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Streamlined One-Pot Synthesis of Nitro Fatty Acids

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In memory of Markus Gerhards.

A novel method for the synthesis of nitro fatty acids (NFAs), an intriguing class of endogenously occurring lipid mediators, is reported. This one-pot procedure enables the controlled and stereoselective construction of nitro fatty acids from a simple set of common building blocks in a highly facile manner. Thereby, this methodology offers a streamlined, highly modular access to naturally occurring nitro fatty acids as well as non-natural NFA derivatives.

Introduction

Nitro fatty acids (NFA), nitrated derivatives of unsaturated fatty acids, are highly potent, endogenously generated lipid mediators, with particular relevance in inflammatory processes.[1,2] NFAs are formed by the reaction of unsaturated fatty acids with reactive nitroxide-derived species.[3,4] Furthermore, Mediterranean diet has been identified as a direct and indirect source of NFAs.[5,6] These highly electrophilic nitrolefins can induce post-translational modifications of selected proteins by nitroalkylation of nucleophilic amino acids residues,[7] in particular cysteine thiols.[8] Thereby NFAs can modulate a number of different signaling pathways with relevance for both the induction and resolution of inflammation. NFAs haven been shown to target the peroxisome proliferator-activated receptor γ (PPAR-γ),[9] the pro-inflammatory nuclear factor-κB (NF-κB),[10] the nuclear factor (erythroid-derived 2)-like 2 pathway (Nrf2),[11] or 5-lipoxygenase (5-LO).[12,13] Their potent anti-inflammatory and cell-protective effects have already been demonstrated in several animal studies.[14,15] In addition, we and others have shown, that NFAs are promising candidates for the treatment of cancer.[16,17] In summary, NFAs have emerged as a class of Michael-acceptor containing compounds with a unique therapeutic potential, which is already under investigations in clinical phase II studies.[18]

In order to evaluate the full therapeutic potential of NFAs, it is mandatory to provide an efficient and straightforward synthetic access to both the most common nitro fatty acids, such as 9- or 10-nitrooleic acid (Figure 1), as well as to a whole array of different non-natural NFA analogues or probes.

In 2017 we reported a synthetic route towards NFAs from a simple set of common building blocks (Scheme 1).[19] This method provides a modular, regiospecific and stereoselective approach to (*E*)-nitroalkenoic acids. However, three separate reactions (including aq. work-up and chromatographic purification) are necessary to prepare a specific NFA from the four common starting materials. During the continuation of our studies, we quickly realized, that these three separate steps

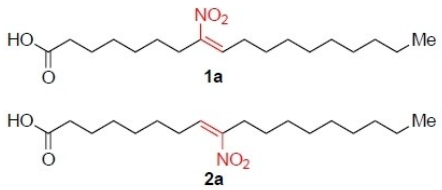
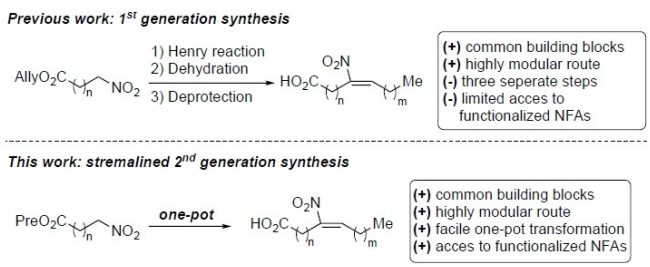


Figure 1. 9- and 10-Nitrooleic acid (**1a** and **2a**) containing an electrophilic nitroalkene unit (marked in red).



Scheme 1. 1st and 2nd generation NFA synthesis.

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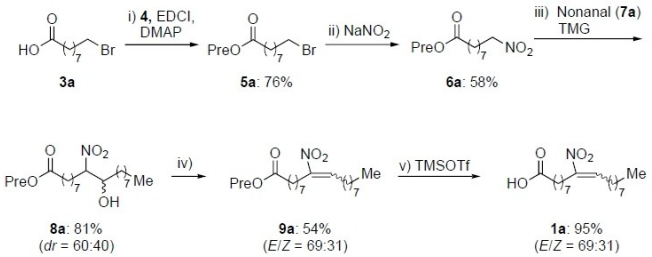
render the overall approach quite time-consuming and waste-intensive.

In addition, the initially selected allyl-protecting group strategy proved to be incompatible with the preparation of alkyne-modified NFA derivatives, valuable probes for biological studies. Preliminary experiments showed, that during the final palladium-catalyzed cleavage of the allyl protecting group, terminal alkynes are not tolerated. From this point of view, a process combining the last three steps from our first-generation route (Henry-reaction, dehydration and final deprotection) in a one-pot operation would greatly facilitate the synthesis of NFAs for further biological studies. Simultaneously, adjustment of the protecting group strategy could provide access to alkyne-labeled NFA-probes. Considering their intriguing therapeutic potential, such a streamlined approach for the synthesis of naturally occurring NFAs and non-natural NFA derivatives in a time- and resource-efficient manner would be highly desirable. Herein, we wish to report the development of a novel one-pot transformation for a streamlined, highly modular synthesis of NFAs. This process enables the direct synthesis of free NFAs from a simple set of four common building blocks and is compatible with side chain functionalities, such as an alkyne label.

Results and Discussion

We commenced our studies with an extensive literature survey of reported carboxylic acid protecting groups.[20] Based on our previously established Henry reaction-dehydration route, the ideal protecting group has to fulfill the following criteria. On the one hand it should be stable towards basic conditions. On the other hand, it should undergo a facile cleavage in the presence of a labile, highly electrophilic nitrolefin moiety. Ideally, the deprotection should be also compatible with additional terminal functionalities, e.g. an alkyne. Considering these aspects, we deemed the prenyl (Pre, 3-methylbut-2-en-1-yl) protecting group as ideal choice for our purposes. It can be easily introduced using readily available prenol (3-methyl-2-buten-1-ol), is stable towards (mild) bases and undergoes facile cleavage upon treatment with I_2, DDQ,[21] or acids[22–24] in the presence of other sensitive functional groups.

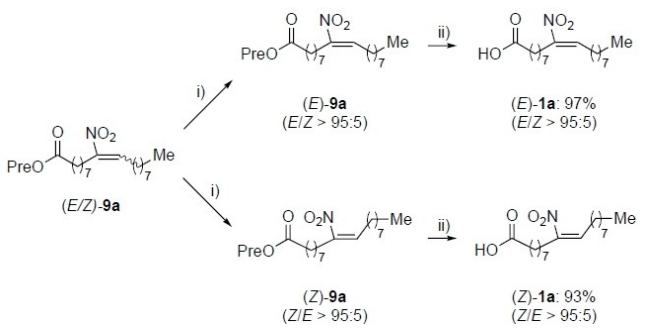
Therefore, we decided to investigate the incorporation of a prenyl protecting group into our previous established route (Scheme 2). Steglich esterification[25] of acid **3a** with prenol (**4**) provided the prenyl-protected acid derivative **5a** in 76% yield. Treatment of ester **5a** with $NaNO_2$ in PEG-400[26] furnished the nitroalkane building block **6a** in 58% yield. 1,1,3,3-Tetramethylguanidine (TMG) catalyzed Henry reaction of nitroalkane **6a** with nonanal (**7a**) afforded the addition product **8a** in 81% yield as mixture of two diastereomers (d.r. = 60:40). Dehydration of nitroalcohol **8a** with the Burgess reagent[27] furnished the prenyl protected 9-NOA **9a** in 54% yield and a *E*/*Z*-ration of 69:31. As in our previous route, the *syn*-specific Burgess dehydration enables an almost complete transfer of stereo-information from the nitroalcohol into the nitroolefin. Compared to the initial route based on an allyl-protecting group,



Scheme 2. Synthesis of 9-NOA (**1a**) using a prenyl protecting group. i) 3-methyl-2-buten-1-ol, EDCI, DMAP, CH_2Cl_2, 0 °C to 23 °C, 3 h; ii) $NaNO_2$, PEG-400, 23 °C, 18 h; iii) nonanal (**7a**) TMG, neat, 0 °C to 23 °C, 18 h; iv) Burgess reagent, benzene, 80 °C, 4 h; v) TMSOTf (3 mol%), CH_2Cl_2, 23 °C, 3 h. (Pre = 3-methylbut-2-en-1-yl; EDCI = 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide; DMAP = 4-Dimethylaminopyridine; TMG = 1,1,3,3-Tetramethylguanidine).

slightly longer reaction times were necessary for the dehydration of the prenyl protected nitro alcohol (4 h vs. 2 h). We assume, that the prolonged reaction times can lead to a partial isomerization towards the thermodynamically more stable *E*-isomer. Removal of the prenyl group proved to be quite facile. Treatment of ester **9a** with only 3 mol% of TMSOTf (TMS = trimethylsilyl)[24] afforded 9-NOA (**1a**) in 95% yield after only 3 h at ambient temperature. Contrary to our previous route, the mild cleavage of the prenyl group did not affect the stereo-integrtity of the nitroolefin moiety. No isomerization was observed and 9-NOA (**1a**) was obtained with an *E*/*Z* ratio of 69:31.

Until now, there has been no procedure for the direct synthesis of (*Z*)-9-NOA (***Z*-1a**) due to facile isomerization of the nitroolefin, either already during the dehydration step or in the final deprotection.[19,28] Only an indirect preparation of (*Z*)-9-NOA (***Z*-1a**) via a three-step isomerization of (*E*)-9-NOA (***E*-1a**) has been reported so far.[29,30] We envisioned, that our new route utilizing the prenyl protecting group might offer a direct access to the less stable (*Z*)-9-NOA isomer. Fortunately, we were able to separate both isomers of the nitroolefin ester **9a** by column chromatography. Treatment of pure (*E*)-**9a** with TMSOTf afforded stereochemically pure (*E*)-9-NOA ***E*-1a**) in 97% yield (Scheme 3). In a similar manner, the reaction of (*Z*)-**9a** lead to the formation of (*Z*)-9-NOA (***Z*-1a**) in 93% yield without isomer-



Scheme 3. Stereospecific access to (*E*)- and (*Z*)-9-NOA. i) separation; ii) TMSOTf (3 mol%), CH_2Cl_2, 23 °C, 3 h. (Pre = 3-methylbut-2-en-1-yl).

ization of the double bond. In conclusion, this represents the first method for a direct synthesis of (*Z*)-9-NOA (***Z*-1 a**). However, one has to emphasize, that for a truly stereoselective synthesis of (*Z*)-9-NOA, one still has to render the Henry reaction diastereoselective.

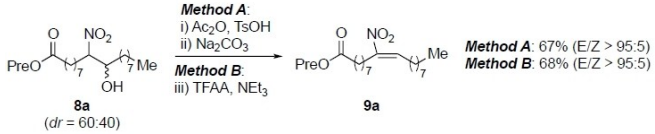
On the other hand, the complete (or partial) transfer of stereoinformation from the nitroalcohol into the final NFAs would be detrimental for our main goal, an efficient one-pot access to a defined product. From a medicinal chemist's point of view, the access to only one stereoisomer would be highly desirable.[31] Therefore, we decided to reinvestigate the dehydration of nitro alcohol **8 a** (Scheme 4). Dehydration via a two-step acetylation-elimination sequence[28,29] afforded exclusively the (*E*)-nitroolefin **9 a** in 67% yield. Dehydration with trifluoroacetic anhydride (TFAA) in the presence of triethylamine[32] provided the (*E*)-nitroolefin **9 a** with almost identical yield and diastereoselectivity. Prolonged reaction times proved to be crucial for the selective formation of the (*E*)-isomer in this case.

Since the TFAA-mediated dehydration takes place in a simple one-flask operation (compared two separate operation for the Ac_2O-route), we decided to proceed with this procedure. In order to evaluate the feasibility of our envisioned one-pot approach, we first investigated the merger of the Henry reaction with the dehydration step in a one-pot operation. Therefore, after dilution with CH_2Cl_2, TFAA and NEt_3 were added directly at 0 °C into the reaction vessel containing the mixture from the Henry reaction (Scheme 5). After warming to ambient temperature and stirring for 22 h, the desired (*E*)-configured nitroolefin **9 a** was obtained in 63% yield. These results show, that the first two out of three separate operations can be performed in a one-pot fashion. One has to emphasize, that the isolated yield for the sequential two-pot operation is slightly higher than the combined yield of the two separate transformations (63% vs. 55% overall yield, compare Scheme 2 and 4).[33]

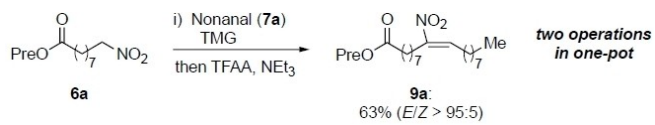
Finally, we turned our attention towards the incorporation of the final deprotection step into a one-pot operation. Therefore, we studied the direct addition of different acids after the Henry-reaction/dehydration sequence. Both the Henry reaction and the TFAA-mediated dehydration employ nitrogen-containing bases. The presence of these bases will certainly interfere in the final acid-catalyzed removal of the prenyl group. As expected, addition of TMSOTf, neither in catalytic nor stoichiometric amounts, afforded any free acid **1 a**. In a similar manner, addition of TFA or iodine proved to be unsuccessful.[21] To our delight, cleavage of the prenyl group was observed after treatment with 3.2 equivalents of $BF_3{\cdot}OEt_2$. Elevated temperatures (55–70 °C) were necessary for complete conversion of ester **9 a**. Therefore, we decided to switch to 1,2-dichloroethane (DCE) as solvent in the dehydration step. With this optimized deprotection procedure, we were able to synthesize (*E*)-9-NOA (**1 a**) in 62% yield directly from the two building blocks **6 a** and **7 a** in a straightforward, sequential one-pot transformation (Scheme 6).

