Rheinland-Pfälzische Technische Universität Kaiserslautern Landau

Synthesis and Biological Evaluation of Non-Natural Analogues of Nitro-Fatty Acids

Dissertation

Vom Fachbereich Chemie der Rheinland-Pfälzischen Technischen Universität Kaiserslautern-Landau zur Verleihung des akademischen Grades „**Doktor der Naturwissenschaften**“ genehmigte Dissertation

Vorgelegt von

Cedric NDEFO NDE, M. Sc.,

Geboren in Zoétélé - Kamerun

Betreuer: Prof. Dr. Georg Manolikakes

begutachtet von: Prof. Dr. Georg Manolikakes, Prof. Dr. Stefan Kubik

Tag der wissenschaftlichen Aussprache: 16.02.2024

DE - 386

Vom Fachbereich Chemie der Rheinland-Pfälzischen Technischen Universität Kaiserslautern Landau als Dissertation angenommen.

Dekan: Prof. Dr. Antonio Pierik

Vorsitzender: Prof. Dr. Jörg Fahrer

1. Gutachter: Prof. Dr. Georg Manolikakes

2. Gutachter: Prof. Dr. Stefan Kubik

The present research work was carried out from October 2019 to November 2023 under the scientific supervision of Prof. Dr. Georg Manolikakes, at the Institute of Organic Chemistry, Department of Chemistry, Rhineland-Palatinate Technical University Kaiserslautern-Landau.

Date of submission: 19.12.2023

Date of Defense: 16.02.2024

STATUTORY DECLARATION

I hereby declare that I have written this doctoral thesis independently and have not used any aids or sources other than those specified. The passages taken from other sources, either literally or analogously, are marked as such.

This thesis has not been submitted in the same or a similar form to any other examining authority or faculty.

Kaiserslautern, _____ _____

Cedric Ndefo Nde

ACKNOWLEDGMENTS

From the bottom of my heart, I would like to thank all the people who supported and guided me throughout my PhD journey.

My special thanks goes to my exceptional *"Doktorvater"* Prof. Dr. Georg Manolikakes, for giving me the opportunity to carry out this interesting topic in his working group, as well as for the support and trust placed in me throughout this journey. Georg, thank you very much for your availability, Kindness, dedicated support, guidance, and for sharing your scientific knowledge. Without you, it would not have been possible to complete this doctoral thesis.

I would like to thank Prof. Dr. Stefan Kubik for agreeing to referee this thesis and Prof. Dr. Jörg Fahrer for agreeing to chair the doctoral committee.

I am extremely grateful to the German Academic Exchange Service (DAAD) for its financial support.

I would like to thank the TU-Nachwuchsring (RPTU) for their support.

I am also thankful to all current and former members of the working group, Dr. Mohamed Hassan, Dr. Kamil Hofman, Dr. Sara-Cathrin Krieg, Dr. Bastian Klaus Jakob, Marius Friedrich, Oluwaseun Olu-Igbiloba, Miro Halaczkiewicz, Julian Keller, Jan Philipp Nau, Thaís Rodrigues Arroio, Christina Wiedermann, Esin Memisler, and Nils Frejack for the friendly working atmosphere and enriching discussions.

I would like to thank Miro Halaczkiewicz for proofreading the experimental section.

I would also like to thank Dr. Lukas Marius Müller for proofreading the "Kurzfassung".

I also want to thank my hard-working research interns and undergraduate students, Kevin Richard Thomas Wallinger, Marvin Krauss, Fabian Casalino, Lea Thullen, Lukas Reinhard, and Yannick Lukas Jahn for their active support and excellent cooperation.

Furthermore, I want to express my gratitude to Ms. Christiane Müller for measuring countless paramagnetic NMR spectra. Many thanks to Ms. Ruth Maria Bergsträßer for recording various high-resolution masses. My gratitude also go to Ms. Birgit Dusch and Ms. Jana Ellmer for the measurement of valuable Elemental Analyses.

I would also like to express my gratitude to Ms. Susanne Zeigner for her support in all administrative and organizational aspects.

I am very grateful to the staff at the Chemicals Warehouse, Mr. Ludvik Napast, Mr. Jürgen Rahm, and Mr. Frank Schröer, for their immense help in ordering chemicals and interesting technical discussions.

Finally, I would like to express my deepest gratitude and love to my family, My dad, Joseph Nde, always prays for and encourages me. My mother, Sara Danielle Mahagoum Ndefo, may she rest in peace. Thanks to my sisters Floriane Mapa, Diane Djoussi, Pauline Joëlle Fogang, and my brother Pascal Nixon Tadjo for their prayers, constant support, unwavering love, and encouragement during good, difficult, and stressful times. My uncles, Réné Fotsing, may he rest in peace, and Flobert Fogang, who always believed in and supported me throughout my studies and doctorate. Many thanks to all my friends.

"Winners are not afraid of losing. But losers are. Failure is part of the process of success. People who avoid failure also avoid success."

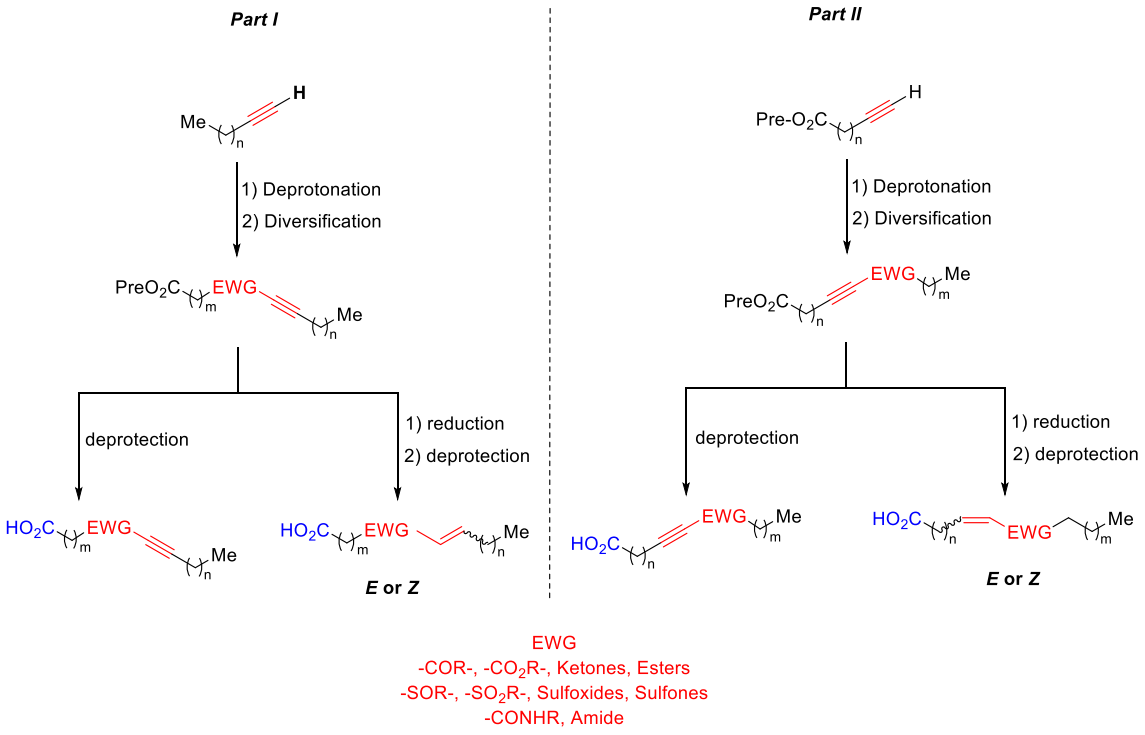
- Robert T. Kiyosaki -

Dedicated to my parents Joseph & Sara Danielle

ABSTRACT

Nitroalkene fatty acids, so-called nitrated or nitro-fatty acids (NO_2-FAs or NFAs), and the corresponding nitrated lipids are naturally occurring electrophiles. They are produced by the nitration of unsaturated fatty acids with nitric oxide-derived radicals, especially during inflammation processes. Nitro-fatty acids have emerged as a novel class of signaling molecules with strong anti-inflammatory and also anti-tumorigenic effects. As potent electrophiles, NFAs mainly act by post-translational modification of proteins through the addition of nucleophilic amino acid side chains to reactive nitroolefin.

Within the framework of this doctoral thesis, it was possible to synthesize non-natural analogues of nitro fatty acids containing different electron-withdrawing groups incorporated into the fatty acid chain in proximal (part I) and distal (part II) position to the terminal carboxyl group via alkyne-based approach (Scheme). Using this novel approach, we could synthesize a library of around 30 novel structurally diverse electrophilic fatty acids.

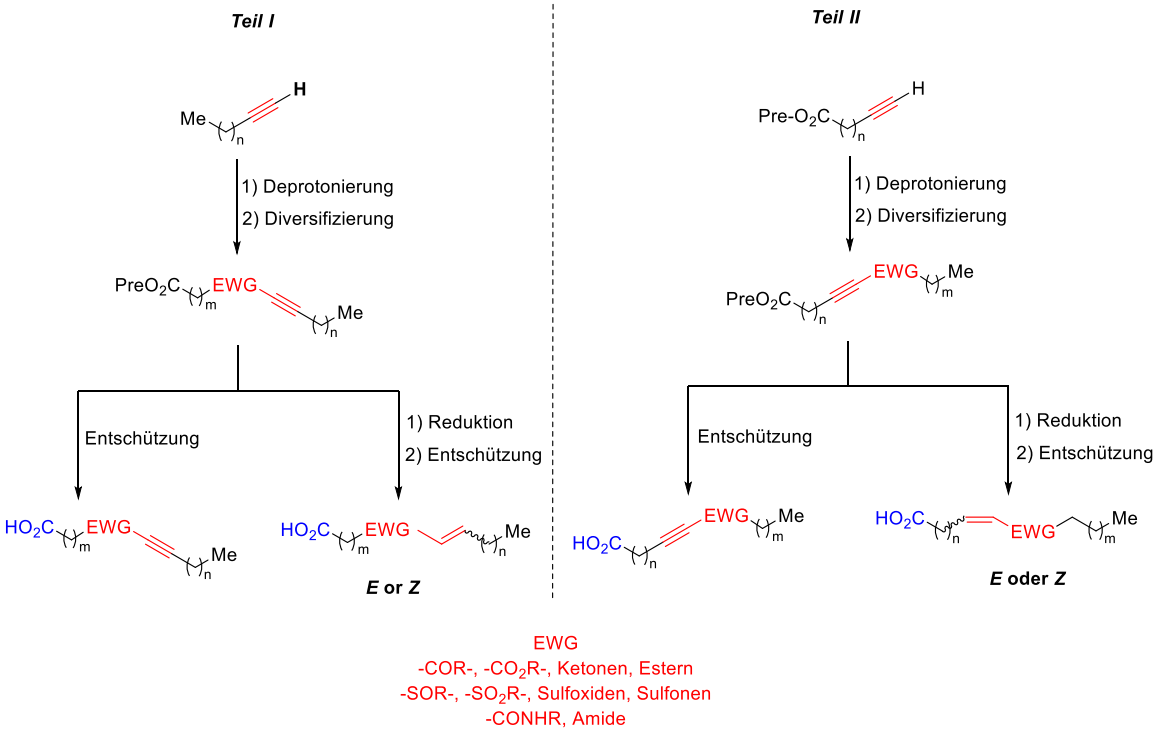


Scheme : Overview of the Dissertation. (EWG = electron-withdrawing group).

KURZFASSUNG

Nitroalkenfettsäuren, sogenannte nitrierte oder Nitrofettsäuren (NO_2-FAs oder NFAs), und die entsprechenden nitrierten Lipide sind natürlich vorkommende Elektrophile. Sie entstehen durch die Nitrierung von ungesättigten Fettsäuren mit aus Stickstoffmonoxid gewonnenen Radikalen, insbesondere bei Entzündungsprozessen. Es hat sich gezeigt, dass Nitrofettsäuren eine neue Klasse von Signalmolekülen mit starker entzündungshemmender und auch antitumoraler Wirkung sind. Als potente Elektrophile wirken NFAs hauptsächlich durch posttranslationale Modifikation von Proteinen durch die Addition von nukleophilen Aminosäureseitenketten an reaktive Nitroolefine.

Im Rahmen dieser Doktorarbeit war es möglich, nicht-natürliche Derivate von Nitrofettsäuren zu synthetisieren, die verschiedene elektronenziehende Gruppen enthalten, die in proximaler (Teil I) oder distaler (Teil II) Position zur terminalen Carboxylgruppe in die Fettsäurekette eingebaut sind, und zwar über einen Ansatz auf Alkinbasis (Schema). Mit diesem neuen Ansatz konnten wir etwa 30 neue, strukturell unterschiedliche elektrophile Fettsäuren synthetisieren.



Schema : Übersicht der Dissertation. (EWG = elektronenziehende Gruppe).

I. TABLE OF CONTENTS

I. TABLE OF CONTENTS xvii

II. ABBREVIATIONS xx

III. LIST OF FIGURES xxv

IV. LIST OF SCHEMES xxvi

1 INTRODUCTION 1-1

1.1 Mode of Action of Covalent Inhibitors 1-3

1.2 Reversible and Irreversible Covalent Inhibitors 1-4

1.3 Historical Overview of Covalent Inhibitors 1-7

1.4 Advantages and Disadvantages of Covalent Inhibitors 1-10

1.5 Nitro-Fatty Acids 1-11

1.5.1 Introduction 1-11

1.5.2 Mode of Action of Nitro-Fatty Acids 1-12

2 OBJECTIVES 2-14

3 RESULTS AND DISCUSSION 3-16

3.1 Attempted hydrozirconation of octadic-9-ynoic acid derivatives 3-16

3.2 Evaluation of the hydrozirconation route with terminal alkyne 3-17

3.3 Implementation of a 2nd generation route 3-18

3.3.1 Alkyne-based approach 3-18

3.3.1.1 Introduction 3-18

3.3.1.2 Access to Keto-modified fatty acids 3-20

3.3.1.3 Access to alkynyl ester-modified fatty acid 3-22

3.3.1.4 Access to Amide-modified fatty acid 3-22

3.3.1.5 Access to Sulfoxide and Sulfone-modified fatty acids 3-23

3.4 Stereoselective Semi-Hydrogenation of Alkynes 3-24

3.4.1 Access to *(Z)*-Configured Alkenyl ester-modified fatty acid 3-24

3.4.2 Access to (*E*)-Configured enone-modified fatty acids 3-25

3.4.3 Access to *(E)*- and *(Z)*- Configured Amide-modified fatty acids 3-26

3.4.4 Access to (*Z*)- and (*E*)-Configured Alkenyl Sulfoxide and Alkenyl Sulfone-modified fatty acids……. 3-26

3.5 Conclusion.....3-27

3.6 Synthesis of fatty acids bearing different electron-withdrawing groups incorporated into the fatty acid chain in distal position to the terminal carboxyl group.....3-28

3.6.1 Introduction..... 3-28

3.6.2 Access to Keto-modified fatty acids 3-29

3.6.3 Access to Alkynyl Ester-modified fatty acid 3-31

3.6.4 Access to Sulfoxide and Sulfone-modified fatty acids..... 3-31

3.7 Stereoselective Semi-Hydrogenation of Alkynes 3-33

3.7.1 Access to (*E*)-Configured enone-modified fatty acids 3-33

3.7.2 Access to *(Z)*-Configured Alkenyl ester-modified fatty acid 3-34

3.7.3 Access to (*Z*)- and (*E*)-Configured Alkenyl Sulfoxide and Alkenyl Sulfone-modified fatty acids……..3-34

3.8 Synthesis of 11-hydroxyoctadec-9-ynoic acid.....3-35

3.9 Conclusion.....3-35

3.10 Biological Studies 3-36

4 GENERAL CONCLUSION 4-37

5 OUTLOOK 5-39

6 EXPERIMENTAL SECTION 6-40

6.1 General information 6-40

6.2 Analytical data and Instrumentation. 6-41

6.3 General Procedures (GP).....6-42

6.3.1 GP1: Prenyl Protection 6-42

6.3.2 GP2: Kornblum Oxidation..... 6-42

6.3.3 GP3: Condensation 6-42

6.3.4 GP4: DMP Oxidation..... 6-43

6.3.5 GP5: Stereoselective semi-hydrogenation of alkynes..... 6-43

6.3.6 GP6: Deprotection with TMSOTf..... 6-43

6.3.7 GP7: Deprotection with $BF_3{\cdot}OEt_2$ 6-43

6.4 Synthesis 6-44

6.4.1 Synthesis of Prenylbromoalkanoates 6-44

6.4.2 Synthesis of Prenyloxoalkanoates 6-46

6.4.3 Synthesis of Acetylenic Carboxylic Acids 6-48

6.4.4 Synthesis of Prenylalkynoates 6-49

6.4.5 Synthesis of Bunte Salts 6-51

6.4.6 Synthesis of *S*-heptyl 4-methylbenzenesulfonothioate 6-52

6.4.7 Synthesis of Propargylic Alcohols 6-53

6.4.8 Synthesis of Alkynyl Sulfide Esters 6-62

6.4.9 Synthesis of Keto-Esters 6-64

6.4.10 Synthesis of Alkynoic Esters 6-73

6.4.11 Synthesis of Amides 6-75

6.4.12 Synthesis of Alkynyl Sulfoxide and Alkynyl Sulfone Esters 6-77

6.4.13 Synthesis of *(Z)*- and *(E)*-Enone Esters 6-80

6.4.14 Synthesis of *(Z)*-Alkenyl Esters 6-88

6.4.15 Synthesis of *(E* and *Z)* Amides 6-89

6.4.16 Synthesis of *(Z)*-Alkenyl Sulfoxide and Alkenyl Sulfone 6-91

6.4.17 Synthesis of *(E)*-Alkenyl Sulfoxide and Alkenyl Sulfone 6-93

6.5 Synthesis of Fatty Acids 6-95

6.5.1 Synthesis of Alkynoic Fatty Acids 6-95

6.5.2 Synthesis of *(E)*-Alkenyl Fatty Acids 6-109

6.5.3 Synthesis of *(Z)*-Alkenyl Fatty Acids 6-121

6.6 ^{1}H and ^{13}C NMR Spectra 6-126

7 CURRICULUM VITAE 7-251

8 REFERENCES 8-252

II. ABBREVIATIONS

5-FU	5-Fluorouracil
5-LO	5-Lipoxygenase
9-NOA	9-Nitrooleic Acid
%	Percentage
^{o}C	Degree Celsius
AcOH	Acetic Acid
Aq	Aqueous
ASA	Acetylsalicylic Acid
Asp	Aspartate
BCB	Bicyclo[1.1.0]butane
$BF_3{\cdot}OEt_2$	Boron Trifluoride Etherate
BTK	Bruton's Tyrosine Kinase
CDDO	2-cyano-3,12-dioxooleana-1,9(11)-dien-28-oic acid
CDDO-Me	Bardoxolone Methyl
$CDCl_3$	Deuterated Chloroform
CNS	Central Nervous System
CO_2	Carbon Dioxide
COX	Cyclooxygenase
$Cp_2Zr(H)Cl$	Schwartz's Reagent, Zirconocene Chloride Hydride
Cu-H	Copper Hydride
Cys	Cysteine
DABSO	1,4-diazabicyclo[2.2.2]octane bis(sulfur dioxide) Adduct
DCE	1,2-Dichloroethane
DCM	Dichloromethane

DIBAL-H	Diisobutylaluminium Hydride
DMAP	4-Dimethylaminopyridine
DMF	Dimethyl Fumarate
DMF	Dimethylformamide
DMP	Dess-Martin periodinane
DMSO	Dimethyl Sulfoxide
DPP IV	Dipeptidyl Peptidase IV
dppb	1,4-Bis(diphenylphosphino)butane
EDA	Ethylenediamine
EDC·HCl	1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide Hydrochloride
EGFR-TKIs	Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors
EtOAc	Ethyl Acetate
Et_2O	Diethylether
equiv	Equivalent
EWG	Electron-withdrawing group
FDA	Food and Drug Administration
G12C	Glycine-to-Cysteine Mutation at Codon 12
GLP-1	Glucagon-Like Peptide-1
GSH	Glutathione
h	Hour
H^+/K^+-ATPase	Gastric Hydrogen-Potassium Adenosine Triphosphatase
HCV	Hepatitis C Virus
HCO_2H	Formic Acid
HCT116	Human Colorectal Carcinoma Cell Line
HCl	Hydrochloride

His	Histidine
H_2O	Water
IC_{50}	Half-Maximal Inhibitory Concentration
*i*PrMgCl	Isopropylmagnesium Chloride
JAK3	Janus Tyrosine Kinase 3
Keap 1	Kelch-like ECH-associated protein 1
KI	Potassium Iodide
k_{-2}	Dissociation Rate
K_i	Dissociation Constant
K_i*	Overall Inhibition Constant
KRAS	Kirsten Rat Sarcoma Viral Oncogene Homologue
MAO-B	Monoamine Oxidase Type B
m-CPBA	meta-Chloroperoxybenzoic Acid
MeOH	Methanol
MeI	Iodomethane
MM	Multiple Myeloma
MMF	Monomethyl Fumarate
MS	Multiple Sclerosis
MurA	Uridine Diphosphate *N*-acetylglucosamine Enolpyruvyl Transferase
MRSA	Methicillin-Resistant Staphylococcus Aureus
Na_2CO_3	Sodium Carbonate
$NaHCO_3$	Sodium Bicarbonate
$Na_2S_2O_3 \cdot 5H_2O$	Sodium Thiosulfate Pentahydrate
Na_2SO_4	Sodium Sulfate
NaH	Sodium Hydride

NaCl	Sodium Chloride
n-BuLi	*n*-Butyllithium
NFA	Nitrated Fatty Acids
NF-κB	Nuclear factor kappa-light-chain-enhancer of activated B cells
NH_4Cl	Ammonium Chloride
NH_4OH	Ammonium Hydroxide
NEt_3	Triethylamine
$NO^{\cdot}$	Nitric Oxide
$NO_2^{\cdot}$	Nitrogen Dioxide
Nrf2	Nuclear factor (erythroid-derived 2)-like 2
NSCLC	Non-Small Cell Lung Cancer
$ONOO^{-2}$	Peroxynitrite
PEI	Paul-Ehrlich-Institut
$P2Y_{12}$	Purinoreceptor
PMB	4-Methoxybenzyl
$Pd/BaSO_4$	Palladium on Barium Sulfate
$Pd_2(dba)_3$	Tris(dibenzylideneacetone)dipalladium(0)
PG	Protecting Group
PPARγ	Peroxisome Proliferator-activated Receptor γ
RRMM	Relapsed and Refractory Multiple Myeloma
R_f	Retention Factor
RT	Room Temperature
Sat	Saturated
Ser	Serine
SO_2	Sulfur Dioxide

TBDMS	Tert-Butyldimethylsilyl
THF	Tetrahydrofuran
THP	Tetrahydropyran
TMSOTf	Trimethylsilyl Trifluoromethanesulfonate
Tyr	Tyrosine
US	United States
Vol	Volume

III. LIST OF FIGURES

Figure 1.1: Approved covalent drugs by therapeutic medication.[6] 1-1

Figure 1.2: Structures of known covalent inhibitors. Warheads are highlighted in red. 1-2

Figure 1.3: General mechanism of action of covalent inhibitors.[42, 43] 1-3

Figure 1.4: Historic overview of covalent drugs. Each covalent drug is provided along with its biological target. Electrophilic warheads are highlighted in red. 1-7

Figure 1.5: Different electrophilic unsaturated fatty aids 1-12

Figure 3.1: Western blot: densitometric analysis. Cell-line: HCT-116; Treatment time: 4h; Conc.: 10 µM. 3-36

IV. LIST OF SCHEMES

Scheme 1.1: Mechanism of action of α-Cyanoacrylamide-based reversible covalent inhibitors. 1-4

Scheme 1.2: Mechanism of action of covalent reversible peptide-based vinylsulfone **19**.[49] 1-5

Scheme 1.3: Mechanism of action of Irreversible peptide-based vinylsulfones **20** and **21**.[49] 1-5

Scheme 1.4: Mechanism of action of acrylamide-based irreversible covalent inhibitor **22** 1-6

Scheme 1.5: Mechanism of action of acrylamide-based Irreversible covalent inhibitor **23**. 1-6

Scheme 1.6: Mechanism of action of Aspirin **1.**[1] 1-8

Scheme 1.7: Mechanism of action of Penicillin **24**.[1] 1-8

Scheme 1.8: Mechanism of action of Fosfomycin **25.**[70] 1-8

Scheme 1.9: Mechanism of action of Omeprazole **26**.[73, 74] 1-9

Scheme 1.10: Mechanism of action of Clopidogrel **27.**[77] 1-10

Scheme 1.11: 9-Nitrooleic acid **31** and its main mechanism of action. 1-11

Scheme 1.12: Inhibition of NF-kB by 9-nitrooleic acid **31a**. 1-12

Scheme 1.13: Inhibition of 5-Lipoxygenase (5-LO) by 9-nitrooleic acid **31a**.[94] 1-13

Scheme 1.14: Induction of the Keap1-Nrf2 pathway by 9-nitrooleic acid **31a**. 1-13

Scheme 2.1: Dissertation Outline. (EWG = electron-withdrawing group; NFAs = Nitro-Fatty Acids; FG = Functional group). 2-14

Scheme 2.2: Initially envisioned synthetic route. (EWG = electron-withdrawing group). 2-15

Scheme 3.1: Failed chemoselective hydrozirconation of octadic-9-ynoic acid derivatives **44a-f**. 3-16

Scheme 3.2: Envisioned route from dec-1-yne **48a** to the NFA analogues **E-50a**, **E-52b,** and **E-53a.** 3-17

Scheme 3.3: Synthesis of building block **55b.** 3-17

Scheme 3.4: Attempted synthesis of vinyl sulfone fatty acid. 3-18

Scheme 3.5: 2nd Generation alkyne-based approach to NFA derivatives **50-54.** 3-19

Scheme 3.6: 2nd Generation alkyne-based approach to NFA derivatives **69-73.** 3-19

Scheme 3.7: Synthesis of building blocks **55a** and **56a-d.** 3-20

Scheme 3.8: Synthesis of propargylic alcohols **74a-h.** 3-20

Scheme 3.9: Synthesis of alkynes **67a-h.** 3-21

Scheme 3.10: Successful synthesis of alkynoic acid **72a-h.** 3-21

Scheme 3.11: Successful synthesis of alkynyl fatty acid **69a**. 3-22

Scheme 3.12: Successful synthesis of alkynoic acid **73a.** 3-22

Scheme 3.13: Synthesis of Bunte salt **61a.** 3-23

Scheme 3.14: Successful synthesis of alkynoic acids **70a** and **71a.** 3-23

Scheme 3.15: Unsuccessful optimization of stereoselective semi-hydrogenation of alkyne **64a.** 3-24

Scheme 3.16: Successful synthesis of (Z)-configured fatty acid **50b.** 3-24

Scheme 3.17: Synthesis of (Z)-configured enones **77a-h.** 3-25
Scheme 3.18: Successful synthesis of (E)-configured fatty acids **53a-h.** 3-25
Scheme 3.19: Successful synthesis of (Z)- and (E)-configured fatty acids **54a** and **54b.** 3-26
Scheme 3.20: Successful synthesis of (Z)-configured fatty acids **51a** and **52a.** 3-26
Scheme 3.21: Successful synthesis of (E)-configured fatty acids **51b** and **52b.** 3-27
Scheme 3.22: 2nd Generation alkyne-based approach to NFA derivatives of types **91, 92, 93,** and **94.** 3-28
Scheme 3.23: 2nd Generation alkyne-based approach to NFA derivatives **95-98**. 3-29
Scheme 3.24: Synthesis of building blocks **82a-c.** 3-29
Scheme 3.25: Synthesis of propargylic alcohols **99a-f.** 3-30
Scheme 3.26: Synthesis of ketones **90a-f.** 3-30
Scheme 3.27: Successful synthesis of keto fatty acids **98a-f.** 3-30
Scheme 3.28: Successful synthesis of alkynyl fatty acid **95a.** 3-31
Scheme 3.29: Synthesis of building block **85a**. 3-31
Scheme 3.30: Failed synthesis of sulfide **101**. 3-31
Scheme 3.31: Synthesis of building block **102.** 3-32
Scheme 3.32: Successful synthesis of alkynoic acids **96a** and **97a.** 3-32
Scheme 3.33: Synthesis of (Z)-configured enones **104a-f.** 3-33
Scheme 3.34: Successful synthesis of (E)-configured fatty acids **94a-f.** 3-33
Scheme 3.35: Successful synthesis of (Z)-configured fatty acid **91a.** 3-34
Scheme 3.36: Successful synthesis of (Z)-configured fatty acids **92a** and **93a.** 3-34
Scheme 3.37: Successful synthesis of (E)-configured fatty acid **92b.** 3-35
Scheme 3.38: Successful synthesis of 11-hydroxyotadec-9-ynoic acid **107.** 3-35
Scheme 4.1: Part 1a - Summary of all NFAs analogues bearing an alkyne-derived Michael acceptor unit. (EWG = electron-withdrawing group). 4-37
Scheme 4.2: Part 1b - Summary of all NFAs derivatives bearing an alkene moiety. (EWG = electron-withdrawing group). 4-37
Scheme 4.3: Part 2a - Summary of all NFAs analogues bearing an alkyne-derived Michael acceptor unit. (EWG = electron-withdrawing group). 4-38
Scheme 4.4: Part 2b - Summary of all NFAs analgues bearing an alkene moiety. (EWG = electron-withdrawing group). 4-38
Scheme 5.1: 2nd Generation alkyne-based approach to NFA of type **110**. (EWG = electron-withdrawing group). 5-39
Scheme 5.2: 2nd Generation alkyne-based approach to NFA derivatives of type **113.** (EWG = electron-withdrawing group). 5-39

1 INTRODUCTION

Covalent inhibitors are compounds that bind covalently to their specific biological targets and thereby inactivate them temporarily or permanently.[1, 2] They are widely used as biochemical tools and potential therapeutic agents.[3, 4] Generally, covalent inhibitors contain an electrophilic functional group moiety often called “warhead” that reacts with nucleophilic residues, typically the side chain of amino acids such as cysteine, lysine, serine, tyrosine, and threonine located on targeted proteins.[2, 5, 6] To date, covalent inhibitors bearing a variety of electrophilic warheads such as Michael acceptors[7-12] (e.g. acrylamides and other α,β-unsaturated carbonyl compounds), heteroatomics motifs[13-15] (e.g. sulfoxides, sulfones, and heterocyclic electrophiles), sulfur(VI) motifs [16-18] (e. g. aryl fluorosulfates and sulfuramidimidoyl fluorides), aziridines,[19, 20] bicyclo[1.1.0]butane (BCB),[21, 22] terminal alkynes,[23, 24] nitriles, ketones, esters, and epoxides[25] are widely used in medicine to treat various diseases.

Among drugs on the market, about 30% act via a covalent mechanism of action.[26] An analysis of FDA-approved covalent drugs shows that approximately 28% of these drugs are used in oncology-related targets, 23% treat central nervous system (CNS) and cardiovascular disorders, 21% are anti-infectives (mainly the β-lactam class of antibiotics), and 11% treat gastrointestinal disorders[6] (Figure 1.1).

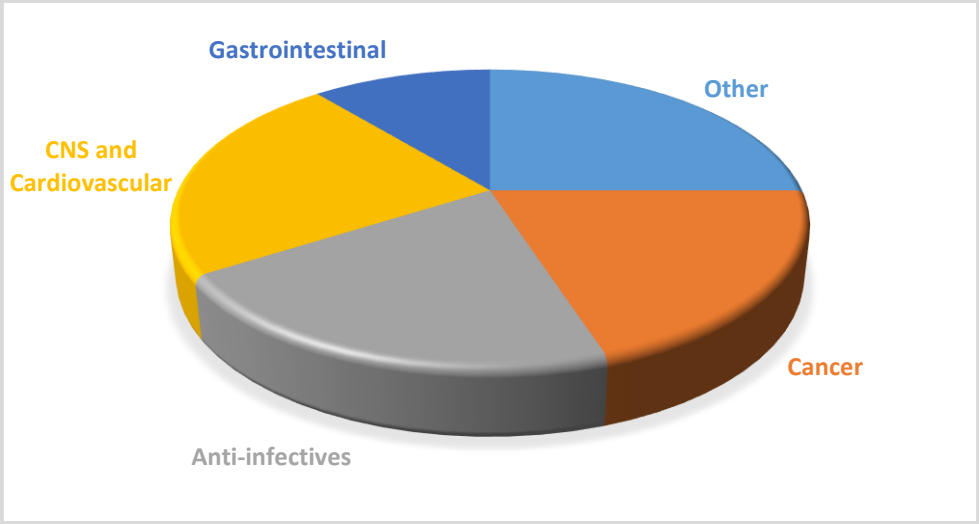


Figure 1.1: Approved covalent drugs by therapeutic medication.[6]

For instance, Aspirin **1** is the earliest marketed covalent drug. Aspirin **1** is an inhibitor of cyclooxygenases.[27] Covalent drugs such as 5-Fluorouracil **2** (5-FU) and Gemcitabine **3** have a significant impact in oncology as inhibitors of thymidylate synthase[28, 29] and ribonucleotide reductase[30] respectively. Rasagiline **4** and Selegiline **5** are potent, selective, and irreversible inhibitors of monoamine oxidase type B (MAO-B) bearing a terminal alkyne warhead. They are widely used to treat depression and Parkinson's disease.[31, 32] Ibrutinib[33] **6** and Tirabrutinib[34] **7** are selective and covalent inhibitors of the enzyme Bruton’s tyrosine kinase (BTK) used to treat a wide range of cancers.

Ibrutinib **6** contains the α,β-unsaturated carbonyl warhead, whereas Tirabrutinib **7** contains a α,β-unsaturated propargylamide warhead. Dacomitinib[35] **8** and Osimertinib[36] **9** are selective and irreversible epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) used to treat non-small-cell lung cancer (NSCLC). Both contain the α,β-unsaturated carbonyl warhead. Boceprevir[37] **10** and Telaprevir[38] **11** are two examples of covalent inhibitors bearing the α-ketoamide warhead. They are potent protease inhibitors used to treat hepatitis C virus (HCV) infection. Carfilzomib[39] **12** is a proteasome inhibitor containing an epoxide warhead. The drug is used to treat relapsed and refractory multiple myeloma (RRMM). Dimethyl fumarate **13a** (DMF) and its primary metabolite, monomethyl fumarate **13b** (MMF), are well-known Nrf2 inducers used for the treatment of multiple sclerosis (MS). The primary metabolite, monomethyl fumarate **13b** (MMF), covalently modifies Cys_{151} of the Keap1 protein.[40, 41] (Figure 1.2).

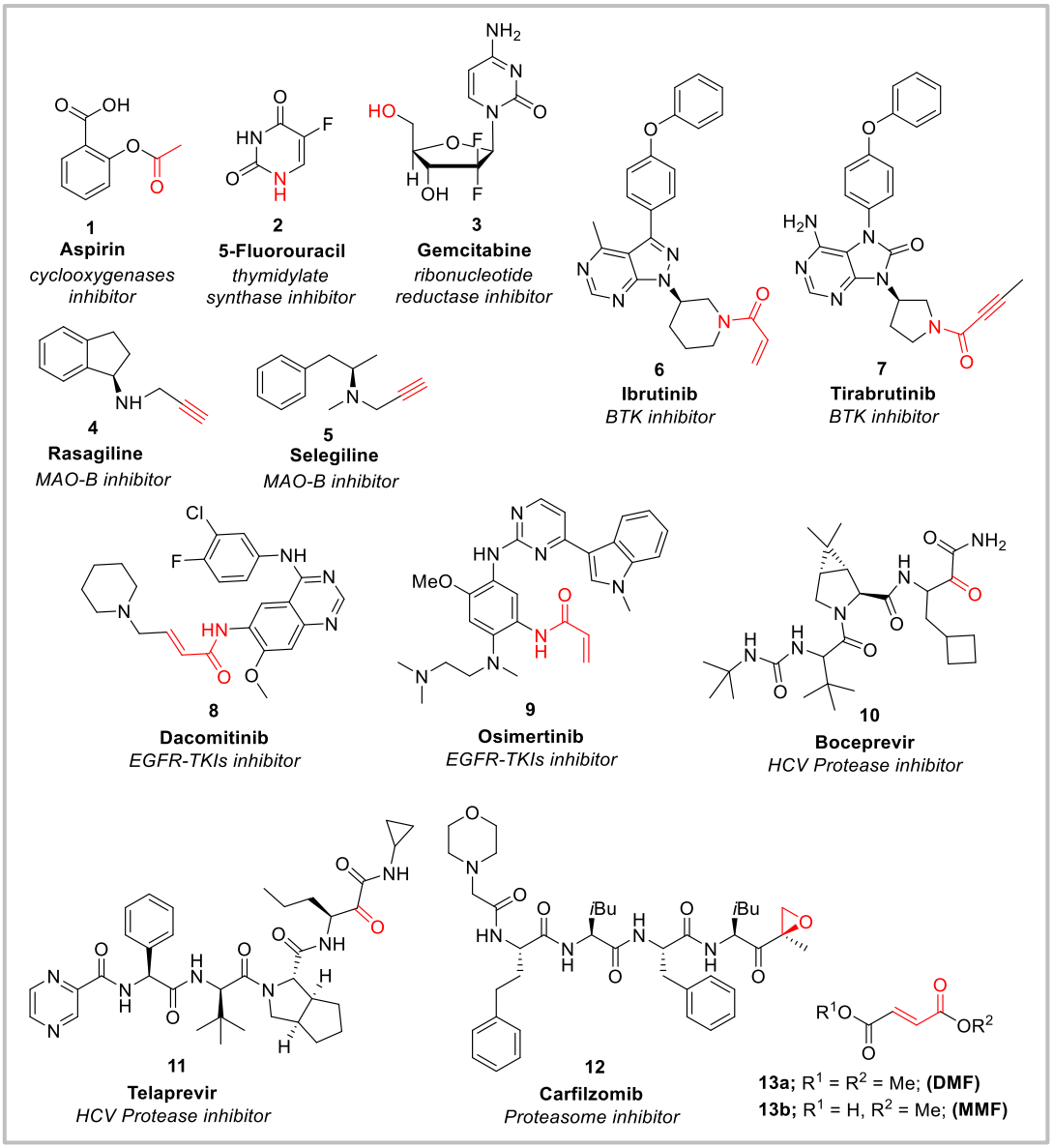


Figure 1.2: Structures of known covalent inhibitors. Warheads are highlighted in red.

1.1 Mode of Action of Covalent Inhibitors

Inhibition of a target enzyme by a covalent inhibitor occurs in two steps, starting with the specific non-covalent complex formation and ending with the specific covalent complex formation between the electrophilic warhead of the ligand and the nucleophilic residue located on the target. In the first step, the ligand and the target protein are in an equilibrium state governed by the dissociation constant (K_i) of the non-covalent complex,[42] and the second step is a non-equilibrium state used to determine the nature (reversible or irreversible) of the covalent bond formed[43] (figure 1.3). If the dissociation rate (k_{-2}) of the covalent ligand-protein complex is defined, the covalent bond formed is reversible, and the inhibitor is called a reversible covalent inhibitor (figure 1.3a). In contrast to a reversible covalent inhibitor, the dissociation rate (k_{-2}) of the covalent ligand-protein complex for an irreversible covalent inhibitor is close to or equal to zero. In this case, the covalent bond formed is irreversible[42,43] (figure 1.3b). As a consequence of the time-dependent half-maximal inhibitory concentration (IC_{50}) values,[44] the overall inhibition constant (K_i*), which takes both steps into account, is the most accurate indicator for measuring the potency of covalent inhibitors.[42, 43]

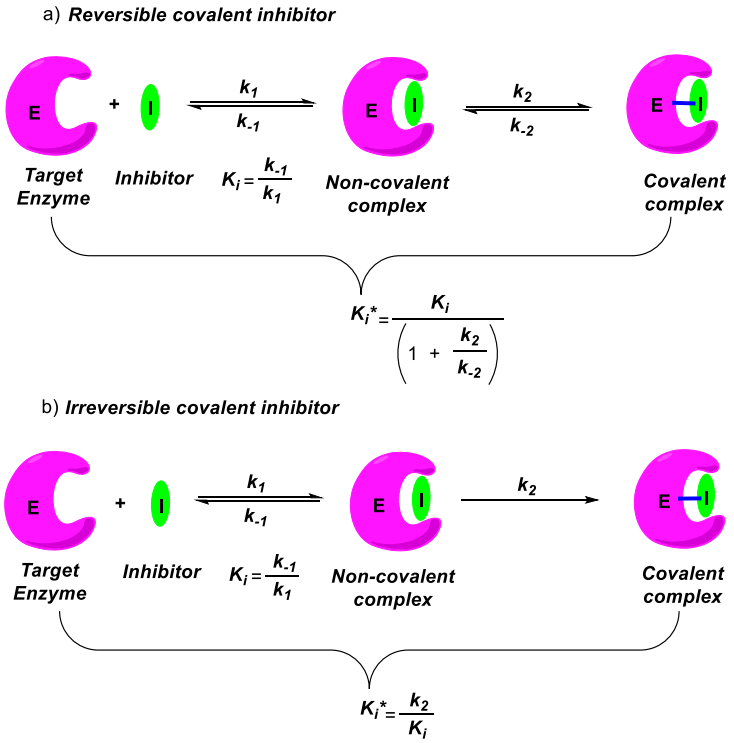
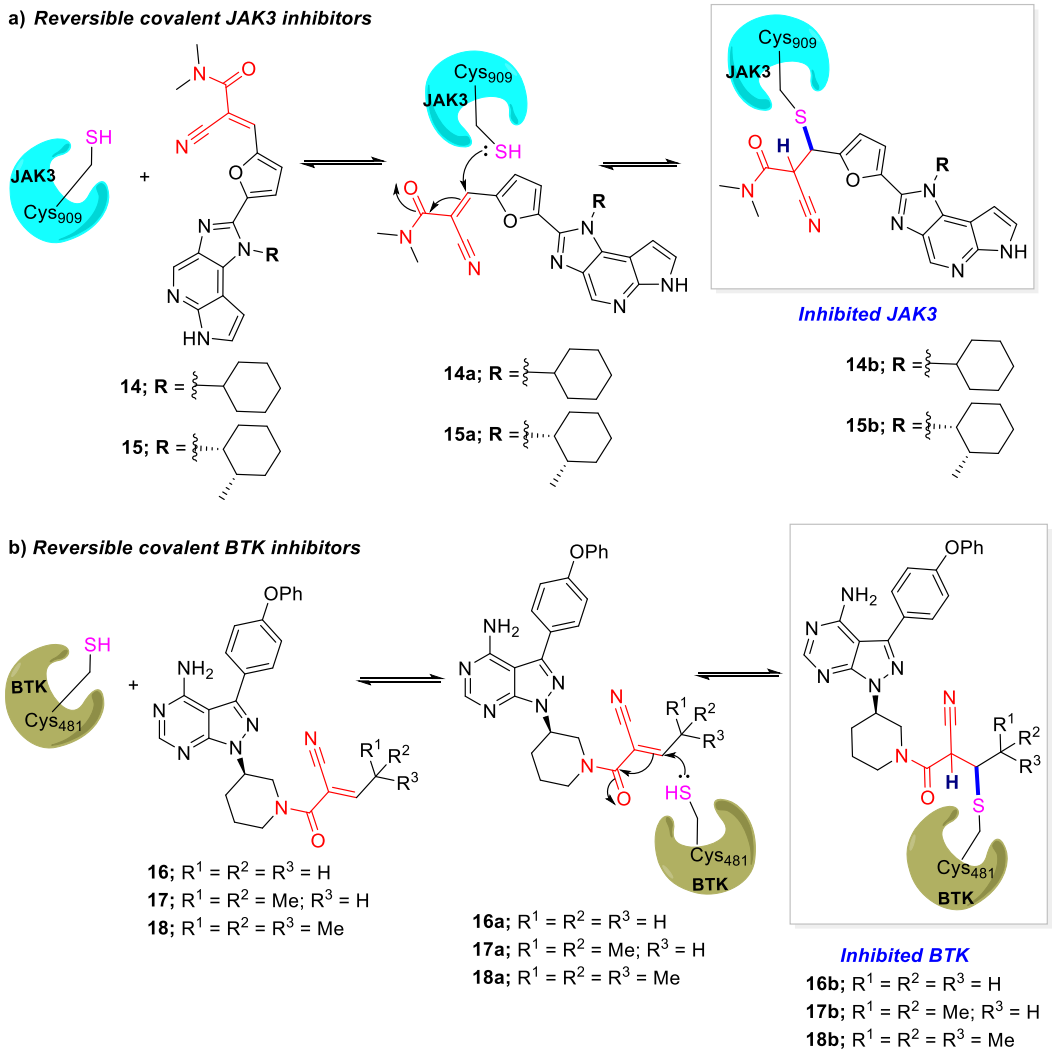


Figure 1.3: General mechanism of action of covalent inhibitors.[42, 43]

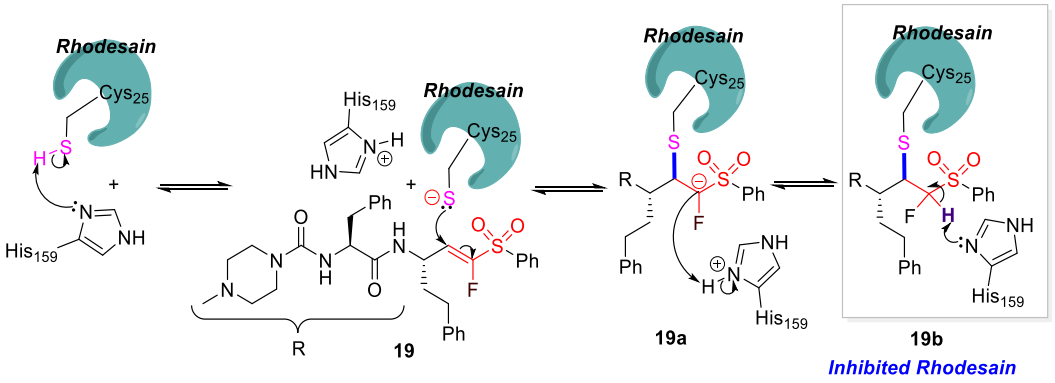
1.2 Reversible and Irreversible Covalent Inhibitors

Covalent inhibitors are classified into two broad categories according to whether inhibition is reversible or irreversible on the biological timescale.[1, 3] Reversible covalent inhibitors form adducts with their target proteins and subsequently dissociate from them.[45] This dissociation restores the protein's biological function. Compounds **14** and **15** are α-cyanoacrylamide-based reversible covalent inhibitors of Janus tyrosine kinase 3 (JAK3) by modifying Cys_{909}[46] (Scheme 1.1a). Compounds **16**, **17**, and **18** also contain the electrophilic α-cyanoacrylamide warhead, which binds reversibly to the Cys_{481} residue of Bruton's tyrosine kinase (BTK)[9] (Scheme 1.1b). The target occupancy for compound **18** is 55% after 20 h, probably due to the *tert*-butyl capping group. While **17** and **16** showed significantly reduced and negligible target occupancy after 20 h respectively.[9] The nitrile group at the α-position of acrylamide highly accelerates the formation of the covalent bond, while the acidic proton at the α-position facilitates the cleavage of this bond.[47]



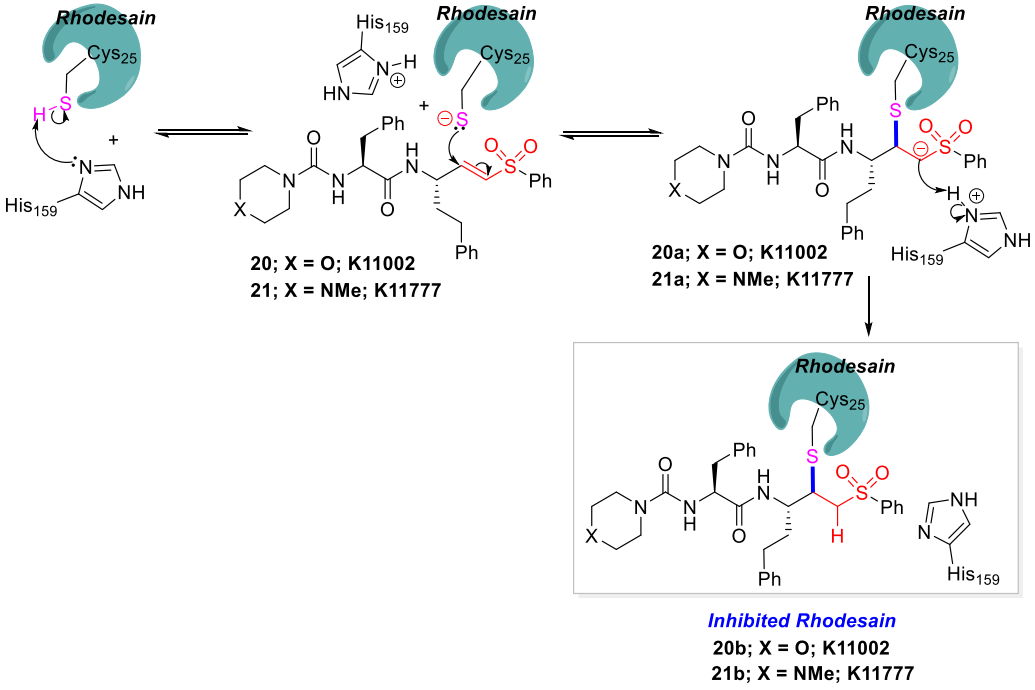
Scheme 1.1: Mechanism of action of α-Cyanoacrylamide-based reversible covalent inhibitors.

Another illustrative example of a reversible covalent inhibitor is the α-fluorovinylsulfone **19** (K_i = 190 nM), an inhibitor of the trypanosomal cysteine protease rhodesain.[48, 49] The inhibition starts with the deprotonation of the Cys_{25} residue of rhodesain by His_{159} residue. The resulting thiolate undergoes a reversible Michael addition to the electrophilic α-fluorovinylsulfone warhead, furnishing the carbanion **19a.** The inhibition is completed by the protonation of **19a** by the protonated His_{159} residue to **19b**, resulting in the formation of the Rhodesain-**19b** complex.[48, 49] The acidic proton at the α-position of sulfone facilitates the cleavage of the C-S bond (Scheme 1.2).



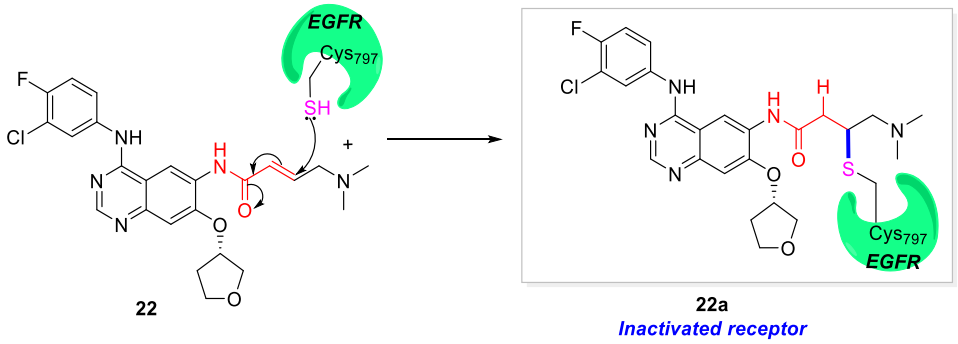
Scheme 1.2: Mechanism of action of covalent reversible peptide-based vinylsulfone **19**.[49]

Irreversible covalent inhibitors bind covalently to their target protein and do not dissociate from it.[45] K11002 **20** and K11777 **21** are peptide-based vinyl sulfones that irreversibly inhibit rhodesain by modification of Cys_{25}.[49-54] The inhibition starts with the reversible Michael addition of the deprotonated Cys_{25} residue of rhodesain to the reactive vinyl sulfone. The final irreversible step is the protonation of **20a** and **21a** by the protonated His_{159} residue to **20b** and **21b** (Scheme 1.3).



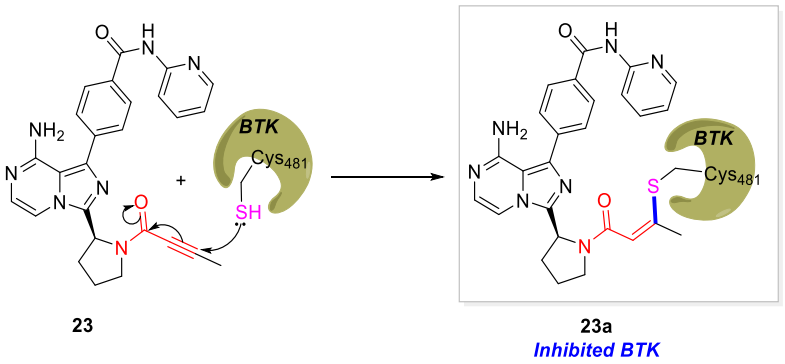
Scheme 1.3: Mechanism of action of Irreversible peptide-based vinylsulfones **20** and **21**.[49]

Afatinib **22** is a potent, selective, and irreversible small molecule inhibitor of the epidermal growth factor receptor (EGFR) tyrosine kinase (TK).[55, 56] Afatinib **22** achieves irreversible inhibition via the Michael addition of the nucleophilic cysteine (Cys_{797}) residue of EGFR to the reactive olefin moiety of the acrylamide warhead[57] (Scheme 1.4).



Scheme 1.4: Mechanism of action of acrylamide-based irreversible covalent inhibitor **22**.

Acalabrutinib **23** is a potent and selective second-generation irreversible Bruton's tyrosine kinase (BTK) inhibitor.[58, 59] Acalabrutinib **23** contains a propargylamide moiety as the electrophilic warhead, which targets Cys_{481} in the BTK active site (Scheme 1.5).



Scheme 1.5: Mechanism of action of acrylamide-based Irreversible covalent inhibitor **23**.

1.3 Historical Overview of Covalent Inhibitors

An overview of the development of covalent inhibitors is shown in Figure 1.4.

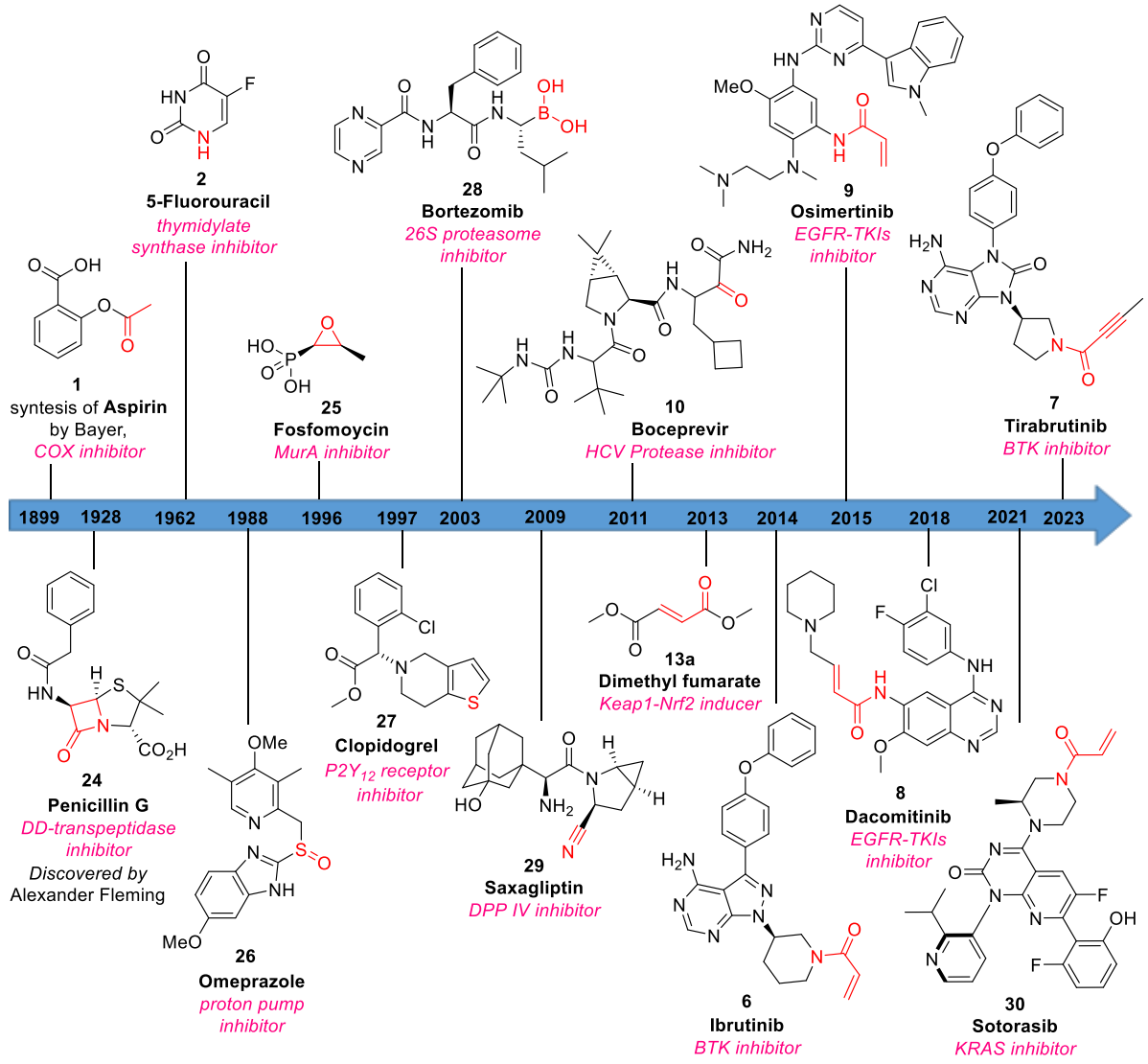
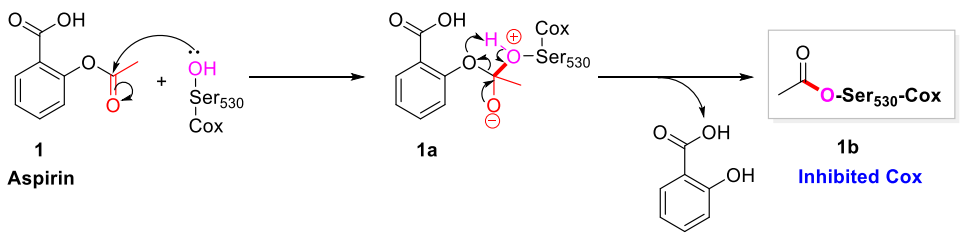


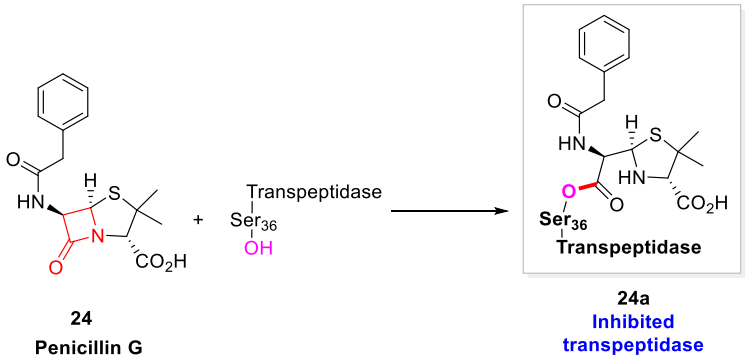
Figure 1.4: Historic overview of covalent drugs. Each covalent drug is provided along with its biological target. Electrophilic warheads are highlighted in red.

The use of small molecules as covalent inhibitors of biological targets started during the late 1800s, when Bayer began investigating and manufacturing aspirin **1** (ASA, acetylsalicylic acid), as a strong painkiller and anti-inflammatory drug.[2, 60] Aspirin **1** irreversibly acetylates an active site serine (Ser_{530}) of cyclooxygenases (COX-1 and COX-2), two key enzymes involved in the biosynthesis of prostaglandins[27, 61] (Scheme 1.6).



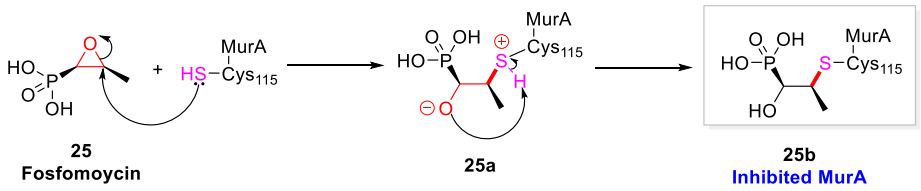
Scheme 1.6: Mechanism of action of Aspirin **1**.[1]

Penicillin **24** is a naturally derived antibiotic, which is produced by *Penicillium* fungi and discovered in 1928 by Alexander Fleming.[62] It bears a β-lactam warhead, which covalently binds to the active site serine (Ser_{36}) of bacterial DD-transpeptidase, an enzyme that plays an important role in cell-wall synthesis[63] (Scheme 1.7).



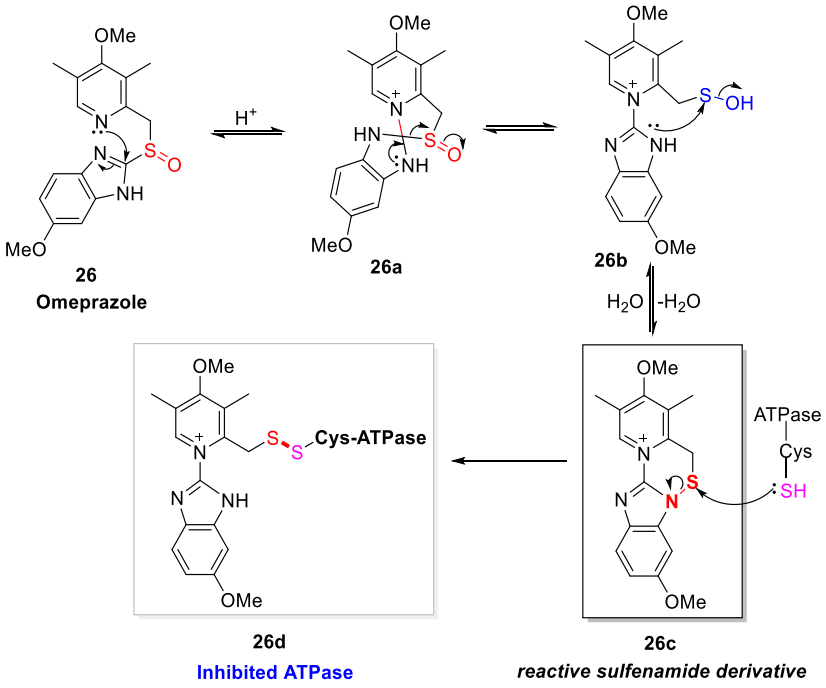
Scheme 1.7: Mechanism of action of Penicillin **24**.[1]

Another interesting example of a natural antibiotic is Fosfomycin **25**, produced by certain types of *Streptomyces* and *Pseudomonas* bacteria,[64, 65] discovered in 1969[66] and approved by the US Food and Drug Administration (FDA) in 1996. The epoxide warhead (oxirane ring) of Fosfomycin **25** reacts irreversibly with the active site cysteine (Cys_{115}) residue of UDP-*N*-acetylglucosamine Enolpyruvyl Transferase (MurA), leading to an inactive enzyme, thus making it unable to biosynthesize peptidoglycan, a key component of the bacterial cell wall[67-69] (Scheme 1.8).



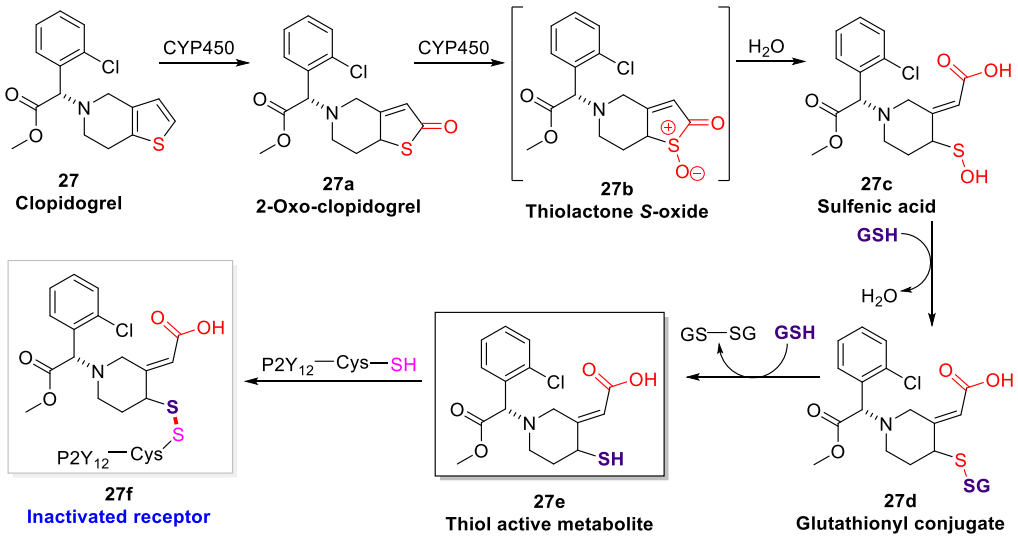
Scheme 1.8: Mechanism of action of Fosfomycin **25**.[70]

Some covalent drugs are activated *in vivo* by the action of chemicals or enzymes into the pharmacologically active metabolite.[71] They are usually called Prodrugs. Omeprazole **26**, a proton pump inhibitor, is an example of a prodrug metabolized in the stomach into the bioactive sulfenamide **26c**. The latter then forms a disulfide bridge with a cysteine residue of the gastric hydrogen-potassium adenosine triphosphatase (H^+/K^+-ATPase) and thereby inactivates the enzyme.[72-75] The drug was discovered in 1979 and approved in 1988 to treat gastrointestinal reflux disease (Scheme 1.9).



Scheme 1.9: Mechanism of action of Omeprazole **26**.[73, 74]

The platelet inhibitor Clopidogrel **27**, approved by the US Food and Drug Administration (FDA) in 1997 to prevent heart attacks and strokes, is another example of a prodrug that undergoes a two-step activation by cytochrome P450 enzymes in the liver to release the pharmacologically active thiol-containing metabolite **27e**.[76, 77] The thiophene ring is first oxidized to 2-oxo-clopidogrel **27a** and then to thiolactone *S*-oxide **27b**. Subsequent hydrolysis of the thioester leads to the thiolactone ring opening into a sulfenic acid intermediate **27c**, which undergoes glutathione (GSH)-mediated reduction to a thiol-containing active metabolite **27e**. This thiol then reacts irreversibly with an active site cysteine residue in the $P2Y_{12}$ purinoreceptor and thus inactivates the receptor[77, 78] (Scheme 1.10).



Scheme 1.10: Mechanism of action of Clopidogrel **27.**[77]

Bortezomib **28** is the first-in-class reversible covalent drug containing a boronic acid as the electrophilic warhead, which covalently binds to the threonine residue of the 26S proteasome.[79] The drug was approved in 2003 by the FDA as an anticancer medication for the treatment of multiple myeloma[79] (MM). The antidiabetic drug Saxagliptin **29** was approved in 2009 by the FDA for the treatment of patients with type 2 diabetes mellitus. Saxagliptin **29** contains a nitrile group as the electrophilic warhead, which reversibly binds to the Ser_{630} residue of dipeptidyl peptidase IV (DPP IV), an enzyme that plays a major role in the regulation of blood glucose levels through the degradation of the hormone Glucagon-like peptide-1 (GLP-1).[80] Sotorasib **30** is the first covalent inhibitor of mutant KRAS G12C, bearing an acrylamide warhead and approved by the FDA in 2021 to treat patients with non-small-cell lung cancer.[81, 82]

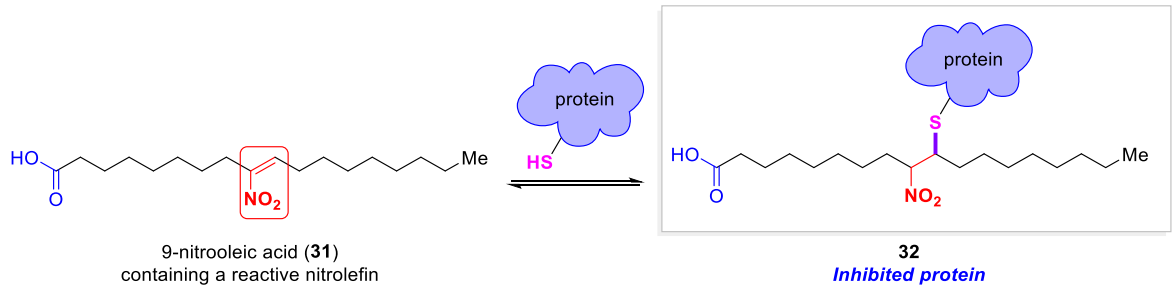
1.4 Advantages and Disadvantages of Covalent Inhibitors

Covalent inhibitors offer several advantages over conventional non-covalent inhibitors, including higher efficiency and reduced risk of drug resistance.[6] The formation of the covalent bond enables a prolonged duration of therapeutic response and enhances the potency of covalent inhibitors, leading to lower and less frequent doses of drug administration.[6, 60] In addition, covalent inhibitors can achieve higher selectivity, enabling them to target undruggable proteins such as KRAS.[6, 82] However, potential toxicity and immunogenicity concerns are the major challenges of covalent inhibitors. The toxicity is associated with their potential for off-target reactivity, which may lead to the permanent modifications of proteins.[43, 60, 83] Also, covalent inhibitors may not be suitable for targets with fast turnover or enzyme degradation.[6]

1.5 Nitro-Fatty Acids

1.5.1 Introduction

Unsaturated nitrated fatty acids (NFAs) are naturally occurring electrophilic lipids,[84-87] which are produced endogenously by the reaction of unsaturated fatty acids with reactive nitrogen species e.g. nitric oxide ($NO^{\cdot}$), nitrogen dioxide ($NO_2^{\cdot}$) or peroxynitrite ($ONOO^-$)[2] during inflammation processes and also after the consumption of unsaturated fatty acids together with nitrite or nitrate.[88, 89] In addition, olives and native olive oil have been identified as natural sources of NFAs.[90] NFAs, such as 9-nitrooleic acid (9-NOA, **31**) are pluripotent signaling mediators, which can modulate various targets and pathways. NFAs mainly act by the post-translational modification of proteins via the reversible Michael addition of nucleophilic cysteine or histidine residues to the reactive nitroolefin (Scheme 1.11).[91, 92]



9-nitrooleic acid (**31**)
containing a reactive nitrolefin

32
Inhibited protein

Scheme 1.11: 9-Nitrooleic acid **31** and its main mechanism of action.

For instance, NFAs inhibit nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB)[93] or 5-Lipoxygenase (5-LO),[94] two key enzymes in inflammation processes, by nitroalkylation of critical cysteines. Also, the covalent modification of Kelch-like ECH-associated protein 1 (Keap 1), important for the regulation of the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway, has been reported.[95] Furthermore, NFAs are potent activators of the peroxisome proliferator-activated receptor γ (PPARγ).[96, 97]

NFAs have emerged as attractive drug candidates for the treatment of inflammatory diseases, such as allergic airways,[98] atherosclerosis,[99] or inflammatory bowel disease.[100] Recently, potent anti-tumorigenic activities of nitrooleic acid against triple-negative breast cancer [101] and colorectal cancer cells,[102] both *in vitro* and in murine xenograft models, have been reported.

Interestingly, the biological activities of unsaturated fatty acids containing other reactive Michael acceptor units have been studied scarcely so far. Biological activities of regiomers of nitrooleic acids **31a**, **31b**[103] and nitrolinoleic acids **33a**, **33b**[85] have been reported. Different fatty acids bearing an electrophilic enone moiety, such as keto fatty acid **34**, have been isolated from different natural sources.[104] They display anti-inflammatory activities and seem to modulate similar targets, such as NF-κB.[105, 106] Unsaturated fatty acids containing other electron-withdrawing groups within the alkyl

chain or as an additional substituent on the double bond were either not evaluated for potential biological activities or have not been reported up to date (Figure 1.5).

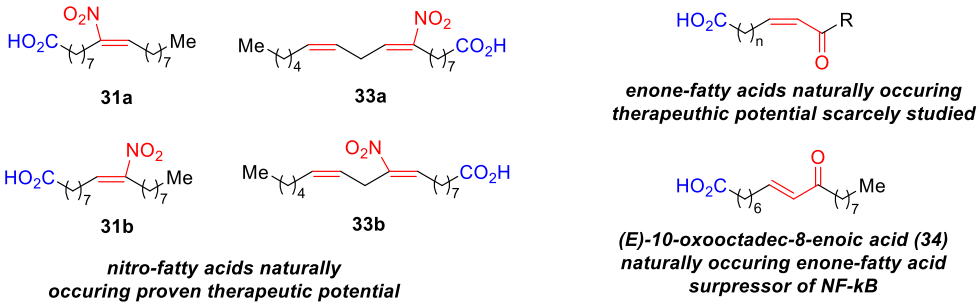
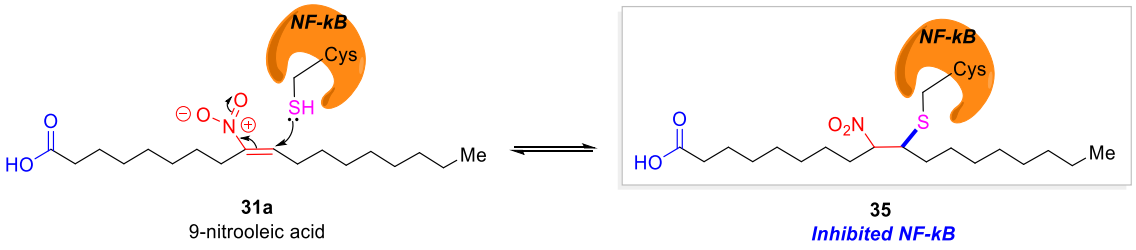


Figure 1.5: Different electrophilic unsaturated fatty aids.

Considering the key role of the Michael acceptor unit in the post-translational protein modification, a controlled modification of its electrophilicity would provide a promising approach for the development of a novel class of drugs based on the NFA-scaffold.

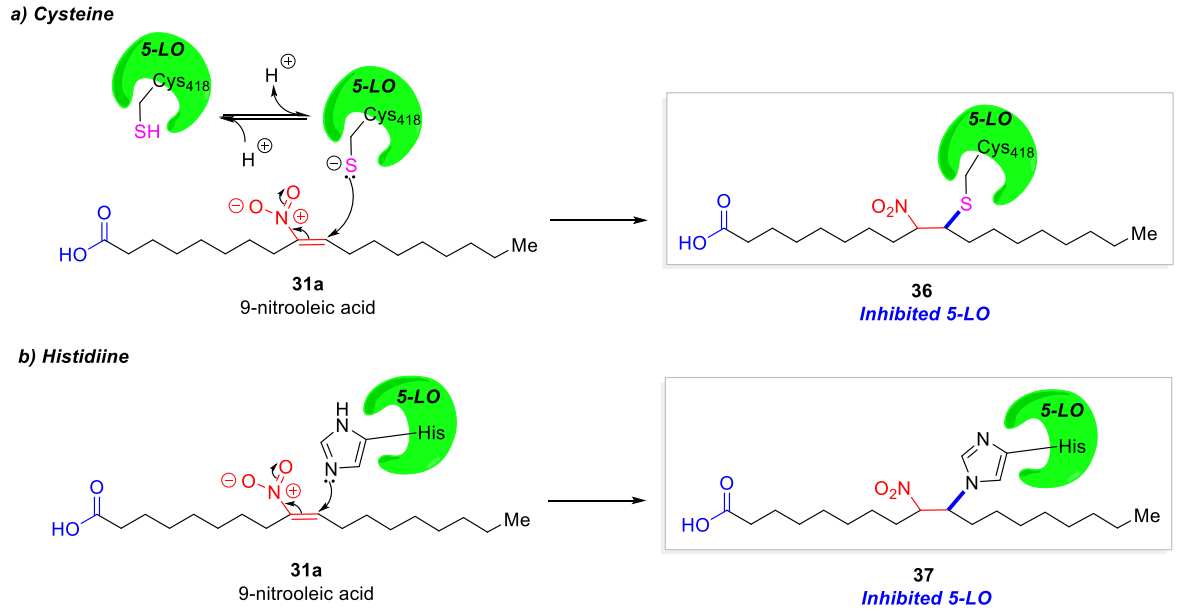
1.5.2 Mode of Action of Nitro-Fatty Acids

The post-translational modification of targeted proteins by nitro-fatty acids *in vitro* and *in vivo* represents an emerging pathway for regulating protein function and cell signaling.[91] The lead structure, 9-nitrooleic acid (9-NOA, **31a**), binds covalently to nucleophilic Cysteine residues such as Cys_{38} and Cys_{62} of p65 and p50 subunits of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), resulting in a loss of its pro-inflammatory and tumorigenic activities[93, 107] (Scheme 1.12).



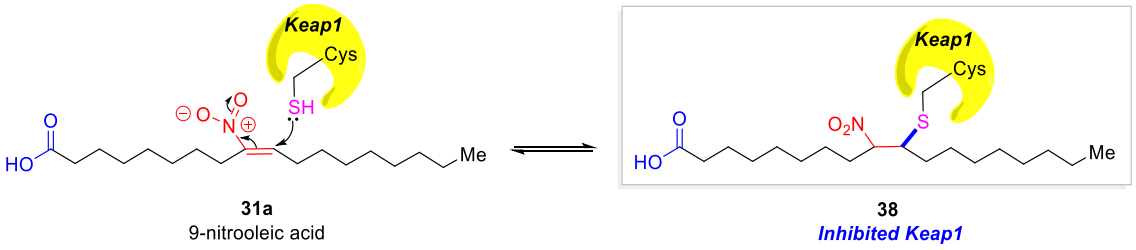
Scheme 1.12: Inhibition of NF-kB by 9-nitrooleic acid **31a**.

Also, 9-nitrooleic acid (9-NOA, **31a**) irreversibly inhibits 5-Lipoxygenase (5-LO) enzyme activity via the formation of covalent adducts with critical nucleophilic Cysteine (Cys_{418}) and Histidines (His_{367} and His_{372}) residues[94] (Scheme 1.13).



Scheme 1.13: Inhibition of 5-Lipoxygenase (5-LO) by 9-nitrooleic acid **31a**.[94]

Furthermore, 9-nitrooleic acid (9-NOA, **31a**) behaves as an activator of the transcription factor Nrf2 by reversible nitroalkylation of relevant Cysteine residues, Cys_{273} and Cys_{288} of Kelch-like ECH-associated protein 1 (Keap 1)[95] (Scheme 1.14).



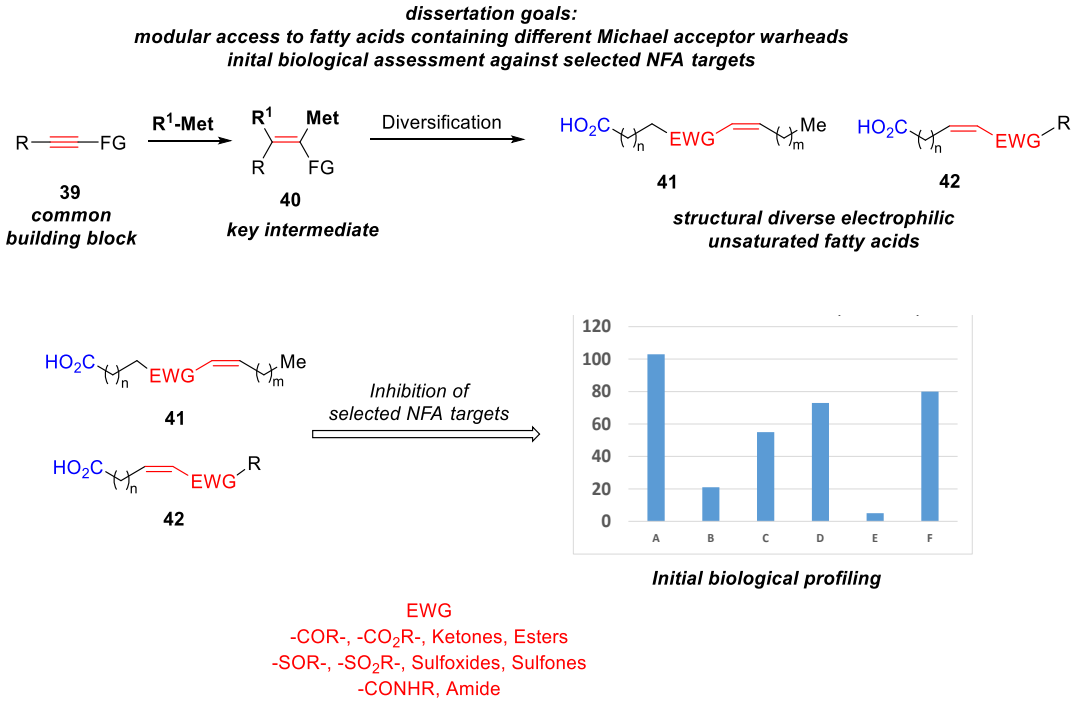
Scheme 1.14: Induction of the Keap1-Nrf2 pathway by 9-nitrooleic acid **31a**.

2 OBJECTIVES

The aim of this research project is the synthesis of a structurally diverse set of unnatural nitro-fatty acid analogues bearing different Michael acceptor units and the evaluation of their biological activities against selected NFA targets in cooperation with the Paul-Ehrlich-Institute (PEI) in Langen and the Goethe-University Frankfurt/Main.

Thus, unsaturated fatty acids bearing different electron-withdrawing groups, either incorporated into the fatty acid chain in proximal (part I) or distal (part II) position to the terminal carboxyl group or as an additional substituent on the double bond, will be prepared.

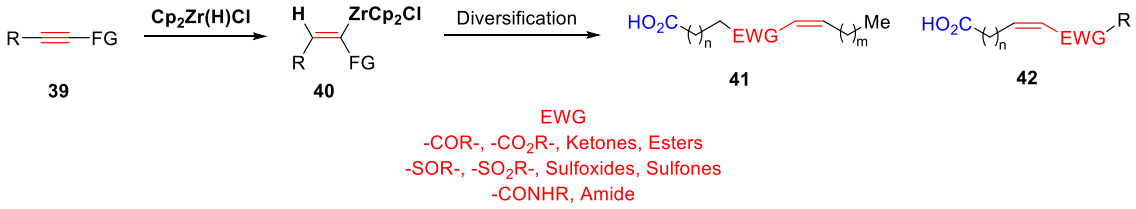
The goal of this dissertation is the development of a highly modular approach enabling the synthesis of structurally diverse fatty acids containing different Michael acceptor warheads from a simple set of common building blocks. Therefore, a route based on the metalation of both internal and terminal alkynes and the diversification of the corresponding metal species will be evaluated. For an initial assessment of their biological activities, the inhibitory effects of all newly synthesized compounds against selected NFA targets will be investigated (Scheme 2.1).



Scheme 2.1: Dissertation Outline. (EWG = electron-withdrawing group; NFAs = Nitro-Fatty Acids; FG = Functional group).

This approach could enable a selective introduction of the key Michael acceptor unit, thereby providing a versatile for chemical modulation of the biological profile.

Initially, the synthesis of a variety of fatty acids bearing different electron-withdrawing groups based on a hydrozirconation-alkynyl metal-diversification route was planned and evaluated (Scheme 2.2).



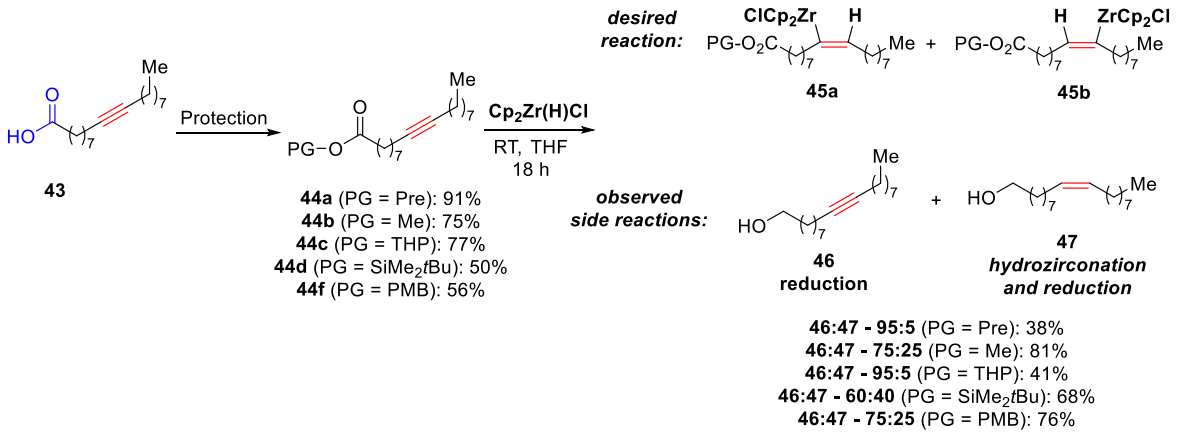
Scheme 2.2: Initially envisioned synthetic route. (EWG = electron-withdrawing group).

3 Results And Discussion

3.1 Attempted hydrozirconation of octadic-9-ynoic acid derivatives

The design of this work were done in collaboration with Prof. Dr. Georg Manolikakes at the Technical University of Kaiserslautern-Landau (RPTU). The experiments were carried out by myself and by Dr. Sara-Cathrin Krieg as part of her master's thesis (hydrozirconation of internal alkynes).

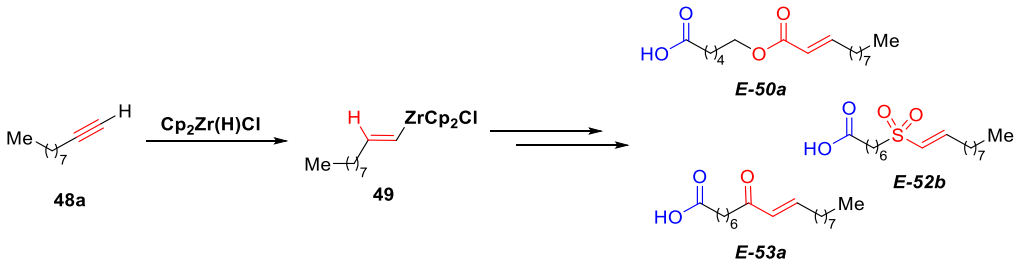
Although different procedures for the hydrometalation step[108] were envisioned, we have identified a hydrozirconation using Schartz's reagent ($Cp_2Zr(H)Cl$)[109] as the most promising approach for our purposes. $Cp_2Zr(H)Cl$ is commercially available and displays the required balance between the reactivity and (chemo)selectivity.[109] Alkenylzirconium reagents are versatile synthetic intermediates, which can undergo reactions with various electrophiles. In addition, a transmetalation to various other metals, such as copper, zinc, nickel, or palladium is feasible, which considerably expands their synthetic utility.[109] In the first phase of this dissertation, the synthesis of NFA analogous via hydrozirconation-electrophilic trapping of octadic-9-ynoic acid derivatives was investigated. Although this route leads to a mixture of regioisomers (**45a** and **45b**), it would provide a first testing ground for the development of the envisioned diversification reactions and generate the first samples for biological testing. Therefore, octadic-9-ynoic acid **43** was converted into the octadic-9-ynoic acid derivatives **44a-f** bearing different protecting groups e.g. Prenyl,[110] Methyl,[111] THP,[112] TBDMS[113] and PMB[114] (Scheme 3.1). Unfortunately, hydrozirconation of all five derivatives using $Cp_2Zr(H)Cl$[109] did not lead to the desired outcome. Instead, a competing reduction of the ester functionality was observed in all cases, leading to a complex mixture of different products **46-47**. It seems that selective hydrozirconation of an internal alkyne in the presence of an ester functionality is not possible (contrary to reported reactions with terminal alkynes). Indeed, product distributions indicated a faster reduction of the ester over the hydrozirconation of the alkyne.



Scheme 3.1: Failed chemoselective hydrozirconation of octadic-9-ynoic acid derivatives **44a-f**.

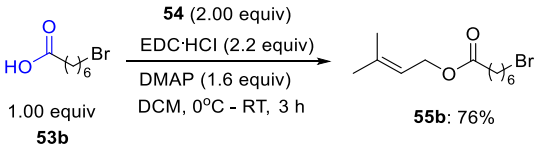
3.2 Evaluation of the hydrozirconation route with terminal alkyne

In the light of these results, we turned our attention to the synthesis of NFA analogues from terminal alkynes. To verify the viability of the initially proposed route, we decided to investigate the conversion of dec-1-yne **48a** to the three fatty acid derivatives ***E-50a***, ***E-52b,*** and ***E-53a*** via a hydrozirconation-SO_2 or CO_2 or aldehyde trapping approach (Scheme 3.2).



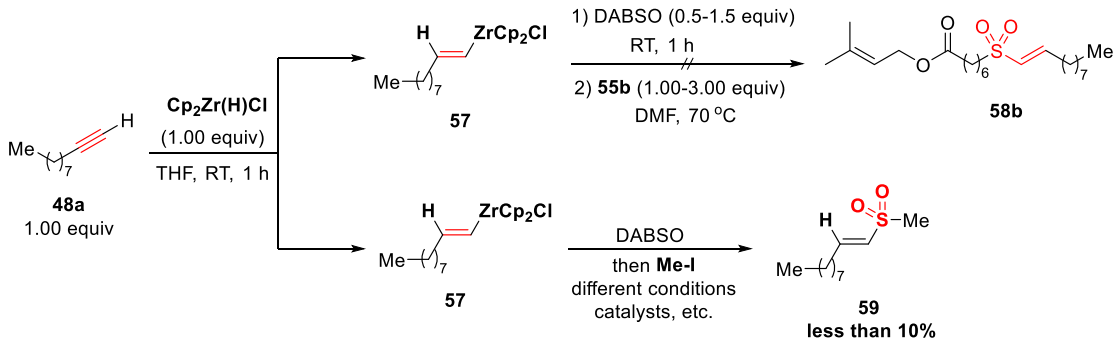
Scheme 3.2: Envisioned route from dec-1-yne **48a** to the NFA analogues ***E-50a***, ***E-52b,*** and ***E-53a.***

Towards this end, the required prenyl-protected building block **55b** was synthesized from the corresponding acid over one step. Steglich esterification[110] of 7-bromoheptanoic acid **53b** with 3-methylbut-2-en-1-ol **54**, DMAP, and EDC·HCl furnished the desired prenyl-protected acid derivative **55b** in 76% yield. (Scheme 3.3).



Scheme 3.3: Synthesis of building block **55b.**

Then, dec-1-yne **48a** was hydrozirconated with $Cp_2Zr(H)Cl$. A complete hydrozirconation occurred after approximately 1 h at room temperature as judged by iodolysis of alkenylmetal species **57**. The formed alkenylzirconium reagent **57** was treated with the 1,4-diazabicyclo[2.2.2]octane bis(sulfur dioxide) adduct DABSO and afterward with alkyl bromide **55b**.[115] Unfortunately, no desired product could be observed. Instead, various unidentified decomposition products were formed. In order, to identify problems in the two-step SO_2 trapping-sulfinate alkylation sequence and optimize the reaction conditions, a model system with methyl iodide as more reactive alkylating agent was studied (Scheme 3.4).



Scheme 3.4: Attempted synthesis of vinyl sulfone fatty acid.

However, even after considerable experimentation, the desired vinyl sulfone **59** could be obtained less than 10% yield. Control experiments revealed, that the zirconium sulfinate formed after trapping of **57** with DABSO, is not stable at the temperature required for the subsequent alkylation. These control studies confirmed, that the initially envisioned general route towards NFA analogous via alkenylzirconium intermediates might not be possible.

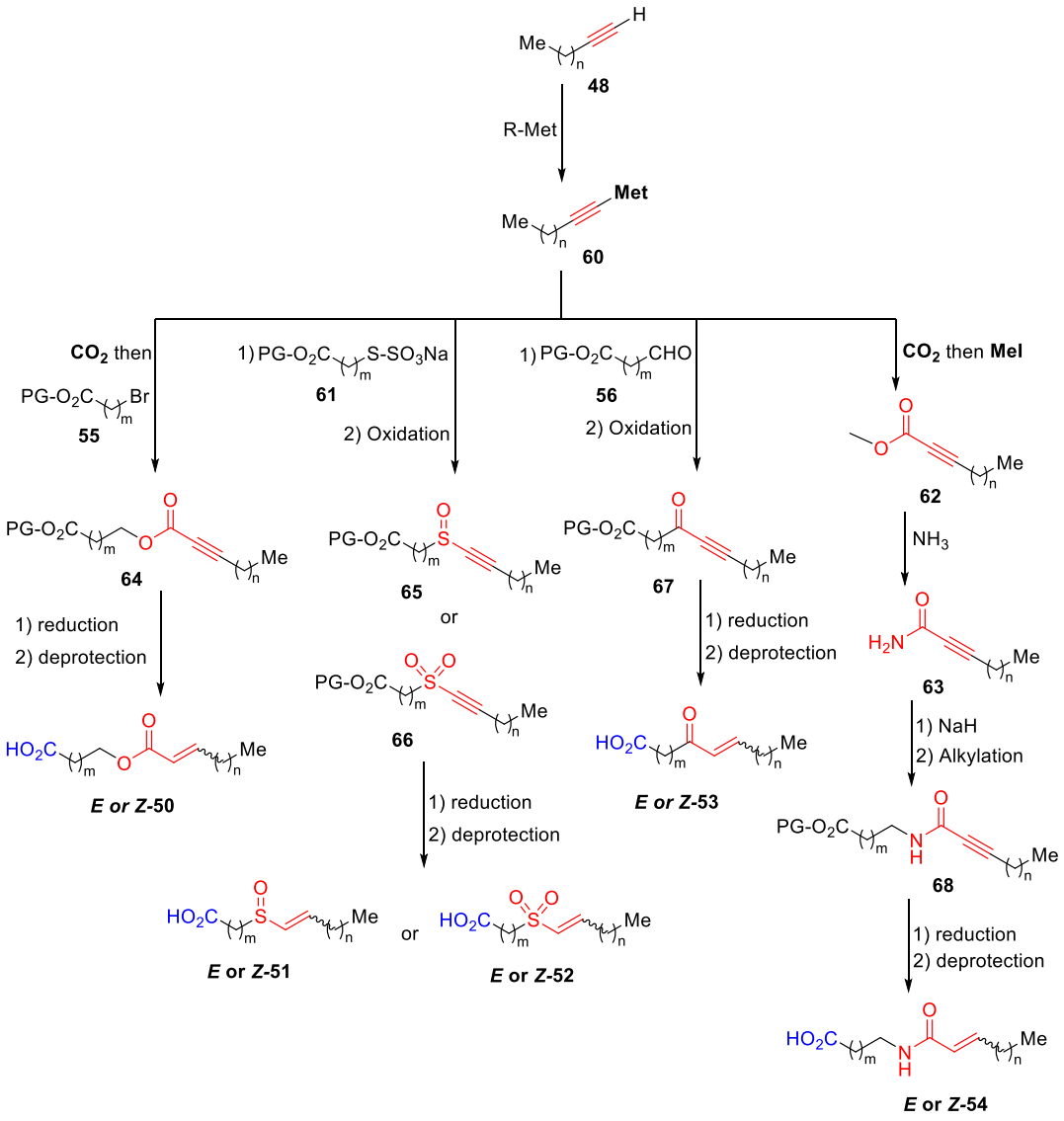
3.3 Implementation of a 2nd generation route

3.3.1 Alkyne-based approach

The results discussed in this part are unpublished. The design and planning of this work were done in collaboration with Prof. Dr. Georg Manolikakes at the Technical University of Kaiserslautern-Landau (RPTU). The experiments were carried out in collaboration with Dr. Mohamed Hassan as part of his Ph.D. thesis (synthesis of sulfone- and sulfoxide-modified fatty acids) from Aswan University in Egypt.

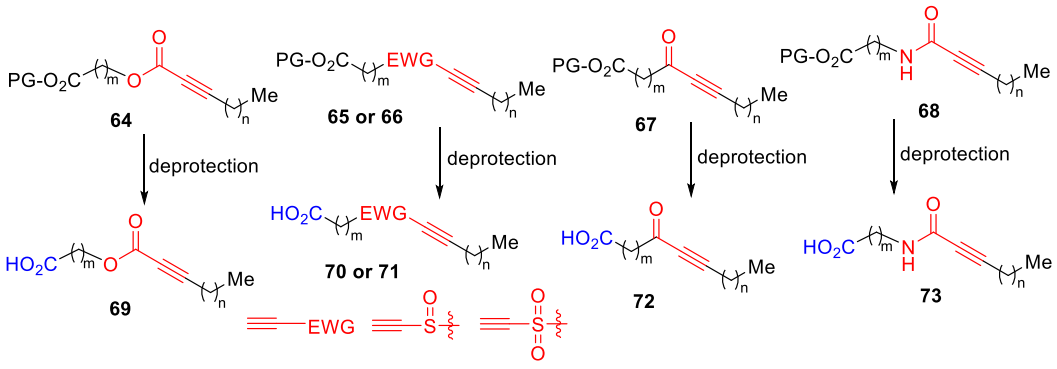
3.3.1.1 Introduction

In the light of the previous results, different alternative routes were evaluated. After extensive literature research, a route via alkynyl metal species was considered as an alternative with the highest chances of success and the same modularity as the first route. Indeed, it would also allow the use of the same building blocks as before, which were already partially prepared. The overall approach is outlined in **scheme 3.5**. Deprotonation of a terminal alkyne **48** leads to the alkynylmetal species **60.** Trapping with CO_2 followed by alkylation with the alkyl bromide **55** affords the conjugated alkyne **64**. The reaction of **60** with Bunte salt **61** followed by oxidation can lead either to a sulfoxide **65** or a sulfone **66.** The reaction of **60** with an aldehyde **56** followed by oxidation furnishes the ketone **67**. Alkylation of amide **63**, accessible from the corresponding methyl ester **62**, furnishes the amide-analogue **68.** Stereoselective semi-hydrogenation of the alkynes **64-68** followed by deprotection of the prenyl group would give access to either the ***E***- or the ***Z***-configured electrophilic fatty acids **50-54** in a highly modular manner.



Scheme 3.5: 2nd Generation alkyne-based approach to NFA derivatives **50-54.**

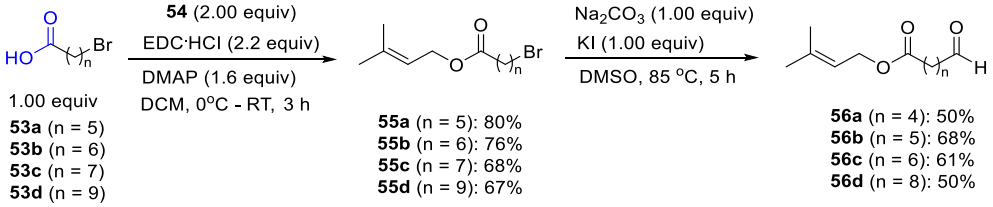
This route has two advantages over the initially envisioned one. Both the *E*- and the *Z*-isomers can be accessed from the same intermediate. The direct deprotection of the alkynoic esters **64-68** would allow the synthesis of an additional class of electrophilic fatty acids **69-73** containing an alkyne-containing Michael acceptor, with a potentially more favorable biological profile (Scheme 3.6).



Scheme 3.6: 2nd Generation alkyne-based approach to NFA derivatives **69-73.**

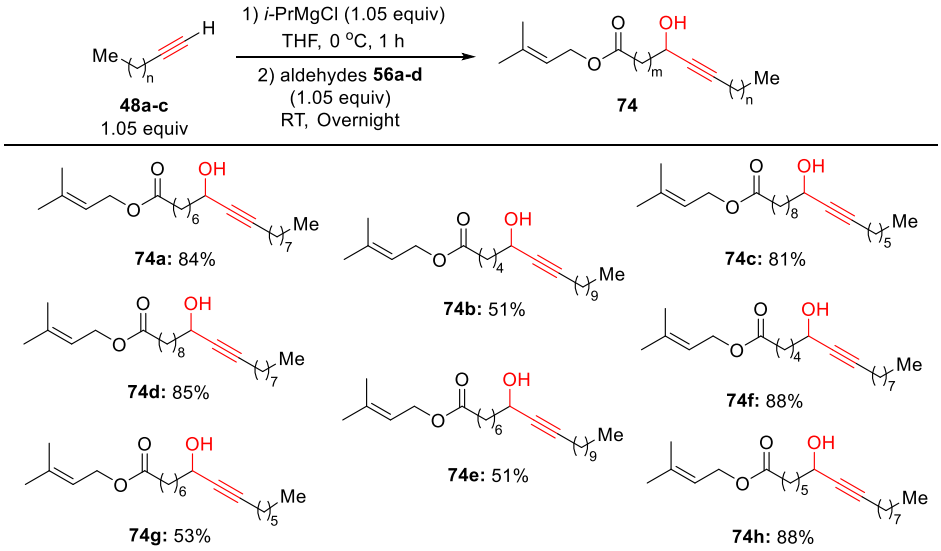
3.3.1.2 Access to Keto-modified fatty acids

In order to evaluate the feasibility of the 2nd generation approach, the required prenyl-protected building blocks were synthesized from the corresponding acids over one or two steps. For the incorporation of the prenyl-protecting group, Steglich esterification[110] of ω-bromofatty acids **53a-d** with 3-methylbut-2-en-1-ol **54**, DMAP, and EDC·HCl furnished the prenyl-protected acid derivatives **55a-d.** Kornblum oxidation[116] of esters **55a-d** with Na_2CO_3 and KI provided the desired Prenyloxoalkanoate derivatives **56a-d** (Scheme 3.7).

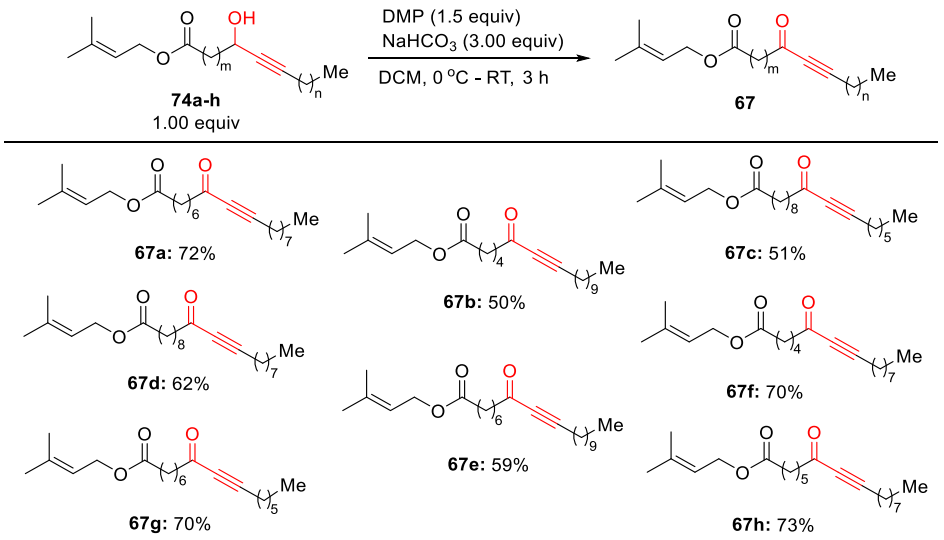


Scheme 3.7: Synthesis of building blocks **55a** and **56a-d.**

Then, alkynes **48a-c** was deprotonated with *i*-PrMgCl. Reaction with aldehydes **56a-d** afforded the desired propargylic alcohols **74a-h** in 51-88% yield (Scheme 3.8). Oxidation of alcohols **74a-h** with Dess-Martin periodinane (DMP)[117] furnishes ketones **67a-h** in 50-73% yield (Scheme 3.9).

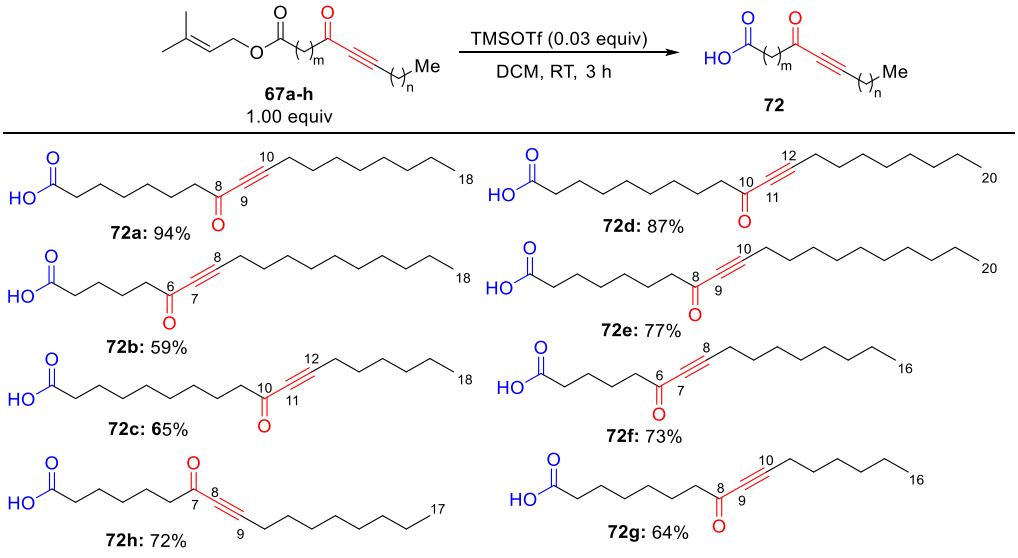


Scheme 3.8: Synthesis of propargylic alcohols **74a-h.**



Scheme 3.9: Synthesis of alkynes **67a-h.**

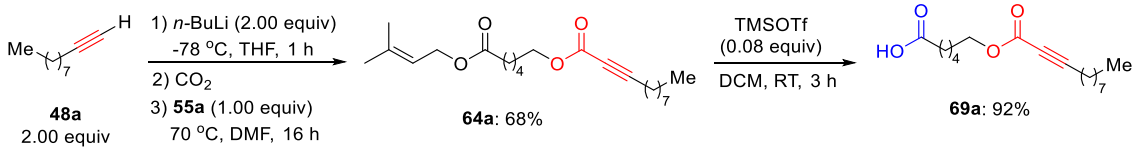
Subsequent removal of the prenyl protecting group with TMSOTf[118] afforded the keto fatty acid derivatives **72a-h** in good to excellent yield of 59-94%. This route enabled the successful synthesis of eight non-natural unsaturated nitrated fatty acids analogs by the variation of the aldehydes and alkynes. The terminal chain length varies between sixteen to twenty carbon atoms, bearing ketone as an electron-withdrawing group close to the terminal carboxyl group and conjugated to a triple bond at different positions, such as C_7-C_8, C_8-C_9, C_9-C_{10}, and C_{11}-C_{12} (Scheme 3.10).



Scheme 3.10: Successful synthesis of alkynoic acid **72a-h.**

3.3.1.3 Access to alkynyl ester-modified fatty acid

Using the planned alkyne-based approach, dec-1-yne **48a** was deprotonated with *n*-BuLi.[119] Reaction with CO_2 followed by alkylation with the bromide **55a** of the formed carboxylate gave the desired ester **64a** in 68% yield over in a simple one-pot operation. Removal of the prenyl group with TMSOTf[118] afforded fatty acid derivative **69a** in 92% yield (Scheme 3.11).

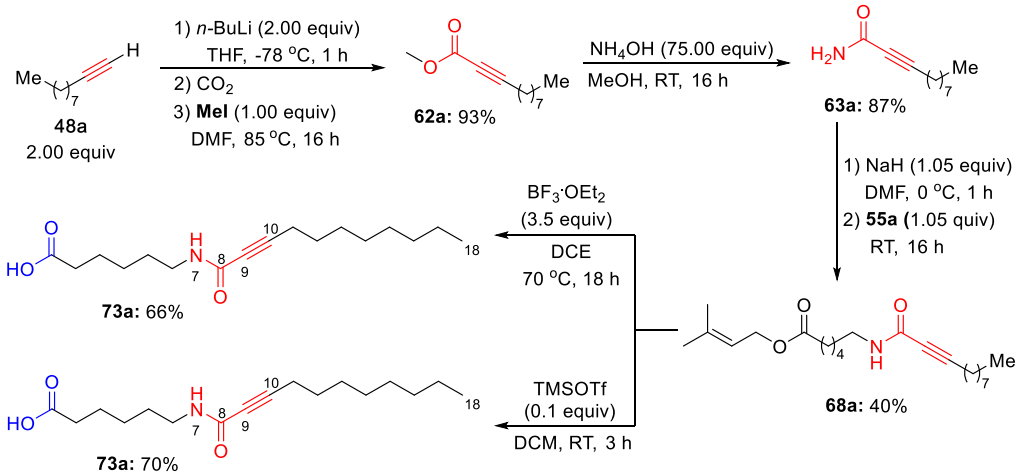


Scheme 3.11: Successful synthesis of alkynyl fatty acid **69a**.

The desired non-natural NFA analog **69a** was obtained in 92% yield in two steps from the appropriate building blocks **55a** and **48a**. It bears an ester as an electron-withdrawing group in a proximal position to the terminal carboxyl group and conjugated to a triple bond.

3.3.1.4 Access to Amide-modified fatty acid

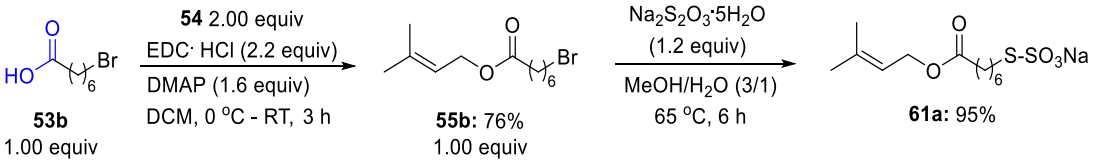
In the same manner, deprotonation of 1-decyne **48a** with *n*-BuLi and then reaction with CO_2 followed by alkylation with MeI of the formed carboxylate gave the desired ester **62a**[120] in 93% yield in a simple one-pot operation. The reaction of ester **62a** with ammonium hydroxide (NH_4OH aq, 28-30%)[121] furnishes amide **63a** in 87% yield. Deprotonation of amide **63a** with sodium hydride (NaH, 60% dispersion in mineral oil)[122] followed by alkylation with alkyl bromide **55a** gave the desired amide-analouge **68a** in 40% yield. Deprotection of **68a** with either TMSOTf[118] or $BF_3{\cdot}OEt_2$[123] furnished the desired fatty acid **73a** in 70% and 66% yield respectively (Scheme 3.12). This route led to the successful synthesis of the desired non-natural NFA analog **73a** bearing amide as an electron-withdrawing group close to the terminal carboxyl group and conjugated to a triple bond.



Scheme 3.12: Successful synthesis of alkynoic acid **73a.**

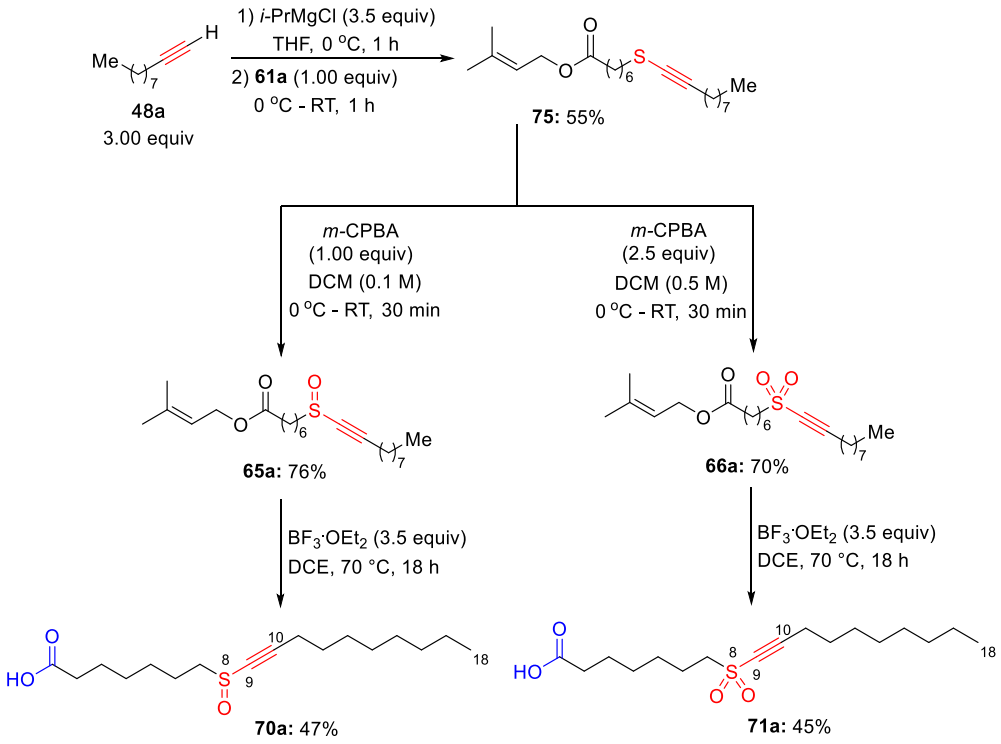
3.3.1.5 Access to Sulfoxide and Sulfone-modified fatty acids

The required Bunte salt[124] building block **61a**, was synthesized from the corresponding acid **53b** over two steps. First, steglich esterification[110] of 7-bromoheptanoic acid **53b** with 3-methylbut-2-en-1-ol **54**, DMAP, and EDC·HCl furnished the prenyl-protected acid derivative **55b**. Then, the reaction of ester **55b** with sodium thiosulfate pentahydrate ($Na_2S_2O_3{\cdot}5H_2O$) provided the desired Bunte salt **61a** in 95% yield (Scheme 3.13).



Scheme 3.13: Synthesis of Bunte salt **61a.**

Next, 1-decyne **48a** was deprotonated with *i*-PrMgCl. Reaction with Bunte salt **61a** afforded the desired sulfide **75** in 55% yield. Oxidation of sulfide **75** with one or 2.5 equivalents of *m*-CPBA[125] furnished sulfoxide **65a** and sulfone **66a** in 76% and 70% yield respectively. Removal of the prenyl-protecting group with $BF_3{\cdot}OEt_2$[123] afforded the desired non-natural unsaturated nitrated fatty acids analogues **70a** and **71a** bearing sulfoxide and sulfone as an electron-withdrawing group close to the terminal carboxyl group and conjugated to a triple bond (Scheme 3.14).

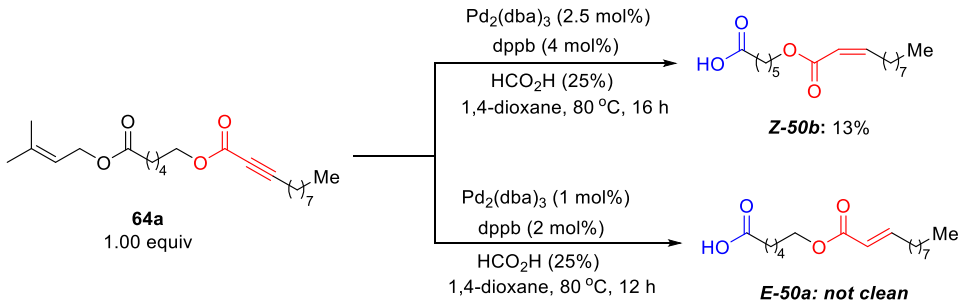


Scheme 3.14: Successful synthesis of alkynoic acids **70a** and **71a.**

3.4 Stereoselective Semi-Hydrogenation of Alkynes

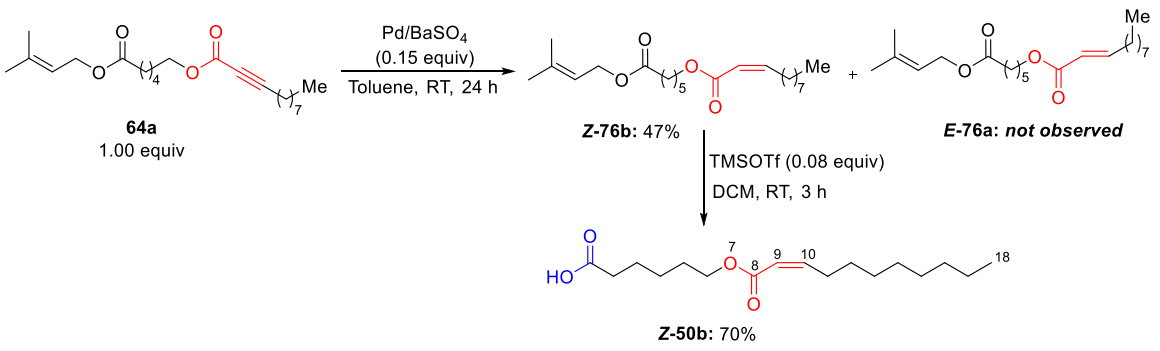
3.4.1 Access to *(Z)*-Configured Alkenyl ester-modified fatty acid

Next, the semi-hydrogenation of alkynes was investigated. After a survey of the existing literature, different methods were applied. First, a Palladium-catalyzed semi-hydrogenation of alkynes with formic acid reported by Han[126] and coworkers was tested. This method gives stereoselective access to the ***E***- or the ***Z***-Isomer by adjusting the Palladium-ligand ratio. In addition, we envisioned that the acidic reaction conditions might lead to a concurrent removal of the prenyl-protecting group. Indeed, a first test reaction using the reported procedure for the ***Z***-selective semi-hydrogenation afforded directly the free acid ***Z*-50b** in 13% yield. Unfortunately, the corresponding *E*-selective version did not afford the desired product in a purity sufficient for biological testing (Scheme 3.15). Unfortunately, all efforts to optimize the Method of Han to our system were unsuccessful.



Scheme 3.15: Unsuccessful optimization of stereoselective semi-hydrogenation of alkyne **64a.**

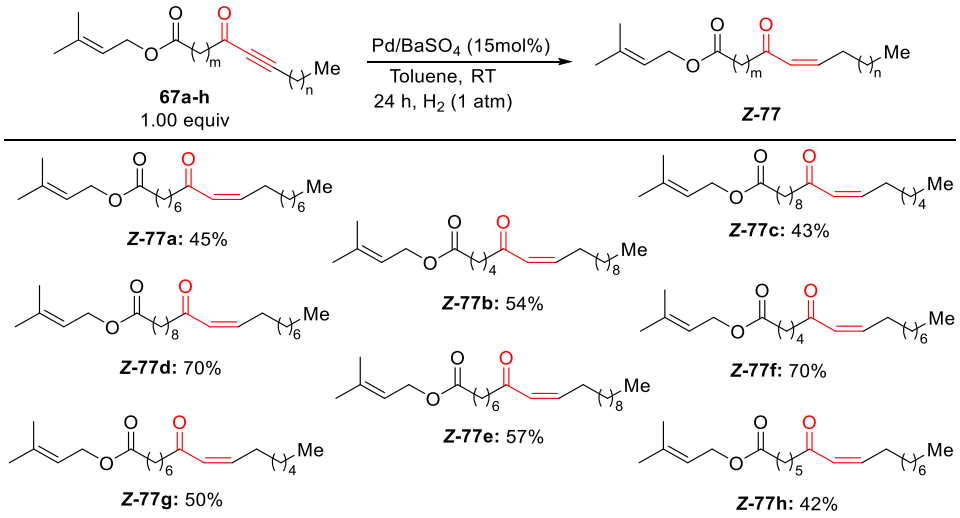
Therefore, alternative routes for the stereoselective semi-hydrogenation of alkynes were evaluated. A ***Z***-selective semi-hydrogenation of alkyne **64a** was achieved with Lindlar catalyst,[127] furnishing ***Z*-76b** in 47% yield. Subsequent removal of the prenyl group with TMSOTf[118] gave NFA derivative ***Z*-50b** in 70% yield. The non-natural NFA derivative ***Z*-50b** contains an ester as an electron-withdrawing group conjugated to a double bond (Scheme 3.16).



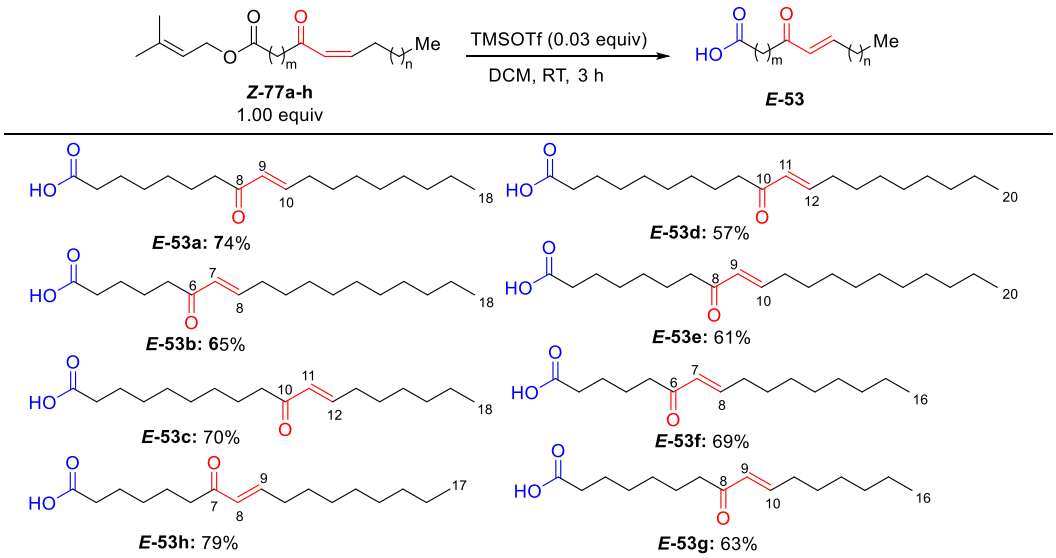
Scheme 3.16: Successful synthesis of *(Z)*-configured fatty acid **50b.**

3.4.2 Access to (*E*)-Configured enone-modified fatty acids

A *Z*-selective, semi-hydrogenation of alkynes **67a-h** was achieved with Lindlar catalyst,[127] furnishing the enones ***Z*-77a-h** in 42-70% yield (Scheme 3.17). However, complete isomerization to the thermodynamically more stable *E*-isomers **53a-h** was observed in the final deprotection step. The same isomerization was also observed for the synthesis of *(E)*-9-NOA **31a**.[128] The C_{16}-, C_{17}-, C_{18}-, and C_{20}-fatty acids derivatives ***E*-53a-h** contain an enone as a Michael acceptor unit incorporated into the aliphatic carbon chain in different positions to the terminal carboxyl group (Scheme 3.18).



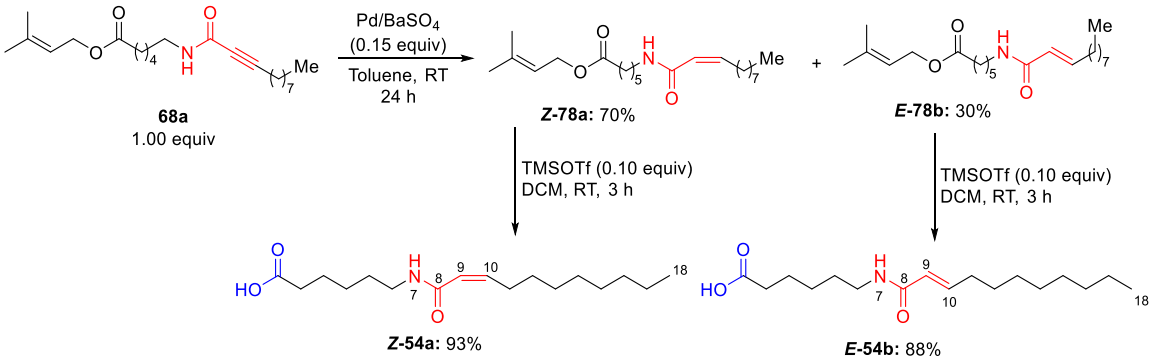
Scheme 3.17: Synthesis of *(Z)*-configured enones **77a-h.**



Scheme 3.18: Successful synthesis of *(E)*-configured fatty acids **53a-h.**

3.4.3 Access to *(E)*- and *(Z)*- Configured Amide-modified fatty acids

Reduction of amide **68a** in the presence of Lindlar catalyst[127] furnishes both isomers ***Z*-78a** and ***E*-78b** in 80% overall yield. Fortunately, both isomers could be separated by column chromatography. The final deprotection of either ***Z*-78a** or ***E*-78b** with TMSOTf[118] furnished the corresponding stereochemically defined NFA derivatives ***Z*-54a** and ***E*-54b** in 93% and 88% yield respectively (Scheme 3.19).

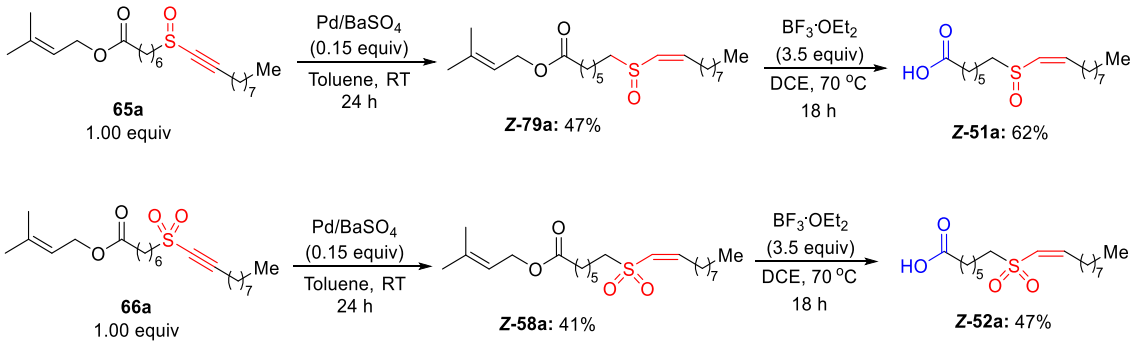


Scheme 3.19: Successful synthesis of *(Z)*- and *(E)*-configured fatty acids **54a** and **54b.**

The stereoselective semi-hydrogenation of alkyne **68a** enabled the successful synthesis of unsaturated fatty acids derivatives ***Z*-54a** and ***E*-54b** bearing amide as an electron-withdrawing group conjugated to a double bond.

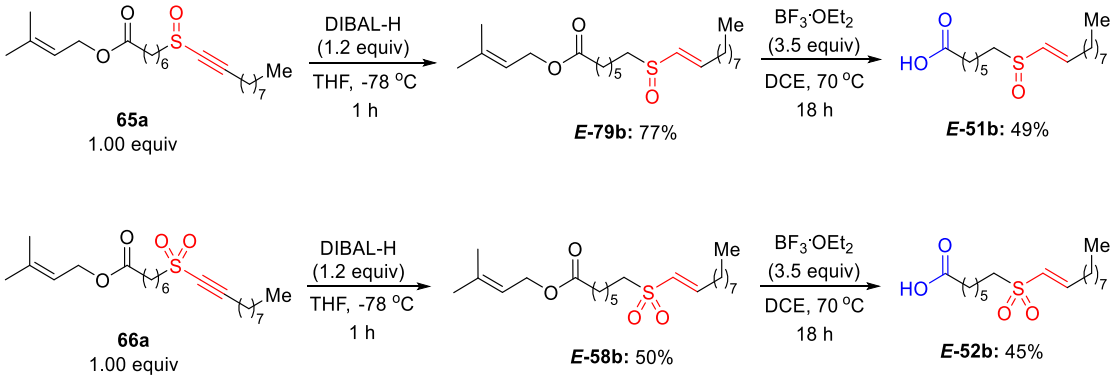
3.4.4 Access to (*Z*)- and (*E*)-Configured Alkenyl Sulfoxide and Alkenyl Sulfone-modified fatty acids

In the same manner, the reduction of sulfoxide **65a** and sulfone **66a** with Lindlar catalyst[127] afforded the ***Z*-**olefins ***Z*-79a** and ***Z*-58a** in acceptable yield. Removal of the prenyl group with $BF_3{\cdot}OEt_2$[123] gave the free acids ***Z*-51a** and ***Z*-52a** in 62% and 47% yield respectively (Scheme 3.20).



Scheme 3.20: Successful synthesis of *(Z)*-configured fatty acids **51a** and **52a.**

An *E*-stereoselective reduction of sulfoxide **65a** and sulfone **66a** was achieved with DIBAL-H,[127] furnishing the ***E*-olefins *E*-79b** in 77% and ***E*-58b** in 50% yield. Deprotection of the prenyl group with $BF_3{\cdot}OEt_2$[123] afforded the NFA analogues ***E*-51b** and ***E*-52b** in 49% and 45% yield respectively (Scheme 3.21).



Scheme 3.21: Successful synthesis of *(E)*-configured fatty acids **51b** and **52b.**

The stereoselective semi-hydrogenation of alkynes **65a** and **66a** led to the synthesis of four unsaturated fatty acids derivatives bearing vinyl sulfoxide ***Z*-51a** and ***E*-51b**, vinyl sulfone ***Z*-52a** and ***E*-52b** as Michael acceptor units.

3.5 Conclusion

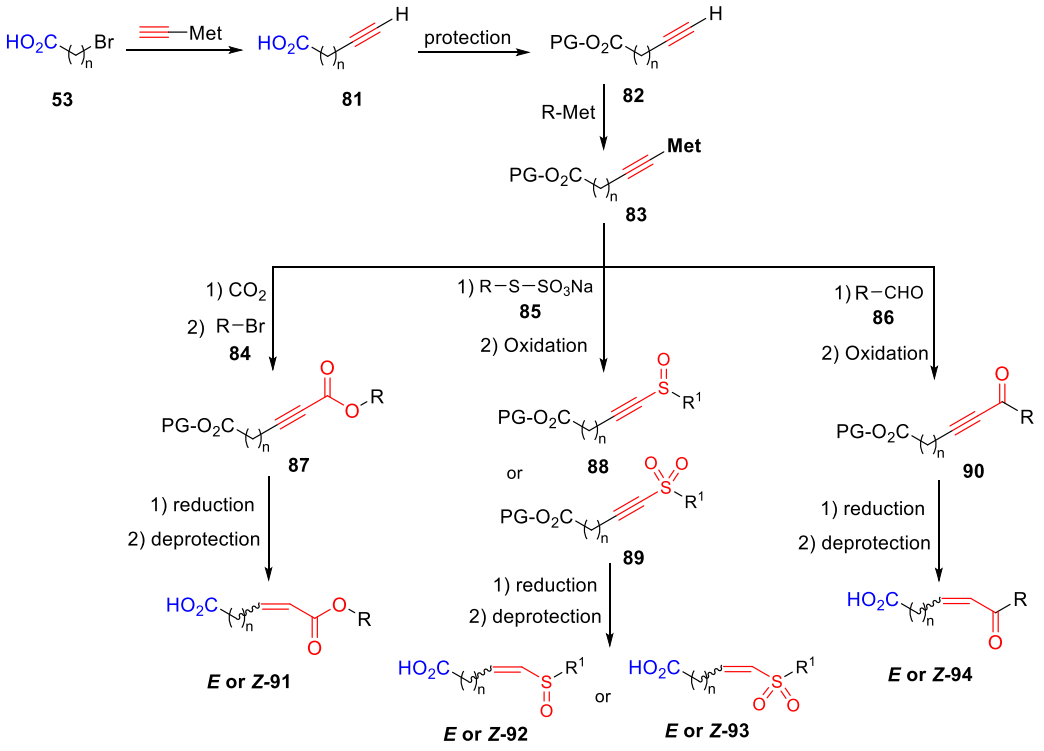
In the first part of this work, we could prove that the envisioned 1st generation synthesis route via hydrozirconation and alkenyl zirconium reagents is not viable. The hydrozirconation of internal alkynes with Schwartz's reagent is not compatible with an ester functionality. In addition, alkenyl zirconium reagents cannot be trapped with sulfur dioxide in a productive manner, presumably due to the instability of the corresponding zirconium sulfinates. In the light of these results, we devised a 2nd generation route via alkynyl metal species as a key intermediate. We demonstrated the viability of the new approach and synthesized twenty-seven (27) non-natural NFAs analogues. The 2nd generation route has two clear advantages: *i*) it greatly simplifies the preparation of both double bond isomers; *ii*) it gives access to an additional class of alkyne-derived Michael acceptors units.

3.6 Synthesis of fatty acids bearing different electron-withdrawing groups incorporated into the fatty acid chain in distal position to the terminal carboxyl group

The results presented in this part of the thesis are unpublished. The design and planning of this work were done in collaboration with Prof. Dr. Georg Manolikakes at the Technical University of Kaiserslautern-Landau (RPTU). All experiments were carried out by myself.

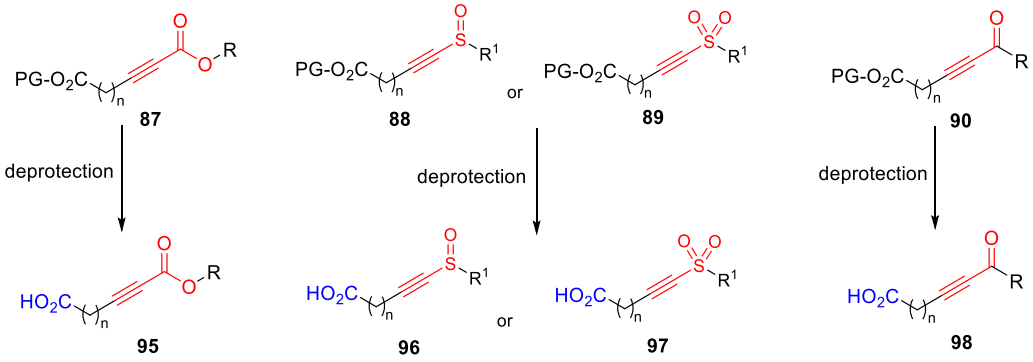
3.6.1 Introduction

Starting from alkynes of type **81** accessible from the corresponding acids **53**, a second series of NFA derivatives bearing the electron-withdrawing group on the alkyl terminus can be accessed in the same manner. In this part, we focused mainly on the construction of ester-, sulfoxide-, sulfone-, and keto-modified fatty acids adopting the previously established route. The overall approach is outlined in **Scheme 3.22**. Protection of alkynoic acid **81** furnishes the corresponding ester-functionalized alkyne **82**. Deprotonation of **82** leads to the alkynylmetal species **83**. Trapping of **83** with CO_2 followed by alkylation with the alkyl bromide **84** affords the diester **87.** The reaction of **83** with Bunte salt **85** followed by oxidation would provide either a sulfoxide **88** or sulfone **89**. The reaction of **83** with aldehydes **86** followed by oxidation furnishes the ketones **90**. Stereoselective semi-hydrogenation of the alkynes **87-90** and subsequent deprotection would give access to either the ***E*-** or the ***Z*-**configured electrophilic fatty acids **91-94.**



Scheme 3.22: 2nd Generation alkyne-based approach to NFA derivatives of types **91, 92, 93,** and **94.**

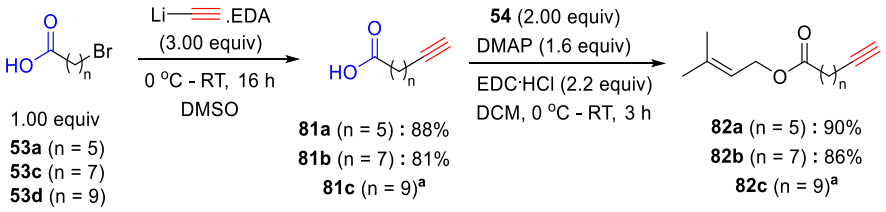
The direct removal of the protecting group of alkynoic esters **87-90** would allow the synthesis of alkyne-derived Michael acceptor units of types **95-98** (Scheme 3.23).



Scheme 3.23: 2nd Generation alkyne-based approach to NFA derivatives **95-98**.

3.6.2 Access to Keto-modified fatty acids

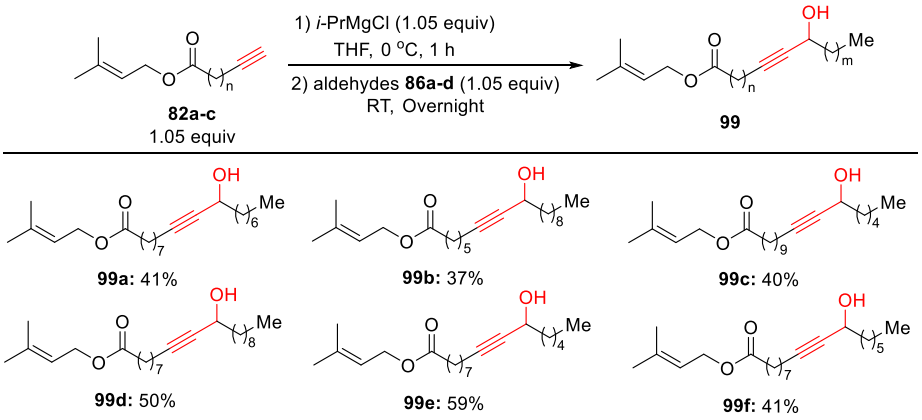
To assess the viability of the planned alkyne approach, the required ester-functionalized alkynes building blocks were synthesized in two steps from the corresponding, commercially available acids. Nucleophilic substitution of acids **53a-d** by lithium acetylide-ethylenediamine complex[129] gave the corresponding alkynoic acids **81a-c** in 81-88% yield. Steglich esterification[110] of acids **81a-c** with 3-methylbut-2-en-1-ol **54**, DMAP, and EDC·HCl provided the desired ester-functionalized alkynes derivatives **82a-c** (Scheme 3.24).



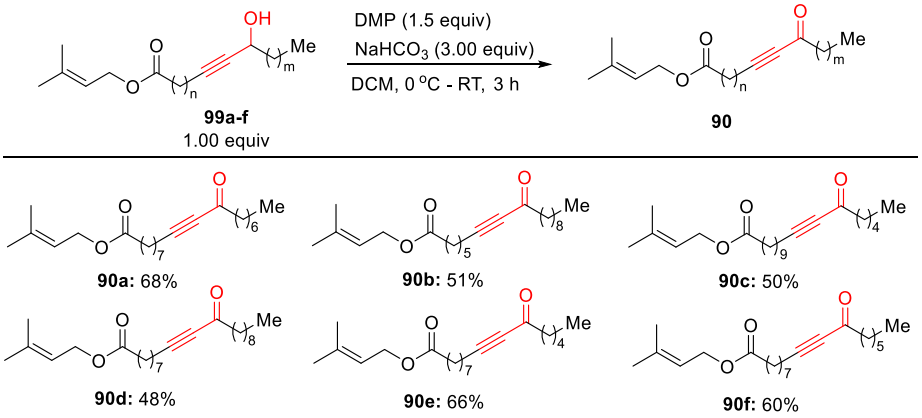
Scheme 3.24: Synthesis of building blocks **82a-c.**

Then, alkynes **82a-c** was deprotonated with *i*-PrMgCl. The reaction with an aldehyde (Hexanal **86a**, Heptanal **86b**, Octanal **86c**, or Decanal **86d**) afforded the propargylic alcohols **99a-f** in 37-59% yield (Scheme 3.25). Oxidation of **99a-f** with Dess-Martin periodinane (DMP)[117] furnishes ketones **90a-f** in 48-68% yield (Scheme 3.26).