With this streamlined procedure at hand, we were able to prepare four different terminal chain-length analogs of 9-nitro oleic acid within a short timeframe by variation of the aldehyde (Scheme 7). The C_{12}-, C_{14}-, C_{16}- and C_{20}-analouges **10 a**–**10 d** were synthesized in 50–61% yield in a single-flask operation from the common building block **6 a** and the corresponding aldehydes **7 b**–**7 e**. The desired (*E*)-configured NFAs were obtained with consistently high diastereoselectivities (E/Z ≥ 92:8).

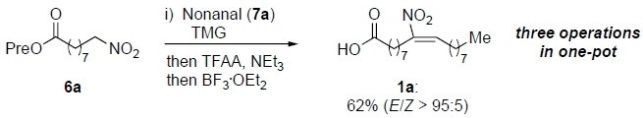
Afterwards we turned our attention to the synthesis of NFA derivatives, bearing a variation of the spatial distance between the carboxylic acid terminus and the nitroolefin acceptor. To this end, we prepared the six prenyl-protected building blocks



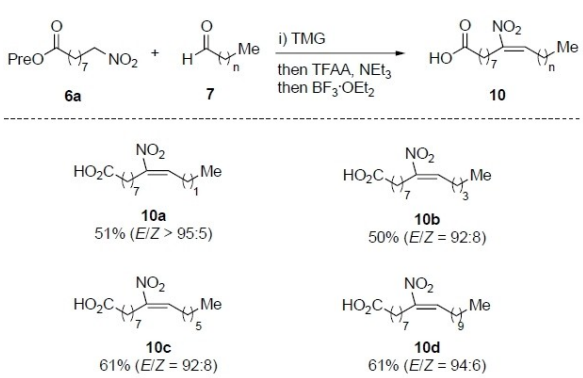
Scheme 4. Stereoselective access to (*E*)-**9 a**. i) Ac_2O, TsOH, neat, 23 °C, 16 h; ii) Na_2CO_3, toluene, 90 °C, 48 h; iii) TFAA, NEt_3, CH_2Cl_2, 0 °C to 23 °C, 22 h. (Pre = 3-methylbut-2-en-1-yl; TFAA = trifluoroacetic anhydride).



Scheme 5. One-pot synthesis of protected (*E*)-9-NOA (**9 a**). i) nonanal (**7 a**) TMG, neat, 0 °C to 23 °C, 18 h; then CH_2Cl_2, TFAA, NEt_3, 0 °C to 23 °C, 22 h: (Pre = 3-methylbut-2-en-1-yl; TMG = 1,1,3,3-Tetramethylguanidine; TFAA = trifluoroacetic anhydride).



Scheme 6. Sequential one-pot synthesis of (*E*)-9-NOA (**1 a**). i) nonanal (**7 a**), TMG, neat, 0 °C to 23 °C, 18 h; then DCE, TFAA, NEt_3, 0 °C to 23 °C, 22 h; then $BF_3{\cdot}OEt_2$, 70 °C, 16 h. (Pre = 3-methylbut-2-en-1-yl; TMG = 1,1,3,3-Tetramethylguanidine; TFAA = trifluoroacetic anhydride).

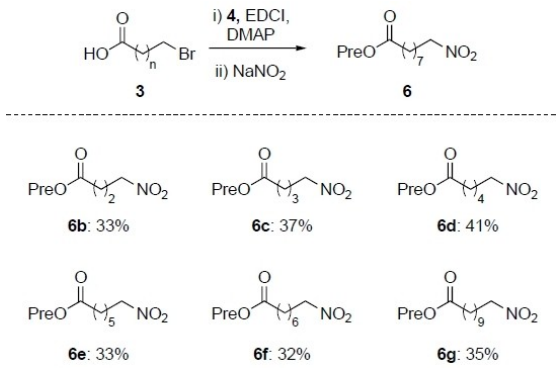


Scheme 7. One-pot synthesis of terminal chain-length analogs **10 a**–**10 d**. i) aldehyde **7**, TMG, neat, 0 °C to 23 °C, 18 h; then DCE, TFAA, NEt_3, 0 °C to 23 °C, 22 h; then $BF_3{\cdot}OEt_2$, 70 °C, 16 h. (Pre = 3-methylbut-2-en-1-yl; TMG = 1,1,3,3-Tetramethylguanidine; TFAA = trifluoroacetic anhydride).

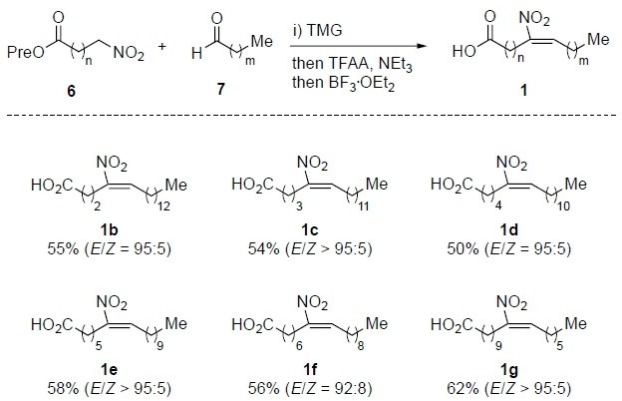
6b–**6g** in two steps from the corresponding bromoalkanoic acids **3a**–**3g** in 32–41% yield over two steps (Scheme 8).

(Pre = 3-methylbut-2-en-1-yl; EDCI = 1-Ethyl-3-(3-dimethylaminopropyl)-carbodiimide; DMAP = 4-Dimethylaminopyridine).

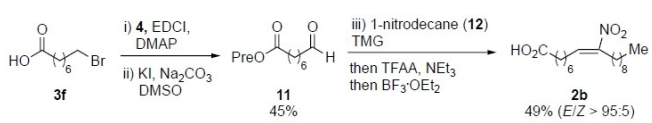
One-pot reaction of these building blocks with the appropriate aldehyde components (**7**) directly furnished the six different C-18 acids **1b**–**1g** bearing a nitroolefin acceptor unit in different positions within the aliphatic chain (Scheme 9). The



Scheme 8. Synthesis of 9-nitroalkanoic acid building blocks **6b**–**6g**. i) 3-methyl-2-buten-1-ol (**4**), EDCI, DMAP, CH_2Cl_2, 0 °C to 23 °C, 3 h; ii) $NaNO_2$, PEG-400, 23 °C, 18 h. Yields refer to overall isolated yield after two steps.



Scheme 9. One-pot synthesis of different C18-NFA analogues **1b**–**1g**. i) aldehyde **7**, TMG, neat, 0 °C to 23 °C, 18 h; then DCE, TFAA, NEt_3, 0 °C to 23 °C, 22 h; then $BF_3{\cdot}OEt_2$, 70 °C, 16 h. (Pre = 3-methylbut-2-en-1-yl; TMG = 1,1,3,3-Tetramethylguanidine; TFAA = trifluoroacetic anhydride).



Scheme 10. Synthesis of NFA **2b**. i) 3-methyl-2-buten-1-ol (**4**), EDCI, DMAP, CH_2Cl_2, 0 °C to 23 °C, 3 h; ii) KI, Na_2CO_3, THF/DMSO, 85 °C, 5 h; iii) 1-nitrodecane (**12**), TMG, neat, 0 °C to 23 °C, 18 h; then DCE, TFAA, NEt_3, 0 °C to 23 °C, 22 h; then $BF_3{\cdot}OEt_2$, 70 °C, 16 h. (Pre = 3-methylbut-2-en-1-yl; EDCI = 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide; DMAP = 4-Dimethylaminopyridine; TMG = 1,1,3,3-Tetramethylguanidine; TFAA = trifluoroacetic anhydride).

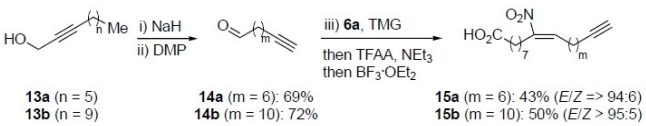
desired (*E*)-NFAs were obtained in 50–62% yield and high stereoselectivities ($E/Z \geq 92:8$).

In parallel, we studied the synthesis of a NFA analog containing the nitroolefin with the nitro group positioned towards the alkyl terminus. The required aldehyde building block **11** was prepared from the prenyl-protected bromoalkanoic acid **3f** via Kornblum oxidation[34] in 45% yield over two steps (Scheme 10). One-pot reaction of aldehyde **11** with 1-nitrodecane (**12**) afforded the desired NFA **2b** in 49% yield.

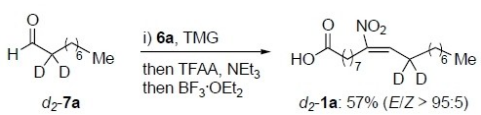
These twelve representative examples showcase the utility of our novel one-pot procedure for the streamlined production of NFAs with a great structural variety from a simple set of common building blocks. To further demonstrate the potential of our novel method, we decided to prepare several unnatural NFA derivatives. At first, we investigated the synthesis of two probes bearing a terminal alkyne label for further biological studies.[35] The required aldehydes **14a** and **14b** were prepared in 69% and 72% overall yield from the propargylic alcohols **13a** and **13b** via base-promoted isomerization[36] and oxidation with Dess-Martin-periodinane (DMP)[37] (Scheme 11). The labile alkyne aldehydes were directly converted into the desired alkyne-labeled NFAs **15a** and **15b** in 43% and 50% yield. As envisioned, facile cleavage of the prenyl group did not affected the terminal alkyne functionality.

As additional probe, a deuterated version of 9-NOA was synthesized. One-pot reaction of nonanal-*2,2-d*$_2$ (d_2-**7a**), prepared via base-mediated deuterium exchange from nonanal (**7a**),[38] afforded 9-NOA-*11,11-d*$_2$ (d_2-**1a**), a useful probe for mass spectrometric studies, in 57% yield (Scheme 12).

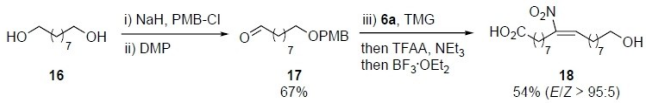
Furthermore, we decided to prepare a 9-NOA derivative bearing a polar hydroxy-terminus on the alkyl chain. Therefore, the *para*-methoxybenzyl (PMB) protected aldehyde **17** was synthesized in two steps from nona-1,9-diol (**16**) (Scheme 13).[39] One-pot reaction of aldehyde **17** with our common building block **6a** directly afforded 18-OH-9-NOA (**18**) in 54% yield. To our delight, concurrent cleavage of both the prenyl and the



Scheme 11. Synthesis of alkyne-labeled NFA **15a** and **15b**. i) NaH, ethylendiamine, 60 °C, 2 h; ii) DMP, CH_2Cl_2, 0 °C to 23 °C, 3 h; iii) **6a**, TMG, neat, 0 °C to 23 °C, 18 h; then DCE, TFAA, NEt_3, 0 °C to 23 °C, 22 h; then $BF_3{\cdot}OEt_2$, 70 °C, 16 h. Yields for compounds **14** refer to isolated overall yield after two steps. (DMP=Dess-Martin periodinane; TMG = 1,1,3,3-Tetramethylguanidine; TFAA = trifluoroacetic anhydride).



Scheme 12. Synthesis of deuterium-labeled 9-NOA (d_2-**1a**). i) **6a**, TMG, neat, 0 °C to 23 °C, 18 h; then DCE, TFAA, NEt_3, 0 °C to 23 °C, 22 h; then $BF_3{\cdot}OEt_2$, 70 °C, 16 h. (TMG = 1,1,3,3-Tetramethylguanidine; TFAA = trifluoroacetic anhydride).

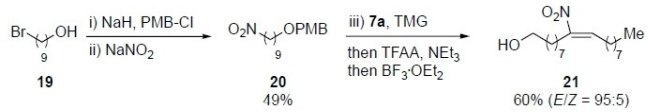


Scheme 13. Synthesis of 18-OH-9-NOA (**18**). i) NaH, PMB–Cl, nBu$_4$NI, THF, 0 °C to 23 °C, 21 h; ii) DMP, CH_2Cl_2, 0 °C to 23 °C, 3 h; iii) **16a**, TMG, neat, 0 °C to 23 °C, 18 h; then DCE, TFAA, NEt_3, 0 °C to 23 °C, 22 h; then $BF_3{\cdot}OEt_2$, 70 °C, 16 h. Yield for compounds **17** refers to isolated overall yield after two steps (PMB = *para*-methoxybenzyl; DMP=Dess-Martin periodinane; TMG = 1,1,3,3-Tetramethylguanidine; TFAA = trifluoroacetic anhydride).

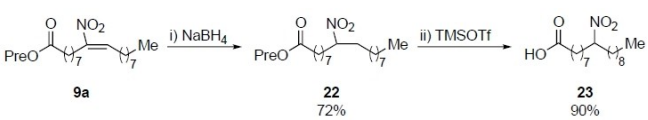
PMB protecting group occurred in the final step. The terminal OH-functionality cannot only alter the pharmacokinetic profile of this NFA derivative but might also serve as useful handle for further modifications of the alkyl side chain.

In a similar manner, a modified version of our one-pot approach was utilized for the construction of 9-nitrooleyl alcohol (**21**). Starting from 9-bromonona-1-ol (**19**) the PMB-protected nitroalcohol **20** was prepared in 49% yield over two steps (scheme 14). To our delight, this modified nitroalkane underwent a smooth one-pot reaction with nonanal (**7a**), furnishing the desired unprotected alcohol 9-nitrooleyl alcohol (**21**) in 60% yield.

With ample amounts of 9-NOA at hand, we turned our attention towards 9-nitrostearic acid (**23**) as control compound lacking the electrophilic nitroolefin moiety. As a selective reduction of the nitroolefin in free 9-NOA failed in our hands, we resorted to a modified route (Scheme 15). Chemoselective reduction of nitroalkenoic ester **9a** with $NaBH_4$ afforded protected nitrostearic acid (**22**) in 72% yield.[40] Removal of the prenyl group with TMSOTf furnished the desired free acid **23** in 90% yield.



Scheme 14. Synthesis of 9-Nitrololeyl alcohol (**21**). i) NaH, PMB–Cl, nBu$_4$NI, THF, 0 °C to 23 °C, 24 h; ii) $NaNO_2$, PEG-400, 23 °C, 18 h; iii) **7a**, TMG, neat, 0 °C to 23 °C, 18 h; then DCE, TFAA, NEt_3, 0 °C to 23 °C, 22 h; then $BF_3{\cdot}OEt_2$, 70 °C, 16 h. Yields for compounds **20** refers to isolated overall yield after two steps (PMB = *para*-methoxybenzyl; TMG = 1,1,3,3-Tetramethylguanidine; TFAA = trifluoroacetic anhydride).



Scheme 15. Synthesis of 9-nitrostearic acid (**23**). i) $NaBH_4$, THF/MeOH, 23 °C, 13 h; ii) ii) TMSOTf (3 mol%), CH_2Cl_2, 23 °C, 3 h. (Pre = 3-methylbut-2-en-1-yl).

Conclusion

In summary, we have developed a novel one-pot protocol for the synthesis of nitro fatty acids. This method provides a facile, highly modular and stereoselective access to a plethora of different natural and non-natural NFA-derivatives. By merging the last three steps (Henry reaction, condensation and final deprotection) into a sequential one-pot operation, various NFAs can be prepared in a highly streamlined manner from a simple set of common building blocks. The established prenyl-protecting group strategy offers the opportunity to prepare various useful probes, e.g. so far inaccessible alkyne-labeled NFAs. In addition, facile removal of the prenyl protecting group opens new possibilities for the direct synthesis of both configurational isomers of the key nitroolefin moiety. Therefore, our novel protocol will provide a highly enabling tool for the evaluation of the full therapeutic potential of nitro fatty acids.

Experimental Section

General Remarks

Experimental: Unless otherwise noted, all reactions were carried out without any precautions to exclude ambient air or moisture. All reactions including moisture- or air-sensitive reagents were carried out under a nitrogen atmosphere. Reaction solvents were dried by standard procedures prior to use when necessary. Thin layer chromatography (TLC) was performed on precoated aluminium sheets (TLC silica gel 60 F254). The spots were visualized by ultraviolet light, iodine, cerium ammonium molybdate (CAM) or $KMnO_4$. Regular column chromatography was performed with Silica 60 (0.04–0.063 mm, 230–400 mesh) and the specified solvent mixture. Flash column chromatography was performed using a puriflash XS 420+ Flash purifier machine from Interchim with prepacked flash colums (Puriflsh_Silica HP_15 μm_F0025 or Puriflsh_Silica HP_30 μm_F0025) and the respectively specified solvent mixture. All yields refer to isolated yields of compounds estimated to be > 95% pure as determined by 1H NMR.

Materials. Unless noted, all starting materials were purchased from different commercial sources and used without further purification. All solvents for reactions and flash column chromatography were obtained from commercial suppliers in p.a. purity and used as received.

Analytical Data and Instrumentation: Proton nuclear magnetic resonance spectra (^{1}H NMR) and carbon spectra (^{13}C NMR) were recorded at a frequency of 400 or 500 MHz (^{1}H) and 101 or 126 MHz (^{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). 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 spectra (MS) were measured using ESI (electrospray ionization) techniques. High resolution mass spectra (HRMS) were measured using electron ionization mass spectroscopy (EI-MS-TOF). Infrared spectra (IR) were recorded on a FT-IR (Fourier transform infrared spectroscopy) spectrometer including a diamond universal ATR sampling technique (attenuated total reflectance) from 4000–400 cm^{-1}. The absorption bands were reported in wave numbers (cm^{-1}). Melting points. Melting Points are uncorrected.

General procedures (GP)

GP1 (Prenyl proection)

A round bottom flask was charged with a magnetic stirring bar, bromoalkanoic acid **3** (1.0 equiv), 3-methyl-2-buten-1-ol **4** (2.0 equiv), DMAP (1.6 equiv) and CH_2Cl_2 (2 ml/mmol bromoalkanoic acid). The resulting mixture was cooled to 0 °C. Then EDCI·HCl (2.2 equiv) was added to the solution in small portions. The resulting solution was stirred for 30 min at 0 °C and then for 3 h at ambient temperature. Then the reaction mixture was diluted with H_2O (20 ml) and extracted with EtOAc (3×25 mL). The combined organic phases were washed with 1 M HCl (50 mL), H_2O (50 mL), sat. aq. NaCl (50 mL) and dried over Na_2SO_4. After concentration under reduced pressure, the crude residue was purified by flash column chromatography affording the desired analytically pure product.

GP2 (Nitration)

A round bottom flask was charged with a magnetic stirring bar, $NaNO_2$ (3.0 equiv) and PEG-400 (2 ml/mmol, 0.5 M). The resulting solution was stirred for 3 h at ambient temperature. Then alkyl bromide **5** (1.0 equiv) was added and the resulting solution was stirred at ambient temperature for 16 h. Then the reaction mixture was diluted with H_2O (20 ml) and extracted with Et_2O (25 ml). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the crude residue by flash column chromatography afforded the desired analytically pure product.

GP3 (One-Pot condensation-dehydration-deprotection)

A solution of nitroalkane (**6** or **12**, 1.0 equiv) and aldehyde (**7**, **11** or **14**, 1.2 equiv) was cooled at 0 °C and then TMG (0.2 equiv) was added. The reaction was stirred for 23 h at ambient temperature. Afterwards the reaction mixture was diluted with DCE (2 mL/mmol) and cooled to 0 °C. TFAA (1.5 equiv) and NEt_3 (3.0 equiv) were added and the reaction mixture was stirred first at 0 °C for 8 h and then at ambient temperature for 22 h. Afterwards $BF_3{\cdot}OEt_2$ (3.5 equiv) was added and the reaction mixture was stirred for 16 h at 70 °C. After cooling to ambient temperature H_2O (3 mL) was added and the resulting mixture was extracted with EtOAc (3× 5 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.

GP4 (DMP oxidation)

To an ice-cooled solution of the alcohol (***I–III***, 1.0 equiv) in CH_2Cl_2 (5 ml/mmol alcohol) Dess-Martin-Periodinan (1.5 equiv) was added. The resulting mixture was warmed to ambient temperature and stirred for 2 h. The reaction was quenched by adding 1:1 mixture of aq. sat. $NaHCO_3$ solution and aq. sat. $Na_2S_2O_3$ solution (60 mL). Then the mixture was extracted with EtOAc (3×60 mL). The combined organic phases were washed with H_2O (150 mL), sat. aq. NaCl (150 mL). After the combined organic phase was dried over sodium sulfate and concentrated, the residue was purified by silica column to afford the product.

Prenyl 9-Bromononanoate (5 a)

Prepared from 9-bromnonanoic acid **3 a** (1.0 equiv, 15.0 mmol, 3.56 g), 3-methyl-2-buten-1-ol **4** (2.0 equiv, 30.0 mmol, 3.0 ml), DMAP (1.6 equiv, 24.0 mmol, 2.93 g) and EDCI·HCl (2.2 equiv, 33.0 mmol, 6.32 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 (3.47 g, 76%). R_f: 0.69 (9:1 *n*-Hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.35–5.31 (m,1H), 4.56 (d, J = 7.2 Hz, 2H), 3.38 (t, J = 7.0 Hz, 2H), 2.28 (t, J = 7.5 Hz, 2H),1.87–1.79 (m, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.65–1.55 (m, 2H), 1.44–1.27 (m, 8H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.9, 139.0, 118.8, 61.3, 34.4, 34.0, 32.9, 29.1, 29.1, 28.8, 28.7, 25.9, 25.0, 18.1 ppm. IR (ν̃ in cm^{-1}): 2929 (m), 2856 (m), 1731 (s), 1700 (w), 1560 (w), 1555 (w), 1440 (w), 1378 (m), 1354 (w), 1304 (w), 1242 (m), 1231 (w), 1167 (m), 1116 (w), 1076 (w), 1066 (w), 1048 (w), 957 (m), 805 (w), 785 (w), 769 (w), 725 (w), 645 (w). MS (ESI) m/z calcd for $C_{14}H_{25}BrNaO_2$: 327.0 $[M+Na]^+$, found 327.1 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{14}H_{27}BrO_2$: 304.1038; found: 304.1036.

Prenyl 4-Bromobutanoate (5 b)

Prepared from 4-bromobutanoic acid **3 b** (1.0 equiv, 15.0 mmol, 2.50 g), 3-methyl-2-buten-1-ol **4** (2.0 equiv, 30.0 mmol, 3.0 ml), DMAP (1.6 equiv, 24.0 mmol, 2.93 g) and EDCI·HCl (2.2 equiv, 33.0 mmol, 6.32 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 (2.39 g, 68%). R_f: 0.59 (9:1 *n*-Hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.37–5.31 (m, J = 7.2 Hz, 1H), 4.58 (d, J = 7.2 Hz, 2H), 3.46 (t, J = 6.5 Hz, 2H), 2,50 (t, J = 14.7, 7.2 Hz, 2H), 2,17 (p, J = 14.7, 6.8 Hz, 2H), 1.76 (s, 3H), 1.71 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 172.7, 139.4, 118.5, 61.6, 32.8, 27.9, 25.9, 25.9, 18.1 ppm. IR (ν̃ in cm^{-1}): 2967 (m), 1728 (s), 1700 (w), 1439 (w), 1418 (w), 1378 (m), 1358 (w), 1279 (w), 1166 (w), 1128 (w), 951 (m), 775(w), 562 (w). MS (ESI) m/z calcd for $C_9H_{15}BrNaO_2$: 257.0 $[M+Na]^+$, found 257.1 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_9H_{15}BrO_2$: 234.0255; found: : 234.0254.

Prenyl 5-Bromopentanoate (5 c)

Prepared from 5-bromopentanoic acid **3 c** (1.0 equiv, 15.0 mmol, 2.71 g), 3-methyl-2-buten-1-ol **4** (2.0 equiv, 30.0 mmol, 3.0 ml), DMAP (1.6 equiv, 24.0 mmol, 2.93 g) and EDCI·HCl (2.2 equiv, 33.0 mmol, 6.32 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 (2.61 g, 70%). R_f: 0.60 (9:1 *n*-Hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.35–5.31 (m, J = 7.2 Hz, 1H), 4.56 (d, J = 7.2 Hz, 2H), 3.40 (t, J = 6.6 Hz, 2H), 2.33 (t, *J* = 7.3 Hz, 2H), 1.89 (dt, J = 14.7, 6.6 Hz, 2H), 1.81–1.76 (m, 2H), 1.75 (s, 3H), 1.70 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.6, 139.6, 118.9, 61.8, 33.9, 33.5, 32.3, 26.2, 23.9, 18.4 ppm. IR (ν̃ in cm^{-1}): 2935 (m), 1728 (s), 1700 (w),1444 (w), 1419 (w), 1378 (m), 1354 (w), 1329 (w), 1312 (w), 1291 (w), 1221 (w), 1168 (m), 1126 (w), 951 (m), 829 (w), 776 (w), 650 (w), 562 (w). MS (ESI) m/z calcd for $C_{10}H_{17}BrNaO_2$: 271.0 $[M+Na]^+$, found 271.1 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{10}H_{17}BrO_2$: 248.0412; found: 248.0422.

Prenyl 6-Bromohexanoate (5 d)

Prepared from 6-bromohexanoic acid **3 d** (1.0 equiv, 15.0 mmol, 2.92 g), 3-methyl-2-buten-1-ol **4** (2.0 equiv, 30.0 mmol, 3 ml), DMAP (1.6 equiv, 24.0 mmol, 2.93 g) and EDCI·HCl (2.2 equiv, 33.0 mmol,

6.32 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 (2.73 g, 70%). R_f: 0.62 (9:1 *n*-Hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.34–5.31 (m, J = 7.2 Hz, 1H), 4.56 (d, J = 7.2 Hz, 2H), 3.39 (t, J = 6.8 Hz, 2H), 2.31 (t, J = 7.4 Hz, 2H), 1.91–1.81 (m, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.67–1.60 (m, 2H), 1.51–1.42 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$): δ 173.6, 139.2, 118.7, 61.4, 34.2, 33.6, 32.5, 27.8, 25.9, 24.2, IR (ν̃ in cm^{-1}): 2935 (m), 2862 (m), 1731 (s), 1700 (w), 1441 (w), 1419 (w), 1378 (m), 1354 (w), 1252 (w), 1168 (m), 1126 (w), 969 (m), 829 (w), 776 (w), 645 (w), 563 (w). MS (ESI) m/z calcd for $C_{11}H_{19}BrNaO_2$: 285.0 $[M+Na]^+$, found 285.1 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{11}H_{19}BrO_2$: 262.0568; found: 262.0567.

Prenyl 7-Bromoheptanoate (5e)

Prepared from 7-bromoheptanoic acid **3e** (1.0 equiv, 15.0 mmol, 3.13 g), 3-methyl-2-buten-1-ol **4** (2.0 equiv, 30.0 mmol, 3 ml), DMAP (1.6 equiv, 24.0 mmol, 2.93 g) and EDCI·HCl (2.2 equiv, 33.0 mmol, 6.32 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 (2.82 g, 68%). R_f: 0.64 (9:1 *n*-Hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.34–5.32 (m, J = 7.2 Hz, 1H), 4.55 (d, J = 7.2 Hz, 2H), 3.38 (t, J = 6.8 Hz, 2H), 2.29 (t, J = 7.4 Hz, 2H), 1.89–1.79 (m, 2H), 1.75 (s, 3H), 1.69 (s, 3H), 1.67–1.57 (m, 2H), 1.48–1.27 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.8, 139.1, 118.8, 61.3, 34.3, 33.9, 32.6, 32.5, 28.3, 27.9, 25.9, 24.8, 18.1 ppm. IR (ν̃ in cm^{-1}): 2935 (m), 2859 (m), 1731 (s), 1682 (m), 1444 (w), 1419 (w),1378 (m), 1354 (w), 1275 (w), 1241 (m),1168 (m), 645 (w), 560 (w). MS (ESI) m/z calcd for $C_{12}H_{21}BrNaO_2$: 299.0 $[M+Na]^+$, found 299.1 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{12}H_{21}BrO_2$: 278.0704; found: 276.0711.