[a] *Used directly for the next step without further purification*

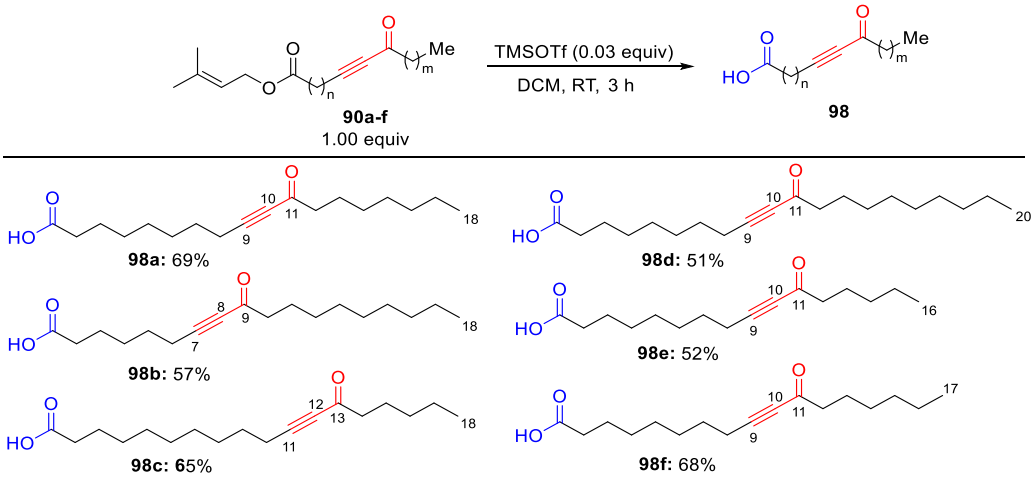


Scheme 3.25: Synthesis of propargylic alcohols **99a-f.**



Scheme 3.26: Synthesis of ketones **90a-f.**

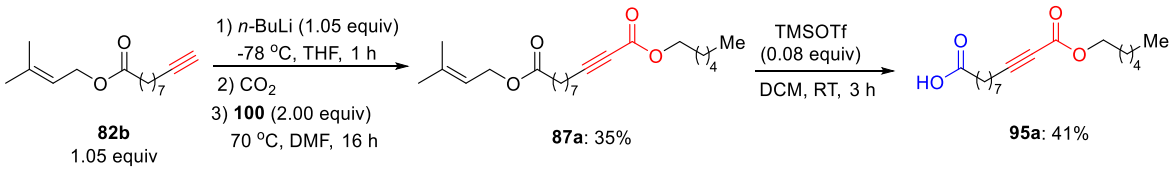
Removal of the prenyl-protecting group with TMSOTf[118] afforded the keto fatty acids derivatives **98a-f** in 51-69% yield (Scheme 3.27). This route enabled the successful synthesis of six different C_{16}-, C_{17}-, C_{18}-, and C_{20}- unsaturated fatty acids derivatives **99a-f** bearing ketone as an electron-withdrawing group conjugated to a triple bond in different positions to the terminal carboxyl group.



Scheme 3.27: Successful synthesis of keto fatty acids **98a-f.**

3.6.3 Access to Alkynyl Ester-modified fatty acid

In the same manner, alkyne **82b** was deprotonated with *n*-BuLi. Reaction with CO_2 followed by alkylation with 1-Bromohexane **100** of the formed carboxylate gave the desired diester **87a** in 35% yield over in a simple one-pot operation. Removal of the prenyl group with TMSOTf[118] directly afforded the fatty acid derivative **95a** in 41% yield (Scheme 3.28).

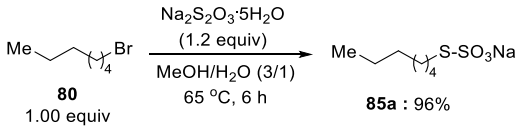


Scheme 3.28: Successful synthesis of alkynyl fatty acid **95a.**

The analog **95a** contains an ester as an electron-withdrawing group in a distal position to the terminal carboxyl group and conjugated to a triple bond.

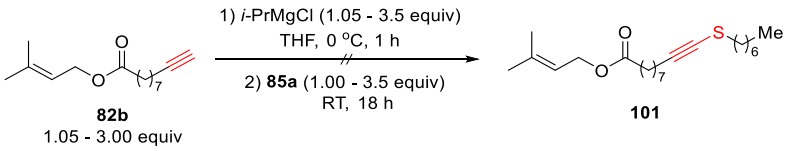
3.6.4 Access to Sulfoxide and Sulfone-modified fatty acids

The required Bunte salt[124] building block **85a**, was synthesized from the corresponding alkyl halide over one step. Treatment of 1-Bromoheptane **80** with sodium thiosulfate pentahydrate ($Na_2S_2O_3{\cdot}5H_2O$) provided the desired Bunte salt **85a** in 96% yield (Scheme 3.29).



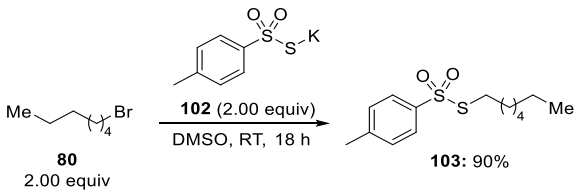
Scheme 3.29: Synthesis of building block **85a**.

Unfortunately, deprotonation of alkyne **82b** with *i*-PrMgCl followed by the addition of Bunte salt **85a** did not afford the desired alkynyl sulfide **101** (Scheme 3.30). The presence of water in the Bunte salt **85a** certainly interferes in the alkylation step by protonating acetylide anion intermediate, leading to the recovery of the starting material **82b**.



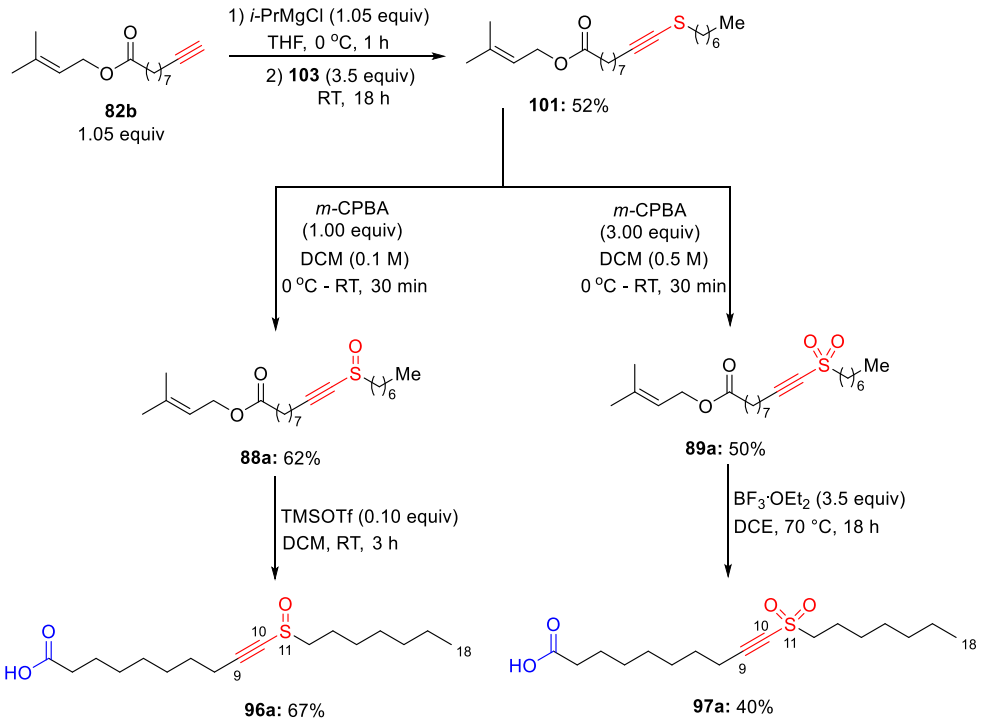
Scheme 3.30: Failed synthesis of sulfide **101**.

In light of the previous result, we turned our attention to the synthesis of alkynyl sulfide **101** from thiosulfonate[130] as an S-alkylating agent. Therefore, *S*-heptyl 4-methylbenzenesulfonothioate[131] building block **103** was prepared from the corresponding alkyl halide **80** in 90% yield by reaction with potassium *p*-toluenethiosulfonate **102** (Scheme 3.31).



Scheme 3.31: Synthesis of building block **102.**

Then, alkyne **82b** was deprotonated with *i*-PrMgCl. Reaction with the sulfur-containing building block **103** gave the desired alkynyl sulfide **101** in 52% yield. Oxidation of sulfide **101** with one or three equivalents of *m*-CPBA furnished sulfoxide **88a** and sulfone **89a** in 62% and 50% yield respectively. Deprotection with TMSOTf[118] or $BF_3{\cdot}OEt_2$[123] directly furnished NFA derivatives **96a** and **97a** in 67% and 40% yield respectively (Scheme 3.32). The planned route enabled the successful synthesis of two non-natural unsaturated fatty acids analogues **96a** and **97a** bearing sulfoxide and sulfone as electron-withdrawing groups conjugated to a triple bond.

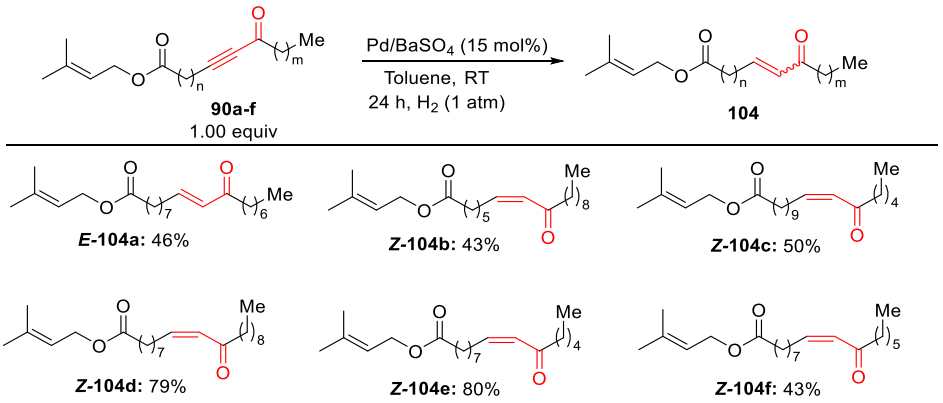


Scheme 3.32: Successful synthesis of alkynoic acids **96a** and **97a.**

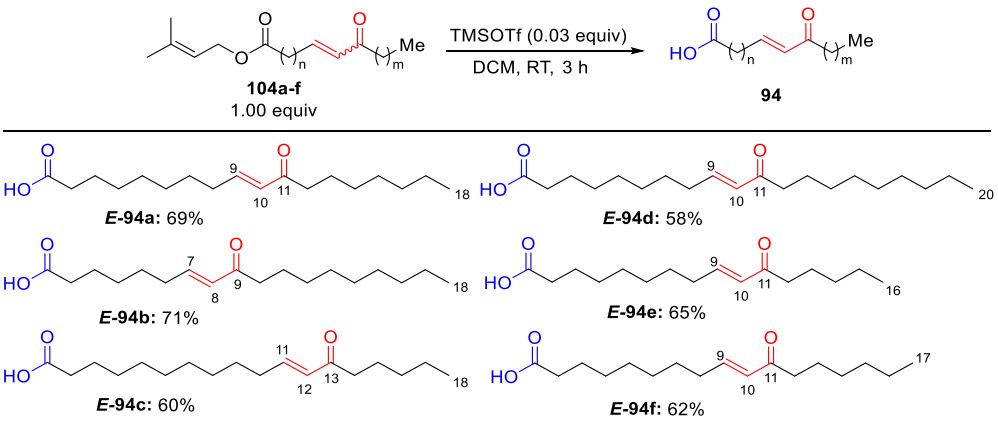
3.7 Stereoselective Semi-Hydrogenation of Alkynes

3.7.1 Access to (*E*)-Configured enone-modified fatty acids

Next, the semi-hydrogenation of the obtained alkynes was investigated. A *Z*-selective, semi-hydrogenation of alkynes **90b-f** was achieved with Lindlar catalyst,[127] furnishing the enones ***Z*-104b** - ***Z*-104f** in 43-80% yield. Semi-hydrogenation of alkyne **90a** furnished directly the thermodynamically more stable *E*-isomer (***E*-104a**) in 46% yield (Scheme 3.33). As before, complete isomerization to the thermodynamically more stable *E*-isomers (***E*-94b** - ***E*-94f**) was observed in the final deprotection step with TMSOTf[118]. Deprotection of ***E*-104a** gave the fatty acid ***E*-94a** in 69% yield (Scheme 3.34). Stereoselective semi-hydrogenation of alkynes **90a-f** led to the successful synthesis of six NFA derivatives ***E*-94a-f** bearing enone as Michael acceptor unit incorporated into the fatty acid chain in distal position to the terminal carboxyl group. The analogs ***E*-94a-f** will provide an overview of structures with comparison to NOA.



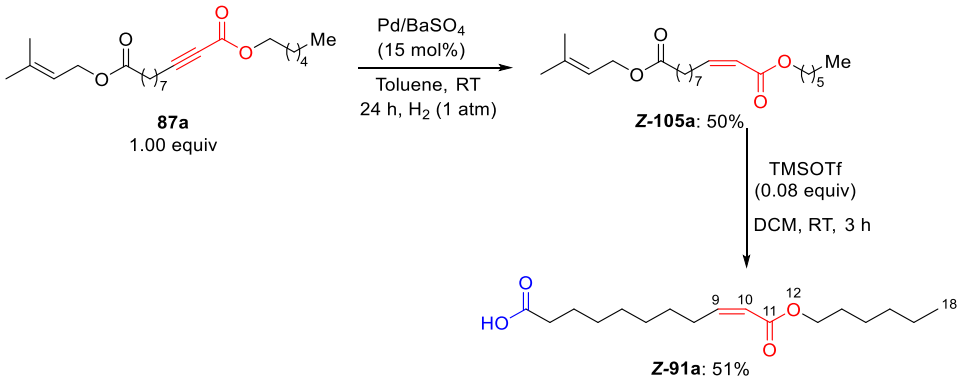
Scheme 3.33: Synthesis of *(Z)*-configured enones **104a-f.**



Scheme 3.34: Successful synthesis of *(E)*-configured fatty acids **94a-f.**

3.7.2 Access to *(Z)*-Configured Alkenyl ester-modified fatty acid

Semi-hydrogenation of ester **87a** with Lindlar catalyst,[127] furnished ***Z*-105a** in 50% yield. Deprotection of the prenyl-protecting group with TMSOTf[118] gave the free acid ***Z*-91a** in 51% yield (Scheme 3.35).

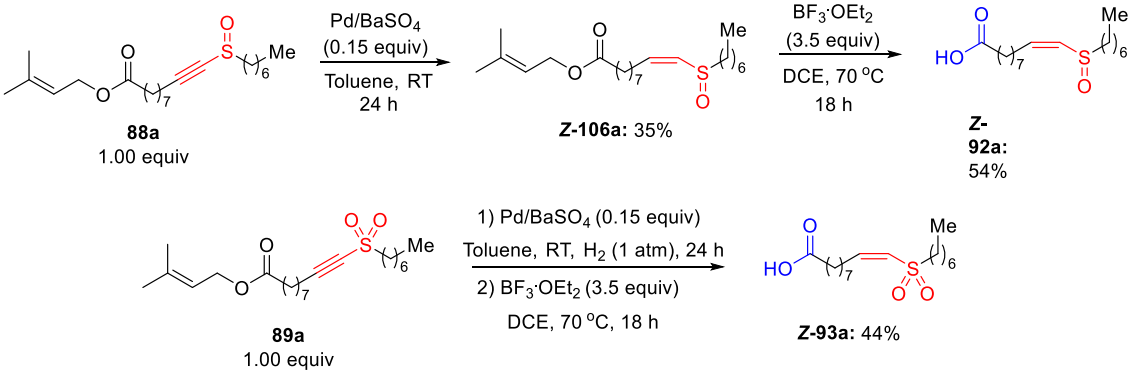


Scheme 3.35: Successful synthesis of *(Z)*-configured fatty acid **91a.**

The stereoselective reduction of alkyne **87a** led to the successful synthesis of a non-natural NFA derivative ***Z*-91a** bearing ester as an electron-withdrawing group conjugated to a double bond in a distal position to the terminal carboxyl group.

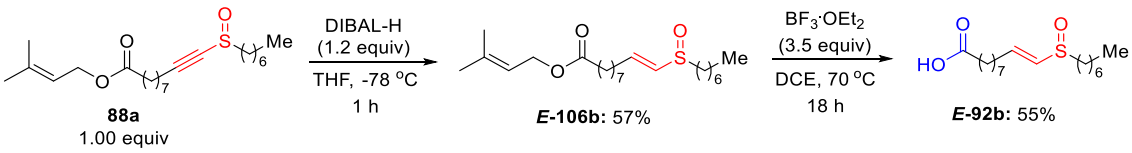
3.7.3 Access to (*Z*)- and (*E*)-Configured Alkenyl Sulfoxide and Alkenyl Sulfone-modified fatty acids

In the same manner, a *Z*-selective semi-hydrogenation of sulfoxide **88a** was achieved with Lindlar catalyst[127] furnishing the *Z*-olefin ***Z*-106a** in 35% yield. Removal of the prenyl-protecting group with $BF_3{\cdot}OEt_2$[123] gave the free acid ***Z*-92a** in 54% yield. Reduction of sulfone **89a** with Lindlar catalyst,[127] followed by direct deprotection of prenyl-protecting group with $BF_3{\cdot}OEt_2$[123] of the resulting *Z*-olefin afforded the free acid ***Z*-93a** in 44% yield (Scheme 3.36).



Scheme 3.36: Successful synthesis of *(Z)*-configured fatty acids **92a** and **93a.**

An *E*-stereoselective semi-hydrogenation of sulfoxide **88a** was achieved with DIBAL-H,[127] furnishing the *E*-isomer ***E*-106b** in 57% yield. Deprotection with $BF_3{\cdot}OEt_2$[123] afforded the NFA analogue ***E*-92b** in 55% yield (Scheme 3.37).

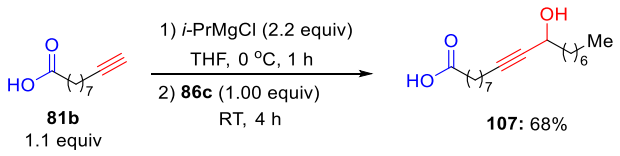


Scheme 3.37: Successful synthesis of *(E)*-configured fatty acid **92b.**

The stereoselective semi-hydrogenation of alkynes **88a** and **89a** led to the successful synthesis of three non-natural NFA derivatives bearing sulfoxide ***Z*-92a**, ***E*-92b**, or sulfone ***Z*-93a** as an electron-withdrawing group conjugated to a double bond in a distal position to the terminal carboxyl group. Although the *E*-isomer of sulfone could not be synthesized (not enough material of alkyne **89a**), the synthesis of a single stereoisomer (***Z*-93a**) is sufficient for biological studies.

3.8 Synthesis of 11-hydroxyoctadec-9-ynoic acid

As an additional probe, unsaturated hydroxy fatty acid **107** was synthesized for further biological studies. Therefore, alkynoic acid **81b** was deprotonated with *i*-PrMgCl. Reaction with Octanal **86c** afforded the desired 11-hydroxyoctadec-9-ynoic acid **107** in 68% yield (Scheme 3.38).



Scheme 3.38: Successful synthesis of 11-hydroxyotadec-9-ynoic acid **107.**

3.9 Conclusion

In the second part of this work, we successfully synthesized twenty (20) non-natural NFAs derivatives via the previously developed modular alkyne approach. Although not all isomers were accessible, these results demonstrate the viability of the proposed 2nd generation route. The synthesized compounds will be useful tools for the post-translational modification of proteins and can serve as lead compounds for the development of new drugs.

3.10 Biological Studies

Evaluation of the biological properties of NFAs analogues prepared within this dissertation is still ongoing at the Paul-Ehrlich Institute in Langen. Initial studies showed promising activities of some compounds such as **72a** (KY-2), **72h** (KY-1), ***E*-53a** (KE-E2), and ***E*-53h** (KE-E1), in the induction of the nuclear factor erythroid 2-related factor 2 (NrF2) protein, a key regulator of the antioxidant response in inflammation (figure 3.1).

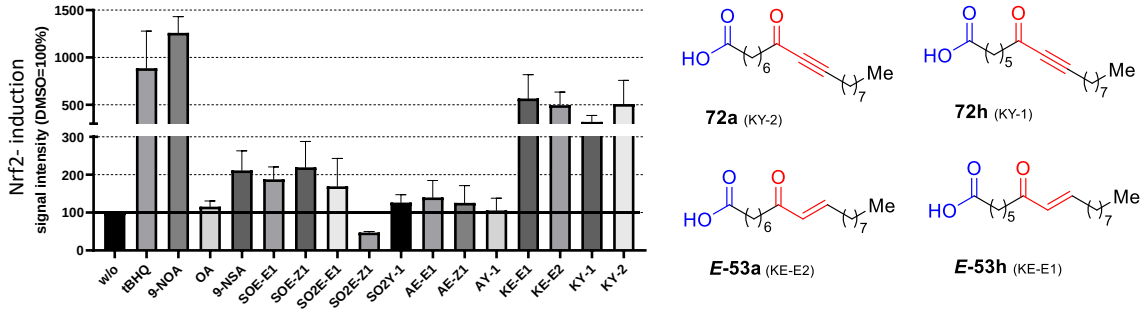
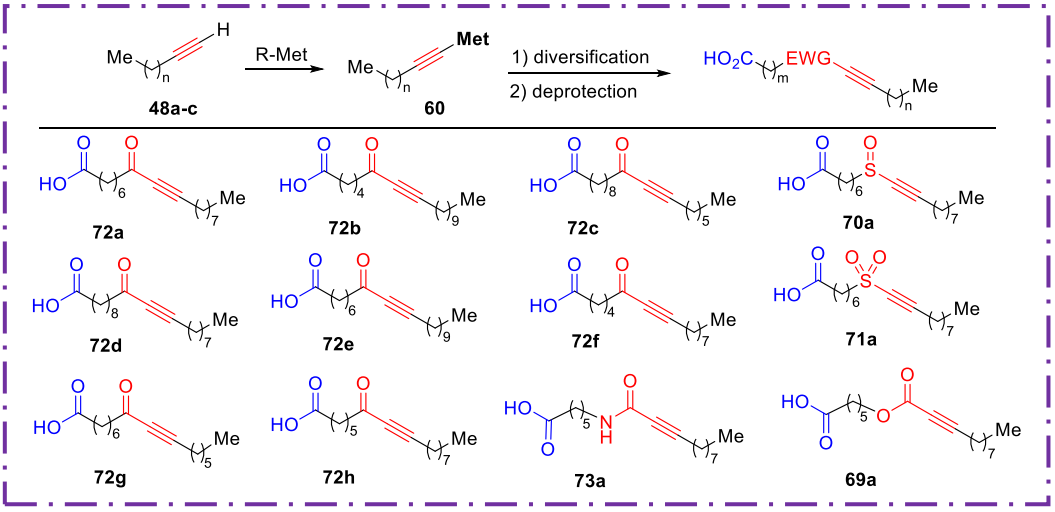


Figure 3.1: Western blot: densitometric analysis. Cell-line: HCT-116; Treatment time: 4h; Conc.: 10 µM.

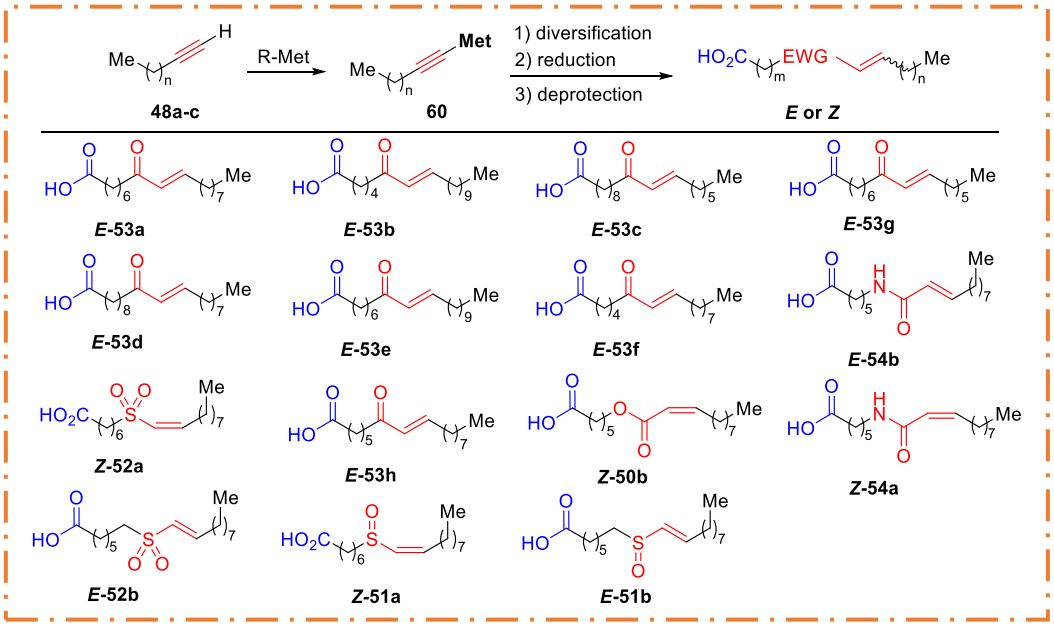
Further biological studies to validate these preliminary results and evaluate the effects of compounds against other 5-lipoxygenase (5-LO) and nuclear factor 'kappa-light-chain-enhancer' of activated B-cells (NF-κB) are still ongoing.

4 General Conclusion

This dissertation describes the successful synthesis of unnatural nitro-fatty acid analogues bearing different Michael acceptor units and the evaluation of their biological activities against selected NFA targets. In the first part of this dissertation, we showed that the synthesis of unsaturated fatty acids bearing different electron withdrawing groups via hydrozirconation-alkynylmetal-diversification-route of both terminal and internal alkynes is not viable. In the light of these results, we devised a 2nd generation route via alkynyl metal species as a key intermediate. We could demonstrate the viability of the new alkyne-based approach and successfully synthesize forty-seven (47) non-natural NFAs derivatives. This new route has two clear advantages: *i*) it greatly simplifies the preparation of both double bond isomers; *ii*) it gives access to an additional class of alkyne-derived Michael acceptors units.

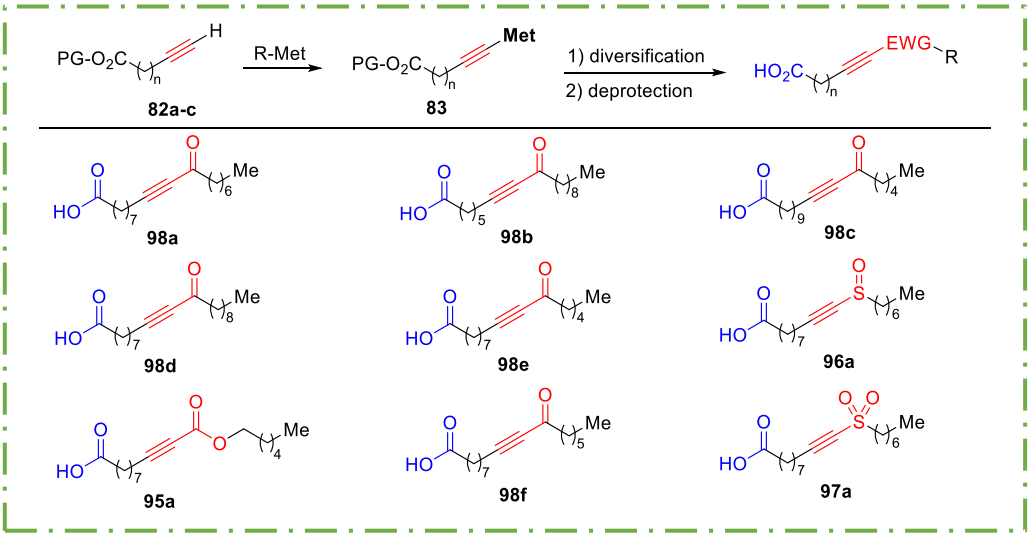


Scheme 4.1: Part 1a - Summary of all NFAs analogues bearing an alkyne-derived Michael acceptor unit. (EWG = electron-withdrawing group).

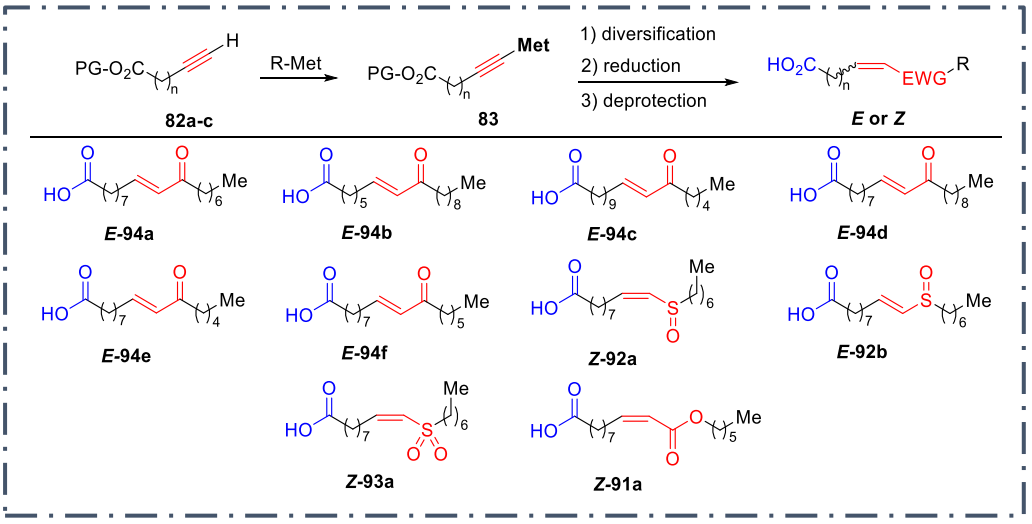


Scheme 4.2: Part 1b - Summary of all NFAs derivatives bearing an alkene moiety. (EWG = electron-withdrawing group).

In the second part of this dissertation, using this modular alkyne approach a second series of NFA analogous bearing the electron-withdrawing group on the alkyl terminus could be synthesized in the same manner (scheme 4.3 and scheme 4.4).



Scheme 4.3: Part 2a - Summary of all NFAs analogues bearing an alkyne-derived Michael acceptor unit. (EWG = electron-withdrawing group).

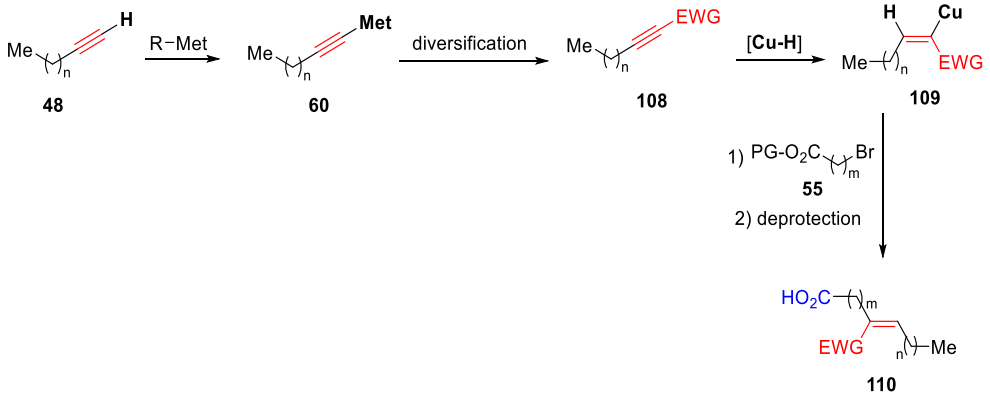


Scheme 4.4: Part 2b - Summary of all NFAs analgues bearing an alkene moiety. (EWG = electron-withdrawing group).

Biological studies are still ongoing, but preliminary results showed some interesting biological activities of novel unnatural NFA analogues against selected targets with particular relevance for inflammatory processes or cancer. These results already indicate an important role of the nature/electrophilicity and position of the Michael acceptor unit in modulating the biological properties. In summary, these studies are already providing some crucial insights into the biological profile of electrophilic fatty acids.

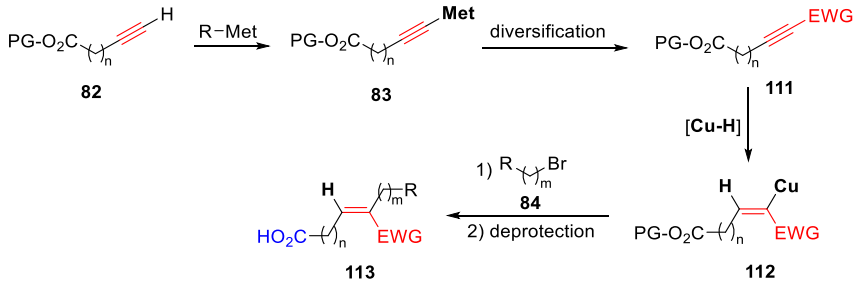
5 OUTLOOK

In this dissertation, we successfully prepared unsaturated fatty acids bearing different electron-withdrawing groups incorporated into the fatty acid chain in a proximal or distal position to the terminal carboxyl group. In the further course of this research project, the synthesis of unsaturated fatty acids bearing different electron-withdrawing groups as an additional substituent on the olefin should be investigated. Therefore, using a slightly adapted version, the alkynyl route can be also used for the synthesis of NFA derivatives bearing the electron-withdrawing groups attached to the carbon chain. In this case, the conjugated alkyne **108** will be reduced with a copper hydride species, either stoichiometric or in a catalytic fashion. Alkylation of the alkenyl copper species **109** with alkyl halide **55** followed by deprotection furnishes the NFAs derivatives of type **110** (Scheme 5.1).



Scheme 5.1: 2nd Generation alkyne-based approach to NFA of type **110**. (EWG = electron-withdrawing group).

In a similar manner, unsaturated fatty acids bearing different electron-withdrawing groups on the olefin in a distal position could be accessed from the ester-functionalized alkynes **82** (Scheme 5.2).



Scheme 5.2: 2nd Generation alkyne-based approach to NFA derivatives of type **113.**
(EWG = electron-withdrawing group).

The biological activities of all novel compounds against various selected NFA targets will be evaluated. The synthesized compounds will provide a valuable toolbox for the elucidation of the role of nitrated fatty acids in the modulation of different signaling pathways and cellular responses. In addition, these results will help to establish a general framework for the design of selective covalent inhibitors.

6 EXPERIMENTAL SECTION

6.1 General Information

Experimental methods: Unless stated, all reactions were carried out without any precautions to exclude air or moisture. All reactions involving moisture or air-sensitive reagents were carried out under a nitrogen atmosphere in flame-dried glassware using standard Schlenk techniques. All yields refer to isolated yields of compounds with an estimated purity of >95 %, determined by ^{1}H NMR analysis.

Chromatography: Thin layer chromatography (TLC) was performed on precoated aluminum sheets (TLC silica gel 60 F254) and the spots were visualized by ultraviolet light or by staining in basic $KMnO_4$-solution, iodine or cerium (IV) ammonium molybdate (CAM). Flash column chromatography was performed using a puriflash XS 420+ Flash purifier machine from Interchim with prepacked flash columns (Puriflash_SilicaHP-JP_30µm_F004 Puriflash_SilicaHP-JP_15µm_F0012, Puriflash_SilicaHP-JP_30µm_F0040 or Puriflash_SilicaHPJP_30µm_F0025) and the respectively specified solvent mixture. Column chromatography was performed with Silica 60 (0.04 – 0.063mm, 230 – 400 mesh) and the specified solvent mixture.

Iodine: Iodine taken up by silica.

$KMnO_4$-solution: Potassium hydrogen carbonate (10 g), Potassium permanganate (1.5 g), and 1.25 mL of 10% NaOH solution in 200 mL of distilled water.

CAM-solution: Cerium (IV) sulfate (2.0 g), Molybdophosphoric acid (5.0 g), and 12 mL of concentrated sulphuric acid in 230 mL of distilled water.

Solvents: All solvents for reactions and column chromatography were purchased from different commercial suppliers in >99% purity and used as received.

Materials: Unless noted, all starting materials were purchased from different commercial suppliers and used without further purification.

6.2 Analytical data and Instrumentation.

NMR spectroscopy: Proton nuclear magnetic resonance spectra (^{1}HNMR) and carbon spectra (^{13}CNMR) were recorded at a frequency of 400 or 600 MHz for ^{1}H and 101 or 151 MHz for ^{13}C respectively. Chemical shifts are reported as δ-values relative to the residual $CDCl_3$ (δ = 7.26 ppm for ^{1}H and δ = 77.16 ppm for ^{13}C), DMSO-d_6 (δ = 2.50 ppm for ^{1}H and δ = 39.51 ppm for ^{13}C). Coupling constants (*J*) are given in Hz and multiplicities of the signals are abbreviated as follows: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet; dd = doublet of doublets and dt = doublet of triplets.

Mass spectrometry: Mass spectra (MS) were measured using a TLC–MS system with electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI) techniques. High-resolution mass spectra were measured on a Waters GCT Premium using electron ionization mass spectroscopy (EI-MS-TOF).

Infrared spectroscopy: Infrared spectra (IR) were recorded on a Shimadzu IRSpirit (QATR-S) equipped with a diamond universal ATR sampling technique (attenuated total reflectance) from 4000-400 cm^{-1}. The absorption bands are reported in wave numbers (cm^{-1}).

6.3 General Procedures (GP)

6.3.1 GP1: Prenyl Protection

A 100 mL round bottom flask equipped with a magnetic stirring bar, was charged with the corresponding bromoalkanoic acids **53a-d** (1.00 equiv) or alkynoic acids **81a-c** (1.00 equiv), 3-methyl-2-buten-1-ol **54** (2.00 equiv), DMAP (1.6 equiv) and DCM (2mL/mmol acids) as solvent. After cooling to 0 °C, EDC·HCl (2.2 equiv) was added over 5 minutes. After complete addition, the suspension was stirred for another 30 minutes at 0 °C and then for 3 h at ambient temperature. The reaction was quenched with H_2O (25 mL) and extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with 1 M HCl aq (50 mL), H_2O (50 mL), and NaCl aq (50 mL), dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude residue was purified by flash column chromatography (*n*-hexane:EtOAc) affording the desired analytically pure product.

6.3.2 GP2: Kornblum Oxidation

A 100 mL round bottom flask equipped with a magnetic stirring bar, was charged with the corresponding prenyl ester **55a-d** (1.00 equiv), $NaHCO_3$ (1.00 equiv), KI (1.00 equiv), and DMSO (5 mL/mmol prenyl ester) as solvent. The resulting solution was stirred at 85 °C for 5 h. After cooling to 0 °C, the mixture was extracted with Et_2O (3 × 25 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ (50 mL), H_2O (50 mL), sat. aq. NaCl (50 mL) and dried over Na_2SO_4. The solvents were evaporated under reduced pressure and the crude residue was purified by flash column chromatography (*n*-hexane:EtOAc) affording the desired analytically pure product.

6.3.3 GP3: Condensation

In a dried 50 mL reaction flask, flushed with nitrogen and equipped with a magnetic stirring bar, alkynes **48a-c** or **82a-c** (1.05 equiv) were added and dissolved with anhydrous THF (2 mL/mmol alkyne). The resulting solution was cooled at 0 °C before the dropwise addition of *i*-PrMgCl (1.05 equiv). After complete addition, the suspension was stirred for another 1 h at 0 °C, and aldehyde (1.05 equiv) was added. The ice bath was removed and the reaction mixture was warmed to ambient temperature. After stirring overnight, the reaction mixture was quenched with sat. aq. NH_4Cl (20 mL) and extracted with EtOAc (3 x 30 ml). The combined organic layers were washed with H_2O (50 mL), sat. aq. NaCl (50 mL) and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, the crude residue was purified by flash column chromatography (*n*-hexane:EtOAc) afforded the desired analytically pure product.

6.3.4 GP4: DMP Oxidation

A 100 mL round bottom flask equipped with a magnetic stirring bar, was charged with the corresponding propargylic alcohol **74a-h** or **99a-f** (1.00 equiv), $NaHCO_3$ (3.00 equiv), and CH_2Cl_2 (5 mL/mmol alcohol) as solvent. The resulting solution was cooled at 0 °C before the slow addition of Dess-Martin-Periodinan (1.5 equiv). The reaction mixture was stirred for an additional 10 minutes at 0 °C then, warmed to ambient temperature and stirred for 3 h. The reaction mixture was quenched with 1 : 1 mixture of sat. aq. $NaHCO_3$ solution and sat. aq. $Na_2S_2O_3$ solution (50 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phases were washed with H_2O (70 mL), sat. aq. NaCl (70 mL) and dried over Na_2SO_4. The solvent were evaporated under reduced pressure and the crude residue was purified by flash column chromatography (*n*-hexane:EtOAc) affording the desired analytically pure product.

6.3.5 GP5: Stereoselective semi-hydrogenation of alkynes

To a solution of alkynes **64-68** or **87-90** (1.00 equiv) in dry toluene (0.05 M), Pd on $BaSO_4$ (0.15 equiv) was added and a balloon filled with H_2 gas was applied. The resulting solution was stirred for 24 h at ambient temperature. The reaction mixture was diluted with EtOAc (5 mL), filtered through a short plug of celite and silica gel. The filter pad was rinsed with additional EtOAc and the solvent was evaporated under reduced pressure. The crude product was then purified by flash column chromatography (*n*-hexane:EtOAc) affording the desired analytically pure product.

6.3.6 GP6: Deprotection with TMSOTf

To a solution of prenyl-protected fatty acid (1.00 equiv) in DCM (2 mL/mmol prenyl-protected fatty acid), TMSOTf (0.03-0.1 equiv) was added, and the reaction mixture was stirred at ambient temperature for 3 h. The solvent was evaporated under reduced pressure, and the crude residue was purified by flash column chromatography affording the desired analytically pure product.

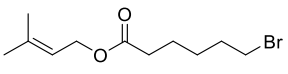
6.3.7 GP7: Deprotection with $BF_3{\cdot}OEt_2$

To a solution of prenyl-protected fatty acid (1.00 equiv) in DCE (2 mL/mmol prenyl-protected fatty acid), $BF_3{\cdot}OEt_2$ (3.5 equiv) was added, and the reaction mixture was stirred for 18 h at 70 °C. After cooling to ambient temperature, H_2O (3 mL) was added, and the resulting mixture was extracted with EtOAc (3 x 10 mL). The combined organic phases were dried over Na_2SO_4. After removal of the solvent, purification of the crude residue by flash column chromatography afforded the desired analytically pure product.

6.4 Synthesis

6.4.1 Synthesis of Prenylbromoalkanoates

Prenyl 6-bromohexanoate (55a)



55a

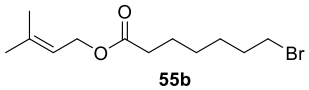
Prepared from 6-bromohexanoic acid **53a** (1.00 equiv, 3.08 mmol, 600 mg), 3-methyl-2-buten-1-ol **54** (2.00 equiv, 6.16 mmol, 0.63 mL) DMAP (1.6 equiv, 4.93 mmol, 602 mg) and EDC·HCl (2.2 equiv, 6.78 mmol, 1.3 g), according to **GP1**. Purification by flash column chromatography (*n*-hexane:EtOAc = 20:1 → 9:1) afforded the desired analytically pure product as a yellow oil (650 mg, 80%). $\mathbf{R_f}$ = 0.62 (9:1 *n*-hexane:EtOAc). Analytical data are in accordance with the literature.[132]

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.32 (ddq, *J* = 8.7, 5.8, 1.4 Hz, 1H), 4.56 (d, *J* = 7.3 Hz, 2H), 3.39 (t, *J* = 6.8 Hz, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 1.91 – 1.80 (m, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.67 – 1.60 (m, 2H), 1.51 – 1.40 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 139.2, 118.6, 61.4, 34.1, 33.6, 32.5, 27.7, 25.8, 24.2, 18.1.

MS (ESI): m/z calcd for $C_{11}H_{19}BrNaO_2$ 285.0 $[M+Na]^+$, found 285.1 $[M+Na]^+$.

Prenyl 7-bromoheptanoate (55b)



55b

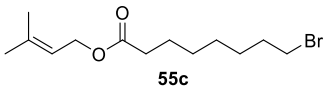
Prepared from 7-bromoheptanoic acid **53b** (1.00 equiv, 3.05 mmol, 640 mg), 3-methyl-2-buten-1-ol **54** (2.00 equiv, 6.10 mmol, 0.63 mL) DMAP (1.6 equiv, 4.88 mmol, 600 mg) and EDC·HCl (2.2 equiv, 6.71 mmol, 1.29 g), according to **GP1**. Purification by flash column chromatography (*n*-hexane:EtOAc = 20:1 → 9:1) afforded the desired analytically pure product as a yellow oil (638 mg, 76%). $\mathbf{R_f}$ = 0.65 (9:1 *n*-hexane:EtOAc). Analytical data are in accordance with the literature.[132]

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.32 (tdt, *J* = 7.3, 2.9, 1.5 Hz, 1H), 4.55 (d, *J* = 7.3 Hz, 2H), 3.38 (t, *J* = 6.8 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.84 (dt, *J* = 14.4, 6.9 Hz, 2H), 1.74 (s, 3H), 1.69 (s, 3H), 1.62 (p, *J* = 7.5 Hz, 2H), 1.49 – 1.27 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 139.1, 118.7, 61.3, 34.2, 33.8, 32.6, 28.3, 27.8, 25.8, 24.8, 18.1.

MS (ESI): m/z calcd for $C_{12}H_{21}BrNaO_2$ 299.0 $[M+Na]^+$, found 299.1 $[M+Na]^+$.

Prenyl 8-bromooctanoate (55c)



55c

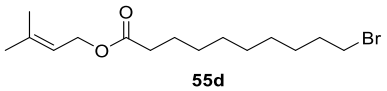
Prepared from 8-bromooctanoic acid **53c** (1.00 equiv, 1.34 mmol, 300 mg), 3-methyl-2-buten-1-ol **54** (2.00 equiv, 2.68 mmol, 0.26 mL) DMAP (1.6 equiv, 2.14 mmol, 262 mg) and EDC·HCl (2.2 equiv, 2.95 mmol, 565 mg), according to **GP1**. Purification by flash column chromatography (*n*-hexane:EtOAc = 20:1 → 9:1) afforded the desired analytically pure product as a yellow oil (265 mg, 68%). $\mathbf{R_f}$ = 0.60 (9:1 *n*-hexane:EtOAc). Analytical data are in accordance with the literature.[132]

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (ddq, *J* = 8.7, 5.8, 1.5 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 3.39 (t, *J* = 6.8 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.84 (p, *J* = 7.0 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.62 (dq, *J* = 9.1, 6.7 Hz, 2H), 1.48 – 1.38 (m, 2H), 1.37 – 1.29 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 139.1, 118.7, 61.3, 34.3, 34.0, 32.8, 29.0, 28.5, 28.0, 25.9, 24.9, 18.1.

MS (ESI): m/z calcd for $C_{13}H_{23}BrNaO_2$ 313.0 $[M+Na]^+$, found 313.1 $[M+Na]^+$.

Prenyl 10-bromodecanoate (55d)



55d

Prepared from 10-bromodecanoic acid **53d** (1.00 equiv, 11.30 mmol, 3.00 g), 3-methyl-2-buten-1-ol **54** (2.00 equiv, 22.70 mmol, 2.33 mL) DMAP (1.6 equiv, 18.20 mmol, 2.22 g) and EDC·HCl (2.2 equiv, 25.00 mmol, 4.80 g), according to **GP1**. Purification by column chromatography (*n*-hexane:EtOAc = 20:1 → 9:1) afforded the desired analytically pure product as a yellow oil (2.5 g, 67%). $\mathbf{R_f}$ = 0.66 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (ddq, *J* = 8.7, 5.8, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 3.39 (t, *J* = 6.9 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H), 1.91 – 1.78 (m, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.61 (dd, *J* = 8.8, 5.5 Hz, 2H), 1.47 – 1.36 (m, 2H), 1.33 – 1.25 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 139.0, 118.8, 61.3, 34.4, 34.1, 32.9, 29.3, 29.2, 29.2, 28.8, 28.2, 25.9, 25.0, 18.1.

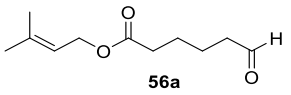
IR (ATR ν in cm^{-1}) 2927 (m), 2856 (m), 1732 (s), 1442 (w), 1378 (w), 1358 (w), 1218 (m), 1166 (m), 961 (w), 723 (w), 648 (w), 529 (w).

MS (APCI): m/z calcd for $C_{15}H_{28}BrO_2$ 319.1 $[M+H]^+$, found 319.1 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{15}H_{27}BrO_2$ 318.1194 $[M]^+$, found 318.1194 $[M]^+$.

6.4.2 Synthesis of Prenyloxoalkanoates

Prenyl 6-oxohexanoate (56a)



56a

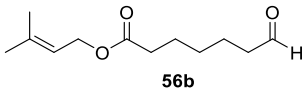
Prepared from prenyl 6-bromohexanoate **55a** (1.00 equiv, 8.36 mmol, 2.20 g), sodium carbonate Na_2CO_3 (1.00 equiv, 8.36 mmol, 886 mg), and potassium iodide KI (1.00 equiv, 8.36 mmol, 1.40 g), according to **GP2**. Purification by column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (830 mg, 50%). $\mathbf{R_f}$ = 0.28 (9:1 *n*-hexane: EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (t, *J* = 1.7 Hz, 1H), 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.51 – 2.40 (m, 2H), 2.32 (q, *J* = 3.7 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.66 (p, *J* = 3.7 Hz, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 202.2, 173.3, 139.3, 118.6, 61.4, 43.6, 34.1, 25.9, 24.5, 21.6, 18.1.

MS (APCI): m/z calcd for $C_{11}H_{19}O_3$ 199.1 $[M+H]^+$, found 199.1 $[M+H]^+$.

Prenyl 7-oxoheptanoate (56b)



56b

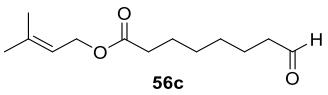
Prepared from prenyl 7-bromoheptanoate **55b** (1.00 equiv, 3.61 mmol, 1.00 g), sodium carbonate Na_2CO_3 (1.00 equiv, 3.61 mmol, 383 mg), and potassium iodide KI (1.00 equiv, 3.61 mmol, 605 mg), according to **GP2**. Purification by column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a colorless oil (520 mg, 68%). $\mathbf{R_f}$ = 0.42 (9:1 *n*-hexane: EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (t, *J* = 1.7 Hz, 1H), 5.33 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.43 (td, *J* = 7.3, 1.7 Hz, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 1.76 (s, 3H), 1.70 (s, 3H), 1.67 – 1.60 (m, 4H), 1.41 – 1.30 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 202.6, 173.7, 139.2, 118.7, 61.4, 43.8, 34.1, 28.7, 25.9, 24.8, 21.8, 18.1.

MS (APCI): m/z calcd for $C_{12}H_{21}O_3$ 213.3 $[M+H]^+$, found 213.3 $[M+H]^+$.

Prenyl 8-oxooctanoate (56c)



56c

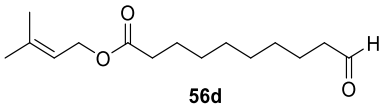
Prepared from prenyl 8-bromooctanoate **55c** (1.00 equiv, 6.25 mmol, 1.82 g), sodium carbonate Na_2CO_3 (1.00 equiv, 6.25 mmol, 662 mg), and potassium iodide KI (1.00 equiv, 6.25 mmol, 1.05 g), according to **GP2**. Purification by column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a colorless oil (860 mg, 61%). $\mathbf{R_f}$ = 0.20 (9:1 *n*-hexane:EtOAc). Analytical data are in accordance with the literature.[132]

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (t, *J* = 1.7 Hz, 1H), 5.33 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.42 (td, *J* = 7.4, 1.8 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.63 (qd, *J* = 6.6, 4.2 Hz, 4H), 1.33 (p, *J* = 3.6 Hz, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 202.8, 173.8, 139.1, 118.7, 61.3, 43.9, 34.3, 28.9, 28.9, 25.9, 24.8, 21.9, 18.1.

MS (ESI): m/z calcd for $C_{13}H_{22}NaO_3$ 249.1 $[M+Na]^+$, found 249.2 $[M+Na]^+$.

Prenyl 10-oxodecanoate (56d)



56d

Prepared from prenyl 10-bromodecanoate **55d** (1.00 equiv, 6.89 mmol, 2.20 g), sodium carbonate Na_2CO_3 (1.00 equiv, 6.89 mmol, 730 mg) and potassium iodide (1.00 equiv, 6.89 mmol, 1.16 g), according to **GP2**. Purification by column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (880 mg, 50%). $\mathbf{R_f}$ = 0.37 (9:1 *n*-hexane: EtOAc).

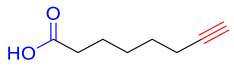
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (t, *J* = 1.8 Hz, 1H), 5.33 (tt, *J* = 7.2, 1.5 Hz, 1H), 4.55 (d, *J* = 7.2 Hz, 2H), 2.41 (td, *J* = 7.4, 1.9 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.66 – 1.58 (m, 4H), 1.32 – 1.28 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 203.0, 174.0, 139.0, 118.7, 61.3, 44.0, 34.4, 29.2, 29.1, 29.1, 25.9, 25.0, 22.1, 18.1.

MS (APCI): m/z calcd for $C_{15}H_{27}O_3$ 255.2 $[M+H]^+$, found 255.1 $[M+H]^+$.

6.4.3 Synthesis of Acetylenic Carboxylic Acids

Oct-7-ynoic acid (81a)



81a

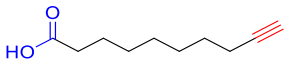
In a dried two-necked flask, equipped with a magnetic stirring bar, was charged lithium acetylide-ethylenediamine complex (3.00 equiv, 46.10 mmol, 4.25 g) in dry DMSO (10 mL). To this, a solution of 6-bromohexanoic acid **53a** (1.00 equiv, 15.40 mmol, 3.00 g) in dry DMSO (6 mL) was added dropwise over a period of 5 - 10 minutes at 0 °C. The resulting solution was slowly warmed to room temperature and stirred overnight. Then, the reaction mixture was poured into ice and acidified with 2 M HCl .aq to pH = 1. The mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine (2 × 30 mL), dried over Na_2SO_4, and filtered. After removing the solvent under reduced pressure, the crude residue was purified by column chromatography (*n*-hexane:EtOAc + 0.5 Vol % HOAc = 95:5 → 80:20) afforded the desired analytically pure product as a yellow oil (1.90 g, 88%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol % HOAc). Analytical data are in accordance with the literature.[133]

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (t, *J* = 7.5 Hz, 2H), 2.20 (td, *J* = 6.9, 2.6 Hz, 2H), 1.94 (t, *J* = 2.6 Hz, 1H), 1.65 (p, *J* = 7.4 Hz, 2H), 1.60 – 1.51 (m, 2H), 1.51 – 1.41 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 180.2, 84.4, 68.5, 34.0, 28.2, 28.1, 24.2, 18.3.

MS (APCI): m/z calcd for $C_8H_{13}O_2$ 141.2 $[M+H]^+$, found 141.0 $[M+H]^+$.

Dec-9-ynoic acid (81b)



81b

In a dried two-necked flask, equipped with a magnetic stirring bar, was charged lithium acetylide-ethylenediamine complex (3.00 equiv, 16.10 mmol, 1.49 g) in dry DMSO (5 mL). To this, a solution of 8-bromooctanoic acid **53c** (1.00 equiv, 5.38 mmol, 1.20 g) in dry DMSO (6 mL) was added dropwise over a period of 5 - 10 minutes at 0 °C. The resulting solution was slowly warmed to room temperature and stirred overnight. Then, the reaction mixture was poured into ice and acidified with 2 M HCl aq to pH=1. The mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine (2 × 30 mL) dried over Na_2SO_4 and filtered. After removing the solvent under reduced pressure, the crude residue was purified by column chromatography (*n*-hexane:EtOAc + 0.5 Vol % HOAc = 95:5 → 80:20) afforded the desired analytically pure product as a yellow oil (730 mg, 81%).

R_f = 0.30 (8:2 *n*-hexane:EtOAc + 0.5 Vol % HOAc). Analytical data are in accordance with the literature.[134]

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (t, *J* = 7.4 Hz, 2H), 2.18 (td, *J* = 7.0, 2.7 Hz, 2H), 1.94 (t, *J* = 2.6 Hz, 1H), 1.63 (p, *J* = 7.4 Hz, 2H), 1.57 – 1.47 (m, 2H), 1.45 – 1.31 (m, 6H).

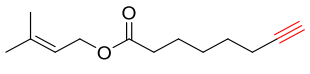
^{13}C NMR (101 MHz, $CDCl_3$) δ 180.3, 84.7, 68.3, 34.1, 29.0, 28.8, 28.6, 28.5, 24.7, 18.4.

MS (APCI): m/z calcd for $C_{10}H_{17}O_2$ 169.1 $[M+H]^+$, found 169.0 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{10}H_{16}O_2$ 168.1150 $[M]^+$, found 168.1139 $[M]^+$.

6.4.4 Synthesis of Prenylalkynoates

Prenyl oct-7-ynoate (82a)



82a

Prepared from oct-7-ynoic acid **81a** (1.00 equiv, 21.9 mmol, 3.07 g), 3-methyl-2-buten-1-ol **54** (2.00 equiv, 43.8 mmol, 4.49 mL) DMAP (1.6 equiv, 35.00 mmol, 4.28 g) and EDC·HCl (2.2 equiv, 48.2 mmol, 9.24 g), according to **GP1**. Purification by column chromatography (*n*-hexane:EtOAc = 20:1 → 9:1) afforded the desired analytically pure product as a colorless oil (4.11 g, 90%). **R_f** = 0.60 (9:1 *n*-hexane: EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.38 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 2.18 (td, *J* = 7.0, 2.6 Hz, 2H), 1.93 (t, *J* = 2.6 Hz, 1H), 1.75 (s, 3H), 1.70 (s, 3H), 1.66 – 1.59 (m, 2H), 1.58 – 1.49 (m, 2H), 1.47 – 1.38 (m, 2H).

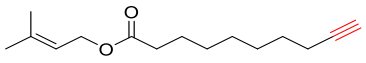
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 139.1, 118.7, 84.4, 68.4, 61.3, 34.3, 28.3, 28.2, 25.9, 24.5, 18.3, 18.1.

IR (ATR ν in cm^{-1}) 3295 (w), 2937 (m), 2863 (m), 1731 (s), 1445 (w), 1378 (m), 1168 (s), 1139 (w), 1083 (w), 969 (m), 949 (m), 776 (w), 629 (s).

MS (APCI): m/z calcd for $C_{13}H_{21}O_2$ 209.1 $[M+H]^+$, found 209.1 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{13}H_{20}O_2$ 208.1463 $[M]^+$, found 208.1459 $[M]^+$.

Prenyl dec-9-ynoate (82b)



82b

Prepared from dec-9-ynoic acid **81b** (1.00 equiv, 4.34 mmol, 730 mg), 3-methyl-2-buten-1-ol **54** (2.00 equiv, 8.68 mmol, 0.89 mL), DMAP (1.6 equiv, 6.94 mmol, 848 mg) and EDC·HCl (2.2 equiv, 9.55 mmol, 1.83 g), according to **GP1**. Purification by column chromatography (*n*-hexane:EtOAc = 20:1 → 9:1) afforded the desired analytically pure product as a yellow oil (880 mg, 86%). $\mathbf{R_f}$ = 0.57 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.17 (td, *J* = 7.1, 2.7 Hz, 2H), 1.93 (t, *J* = 2.6 Hz, 1H), 1.76 (s, 3H), 1.70 (s, 3H), 1.62 (p, *J* = 7.4 Hz, 2H), 1.56 – 1.46 (m, 2H), 1.44 – 1.28 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 139.1, 118.8, 84.8, 68.2, 61.3, 34.4, 29.1, 28.8, 28.6, 28.5, 25.9, 25.0, 18.5, 18.1.

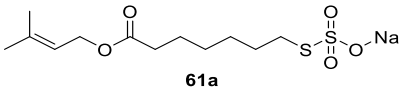
IR (ATR ν in cm^{-1}) 3296 (w), 2933 (m), 2857 (m), 1731 (s), 1445 (w), 1378 (m), 1166 (s), 1095 (w), 955 (w), 778 (m), 725 (w), 629 (s).

MS (ESI): m/z calcd for $C_{15}H_{24}NaO_2$ 259.2 $[M+Na]^+$, found 259.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{15}H_{24}O_2$ 236.1776 $[M]^+$, found 236.1768 $[M]^+$.

6.4.5 Synthesis of Bunte Salts

Sodium *S*-(7-((prenyl)oxy)-7-oxoheptyl) sulfurothioate (61a).



61a

A round bottom flask was charged with a magnetic stirring bar, prenyl 7-bromoheptanoate **55b** (1.00 equiv, 10.00 mmol, 2.77 g), sodium thiosulfate pentahydrate (1.2 equiv, 12.0 mmol, 2.98 g), MeOH and water (3:1). The resulting mixture was heated for 6 h at 65 °C. Then the reaction mixture was cooled to ambient temperature. After evaporation of the solvent using a rotovap at a bath temperature of 40 - 45 °C, the resulting solid was treated with MeOH (100 mL), heated to 50 °C, and filtrated. The filtrate was concentrated to a white solid, which was triturated with hexanes, filtrated, and dried under vacuum at 50 °C to afford the desired Bunte salt **61a** as a white solid (3.15 g, 95%).

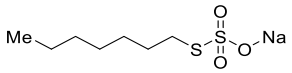
^{1}H NMR (400 MHz, D_2O): δ 5.40 - 5.35 (m, 1H), 4.60 (d, *J* = 7.4 Hz, 2H), 3.08 (t, *J* = 7.3 Hz, 2H), 2.35 (t, *J* = 7.3 Hz, 2H), 1.78 – 1.69 (m, 8H), 1.64 – 1.56 (m, 2H), 1.45 – 1.27 (m, 4H).

^{13}C NMR (101 MHz, D_2O): δ 175.5, 139.7, 118.2, 61.5, 34.8, 34.1, 28.6, 28.1, 27.8, 25.2, 24.5, 17.5.

IR (ATR ν in cm^{-1}): 2970 (m), 2931 (m), 2857 (m), 1732 (s), 1622 (s), 1467 (w), 1443 (m), 1377 (m), 1347 (m), 1184 (w), 1033 (w), 952 (m), 639 (w).

HRMS (TOF MS EI+): m/z calcd for $C_{12}H_{21}NaO_5S_2$ 332.0728 $[M]^+$, found 332.0730 $[M]^+$.

Sodium *S*-heptyl sulfurothioate (85a)



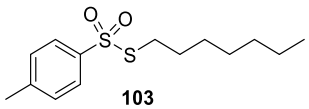
85a

A round bottom flask was charged with a magnetic stirring bar, 1-bromoheptane **80** (1.00 equiv, 1.40 mmol, 250 mg), sodium thiosulfate pentahydrate (1.2 equiv, 1.47 mmol, 364 mg), MeOH and water (3:1). The resulting mixture was heated for 6 h at 65 °C. Then the reaction mixture was cooled to ambient temperature. After evaporation of the solvent using a rotovap at a bath temperature of 40 - 45 °C, the resulting solid was treated with MeOH (100 mL), heated to 50 °C, and filtrated. The filtrate was concentrated to a white solid, which was triturated with hexanes, filtrated, and dried under vacuum at 50 °C to afford the desired Bunte salt **85a** as a white solid (315 mg, 96%).

^{1}H NMR (400 MHz, D_2O) δ 3.11 (t, *J* = 7.4 Hz, 2H), 1.84 – 1.68 (m, 2H), 1.48 – 1.22 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, D_2O) δ 35.1, 30.9, 28.6, 27.8, 27.7, 21.9, 13.4.

6.4.6 Synthesis of *S*-heptyl 4-methylbenzenesulfonothioate



103

In a dried two-necked flask equipped with a magnetic stirring bar, potassium *p*-toluenethiosulfonate **102** (2.00 equiv, 6.36 mmol, 1.43 g), and 1-Bromoheptane **80** (2.00 equiv, 6.36 mmol, 1 mL), was added and diluted with anhydrous DMSO (6 mL). After stirring at room temperature for 18 h, the reaction mixture was quenched with H_2O (50 mL) and extracted with EtOAc (3 x 50 mL). The organic layers were combined and washed with saturated aqueous NaCl (90 mL) and dried over Na_2SO_4. After removing the solvent under reduced pressure, the crude residue was purified by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) to afford the desired analytically pure product as a colorless oil (820 mg, 90%). $\mathbf{R_f}$ = 0.48 (9:1 *n*-hexane:EtOAc). Analytical data are in accordance with the literature.[131]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 2.98 (t, *J* = 6.9, 2H), 2.45 (s, 3H), 1.58 (p, *J* = 7.1 Hz, 2H), 1.33 – 1.17 (m, 8H), 0.86 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 142.2, 129.9, 127.1, 36.1, 31.6, 28.6, 28.5, 22.6, 21.7, 14.1.

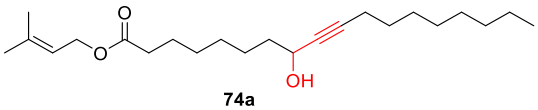
IR (ATR ν in cm^{-1}) 2955 (w), 2925 (m), 2854 (m), 1594 (w), 1492 (w), 1379 (w), 1325 (s), 1292 (m), 1184 (w2), 1139 (s), 1118 (w), 1076 (m), 1018 (w), 812 (m), 703 (m), 652 (s), 585 (s), 519 (s).

MS (ESI): m/z calcd for $C_{14}H_{22}NaO_2S_2$ 309.1 $[M+Na]^+$, found 595.2 $[2M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{14}H_{22}O_2S_2$ 286.1061 $[M]^+$, found 286.1065 $[M]^+$.

6.4.7 Synthesis of Propargylic Alcohols

Prenyl 8-hydroxyoctadec-9-ynoate (74a)



74a

Prepared from 1-Decyne **48a** (1.00 equiv, 3.58 mmol, 0.65 mL), *i*-PrMgCl (1.05 equiv, 3.76 mmol, 1.88 mL, 2 M in THF), and prenyl 8-oxooctanoate **56c** (1.00 equiv, 3.58 mmol, 810 mg), according to **GP3**. Purification by column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a colorless oil (1.10 g, 84%). $\mathbf{R_f}$ = 0.24 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.33 (tt, *J* = 6.5, 1.9 Hz, 1H), 2.29 (t, *J* = 7.6 Hz, 2H), 2.18 (td, *J* = 6.1, 3.7 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.63 (p, *J* = 6.5 Hz, 4H), 1.47 (dt, *J* = 14.2, 6.7 Hz, 4H), 1.36 – 1.25 (m, 14H), 0.87 (t, *J* = 6.2 Hz, 3H).

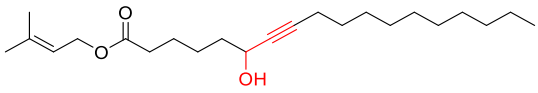
^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 139.1, 118.7, 85.7, 81.3, 62.8, 61.3, 38.2, 34.4, 31.9, 29.3, 29.2, 29.1, 29.1, 28.9, 28.8, 25.9, 25.1, 25.0, 22.7, 18.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 3468 (w), 2926 (s), 2855 (s), 1734 (s), 1462 (m), 1378 (m), 1244 (w), 1169 (m), 1091 (w), 1037 (w), 981 (w), 959 (w), 753 (w), 724 (w), 673 (w), 645 (w).

MS (ESI): m/z calcd for $C_{23}H_{40}NaO_3$ 387.3 $[M+Na]^+$, found 387.1 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{39}O_3$ 363.2899 $[M-H]^+$, found 363.2880 $[M-H]^+$.

Prenyl 6-hydroxyoctadec-7-ynoate (74b)



74b

Prepared from 1-Dodecyne **48b** (1.00 equiv, 4.80 mmol, 1.02 mL), *i*-PrMgCl (1.05 equiv, 5.04 mmol, 2.52 mL, 2 M in THF) and prenyl 6-oxohexanoate **56a** (1.05 equiv, 5.04 mmol, 1 g), according to **GP3**. Purification by column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (890 mg, 51%). $\mathbf{R_f}$ = 0.28 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.3, 1.5 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.35 (tt, *J* = 6.5, 1.9 Hz 1H), 2.32 (t, *J* = 7.5 Hz, 2H), 2.18 (td, *J* = 7.1, 1.9 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.69 – 1.61 (m, 4H), 1.48 (q, *J* = 7.4 Hz, 4H), 1.39 - 1.26 (m, 14H), 0.87 (t, *J* = 6.7 Hz, 3H).

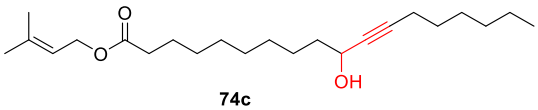
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 139.1, 118.7, 85.8, 81.1, 62.6, 61.4, 37.9, 34.4, 32.0, 29.7, 29.6, 29.4, 29.2, 29.0, 28.8, 25.9, 24.9, 24.7, 22.8, 18.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 3468 (w), 2926 (s), 2856 (s), 1734 (s), 1462 (m), 1378 (m), 1246 (w), 1170 (m), 1095 (w), 1037 (w), 981 (w), 959 (w), 753 (w), 722 (w), 673 (w), 645 (w).

MS (APCI): m/z calcd for $C_{23}H_{41}O_3$ 365.3 $[M+H]^+$, found 365.7 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{40}O_3$ 364.2977 $[M]^+$, found 364.2968 $[M]^+$.

Prenyl 10-hydroxyoctadec-11-ynoate (74c)



74c

Prepared from 1-Octyne **48c** (1.00 equiv, 4.72 mmol, 0.70 mL), *i*-PrMgCl (1.05 equiv, 4.95 mmol, 2.48 mL, 2 M in THF), and prenyl 10-oxodecanoate **56d** (1.05 equiv, 4.72 mmol, 1.2 g), according to **GP3**. Purification by column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (1.40 g, 81%). $\mathbf{R_f}$ = 0.30 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.38 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.33 (d, *J* = 6.6 Hz, 1H), 2.29 (t, *J* = 7.6 Hz, 2H), 2.19 (dd, *J* = 8.1, 5.8 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.66 – 1.60 (m, 4H), 1.54 – 1.43 (m, 4H), 1.40 - 1.29 (m, 14H), 0.88 (t, *J* = 6.2 Hz, 3H).

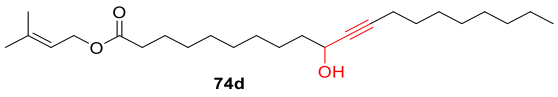
^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 139.1, 118.8, 85.6, 81.4, 62.8, 61.3, 38.3, 34.5, 31.4, 29.4, 29.3, 29.3, 29.2, 28.7, 28.6, 25.9, 25.3, 25.1, 22.6, 18.8, 18.1, 14.1.

IR (ATR ν in cm^{-1}) 3465 (w), 2927 (s), 2856 (s), 1735 (s), 1457 (m), 1378 (m), 1236 (w), 1166 (m), 1095 (w), 1046 (w), 969 (w), 725 (w).

MS (APCI): m/z calcd for $C_{23}H_{41}O_3$ 365.3 $[M+H]^+$, found 365.6 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{40}O_3$ 364.2977 $[M]^+$, found 364.2968 $[M]^+$.

Prenyl 10-hydroxyicos-11-ynoate (74d)



74d

Prepared from 1-decyne **48a** (1.00 equiv, 3.30 mmol, 0.61 mL), *i*-PrMgCl (1.05 equiv, 3.47 mmol, 1.73 mL, 2 M in THF), and prenyl 10-oxodecanoate **56d** (1.05 equiv, 3.30 mmol, 840 mg), according to **GP3**. Purification by column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (1.10 g, 85%). $\mathbf{R_f}$ = 0.28 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.33 (t, *J* = 6.6 Hz, 1H), 2.28 (t, *J* = 7.5 Hz, 2H), 2.21 – 2.17 (m, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.63 (ddd, *J* = 16.1, 9.0, 7.0 Hz, 4H), 1.52 - 1.49 (m, 2H), 1.39 - 1.28 (m, 20H), 0.87 (t, *J* = 6.2 Hz, 3H).

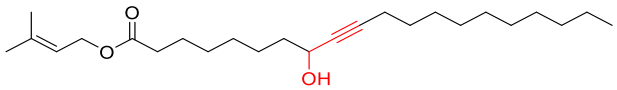
^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 139.1, 118.8, 85.6, 81.4, 62.8, 61.3, 38.3, 34.5, 31.9, 29.4, 29.3, 29.3, 29.3, 29.2, 29.2, 28.9, 28.8, 25.9, 25.3, 25.1, 22.7, 18.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 3458 (w), 2925 (s), 2854 (s), 1735 (s), 1457 (m), 1377 (m), 1229 (m), 1216 (m), 1169 (w), 1093 (w), 1046 (w), 1012 (w), 982 (w), 723 (w), 527 (w), 515 (w).

MS (APCI): m/z calcd for $C_{25}H_{45}O_3$ 393.6 $[M+H]^+$, found 393.8 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{25}H_{44}O_3$ 392.3290 $[M]^+$, found 392.3295 $[M]^+$.

Prenyl 8-hydroxyicos-9-ynoate (74e)



74e

Prepared from 1-dodecyne **48b** (1.00 equiv, 2.78 mmol, 0.60 mL), *i*-PrMgCl (1.05 equiv, 2.92 mmol, 1.46 mL, 2 M in THF), and prenyl 8-oxooctanoate **56c** (1.05 equiv, 2.78 mmol, 630 mg), according to **GP3**. Purification by flash column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (560 mg, 51%). $\mathbf{R_f}$ = 0.28 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.33 (tt, *J* = 6.6, 1.9 Hz, 1H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.19 (dd, *J* = 7.2, 5.2 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.64 (q, *J* = 7.6 Hz, 4H), 1.50 – 1.47 (m, 2H), 1.36 – 1.26 (m, 20H), 0.87 (t, *J* = 6.2 Hz, 3H).

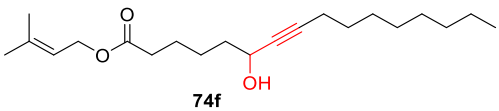
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 139.1, 118.8, 85.7, 81.3, 62.8, 61.3, 38.2, 34.4, 32.0, 29.7, 29.6, 29.4, 29.2, 29.1, 29.1, 29.0, 28.8, 25.9, 25.2, 25.0, 22.8, 18.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 3455 (w), 2925 (s), 2854 (s), 1735 (s), 1715 (s), 1457 (m), 1377 (m), 1361 (m), 1218 (m), 1169 (m), 1091 (w), 1036 (w), 982 (w), 723 (w).

MS (APCI): m/z calcd for $C_{25}H_{45}O_3$ 393.6 $[M+H]^+$, found 393.5 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{25}H_{44}O_3$ 392.3290 $[M]^+$, found 392.3292 $[M]^+$.

Prenyl 6-hydroxyhexadec-7-ynoate (74f)



74f

Prepared from 1-decyne **48a** (1.00 equiv, 3.73 mmol, 0.67 mL), *i*-PrMgCl (1.05 equiv, 3.92 mmol, 1.96 mL, 2 M in THF), and prenyl 6-oxohexanoate **56a** (1.00 equiv, 3.73 mmol, 740 mg), according to **GP3**. Purification by column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (1.10 g, 88%). $\mathbf{R_f}$ = 0.28 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.34 (tt, *J* = 6.6, 2.0 Hz, 1H), 2.35 – 2.28 (m, 2H), 2.18 (td, *J* = 7.0, 2.0 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.66 (dd, *J* = 10.4, 5.1 Hz, 2H), 1.48 (p, *J* = 7.1 Hz, 4H), 1.40 – 1.26 (m, 12H), 0.88 (t, *J* = 6.4 Hz, 3H).

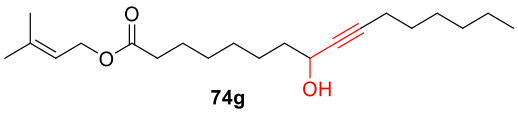
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 139.1, 118.7, 85.8, 81.2, 62.6, 61.4, 37.9, 34.4, 31.9, 29.3, 29.2, 29.0, 28.8, 25.9, 24.9, 24.7, 22.7, 18.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 3441 (w), 2926 (s), 2856 (m), 1735 (s), 1457 (m), 1378 (m), 1229 (m), 1218 (m), 1162 (m), 1083 (w), 1016 (w), 959 (w), 723 (w).

MS (APCI): m/z calcd for $C_{21}H_{37}O_3$ 337.5 $[M+H]^+$, found 337.7 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{21}H_{36}O_3$ 336.2664 $[M]^+$, found 336.2683 $[M]^+$.

Prenyl 8-hydroxyhexadec-9-ynoate (74g)



74g

Prepared from 1-Octyne **48c** (1.00 equiv, 2.78 mmol, 0.42 mL), *i*-PrMgCl (1.05 equiv, 2.92 mmol, 1.46 mL, 2 M in THF), and prenyl 8-oxooctanoate **56c** (1.00 equiv, 2.78 mmol, 630 mg), according to **GP3**. Purification by flash column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (500 mg, 53%). $\mathbf{R_f}$ = 0.28 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 6.0, 1.5 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.33 (tt, *J* = 6.5, 2.0 Hz, 1H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.19 (td, *J* = 7.1, 2.0 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.68 – 1.60 (m, 4H), 1.52 – 1.28 (m, 14H), 0.88 (t, *J* = 6.9 Hz, 3H).

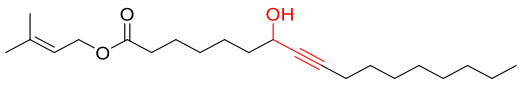
^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 139.1, 118.8, 85.7, 81.3, 62.8, 61.3, 38.2, 34.4, 31.4, 29.1, 29.1, 28.7, 28.6, 25.9, 25.1, 25.0, 22.6, 18.8, 18.1, 14.1.

IR (ATR ν in cm^{-1}) 3458 (w), 2930 (m), 2859 (m), 1735 (s), 1717 (s), 1442 (w), 1365 (m), 1218 (m), 1171 (w), 1091 (w), 1039 (w), 982 (w), 959 (w), 778 (w), 726 (w).

MS (APCI): m/z calcd for $C_{21}H_{37}O_3$ 337.5 $[M+H]^+$, found 337.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{21}H_{36}O_3$ 336.2664 $[M]^+$, found 336.2675 $[M]^+$.

Prenyl 7-hydroxyheptadec-8-ynoate (74h)



74h

Prepared from 1-decyne **48a** (1.00 equiv, 3.96 mmol, 0.72 mL), *i*-PrMgCl (1.05 equiv, 4.16 mmol, 2.08 mL, 2 M in THF), and prenyl 7-oxoheptanoate **56b** (1.00 equiv, 3.96 mmol, 840 mg), according to **GP3**. Purification by column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (1.22 g, 88%). $\mathbf{R_f}$ = 0.26 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.3, 1.5 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.33 (t, *J* = 6.5 Hz, 1H), 2.30 (t, *J* = 7.5 Hz, 2H), 2.18 (td, *J* = 7.1, 2.0 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.65 (q, *J* = 7.3 Hz, 4H), 1.48 (dq, *J* = 13.7, 6.8 Hz, 4H), 1.39 – 1.22 (m, 12H), 0.87 (t, *J* = 6.7 Hz, 3H).

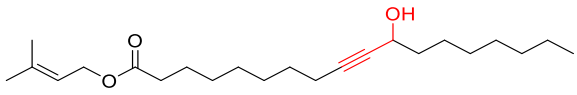
^{13}C NMR (151 MHz, $CDCl_3$) δ 173.9, 139.1, 118.8, 85.8, 81.3, 62.7, 61.3, 38.1, 34.3, 31.9, 29.3, 29.2, 29.0, 28.9, 28.8, 25.9, 25.0, 24.9, 22.7, 18.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 3411 (w), 2926 (s), 2856 (m), 2211 (m), 1734 (s), 1673 (s), 1459 (m), 1375 (m), 1231 (w), 1167 (m), 1082 (w), 1046 (w), 981 (w), 775 (w), 724 (w).

MS (ESI): m/z calcd for $C_{22}H_{38}NaO_3$ 373.3 $[M+Na]^+$, found 373.5 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{38}O_3$ 350.2821 $[M]^+$, found 350.2848 $[M]^+$.

Prenyl 11-hydroxyoctadec-9-ynoate (99a)



99a

Prepared from prenyl dec-9-ynoate **82b** (1.05 equiv, 2.80 mmol, 662.60 mg), *i*-PrMgCl (1.20 equiv, 3.20 mmol, 1.60 mL, 2 M in THF) and Octanal **86c** (1.05 equiv, 2.80 mmol, 359.00 mg), according to **GP3**. Purification by flash column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (400 mg, 41%). $\mathbf{R_f}$ = 0.38 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.57 (d, *J* = 7.2 Hz, 2H), 4.34 (tt, *J* = 6.6, 2.0 Hz, 1H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.19 (td, *J* = 7.0, 1.9 Hz, 2H), 1.76 (s, 3H), 1.71 (s, 3H), 1.69 – 1.59 (m, 4H), 1.52 – 1.38 (m, 6H), 1.33 – 1.26 (m, 12H), 0.88 (t, *J* = 6.5 Hz, 3H).

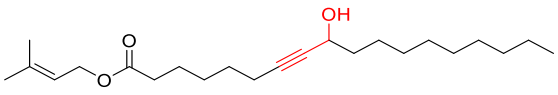
^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 139.1, 118.7, 85.4, 81.5, 62.9, 61.3, 38.3, 34.4, 31.9, 29.4, 29.3, 29.3, 29.1, 28.6, 28.6, 25.9, 25.3, 25.0, 22.7, 18.7, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 3453 (w), 2929 (s), 2857 (s), 2211 (m), 1735 (s), 1712 (s), 1672 (s), 1459 (m), 1364 (m), 1219 (w), 1164 (m), 1095 (w), 725 (w), 530 (w).

MS (ESI): m/z calcd for $C_{23}H_{40}NaO_3$ 387.3 $[M+Na]^+$, found 387.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{40}O_3$ 364.2977 $[M]^+$, found 364.2986 $[M]^+$.

Prenyl 9-hydroxyoctadec-7-ynoate (99b)



99b

Prepared from prenyl oct-7-ynoate **82a** (1.00 equiv, 4.80 mmol, 1.00 g), *i*-PrMgCl (1.05 equiv, 5.04 mmol, 2.52 mL, 2 M in THF), and Decanal **86d** (1.05 equiv, 5.04 mmol, 0.95 mL), according to **GP3**. Purification by column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (650 mg, 37%). $\mathbf{R_f}$ = 0.28 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.34 (tt, *J* = 6.6, 2.0 Hz, 1H)2, 2.31 (t, *J* = 7.5 Hz, 2H), 2.21 (td, *J* = 7.0, 2.0 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.68 – 1.59 (m, 4H), 1.54 – 1.49 (m, 2H), 1.45 – 1.39 (m, 4H), 1.31 – 1.25 (m, 12H), 0.87 (t, *J* = 6.7 Hz, 3H).

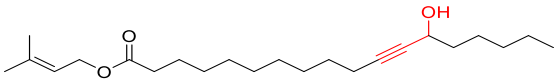
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 139.2, 118.7, 85.2, 81.7, 62.8, 61.4, 38.3, 34.3, 32.0, 29.7, 29.6, 29.4, 29.4, 28.3, 28.3, 25.9, 25.3, 24.5, 22.8, 18.6, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 3461 (w), 2926 (s), 2856 (s), 2211 (m), 1735 (s), 1672 (s), 1459 (m), 1371 (m), 1218 (s), 1166 (s), 1086 (w), 979 (w), 723 (w), 636 (w), 527 (w), 517 (w).

MS (APCI): m/z calcd for $C_{23}H_{41}O_3$ 365.5 $[M+H]^+$, found 365.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{39}O_3$ 363.2899 $[M-H]^+$, found 363.2891 $[M-H]^+$.

Prenyl 13-hydroxyoctadec-11-ynoate (99c)



99c

In a dried two-necked flask, equipped with a magnetic stirring bar was charged lithium acetylide-ethylenediamine complex (3.00 equiv, 34.00 mmol, 3.13 g) in dry DMSO (10 mL). To this, a solution of 10-Bromodecanoic acid **53d** (1.00 equiv, 11.13 mmol, 3.00 g) in dry DMSO (6 mL) was added dropwise over a period of 5 - 10 minutes at 0 °C. The resulting solution was slowly warmed to room temperature and stirred overnight. Then, the reaction mixture was poured into ice and acidified with 2 M HCl .aq to pH=1. The mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine (2 × 30 mL), dried over Na_2SO_4, and filtered. After removing the solvent under reduced pressure, the crude material was treated with 3-methyl-2-buten-1-ol **54** (2.00 equiv, 30.6 mmol, 3.13 mL), DMAP (1.6 equiv, 24.5 mmol, 2.99 g) and EDC·HCl (2.2 equiv, 33.6 mmol, 6.45 g), according to **GP1**. The resulting product, prenyl dodec-11-ynoate **82c** (1.00 equiv, 1.13 mmol, 300 mg) was carried on directly to the next step and treated with *i*-PrMgCl (1.05 equiv, 1.19 mmol, 0.60 mL, 2 M in THF), and Hexanal **86a** (1.05 equiv, 1.19 mmol, 0.15 mL), according to **GP3**. Purification by flash column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (166 mg, 40%). $\mathbf{R_f}$ = 0.28 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.34 (tt, *J* = 6.6, 2.0 Hz, 1H), 2.29 (t, *J* = 7.6 Hz, 2H), 2.19 (td, *J* = 7.1, 2.0 Hz, 2H), 1.76 (s, 3H), 1.70 (s, 3H), 1.68 – 1.59 (m, 4H), 1.47 (dp, *J* = 12.6, 6.7 Hz, 6H), 1.32 – 1.26 (m, 12H), 0.88 (t, *J* = 6.7 Hz, 3H).

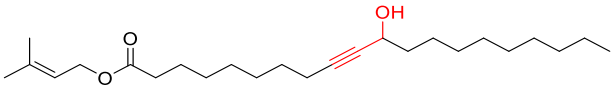
^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 139.1, 118.8, 85.6, 81.5, 62.9, 61.3, 38.3, 34.5, 31.6, 29.4, 29.3, 29.2, 29.2, 28.9, 28.7, 25.9, 25.1, 25.0, 22.7, 18.8, 18.1, 14.1.

IR (ATR ν in cm^{-1}) 3468 (w), 2927 (s), 2857 (m), 2211 (m), 1735 (s), 1672 (m), 1458 (m), 1378 (m), 1229 (m), 1166 (s), 1099 (w), 963 (w), 725 (w), 515 (w).

MS (APCI): m/z calcd for $C_{23}H_{41}O_3$ 365.6 $[M+H]^+$, found 365.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{39}O_3$ 363.2899 $[M-H]^+$, found 363.2877 $[M-H]^+$.

Prenyl 11-hydroxyicos-9-ynoate (99d)



99d

Prepared from prenyl dec-9-ynoate **82b** (1.00 equiv, 5.08 mmol, 1.20 g), *i*-PrMgCl (1.05 equiv, 6.09 mmol, 2.67 mL, 2 M in THF), and Decanal **86d** (1.05 equiv, 6.09 mmol, 1.00 mL), according to **GP3**. Purification by column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (1.00 g, 50%). $\mathbf{R_f}$ = 0.37 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.33 (tt, *J* = 6.7, 2.0 Hz, 1H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.19 (td, *J* = 7.0, 2.0 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.67 – 1.59 (m, 4H), 1.51 – 1.37 (m, 6H), 1.31 – 1.25 (m, 16H), 0.85 (t, *J* = 6.7 Hz,, 3H).

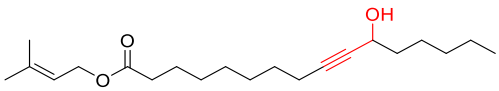
^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 139.1, 118.7, 85.4, 81.5, 62.8, 61.3, 38.3, 34.4, 32.0, 29.7, 29.6, 29.4, 29.4, 29.1, 28.7, 28.6, 28.6, 25.9, 25.3, 25.0, 22.8, 18.7, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 3453 (w), 2925 (s), 2854 (s), 2210 (m), 1735 (s), 1672 (s), 1457 (m), 1377 (m), 1231 (w), 1164 (s), 1098 (w), 981 (w), 723 (w), 527 (w).

MS (APCI): m/z calcd for $C_{25}H_{45}O_3$ 393.6 $[M+H]^+$, found 393.4 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{25}H_{44}O_3$ 392.3290 $[M]^+$, found 392.3309 $[M]^+$.

Prenyl 11-hydroxyhexadec-9-ynoate (99e)



99e

Prepared from prenyl dec-9-ynoate **82b** (1.00 equiv, 5.08 mmol, 1.20 g), *i*-PrMgCl (1.05 equiv, 6.09 mmol, 2.67 mL, 2 M in THF), and Hexanal **86a** (1.05 equiv, 6.09 mmol, 0.66 mL), according to **GP3**. Purification by column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (1.00 g, 59%). $\mathbf{R_f}$ = 0.36 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.34 (t, *J* = 6.7 Hz, 1H), 2.29 (t, *J* = 7.6 Hz, 2H), 2.19 (td, *J* = 7.0, 1.9 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.63 (p, *J* = 6.6 Hz, 4H), 1.52 – 1.36 (m, 6H), 1.32 – 1.28 (m, 8H), 0.89 (t, *J* = 6.3 Hz, 3H).

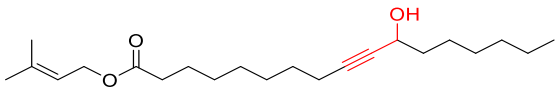
^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 139.1, 118.7, 85.4, 81.5, 62.8, 61.3, 38.3, 34.4, 31.6, 29.1, 28.8, 28.6, 28.6, 25.9, 25.0, 25.0, 22.7, 18.7, 18.1, 14.1.

IR (ATR ν in cm^{-1}) 3465 (w), 2930 (s), 2859 (s), 2211 (m), 1732 (s), 1672 (s), 1459 (m), 1378 (m), 1231 (w), 1168 (s), 1096 (w), 982 (w), 728 (w), 629 (w), 529 (w), 516 (w).

MS (APCI): m/z calcd for $C_{21}H_{37}O_3$ 337.5 $[M+H]^+$, found 337.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{21}H_{34}O_3$ 334.2508 $[M-2H]^+$, found 334.2509 $[M-2H]^+$.

Prenyl 11-hydroxyheptadec-9-ynoate (99f)



99f

Prepared from prenyl dec-9-ynoate **82b** (1.05 equiv, 2.12 mmol, 500 mg), *i*-PrMgCl (1.20 equiv, 2.41 mmol, 1.21 mL, 2 M in THF), and Heptanal **86b** (1.05 equiv, 2.11 mmol, 0.30 mL), according to **GP3**. Purification by flash column chromatography (*n*-hexane:EtOAc = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (290 mg, 41%). $\mathbf{R_f}$ = 0.38 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (tt, *J* = 7.1, 1.5 Hz, 1H), 4.56 (d, *J* = 7.3 Hz, 2H), 4.38 – 4.30 (m, 1H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.19 (td, *J* = 7.1, 2.1 Hz, 2H), 1.76 (s, 3H), 1.71 (s, 3H), 1.67 – 1.60 (m, 4H), 1.51 – 1.38 (m, 6H), 1.33 – 1.28 (m, 10H), 0.88 (t, *J* = 6.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 139.1, 118.7, 85.5, 81.5, 62.9, 61.3, 38.3, 34.4, 31.9, 29.1, 29.1, 28.8, 28.6, 28.6, 25.9, 25.3, 25.0, 22.7, 18.7, 18.1, 14.2.

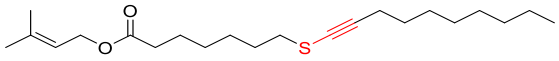
IR (ATR ν in cm^{-1}) 3442 (w), 2929 (s), 2857 (s), 2211 (m), 1717 (s), 1675 (m), 1464 (m), 1378 (m), 1231 (w), 1168 (s), 1099 (w), 978 (w), 725 (w), 628 (w).

MS (ESI): m/z calcd for $C_{22}H_{38}NaO_3$ 373.3 $[M+Na]^+$, found 373.4 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{38}O_3$ 350.2821 $[M]^+$, found 350.2801 $[M]^+$.

6.4.8 Synthesis of Alkynyl Sulfide Esters

Prenyl 7-(dec-1-yn-1-ylthio)heptanoate (75)



75

In a dried two-necked flask, 1-decyne **48a** (3.50 equiv, 17.50 mmol, 3.16 mL) was added and diluted with anhydrous THF (0.65 M). The resulting solution was cooled to 0 °C before dropwise addition of *i*-PrMgCl (3.00 equiv, 15.00 mmol, 7.50 mL). The reaction mixture was stirred for 1 h at 0 °C and Bunte salt **61a** (1.00 equiv, 5.00 mmol, 1.66 g) was then added. The ice bath was removed, and the reaction mixture was allowed to warm to ambient temperature. After stirring for 1 h, the reaction mixture was quenched with saturated aqueous NH_4Cl (75 mL) and extracted with EtOAc (3 x 80 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (90 mL), saturated aqueous NaCl (90 mL), and dried over Na_2SO_4. After concentration under reduced pressure, the crude residue was purified by flash column chromatography (*n*-hexane:EtOAc = 50:1 → 20:1) to afford the desired analytically pure product as a yellow oil (1.0 g, 55%). $\mathbf{R_f}$: 0.59 (19:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.34 – 5.31 (m, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.64 (t, *J* = 7.3 Hz, 2H), 2.29 (q, *J* = 7.4 Hz, 4H), 1.76 (s, 3H), 1.70 (s, 3H), 1.62 (dd, *J* = 15.7, 8.2 Hz, 2H), 1.54 – 1.26 (m, 18H), 0.87 (t, *J* = 6.8 Hz, 3H).

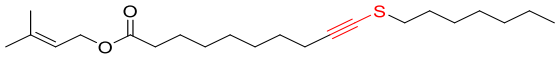
^{13}C NMR (101 MHz, $CDCl_3$): δ 174.1, 139.4, 119.1, 94.8, 68.5, 61.6, 35.7, 34.6, 32.2, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 28.3, 26.2, 25.2, 23.1, 20.5, 18.4, 14.5.

IR (ATR ν in cm^{-1}): 2925 (m), 2854 (m), 1733 (s), 1675 (m), 1457 (w), 1377 (m), 1236 (m), 1167 (w), 1122 (w), 1068 (w), 802 (m), 726 (w).

MS (ESI): m/z calcd for $C_{22}H_{38}NaO_2S$ 389.2 $[M+Na]^+$, found 389.3 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{38}O_2S$ 366.2593 $[M]^+$, found 366.2599 $[M]^+$.

Prenyl 10-(heptylthio)dec-9-ynoate (101)



101

In a dried two-necked flask, prenyl dec-9-ynoate **82b** (1.05 equiv, 1.77 mmol, 420 mg), was added and diluted with anhydrous THF (1 mL). The resulting solution was cooled to 0 °C before dropwise addition of *i*-PrMgCl (1.05 equiv, 1.77 mmol, 2 M in THF, 766 µl). The reaction mixture was stirred for 1 h at 0 °C and *S*-heptyl 4-methylbenzenesulfonothioate **103** (3.50 equiv, 5.92 mmol, 1.70 g) was added. After stirring at room temperature overnight, the reaction mixture was quenched with saturated aqueous NH_4Cl (60 mL) and extracted with EtOAc (3 x 30 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (60 mL), saturated aqueous NaCl (50 mL), and dried over Na_2SO_4. After concentration under reduced pressure, the crude residue was purified by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) to afford the desired analytically pure product as a yellow oil (321 mg, 52%). $\mathbf{R_f}$ = 0.57 (20:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.1 Hz, 2H), 2.65 (t, *J* = 7.3 Hz, 2H), 2.28 (td, *J* = 7.2, 3.6 Hz, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.65 – 1.58 (m, 2H), 1.53 – 1.46 (m, 2H), 1.42 – 1.25 (m, 16H), 0.86 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 139.1, 118.7, 94.2, 68.5, 61.3, 35.5, 34.4, 31.8, 29.3, 29.1, 28.9, 28.8, 28.8, 28.7, 28.3, 25.9, 25.1, 22.7, 20.2, 18.1, 14.2.

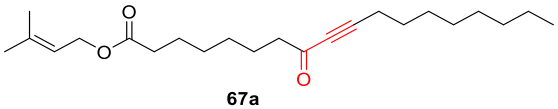
IR (ATR ν in cm^{-1}) 2927 (m), 2856 (m), 1735 (s), 1448 (m), 1377 (m), 1276 (w), 1229 (w), 1218 (m), 1166 (m), 1093 (w), 1048 (w), 959 (w), 725 (w), 635 (w).

MS (ESI): m/z calcd for $C_{22}H_{38}NaO_2S$ 389.2 $[M+Na]^+$, found 389.3 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{38}O_2S$ 366.2593 $[M]^+$, found 366.2611 $[M]^+$,

6.4.9 Synthesis of Keto-Esters

Prenyl 8-oxooctadec-9-ynoate (67a)



67a

Prepared from prenyl 8-hydroxyoctadec-9-ynoate **74a** (1.00 equiv, 2.88 mmol, 1.05 g), $NaHCO_3$ (3.00 equiv, 8.64 mmol, 0.72 mg) and Dess-Martin-Periodinan (1.50 equiv, 4.32 mmol, 1.83 g), according to **GP4**. Purification by column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (750 mg, 72%). $\mathbf{R_f}$ = 0.57 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.51 (t, *J* = 7.4 Hz, 2H), 2.32 (dt, *J* = 24.1, 7.3 Hz, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.66 – 1.52 (m, 6H), 1.44 – 1.26 (m, 14H), 0.87 (t, *J* = 6.7 Hz, 3H).

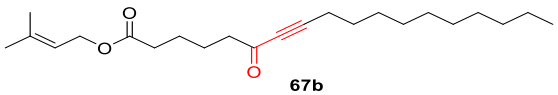
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.5, 173.8, 139.1, 118.7, 94.5, 81.0, 61.3, 45.5, 34.4, 31.9, 29.2, 29.1, 29.0, 28.9, 28.7, 27.8, 25.9, 24.9, 24.1, 22.7, 19.1, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2927 (s), 2857 (m), 2210 (m), 1733 (s), 1672 (s), 1458 (m), 1378 (m), 1354 (w), 1328 (w), 1276 (w), 1231 (w), 1167 (s), 1086 (w), 1048 (w), 959 (m), 777 (w), 725 (w).

MS (ESI): m/z calcd for $C_{23}H_{38}NaO_3$ 385.3 $[M+Na]^+$, found 385.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{38}O_3$ 362.2821 $[M]^+$, found 362.2832 $[M]^+$.

Prenyl 6-oxooctadec-7-ynoate (67b)



67b

Prepared from prenyl 6-hydroxyoctadec-7-ynoate **74b** (1.00 equiv, 1.65 mmol, 600 mg), $NaHCO_3$ (3.00 equiv, 4.94 mmol, 415 mg) and Dess-Martin-Periodinan (1.50 equiv, 2.47 mmol, 1.05 g), according to **GP4**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (300 mg, 50%). $\mathbf{R_f}$ = 0.54 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.37 – 5.28 (m, 1H), 4.55 (d, *J* = 7.2 Hz, 2H), 2.54 (t, *J* = 7.0 Hz, 2H), 2.32 (dt, *J* = 11.3, 7.1 Hz, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.68 – 1.62 (m, 4H), 1.56 (t, *J* = 6.8 Hz, 2H), 1.27 (m, 14H), 0.87 (t, *J* = 6.8 Hz, 3H).

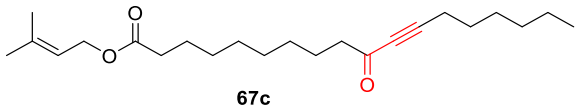
^{13}C NMR (101 MHz, $CDCl_3$) δ 187.8, 173.4, 139.2, 118.6, 94.7, 80.9, 61.4, 45.2, 34.1, 32.0, 29.6, 29.5, 29.4, 29.1, 28.9, 27.8, 25.8, 24.3, 23.5, 22.8, 19.1, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2925 (s), 2854 (m), 2210 (m), 1735 (s), 1715 (s), 1672 (s), 1458 (m), 1377 (m), 1361 (m), 1218 (m), 1164 (s), 963 (w), 776 (w), 722 (w), 529 (m).

MS (APCI): m/z calcd for $C_{23}H_{39}O_3$ 363.3 $[M+H]^+$, found 363.3 $[M]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{38}O_3$ 362.2821 $[M]^+$, found 362.2835 $[M]^+$.

Prenyl 10-oxooctadec-11-ynoate (67c)



67c

Prepared from prenyl 10-hydroxyoctadec-11-ynoate **74c** (1.00 equiv, 3.51 mmol, 1.28 g), $NaHCO_3$ (3.00 equiv, 10.50 mmol, 885 mg) and Dess-Martin-Periodinan (1.50 equiv, 5.27 mmol, 2.23 g), according to **GP4.** Purification by column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (650 mg, 51%). $\mathbf{R_f}$ = 0.54 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.32 (ddd, *J* = 8.6, 4.8, 1.9 Hz, 1H), 4.55 (d, *J* = 7.2 Hz, 2H), 2.53 – 2.48 (m, 2H), 2.34 (t, *J* = 7.1 Hz, 2H), 2.28 (t, *J* = 7.5 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.57 (dq, *J* = 14.9, 7.3 Hz, 6H), 1.28 (m, 14H), 0.89 (t, *J* = 6.8 Hz, 3H).

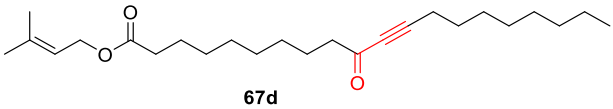
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.7, 174.0, 139.1, 118.7, 94.5, 81.0, 61.3, 45.6, 34.4, 31.3, 29.2, 29.1, 29.0, 28.6, 27.8, 25.9, 25.1, 24.2, 22.6, 19.1, 18.1, 14.1.

IR (ATR ν in cm^{-1}) 2929 (s), 2857 (m), 2211 (m), 1735 (s), 1671 (s), 1457 (m), 1365 (m), 1218 (m), 1166 (s), 978 (w), 725 (w), 529 (w).

MS (APCI): m/z calcd for $C_{23}H_{39}O_3$ 363.5 $[M+H]^+$, found 363.4 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{38}O_3$ 362.2821 $[M]^+$, found 362.2828 $[M]^+$.

Prenyl 10-oxoicos-11-ynoate (67d)



67d

Prepared from prenyl 10-hydroxyicos-11-ynoate **74d** (1.00 equiv, 3.01 mmol, 1.18 g), $NaHCO_3$ (3.00 equiv, 9.02 mmol, 757 mg) and Dess-Martin-Periodinan (1.50 equiv, 4.51 mmol, 1.91 g), according to **GP4**. Purification by column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (730 mg, 62%). $\mathbf{R_f}$ = 0.57 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.2, 1.5 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.50 (t, *J* = 7.4 Hz, 2H), 2.31 (dt, *J* = 26.5, 7.3 Hz, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.59 (td, *J* = 14.8, 7.4 Hz, 6H), 1.44 – 1.26 (m, 18H), 0.85(t, *J* = 6.8 Hz, 3H).

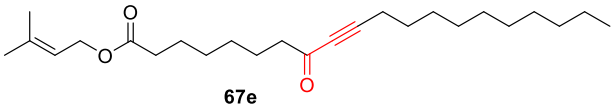
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.6, 174.0, 139.1, 118.8, 94.4, 81.0, 61.3, 45.6, 34.4, 31.9, 29.3, 29.2, 29.2, 29.1, 29.0, 29.0, 27.8, 25.9, 25.1, 24.2, 22.7, 19.1, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2926 (s), 2854 (m), 2211 (m), 1735 (s), 1672 (s), 1457 (m)6, 1378 (m), 1231 (w), 1166 (s), 1093 (w), 962 (m), 723 (w), 576 (w), 515 (w).

MS (APCI): m/z calcd for $C_{25}H_{43}O_3$ 391.6 $[M+H]^+$, found 391.8 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{25}H_{42}O_3$ 390.3134 $[M]^+$, found 390.3147 $[M]^+$.

Prenyl 8-oxoicos-9-ynoate (67e)



67e

Prepared from prenyl 8-hydroxyicos-9-ynoate **74e** (1.00 equiv, 1.30 mmol, 510 mg), $NaHCO_3$ (3.00 equiv, 3.90 mmol, 327 mg) and Dess-Martin-Periodinan (1.50 equiv, 1.95 mmol, 826 mg), according to **GP4**. Purification by column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (300 mg, 59%). $\mathbf{R_f}$ = 0.45 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.3, 1.5 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.51 (t, *J* = 7.5 Hz, 2H), 2.31 (dt, *J* = 23.8, 7.3 Hz, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.65 – 1.52 (m, 6H), 1.44 – 1.25 (m, 18H), 0.87 (t, *J* = 6.8 Hz, 3H).

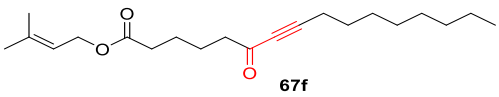
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.5, 173.8, 139.1, 118.7, 94.5, 81.0, 61.3, 45.5, 34.4, 32.0, 29.6, 29.5, 29.4, 29.1, 29.0, 28.9, 28.7, 27.8, 25.9, 24.9, 24.0, 22.8, 19.1, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2925 (s), 2854 (m), 2210 (m), 1735 (s), 1672 (s), 1457 (m), 1377 (m), 1361 (m), 1218 (w), 1166 (s), 1089 (w), 978 (w), 723 (w), 529 (w).

MS (APCI): m/z calcd for $C_{25}H_{43}O_3$ 391.6 $[M+H]^+$, found 391.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{25}H_{42}O_3$ 390.3134 $[M]^+$, found 390.3144 $[M]^+$.

Prenyl 6-oxohexadec-7-ynoate (67f)



67f

Prepared from prenyl 6-hydroxyhexadec-7-ynoate **74f** (1.00 equiv, 2.97 mmol, 1.00 g), $NaHCO_3$ (3.00 equiv, 8.91 mmol, 749 mg) and Dess-Martin-Periodinan (1.50 equiv, 4.46 mmol, 4.89 g), according to **GP4**. Purification by column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (700 mg, 70%). $\mathbf{R_f}$ = 0.55 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.54 (t, *J* = 6.9 Hz, 2H), 2.33 (dt, *J* = 11.6, 7.0 Hz, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.68 – 1.52 (m, 6H), 1.44 – 1.26 (m, 10H), 0.85 (t, *J* = 6.8 Hz, 3H).

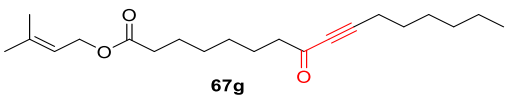
^{13}C NMR (101 MHz, $CDCl_3$) δ 187.8, 173.4, 139.2, 118.7, 94.7, 80.9, 61.4, 45.2, 34.1, 31.9, 29.2, 29.1, 29.0, 27.8, 25.9, 24.4, 23.6, 22.7, 19.1, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2927 (s), 2856 (m), 2210 (m), 1735 (s), 1672 (s), 1455 (m), 1377 (m), 1229 (m), 1218 (w), 1162 (m), 1136 (w), 962 (w), 778 (w), 723 (w), 527 (w).

MS (APCI): m/z calcd for $C_{21}H_{35}O_3$ 335.5 $[M+H]^+$, found 335.7 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{21}H_{34}O_3$ 334.2508 $[M]^+$, found 334.2519 $[M]^+$.

Prenyl 8-oxohexadec-9-ynoate (67g)



67g

Prepared from prenyl 8-hydroxyhexadec-9-ynoate **74g** (1.00 equiv, 1.37 mmol, 460 mg), $NaHCO_3$ (3.00 equiv, 4.10 mmol, 345 mg) and Dess-Martin-Periodinan (1.50 equiv, 2.05 mmol, 870 mg), according to **GP4**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (320 mg, 70%). $\mathbf{R_f}$ = 0.45 (9:1 *n*-hexane: EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.51 (t, *J* = 7.4 Hz, 2H), 2.32 (dt, *J* = 25.1, 7.3 Hz, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.65 – 1.53 (m, 6H), 1.44 – 1.28 (m, 10H), 0.89 (t, *J* = 6.9 Hz, 3H).

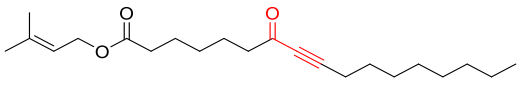
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.5, 173.8, 139.1, 118.7, 94.5, 81.0, 61.3, 45.5, 34.3, 31.3, 28.9, 28.7, 28.6, 27.8, 25.9, 24.8, 24.1, 22.6, 19.1, 18.1, 14.1.

IR (ATR ν in cm^{-1}) 2930 (s), 2859 (m), 2210 (m), 1732 (s), 1671 (s), 1457 (m), 1378 (m), 1359 (m), 1219 (w), 1166 (s), 1089 (w), 1048 (w), 1978 (m), 726 (w), 529 (m).

MS (APCI): m/z calcd for $C_{21}H_{35}O_3$ 335.5 $[M+H]^+$, found 335.4 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{21}H_{34}O_3$ 334.2508 $[M]^+$, found 334.2523 $[M]^+$,

Prenyl 7-oxoheptadec-8-ynoate (67h)



67h

Prepared from prenyl 7-hydroxyheptadec-8-ynoate **74h** (1.00 equiv, 2.57 mmol, 900 mg), $NaHCO_3$ (3.00 equiv, 7.71 mmol, 648 mg) and Dess-Martin-Periodinan (1.50 equiv, 3.86 mmol, 1.64 g), according to **GP4**. Purification by column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (680 mg, 73%). $\mathbf{R_f}$ = 0.57 (9:1 *n*-hexane:EtOAc).

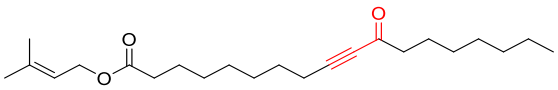
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.52 (t, *J* = 7.4 Hz, 2H), 2.32 (dt, *J* = 20.0, 7.3 Hz, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.67 – 1.52 (m, 6H), 1.43 – 1.25 (m, 12H), 0.85 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.3, 173.7, 139.1, 118.7, 94.6, 80.9, 61.3, 45.3, 34.2, 31.9, 29.2, 29.1, 29.0, 28.5, 27.8, 25.9, 24.8, 23.8, 22.7, 19.1, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2926 (s), 2856 (m), 2209 (m), 1732 (s), 1672 (s), 1456 (m), 1378 (m), 1354 (w), 1328 (w), 1240 (w), 1168 (s), 1079 (w), 967 (w), 775 (w), 726 (w).

MS (APCI): m/z calcd for $C_{22}H_{37}O_3$ 349.3 $[M+H]^+$, found 349.2 $[M+H]^+$.

Prenyl 11-oxooctadec-9-ynoate (90a)



90a

Prepared from prenyl 11-hydroxyoctadec-9-ynoate **99a** (1.00 equiv, 1.10 mmol, 400 mg), $NaHCO_3$ (3.00 equiv, 3.30 mmol, 277 mg) and Dess-Martin-Periodinan (1.50 equiv, 1.65 mmol, 700 mg), according to **GP4**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (270 mg, 68%). $\mathbf{R_f}$ = 0.54 (9:1 *n*-hexane: EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (ddt, *J* = 8.6, 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.3 Hz, 2H), 2.51 (t, *J* = 7.4 Hz, 2H), 2.32 (dt, *J* = 21.5, 7.3 Hz, 4H), 1.76 (s, 3H), 1.70 (s, 3H), 1.65 – 1.53 (m, 6H), 1.44 – 1.27 (m, 14H), 0.86 (t, *J* = 6.6 Hz, 3H).

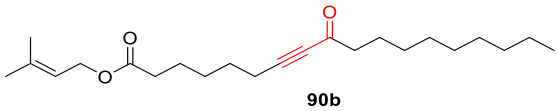
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.7, 173.9, 139.1, 118.7, 94.2, 81.1, 61.3, 45.6, 34.4, 31.7, 29.1, 29.1, 29.1, 28.8, 28.8, 27.7, 25.9, 25.0, 24.2, 22.7, 19.1, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2929 (s), 2857 (m), 2211 (m), 1732 (s), 1671 (s), 1458 (m), 1364 (m), 1219 (m), 1164 (m), 1093 (w), 725 (w), 530 (w).

MS (ESI): m/z calcd for $C_{23}H_{38}NaO_3$ 385.3 $[M+Na]^+$, found 385.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{38}O_3$ 362.2821 $[M]^+$, found 362.2832 $[M]^+$.

Prenyl 9-oxooctadec-7-ynoate (90b)



90b

Prepared from prenyl 9-hydroxyoctadec-7-ynoate **99b** (1.00 equiv, 4.11 mmol, 1.50 g), $NaHCO_3$ (3.00 equiv, 12.30 mmol, 1.04 g) and Dess-Martin-Periodinan (1.50 equiv, 6.17 mmol, 2.62 g), according to **GP4**. Purification by column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (765 mg, 51%). $\mathbf{R_f}$ = 0.55 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (t, *J* = 7.3 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.56 – 2.47 (m, 2H), 2.34 (dt, *J* = 20.1, 7.3 Hz, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.61 (dd, *J* = 19.4, 7.9 Hz, 6H), 1.47 – 1.40 (m, 2H), 1.30 – 1.25 (m, 12H), 0.87 (t, *J* = 7.0 Hz, 3H).

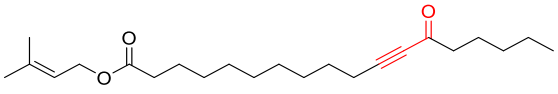
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.7, 173.6, 139.2, 118.6, 93.8, 81.1, 61.4, 45.6, 34.2, 32.0, 29.5, 29.4, 29.3, 29.1, 28.4, 27.5, 25.9, 24.4, 24.2, 22.8, 18.9, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2925 (s), 2854 (m), 2211 (m), 1735 (s), 1672 (s), 1459 (m), 1378 (m), 1229 (w), 1164 (s), 963 (w), 723 (w), 629 (w), 526 (w).

MS (APCI): m/z calcd for $C_{23}H_{39}O_3$ 363.3 $[M+H]^+$, found 363.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{38}O_3$ 362.2821 $[M]^+$, found 362.2840 $[M]^+$.

Prenyl 13-oxooctadec-11-ynoate (90c)



90c

Prepared from prenyl 13-hydroxyoctadec-11-ynoate **99c** (1.00 equiv, 1.78 mmol, 650 mg), $NaHCO_3$ (3.00 equiv, 5.35 mmol, 449 mg) and Dess-Martin-Periodinan (1.50 equiv, 2.67 mmol, 1.13 g), according to **GP4**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (325 mg, 50%). $\mathbf{R_f}$ = 0.55 (9:1 *n*-hexane: EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (t, *J* = 7.2 Hz, 1H), 4.56 (d, *J* = 7.3 Hz, 2H), 2.51 (t, *J* = 7.5 Hz, 2H), 2.31 (dt, *J* = 23.6, 7.3 Hz, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.66 – 1.52 (m, 6H), 1.43 – 1.27 (m, 14H), 0.89 (t, *J* = 6.6 Hz, 3H).

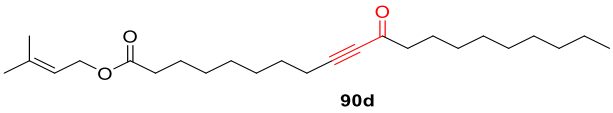
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.7, 174.0, 139.1, 118.8, 94.3, 81.0, 61.3, 45.6, 34.4, 31.2, 29.3, 29.3, 29.2, 29.1, 28.9, 27.8, 25.9, 25.1, 23.9, 22.5, 19.1, 18.1, 14.0.

IR (ATR ν in cm^{-1}) 2927 (s), 2856 (m), 2211 (m), 1732 (s), 1671 (s), 1459 (m), 1378 (m), 1356 (w), 1235 (m), 1219 (w), 1165 (s), 1093 (w), 962 (m), 725 (w), 655 (w), 590 (m), 520 (w).

MS (APCI): m/z calcd for $C_{23}H_{39}O_3$ 363.5 $[M+H]^+$, found 363.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{38}O_3$ 362.2821 $[M]^+$, found 362.2835 $[M]^+$.

Prenyl 11-oxoicos-9-ynoate (90d)



90d

Prepared from prenyl 11-hydroxyicos-9-ynoate **99d** (1.00 equiv, 1.91 mmol, 750 mg), $NaHCO_3$ (3.00 equiv, 5.73 mmol, 481 mg) and Dess-Martin-Periodinan (1.50 equiv, 2.87 mmol, 1.22 g), according to **GP4**. Purification by column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (360 mg, 48%). $\mathbf{R_f}$ = 0.41 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.3, 1.5 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.51 (t, *J* = 7.4 Hz, 2H), 2.32 (dt, *J* = 21.2, 7.3 Hz, 4H), 1.76 (s, 3H), 1.70 (s, 3H), 1.64 – 1.53 (m, 6H), 1.44 – 1.25 (m, 18H), 0.85 (t, *J* = 7.0 Hz, 3H).

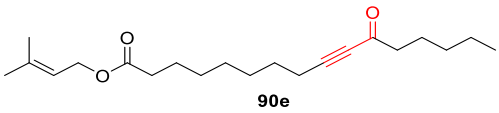
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.7, 173.9, 139.1, 118.7, 94.2, 81.1, 61.3, 45.6, 34.4, 31.9, 29.5, 29.4, 29.3, 29.1, 29.0, 28.8, 28.7, 27.7, 25.9, 25.0, 24.2, 22.8, 19.0, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2926 (s), 2856 (m), 2211 (m), 1735 (s), 1671 (s), 1464 (m), 1378 (m), 1232 (w), 1164 (s), 982 (w), 962 (w), 912 (m), 730 (s), 648 (w).

MS (APCI): m/z calcd for $C_{25}H_{43}O_3$ 391.6 $[M+H]^+$, found 391.4 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{25}H_{42}O_3$ 390.3134 $[M]^+$, found 390.3152 $[M]^+$.

Prenyl 11-oxohexadec-9-ynoate (90e)



90e

Prepared from prenyl 11-hydroxyhexadec-9-ynoate **99e** (1.00 equiv, 1.28 mmol, 430 mg), $NaHCO_3$ (3.00 equiv, 3.83 mmol, 322 mg) and Dess-Martin-Periodinan (1.50 equiv, 1.92 mmol, 813 mg), according to **GP4**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (281 mg, 66%). $\mathbf{R_f}$ = 0.41 (9:1 *n*-hexane: EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.2, 1.5 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.51 (t, *J* = 7.4 Hz, 2H), 2.32 (dt, *J* = 21.7, 7.3 Hz, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.65 – 1.53 (m, 6H), 1.42 – 1.29 (m, 10H), 0.86 (t, *J* = 6.9 Hz, 3H).

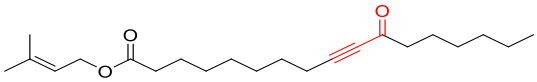
^{13}C NMR (101 MHz, $CDCl_3$) δ 188.7, 173.9, 139.1, 118.7, 94.2, 81.1, 61.3, 45.6, 34.4, 31.2, 29.1, 28.8, 28.7, 27.7, 25.9, 25.0, 23.9, 22.5, 19.0, 18.1, 14.0.

IR (ATR ν in cm^{-1}) 2930 (s), 2859 (m), 2211 (m), 1732 (s), 1671 (s), 1457 (m), 1378 (m), 1355 (w), 1278 (w), 1236 (m), 1165 (s), 1095 (w), 961 (m), 726 (w), 530 (w).

MS (APCI): m/z calcd for $C_{21}H_{35}O_3$ 335.5 $[M+H]^+$, found 335.4 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{21}H_{34}O_3$ 334.2508 $[M]^+$, found 334.2517 $[M]^+$.

Prenyl 11-oxoheptadec-9-ynoate (90f)



90f

Prepared from prenyl 11-hydroxyheptadec-9-ynoate **99f** (1.00 equiv, 0.57 mmol, 200 mg), $NaHCO_3$ (3.00 equiv, 1.71 mmol, 143.90 mg) and Dess-Martin-Periodinan (1.50 equiv, 0.87 mmol, 363.27 mg), according to **GP4**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (120 mg, 60%). $\mathbf{R_f}$ = 0.53 (9:1 *n*-hexane: EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.51 (t, *J* = 7.4 Hz, 2H), 2.32 (dt, *J* = 21.5, 7.4 Hz, 4H), 1.76 (s, 3H), 1.71 (s, 3H), 1.65 – 1.53 (m, 6H), 1.42 – 1.29 (m, 12H), 0.87 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.7, 173.9, 139.1, 118.7, 94.2, 81.1, 61.3, 45.7, 34.4, 31.6, 29.1, 28.8, 28.8, 28.7, 27.7, 25.9, 25.0, 24.2, 22.6, 19.1, 18.1, 14.1.

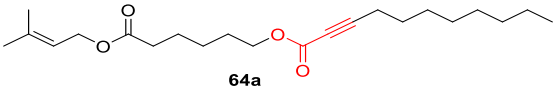
IR (ATR ν in cm^{-1}) 2930 (s), 2859 (m), 2211 (m), 1735 (s), 1671 (s), 1457 (m), 1419 (w), 1365 (s), 1218 (m), 1165 (m), 1093 (w), 726 (w), 529 (w).

MS (ESI): m/z calcd for $C_{22}H_{36}NaO_3$ 371.3 $[M+Na]^+$, found 371.3 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{36}O_3$ 348.2664 $[M]^+$, found 348.2650 $[M]^+$**.**

6.4.10 Synthesis of Alkynoic Esters

6-((Prenyl)oxy)-6-oxohexyl undec-2-ynoate (64a)



64a

In a dried two-necked flask, 1-decyne **48a** (2.00 equiv, 3.40 mmol, 614 µl) was added and diluted with anhydrous THF (6 mL). The resulting solution was cooled to -78 °C before dropwise addition of *n*-BuLi (2.00 equiv, 3.40 mmol, 2.56 mL 1.55 M in hexanes). The reaction mixture was stirred for 1 h at -78 °C Carbon dioxide (dry-ice), was then added and the mixture was stirred at 0 °C for 10-15 minutes. To the resulting solution, prenyl 6-bromohexanoate **55a** (1.00 equiv, 1.70 mmol, 448 mg), was added and the mixture was diluted with DMF (8 mL). After stirring at 70 °C for 16 h, the reaction mixture was quenched with H_2O (30 mL) and extracted with EtOAc (3 x 25 mL). The organic layers were washed with H_2O (50 mL), sat. aq. NaCl (50 ml) and dried over Na_2SO_4. After removing the solvent under reduced pressure, the crude residue was purified by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (423 mg, 68%). $\mathbf{R_f}$ = 0.39 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.3, 1.5 Hz, 1H), 4.57 (d, *J* = 7.2 Hz, 2H), 4.14 (t, *J* = 6.6 Hz, 2H), 2.32 (td, *J* = 7.3, 1.8 Hz, 4H), 1.76 (s, 3H), 1.71 (s, 3H), 1.68 – 1.54 (m, 6H), 1.45 – 1.34 (m, 4H), 1.32 – 1.22 (m, 8H), 0.84 (t, *J* = 6.9 Hz, 3H).

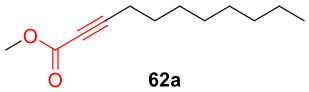
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 154.1, 139.2, 118.7, 89.8, 73.2, 65.6, 61.4, 34.2, 31.9, 29.2, 29.1, 29.0, 28.2, 27.6, 25.9, 25.5, 24.6, 22.7, 18.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2927 (s), 2857 (m), 2234 (m), 1733 (s), 1709 (s), 1459 (m), 1379 (m), 1355 (w), 1328 (w), 1244 (s), 1161 (m), 1072 (m), 951 (w), 828 (w), 775 (w), 750 (m).

MS (ESI): m/z calcd for $C_{22}H_{36}NaO_4$ 387.5 $[M+Na]^+$, found 387.5 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{36}O_4$ 364.2614 $[M]^+$, found 364.2617 $[M]^+$.

Methyl undec-2-ynoate (62a)



62a

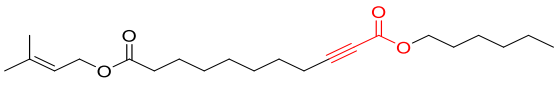
In a dried two-necked flask, 1-decyne **48a** (2.00 equiv, 15.50 mmol, 2.80 mL) was added and diluted with anhydrous THF (10 mL). The resulting solution was cooled to -78 °C before dropwise addition of *n*-BuLi (2.00 equiv, 15.50 mmol, 10 mL, 1.55 M in hexanes). The reaction mixture was stirred for 1 h at -78 °C Carbon dioxide (dry-ice), was then added and the mixture was stirred at 0 °C for 10-15 minutes. To the resulting solution, **MeI** (1.00 equiv, 7.75 mmol, 480 µl), was added and the mixture was diluted with DMF (10 mL). After stirring at 70 °C for 16 h, the reaction mixture was quenched with H_2O (50 mL) and extracted with EtOAc (3 x 30 mL). The organic layers were washed with H_2O (50 mL), sat. aq. NaCl (50 ml) and dried over Na_2SO_4. After removing the solvent under reduced pressure, the crude residue was purified by column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (1.42 g, 93%). $\mathbf{R_f}$ = 0.60 (9:1 *n*-hexane:EtOAc). Analytical data are in accordance with the literature. [120]

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 3H), 2.32 (t, *J* = 7.1 Hz, 2H), 1.57 (p, *J* = 7.5 Hz, 2H), 1.45 – 1.20 (m, 10H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4, 90.1, 72.9, 52.7, 31.9, 29.2, 29.1, 28.9, 27.6, 22.7, 18.7, 14.2.

MS (ESI): m/z calcd for $C_{12}H_{20}NaO_2$ 219.1 $[M+Na]^+$, found 219.4 $[M+Na]^+$.

1-hexyl 11-(prenyl) undec-2-ynedioate (87a)



87a

In a dried two-necked flask, prenyl dec-9-ynoate **82b** (1.05 equiv, 1.69 mmol, 400 mg) was added and diluted with anhydrous THF (6 mL). The resulting solution was cooled to -78 °C before dropwise addition of *n*-BuLi (1.05 equiv, 1.69 mmol, 676 µL, 2.5 M in hexanes). The reaction mixture was stirred for 1 h at -78 °C. Carbon dioxide (dry ice), was then added and the mixture was stirred at 0 °C for 10-15 minutes. To the resulting solution, 1-Bromhexane **100** (2.00 equiv, 3.22 mmol, 454 µL), was added and the mixture was diluted with DMF (8 mL). After stirring at 70 °C for 16h, the reaction mixture was quenched with H_2O (30 mL) and extracted with EtOAc (3 x 30 mL). The organic layers were washed with H_2O (50 mL), sat. aq. NaCl (50 ml) and dried over Na_2SO_4. After removing the solvent under reduced pressure, the crude residue was purified by flash column chromatography (*n*-hexane:EtOAc =

99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (206 mg, 35%). **R_f** = 0.45 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.14 (t, *J* = 6.8 Hz, 2H), 2.30 (dt, *J* = 10.2, 7.3 Hz, 4H), 1.76 (s, 3H), 1.71 (s, 3H), 1.66 – 1.55 (m, 6H), 1.45 – 1.29 (m, 12H), 0.86 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 154.1, 139.1, 118.8, 89.4, 73.3, 66.1, 61.3, 34.4, 31.5, 29.0, 28.8, 28.8, 28.5, 27.6, 25.9, 25.6, 25.0, 22.6, 18.8, 18.1, 14.1.

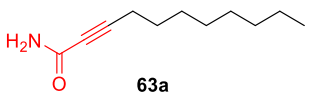
IR (ATR ν in cm^{-1}) 2932 (s), 2859 (m), 2236 (m), 1732 (s), 1710 (s), 1457 (m), 1378 (m), 1245 (s), 1166 (w), 1076 (m), 979 (w), 955 (w), 806 (w), 752 (m), 726 (w).

MS (APCI): m/z calcd for $C_{22}H_{37}O_4$ 365.5 $[M+H]^+$, found 365.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{36}O_4$ 364.2614 $[M]^+$, found 364.2610 $[M]^+$.

6.4.11 Synthesis of Amides

Undec-2-ynamide (63a)



63a

To a solution of Methyl undec-2-ynoate **62a** (1.00 equiv, 6.11 mmol, 1.20 g) in dry MeOH (0.1 M), an excess of ammonium hydroxide (28 – 30%, 75.00 equiv, 458 mmol, 50.10 mL) was added slowly. The reaction mixture was stirred at room temperature overnight. The reaction mixture was diluted with H_2O (30 ml) and extracted with EtOAc (3 × 25 mL). The combined organic phases were washed with NaCl (50 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (*n*-hexane:EtOAc + 0.2% Vol NEt_3 = 95:5 → 70:30) afforded the desired analytically pure product as a white powder (961mg, 87%). **R_f** = 0.27 (7:3 *n*-hexane: EtOAc + 0.2% Vol NEt_3).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (d, *J* = 105.8 Hz, 2H), 2.29 (t, *J* = 7.1 Hz, 2H), 1.62 – 1.50 (m, 2H), 1.44 – 1.23 (m, 10H), 0.85 (t, *J* = 6.9 Hz, 3H).

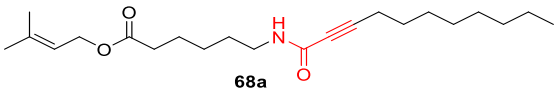
^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5, 89.1, 75.0, 31.9, 29.2, 29.1, 28.9, 27.7, 22.7, 18.7, 14.1.

IR (ATR ν in cm^{-1}) 3381 (s), 3170 (s), 2955 (w), 2924 (s), 2852 (m), 2242 (s), 1634 (s), 1612 (s), 1464 (m), 1392 (s), 1293 (w), 1129 (m), 788 (w), 763 (w), 721 (w), 640 (s).

MS (ESI): m/z calcd for $C_{11}H_{19}NNaO$ 204.1 $[M+Na]^+$, found 204.1 $[M+Na]^+$.

HRMS (TOF ME EI+): m/z calcd for $C_{11}H_{20}NO$ 182.1545 $[M+H]^+$, found 182.1546 $[M+H]^+$.

Prenyl 6-(undec-2-ynamido)hexanoate (68a)



68a

In a dried two-necked flask, undec-2-ynamide **63a** (1.00 equiv, 0.83 mmol, 150 mg) was added and dissolved with anhydrous DMF (2 mL). The resulting solution was cooled to 0 °C before the slow addition of NaH (1.05 equiv, 870 µmol, 20.90 mg, 60% dispersion in mineral oil). The reaction mixture was stirred for 1 h at 0 °C and Prenyl 6-bromohexanoate **55a** (1.05 equiv, 0.87 mmol, 229 mg) was then added and the mixture was stirred at room temperature overnight. The reaction mixture was quenched with H_2O (20 mL) and extracted with EtOAc (3 x 25 ml). The organic layers were washed with saturated aqueous NaCl (50 ml) and dried over Na_2SO_4. After concentration under reduced pressure, the crude residue was purified by flash column chromatography (*n*-hexane:EtOAc + 0.2% Vol NEt_3 = 95:5 → 70:30) afforded the desired analytically pure product as a yellow oil (121 mg, 40%). $\mathbf{R_f}$ = 0.42 (7:3 *n*-hexane:EtOAc + 0.2% Vol NEt_3).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.75 (s, 1H), 5.33 (t, *J* = 7.1 Hz, 1H), 4.56 (d, *J* = 7.4 Hz, 2H), 3.28 (t, *J* = 6.8 Hz, 2H), 2.36 – 2.25 (m, 4H), 1.76 (s, 3H), 1.71 (s, 3H), 1.65 – 1.52 (m, 6H), 1.39 – 1.27 (m, 12H), 0.88 (t, *J* = 6.6 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.7, 153.7, 139.2, 118.6, 87.4, 75.6, 61.4, 39.6, 34.2, 31.9, 29.2, 29.1, 29.0, 27.9, 26.4, 25.9, 24.6, 22.7, 18.7, 18.1, 14.2.

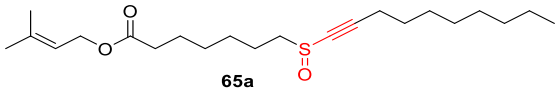
IR (ATR ν in cm^{-1}) 3278 (w), 2927 (s), 2857 (m), 2243 (w), 1732 (s), 1632 (s), 1530 (m)6, 1456 (m), 1379 (m), 1355 (w), 1275 (m), 1159 (s), 1104 (w), 1048 (w), 953 (m), 725 (w).

MS (ESI): m/z calcd for $C_{22}H_{37}NNaO_3$ 386.3 $[M+Na]^+$, found 386.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{37}NO_3$ 363.2773 $[M]^+$, found 363.2773 $[M]^+$.

6.4.12 Synthesis of Alkynyl Sulfoxide and Alkynyl Sulfone Esters

Prenyl 7-(dec-1-yn-1-ylsulfinyl)heptanoate (65a)



65a

To a solution of Prenyl 7-(dec-1-yn-1-ylthio)heptanoate **75** (1.00 equiv, 5.00 mmol, 1.83 g) in DCM (0.1 M) at 0 °C, *m*-CPBA (1.00 equiv, 5.00 mmol, 863 mg) was added in portions. The reaction mixture was allowed to stir for 30 minutes at ambient temperature. Then, the resulting slurry was quenched with saturated aqueous $Na_2S_2O_3$ (20 mL) and extracted with DCM (3 x 25 mL). The organic layers were washed with saturated aqueous $NaHCO_3$ (3 x 20 mL), saturated aqueous NaCl (50 mL), dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (*n*-hexane: Acetone = 19:1 → 9:1) to afford the desired analytically pure product as a yellow oil (1.0 g, 55%). $\mathbf{R_f}$: 0.30 (8:2 *n*-hexanel:Acetone).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.35 – 5.29 (m, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 3.03 – 2.96 (m, 2H), 2.42 (t, *J* = 7.1 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 1.93 – 1.77 (m,2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.61 (ddt, *J* = 27.0, 14.9, 7.3 Hz, 4H), 1.52 – 1.26 (m, 14H), 0.87 (t, *J* = 6.8 Hz, 3H).

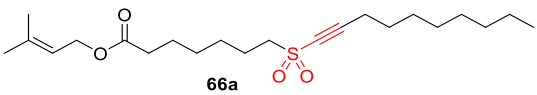
^{13}C NMR (101 MHz, $CDCl_3$): δ 173.6, 139.1, 118.7, 105.7, 61.3, 56.3, 34.2, 31.8, 29.1, 29.1, 28.9, 28.8, 28.3, 27.7, 25.8, 25.8, 24.7, 22.7, 22.2, 19.7, 18.1, 14.2.

IR (ATR ν in cm^{-1}): 2924 (m), 2855 (m), 2179 (w), 1730 (s), 1674 (m), 1455 (w), 1377 (s), 1274 (m), 1167 (w), 1068 (w), 972 (m), 726 (m), 650 (w).

MS (ESI): m/z calcd for $C_{22}H_{38}NaO_3S$ 405.2 $[M+Na]^+$, found 405.3 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{38}O_3S$ 382.2542 $[M]^+$, found 382.2542 $[M]^+$.

Prenyl 7-(dec-1-yn-1-ylsulfonyl)heptanoate (66a).



66a

To a solution of Prenyl 7-(dec-1-yn-1-ylthio)heptanoate **75** (1.00 equiv, 2.00 mmol, 733 mg) in DCM (0.5 M) at 0 °C, *m*-CPBA (2.50 equiv, 5.00 mmol, 1.12 g) was added in portions. The reaction mixture was allowed to stir for 30 minutes at ambient temperature. The precipitate was filtered off and the filtrate was extracted with DCM (3 x 25 mL). The organic phases were washed with 1 M NaOH (2 X 25 mL) and saturated aqueous NaCl (20 mL). After drying with Na_2SO_4, the solvent was removed under

reduced pressure. The crude product was then purified by flash column chromatography (*n*-hexane:EtOAc = 19:1 → 9:1) to produce the desired analytically pure product as a colorless oil (558 mg, 70%). **R_f**: 0.23 (8:2 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.33 – 5.30 (m,1H), 4.57 (d, *J* = 7.2 Hz, 2H), 3.16 – 3.09 (m, 2H), 2.43 – 2.25 (m, 4H), 1.94 – 1.85(m, 2H), 1.76 (s, 3H), 1.71 (s, 3H), 1.68 – 1.55 (m, 4H), 1.51 – 1.27 (m, 14H), 0.87 (t, *J* = 6.8 Hz, 3H).

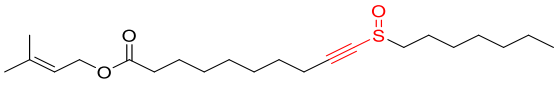
^{13}C NMR (101 MHz, $CDCl_3$): δ 173.6, 139.2, 118.6, 96.6, 61.4, 58.1, 34.2, 31.8, 29.1, 29.0, 28.9, 28.6, 27.8, 27.1, 25.9, 24.6, 22.9, 22.7, 18.9, 18.1, 14.2.

IR (ATR ν in cm^{-1}): 2925 (m), 2855 (m), 2201 (w), 1730 (s), 1672 (m), 1459 (w), 1378 (s), 1327 (s), 1244 (w), 1144 (w), 1070 (w), 876 (w), 786 (m), 668 (m), 650 (w).

MS (ESI): m/z calcd for $C_{22}H_{38}NaO_4S$ 421.2 $[M+Na]^+$, found 421.3 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{38}O_4S$ 398.2491 $[M]^+$, found 398.2485 $[M]^+$.

Prenyl 10-(heptylsulfinyl)dec-9-ynoate (88a)



88a

To a solution of prenyl 10-(heptylthio)dec-9-ynoate **101** (1.00 equiv, 0.93 mmol, 340 mg) in DCM (10 mL) at 0 °C, *m*-CPBA (1.00 equiv, 1.33 mmol, 229 mg) was added in portions and the reaction mixture was stirred at the same temperature for 5 minutes. The reaction mixture was then allowed to warm up to ambient temperature and was stirred for 30 minutes. Then, the resulting slurry was quenched with saturated aqueous $Na_2S_2O_3$ (20 mL) and extracted with DCM (3 x 25 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (3 x 30 mL), saturated aqueous NaCl (50 mL), dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was then purified by flash column chromatography (*n*-hexane: Acetone = 95:5 → 80:20) to afford the desired analytically pure product as a yellow oil (220 mg, 62%). **R_f** = 0.40 (8:2 *n*-hexane:Acetone).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.3, 1.5 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 3.01 (ddd, *J* = 8.7, 6.8, 1.9 Hz, 2H), 2.42 (t, *J* = 7.1 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.92 – 1.78 (m, 2H), 1.76 (s, 3H), 1.70 (s, 3H), 1.58 (dq, *J* = 15.1, 7.3 Hz, 4H), 1.50 – 1.29 (m, 14H), 0.86 (t, *J* = 6.8 Hz, 3H).

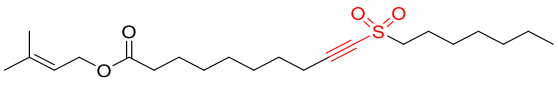
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 139.1, 118.7, 105.4, 61.3, 56.6, 34.4, 31.6, 29.0, 29.0, 28.7, 28.7, 28.6, 27.6, 25.9, 25.0, 22.6, 22.4, 19.7, 18.1, 14.1.

IR (ATR ν in cm^{-1}) 2927 (s), 2856 (m), 2181 (w), 1731 (s), 1459 (m), 1378 (m), 1325 (w), 1276 (w), 1236 (w), 1168 (m), 1142 (w), 1061 (m), 778 (w), 725 (w), 602(w).

MS (ESI): m/z calcd for $C_{22}H_{38}O_3NaS$ 405.2 $[M+Na]^+$, found 405.1 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{38}O_3S$ 382.2542 $[M]^+$, found 382.2562 $[M]^+$.

Prenyl 10-(heptylsulfonyl)dec-9-ynoate (89a)



89a

To a solution of prenyl 10-(heptylthio)dec-9-ynoate **101** (1.00 equiv, 0.90 mmol, 330 mg) in DCM (12 mL) at 0 °C, *m*-CPBA (3.00 equiv, 2.70 mmol, 666 mg) was added in portions and the resulting mixture was stirred at the same temperature for 5 minutes. After stirring at room temperature for 30 minutes, the precipitate was filtered off and the filtrate was extracted with DCM (3 x 25 mL). The organic phases were washed with 1 M NaOH (2 X 25 mL), saturated aqueous NaCl (30 mL), and dried over Na_2SO_4. After removing the solvent under reduced pressure, the crude product was then purified by flash column chromatography (*n*-hexane:Acetone = 98:2 → 90:10) afforded the desired analytically pure product as a yellow oil (180 mg, 50%). $\mathbf{R_f}$ = 0.40 (9:1 *n*-hexane:Acetone).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 3.20 – 3.09 (m, 2H), 2.40 (t, *J* = 7.1 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.93 – 1.84 (m, 2H), 1.76 (s, 3H), 1.70 (s, 3H), 1.64 – 1.58 (m, 4H), 1.48 – 1.29 (m, 14H), 0.86 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 139.1, 118.7, 96.2, 76.3, 61.3, 58.2, 34.3, 31.5, 28.9, 28.8, 28.7, 28.7, 28.1, 27.1, 25.9, 24.9, 23.0, 22.6, 18.9, 18.1, 14.1.