Prenyl 8-Bromooctanoate (5f)

Prepared from 8-bromooctanoic acid **3f** (1.0 equiv, 15.0 mmol, 3.34 g), 3-methyl-2-buten-1-ol **4** (2.0 equiv, 30.0 mmol, 3 ml), DMAP (1.6 equiv, 24.0 mmol, 2.93 g) and EDCI·HCl (2.2 equiv, 33.0 mmol, 6.32 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 (2.82 g, 71%). R_f: 0.66 (9:1 *n*-Hexane:EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.35–5.31 (m, J = 7.2 Hz, 1H), 4.55 (d, J = 7.2 Hz, 2H), 3.38 (t, J = 6.8 Hz, 2H), 2.28 (t, J = 7.4 Hz, 2H), 1.88–1.79 (m, 2H), 1.74 (s, 3H), 1.69 (s, 3H), 1.65–1.57 (m, 2H), 1.47–1.36 (m, 2H), 1.35–1.23 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.9, 139.1, 118.8, 61.3, 34.4, 33.9, 32.8, 29.0, 28.5, 28.1, 25.9, 24.9, 18.1 ppm. IR (ν̃ in cm^{-1}): 2932 (m), 2857 (m), 1731 (s), 1561 (w), 1551 (w), 1444 (w), 1378 (m), 1355 (w), 1235 (w), 1168 (m), 952 (m), 769 (w), 726 (w), 645 (w), 560 (w). MS (ESI) m/z calcd for $C_{13}H_{23}BrNaO_2$: 313.0 $[M+Na]^+$, found 313.1 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{13}H_{23}BrO_2$: 290.0881; found: 290.0886.

Prenyl 11-Bromoundecanoate (5g)

Prepared from 11-bromoundecanoic acid **3g** (1.0 equiv, 15.0 mmol, 3.97 g), 3-methyl-2-buten-1-ol **4** (2.0 equiv, 30.0 mmol, 3 ml), DMAP (1.6 equiv, 24.0 mmol, 2.93 g) and EDCI·HCl (2.2 equiv, 33.0 mmol, 6.32 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 (3.57 g, 72%). R_f: 0.68 (9:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.37–5.31 (m, J = 7.2 Hz, 1H), 4.56 (d, J = 7.2 Hz, 2H), 3.40 (t, J = 6.9 Hz, 2H), 2.29 (t, J = 7.6 Hz, 2H),1.89–1.80 (m, 2H), 1.76 (s, 3H), 1.71 (s, 3H), 1.65–1.56 (m, 2H), 1.45–1.26 (m, 12H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 174.1, 139.1, 118.8, 61.3, 34.5, 34.2, 32.9, 29.5, 29.4, 29.3, 29.2, 28.9, 28.3, 25.9, 25.1, 18.1 ppm. IR (ν̃ in cm^{-1}): 2926 (m), 2854 (m), 2158 (w), 2004 (w), 1728 (s), 1554 (w), 1444 (w), 1378 (m), 1354 (w), 1303 (w), 1242 (m), 1165 (m), 956 (m), 722 (w), 646 (w), 563 (w). MS (ESI) m/z calcd for $C_{16}H_{29}BrNaO_2$: 355.1 $[M+Na]^+$, found 355.2 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{16}H_{29}BrO_2$: 332.1351; found: 332.1358.

Prenyl 9-Nitrononanoate (6a)

Prepared from prenyl 9-bromononanoate **5a** (1.0 equiv, 5.0 mmol, 1.53 g), and $NaNO_2$ (3.0 equiv, 15.0 mmol, 1.03 g) according to GP2. Purification by flash column chromatography (*n*-Hexane:EtOAc = 50:1→20:1) afforded the desired analytically pure product as a colourless liquid (781 mg, 58%). R_f: 0.15 (9:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.36–5.30(m, 1H), 4.56 (d, J = 7.2 Hz, 2H), 4.37 (t, J = 7.0 Hz, 2H), 2.29 (t, J = 7.5 Hz, 2H), 2.04–1.92 (m, 2H), 1.76 (s, 3H), 1.70 (s, 3H), 1.66–1.57 (m, 2H), 1.41–1.28 (m, 8H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.9, 139.1, 118.8, 75.8, 61.4, 34.3, 29.1, 29.0, 28.9, 27.4, 26.2, 25.9, 24.9, 18.1 ppm. IR (ν̃ in cm^{-1}): 2930 (m), 2857 (m), 1729 (s), 1676 (w), 1560 (s), 1463 (w), 1441 (m), 1380 (m), 1352 (w), 1232 (w), 1167 (m), 1109 (w), 1048 (w), 958 (m), 775 (w). MS (ESI): m/z calcd for $C_{14}H_{25}NNaO_4$: 294.1 $[M+Na]^+$, found 294.2 $[M+Na]^+$ HRMS: m/z $[M+Na]^+$ calcd for $C_{14}H_{25}NNaO_4$: 294.1681; found: 294.1679.

Prenyl 4-Nitrobutanoate (6b)

Prepared from prenyl 4-bromobutanoate **5b** (1.0 equiv, 5.0 mmol, 1.17 g), and $NaNO_2$ (3.0 equiv, 15.0 mmol, 1.03 g) according to GP2. Purification by flash column chromatography (*n*-Hexane:EtOAc = 50:1→20:1) afforded the desired analytically pure product as a colourless liquid (492 mg, 49%). R_f: 0.10 (9:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.35–5.29 (m, 1H), 4.60 (d, J = 7.3 Hz, 2H), 4.48 (t, J = 6.7 Hz, 2H), 2.46 (t, J = 6.9 Hz, 2H), 2.35–2.28 (m, 2H), 1.76 (s, 3H), 1.71 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 172.0, 139.8, 118.3, 74.5, 61.9, 30.6, 25.9, 22.4, 18.2 ppm. IR (ν̃ in cm^{-1}): 3003 (m), 1727 (s), 1555 (w), 1437 (m), 1419 (w), 1382 (m), 1359 (w),1171 (m), 1221 (w), 955 (m), 735 (w). MS (ESI): m/z calcd for $C_9H_{15}NNaO_4$: 224.0 $[M+Na]^+$, found 224.1 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_9H_{15}NO_4$: 201.1001; found: 201.1013.

Prenyl 5-Nitropentanoate (6c)

Prepared from prenyl 5-bromopentanoate **5c** (1.0 equiv, 5.0 mmol, 1.24 g), and $NaNO_2$ (3.0 equiv, 15.0 mmol, 1.03 g) according to GP2. Purification by flash column chromatography (*n*-Hexane:EtOAc = 50:1→20:1) afforded the desired analytically pure product as a colourless liquid (570 mg, 53%). R_f: 0.16 (9:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.35–5.29 (m, 1H), 4.57 (d, J = 7.2 Hz, 2H), 4.39 (t, J = 6.9 Hz, 2H), 2.37 (t, J = 7.2 Hz, 2H), 2.09–2.01 (m, 2H), 1.75 (s, 3H), 1.73 (dt, *J* = 4.9, 2.1 Hz, 2H), 1.70 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.1, 139.9, 118.8, 75.6, 61.9, 33.7, 27.1, 26.2, 22.1, 18.4 ppm. IR (ν̃ in cm^{-1}): 2936 (m), 2919 (m), 1728 (s), 1678 (m), 1549 (w), 1437 (m), 1379 (m), 1239 (w), 1159 (w), 1086 (w), 949 (m), 775 (w). MS (ESI): m/z calcd for $C_{10}H_{17}NNaO_4$: 238.1 $[M+Na]^+$, found 238.2 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{10}H_{17}NO_4$: 215.1158; found: 215.1150.

Prenyl 6-Nitrohexanoate (6d)

Prepared from prenyl 6-bromohexanoate **5d** (1.0 equiv, 5.0 mmol, 1.31 g), and $NaNO_2$ (3.0 equiv, 15.0 mmol, 1.03 g) according to GP2.

Purification by flash column chromatography (*n*-Hexane:EtOAc = 50:1→20:1) afforded the desired analytically pure product as a colourless liquid (676 mg, 59%). R_f: 0.15 (9:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.33–5.27 (m, 1H), 4.54 (d, J = 7.2 Hz, 2H), 4.36 (t, J = 7.0 Hz, 2H), 2.30(t, J = 7.4 Hz, 2H), 2.05 - 1.95 (m, 2H), 1.73 (s, 3H), 1.68 (s, 3H), 1.67–1.60 (m, 2H), 1.40(tt, J = 10.1, 6.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.3, 139.3, 118.6, 75.5, 61.5, 33.9, 27.1, 25.8, 25.8, 24.2, 18.1 ppm. IR (ν̃ in cm^{-1}): 2933 (m), 2866 (m), 1728 (s), 1678 (m), 1549 (w), 1435 (m), 1378 (m), 1156 (w), 1049 (w), 966 (m), 738 (w). MS (ESI): m/z calcd for $C_{11}H_{19}NNaO_4$: 252.1 $[M+Na]^+$, found 252.2 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{11}H_{19}NO_4$: 229.1314; found: 215.1325.

Prenyl 7-Nitroheptanoate (6e)

Prepared from prenyl 7-bromoheptanoate **5e** (1.0 equiv, 5.0 mmol, 1.38 g), and $NaNO_2$ (3.0 equiv, 15.0 mmol, 1.03 g) according to GP2. Purification by flash column chromatography (*n*-Hexane:EtOAc = 50:1→20:1) afforded the desired analytically pure product as a colourless liquid (580 mg, 48%).

R_f: 0.17 (9:1 *n*-Hexane:EtOAc).ν^{1}H NMR (400 MHz, $CDCl_3$): δ 5.33–5.27 (m, 1H), 4.55 (d, J = 7.2 Hz, 2H), 4.36 (t, J = 7.0 Hz, 2H), 2.29(t, J = 7.4 Hz, 2H), 2.06 - 1.94 (m, 2H), 1.74 (s, 3H), 1.69 (s, 3H), 1.66–1.57 (m, 2H), 1.43–1.30 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.6, 139.2, 118.7, 75.6, 61.4, 34.1, 29.8, 28.7, 27.2, 25.9, 24.8, 18.1 ppm. IR (ν̃ in cm^{-1}): 2932 (m), 2862 (m), 1728 (s), 1678 (m), 1549 (w), 1462 (w), 1435 (m), 1379 (m), 1222 (w), 1172 (w), 1048 (w), 952 (m), 779 (w). MS (ESI): m/z calcd for $C_{12}H_{21}NNaO_4$: 266.1 $[M+Na]^+$, found 266.2 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{12}H_{21}NO_4$: 243.1471; found: 243.1462.

Prenyl 8-Nitrooctanoate (6f)

Prepared from prenyl 8-bromooctanoate **5f** (1.0 equiv, 5.0 mmol, 1.45 g), and $NaNO_2$ (3.0 equiv, 15.0 mmol, 1.03 g) according to GP2. Purification by flash column chromatography (*n*-Hexane:EtOAc = 50:1→20:1) afforded the desired analytically pure product as a colourless liquid (570 mg, 45%).

R_f: 0.18 (9:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.35–5.29 (m, 1H), 4.55 (d, J = 7.2 Hz, 2H), 4.36 (t, J = 7.0 Hz, 2H), 2.28(t, J = 7.5 Hz, 2H), 2.05 - 1.94 (m, 2H), 1.75 (s, 3H), 1.69 (s, 3H), 1.66–1.56 (m, 2H), 1.43–1.30 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.8, 139.1, 118.7, 75.7, 61.3, 34.3, 28.8, 28.6, 27.4, 26.1, 25.9, 24.8, 18.1 ppm. IR (ν̃ in cm^{-1}): 2932 (m), 2855 (m), 1728 (s), 1549 (w), 1462 (w), 1435 (w), 1379 (m), 1354 (w), 1222 (w), 1169 (m), 1095 (w), 953 (m), 728 (w). MS (ESI): m/z calcd for $C_{13}H_{23}NNaO_4$: 280.1 $[M+Na]^+$, found 280.2 $[M+Na]^+$ HRMS: m/z $[M+H]^+$ calcd for $C_{13}H_{23}NO_4$: 257.1627; found: 257.1644.

Prenyl 11-Nitroundecanoate (6g)

Prepared from prenyl 11-undecanoate **5g** (1.0 equiv, 5.0 mmol, 1.66 g), and $NaNO_2$ (3.0 equiv, 15.0 mmol, 1.03 g) according to GP2. Purification by flash column chromatography (*n*-Hexane:EtOAc = 50:1→20:1) afforded the desired analytically pure product as a colourless liquid (720 mg, 48%). R_f: 0.15 (9:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.36–5.30(m, 1H), 4.56 (d, J = 7.2 Hz, 2H), 4.37 (t, J = 7.1 Hz, 2H), 2.29 (t, J = 7.5 Hz, 2H), 2.05–1.96 (m, 2H), 1.76 (s, 3H), 1.71 (s, 3H), 1.65–1.57 (m, 2H), 1.41–1.25 (m, 12H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.9, 139.0, 118.7, 75.8, 61.3, 34.4, 29.3, 29.2, 29.2, 29.1, 28.9, 27.5, 26.3, 25.9, 25.0, 18.1 ppm. IR (ν̃ in cm^{-1}): 2926 (m), 2856 (m), 1731 (s), 1551 (w), 1464 (w), 1455 (w), 1451 (m), 1379 (m), 1354 (w), 1224 (w), 1168 (m), 976 (m), 776 (w), 723 (w). MS (ESI): m/z calcd for $C_{16}H_{29}NNaO_4$: 322.1 $[M+Na]^+$, found 322.2 $[M+Na]^+$ HRMS: m/z $[M+H]^+$ calcd for $C_{16}H_{29}NO_4$: 299.2097; found: 299.2085.