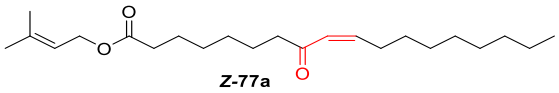
IR (ATR ν in cm^{-1}) 2953 (w), 2925 (m), 2850 (m), 2208 (m), 1737 (s), 1694 (s), 1428 (w), 1405 (w), 1328 (s), 1292 (m), 1266 (m), 1229 (m), 1132 (s), 1092 (w), 1059 (w), 757 (s), 726 (m), 676 (s), 566 (m).

MS (ESI): m/z calcd for $C_{22}H_{37}O_4S$ 397.2 $[M-H]^+$, found 397.6 $[M-H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{38}O_4S$ 398.2491 $[M]^+$, found 398.2504 $[M]^+$.

6.4.13 Synthesis of *(Z)*- and *(E)*-Enone Esters

***(Z)*-Prenyl-8-oxooctadec-9-enoate (*Z*-77a)**



Z-77a

Prepared from Prenyl 8-oxooctadec-9-ynoate **67a** (1.00 equiv, 1.05 mmol, 380 mg) and Pd on $BaSO_4$ (0.15 equiv, 158 µmol, 53.50 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a colorless oil (170 mg, 45%). $\mathbf{R_f}$ = 0.6 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.21 – 5.90 (m, 2H), 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.59 (qd, *J* = 7.0, 1.2 Hz, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.65 – 1.55 (m, 4H), 1.45 – 1.24 (m, 16H), 0.87 (t, *J* = 6.8 Hz, 3H).

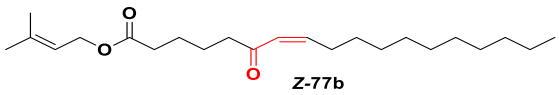
^{13}C NMR (101 MHz, $CDCl_3$) δ 201.9, 173.9, 148.8, 139.1, 126.7, 118.8, 61.3, 44.2, 34.4, 31.9, 29.6, 29.5, 29.4, 29.3, 29.3, 29.1, 28.9, 25.9, 24.9, 23.9, 22.7, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2970 (w), 2927 (m), 2856 (m), 1735 (s), 1631 (w), 1465 (w), 1457 (w), 1376 (m), 1366 (w), 1229 (w), 1217 (m), 1168 (m), 978 (w), 725 (w).

MS (ESI): m/z calcd for $C_{23}H_{40}NaO_3$ 387.3 $[M+Na]^+$, found 387.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{40}O_3$ 364.2977 $[M]^+$, found 364.2959 $[M]^+$.

***(Z)*-Prenyl-6-oxooctadec-7-enoate (*Z*-77b)**



Z-77b

Prepared from Prenyl 6-oxooctadec-7-ynoate **67b** (1.00 equiv, 965 µmol, 350 mg) and Pd on $BaSO_4$ (0.15 equiv, 145 µmol, 49.20 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (190 mg, 54%). $\mathbf{R_f}$ = 0.57 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 – 5.94 (m, 2H), 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.63 – 2.52 (m, 2H), 2.50 – 2.43 (m, 2H), 2.32 (td, *J* = 7.0, 3.6 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.65 – 1.60 (m, 4H), 1.39 (q, *J* = 7.2 Hz, 2H), 1.26 (d, *J* = 8.6 Hz, 14H), 0.87 (t, *J* = 6.8 Hz, 3H).

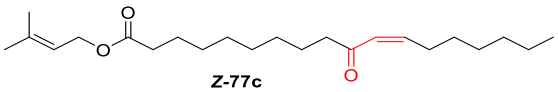
^{13}C NMR (101 MHz, $CDCl_3$) δ 201.3, 173.6, 149.1, 139.2, 126.5, 118.7, 61.4, 43.8, 34.2, 32.0, 29.7, 29.6, 29.5, 29.4, 29.4, 29.3, 27.8, 25.9, 24.6, 23.4, 22.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2925 (s), 2854 (m), 2211 (w), 1732 (s), 1714 (s), 1458 (m), 1377 (m), 1364 (w), 1218 (w), 1168 (s), 978 (m), 722 (w), 530 (w).

MS (ESI): m/z calcd for $C_{23}H_{40}NaO_3$ 387.3 $[M+Na]^+$, found 387.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{40}O_3$ 364.2977 $[M]^+$, found 364.2995 $[M]^+$

***(Z)*-Prenyl-10-oxooctadec-11-enoate (*Z*-77c)**



Z-77c

Prepared from Prenyl 10-oxooctadec-11-ynoate **67c** (1.00 equiv, 993 µmol, 360 mg) and Pd on $BaSO_4$ (0.15 equiv, 149 µmol, 51 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (155 mg, 43%). R_f = 0.57 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.15 – 6.00 (m, 2H), 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.59 (qd, *J* = 7.0, 1.3 Hz, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 2.28 (t, *J* = 7.5 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.62 – 1.56 (m, 4H), 1.43 – 1.37 (m, 2H), 1.28 (q, *J* = 3.5 Hz, 14H), 0.84 (t, *J* = 6.8 Hz, 3H).

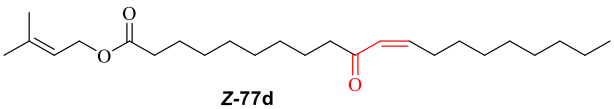
^{13}C NMR (101 MHz, $CDCl_3$) δ 202.1, 174.1, 148.7, 139.1, 126.7, 118.8, 61.3, 44.3, 34.5, 31.7, 29.6, 29.4, 29.3, 29.3, 29.2, 29.1, 25.9, 25.1, 24.1, 22.7, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2929 (s), 2857 (m), 1735 (s), 1712 (s), 1457 (w), 1419 (w), 1365 (m), 1218 (s), 1169 (m), 1092 (w), 978 (w), 725 (w), 529 (w).

MS (ESI): m/z calcd for $C_{23}H_{40}NaO_3$ 387.5 $[M+Na]^+$, found 387.3 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{40}O_3$ 364.2977 $[M]^+$, found 364.2978 $[M]^+$.

(*Z*)-Prenyl-10-oxoicos-11-enoate (*Z*-77d)



Z-77d

Prepared from Prenyl 10-oxoicos-11-ynoate **67d** (1.00 equiv, 1.41 mmol, 550 mg) and Pd on $BaSO_4$ (0.15 equiv, 211 µmol, 71.80 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (310 mg, 70%). R_f = 0.6 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.15 – 6.00 (m, 2H), 5.33 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.63 – 2.55 (m, 2H), 2.42 (t, *J* = 7.4 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.62 – 1.54 (m, 4H), 1.40 (p, *J* = 6.7 Hz, 2H), 1.30 – 1.23 (m, 18H), 0.87 (t, *J* = 6.7 Hz, 3H).

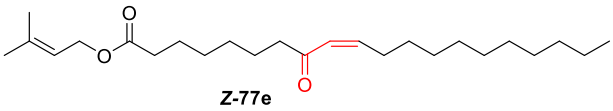
^{13}C NMR (101 MHz, $CDCl_3$) δ 202.1, 174.1, 148.7, 139.1, 126.7, 118.7, 61.3, 44.3, 34.4, 31.9, 29.6, 29.5, 29.4, 29.4, 29.3, 29.3, 29.2, 29.2, 25.9, 25.1, 24.1, 22.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2926 (s), 2854 (m), 1732 (s), 1710 (s), 1458 (w), 1377 (m), 1218 (w), 1166 (s), 1096 (w), 979 (w), 723 (w), 529 (w), 510 (w).

MS (APCI): m/z calcd for $C_{25}H_{45}O_3$ 393.3 $[M+H]^+$, found 393.4 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{25}H_{44}O_3$ 392.3290 $[M]^+$, found 392.3287 $[M]^+$.

***(Z)*-Prenyl-8-oxoicos-9-enoate (*Z*-77e)**



***Z*-77e**

Prepared from Prenyl 8-oxoicos-9-ynoate **67e** (1.00 equiv, 870 µmol, 340 mg) and Pd on $BaSO_4$ (0.15 equiv, 131 µmol, 44.40 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (190 mg, 57%). $\mathbf{R_f}$ = 0.6 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.15 – 6.00 (m, 2H), 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.59 (q, *J* = 6.5 Hz, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 2.28 (t, *J* = 7.5 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.58 (dt, *J* = 14.5, 6.6 Hz, 4H), 1.39 (q, *J* = 7.2 Hz, 2H), 1.28 (d, *J* = 26.5 Hz, 18H), 0.87 (t, *J* = 6.8 Hz, 3H).

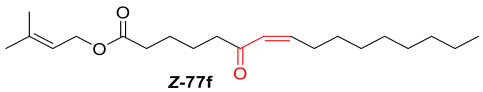
^{13}C NMR (101 MHz, $CDCl_3$) δ 201.9, 173.9, 148.8, 139.1, 126.6, 118.7, 61.3, 44.2, 34.4, 32.0, 29.7, 29.7, 29.6, 29.5, 29.4, 29.4, 29.3, 29.1, 28.9, 25.9, 24.9, 23.9, 22.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2926 (s), 2854 (m), 1735 (s), 1712 (s), 1457 (w), 1441 (w), 1365 (m), 1218 (s), 1168 (w), 1092 (w), 979 (w), 723 (w), 529 (w).

MS (APCI): m/z calcd for $C_{25}H_{45}O_3$ 393.6 $[M+H]^+$, found 393.5 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{25}H_{44}O_3$ 392.3290 $[M]^+$, found 392.3272 $[M]^+$.

***(Z)*-Prenyl-6-oxohexadec-7-enoate (*Z*-77f)**



Z-77f

Prepared from Prenyl 6-oxohexadec-7-ynoate **67f** (1.00 equiv, 1.41 mmol, 470 mg) and Pd on $BaSO_4$ (0.15 equiv, 211 µmol, 71.60 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (330 mg, 70%). $\mathbf{R_f}$ = 0.55 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.16 – 6.00 (m, 2H), 5.32 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.59 (q, *J* = 7.0 Hz, 2H), 2.49 – 2.43 (m, 2H), 2.31 (t, *J* = 7.1 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.62 (t, *J* = 3.6 Hz, 4H), 1.39 (q, *J* = 6.4 Hz, 2H), 1.31 – 1.24 (m, 10H), 0.86 (t, *J* = 6.8 Hz, 3H).

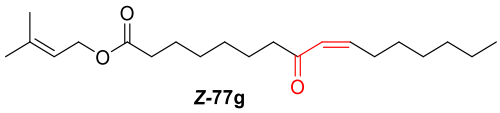
^{13}C NMR (101 MHz, $CDCl_3$) δ 201.3, 173.6, 149.1, 139.1, 126.5, 118.7, 61.4, 43.8, 34.2, 31.9, 29.6, 29.5, 29.4, 29.3, 29.3, 25.9, 24.6, 23.5, 22.7, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2926 (s), 2856 (m), 1728 (s), 1712 (s), 1457 (w), 1375 (m), 1216 (w), 1168 (s), 979 (w), 723 (w), 527 (w).

MS (APCI): m/z calcd for $C_{21}H_{37}O_3$ 337.3 $[M+H]^+$, found 337.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{21}H_{36}O_3$ 336.2664 $[M]^+$, found 336.2668 $[M]^+$.

***(Z)*-Prenyl-8-oxohexadec-9-enoate (*Z*-77g)**



Z-77g

Prepared from Prenyl 8-oxohexadec-9-ynoate **67g** (1.00 equiv, 957 µmol, 320 mg) and Pd on $BaSO_4$ (0.15 equiv, 143 µmol, 48.80 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (160 mg, 50%). $\mathbf{R_f}$ = 0.57 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.15 – 5.98 (m, 2H), 5.38 – 5.28 (m, 1H), 4.55 (d, *J* = 7.2 Hz, 2H), 2.59 (q, *J* = 7.2 Hz, 2H), 2.43 (t, *J* = 7.6 Hz, 2H), 2.28 (t, *J* = 7.5 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.64 – 1.57 (m, 4H), 1.43 – 1.36 (m, 2H), 1.33 – 1.26 (m, 10H), 0.86 (t, *J* = 6.4 Hz, 3H).

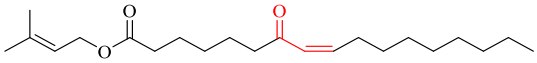
^{13}C NMR (101 MHz, $CDCl_3$) δ 201.9, 173.9, 148.8, 139.1, 126.7, 118.7, 61.3, 44.2, 34.4, 31.7, 29.6, 29.3, 29.1, 29.1, 28.9, 25.9, 24.9, 23.9, 22.7, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2930 (s), 2859 (m), 1728 (s), 1712 (s), 1457 (w), 1415 (w), 1371 (m), 1218 (w), 1205 (w), 1168 (s), 1093 (w), 978 (w), 728 (w), 527 (w).

MS (APCI): m/z calcd for $C_{21}H_{37}O_3$ 337.3 $[M+H]^+$, found 337.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{21}H_{36}O_3$ 336.2664 $[M]^+$, found 336.2682 $[M]^+$.

***(Z)*-Prenyl-7-oxoheptadec-8-enoate (*Z*-77h)**



***Z*-77h**

Prepared from Prenyl 7-oxoheptadec-8-ynoate **67h** (1.00 equiv, 861 mmol, 300 mg) and Pd on $BaSO_4$ (0.15 equiv, 155 µmol, 52.70 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a colorless oil (125 mg, 42%). $\mathbf{R_f}$ = 0.61 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.15 – 6.00 (m, 2H), 5.33 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.59 (q, *J* = 7.1 Hz, 2H), 2.44 (t, *J* = 7.4 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 1.76 (s, 3H), 1.70 (s, 3H), 1.66 – 1.58 (m, 4H), 1.45 – 1.25 (m, 14H), 0.84 (t, *J* = 6.4 Hz, 3H).

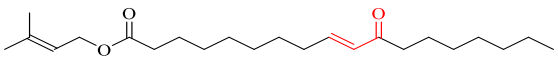
^{13}C NMR (101 MHz, $CDCl_3$) δ 201.7, 173.8, 148.9, 139.1, 126.6, 118.7, 61.3, 44.1, 34.3, 32.0, 29.6, 29.5, 29.4, 29.4, 29.3, 28.8, 25.9, 24.9, 23.7, 22.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2925 (s), 2854 (m), 1733 (s), 1675 (m), 1458 (w), 1374 (m), 1231 (w), 1211 (m), 1169 (m), 1108 (w), 1055 (w), 978 (w), 776 (w), 727 (w).

MS (APCI): m/z calcd for $C_{22}H_{39}O_3$ 351.3 $[M+H]^+$, found 351.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{37}O_3$ 349.2743 $[M-H]^+$, found 349.2758 $[M-H]^+$.

***(E)*-Prenyl-11-oxooctadec-9-enoate (*E*-104a)**



***E*-104a**

Prepared from Prenyl 11-oxooctadec-9-ynoate **90a** (1.00 equiv, 600 µmol, 218 mg) and Pd on $BaSO_4$ (0.15 equiv, 90 µmol, 30.60 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (100 mg, 46%). $\mathbf{R_f}$ = 0.45 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (dt, *J* = 15.8, 6.9 Hz, 1H), 6.08 (dt, *J* = 15.9, 1.5 Hz, 1H), 5.34 (tt, *J* = 5.8, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.56 – 2.48 (m, 2H), 2.29 (t, *J* = 7.5 Hz, 2H),

2.19 (qd, *J* = 7.0, 1.9 Hz, 2H), 1.76 (s, 3H), 1.71 (s, 3H), 1.64 – 1.57 (m, 4H), 1.45 (t, *J* = 7.2 Hz, 2H), 1.34 – 1.26 (m, 14H), 0.85 (t, *J* = 6.8 Hz, 3H).

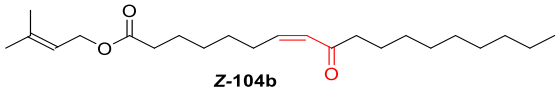
^{13}C NMR (101 MHz, $CDCl_3$) δ 201.1, 173.9, 147.3, 139.1, 130.4, 118.7, 61.3, 40.3, 34.5, 32.5, 31.8, 29.4, 29.2, 29.1, 29.1, 28.1, 25.9, 25.1, 24.4, 22.7, 18.2, 14.2.

IR (ATR ν in cm^{-1}) 2927 (s), 2856 (m), 1735 (s), 1708 (s), 1459 (w), 1412 (w), 1375 (m), 1218 (m), 1168 (m), 1101 (w), 978 (w), 725 (w).

MS (ESI): m/z calcd for $C_{23}H_{40}NaO_3$ 387.3 $[M+Na]^+$, found 387.4 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{40}O_3$ 364.2977 $[M]^+$, found 364.2978 $[M]^+$.

***(Z)*-Prenyl-9-oxooctadec-7-enoate (*Z*-104b)**



***Z*-104b**

Prepared from Prenyl 9-oxooctadec-7-ynoate **90b** (1.00 equiv, 1.16 mmol, 420 mg) and Pd on $BaSO_4$ (0.15 equiv, 174 µmol, 59 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (182 mg, 43%). R_f = 0.57 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 – 5.93 (m, 2H), 5.33 (tt, *J* = 5.8, 1.0 Hz, 1H), 4.55 (d, *J* = 7.3 Hz, 2H), 2.60 (q, *J* = 7.3 Hz, 2H), 2.42 (t, *J* = 7.4 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.60 (dt, *J* = 14.5, 7.3 Hz, 4H), 1.42 – 1.25 (m, 16H), 0.87 (t, *J* = 6.8 Hz, 3H).

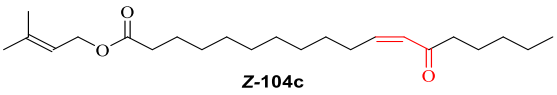
^{13}C NMR (101 MHz, $CDCl_3$) δ 202.1, 173.8, 148.2, 139.1, 126.9, 118.7, 61.3, 44.4, 34.3, 31.9, 29.5, 29.5, 29.4, 29.3, 28.9, 28.9, 25.9, 24.9, 24.1, 22.7, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2925 (s), 2854 (m), 1735 (s), 1457 (w), 1377 (m), 1229 (w), 1216 (m), 1168 (m), 979 (w), 723 (w), 527 (w), 517 (w).

MS (APCI): m/z calcd for $C_{23}H_{41}O_3$ 365.3 $[M+H]^+$, found 365.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{40}O_3$ 364.2977 $[M]^+$, found 364.2985 $[M]^+$.

***(Z)*-Prenyl 13-oxooctadec-11-enoate (*Z*-104c)**



***Z*-104c**

Prepared from prenyl 13-oxooctadec-11-ynoate **90c** (1.00 equiv, 883 µmol, 320 mg) and Pd on $BaSO_4$ (0.15 equiv, 133 µmol, 45 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (161 mg, 50%). $\mathbf{R_f}$ = 0.58 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 – 5.85 (m, 2H), 5.33 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.60 (qd, *J* = 7.3, 1.6 Hz, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 2.29 (t, *J* = 7.6 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.65 – 1.58 (m, 4H), 1.49 – 1.32 (m, 6H), 1.28 – 1.25 (m, 10H), 0.87 (t, *J* = 6.6 Hz, 3H).

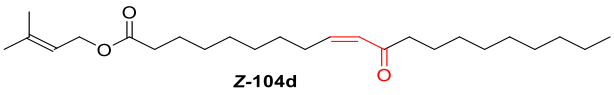
^{13}C NMR (101 MHz, $CDCl_3$) δ 202.1, 173.9, 148.1, 139.1, 126.9, 118.8, 61.3, 44.4, 34.3, 32.0, 29.6, 29.5, 29.4, 29.3, 29.3, 28.9, 28.9, 25.9, 24.9, 24.1, 22.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2927 (s), 2856 (m), 1735 (s), 1715 (s), 1459 (w), 1378 (m), 1362 (m), 1218 (w), 1169 (m), 979 (w), 725 (w), 530 (w).

MS (APCI): m/z calcd for $C_{23}H_{41}O_3$ 365.3 $[M+H]^+$, found 365.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{23}H_{40}O_3$ 364.2977 $[M]^+$, found 364.3016 $[M]^+$.

***(Z)*-Prenyl-11-oxoicos-9-enoate (*Z*-104d)**



***Z*-104d**

Prepared from Prenyl 11-oxoicos-9-ynoate **90d** (1.00 equiv, 1.10 mmol, 430 mg) and Pd on $BaSO_4$ (0.15 equiv, 166 µmol, 56.10 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a colorless oil (340 mg, 79%). $\mathbf{R_f}$ = 0.47 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.16 – 5.98 (m, 2H), 5.39 – 5.27 (m, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.63 – 2.55 (m, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H), 1.76 (s, 3H), 1.70 (s, 3H), 1.58 (dt, *J* = 10.0, 4.4 Hz, 4H), 1.40 (t, *J* = 7.3 Hz, 2H), 1.27 (dd, *J* = 12.1, 6.5 Hz, 18H), 0.85 (t, *J* = 6.8 Hz, 3H).

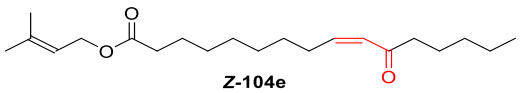
^{13}C NMR (101 MHz, $CDCl_3$) δ 202.1, 174.0, 148.5, 139.1, 126.8, 118.8, 61.3, 44.4, 34.4, 32.0, 29.6, 29.5, 29.5, 29.4, 29.3, 29.2, 29.1, 25.9, 25.1, 24.1, 22.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2925 (s), 2854 (m), 1735 (s), 1717 (s), 1457 (w), 1419 (w), 1365 (m), 1218 (m), 1169 (m), 1092 (w), 978 (w), 723 (w), 529 (w).

MS (APCI): m/z calcd for $C_{25}H_{45}O_3$ 393.3 $[M+H]^+$, found 393.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{25}H_{44}O_3$ 392.3290 $[M]^+$, found 392.3302 $[M]^+$.

***(Z)*-Prenyl-11-oxohexadec-9-enoate (*Z*-104e)**



Z-104e

Prepared from Prenyl 11-oxohexadec-9-ynoate **90e** (1.00 equiv, 1.05 mmol, 350 mg) and Pd on $BaSO_4$ (0.15 equiv, 157 µmol, 53.30 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a colorless oil (280 mg, 80%). $\mathbf{R_f}$ = 0.46 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.16 – 5.98 (m, 2H), 5.33 (tt, *J* = 7.6, 1.6 Hz, 1H), 4.55 (d, *J* = 7.2 Hz, 2H), 2.59 (q, *J* = 7.2 Hz, 2H), 2.43 (t, *J* = 7.5 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.59 (dd, *J* = 14.8, 7.5 Hz, 4H), 1.34 (dd, *J* = 41.5, 4.9 Hz, 12H), 0.88 (t, *J* = 7.1 Hz, 3H).

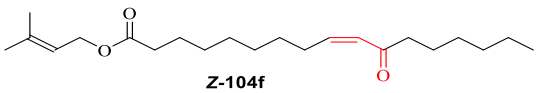
^{13}C NMR (101 MHz, $CDCl_3$) δ 202.1, 174.0, 148.5, 139.1, 126.8, 118.8, 61.3, 44.4, 34.4, 31.5, 29.5, 29.2, 29.1, 25.9, 25.1, 23.8, 22.6, 18.1, 14.1.

IR (ATR ν in cm^{-1}) 2930 (s), 2857 (m), 1732 (s), 1714 (s), 1457 (w), 1377 (m), 1365 (m), 1218 (w), 1169 (s), 1093 (w), 978 (w), 726 (w), 529 (w).

MS (APCI): m/z calcd for $C_{21}H_{37}O_3$ 337.3 $[M+H]^+$, found 337.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{21}H_{36}O_3$ 336.2664 $[M]^+$, found 336.2672 $[M]^+$.

***(Z)*-Prenyl-11-oxoheptadec-9-enoate (*Z*-104f)**



Z-104f

Prepared from Prenyl 11-oxoheptadec-9-ynoate **90f** (1.00 equiv, 460 µmol, 160 mg) and Pd on $BaSO_4$ (0.15 equiv, 69 µmol, 23.40 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (70 mg, 43%). $\mathbf{R_f}$ = 0.46 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 – 5.91 (m, 2H), 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.3 Hz, 2H), 2.64 – 2.54 (m, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.63 – 1.55 (m, 4H), 1.43 – 1.27 (m, 14H), 0.89 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 202.1, 174.0, 148.5, 139.1, 126.8, 118.8, 61.3, 44.4, 34.4, 31.8, 29.5, 29.3, 29.2, 29.1, 25.9, 25.1, 24.1, 22.6, 18.2, 14.2.

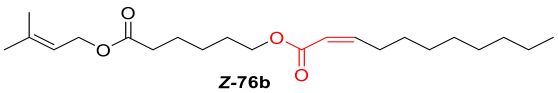
IR (ATR ν in cm^{-1}) 2930 (s), 2859 (m), 1735 (s), 1712 (s), 1457 (w), 1419 (w), 1365 (m), 1218 (m), 1165 (m), 1093 (w), 726 (w), 529 (w).

MS (ESI): m/z calcd for $C_{22}H_{38}NaO_3$ 373.5 $[M+Na]^+$, found 373.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{38}O_3$ 350.2821 $[M]^+$, found 350.2801 $[M]^+$.

6.4.14 Synthesis of *(Z)*-Alkenyl Esters

***(Z)*-6-((Prenyl)oxy)-6-oxohexyl-undec-2-enoate (*Z*-76b)**



***Z*-76b**

Prepared from 6-((prenyl)oxy)-6-oxohexyl undec-2-ynoate **64a** (1.00 equiv, 411 µmol, 150 mg) and Pd on $BaSO_4$ (0.15 equiv, 62 µmol, 18.75 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a yellow oil (70 mg, 47%). $\mathbf{R_f}$ = 0.64 (9:1 *n*-hexane:EtOAc).

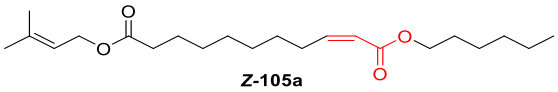
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.21 (dt, *J* = 11.5, 7.5 Hz, 1H), 5.74 (dt, *J* = 11.5, 1.7 Hz, 1H), 5.38 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.09 (t, *J* = 6.6 Hz, 2H), 2.63 (qd, *J* = 7.4, 1.7 Hz, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 1.76 (s, 3H), 1.70 (s, 3H), 1.66 (q, *J* = 7.1 Hz, 4H), 1.48 – 1.37 (m, 4H), 1.27 (d, *J* = 11.5 Hz, 10H), 0.81 (t, *J* = 6.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 166.7, 150.9, 139.2, 119.6, 118.7, 63.7, 61.4, 34.3, 31.9, 29.5, 29.4, 29.3, 29.2, 28.5, 25.9, 25.7, 24.7, 22.8, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 2955 (m), 2926 (s), 2858 (m), 1735 (s), 1720 (s), 1458 (m), 1378 (m), 1361 (w), 1218 (w), 1174 (s), 982 (w), 905 (w), 728 (w), 529 (w).

MS (ESI): m/z calcd for $C_{22}H_{38}NaO_4$ 389.5 $[M+Na]^+$, found 389.6 $[M+Na]^+$.

***(Z)*-1-hexyl-11-(Prenyl)-undec-2-enedioate (*Z*-105a)**



***Z*-105a**

Prepared from 1-hexyl 11-(prenyl) undec-2-ynedioate **87a** (1.00 equiv, 1.76 mmol, 640 mg) and Pd on $BaSO_4$ (0.15 equiv, 263 µmol, 89.50 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 99:1 → 90:10) afforded the desired analytically pure product as a colorless oil (358 mg, 50%). $\mathbf{R_f}$ = 0.34 (9:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (dt, *J* = 11.5, 7.5 Hz, 1H), 5.75 (dt, *J* = 11.5, 1.7 Hz, 1H), 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.09 (t, *J* = 6.7 Hz, 2H), 2.63 (qd, *J* = 7.5, 1.7 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.66 – 1.58 (m, 4H), 1.47 – 1.28 (m, 14H), 0.85 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 166.7, 150.5, 139.1, 119.8, 118.8, 64.2, 61.3, 34.4, 31.5, 29.2, 29.1, 29.1, 28.7, 25.9, 25.8, 25.1, 22.6, 18.1, 14.1.

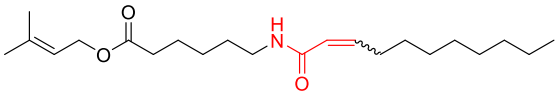
IR (ATR ν in cm^{-1}) 2955 (m), 2929 (s), 2857 (m), 1735 (s), 1720 (s), 1458 (m), 1378 (m), 1361 (w), 1218 (w), 1174 (s), 982 (w), 905 (w), 728 (w), 529 (w).

MS (APCI): m/z calcd for $C_{22}H_{39}O_4$ 367.3 $[M+H]^+$, found 367.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{38}O_4$ 366.2770 $[M]^+$, found 366.2759 $[M]^+$.

6.4.15 Synthesis of *(E* and *Z)* Amides

***(E* and *Z)* Prenyl -6-(undec-2-enamido)hexanoate**



Prepared from prenyl 6-(undec-2-ynamido)hexanoate **68a** (1.00 equiv, 610 µmol, 222 mg) and Pd on $BaSO_4$ (0.15 equiv, 92 µmol, 31.10 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.2 Vol% NEt_3 = 95:5 → 70:30) afforded the desired product (yellow oil) as a mixture of both isomers *E:Z* = 70:30, 180 mg, 81%.

***(Z)*-Prenyl-6-(undec-2-enamido)hexanoate (*Z*-78a)**

126 mg (70% of the total yield of 81%). $\mathbf{R_f}$ = 0.42 (7:3 *n*-hexane:EtOAc + 0.2 Vol% NEt_3).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96 (dt, *J* = 11.5, 7.5 Hz, 1H), 5.64 (dt, *J* = 11.5, 1.7 Hz, 1H), 5.51 (s, 1H), 5.36 – 5.30 (m, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 3.33 – 3.23 (m, 2H), 2.63 (q, *J* = 7.7 Hz, 2H), 2.30 (t, *J* = 7.4

Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.67 – 1.60 (m, 2H), 1.53 (p, *J* = 7.3 Hz, 2H), 1.43 – 1.24 (m, 14H), 0.86 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.7, 166.7, 145.8, 139.2, 122.2, 118.7, 61.4, 39.1, 34.2, 31.9, 29.5, 29.5, 29.4, 29.4, 29.4, 28.9, 26.5, 25.9, 24.6, 22.7, 18.1, 14.2.

IR (ATR ν in cm^{-1}) 3300 (m), 2923 (s), 2854 (m), 1733 (s), 1657 (m), 1629 (m), 1537 (m), 1442 (m), 1378 (w), 1356 (w), 1232 (w), 1160 (s), 1102 (w), 1048 (w), 976 (w), 813 (w), 774 (w), 723 (w).

MS (ESI): m/z calcd for $C_{22}H_{39}NNaO_3$ 388.3 $[M+Na]^+$, found 388.1 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{39}NO_3$ 365.2930 $[M]^+$, found 365.2933 $[M]^+$.

***(E)*-Prenyl-6-(undec-2-enamido)hexanoate (*E*-78b)**

54 mg (30% of the total yield of 81%). R_f = 0.32 (7:3 *n*-hexane:EtOAc + 0.2 Vol% NEt_3).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 – 6.76 (m, 1H), 5.73 (dt, *J* = 15.2, 1.5 Hz, 1H), 5.51 (s, 1H), 5.33 (tt, *J* = 7.3, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 3.31 (q, *J* = 6.7 Hz, 2H), 2.30 (t, *J* = 7.4 Hz, 2H), 2.21 – 2.11 (m, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.63 (q, *J* = 7.6 Hz, 2H), 1.54 (p, *J* = 7.3 Hz, 2H), 1.46 – 1.24 (m, 14H), 0.87 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.8, 166.2, 145.0, 139.2, 123.5, 118.7, 61.4, 39.3, 34.2, 32.1, 31.9, 29.5, 29.4, 29.3, 29.3, 28.4, 26.5, 25.9, 24.6, 22.7, 18.1, 14.2.

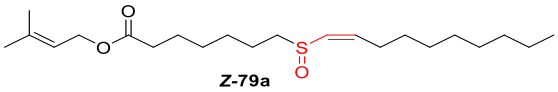
IR (ATR ν in cm^{-1}) 3299 (m), 2956 (m), 2920 (s), 2852 (m), 1720 (s), 1664 (m), 1614 (s), 1539 (s), 1469 (m), 1389 (w), 1361 (m), 1239 (m), 1163 (s), 1104 (w), 978 (w), 948 (w), 734 (w), 643 (m).

MS (ESI): m/z calcd for $C_{22}H_{39}NNaO_3$ 388.3 $[M+Na]^+$, found 388.1 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{39}NO_3$ 365.2930 $[M]^+$, found 365.2924 $[M]^+$.

6.4.16 Synthesis of *(Z)*-Alkenyl Sulfoxide and Alkenyl Sulfone

***(Z)*-Prenyl-7-(dec-1-en-1-ylsulfinyl)heptanoate (*Z*-79a)**



Z-79a

Prepared from Prenyl 7-(dec-1-yn-1-ylsulfinyl)heptanoate **65a** (1.00 equiv, 780 µmol, 300 mg) and Pd on $BaSO_4$ (0.15 equiv, 120 µmol, 250 mg), according to **GP5**. Purification by flash column chromatography (*n*-hexane:EtOAc = 90:10 → 70:30) afforded the desired analytically pure product as a colorless oil (141 mg, 47%). $\mathbf{R_f}$: 0.29 (1:1 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.24 – 6.15 (m, 2H), 5.32 (dddd, *J* = 7.2, 5.9, 2.7, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.88 – 2.56 (m, 2H), 2.47 – 2.24 (m, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.68 – 1.57 (m, 2H), 1.53 – 1.24 (m, 18H), 0.87 (t, *J* = 6.9 Hz, 3H).

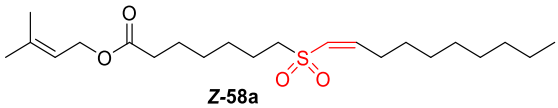
^{13}C NMR (101 MHz, $CDCl_3$): δ 173.7, 143.4, 139.1, 134.5, 118.7, 61.3, 54.0, 34.2, 31.9, 29.6, 29.3, 29.2, 29.2, 29.1, 28.8, 28.6, 25.9, 24.7, 22.7, 22.3, 18.1, 14.2.

IR (ATR ν in cm^{-1}): 2925 (m), 2855 (m), 1731 (s), 1676 (m), 1620(w), 1377 (m), 1276(w), 1234 (w), 1167 (w), 1121 (w), 1033 (s), 888 (m), 723 (w).

MS (ESI): m/z calcd for $C_{22}H_{40}NaO_3S$ 407.2 $[M+Na]^+$, found 407.3 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{41}O_3S$ 384.2698 $[M+H]^+$, found 384.2695 $[M+H]^+$.

***(Z)*-Prenyl 7-(dec-1-en-1-ylsulfonyl)heptanoate (*Z*-58a)**



Z-58a

Prepared from Prenyl 7-(dec-1-yn-1-ylsulfonyl)heptanoate **66a** (1.00 equiv, 700 µmol, 280 mg) and Pd on $BaSO_4$ (0.15 equiv, 110 µmol, 224 mg), according to **GP5**. purification by flash column chromatography (*n*-hexane:EtOAc = 19:1 → 9:1) afforded the desired analytically pure product as a colorless oil (117 mg, 41%). $\mathbf{R_f}$: 0.22 (8:2 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.38 (dt, *J* = 11.2, 7.8 Hz, 1H), 6.14 (dt, *J* = 11.2, 1.6 Hz, 1H), 5.35 – 5.29 (m, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.99 – 2.89 (m, 2H), 2.63 (ddd, *J* = 15.3, 7.8, 1.6 Hz, 2H), 2.99 (t, *J* = 7.4 Hz, 2H), 1.85–1.77 (m, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.66 – 1.56 (m, 2H), 1.52 – 1.21 (m, 16H), 0.87 (t, *J* = 6.9 Hz, 3H).

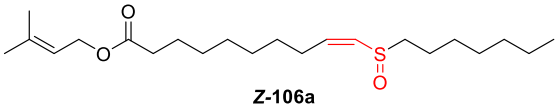
^{13}C NMR (101 MHz, $CDCl_3$): δ 173.6, 149.6, 139.2, 127.8, 118.6, 61.4, 55.7, 34.2, 31.9, 29.4, 29.3, 29.2, 29.0, 28.7, 28.2, 28.0, 25.9, 24.6, 22.7, 22.3, 18.1, 14.2.

IR (ATR ν in cm^{-1}): 2924 (m), 2855 (m), 2354 (w), 1730 (s), 1624 (m), 1456 (w), 1375 (s), 1301 (s), 1238 (w), 1168 (w), 1126 (w), 1021 (w), 976 (w), 873 (m), 799 (m), 725 (w).

MS (ESI): m/z calcd for $C_{22}H_{40}NaO_4S$ 423.2 $[M+Na]^+$, found 423.3 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{40}O_4S$ 400.2647 $[M]^+$, found 400.2633 $[M]^+$.

***(Z)*-Prenyl-10-(heptylsulfinyl)dec-9-enoate (*Z*-106a)**



***Z*-106a**

Prepared from Prenyl 10-(heptylsulfinyl)dec-9-ynoate **88a** (1.00 equiv, 1.05 mmol, 401 mg) and Pd on $BaSO_4$ (0.15 equiv, 160 µmol, 53.50 mg), according to **GP5** Purification by flash column chromatography (*n*-hexane:EtOAc = 95:5 → 80:20) afforded the desired analytically pure product as a yellow oil (140 mg, 35%). $\mathbf{R_f}$ = 0.22 (8:2 *n*-hexane:Acetone).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.26 – 6.13 (m, 2H), 5.33 (tt, *J* = 7.2, 1.4 Hz, 1H), 4.55 (d, *J* = 7.2 Hz, 2H), 2.83 (dt, *J* = 12.9, 7.3 Hz, 1H), 2.61 (dt, *J* = 12.7, 7.9 Hz, 1H), 2.34 (dt, *J* = 48.7, 7.2 Hz, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.61 (dd, *J* = 13.6, 6.5 Hz, 2H), 1.41 (q, *J* = 7.4 Hz, 4H), 1.35 – 1.25 (m, 14H), 0.89 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 143.1, 139.1, 134.8, 118.7, 61.3, 54.2, 34.4, 31.6, 29.5, 29.1, 29.0, 29.0, 28.9, 25.9, 25.0, 22.6, 22.5, 18.1, 14.1.

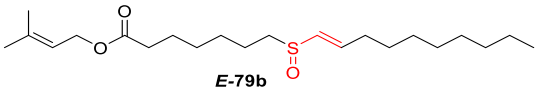
IR (ATR ν in cm^{-1}): 2926 (s), 2856 (m), 1731 (s), 1457 (w), 1378 (w), 1257 (w), 1172 (m), 1001 (m), 723 (w), 529 (w).

MS (ESI): m/z calcd for $C_{22}H_{40}O_3NaS$ 407.3 $[M+Na]^+$, found 407.3 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{40}O_3S$ 384.2698 $[M]^+$, found 384.2704 $[M]^+$.

6.4.17 Synthesis of *(E)*-Alkenyl Sulfoxide and Alkenyl Sulfone

***(E)*-Prenyl-7-(dec-1-en-1-ylsulfinyl)heptanoate (*E*-79b).**



***E*-79b**

To a cold (-78 °C) solution of Prenyl 7-(dec-1-yn-1-ylsulfinyl)heptanoate **65a** (1.00 equiv, 0.52 mmol, 200 mg) in dry THF (0.1 M), DIBAL-H (1.20 equiv, 0.63 mmol, 523 µl, 1 M in hexane) was added dropwise. The resulting mixture was stirred at -78 °C for 1 h before the addition of saturated aqueous NH_4Cl (10 mL). The mixture was diluted with a (1:1) mixture of ether and saturated Potassium sodium tartrate solution and stirred for 1 h at ambient temperature. The organic layers were separated, washed with H_2O (10 mL), and dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product was then purified by flash column chromatography (*n*-hexane:EtOAc = 19:1 → 9:1) to produce the desired analytically pure product as a colorless oil (155 mg, 77%). **R_f**: 0.23 (7:3 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.45 (dt, *J* = 15.1, 6.8 Hz, 1H), 6.17 (dt, *J* = 15.2, 1.4 Hz, 1H), 5.33 (dddd, *J* = 7.2, 5.8, 2.8, 1.4 Hz, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.68 (t, *J* = 7.7 Hz, 2H), 2.32 – 3.19 (m, 4H), 1.76 (s, 3H), 1.70 (s, 3H), 1.69 – 1.57 (m, 4H), 1.52 – 1.24 (m, 16H), 0.87 (t, *J* = 6.9 Hz, 3H).

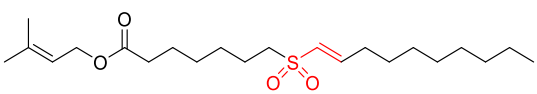
^{13}C NMR (101 MHz, $CDCl_3$): δ 173.7, 141.7, 139.1, 132.1, 118.7, 61.3, 53.9, 34.2, 32.2, 31.9, 29.4, 29.3, 29.1, 28.8, 28.5, 28.2, 25.8, 24.7, 22.7, 22.1, 18.1, 14.2.

IR (ATR ν in cm^{-1}): 2925 (m), 2855 (m), 1730 (s), 1673 (m), 1455 (w), 1377 (m), 1169 (w), 1037 (s), 965 (w), 916 (m), 805 (m), 730 (w), 645 (w).

MS (ESI) m/z calcd for $C_{22}H_{40}NaO_3S$ 407.2 $[M+Na]^+$, found 407.3 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{40}O_3S$ 384.2698 $[M]^+$, found 384.2714 $[M]^+$.

***(E)*-Prenyl-7-(dec-1-en-1-ylsulfonyl)heptanoate (*E*-58b)**



***E*-58b**

To a cold (-78 °C) solution of Prenyl 7-(dec-1-yn-1-ylsulfonyl)heptanoate **66a** (1.00 equiv,0.75 mmol, 300 mg) in dry THF (0.1 M), DIBAL-H (1.20 equiv, 0.90 mmol, 753 µl, 1 M in hexane) was added dropwise. The resulting mixture was stirred at -78 °C for 1 h before the addition of saturated aqueous NH_4Cl (10 mL). The reaction mixture was diluted with a (1:1) mixture of ether and saturated Potassium sodium tartrate solution and stirred for 1 h at ambient temperature. The organic layers were

separated, washed with H_2O (10 mL), and dried with Na_2SO_4. The solvent was removed under reduced pressure and the crude product was then purified by flash column chromatography (*n*-hexane:EtOAc = 19:1 → 9:1) to produce the desired analytically pure product as a colorless oil (151 mg, 50%). **R_f**: 0.31 (8:2 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95–6.85 (m, 1H), 6.24 (d, *J* = 15.1, 1H), 5.36–5.30 (m, 1H), 4.56 (d, *J* = 7.1 Hz, 2H), 2.96–2.89 (m, 2H), 2.33–2.23 (m, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.66–1.58 (m, 2H), 1.50–1.25 (m, 18H), 0.87 (t, *J* = 6.2 Hz, 3H).

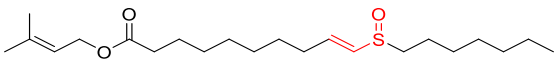
^{13}C NMR (101 MHz, $CDCl_3$): δ 173.6, 149.9, 139.2, 127.8, 118.6, 61.4, 54.7, 34.2, 31.9, 31.7, 29.3, 29.2, 29.1, 28.6, 28.1, 27.7, 25.9, 24.6, 22.7, 22.4, 18.1, 14.2.

IR (ATR ν in cm^{-1}): 2925 (m), 2855 (m), 2354 (w), 1731 (s), 1624 (m), 1456 (w), 1374 (s), 1304 (s), 1237 (w), 1167 (w), 1125 (w), 1021 (w), 976 (w), 875 (m), 730 (w).

MS (ESI) m/z calcd for $C_{22}H_{40}NaO_4S$ 423.2 $[M+Na]^+$, found 423.3 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{40}O_4S$ 400.2647 $[M]^+$, found 400.2665 $[M]^+$.

(*E*)-Prenyl-10-(heptylsulfinyl)dec-9-enoate (*E*-106b)



***E*-106b**

To a cold (-78 °C) solution of Prenyl 10-(heptylsulfinyl)dec-9-ynoate **88a** (1.00 equiv, 0.92 mmol, 350 mg) in dry THF (0.1 M), DIBAL-H (1.20 equiv, 1.10 mmol, 1.10 mL, 1 M in hexane) was added dropwise. The resulting mixture was stirred at -78 °C for 1 h before the addition of saturated aqueous NH_4Cl (20 mL). The reaction mixture was diluted with a (1:1) mixture of ether and saturated Potassium sodium tartrate solution and stirred for 1 h at ambient temperature. The organic layers were separated, washed with H_2O (20 mL), and dried with Na_2SO_4. The solvent was removed under reduced pressure and the crude product was then purified by flash column chromatography (*n*-hexane:EtOAc = 95:5 → 60:40) afforded the desired analytically pure product as a yellow oil (200 mg, 57%). **R_f** = 0.28 (6:4 *n*-hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 – 6.38 (m, 1H), 6.19 (dd, *J* = 15.2, 1.7 Hz, 1H), 5.38 – 5.29 (m, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.74 – 2.66 (m, 2H), 2.34 – 2.17 (m, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.61 (t, *J* = 6.7 Hz, 2H), 1.45 – 1.28 (m, 18H), 0.87 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 141.5, 139.1, 132.3, 118.7, 61.3, 54.1, 34.4, 32.2, 31.6, 29.1, 29.0, 28.8, 28.2, 25.9, 25.0, 22.6, 22.2, 18.1, 14.1.

IR (ATR ν in cm^{-1}): 2926 (s), 2854 (m), 1728 (s), 1459 (m), 1378 (w), 1172 (w), 1131 (w), 1001 (w), 963 (w), 725 (w), 510 (w).

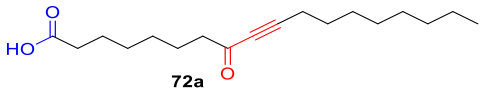
MS (APCI): m/z calcd for $C_{22}H_{41}O_3S$ 385.6 $[M+H]^+$, found 385.6 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{22}H_{40}O_3S$ 384.2698 $[M]^+$, found 384.2709 $[M]^+$.

6.5 Synthesis of Fatty Acids

6.5.1 Synthesis of Alkynoic Fatty Acids

8-oxooctadec-9-ynoic acid (72a)



72a

Prepared from Prenyl 8-oxooctadec-9-ynoate **67a** (1.00 equiv, 552 µmol, 200 mg) and TMSOTf (0.03 equiv, 17 µmol, 3 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (153 mg, 94%). $\mathbf{R_f}$ = 0.25 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52 (t, *J* = 7.4 Hz, 2H), 2.34 (dd, *J* = 11.5, 4.4 Hz, 4H), 1.62 (dtt, *J* = 26.6, 15.0, 7.3 Hz, 6H), 1.45 – 1.22 (m, 14H), 0.88 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.5, 179.6, 94.6, 81.0, 45.5, 33.9, 31.9, 29.2, 29.1, 29.0, 28.8, 28.7, 27.8, 24.5, 24.0, 22.7, 19.1, 14.2.

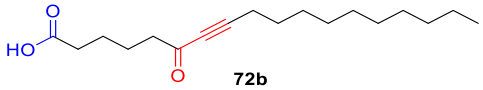
IR (ATR ν in cm^{-1}): 2926 (s), 2856 (m), 2210 (m), 1737 (w), 1708 (s), 1672 (s), 1459 (w), 1410 (w), 1360 (w), 1326 (w), 1275 (w), 1219 (w), 1161 (w), 1082 (w), 1006 (w), 943 (w), 851 (w), 725 (w).

MS (ESI): m/z calcd for $C_{18}H_{30}NaO_3$ 317.2 $[M+Na]^+$, found 317.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{18}H_{30}O_3$ 294.2195 $[M]^+$, found 294.2193 $[M]^+$.

Elm Anal. Calcd for $C_{18}H_{30}O_3$ C: 73.43%, H: 10.27; found C: 73.64%, H: 10.07%.

6-oxooctadec-7-ynoic acid (72b)



72b

Prepared from Prenyl 6-oxooctadec-7-ynoate **67b** (1.00 equiv, 552 µmol, 200 mg) and TMSOTf (0.03 equiv, 17 µmol, 3 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (95 mg, 59%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56 (t, *J* = 6.9 Hz, 2H), 2.41 – 2.32 (m, 4H), 1.76 – 1.52 (m, 6H), 1.44 – 1.24 (m, 14H), 0.92 – 0.84 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 187.8, 179.1, 94.9, 80.9, 45.1, 33.8, 32.0, 29.6, 29.5, 29.4, 29.1, 29.0, 27.8, 24.1, 23.4, 22.8, 19.1, 14.2.

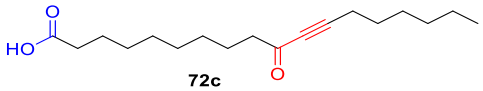
IR (ATR ν in cm^{-1}): 2925 (s), 2854 (m), 2210 (m), 1710 (s), 1671 (s), 1458 (w), 1411 (w), 1361 (w), 1219 (w), 1162 (w), 936 (w), 722 (w), 529 (w).

MS (APCI): m/z calcd for $C_{18}H_{31}O_3$ 295.4 $[M+H]^+$, found 295.2 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{18}H_{30}O_3$ 294.2195 $[M]^+$, found 294.2191 $[M]^+$.

Elm Anal. Calcd for $C_{18}H_{30}O_3$ C: 73.43%, H: 10.27; found C: 73.80%, H: 10.30%.

10-oxooctadec-11-ynoic acid (72c)



72c

Prepared from Prenyl 10-oxooctadec-11-ynoate **67c** (1.00 equiv, 496 µmol, 180 mg) and TMSOTf (0.03 equiv, 15 µmol, 2.70 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (95 mg, 65%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (t, *J* = 7.4 Hz, 2H), 2.34 (td, *J* = 7.3, 5.1 Hz, 4H), 1.58 (dq, *J* = 22.2, 8.3 Hz, 6H), 1.44 – 1.27 (m, 14H), 0.89 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.7, 179.9, 94.5, 81.0, 45.6, 34.1, 31.3, 29.2, 29.1, 29.1, 29.0, 28.6, 27.8, 24.7, 24.2, 22.6, 19.1, 14.1.

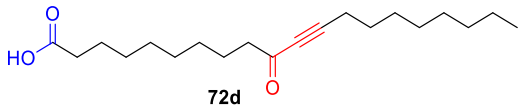
IR (ATR ν in cm^{-1}): 2927 (s), 2856 (m), 2211 (m), 1705 (s), 1671 (s), 1458 (w), 1409 (w), 1231 (w), 1169 (w), 936 (w), 725 (w).

MS (APCI): m/z calcd for $C_{18}H_{31}O_3$ 295.2 $[M+H]^+$, found 295.2 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{18}H_{30}O_3$ 294.2195 $[M]^+$, found 294.2199 $[M]^+$.

Elm Anal. Calcd for $C_{18}H_{30}O_3$ C: 73.43%, H: 10.27; found C: 73.19%, H: 10.37%.

10-oxoicos-11-ynoic acid (72d)



72d

Prepared from Prenyl 10-oxoicos-11-ynoate **67d** (1.00 equiv, 358 µmol, 140 mg) and TMSOTf (0.03 equiv, 11 µmol, 2.00 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (100 mg, 87%). $\mathbf{R_f}$ = 0.27 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (t, *J* = 7.4 Hz, 2H), 2.35 (td, *J* = 7.3, 3.3 Hz, 4H), 1.60 (ddd, *J* = 29.2, 14.7, 7.2 Hz, 6H), 1.44 – 1.26 (m, 18H), 0.88 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.7, 179.7, 94.5, 81.0, 45.6, 34.1, 31.9, 29.2, 29.1, 29.1, 29.1, 29.0, 28.9, 27.8, 24.7, 24.2, 22.7, 19.1, 14.2.

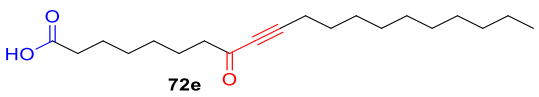
IR (ATR ν in cm^{-1}): 2926 (s), 2854 (m), 2211 (m), 1705 (s), 1671 (s), 1458 (w), 1411 (w), 1286 (w), 1231 (w), 1169 (w), 936 (w), 755 (w), 723 (w).

MS (APCI): m/z calcd for $C_{20}H_{35}O_3$ 323.3 $[M+H]^+$, found 323.3 $[M+H]^+$

HRMS (TOF MS EI+): m/z calcd for $C_{20}H_{34}O_3$ 322.2508 $[M]^+$, found 322.2520 $[M]^+$.

Elm Anal. Calcd for $C_{20}H_{34}O_3$ C: 74.49%, H: 10.63; found C: 74.23%, H: 10.62%.

8-oxoicos-9-ynoic acid (72e)



72e

Prepared from Prenyl 8-oxoicos-9-ynoate **67e** (1.00 equiv, 384 µmol, 150 mg) and TMSOTf (0.03 equiv, 12 µmol, 2.09 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow solid (95 mg, 77%). $\mathbf{R_f}$ = 0.2 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52 (t, *J* = 7.4 Hz, 2H), 2.34 (dd, *J* = 11.2, 4.1 Hz, 4H), 1.62 (dtt, *J* = 27.1, 14.9, 7.3 Hz, 6H), 1.43 – 1.24 (m, 18H), 0.88 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.5, 179.6, 94.6, 80.9, 45.5, 33.9, 32.0, 29.6, 29.5, 29.4, 29.1, 29.0, 28.8, 28.7, 27.8, 24.5, 24.0, 22.8, 19.1, 14.2.

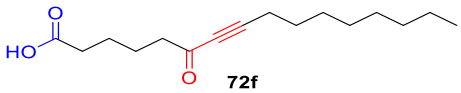
IR (ATR ν in cm^{-1}): 2932 (m), 2907 (m), 2849 (m), 2214 (m), 1694 (s), 1667 (s), 1471 (m), 1435 (w), 1404 (w), 1371 (w), 1285 (w), 1262 (w), 1242 (m), 1164 (m), 1035 (w), 978 (w), 955 (w), 909 (w), 789 (m), 716 (m), 682 (w), 603 (w), 555 (w), 536 (w), 502 (w).

MS (APCI): m/z calcd for $C_{20}H_{35}O_3$ 323.3 $[M+H]^+$, found 323.5 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{20}H_{34}O_3$ 322.2508 $[M]^+$, found 322.2513 $[M]^+$.

Elm Anal. Calcd for $C_{20}H_{34}O_3$ C: 74.49%, H: 10.63; found C: 74.23%, H: 10.60%.

6-oxohexadec-7-ynoic acid (72f)



72f

Prepared from Prenyl 6-oxohexadec-7-ynoate **67f** (1.00 equiv, 568 µmol, 190 mg) and TMSOTf (0.03 equiv, 17 µmol, 3.08 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (110 mg, 73%). $\mathbf{R_f}$ = 0.37 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56 (t, *J* = 7.0 Hz, 2H), 2.37 (dt, *J* = 11.4, 7.2 Hz, 4H), 1.78 – 1.51 (m, 6H), 1.43 – 1.23 (m, 10H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 187.8, 179.2, 94.9, 80.9, 45.1, 33.7, 31.9, 29.2, 29.1, 29.0, 27.8, 24.0, 23.4, 22.7, 19.1, 14.2.

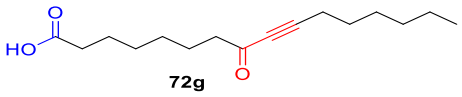
IR (ATR ν in cm^{-1}): 2926 (s), 2856 (m), 2210 (m), 1708 (s), 1671 (s), 1458 (w), 1409 (w), 1365 (w), 1218 (m), 1162 (w), 1072 (w), 941 (w), 723 (w), 529 (w).

MS (APCI): m/z calcd for $C_{16}H_{27}O_3$ 267.2 $[M+H]^+$, found 267.2 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{16}H_{26}O_3$ 266.1882 $[M]^+$, found 266.1873 $[M]^+$.

Elm Anal. Calcd for $C_{16}H_{26}O_3$ C: 72.14%, H: 9.84; found C: 71.62%, H: 9.95%.

8-oxohexadec-9-ynoic acid (72g)



72g

Prepared from Prenyl 8-oxohexadec-9-ynoate **67g** (1.00 equiv, 538 µmol, 180 mg) and TMSOTf (0.03 equiv, 16 µmol, 2.92 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane: Acetone + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (92 mg, 64%). $\mathbf{R_f}$ = 0.20 (8:2 *n*-hexane:Acetone + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52 (t, *J* = 7.4 Hz, 2H), 2.35 (td, *J* = 7.3, 2.5 Hz, 4H), 1.71 – 1.52 (m, 6H), 1.44 – 1.26 (m, 10H), 0.89 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.5, 179.4, 94.6, 80.9, 45.5, 33.9, 31.3, 28.8, 28.7, 28.6, 27.8, 24.5, 24.0, 22.6, 19.1, 14.1.

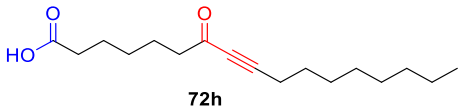
IR (ATR ν in cm^{-1}): 2930 (s), 2859 (m), 2210 (m), 1707 (s), 1671 (s), 1458 (w), 1409 (w), 1236 (w), 1161 (w), 933 (w).

MS (APCI): m/z calcd for $C_{16}H_{27}O_3$ 267.2 $[M+H]^+$, found 267.2 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{16}H_{26}O_3$ 266.1882 $[M]^+$, found 266.1895 $[M]^+$.

Elm Anal. Calcd for $C_{16}H_{26}O_3$ C: 72.14%, H: 9.84; found C: 71.69%, H: 9.88%.

7-oxoheptadec-8-ynoic acid (72h)



72h

Prepared from Prenyl 7-oxoheptadec-8-ynoate **67h** (1.00 equiv, 224 µmol, 78 mg) and TMSOTf (0.03 equiv, 6.00 µmol, 1.21 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (45 mg, 72%). $\mathbf{R_f}$ = 0.2 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.54 (t, *J* = 7.4 Hz, 2H), 2.36 (td, *J* = 7.3, 3.2 Hz, 4H), 1.73 – 1.53 (m, 6H), 1.43 – 1.25 (m, 12H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.2, 179.2, 94.7, 80.9, 45.3, 33.8, 31.9, 29.2, 29.1, 29.0, 28.4, 27.8, 24.5, 23.8, 22.7, 19.1, 14.2.

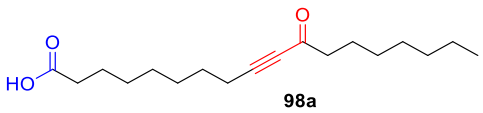
IR (ATR ν in cm^{-1}): 2925 (s), 2855 (m), 2209 (m), 1707 (s), 1672 (s), 1459 (w), 1410 (w), 1372 (m), 1324 (w), 1231 (w), 1161 (w), 1006 (w), 945 (w), 851 (w), 726 (w).

MS (ESI): m/z calcd for $C_{17}H_{28}NaO_3$ 303.2 $[M+Na]^+$, found 303.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{27}O_3$ 279.1960 $[M-H]^+$, found 279.1978 $[M-H]^+$.

Elm Anal. Calcd for $C_{17}H_{28}O_3$ C: 72.82%, H: 10.07%; found C: 72.82%, H: 9.82%.

11-oxooctadec-9-ynoic acid (98a)



98a

Prepared from Prenyl 11-oxooctadec-9-ynoate **90a** (1.00 equiv, 276 µmol, 100 mg) and TMSOTf (0.03 equiv, 8.00 µmol, 1.50 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 70:30) afforded the desired analytically pure product as a yellow oil (56 mg, 69%). $\mathbf{R_f}$ = 0.2 (7:3 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (t, *J* = 7.5 Hz, 2H), 2.35 (t, *J* = 7.1 Hz, 4H), 1.71 – 1.51 (m, 6H), 1.47 – 1.22 (m, 14H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.8, 179.7, 94.2, 81.1, 45.6, 34.0, 31.7, 29.1, 29.1, 28.9, 28.7, 28.7, 27.7, 24.6, 24.2, 22.7, 19.0, 14.2.

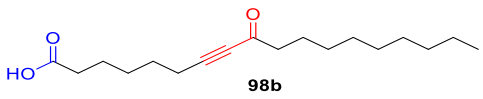
IR (ATR ν in cm^{-1}): 2927 (s), 2856 (m), 2211 (m), 1710 (s), 1671 (s), 1458 (w), 1411 (w), 1361 (m), 1219 (m), 1164 (m), 1093 (w), 935 (w), 725 (w), 529 (w).

MS (ESI): m/z calcd for $C_{18}H_{30}NaO_3$ 317.2 $[M+Na]^+$, found 317.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{18}H_{30}O_3$ 294.2195 $[M]^+$, found 294.2201 $[M]^+$.

Elm Anal. Calcd for $C_{18}H_{30}O_3$ C: 73.43%, H: 10.27; found C: 73.64%, H: 10.39%.

9-oxooctadec-7-ynoic acid (98b)



98b

Prepared from Prenyl 9-oxooctadec-7-ynoate **90b** (1.00 equiv, 717 µmol, 260 mg) and TMSOTf (0.03 equiv, 22 µmol, 3.89 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (121 mg, 57%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (t, *J* = 7.4 Hz, 2H), 2.42 – 2.32 (m, 4H), 1.71 – 1.56 (m, 6H), 1.52 – 1.41 (m, 2H), 1.33 – 1.23 (m, 12H), 0.87 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.8, 179.6, 93.7, 81.1, 45.6, 33.8, 31.9, 29.5, 29.4, 29.3, 29.1, 28.3, 27.4, 24.2, 24.1, 22.7, 18.9, 14.2.

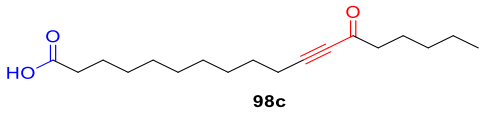
IR (ATR ν in cm^{-1}): 2925 (s), 2854 (m), 2211 (m), 1708 (s), 1671 (s), 1458 (w), 1411 (w), 1275 (w), 1231 (w), 1162 (w), 935 (w), 723 (w), 636 (w).

MS (APCI): m/z calcd for $C_{18}H_{31}O_3$ 295.2 $[M+H]^+$, found 295.2 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{18}H_{30}O_3$ 294.2195 $[M]^+$, found 294.2202 $[M]^+$.

Elm Anal. Calcd for $C_{18}H_{30}O_3$ C: 73.43%, H: 10.27; found C: 73.13%, H: 10.21%.

13-oxooctadec-11-ynoic acid (98c)



98c

Prepared from Prenyl 13-oxooctadec-11-ynoate **90c** (1.00 equiv, 469 µmol, 170 mg) and TMSOTf (0.03 equiv, 14 µmol, 2.55 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (90 mg, 65%). $\mathbf{R_f}$ = 0.30 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (t, *J* = 7.4 Hz, 2H), 2.34 (td, *J* = 7.3, 2.5 Hz, 4H), 1.60 (ddt, *J* = 31.2, 14.9, 7.3 Hz, 6H), 1.43 – 1.26 (m, 14H), 0.88 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.9, 180.1, 94.4, 81.0, 45.6, 34.1, 31.2, 29.3, 29.2, 29.1, 29.1, 28.9, 27.8, 24.7, 23.9, 22.5, 19.1, 14.0.

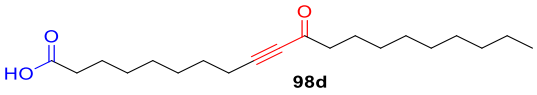
IR (ATR ν in cm^{-1}): 2927 (s), 2856 (m), 2211 (m), 1708 (s), 1671 (s), 1465 (w), 1411 (w), 1361 (w), 1235 (m), 1166 (m), 1105 (w), 928 (w), 725 (w), 590 (w), 529 (w).

MS (APCI): m/z calcd for $C_{18}H_{31}O_3$ 295.2 $[M+H]^+$, found 295.2 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{18}H_{30}O_3$ 294.2195 $[M]^+$, found 294.2190 $[M]^+$.

Elm Anal. Calcd for $C_{18}H_{30}O_3$ C: 73.43%, H: 10.27; found C: 73.65%, H: 10.36%.

11-oxoicos-9-ynoic acid (98d)



98d

Prepared from Prenyl 11-oxoicos-9-ynoate **90d** (1.00 equiv, 23 µmol, 110 mg) and TMSOTf (0.03 equiv, 8 µmol, 1.53 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (46 mg, 51%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (t, *J* = 7.4 Hz, 2H), 2.42 – 2.28 (m, 4H), 1.61 (dddd, *J* = 22.2, 20.2, 10.1, 5.5 Hz, 6H), 1.46 – 1.23 (m, 18H), 0.80 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.8, 179.6, 94.2, 81.1, 45.6, 34.0, 32.0, 29.5, 29.4, 29.3, 29.1, 28.9, 28.7, 28.7, 27.7, 24.6, 24.2, 22.8, 19.0, 14.2.

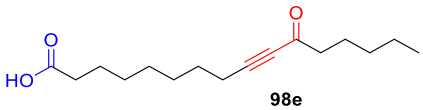
IR (ATR ν in cm^{-1}): 2925 6(s), 2854 (m), 2210 (m), 1708 (s), 1671 (s), 1457 (w), 1409 (w), 1231 (w), 1216 (w), 1161 (w), 932 (w), 723 (w).

MS (APCI): m/z calcd for $C_{20}H_{35}O_3$ 323.3 $[M+H]^+$, found 323.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{20}H_{34}O_3$ 322.2508 $[M]^+$, found 322.2526 $[M]^+$.

Elm Anal. Calcd for $C_{20}H_{34}O_3$ C: 74.49%, H: 10.63; found C: 74.62%, H: 10.66%.

11-oxohexadec-9-ynoic acid (98e)



98e

Prepared from Prenyl 11-oxohexadec-9-ynoate **90e** (1.00 equiv, 359 µmol, 120 mg) and TMSOTf (0.03 equiv, 11 µmol, 1.95 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:Acetone + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (50 mg, 52%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:Acetone + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (t, *J* = 7.4 Hz, 2H), 2.35 (td, *J* = 7.3, 1.8 Hz, 4H), 1.60 (dq, *J* = 32.8, 7.3 Hz, 6H), 1.45 – 1.26 (m, 10H), 0.89 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 188.8, 179.6, 94.2, 81.1, 45.6, 34.1, 31.2, 28.9, 28.7, 28.7, 27.7, 24.7, 23.9, 22.5, 19.0, 14.0.

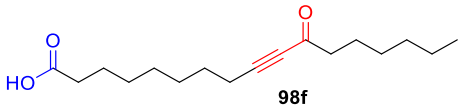
IR (ATR ν in cm^{-1}): 2930 (s), 2857 (m), 2210 (m), 1708 (s), 1671 (s), 1458 (w), 1409 (w), 1365 (w), 1234 (m), 1166 (m), 1093 (w), 923 (w), 726 (w), 633 (w).

MS (APCI): m/z calcd for $C_{16}H_{27}O_3$ 267.2 $[M+H]^+$, found 267.2 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{16}H_{26}O_3$ 266.1882 $[M]^+$, found 266.1865 $[M]^+$.

Elm Anal. Calcd for $C_{16}H_{26}O_3$ C: 72.14%, H: 9.84; found C: 71.99%, H: 9.68%.

11-oxoheptadec-9-ynoic acid (98f)



98f

Prepared from Prenyl 11-oxoheptadec-9-ynoate **90f** (1.00 equiv, 287 µmol, 100 mg) and TMSOTf (0.03 equiv, 8.60 µmol, 1.55 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (55 mg, 68%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52 (t, *J* = 7.4 Hz, 2H), 2.35 (t, *J* = 7.2 Hz, 4H), 1.70 – 1.53 (m, 6H), 1.45 – 1.28 (m, 12H), 0.88 (t, *J* = 8.4, 5.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 188.8, 179.1, 94.2, 81.1, 45.6, 33.9, 31.6, 28.9, 28.7, 28.7, 27.7, 24.6, 24.2, 22.6, 19.1, 14.1.

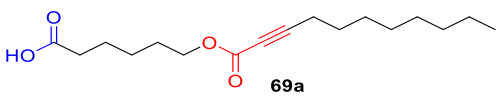
IR (ATR ν in cm^{-1}): 2930 (s), 2857 (m), 2211 (m), 1708 (s), 1671 (s), 1458 (w), 1411 (w), 1362 (w), 1219 (m), 1165 (m), 1095 (w), 936 (w), 726 (w), 529 (w).

MS (ESI): m/z calcd for $C_{17}H_{28}NaO_3$ 303.2 $[M+Na]^+$, found 303.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{28}O_3$ 280.2038 $[M]^+$, found 280.2028 $[M]^+$.

Elm Anal. Calcd for $C_{17}H_{28}O_3$ C: 72.82%, H: 10.07; found C: 72.76%, H: 10.19%.

6-(undec-2-ynoyloxy)hexanoic acid (69a)



69a

Prepared from 6-((Prenyl)oxy)-6-oxohexyl undec-2-ynoate **64a** (1.00 eqiuv, 447 µmol, 163 mg) and TMSOTf (0.08 equiv, 35.80 µmol, 6.46 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 90:10) afforded the desired analytically pure product as a yellow oil (122 mg, 92%). $\mathbf{R_f}$ = 0.26 (9:1 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.15 (t, *J* = 6.6 Hz, 2H), 2.41 – 2.29 (m, 4H), 1.74 – 1.53 (m, 6H), 1.48 – 1.25 (m, 12H), 0.88 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.16, 154.12, 89.95, 73.18, 65.62, 33.83, 31.93, 29.22, 29.12, 29.00, 28.26, 27.66, 25.48, 24.36, 22.78, 18.84, 14.24.

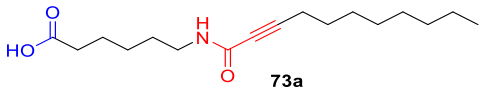
IR (ATR ν in cm^{-1}): 2925 (m), 2856 (m), 2234 (m), 1706 (s), 1461 (w), 1415 (w), 1325 (w), 1245 (s), 1073 (m), 944 (w), 872 (w), 751 (w), 675 (w).

MS (ESI): m/z calcd for $C_{17}H_{28}NaO_4$ 319.4 $[M+Na]^+$, found 319.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{28}O_4$ 296.1988 $[M]^+$, found 296.1981 $[M]^+$.

Elm Anal. Calcd for $C_{17}H_{28}O_4$ C: 68.89%, H: 9.52%; found C: 69.32%, H: 9.48%.

6-(undec-2-ynamido)hexanoic acid (73a)



73a

a) With $BF_3{\cdot}OEt_2$: Prepared from Prenyl 6-(undec-2-ynamido)hexanoate **68a** (1.00 equiv, 261 µmol, 95 mg) and $BF_3{\cdot}OEt_2$ (3.50 equiv, 944 µmol, 115 µL), according to **GP7**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 95:5 → 50:50) afforded the desired analytically pure product as a white powder (56 mg, 66%). $\mathbf{R_f}$ = 0.32 (1:1 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

b) With TMSOTf: Prepared from Prenyl 6-(undec-2-ynamido)hexanoate **68a** (1.00 equiv, 385 µmol, 140 mg) and TMSOTf (0.1 equiv, 38.5 µmol, 7.00 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 95:5 → 50:50) afforded the desired analytically pure product as a white powder (80 mg, 70%). $\mathbf{R_f}$ = 0.32 (1:1 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, DMSO_d_6) δ 8.42 (t, *J* = 5.6 Hz, 1H), 3.02 (dd, *J* = 12.9, 6.8 Hz, 2H), 2.30 (t, *J* = 7.0 Hz, 2H), 2.18 (dd, *J* = 9.0, 5.8 Hz, 2H), 1.51 – 1.23 (m, 18H), 0.86 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, DMSO_d_6) δ 174.4, 152.4, 85.6, 76.4, 38.6, 33.5, 31.2, 28.6, 28.5, 28.4, 28.2, 27.4, 25.9, 24.1, 22.1, 17.7, 13.9.

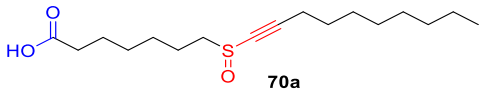
IR (ATR ν in cm^{-1}): 3276 (m), 2920 (s), 2854 (m), 2249 (w), 2223 (w), 1698 (s), 1614 (s), 1528 (s), 1463 (w), 1414 (w), 1351 (w), 1319 (w), 1273 (m), 1229 (w), 1105 (w), 1054 (w), 947 (w), 853 (w), 670 (s).

MS (ESI): m/z calcd for $C_{17}H_{29}NNaO_3$ 318.2 $[M+Na]^+$, found 318.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{29}NO_3$ 295.2147 $[M]^+$, found 295.2144 $[M]^+$.

Elm Anal. Calcd for $C_{17}H_{29}NO_3$ C: 69.12%, H: 9.89%, N: 4.74%; found C: 68.79%, H: 9.87%, N: 4.74%.

7-(dec-1-yn-1-ylsulfinyl)heptanoic acid (70a)



70a

Prepared from Prenyl 7-(dec-1-yn-1-ylsulfinyl)heptanoate **65a** (1.00 equiv, 340 µmol, 130 mg) and $BF_3 \cdot OEt_2$ (3.50 equiv, 1.19 mmol, 72 µL) according to **GP7**. Purification by flash column chromatography (*n*-hexan:EtOAc + 0.5 Vol% HOAc = 9:1 → 8:2) afforded the desired analytically pure product as a white solid (51 mg, 47%). $\mathbf{R_f}$: 0.21 (7:3 *n*-Hexan:EtOAc+ 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.02 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 2H), 2.40 (dt, *J* = 23.9, 7.3 Hz, 4H), 1.95–1.80 (m, 2H), 1.71–1.27 (m, 18H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.9, 106.0, 56.3, 33.9, 31.9, 29.2, 29.1, 28.9, 28.7, 28.3, 27.7, 24.5, 22.7, 22.2, 19.7, 14.2.

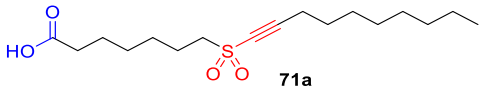
IR (ATR ν in cm^{-1}): 2937 (m), 2922 (m), 2870 (m), 2180 (w), 1464 (s), 1438 (w), 1410 (w), 1344 (s), 1313 (s), 1286 (w), 1274 (w), 1260 (w), 1209 (m), 1073 (s), 1043 (s), 975 (w), 913 (m), 725 (m), 606 (m).

MS (ESI) m/z calcd for $C_{17}H_{30}NaO_3S$ 337.1 $[M+Na]^+$, found 337.3 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{30}O_3S$ 314.1916 $[M]^+$, found 314.1905 $[M]^+$.

Elm Anal. Calcd for $C_{17}H_{30}O_3S$ C: 64.93, H: 9.62, S: 10.19; Found: C: 64.82, H: 9.38, S: 9.88.

7-(dec-1-yn-1-ylsulfonyl)heptanoic acid (71a)



71a

Prepared from Prenyl 7-(dec-1-yn-1-ylsulfonyl)heptanoate **66a** (1.00 equiv, 304 µmol, 121 mg), and $BF_3 \cdot OEt_2$ (3.50 equiv, 1.10 mmol, 65 µL) according to **GP7**. Purification by flash column chromatography (*n*-hexane:EtOAc+ 0.5 Vol% HOAc = 9:1 → 8:2) afforded the desired analytically pure product as a white solid (46 mg, 45%). $\mathbf{R_f}$: 0.27 (7:3 *n*-Hexan:EtOAc+ 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.15 (dd, *J* = 9.0, 6.2 Hz, 2H), 2.39 (dt, *J* = 15.8, 7.3 Hz, 4H), 1.96–1.87 (m, 2H), 1.71–1.28 (m, 18H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.8, 96.6, 58.1, 33.7, 31.8, 29.1, 29.0, 28.9, 28.6, 27.8, 27.1, 24.3, 22.8, 22.7, 18.9, 14.2.

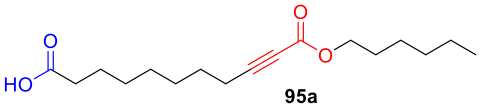
IR (ATR ν in cm^{-1}): 2954 (m), 2920 (m), 2849 (m), 2211 (m), 1718 (m), 1467 (m), 1419 (w), 1404 (w), 1330 (s), 1303 (s), 1244 (w), 1208 (m), 1131 (s), 1055 (m), 774 (m), 723 (m), 676 (m).

MS (ESI) m/z calcd for $C_{17}H_{32}NaO_3S$ 353.1 $[M+Na]^+$, found 353.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{30}O_4S$ 330.1865 $[M]^+$, found 330.1860 $[M]^+$.

Elm Anal. Calcd for $C_{17}H_{30}O_4S$ C: 61.78, H: 9.15, S: 9.70; Found C: 62.14, H: 9.14, S: 8.93.

11-(hexyloxy)-11-oxoundec-9-ynoic acid (95a)



95a

Prepared from 1-hexyl 11-(prenyl) undec-2-ynedioate **87a** (1.00 equiv, 329 µmol, 120 mg) and TMSOTf (0.08 equiv, 26.30 µmol, 4.76 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (40 mg, 41%). $\mathbf{R_f}$ = 0.4 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14 (t, *J* = 6.8 Hz, 2H), 2.33 (dt, *J* = 10.2, 7.3 Hz, 4H), 1.69 – 1.54 (m, 6H), 1.42 – 1.29 (m, 12H), 0.89 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.5, 154.2, 89.4, 73.3, 66.1, 34.0, 31.5, 28.9, 28.7, 28.7, 28.5, 27.5, 25.6, 24.6, 22.6, 18.7, 14.1.

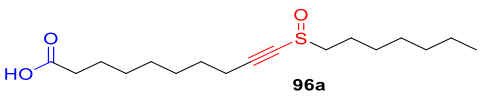
IR (ATR ν in cm^{-1}): 2929 (s), 2857 (m), 2236 (w), 1708 (s), 1458 (w), 1412 (w), 1365 (w), 1246 (s), 1078 (m), 935 (w), 905 (w), 752 (w), 725 (w), 629 (w), 529 (w).

MS (APCI): m/z calcd for $C_{17}H_{29}O_4$ 297.4 $[M+H]^+$, found 297.2 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{27}O_4$ 295.1909 $[M-H]^+$, found 295.1924 $[M-H]^+$.

Elm Anal. Calcd for $C_{17}H_{28}O_4$ C: 68.89%, H: 9.52; found C: 68.62%, H: 9.64%.

10-(heptylsulfinyl)dec-9-ynoic acid (96a)



96a

Prepared from Prenyl 10-(heptylsulfinyl)dec-9-ynoate **88a** (1.00 equiv, 340 µmol, 130 mg) and TMSOTf (0.1 equiv, 27.20 µmol, 6.15 µL) according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 70:30) afforded the desired analytically pure product as a yellow oil (72 mg, 67%). $\mathbf{R_f}$ = 0.40 (7:3 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.11 – 2.98 (m, 2H), 2.43 (t, *J* = 7.0 Hz, 2H), 2.35 (t, *J* = 7.4 Hz, 2H), 1.93 – 1.75 (m, 2H), 1.68 – 1.54 (m, 4H), 1.49 – 1.25 (m, 14H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.1, 105.7, 56.4, 34.1, 31.6, 28.9, 28.9, 28.6, 28.5, 27.6, 24.6, 22.6, 22.4, 19.7, 14.1.

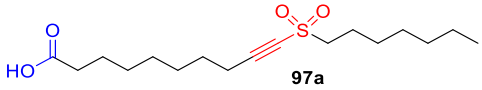
IR (ATR ν in cm^{-1}): 2926 (s), 2856 (m), 2184 (m), 1708 (s), 1458 (w), 1411 (w), 1279 (w), 1242 (w), 1201 (m), 1023 (s), 886 (w), 725 (w), 597 (w).

MS (ESI): m/z calcd for $C_{17}H_{30}NaO_3S$ 337.2 $[M+Na]^+$, found 337.1 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{30}O_3S$ 314.1916 $[M]^+$, found 314.1901 $[M]^+$.

Elm Anal. Calcd for $C_{17}H_{30}O_3S$ C: 64.93%, H: 9.62, S: 10.19%; found C: 64.78%, H: 9.86%, S: 9.61%.

10-(heptylsulfonyl)dec-9-ynoic acid (97a)



97a

Prepared from Prenyl 10-(heptylsulfonyl)dec-9-ynoate **89a** (1.00 equiv, 376 µmol, 150 mg), and $BF_3{\cdot}OEt_2$ (3.50 equiv, 1.88 mmol, 237 µL) according to **GP7**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow solid (50 mg, 40%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.17 – 3.13 (m, 2H), 2.38 (dt, *J* = 22.9, 7.3 Hz, 4H), 1.93 – 1.84 (m, 2H), 1.68 – 1.57 (m, 4H), 1.48 – 1.27 (m, 14H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.5, 96.2, 58.2, 33.9, 31.5, 28.8, 28.8, 28.7, 28.7, 28.1, 27.1, 24.6, 23.0, 22.6, 18.9, 14.1.

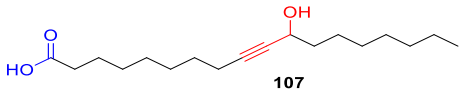
IR (ATR ν in cm^{-1}): 2953 (m), 2923 (s), 2852 (m), 2208 (m), 1694 (s), 1467 (m), 1427 (w), 1404 (w), 1328 (m), 1302 (m), 1292 (m), 1266 (m), 1228(m), 1134 (m), 773 (m), 725 (m), 675 (s), 566 (m), 523 (m).

MS (APCI): m/z calcd for $C_{17}H_{31}O_4NaS$ 331.5 $[M+H]^+$, found 331.5 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{30}O_4S$ 330.1865 $[M]^+$, found 330.1875 $[M]^+$.

Elm Anal. Calcd for $C_{17}H_{30}O_4S$ C: 61.78%, H: 9.15, S: 9.70%; found C: 62.35%, H: 9.17%, S: 9.24%.

11-hydroxyoctadec-9-ynoic acid (107)



107

In a dried two-necked flask, dec-9-ynoic acid **81b** (1.10 equiv, 654 µmol, 110 mg) was added and diluted with anhydrous THF (2 mL). The resulting solution was cooled at 0 °C before dropwise addition of *i*-PrMgCl (2.20 equiv, 1.31 mmol, 653 µL). The reaction mixture was stirred for 1 h at 0 °C and Octanal **86c** (1.00 equiv, 594 µmol, 305 µL) was then added. The ice bath was removed, and the reaction mixture was allowed to warm up to ambient temperature. After stirring for 4 h, the reaction mixture was quenched with saturated aqueous NH_4Cl (30 mL) and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with H_2O (30 mL), saturated aqueous NaCl (30 mL), and dried over Na_2SO_4. After concentration under reduced pressure, the crude residue was purified by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 95:5 → 70:30) to afford the desired analytically pure product as a white solid (120 mg, 68%). $\mathbf{R_f}$ = 0.28 (7:3 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.34 (tt, *J* = 6.6, 1.9 Hz, 1H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.20 (td, *J* = 7.0, 1.9 Hz, 2H), 1.71 – 1.59 (m, 4H), 1.54 – 1.27 (m, 18H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.6, 85.5, 81.5, 62.9, 38.3, 34.1, 31.9, 29.3, 29.3, 29.0, 28.7, 28.6, 25.3, 24.6, 22.7, 18.7, 14.2.

IR (ATR ν in cm^{-1}): 3363 (m), 3295 (w), 2955 (m), 2925 (s), 2847 (s), 1691 (s), 1421 (w), 1439 (w), 1414 (w), 1302 (w), 1269 (m), 1196 (w), 1062 (m), 939 (m), 888 (w), 799 (w), 725 (m), 633 (m), 553 (w).

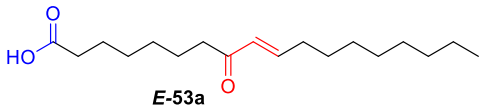
MS (ESI): m/z calcd for $C_{18}H_{32}NaO_3$ 319.2 $[M+Na]^+$, found 319.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{18}H_{32}O_3$ 296.2351 $[M]^+$, found 296.2356 $[M]^+$**.**

Elm Anal. Calcd for $C_{18}H_{32}O_3$ C: 72.93%, H: 10.88; found C: 72.60%, H: 10.88%.

6.5.2 Synthesis of *(E)*-Alkenyl Fatty Acids

(*E*)-8-Oxooctadec-9-enoic acid (*E*-53a)



***E*-53a**

Prepared from (*Z*)-Prenyl-8-oxooctadec-9-enoate ***Z*-77a** (1.00 equiv, 55 µmol, 200 mg) and TMSOTf (0.03 equiv, 166 µmol, 3.00 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a white solid (90 mg, 74%). $\mathbf{R_f}$ = 0.24 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc). Analytical data are in accordance with the literature.[104, 135]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (dt, *J* = 15.8, 6.9 Hz, 1H), 6.08 (dt, *J* = 15.9, 1.5 Hz, 1H), 2.52 (t, *J* = 7.4 Hz, 2H), 2.34 (t, *J* = 7.5 Hz, 2H), 2.24 – 2.16 (m, 2H), 1.62 (dp, *J* = 9.7, 7.4 Hz, 4H), 1.50 – 1.25 (m, 16H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 201.0, 179.3, 147.7, 130.4, 40.0, 33.9, 32.6, 31.9, 29.4, 29.3, 29.3, 29.0, 28.9, 28.2, 24.6, 24.1, 22.7, 14.2.

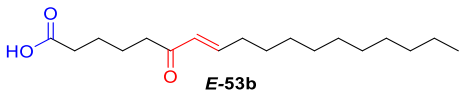
IR (ATR ν in cm^{-1}): 3029 (w), 2954 (m), 2915 (s), 2848 (m), 1740 (s), 1687 (s), 1656 (m), 1469 (m), 1439 (w), 1415 (w), 1381 (w), 1366 (m), 1342 (w), 1295 (w), 1253 (m), 1229 (w), 1174 (m), 1080 (w), 979 (m), 910 (m), 890 (w), 846 (w), 718 (w), 702 (w), 683 (w).

MS (ESI): m/z calcd for $C_{18}H_{32}NaO_3$ 319.2 $[M+Na]^+$, found 319.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{18}H_{32}O_3$ 296.2351 $[M]^+$, found 296.2354 $[M]^+$.

Elm Anal. Calcd for $C_{18}H_{32}O_3$ C: 72.93%, H: 10.88%; found C: 72.85%, H: 10.83%.

(*E*)-6-Oxooctadec-7-enoic acid (*E*-53b)



***E*-53b**

Prepared from (*Z*)-Prenyl-6-oxooctadec-7-enoate ***Z*-77b** (1.00 equiv, 439 µmol, 160 mg) and TMSOTf (0.03 equiv, 13 µmol, 2.38 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a white solid (85 mg, 65%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (dt, *J* = 15.9, 6.9 Hz, 1H), 6.08 (dt, *J* = 15.9, 1.5 Hz, 1H), 2.56 (dq, *J* = 6.4, 3.2 Hz, 2H), 2.41 – 2.34 (m, 2H), 2.20 (qd, *J* = 7.0, 1.5 Hz, 2H), 1.71 – 1.62 (m, *J* = 5.2 Hz, 4H), 1.49 – 1.40 (m, 2H), 1.27 (d, *J* = 8.3 Hz, 14H), 0.85 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 200.3, 179.1, 147.9, 130.3, 39.5, 33.8, 32.6, 32.0, 29.7, 29.6, 29.5, 29.4, 29.3, 28.2, 24.3, 23.5, 22.8, 14.2.

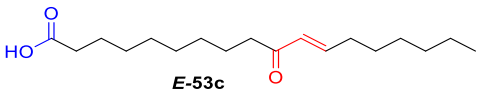
IR (ATR ν in cm^{-1}): 3026 (w), 2920 (s), 2849 (m), 1698 (s), 1674 (s), 1657 (s), 1471 (m), 1411 (w), 1378 (w), 1309 (w), 1272 (w), 1232 (m), 1176 (m), 1099 (w), 992 (m), 916 (w), 718 (w), 682 (w), 520 (w).

MS (APCI): m/z calcd for $C_{18}H_{33}O_3$ 297.2 $[M+H]^+$, found 297.2 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{18}H_{32}O_3$ 296.2351 $[M]^+$, found 296.2333 $[M]^+$.

Elm Anal. Calcd for $C_{18}H_{32}O_3$ C: 72.93%, H: 10.88%; found C: 72.94%, H: 10.80%.

(*E*)-10-Oxooctadec-11-enoic acid (*E*-53c)



***E*-53c**

Prepared from (*Z*)-Prenyl-10-oxooctadec-11-enoate ***Z*-77c** (1.00 equiv, 192 µmol, 70 mg) and TMSOTf (0.03 equiv, 5.80 µmol, 1.04 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a white solid (40 mg, 70%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc). Analytical data are in accordance with the literature.[136]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (dt, *J* = 15.9, 6.9 Hz, 1H), 6.08 (dt, *J* = 15.8, 1.5 Hz, 1H), 2.52 (t, *J* = 7.5 Hz, 2H), 2.34 (t, *J* = 7.5 Hz, 2H), 2.20 (qd, *J* = 7.1, 1.6 Hz, 2H), 1.65 – 1.57 (m, 4H), 1.50 – 1.40 (m, 2H), 1.30 (td, *J* = 7.5, 2.9 Hz, 14H), 0.86 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 201.2, 179.6, 147.6, 130.4, 40.1, 34.1, 32.6, 31.7, 29.3, 29.3, 29.2, 29.1, 29.0, 28.2, 24.7, 24.4, 22.6, 14.1.

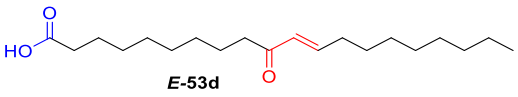
IR (ATR ν in cm^{-1}): 2926 (s), 2853 (m), 1701 (s), 1690 (s), 1625 (m), 1471 (w), 1428 (w), 1409 (w), 1377 (w), 1292 (w), 1218 (m), 1191 (m), 1115 (w), 1082 (w), 976 (w), 915 (w), 719 (w), 679 (w), 536 (w).

MS (APCI): m/z calcd for $C_{18}H_{33}O_3$ 297.2 $[M+H]^+$, found 297.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{18}H_{32}O_3$ 296.2351 $[M]^+$, found 296.2361 $[M]^+$.

Elm Anal. Calcd for $C_{18}H_{32}O_3$ C: 72.93%, H: 10.88%; found C: 72.96%, H: 10.81%.

(*E*)-10-Oxoicos-11-enoic acid (*E*-53d)



***E*-53d**

Prepared from (*Z*)-Prenyl-10-oxoicos-11-enoate ***Z*-77d** (1.00 equiv, 688 µmol, 270 mg) and TMSOTf (0.03 equiv, 21 µmol, 3.73 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a white solid (127 mg, 57%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (dt, *J* = 15.9, 6.9 Hz, 1H), 6.08 (dt, *J* = 15.9, 1.5 Hz, 1H), 2.51 (t, *J* = 7.5 Hz, 2H), 2.33 (t, *J* = 7.5 Hz, 2H), 2.19 (qd, *J* = 7.0, 1.5 Hz, 2H), 1.60 (dtd, *J* = 11.8, 8.3, 4.7 Hz, 4H), 1.45 (p, *J* = 7.2 Hz, 2H), 1.33 – 1.25 (m, 18H), 0.84 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 201.2, 180.0, 147.7, 130.3, 40.1, 34.1, 32.6, 31.9, 29.4, 29.3, 29.3, 29.1, 29.1, 28.2, 24.7, 24.4, 22.7, 14.2.

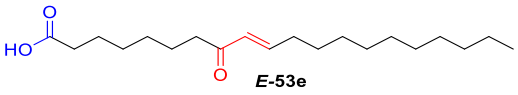
IR (ATR ν in cm^{-1}): 2956 (w), 2916 (s), 2850 (m), 1688 (s), 1625 (m), 1471 (m), 1428 (w), 1409 (w), 1377 (w), 1291 (m), 1256 (w), 1219 (m), 1191 (w), 1118 (w), 1071 (w), 1036 (w), 1021 (w), 976 (m), 915 (m), 868 (w), 769 (w), 722 (m), 679 (w), 536 (w).

MS (APCI): m/z calcd for $C_{20}H_{37}O_3$ 325.3 $[M+H]^+$, found 325.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{20}H_{36}O_3$ 324.2664 $[M]^+$, found 324.2661 $[M]^+$.

Elm Anal. Calcd for $C_{20}H_{36}O_3$ C: 74.03%, H: 11.18%; found C: 73.87%, H: 11.05%.

(*E*)-8-oxoicos-9-enoic acid (*E*-53e)



***E*-53e**

Prepared from (*Z*)-Prenyl-8-oxoicos-9-enoate ***Z*-77e** (1.00 equiv, 408 µmol, 180 mg) and TMSOTf (0.03 equiv, 13.80 µmol, 2.49 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a white solid (90 mg, 61%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 – 6.78 (m, 1H), 6.08 (dt, *J* = 15.9, 1.5 Hz, 1H), 2.53 (t, *J* = 7.4 Hz, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.24 – 2.16 (m, 2H), 1.62 (qd, *J* = 7.3, 3.4 Hz, 4H), 1.49 – 1.24 (m, 20H), 0.91 – 0.84 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 201.0, 179.6, 147.7, 130.3, 40.0, 34.0, 32.6, 32.0, 29.7, 29.6, 29.5, 29.4, 29.3, 29.0, 28.9, 28.2, 24.6, 24.1, 22.8, 14.2.

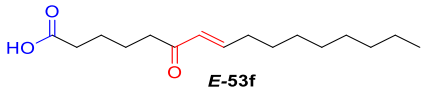
IR (ATR ν in cm^{-1}): 2953 (w), 2915 (s), 2849 (m), 1695 (s), 1661 (m), 1471 (m), 1412 (w), 1381 (w), 1325 (w), 1285 (w), 1248 (m), 1219 (w), 1174 (m), 1116 (w), 983 (w), 968 (w), 912 (w), 716 (w), 678 (w).

MS (APCI): m/z calcd for $C_{20}H_{37}O_3$ 325.3 $[M+H]^+$, found 325.3 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{20}H_{36}O_3$ 324.2664 $[M]^+$, found 324.2672 $[M]^+$.

Elm Anal. Calcd for $C_{20}H_{36}O_3$ C: 74.03%, H: 11.18%; found C: 73.94%, H: 11.14%.

(*E*)-6-Oxohexadec-7-enoic acid (*E*-53f)



***E*-53f**

Prepared from (*Z*)-Prenyl-6-oxohexadec-7-enoate ***Z*-77f** (1.00 equiv, 951 µmol, 320 mg) and TMSOTf (0.03 equiv, 28.50 µmol, 5.16 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow solid (176 mg, 69%). $\mathbf{R_f}$ = 0.37 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (dt, *J* = 15.9, 6.9 Hz, 1H), 6.08 (dt, *J* = 15.9, 1.5 Hz, 1H), 2.61 – 2.51 (m, 2H), 2.40 – 2.34 (m, 2H), 2.20 (qd, *J* = 7.0, 1.5 Hz, 2H), 1.66 (p, *J* = 3.1 Hz, 4H), 1.45 (p, *J* = 7.1 Hz, 2H), 1.32 – 1.24 (m, 10H), 0.85 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 200.4, 179.5, 147.9, 130.3, 39.5, 33.9, 32.6, 31.9, 29.4, 29.3, 29.3, 28.2, 24.3, 23.6, 22.7, 14.2.

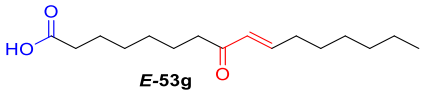
IR (ATR ν in cm^{-1}): 3032 (w), 2950 (w), 2917 (s), 2850 (m), 1685 (s), 1622 (m), 1464 (m), 1428 (w), 1401 (m), 1378 (w), 1256 (w), 1198 (m), 1112 (w), 1012 (w), 979 (w), 906 (w), 710 (w), 675 (w), 513 (w).

MS (APCI): m/z calcd for $C_{16}H_{29}O_3$ 269.2 $[M+H]^+$, found 269.1 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{16}H_{28}O_3$ 268.2038 $[M]^+$, found 268.2049 $[M]^+$.

Elm Anal. Calcd for $C_{16}H_{28}O_3$ C: 71.60%, H: 10.52%; found C: 71.55%, H: 10.56%.

(*E*)-8-Oxohexadec-9-enoic acid (*E*-53g)[137]



***E*-53g**

Prepared from (*Z*)-Prenyl-8-oxohexadec-9-enoate ***Z*-77g** (1.00 equiv, 446 µmol, 150 mg) and TMSOTf (0.03 equiv, 13.40 µmol, 2.42 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a white solid (75 mg, 63%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (dt, *J* = 15.8, 6.9 Hz, 1H), 6.08 (dt, *J* = 15.8, 1.5 Hz, 1H), 2.52 (t, *J* = 7.4 Hz, 2H), 2.34 (t, *J* = 7.5 Hz, 2H), 2.20 (qd, *J* = 7.0, 1.5 Hz, 2H), 1.61 (dtd, *J* = 14.4, 7.3, 3.2 Hz, 4H), 1.50 – 1.27 (m, 12H), 0.84 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 201.1, 179.5, 147.7, 130.3, 40.0, 34.0, 32.6, 31.7, 29.0, 29.0, 28.9, 28.2, 24.6, 24.1, 22.6, 14.2.

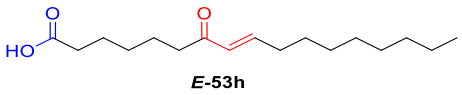
IR (ATR ν in cm^{-1}): 2926 (s), 2856 (m), 1734 (m), 1705 (s), 1628 (m), 1457 (w), 1411 (w), 1378 (w), 1229 (w), 1171 (m), 975 (w), 935 (w), 725 (w).

MS (APCI): m/z calcd for $C_{16}H_{29}O_3$ 269.4 $[M+H]^+$, found 269.5 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{16}H_{28}O_3$ 268.2038 $[M]^+$, found 268.2045 $[M]^+$.

Elm Anal. Calcd for $C_{16}H_{28}O_3$ C: 71.60%, H: 10.52%; found C: 71.64%, H: 10.44%.

(*E*)-7-Oxoheptadec-8-enoic acid (*E*-53h)



***E*-53h**

Prepared from (*Z*)-Prenyl-7-oxoheptadec-8-enoate ***Z*-77h** (1.00 equiv, 305 µmol, 107 mg) and TMSOTf (0.03 equiv, 9.15 µmol, 1.65 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a white solid (68 mg, 79%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (dt, *J* = 15.8, 6.9 Hz, 1H), 6.08 (dt, *J* = 15.8, 1.4 Hz, 1H), 2.54 (t, *J* = 7.4 Hz, 2H), 2.36 (t, *J* = 7.5 Hz, 2H), 2.24 – 2.17 (m, 2H), 1.64 (dq, *J* = 15.7, 7.8 Hz, 4H), 1.48 – 1.25 (m, 14H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 200.7, 179.2, 147.8, 130.3, 39.8, 33.8, 32.6, 31.9, 29.4, 29.3, 29.3, 28.8, 28.2, 24.6, 23.9, 22.7, 14.2.

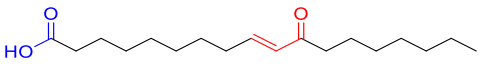
IR (ATR ν in cm^{-1}): 3029 (w), 2950 (w), 2915 (s), 2850 (m), 1687 (s), 1655 (s), 1469 (w), 1438 (w), 1414 (w), 1382 (w), 1341 (w), 1299 (w), 1251 (m), 1203 (w), 1173 (m), 1085 (w), 979 (m), 923 (m), 873 (w), 718 (w), 700 (w), 684 (w).

MS (ESI): m/z calcd for $C_{17}H_{30}NaO_3$ 305.2 $[M+Na]^+$, found 305.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{29}O_3$ 281.2117 $[M-H]^+$, found 281.2129 $[M-H]^+$

Elm Anal. Calcd for $C_{17}H_{30}O_3$ C: 72.30%, H: 10.71%; found C: 72.21%, H: 10.66%.

(*E*)-11-Oxooctadec-9-enoic acid (*E*-94a)



***E*-94a**

Prepared from (*E*)-Prenyl-11-oxooctadec-9-enoate ***E*-104a** (1.00 equiv, 274 µmol, 100 mg) and TMSOTf (0.03 equiv, 8.22 µmol, 1.48 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow solid (56 mg, 69%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc). Analytical data are in accordance with the literature.[104, 135]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (dt, *J* = 15.8, 6.9 Hz, 1H), 6.08 (dt, *J* = 15.8, 1.4 Hz, 1H), 2.56 – 2.49 (m, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.20 (td, *J* = 8.1, 1.3 Hz, 2H), 1.65 – 1.57 (m, 4H), 1.49 – 1.42 (m, 2H), 1.29 (dd, *J* = 10.4, 6.7 Hz, 14H), 0.87 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 201.3, 147.3, 130.5, 40.2, 33.9, 32.5, 31.8, 29.4, 29.2, 29.1, 29.1, 29.0, 28.1, 24.7, 24.4, 22.7, 14.2.

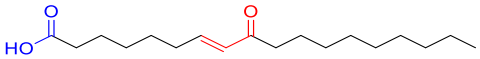
IR (ATR ν in cm^{-1}): 3029 (w), 2920 (s), 2906 (s), 2850 (m), 1697 (s), 1671 (s), 1658 (s), 1471 (m), 1431 (w), 1411 (w), 1378 (w), 1312 (w), 1272 (w), 1234 (m), 1211 (w), 1175 (m), 1101 (w), 992 (w), 978 (w), 931 (w), 792 (w), 718 (w), 682 (w), 519 (w).

MS (ESI): m/z calcd for $C_{18}H_{32}NaO_3$ 319.2 $[M+Na]^+$, found 319.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{18}H_{32}O_3$ 296.2351 $[M]^+$, found 296.2370 $[M]^+$.

Elm Anal. Calcd for $C_{18}H_{32}O_3$ C: 72.93%, H: 10.88; found C: 72.67%, H: 10.75%.

(*E*)-9-Oxooctadec-7-enoic acid (*E*-94b)



***E*-94b**

Prepared from (*Z*)-Prenyl-9-oxooctadec-7-enoate ***Z*-104b** (1.00 equiv, 439 µmol, 160 mg) and TMSOTf (0.03 equiv, 13.20 µmol, 2.38 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a white solid (92 mg, 71%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc). Analytical data are in accordance with the literature.[138]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (dt, *J* = 15.8, 7.0 Hz, 1H), 6.09 (dq, *J* = 15.9, 1.5 Hz, 1H), 2.52 (t, *J* = 7.5 Hz, 2H), 2.36 (t, *J* = 7.4 Hz, 2H), 2.22 (qd, *J* = 7.1, 1.5 Hz, 2H), 1.70 – 1.25 (m, 20H), 0.83 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 201.2, 179.0, 146.8, 130.6, 40.3, 33.8, 32.3, 32.0, 29.5, 29.4, 29.4, 28.6, 27.8, 24.5, 24.4, 22.8, 14.2.

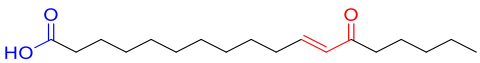
IR (ATR ν in cm^{-1}): 3026 (w), 2920 (s), 2849 (m), 1698 (s), 1674 (s), 1657 (m), 1471 (m), 1411 (w), 1378 (w), 1309 (w), 1272 (w), 1232 (m), 1176 (m), 1099 (w), 992 (w), 916 (w), 718 (w), 682 (w), 520 (w).

MS (APCI): m/z calcd for $C_{18}H_{33}O_3$ 297.2 $[M+H]^+$, found 297.2 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{18}H_{32}O_3$ 296.2351 $[M]^+$, found 296.2365 $[M]^+$**.**

Elm Anal. Calcd for $C_{18}H_{32}O_3$ C: 72.93%, H: 10.88; found C: 72.72%, H: 11.06%.

***(E)*-13-Oxooctadec-11-enoic acid (*E*-94c)**



***E*-94c**

Prepared from *(Z)*-prenyl 13-oxooctadec-11-enoate ***Z*-104c** (1.00 equiv, 439 µmol, 160 mg) and TMSOTf (0.03 equiv, 13.20 µmol, 2.38 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a white solid (78 mg, 60%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc). Analytical data are in accordance with the literature.[139, 140]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (dt, *J* = 15.9, 6.9 Hz, 1H), 6.08 (dt, *J* = 15.8, 1.6 Hz, 1H), 2.52 (t, *J* = 7.5 Hz, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.20 (qd, *J* = 7.1, 1.5 Hz, 2H), 1.62 (qd, *J* = 7.2, 2.3 Hz, 4H), 1.48 – 1.41 (m, 2H), 1.31 – 1.25 (m, 14H), 0.89 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 201.3, 179.4, 147.5, 130.4, 40.2, 34.1, 32.5, 31.6, 29.4, 29.3, 29.2, 29.2, 29.1, 28.2, 24.7, 24.1, 22.6, 14.1.

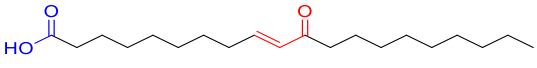
IR (ATR ν in cm^{-1}): 3026 (w), 2925 (s), 2854 (m), 1735 (s), 1712 (s), 1624 (m), 1541 (w), 1457 (w), 1438 (w), 1419 (w), 1364 (m), 1218 (m), 1092 (w), 979 (w), 725 (w), 529 (w).

MS (APCI): m/z calcd for $C_{18}H_{33}O_3$ 297.2 $[M+H]^+$, found 297.2 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{18}H_{32}O_3$ 296.2351 $[M]^+$, found 296.2417 $[M]^+$**.**

Elm Anal. Calcd for $C_{18}H_{32}O_3$ C: 72.93%, H: 10.88; found C: 72.68%, H: 10.59%.

(*E*)-11-Oxoicos-9-enoic acid (*E*-94d)



***E*-94d**

Prepared from (*Z*)-Prenyl-11-oxoicos-9-enoate ***Z*-104d** (1.00 equiv, 637 µmol, 250 mg) and TMSOTf (0.03 equiv, 19.10 µmol, 3.46 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a white solid (120 mg, 58%). $\mathbf{R_f}$ = 0.30 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (dt, *J* = 15.9, 6.9 Hz, 1H), 6.08 (dt, *J* = 15.9, 1.5 Hz, 1H), 2.52 (t, *J* = 7.5 Hz, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.20 (qd, *J* = 7.0, 1.5 Hz, 2H), 1.61 (dt, *J* = 14.8, 7.2 Hz, 4H), 1.45 (p, *J* = 6.9 Hz, 2H), 1.29 (dd, *J* = 24.1, 6.0 Hz, 18H), 0.87 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 201.3, 179.5, 147.3, 130.4, 40.2, 34.0, 32.5, 32.0, 29.5, 29.4, 29.4, 29.1, 29.1, 29.0, 28.1, 24.7, 24.5, 22.8, 14.2.

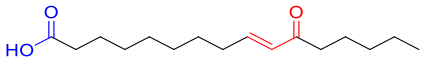
IR (ATR ν in cm^{-1}): 3026 (w), 2952 (w), 2910 (s), 2849 (m), 1694 (s), 1661 (s), 1645 (m), 1471 (m), 1425 (w), 1411 (w), 1382 (w), 1345 (w), 1325 (w), 1309 (w), 1275 (w), 1252 (w), 1231 (w), 1215 (w), 1175 (m), 1098 (w), 1071 (w), 993 (w), 979 (m), 911 (w), 888 (w), 848 (w), 716 (m), 702 (w), 683 (w), 523 (w).

MS (APCI): m/z calcd for $C_{20}H_{37}O_3$ 325.3 $[M+H]^+$, found 325.2 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{20}H_{36}O_3$ 324.2664 $[M]^+$, found 324.2678 $[M]^+$**.**

Elm Anal. Calcd for $C_{20}H_{36}O_3$ C: 74.03%, H: 11.18; found C: 73.98%, H: 11.12%.

(*E*)-11-Oxohexadec-9-enoic acid (*E*-94e)



***E*-94e**

Prepared from (*Z*)-Prenyl-11-oxohexadec-9-enoate ***Z*-104e** (1.00 equiv, 624 µmol, 210 mg) and TMSOTf (0.03 equiv, 18.70 µmol, 3.39 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a white solid (109 mg, 65%). $\mathbf{R_f}$ = 0.30 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc). Analytical data are in accordance with the literature.[137, 141]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (dt, *J* = 16.0, 6.9 Hz, 1H), 6.08 (dt, *J* = 15.9, 1.6 Hz, 1H), 2.51 (t, *J* = 7.5 Hz, 2H), 2.34 (td, *J* = 7.4, 1.9 Hz, 2H), 2.25 – 2.14 (m, 2H), 1.61 (dt, *J* = 14.8, 7.6 Hz, 4H), 1.44 (q, *J* = 7.0 Hz, 2H), 1.31 (qd, *J* = 8.1, 5.1 Hz, 10H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 201.3, 179.8, 147.4, 130.4, 40.2, 34.1, 32.5, 31.6, 29.1, 29.1, 29.0, 28.1, 24.7, 24.1, 22.6, 14.1.

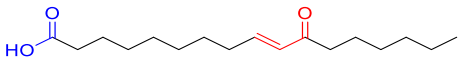
IR (ATR ν in cm^{-1}): 3026 (w), 2952 (w), 2922 (s), 2850 (m), 1695 (s), 1670 (s), 1654 (m), 1471 (m), 1457 (w), 1432 (w), 1412 (w), 1372 (w), 1319 (w), 1309 (w), 1276 (w), 1251 (m), 1231 (w), 1115 (w), 1099 (w), 999 (w), 978 (w), 942 (m), 860 (w), 793 (w), 722 (w), 700 (w), 683 (w), 515 (w).

MS (APCI): m/z calcd for $C_{16}H_{29}O_3$ 269.2 $[M+H]^+$, found 269.1 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{16}H_{28}O_3$ 268.2038 $[M]^+$, found 268.2054 $[M]^+$**.**

Elm Anal. Calcd for $C_{16}H_{28}O_3$ C: 71.60% H: 10.52; found C: 71.67%, H: 10.53%.

(*E*)-11-Oxoheptadec-9-enoic acid (*E*-94f)



***E*-94f**

Prepared from (*Z*)-Prenyl-11-oxoheptadec-9-enoate ***Z*-104f** (1.00 equiv, 200 µmol, 70.10 mg) and TMSOTf (0.03 equiv, 6.00 µmol, 1.09 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow solid (35 mg, 62%). $\mathbf{R_f}$ = 0.28 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (dt, *J* = 15.8, 6.9 Hz, 1H), 6.08 (d, *J* = 15.9 Hz, 1H), 2.52 (t, *J* = 7.5 Hz, 2H), 2.35 (t, *J* = 3.6 Hz, 2H), 2.20 (q, *J* = 7.4 Hz, 2H), 1.60 (dd, *J* = 14.8, 7.4 Hz, 4H), 1.45 (dd, *J* = 14.9, 8.4 Hz, 2H), 1.30 (dd, *J* = 14.6, 6.2 Hz, 12H), 0.88 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 200.8, 179.6, 147.8, 130.3, 39.8, 33.9, 32.6, 31.9, 29.4, 29.3, 29.3, 28.7, 28.2, 24.5, 23.9, 22.7, 14.2.

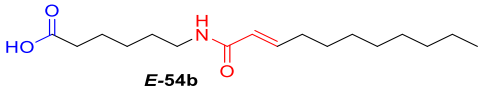
IR (ATR ν in cm^{-1}): 3026 (w), 2927 (s), 2856 (m), 1708 (s), 1674 (m), 1458 (w), 1411 (w), 1371 (w), 1216 (m), 978 (w), 935 (w), 725 (w).

MS (ESI): m/z calcd for $C_{17}H_{30}NaO_3$ 305.2 $[M+Na]^+$, found 305.1 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{30}O_3$ 282.2195 $[M]^+$, found 282.2207 $[M]^+$**.**

Elm Anal. Calcd for $C_{17}H_{30}O_3$ C: 72.30%, H: 10.71; found C: 72.71%, H: 10.59%.

(*E*)-6-(undec-2-enamido)hexanoic acid (*E*-54b)



***E*-54b**

Prepared from (*E*)-Prenyl-6-(undec-2-enamido)hexanoate ***E*-78b** (1.00 equiv, 274 µmol, 100 mg) and TMSOTf (0.10 equiv, 27.40 µmol, 4.96 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 95:5 → 50:50) afforded the desired analytically pure product as a white solid (72 mg, 88%). $\mathbf{R_f}$ = 0.22 (1:1 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (dt, *J* = 15.2, 7.0 Hz, 1H), 5.75 (dt, *J* = 15.2, 1.4 Hz, 1H), 5.66 (t, *J* = 5.0 Hz, 1H), 3.31 (dd, *J* = 13.2, 7.0 Hz, 2H), 2.35 (t, *J* = 7.3 Hz, 2H), 2.15 (td, *J* = 8.2, 1.3 Hz, 2H), 1.67 – 1.52 (m, 4H), 1.45 – 1.25 (m, 14H), 0.87 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.5, 166.5, 145.3, 123.4, 39.4, 33.9, 32.2, 31.9, 29.5, 29.3, 29.3, 29.3, 28.3, 26.4, 24.4, 22.7, 14.2.

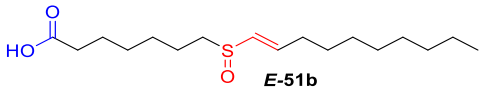
IR (ATR ν in cm^{-1}): 3298 (m), 3050 (w), 2920 (s), 2853 (m), 1697 (s), 1663 (w), 1614 (s), 1537 (s), 1467 (w), 1431 (w), 1353 (w), 1303 (w), 1256 (m), 1201 (m), 976 (m), 940 (m), 871 (w), 728 (w), 643 (m).

MS (ESI): m/z calcd for $C_{17}H_{31}NNaO_3$ 320.2 $[M+Na]^+$, found 320.1 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{31}NO_3$ 297.2304 $[M]^+$, found 297.2295 $[M]^+$.

Elm Anal. Calcd for $C_{17}H_{31}NO_3$ C: 68.65%, H: 10.51%, N: 4.71%; found C: 68.65%, H: 10.37%, N: 4.68%.

***(E)*-7-(dec-1-en-1-ylsulfinyl)heptanoic acid (*E*-51b)**



***E*-51b**

Prepared from Prenyl *(E)*-7-(dec-1-en-1-ylsulfinyl)heptanoate ***E*-79b** (1.00 equiv, 312 µmol, 120 mg), and $BF_3{\cdot}OEt_2$ (3.50 equiv, 1.09 mmol, 66.10 µL), according to **GP7**. Purification by flash column chromatography (*n*-hexane:Acetone = 19:1 → 9:1) afforded the desired analytically pure product as a white solid (49 mg, 49%). $\mathbf{R_f}$: 0.23 (7:3 *n*-hexane:Acetone).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.47 (dt, *J* = 15.1, 6.8 Hz, 1H), 6.20 (dt, *J* = 15.2, 1.3 Hz, 1H), 2.72 (qdd, *J* = 13.0, 8.6, 6.7 Hz, 2H), 2.33 (t, *J* = 7.4 Hz, 2H), 2.23 (td, *J* = 8.1, 1.2 Hz, 2H), 1.77 – 1.58 (m, 4H), 1.52 – 1.23 (m, 16H), 0.87 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.2, 142.5, 131.7, 53.7, 33.9, 32.2, 31.9, 29.4, 29.3, 29.2, 28.7, 28.5, 28.2, 24.5, 22.7, 22.1, 14.2.

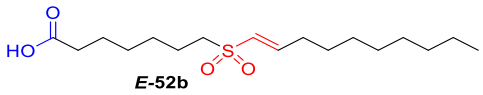
IR (ATR ν in cm^{-1}): 3054 (m), 2957 (m), 2854 (m), 1710 (s), 1640 (m), 1467 (w), 1444 (w), 1404 (m), 1338 (m), 1302 (5), 1265 (w), 1248 (w), 1226 (w), 1104 (w), 1068 (w), 995 (w), 960 (m), 923 (m), 864 (m), 725 (w).

MS (ESI) m/z calcd for $C_{17}H_{32}NaO_3S$ 339.1 $[M+Na]^+$, found 339.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{33}O_3S$ 316.2072 $[M+H]^+$, found 316.2077 $[M+H]^+$.

Elm Anal. Calcd for $C_{17}H_{32}O_3S$ C: 64.51, H: 10.19, S: 10.13; Found: C: 64.61, H: 10.10, S: 9.83.

***(E)*-7-(dec-1-en-1-ylsulfonyl)heptanoic acid (*E*-52b)**



***E*-52b**

Prepared from Prenyl *(E)*-7-(dec-1-en-1-ylsulfonyl)heptanoate ***E*-58b** (1.00 equiv, 374 µmol, 150 mg), and $BF_3{\cdot}OEt_2$ (3.50 equiv, 1.31 mmol, 79.30 µL), according to **GP7**. Purification by flash column chromatography (*n*-hexane:EtOAc+ 0.5 Vol% HOAc = 19:1 → 9:1) afforded the desired analytically pure product as a colorless solid (56 mg, 45%). $\mathbf{R_f}$: 0.31 (8:2 *n*-hexane:EtOAc+ 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95 – 6.87(m, 1H), 6.25 (d, *J* = 15.2 Hz, 1H), 2.98 – 2.91(m, 2H), 2.39 – 2.22 (m, 4H), 1.77 (dt, *J* = 15.6, 7.6 Hz, 2H), 1.69 – 1.59 (m, 2H), 1.52 – 1.25 (m, 16H), 0.87 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 179.5, 150.0, 127.8, 54.7, 33.8, 31.9, 31.7, 29.3, 29.2, 29.1, 28.5, 28.1, 27.7, 24.3, 22.7, 22.4, 14.2.

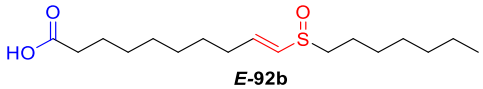
IR (ATR ν in cm^{-1}): 2955 (m), 2920 (m), 2869 (m), 1695 (s), 1649 (m), 1467 (w), 1433 (w), 1412 (m), 1325 (s), 1316 (s), 1274 (w), 1254 (w), 1231 (w), 1211 (w), 1116 (s), 1084 (w), 998 (w), 973 (m), 956 (m), 864 (m), 731 (w), 724 (w), 612 (m).

MS (ESI) m/z calcd for $C_{17}H_{32}NaO_4S$ 355.1 $[M+Na]^+$, found 355.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{33}O_4S$ 332.2021 $[M+H]^+$, found 332.2038 $[M+H]^+$.

Elm Anal. Calcd for $C_{17}H_{32}O_4S$ C: 61.41, H: 9.70, S: 9.64; Found C: 61.68, H: 9.70, S: 9.17.

(*E*)-10-(heptylsulfinyl)dec-9-enoic acid (*E*-92b)



***E*-92b**

Prepared from (*E*)-Prenyl-10-(heptylsulfinyl)dec-9-enoate ***E*-106b** (1.00 equiv, 260 µmol, 100 mg), and $BF_3{\cdot}OEt_2$ (3.50 equiv, 910 µmol, 115 µL), according to **GP7.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 50:50) afforded the desired analytically pure product as a yellow solid (46 mg, 55%). $\mathbf{R_f}$ = 0.28 (1:1 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 (dt, *J* = 15.1, 6.8 Hz, 1H), 6.22 (dd, *J* = 13.9, 1.3 Hz, 1H), 2.81 – 2.66 (m, 2H), 2.34 (dd, *J* = 15.4, 8.0 Hz, 2H), 2.24 (td, *J* = 8.0, 1.2 Hz, 2H), 1.75 – 1.59 (m, 4H), 1.50 – 1.26 (m, 16H), 0.88 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.1, 142.1, 132.1, 53.9, 34.0, 32.1, 31.6, 29.0, 29.0, 28.9, 28.8, 28.8, 28.1, 24.7, 22.6, 22.3, 14.1.

IR (ATR ν in cm^{-1}): 3029 (w), 2909 (s), 2847 (s), 1695 (s), 1635 (w), 1469 (m), 1429 (w), 1411 (w), 1377 (w), 1335 (w), 1309 (w), 1285 (w), 1266 (m), 1234 (m), 1218 (w), 1202 (w), 1186 (w), 1093 (w), 1078 (m), 1032 (m), 1023 (w), 985 (w), 961 (m), 926 (w), 903 (w), 792 (w), 719 (m), 680 (w), 526 (w).

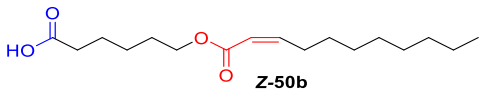
MS (ESI): m/z calcd for $C_{17}H_{32}NaO_3S$ 339.2 $[M+Na]^+$, found 339.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{32}O_3S$ 316.2072 $[M]^+$, found 316.2085 $[M]^+$.

Elm Anal. Calcd for $C_{17}H_{32}O_3S$ C: 64.51%, H: 10.19, S: 10.13%; found C: 64.48%, H: 9.92%, S: 10.08%.

6.5.3 Synthesis of *(Z)*-Alkenyl Fatty Acids

(*Z*)-6-(undec-2-enoyloxy)hexanoic acid (*Z*-50b)



***Z*-50b**

Prepared from (*Z*)-6-((Prenyl)oxy)-6-oxohexyl-undec-2-enoate ***Z*-76b** (1.00 equiv, 1.37 mmol, 501 mg), and TMSOTf (0.08 equiv, 110 µmol, 19.80 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 →90:10) afforded the desired analytically pure product as a white solid (353 mg, 86%). $\mathbf{R_f}$ = 0.29 (9:1 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.22 (dt, *J* = 11.5, 7.5 Hz, 1H), 5.74 (dt, *J* = 11.5, 1.7 Hz, 1H), 4.10 (t, *J* = 6.6 Hz, 2H), 2.63 (qd, *J* = 7.5, 1.7 Hz, 2H), 2.37 (t, *J* = 7.5 Hz, 2H), 1.73 – 1.61 (m, 4H), 1.48 – 1.23 (m, 14H), 0.87 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.6, 166.7, 151.0, 119.5, 63.7, 33.9, 31.9, 29.5, 29.4, 29.3, 29.2, 29.1, 28.4, 25.6, 24.4, 22.8, 14.2.

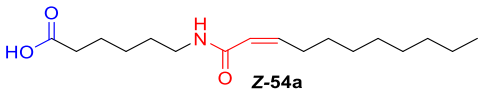
IR (ATR ν in cm^{-1}): 3037 (w), 2952 (w), 2922 (s), 2853 (m), 1704 (s), 1643 (m), 1474 (w), 1417 (m), 1351 (w), 1307 (w), 1254 (m), 1186 (s), 1111 (w), 1034 (w), 933 (w), 815 (m), 729 (w), 673 (w), 647 (w).

MS (ESI): m/z calcd for $C_{17}H_{30}NaO_4$ 321.4 $[M+Na]^+$, found 321.5 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{30}O_4$ 298.2144 $[M]^+$, found 298.2153 $[M]^+$.

Elm Anal. Calcd for $C_{17}H_{30}O_4$ C: 68.42%, H: 10.13%; found C: 68.75%, H: 9.94%.

***(Z)*-6-(undec-2-enamido)hexanoic acid (*Z*-54a)**



***Z*-54a**

Prepared from (*Z*)-Prenyl-6-(undec-2-enamido)hexanoate ***Z*-78a** (1.00 equiv, 399 µmol, 146 mg) and TMSOTf (0.10 equiv, 39.90 µmol, 7.22 µL), according to **GP6**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 95:5 → 50:50) afforded the desired analytically pure product as a white solid (110 mg, 93%). $\mathbf{R_f}$ = 0.28 (1:1 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96 (dt, *J* = 11.5, 7.4 Hz, 1H), 5.66 (dt, *J* = 11.5, 1.6 Hz, 1H), 5.61 (s, 1H), 3.28 (dd, *J* = 13.2, 7.0 Hz, 2H), 2.61 (qd, *J* = 7.5, 1.5 Hz, 2H), 2.35 (t, *J* = 7.4 Hz, 2H), 1.60 (ddt, *J* = 43.3, 14.7, 7.4 Hz, 4H), 1.45 – 1.23 (m, 14H), 0.86 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.9, 166.9, 145.9, 122.1, 39.1, 33.9, 31.9, 29.5, 29.4, 29.4, 29.4, 29.3, 28.9, 26.4, 24.3, 22.7, 14.2.

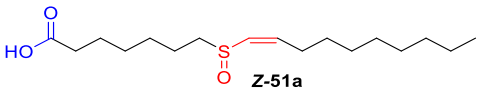
IR (ATR ν in cm^{-1}): 3283 (m), 3055 (w), 2950 (w), 2919 (s), 2851 (m), 1692 (s), 1658 (m), 1623 (s), 1539 (s), 1461 (w), 1430 (m), 1325 (w), 1276 (w), 1236 (m), 1200 (w), 931 (m), 813 (w), 724 (w), 677 (m).

MS (ESI): m/z calcd for $C_{17}H_{31}NNaO_3$ 320.2 $[M+Na]^+$, found 320.1 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{31}NO_3$ 297.2304 $[M]^+$, found 297.2295 $[M]^+$.

Elm Anal. Calcd for $C_{17}H_{31}NO_3$ C: 68.65%, H: 10.51%, N: 4.71%; found C: 68.58%, H: 10.51%, N: 4.70%.

(*Z*)-7-(dec-1-en-1-ylsulfinyl)heptanoic acid (*Z*-51a)



***Z*-51a**

Prepared from Prenyl *(Z)*-7-(dec-1-en-1-ylsulfinyl)heptanoate ***Z*-79a** (1.00 equiv, 263 µmol, 101 mg), and $BF_3{\cdot}OEt_2$ (3.50 equiv, 921 µmol, 55.70 µL), according to **GP7**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 9:1 → 7:3) afforded the desired analytically pure product as a colorless liquid (52 mg, 62%). $\mathbf{R_f}$: 0.15 (1:1 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.26 – 6.18 (m, 2H), 2.93 – 2.60 (m, 2H), 1.77 – 1.58 (m, 4H), 1.47 – 1.25 (m, 4H), 1.76 – 1.59 (m, 4H), 1.55 – 1.24 (m, 16H), 0.87 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 178.0, 143.8, 134.0, 53.7, 33.9, 31.9, 29.6, 29.4, 29.2, 29.2, 29.1, 28.7, 28.5, 24.5, 22.7, 22.3, 14.2.

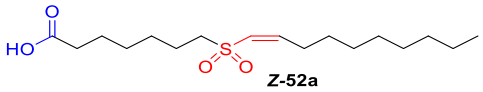
IR (ATR ν in cm^{-1}): 2923 (m), 2854 (m), 2361 (w), 1719 (s), 1621 (w), 1459 (w), 1406 (w), 1377 (m), 1245 (w), 1196 (w), 1120 (w), 997 (s), 808 (m), 724 (w).

MS (ESI) m/z calcd for $C_{17}H_{32}NaO_3S$ 339.2 $[M+Na]^+$, found 339.3 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{33}O_3S$ 316.2072 $[M+H]^+$, found 316.2081 $[M+H]^+$.

Elm Anal. Calcd for $C_{17}H_{32}O_3S$ C: 64.51, H: 10.19, S: 10.13; Found C: 64.61, H: 10.16, S: 9.82.

(*Z*)-7-(dec-1-en-1-ylsulfonyl)heptanoic acid (*Z*-52a)



***Z*-52a**

Prepared from Prenyl *(Z)*-7-(dec-1-en-1-ylsulfonyl)heptanoate ***Z*-58a** (1.00 equiv, 320 µmol, 128 mg), and $BF_3{\cdot}OEt_2$ (3.50 equiv, 1.12 mmol, 67.80 µL) according to **GP7**. Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 19:1 → 9:1) afforded the desired analytically pure product as a colorless liquid (50 mg, 47%). $\mathbf{R_f}$: 0.22 (7:3 *n*-hexane:EtOAc+ 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.39 (dt, *J* = 11.2, 7.9 Hz, 1H), 6.14 (dt, *J* = 11.2, 1.4 Hz, 1H), 3.00 – 2.91(m, 2H), 2.69 – 2.59 (m, 2H), 2.35 (t, *J* = 7.4 Hz, 2H), 1.81 (dt, *J* = 11.3, 7.6 Hz, 2H), 1.69 – 1.59 (m, 2H), 1.50 – 1.24 (m, 16H), 0.87 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 179.7, 149.7, 127.8, 55.6, 33.9, 31.9, 29.4, 29.3, 29.2, 29.0, 28.6, 28.2, 28.0, 24.3, 22.7, 22.2, 14.2.

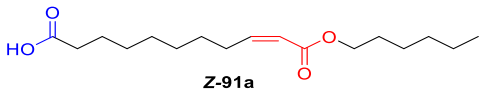
IR (ATR ν in cm^{-1}): 3060 (w), 2952 (m), 2870 (m), 1690(s), 1625 (m), 1469 (w), 1427 (w), 1412 (m), 1308 (s), 1287 (w), 1270 (w), 1228 (w), 1194 (w), 1113 (s), 1086 (w), 1071 (w), 960 (m), 931 (m), 864 (m), 820 (w), 720 (w), 621 (m).

MS (ESI) m/z calcd for $C_{17}H_{32}NaO_4S$ 355.1 $[M+Na]^+$, found 355.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{33}O_4S$ 332.2021 $[M+H]^+$, found 332.2013 $[M+H]^+$.

Elm Anal. Calcd for $C_{17}H_{32}O_4S$ C: 61.41, H: 9.70, S: 9.64; Found C: 61.79, H: 9.89, S: 9.13.

***(Z)*-11-(hexyloxy)-11-oxoundec-9-enoic acid (*Z*-91a)**



***Z*-91a**

Prepared from (*Z*)-1-hexyl-11-(Prenyl)-undec-2-enedioate ***Z*-105a** (1.00 equiv, 273 µmol, 100 mg), and TMSOTf (0.08 equiv, 21.80 µmol, 3.95 µL), according to **GP6.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 80:20) afforded the desired analytically pure product as a yellow oil (120 mg, 51%). $\mathbf{R_f}$ = 0.34 (8:2 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 (dt, *J* = 11.5, 7.5 Hz, 1H), 5.75 (dd, *J* = 11.5, 1.5 Hz, 1H), 4.10 (t, *J* = 6.7 Hz, 2H), 2.63 (q, *J* = 7.4 Hz, 2H), 2.33 (q, *J* = 7.4 Hz, 2H), 1.69 – 1.59 (m, 4H), 1.47 – 1.28 (m, 14H), 0.88 (t, *J* = 6.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.9, 166.8, 150.5, 119.8, 64.2, 34.1, 31.5, 29.2, 29.1, 29.1, 29.1, 28.7, 25.8, 24.7, 22.6, 14.1.

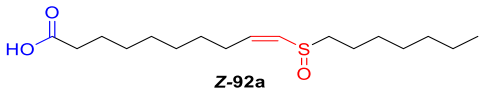
IR (ATR ν in cm^{-1}): 3026 (w), 2926 (s), 2856 (m), 1708 (s), 1644 (w), 1458 (w), 1415 (w), 1379 (w), 1284 (w), 1172 (s), 993 (w), 935 (w), 818 (w), 725 (w).

MS (APCI): m/z calcd for $C_{17}H_{31}O_4$ 299.4 $[M+H]^+$, found 299.5 $[M+H]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{30}O_4$ 298.2144 $[M]^+$, found 298.2155 $[M]^+$.

Elm Anal. Calcd for $C_{17}H_{30}O_4$ C: 68.42%, H: 10.13; found C: 68.48%, H: 10.04%.

(*Z*)-10-(heptylsulfinyl)dec-9-enoic acid (*Z*-92a)



***Z*-92a**

Prepared from (*Z*)-Prenyl-10-(heptylsulfinyl)dec-9-enoate ***Z*-106a** (1.00 equiv, 442 µmol, 170 mg), and $BF_3{\cdot}OEt_2$ (3.50 equiv, 1.55 mmol, 195 µL), according to **GP7.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 50:50) afforded the desired analytically pure product as a yellow oil (75 mg, 54%). $\mathbf{R_f}$ = 0.28 (1:1 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.26 – 6.18 (m, 2H), 2.95 – 2.85 (m, 1H), 2.71 – 2.60 (m, 1H), 2.48 – 2.26 (m, 4H), 1.71 – 1.59 (m, 4H), 1.48 – 1.28 (m, 16H), 0.87 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.3, 143.7, 134.1, 53.8, 34.1, 31.6, 29.5, 29.0, 28.9, 28.8, 28.8, 24.7, 22.6, 22.5, 14.1.

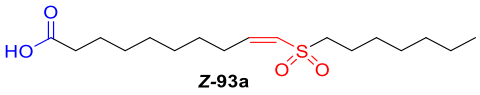
IR (ATR ν in cm^{-1}): 3026 (w), 2926 (s), 2854 (m), 1714 (s), 1622 (w), 1458 (w), 1362 (w), 1218 (m), 1129 (w), 1089 (w), 991 (s), 723 (m), 529 (w).

MS (ESI): m/z calcd for $C_{17}H_{32}NaSO_3$ 339.2 $[M+Na]^+$, found 339.2 $[M+Na]^+$.

HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{32}O_3S$ 316.2072 $[M]^+$, found 316.2083 $[M]^+$.

Elm Anal. Calcd for $C_{17}H_{32}O_3S$ C: 64.51%, H: 10.19, S: 10.13%; found C: 64.91%, H: 10.20%, S: 9.92%.

***(Z)*-10-(heptylsulfonyl)dec-9-enoic acid (*Z*-93a)**



Z-93a

To a solution of Prenyl 10-(heptylsulfonyl)dec-9-ynoate **89a** (1.00 equiv, 1.00 mmol, 400 mg) in dry toluene (0.05 M), Pd on $BaSO_4$ (0.15 equiv, 150 µmol, 51 mg) was added and a balloon filled with H_2 gas was applied. The reaction mixture was allowed to stir for 24 h at ambient temperature. After removal of the solvent under reduced pressure, DCM (5 ml) was added to the residue, filtrated, and then evacuated. The crude product was carried on directly to the next step and treated with $BF_3{\cdot}OEt_2$ (3.50 equiv, 1.57 mmol, 200 µL), according to **GP7.** Purification by flash column chromatography (*n*-hexane:EtOAc + 0.5 Vol% HOAc = 97:3 → 70:30) afforded the desired analytically pure product as a yellow solid (65 mg, 44%). $\mathbf{R_f}$ = 0.38 (7:3 *n*-hexane:EtOAc + 0.5 Vol% HOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.37 (dt, *J* = 11.1, 7.9 Hz, 1H), 6.14 (d, *J* = 11.2 Hz, 1H), 2.99 – 2.92 (m, 2H), 2.63 (q, *J* = 7.2 Hz, 2H), 2.33 (t, *J* = 7.4 Hz, 2H), 1.83 – 1.75 (m, 2H), 1.65 – 1.58 (m, 2H), 1.38 (ddd, *J* = 45.2, 16.9, 8.0 Hz, 16H), 0.87 (t, *J* = 6.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 179.7, 149.2, 127.9, 55.8, 34.1, 31.5, 29.1, 29.0, 28.9, 28.8, 28.8, 28.4, 27.9, 24.6, 22.6, 22.4, 14.1.

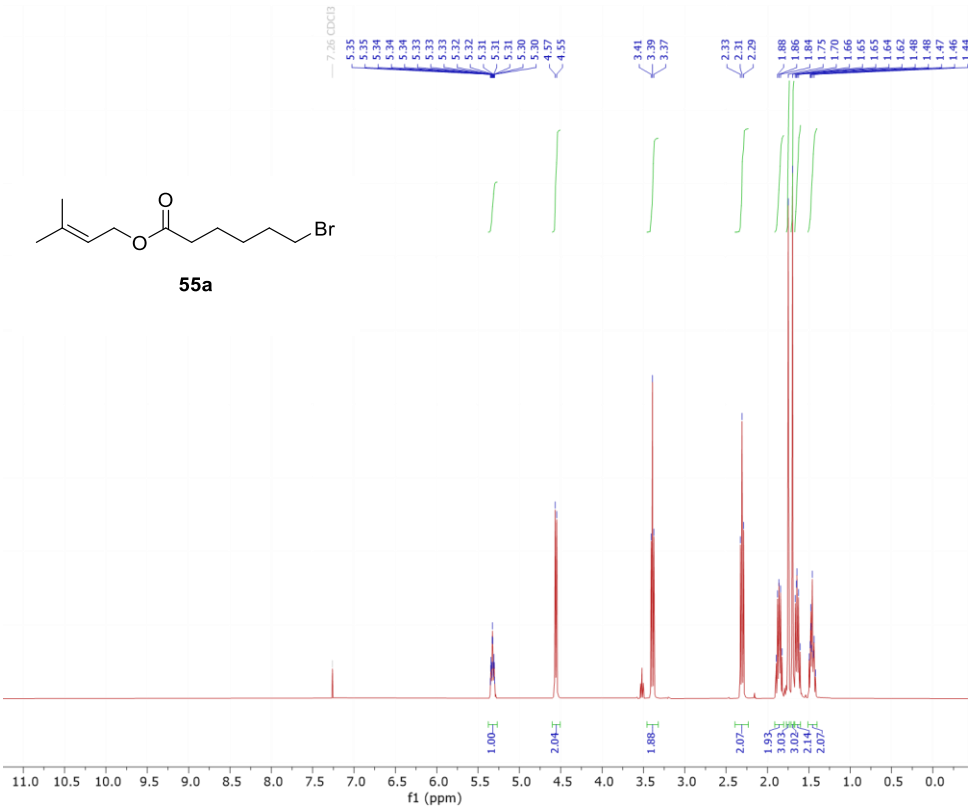
IR (ATR ν in cm^{-1}): 3057 (w), 2952 (w), 2917 (s), 2849 (m), 1691 (s), 1621 (w), 1468 (m), 1425 (w), 1409 (m), 1315 (m), 1285 (s), 1256 (m), 1215 (m), 1115 (s), 948 (w), 905 (w), 830 (m), 816 (w), 792 (w), 763 (w), 679 (w), 662 (m), 613 (m), 543 (w), 522 (w).

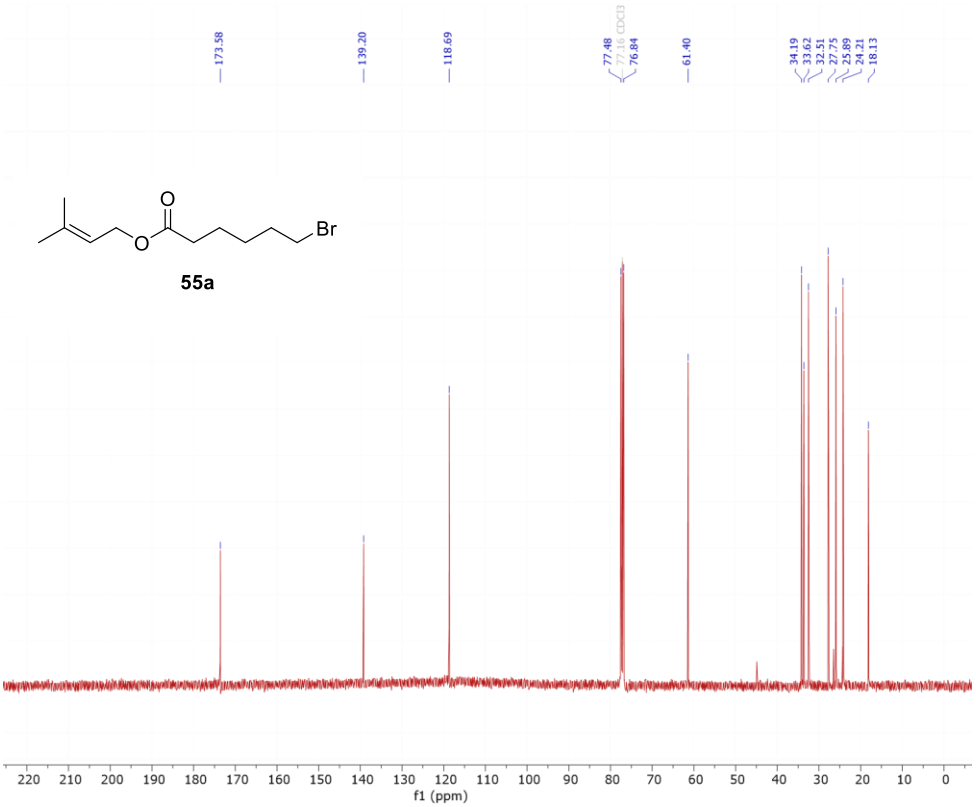
MS (APCI): m/z calcd for $C_{17}H_{33}O_4S$ 333.5 $[M+H]^+$, found 333.6 $[M+H]^+$.