Prenyl-10-hydroxy-9-nitrooctadecanoat (8a)

1,1,3,3-tetramethylguanidine (0.2 equiv, 300 μmol, 38.4 μL) was added to a mixture of prenyl 9-nitrononanoate **6a** (1.0 equiv, 1.50 mmol, 407 mg) and nonanal **7a** (1.2 equiv, 1.8 μmol, 310 μL) at 0 °C. The reaction was stirred for 18 h at ambient temperature. The crude product was purified by flash column chromatography (*n*-Hexane:EtOAc = 50:1→19:1) to afford the desired analytically pure product as a yellow oil as a mixture of diastereoisomers (d.r. = 60:40) (499 mg, 81%). R_f: 0.17 (9:1 *n*-Hexane:EtOAc).^{1}H NMR (400 MHz, $CDCl_3$): δ 5.35 (m, 1H), 4.56 (d, J = 7.2 Hz, 2H), 4.48–4.38 (m, 1H), 4.04–3.81 (m, 1H), 2.29 (t, J = 7.5 Hz, 2H), 2.15–1.198 (m, 2H), 1.76 (s, 3H), 1.71 (s, 3H), 1.65–1.55 (m, 2H), 1.55–1.21 (m, 23H), 0.88 (t, J = 6.8 Hz, 3H). (Individual isomers could not be assigned.) ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.9, 139.2, 118.8, 92.9, 72.5, 61.4, 34.4, 33.8, 33.3, 31.9, 30.6, 29.6, 29.5, 29.3, 29.0, 28.9, 28.9, 28.0, 26.0, 25.9, 25.8, 25.6, 24.9, 22.8, 18.2, 14.2 ppm. IR (ν̃ in cm-1): 2924 (m), 2855 (m), 1732 (s), 1561 (s), 1461 (w), 1378 (m), 1270 (w), 1204 (w), 1171 (m), 1104 (w), 1059 (w), 978 (w), 959 (m), 772 (w), 724 (m). MS (ESI) m/z calcd for $C_{23}H_{43}NNaO_5$: 436.3 $[M+Na]^+$, found 436.4 $[M+Na]^+$. HRMS: m/z $[M+Na]^+$ calcd for $C_{23}H_{43}NNaO_5$: 436.3039; found: 436.3030.

(*E*- and *Z*-) -Prenyl-9-nitrooctadec-9-enoate (9a)

To a suspension of Burgess reagent (1.7 equiv, 1.80 mmol, 429 mg) in Benzene (4.5 mL) prenyl 10-hydroxy-9-nitrooctadecanoate **8a** (1.0 equiv, 1.06 mmol, 440 mg) was added and the mixture was stirred at 80 ° C for 4 h. The reaction was stopped by adding sat. aq. NH_4Cl solution and extracted with EtOAc (3×5 mL). The combined organic phases were dried over Na_2SO_4 and the solvent was removed under reduced pressure. Purification by flash column chromatography (*n*-Hexane:EtOAc = 50:1→19:1) afforded the desired product as a diastereoisomeric mixture (E/Z = 69:31) (223 mg, 54%). Careful purification of this mixture using the Interchim Flash purifier machine (*n*-Hexane: CH_2Cl_2 = 20:1→1:1) afforded the two analytically pure isomers (148 mg of ***E*-9a** and 74 mg of ***Z*-9a**).

(E)-Prenyl-9-nitrooctadec-9-enoat (E-9a)

R_f: 0.11 (1:1 *n*-Hexane:CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (t, J = 7.9 Hz, 1H), 5.41–5.26 (m, 1H), 4.56 (d, J = 7.2 Hz, 2H), 2.63–2.52 (m, 2H), 2.29 (t, J = 7.5 Hz, 2H), 2.21 (dd, J = 15.1, 7.6 Hz, 2H), 1.76 (s, 3H), 1.71 (s, 3H), 1.65–1.58 (m, 2H), 1.51–1.45 (m, 4H), 1.38–1.23 (m, 16H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): 173.9, 151.9, 139.1, 136.7, 118.8, 61.4, 34.4, 31.9, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 28.7, 28.2, 28.0, 26.5, 25.9, 25.1, 22.8, 18.2, 14.2 ppm. IR (ν̃ in cm^{-1}): 2925 (m), 2856 (m), 1733 (s), 1549 (w), 1520 (s), 1461 (w), 1376 (w), 1335 (m), 1273 (w), 1214 (w), 1167 (m), 1109 (w), 957 (m), 771 (w), 726 (m). MS (ESI) m/z calcd for $C_{23}H_{41}NNaO_4$: 418.3 $[M+Na]^+$, found 418.4 $[M+Na]^+$. HRMS: m/z $[M+Na]^+$calcd for $C_{23}H_{41}NNaO_4$: 418.2933; found: 418.2925.

(Z)-Prenyl-9-nitrooctadec-9-enoat (Z-9a)

R_f : 0.18 (1:1 *n*-Hexane: CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.67 (t, *J* = 7.4 Hz, 1H), 5.37–5.29 (m, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 2.49 (t, *J* = 7.4 Hz, 2H), 2.37–2.27 (m, 4H), 1.76 (s, 3H), 1.71 (s, 3H), 1.67–1.56 (m, 2H), 1.50–1.39 (m, 4H), 1.35–1.24 (m, 16H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.9, 151.3, 139.1, 132.1, 118.8, 61.4, 34.4, 32.9, 31.9, 29.4, 29.4, 29.3, 29.1, 29.1, 29.0, 28.9, 28.4, 27.3, 25.9, 25.0,

22.8, 18.2, 14.2 ppm. IR ($\tilde{\nu}$ in cm^{-1}): 2915 (m), 2849 (m), 1689 (s), 1514 (s), 1467 (w), 1434 (m), 1411 (w), 1335 (m), 1309 (m), 1274 (m), 1235 (m), 1201 (w), 1093 (w), 913 (m), 725 (m). MS (ESI) m/z calcd for $C_{23}H_{41}NNaO_4$: 418.3 $[M+Na]^+$, found 418.4 $[M+Na]^+$. HRMS: m/z $[M+Na]^+$calcd for $C_{23}H_{41}NNaO_4$: 418.2933; found: 418.2925.

(*E*)-Prenyl-9-nitrooctadec-9-enoat

Method A: Prenyl 10-hydroxy-9-nitrooctadecanoate **8a** (1.0 equiv, 817 µmol, 338 mg) and *p*-toluenesulfonic acid monohydrate (0.01 equiv, 8.17 µmol, 1.55 mg) were dissolved in Ac_2O and left for 16 h stirred at ambient temperature. The solvent was removed under reduced pressure and the acetic acid produced in the reaction was removed with toluene. The residue was dissolved in toluene (7.5 mL) without further purification. Molecular sieve (4 Å, 1.2 g) and Na_2CO_3 (1.0 equiv, 817 µmol, 86.6 mg) were added and the mixture was stirred at 90 ° C for 22 h. The reaction mixture was then filtered through silica gel and Celite, washed with EtOAc (30 mL). The solvent was removed under reduced pressure. Purification by column chromatography (*n*-Hexane: EtOAc = 50: 1→19: 1) afforded the product as a yellow oil (217 mg, 67%). Analytical data match those of the ***E*-9a** prepared above.

Method B: 1,1,3,3-Tetramethylguanidine (0.2 equiv, 332 µmol, 42.4 µL) was added to a solution of prenyl 9-nitrononanoate **6a** (1.0 equiv, 1.66 mmol, 450 mg) and nonanal **7a** (1.2 equiv, 1.99 mmol, 340 µL) at 0 °C and the mixture was stirred at ambient temperature for 23 h. The reaction mixture was then diluted with CH_2Cl_2 (6.5 mL) and cooled to 0 °C. Afterwards TFAA (1.5 equiv, 2.49 µmol, 350 µL) and NEt_3 (3.0 equiv, 4.98 mmol, 690 µL) were added and the mixture was stirred at ambient temperature for 22 h. The solvent was removed under reduced pressure. Purification of the crude product by flash column chromatography (*n*-Hexane: EtOAc = 19:1→9:1) afforded the desired analytically pure product as a yellow oil (411 mg, 63%). Analytical data match those of the ***E*-9a** prepared above.

(*E*)-9-Nitrooctadec-9-enoic Acid (*E*-1a)

Method A: A solution of (*E*)-prenyl-9-nitrooctadec-9-enoate **9a** (1.0 equiv, 533 µmol, 211 mg) and TMSOTf (2.9 µL, 16.0 µmol, 0.03 equiv) in CH_2Cl_2 (1.5 mL) was stirred for 3 h at ambient temperature. The solvent was then removed under reduced pressure. Purification of the crude product by flash column chromatography (*n*-Hexane:EtOAc + 0.5 vol% HOAc = 19:1→9:1) afforded the desired analytically pure product as a yellow oil (169 mg, 97%). Analytical data match those reported in the literature.[19]

Method B: Prepared from Prenyl-9-nitronanoat **6a** (1.0 equiv, 490 µmol, 133 mg), nonanal **7a** (1.2 equiv, 588 µmol, 101 µL), TMG (0.2 equiv, 98 µmol, 12.5 µL), TFAA (1.5 eq, 735 µmol, 102 µL), NEt_3 (3.0 equiv, 1.47 mmol, 204 µL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 µL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19:1→9:1) afforded the desired analytically pure product as a yellow oil (98 mg, 62%, E/Z > 95:5). Analytical data match those reported in the literature.[19]

R_f: 0.19 (9:1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (t, J = 7.9 Hz, 1H), 2.59–2.53 (m, 2H), 2.35 (t, J = 7.5 Hz, 2H), 2.21 (q, J = 7.6 Hz, 2H), 1.68–1.58 (m, 2H), 1.53–1.43 (m, 4H), 1.38–1.21 (m, 16H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.9, 151.9, 136.7, 34.1, 31.9, 29.8, 29.5, 29.4, 29.3, 29.2, 29.0, 28.7, 28.2, 27.9, 26.4, 24.7, 22.8, 14.2 ppm. MS (ESI) m/z calcd for $C_{18}H_{33}NNaO_4$: 350.2 $[M+Na]^+$, found 350.3 $[M+Na]^+$.

(*Z*)-9-Nitrooctadec-9-enoic Acid (1a)

A solution of (*Z*)-prenyl-9-nitrooctadec-9-enoate***Z*-9a** (1.0 equiv, 180 µmol, 71.4 mg) and TMSOTf (1.0 µL, 5.40 µmol, 0.03 equiv) in CH_2Cl_2 (0.5 mL) was stirred for 3 h at ambient temperature. The solvent was then removed under reduced pressure. Purification of the crude product by flash column chromatography (*n*-Hexane:EtOAc + 0.5 vol% HOAc = 19:1→9:1) afforded the desired analytically pure product as a yellow oil (54.9 mg, 93%). Analytical data match those reported in the literature.[29] R_f: 0.19 (9:1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.67 (t, J = 7.4 Hz, 1H), 2.50 (t, J = 7.4 Hz, 2H), 2.34 (dd, J = 13.9, 6,5 Hz, 4H), 1.62 (dd, J = 14.3, 7.1 Hz, 2H), 1.51–1.39 (m, 4H), 1.37–1.23 (m, 16H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.5, 151.3, 132.1, 33.9, 32.9, 31.9, 29.4, 29.3, 29.2, 29.1, 29.0, 28.9, 28.7, 28.4, 27.3, 24.7, 22.8, 14.2 ppm. MS (ESI) m/z calcd for $C_{18}H_{33}NNaO_4$: 350.2 $[M+Na]^+$, found 350.3 $[M+Na]^+$.

(*E*)-9-Nitrododec-9-enoic Acid (10a)

Prepared from Prenyl-9-nitronanoat **6a** (1.0 equiv, 490 µmol, 133 mg), propanal **7b** (1.2 equiv, 588 µmol, 43 µL), TMG (0.2 equiv, 98 µmol, 12.5 µL), TFAA (1.5 equiv, 735 µmol, 102 µL), NEt_3 (3.0 equiv, 1.47 mmol, 204 µL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 µL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19:1→9:1) afforded the desired analytically pure product as a yellow oil (61 mg, 51%, E/Z > 95:5). Analytical data match those reported in the literature.[19] R_f: 0.2 (9:1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06 (t, J = 7.9 Hz, 1H), 2.59–2.53 (m, 2H), 2.34 (t, J = 7.5 Hz, 2H), 2.24 (p, J = 7.6 Hz, 2H), 1.67–1.58 (m, 2H), 1.54–1.42 (m, 2H), 1.41–1.24 (m, 6H), 0.88 (t, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 180.2, 151.5, 137.8, 34.1, 29.1, 28.9, 27.9, 26.4, 24.7, 21.6, 13.2 ppm. MS (ESI) m/z calcd for $C_{12}H_{21}NNaO_4$: 266.1 $[M+Na]^+$, found 266.2 $[M+Na]^+$.

(*E*)-9-Nitrotetradec-9-enoic Acid (10b)

Prepared from Prenyl-9-nitronanoat **6a** (1.0 equiv, 490 µmol, 133 mg), pentanal **7c** (1.2 equiv, 588 µmol, 63 µL), TMG (0.2 equiv, 98 µmol, 12.5 µL), TFAA (1.5 equiv, 735 µmol, 102 µL), NEt_3 (3.0 equiv, 1.47 mmol, 204 µL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 µL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19:1→9:1) afforded the desired analytically pure product as a yellow oil (66 mg, 50%, E/Z = 92:8). Analytical data match those reported in the literature.[19] R_f: 0.2 (9:1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (t, J = 7.9 Hz, 1H), 2.60–2.53 (m, 2H), 2.35 (t, J = 7.5 Hz, 2H), 2.22 (dd, J = 15.0, 7.6 Hz, 2H), 1.70–1.58 (m, 2H), 1.54–1.42 (m, 4H), 1.41–1.24 (m, 8H), 0.88 (t, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 178.4, 151.9, 136.6, 33.8, 30.8, 29.2, 29.0, 27.9, 27.9, 26.5, 24.7, 22.6, 13.9 ppm. MS (ESI) m/z calcd for $C_{14}H_{25}NNaO_4$: 294.1 $[M+Na]^+$, found 294.2 $[M+Na]^+$.

(*E*)-9-Nitrohexadec-9-enoic Acid (10c)

Prepared from Prenyl-9-nitronanoat **6a** (1.0 equiv, 490 µmol, 133 mg), heptanal **7d** (1.2 equiv, 588 µmol, 79 µL), TMG (0.2 equiv, 98 µmol, 12.5 µL), TFAA (1.5 equiv, 735 µmol, 102 µL), NEt_3 (3.0 equiv, 1.47 mmol, 204 µL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 µL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19:1→9:1) afforded the desired analytically pure product as a yellow oil (90 mg, 61%, E/Z = 92:8). Analytical data match those reported in the literature.[19] R_f: 0.2 (9:1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz,

$CDCl_3$): δ 7.08 (t, J = 7.9 Hz, 1H), 2.60–2.53 (m, 2H), 2.35 (t, J = 7.5 Hz, 2H), 2.21 (dd, J = 15.1, 7.6 Hz, 2H), 1.69–1.57 (m, 2H), 1.54–1.42 (m, 4H), 1.39–1.24 (m, 12H), 0.88 (t, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 180.1, 151.9, 136.7, 34.1, 31.7, 29.1, 29.1, 29.0, 28.6, 28.2, 27.9, 26.4, 24.7, 22.6, 14.2 ppm. MS (ESI) m/z calcd for $C_{16}H_{29}NNaO_4$: 322.1 $[M+Na]^+$, found 322.2 $[M+Na]^+$.

(*E*)-9-Nitroicos-9-enoic Acid (10 d)

Prepared from Prenyl-9-nitrononaoat **6 a** (1.0 equiv, 490 μmol, 133 mg), undecanal **7 e** (1.2 equiv, 588 μmol, 122 μL), TMG (0.2 equiv, 98 μmol, 12.5 μL), TFAA (1.5 equiv, 735 μmol, 102 μL), NEt_3 (3.0 equiv, 1.47 mmol, 204 μL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 μL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19 : 1→9 : 1) afforded the desired analytically pure product as a yellow oil (98 mg, 61 %, E/Z = 94 : 6). Analytical data match those reported in the literature.[19] R_f: 0.18 (9 : 1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (t, J = 7.9 Hz, 1H), 2.59–2.53 (m, 2H), 2.34 (t, J = 7.5 Hz, 2H), 2.21 (q, J = 7.6 Hz, 2H), 1.65–1.60 (m, 2H), 1.51–1.44 (m, 4H), 1.33–1.25 (m, 20H), 0.87 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.6, 151.9, 136.7, 34.0, 32.0, 29.7, 29.6, 29.5, 29.4, 29.2, 29.0, 28.7, 28.2, 27.9, 26.5, 24.7, 22.8, 14.3 ppm. MS (ESI) m/z calcd for $C_{20}H_{37}NNaO_4$: 387.2 $[M+Na]^+$, found 387.3 $[M+Na]^+$.

(*E*)-4-Nitrooctadec-4-enoic Acid (1 b)

Prepared from prenyl 4-nitrobutanoate **6 b** (1.0 equiv, 490 μmol, 99 mg), tetradecanal **7 i** (1.2 equiv, 588 μmol, 150 μL), TMG (0.2 equiv, 98 μmol, 12.5 μL), TFAA (1.5 equiv, 735 μmol, 102 μL), NEt_3 (3.0 equiv, 1.47 mmol, 204 μL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 μL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19 : 1→9 : 1) afforded the desired analytically pure product as a yellow oil (88 mg, 55 %, E/Z = 95 : 5). Analytical data match those reported in the literature.[19] R_f: 0.2 (9 : 1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (t, J = 7.9 Hz, 1H), 2.91 (t, J = 7.5 Hz, 2H), 2.62 (t, J = 7.5 Hz, 2H), 2.28 (dd, J = 15.1, 7.6 Hz, 2H), 1.54–1.39 (m, 4H), 1.31–1.24 (m, 20H), 0.87 (t, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 177.9, 149.3, 139.1, 32.1, 29.8, 29.7, 29.7, 29.6, 29.5, 28.6, 28.3, 22.8, 21.8, 14.3. ppm. MS (ESI) m/z calcd for $C_{18}H_{33}NNaO_4$: 350.2 $[M+Na]^+$, found 350.3 $[M+Na]^+$.

(*E*)-5-Nitrooctadec-5-enoic Acid (1 c)

Prepared from prenyl 5-nitropentanoate **6 c** (1.0 equiv, 490 μmol, 105 mg), tridecanal **7 h** (1.2 equiv, 588 μmol, 140 μL), TMG (0.2 equiv, 98 μmol, 12.5 μL), TFAA (1.5 equiv, 735 μmol, 102 μL), NEt_3 (3.0 equiv, 1.47 mmol, 204 μL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 μL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19 : 1→9 : 1) afforded the desired analytically pure product as a yellow oil (86 mg, 54 %, E/Z > 95 : 5). Analytical data match those reported in the literature.[19] R_f: 0.2 (9 : 1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16 (t, J = 7.9 Hz, 1H), 2.69 - 2.63 (m, 2H), 2.42 (t, J = 7.2 Hz, 2H), 2.24 (dd, J = 15.1, 7.6 Hz, 2H), 1.89–1.80 (m, 2H), 1.55–1.41 (m, 2H), 1.36–1.25 (m, 20H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 178.3, 150.7, 137.9, 32.9, 32.1, 29.8, 29.8, 29.7, 29.6, 29.5, 28.6, 28.2, 25.7, 22.9, 22.8, 14.3 ppm. MS (ESI) m/z calcd for $C_{18}H_{33}NNaO_4$: 350.2 $[M+Na]^+$, found 350.4 $[M+Na]^+$.

(*E*)-6-Nitrooctadec-6-enoic Acid (1 d)

Prepared from prenyl 6-nitrohexanoate **6 d** (1.0 equiv, 490 μmol, 112 mg), dodecanal **7 f** (1.2 equiv, 588 μmol, 130 μL), TMG (0.2 equiv, 98 μmol, 12.5 μL), TFAA (1.5 equiv, 735 μmol, 102 μL), NEt_3 (3.0 equiv, 1.47 mmol, 204 μL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 μL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19 : 1→9 : 1) afforded the desired analytically pure product as a yellow oil (80 mg, 50 %, E/Z = 95 : 5). Analytical data match those reported in the literature.[19] R_f: 0.2 (9 : 1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12 (t, *J* = 7.9 Hz, 1 H), 2.63–2.58 (m, 2H), 2.38 (t, *J* = 7.3 Hz, 2 H), 2.22 (dd, J = 15.1, 7.6 Hz, 2H), 1.72–1.63 (m, 2 H), 1.60–1.25 (m, 20 H), 0.87 (t, *J* = 6.7 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.1, 151.3, 137.2, 33.7, 32.0, 29.7, 29.6, 29.5, 29.4, 29.3, 28.6, 28.2, 27.4, 26.2, 24.3, 22.8, 14.3 ppm. MS (ESI) m/z calcd for $C_{18}H_{33}NNaO_4$: 350.2 $[M+Na]^+$, found 350.3 $[M+Na]^+$.

(*E*)-7-Nitrooctadec-7-enoic Acid (1 e)

Prepared from prenyl 7-nitroheptanoate **6 e** (1.0 equiv, 490 μmol, 119 mg), Undecanal **7 e** (1.2 equiv, 588 μmol, 121 μL), TMG (0.2 equiv, 98 μmol, 12.5 μL), TFAA (1.5 equiv, 735 μmol, 102 μL), NEt_3 (3.0 equiv, 1.47 mmol, 204 μL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 μL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19 : 1→9 : 1) afforded the desired analytically pure product as a yellow oil (93 mg, 58 %, E/Z > 95 : 5). Analytical data match those reported in the literature.[19] R_f: 0.2 (9 : 1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10 (t, *J* = 7.9 Hz, 1 H), 2.61–2.53 (m, 2H), 2.36 (t, *J* = 7.4 Hz, 2 H), 2.21 (dd, J = 15.1, 7.6 Hz, 2H), 1.66 (dt, *J* = 15.1, 7.5 Hz, 2H), 1.55–1.46 (m, 4 H), 1.43–1.25 (m, 16 H), 0.88 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.8, 151.9, 137.3, 34.2, 32.3, 30.0, 29.9, 29.8, 29.8, 29.7, 29.1, 28.9, 28.5, 28.0, 26.6, 24.7, 23.1, 14.6 ppm. MS (ESI) m/z calcd for $C_{18}H_{33}NNaO_4$: 350.2 $[M+Na]^+$, found 350.3 $[M+Na]^+$.

(*E*)-8-Nitrooctadec-8-enoic Acid (1 f)

Prepared from prenyl 8-nitrooctanoate **6 f** (1.0 equiv, 490 μmol, 126 mg), decanal **7 f** (1.2 equiv, 588 μmol, 111 μL), TMG (0.2 equiv, 98 μmol, 12.5 μL), TFAA (1.5 equiv, 735 μmol, 102 μL), NEt_3 (3.0 equiv, 1.47 mmol, 204 μL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 μL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19 : 1→9 : 1) afforded the desired analytically pure product as a yellow oil (89 mg, 56 %, E/Z = 92 : 8). Analytical data match those reported in the literature.[19] R_f: 0.2 (9 : 1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (t, *J* = 7.9 Hz, 1H), 2.58–2.54 (m, 2H), 2.35 (t, *J* = 7.5 Hz, 3H), 2.21 (dd, *J* = 15.1, 7.6 Hz, 2H), 1.62 (dd, *J* = 14.5, 7.2 Hz, 3H), 1.52–1.43 (m, 4H), 1.29 (ddd, *J* = 21.1, 17.3, 9.7 Hz, 16H), 0.88 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.8, 151.8, 136.8, 34.0, 31.9, 29.6, 29.5, 29.5, 29.4, 29.0, 28.8, 28.7, 28.2, 27.9, 26.4, 24.6, 22.8, 14.2 ppm. MS (ESI) m/z calcd for $C_{18}H_{33}NNaO_4$: 350.2 $[M+Na]^+$, found 350.3 $[M+Na]^+$.

(*E*)-11-Nitrooctadec-11-enoic Acid (1 g)

Prepared from prenyl 11-nitroundecanoate **6 g** (1.0 equiv, 490 μmol, 147 mg), heptanal **7 d** (1.2 equiv, 588 μmol, 82 μL), TMG (0.2 equiv, 98 μmol, 12.5 μL), TFAA (1.5 equiv, 735 μmol, 102 μL), NEt_3 (3.0 equiv, 1.47 mmol, 204 μL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 μL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19 : 1→9 : 1) afforded the desired analytically pure product as a yellow oil (100 mg, 62 %, E/

Z > 95:5). Analytical data match those reported in the literature.[19] R_f: 0.2 (9:1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (t, *J* = 7.9 Hz, 1 H), 2.58–2.55 (m, 2H), 2.35 (t, *J* = 7.5 Hz, 2 H), 2.21 (dd, *J* = 15.1, 7.6 Hz, 2 H), 1.67–1.58 (m, 2 H), 1.52–1.42 (m, 4 H), 1.37–1.25 (m, 16 H), 0.89 (t, *J* = 6.9 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.6, 152.0, 136.6, 34.1, 31.7, 29.8, 29.4, 29.3, 29.3, 29.2, 28.6, 28.1, 28.0, 26.3, 24.8, 22.7, 14.2 ppm. MS (ESI) m/z calcd for $C_{18}H_{33}NNaO_4$: 350.2 $[M+Na]^+$, found 350.3 $[M+Na]^+$.

Prenyl 8-Oxooctanoate (11)

A flask was charged with prenyl 8-bromooctanoate **5f** (1.0 equiv, 10.3 mmol, 3.00 g), Na_2CO_3 (1.0 equiv, 10.3 mmol, 1.09 g), KI (1.0 equiv, 10.3 mmol, 1.70 g) and DMSO (50 ml) as a solvent. The resulting mixture was stirred at 85 °C for 5 h. After cooling to 0 °C, the mixture was extracted with Et_2O (3 × 30 ml) and washed with sat. aq Na_2CO_3 (50 ml), H_2O (50 ml), sat. aq. NaCl (50 mL) and dried over MgSO4. The solvent removed under reduced pressure. Purification of the crude residue by flash column chromatography (*n*-hexane:EtOAc 20:1→9:1) afforded the analytically pure product as a yellow liquid (1.46 g, 63%). R_f: 0.15 (9:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.74 (t, *J* = 1.7 Hz, 1H), 5.32 (t, *J* = 7.2 Hz, 1H), 4.55 (d, *J* = 7.2 Hz, 2H), 2.41 (td, *J* = 7.3, 1.7 Hz, 2H), 2.28 (t, *J* = 7.5 Hz, 2H), 1.74 (s, 3H), 1.69 (s, 3H), 1.62 (dq, *J* = 13.9, 7.1 Hz, 4H), 1.37–1.28 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 202.7, 173.7, 139.0, 118.7, 61.3, 43.8, 34.2, 28.9, 28.8, 25.8, 24.6, 21.9, 18.0 ppm IR ($\tilde{\nu}$ in cm^{-1}): 2931 (m), 1720 (m), 1700 (s), 1695 (m), 1684 (w), 1217 (m), 1206 (w). MS (ESI): m/z calcd for $C_{13}H_{22}NaO_3$: 249.1 $[M+Na]^+$, found 249.2 $[M+Na]^+$ HRMS: m/z $[M+H]^+$ calcd for $C_{13}H_{22}O_3$: 226.1569; found 226.1566.