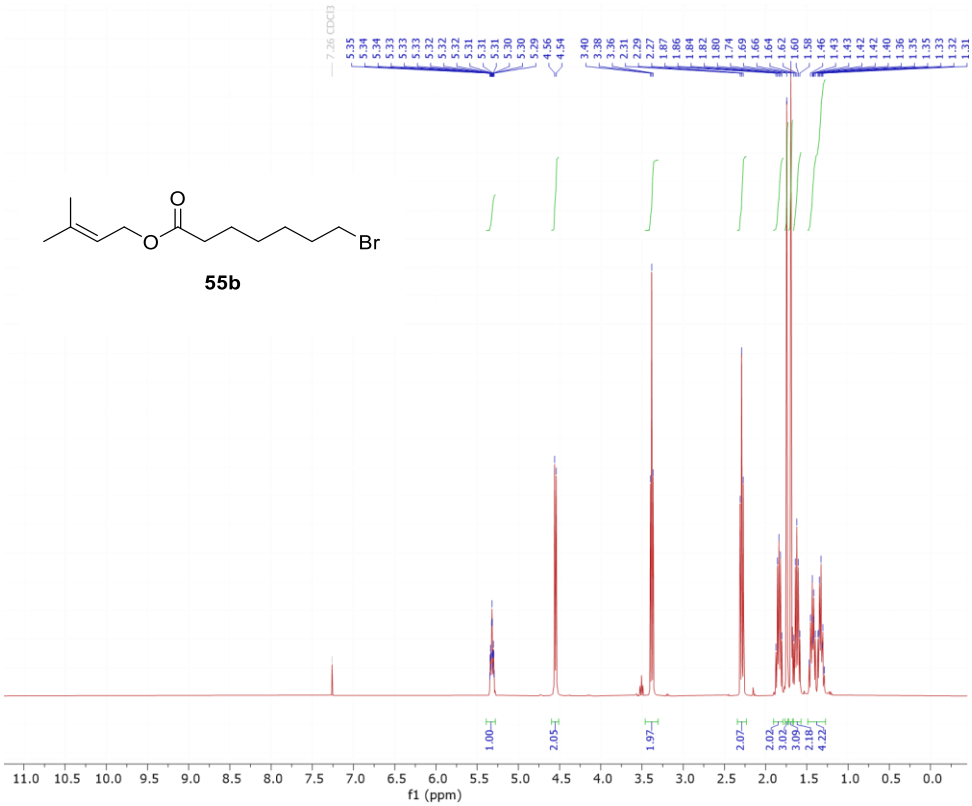
HRMS (TOF MS EI+): m/z calcd for $C_{17}H_{32}O_4S$ 332.2021 $[M]^+$, found 332.2040 $[M]^+$**.**

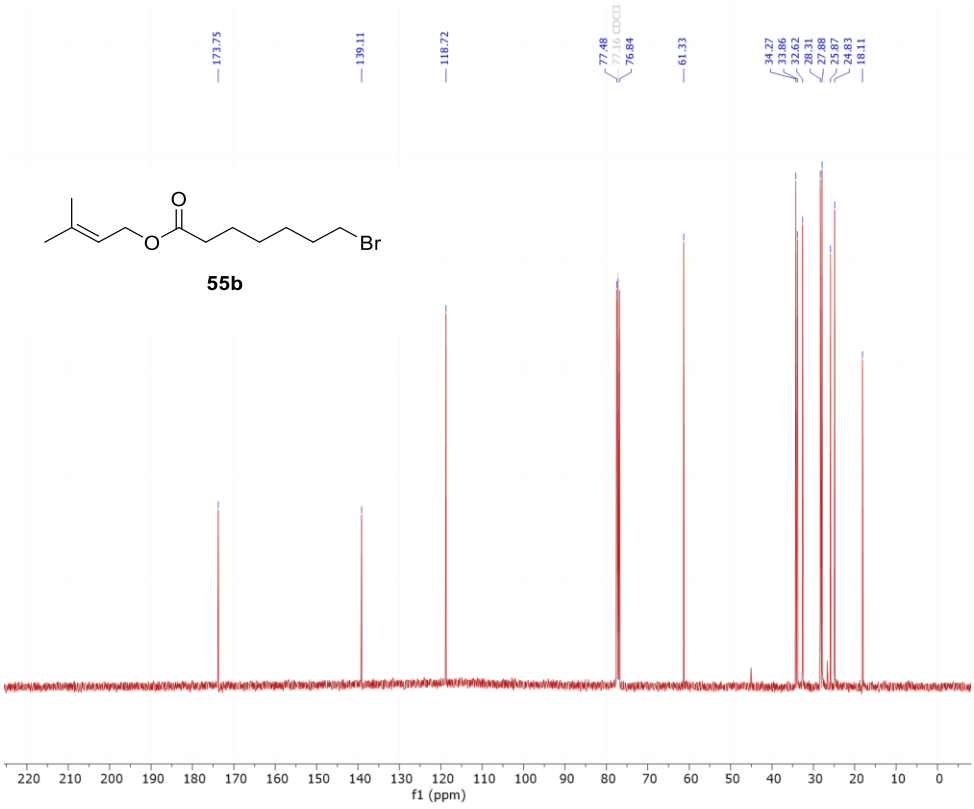
Elm Anal. Calcd for $C_{17}H_{32}O_4S$ C: 61.41%, H: 9.70, S: 9.64%; found C: 61.49%, H: 9.90%, S: 8.99%.

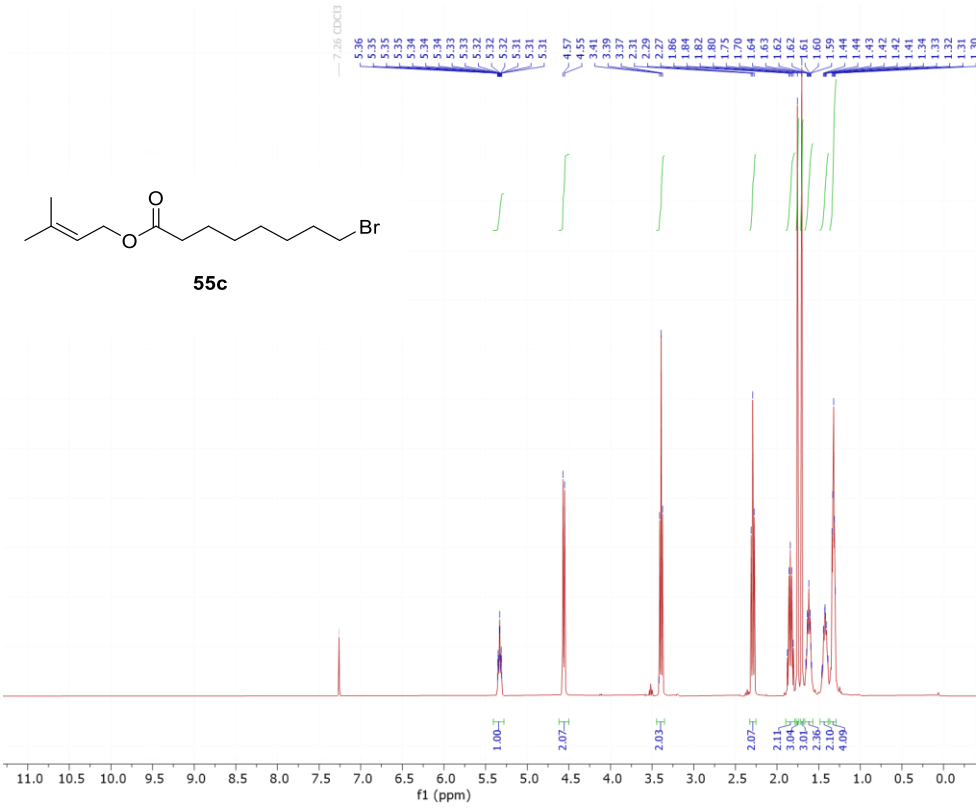
6.6 ^{1}H and ^{13}C NMR Spectra

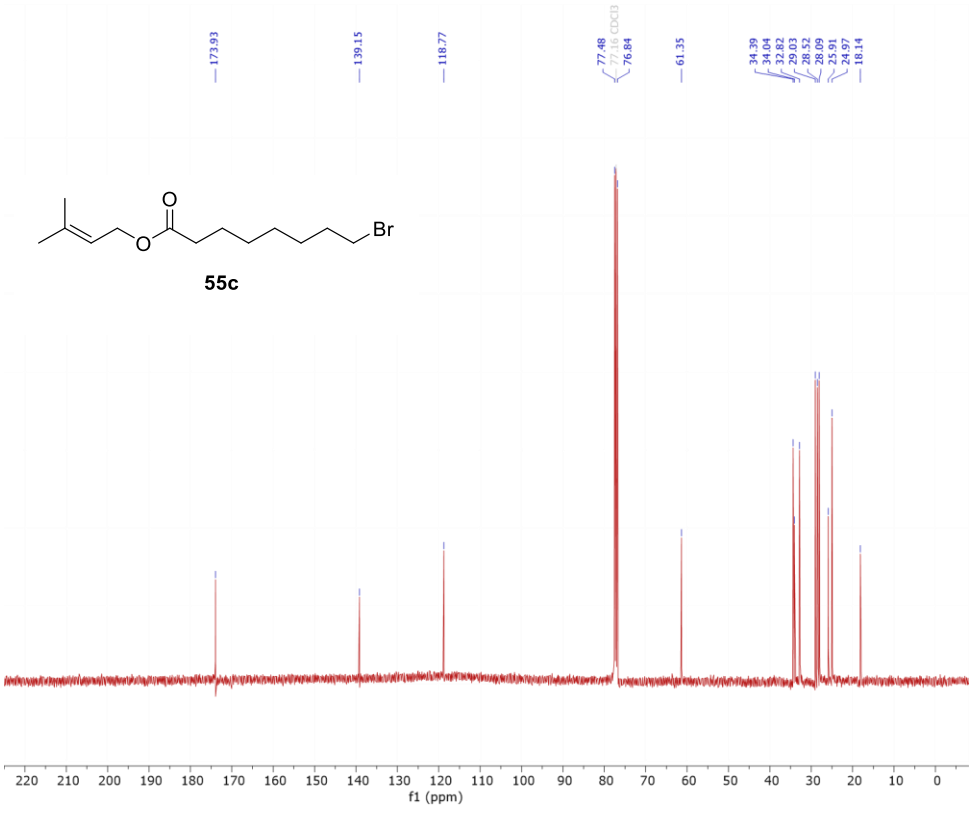


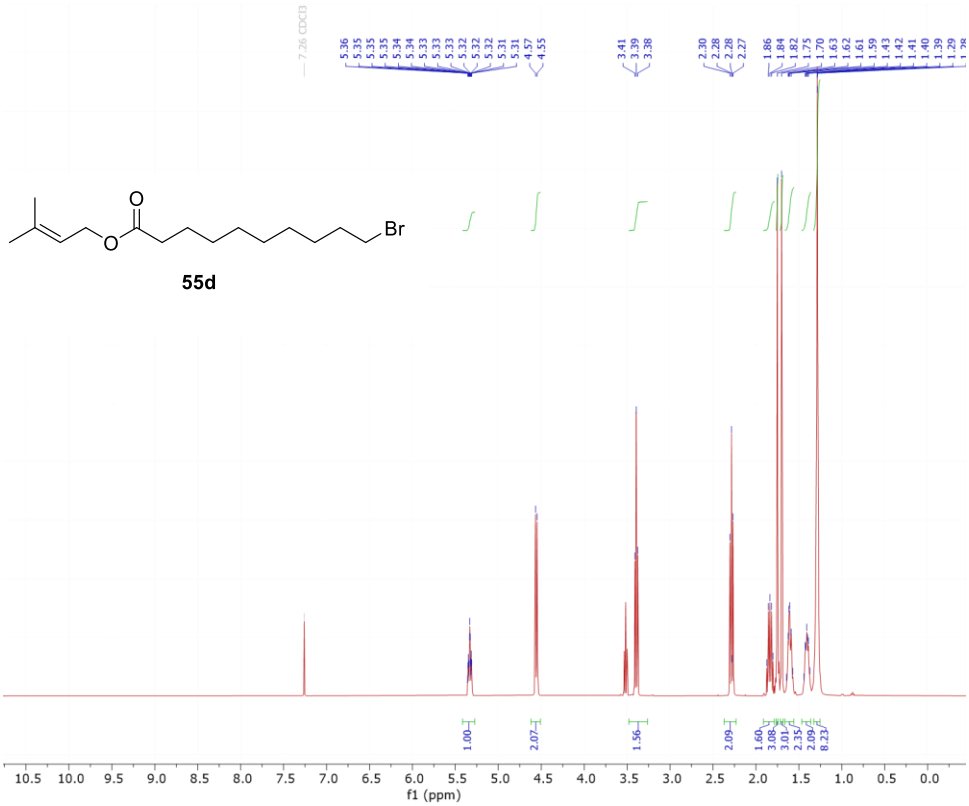


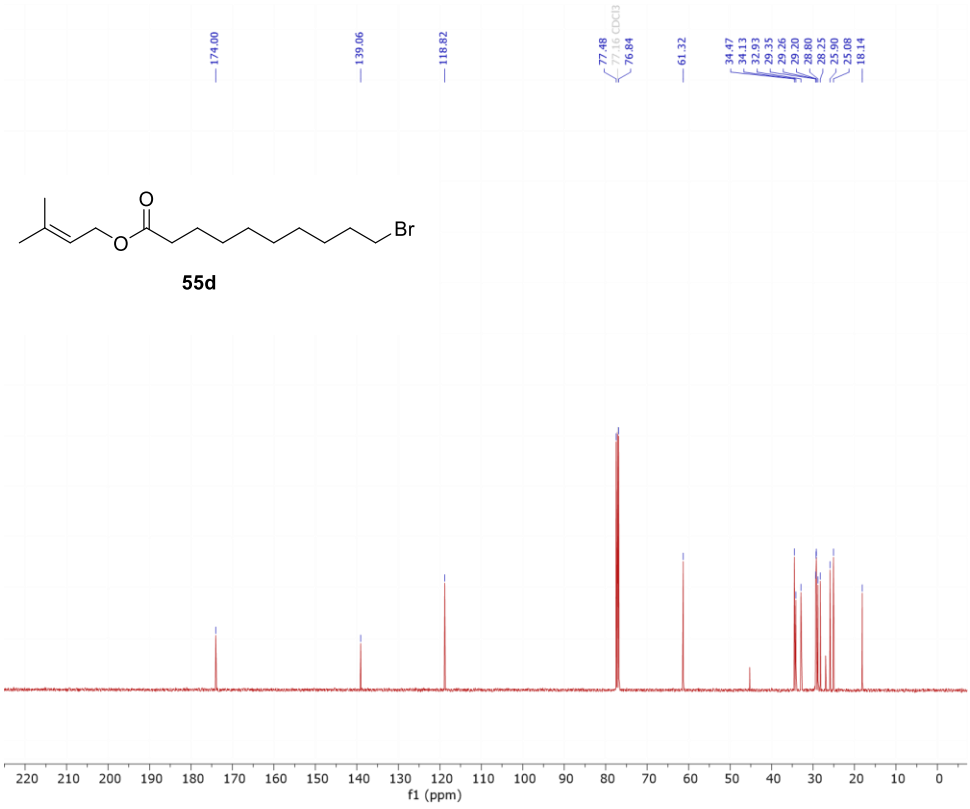

7.26 CDCl3
5.35 5.34 5.34 5.33 5.33 5.32 5.32 5.32 5.31 5.31 5.31 5.30 5.30 5.29 4.56 4.54
3.40 3.38 3.36 2.31 2.29 2.27 1.87 1.86 1.84 1.82 1.80 1.74 1.69 1.66 1.64 1.62 1.60 1.58 1.46 1.43 1.43 1.42 1.42 1.40 1.36 1.35 1.35 1.33 1.32 1.31
O
O
Br
55b
1.00 2.05 1.97 2.07 2.02 3.02 3.09 2.18 4.22
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

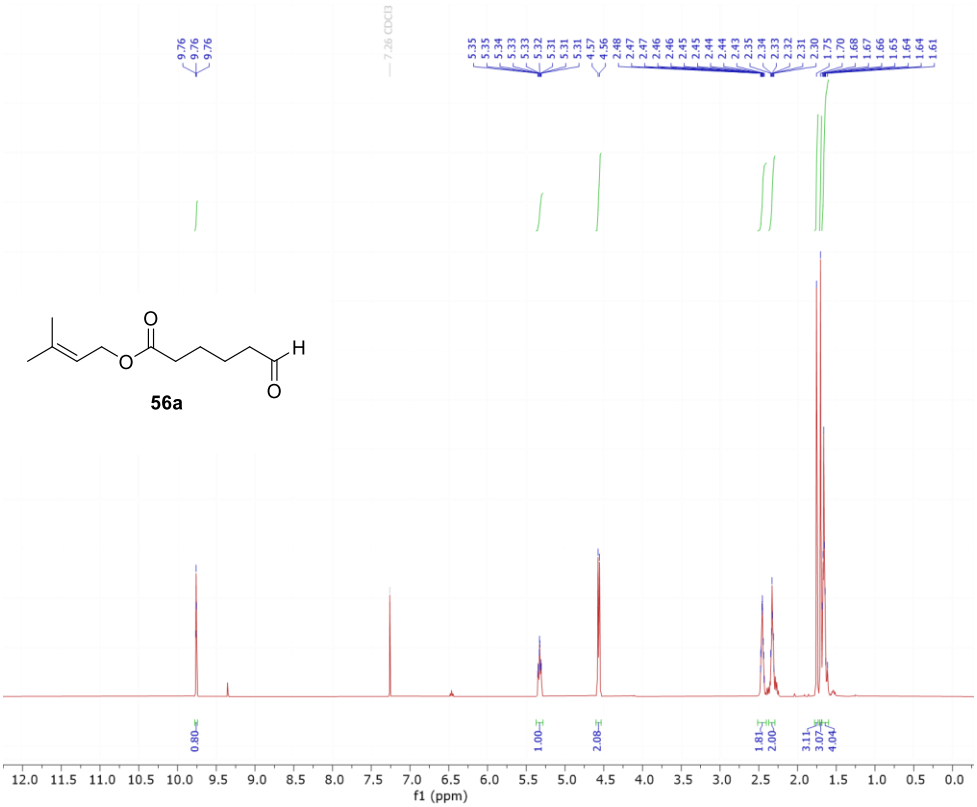

173.75
139.11
118.72
77.48
77.16 CDCl3
76.84
61.33
34.27
33.86
32.62
28.31
27.88
25.87
24.83
18.11
O
O
Br
55b
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

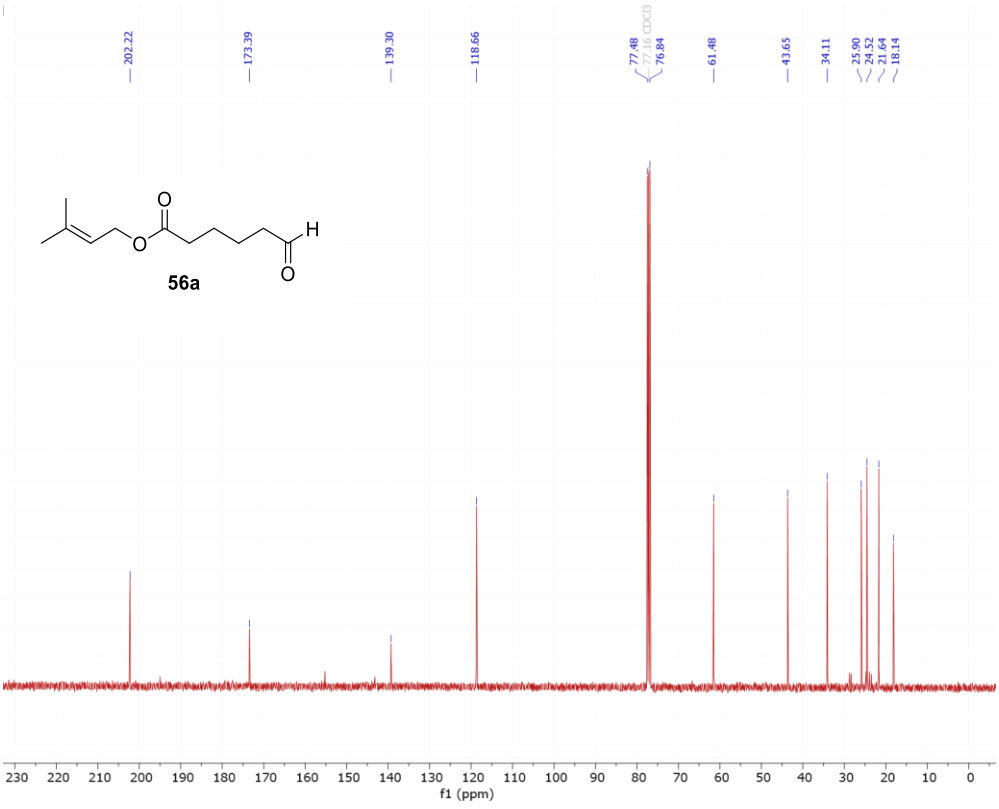

O
O
Br
55c
f1 (ppm)

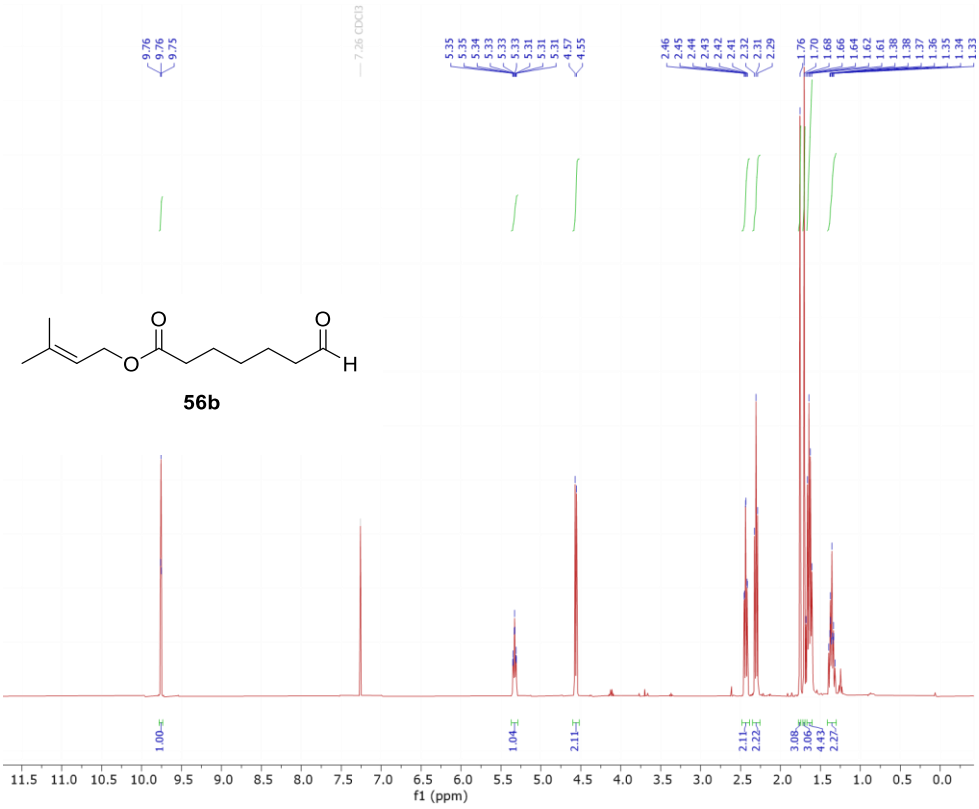

O
O
Br
55c
f1 (ppm)

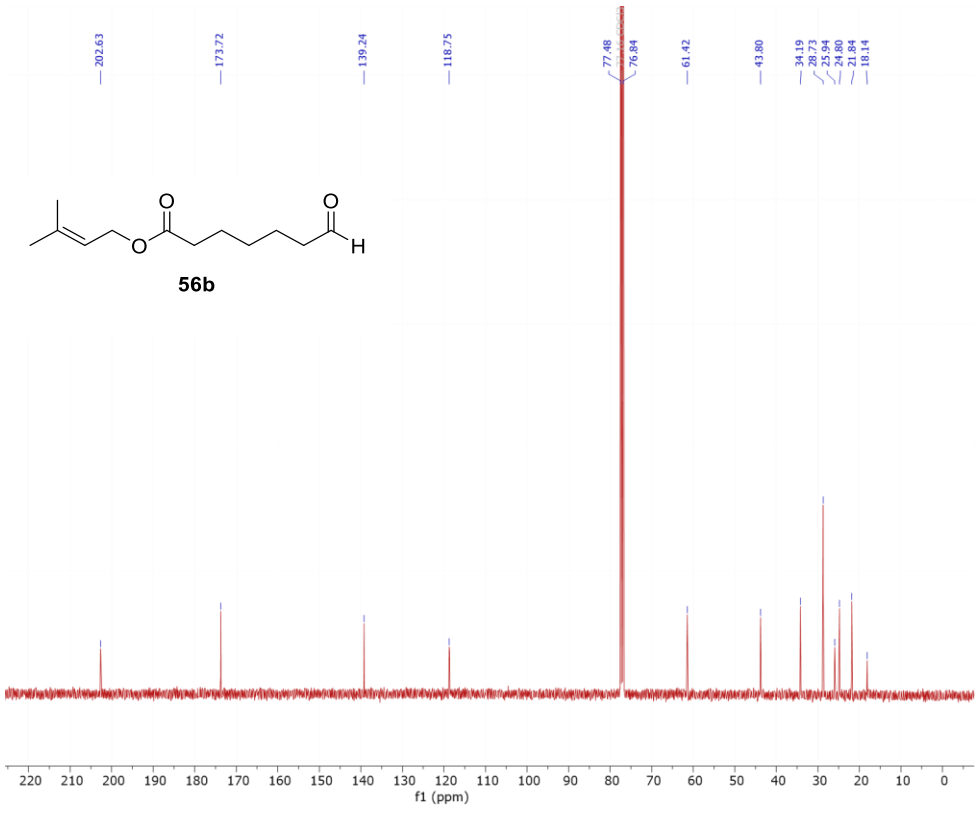

Br
55d
f1 (ppm)

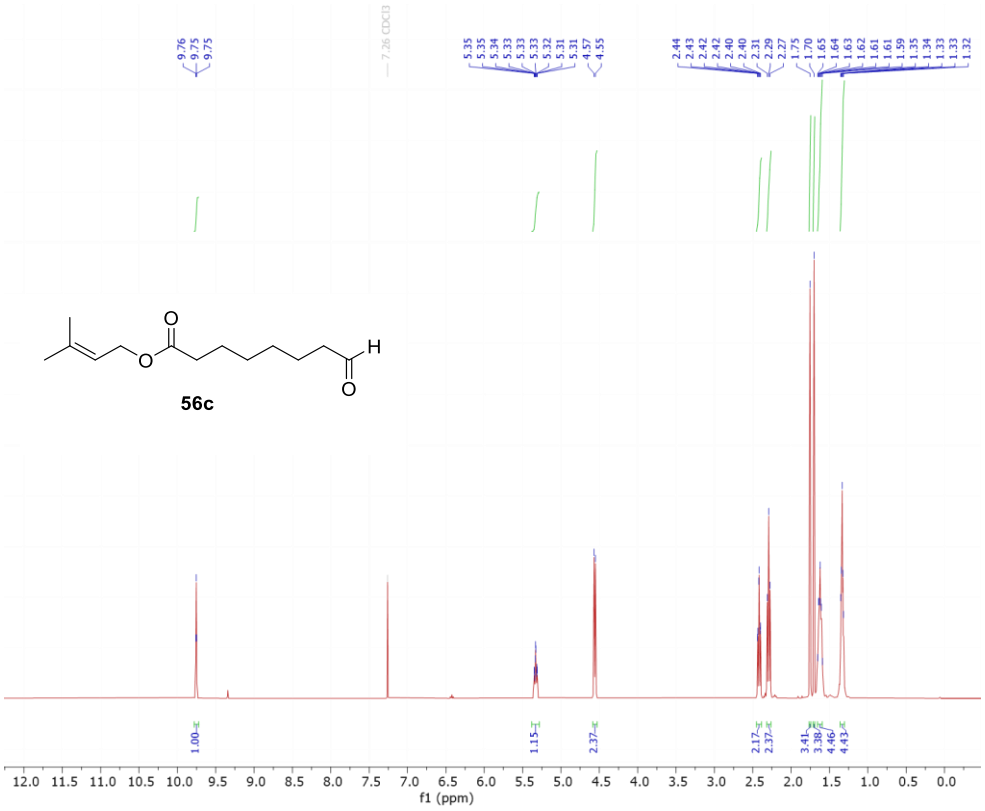

Br
55d
f1 (ppm)

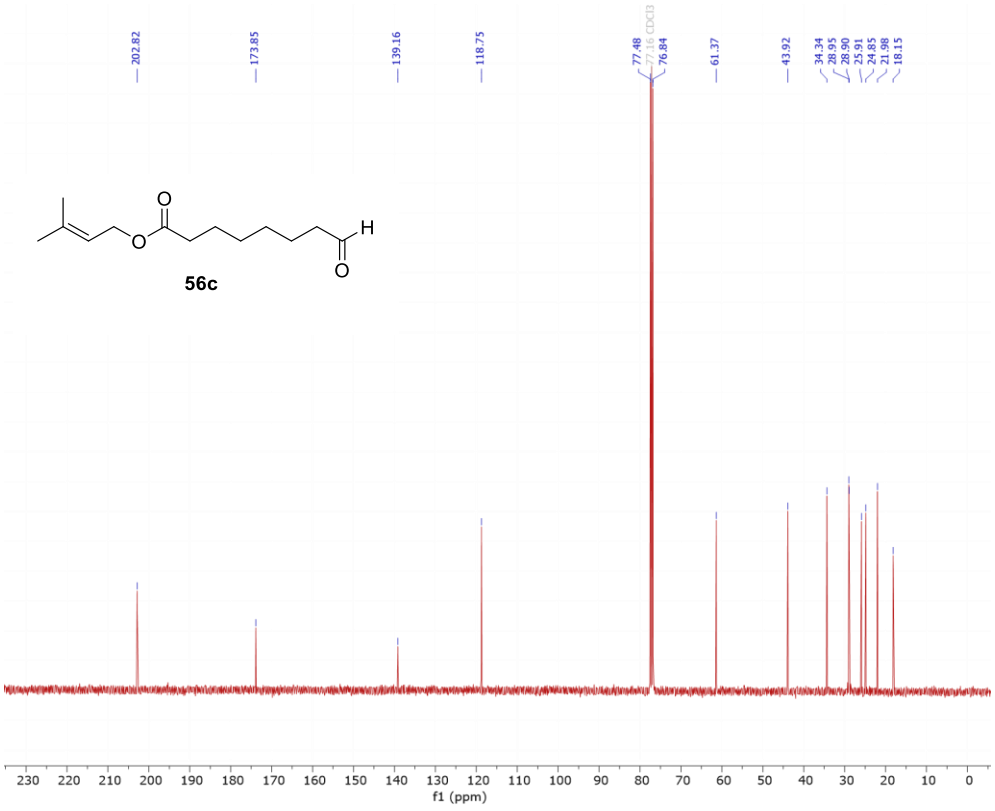

9.76
9.76
9.76
7.26 CDCl3
5.35
5.35
5.34
5.34
5.33
5.33
5.32
5.31
5.31
5.31
4.57
4.56
2.48
2.47
2.47
2.46
2.46
2.45
2.45
2.44
2.44
2.43
2.35
2.34
2.33
2.32
2.31
2.30
1.75
1.70
1.68
1.67
1.66
1.65
1.64
1.64
1.61
O
O
H
O
56a
0.80
1.00
2.08
1.81
2.00
3.11
3.07
4.04
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

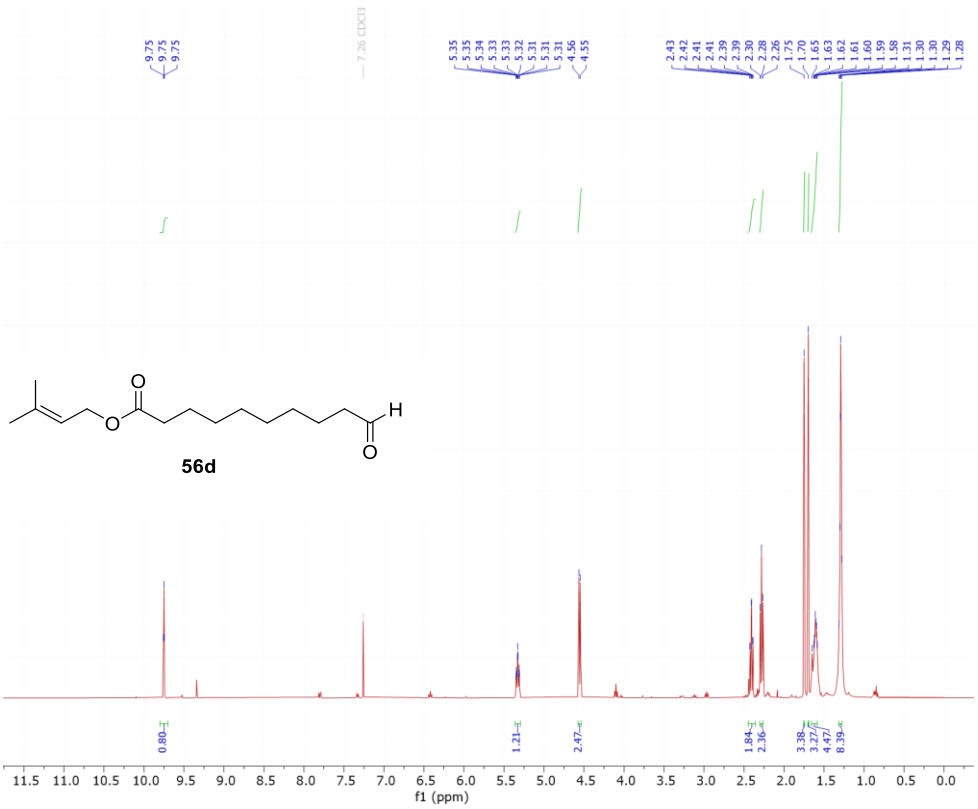

202.22
173.39
139.30
118.66
77.48
77.16 CDCl3
76.84
61.48
43.65
34.11
25.90
24.52
21.64
18.14
O
O
H
O
56a
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

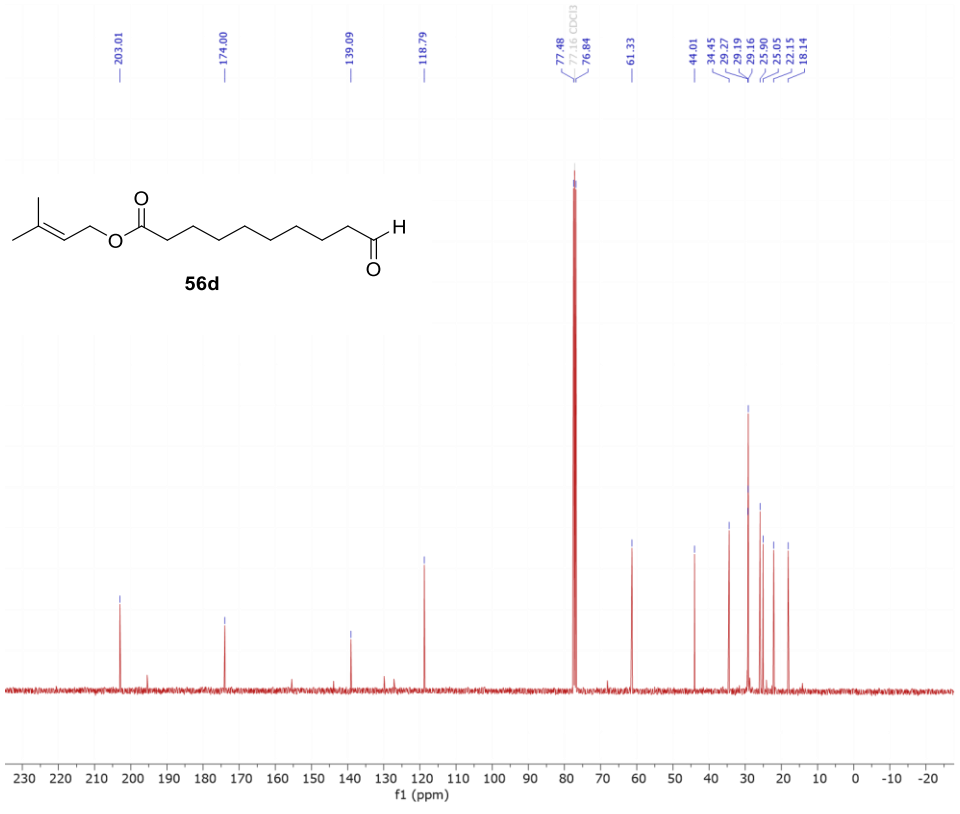

9.76
9.76
9.75
7.26 CDCl3
5.35
5.35
5.34
5.33
5.33
5.31
5.31
5.31
4.57
4.55
2.46
2.45
2.44
2.43
2.42
2.41
2.32
2.31
2.29
1.76
1.70
1.68
1.66
1.64
1.62
1.61
1.38
1.38
1.37
1.36
1.35
1.34
1.33
O
O
O
H
56b
1.00
1.04
2.11
2.11
2.23
3.08
3.06
4.43
2.27
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

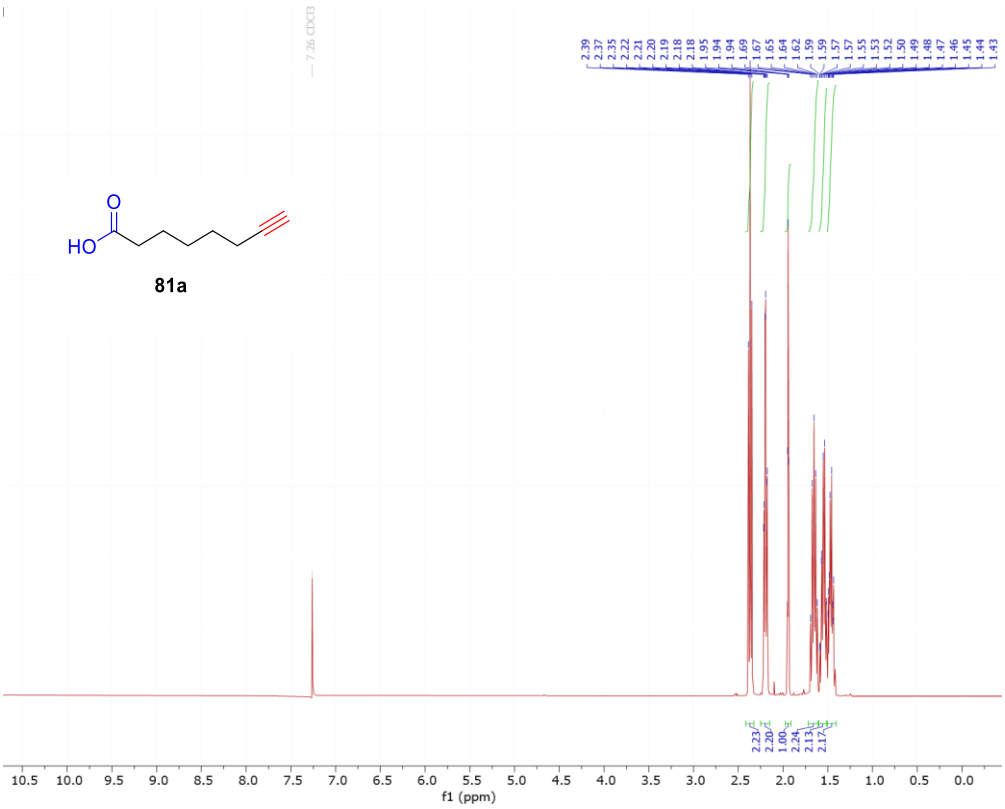

202.63
173.72
139.24
118.75
77.48
76.84
61.42
43.80
34.19
28.73
25.94
24.80
21.84
18.14
O
O
O
H
56b
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

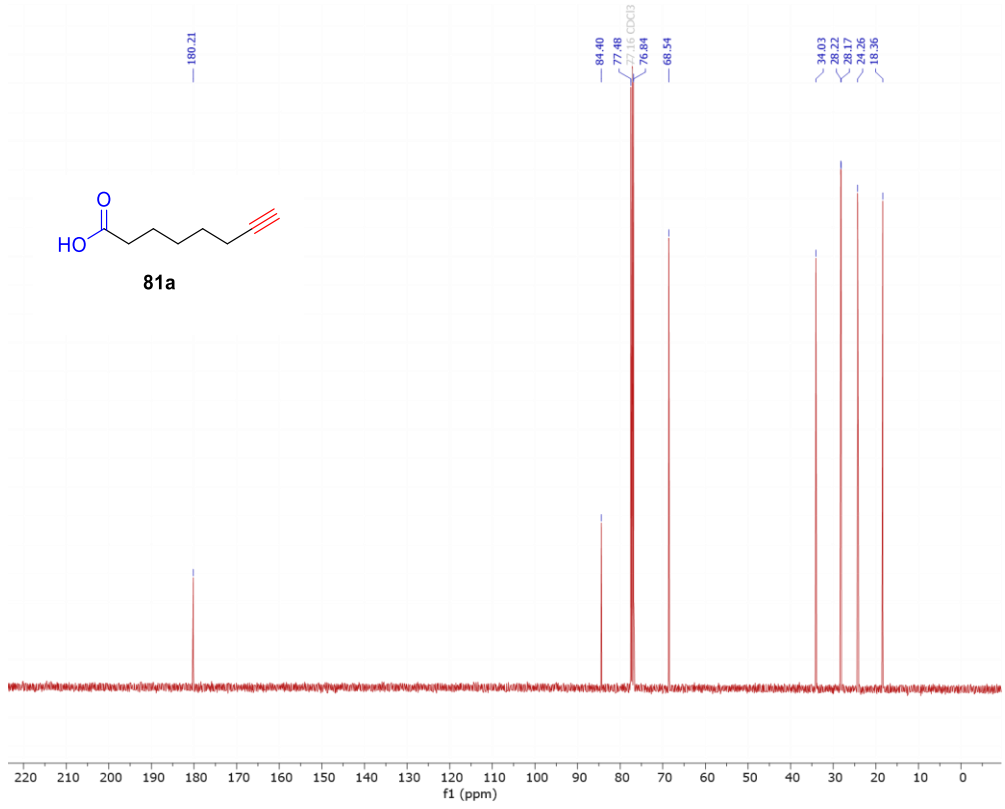

9.76
9.75
9.75
7.26 CDCl3
5.35
5.35
5.34
5.33
5.33
5.32
5.31
5.31
4.57
4.55
2.44
2.43
2.42
2.42
2.40
2.40
2.31
2.29
2.27
1.75
1.70
1.65
1.64
1.63
1.62
1.61
1.61
1.59
1.35
1.34
1.33
1.33
1.32
O
O
H
O
56c
1.00
1.15
2.37
2.17
2.37
3.41
3.38
4.46
4.43
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

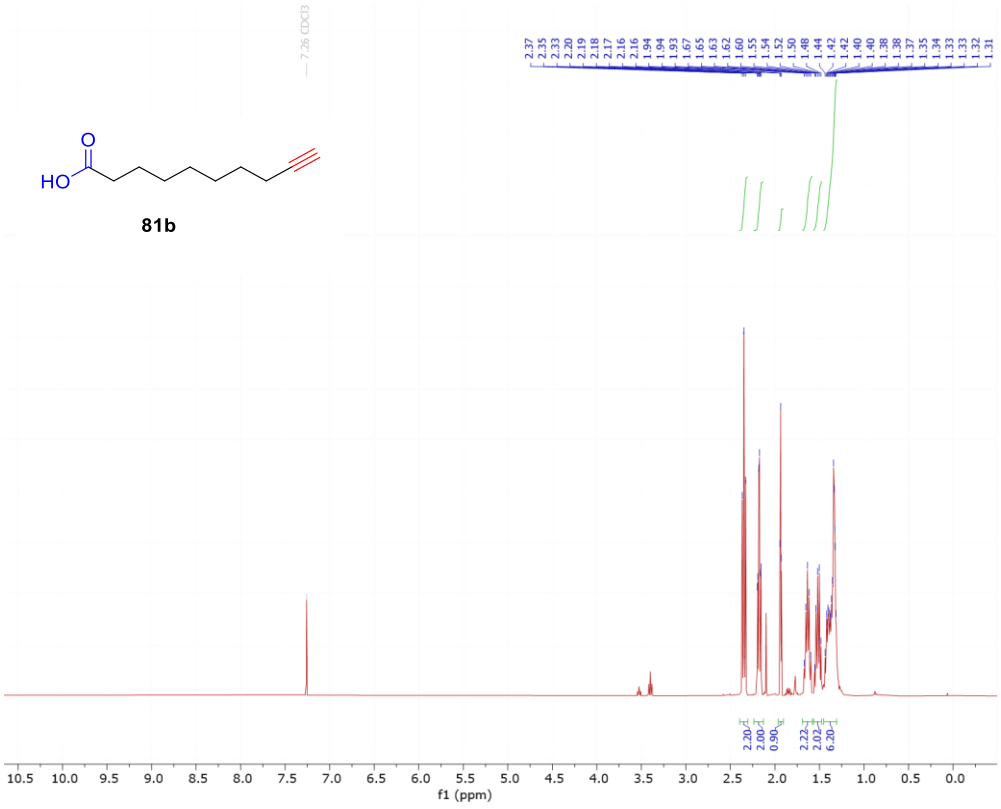

202.82
173.85
139.16
118.75
77.48
77.16 CDCl3
76.84
61.37
43.92
34.34
28.95
28.90
25.91
24.85
21.98
18.15
O
O
H
O
56c
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

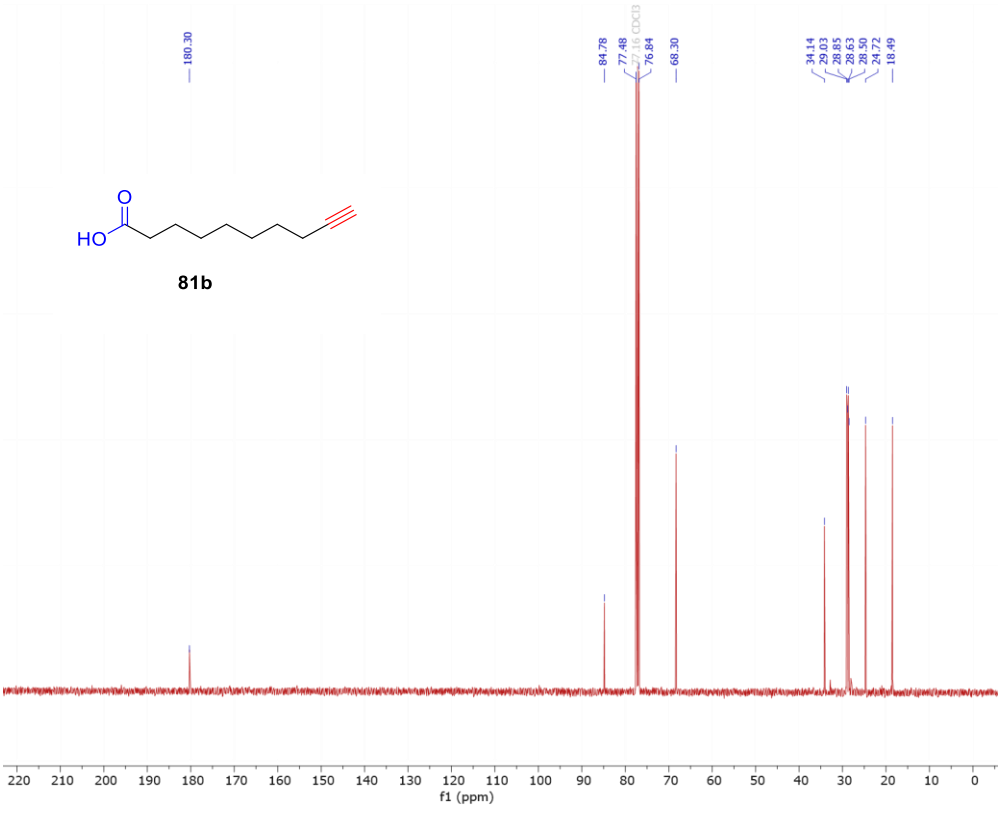

9.75
9.75
9.75
7.26 CDCl3
5.35
5.35
5.34
5.33
5.33
5.32
5.31
5.31
5.31
4.56
4.55
2.43
2.42
2.41
2.41
2.39
2.39
2.30
2.28
2.26
1.75
1.70
1.65
1.63
1.62
1.61
1.60
1.59
1.58
1.31
1.30
1.30
1.29
1.28
O
O
H
O
56d
0.80
1.21
2.47
1.84
2.36
3.38
3.27
4.47
8.39
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

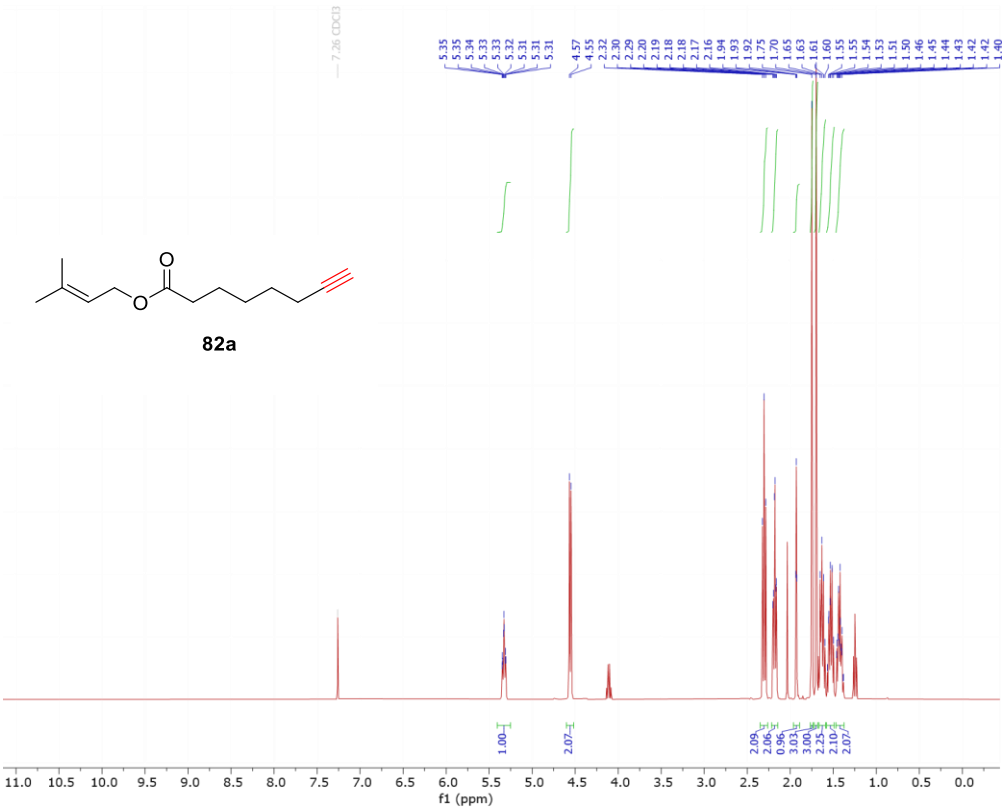

203.01
174.00
139.09
118.79
77.48
77.16 CDCl3
76.84
61.33
44.01
34.45
29.27
29.19
29.16
25.90
25.05
22.15
18.14
O
O
H
O
56d
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

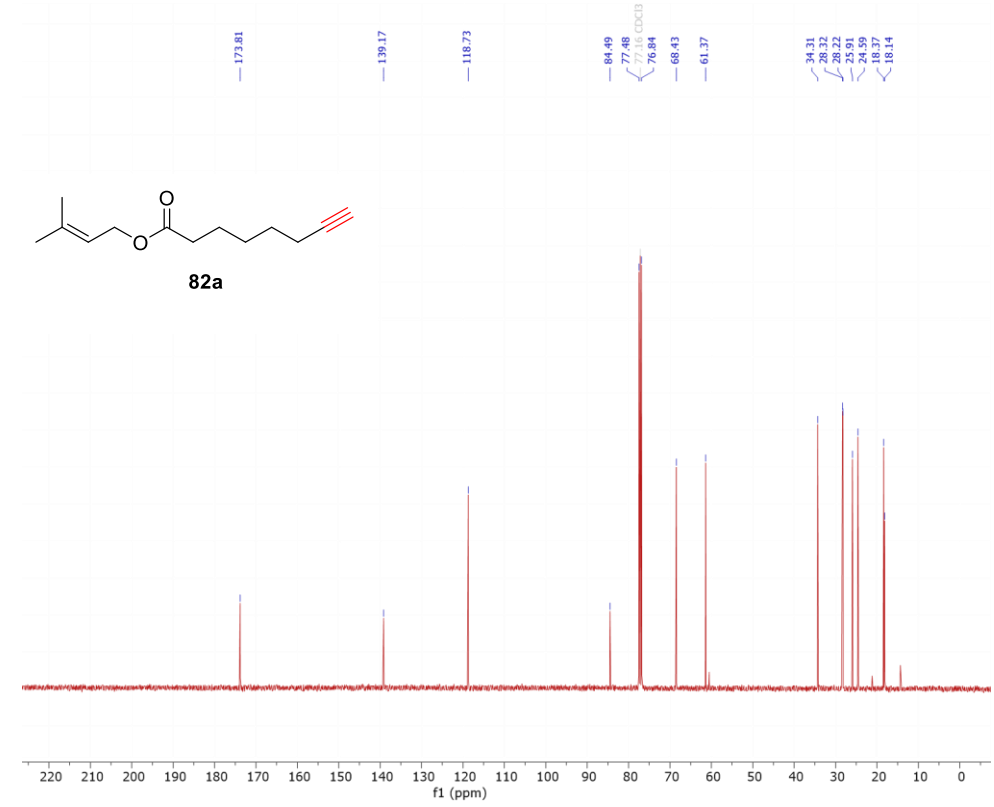

HO
O
81a
f1 (ppm)

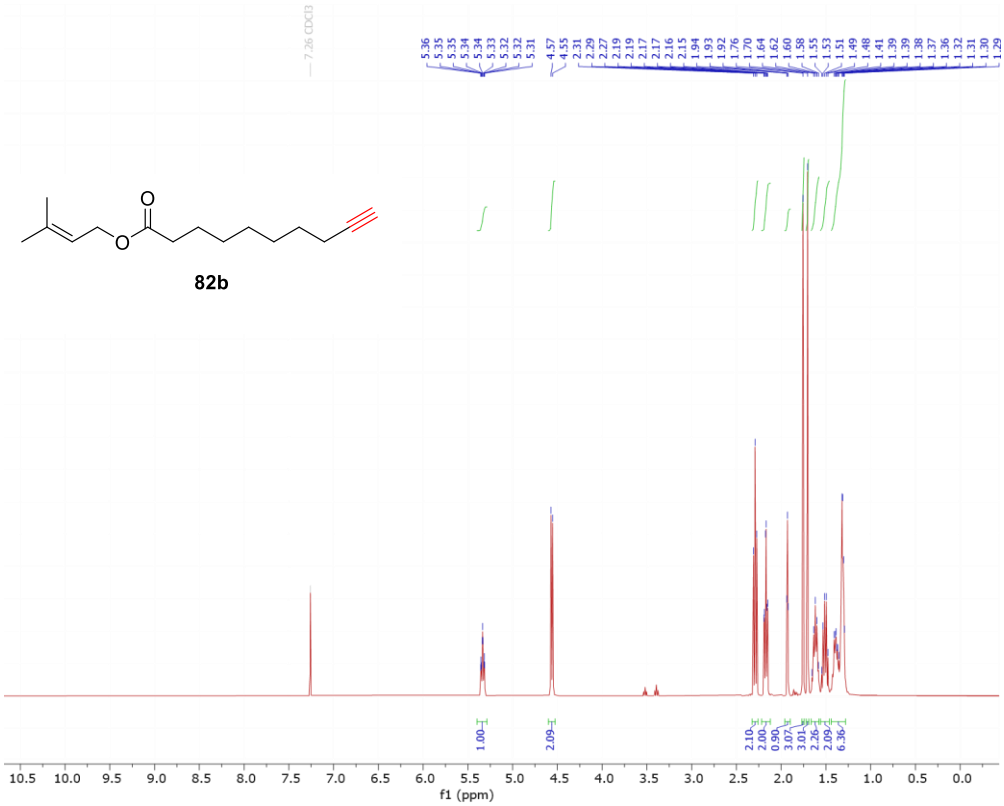

HO
O
81a
f1 (ppm)

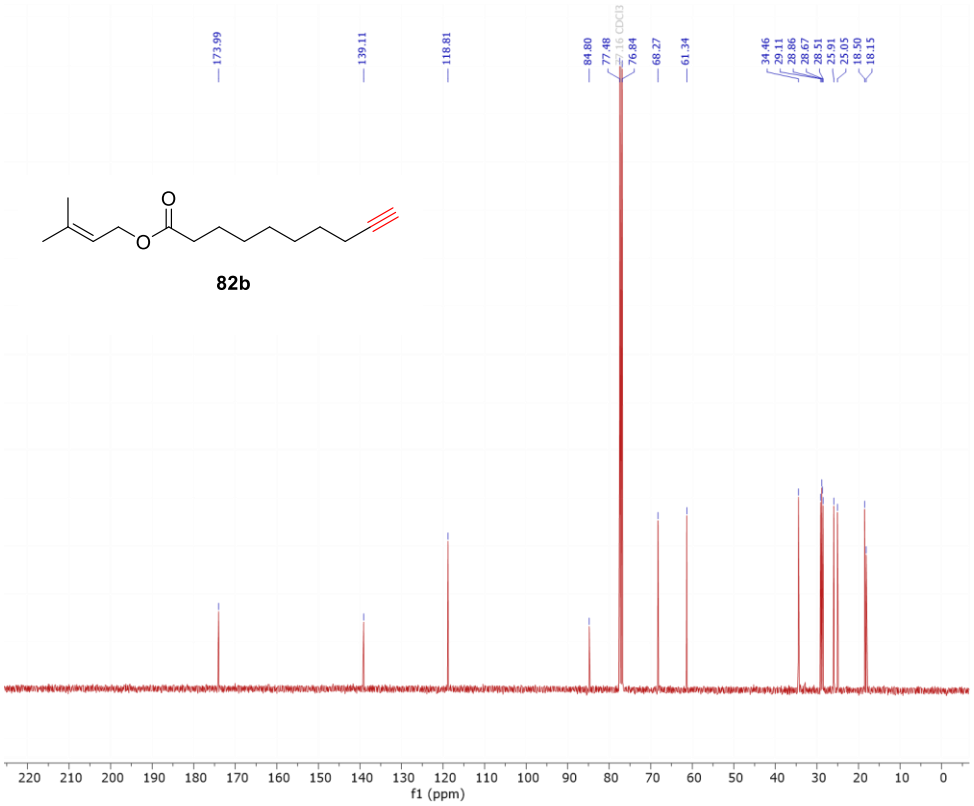

HO
O
81b
f1 (ppm)

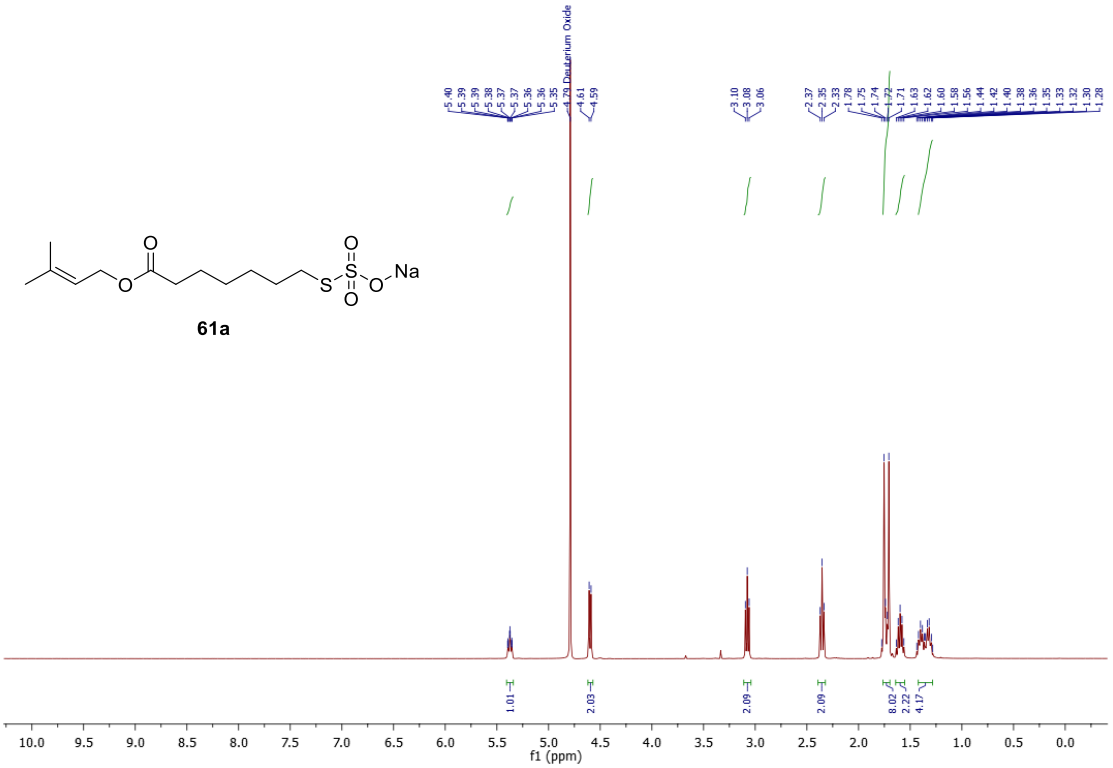

HO
O
81b
f1 (ppm)


82a
f1 (ppm)

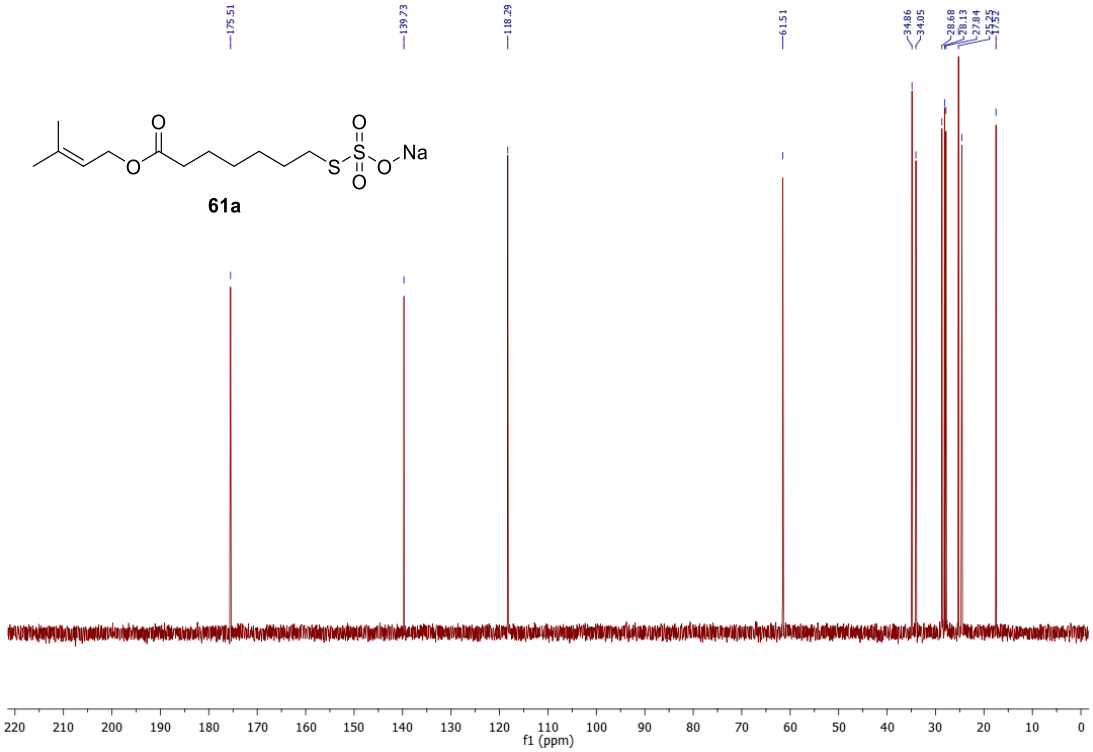

82a
f1 (ppm)


82b
f1 (ppm)

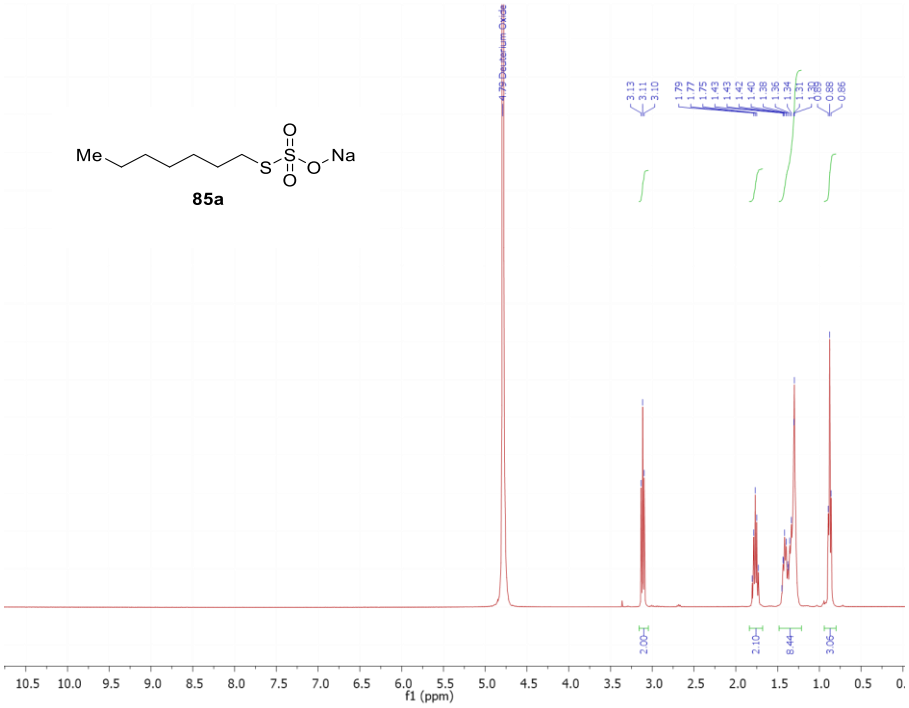

82b
f1 (ppm)

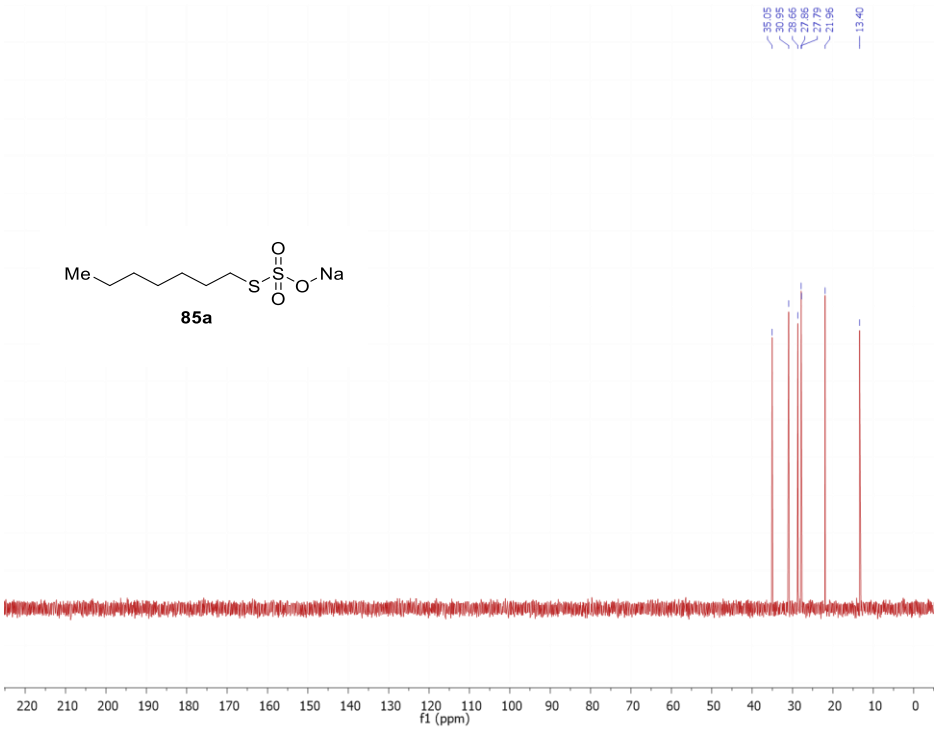

Deuterium Oxide
1.01
2.03
2.09
2.09
8.02
2.22
4.17
f1 (ppm)

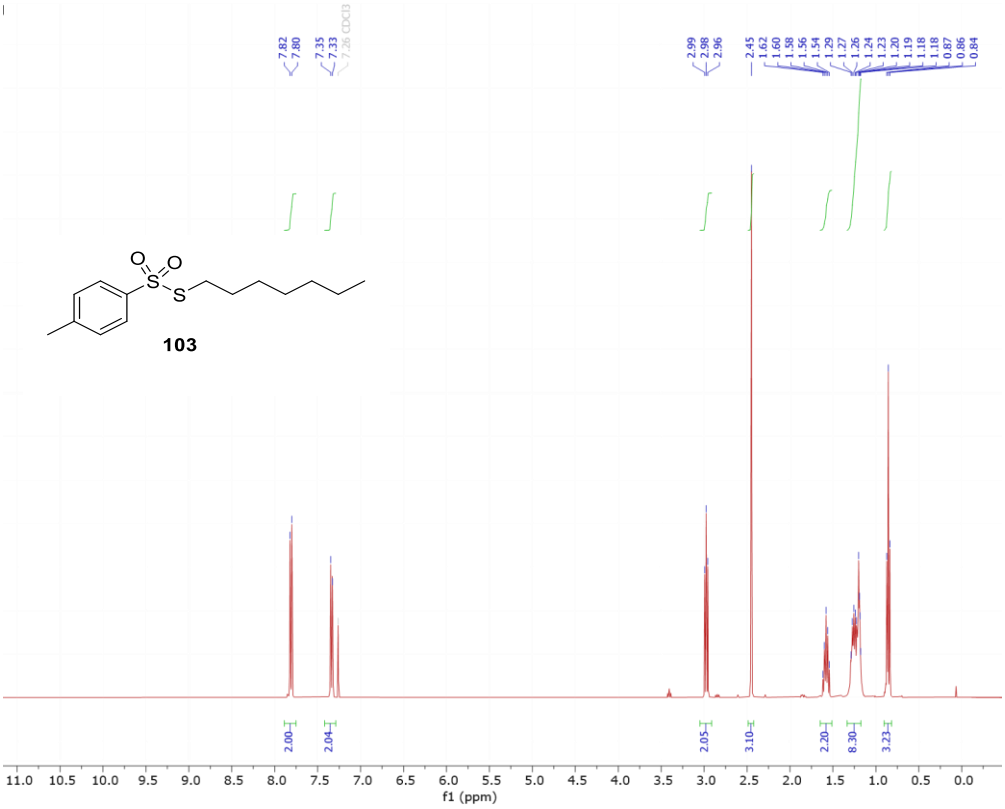
61a

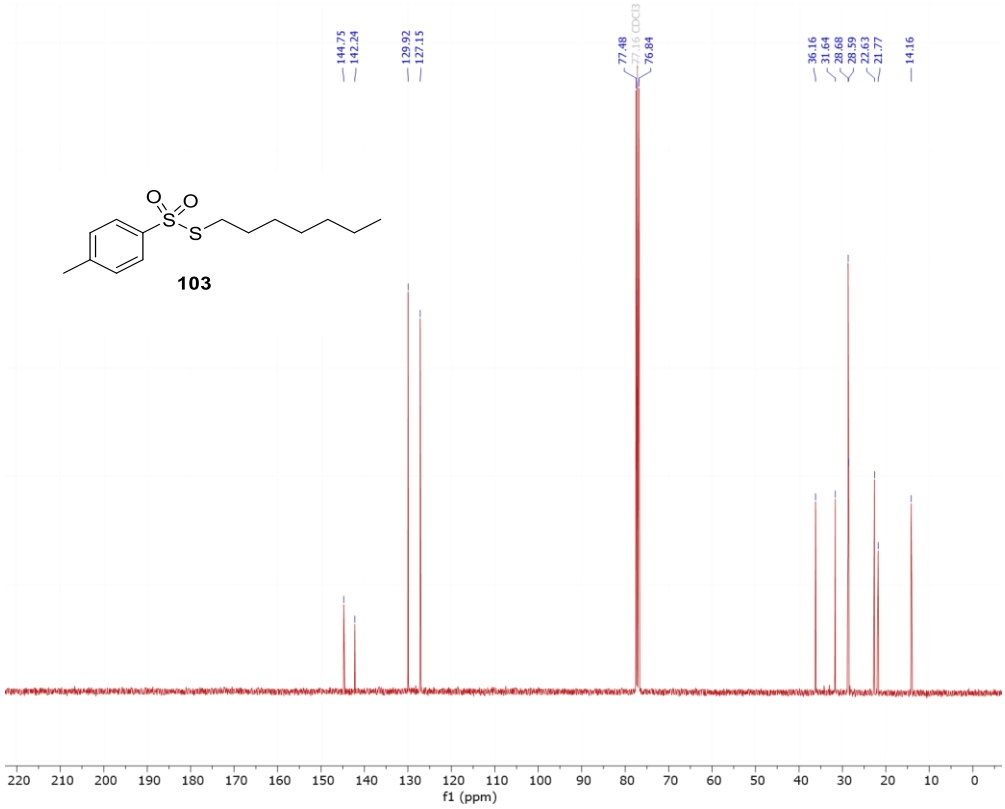

175.51
139.73
118.29
61.51
34.86
34.05
28.68
28.13
27.84
f1 (ppm)

61a

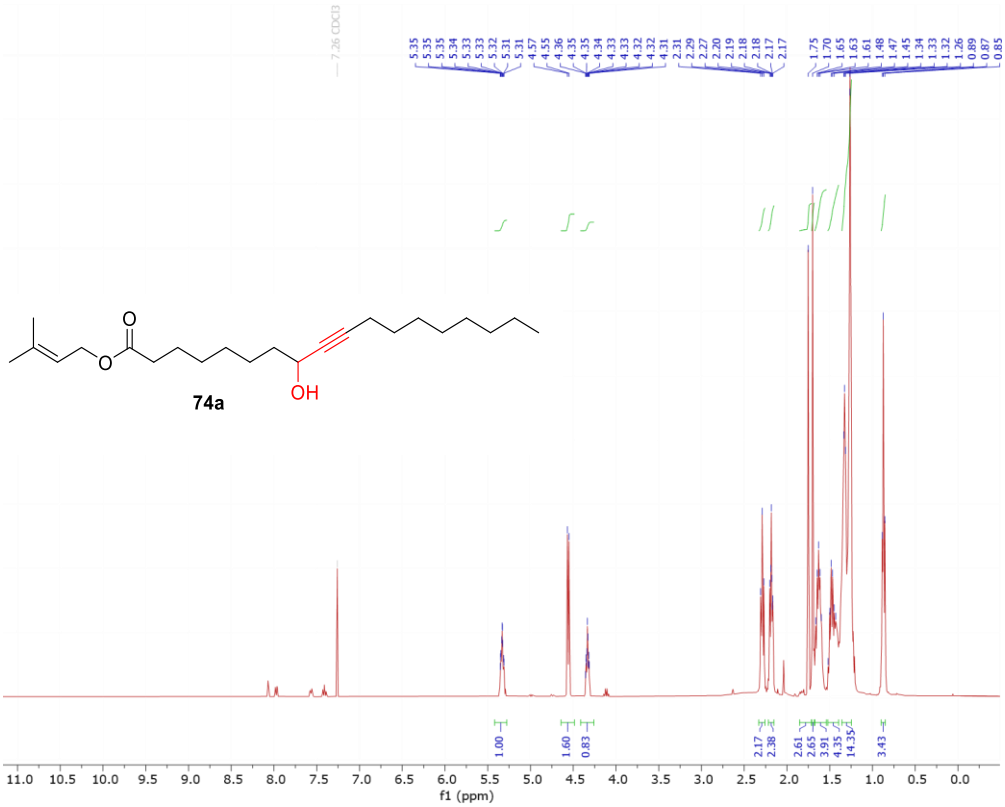

Me
S
O
O
O
Na
85a
4.79 Deuterium Oxide
3.13
3.11
3.10
1.79
1.77
1.75
1.43
1.42
1.40
1.38
1.36
1.34
1.31
0.89
0.88
0.86
2.00
2.10
8.44
3.06
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

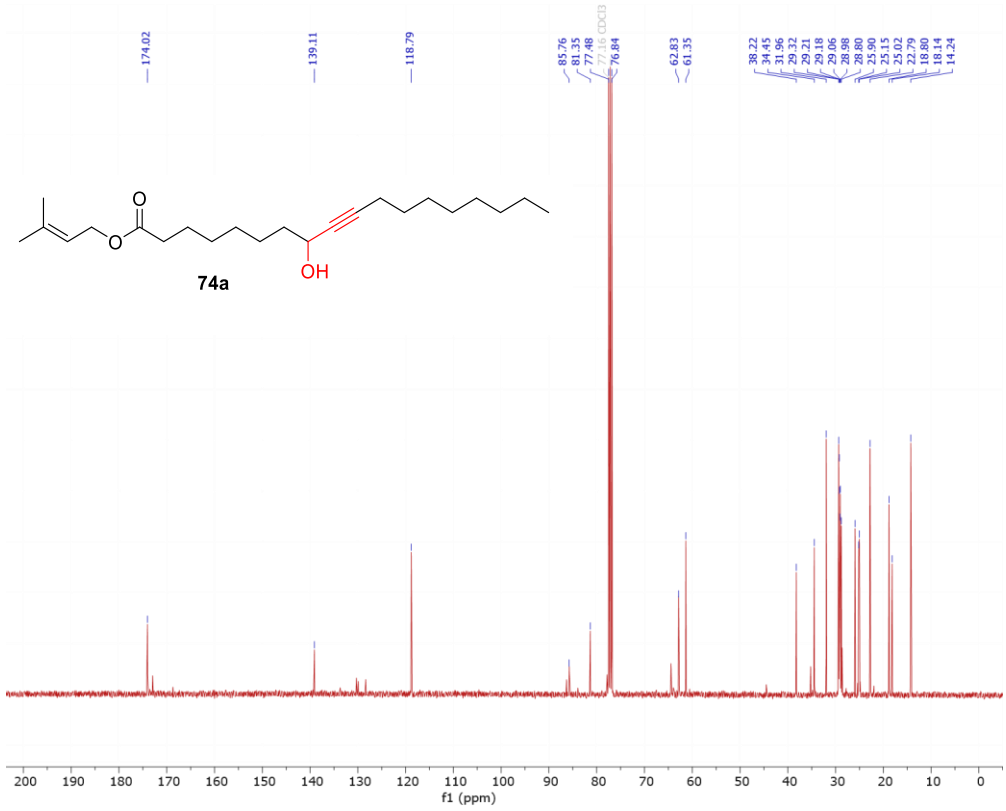

35.05
30.95
28.66
27.86
27.79
21.96
13.40
Me
S
O
O
O
Na
85a
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

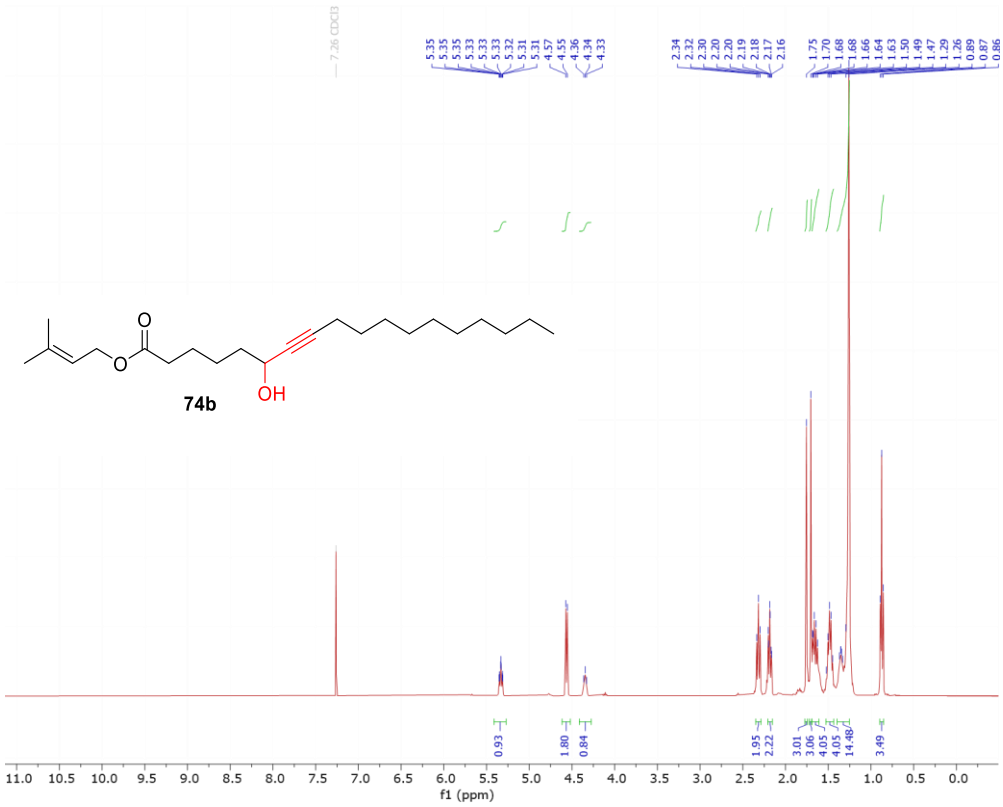

7.82
7.80
7.35
7.33
2.99
2.98
2.96
2.45
1.62
1.60
1.58
1.56
1.54
1.29
1.27
1.26
1.24
1.23
1.20
1.19
1.18
1.18
0.87
0.86
0.84
2.00
2.04
2.05
3.10
2.20
8.30
3.23
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

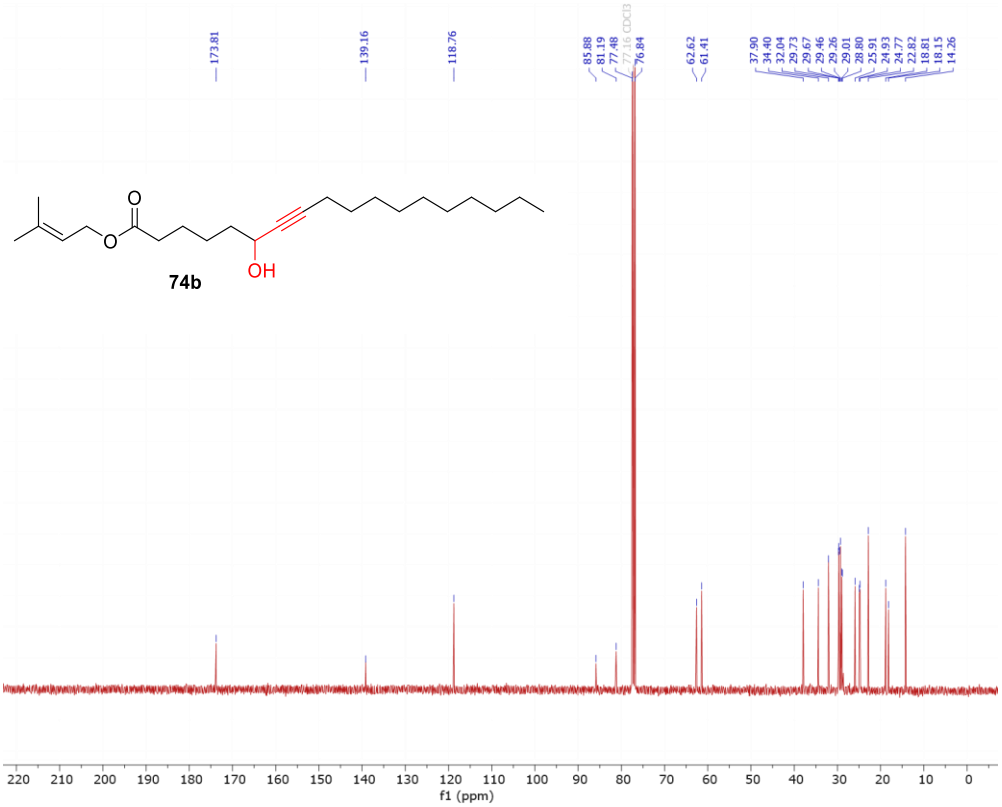

144.75
142.24
129.92
127.15
77.48
76.84
36.16
31.64
28.68
28.59
22.63
21.77
14.16
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

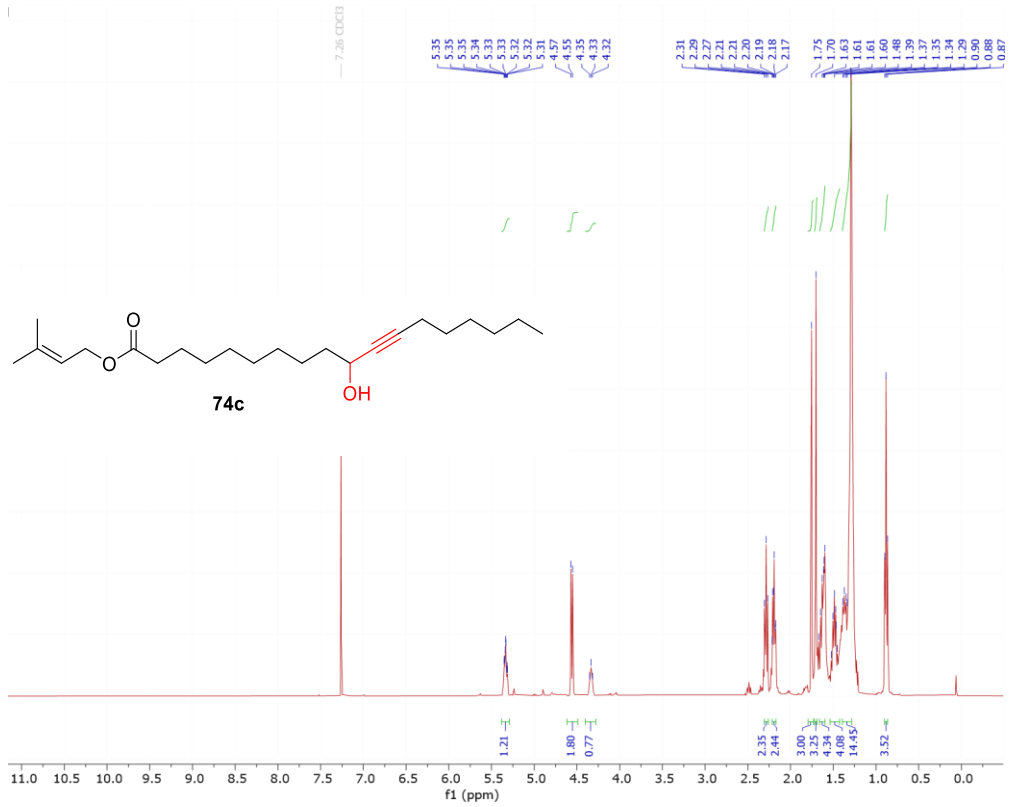
103

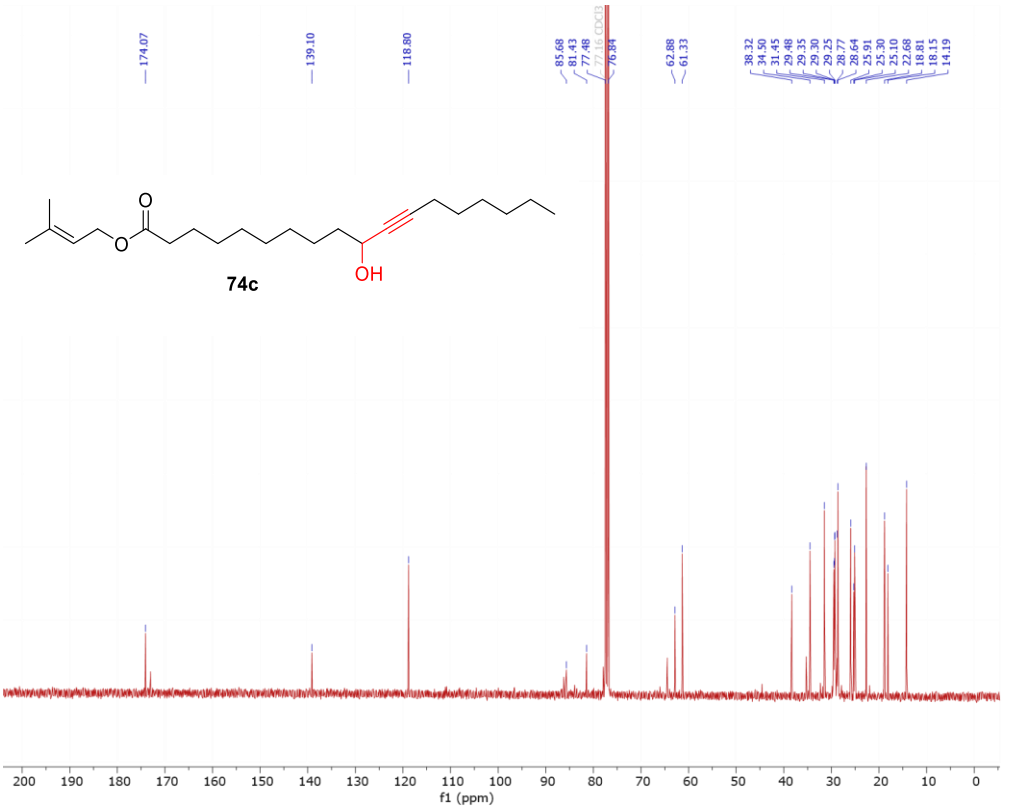

74a
OH
f1 (ppm)

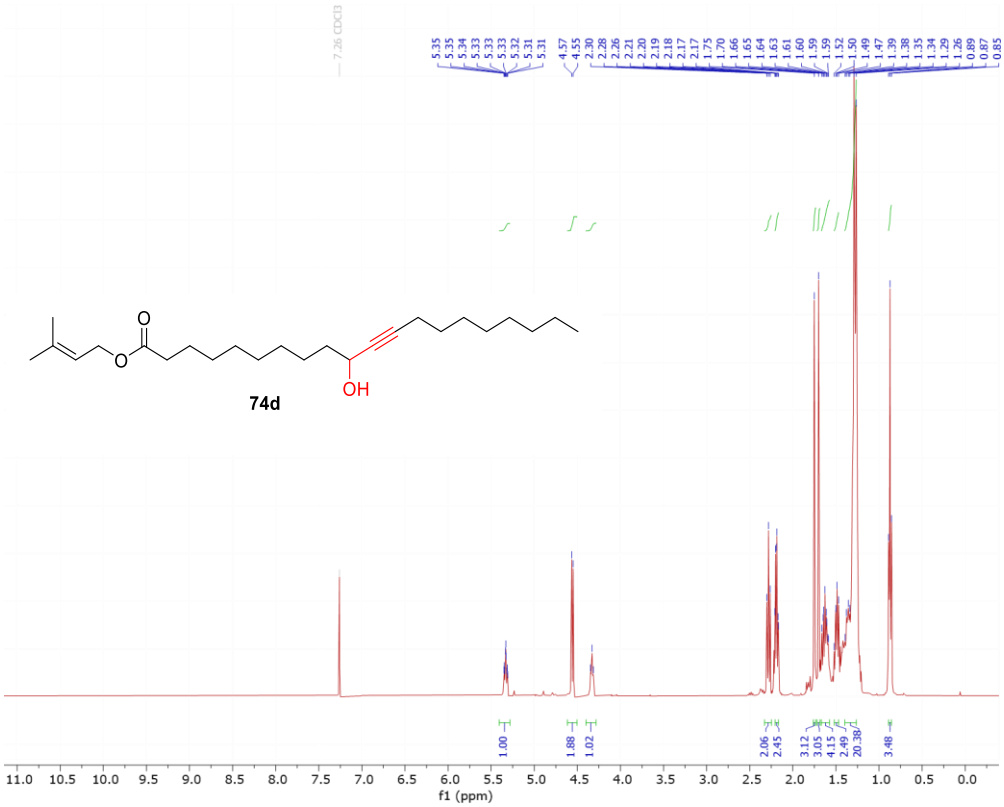

74a
OH
f1 (ppm)

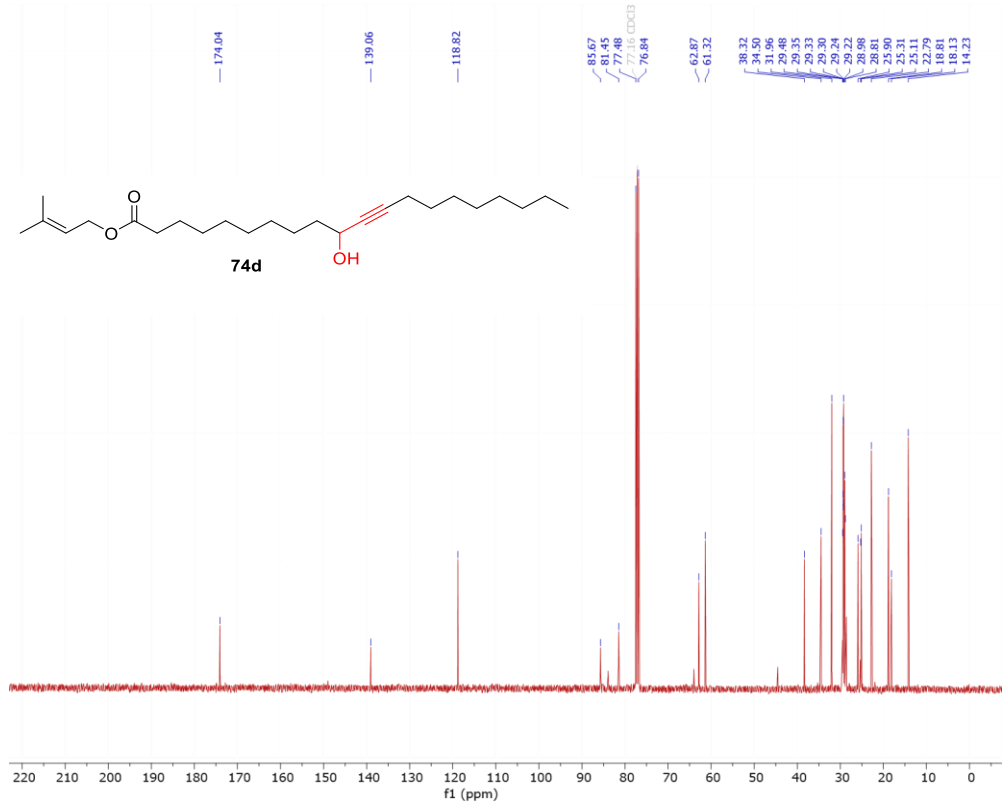

74b
f1 (ppm)

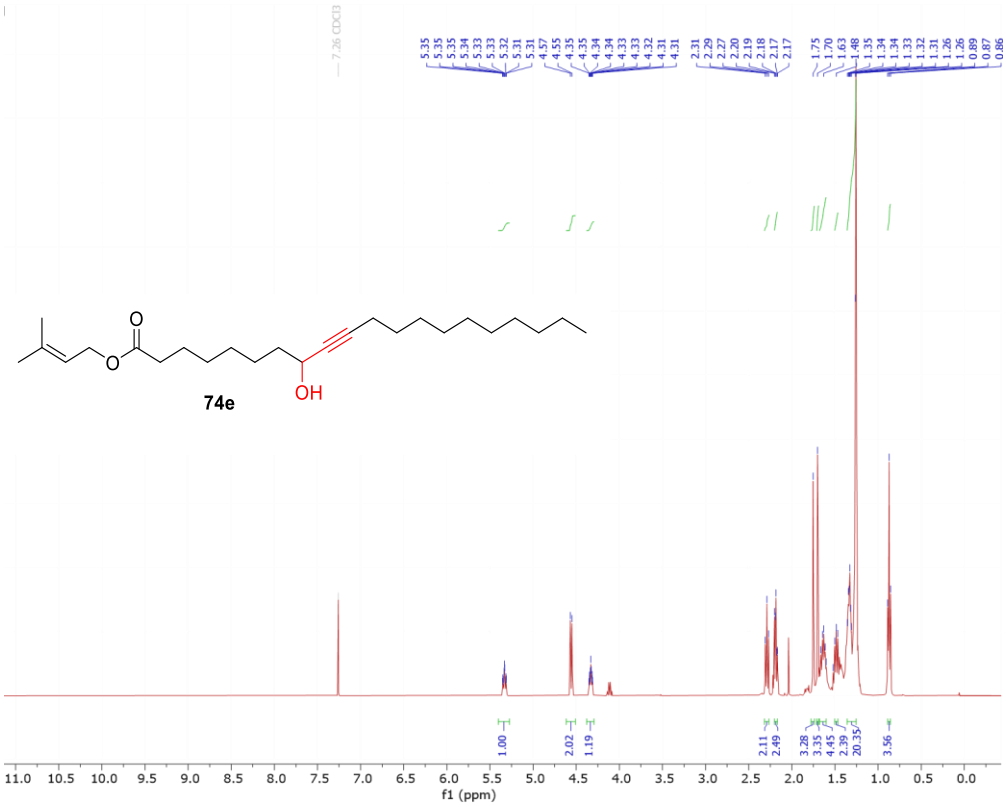

74b
f1 (ppm)

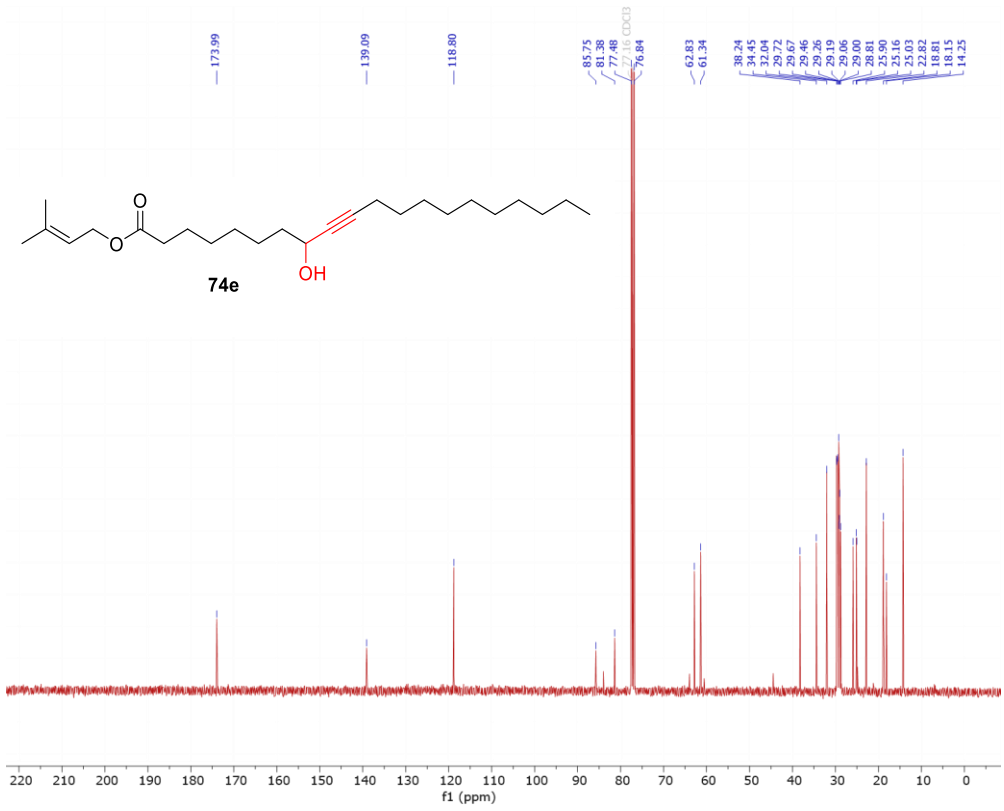

74c
OH
f1 (ppm)

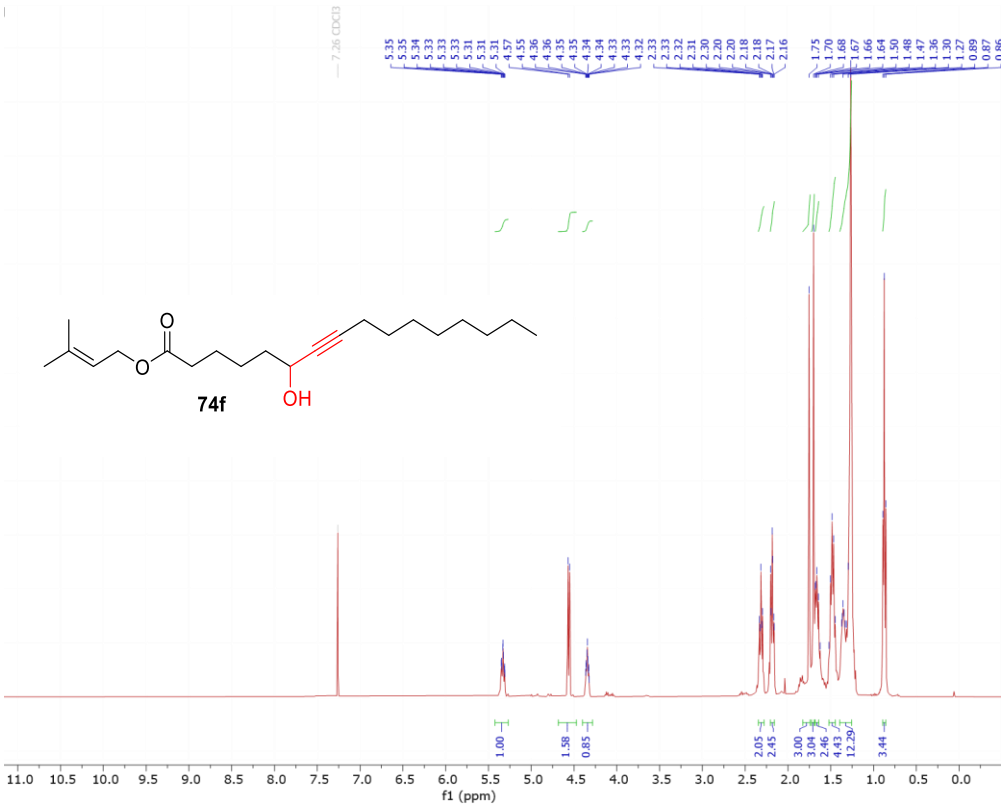

74c
OH
f1 (ppm)

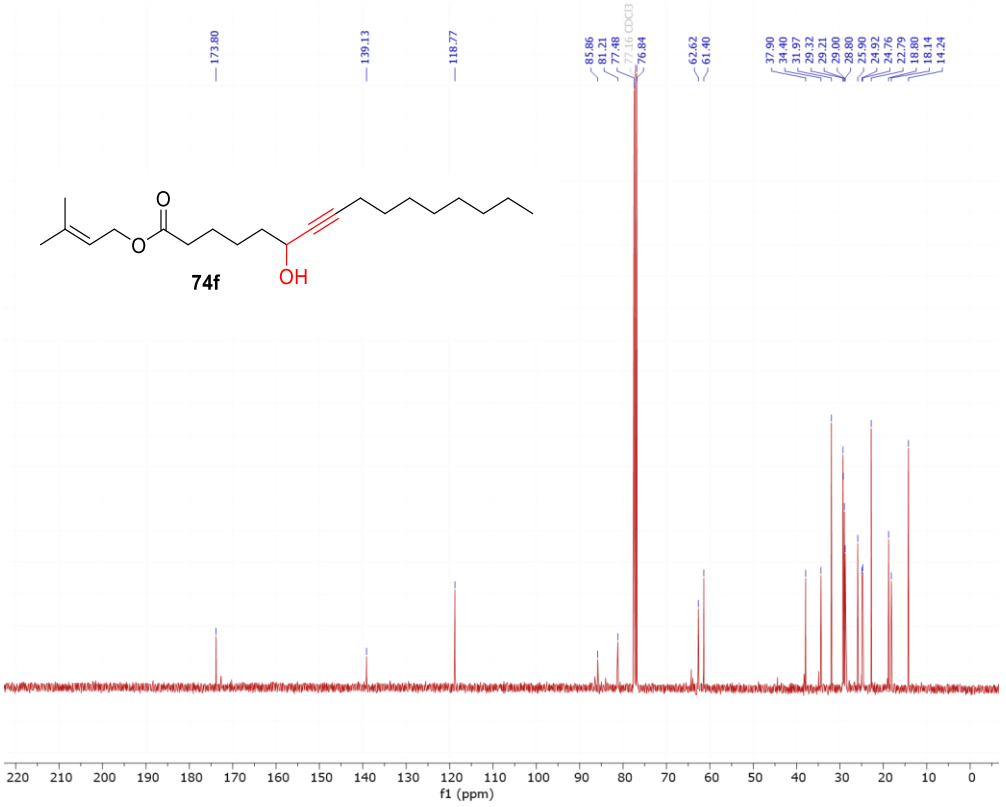

74d
OH
f1 (ppm)

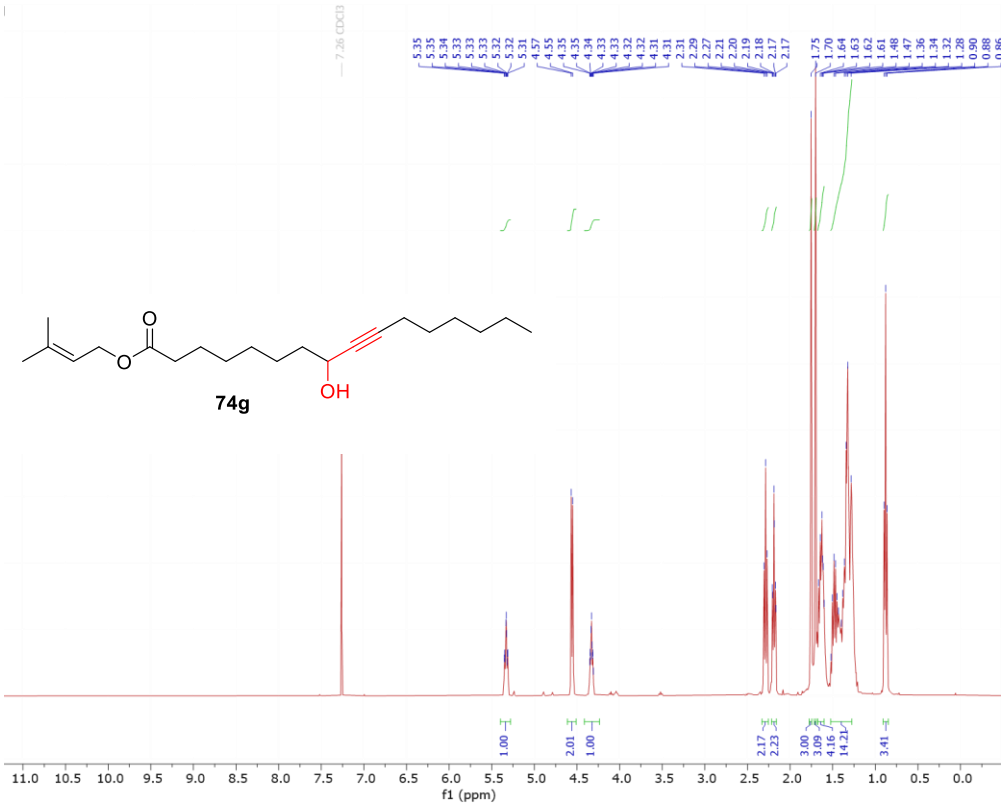

74d
OH
f1 (ppm)

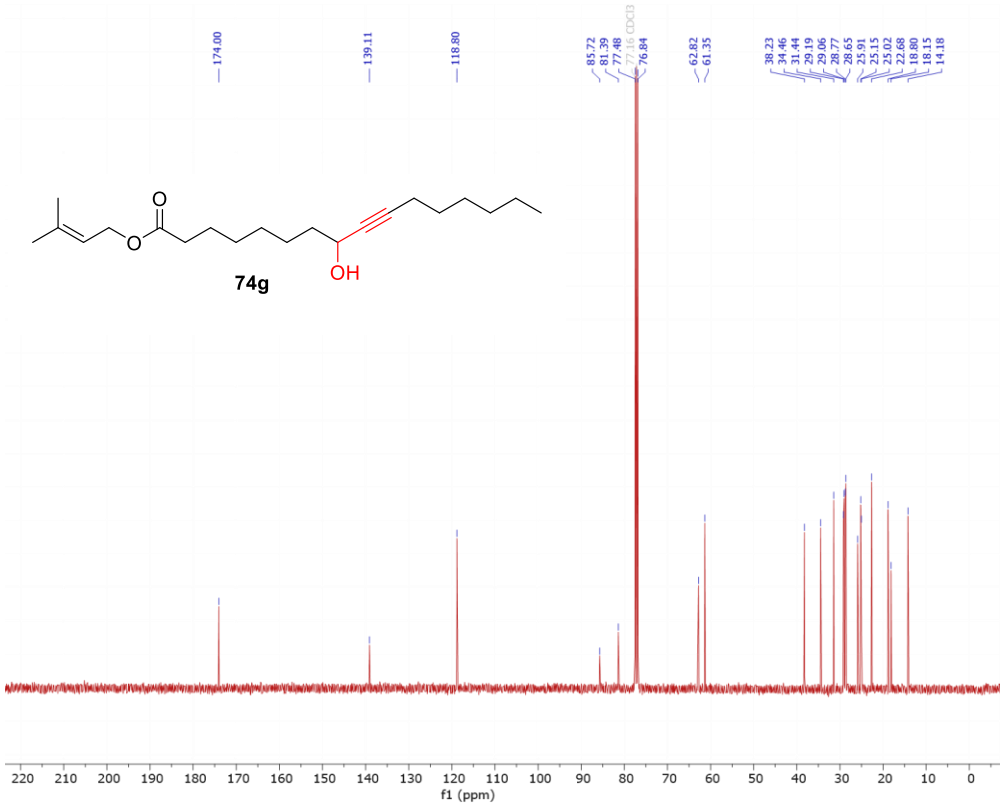

74e
OH
f1 (ppm)

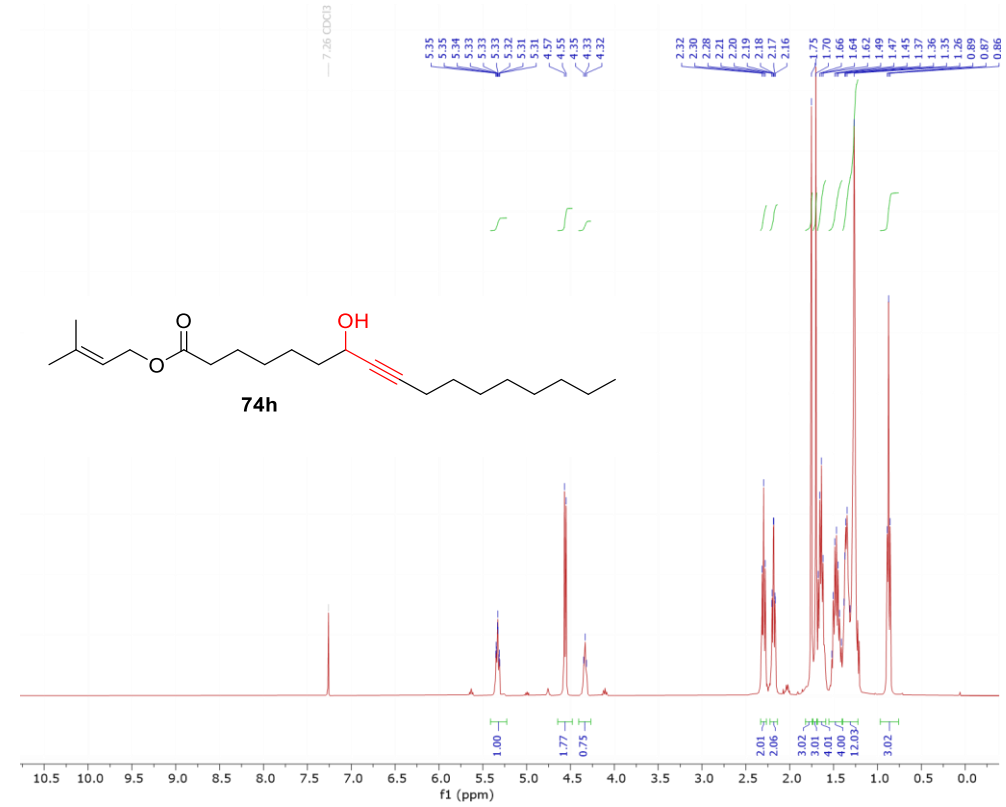

74e
OH
f1 (ppm)

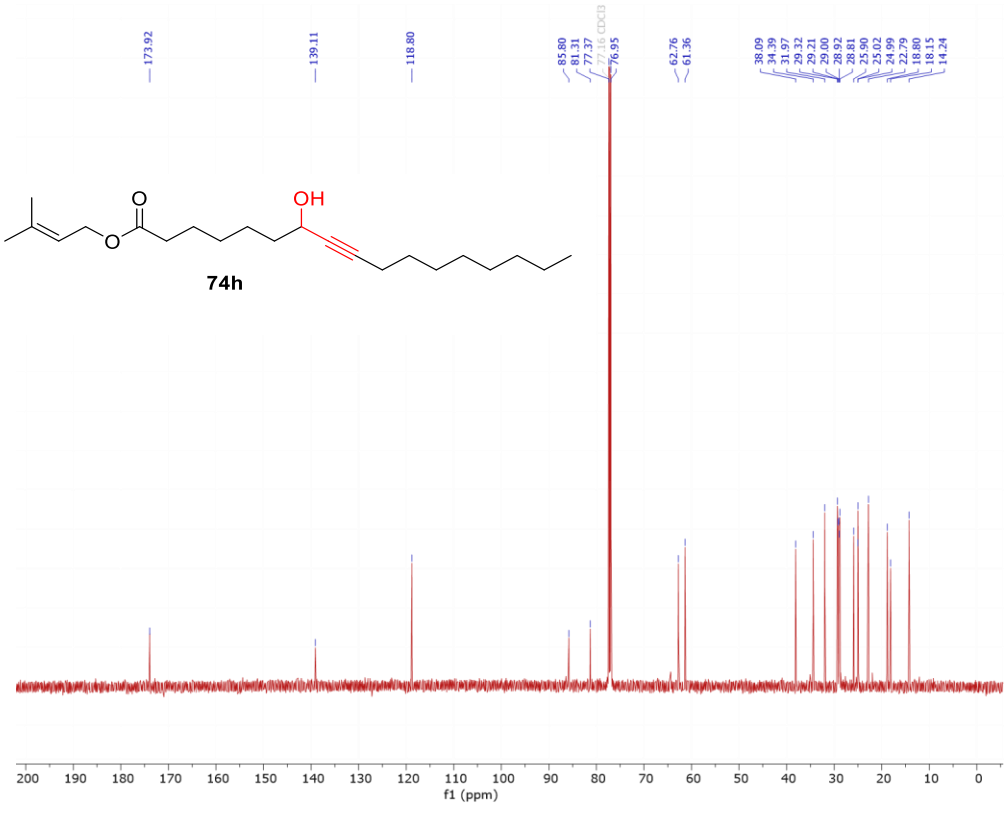

74f
OH
f1 (ppm)

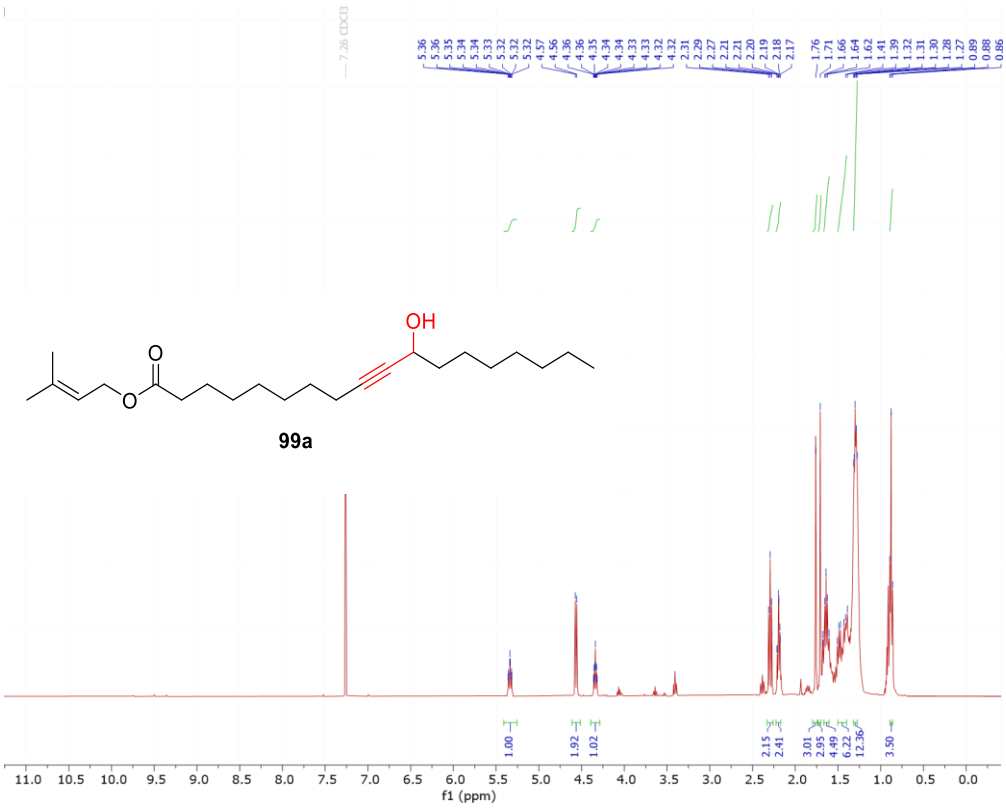

74f
OH
f1 (ppm)

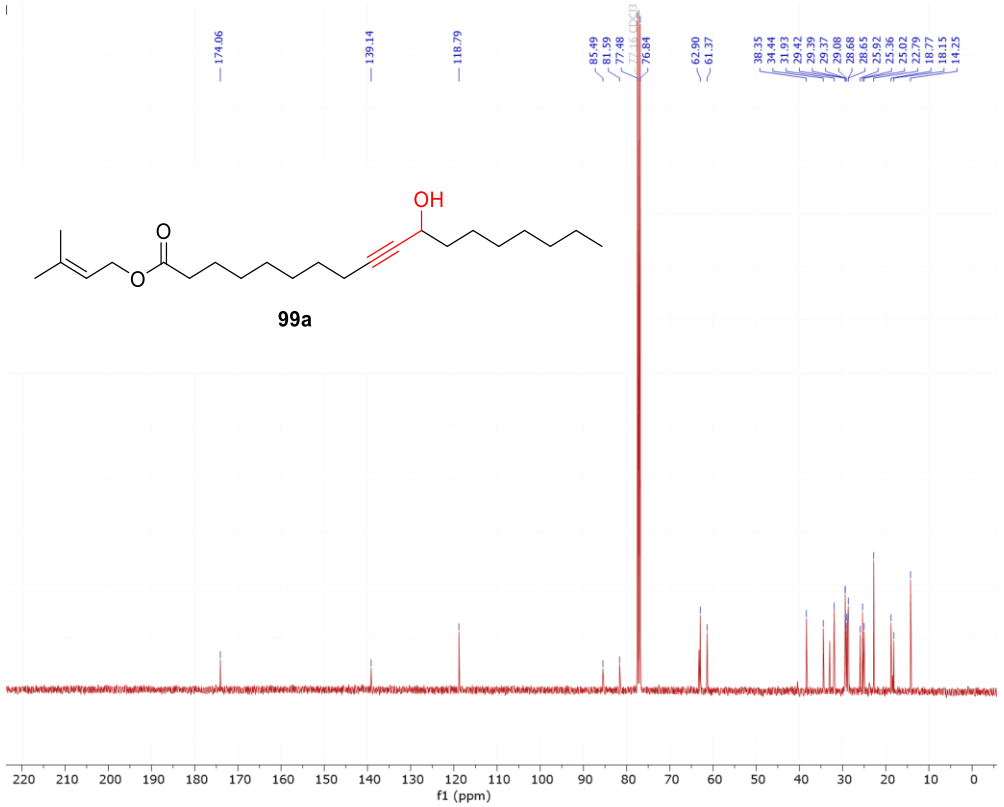

74g
OH
f1 (ppm)

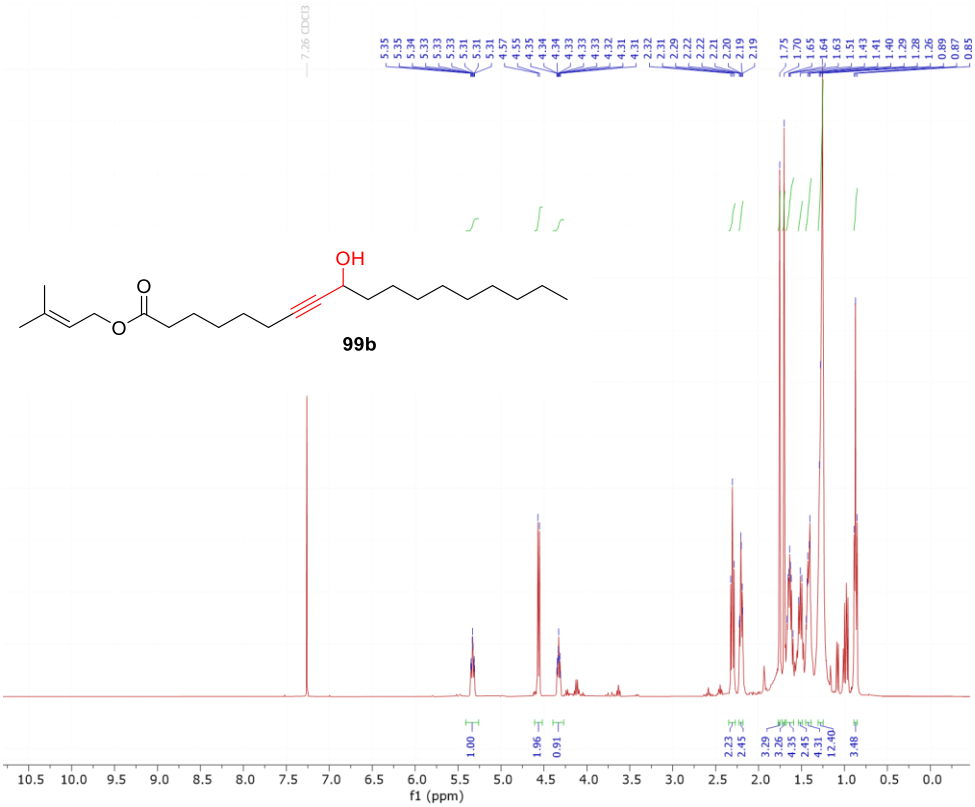

74g
OH
f1 (ppm)

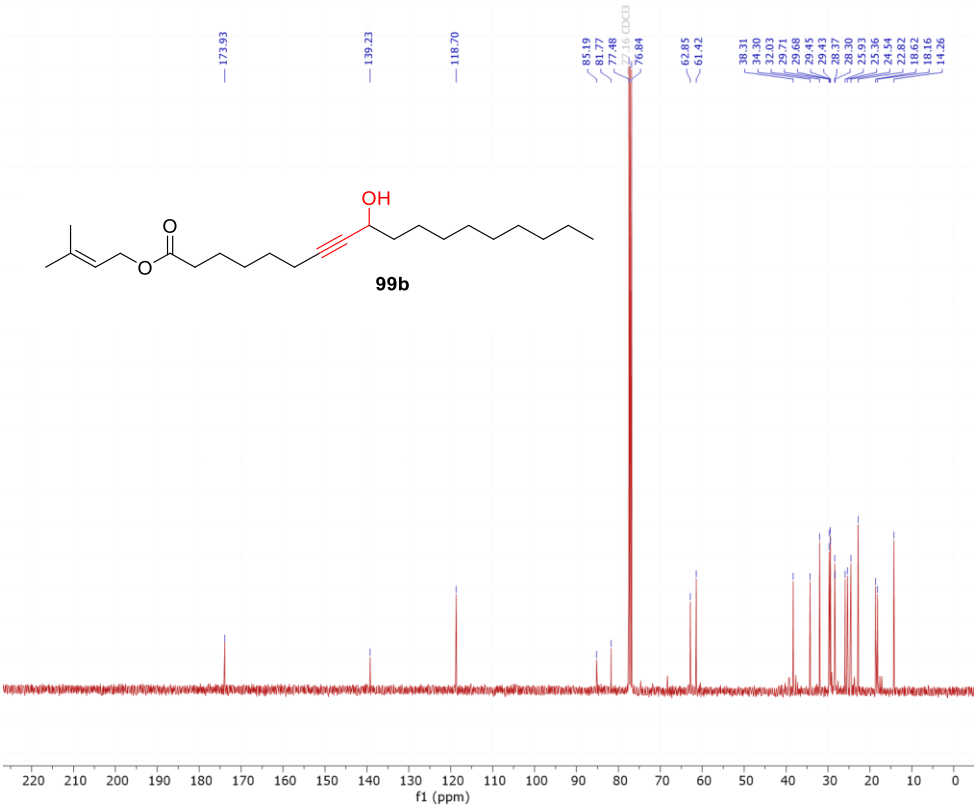

7.26 CDCl3
5.35
5.35
5.34
5.33
5.33
5.32
5.31
5.31
4.57
4.55
4.35
4.33
4.32
2.32
2.30
2.28
2.21
2.20
2.19
2.18
2.17
2.16
1.75
1.70
1.66
1.64
1.62
1.49
1.47
1.45
1.37
1.36
1.35
1.26
0.89
0.87
0.86
O
O
OH
74h
1.00
1.77
0.75
2.01
2.06
3.02
3.01
4.01
4.00
12.03
3.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

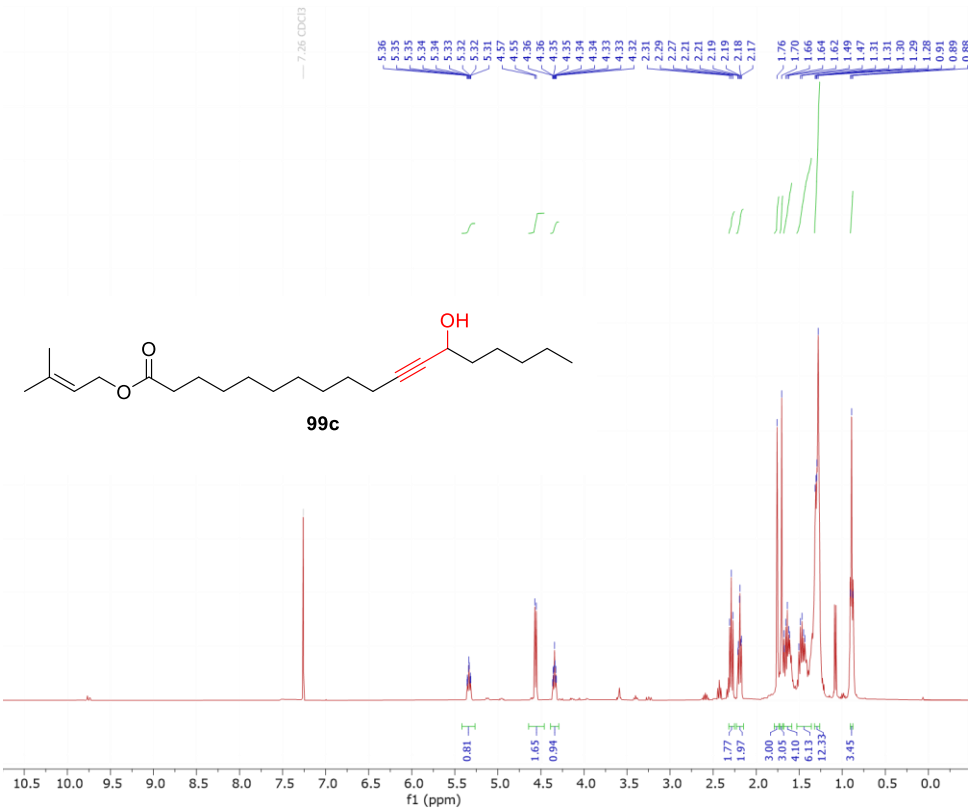

173.92
139.11
118.80
85.80
81.31
77.37
77.05
76.95
CDCl3
62.76
61.36
38.09
34.39
31.97
29.32
29.21
29.00
28.92
28.81
25.90
25.02
24.99
22.79
18.80
18.15
14.24
O
O
OH
74h
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

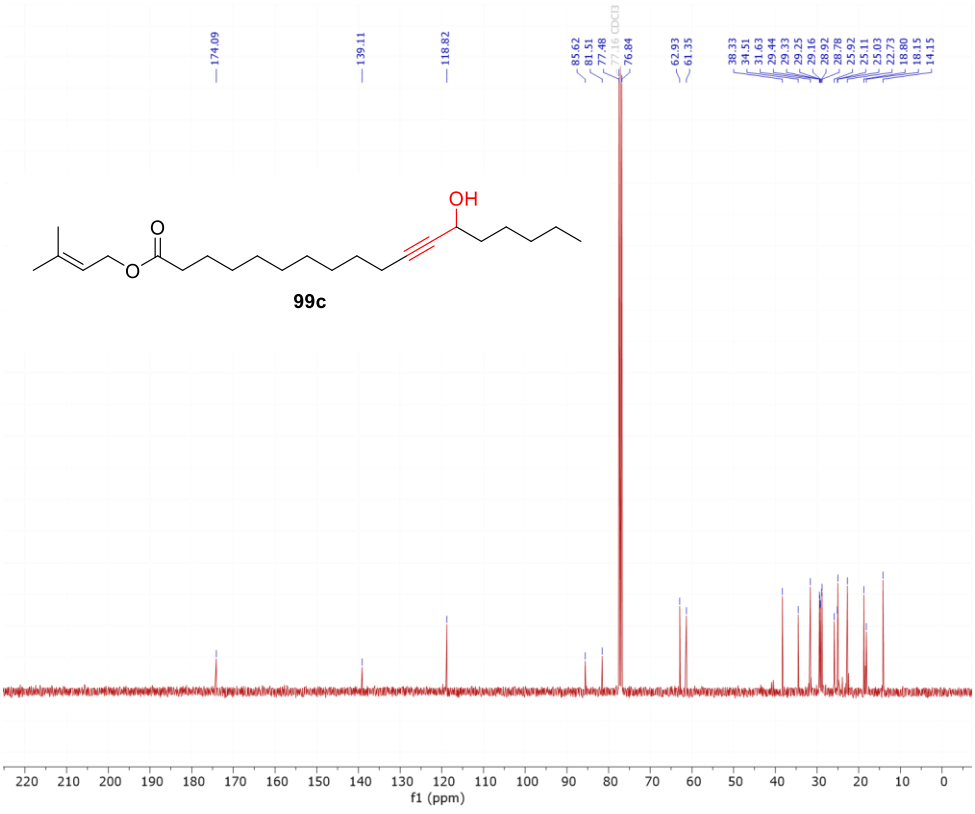

OH
O
O
99a
f1 (ppm)

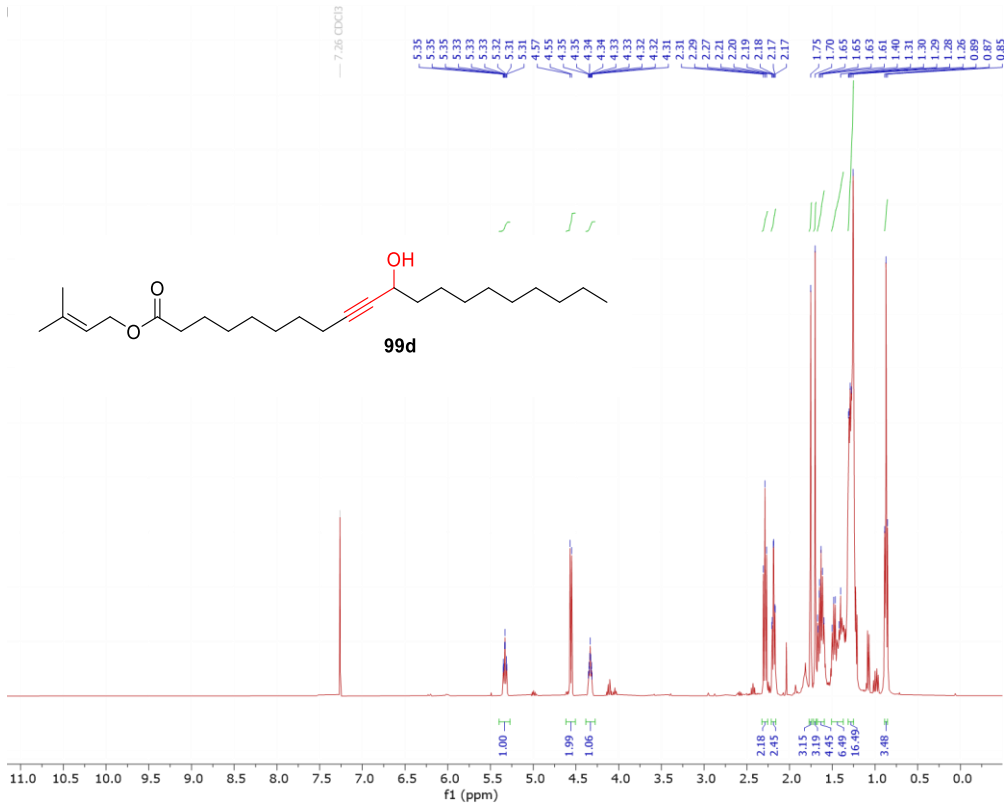

OH
O
O
99a
f1 (ppm)

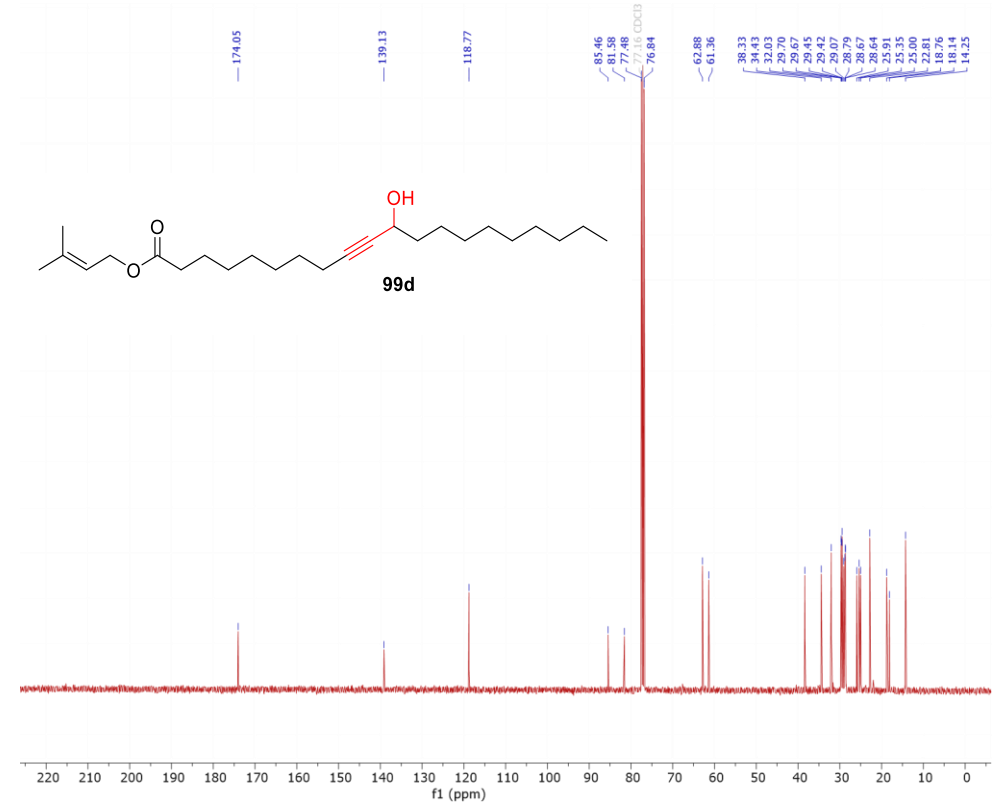

OH
O
O
99b
f1 (ppm)

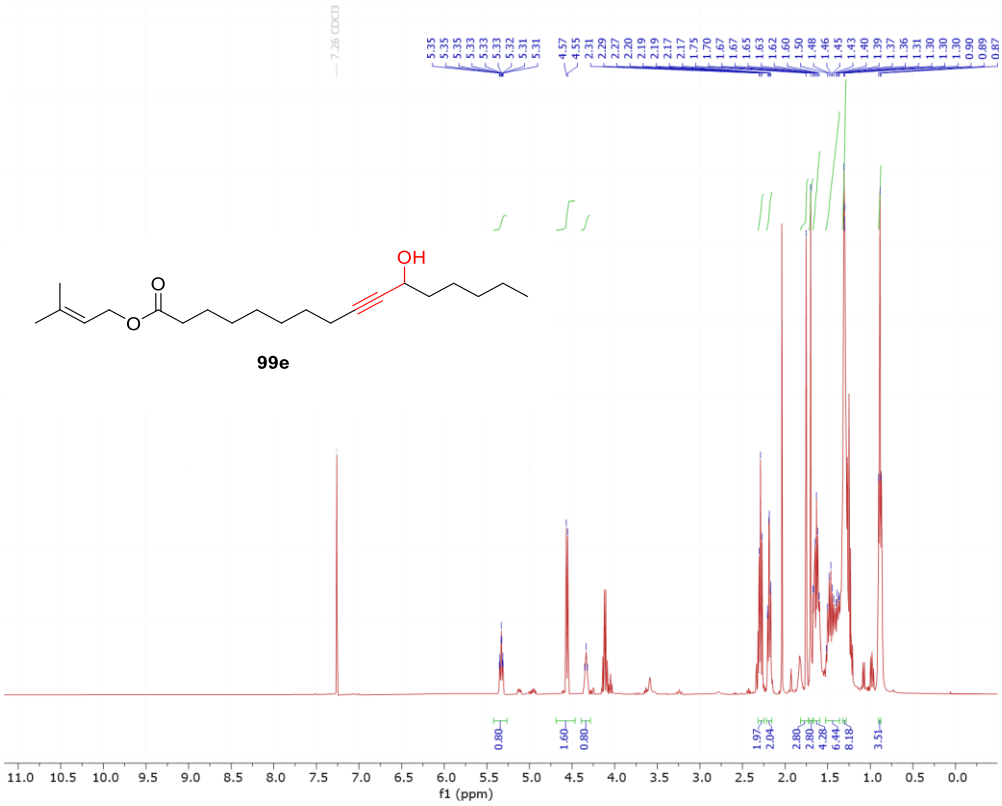

OH
O
O
99b
f1 (ppm)

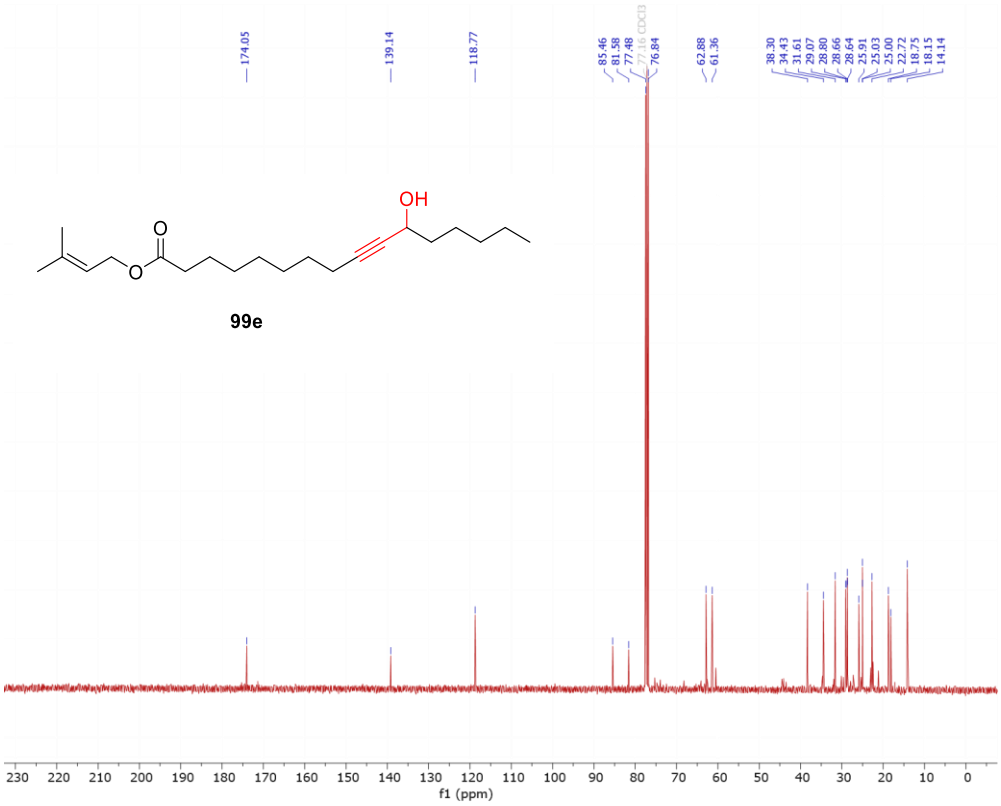

OH
O
O
99c
f1 (ppm)

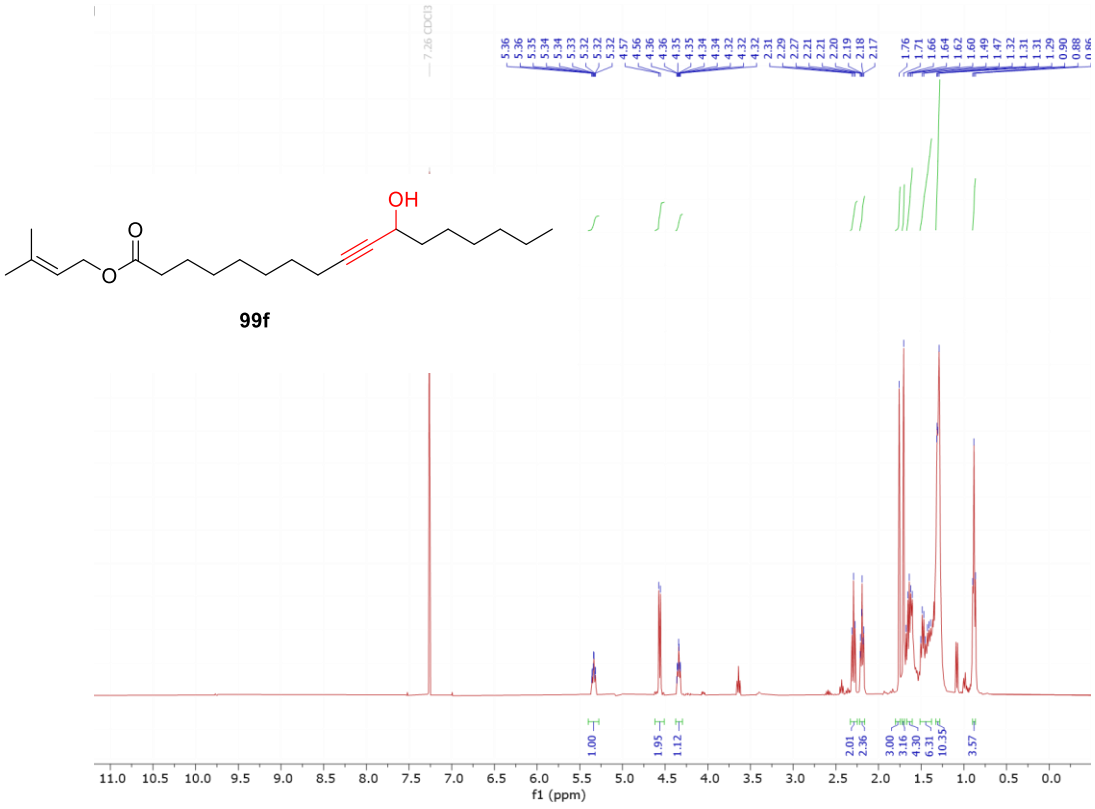

OH
O
O
99c
f1 (ppm)

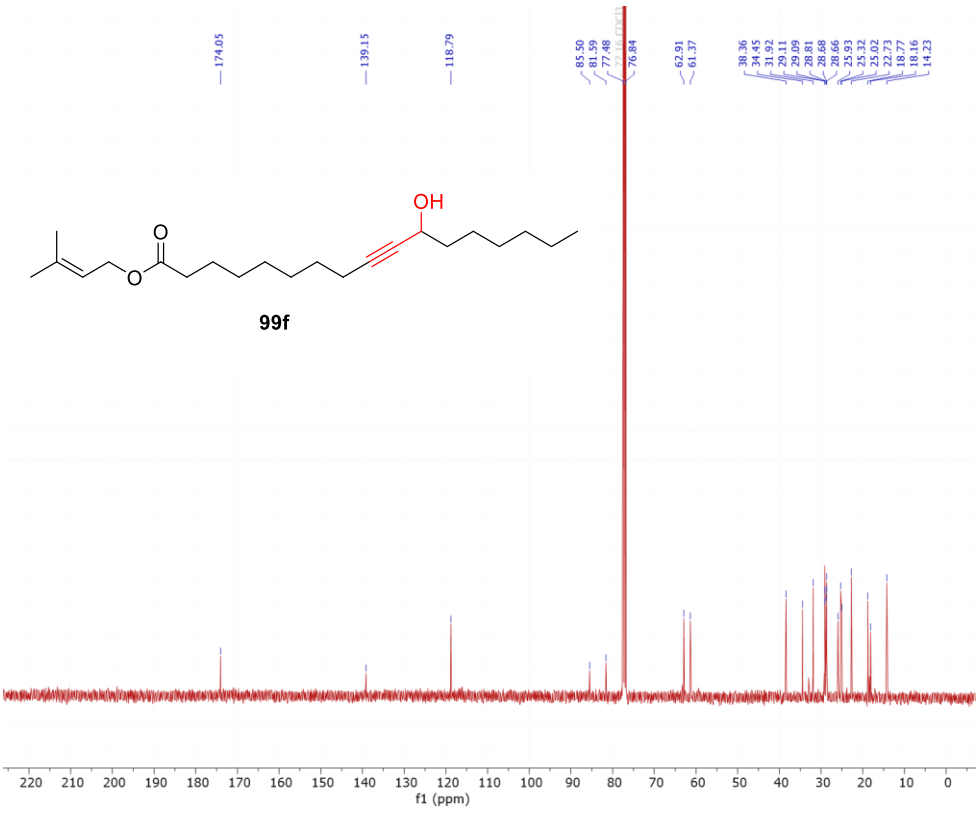

OH
O
O
99d
f1 (ppm)

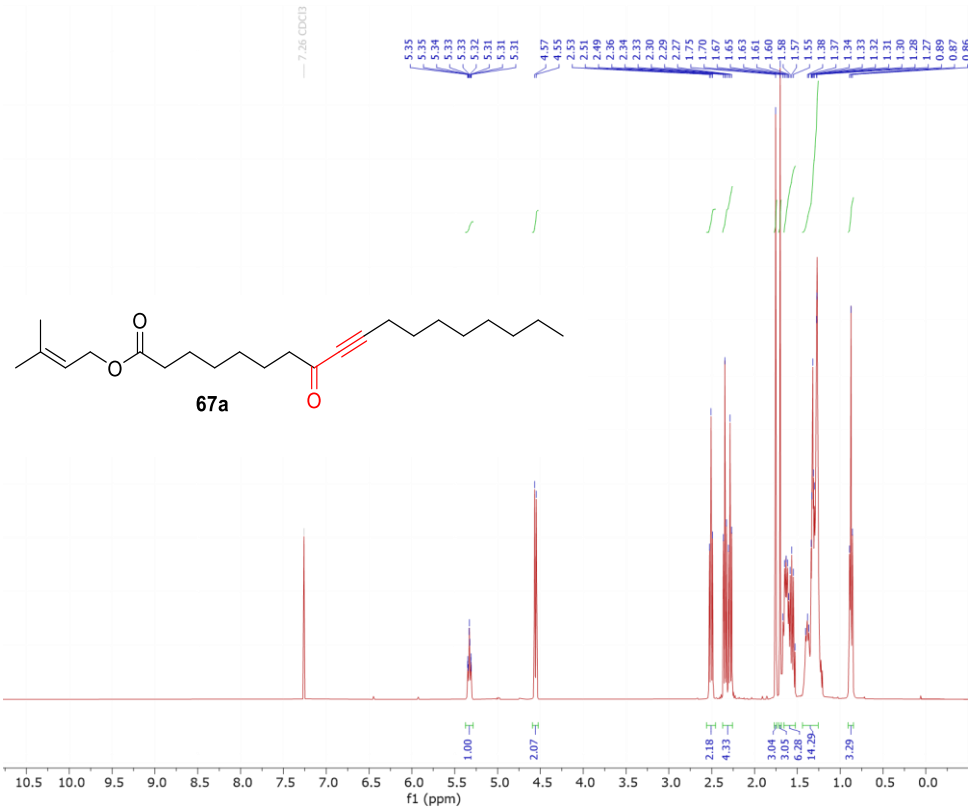

OH
O
O
99d
f1 (ppm)

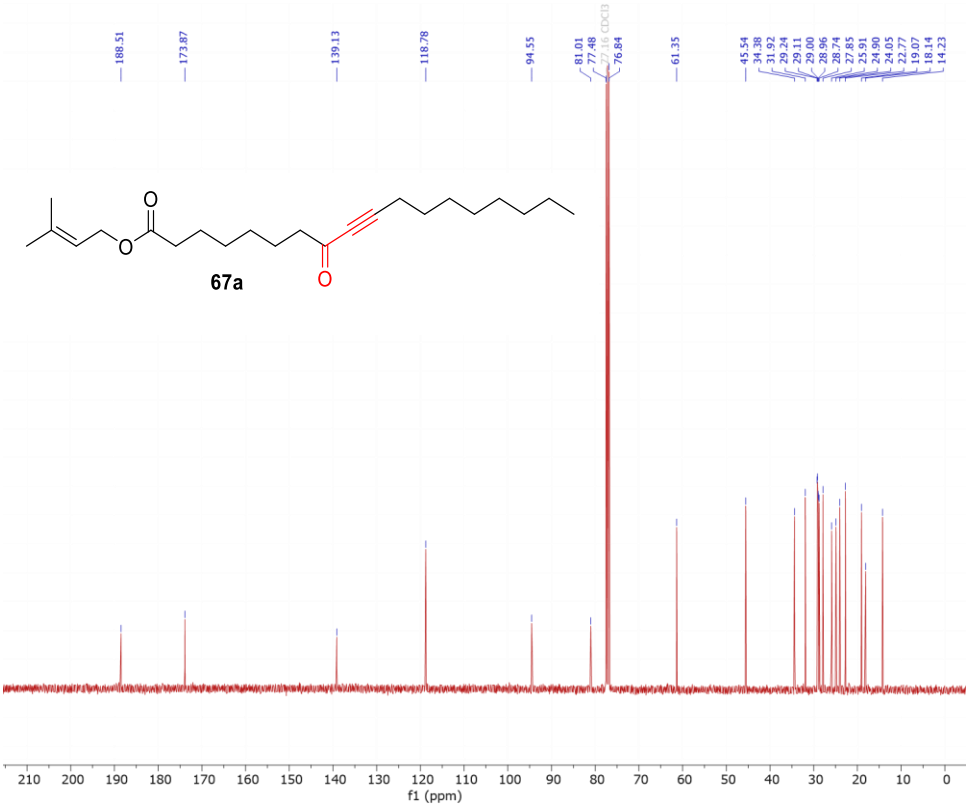

OH
O
O
99e
f1 (ppm)

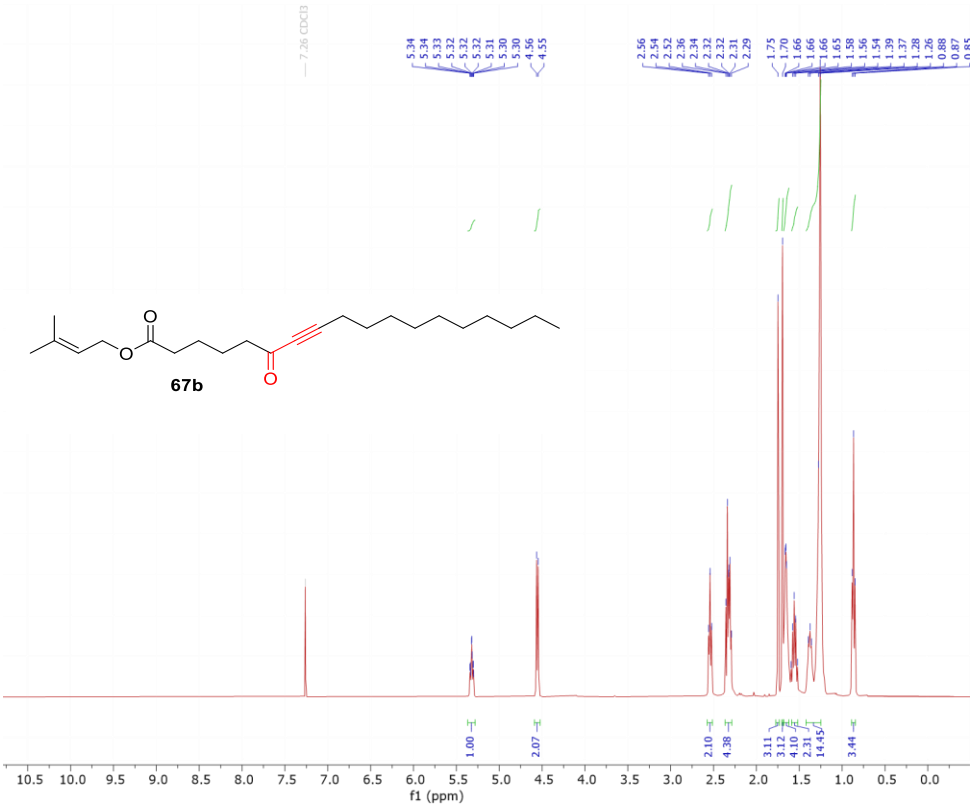

OH
O
O
99e
f1 (ppm)

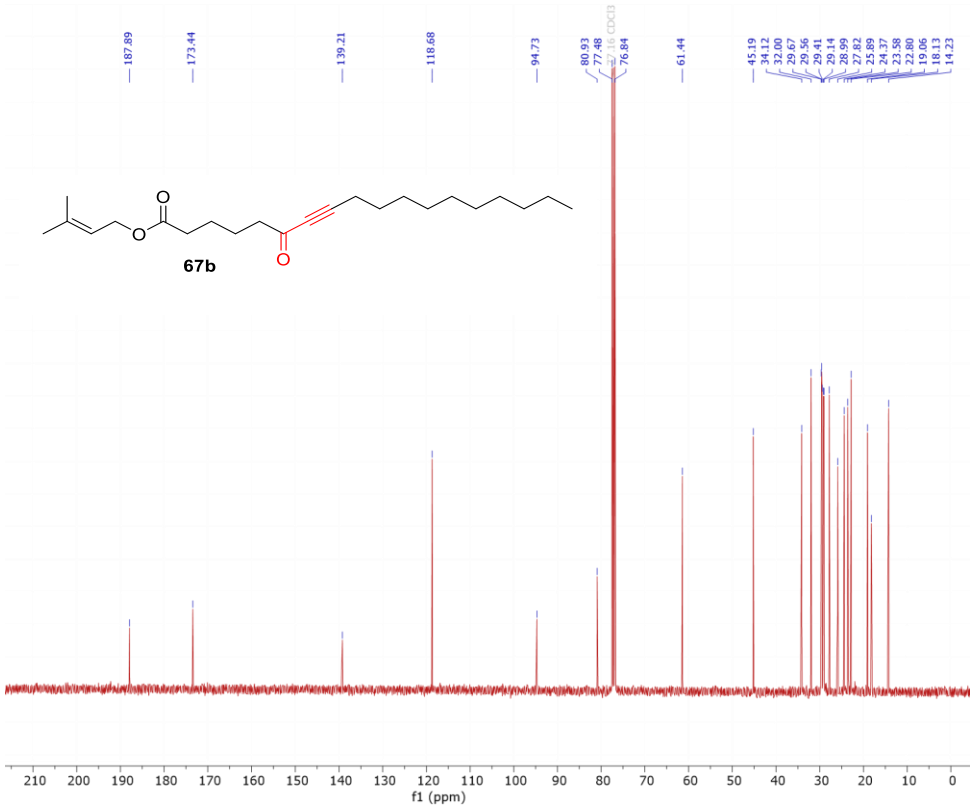

OH
O
O
99f
f1 (ppm)

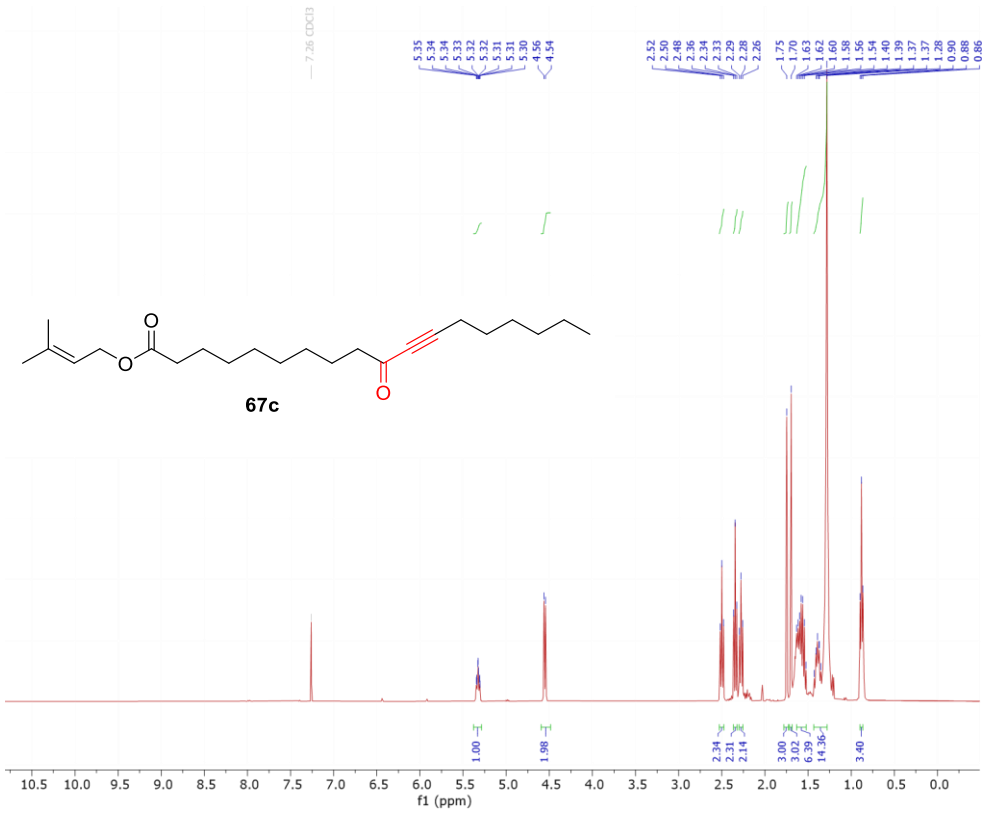

OH
O
O
99f
f1 (ppm)

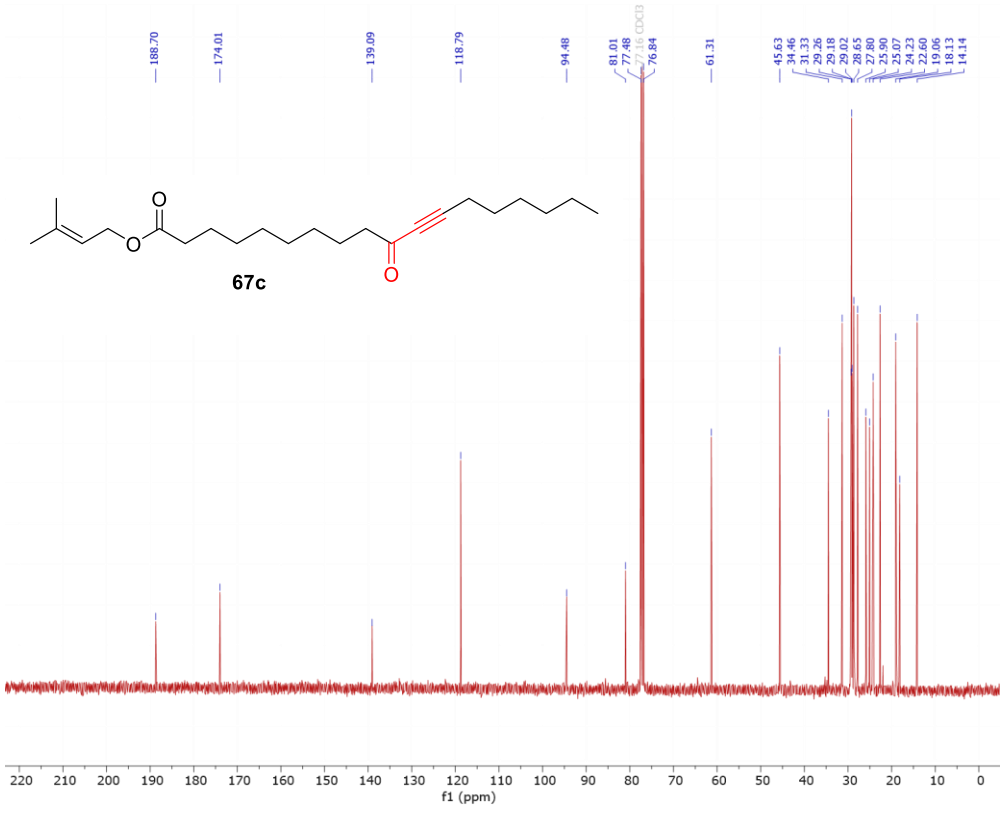

67a
f1 (ppm)

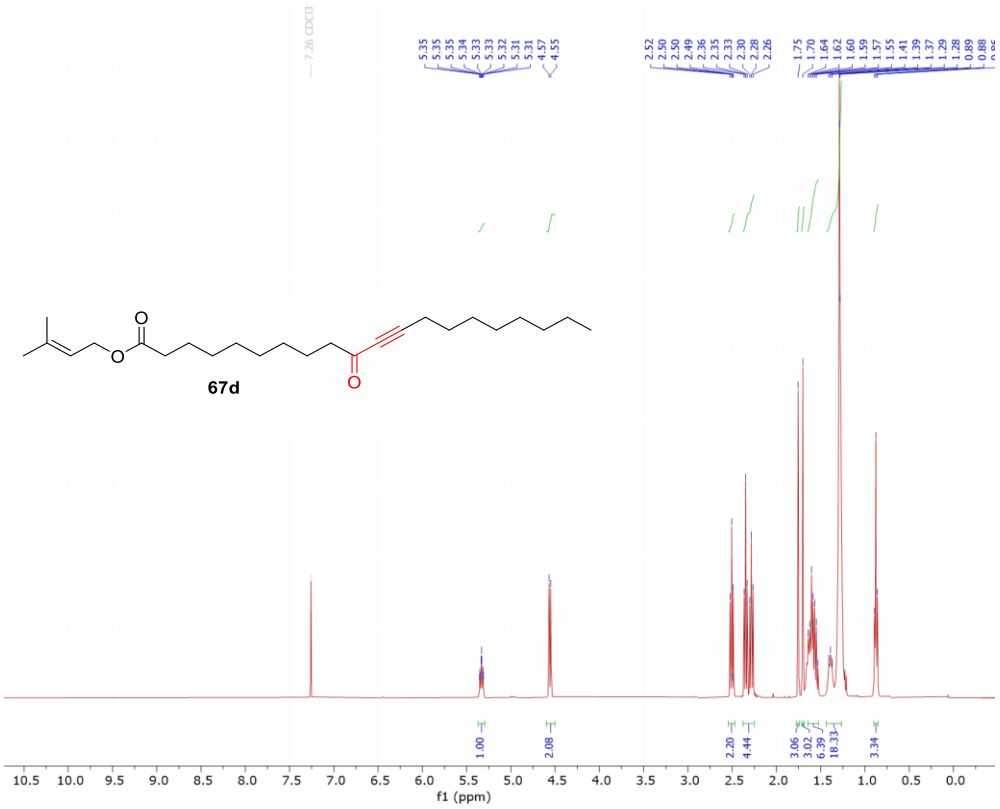

67a
f1 (ppm)

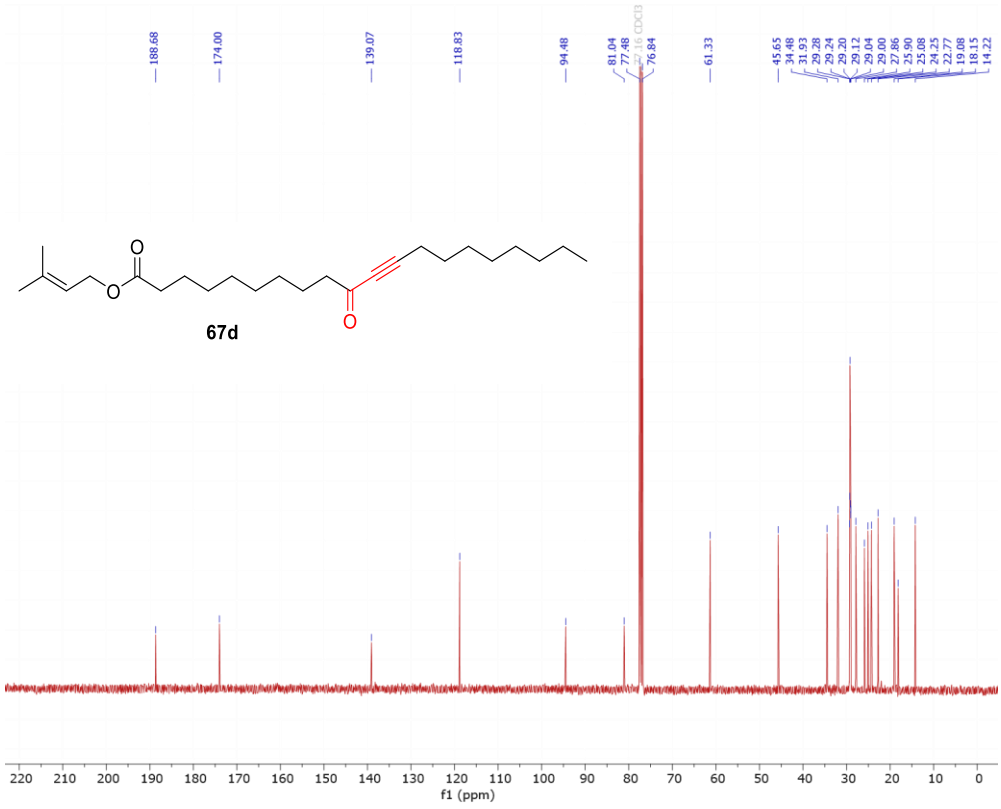

67b
f1 (ppm)

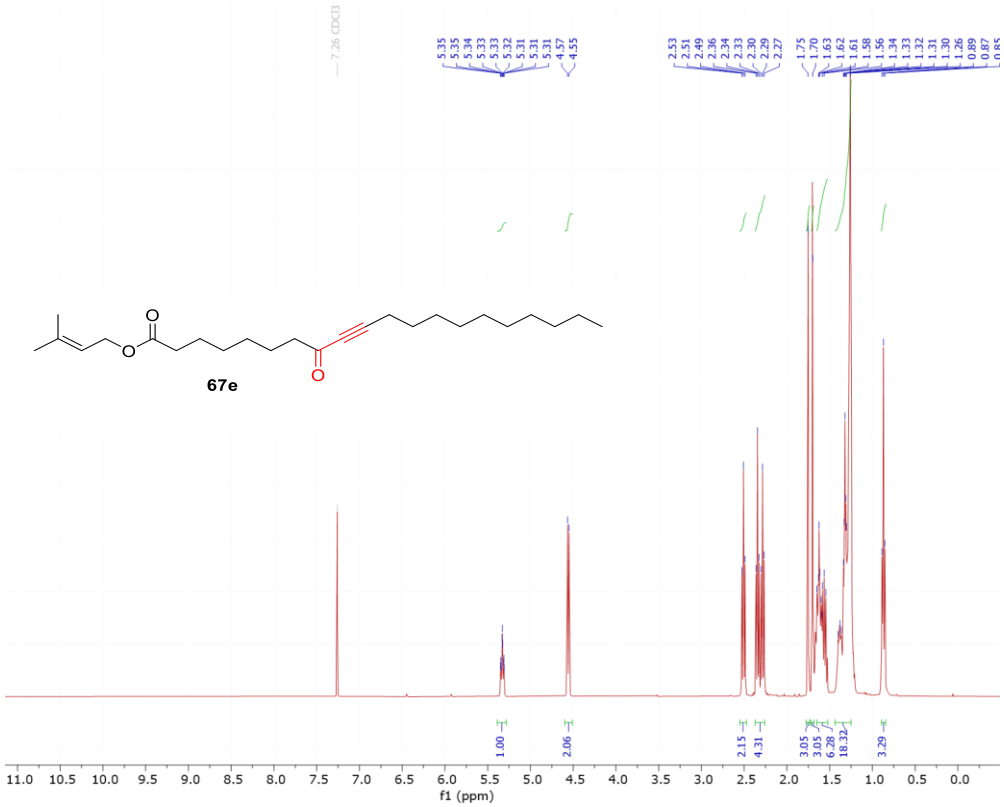

67b
f1 (ppm)

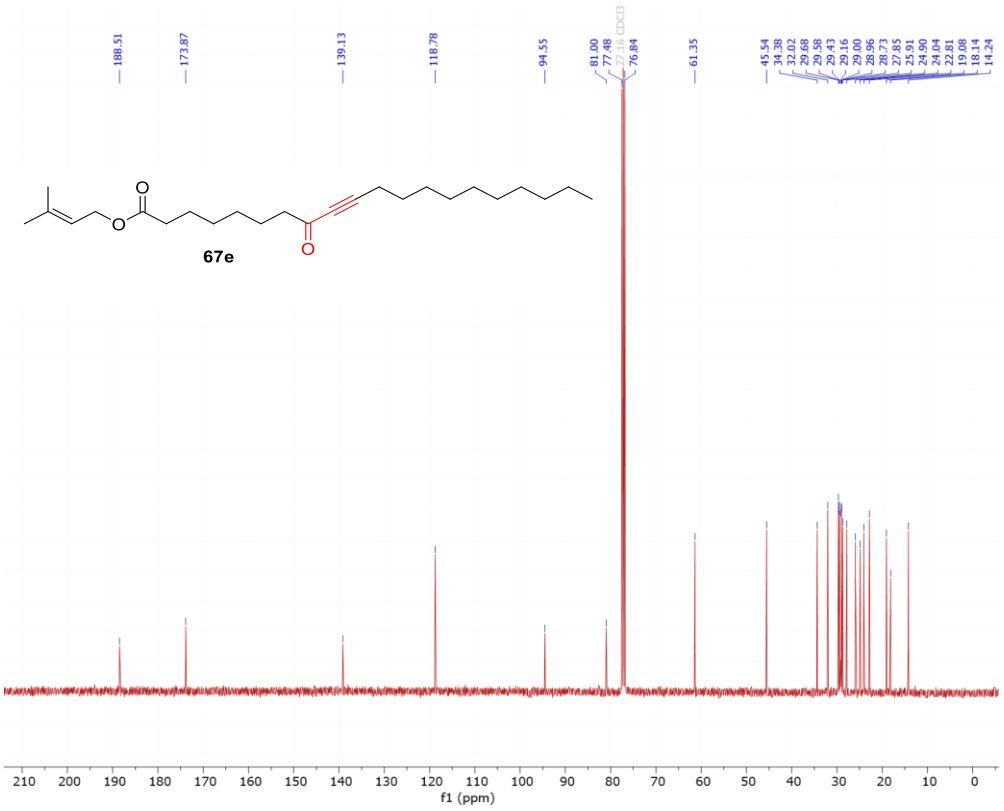

67c
f1 (ppm)

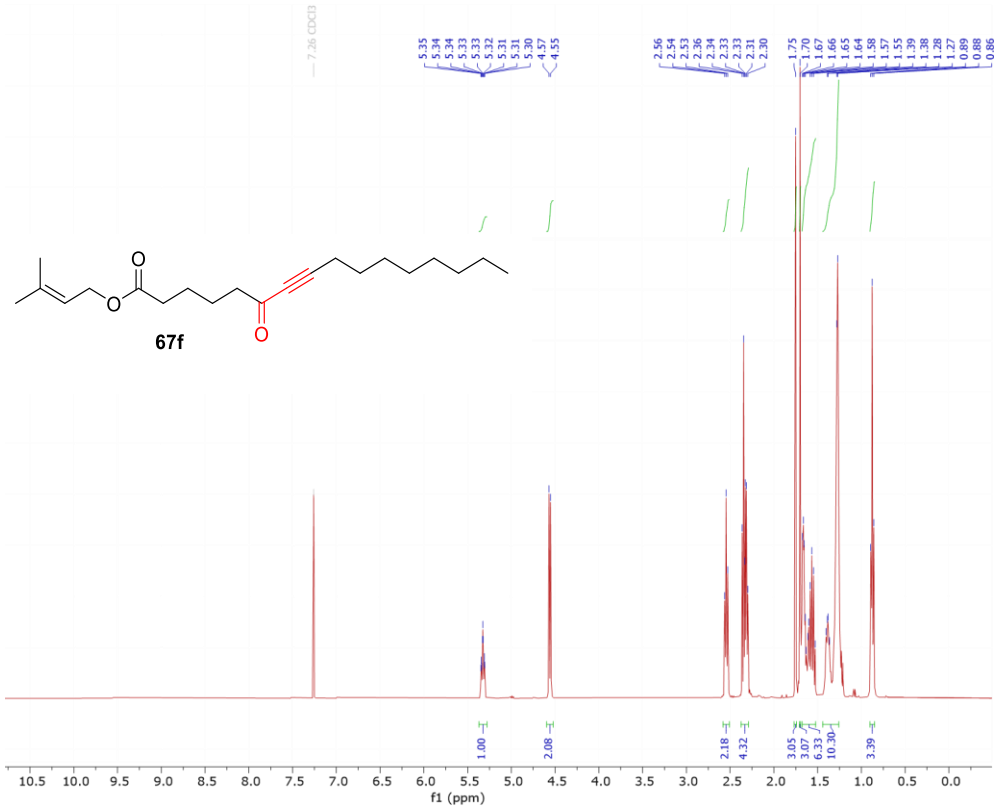

67c
f1 (ppm)

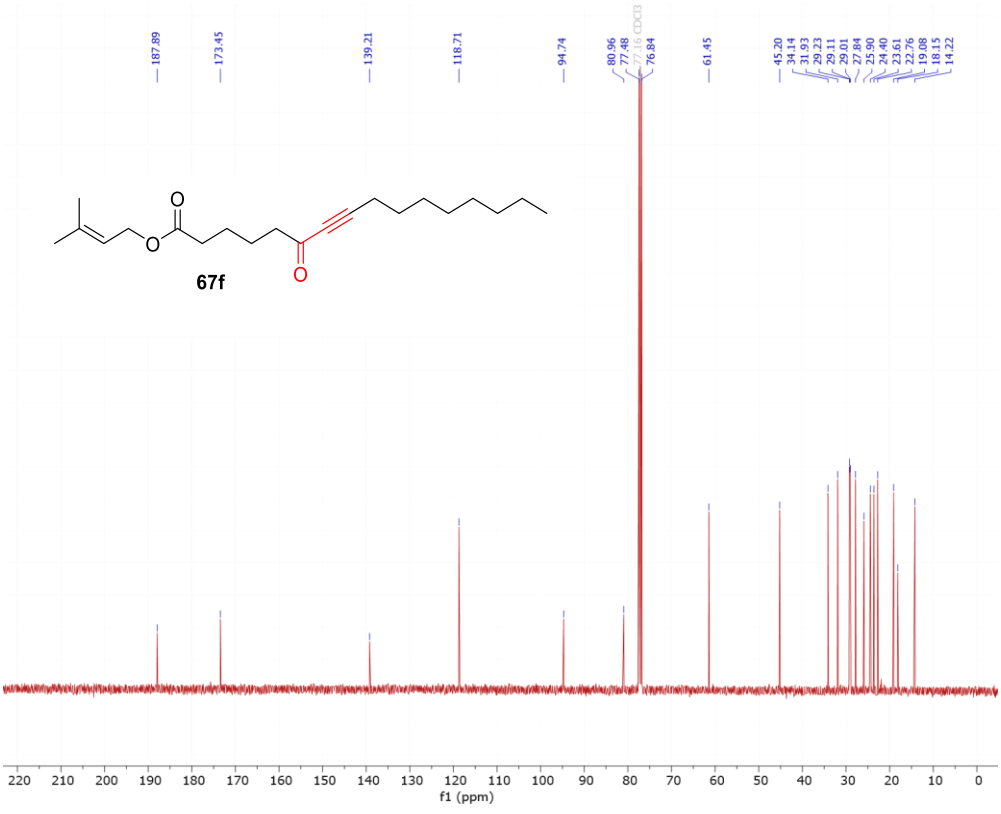

67d
f1 (ppm)

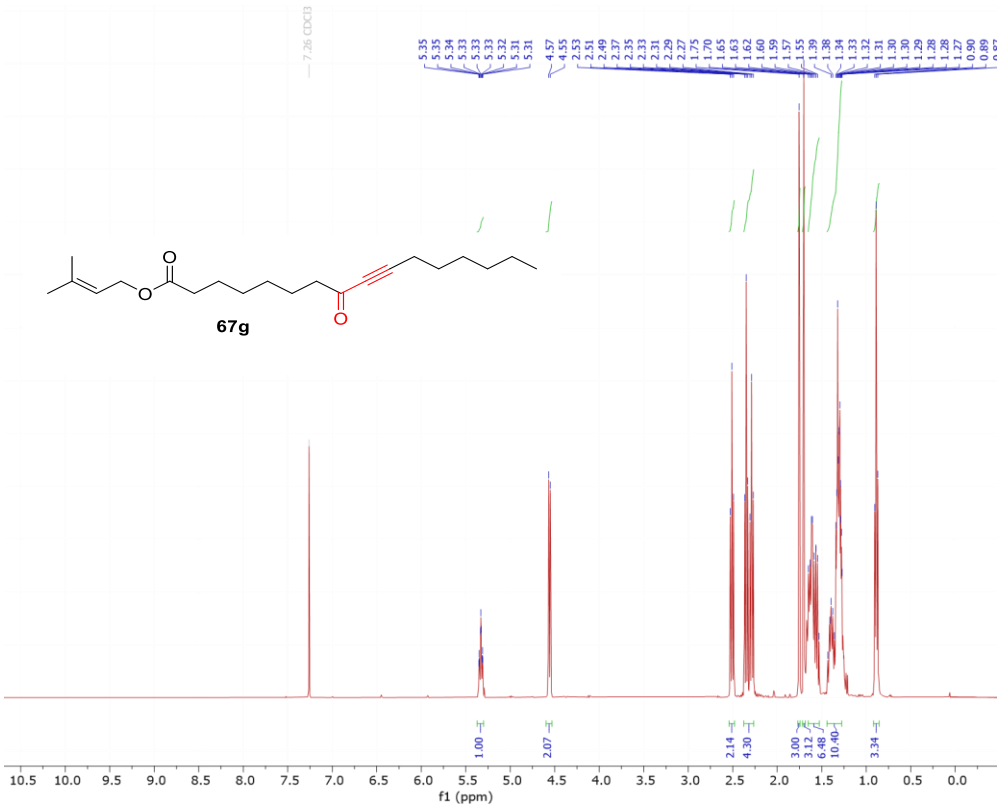

67d
f1 (ppm)

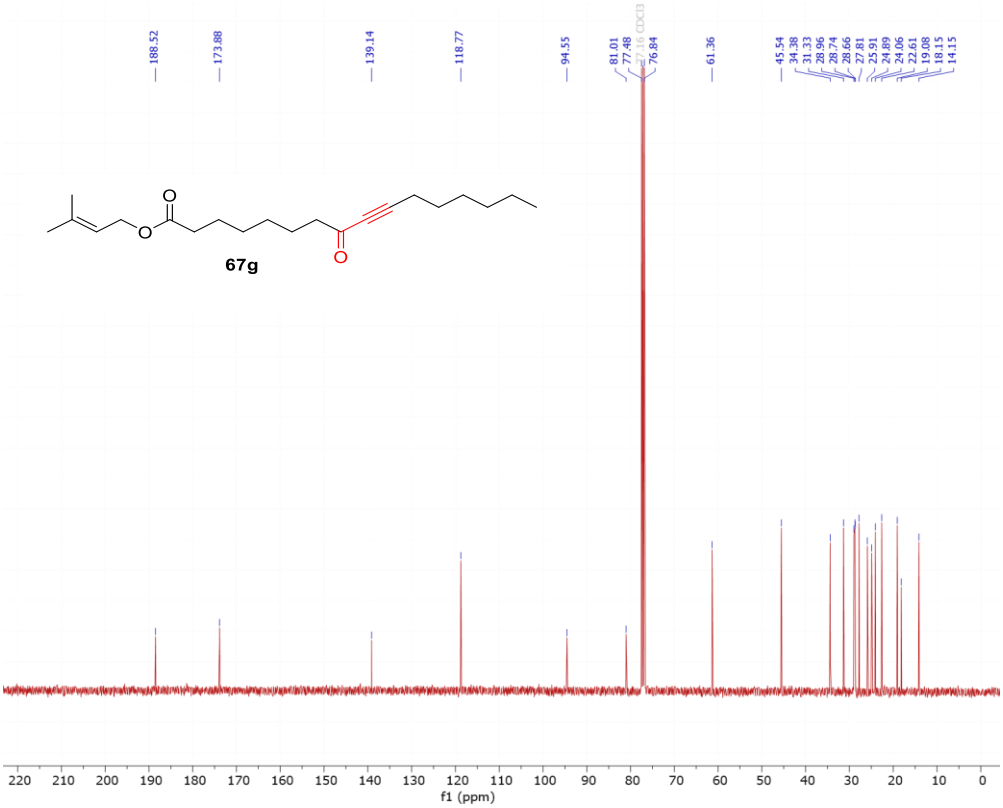

67e
f1 (ppm)

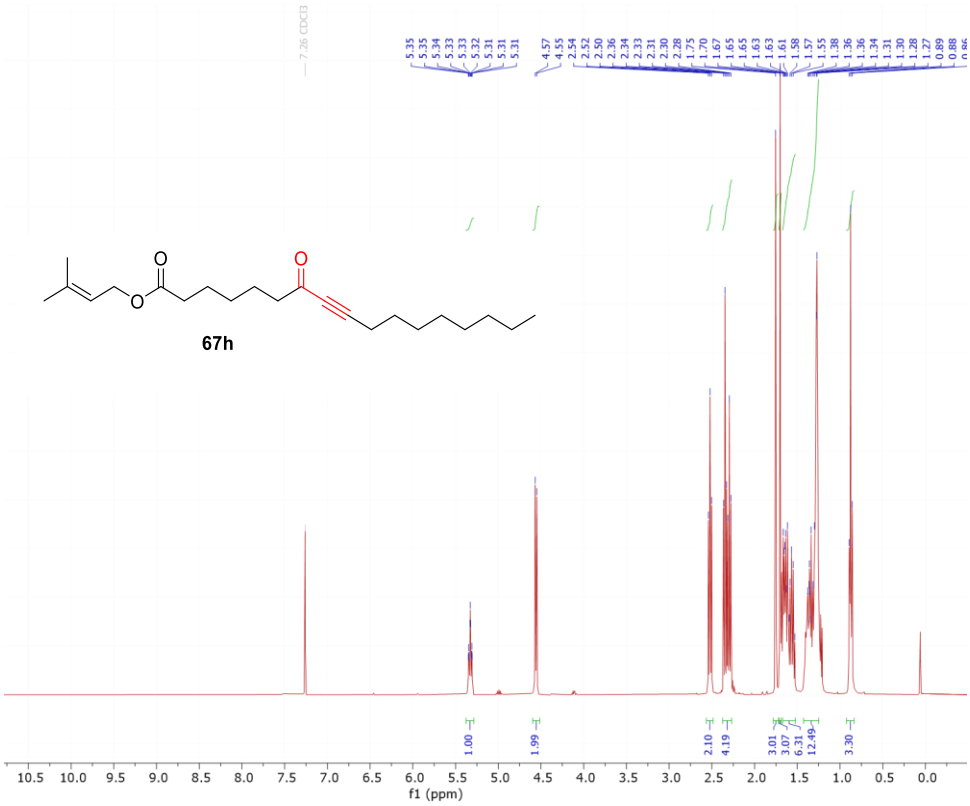

67e
f1 (ppm)

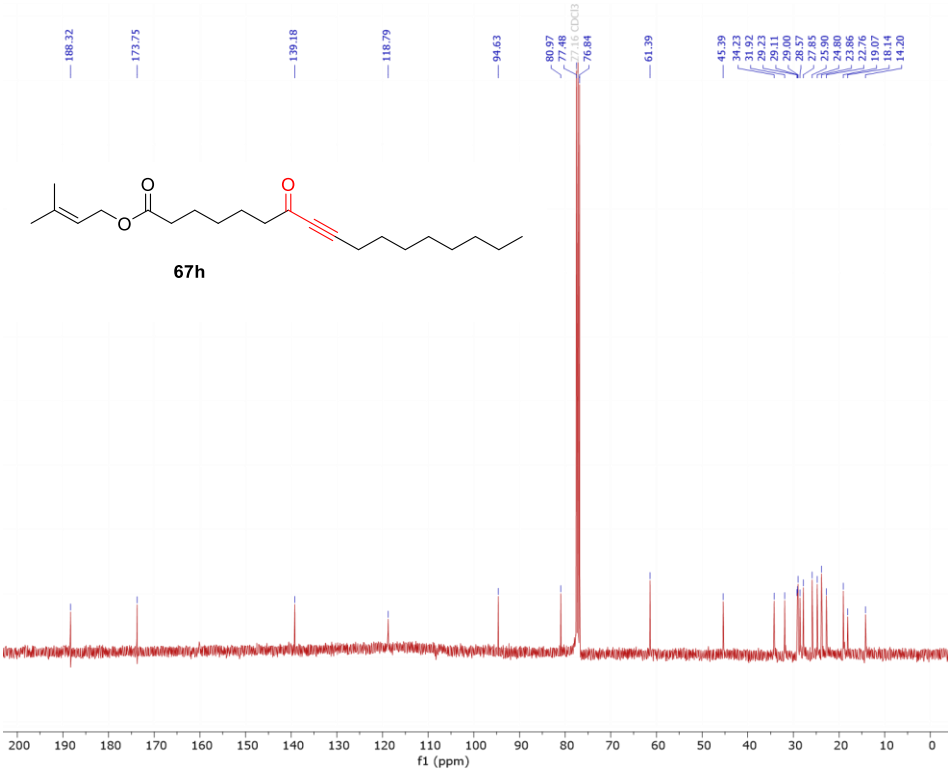

67f
f1 (ppm)

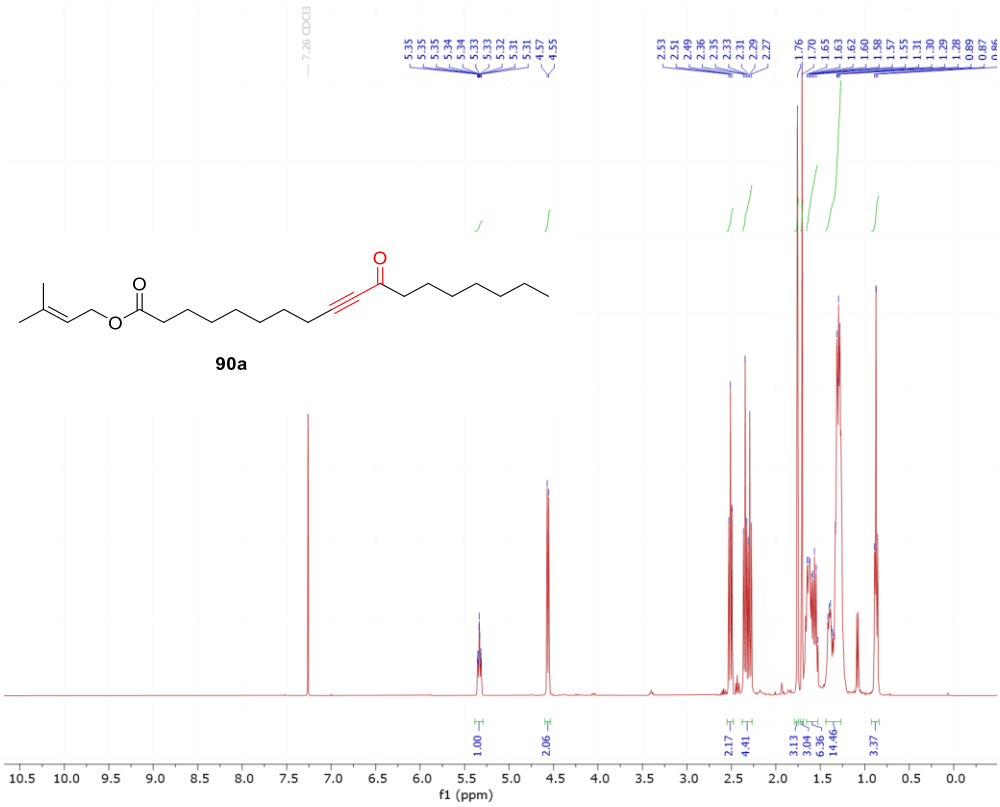

67f
f1 (ppm)

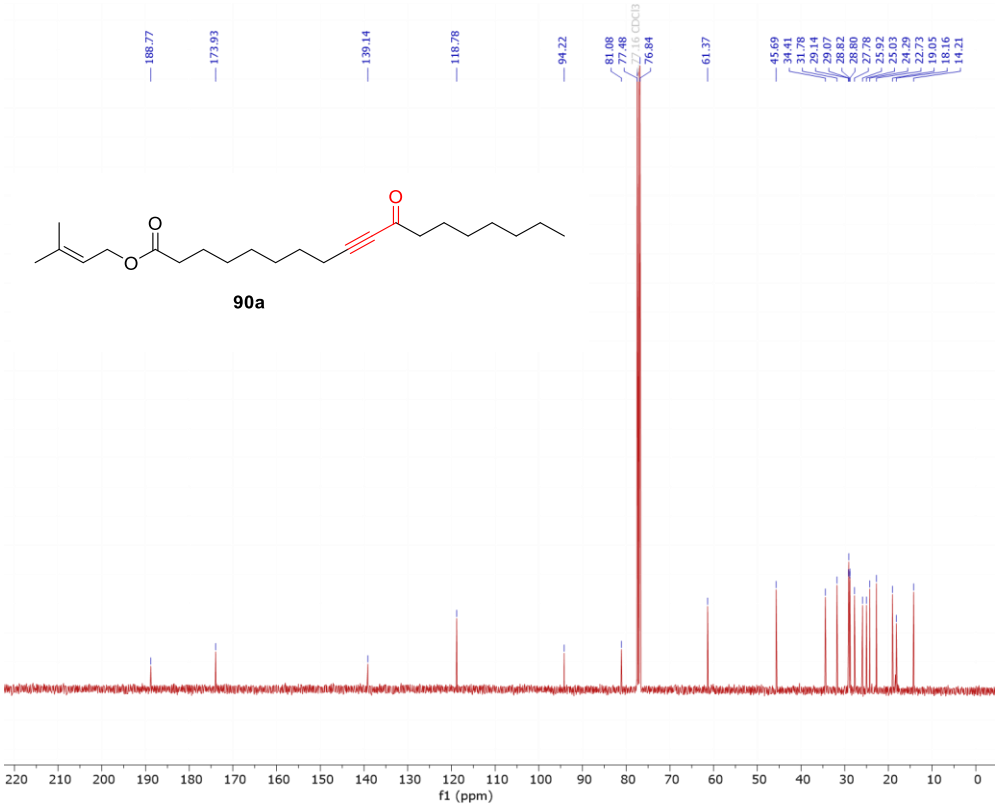

67g
f1 (ppm)

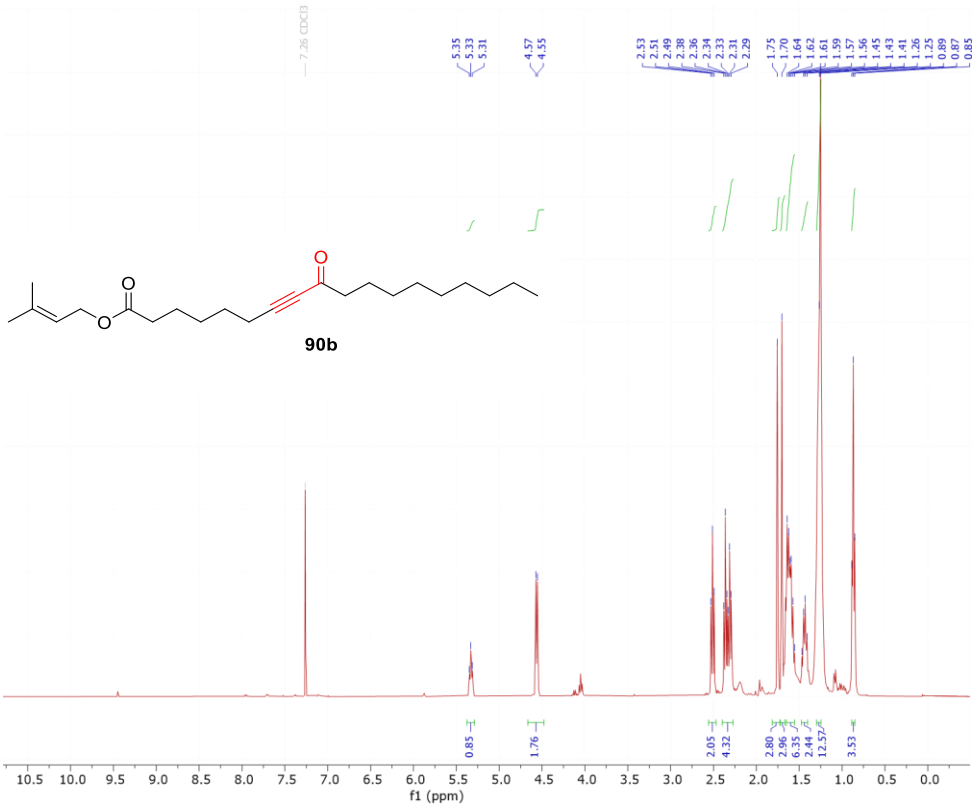

67g
f1 (ppm)

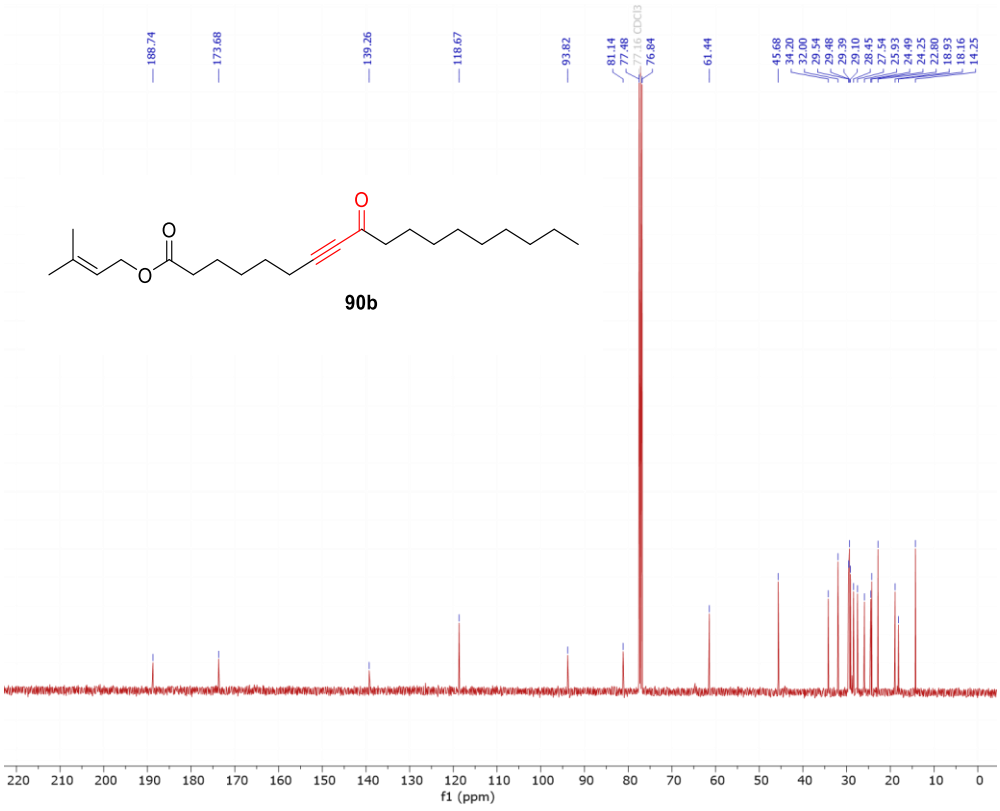

67h
f1 (ppm)

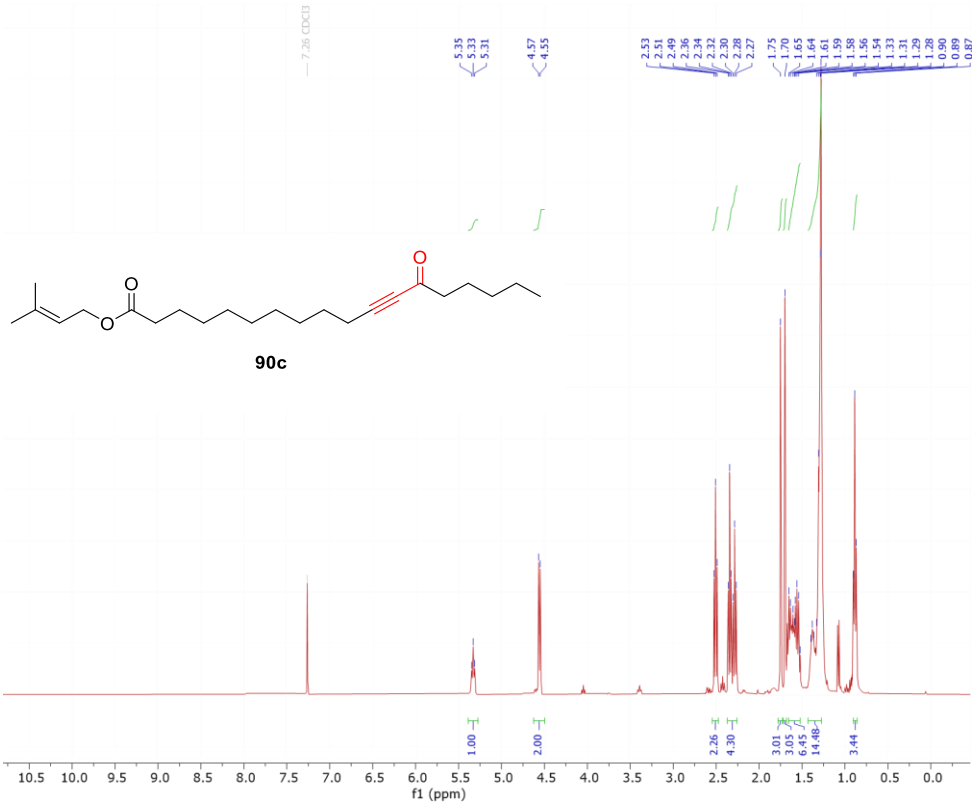

67h
f1 (ppm)

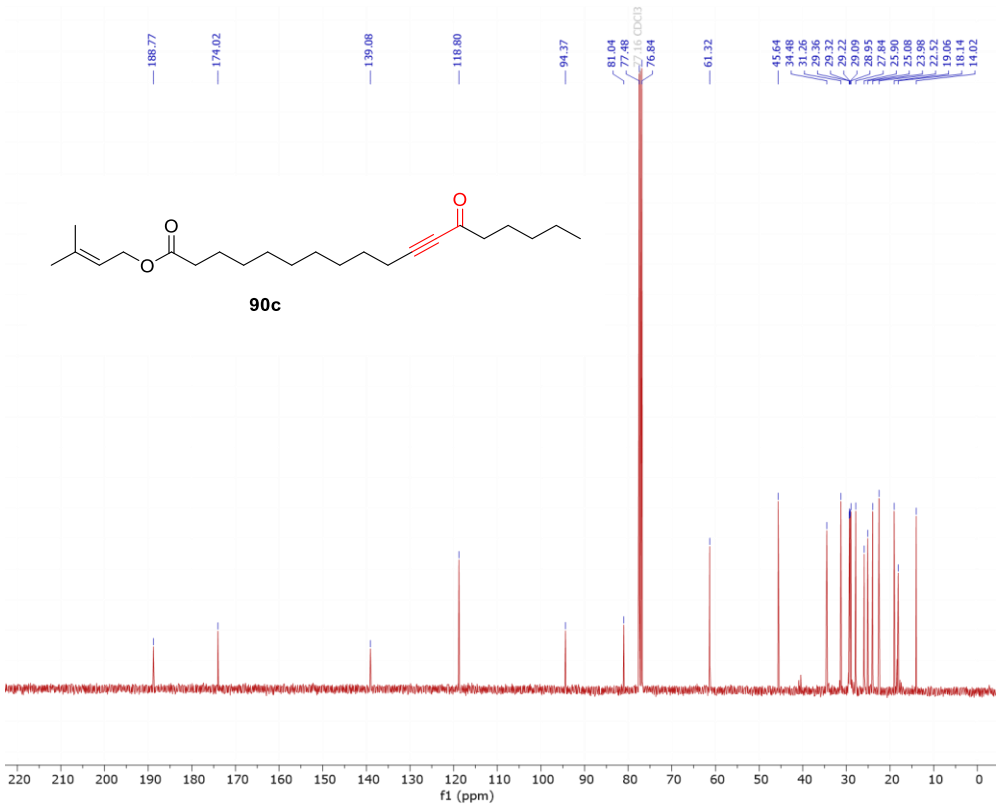

90a
f1 (ppm)

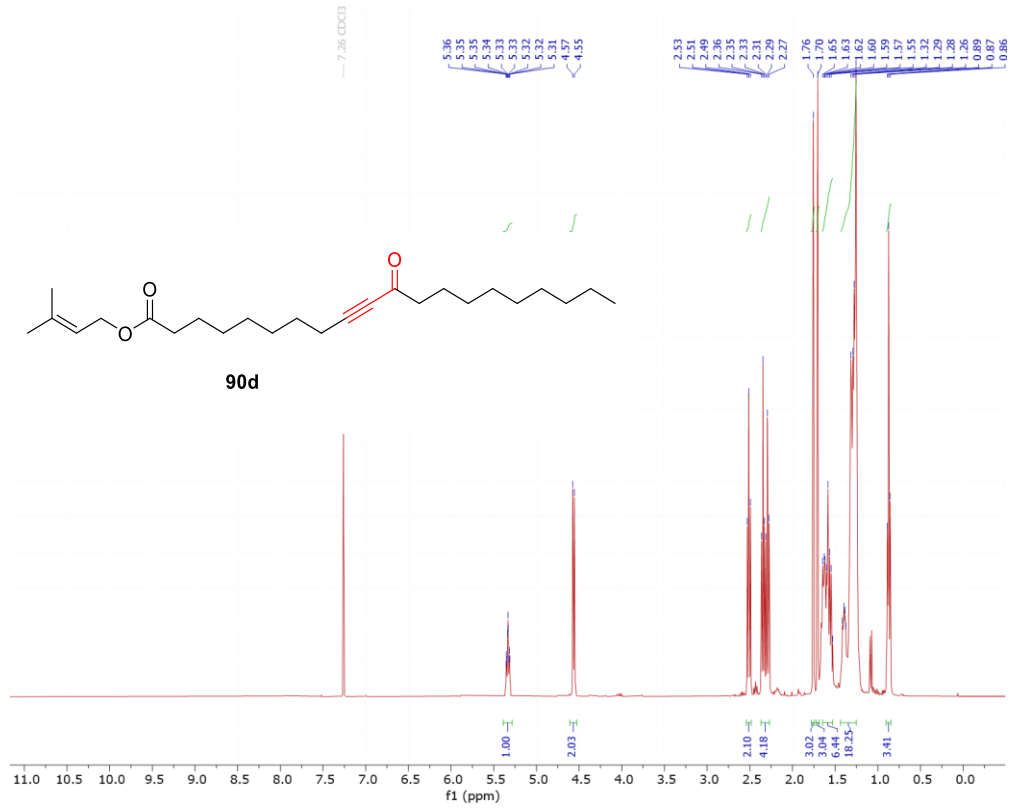

90a
f1 (ppm)

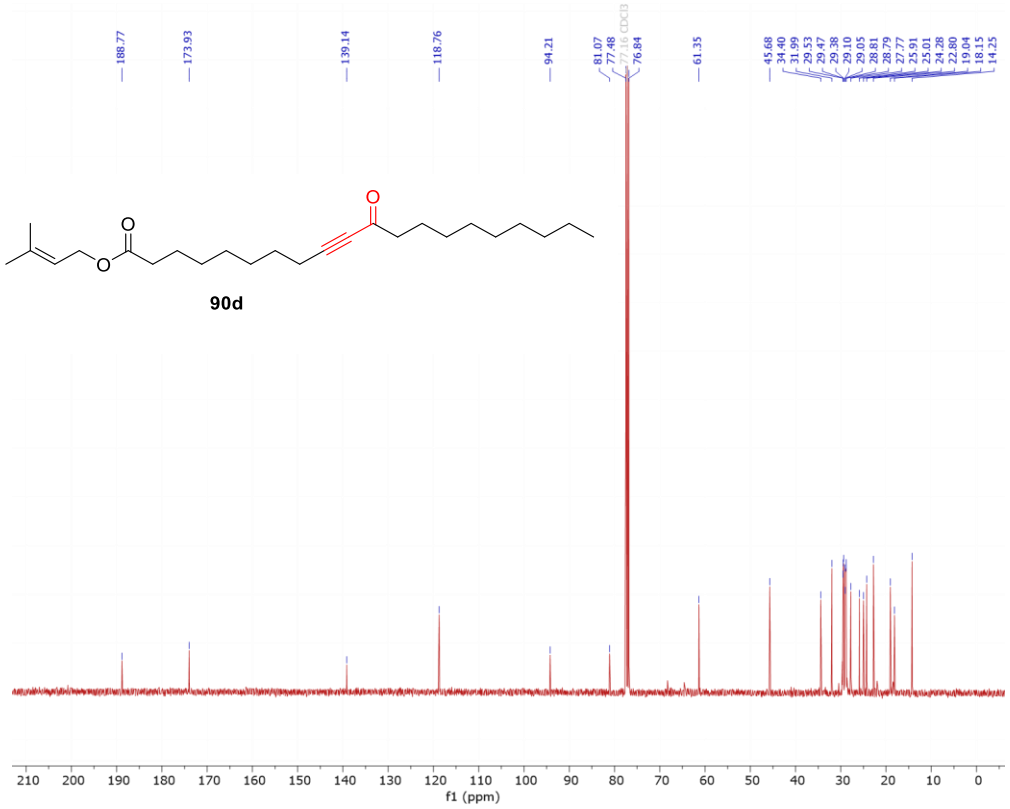

90b
f1 (ppm)

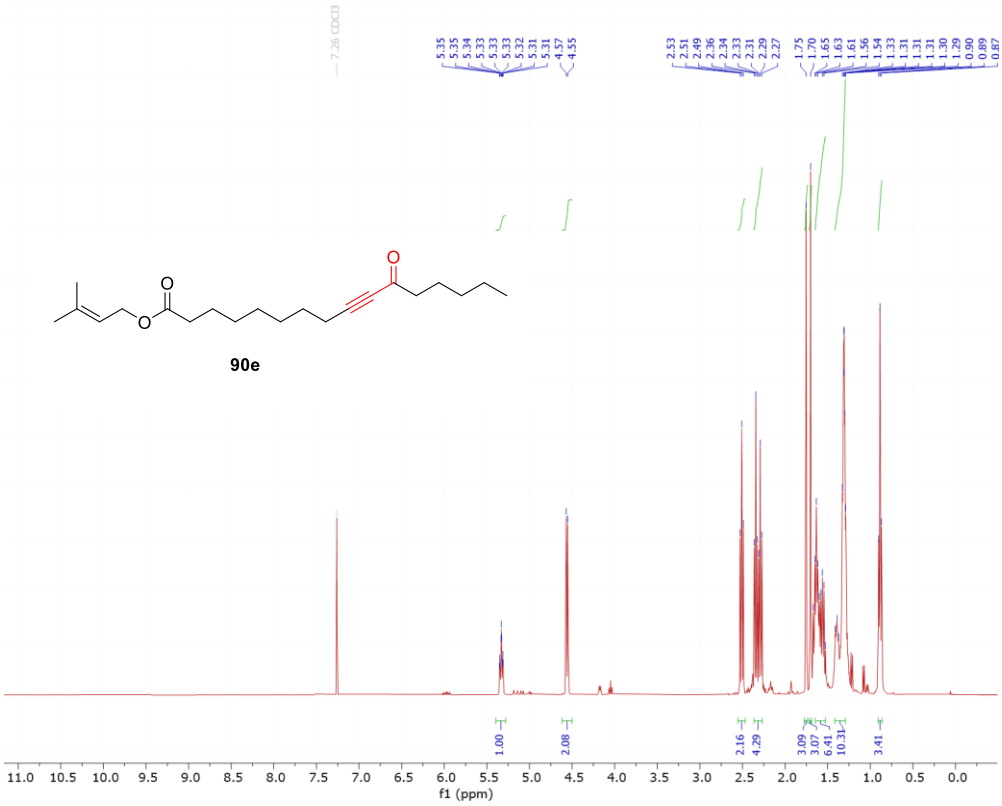

90b
f1 (ppm)

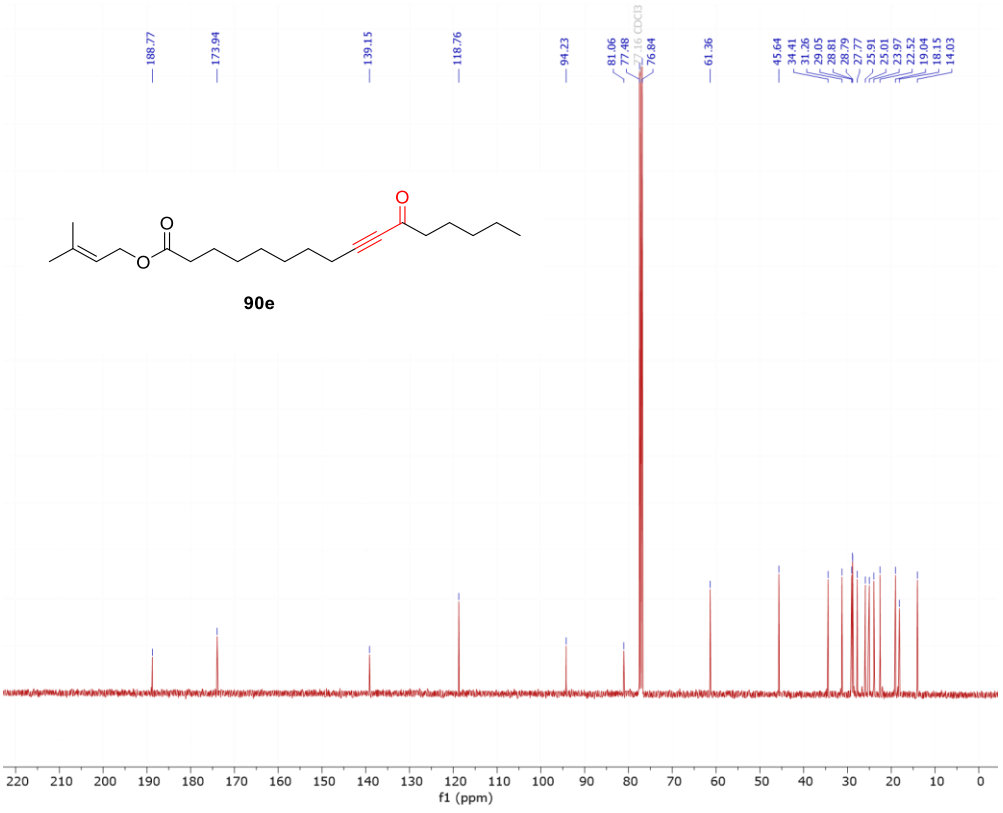

90c
f1 (ppm)

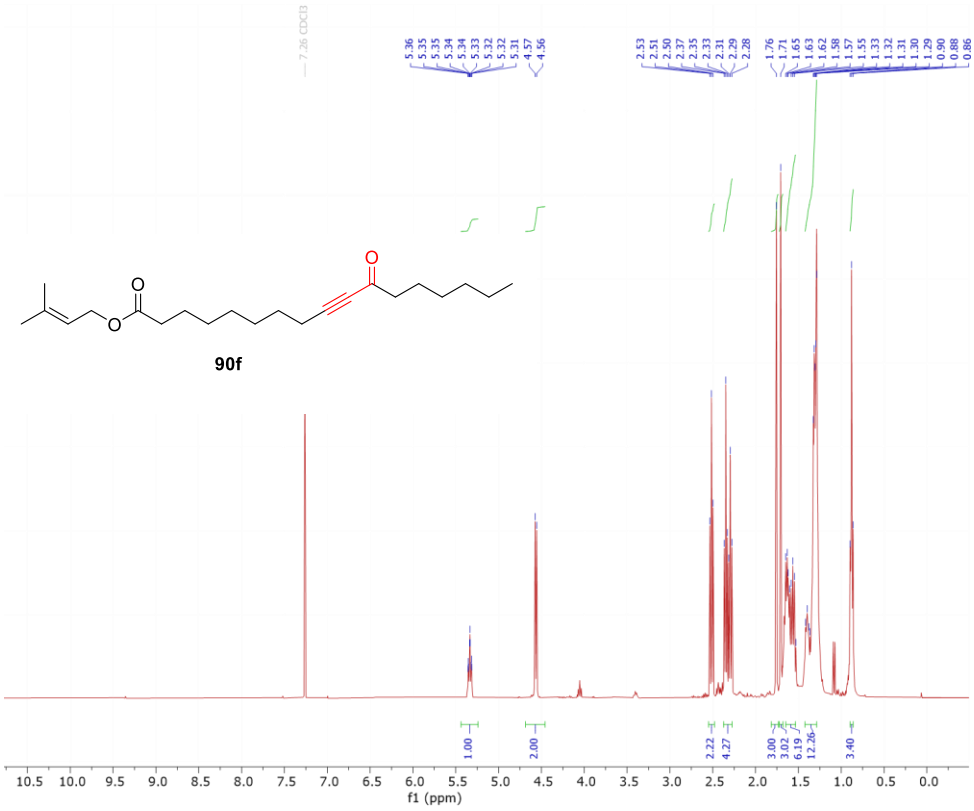

90c
f1 (ppm)

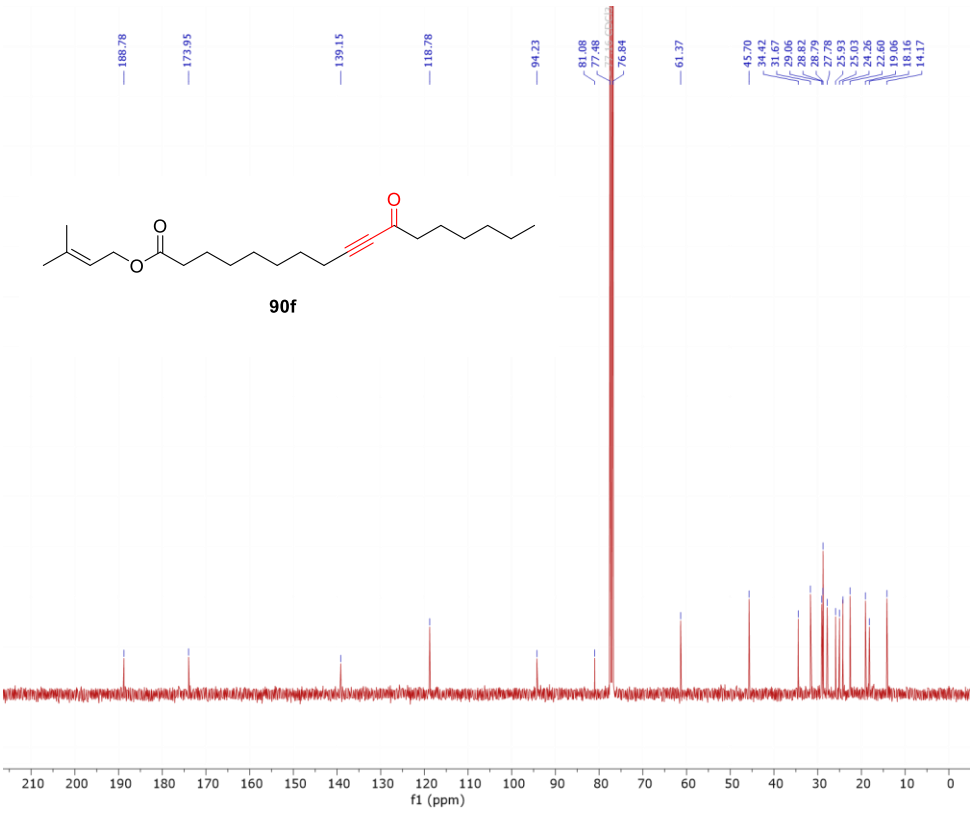

90d
f1 (ppm)

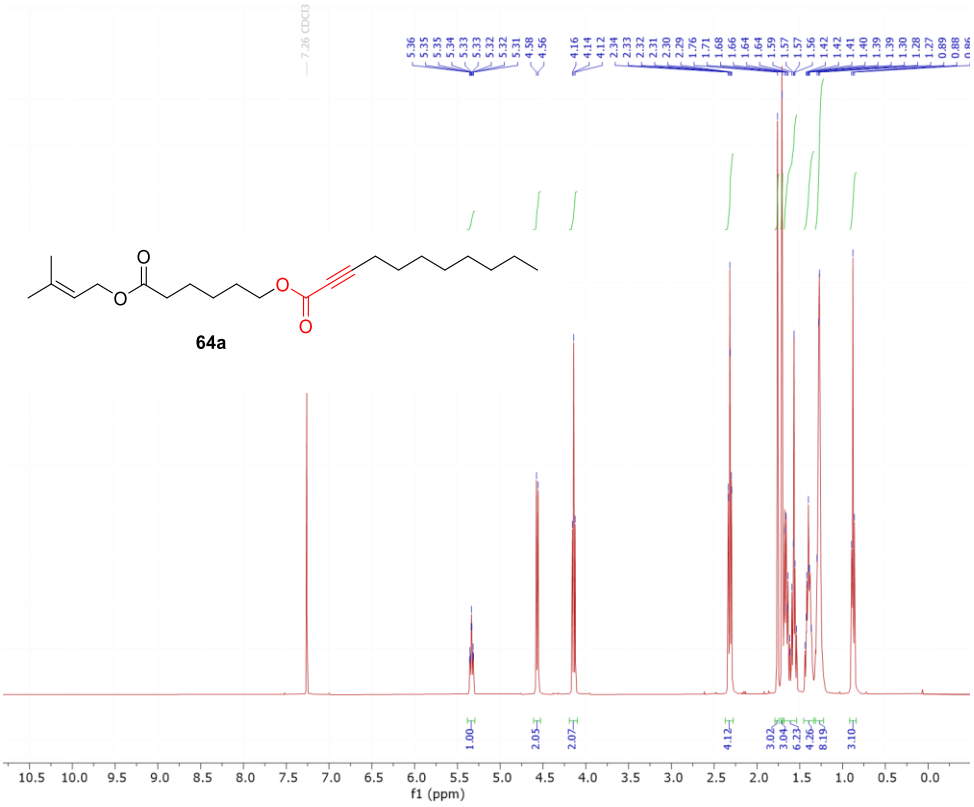

90d
f1 (ppm)

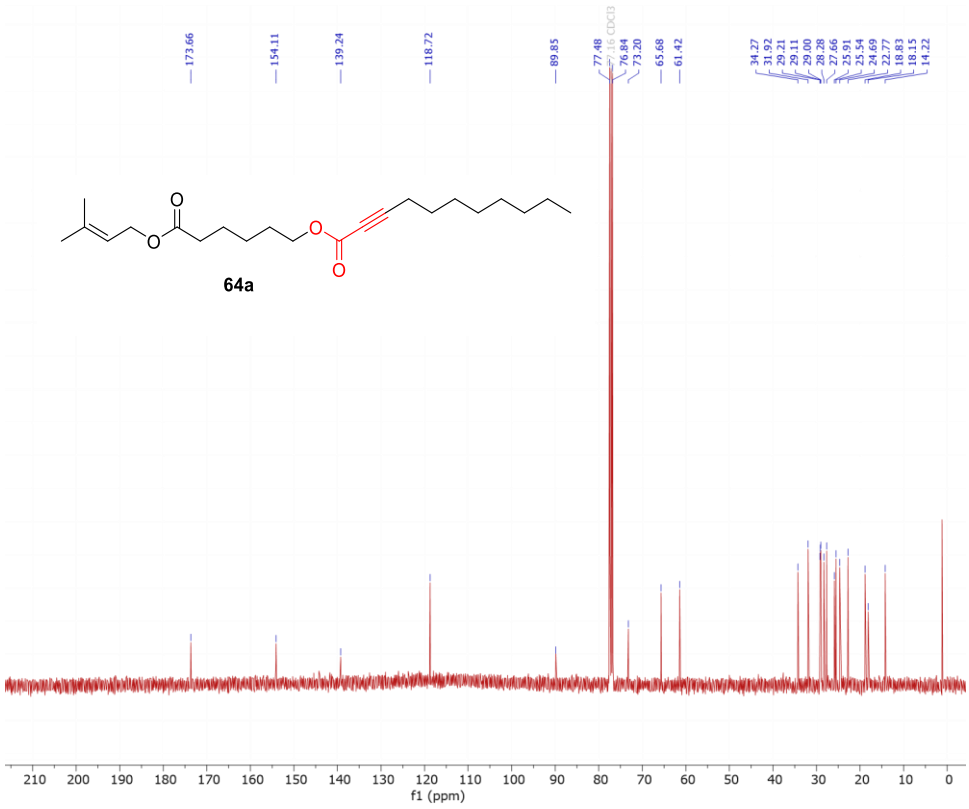

7.26 CDCl3
5.35
5.35
5.34
5.34
5.33
5.33
5.32
5.31
5.31
4.57
4.55
2.53
2.51
2.49
2.36
2.34
2.33
2.31
2.29
2.27
1.75
1.70
1.65
1.63
1.61
1.56
1.54
1.33
1.31
1.31
1.31
1.30
1.29
1.29
0.90
0.89
0.87
O
O
O
90e
1.00
2.08
2.16
4.29
3.09
3.07
6.41
10.31
3.41
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

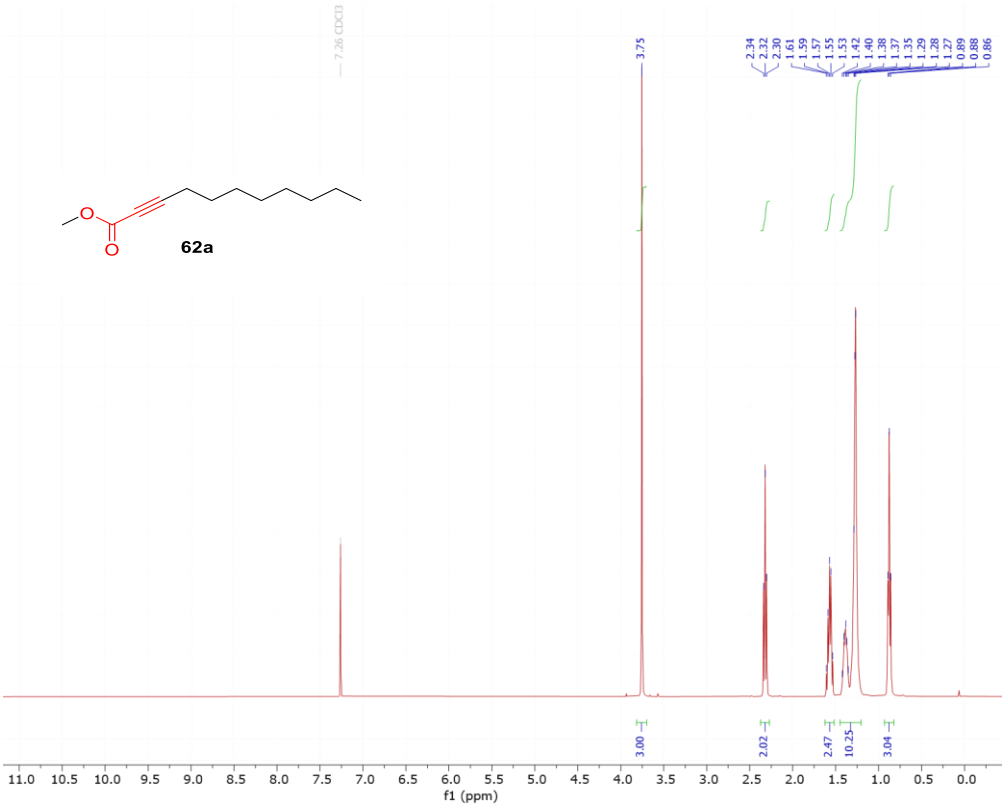

188.77
173.94
139.15
118.76
94.23
81.06
77.48
77.16
CDCl3
76.84
61.36
45.64
34.41
31.26
29.65
29.31
28.79
27.77
25.91
25.01
23.97
22.52
19.04
18.15
14.03
O
O
O
90e
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

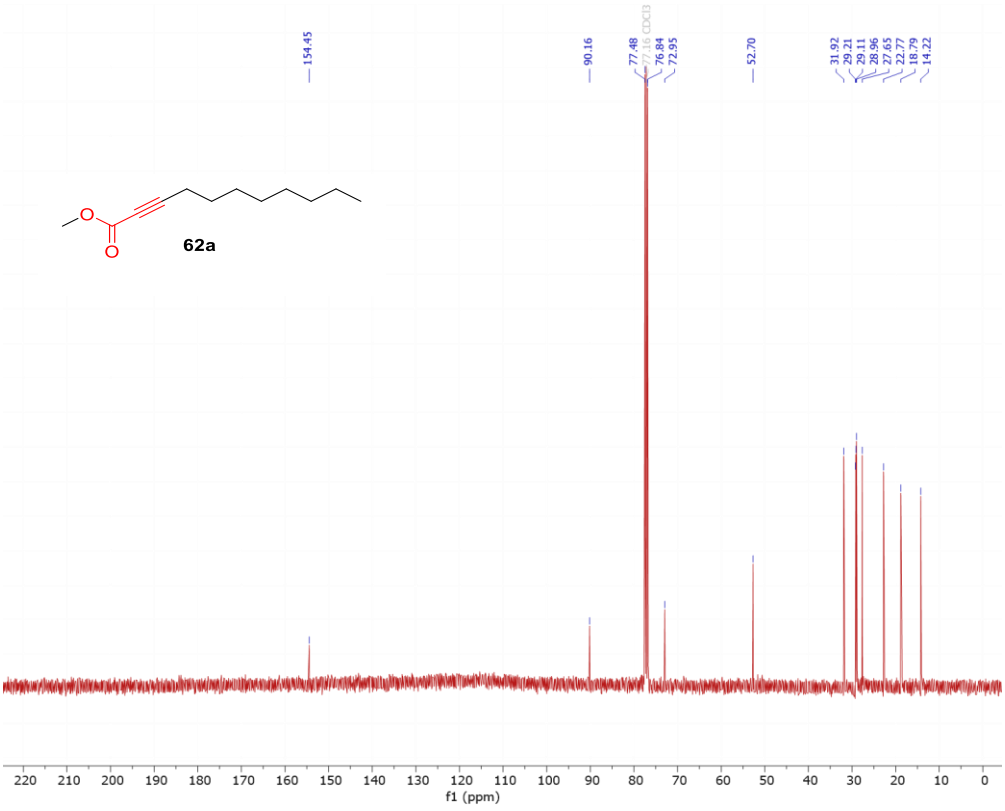

90f
f1 (ppm)

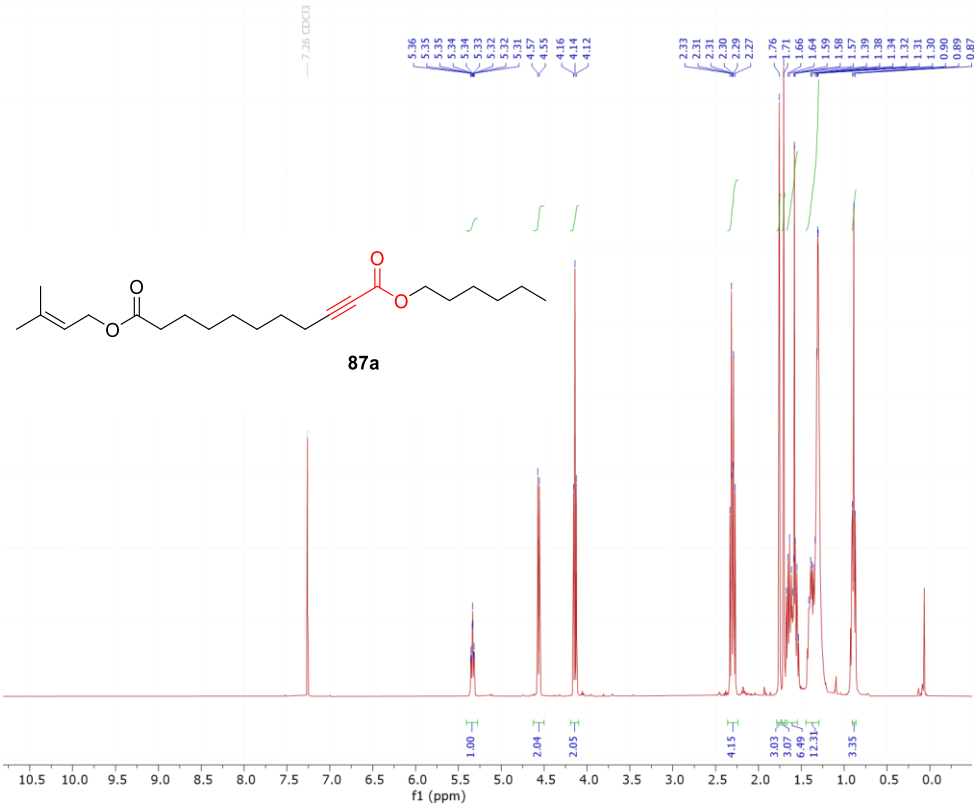

90f
f1 (ppm)

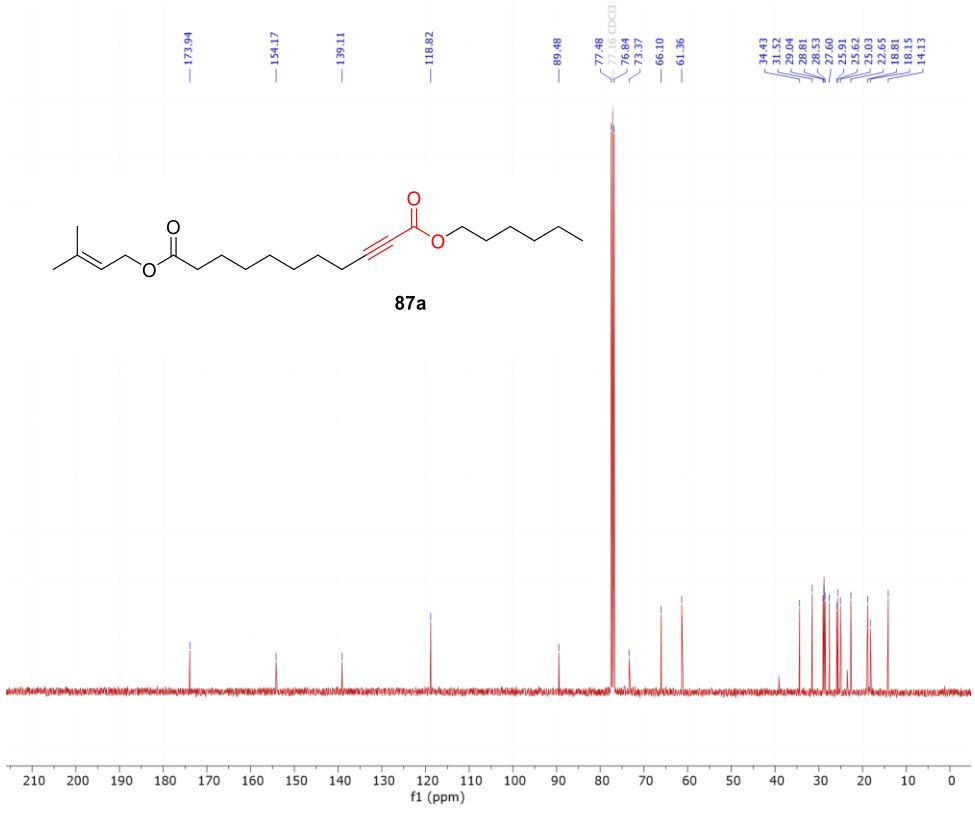

64a
f1 (ppm)

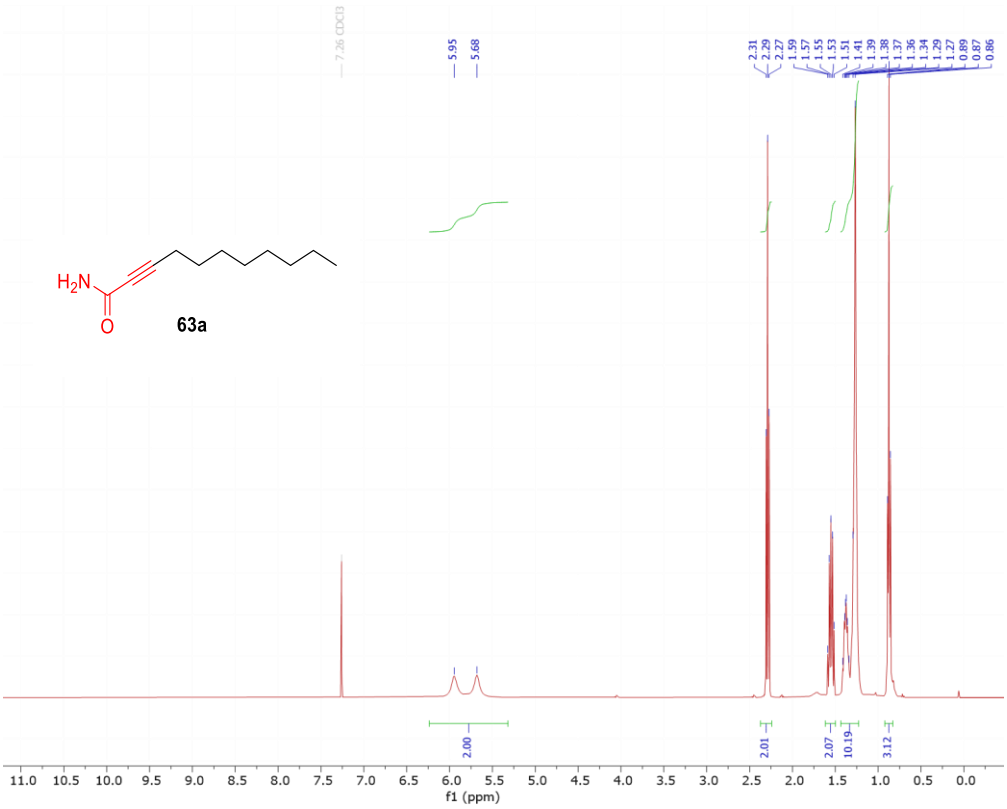

64a
f1 (ppm)

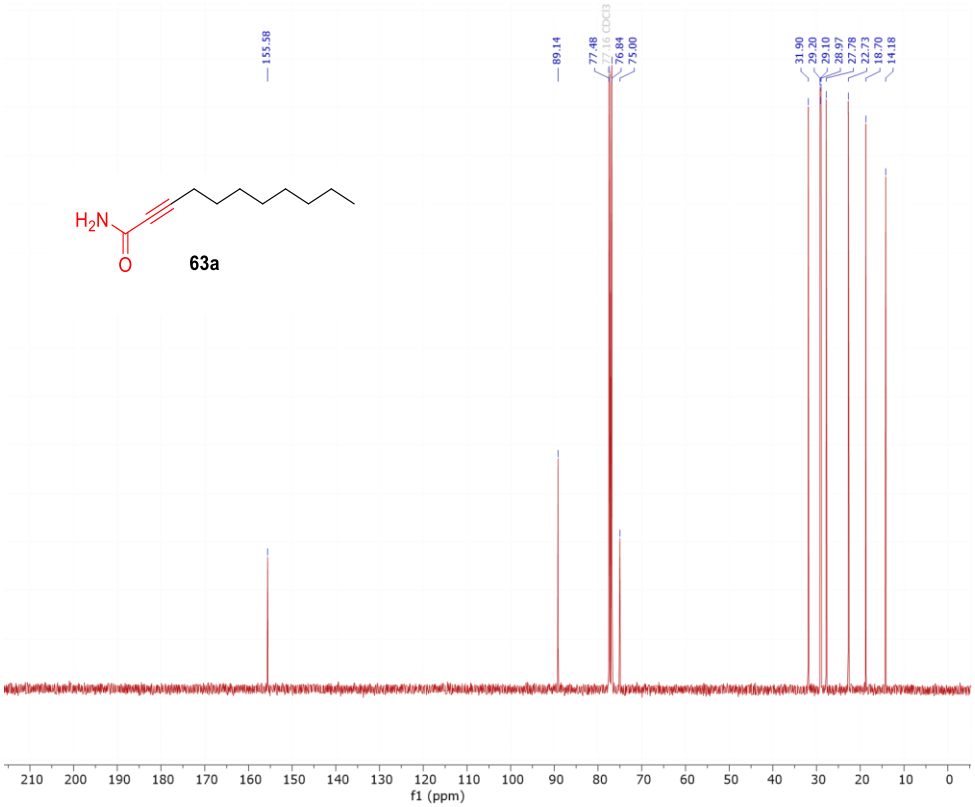

7.26 CDCl3
3.75
2.34
2.32
2.30
2.01
1.59
1.57
1.55
1.53
1.42
1.40
1.38
1.37
1.35
1.29
1.28
1.27
0.89
0.88
0.86
3.00
2.02
2.47
10.25
3.04
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
62a

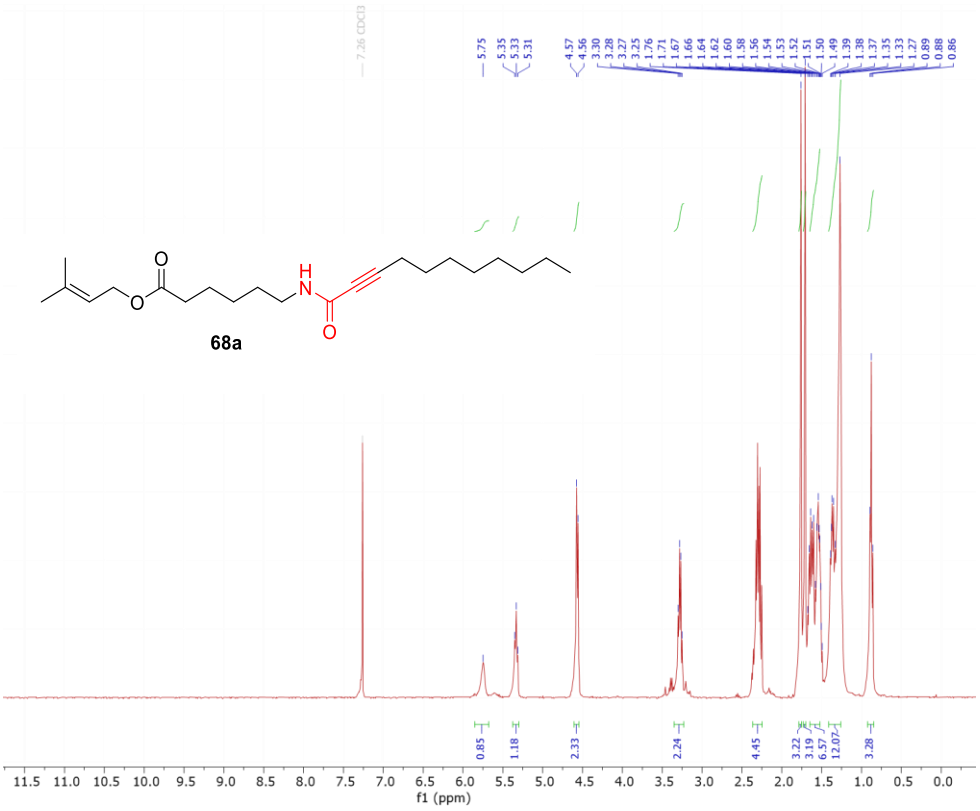

154.45
90.16
77.48
77.16 CDCl3
76.84
72.95
52.70
31.92
29.21
29.11
28.96
27.65
22.77
18.79
14.22
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
62a

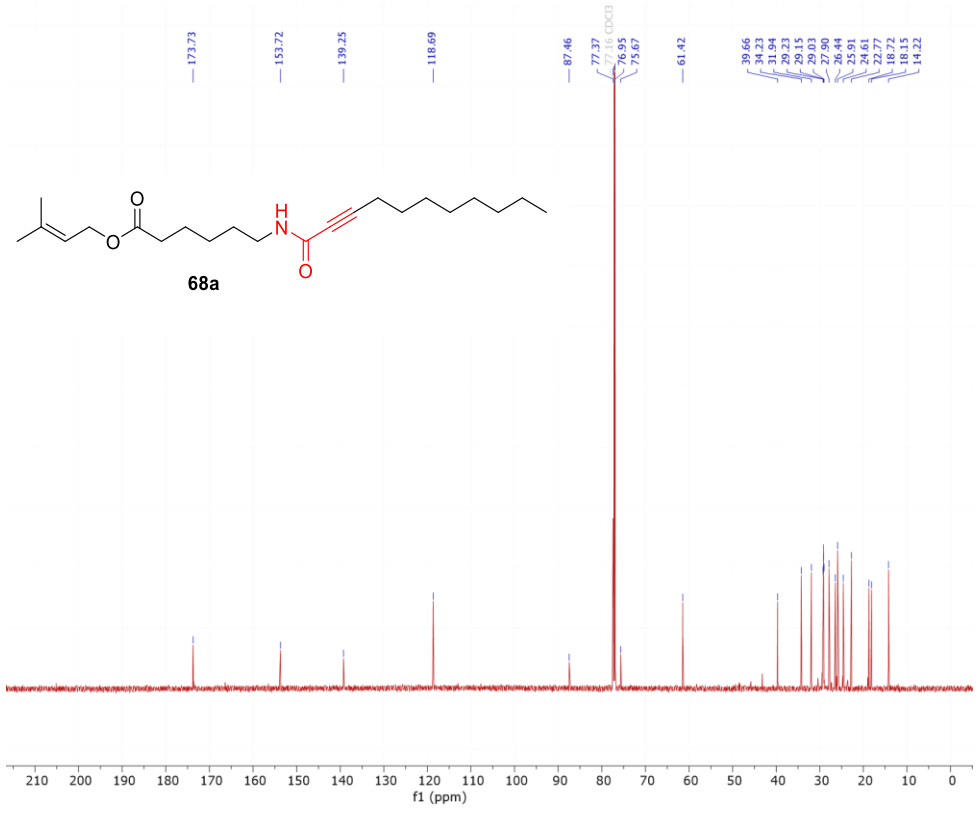

87a
f1 (ppm)

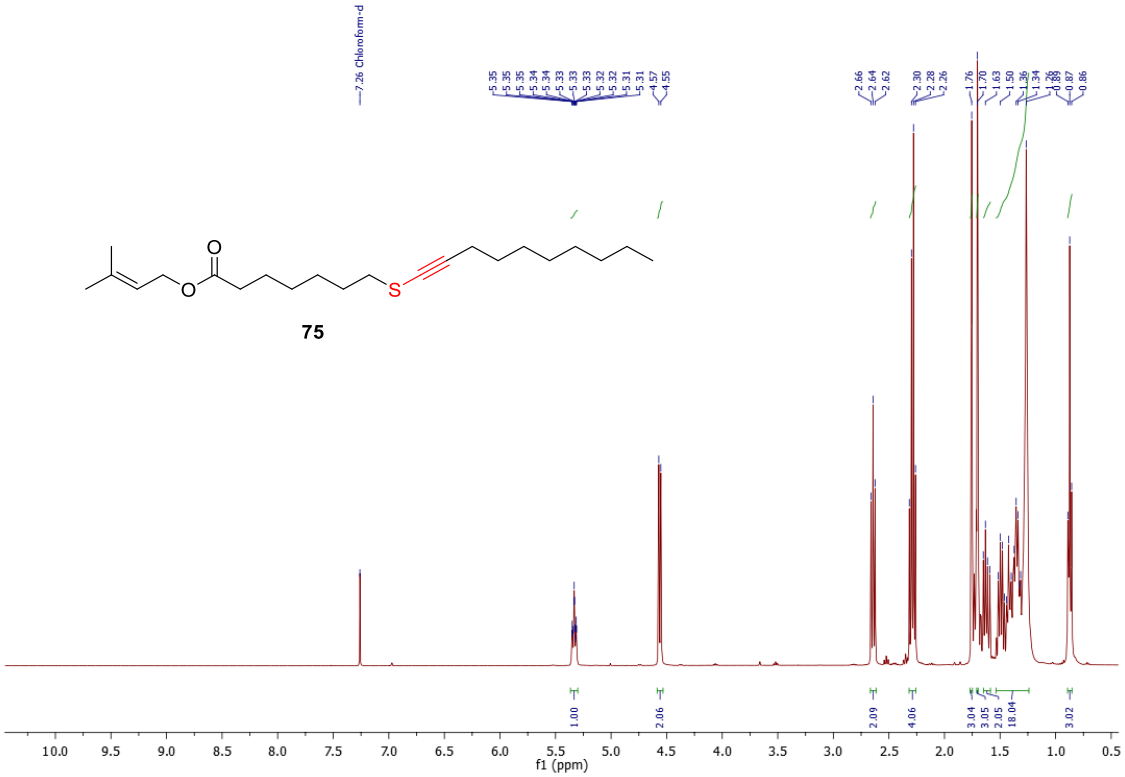

87a
f1 (ppm)


7.26 CDCl3
5.95
5.68
2.31
2.29
2.27
1.59
1.57
1.55
1.53
1.51
1.41
1.39
1.38
1.37
1.36
1.34
1.29
1.27
0.89
0.87
0.86
H2N
O
63a
2.00
2.01
2.07
10.19
3.12
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


155.58
89.14
77.48
77.16 CDCl3
76.84
75.00
31.90
29.20
29.10
28.97
27.78
22.73
18.70
14.18
H2N
O
63a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

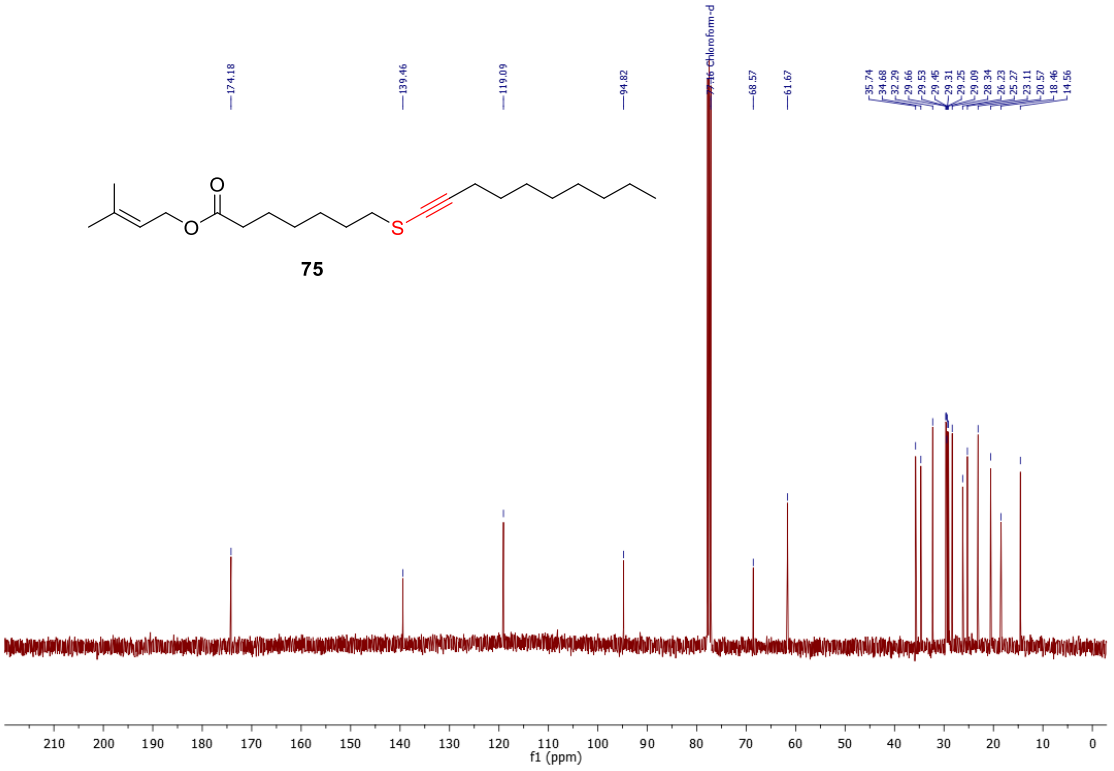

7.26 CDCl3
5.75
5.35
5.33
5.31
4.57
4.56
3.30
3.28
3.27
3.25
1.76
1.71
1.67
1.66
1.64
1.62
1.60
1.58
1.56
1.54
1.53
1.52
1.51
1.50
1.49
1.39
1.38
1.37
1.35
1.33
1.27
0.89
0.88
0.86
O
O
H
N
O
68a
0.85
1.18
2.33
2.24
4.45
3.22
3.19
6.57
12.07
3.28
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


173.73
153.72
139.25
118.69
87.46
77.37
77.16 CDCl3
76.95
75.67
61.42
39.66
34.23
31.94
29.23
29.15
29.03
27.90
26.44
25.91
24.61
22.77
18.72
18.15
14.22
O
O
H
N
O
68a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.26 Chloroform-d
5.35
5.35
5.35
5.34
5.34
5.33
5.33
5.33
5.32
5.32
5.31
5.31
4.57
4.55
2.66
2.64
2.62
2.30
2.28
2.26
1.76
1.70
1.63
1.50
1.39
1.34
1.28
0.87
0.86
1.00
2.06
2.09
4.06
3.04
3.05
2.05
18.04
3.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

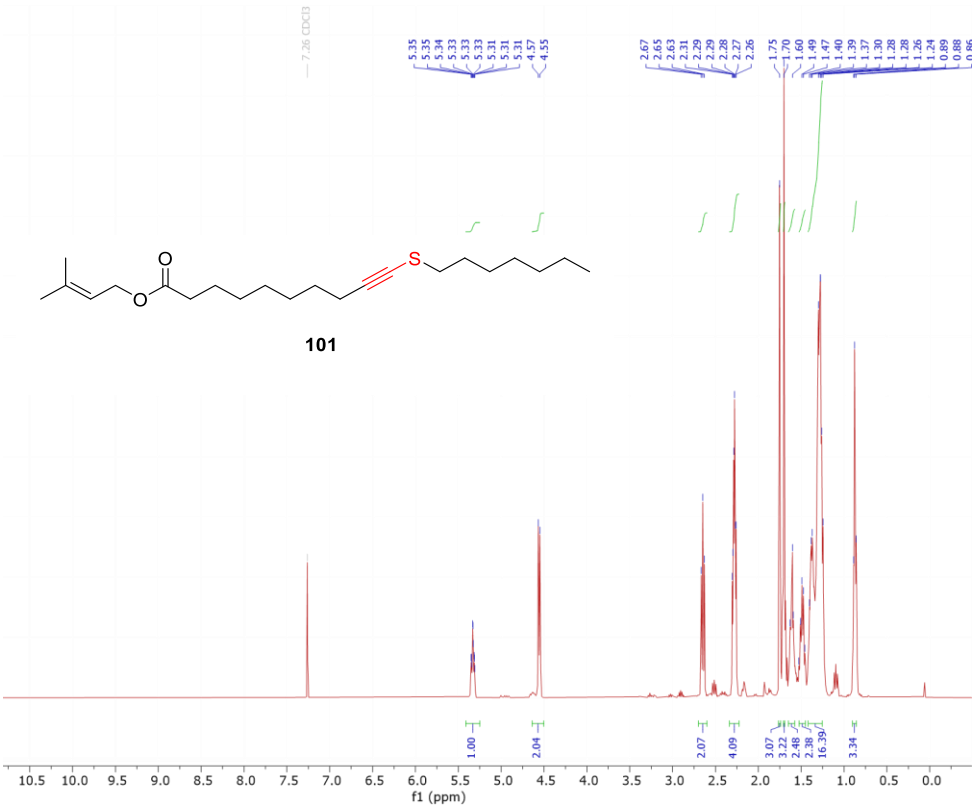
O
O
S

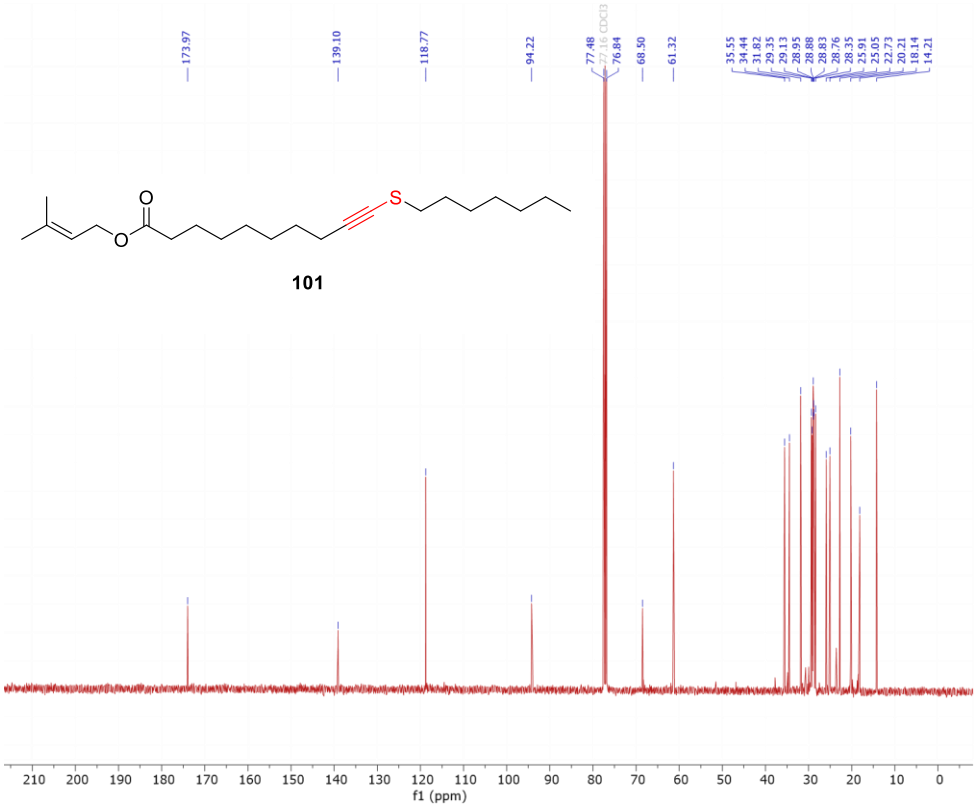
75

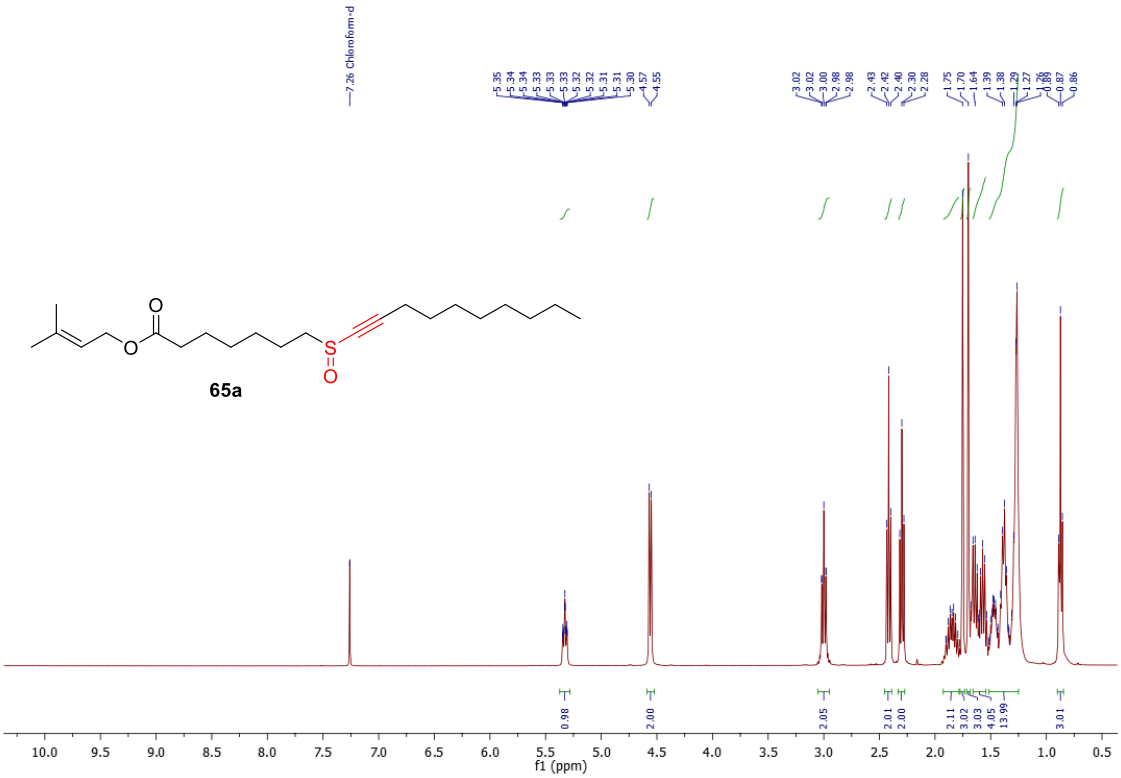

174.18
139.46
119.09
94.82
77.16 Chloroform-d
68.57
61.67
35.74
34.68
32.29
29.66
29.53
29.45
29.31
29.25
29.09
28.34
26.23
25.27
23.11
20.57
18.46
14.56
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

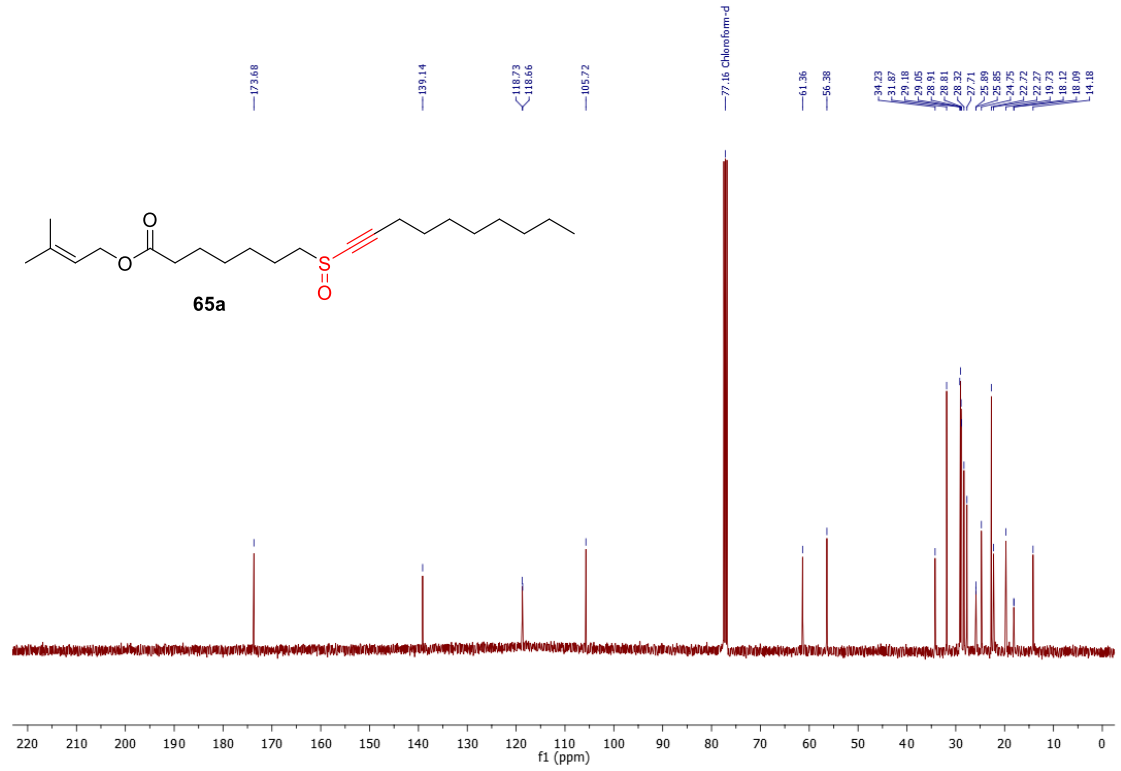
O
O
S

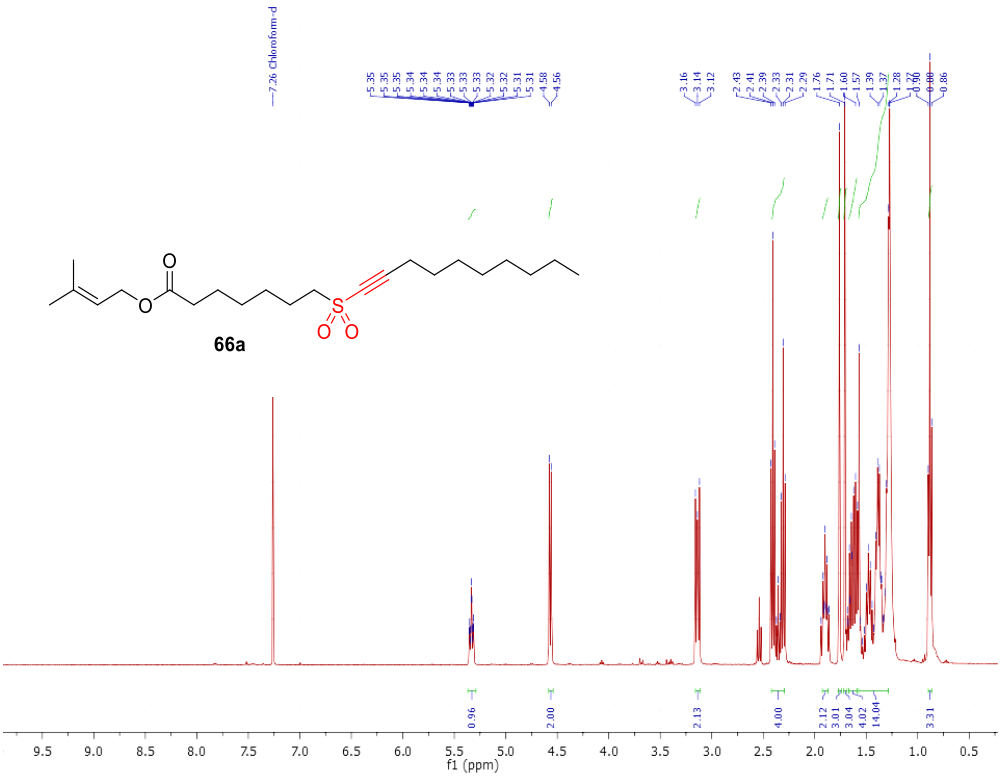
75

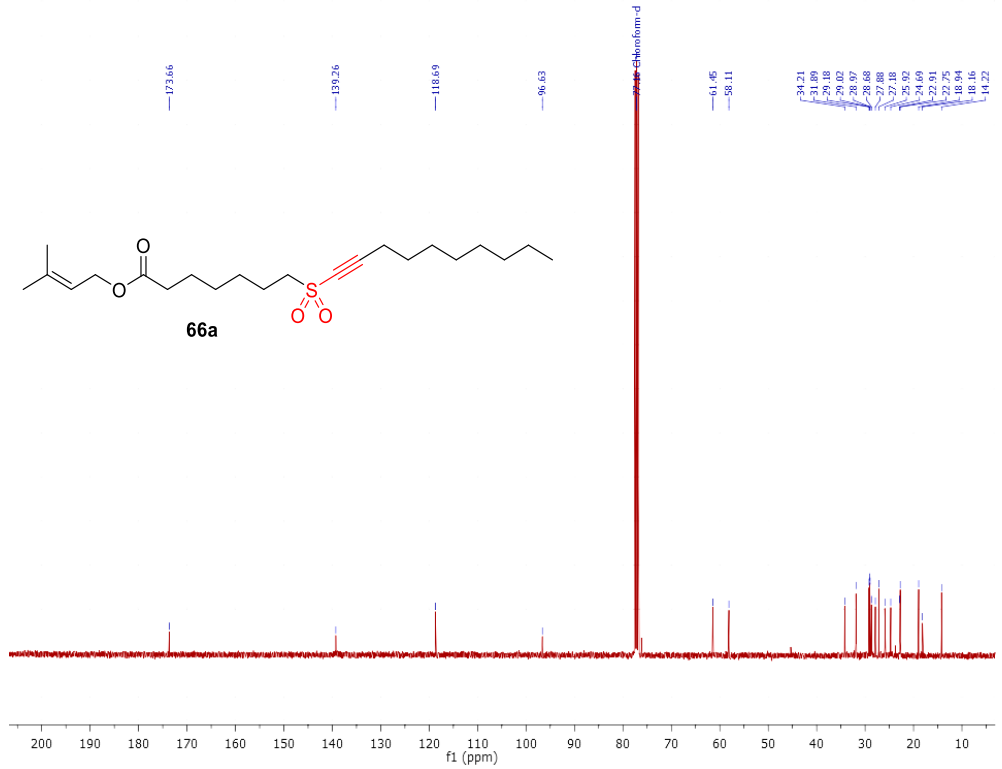

101
f1 (ppm)

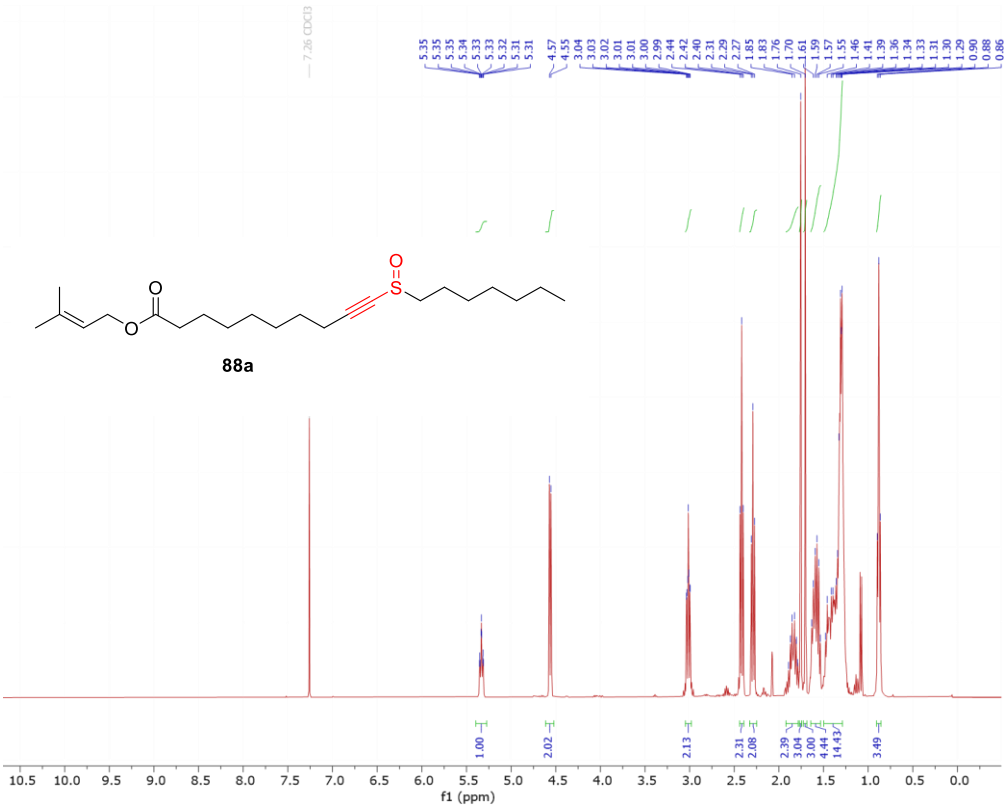

101
f1 (ppm)

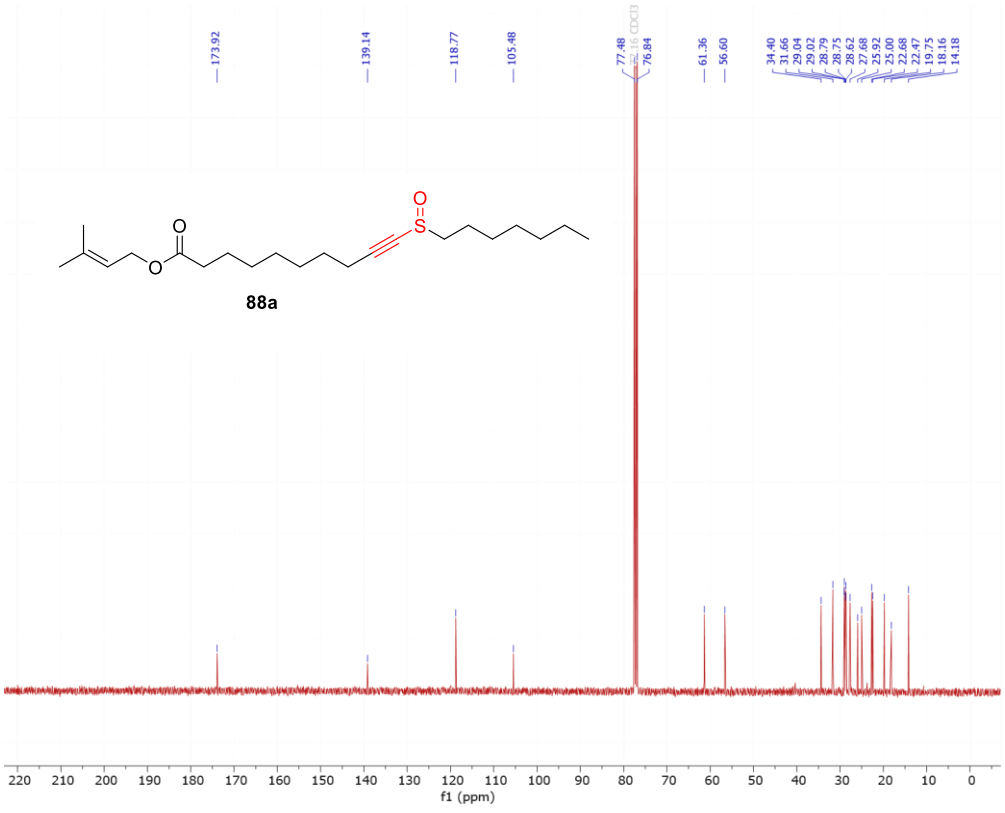

7.26 Chloroform-d
5.35
5.34
5.34
5.33
5.33
5.33
5.32
5.32
5.31
5.31
5.30
4.57
4.55
3.02
3.02
3.00
2.98
2.98
2.43
2.42
2.40
2.30
2.28
1.75
1.70
1.64
1.39
1.38
1.29
1.27
0.89
0.87
0.86
O
O
S
O
65a
0.98
2.00
2.05
2.01
2.00
2.11
3.02
3.03
4.05
13.99
3.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

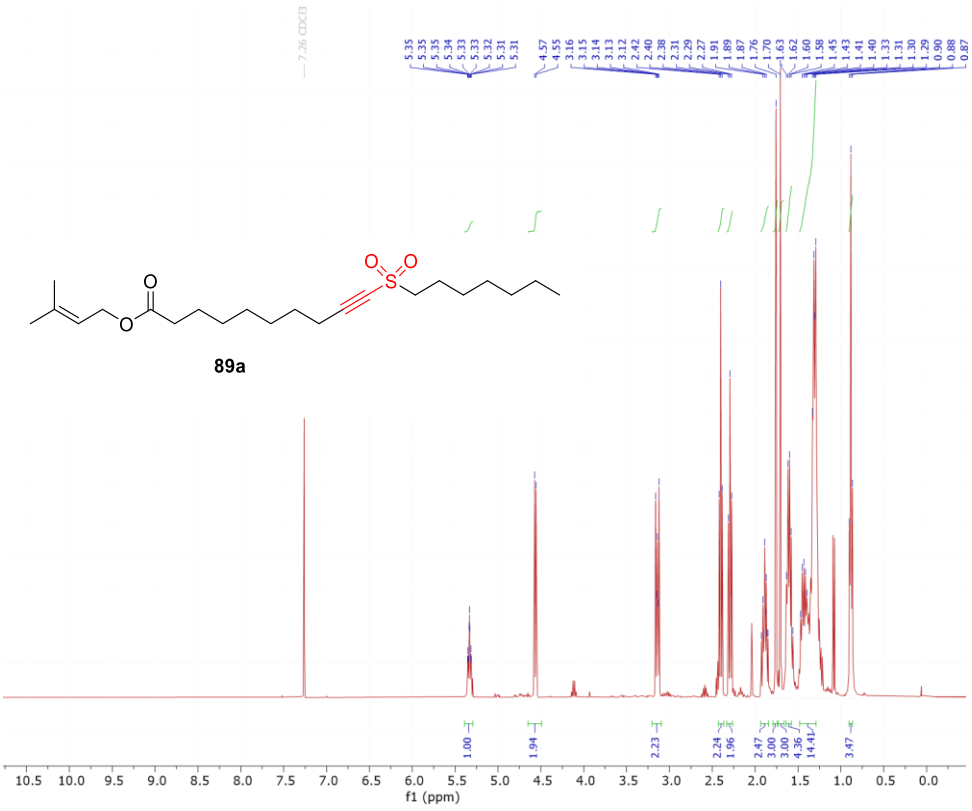

173.68
139.14
118.73
118.66
105.72
77.16 Chloroform-d
61.36
56.38
34.23
31.87
29.18
29.05
28.91
28.81
28.32
27.71
25.89
25.85
24.75
22.72
22.27
19.73
18.12
18.09
14.18
O
O
S
O
65a
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

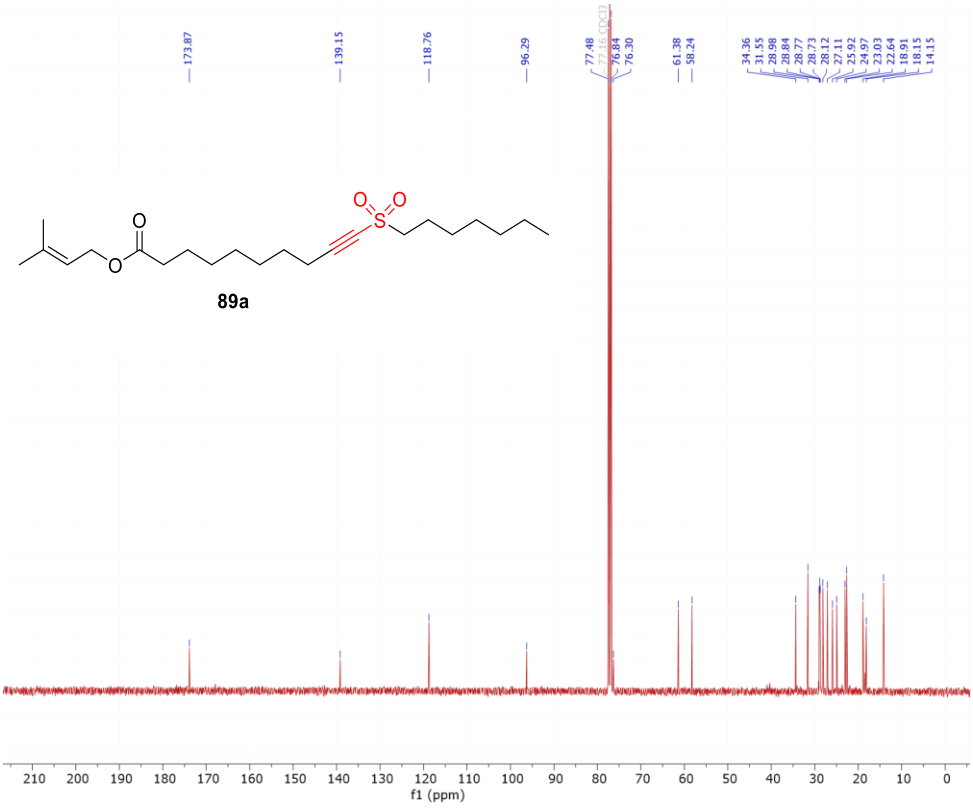

7.26 Chloroform-d
5.35
5.34
5.33
5.32
5.31
4.58
4.56
3.16
3.14
3.12
2.43
2.41
2.39
2.33
2.31
2.29
1.76
1.71
1.60
1.57
1.39
1.37
1.28
1.07
1.00
0.86
O
O
S
O
O
66a
0.96
2.00
2.13
4.00
2.12
3.01
3.04
4.02
14.04
3.31
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

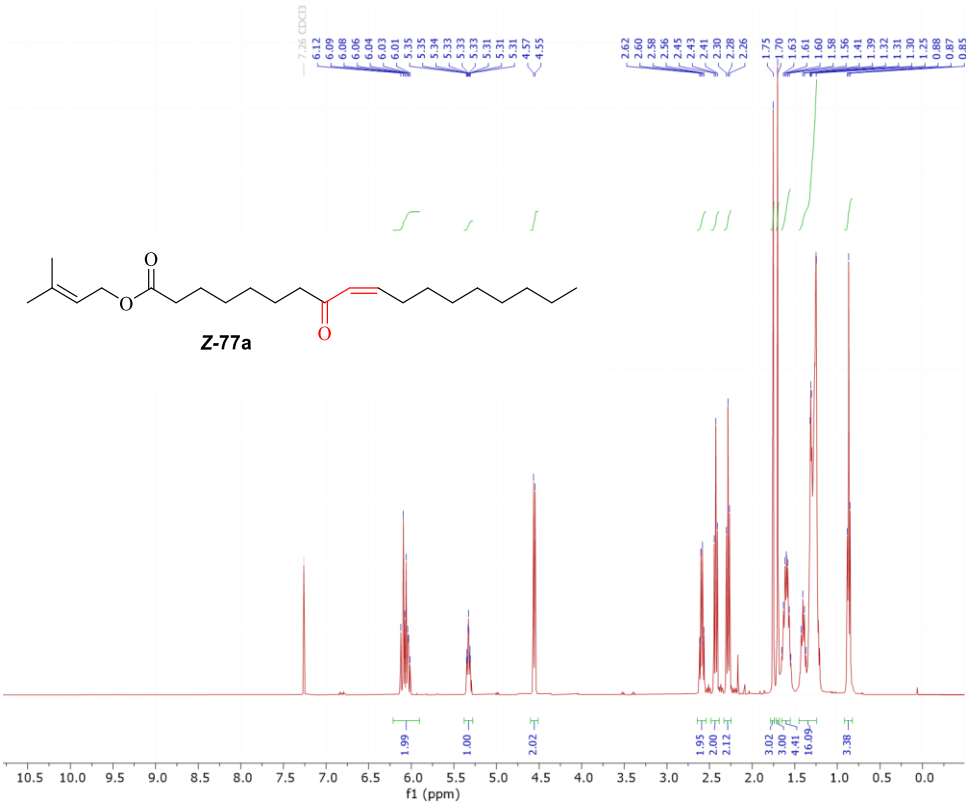

173.66
139.26
118.69
96.63
77.16 Chloroform-d
61.45
58.11
34.21
31.89
29.18
29.02
28.97
28.68
27.88
27.18
25.92
24.69
22.91
22.75
18.94
18.16
14.22
O
O
S
O
O
66a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