(*E*)-9-nitrooctadec-8-enoic acid (2b)

Prepared from 1-Nitrodecane **12** (1.0 equiv, 592 μmol, 111 mg), Prenyl 8-Oxooctanoate **11** (1.2 equiv, 710 μmol, 161 mg), TMG (0.2 equiv, 118 μmol, 15.0 μL), TFAA (1.5 equiv, 888 μmol, 124 μL), NEt_3 (3.0 equiv, 1.77 mmol, 247 μL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 2.11 mmol, 260 μL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19:1→9:1) afforded the desired analytically pure product as a yellow oil (95 mg, 49%, E/Z = 95:5). Analytical data match those reported in the literature.[19] R_f: 0.16 (9:1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (t, *J* = 7.9 Hz, 1 H), 2.59–2.53 (m, 2H), 2.35 (t, *J* = 7.5 Hz, 2 H), 2.21 (dd, J = 15.1, 7.6 Hz, 2H), 1.66–1.60 (m, 2 H)1.48 (dd, *J* = 14.8, 7.4 Hz, 4H), 1.35–1.24 (m, 16 H), 0.87 (t, *J* = 6.7 Hz, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.8, 152.2, 136.1, 34.0, 31.9, 29.6, 29.4, 29.3, 29.1, 28.9, 28.5, 28.0, 26.5, 24.6, 22.8, 14.2 ppm. MS (ESI): m/z calcd for $C_{18}H_{33}NNaO_4$: 350.2 $[M+Na]^+$, found 350.3 $[M+Na]^+$.

Non-8-ynal (14a)

Non-8-yn-1-ol (***I***): Under inert atmosphere, NaH (60% in mineral oil, 8.3 equiv, 125 mmol, 1.99 g) was suspended in ethylendiamin (60 ml) at 0 °C under N_2. The suspension was slowly heated up to 60 °C and stirred for 1 h at this temperature. The mixture was cooled to 40 °C before non-2-yn-1-ol **13a** (1.0 equiv, 15 mmol, 2.5 mL) was added and stirred for 1 h at 60 °C. The reaction was quenched by carefully adding H_2O (75 ml) at 0 °C. The pH of the resulting mixture was adjusted to pH = 1 by adding HCl (1 M). Then the mixture was extracted with Et_2O (3 × 150 mL) and the combined organic phases were dried over Na_2SO_4. The solvent was removed under reduced pressure. Purification by flash column chromatography (*n*-Hexane:EtOAc = 50:1→20:1) afforded the desired analytically pure product as a colourless liquid (1.66 g, 79%). Analytical data match those reported in the literature.[36] R_f: 0.10 (9:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.61 (t, J = 6.6 Hz, 2H), 2.16 (td, J = 7.0, 2.6 Hz, 2H), 1.92 (t, J = 2.6 Hz, 1H), 1.59–1.47 (m, 4H), 1.43–1.27 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 84.8, 68.2, 62.9, 32.7, 28.9, 28.7, 28.4, 25.7, 18.4 ppm. MS (ESI): m/z calcd for $C_9H_{16}NaO$: 163.1 $[M+Na]^+$, found 163.2 $[M+Na]^+$.

Non-8-ynal (***14a***): Prepared from Non-8-yn-1-ol (1.0 equiv, 7.45 mmol, 1.04 g) and Dess-Martin-Periodinan (1.2 equiv, 8.88 mmol, 3.77 g) according to GP4. Purification by flash column chromatography (*n*-Hexane:EtOAc = 19:1→9:1) afforded the desired analytically pure product as a colourless liquid (720 mg, 69%). *Aldehyde **14a** is very unstable and was always used directly in the next step.* R_f: 0.59 (9:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.72 (t, *J* = 1.8 Hz, 1H), 2.40 (td, *J* = 7.3, 1.8 Hz, 2H), 2.14 (td, *J* = 7.0, 2.6 Hz, 2H), 1.91 (t, *J* = 2.6 Hz, 1H), 1.65–1.56 (m, 2H), 1.53–1.44 (m, 2H), 1.43–1.26 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 202.8, 84.5, 68.4, 43.8, 28.7, 28.5, 28.2, 21.9, 18.3 ppm. MS (ESI): m/z calcd for $C_9H_{14}NaO$: 161.0 $[M+Na]^+$, found 161.1 $[M+Na]^+$.

Tridec-12-ynal (14b)

Tridec-12-yn-1-ol (***II***): Under inert atmosphere, NaH (60% in mineral oil, 8.3 equiv, 125 mmol, 1.99 g) was suspended in ethylendiamin (40 ml) at 0 °C under N_2. The suspension was slowly heated up to 60 °C and stirred for 1 h at this temperature. The mixture was cooled to 40 °C before tri-2-yn-1-ol **13b** (1.0 equiv, 10 mmol, 1.96 g) was added and stirred for 1 h at 60 °C. The reaction was quenched by carefully adding H_2O (75 ml) at 0 °C. The pH of the resulting mixture was adjusted to pH = 1 by adding HCl (1 M). Then the mixture was extracted with Et_2O (3 × 150 mL) and the combined organic phases were dried over Na_2SO_4 and evaporated under reduced pressure. Purification of the crude residue by flash column chromatography (*n*-Hexane:EtOAc = 50:1→20:1) afforded the desired analytically pure product as a colourless liquid (1.66 g, 85%). Analytical data match those reported in the literature.[36] R_f: 0.12 (9:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.63 (t, *J* = 6.6 Hz, 2H), 2.17 (td, *J* = 7.1, 2.6 Hz, 2H), 1.93 (t, *J* = 2.6 Hz, 1H), 1.60–1.48 (m, 4H), 1.46–1.26 (m, 14H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 84.9, 68.2, 63.2, 32.9, 29.7, 29.6, 29.6, 29.5, 29.2, 28.9, 28.6, 25.9, 18.5 ppm. MS (ESI): m/z calcd for $C_{13}H_{24}NaO$: 219.1 $[M+Na]^+$, found 219.2 $[M+Na]^+$.

Tridec-12-ynal (***14b***)*:* Prepared from tridec-12-yn-1-ol **II** (1.0 equiv, 3.05 mmol, 600 mg) and Dess-Martin-Periodinan (1.2 equiv, 3.66 mmol, 1.55 g) according to GP4. Purification by flash column chromatography (*n*-Hexane:EtOAc = 19:1→9:1) afforded the desired analytically pure product as a colourless liquid (427 mg, 72%). *Aldehyde **14b** is very unstable and was always used directly in the next step.* R_f: 0.52 (9:1 n-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.76 (t, *J* = 1.8 Hz, 1H), 2.41 (td, *J* = 7.4, 1.7 Hz, 2H), 2.17 (td, *J* = 7.1, 2.6 Hz, 2H), 1.93 (t, *J* = 2.6 Hz, 1H), 1.67–1.57 (m, 2H), 1.55–1.47 (m, 2H), 1.42–1.25 (m, 12H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 202.8, 84.7, 68.0, 43.8, 29.3, 29.3, 29.2, 29.1, 29.0, 28.6, 28.4, 22.0, 18.3 ppm. MS (ESI): m/z calcd for $C_{13}H_{22}NaO$: 217.1 $[M+Na]^+$, found 217.2 $[M+Na]^+$.

(*E*)-9-nitrooctadec-9-en-17-ynoic acid (15a)

Prepared from Prenyl-9-nitronanoat **6a** (1.0 equiv, 490 μmol, 133 mg), non-8-ynal **14a** (1.2 equiv, 588 μmol, 82 mg), TMG (0.2 equiv, 98 μmol, 12.5 μL), TFAA (1.5 eq, 735 μmol, 102 μL), NEt_3 (3.0 equiv, 1.47 mmol, 204 μL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 μL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19:1→9:1) afforded the desired analytically pure product as a yellow oil (68 mg, 43%, E/Z =

94:6). R_f: 0.12 (9:1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06 (t, *J* = 7.9 Hz, 1H), 2.58–2.52 (m, 2H), 2.33 (t, *J* = 7.5 Hz, 2H), 2.24–2.15 (m, 4H), 1.93 (t, *J* = 2.6 Hz, 1H), 1.65–1.57 (m, 2H), 1.54–1.30 (m, 16H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 180.3, 151.9, 136.4, 84.5, 68.5, 34.1, 29.1, 28.9, 28.9, 28.8, 28.4, 28.3, 28.0, 27.9, 26.4, 24.6, 18.4. IR ($\tilde{\nu}$ in cm^{-1}): 3302 (w), 2930 (m), 2858 (m), 1785 (w), 1706 (s), 1558 (w), 1518 (s), 1465 (w), 1435 (m), 1414 (w), 1334 (m), 1284 (w), 1220 (w), 1173 (w), 931 (w), 726 (m). MS (ESI): m/z calcd for $C_{18}H_{29}NNaO_4$: 346.1 $[M+Na]^+$, found 346.2 $[M+Na]^+$ HRMS: m/z $[M+H]^+$ calcd for $C_{18}H_{29}NO_4$: 323.2097; found 323.2099.

(*E*)-9-nitrodocos-9-en-21-ynoic acid (15b)

Prepared from prenyl-9-nitrononanoat **6a** (1.0 equiv, 490 μmol, 133 mg), tridec-12-ynal **14b** (1.2 equiv, 588 μmol, 114 mg), TMG (0.2 equiv, 98 μmol, 12.5 μL), TFAA (1.5 eq, 735 μmol, 102 μL), NEt_3 (3.0 equiv, 1.47 mmol, 204 μL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 μL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19:1→9:1) afforded the desired analytically pure product as a yellow oil (93 mg, 50%, E/Z > 95:5). R_f: 0.13 (9:1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (t, *J* = 7.9 Hz, 1H), 2.59–2.53 (m, 2H), 2.38–2.15 (m, 8H), 1.94 (t, *J* = 2.6 Hz, 1H), 1.67–1.59 (m, 2H), 1.55–1.45 (m, 4H), 1.41–1.25 (m, 18H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.9, 151.9, 136.6, 84.9, 68.2, 34.0, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 28.9, 28.6, 28.5, 28.1, 27.9, 26.4, 24.7, 18.5. IR ($\tilde{\nu}$ in cm^{-1}): 3320 (w), 2930 (m), 2840 (m), 2140 (w), 1760 (w), 1706 (w), 1550 (w), 1464 (w), 1385 (w), 1173 (w), 933 (w), 725 (m). MS (ESI) m/z calcd for $C_{22}H_{37}NNaO_4$: 402.2 $[M+Na]^+$, found 402.3 $[M+Na]^+$. HRMS: m/z $[M - H]^-$ calcd for $C_{22}H_{36}NO_4$: 378.2644; found: 378.2652.

(*E*)-9-Nitrooctadec-9-enoic-11,11-d_2 acid (d_2-1a)

*Nonanal-2,2-d_2 (d_2-**7a**):* To a flamed-dried 25 mL flask equipped with a magnetic stirring bar was added under a N_2 atmosphere, nonanal **7a** (1.0 equiv, 5.81 mmol, 830 mg), D_2O (1.0 equiv, 54.9 mmol, 1 ml), DMAP (0.1 equiv, 0.581 mmol, 71 mg), and was heated to 100 °C for 1 h. Then CH_2Cl_2 (16 ml) and 1 M aq. HCl (4 ml) were added to the resulting mixture at ambient temperature. The layers were separated and the organic layers were then washed with sat. aq. $NaHCO_3$ (20 ml) and sat. aq. NaCl (20 ml), dried over MgSO4, filtered and concentrated carefully under reduced pressure. The resulting yellow oil was then re-subjected to the same reaction condition to afford nonanal-d_2 (d_2-**7a**).[38] The obtained crude Nonanal-d_2 d_2-**7a** was used directly in the next step without further purification.

*(E)-9-Nitrooctadec-9-enoic-11,11-d_2 acid (d_2-**1a**)* To a flamed-dried 10 mL flask was added d_2-**7a** (1.2 equiv, 588 μmol, 85 mg), prenyl-9-nitrononanoat **6a** (1.0 equiv, 490 μmol, 133 mg), TMG (0.2 equiv, 98 μmol, 12.5 μL), TFAA (1.5 eq, 735 μmol, 102 μL), NEt_3 (3.0 equiv, 1.47 mmol, 204 μL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 μL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19:1→9:1) afforded the desired analytically pure product as a yellow oil (92 mg, 57%, E/Z = 96:4). R_f: 0.18 (9:1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07 (s, J = 7.9 Hz, 1H), 2.59–2.53 (m, 2H), 2.34 (t, J = 7.5 Hz, 2H), 1.66–1.59 (m, 2H), 1.51–1.43 (m, 4H), 1.37–1.26 (m, 16H), 0.88 (t, J = 6.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 180.3, 151.9, 136.5, 34.1, 31.9, 29.4, 29.4, 29.3, 29.2, 29.1, 29.0, 28.5, 28.4, 27.9, 26.4, 24.7, 22.7, 14.2 ppm. IR ($\tilde{\nu}$ in cm^{-1}): 2926 (m), 2856 (m), 1735 (w), 1710 (s), 1701 (m), 1652 (w), 1544 (w), 1519 (s), 1462 (m), 1216 (w), 938 (w), 728 (m). MS (ESI) m/z calcd for $C_{18}H_{31}D_2NNaO_4$: 352.2 $[M+Na]^+$, found 352.3 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{18}H_{31}D_2NNaO_4$: 329.2535; found 329.2539.