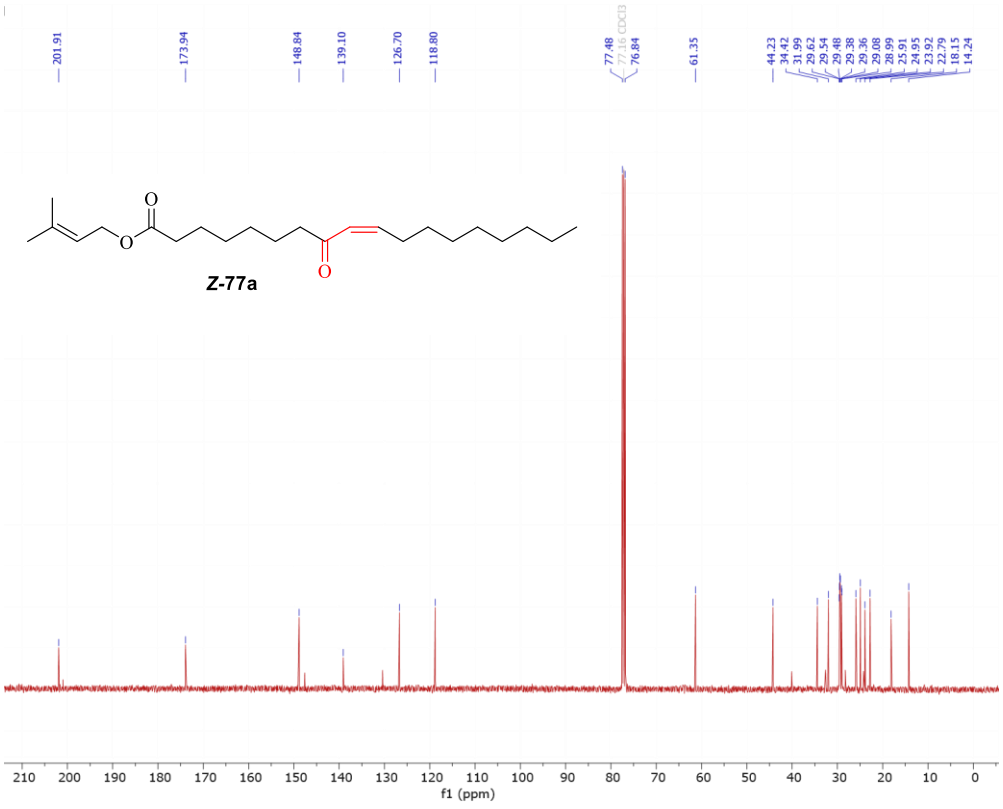

88a
f1 (ppm)

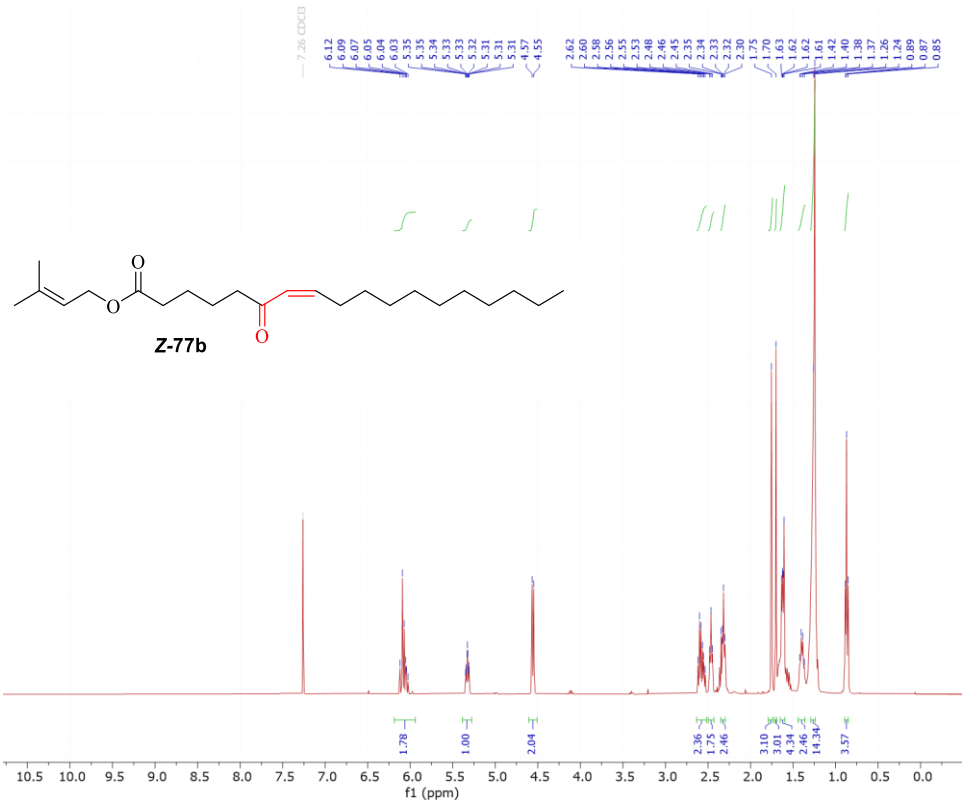

88a
f1 (ppm)

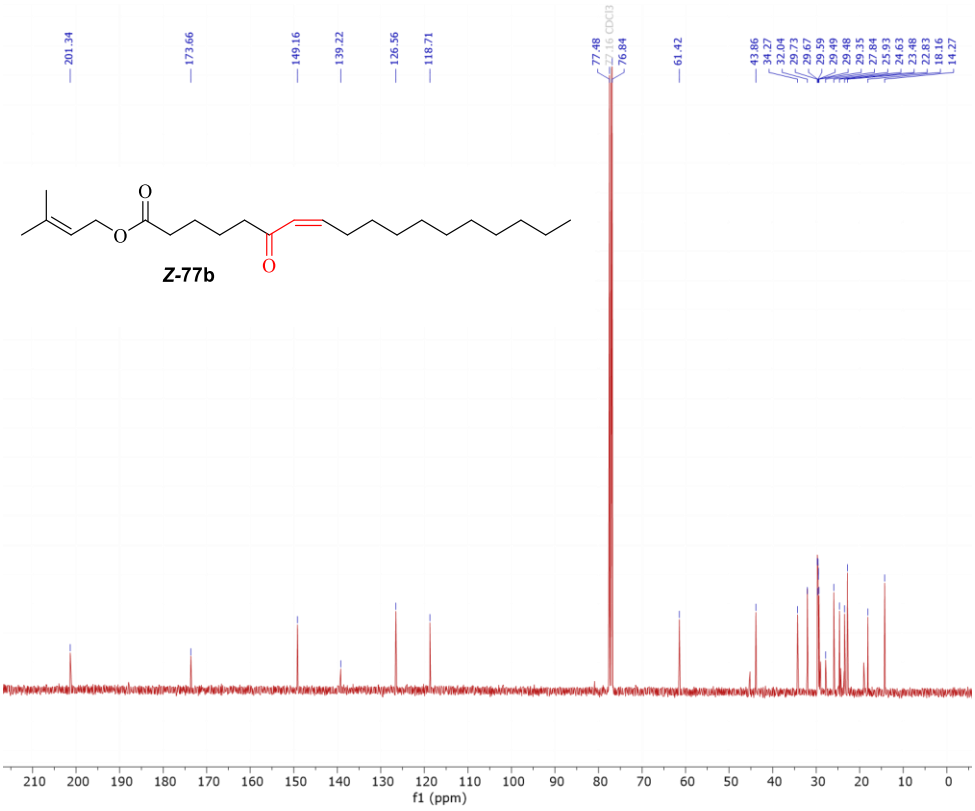

89a
f1 (ppm)

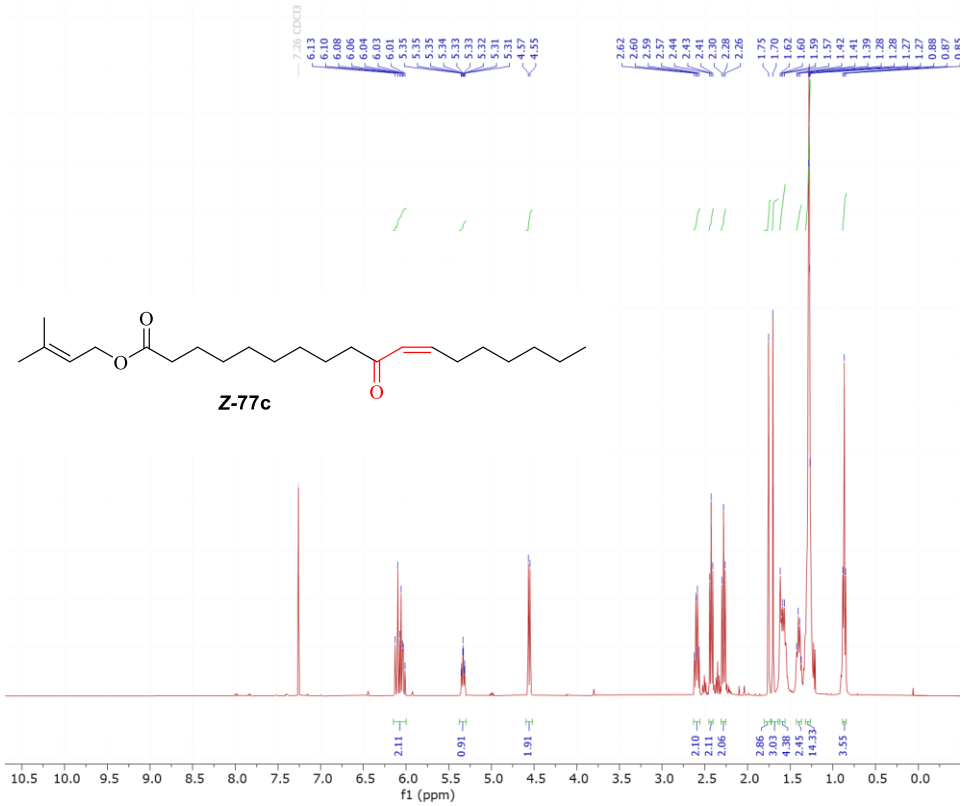

89a
f1 (ppm)

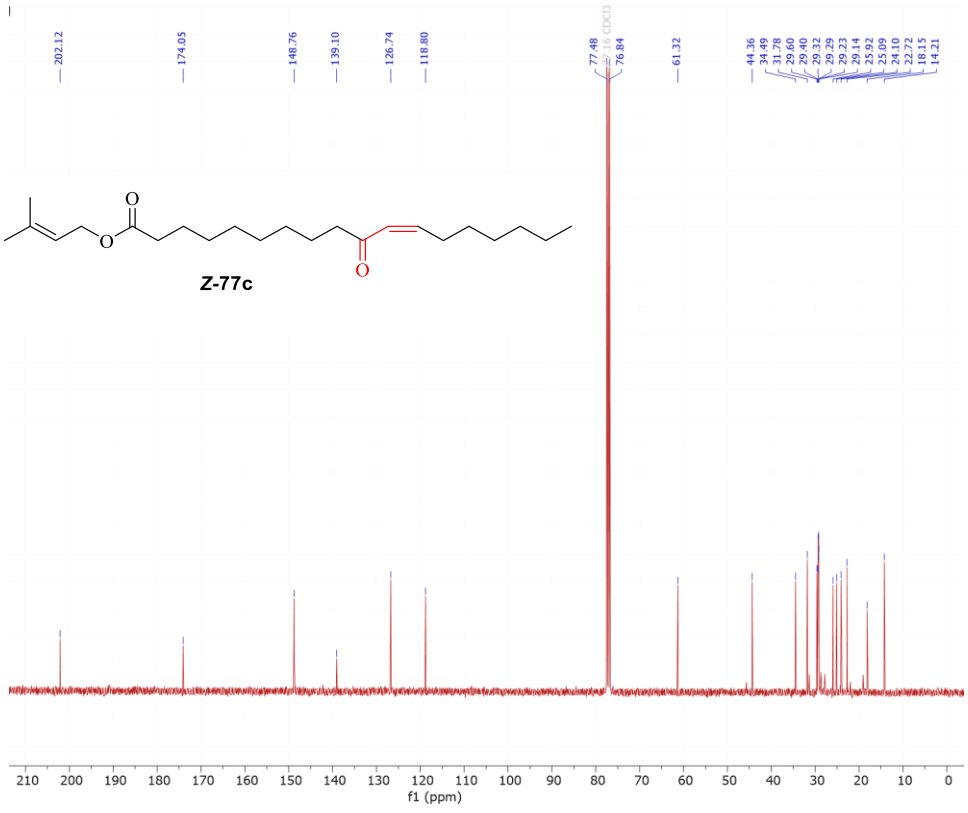

Z-77a
f1 (ppm)

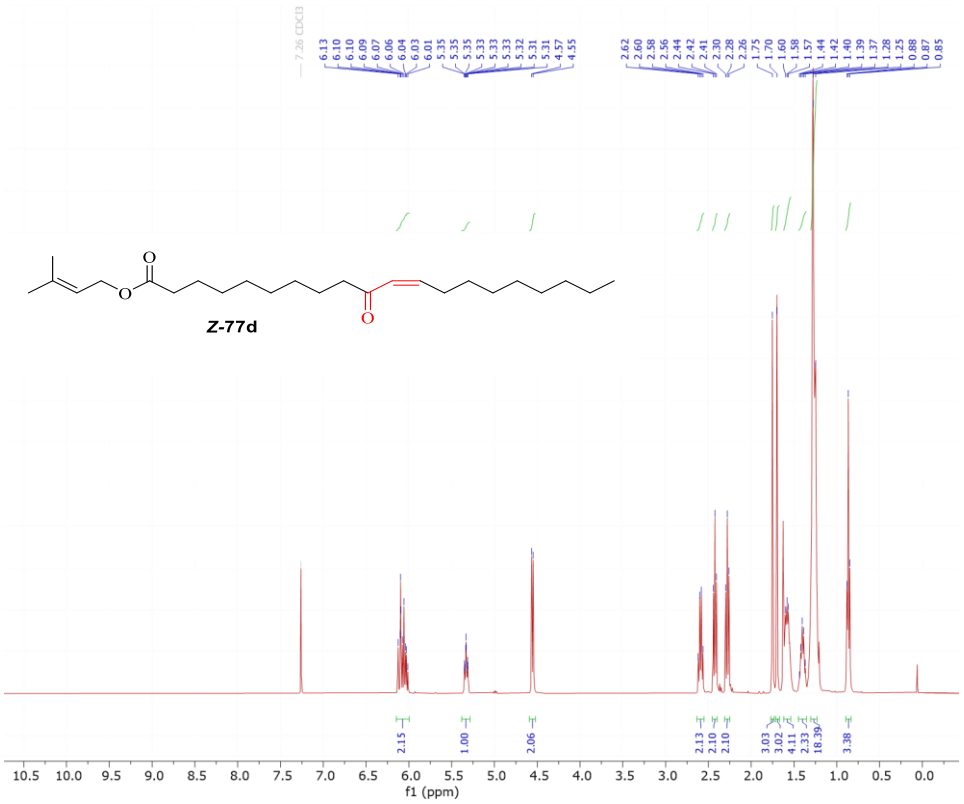

Z-77a
f1 (ppm)

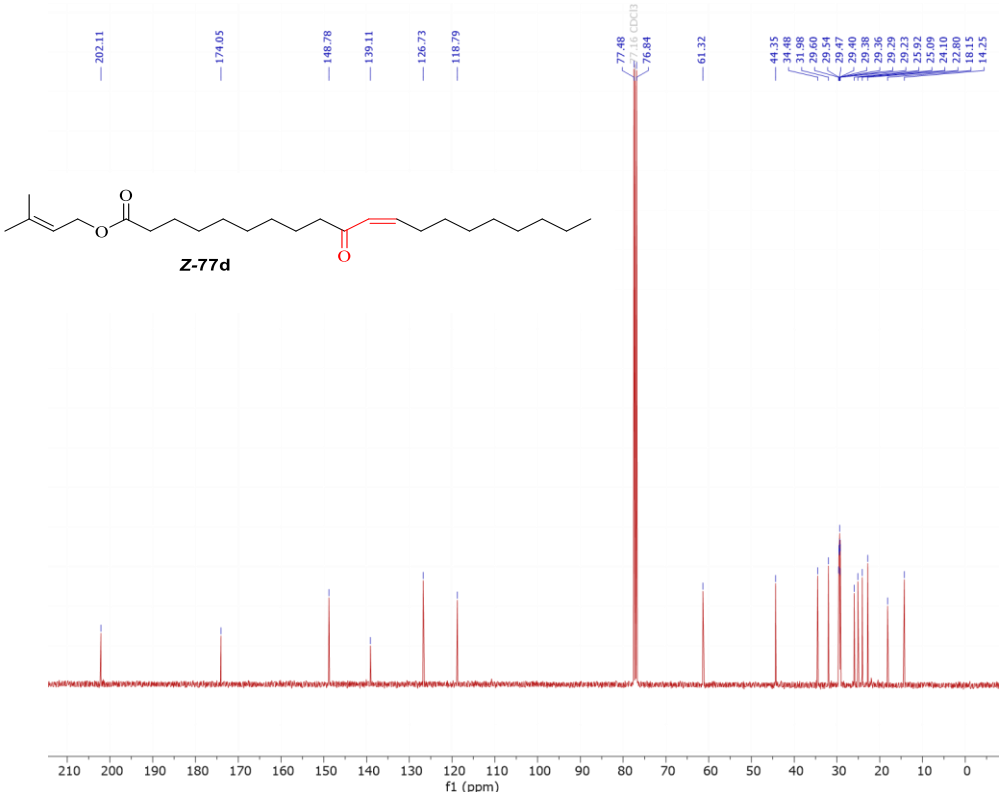

Z-77b
f1 (ppm)

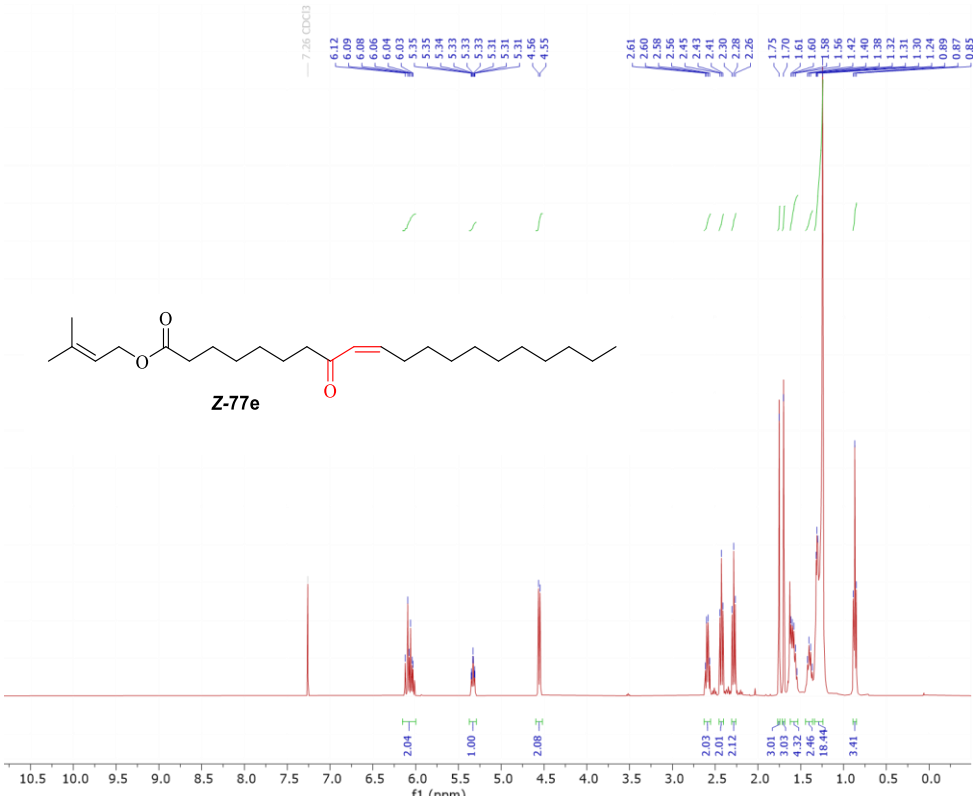

Z-77b
f1 (ppm)

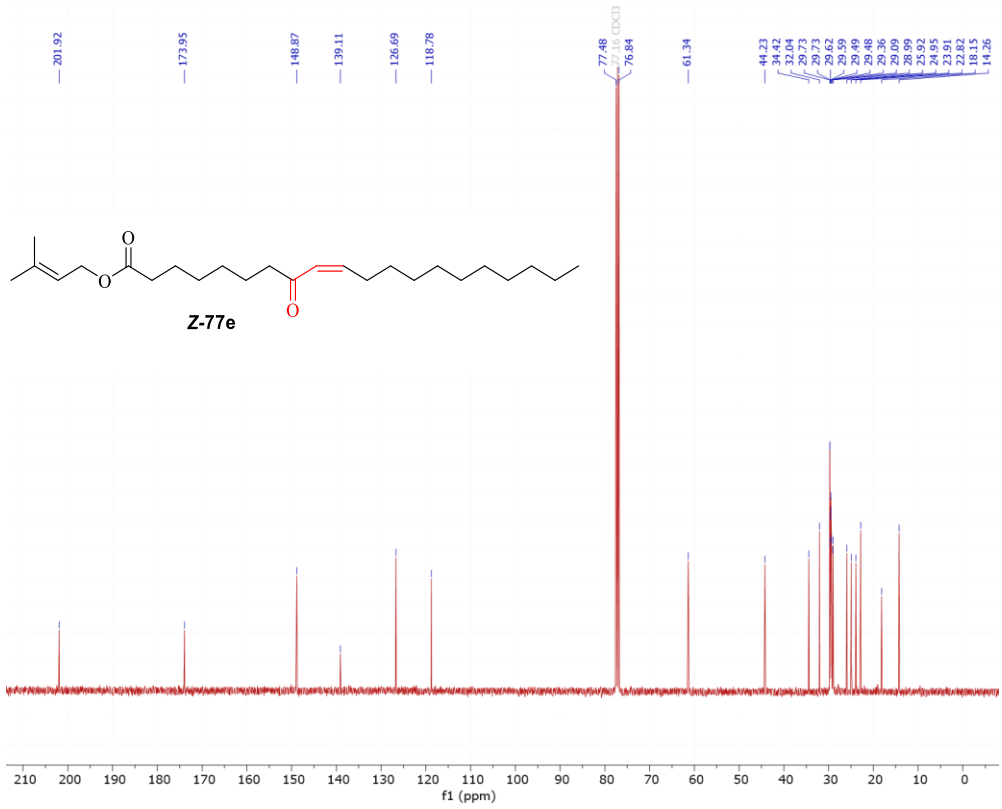

Z-77c
f1 (ppm)

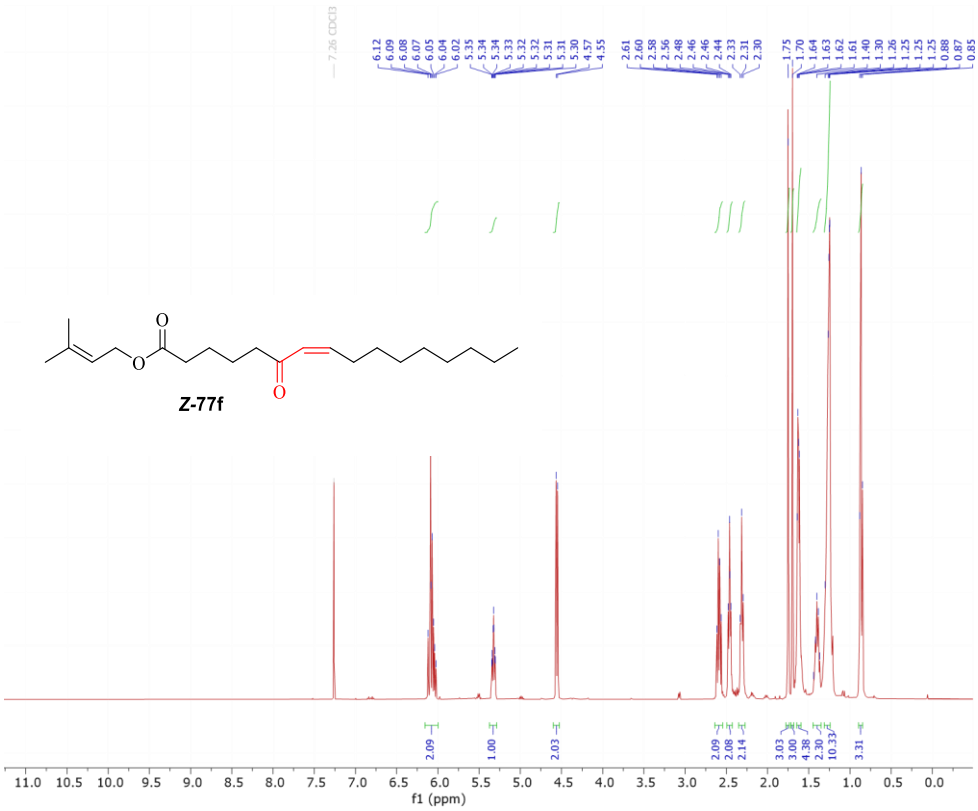

Z-77c
f1 (ppm)

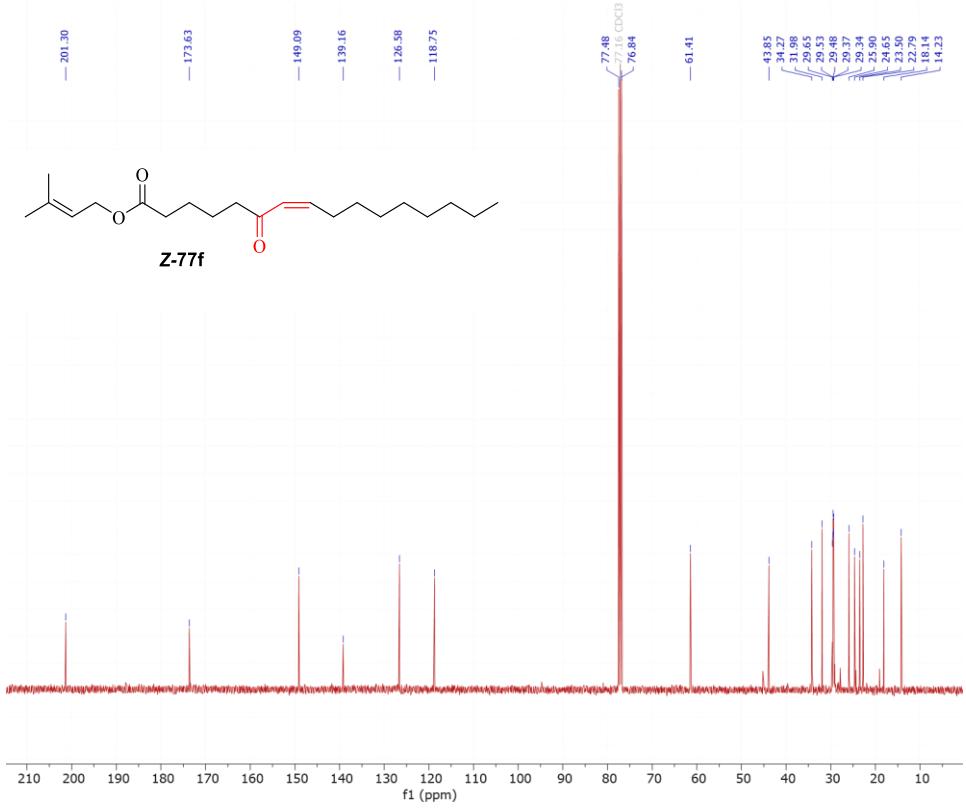

Z-77d
f1 (ppm)

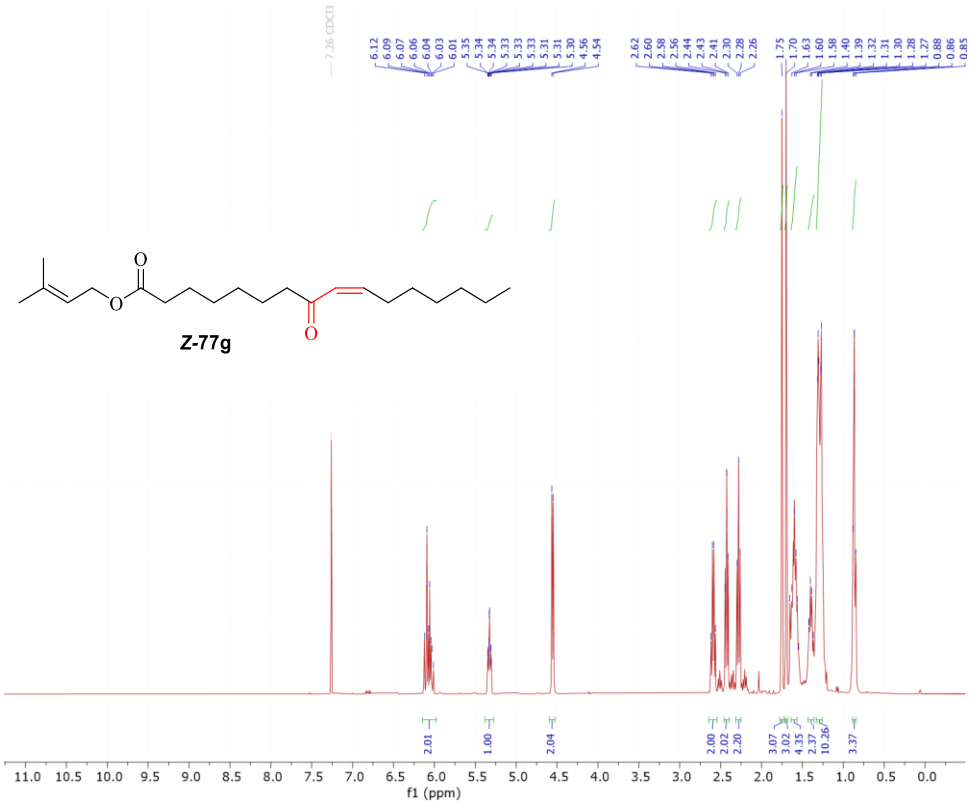

Z-77d
f1 (ppm)

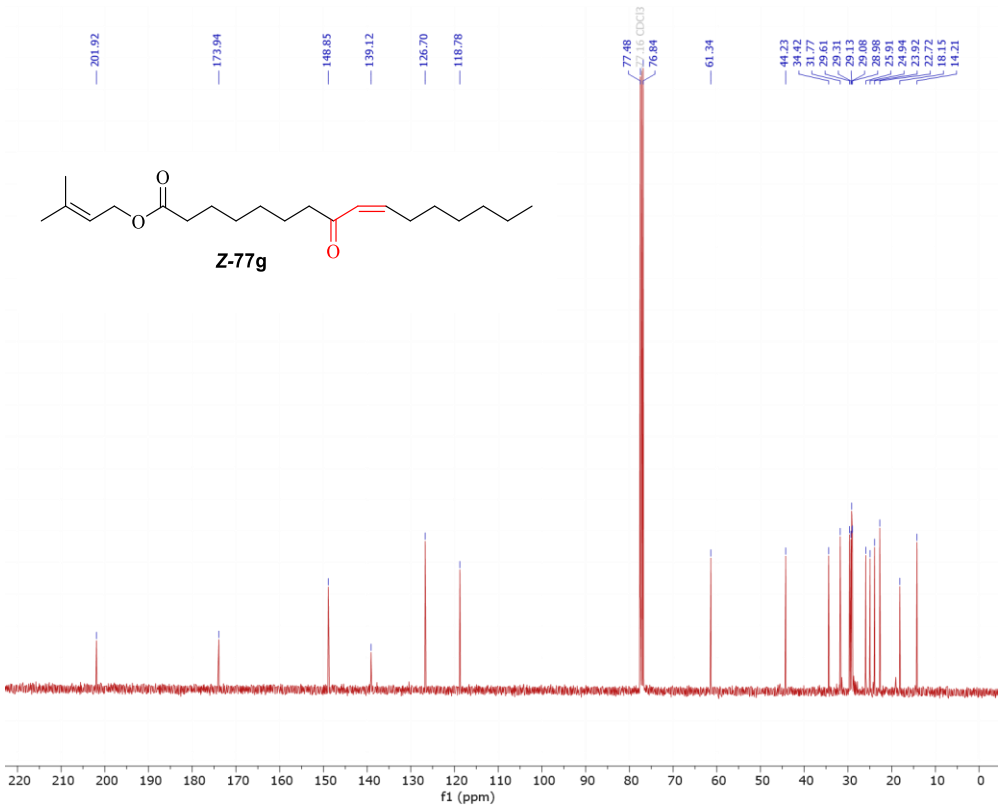

Z-77e
f1 (ppm)

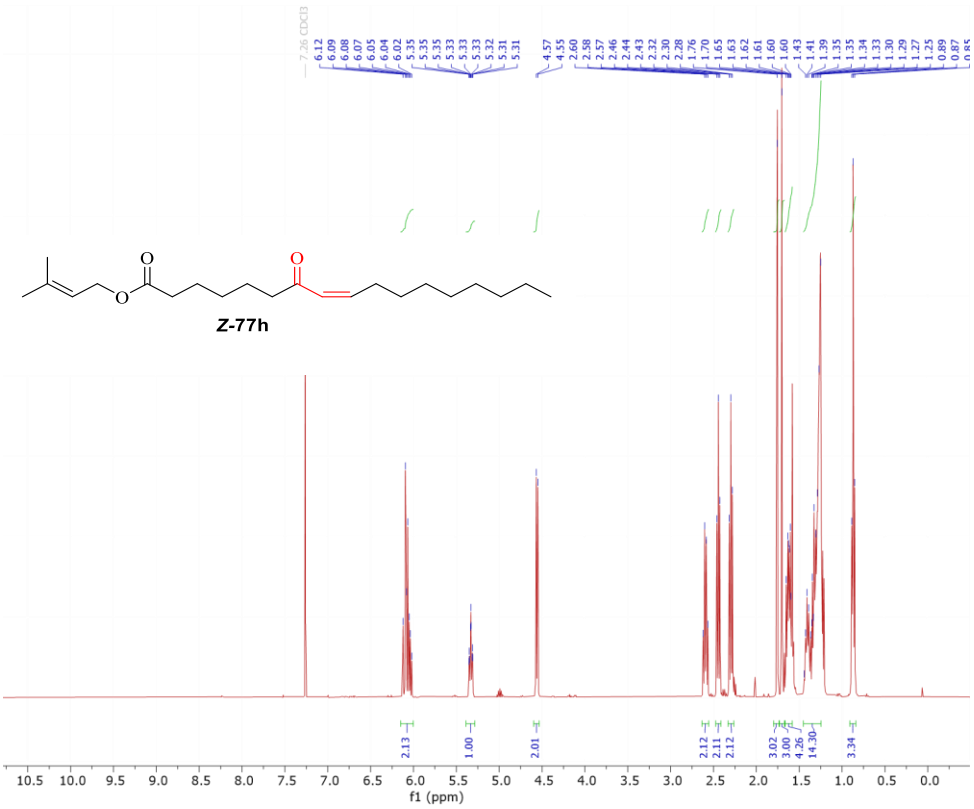

Z-77e
f1 (ppm)

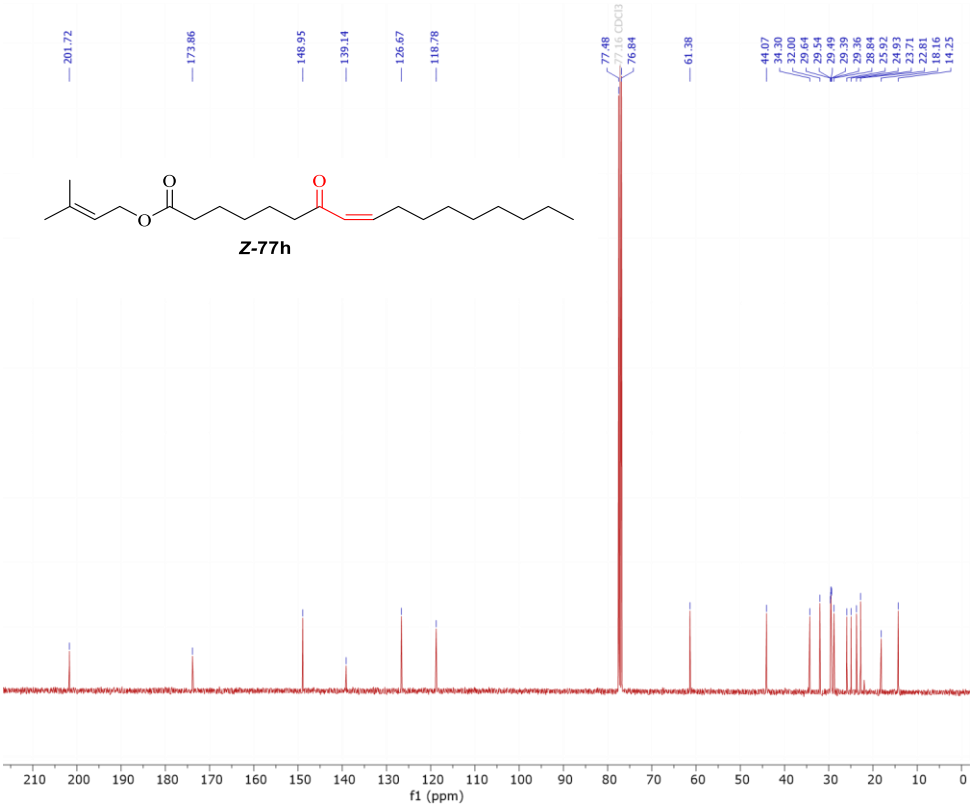

Z-77f
f1 (ppm)

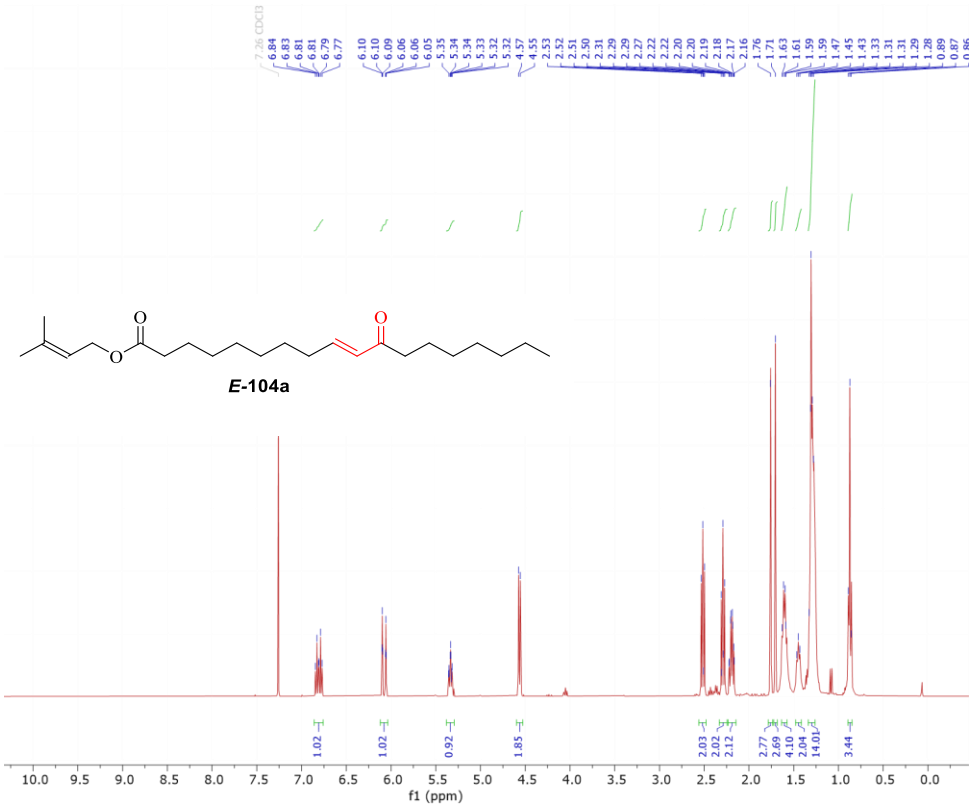

Z-77f
f1 (ppm)

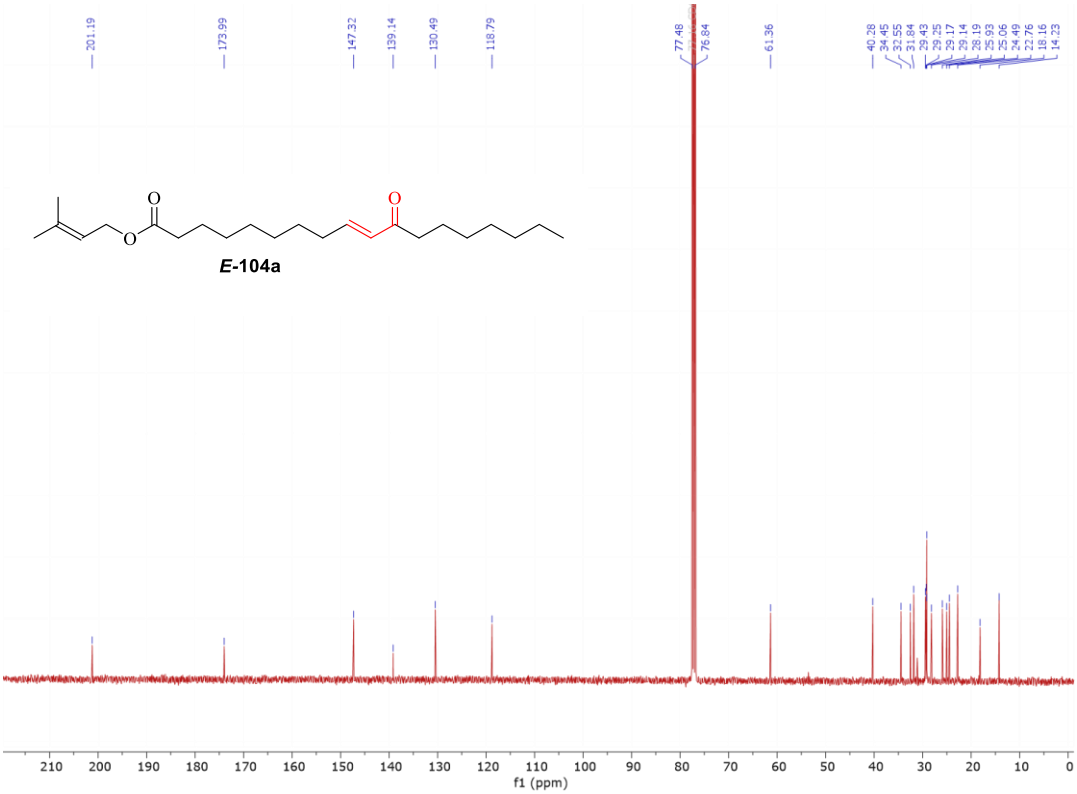

Z-77g
f1 (ppm)

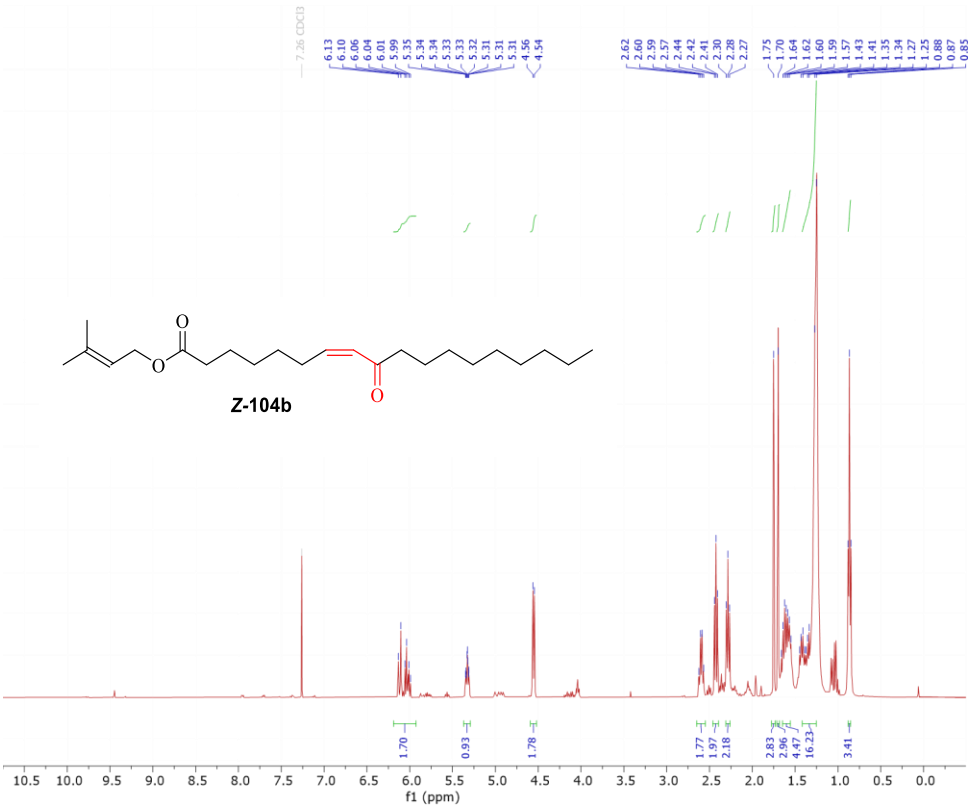

Z-77g
f1 (ppm)

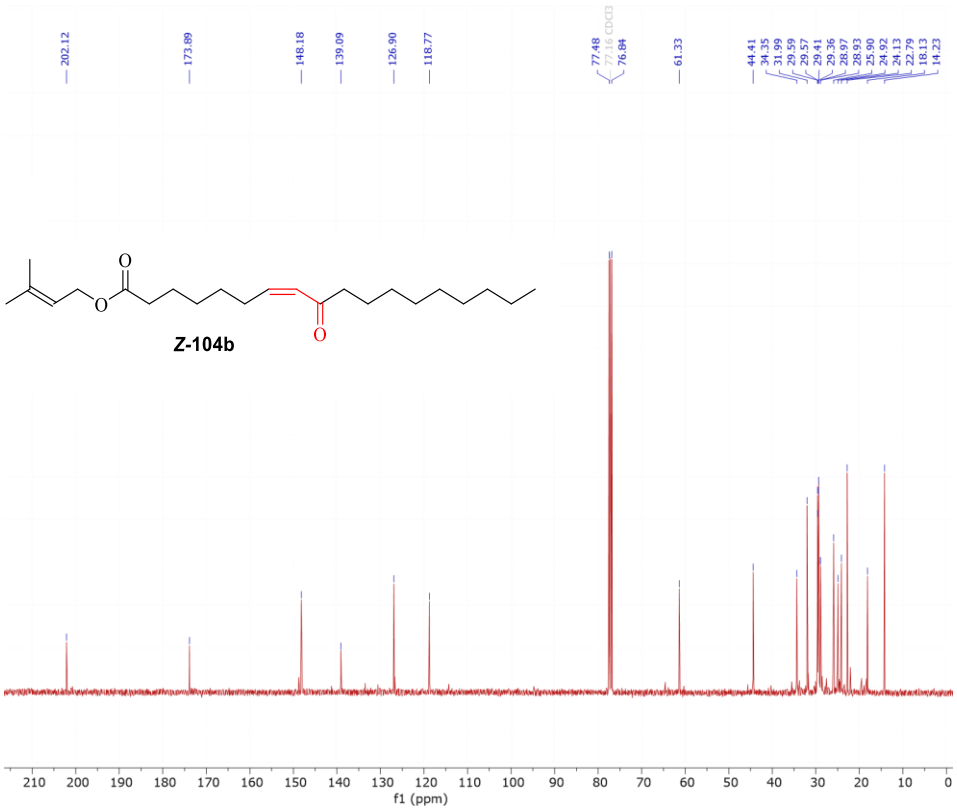

Z-77h
f1 (ppm)

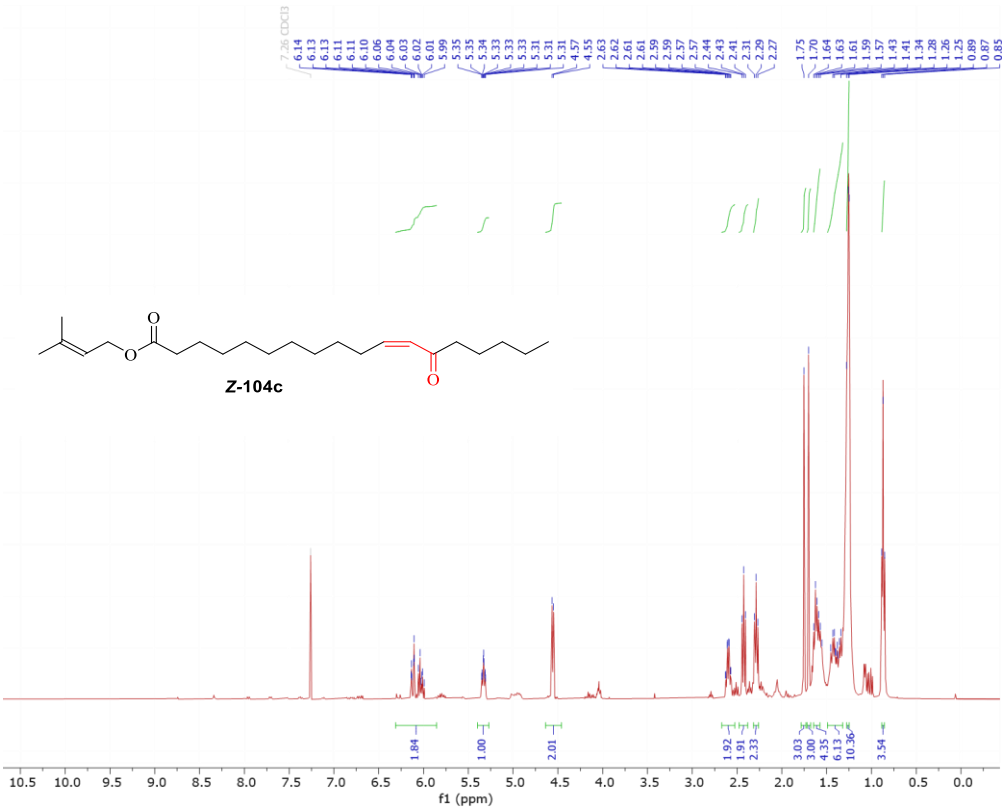

Z-77h
f1 (ppm)

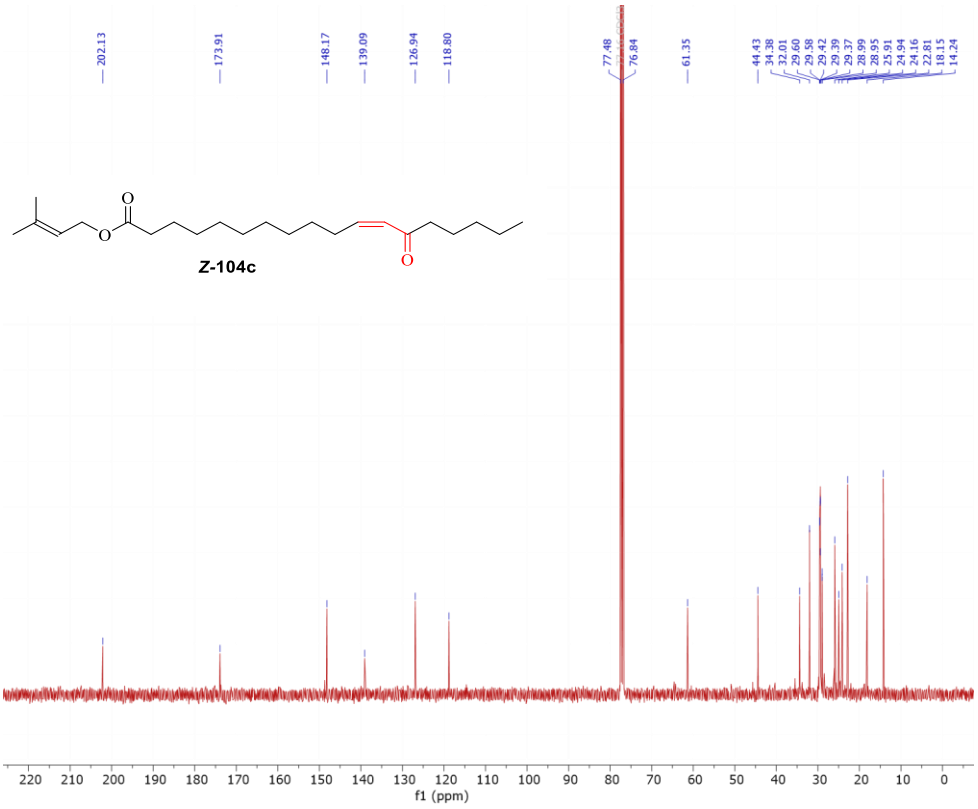

E-104a
f1 (ppm)

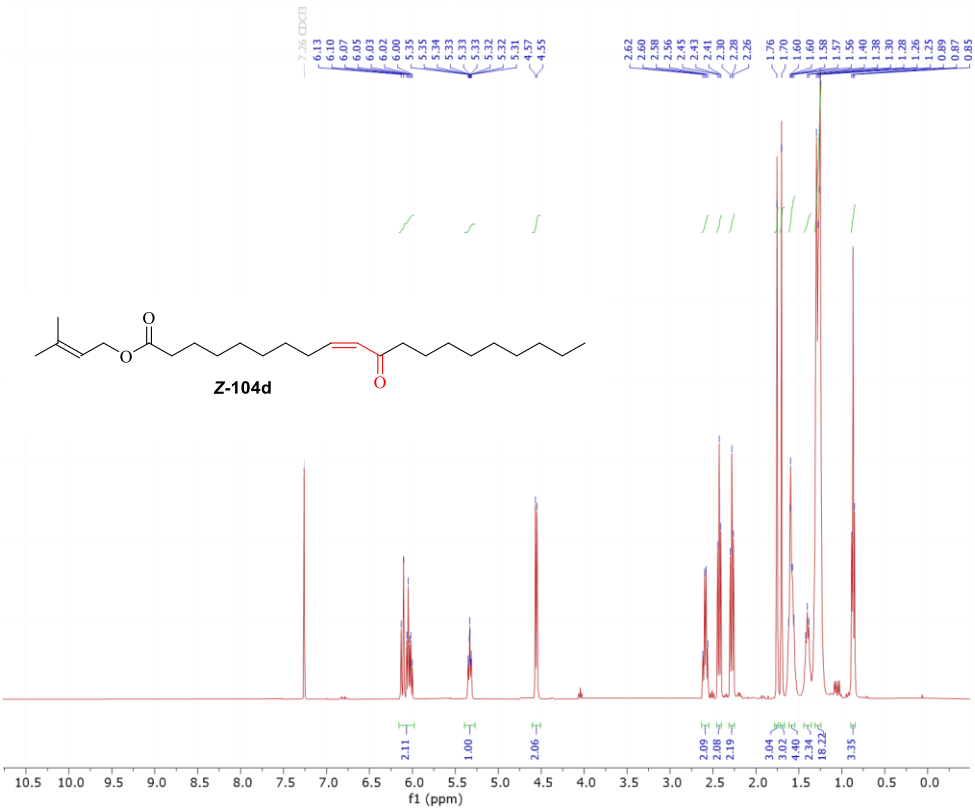

E-104a
f1 (ppm)

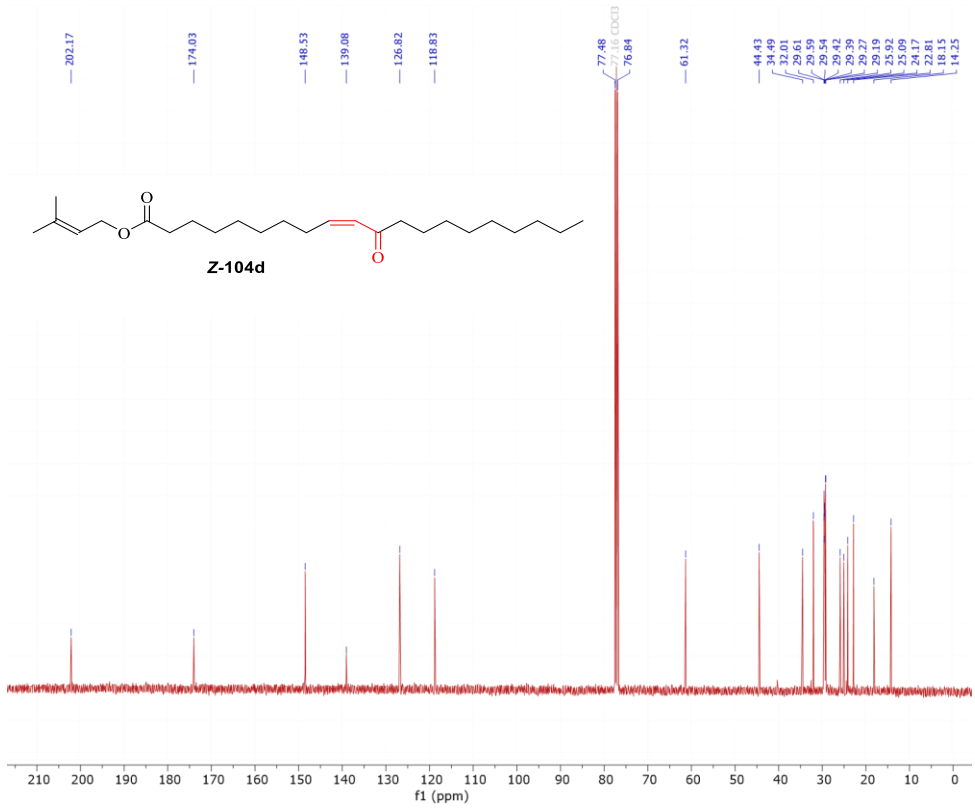

Z-104b
f1 (ppm)

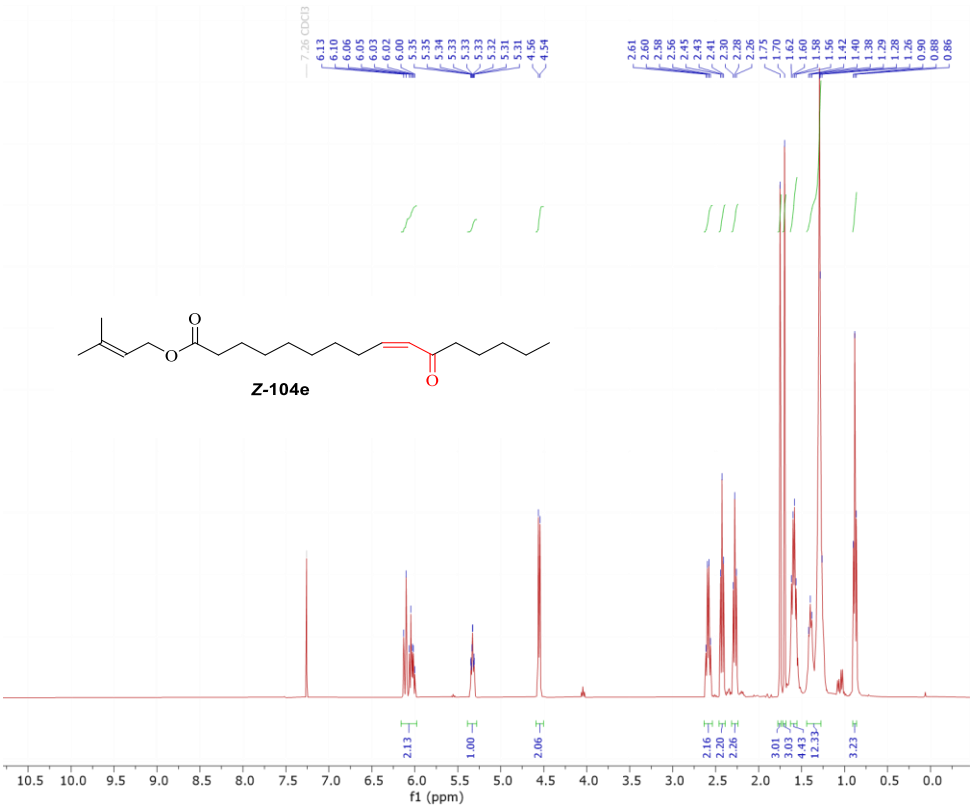

Z-104b
f1 (ppm)

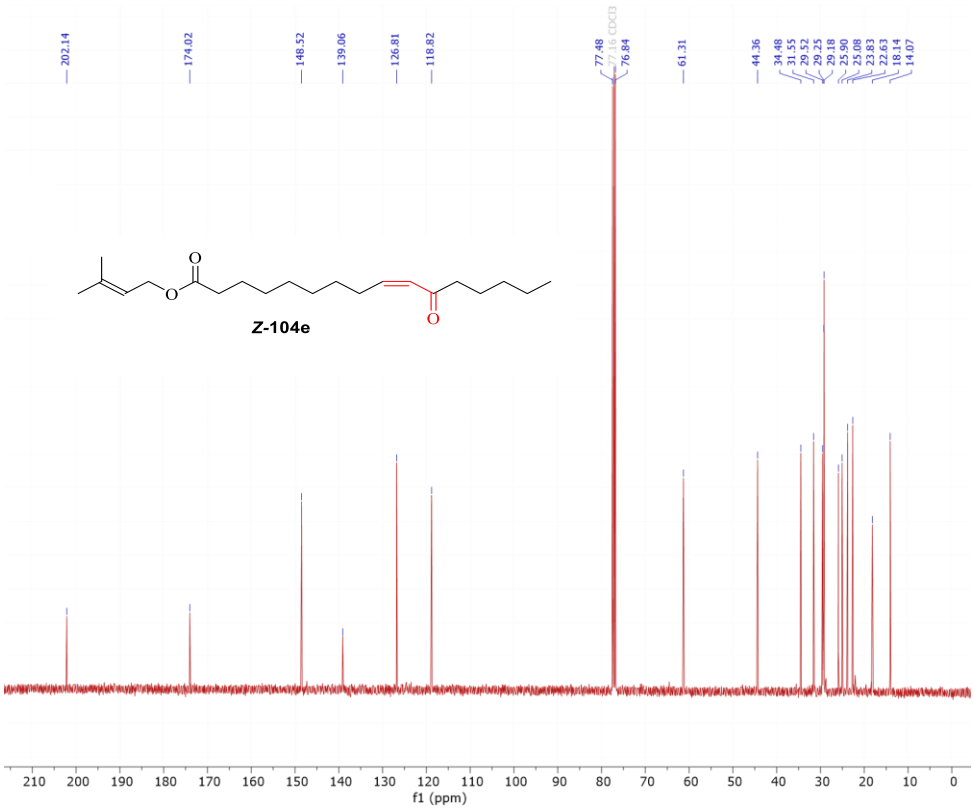

Z-104c
f1 (ppm)

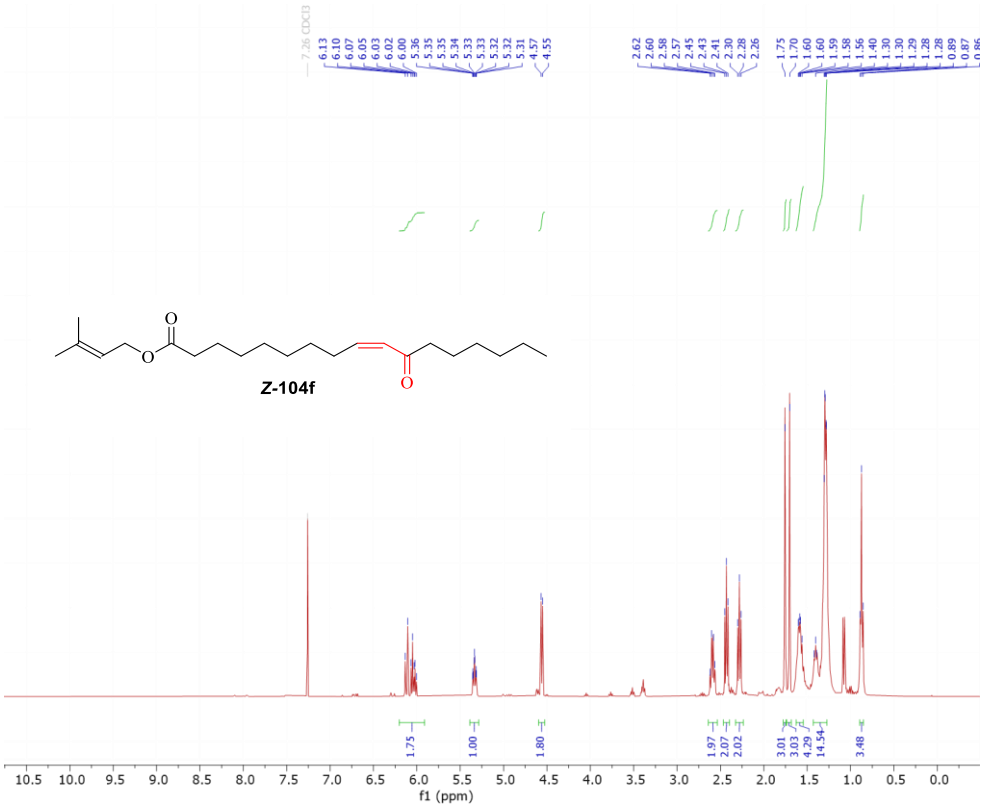

Z-104c
f1 (ppm)

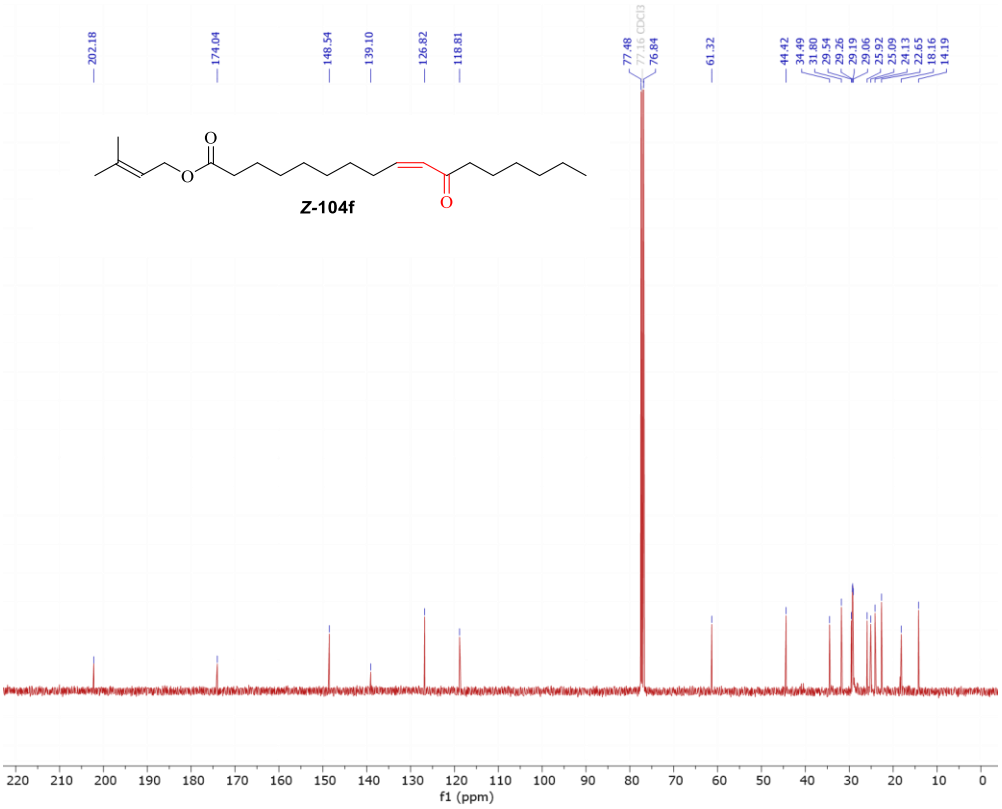

Z-104d
f1 (ppm)

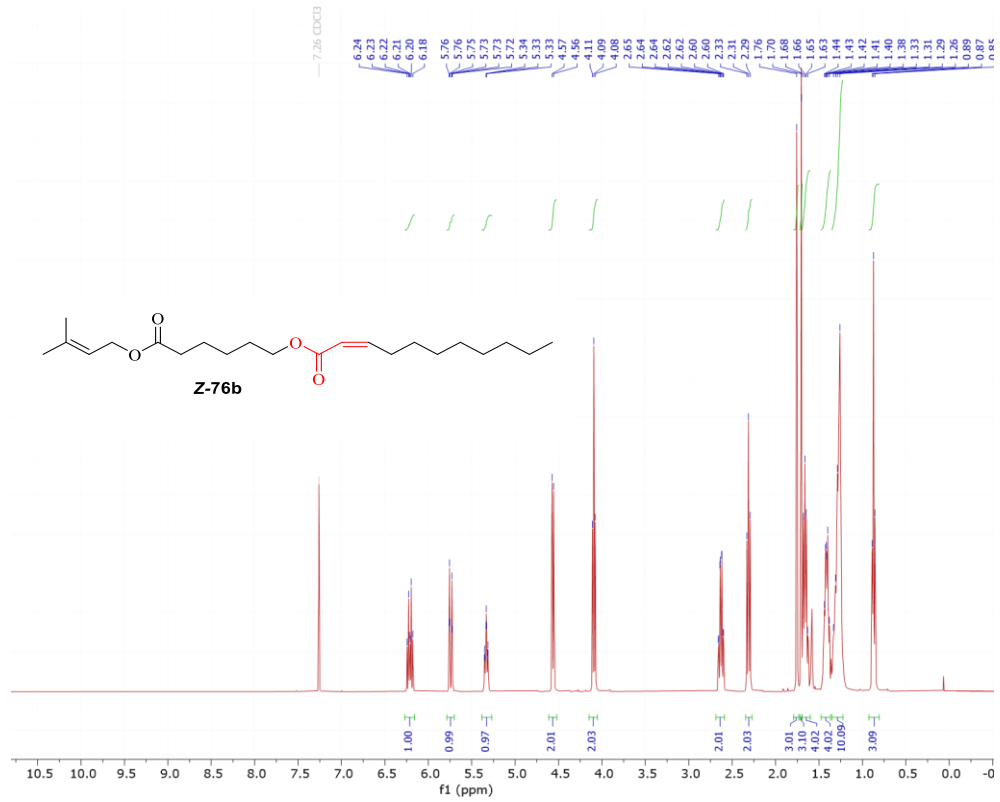

Z-104d
f1 (ppm)

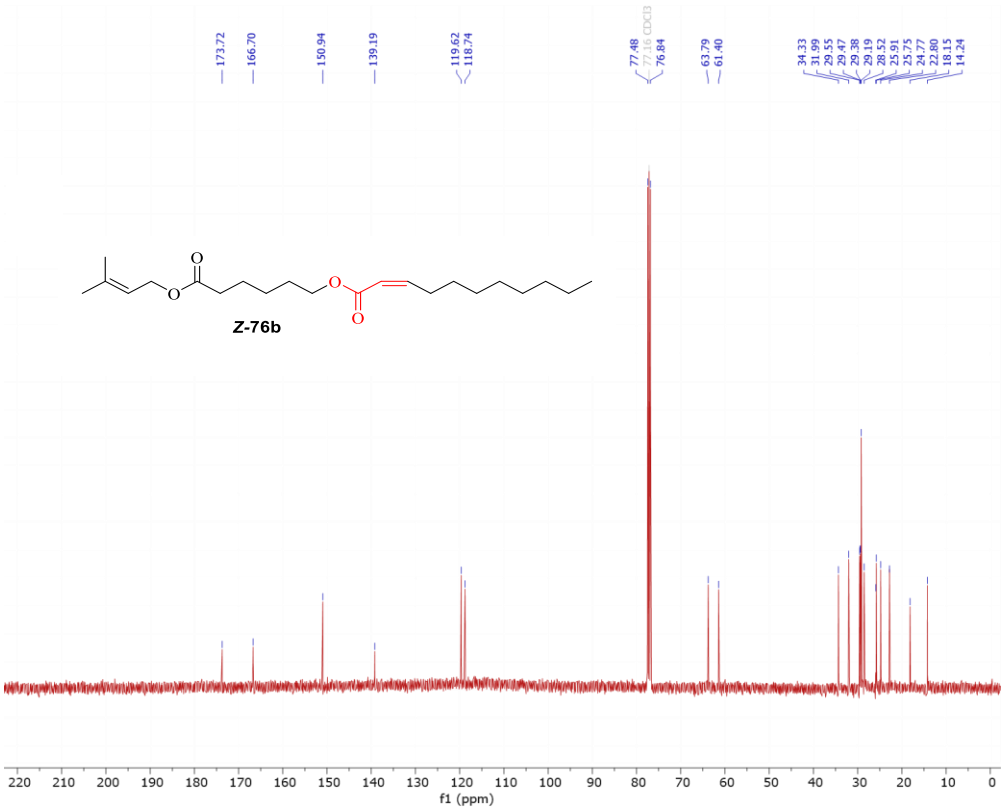

7.26 CDCl3
6.13
6.10
6.06
6.05
6.03
6.02
6.00
5.35
5.34
5.33
5.33
5.32
5.31
5.31
4.56
4.54
2.61
2.60
2.58
2.56
2.45
2.43
2.41
2.30
2.28
2.26
1.75
1.70
1.62
1.60
1.58
1.56
1.42
1.40
1.38
1.29
1.28
1.26
0.90
0.88
0.86
O
O
O
Z-104e
2.13
1.00
2.06
2.16
2.20
2.26
3.01
3.03
4.43
12.33
3.23
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

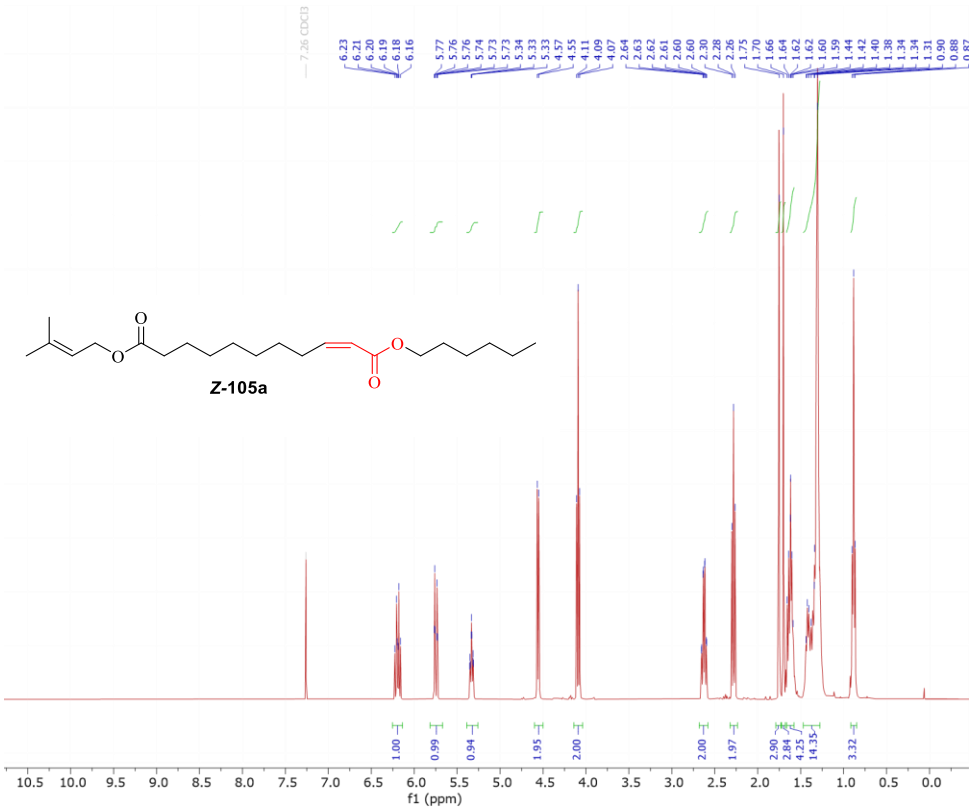

202.14
174.02
148.52
139.06
126.81
118.82
77.48
77.16 CDCl3
76.84
61.31
44.36
34.48
31.55
29.52
29.35
29.18
25.90
25.08
23.83
22.63
18.14
14.07
O
O
O
Z-104e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

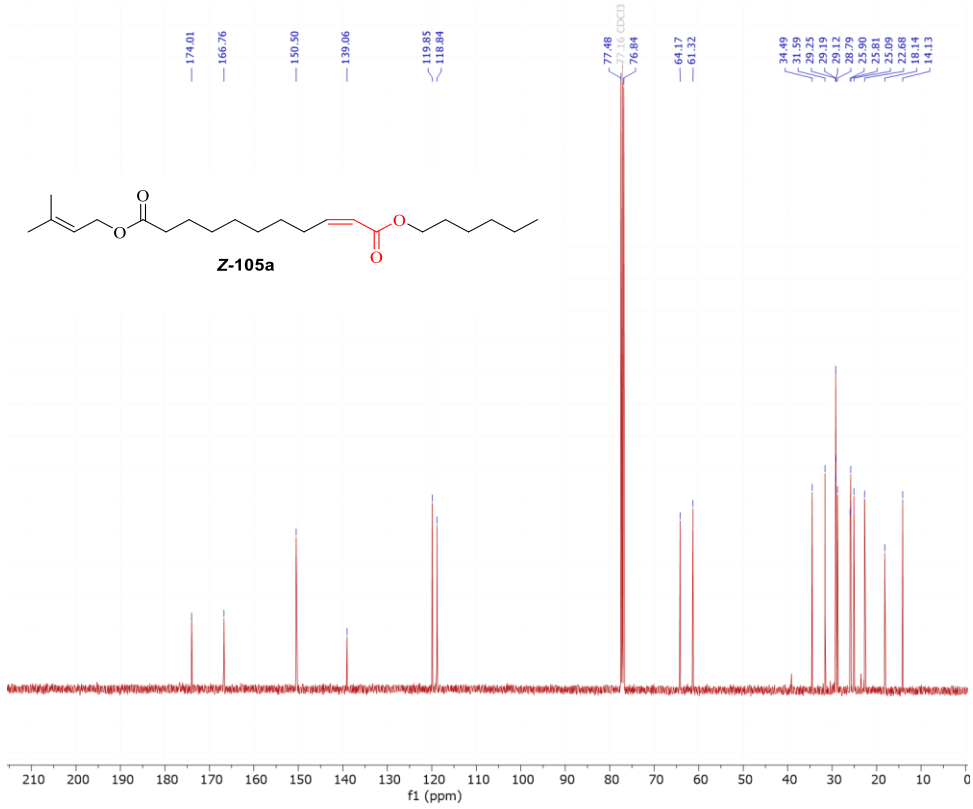

Z-104f
f1 (ppm)

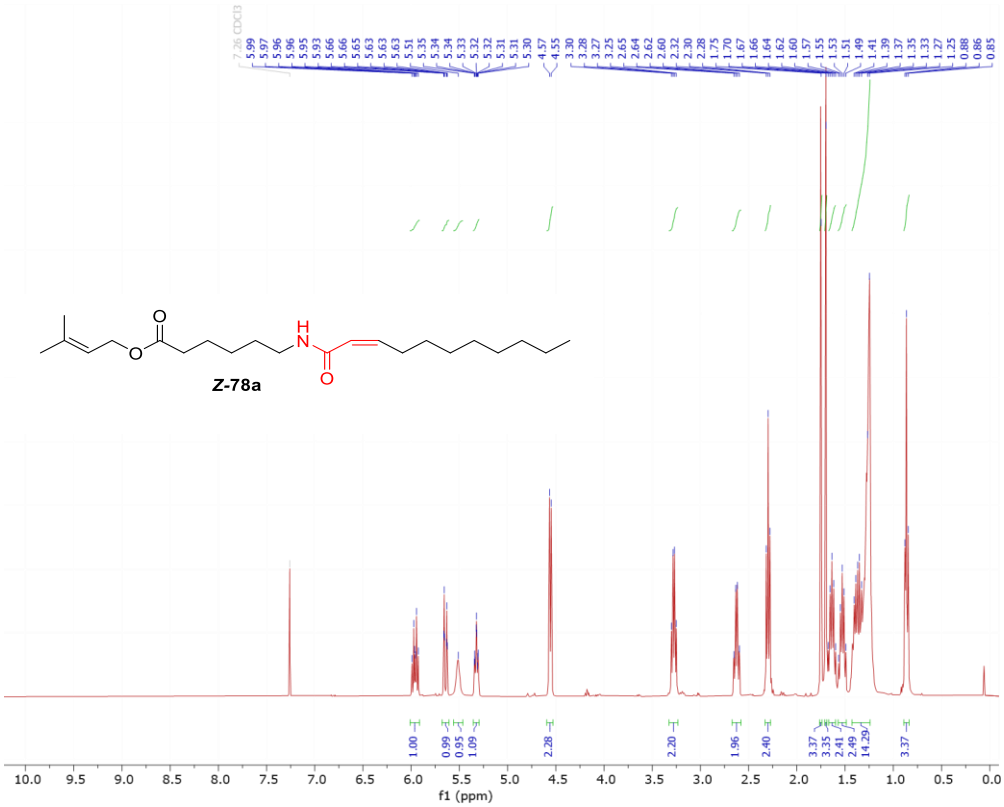

Z-104f
f1 (ppm)

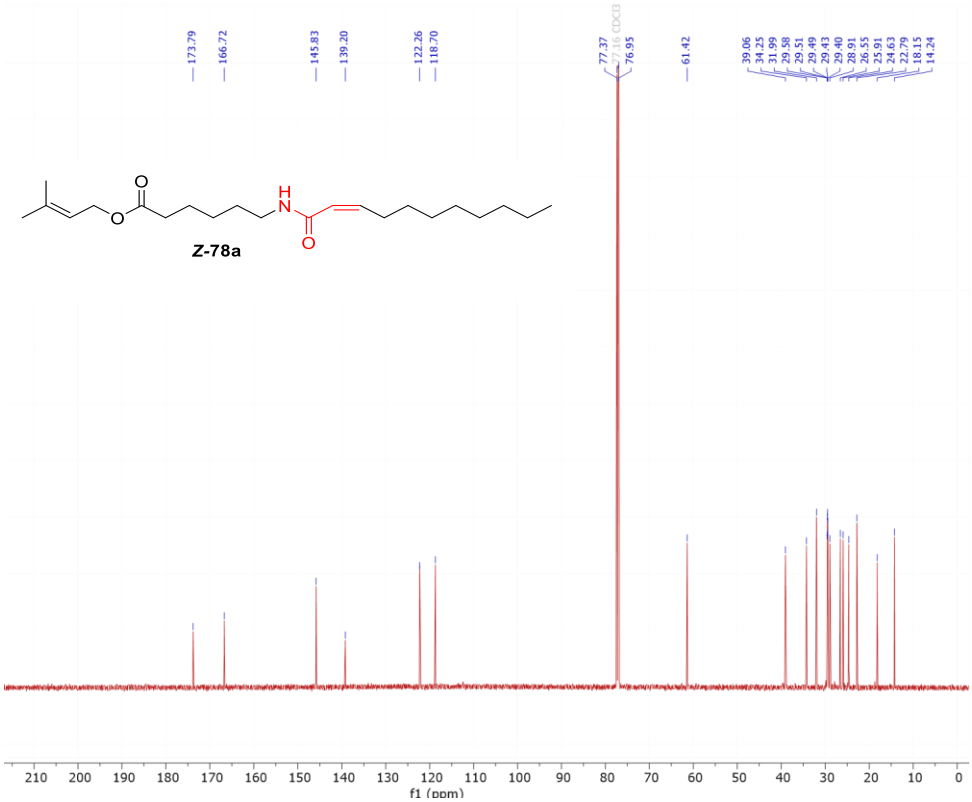

Z-76b
f1 (ppm)

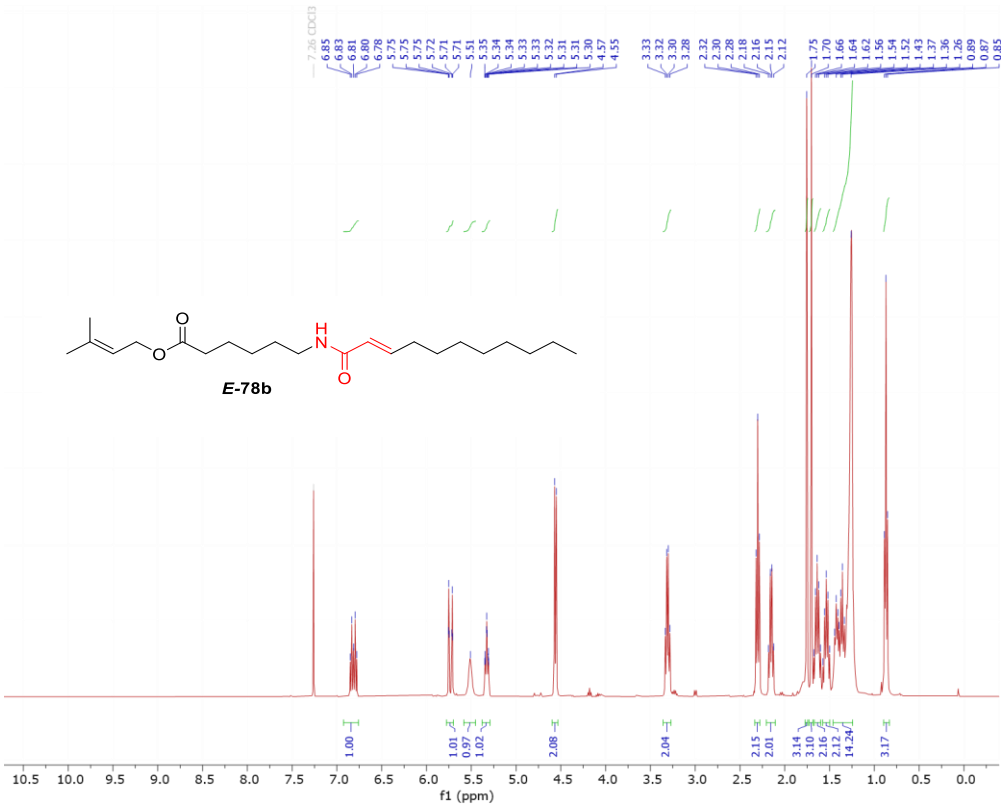

Z-76b
f1 (ppm)

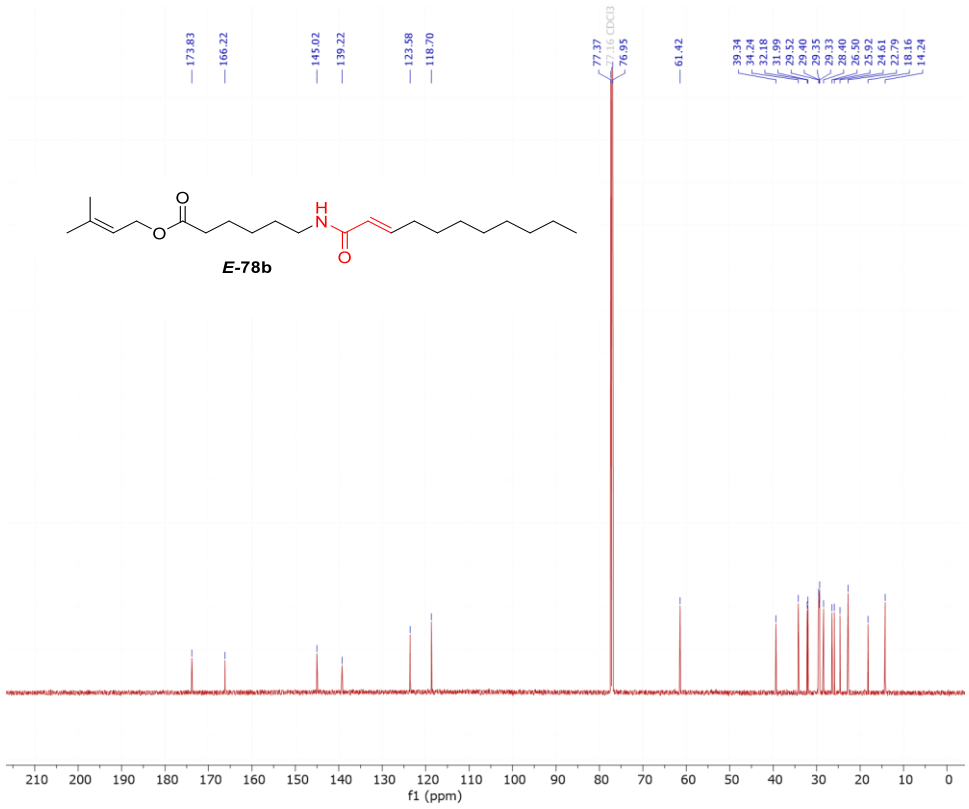

Z-105a
f1 (ppm)

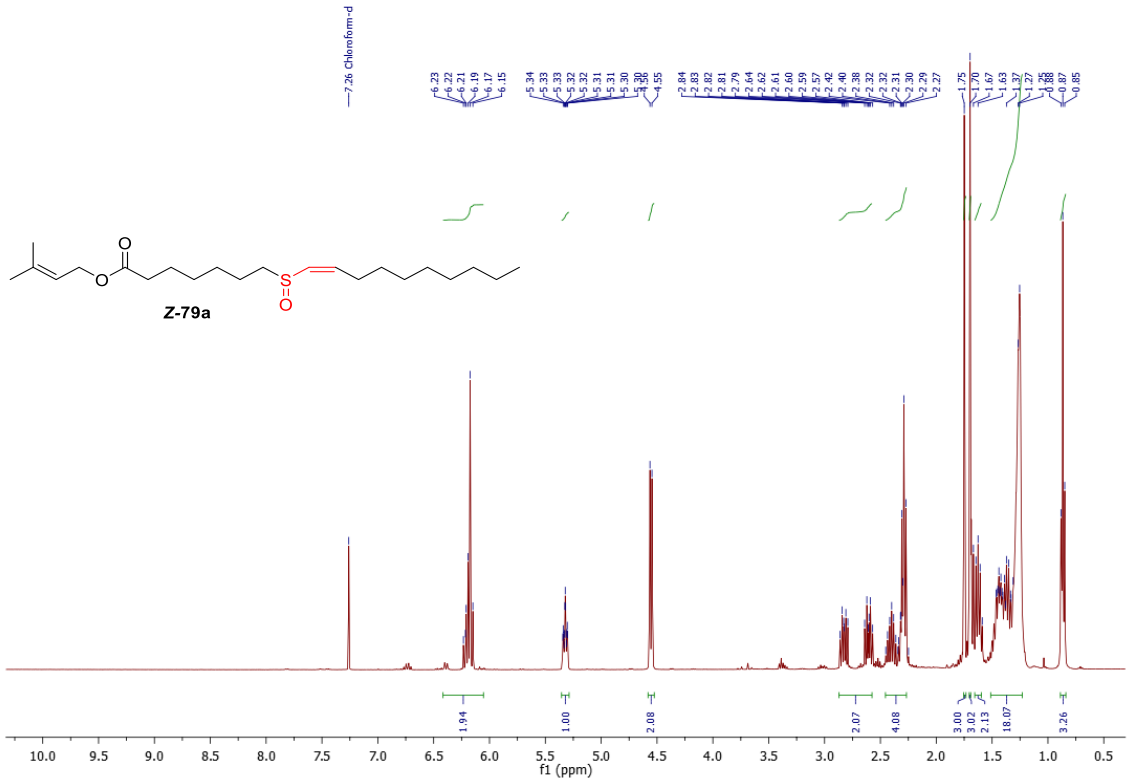

Z-105a
f1 (ppm)

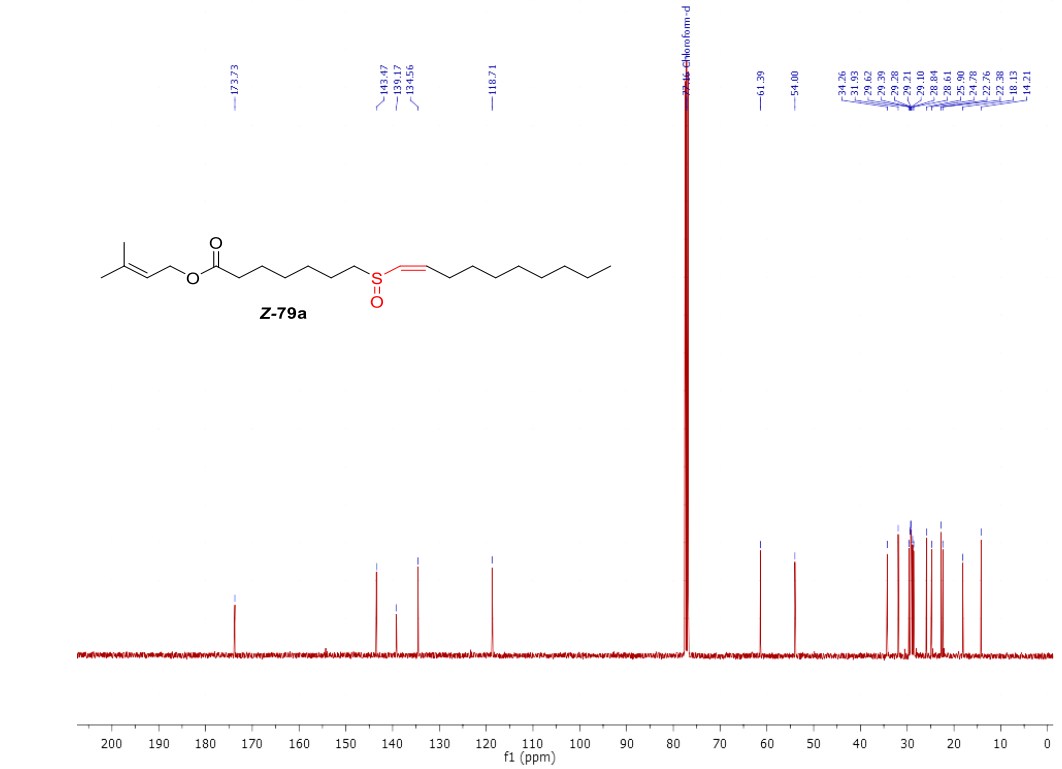

Z-78a
f1 (ppm)

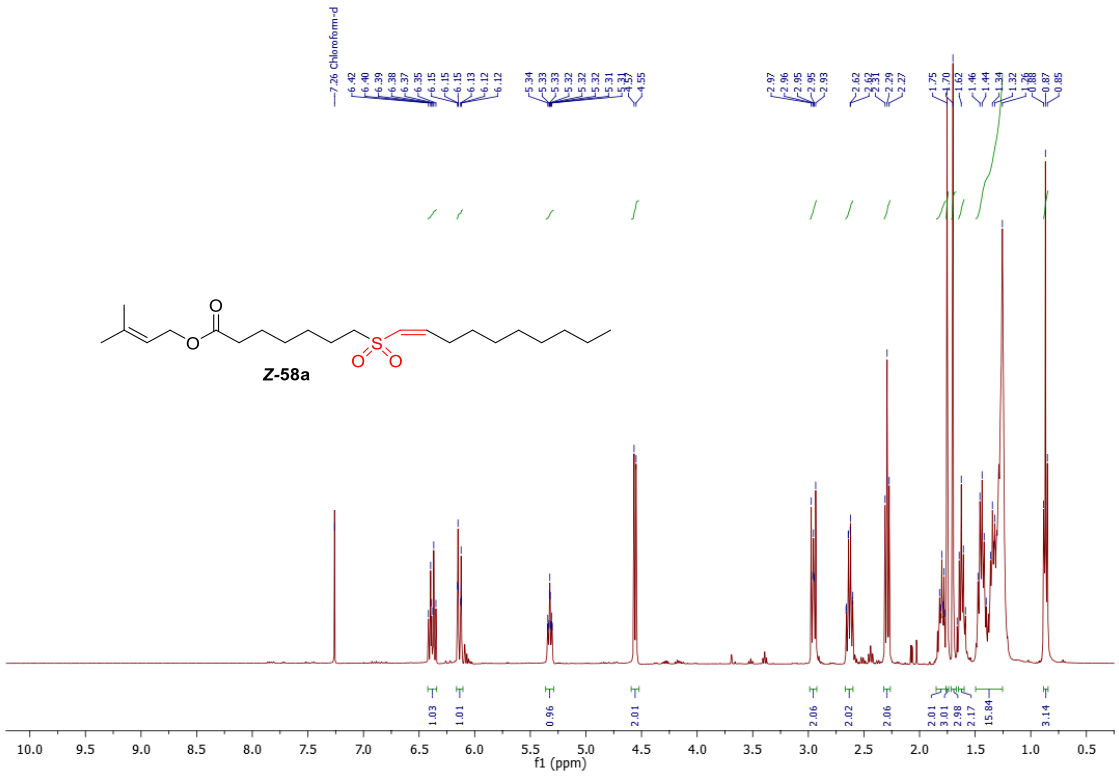

Z-78a
f1 (ppm)

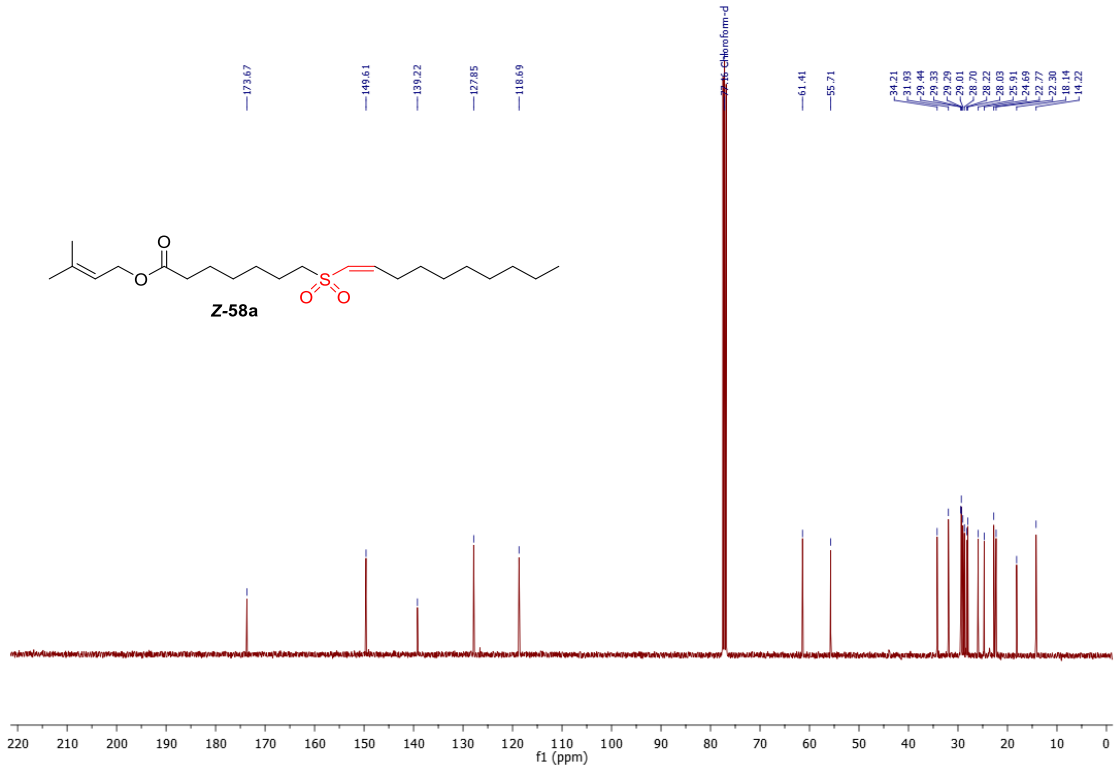

7.26 CDCl3
6.83
6.83
6.81
6.80
6.78
5.75
5.75
5.75
5.72
5.71
5.51
5.35
5.34
5.34
5.33
5.33
5.32
5.31
5.31
5.30
4.57
4.55
3.33
3.32
3.30
3.28
2.32
2.30
2.28
2.18
2.16
2.15
2.12
1.75
1.70
1.66
1.64
1.62
1.56
1.54
1.52
1.43
1.37
1.36
1.26
0.89
0.87
0.85
O
O
H
N
O
E-78b
1.00
1.01
0.97
1.02
2.08
2.04
2.15
2.01
3.14
3.10
2.16
2.12
14.24
3.17
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

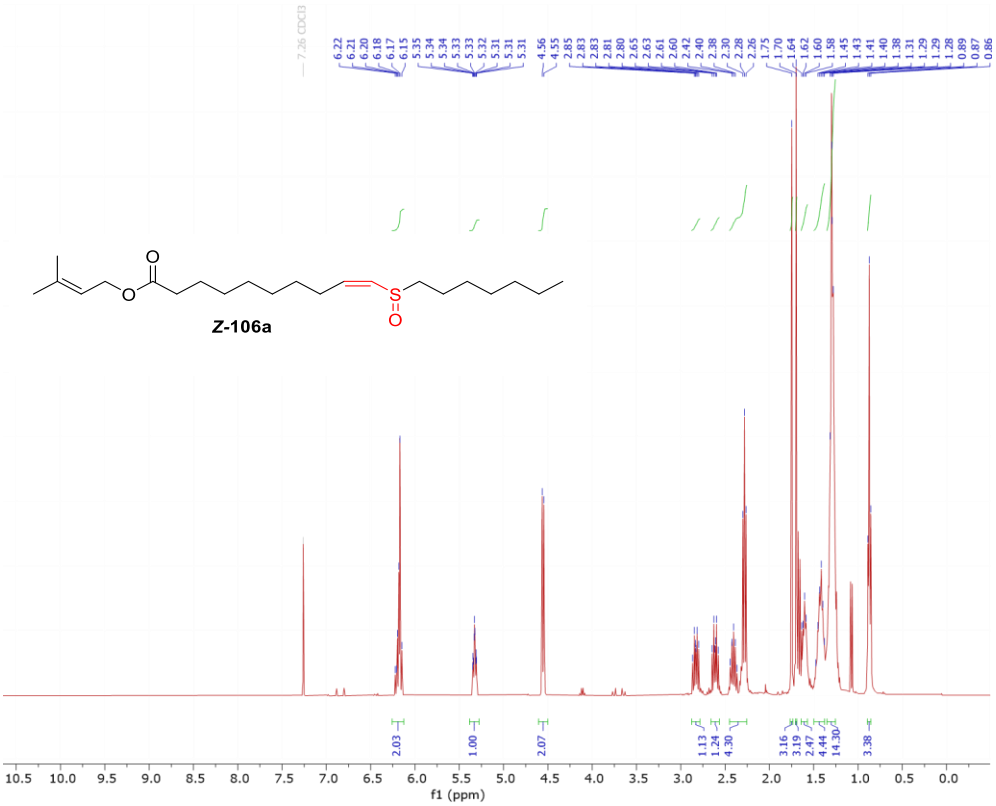

173.83
166.22
145.02
139.22
123.58
118.70
77.37
77.16 CDCl3
76.95
61.42
39.34
34.24
32.18
31.99
29.52
29.40
29.35
29.33
28.40
26.50
25.92
24.61
22.79
18.16
14.24
O
O
H
N
O
E-78b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

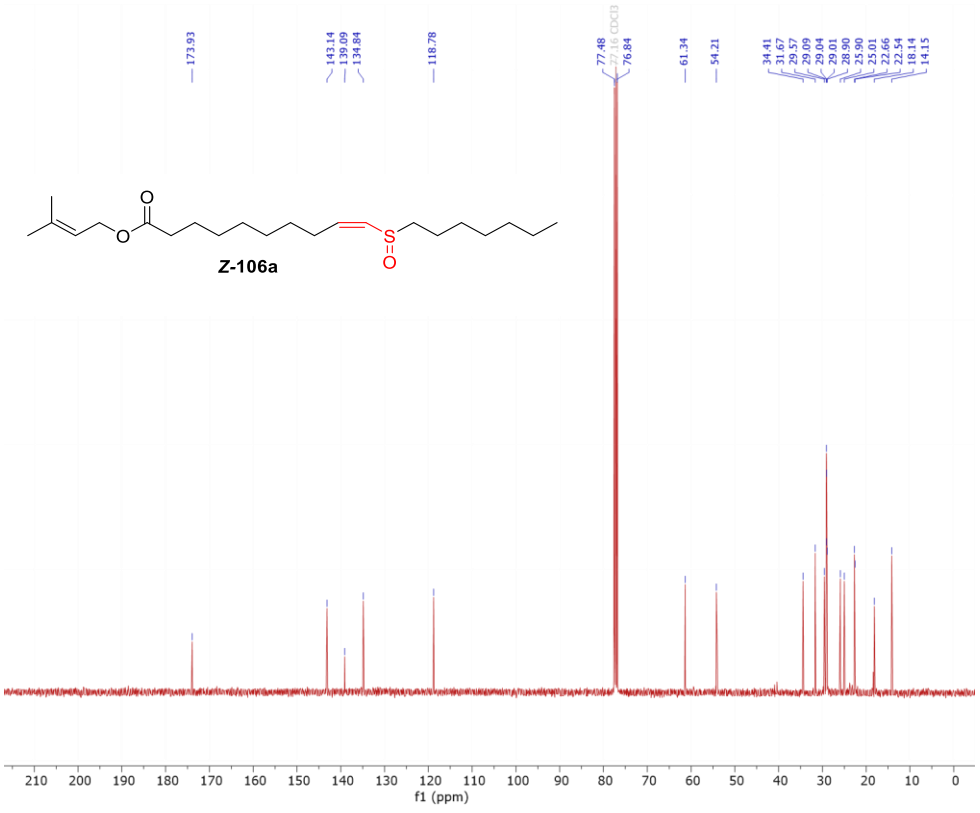

7.26 Chloroform-d
6.23
6.22
6.21
6.19
6.17
6.15
5.34
5.33
5.33
5.32
5.32
5.31
5.31
5.30
5.30
5.30
4.55
2.84
2.83
2.82
2.81
2.79
2.64
2.62
2.61
2.60
2.59
2.57
2.42
2.40
2.38
2.32
2.32
2.31
2.30
2.29
2.27
1.75
1.70
1.67
1.63
1.37
1.27
0.88
0.87
0.85
1.94
1.00
2.08
2.07
4.08
3.00
3.02
2.13
18.07
3.26
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
Z-79a

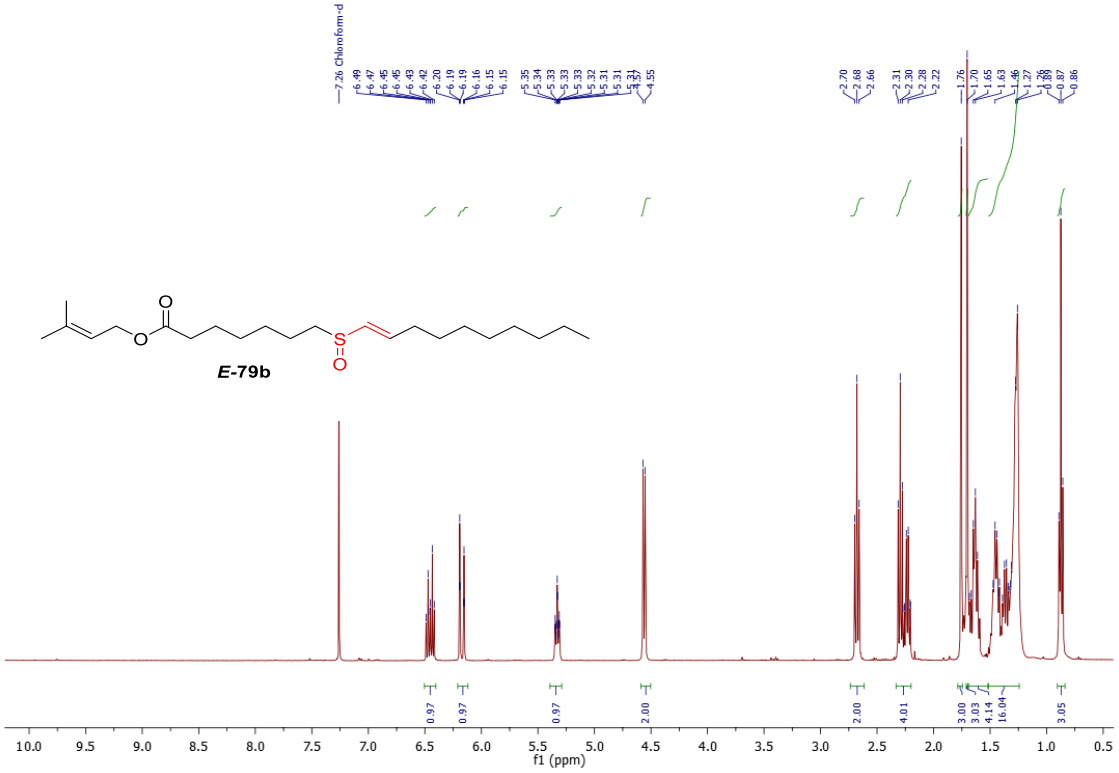

173.73
143.47
139.17
134.56
118.71
77.16 Chloroform-d
61.39
54.00
34.26
31.93
29.62
29.39
29.28
29.21
29.10
28.84
28.61
25.90
24.78
22.76
22.38
18.13
14.21
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
Z-79a

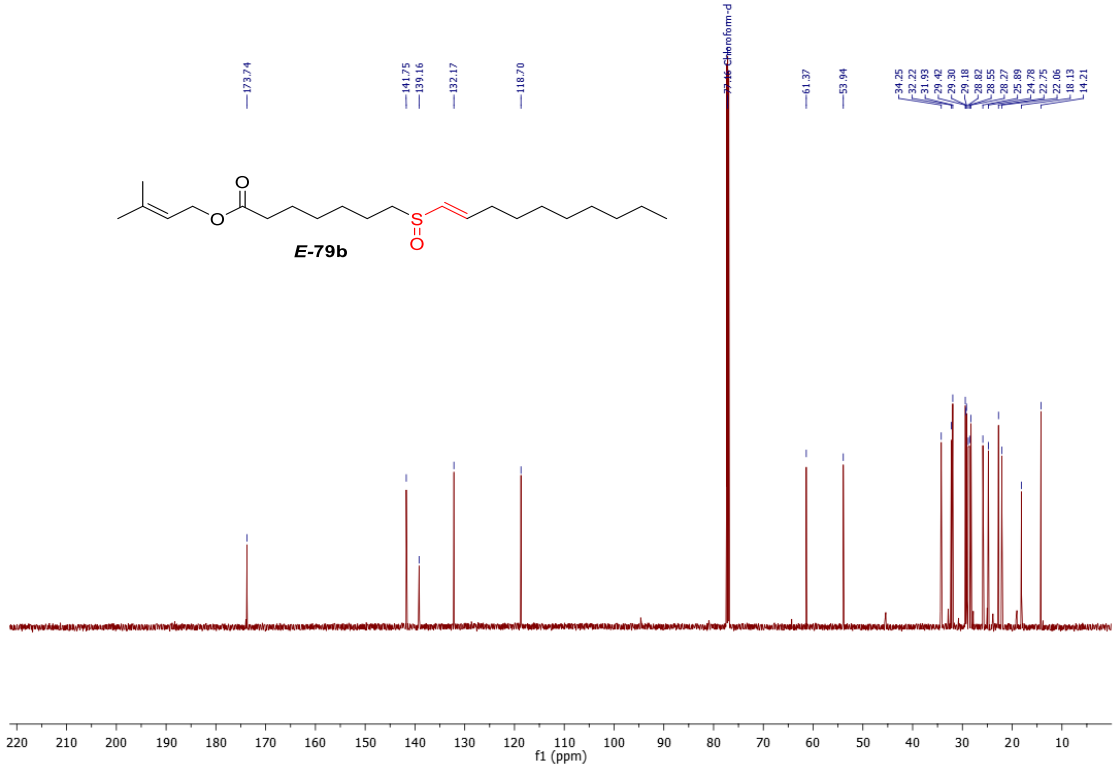

Z-58a
f1 (ppm)

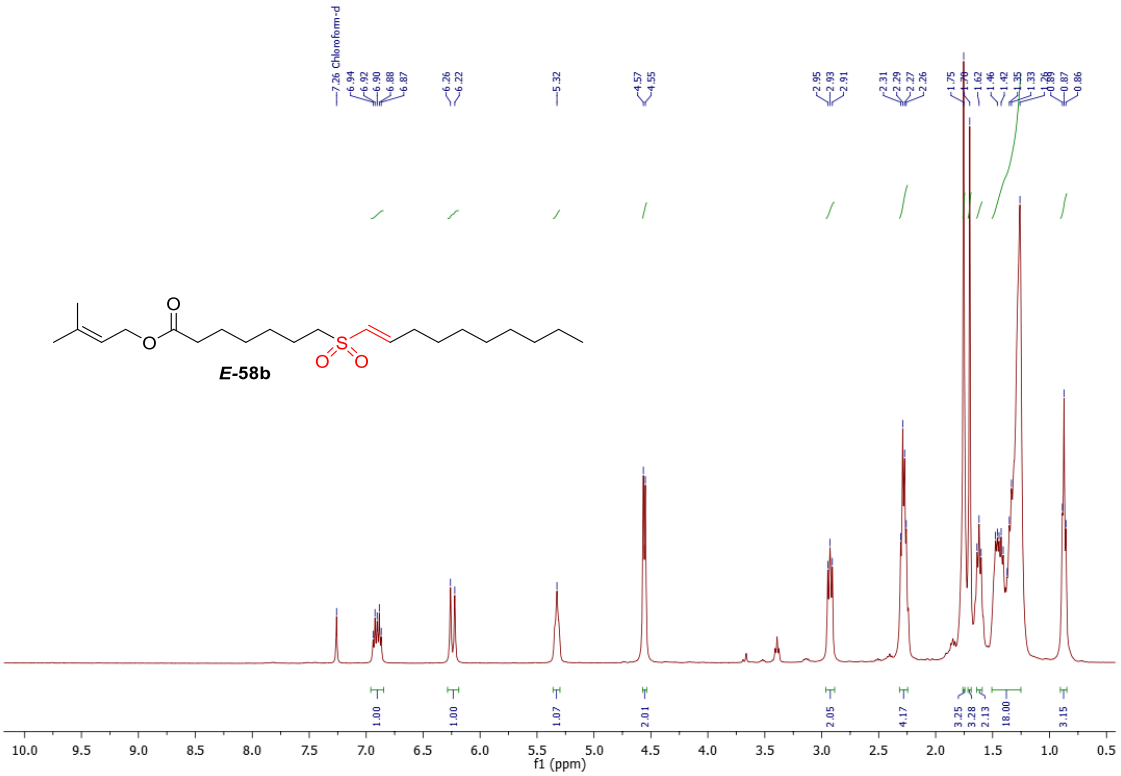

Z-58a
f1 (ppm)


Z-106a
f1 (ppm)

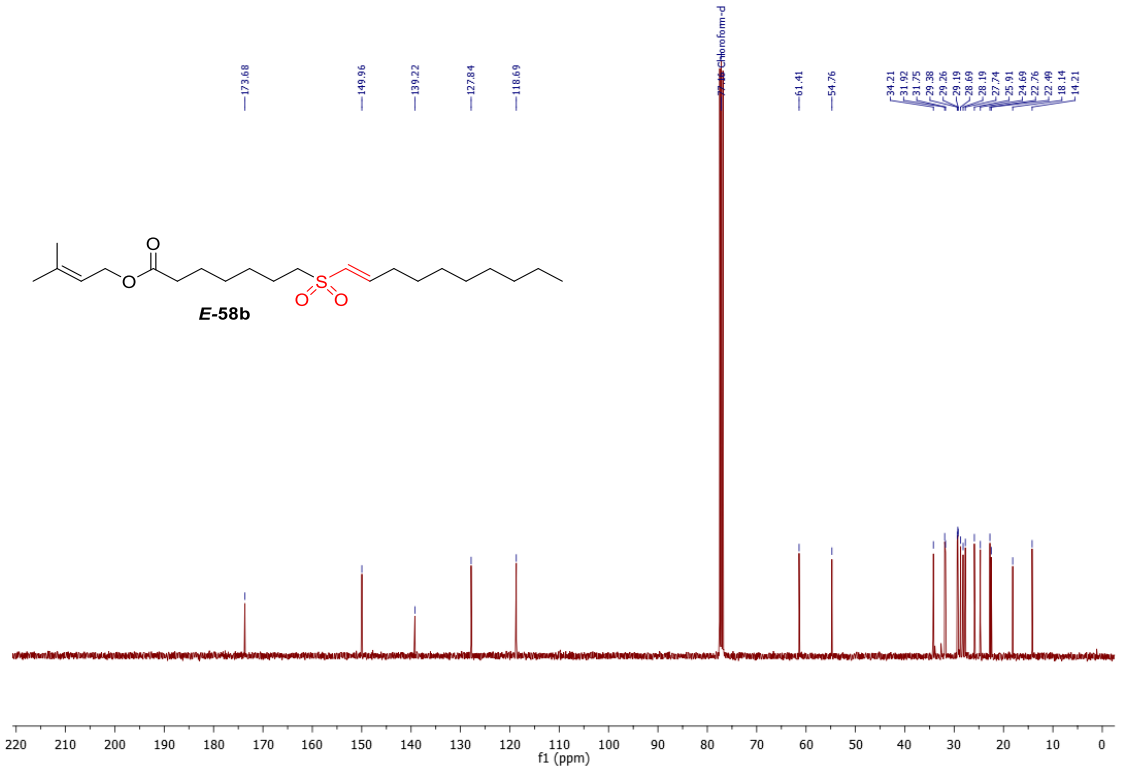

Z-106a
f1 (ppm)


7.26 Chloroform-d
6.49
6.47
6.45
6.43
6.42
6.20
6.19
6.19
6.16
6.15
5.35
5.34
5.33
5.33
5.32
5.31
5.31
5.31
4.55
2.70
2.68
2.66
2.31
2.30
2.28
2.22
1.76
1.70
1.65
1.63
1.46
1.27
1.26
0.89
0.87
0.86
O
O
S
O
E-79b
0.97
0.97
0.97
2.00
2.00
4.01
3.00
3.03
4.14
16.04
3.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

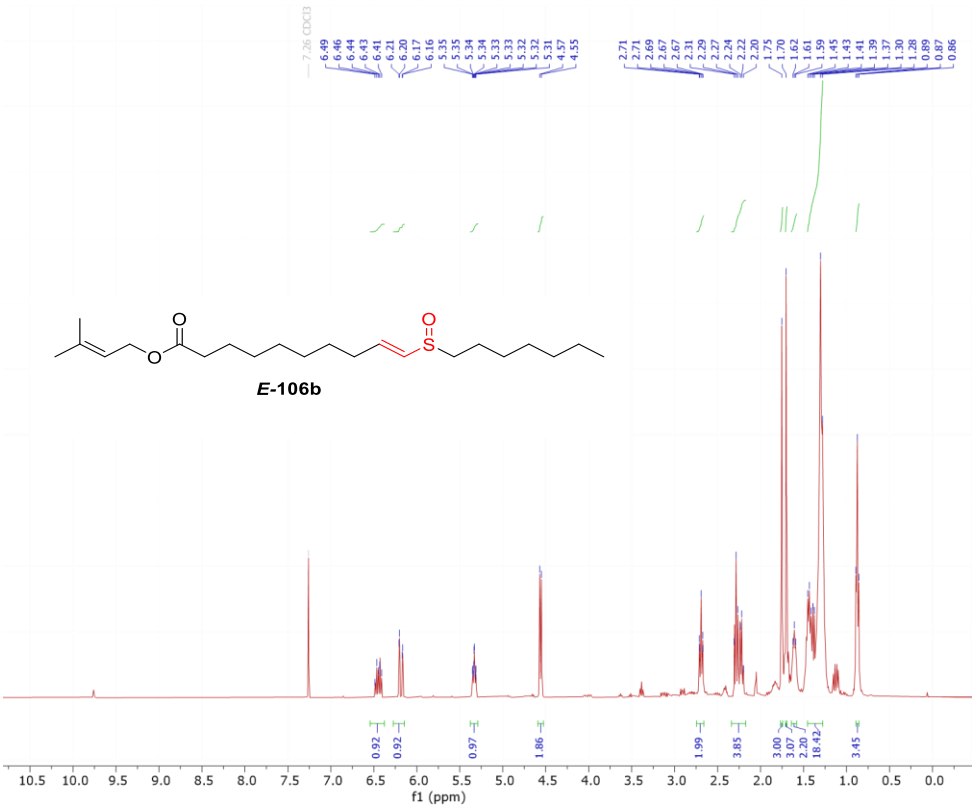

173.74
141.75
139.16
132.17
118.70
77.16 Chloroform-d
61.37
53.94
34.25
32.22
31.93
29.42
29.30
29.18
28.82
28.55
28.27
25.89
24.78
22.75
22.06
18.13
14.21
O
O
S
O
E-79b
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

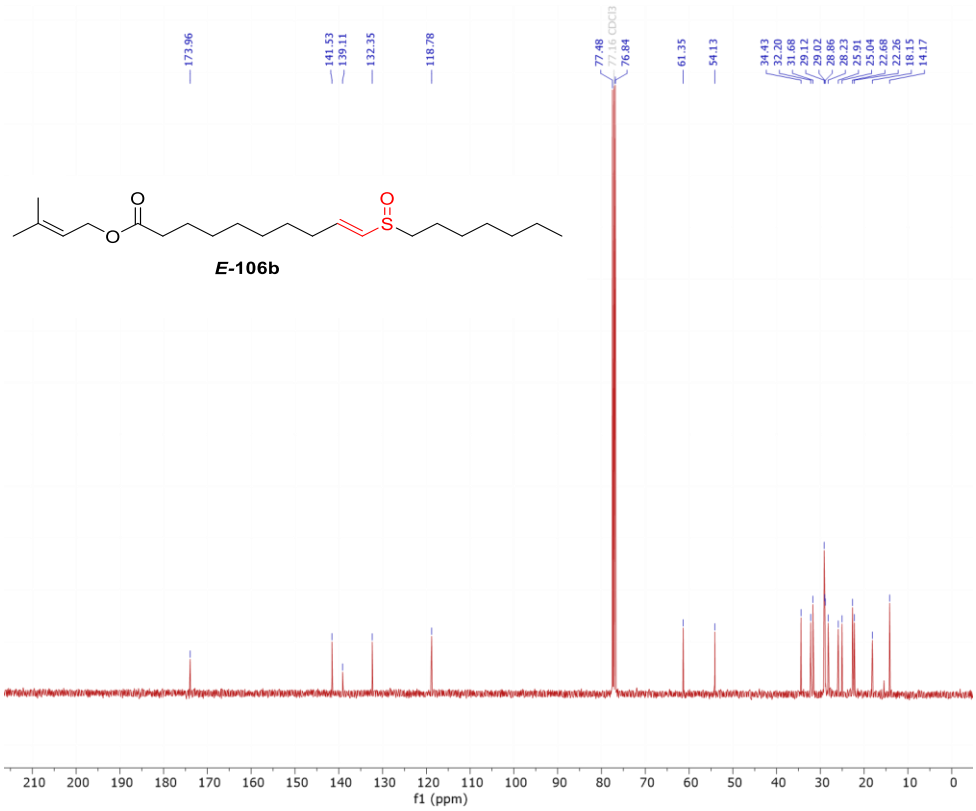

7.26 Chloroform-d
6.94
6.92
6.90
6.88
6.87
6.26
6.22
5.32
4.57
4.55
2.95
2.93
2.91
2.31
2.29
2.27
2.26
1.75
1.70
1.62
1.46
1.42
1.35
1.33
0.89
0.87
0.86
1.00
1.00
1.07
2.01
2.05
4.17
3.25
3.28
2.13
18.00
3.15
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

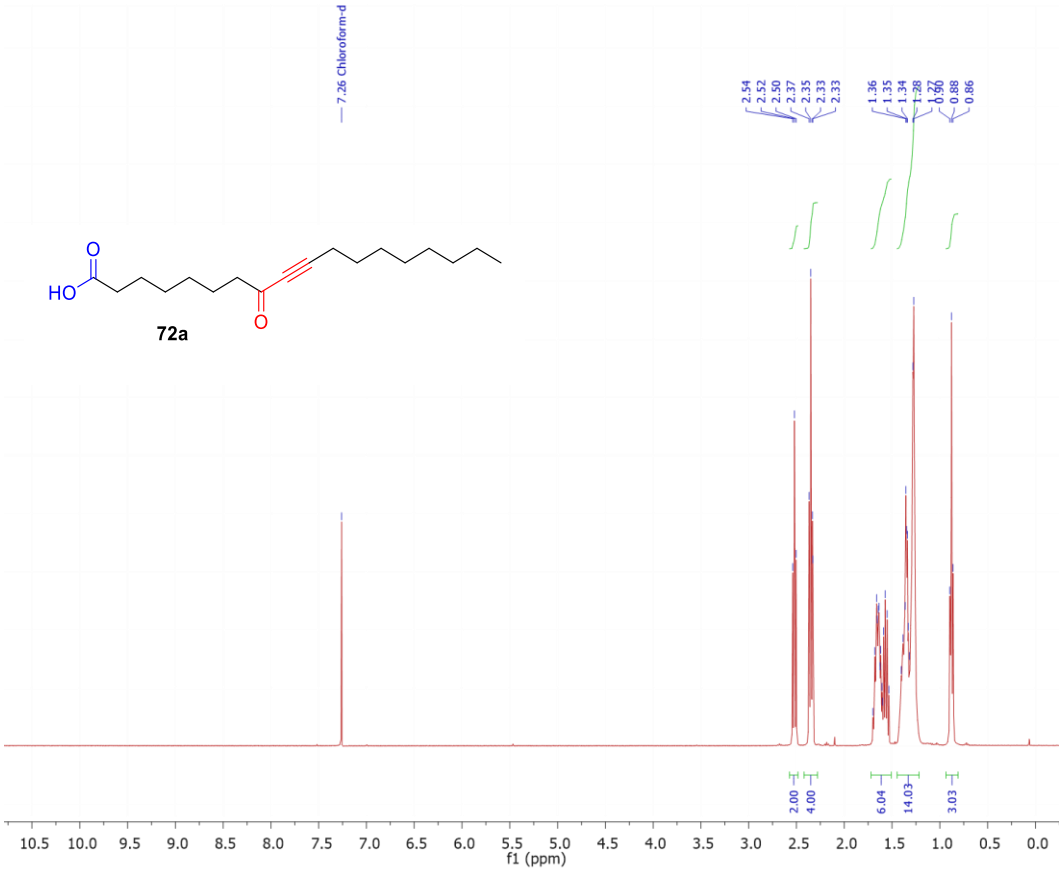
E-58b

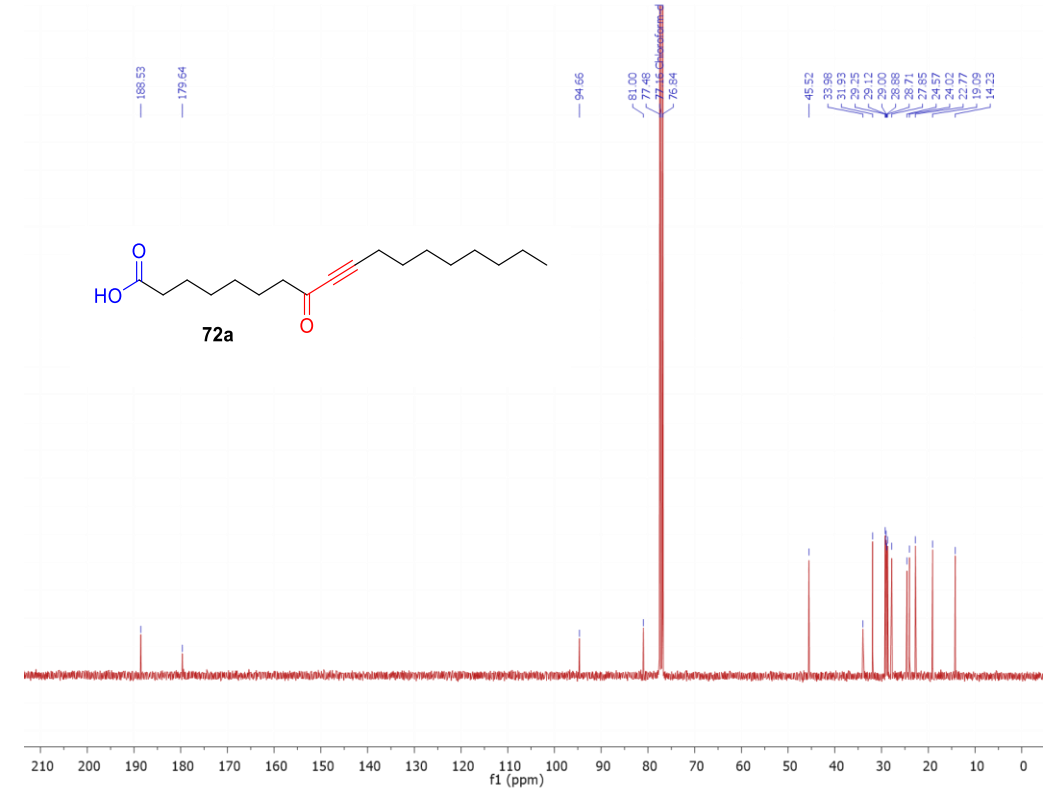

173.68
149.96
139.22
127.84
118.69
77.16 Chloroform-d
61.41
54.76
34.21
31.92
31.75
29.38
29.26
29.19
28.69
28.19
27.74
25.91
24.69
22.76
22.49
18.14
14.21
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

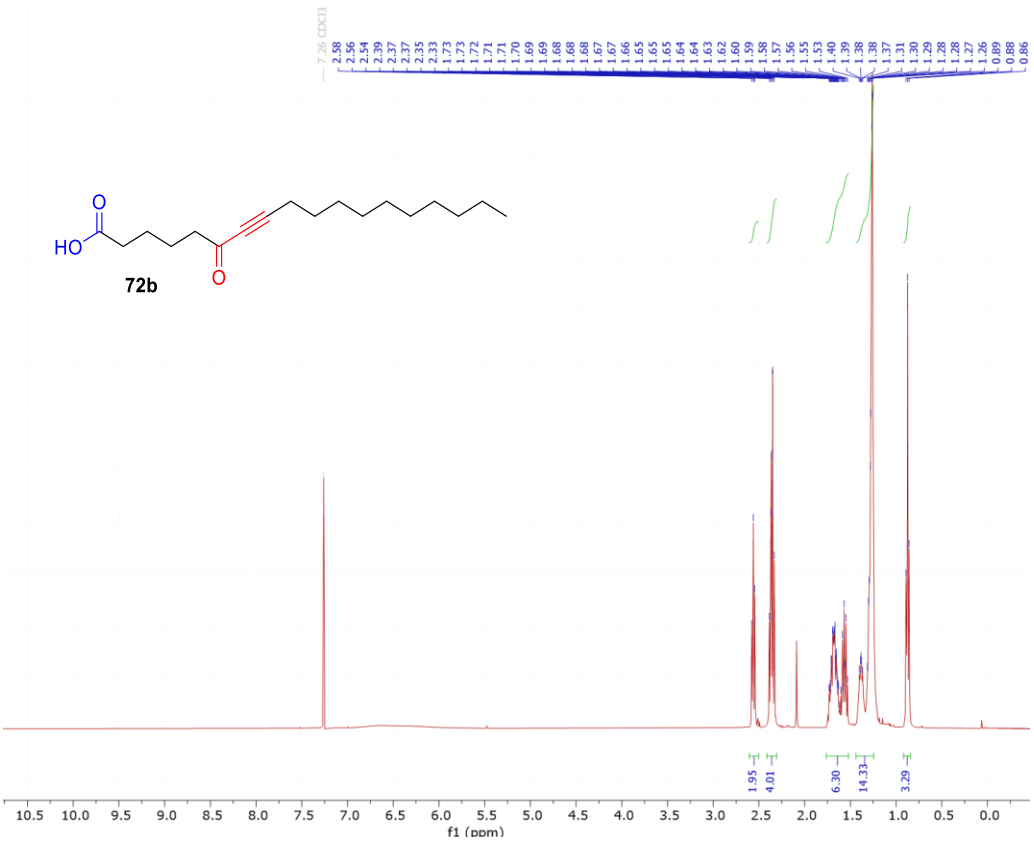
E-58b

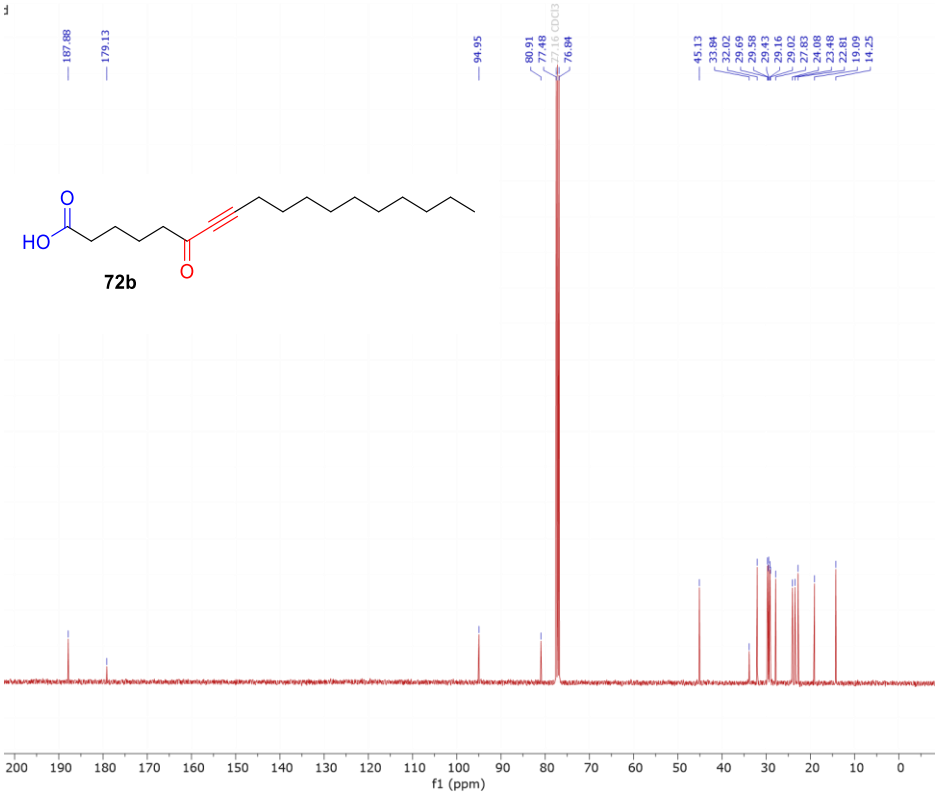

7.26 CDCl3
6.49
6.46
6.44
6.43
6.41
6.21
6.20
6.17
6.16
5.35
5.35
5.34
5.34
5.33
5.33
5.32
5.32
5.31
4.57
4.55
2.71
2.71
2.69
2.69
2.67
2.67
2.31
2.29
2.27
2.24
2.22
2.20
1.75
1.70
1.62
1.61
1.59
1.45
1.43
1.41
1.39
1.37
1.30
1.28
0.89
0.87
0.86
O
O
O
S
E-106b
0.92
0.92
0.97
1.86
1.99
3.85
3.00
3.07
2.07
2.00
18.42
3.45
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

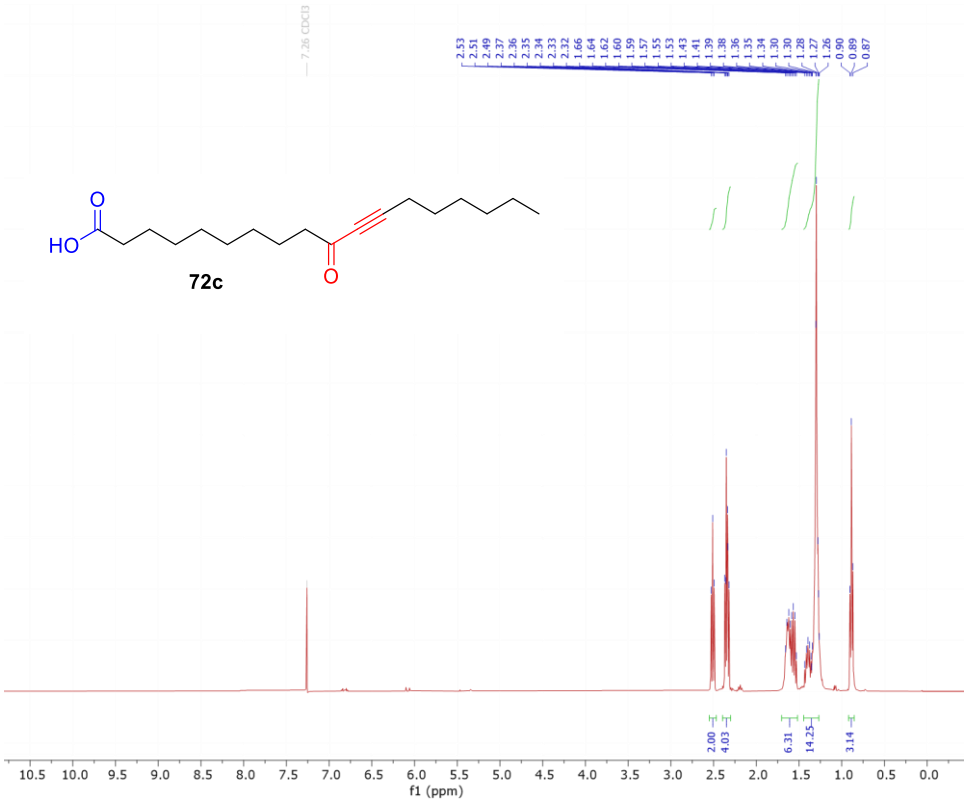

173.96
141.53
139.11
132.35
118.78
77.48
77.16 CDCl3
76.84
61.35
54.13
34.43
32.20
31.68
29.12
29.02
28.86
28.23
25.91
25.04
22.68
22.26
18.15
14.17
O
O
O
S
E-106b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

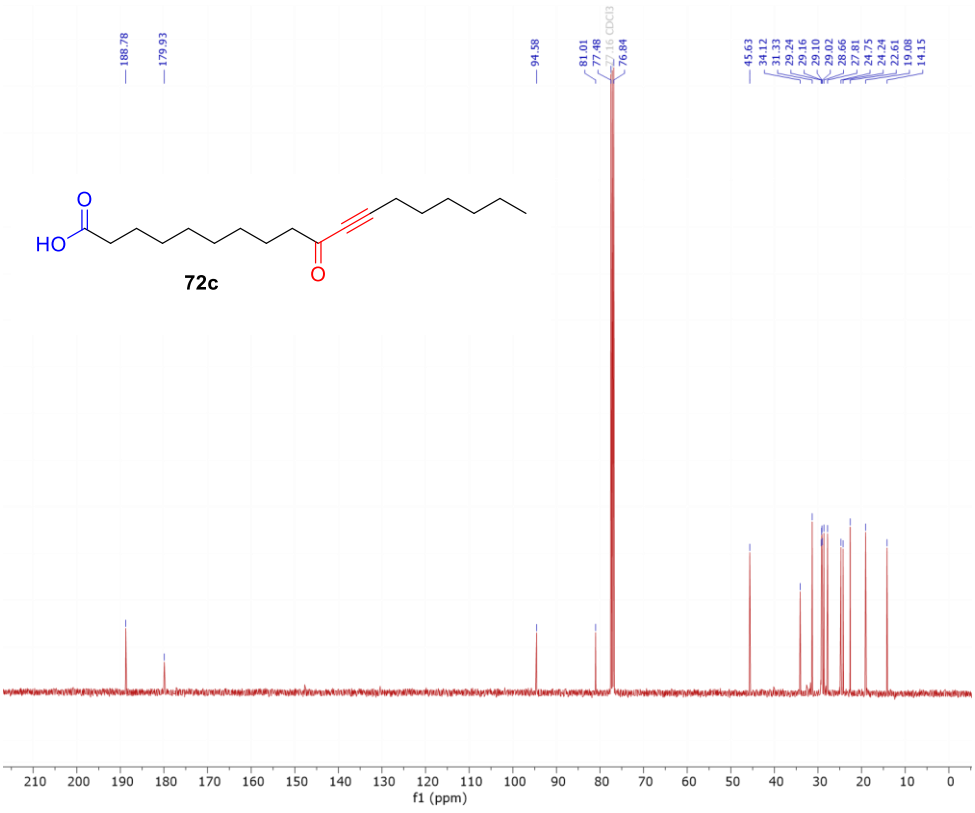

7.26 Chloroform-d
2.54
2.52
2.50
2.37
2.35
2.33
2.33
1.36
1.35
1.34
1.28
1.27
0.90
0.88
0.86
HO
O
O
72a
2.00
4.00
6.04
14.03
3.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