9-((4-Methoxybenzyl)oxy)nonanal (17)

*9-((4-methoxybenzyl)oxy)nonan-1-ol (**III**)*: Under N_2 atmosphere, to a solution of 1,9-nonanediol **16** (3.0 equiv, 21.8 mmol, 3.5 g) in THF (45 mL), NaH (1.1 equiv, 8.0 mmol, 0.19 g, 60% in mineral oil) was added in multiple portions at 0 °C. The resulting suspension was stirred for 1 h at 0 °C. After addition of TBAI (0.1 equiv, 0.727 mmol, 0.26 g), PMBCl (1.0 equiv, 7.27 mmol, 1.02 mL) was added dropwise. The reaction mixture was warmed to ambient temperature and stirred for additional 18 h. After addition of sat. aq. NH_4Cl (25 ml), the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3×30 ml). The combined organic phases were washed with H_2O (3×50 ml) and sat. aq. NaCl (50 ml). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude residue by flash column chromatography (n-Hex:EtOAc = 19:1→9:1) afforded the desired analytically pure product as a white solid (1.7 g, 83%). Analytical data match those reported in the literature.[39] R_f: 0.3 (2:1 *n*-Hexane:EtOAc). Mp.: 32.5 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, J = 8.5 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.43 (s, 2H), 3.80 (s, 3H), 3.63 (t, *J* = 6.6 Hz, 2H), 3.43 (t, *J* = 6.6 Hz, 2H), 1.56 (td, *J* = 14.1, 6.9 Hz, 4H), 1.40–1.27 (m, 10H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 159.2, 130.9, 129.4, 113.9, 72.6, 70.3, 63.2, 55.4, 32.9, 29.9, 29.7, 29.6, 29.5, 29.4, 29., 26.3, 25.9 ppm. MS (ESI) m/z calcd for $C_{17}H_{28}NaO_3$: 303.1 $[M+Na]^+$, found 303.2 $[M+Na]^+$.

*9-((4-Methoxybenzyl)oxy)nonanal (**17**):* 9-((4-methoxybenzyl)oxy) nonan-1-ol ***III*** (1.0 equiv, 3.56 mmol, 1.03 g) in CH_2Cl_2 (18 mL) was treated with Dess-Martin-Periodinan (1.5 equiv, 5,34 mmol, 2,27 g) for 3 h at ambient temperature according to GP4. Purification by flash column chromatography (n-Hex:EtOAc = 19:1→9:1) afforded the desired analytically pure product as a colorless oil (870 mg, 89%). Analytical data match those reported in the literature.[39] *Aldehyde **17** is very unstable and was always used directly in the next step.* R_f: 0.6 (2:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.76 (t, *J* = 1.8 Hz, 1H), 7.25 (d, *J* = 4.7 Hz, 2H), 6.88 (d, *J* = 4.7 Hz 2H), 4.43 (s, 2H), 3.80 (s, 3H), 3.43 (t, *J* = 6.6 Hz, 2H), 2.41 (td, *J* = 7.4, 1.8 Hz, 2H), 1.64–1.55 (m, 4H), 1.30 (m, 8H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 203.1, 159.2, 130.9, 129.3, 113.8, 72.6, 70.2, 55.4, 55.3, 44.0, 29.8, 29.4, 29.3, 29.2, 26.2, 22.1 ppm. MS (ESI) m/z calcd for $C_{17}H_{26}NaO_3$: 301.1 $[M+Na]^+$, found 301.2 $[M+Na]^+$.

(*E*)-18-Hydroxy-9-nitrooctadec-9-enoic acid (18)

Prepared from prenyl-9-nitrononanoat **6a** (1.0 equiv, 490 μmol, 133 mg), 9-[(4-methoxybenzyl)oxy]nonanal **17** (1.2 equiv, 588 μmol, 82 mg), TMG (0.2 equiv, 98 μmol, 12.5 μL), TFAA (1.5 eq, 735 μmol, 102 μL), NEt_3 (3.0 equiv, 1.47 mmol, 204 μL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.71 mmol, 215 μL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19:1→9:1) afforded the desired analytically pure product as a yellow oil (91 mg, 54%, E/Z > 95:5). R_f: 0.13 (9:1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07 (t, *J* = 7.9 Hz, 1H), 4.35 (t, *J* = 6.7 Hz, 2H), 3.86–3.73 (m, 1H), 2.60–2.48 (m, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.21 (dd, *J* = 15.0, 7.6 Hz, 2H), 1.78–1.70 (m, 2H), 1.62 (dd, *J* = 14.3, 7.1 Hz, 2H), 1.53–1.43 (m, 4H), 1.33 (m, 14H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.9, 151.9, 136.4, 68.2, 34.0, 29.3, 29.3, 29.1, 29.0, 29.0, 28.6, 28.2, 28.1, 27.9, 26.4, 25.6, 24.7 ppm. IR ($\tilde{\nu}$ in cm^{-1}): 3585 (w), 2925 (m), 2855 (m), 1766 (w), 1667 (m), 1530 (m), 1462 (w), 1415 (w), 1216 (w), 935 (w), 725 (m). MS (ESI) m/z calcd for $C_{18}H_{33}NNaO_5$: 366.2 $[M+Na]^+$, found 366.3 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{18}H_{33}NO_5$: 343.2359; found 343.2362.

1-Methoxy-4-(((9-nitrononyl)oxy)methyl)benzene (20)

*1-(((9-Bromononyl)oxy)methyl)-4-methoxybenzene (**IV**)*: A solution of 9-bromononan-1-ol **19** (2.5 g, 11.2 mmol, 3.0 equiv) in THF (25 mL) was treated with NaH (164 mg, 4.1 mmol, 1.1 equiv, 60% in mineral oil) at 0 °C. Then TBAI (138 mg, 0.373 mmol, 0.1 equiv) and PMBCl (518 µL, 3.37 mmol, 1.0 equiv) were added. The mixture was warmed to ambient temperature and stirred for 20 h. Then the reaction was quenched by addition of sat. aq. NH_4Cl (15 ml). the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3×20 ml). The combined organic phases were washed with H_2O (3×50 ml) and sat. aq. NaCl (50 ml). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash column chromatography (n-Hex:EtOAc = 19:1→9:1) afforded the desired analytically pure product as a colorless oil (955 mg, 75%). Analytical data match those reported in the literature.[41]

R_f: 0.6 (9:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, J = 8.7 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.43 (s, 2H), 3.80 (s, 3H), 3.42 (dt, *J* = 11.7, 6.8 Hz, 4H), 2.07–1.27 (m, 14H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 159.2, 130.9, 129.4, 114.3, 113.9, 72.6, 70.3, 55.4, 34.2, 33.9, 32.9, 29.9, 29.5, 29.4, 29.2, 28.9, 28.8, 28.3, 26.3 ppm. MS (ESI) m/z calcd for $C_{17}H_{27}BrNaO_2$: 365.1 $[M+Na]^+$, found 365.2 $[M+Na]^+$.

*1-Methoxy-4-(((9-nitrononyl)oxy)methyl)benzene (**20**):* Prepared from 1-(((9-bromononyl)oxy)methyl)-4-methoxybenzene ***IV*** (1.0 equiv, 2.33 mmol, 800 mg), and $NaNO_2$ (3.0 equiv, 6.99 mmol, 482 mg) according to GP2. Purification by flash column chromatography (*n*-Hexane:EtOAc = 50:1→20:1) afforded the desired analytically pure product as a colourless liquid (355 mg, 49%). R_f: 0.35 (9:1 *n*-Hexane:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, J = 8.7 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.42 (s, 2H), 4.35 (t, *J* = 7.1 Hz, 2H), 3.79 (s, 3H), 3.42 (t, *J* = 6.6 Hz, 2H), 2.03–1.93 (m, 2H), 1.59 (td, *J* = 14.4, 7.1 Hz, 2H), 1.38–1.26 (m, 10H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 159.2, 130.9, 129.3, 113.8, 75.8, 72.6, 70.2, 55.4, 29.8, 29.4, 29.3, 28.9, 27.5, 26.3, 26.2 ppm. IR ($\tilde{\nu}$ in cm^{-1}): 2928 (m), 2851 (m), 1613 (w), 1568 (w), 1550 (m), 1512 (m), 1463 (w), 1361 (w), 1302 (w), 1244 (w), 1172 (w), 1078 (m), 1033 (w), 819 (m). MS (ESI) m/z calcd for $C_{17}H_{27}NNaO_4$: 332.1 $[M+Na]^+$, found 332.2 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{17}H_{27}NO_4$: 309.1940; found 309.1945.

(*E*)-9-Nitrooctadec-9-en-1-ol (21)

Prepared from 1-methoxy-4-(((9-nitrononyl)oxy)methyl)benzene **20** (1.0 equiv, 462 µmol, 143 mg), nonanal **7a** (1.2 equiv, 554 µmol, 78.9 mg), TMG (0.2 equiv, 92.4 µmol, 11.7 µL), TFAA (1.5 eq, 693 µmol, 96.4 µL), NEt_3 (3.0 equiv, 1.39 mmol, 193 µL) and $BF_3{\cdot}OEt_2$ (3.5 equiv, 1.62 mmol, 203 µL) according to GP3. Purification by flash column chromatography (*n*-Hexane:EtOAc + 0.5 Vol% HOAc = 19:1→9:1) afforded the desired analytically pure product as a yellow oil (87 mg, 60%, E/Z = 95:5). R_f: 0.12 (9:1 *n*-Hexane:EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (t, J = 7.9 Hz, 1H), 3.63 (t, J = 6.6 Hz, 2H), 2.65–2.49 (m, 2H), 2.21 (dd, J = 15.1, 7.6 Hz, 2H), 1.61–1.43 (m, 6H), 1.29 (d, J = 17.9 Hz, 18H), 0.88 (t, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 151.9, 136.6, 63.1, 32.9, 31.9, 29.5, 29.4, 29.4, 29.4, 29.3, 29.2, 28.7, 28.0, 26.0, 25.8, 22.8, 14.2 ppm. IR ($\tilde{\nu}$ in cm^{-1}): 2925 (m), 2855 (m), 1737 (w), 1666 (w), 1552 (w), 1519 (s), 1461 (m), 1425 (w), 1368 (w), 1334 (s), 1216 (w), 1057 (m), 1044 (w), 904 (w), 724 (m). MS (ESI) m/z calcd for $C_{18}H_{35}NNaO_3$: 336.2 $[M+Na]^+$, found 336.3 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{18}H_{35}NO_3$: 313.2617; found 313.2619.

Prenyl 9-nitrooctadecanoate (22)

To a solution of prenyl-9-nitrooctadec-9-enoate **9a** (80.9 mg, 205 µmol, 1.0 equiv) in a 9: 1 mixture of THF/MeOH (1 mL) $NaBH_4$ (10.0 mg, 256 mmol, 1.25 equiv) was added and stirred for 14 h at ambient temperature. Then H_2O was added, the reaction mixture was extracted with EtOAc (3×5 mL), dried over Na_2SO_4 and the solvent was removed under reduced pressure. After purification by column chromatography (*n*-Hexane: EtOAc = 50: 1→19: 1) the product was obtained as a colorless oil (58.7 mg, 72%). R_f: 0.53 (9:1 n-Hex: EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.39–5.28 (m, 1H), 4.56 (d, *J* = 7.2 Hz, 2H), 4.49–4.39 (m, 1H), 2.28 (t, *J* = 7.5 Hz, 2H), 2.00–1.89 (m, 2H), 1.75 (s, 3H), 1.70 (s, 3H), 1.68–1.55 (m, 4H), 1.38–1.22 (m, 22H), 0.87 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.9, 139.1, 118.8, 89.2, 61.4, 34.4, 34.1, 34.0, 31.9, 29.5, 29.4, 29.4, 29.1, 29.0, 28.9, 25.9, 25.9, 25.8, 25.0, 22.8, 18.1, 14.2 ppm. IR ($\tilde{\nu}$ in cm^{-1}): 2925 (m), 2857 (m), 1734 (s), 1549 (s), 1462 (m), 1453 (w), 1441 (w), 1378 (m), 1232 (m), 1207 (m), 1164 (m), 1115 (w), 971 (w), 951 (m), 724 (m). MS (ESI) m/z calcd for $C_{23}H_{43}NNaO_4$: 420.3 $[M+Na]^+$, found 420.3 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{23}H_{43}NO_4$: 420.3090; found 420.3092.

9-Nitrooctadecanoic acid (23)

A solution of prenyl 9-nitrooctadecanoate **22** (58.7 mg, 147 µmol, 1.0 equiv) and TMSOTf (10 µL, 5.88 µmol, 0.03 equiv) in CH_2Cl_2 (0.5 mL) was stirred for 3 h at ambient temperature. The solvent was then removed under reduced pressure and the crude product was purified by flash column chromatography (*n*-Hexane:EtOAc + 0.5 vol% HOAc = 19:1→9:1) to afford the desired analytically pure product as a yellowish oil (43.5 mg, 90%). R_f: 0.41 (9:1 *n*-Hexane: EtOAc + 0.5 Vol% HOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.47–4.40 (m, 1H), 2.28 (t, *J* = 7.5 Hz, 2H), 1.95–1.80 (m, 2H), 1.64–1.50 (m, 4H), 1.33–1.12 (m, 21H), 0.81 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 179.1, 89.2, 34.1, 34.0, 33.9, 31.9, 29.6, 29.5, 29.4, 29.1, 29.0, 28.9, 28.9, 25.9, 25.8, 24.7, 22.8, 14.2 ppm. IR ($\tilde{\nu}$ in cm^{-1}): 2925 (m), 2855 (m), 1707 (s), 1548 (s), 1460 (m), 1413 (w), 1362 (w), 1337 (w), 1279 (m), 1260 (w), 1214 (w), 1109 (w), 967 (w), 942 (m), 725 (m). MS (ESI) m/z calcd for $C_{18}H_{35}NNaO_4$: 352.2 $[M+Na]^+$, found 352.3 $[M+Na]^+$. HRMS: m/z $[M+H]^+$ calcd for $C_{18}H_{35}NO_4$: 329.2566; found 329.2568.

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Conflict of Interest

The authors declare no conflict of interest.

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