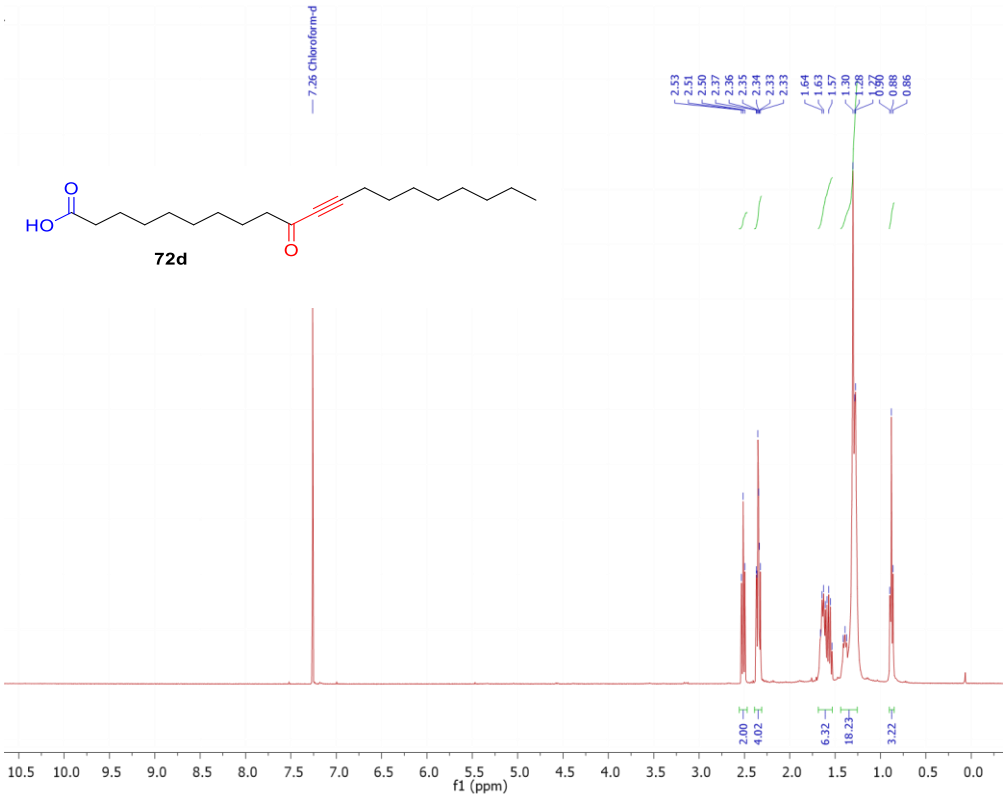

188.53
179.64
94.66
81.00
77.48
77.16 Chloroform-d
76.84
45.52
33.98
31.93
29.25
29.12
29.00
28.88
28.71
27.85
24.57
24.02
22.77
19.29
14.23
HO
O
O
72a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

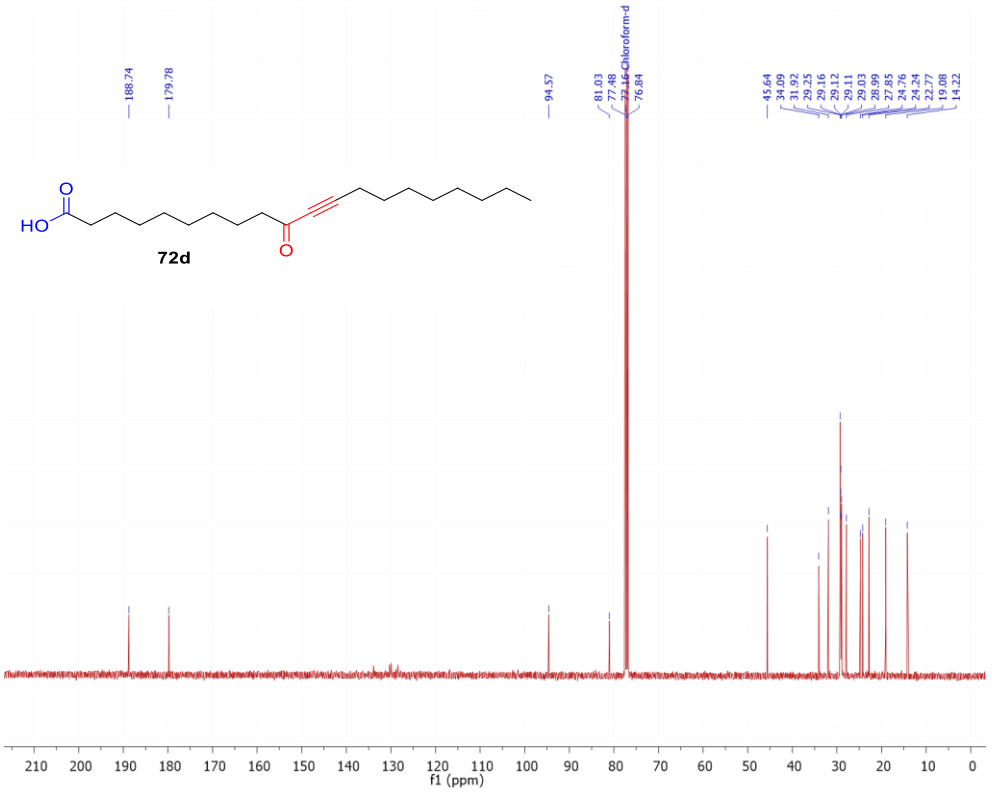

HO
O
O
72b
f1 (ppm)

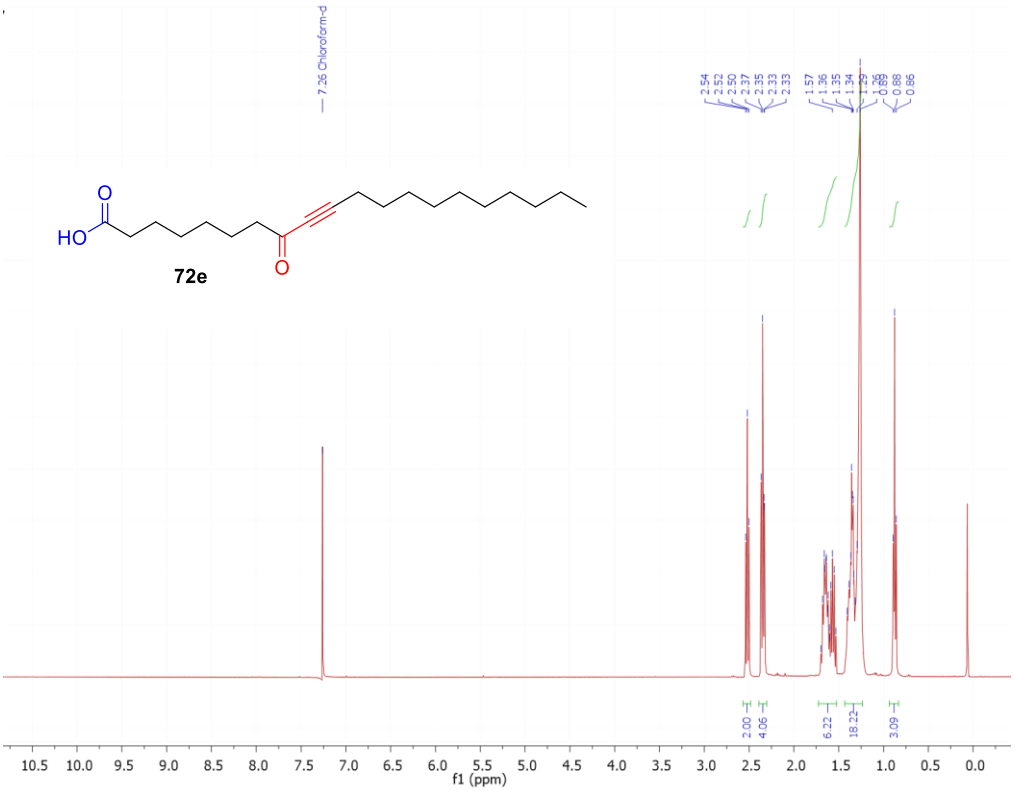

HO
O
O
72b
f1 (ppm)

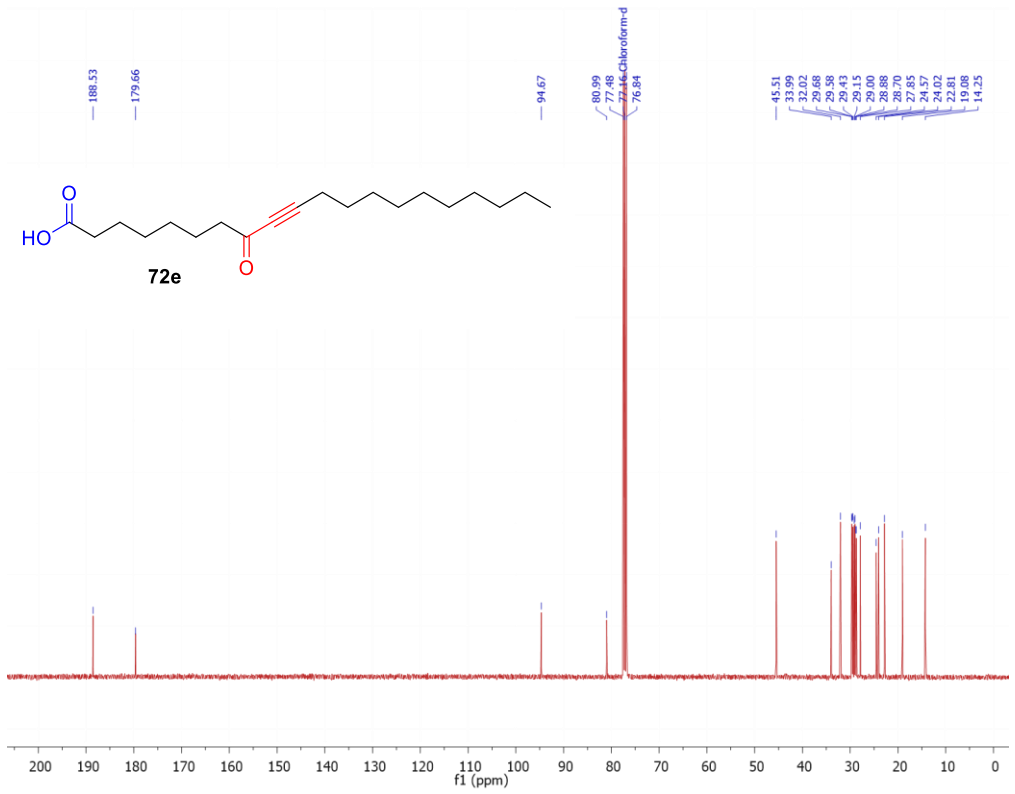

7.26 CDCl3
2.53
2.51
2.49
2.37
2.36
2.35
2.34
2.33
2.32
1.66
1.64
1.62
1.60
1.59
1.57
1.55
1.53
1.43
1.41
1.39
1.38
1.36
1.35
1.34
1.30
1.30
1.28
1.27
1.26
0.90
0.89
0.87
O
HO
O
72c
2.00
4.03
6.31
14.25
3.14
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

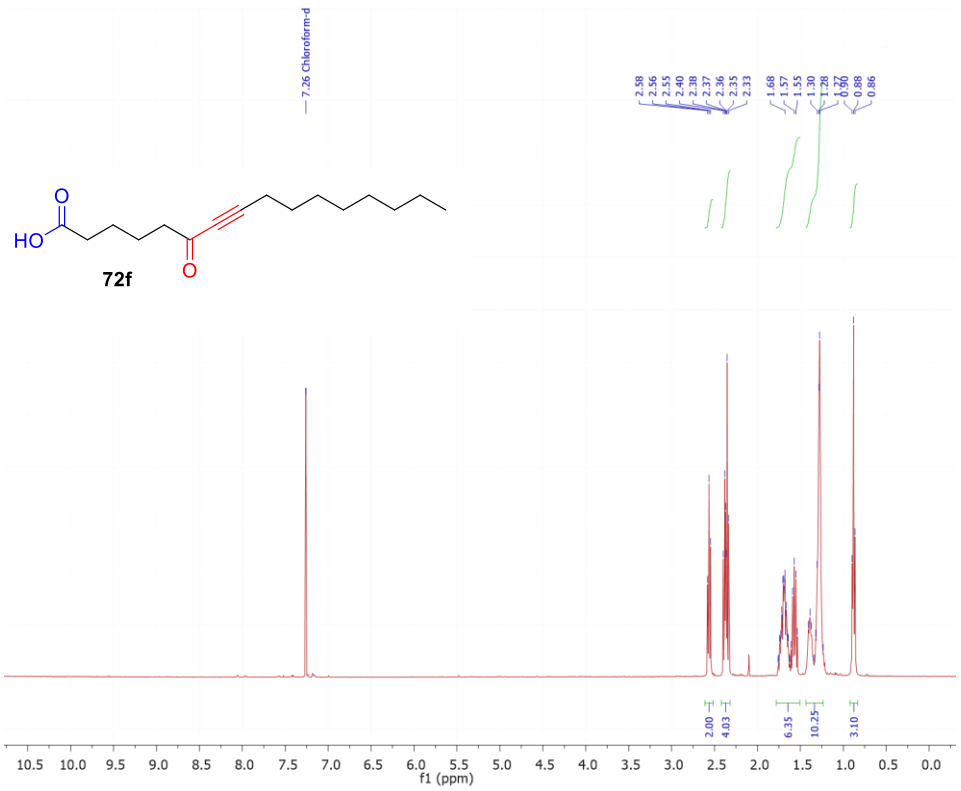

188.78
179.93
94.58
81.01
77.48
77.16 CDCl3
76.84
45.63
34.12
31.33
29.24
29.16
29.10
29.02
28.66
27.81
24.75
24.24
22.61
19.08
14.15
O
HO
O
72c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

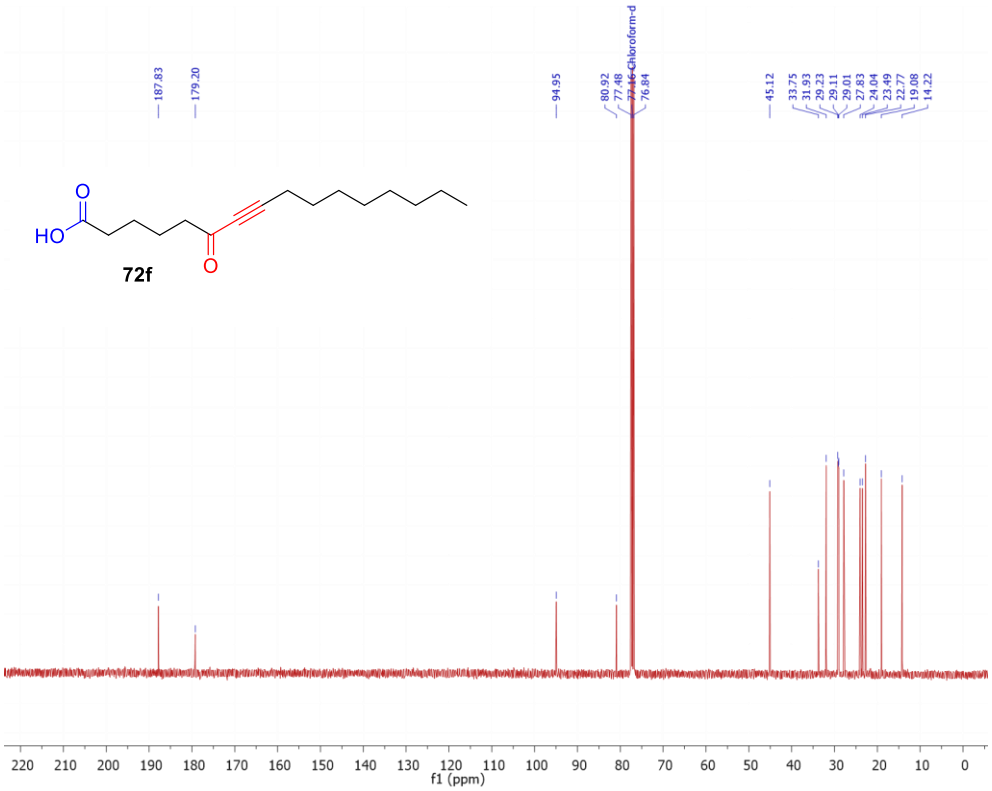

7.26 Chloroform-d
2.53
2.51
2.50
2.37
2.36
2.35
2.34
2.33
2.33
1.64
1.63
1.57
1.30
1.28
0.90
0.88
0.86
HO
O
O
72d
2.00
4.02
6.32
18.23
3.22
f1 (ppm)

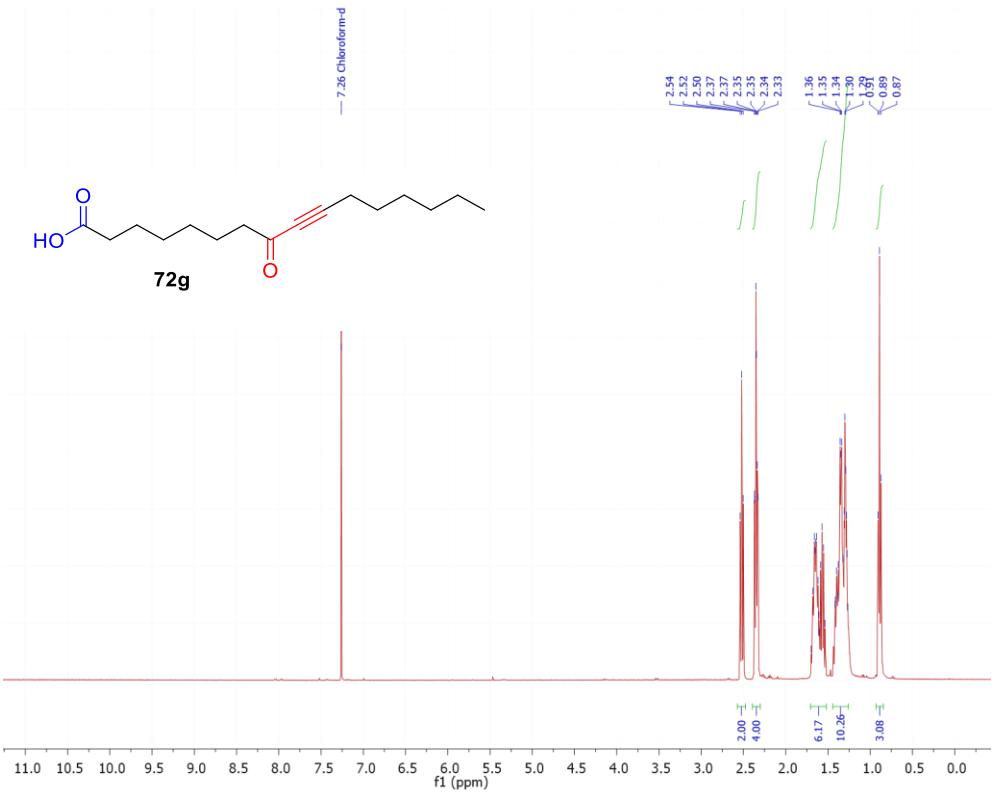

188.74
179.78
94.57
81.03
77.48
77.16 Chloroform-d
76.84
45.64
34.09
31.92
29.25
29.16
29.12
29.11
29.03
28.99
27.85
24.76
24.24
22.77
19.08
14.22
HO
O
O
72d
f1 (ppm)

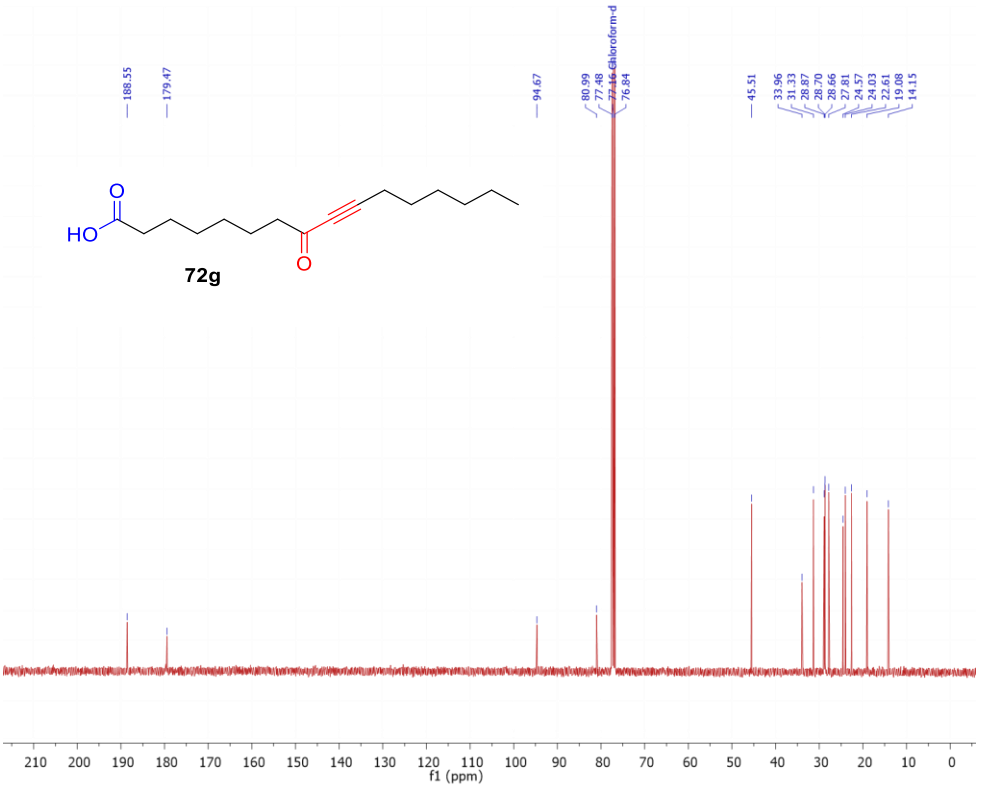

7.26 Chloroform-d
2.54
2.52
2.50
2.37
2.35
2.33
2.33
1.57
1.36
1.35
1.34
1.29
0.89
0.88
0.86
HO
O
O
72e
2.00
4.06
6.22
18.22
3.09
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

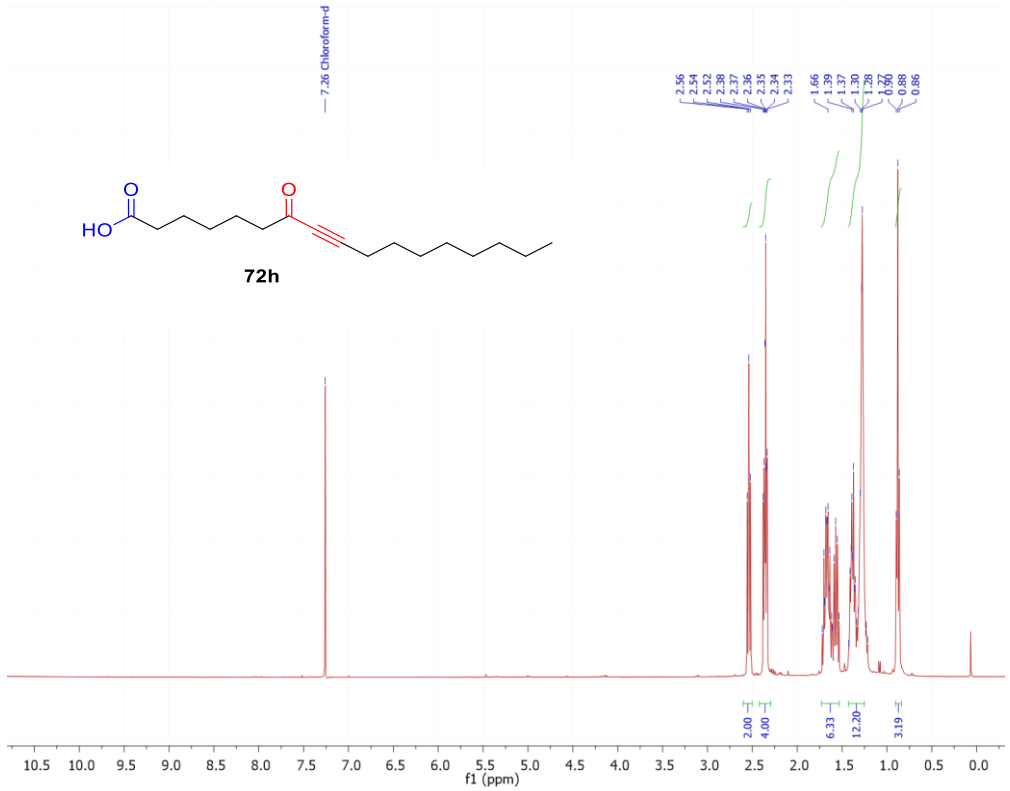

188.53
179.66
94.67
80.99
77.48
77.16 Chloroform-d
76.84
45.51
33.99
32.02
29.68
29.58
29.43
29.15
29.00
28.88
28.70
27.85
24.57
24.02
22.81
19.08
14.25
HO
O
O
72e
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

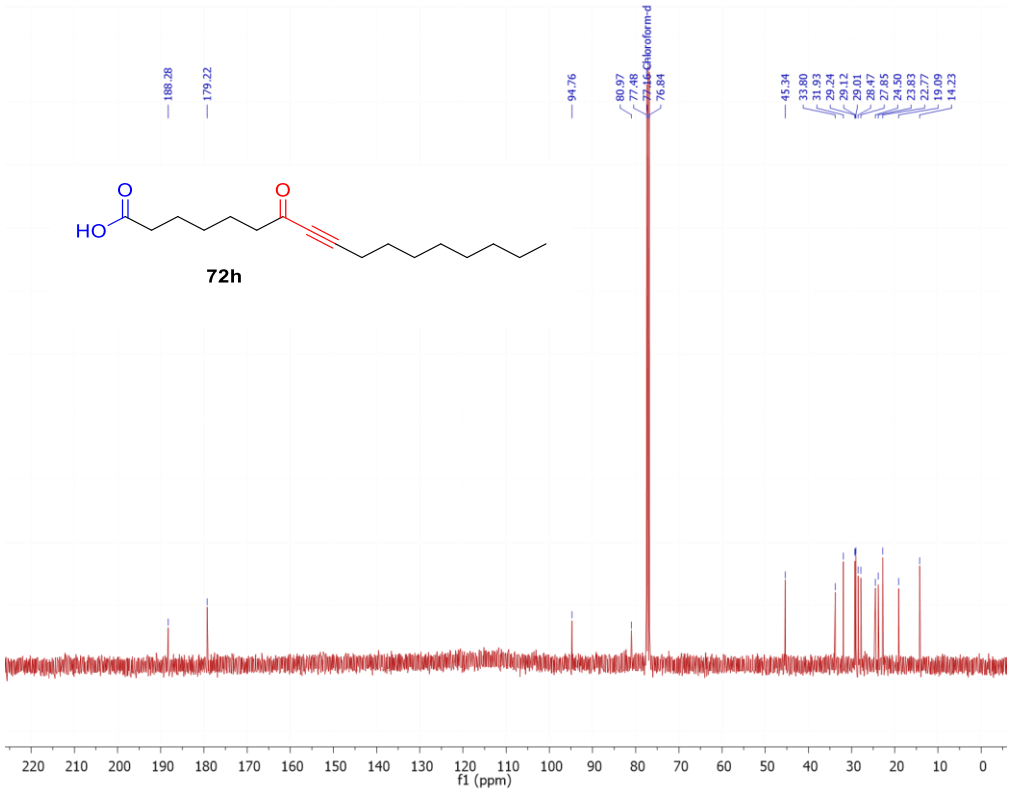

7.26 Chloroform-d
2.58
2.56
2.55
2.40
2.38
2.37
2.36
2.35
2.33
1.68
1.57
1.55
1.30
1.28
0.88
0.86
HO
O
O
72f
2.00
4.03
6.35
10.25
3.10
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

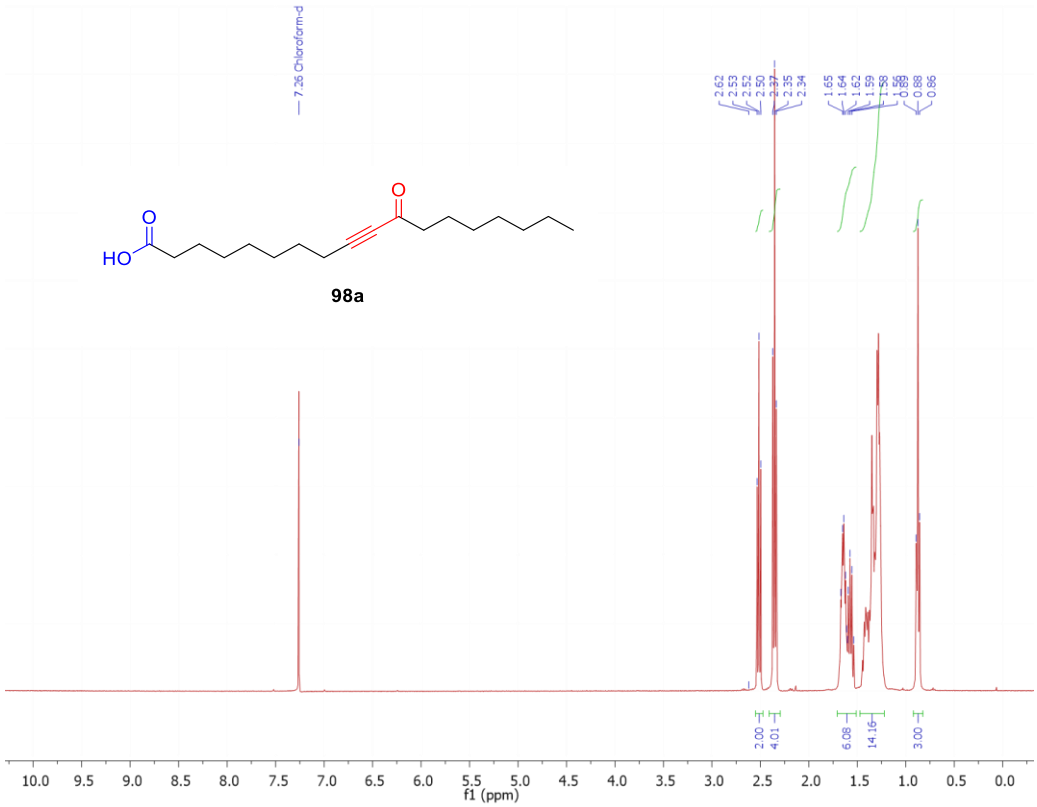

187.83
179.20
94.95
80.92
77.48
77.16 Chloroform-d
76.84
45.12
33.75
31.93
29.23
29.11
29.01
27.83
24.04
23.49
22.77
19.08
14.22
HO
O
O
72f
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

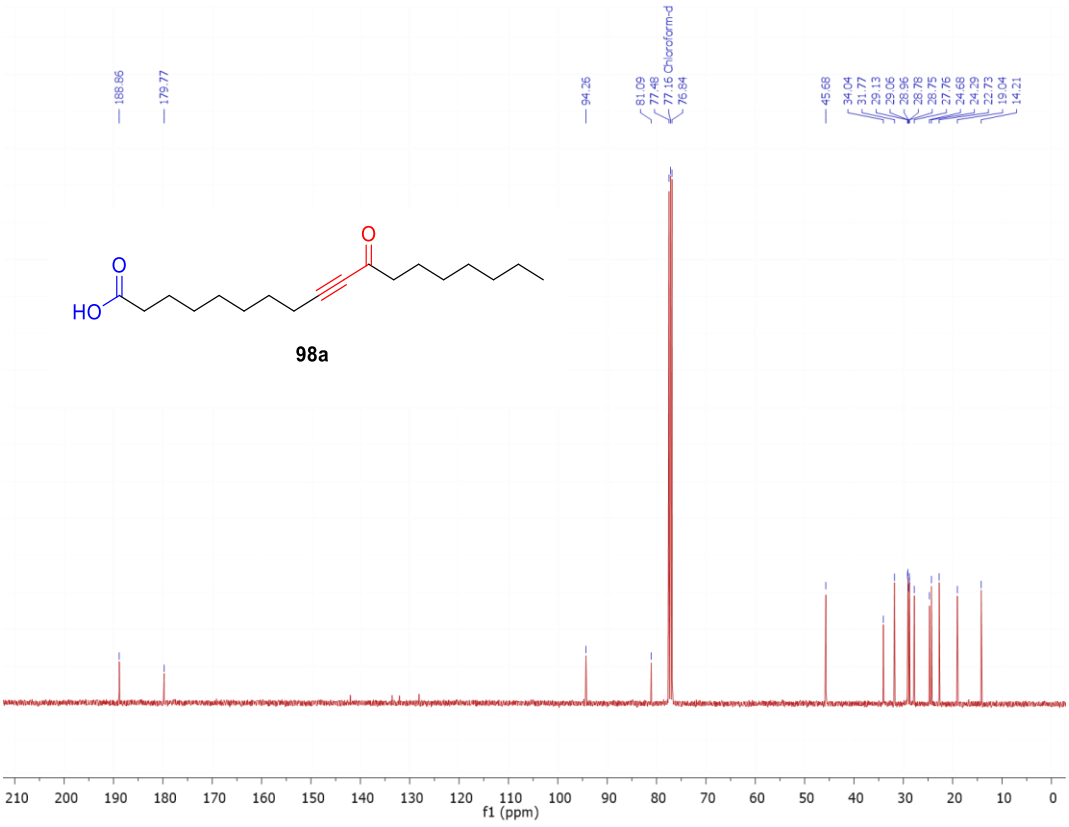

7.26 Chloroform-d
2.54
2.52
2.50
2.37
2.37
2.35
2.35
2.34
2.33
1.36
1.35
1.34
1.30
1.29
0.91
0.89
0.87
HO
O
O
72g
2.00
4.00
6.17
10.26
3.08
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

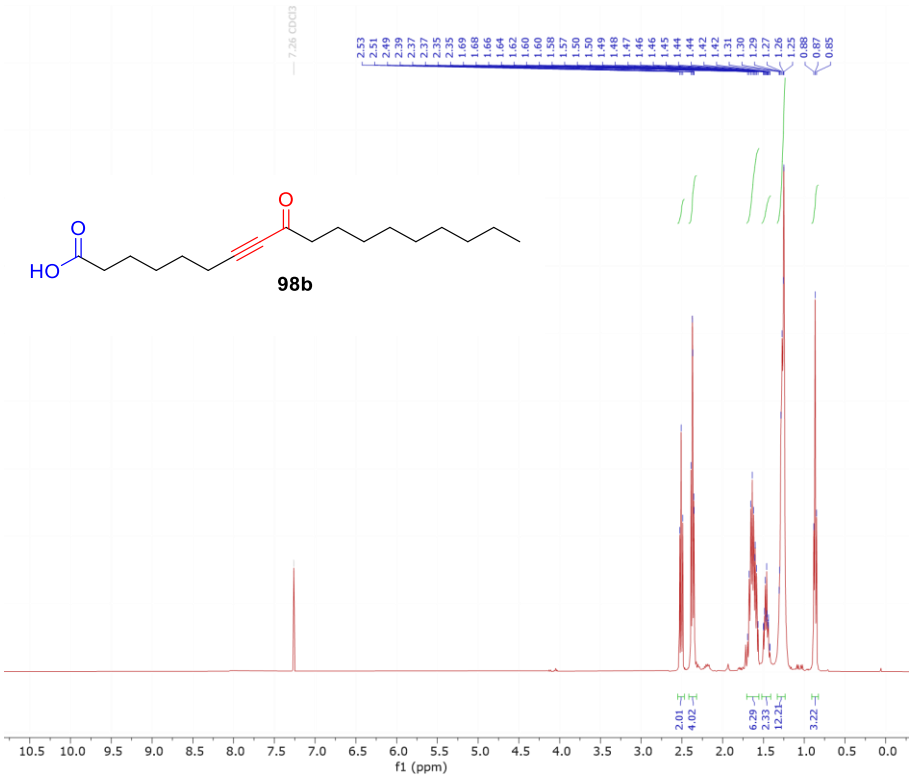

188.55
179.47
94.67
80.99
77.48
77.16 Chloroform-d
76.84
45.51
33.96
31.33
28.87
28.70
28.66
27.81
24.57
24.03
22.61
19.08
14.15
HO
O
O
72g
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

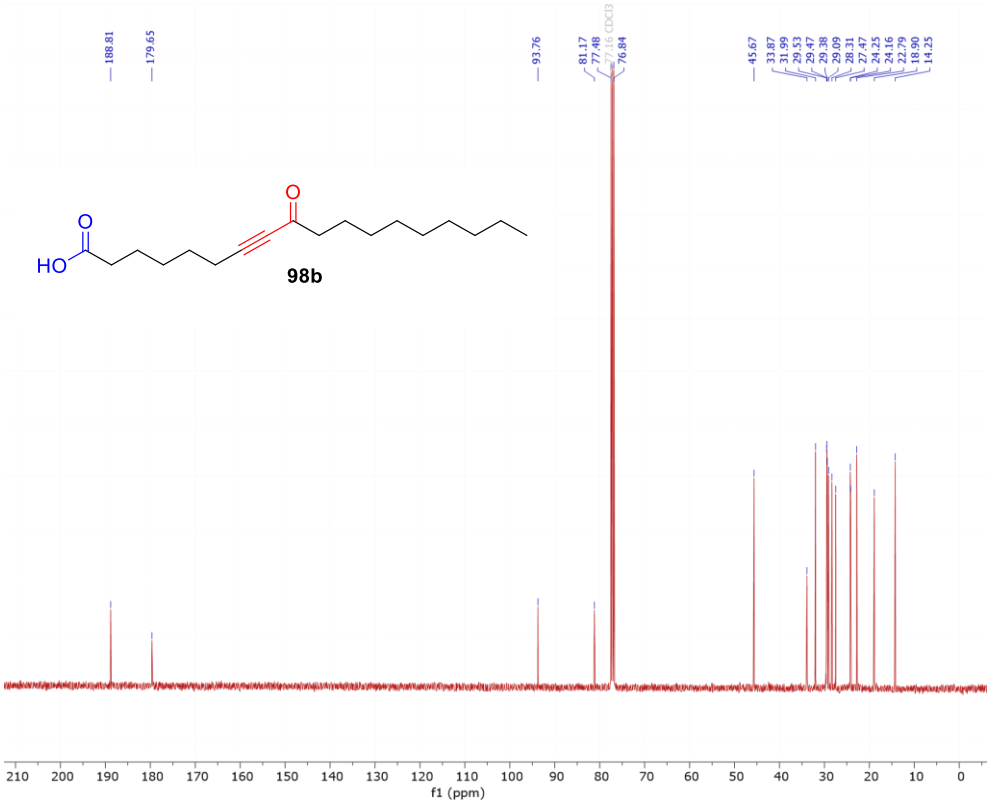

7.26 Chloroform-d
2.56
2.54
2.52
2.38
2.37
2.36
2.35
2.34
2.33
1.66
1.39
1.37
1.30
1.28
0.88
0.86
HO
O
O
72h
2.00
4.00
6.33
12.20
3.19
f1 (ppm)

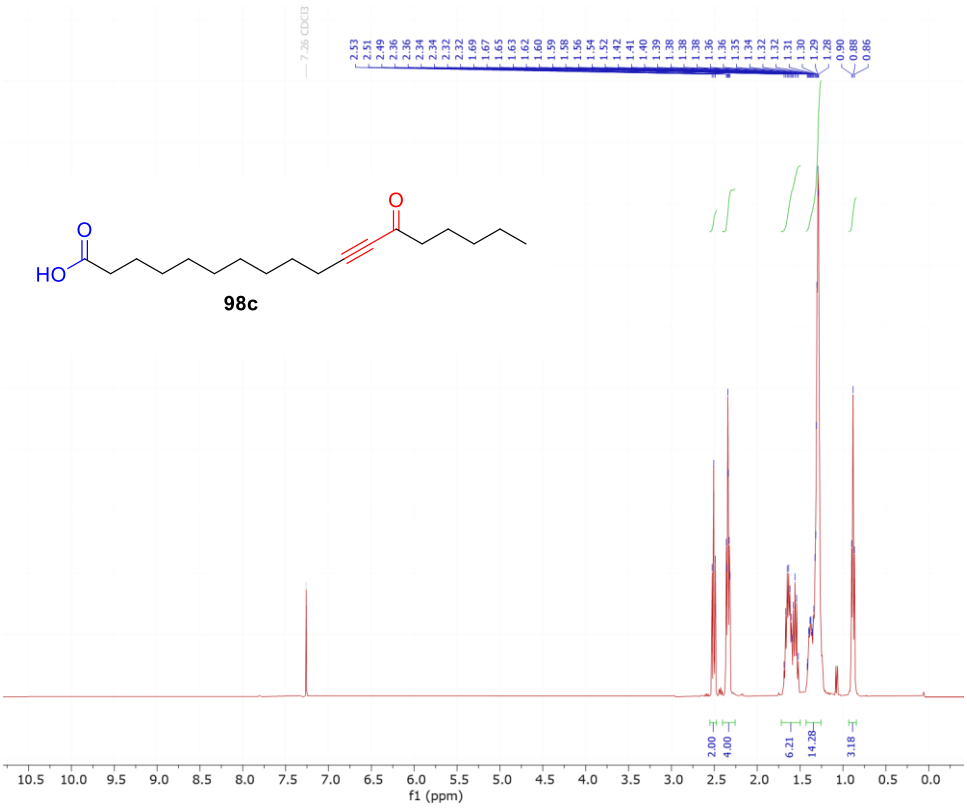

188.28
179.22
94.76
80.97
77.48
77.16 Chloroform-d
76.84
45.34
33.80
31.93
29.24
29.12
29.01
28.47
27.85
24.50
23.83
22.77
19.09
14.23
HO
O
O
72h
f1 (ppm)

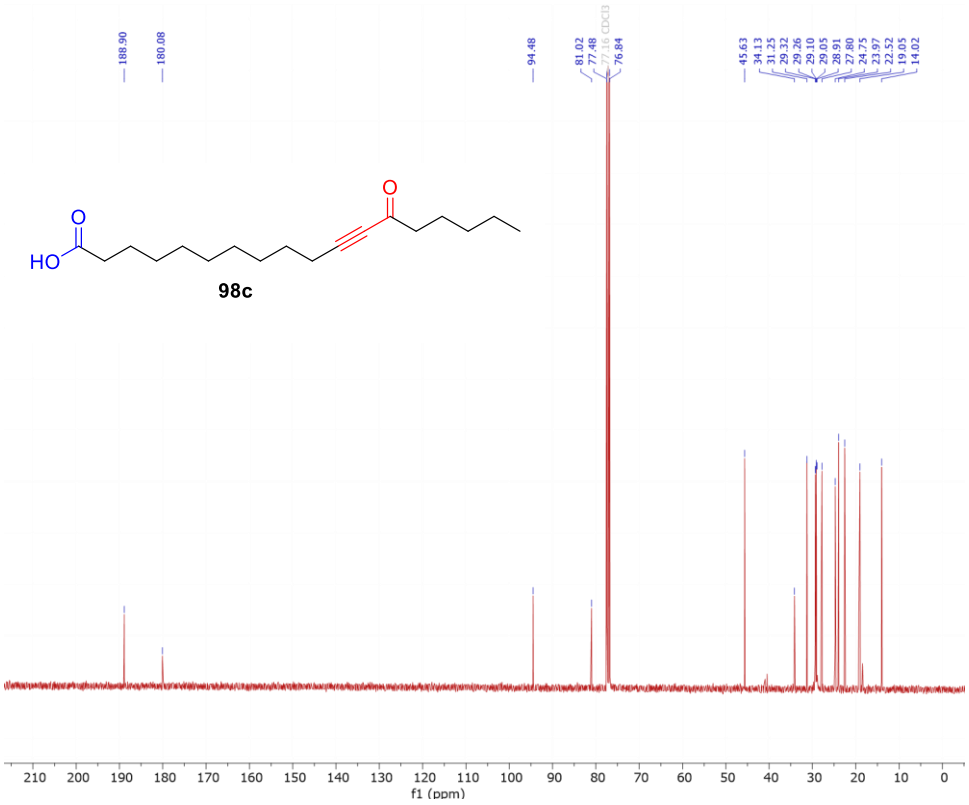

7.26 Chloroform-d
2.62
2.53
2.52
2.50
2.37
2.35
2.34
1.65
1.64
1.62
1.59
1.58
0.89
0.88
0.86
HO
O
O
98a
2.00
4.01
6.08
14.16
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

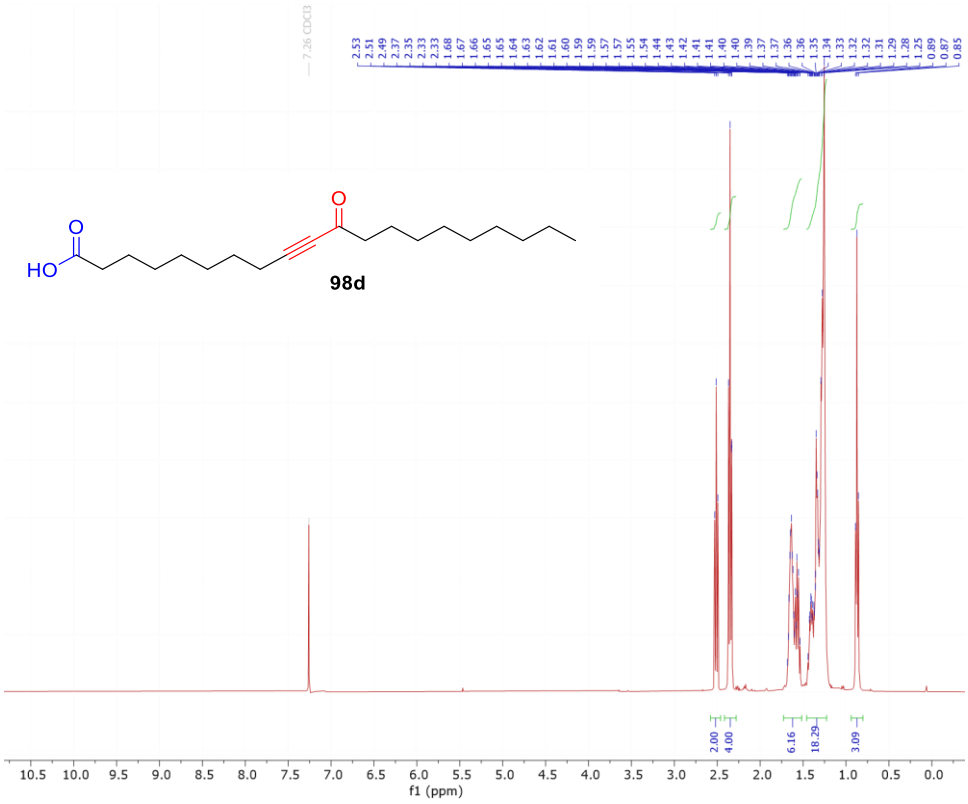

188.86
179.77
94.26
81.09
77.48
77.16 Chloroform-d
76.84
45.68
34.04
31.77
29.13
29.06
28.96
28.78
28.75
27.75
24.68
24.29
21.23
19.04
14.21
HO
O
O
98a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

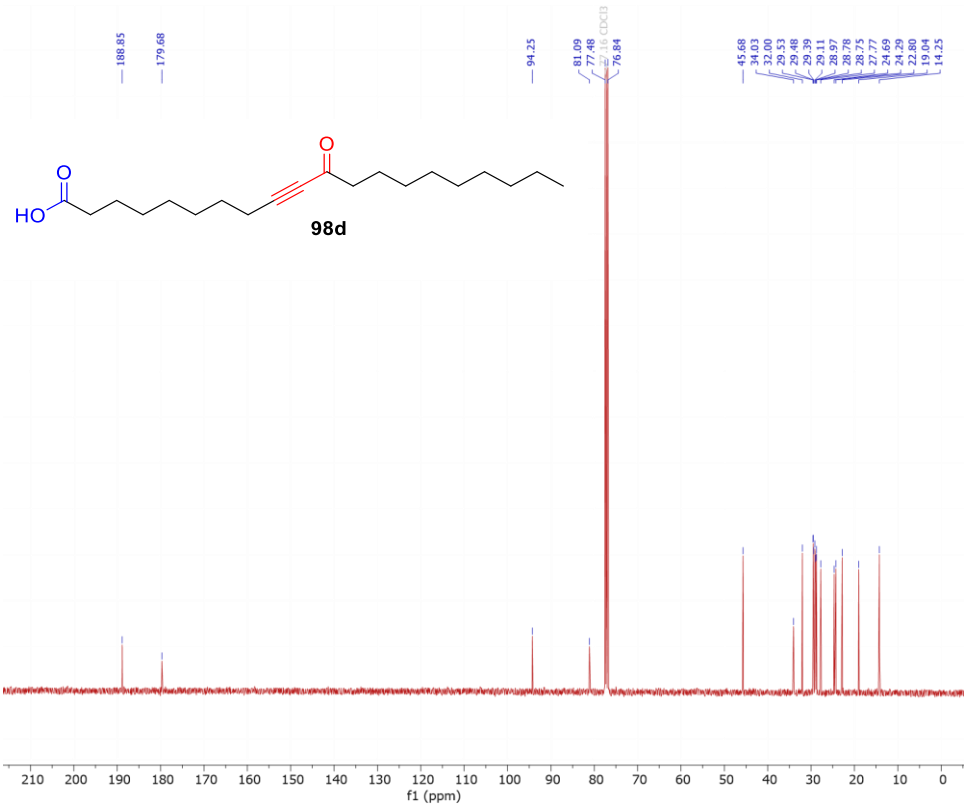

HO
O
O
98b
f1 (ppm)

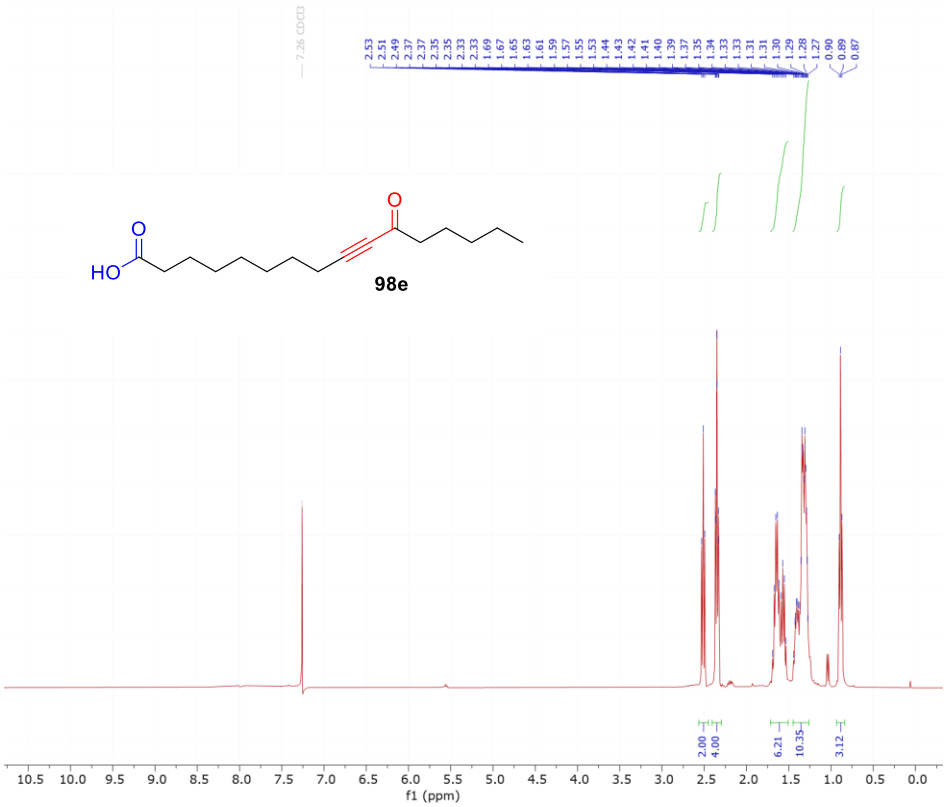

HO
O
O
98b
f1 (ppm)

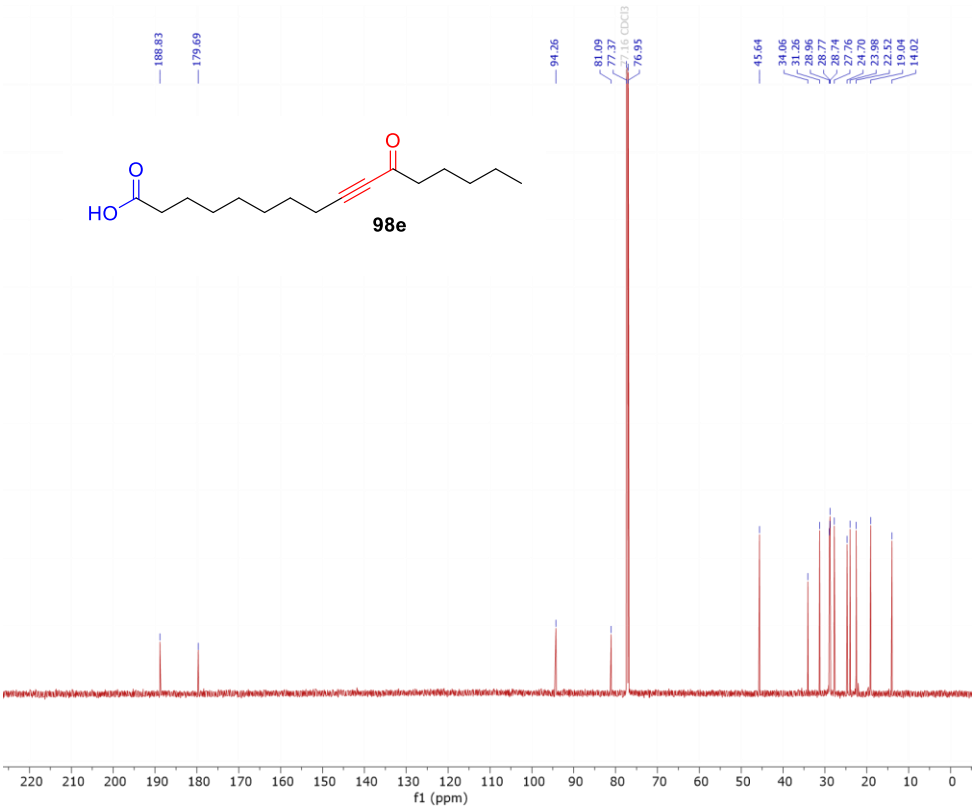

7.26 CDCl3
2.53
2.51
2.49
2.36
2.36
2.34
2.34
2.32
2.32
1.69
1.67
1.65
1.63
1.62
1.60
1.59
1.58
1.56
1.54
1.52
1.42
1.41
1.40
1.39
1.38
1.38
1.38
1.36
1.36
1.35
1.34
1.32
1.31
1.30
1.29
1.28
0.90
0.88
0.86
O
HO
O
98c
2.00
4.00
6.21
14.28
3.18
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

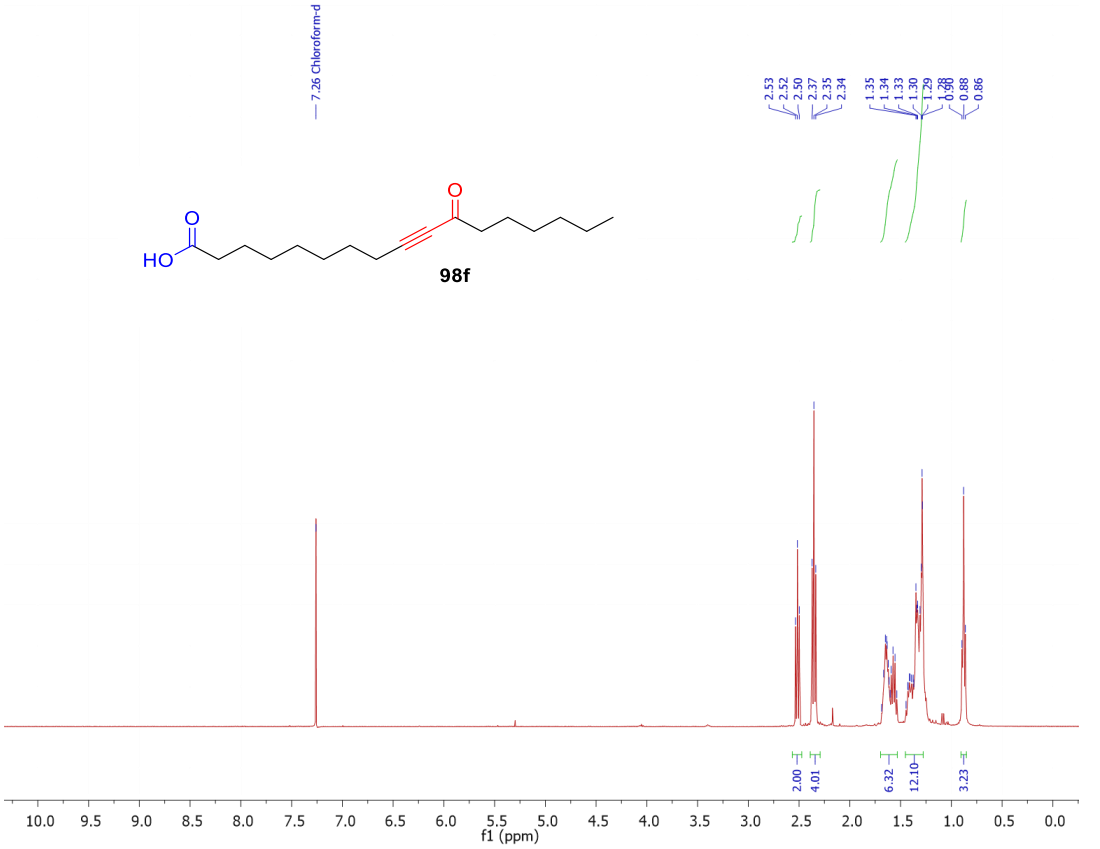

188.90
180.08
94.48
81.02
77.48
77.16 CDCl3
76.84
45.63
34.13
31.25
29.32
29.26
29.10
29.05
28.91
27.80
24.75
23.97
22.52
19.05
14.02
O
HO
O
98c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

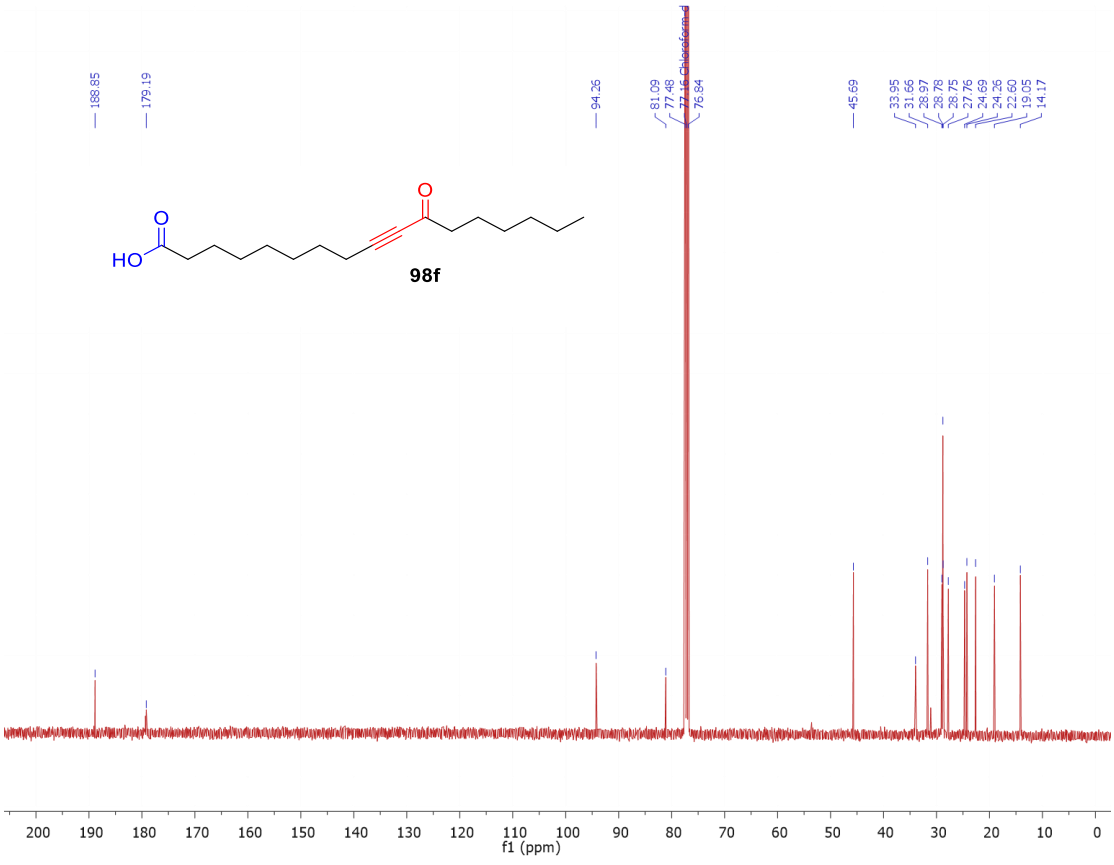

HO
O
O
98d
f1 (ppm)

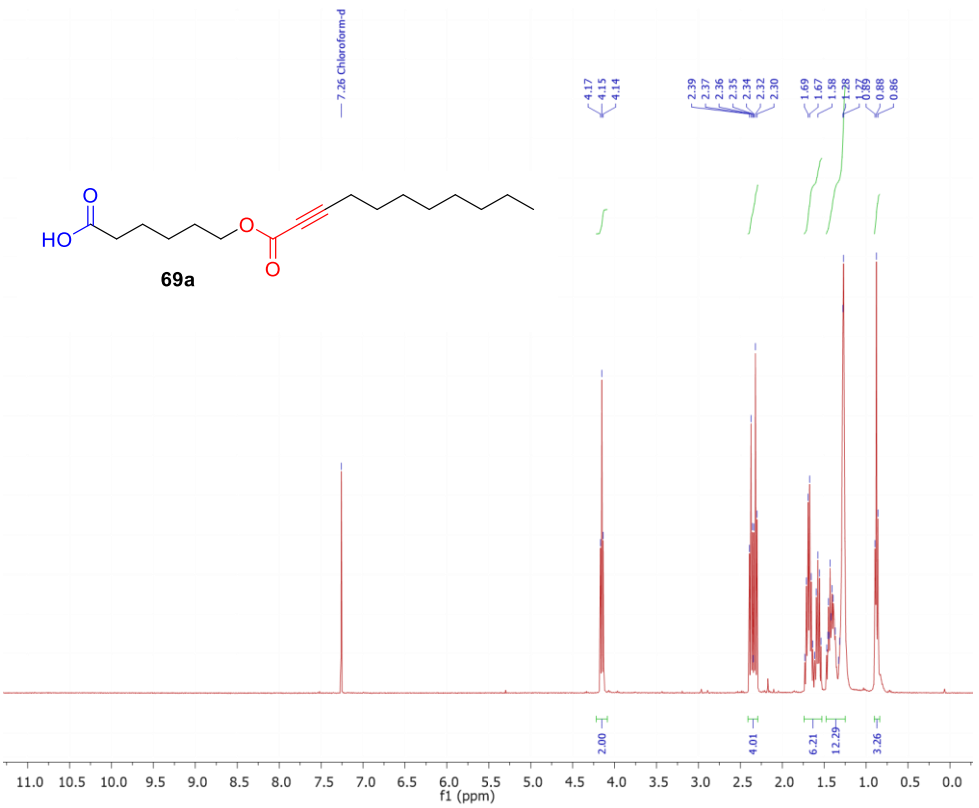

HO
O
O
98d
f1 (ppm)

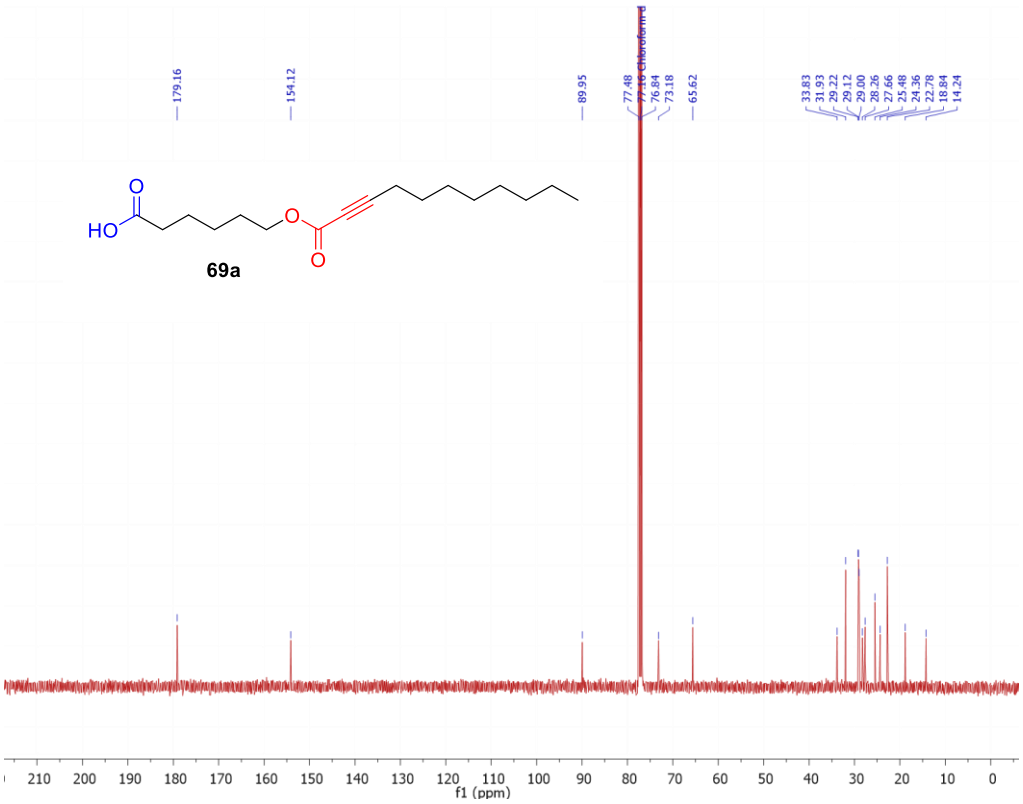

7.26 CDCl3
2.53
2.51
2.49
2.37
2.37
2.35
2.35
2.33
2.33
1.69
1.67
1.65
1.63
1.61
1.59
1.57
1.55
1.53
1.44
1.43
1.42
1.41
1.40
1.39
1.37
1.35
1.34
1.33
1.33
1.31
1.31
1.30
1.29
1.28
1.27
0.90
0.89
0.87
O
HO
O
98e
2.00
4.00
6.21
10.35
3.12
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

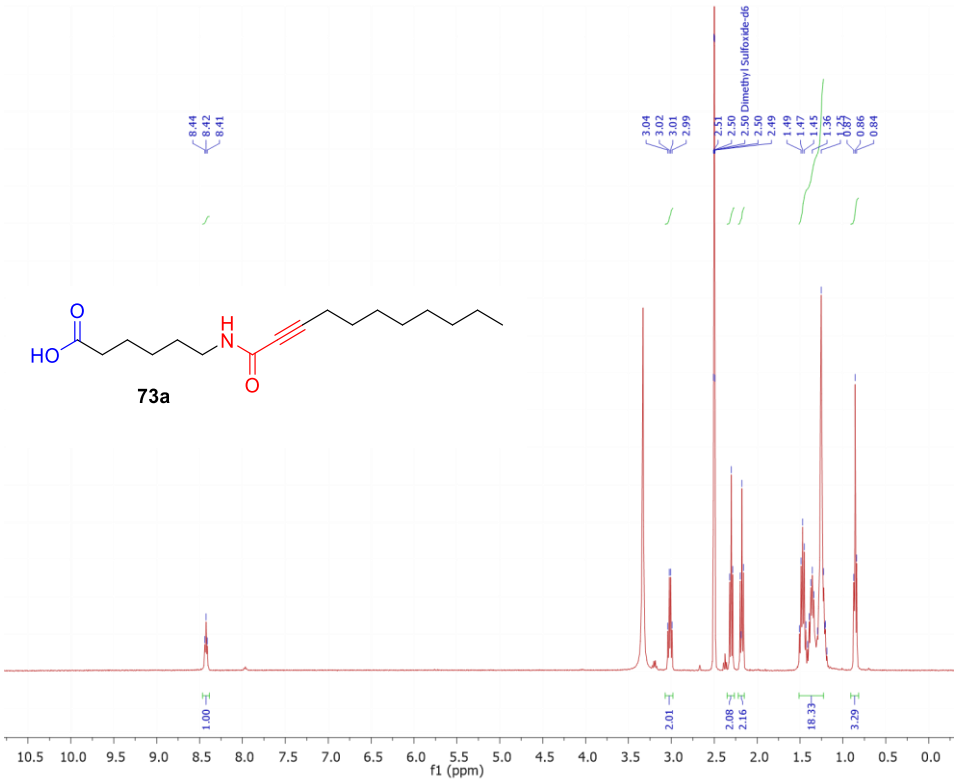

188.83
179.69
94.26
81.09
77.37
77.16 CDCl3
76.95
45.64
34.06
31.26
28.96
28.77
28.74
27.76
24.70
23.98
22.52
19.04
14.02
O
HO
O
98e
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

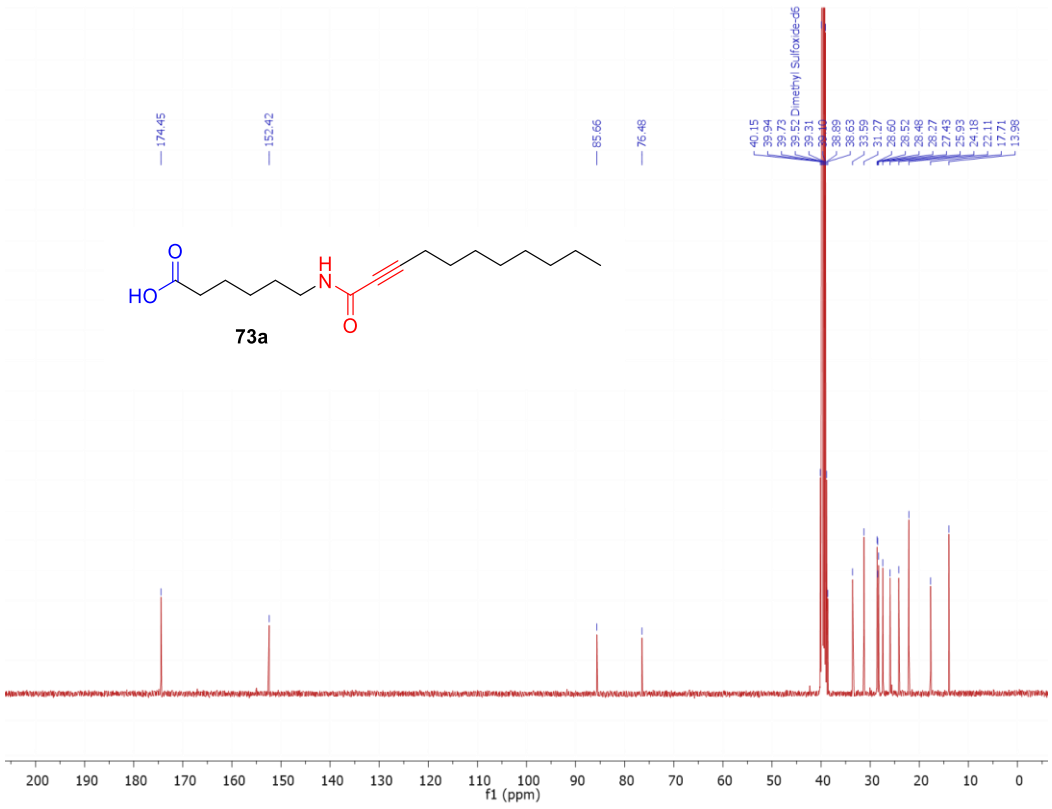

7.26 Chloroform-d
2.53
2.52
2.50
2.37
2.35
2.34
1.35
1.34
1.33
1.30
1.29
0.88
0.86
HO
O
O
98f
2.00
4.01
6.32
12.10
3.23
f1 (ppm)

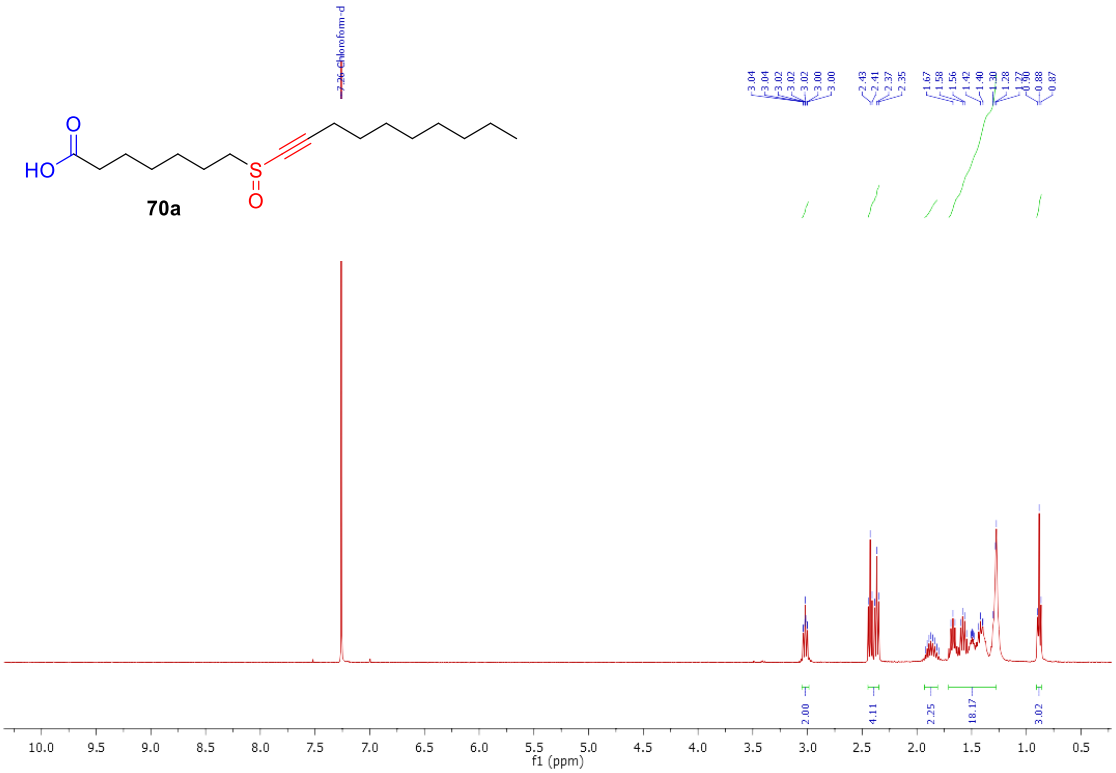

188.85
179.19
94.26
81.09
77.48
77.16 Chloroform-d
76.84
45.69
33.95
31.66
28.97
28.78
28.75
27.76
24.69
24.25
22.60
19.05
14.17
HO
O
O
98f
f1 (ppm)

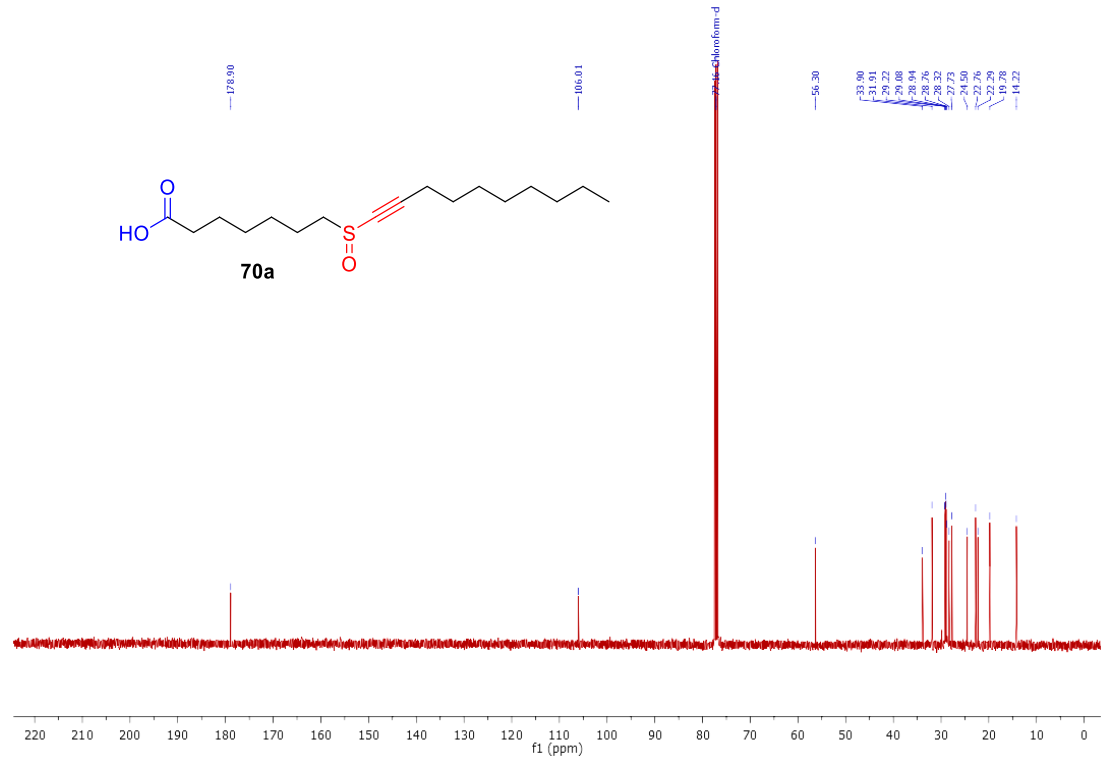

7.26 Chloroform-d
4.17
4.15
4.14
2.39
2.37
2.36
2.35
2.34
2.32
2.30
1.69
1.67
1.58
1.28
0.89
0.88
0.86
HO
O
O
O
69a
2.00
4.01
6.21
12.29
3.26
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

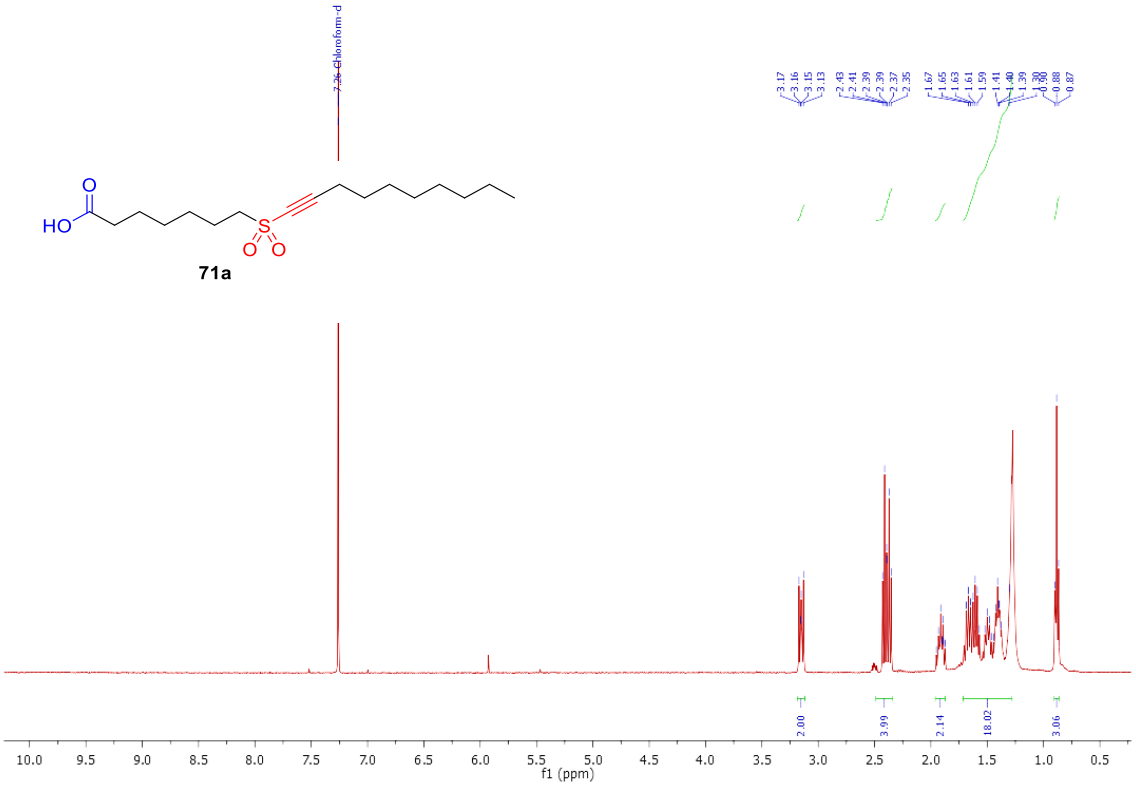

179.16
154.12
89.95
77.48
77.16 Chloroform-d
76.84
73.18
65.62
33.83
31.93
29.22
29.12
29.00
28.26
27.66
25.48
24.36
22.78
18.84
14.24
HO
O
O
O
69a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

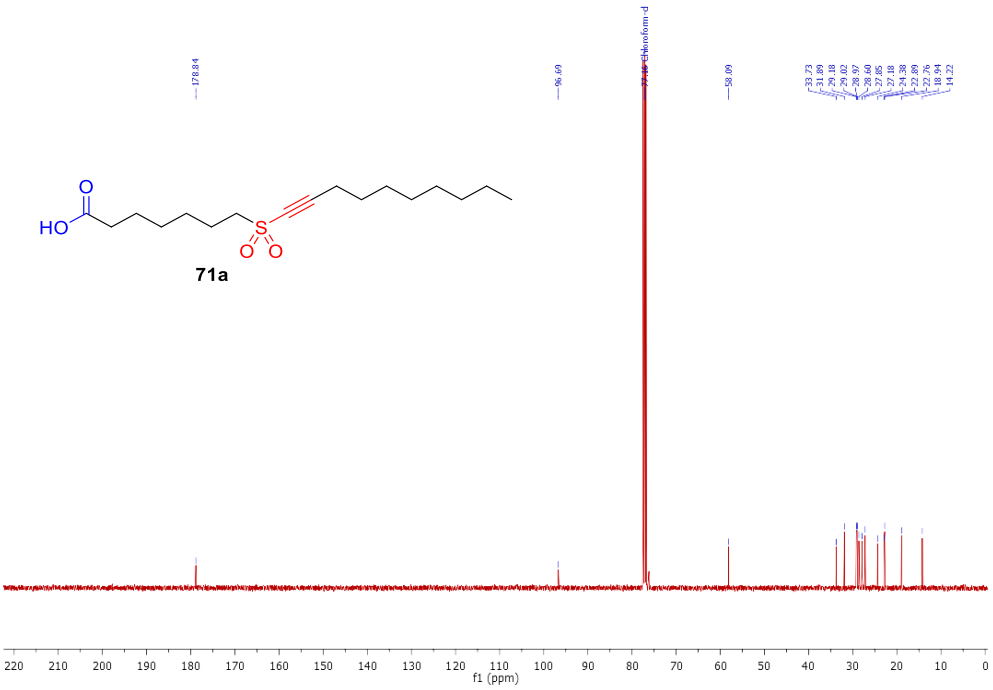

8.44
8.42
8.41
3.04
3.02
3.01
2.99
2.51
2.50
2.50 Dimethyl Sulfoxide-d6
2.50
2.49
1.49
1.47
1.45
1.36
0.87
0.86
0.84
HO
O
H
N
O
73a
1.00
2.01
2.08
2.16
18.33
3.29
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

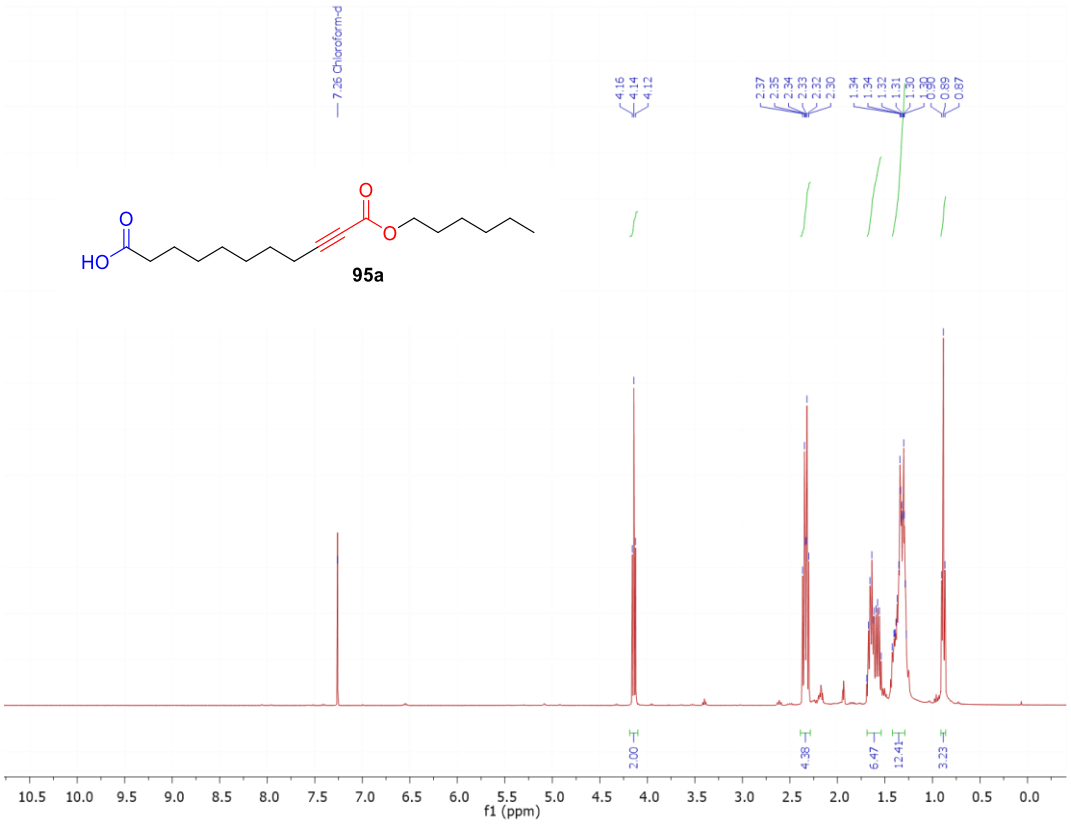

174.45
152.42
85.66
76.48
40.15
39.94
39.73
39.52 Dimethyl Sulfoxide-d6
39.31
38.89
38.63
33.59
31.27
28.60
28.52
28.48
28.27
27.43
25.93
24.18
22.11
17.71
13.98
HO
O
H
N
O
73a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

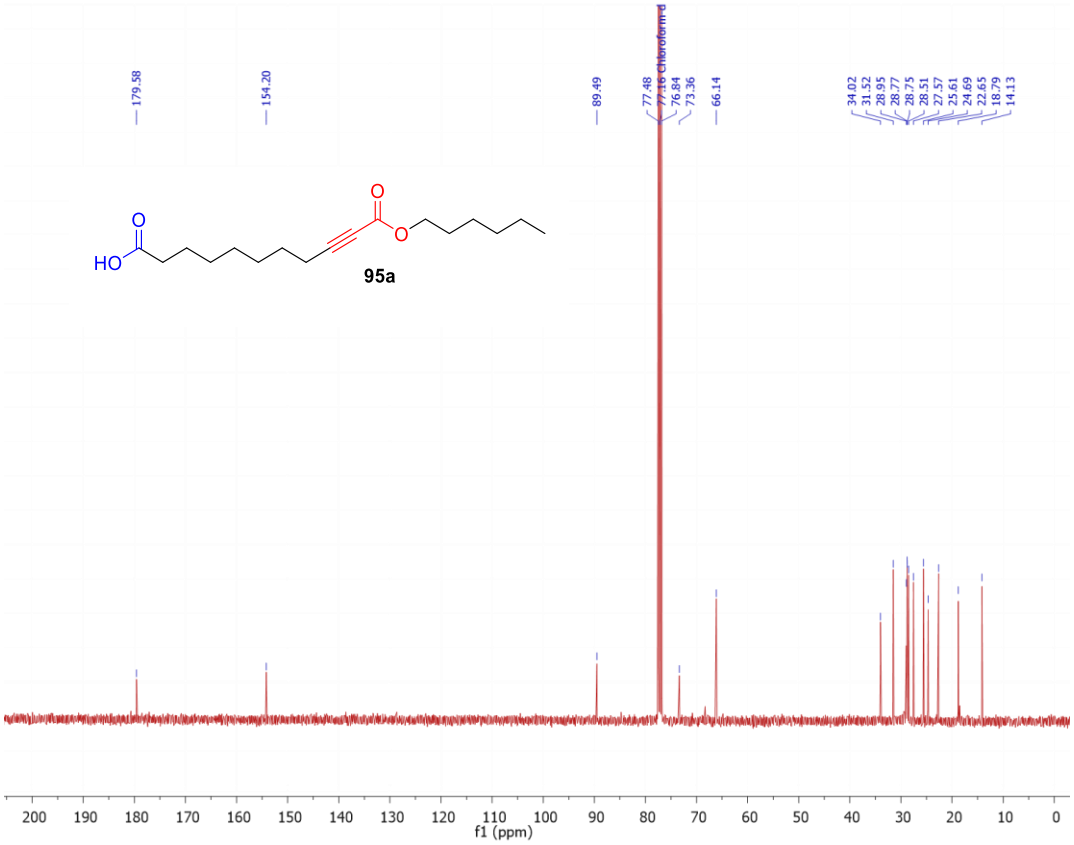

HO
O
S
O
70a
f1 (ppm)

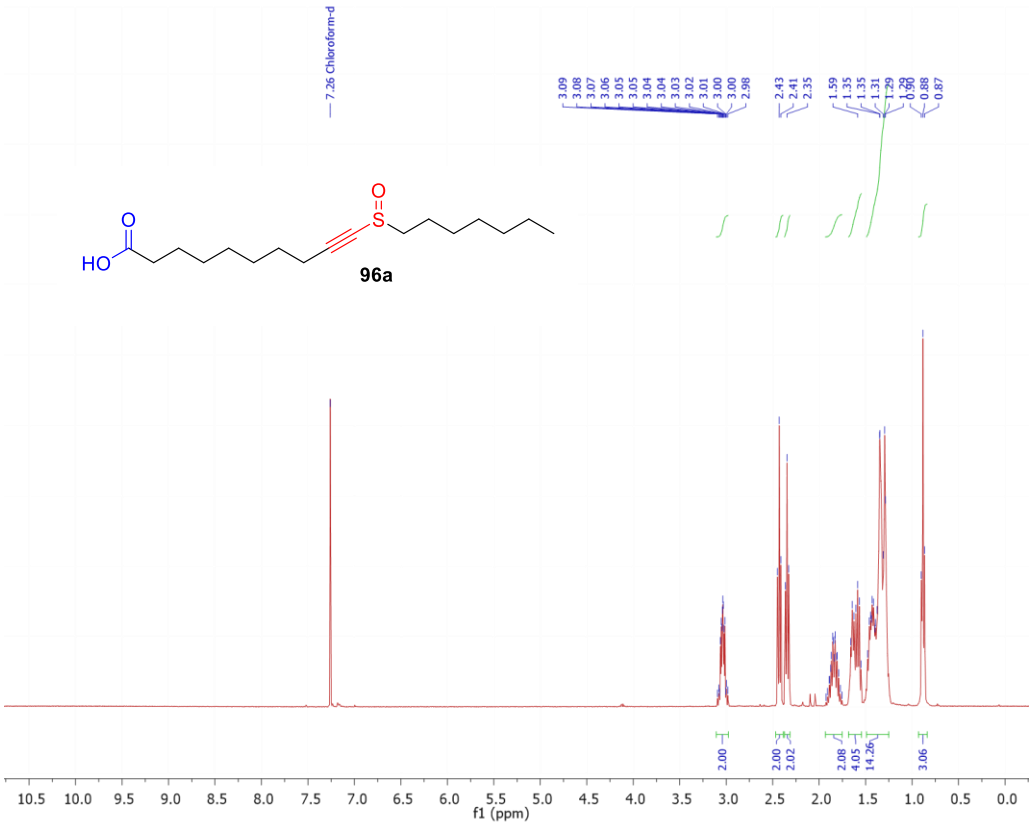

HO
O
S
O
70a
f1 (ppm)

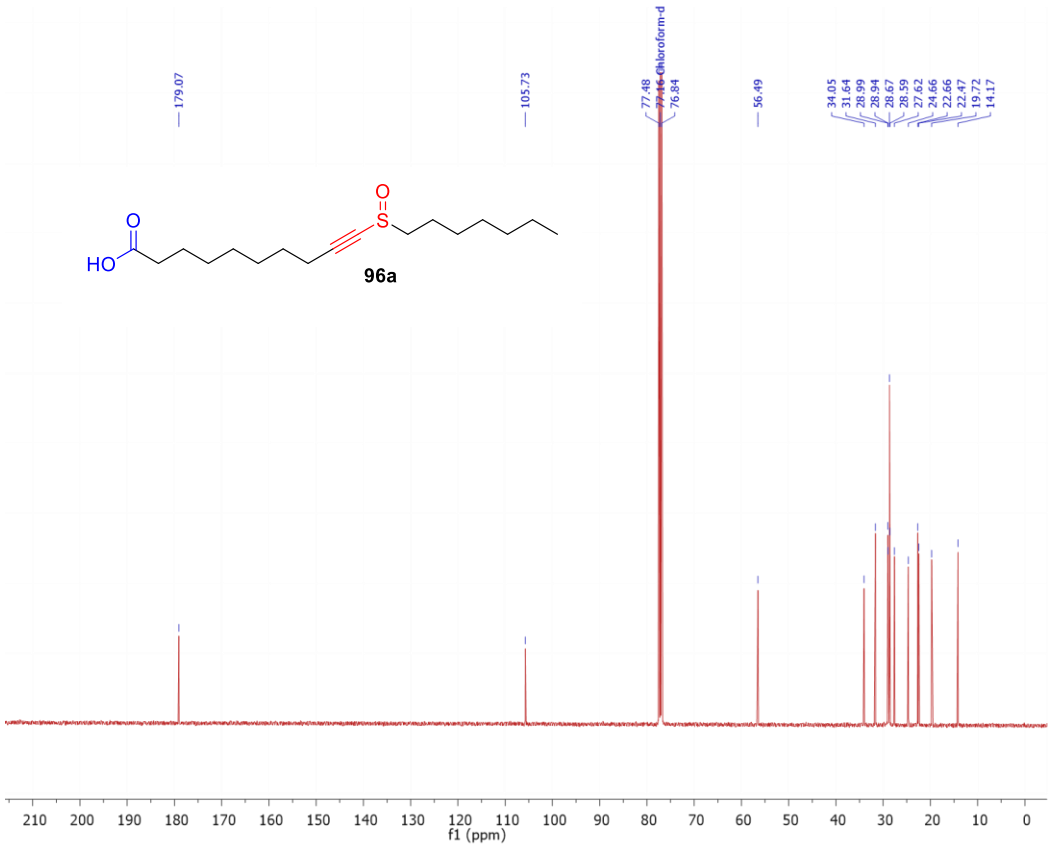

7.26 Chloroform-d
3.17
3.16
3.15
3.13
2.43
2.41
2.39
2.39
2.37
2.35
1.67
1.65
1.63
1.61
1.59
1.41
1.40
1.39
1.30
0.90
0.88
0.87
HO
O
S
O
O
71a
2.00
3.99
2.14
18.02
3.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

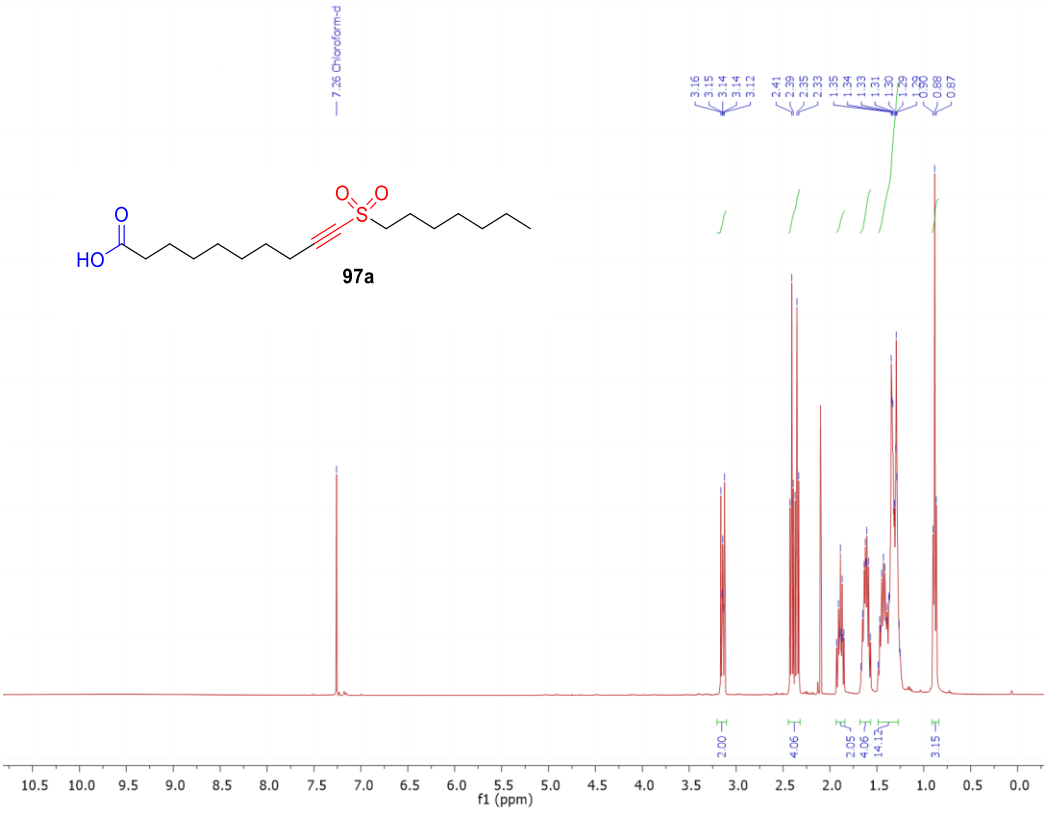

178.84
96.69
77.16 Chloroform-d
58.09
33.73
31.89
29.18
29.02
28.97
28.60
27.85
27.18
24.38
22.89
22.76
18.84
14.22
HO
O
S
O
O
71a
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

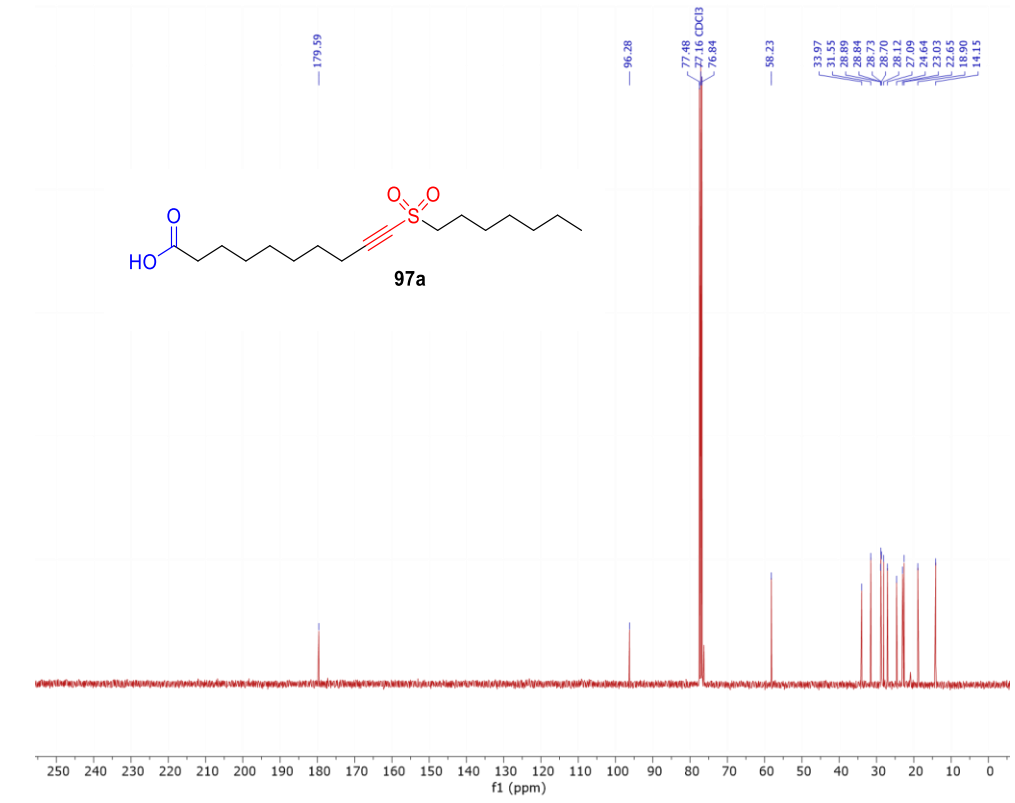

7.26 Chloroform-d
4.16
4.14
4.12
2.37
2.35
2.34
2.33
2.32
2.30
1.34
1.34
1.32
1.31
1.30
0.90
0.89
0.87
HO
O
O
O
95a
2.00
4.38
6.47
12.41
3.23
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

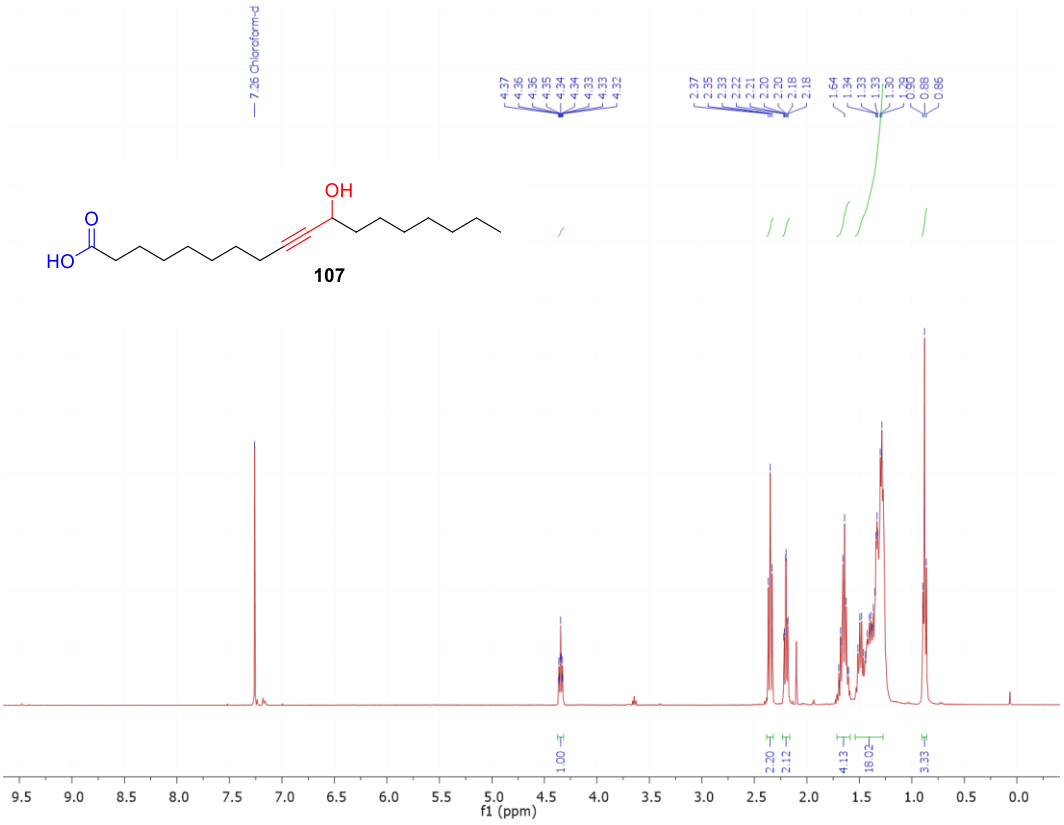

179.58
154.20
89.49
77.48
77.16 Chloroform-d
76.84
73.36
66.14
34.02
31.52
28.95
28.77
28.75
28.51
27.57
25.61
24.69
22.65
18.79
14.13
HO
O
O
O
95a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

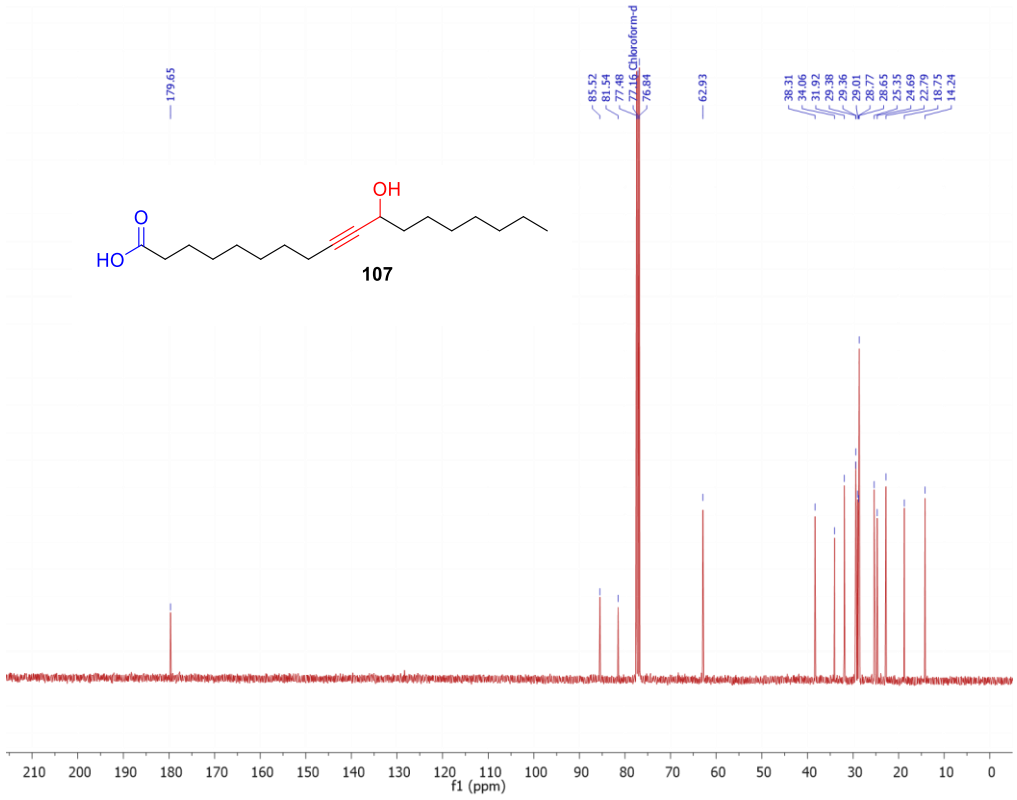

7.26 Chloroform-d
3.09
3.08
3.07
3.06
3.05
3.05
3.04
3.04
3.03
3.02
3.01
3.00
3.00
2.98
2.43
2.41
2.35
1.59
1.35
1.35
1.31
1.29
0.90
0.88
0.87
O
HO
O
S
96a
2.00
2.00
2.02
2.08
4.05
14.26
3.06
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

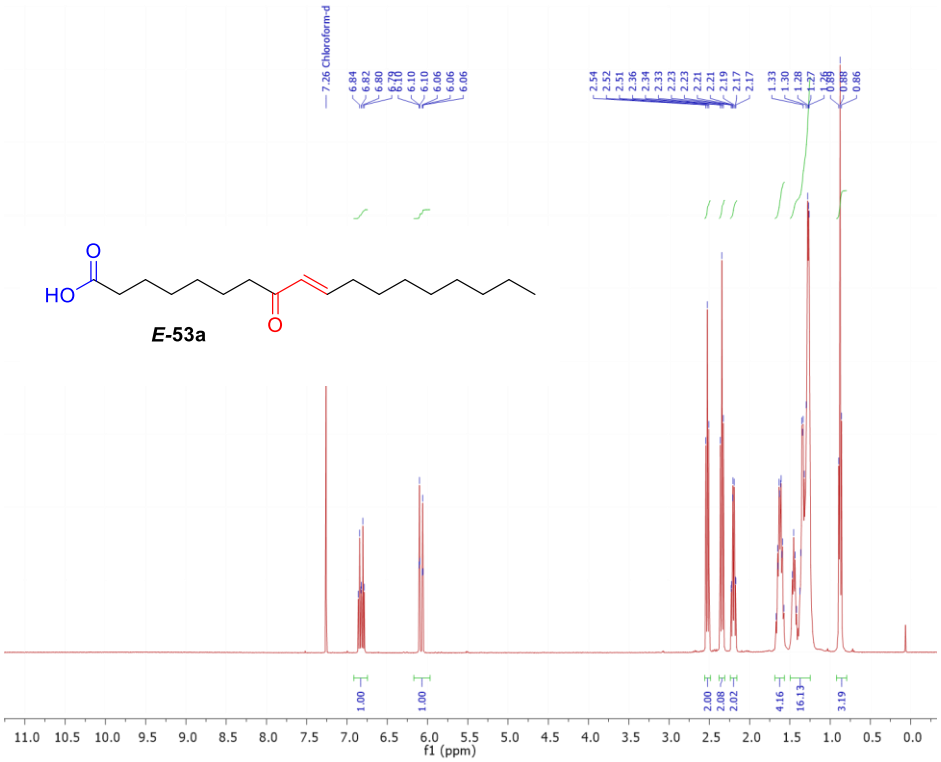

179.07
105.73
77.48
77.16 Chloroform-d
76.84
56.49
34.05
31.64
28.99
28.94
28.67
28.59
27.62
24.66
22.66
22.47
19.72
14.17
O
HO
O
S
96a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

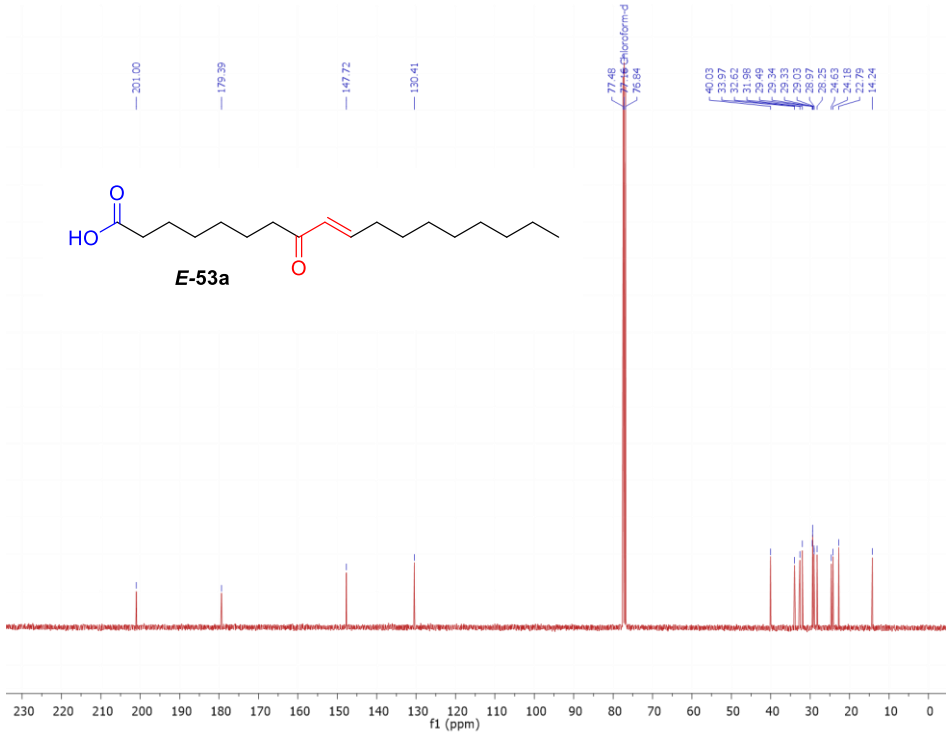

7.26 Chloroform-d
3.16
3.15
3.14
3.14
3.12
2.41
2.39
2.35
2.33
1.35
1.34
1.33
1.31
1.30
1.29
1.29
0.90
0.88
0.87
2.00
4.06
2.05
4.05
14.12
3.15
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
HO
O
O
O
S
97a

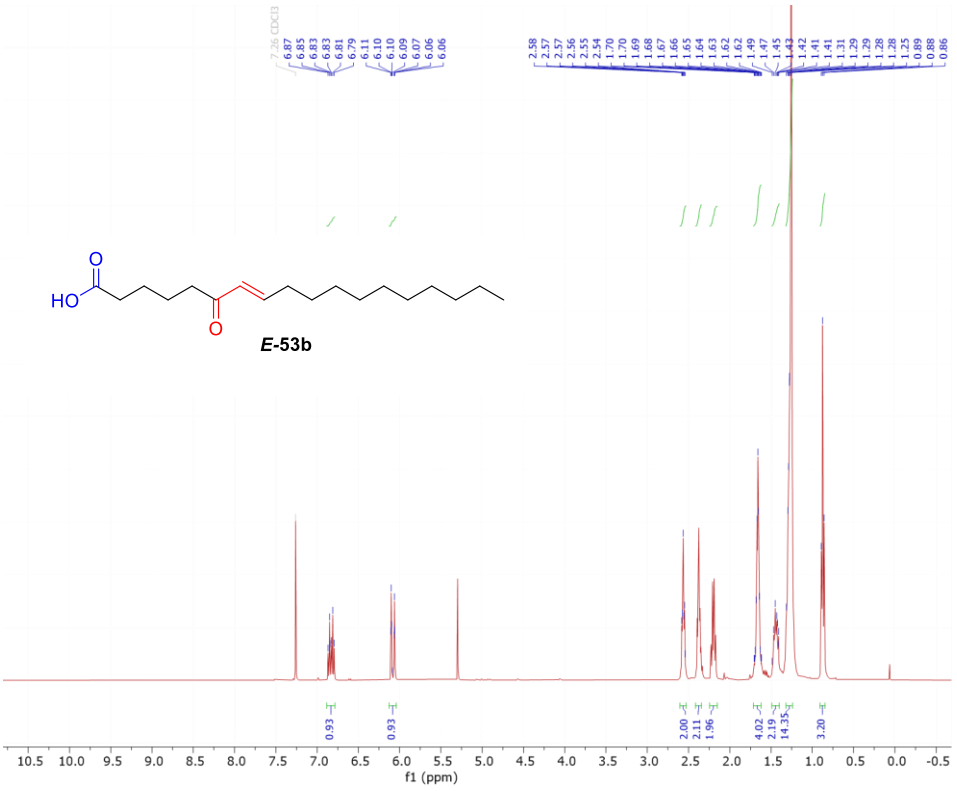

179.59
96.28
77.48
77.16 CDCl3
76.84
58.23
33.97
31.55
28.89
28.84
28.73
28.70
28.12
27.09
24.64
23.03
22.65
18.90
14.15
250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
HO
O
O
O
S
97a

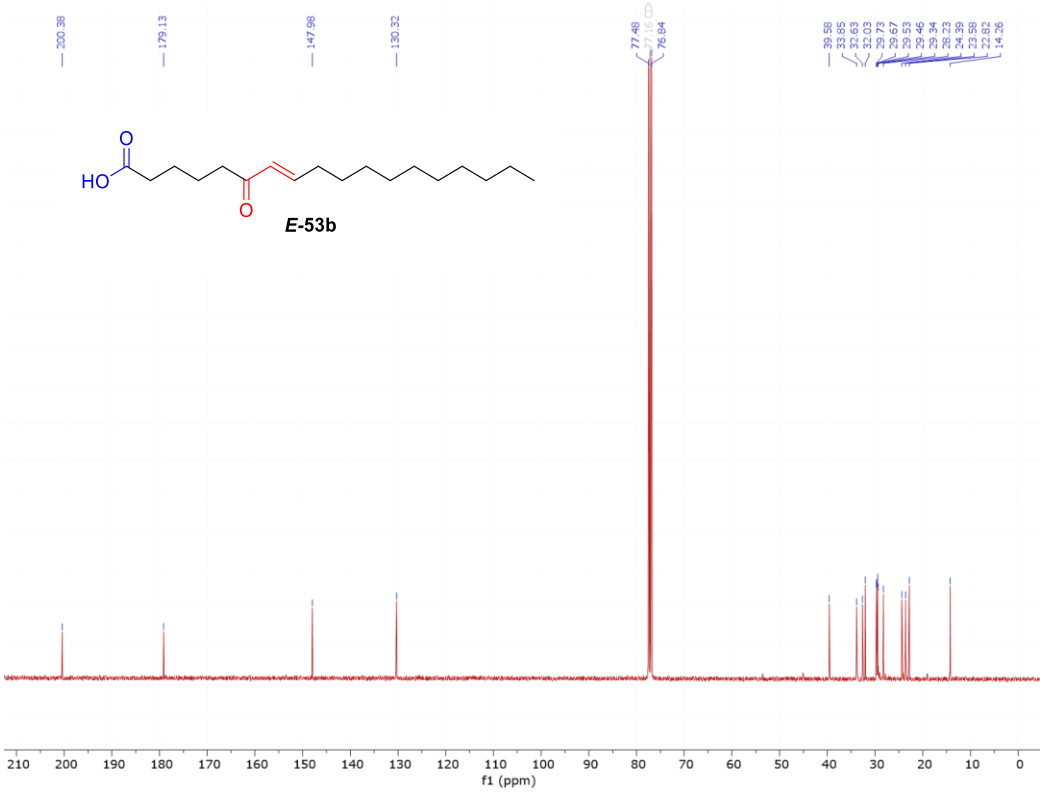

7.26 Chloroform-d
4.37
4.36
4.36
4.35
4.34
4.34
4.33
4.33
4.32
2.37
2.35
2.33
2.22
2.21
2.20
2.20
2.18
2.18
1.64
1.34
1.33
1.33
1.30
0.90
0.88
0.86
OH
O
HO
107
1.00
2.20
2.12
4.13
18.02
3.33
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

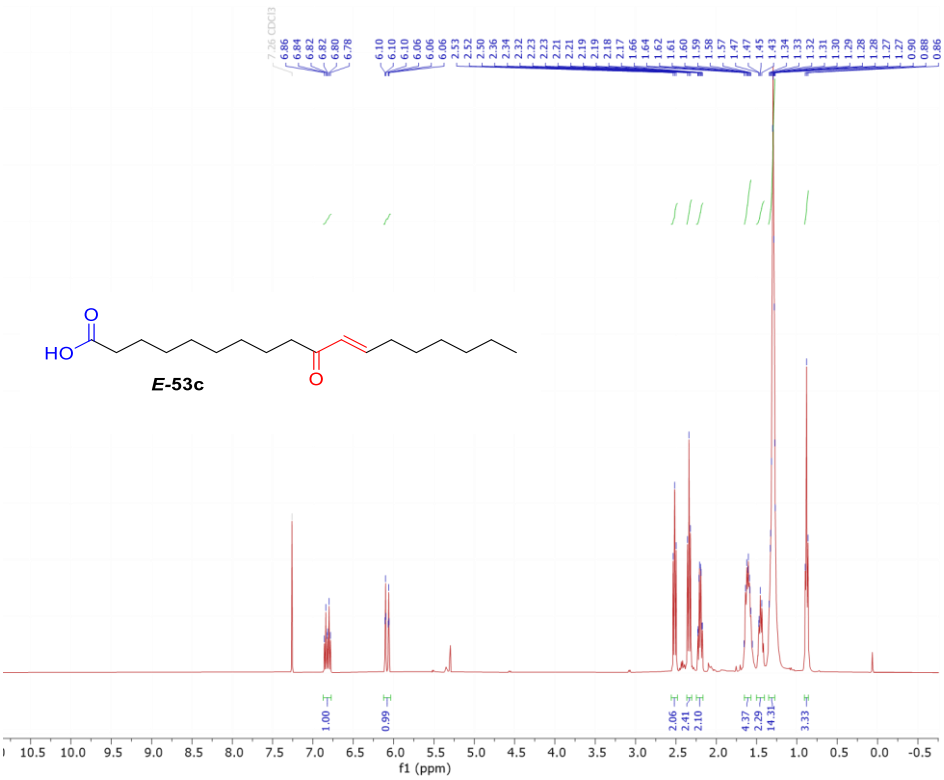

179.65
85.52
81.54
77.48
77.16 Chloroform-d
76.84
62.93
38.31
34.06
31.92
29.38
29.36
29.01
28.77
28.65
25.35
24.69
22.79
18.75
14.24
OH
O
HO
107
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

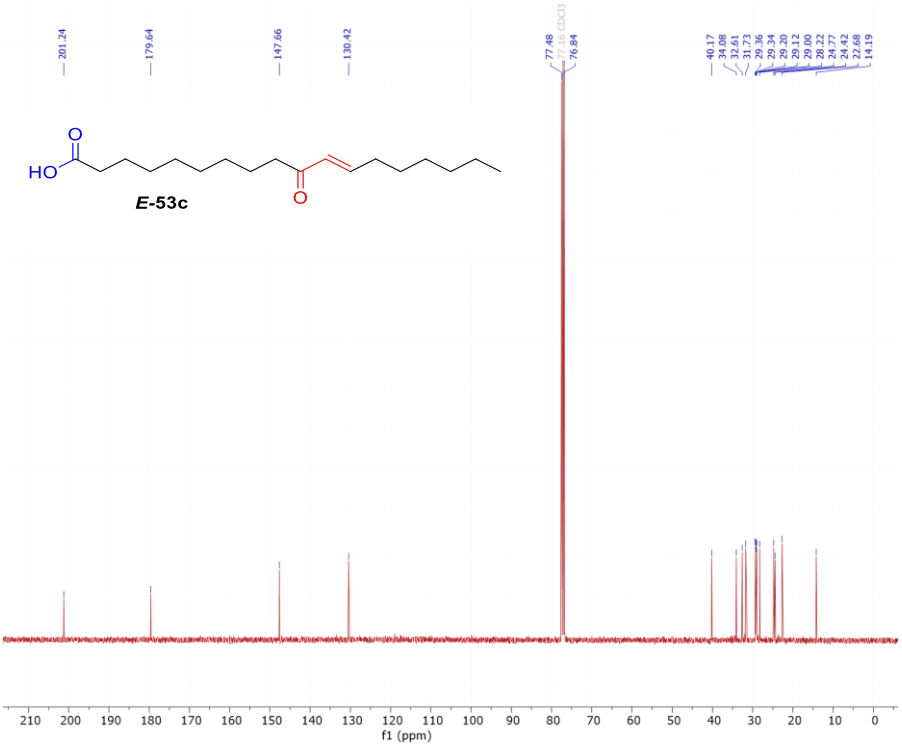

7.26 Chloroform-d
6.84
6.82
6.80
6.78
6.10
6.08
6.06
6.06
6.06
3.54
2.52
2.51
2.36
2.34
2.33
2.23
2.23
2.21
2.21
2.19
2.17
2.17
1.33
1.30
1.28
1.27
0.88
0.86
HO
O
O
E-53a
1.00
1.00
2.00
2.08
2.02
4.16
16.13
3.19
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

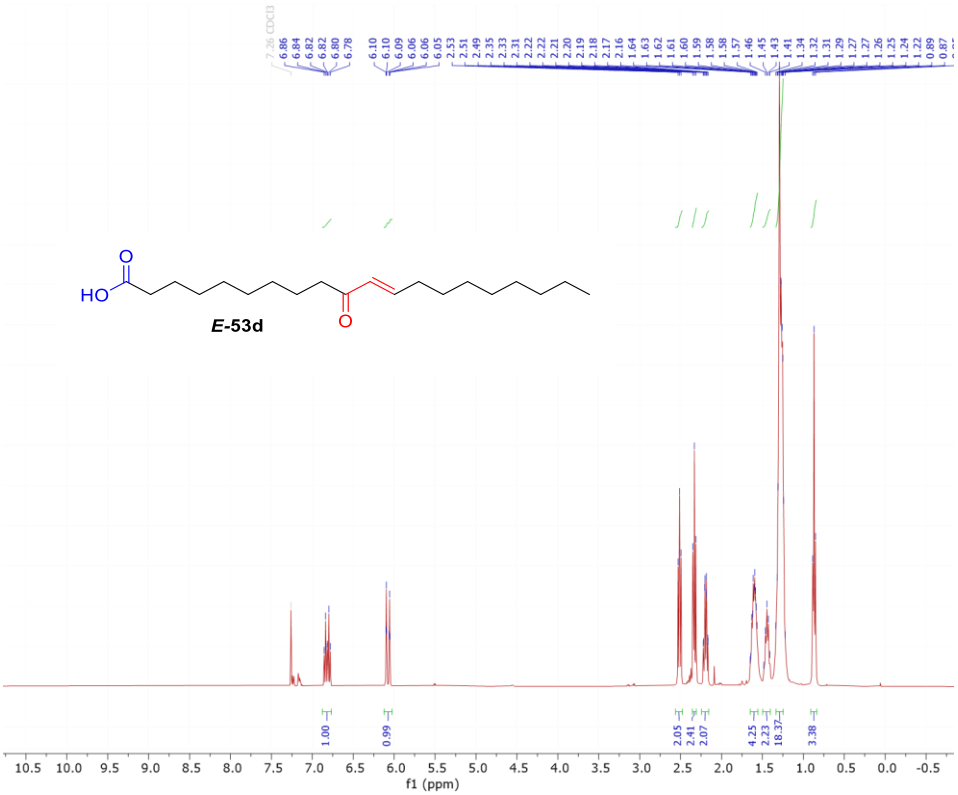

201.00
179.39
147.72
130.41
77.48
77.16 Chloroform-d
76.84
40.03
33.97
32.62
31.88
31.49
29.34
29.33
29.03
28.97
28.25
24.63
24.18
22.79
22.79
14.24
HO
O
O
E-53a
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

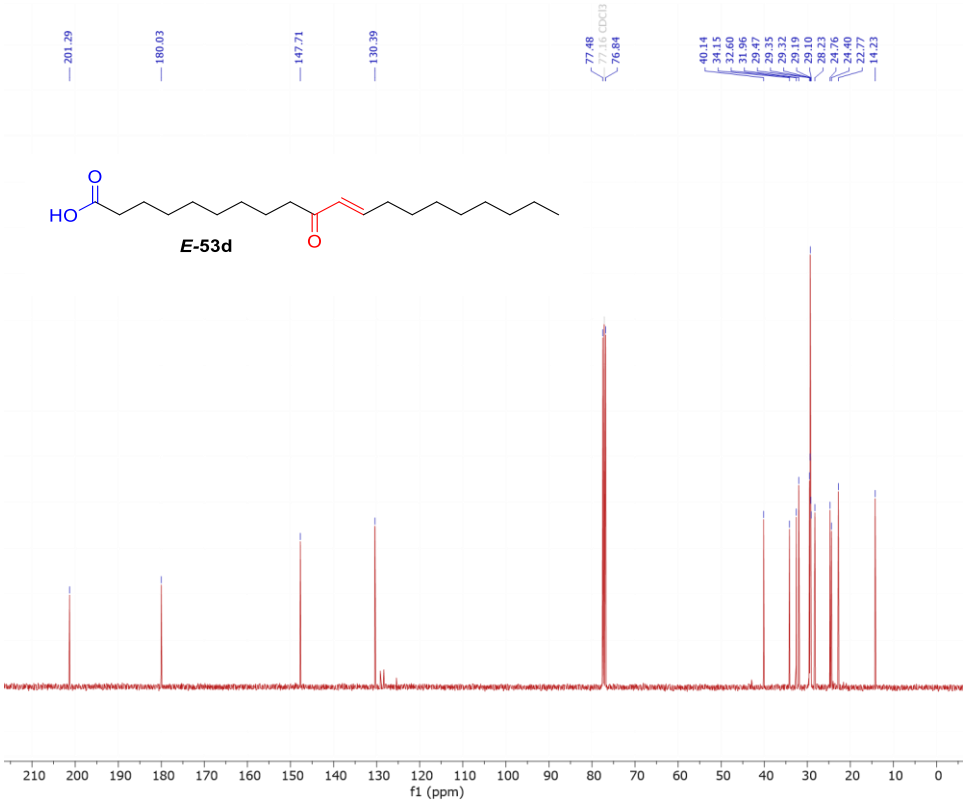

HO
O
O
E-53b
f1 (ppm)

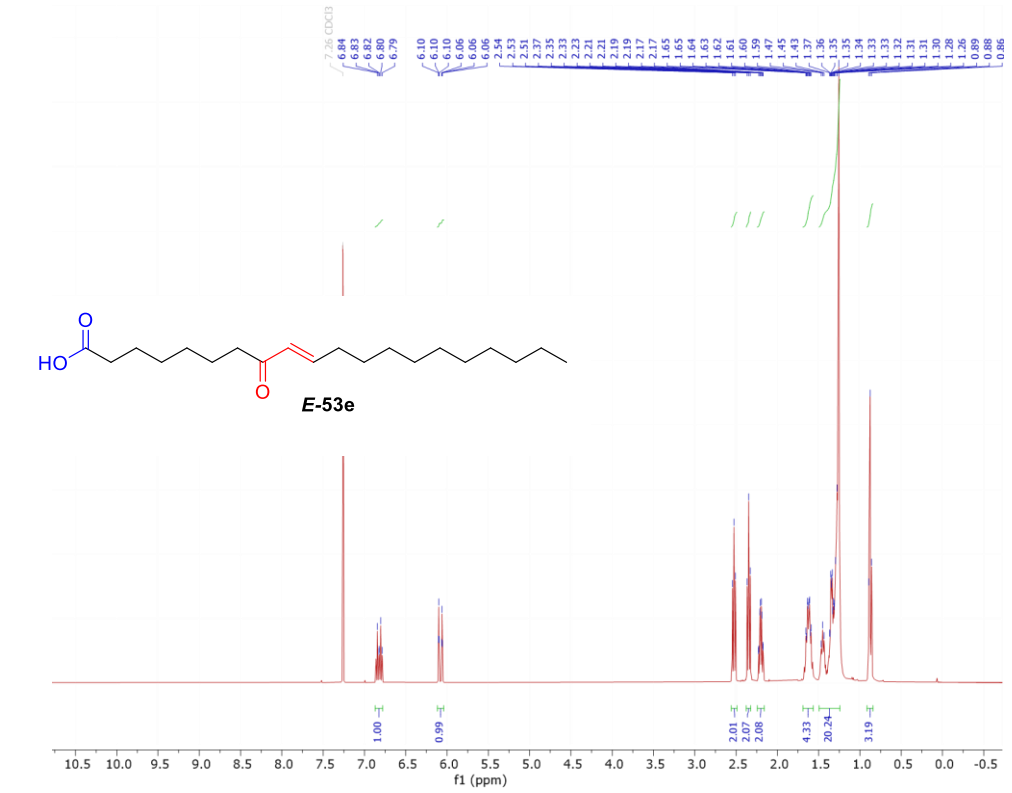

HO
O
O
E-53b
f1 (ppm)

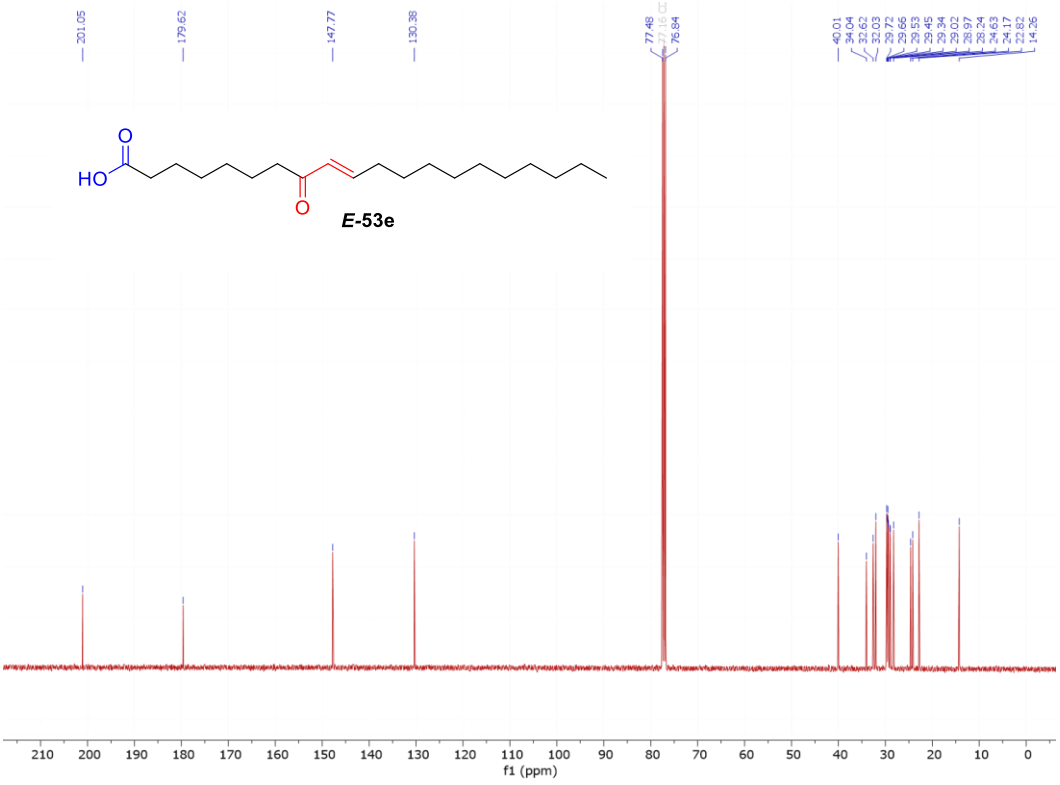

HO
O
O
E-53c
1.00
0.99
2.06
2.41
2.10
4.37
2.29
14.31
3.33
f1 (ppm)

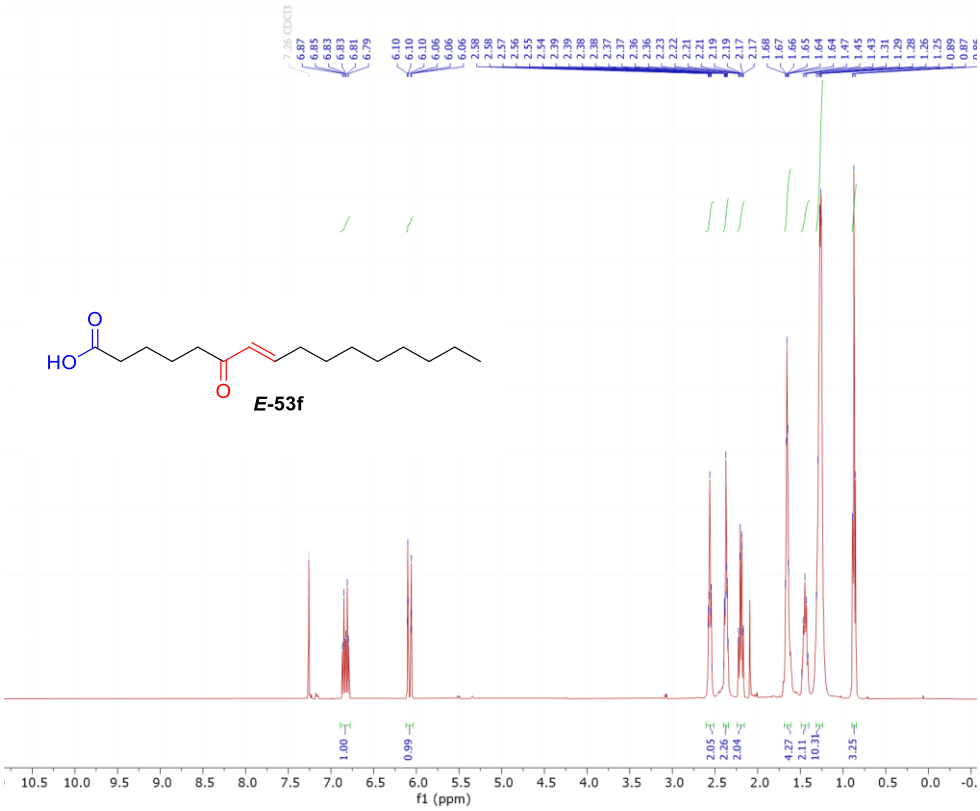

HO
O
O
E-53c
201.24
179.64
147.66
130.42
77.48
76.84
40.17
34.08
32.61
31.73
29.36
29.34
29.20
29.12
29.00
28.22
24.77
24.42
22.68
14.19
f1 (ppm)

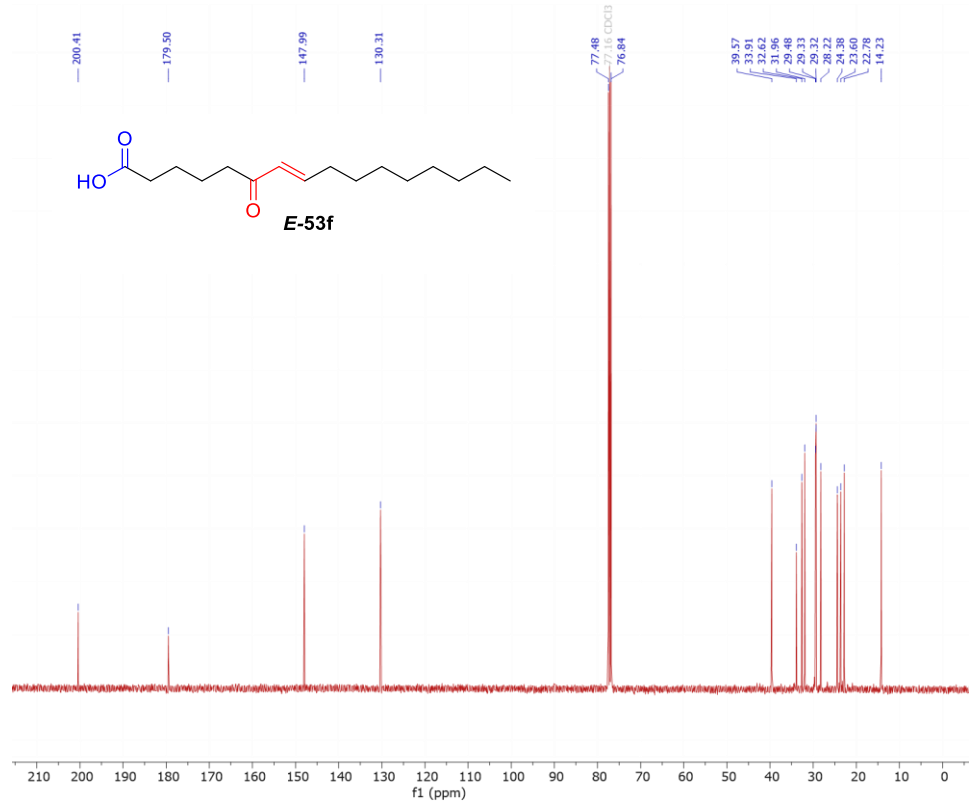

HO
O
O
E-53d
f1 (ppm)

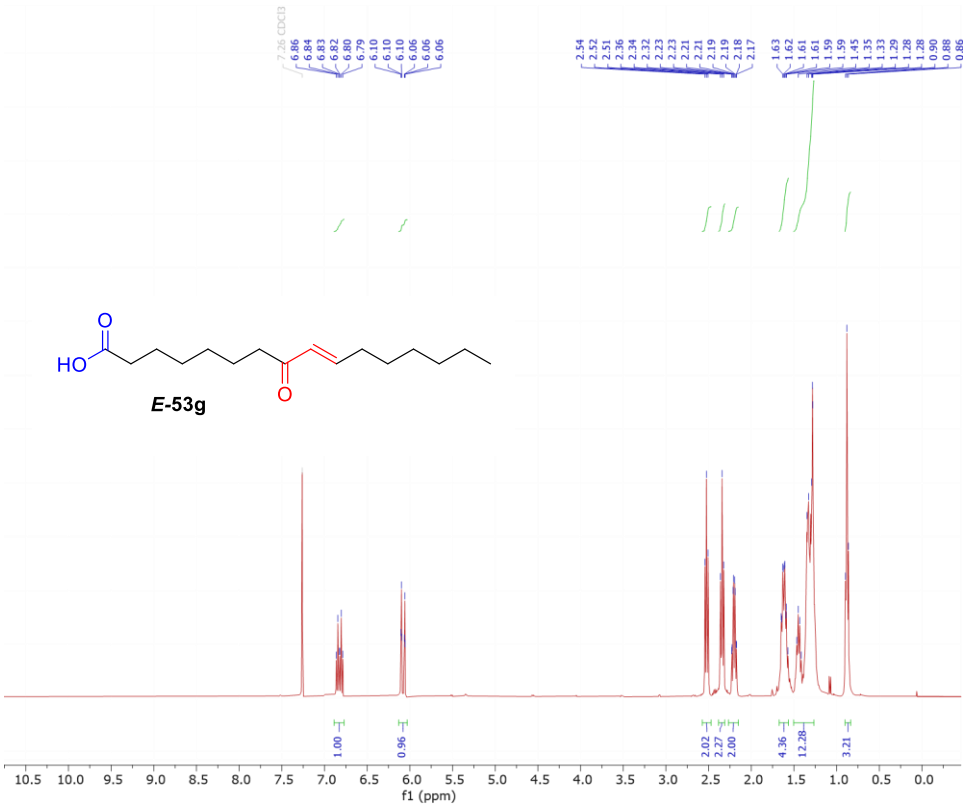

HO
O
O
E-53d
f1 (ppm)

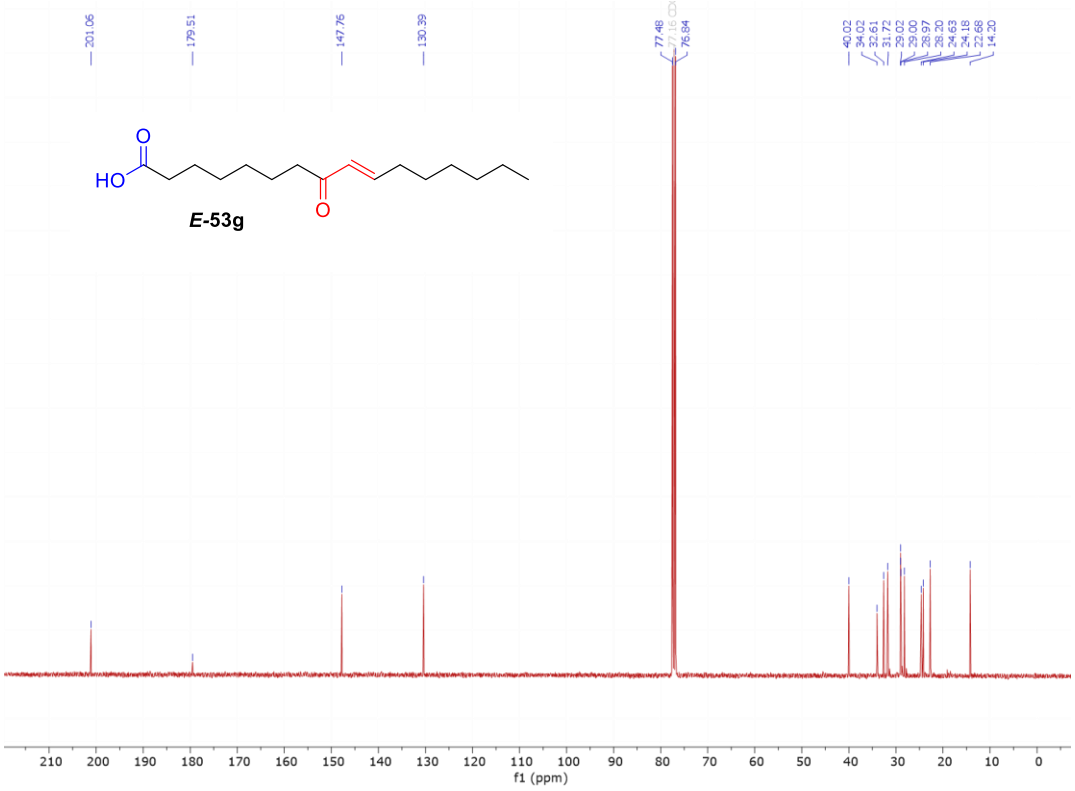

HO
O
O
E-53e
f1 (ppm)

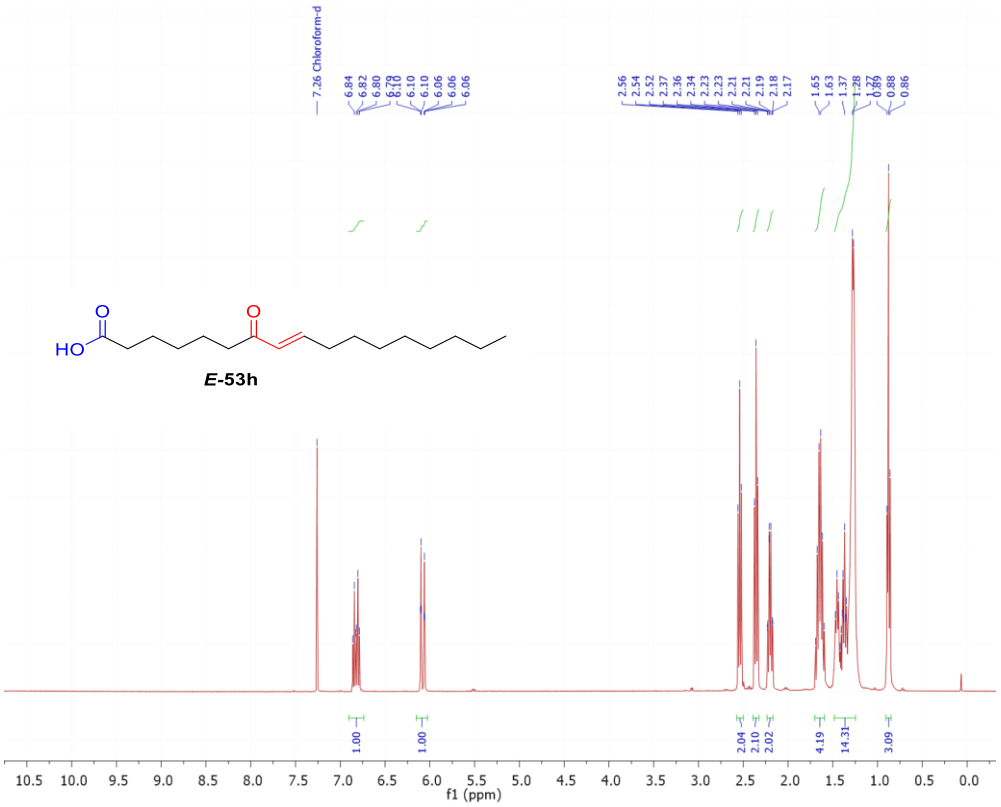

HO
O
O
E-53e
f1 (ppm)

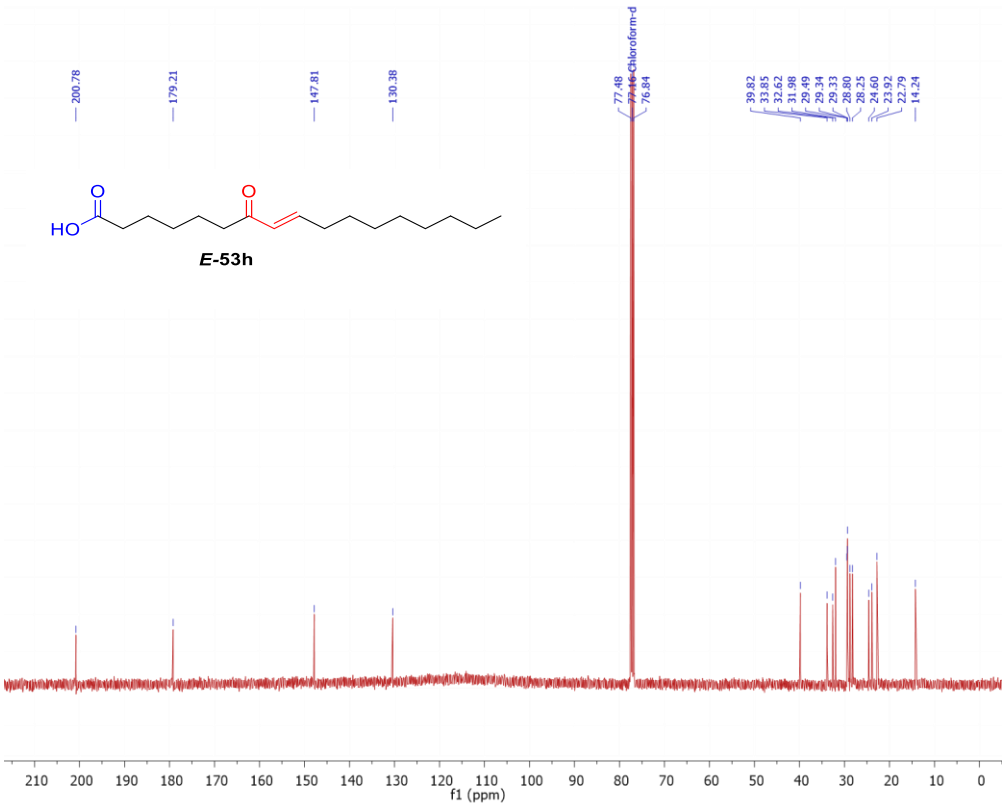

HO
O
O
E-53f
f1 (ppm)

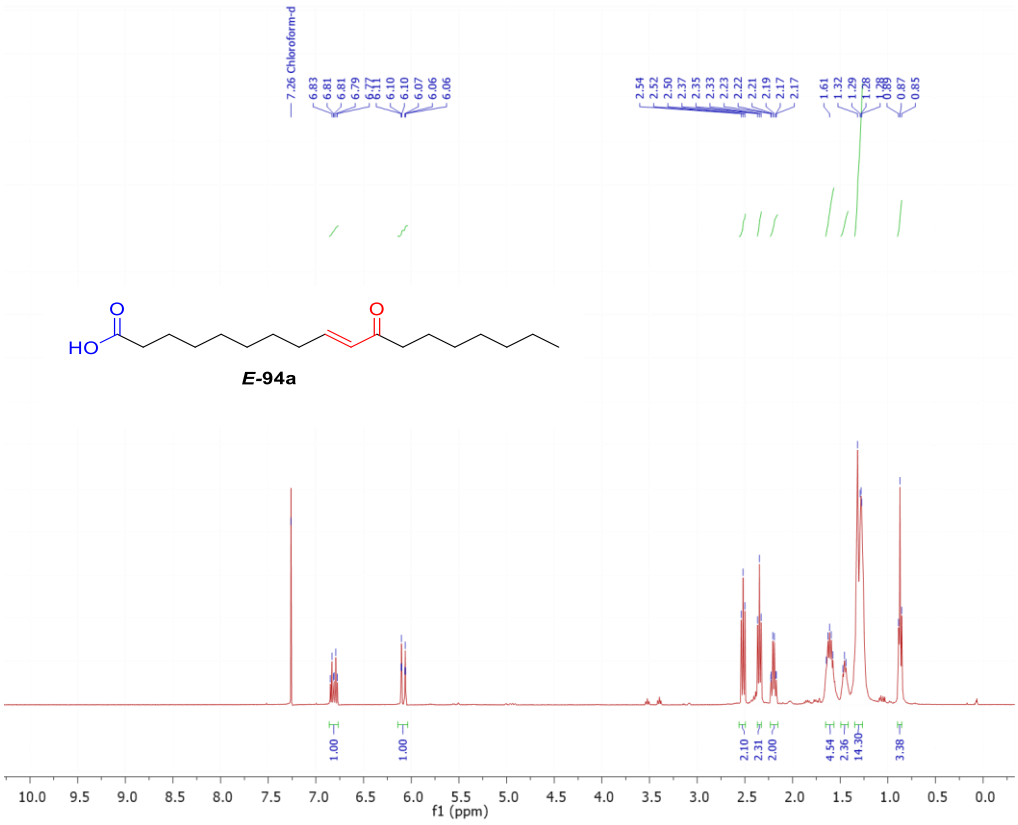

HO
O
O
E-53f
f1 (ppm)


HO
O
O
E-53g
f1 (ppm)

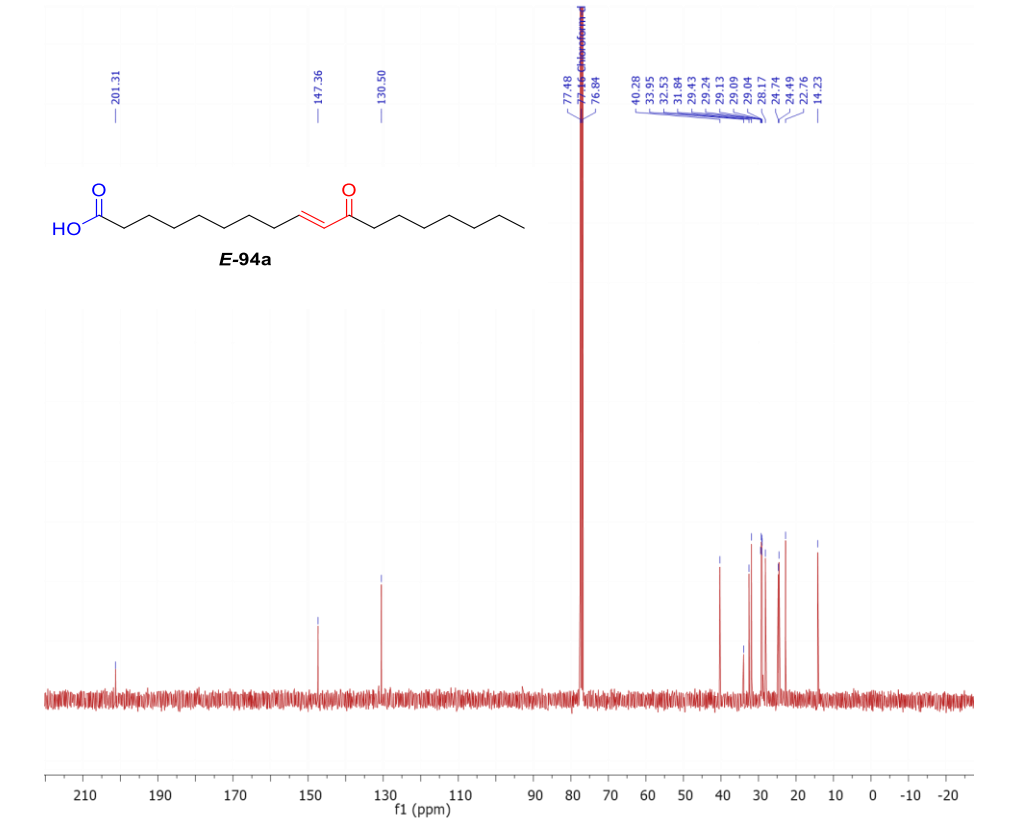

HO
O
O
E-53g
f1 (ppm)


7.26 Chloroform-d
6.84
6.82
6.80
6.78
6.10
6.10
6.06
6.06
6.06
6.06
2.56
2.54
2.52
2.37
2.36
2.34
2.23
2.21
2.21
2.19
2.18
2.17
1.65
1.63
1.37
1.28
0.89
0.88
0.86
O
HO
O
E-53h
1.00
1.00
2.04
2.10
2.02
4.19
14.31
3.09
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

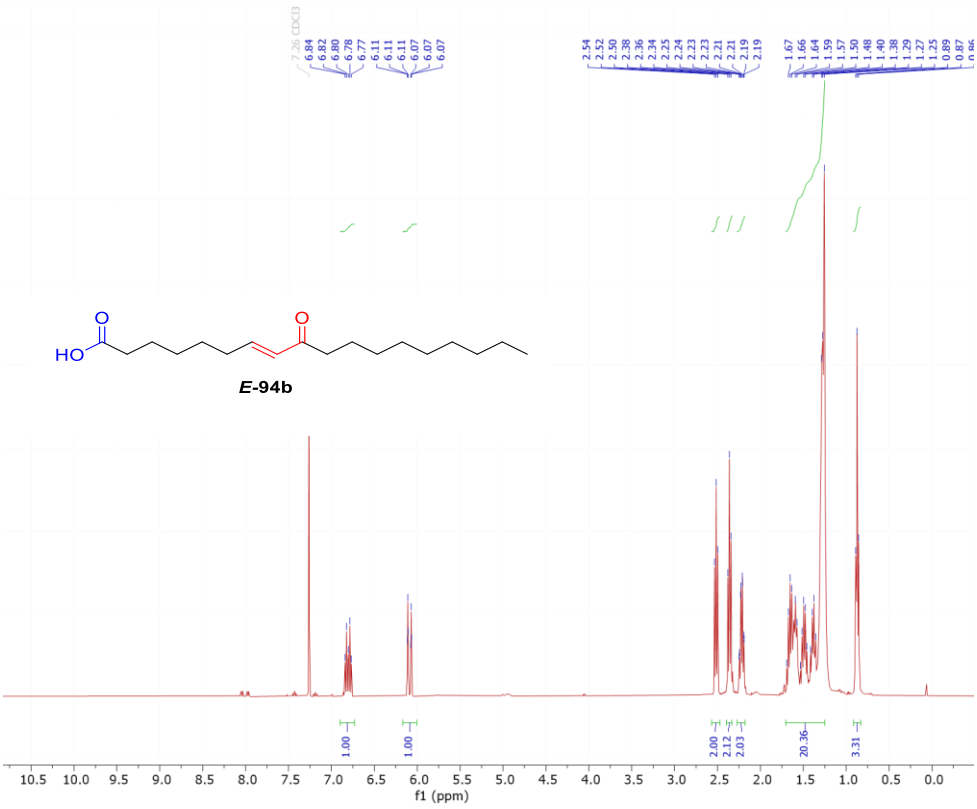

200.78
179.21
147.81
130.38
77.48
77.16 Chloroform-d
76.84
39.82
33.85
32.62
31.98
29.49
29.34
29.33
28.80
28.25
24.60
23.92
22.79
14.24
O
HO
O
E-53h
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

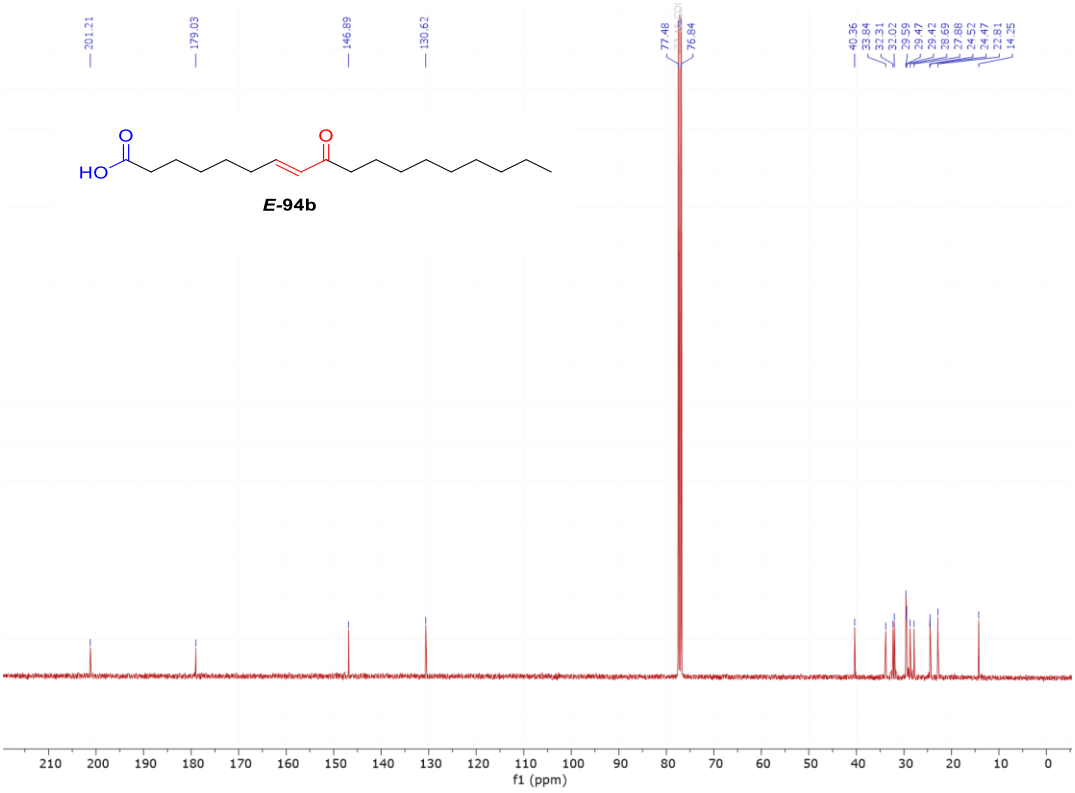

7.26 Chloroform-d
6.83
6.81
6.81
6.79
6.11
6.10
6.10
6.07
6.06
6.06
2.54
2.52
2.50
2.37
2.35
2.33
2.23
2.22
2.21
2.19
2.17
2.17
1.61
1.32
1.29
1.28
0.89
0.87
0.85
HO
O
O
1.00
1.00
2.10
2.31
2.00
4.54
2.36
14.30
3.38
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

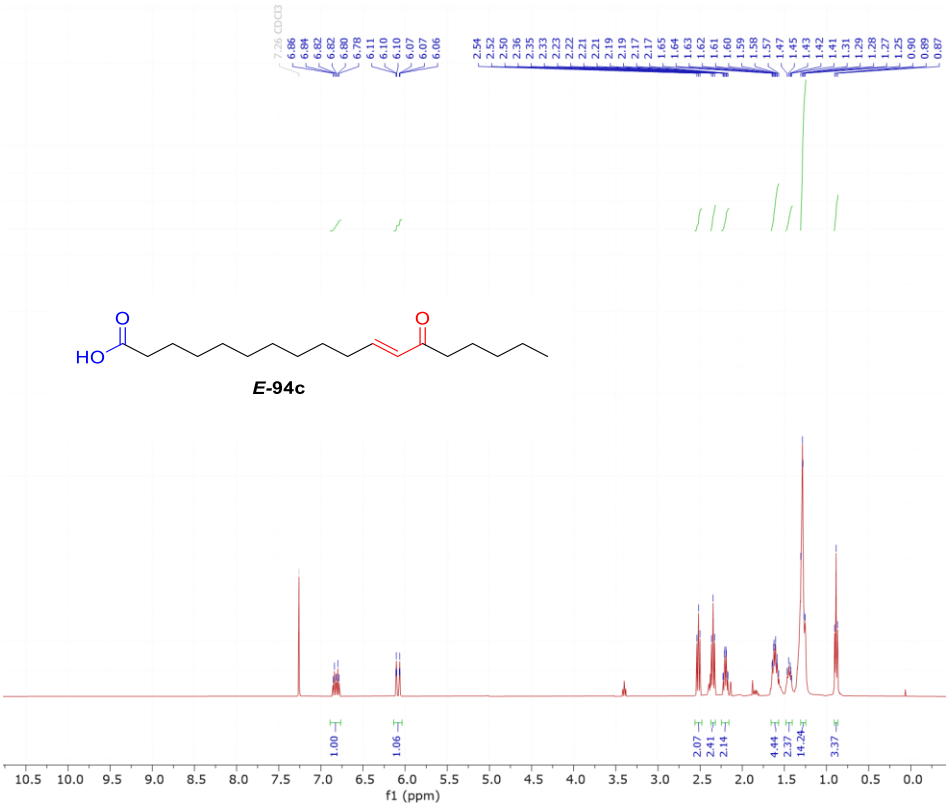
E-94a


201.31
147.36
130.50
77.48
77.16 Chloroform-d
76.84
40.28
33.95
32.53
31.84
29.43
29.24
29.13
29.09
29.04
28.17
24.74
24.49
22.76
14.23
HO
O
O
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

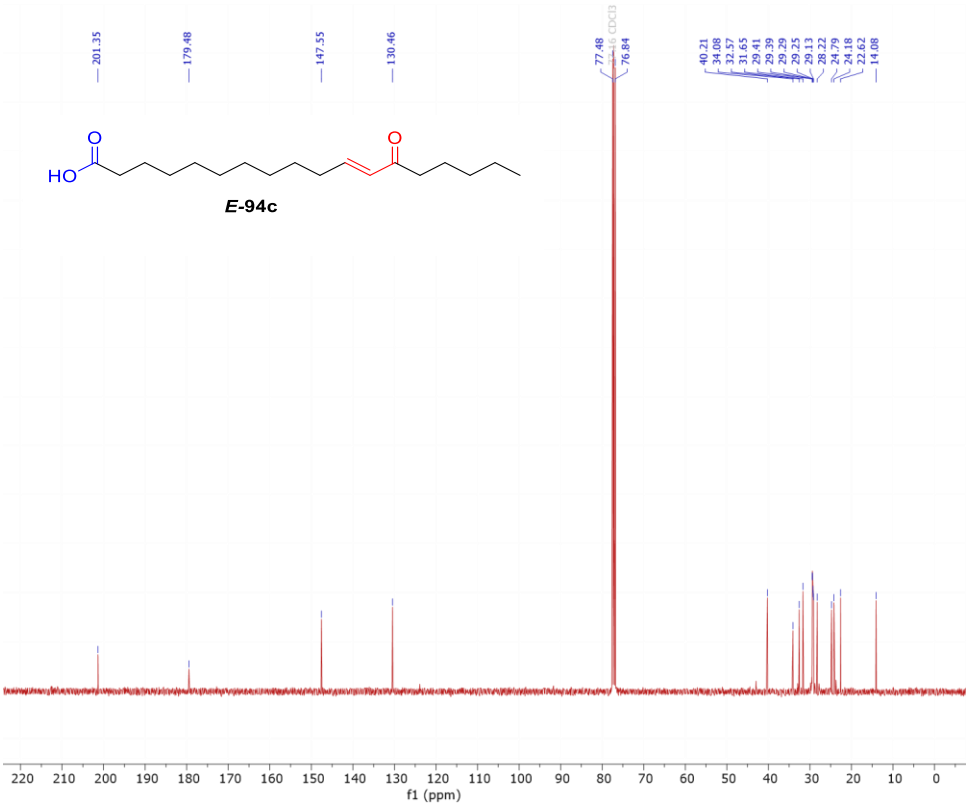
E-94a


HO
O
O
E-94b
f1 (ppm)

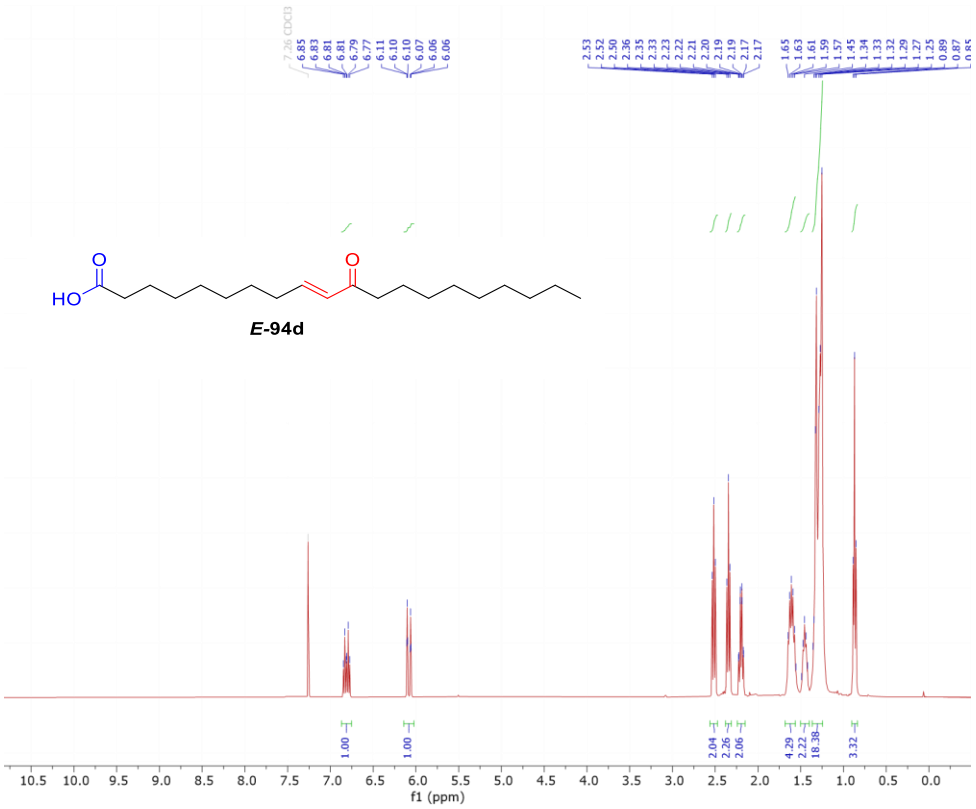

HO
O
O
E-94b
f1 (ppm)

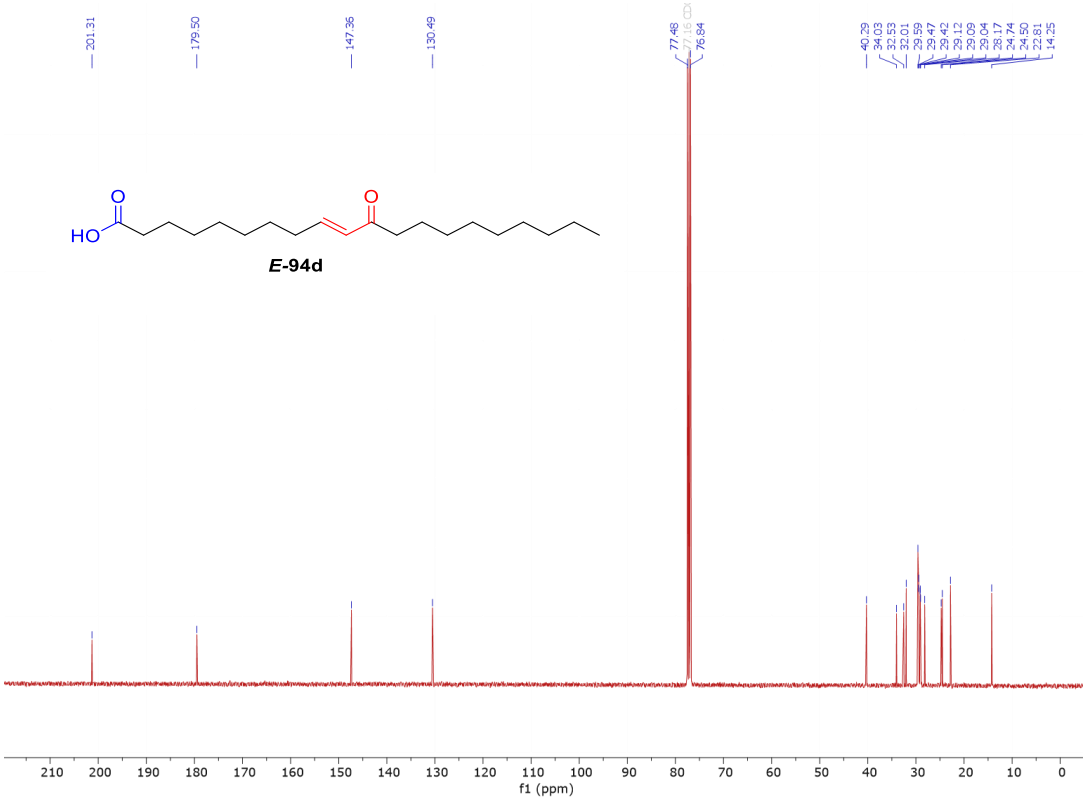

HO
O
O
1.00
1.06
2.07
2.41
2.14
4.44
2.37
14.24
3.37
f1 (ppm)

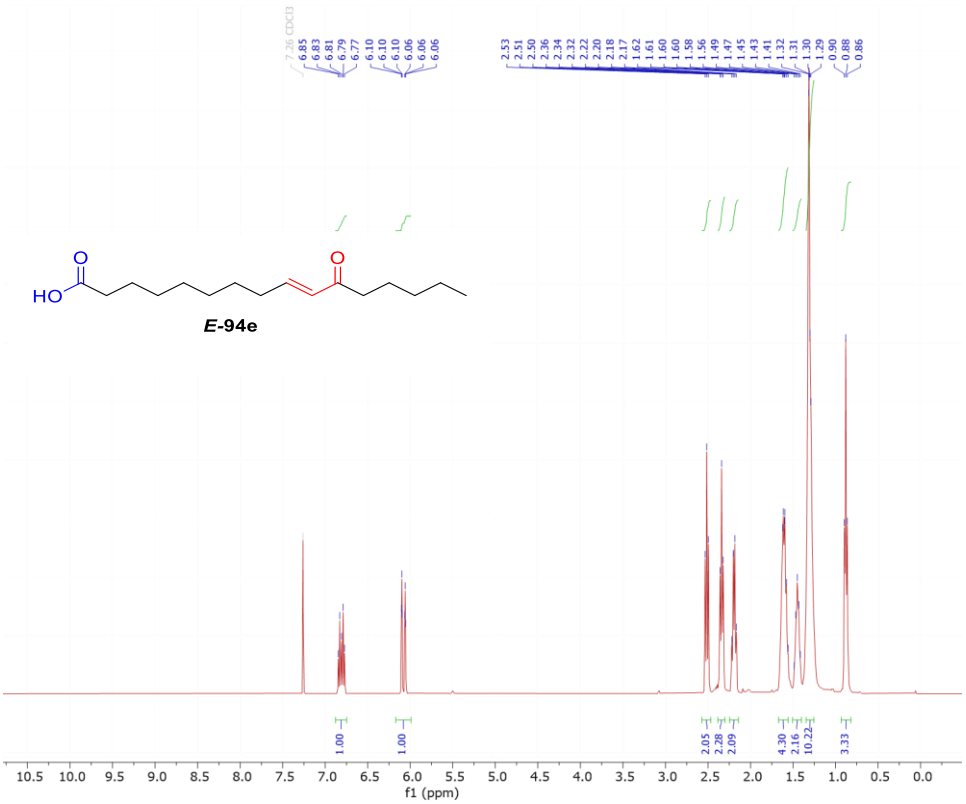
E-94c

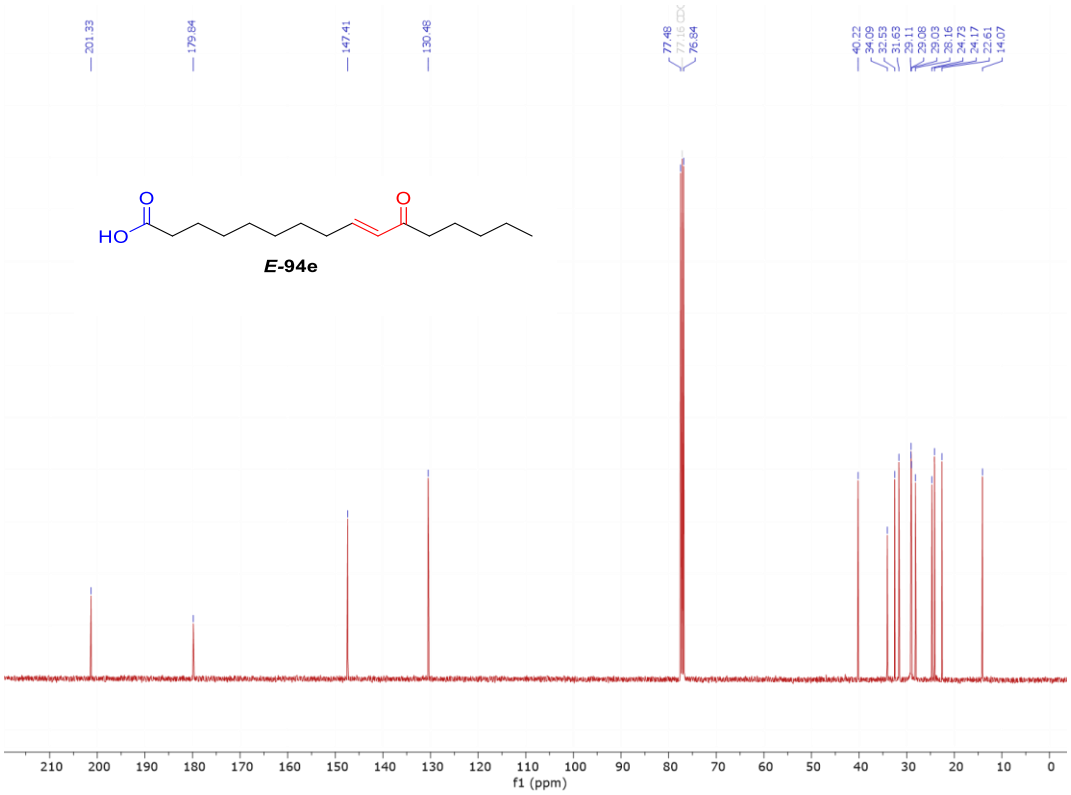

201.35
179.48
147.55
130.46
77.48
76.84
40.21
34.08
32.57
31.65
29.41
29.39
29.29
29.25
29.13
28.22
24.79
24.18
22.62
14.08
HO
O
O
f1 (ppm)

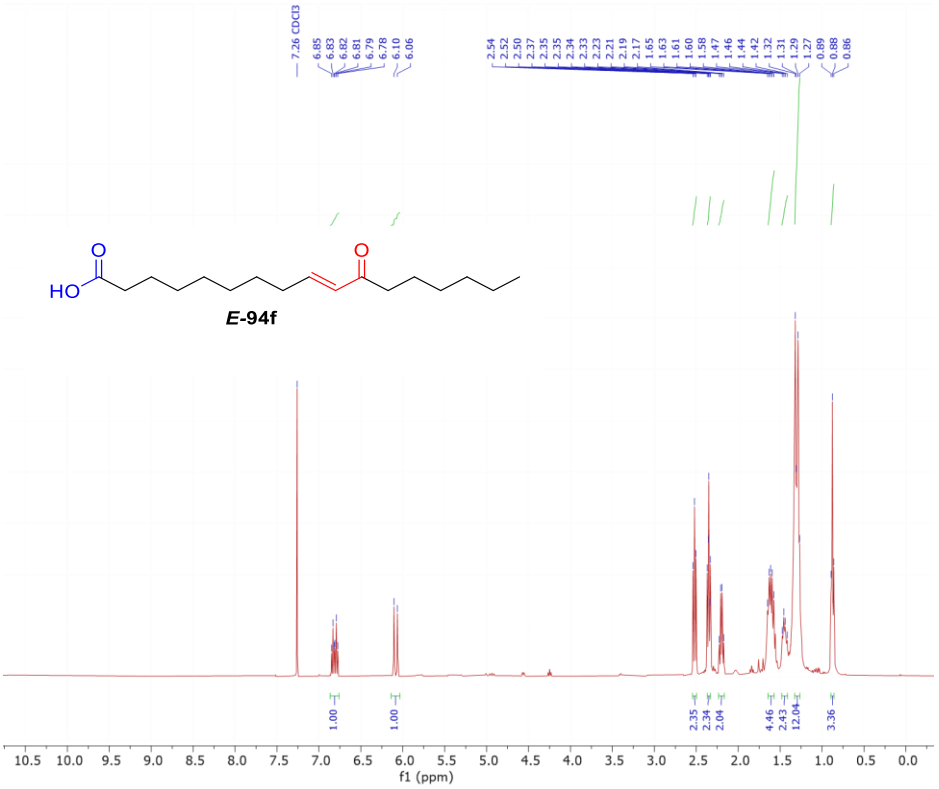
E-94c

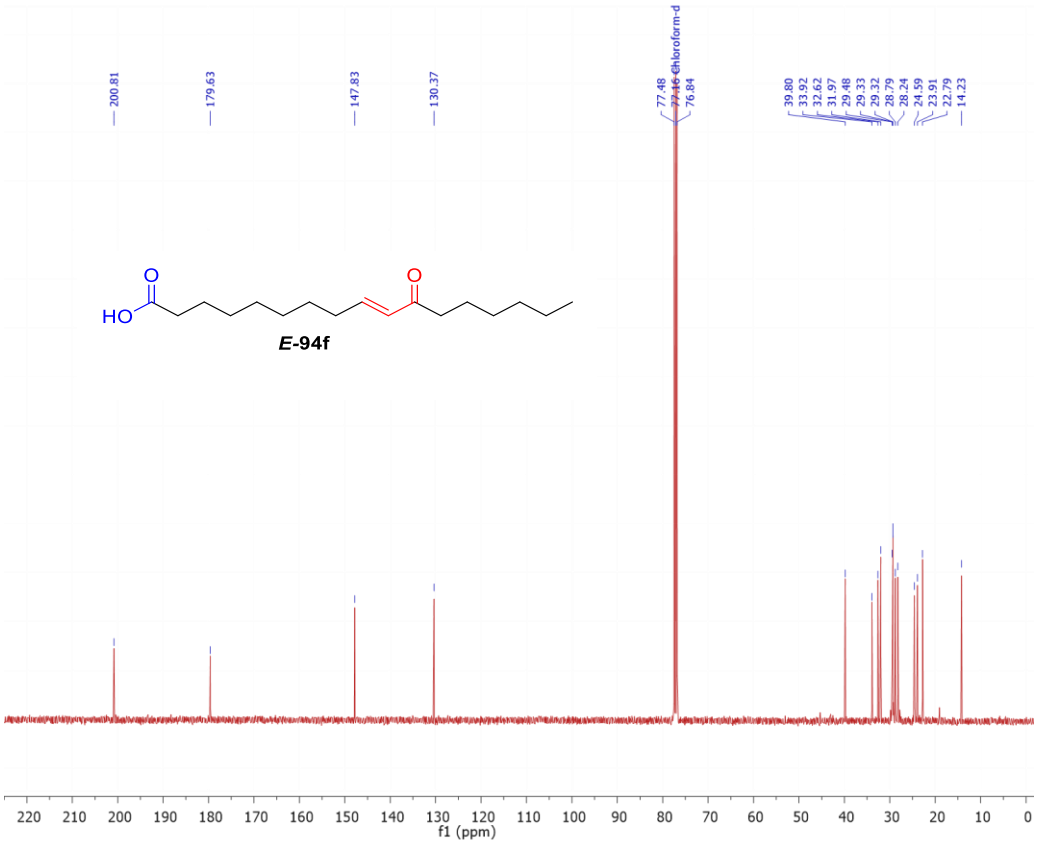

HO
O
O
E-94d
f1 (ppm)

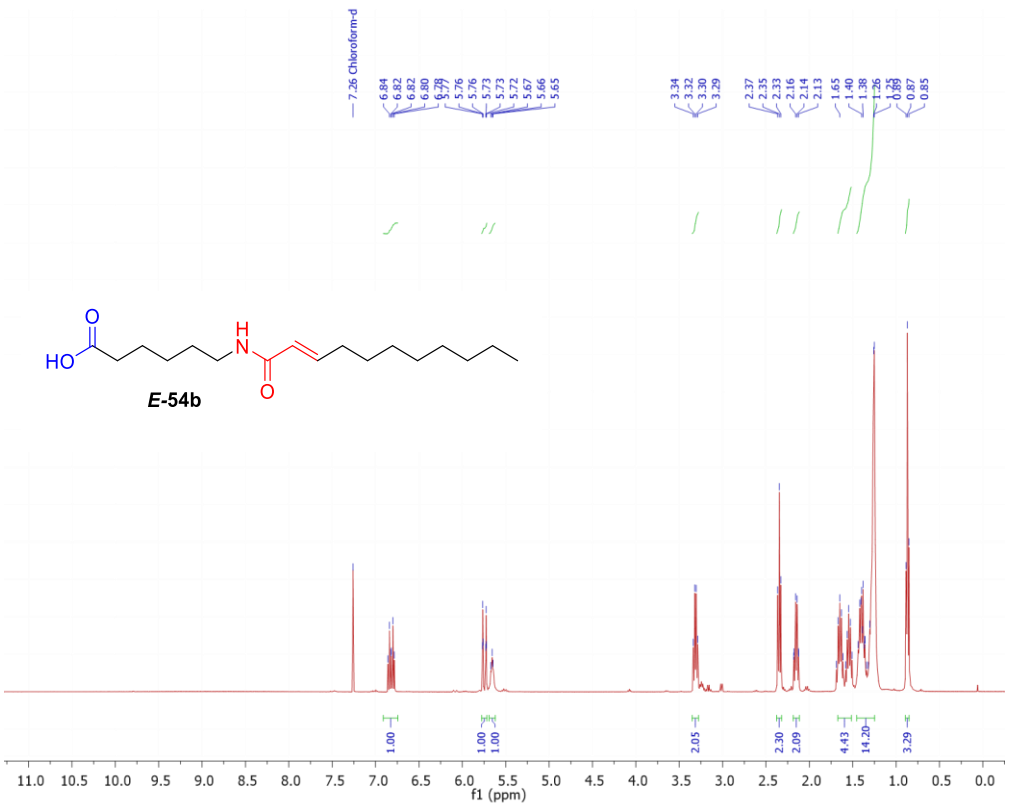

HO
O
O
E-94d
f1 (ppm)

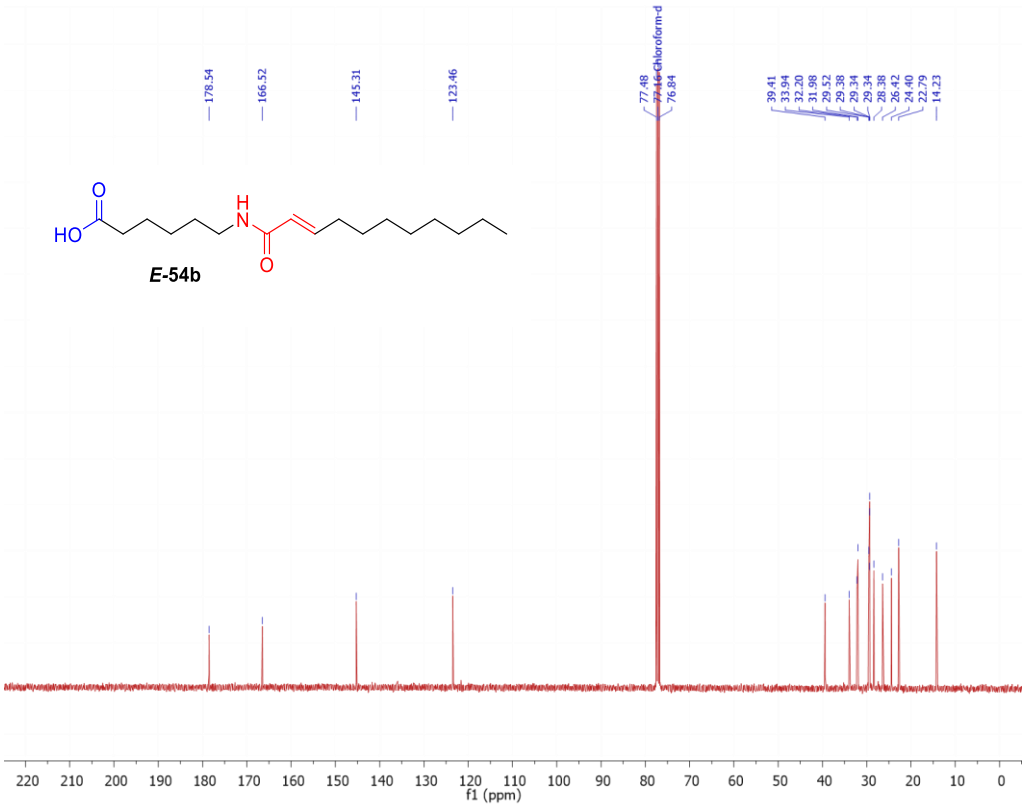

7.26 CDCl3
6.85
6.83
6.81
6.79
6.77
6.10
6.10
6.10
6.06
6.06
6.06
2.53
2.51
2.50
2.36
2.34
2.32
2.22
2.20
2.18
2.17
1.62
1.61
1.60
1.60
1.58
1.56
1.49
1.47
1.45
1.43
1.41
1.32
1.31
1.30
1.29
0.90
0.88
0.86
HO
O
O
E-94e
1.00
1.00
2.05
2.28
2.09
4.30
2.16
10.22
3.33
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

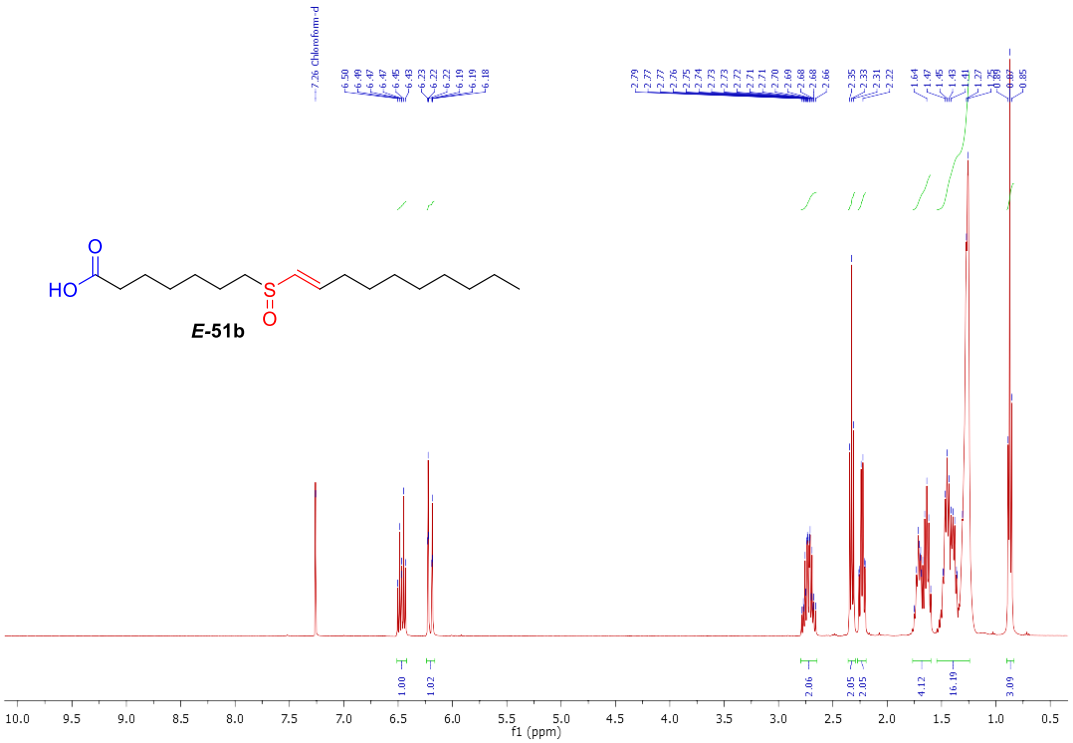

201.33
179.84
147.41
130.48
77.48
77.16 CDCl3
76.84
40.22
34.09
32.53
31.63
29.11
29.08
29.03
28.16
24.73
24.17
22.61
14.07
HO
O
O
E-94e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

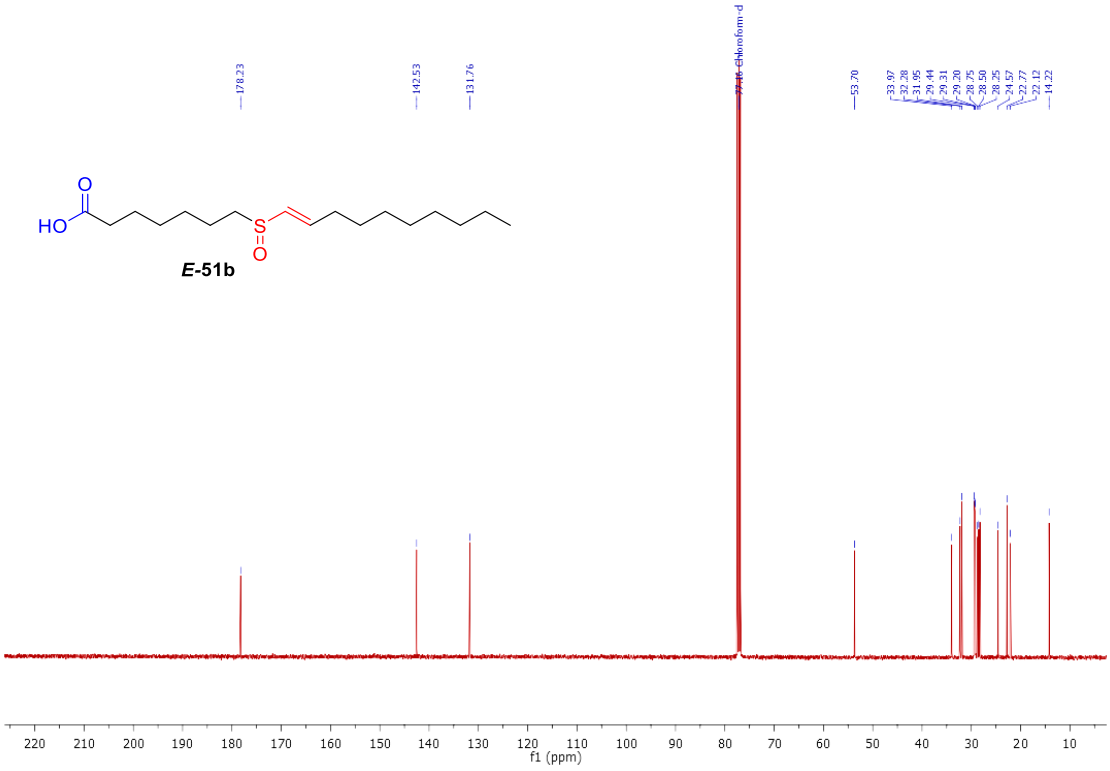

7.26 CDCl3
6.85
6.83
6.82
6.81
6.79
6.78
6.10
6.06
2.54
2.52
2.50
2.37
2.35
2.35
2.34
2.33
2.23
2.21
2.19
2.17
1.65
1.63
1.61
1.60
1.58
1.47
1.46
1.44
1.42
1.32
1.31
1.29
1.27
0.89
0.88
0.86
HO
O
O
E-94f
1.00
1.00
2.35
2.34
2.04
4.46
2.43
12.04
3.36
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

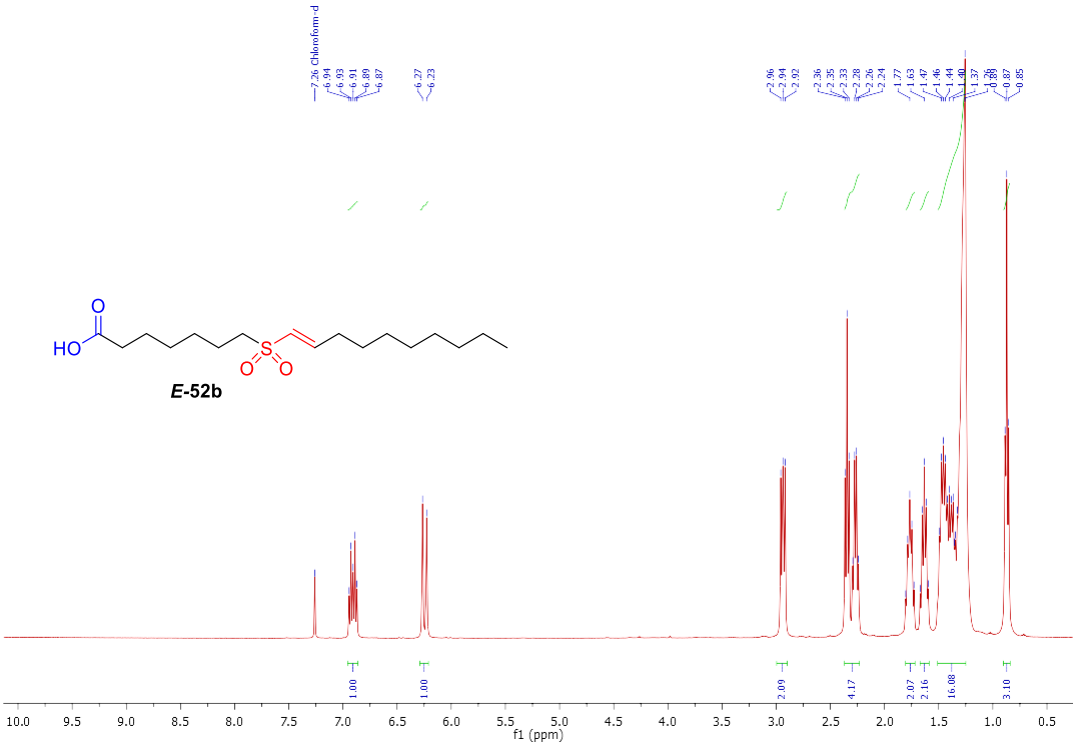

200.81
179.63
147.83
130.37
77.48
77.16 Chloroform-d
76.84
39.80
33.92
32.62
31.97
29.48
29.33
29.32
28.79
28.24
24.59
23.91
22.79
14.23
HO
O
O
E-94f
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.26 Chloroform-d
6.84
6.82
6.82
6.80
5.76
5.76
5.73
5.73
5.72
5.67
5.66
5.65
3.34
3.32
3.30
3.29
2.37
2.35
2.33
2.16
2.14
2.13
1.65
1.40
1.38
1.26
0.89
0.87
0.85
HO
O
H
N
O
E-54b
1.00
1.00
1.00
2.05
2.30
2.09
4.43
14.20
3.29
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

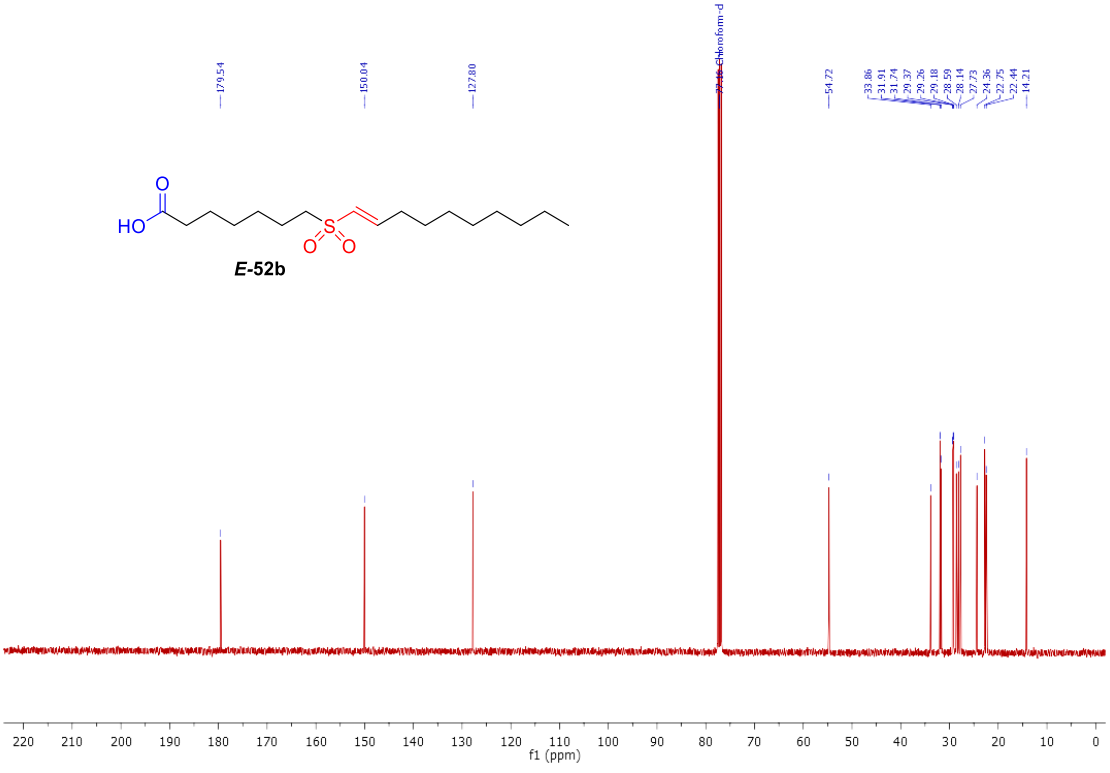

178.54
166.52
145.31
123.46
77.48
77.16 Chloroform-d
76.84
39.41
33.94
32.20
31.98
29.52
29.38
29.34
28.38
26.42
24.40
22.79
14.23
HO
O
H
N
O
E-54b
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.26 Chloroform-d
6.50
6.49
6.47
6.47
6.45
6.43
6.23
6.22
6.22
6.19
6.19
6.18
2.79
2.77
2.77
2.76
2.75
2.74
2.73
2.73
2.72
2.71
2.71
2.70
2.69
2.68
2.68
2.66
1.64
1.47
1.45
1.43
1.41
1.27
0.89
0.88
0.87
0.85
1.00
1.02
2.06
2.05
2.05
4.12
16.19
3.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
HO
O
S
O
E-51b

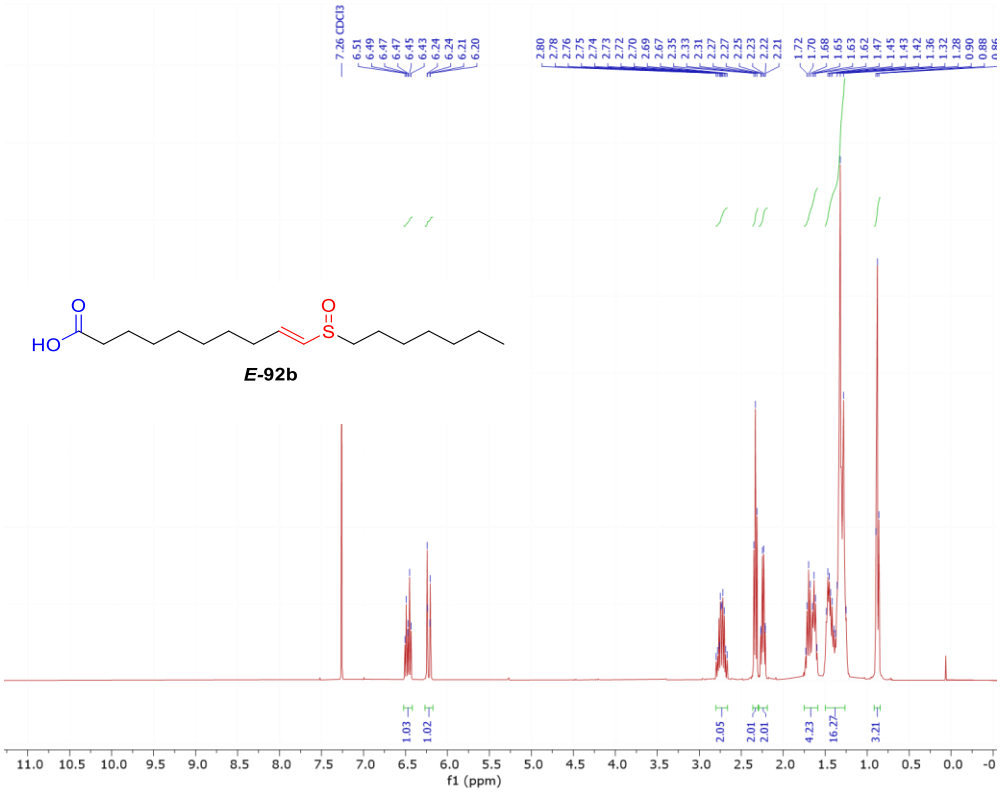

178.23
142.53
131.76
77.16 Chloroform-d
53.70
33.97
32.28
31.95
29.44
29.31
29.20
28.75
28.50
28.25
24.57
22.77
22.12
14.22
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)
HO
O
S
O
E-51b


7.26 Chloroform-d
6.94
6.93
6.91
6.89
6.87
6.27
6.23
2.96
2.94
2.92
2.36
2.35
2.33
2.28
2.26
2.24
1.77
1.65
1.47
1.46
1.44
1.40
1.37
0.88
0.87
0.85
1.00
1.00
2.09
4.17
2.07
2.16
16.08
3.10
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)
HO
O
S
O
O

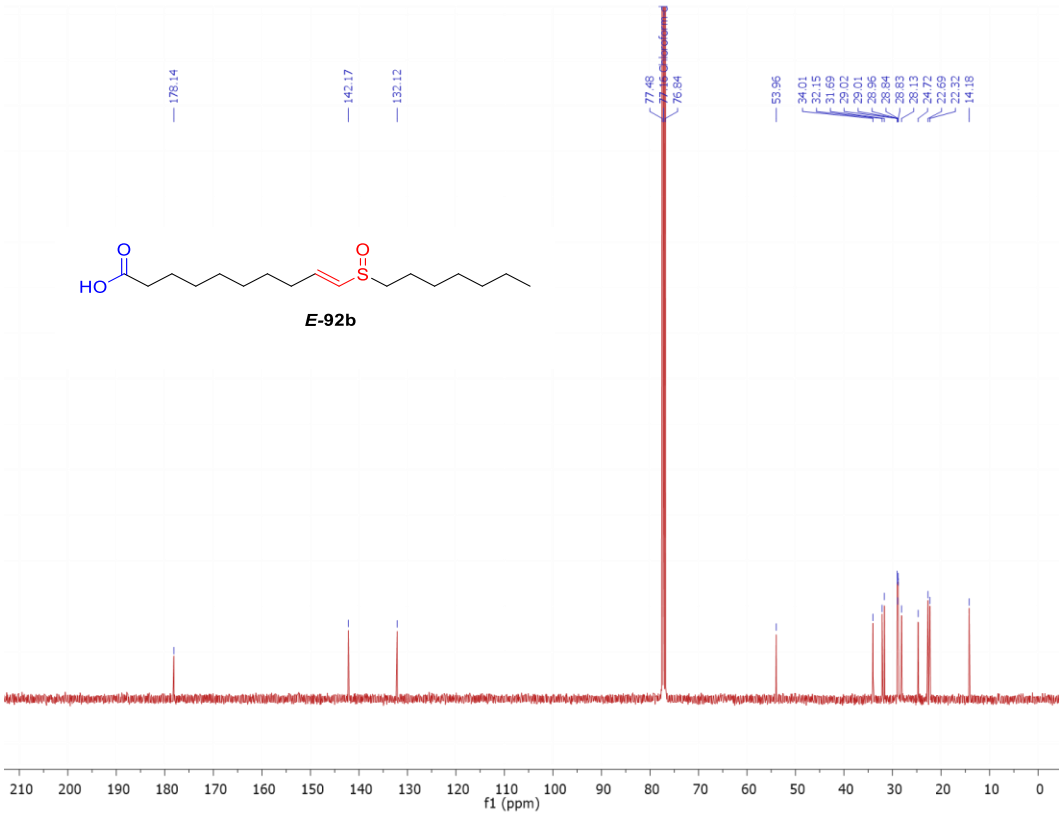
***E*-52b**


179.54
150.04
127.80
77.16 Chloroform-d
54.72
33.86
31.91
31.74
29.37
29.26
29.18
28.59
28.14
27.73
24.36
22.75
22.44
14.21
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
HO
O
S
O
O

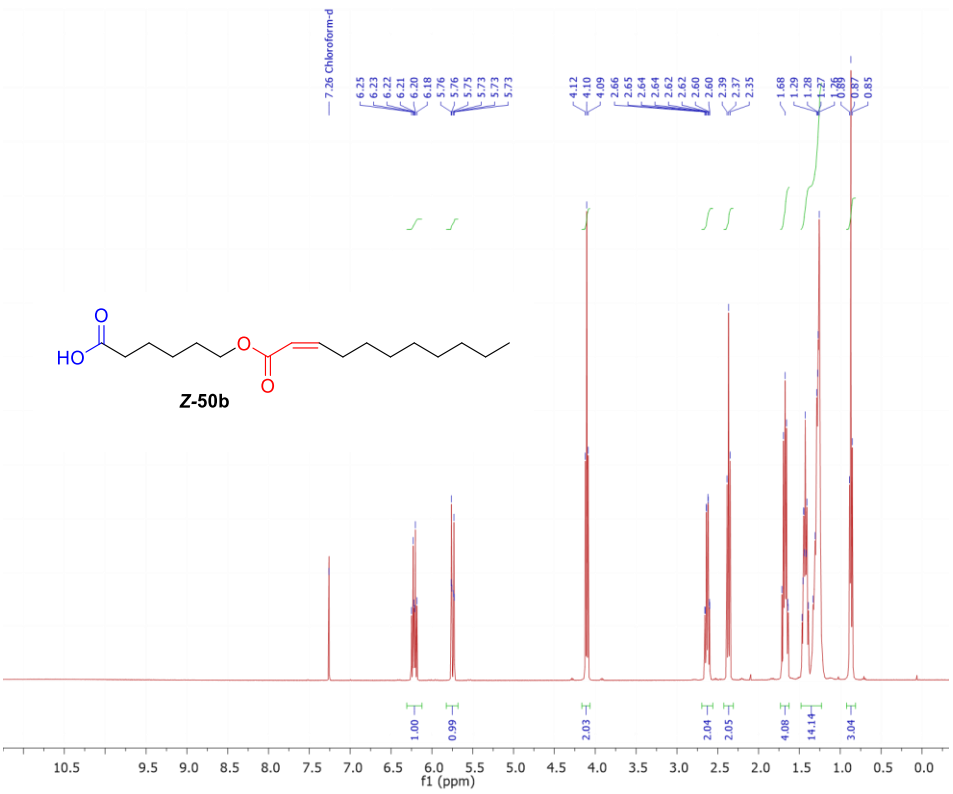
***E*-52b**

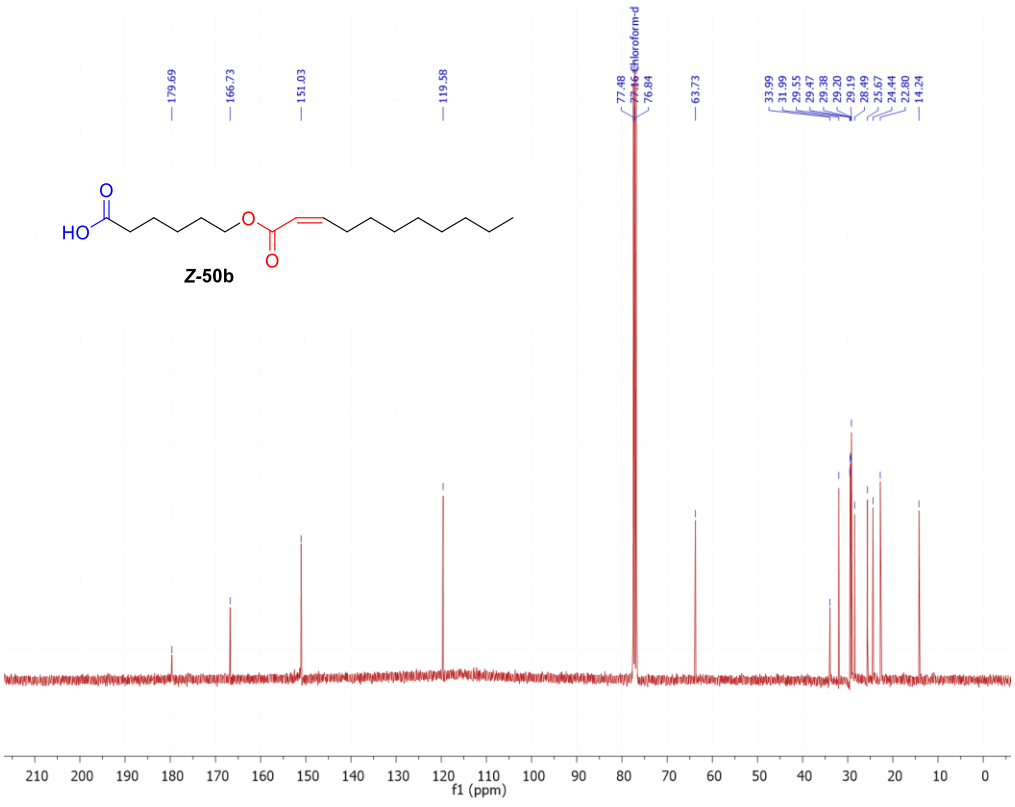

7.26 CDCl3
6.51
6.49
6.47
6.47
6.47
6.45
6.43
6.24
6.24
6.21
6.20
2.80
2.78
2.76
2.75
2.74
2.73
2.72
2.70
2.69
2.67
2.35
2.33
2.31
2.27
2.27
2.25
2.23
2.22
2.21
1.72
1.70
1.68
1.65
1.63
1.62
1.47
1.45
1.43
1.42
1.36
1.32
1.28
0.90
0.88
HO
O
S
1.03
1.02
2.05
2.01
2.01
4.23
16.27
3.21
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

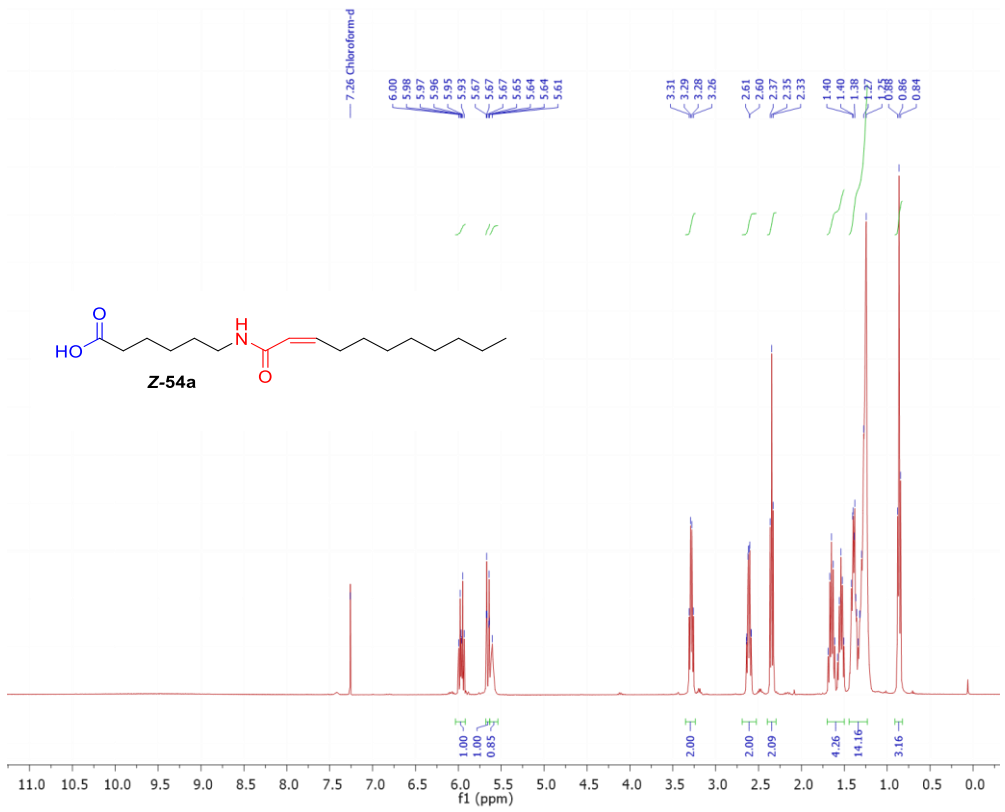
E-92b

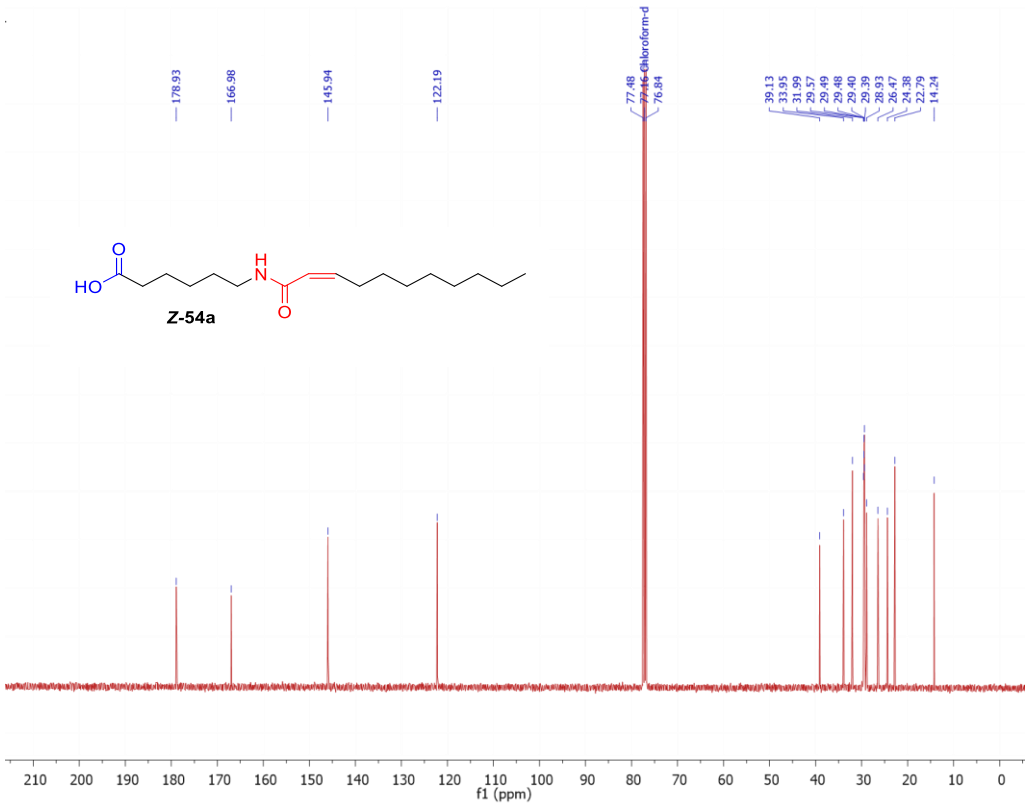

178.14
142.17
132.12
77.48
77.16 CDCl3
76.84
53.96
34.01
32.15
31.69
29.02
29.01
28.96
28.84
28.83
28.13
24.72
22.69
22.32
14.18
HO
O
S
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

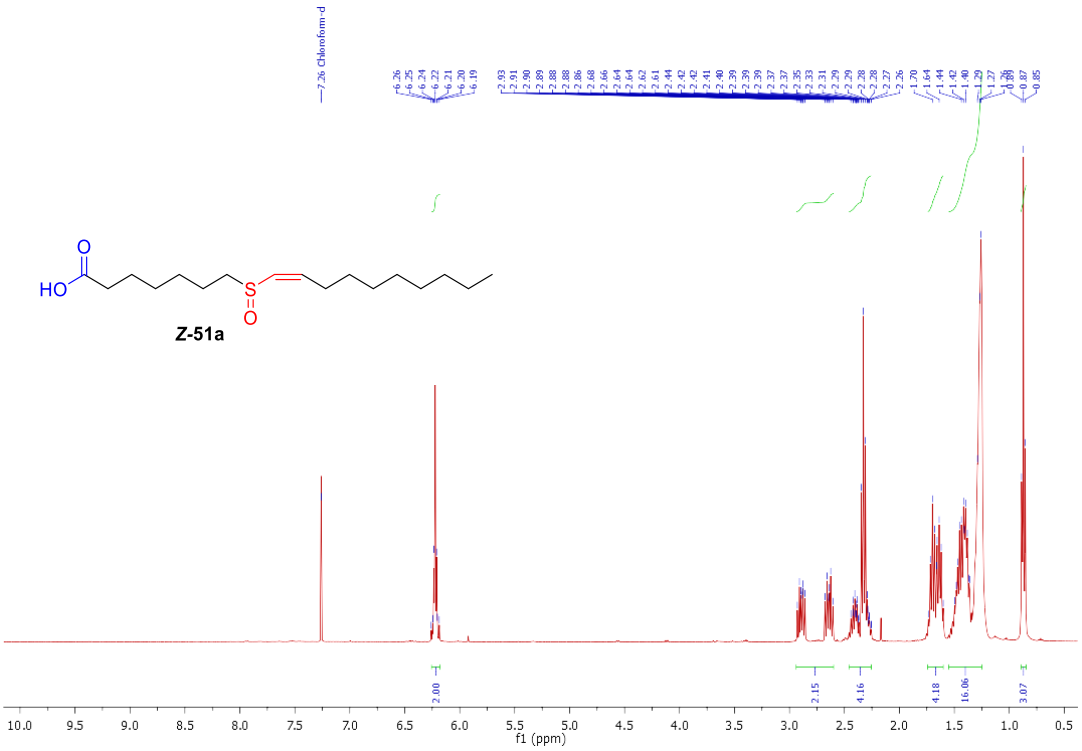
E-92b

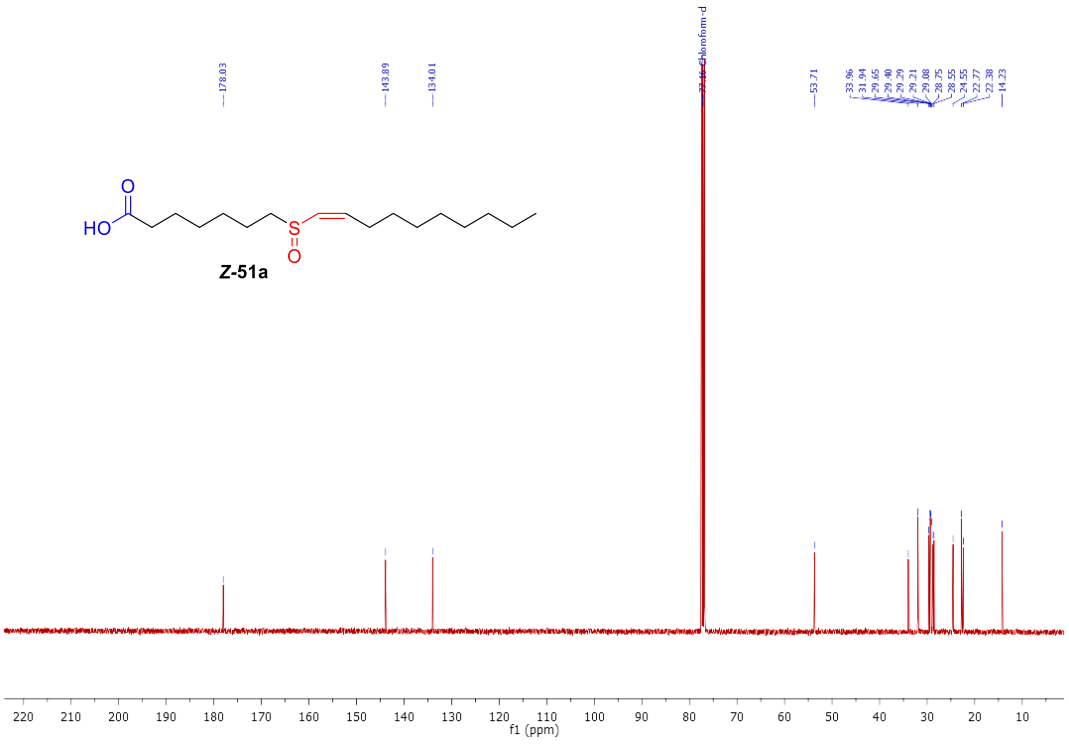

7.26 Chloroform-d
6.25
6.23
6.22
6.21
6.20
6.18
5.76
5.75
5.73
5.73
5.73
4.12
4.10
4.09
2.66
2.65
2.64
2.64
2.62
2.62
2.60
2.60
2.39
2.37
2.35
1.68
1.29
1.28
1.27
0.88
0.87
0.85
HO
O
O
O
Z-50b
1.00
0.99
2.03
2.04
2.05
4.08
14.14
3.04
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

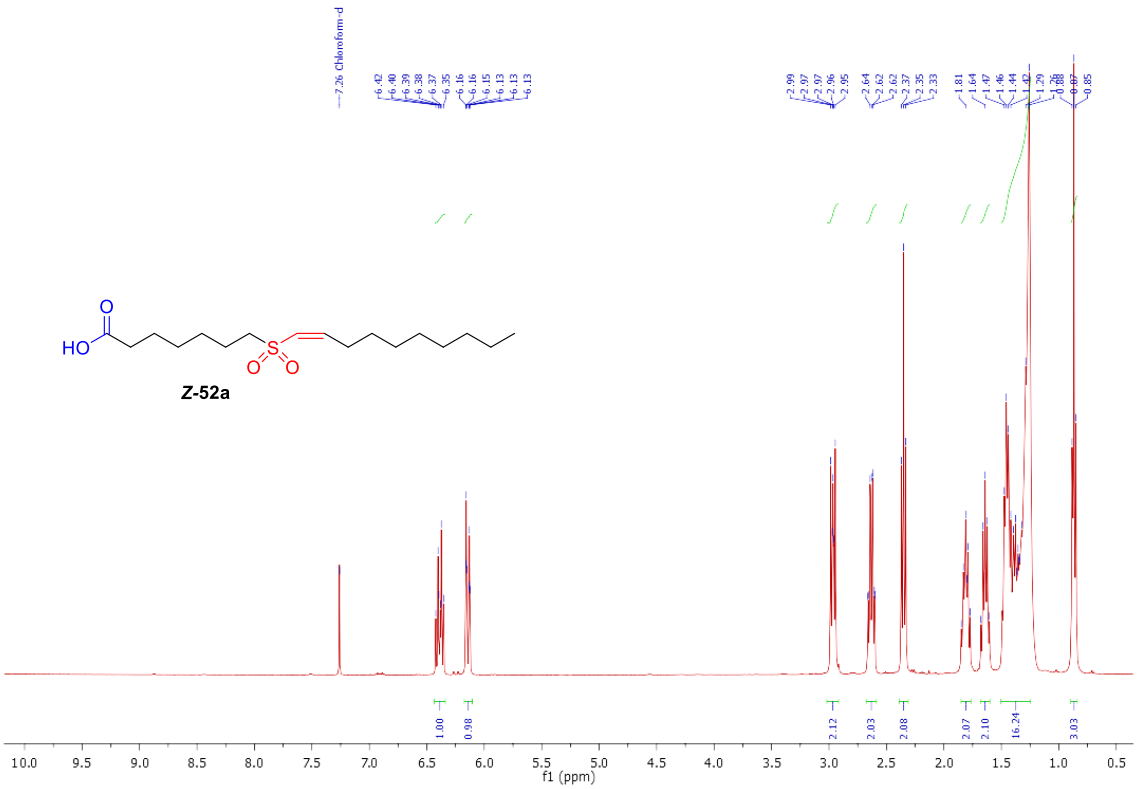

179.69
166.73
151.03
119.58
77.48
77.16 Chloroform-d
76.84
63.73
33.99
31.99
29.55
29.47
29.38
29.20
29.19
28.49
25.67
24.44
22.80
14.24
HO
O
O
O
Z-50b
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.26 Chloroform-d
6.00
5.98
5.97
5.96
5.95
5.93
5.67
5.67
5.67
5.65
5.64
5.64
5.61
3.31
3.29
3.28
3.26
2.61
2.60
2.37
2.35
2.33
1.40
1.40
1.38
1.27
0.88
0.86
0.84
HO
O
H
N
O
Z-54a
1.00
1.00
0.85
2.00
2.00
2.09
4.26
14.16
3.16
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

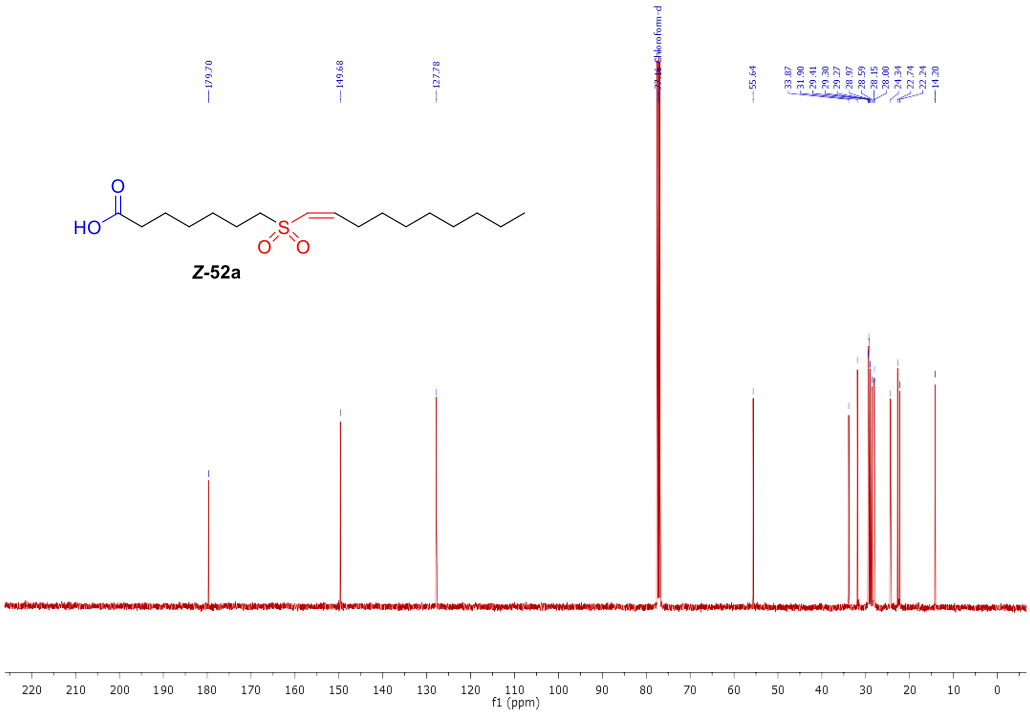

178.93
166.98
145.94
122.19
77.48
77.16 Chloroform-d
76.84
39.13
33.95
31.99
29.57
29.49
29.48
29.40
29.39
28.93
26.47
24.38
22.79
14.24
HO
O
H
N
O
Z-54a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


HO
O
S
O
Z-51a
f1 (ppm)

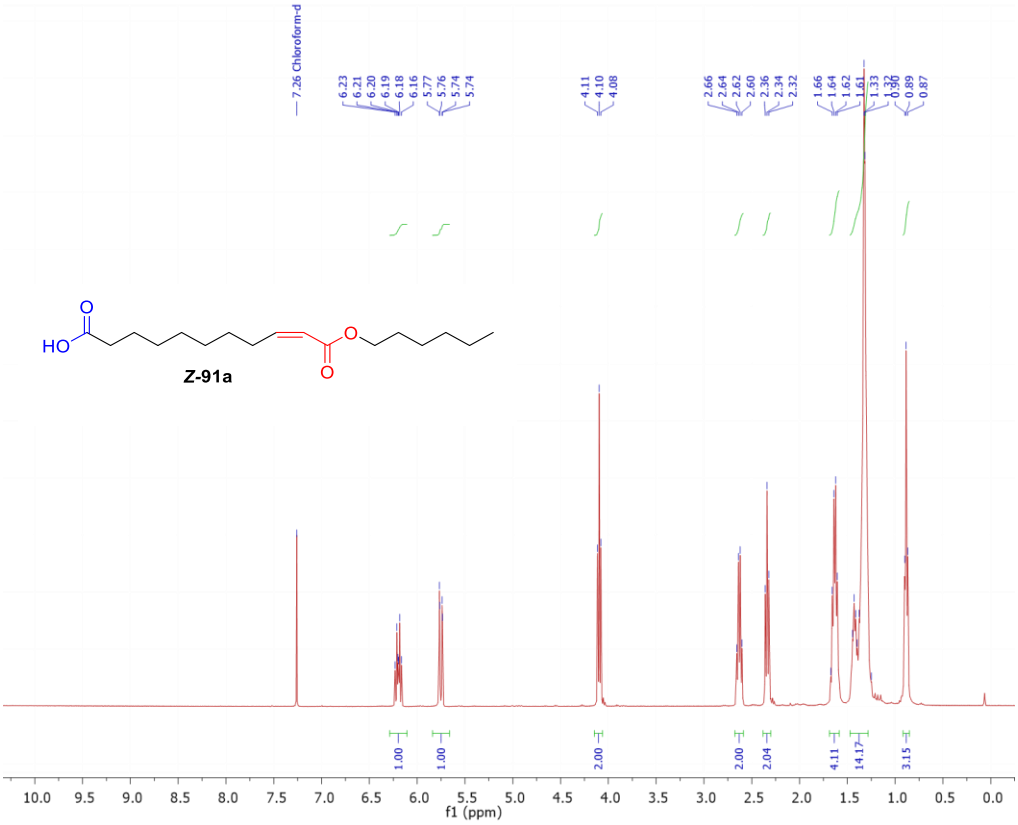

HO
O
S
O
Z-51a
f1 (ppm)

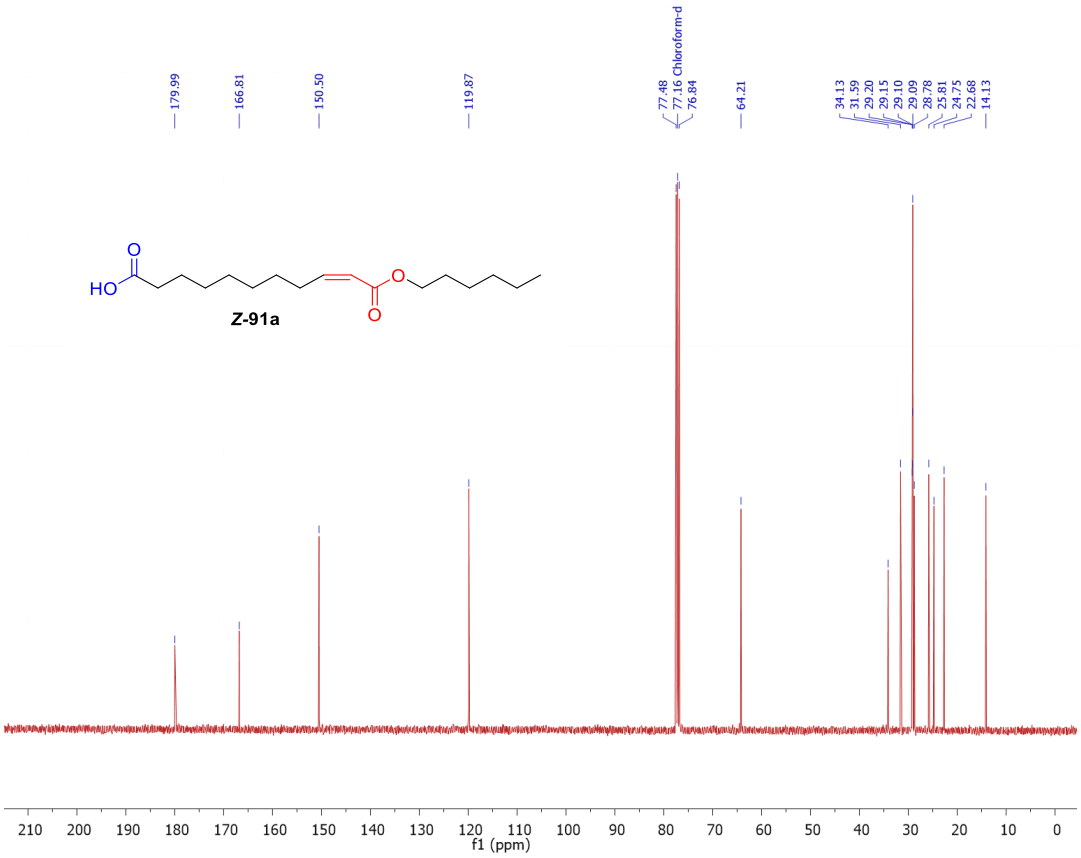

7.26 Chloroform-d
6.42
6.40
6.39
6.38
6.37
6.35
6.16
6.16
6.15
6.13
6.13
6.13
2.99
2.97
2.97
2.96
2.95
2.64
2.62
2.62
2.37
2.35
2.33
1.81
1.64
1.47
1.46
1.44
1.42
1.29
0.88
0.87
0.85
HO
O
S
O
O
1.00
0.98
2.12
2.03
2.08
2.07
2.10
16.24
3.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

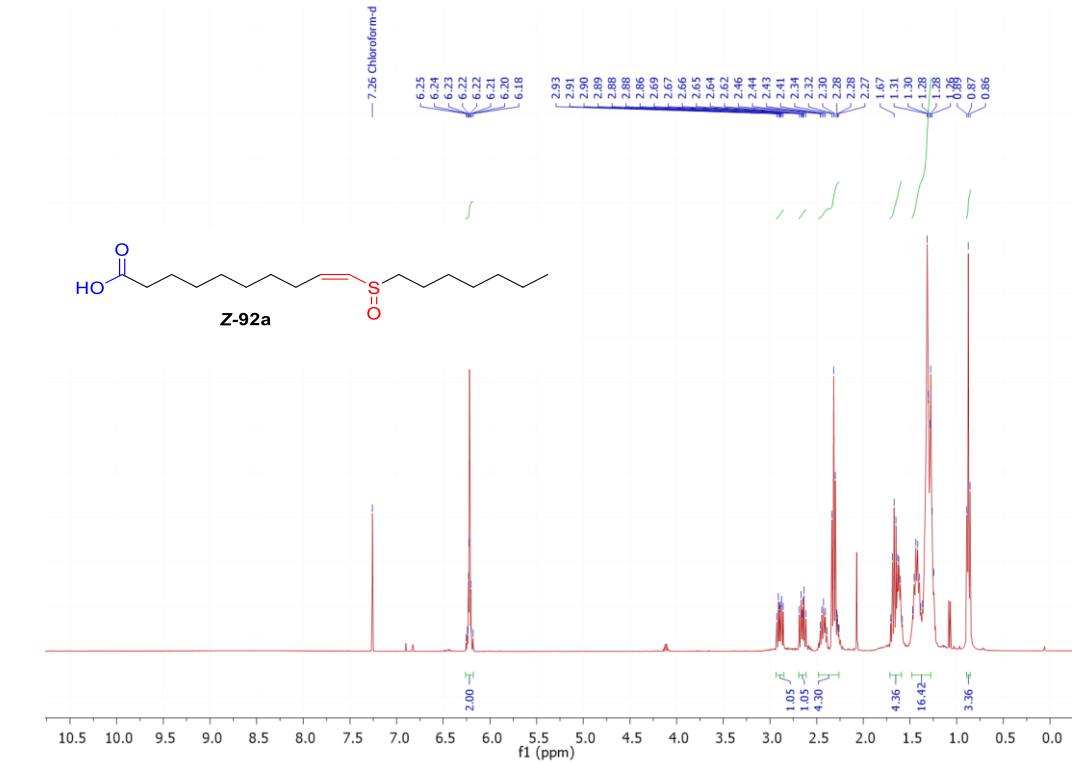
***Z*-52a**

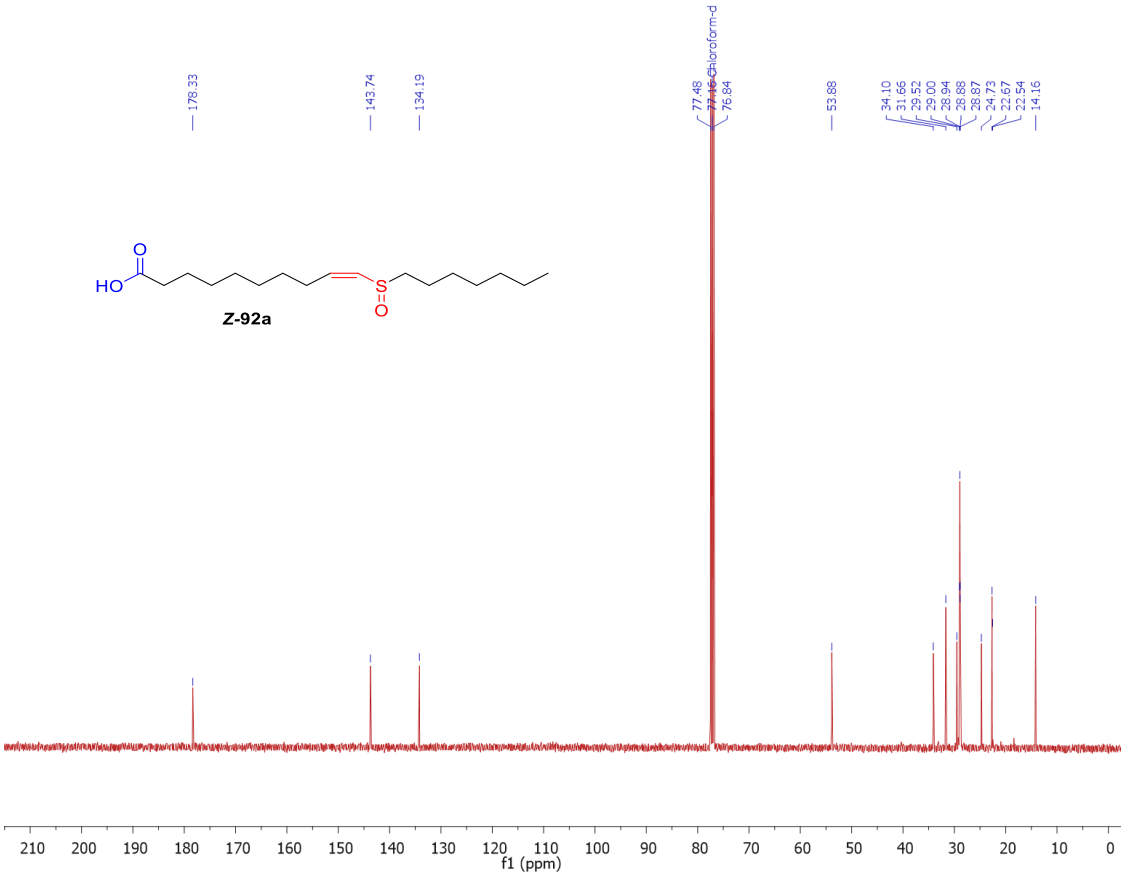

179.70
149.68
127.78
77.16 Chloroform-d
55.64
33.87
31.90
29.41
29.30
29.27
28.97
28.59
28.15
28.06
24.94
22.74
22.24
14.20
HO
O
S
O
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

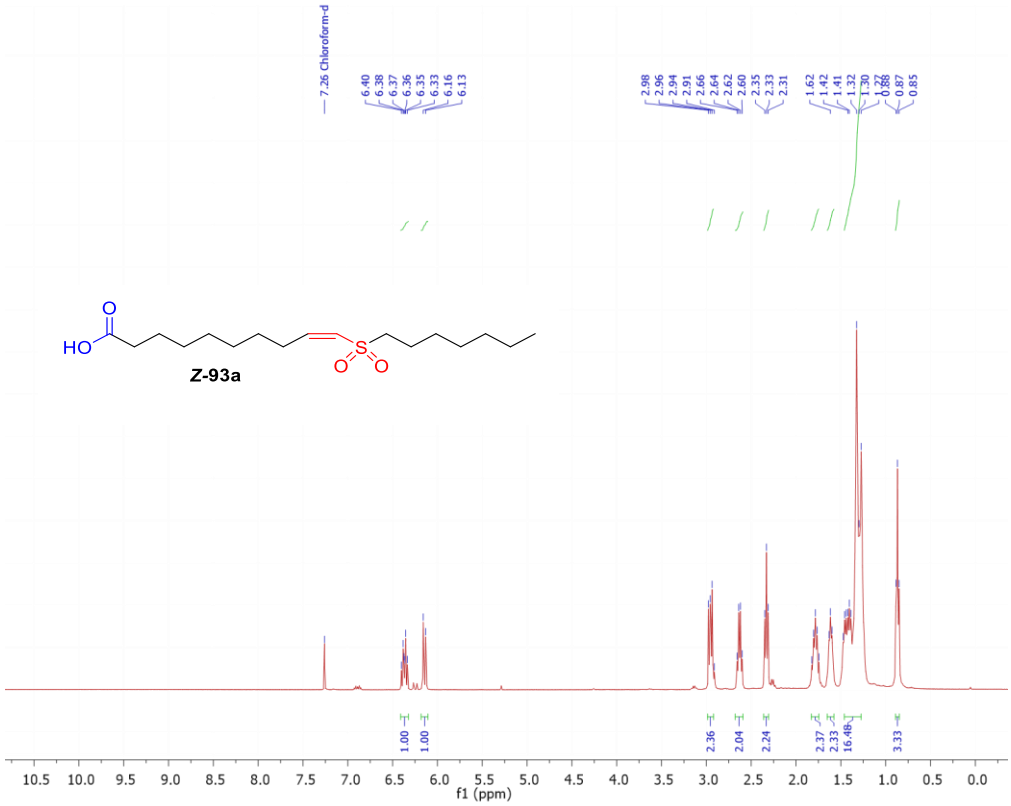
***Z*-52a**

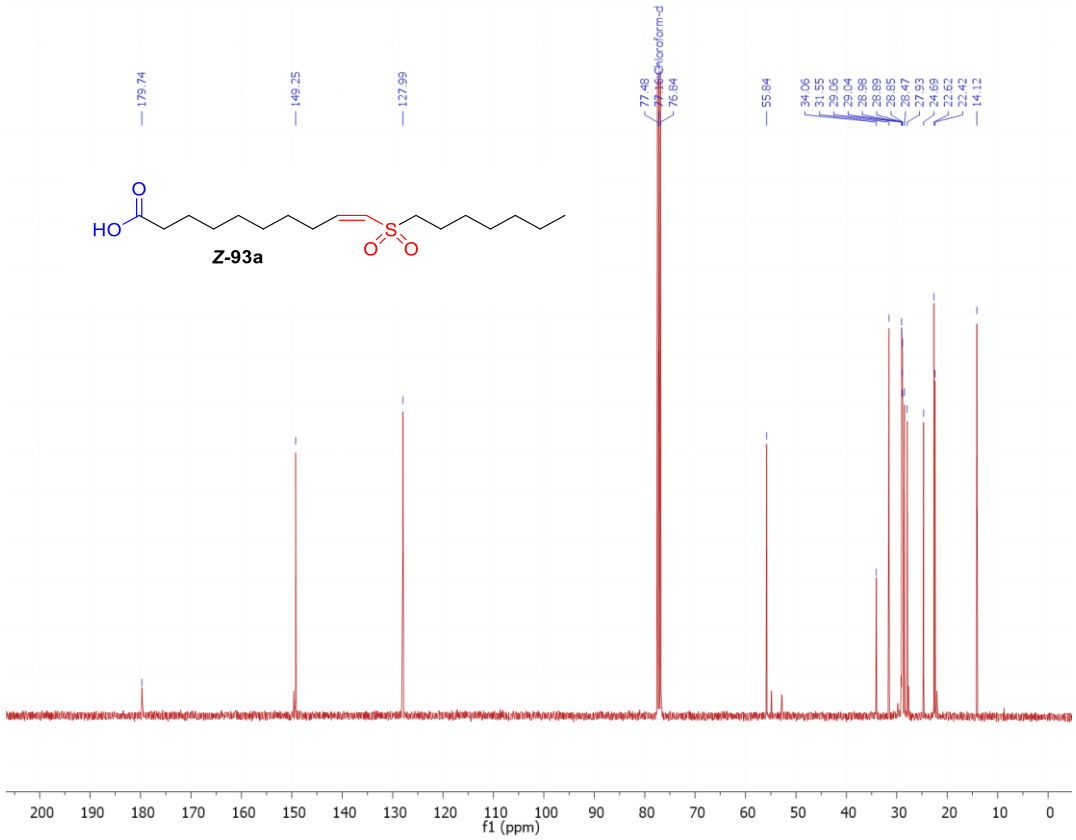

7.26 Chloroform-d
6.23
6.21
6.20
6.19
6.18
6.16
5.77
5.76
5.74
5.74
4.11
4.10
4.08
2.66
2.64
2.62
2.60
2.36
2.34
2.32
1.66
1.64
1.62
1.61
1.33
0.90
0.89
0.87
HO
O
O
O
Z-91a
1.00
1.00
2.00
2.00
2.04
4.11
14.17
3.15
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


179.99
166.81
150.50
119.87
77.48
77.16 Chloroform-d
76.84
64.21
34.13
31.59
29.20
29.15
29.10
29.09
28.78
25.81
24.75
22.68
14.13
HO
O
O
O
Z-91a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.26 Chloroform-d
6.25
6.24
6.23
6.22
6.22
6.21
6.20
6.18
2.93
2.91
2.90
2.89
2.88
2.88
2.86
2.69
2.67
2.66
2.65
2.64
2.62
2.46
2.44
2.43
2.41
2.34
2.32
2.30
2.28
2.28
2.27
1.67
1.31
1.30
1.28
1.28
0.88
0.87
0.86
HO
O
S
O
Z-92a
2.00
1.05
1.05
4.30
4.36
16.42
3.36
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


178.33
143.74
134.19
77.48
77.16 Chloroform-d
76.84
53.88
34.10
31.66
29.52
29.00
28.94
28.88
28.87
24.73
22.67
22.54
14.16
HO
O
S
O
Z-92a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.26 Chloroform-d
6.40
6.38
6.37
6.36
6.35
6.33
6.16
6.13
2.98
2.96
2.94
2.91
2.66
2.64
2.62
2.60
2.35
2.33
2.31
1.62
1.42
1.41
1.32
1.30
0.88
0.87
0.85
HO
O
S
O
O
Z-93a
1.00
1.00
2.36
2.04
2.24
2.37
2.33
16.48
3.33
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


179.74
149.25
127.99
77.48
77.16 Chloroform-d
76.84
55.84
34.06
31.55
29.06
29.04
28.98
28.89
28.85
28.47
27.93
24.69
22.62
22.42
14.12
HO
O
S
O
O
Z-93a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

7 CURRICULUM VITAE



Cedric Ndefo Nde

EDUCATION

PHD IN ORGANIC SYNTHESIS / MEDICINAL CHEMISTRY — Oct 2019 - Nov 2023

Rhineland-Palatinate Technical University Kaiserslautern-Landau

Thesis: "Synthesis and Biological Evaluation of Non-Natural Analogues of Nitro-Fatty Acids"

MASTER OF SCIENCE IN CHEMISTRY — Sep 2015 - Jul 2017

University of Yaounde 1 - Cameroon

Thesis: "Isolation of compounds with antiplasmodial activities from the trunk Bark of *Sterculia Tragacantha* (Sterculiaceae)"

BACHELOR OF SCIENCE IN CHEMISTRY — Oct 2011 - Jul 2015

University of Yaounde 1 - Cameroon

HIGH SCHOOL DIPLOMA — Sep 2004 - Jun 2011

High School Zoétélé - Cameroon

PUBLICATIONS

2. M. Hassan, **C. Ndefo Nde**, G. Manolikakes, (2021). Synthesis of Nitroolefins via the Direct Nitration of Alkenes, *SynOpen*, 5, 229-231.

1. M. Hassan, S.-C. Krieg, **C. Ndefo Nde**, J. Roos. T. J. Maier, E. A. El Rady, M. A. Raslan, K. U. Sadek, G. Manolikakes (2021). Streamlined One-Pot Synthesis of Nitro Fatty Acids *Eur. J. Org. Chem.* 2239. (Highlighted in Chemistry Views and Org. Chem. Highlights: Carbon-Carbon Bond Construction).

8 REFERENCES

[1] T. A. Baillie, *Angew. Chem. Int. Ed.,* **2016**, *55*, 13408-13421.

[2] A. K. Ghosh, I. Samanta, A. Mondal, and W. R. Liu, *ChemMedChem.,* **2019**, *14*, 889-906.

[3] A. Tuley, and W. Fast, *Biochemistry.,* **2018**, *57*, 3326-3337.

[4] P. A. Jackson, J. C. Widen, D. A. Harki, and K. M. Brummond, *J. Med. Chem.,* **2017**, *60*, 839-885.

[5] M. Gehringe, and S. A. Laufer, *J. Med. Chem.,* **2019**, *62*, 5673-5724.

[6] F. Sutanto, M. Konstantinidou, and A. Dömling, *RSC Med. Chem.,* **2020**, *11*, 876-884.

[7] I. M. Serafimova, M. A. Pufall, S. Krishnan, K. Duda, M. S. Cohen, R. L. Maglathlin, J. M. Mc Farland, R. M. Miller, M. Frödin, and J. Taunton, *Nat. Chem. Biol.,* **2012**, *8*, 471-476.

[8] R. M. Miller, V. O. Paavilainen, S. Krishnan, I. M. Serafimova, and J. Taunton, *J. Am. Chem. Soc.,* **2013**, *135*, 5298-5301.

[9] J. M. Bradshaw, J. M. McFarland, V. O. Paavilainen, A. Bisconte, D. Tam, V. T. Phan, S. Romanov, D. Finkle, J. Shu, V. Patel, T. Ton, X. Li, D. G. Loughhead, P. A. Nunn, D. E. Karr, M. E. Gerritsen, J. O. Funk, T. D. Owens, E. Verner, K. A. Brameld, R. J. Hill, D. M. Goldstein, and J. Taunton, *Nat. Chem. Biol.,* **2015**, *11*, 525-531.

[10] J. Y. Jang, H. Kim, H.-J. Kim, S. W. Suh, S. B. Park, and B. W. Han, *Sci. Rep.,* **2019**, *9*, 11168.

[11] H. Kim, A. Jo, S.-S. Choi, H. Nam, W. G. Byun, H. Bae, J. H. Choi, and S. B. Park, *Asian J. Org. Chem.,* **2019**, *8*, 1698-1706.

[12] D. Chen, D. Guo, Z. Yan, and Y. Zhao, *MedChemComm.,* **2018**, *9*, 244-253.

[13] C. Zambaldo, E. V. Vinogradova, X. Qi, J. Iaconelli, R. M. Suciu, M. Koh, K. Senkane, S. R. Chadwick, B. B. Sanchez, J. S. Chen, A. K. Chatterjee, P. Liu, P. G. Schultz, B. F. Cravatt, and M. J. Bollong, *J. Am. Chem. Soc.,* **2020**, *142*, 8972-8979.

[14] H. F. Motiwala, Y. H. Kuo, B. L. Stinger, B. A. Palfey, and B. R. Martin, *J. Am. Chem. Soc.,* **2020**, *142*, 1801-1810.

[15] A. Keeley, P. Ábrányi-Balogh, M. Hrast, T. Imre, J. Ilaš, S. Gobec, and G. M. Keserű, *Arch. Pharm.,* **2018**, *351*, 1800184.

[16] W. Chen, J. Dong, L. Plate, D. E. Mortenson, G. J. Brighty, S. Li, Y. Liu, A. Galmozzi, P. S. Lee, J. J. Hulce, B. F. Cravatt, E. Saez, E. T. Powers, I. A. Wilson, K. B. Sharpless, and J. W. Kelly, *J. Am. Chem*. *Soc.,* **2016**, *138*, 7353-7364.

[17] D. E. Mortenson, G. J. Brighty, L. Plate, G. Bare, W. Chen, S. Li, H. Wang, B. F. Cravatt, S. Forli, E. T. Powers, K. B. Sharpless, I. A. Wilson, and J. W. Kelly, *J. Am. Chem. Soc.,* **2018**, *140*, 200-21.

[18] G. J. Brighty, R. C. Botham, S. Li, L. Nelson, D. E. Mortenson, G. Li, C. Morisseau, H. Wang, B. D. Hammock, K. B. Sharpless, and J. W. Kelly, *Nat. Chem.,* **2020**, *12*, 906-913.

[19] R. Vicik, H. Helten, T. Schirmeister, and B. Engels, *ChemMedChem.,* **2006**, *1*, 1021-1028.

[20] H. Huang, C. A. Howard, S. Zari, H. J. Cho, S. Shukla, H. Li, J. Ndoj, P. González-Alonso, C. Nikolaidis, J. Abbott, D. S. Rogawski, M. A. Potopnyk, K. Kempinska, H. Miao, T. Purohit, A. Henderson, A. Mapp, J. Grembecka, T. Cierpicki *et al., Nat. Chem. Biol.,* **2020**, *16*, 1403-1410.

[21] J. M. Lopchuk, K. Fjelbye, Y. Kawamata, L. R. Malins, C.-M. Pan, R. Gianatassio, J. Wang, L. Prieto, J. Bradow, T. A. Brandt, M. R. Collins, J. Elleraas, J. Ewanicki, W. Farrell, O. O. Fadeyi, G. M. Gallego, J. J. Mousseau, R. Oliver, N. W. Sach, J. K. Smith, J. E. Spangler, H. Zhu, J. Zhu, and P. S. Baran, *J. Am. Chem. Soc.,* **2017**, *139*, 3209-3226.

[22] K. Tokunaga, M. Sato, K. Kuwata, C. Miura, H. Fuchida, N. Matsunaga, S. Koyanagi, S. Ohdo, N. Shindo, and A. Ojida, *J. Am. Chem. Soc.,* **2020**, *142*, 18522-18531.

[23] R. Ekkebus, S. I. van Kasteren, Y. Kulathu, A. Scholten, I. Berlin, P. P. Geurink, A. de Jong, S. Goerdayal, J. Neefjes, A. J. Heck, D. Komander, and H. Ovaa, *J. Am. Chem. Soc.,* **2013**, *135*, 2867-2870.

[24] E. Mons, I. D. C. Jansen, J. Loboda, B. R. van Doodewaerd, J. Hermans, M. Verdoes, C. A. A. van Boeckel, P. A. van Veelen, B. Turk, D. Turk, and H. Ovaa, *J. Am. Chem. Soc.,* **2019**, *141*, 3507-3514.

[25] R. A. Bauer, *Drug Discov. Today.,* **2015**, *20*, 1061-1073.

[26] R. Mah, J. R. Thomas, and Cynthia M. Shafer, *Bioorg. Med. Chem. Lett.,* **2014**, *24*, 33-39.

[27] G. J. Roth, N. Stanford, and P. W. Majerus, *Proc. Natl. Acad. Sci. USA*., **1975**, *72*, 3073-3076.

[28] D. M. Thomas, and J. R. Zalcberg, *Clin. Exp. Pharmacol. Physiol.,* **1998**, *25*, 887-895.

[29] P. V. Danenberg, R. J. Langenbach, and Charles Heidelberger, *Biochemistry.,* **1974**, *13*, 926-933.

[30] H. Xu, C. Faber, T. Uchiki, J. Racca, and Chris Dealwis, *Proc. Natl Acad. Sci. USA.,* **2006**, *103*, 4028-4033.

[31] V. Oldfield, G. M. Keating, and C. M. Perry, *Drugs.,* **2007**, *67*, 1725-1747.

[32] K. I. Hasegawa, Y. Akao, W. Maruyama, and M. Naoi, *J. Neural Transm.,* **2013**, *120*, 435-444.

[33] L. A. Honigberga, A. M. Smitha, M. Sirisawada, E. Vernera, D. Lourya, B. Changa, S. Lib, Z. Panb, D. H. Thamme, R. A. Millera, and J. J. Buggy, *Proc. Natl. Acad. Sci. U. S. A*., **2010**, *107*, 13075-13080.

[34] a) S. Dhillon, *Drugs.* **2020**, *80*, 835-840; b) *Ono Pharma USA's tirabrutinib receives orphan drug designation from the FDA for the treatment of primary central nervous system lymphoma.* News release. Ono Pharma, USA. March 23, **2023**. https://prn.to/40bAWcd.

[35] S. H. I. Ou, *Crit. Rev. Oncol. Hematol.,* **2012**, *83*, 407-421.

[36] G. Gomatou, N. Syrigos, and E. Kotteas, *Cancers.,* **2023**, *15*, 841.

[37] D. P. Rotelle, *Expert Opin. Drug Discov.,* **2013**, *8*, 1439-1447.

[38] A. D Kwong, R. S Kauffman, P. Hurter, and P. Mueller, *Nat. Biotechnol.,* **2011**, *29*, 993-1003.

[39] J. L Thompson, *Ann. Pharmacother.,* **2013**, *47*, 56-62.

[40] Y. Yao, W. Miao, Z. Liu, W. H, K. Shi, Y. Shen, H. Li, Q. Liu, Y. Fu, D. Huang, F. D. Shi, *Transl. Stroke Res.,* **2016**, *7*, 535-547.

[41] R. A. Linker, D. H. Lee, S. Ryan, A. M. van Dam, R. Conrad, P. Bista, W. Zeng, X. Hronowsky, A. Buko, S. Chollate, G. Ellrichmann, and R. Gold *et al., Brain.,* **2011***, 134,* 678-692.

[42] S. De Cesco, J. Kurian, C. Dufresne, A. K. Mittermaier, and N. Moitessier, *Eur. J. Med. Chem.,* **2017**, *138*, 96-114.

[43] H. Kim, Y. S. Hwang, M. Kim, and S. B. Park, *RSC Med. Chem.,* **2021**, *12*, 1037-1045.

[44] B.-F. Krippendorff, R. Neuhaus, P. Lienau, A. Reichel, and W. Huisinga, *J. Biomol. Screening.,* **2009**, *14*, 913-923.

[45] M. C. Noe, A. M. Gilbert, *Annu. Rep. Med. Chem.,* **2012**, *47*, 413 - 439.

[46] M. Forster, A. Chaikuad, S. M. Bauer, J. Holstein, M. B. Robers, C. R. Corona, M. Gehringer, E. Pfaffenrot, K. Ghoreschi, S. Knapp, and S. A. Laufer, *Cell. Chem. Biol.,* **2016**, *23*, 1335-1340.

[47] Faridoon, R. Ng, G. Zhang, and J. J. Li, *Med. Chem. Res.,* **2023**, *32*, 1039-1062.

[48] T. Schirmeister, J. Kesselring, S. Jung, T. H. Schneider, A. Weickert, J. Becker, W. Lee, D. Bamberger, P. R. Wich, U. Distler, S. Tenzer, P. Johe, U. A. Hellmich, and Bernd Engels, *J. Am. Chem. Soc.,* **2016**, *138*, 8332-8335.

[49] S. Jung, N. Fuchs, P. Johe, A. Wagner, E. Diehl, T. Yuliani, C. Zimmer, F. Barthels, R. A. Zimmermann, P. Klein, W. Waigel, J. Meyr, T. Opatz, S. Tenzer, U. Distler, H-J. Räder, C. Kersten, B. Engels, U. A. Hellmich, J. Klein, and T. Schirmeister, *J. Med. Chem.,* **2021**, *64*, 12322-12358.

[50] J. T. Palmer, D. Rasnick, J. L. Klaus, and Dieter Brömme, *J. Med. Chem.,* **1995**, *38*, 3193-3196.

[51] P. Y. Yang, M. Wang, C. Y. He, and S. Q. Yao, *Chem. Commun.,* **2012**, *48*, 835-837.

[52] I. D. Kerr, J. H. Lee, C. J. Farady, R. Marion, M. Rickert, M. Sajid, K. C. Pandey, C. R. Caffrey, J. Legac, E. Hansell, J. H. McKerrow, C. S. Craik, P. J. Rosenthal, and L. S. Brinen, *J. Biol. Chem.,* **2009***, 284,* 25697-25703.

[53] I. D. Kerr, P. Wu, R. Marion-Tsukamaki, Z. B. Mackey, and L. S. Brinen, *PLoS. Negl. Trop. Dis.,* **2010***, 4*, e701.

[54] R. Ettari, L. Tamborini, I. C. Angelo, N. Micale, A. Pinto, C. D. Micheli, and P. Conti, *J. Med. Chem.,* **2013**, *56*, 5637-5658.

[55] F. Solca, G. Dahl, A. Zoephel, G. Bader, M. Sanderson, C. Klein, O. Kraemer, F. Himmelsbach, E. Haaksma, and G. R. Adolf, *J. Pharmacol. Exp. Ther.,* **2012**, *343*, 342-350.

[56] H. Modjtahedi, B. C. Cho, M. C. Michel, and F. Solca, *Naunyn-Schmiedeberg's Arch. Pharmacol.,* **2014**, *387*, 505-521.

[57] M. A. S. Abourehab, A. M. Alqahtani, B. G. M. Youssif, and A. M. Gouda, *Molecules.,* **2021**, *26*, 6677.

[58] D. Y. Lin, and A. H. Andreotti, *PLoS ONE.,* **2023**, *18*, e0290872.

[59] J. C. Byrd, B. Harrington, S. O'Brien, J. A. Jones, A. Schuh, S. Devereux, J. Chaves, W. G. Wierda, F. T. Awan, J. R. Brown, P. Hillmen, D. M. Stephens, P. Ghia, J. C. Barrientos, J. M. Pagel, J. Woyach, Dave Johnson, J. Huang, X. Wang, A. Kaptein, B. J. Lannutti, T. Covey, M. Fardis, J. McGreivy, A. Hamdy, W. Rothbaum, R. Izumi, T. G. Diacovo, A. J. Johnson, and R. R. Furman, *N. Engl. J. Med.,* **2016**, *374*, 323-332.

[60] J. Singh, R. C. Petter, T. A. Baillie, and A. Whitty, *Nat. Rev. Drug Discov.,* **2011**, *10*, 307-317.

[61] T. Shimokawa, and W. L. Smith, *J. Biol. Chem.,* **1992**, *267*, 12387-12392.

[62] a) A. Fleming, *Br. Med. J.,* **1941**, *2*, 386. b) G. Nicola, J. Tomberg, R. F. Pratt, R. A. Nicholas, and C. Davies, *Biochemistry.,* **2010**, *49*, 8094-8104.

[63] D. J. Waxman, and J. L. Strominger, *Annu. Rev. Biochem*., **1983**, *52*, 825-869.

[64] S. Sato, F. Kudo, and T. Eguchi, *Meth. Enzymol*., **2022**, *669*, 45-70.

[65] J. M. Paris, *Comprehensive Chirality.,* **2012**, *1*, 30-53.

[66] A. S. Michalopoulos, I. G. Livaditis, and V. Gougoutas, *Int. J. Infect. Dis.,* **2011**, *15*, e732-e739.

[67] E. D. Brown, E. I. Vivas, C. T. Walsh, and R. Kolter, *J. Bacteriol.,* **1995**, *177*, 4194-4197.

[68] F. M. Kahan, J. S. Kahan, P. J. Cassidy, and H. Kropp, *Ann. NY Acad. Sci.,* **1974**, *235,* 364-386.

[69] A. C. Dijkmans, N. V. O. Zacarías, J. Burggraaf, J. W. Mouton, E. B. Wilms, C. V. Nieuwkoop, D. J. Touw, J. Stevens, and I. M. C. Kamerling, *Antibiotics.,* **2017**, *6*, 24.

[70] M. V. D. de Oliveira, R. M. Furtado, K. S. da Costa, S. Vakal, and Anderson H. Lima, *Front. Mol. Biosci.,* **2022**, *9*, 889825.

[71] J. Rautio, N. A. Meanwell, L. Di, and M. J. Hageman, *Nat. Rev. Drug Discov.,* **2018**, *17*, 559-587.

[72] L. Olbe, E. Carlsson, and P. Lindberg, *Nat. Rev. Drug.Discov.,* **2003***, 2,* 132-139*.*

[73] P Lindberg, P Nordberg, T Alminger, A Brändström, and B Wallmark, *J. Med. Chem.,* **1986**, *29*, 1327-1329.

[74] J. M. Shin, Y. M. Cho, and G. Sachs, *J. Am. Chem. Soc.,* **2004**, *126*, 7800-7811.

[75] K. Munson, R. Garcia, and G. Sachs, *Biochemistry.,* **2005**, *44*, 5267-5284.

[76] P. Savi, J. M. Pereillo, M. F. Uzabiaga, J. Combalbert, C. Picard, J. P. Maffrand et *al., Thromb. Haemost.,* **2000***, 84,* 891-896*.*

[77] Y. Zhu, and J. Zhou, *Chem. Res. Toxicol.,* **2013**, *26*, 179-190.

[78] M. H. Potashman, and M. E. Duggan, *J. Med. Chem.,* **2009**, *52*, 1231-1246.

[79] B. S. Greener, and D. S. Millan, Bortezomib (Velcade): A First-in-Class Proteasome Inhibitor, *Mod. Drug. Synth.,* **2010**, 99-110.

[80] a) Y. H. Wang, F. Zhang, H. Diao, and R. Wu, *ACS Catal.,* **2019**, *9*, 2292-2302. b) W. J. Metzler, J. Yanchunas, C. Weigelt, K. Kish, H. E. Klei, D. Xie, Y. Zhang, M. Corbett, J. K. Tamura, B. He, L. G. Hamann, M. S. Kirby, and J. Marcinkeviciene, *Protein Sci.,* **2008**, *17*, 240-250.

[81] L. Boike, N. J. Henning, and D. K. Nomura, *Nat. Rev. Drug Discov.,* **2022**, *21*, 881-898.

[82] L. Huang, Z. Guo, F. Wang, and L. Fu, *Signal. Transduct. Target. Ther.,* **2021**, *6*, 386.

[83] T. Barf and A. Kaptein, *J. Med. Chem.,* **2012**, *55*, 6243-6262.

[84] H. Rubbo, and R. Radi, Biochim. *Biophys. Acta BBA - Gen. Subj.,* **2008**, *1780*, 1318-1324.

[85] F. J. Schopfer, C. Cipollina, and B. A. Freeman, *Chem. Rev.,* **2011**, *111*, 5997-6021.

[86] P. R. S. Baker, F. J. Schopfer, V. B. O'Donnell and B. A. Freeman, *Free Radic. Biol. Med.,* **2009**, *46*, 989-1003.

[87] A. Trostchansky, and H. Rubbo, *Free Radic. Biol. Med.,* **2008**, *44*, 1887-1896.

[88] V. B. O'Donnell, J. P. Eiserich, P. H. Chumley, M. J. Jablonsky, N. R. Krishna, M. Kirk, S. Barnes, V.M. Darley-Usmar, and B. A. Freeman, *Chem. Res. Toxicol.,* **1999**, *12*, 83-92.

[89] M. D. Greenwood, K. S. Hughan, D. A. Vitturi, S. R. Salvatore, *et al., Free Radic. Biol. Med.,* **2015,** *89,* 333-341.

[90] M. Fazzari, A. Trostchansky, F. J. Schopfer, S. R. Salvatore, B. Sánchez-Calvo, D. Vitturi, R. Valderrama, J. B. Barroso, R. Radi, B. A. Freeman, *et al., PLoS ONE.,* **2014**, *9*, e84884.

[91] C. Batthyany, F. J. Schopfer, P. R. S. Baker, Rosario Durán, L. M. S. Baker, Y Huang, C. Cervenansky, B. P. Branchaud, and B. A. Freeman, *J. Biol. Chem.,* **2006**, *281,* 20450-20463.

[92] I. V. Maucher, M. Rühl, S. B. M. Kretschmer, B. Hofmann, B. Kühn, J. Fettel, A. Vogel, K. T. Flügel, G. Manolikakes, N. Hellmuth, A. K. Häfner, V. Golghalyani, A. K. Ball, M. Piesche, C. Matrone, G. Geisslinger, M. J. Parnham, M. Karas, D. Steinhilber, J. Roos, and Thorsten J. Maier, *Biochem. Pharmacol.,* **2017**, *125*, 55-74.

[93] T. Cui, F. J. Schopfer, J. Zhang, K. Chen, T. Ichikawa, P. R. S. Baker, C. Batthyany, B. K. Chacko, X. Feng, R. P. Patel, A. Agarwal, B. A. Freeman *et al., J. Biol. Chem.,* **2006**, *281,* 35686-35698.

[94] K. Awwad, S. D. Steinbrink, T. Frömel, N. Lill, J. Isaak, A. K. Häfner, J. Roos, B. Hofmann, H. Heide, G. Geisslinger, D. Steinhilber, B. A. Freeman, T. J. Maier, and I. Fleming, *Antioxid. Redox Signaling.,* **2014**, *20*, 2667-2680.

[95] E. Kansanen, G. Bonacci, F. J. Schopfer, S. M. Kuosmanen, K. I. Tong, H. Leinonen, S. R. Woodcock, M. Yamamoto, C. Carlberg, S. Y. Herttuala, B. A. Freeman, and A. L. Levonen, *J. Biol. Chem.,* **2011**, *286*, 14019-14027.

[96] M. J. Gorczynski, P. K. Smitherman, T. E. Akiyama, H. B. Wood, J. P. Berger, S. B. King, and C. S. Morrow, *J. Med. Chem.,* **2009**, *52*, 4631-4639.

[97] a) F. J. Schopfer, Y. Lin, P. R. S. Baker, T. Cui, M. G. Barrio, J. Zhang, K. Chen, Y. E. Chen, and Bruce A. Freeman, *PNAS.,* **2005**, *102,* 2340-2345. b) F. J. Schopfer, M. P. Cole, A. L. Groeger, C. S. Chen, N. K. H. Khoo, S. R. Woodcock, F. G. Bisello, U. N. Motanya, *et al., J. Biol. Chem.,* **2010**, *285*, 12321-12333.

[98] A. T. Reddy, S. P. Lakshmi, S. Dornadula, S. Pinni, D. R. Rampa, and R. C. Reddy, *J. Immunol.,* **2013**, *191*, 2053-2063.

[99] T. K. Rudolph, V. Rudolph, M. M. Edreira, M. P. Cole, G. Bonacci, F. J. Schopfer, S. R. Woodcock, A. Franek, M. Pekarova, *et al., Arterioscler. Thromb. Vasc. Biol.,* **2010**, *30*, 938-945.

[100] S. Borniquel, E. Å. Jansson, M. P. Cole, B. A. Freeman, and J. O. Lundberg, *Free Radic. Biol. Med.,* **2010**, *48*, 499-505.

[101] C. S. C. Woodcock, Y. Huang, S. R. Woodcock, S. R. Salvatore, B. Singh, F. G. Bisello, N. E. Davidson, C. A. Neumann, B. A. Freeman, and S. G. Wendell, *J. Biol. Chem.,* **2018**, *293*, 1120-1137.

[102] B. Kühn, C. Brat, J. Fettel, N. Hellmuth, I. V. Maucher, U Bulut, K. J. Hock, J. Grimmer, G. Manolikakes, M. Rühl, Thorsten J. Maier, *et al., Biochem. Pharmacol.,* **2018**, *155*, 48-60.

[103] P. R. S. Baker, Y. Lin, F. J. Schopfer, S. R. Woodcock, A. L. Groeger, C. Batthyany, S. Sweeney, M. H. Long, K. E. Iles, L. M. S. Baker, *et al., J. Biol. Chem.,* **2005**, *280*, 42464-42475.

[104] H. T. Dang, H. J. Lee, E. S. Yoo, P. B. Shinde, Y. M. Lee, J. Hong, D. K. Kim and J. H. Jung, *J. Nat. Prod.,* **2008**, *71*, 232-240.

[105] H. T. Dang, G. J. Kang, E. S. Yoo, J. Hong, J. S. Choi, H. S. Kim, H. Y. Chung and J. H. Jung, *Bioorg. Med. Chem.,* **2011**, *19*, 1520-1527.

[106] H. J. Lee, H. T. Dang, G. J. Kang, E. J. Yang, S. S. Park, W. J. Yoon, J. H. Jung, H. K. Kang, and E. S. Yoo, *Arch. Pharm. Res.,* **2009**, *32*, 453-462.

[107] N. K. H. **Khoo**, L. Li, S. R. Salvatore, F. J. Schopfer, and B. A. Freeman, *Sci. Rep.,* **2018**, *8,* 2295.

[108] *Comprehensive Organic Synthesis* 2nd Ed., Elsevier, Amsterdam, 838-998.

[109] a) P. Wipt and H. Jahn, *Tetrahedron.,* **1996**, *52*, 12853-12910; b) S. L. Buchwald, S. J. LaMaire, R. B. Nielsen, B. T. Watson, and S. M. King, *Org. Synth.,* **1993**, *71*, 77; c) *Handbook of Functionalized Organometallics: Applications in Synthesis,* Wiley-VCH, Weinheim, **2008**, 503- 540. d) D. Zhang, and J. M. Ready, *J. Am. Chem. Soc.,* **2007**, *129*, 12088-12089.

[110] S. M. Seo, J. Kim, S. H. Koh, Y. J. Ahn, and I. K. Park, *J. Agric. Food Chem.,* **2014**, *62*, 9103-9108.

[111] C. B. Hobuss, D. Venzke, B. S. Pacheco, A. O. Souza, M. A. Z. Santos, S. Moura, F. H. Quina, K. G. Fiametti, J. Vladimir Oliveira, and C. M. P. Pereira, *Ultrason. Sonochem.,* **2012**, *19*, 387-389.

[112] M. Miyashita, A. Yoshikoshi, and P. A. Grieco, *J. Org. Chem.,* **1977**, *42*, 3772-3774.

[113] R. C. Claussen, B. M. Rabatic, and S. I. Stupp, *J. Am. Chem. Soc.,* **2003**, *125*, 12680-12681.

[114] A. Ilangovan, K. Anandhan, and M. P. Kaushik, *Tetrahedron Lett.,* **2015**, *56*, 1080-1084.

[115] B. N. Rocke, K. B. Bahnck, M. Herr, S. Lavergne, V. Mascitti, C. Perreault, J. Polivkova, and A. Shavnya, *Org. Lett.,* **2014**, *16*, 154-157.

[116] N. Kornblum, W. J. Jones, and G. J. Anderson, *J. Am. Chem. Soc.,* **1959**, *81*, 4113-4114.

[117] D. B. Dess, and J. C. Martin, *J. Org.Chem.,* **1983**, *48*, 4155-4156.

[118] M. Nishizawa, H. Yamamoto, K. Seo, H. Imagawa, and T. Sugihara, *Org. Lett.,* **2002**, *4*, 1947-1949.

[119] D. P. Larson, and C. H. Heathcock, *J. Org. Chem.,* **1997**, *62*, 8406-8418.

[120] C. C. Fortes, and C. F. D. Garrote, *Synth. Commun.,* **1997**, *27*, 2993-3026.

[121] R. T. H. Linstadt, C. A. Peterson, D. J. Lippincott, C. I. Jette, and B. H. Lipshutz, *Angew. Chem. Int. Ed.,* **2014**, *53*, 4159 -4163.

[122] W. S. Fones, *J. Org. Chem.,* **1949**, *14*, 1099-1102.

[123] T. Narender, K. Venkateswarlu, G. Madhur, K. P. Reddy, *Synth. Commun.,* **2013**, *43*, 26-33.

[124] J. T. Reeves, K. Camara, Z. S. Han, Y. Xu, H. Lee, C. A. Busacca, and C. H. Senanayake, *Org. Lett.,* **2014**, *16*, 1196-1199.

[125] G. F. Pasha, S. Asghari, M. Tajbakhsh, and M. Mohseni, *Res. Chem. Intermed.,* **2017**, *43*, 7291-7306.

[126] R. Shen, T. Chen, Y. Zhao, R. Qiu, Y. Zhou, S. Yin, X. Wang, M. Goto, and L. B. Han, *J. Am. Chem. Soc.,* **2011**, *133*, 17037-17044.

[127] D. Kaldre, I. Klose, and N. Maulide, *Science.,* **2018**, *361*, 664-667.

[128] K. J. Hock, J. Grimmer, D. Göbel, G. G. T. Gasaya, J. Roos, I. V. Maucher, B. Kühn, J. Fettel, T.J. Maier, and G. Manolikakes, *Synthesis*., **2017**, *49*, 615-636.

[129] M. H. Kaspersen, L. Jenkins, J. Dunlop, G. Milliganb, and T. Ulven, *Med. Chem. Commun.,* **2017**, *8*, 1360-1365.

[130] K. Kanemoto, S. Yoshida, and T. Hosoya, *Org. Lett.,* **2019**, *21*, 3172-3177.

[131] K. Fujiki, N. Tanifuji, Y. Sasaki, and T. Yokoyama, *Synthesis*., **2002**, *3*, 343-348.

[132] M. Hassan, S. C. Krieg, C. N. Nde, J. Roos, T. J. Maier, E. A. El Rady, M. A. Raslan, K. U. Sadek, and G. Manolikakes, *Eur.J. Org.Chem.,* **2021**, 2239-2252.

[133] A. L. Garner, and K. D. Janda, *Angew. Chem. Int. Ed.,* **2010**, *49*, 9630 -9634.

[134] T. V. Hansen, and Y. Stenstrom, *Synth. Commun.,* **2000**, *30*, 2549-2557.

[135] N. A. Porter, and J. S. Wujek, *J. Org. Chem.,* **1987**, *52*, 5085-5089.

[136] K. Kai, J. Takeuchi, T. Kataoka, M. Yokoyama, and N. Watanabe, *Tetrahedron.,* **2008**, *64*, 6760-6769.

[137] J. F. Rontani, R. Amiraux, C. Lalande, M. Babin, H. R. Kim, and S. T. Belt, *Org. Geochem.,* **2018**, *124*, 88-102.

[138] R. Wang, V. J. Paul, H. Luesch, *Free Radic. Biol. Med.,* **2013**, *57*, 141-153.

[139] C. H. Clapp, S. E. Senchak, T. J. Stover, T. C. Potter, P. M. Findeis, and M. J. Novak, *J. Am. Chem. Soc.,* **2001**, *123*, 747-748.

[140] C. H. Clapp, M. Strulson, P. C. Rodriguez, R. Lo, and M. J. Novak, *Biochem*., **2006**, *45*, 15884-15892.

[141] H. Solanki, M. Pierdet, O. P. Thomas, and M. Zubia, *Metabolites.,* **2020**, *10*, 215.