Modern dehydrogenative amination reactions.

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D 386

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Eidesstattliche Erklärung

Hiermit versichere ich, dass ich die vorliegende Arbeit eigenständig verfasst, keine anderen als die angegebenen Quellen und Hilfsmittel verwendet und Literaturzitate kenntlich gemacht habe. Ich erkläre außerdem, dass diese Arbeit weder in gleicher noch in ähnlicher Form bereits in einem anderen Prüfungsverfahren vorgelegen hat.

Kaiserslautern, den_____2015 _____

Marie-Laure Louillat Habermeyer

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Communication of results:

-M.-L. Louillat-Habermeyer, R. Jin, F. W. Patureau, *Angew. Chem. Int. Ed.* **2015**, *54*, 4102-4104.

O_2-mediated dehydrogenative amination of phenols.

-A. W. Jones, M.-L. Louillat-Habermeyer, F. W. Patureau, *Adv. Synth. Catal.* **2015**, DOI: 10.1002/adsc.201401136.

Strained dehydrogenative ring closure of phenyl-carbazoles.

-M.-L. Louillat, A. Biafora, F. Legros, F. W. Patureau, *Angew. Chem. Int. Ed.* **2014**, *53*, 3505-3509.

Ruthenium-Catalyzed Cross-Dehydrogenative *ortho*-N-Carbazolation of Diarylamines: Versatile Access to Unsymmetrical Diamines.

-M.-L. Louillat, F. W. Patureau, *Chem. Soc. Rev.* **2014**, *43*, 901-910.

Oxidative C-H amination reactions.

-M.-L. Louillat, F. W. Patureau, *Org. Lett.* **2013**, *15*, 164-167.

Towards polynuclear Ru-Cu catalytic dehydrogenative C-N bond formation, on the reactivity of carbazoles.

Abbreviations

Products and reagents:

acacH	Acetyl acetone
NFSI	*N*-fluorobenzenesulfonimide
NMO	*N*-methyl morpholine
TEMPO	(2,2,6,6-tetramethypiperidin-1-yl)oxy
TFA	Trifluoroacetic acid

Solvents:

DCE	1,2–Dichloroethane
DCM	Dichloromethane
DMF	*N*,*N*–Dimethylformamide
DMSO	Dimethylsulfoxide
EtOH	Ethanol
*i*PrPh	Cumene
MeCN	Acetonitrile
MeOH	Methanol
NMP	*N*-methyl-2-pyrrolidone
PhCl	Chlorobenzene
Py	Pyridine
THF	Tetrahydrofuran

Groups

AcO	Acetate
Ar	Aryl
Boc	*Tert*-butoxycarbonyle
Cp*	Pentamethylcyclopentadienyl
Cy	Cyclohexyl
Et	Ethyl

Abbreviations

*i*Pr	*Iso*-propyl
Me	Methyl
MeO	Methoxy
Mes	Mesityl
MesO	Mesityl sulfonate
Ph	Phenyl
Pyr	Pyridyl
*t*Bu	*tert*–butyl
TfO	Triflate
Tol	Tolyl

Characterization techniques

COSY	COrrelation SpectroscopY
EI	Electronic impact
ESI	ElectroSpray Ionization
GC	Gas chromatography
HMBC	Heteronuclear Multiple-Bond Correlation spectroscopy
HR	High resolution
IR	Infra–red
MS	Mass spectrometry
NMR	Nuclear Magnetic Resonance
TLC	Thin Layer Chromatography
TOF	Time Of Flight
UV	Ultra–violet
XRD	X–Ray Diffraction

Others

aq.	Aqueous
AUP	Area Under Peak
BZ	Benzoquinone

Abbreviations

EDG	Electro-Donating Group
eq.	Equivalent
EWG	Electro-Withdrawing Group
CDC(s)	Cross Dehydrogenative Coupling(s)
cat.	catalytic
DG	Directing Group
DNA	Deoxyribonucleic acid
h	Hour
HIV	Human Immunodeficiency Virus
min	Minute
Ox.	Oxidant
ppm	Parts per million
RT	Room temperature
S_EAr	Aromatic electrophilic substitution
δ	Chemical shift

The multiplicity of the signals is given by the following abbreviations:

s for singlet, d for doublet, dd for doublet of doublets, t for triplet, dt for doublet of triplets, q for quartet, and m for multiplet.

Structure Numbering.

The chemical structures of each chapter are numbered separately for clarity and readability.

Table of contents.

Foreword

Nitrogen element is preponderant in Nature. Found in its simplest form as diatomic gas in the air, as well as in elaborated molecules such as the double helix of DNA, this element is indisputably essential for life. Indeed, nitrogen is omnipresent in all metabolic pathways. For instance, this element in amino and nucleic acids allows 3D construction of protein thanks to the availability to create intermolecular forces such as Van der Waals or hydrogen bonding with the lone pair of nitrogen.

With the advent of green chemistry, researchers attempt to functionalize arenes without pre-functionalization of the later for the establishment of C-C bond formation. Why not C-N bond formation?

Chapter I:

Introduction on C-N bond formation by C-H activation.

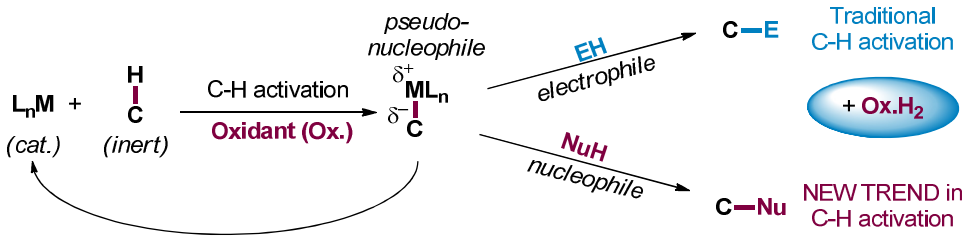
* M.-L. Louillat, and F. W. Patureau, *Chem. Soc. Rev.* **2014**, *43*, 901-910-Reproduced by permission of The Royal Society of Chemistry.
http://pubs.rsc.org/en/content/articlelanding/2014/cs/c3cs60318k#!divAbstract

1.1. Introduction.

With their discovery of copper catalyzed C-O and C-N bond formation from ubiquitous C(sp^2)-X organo-halide compounds, Ullmann and Goldberg[1,2] laid the foundations of modern cross-coupling reactions. Dated from 1905, this breakthrough established a general route to form highly relevant C-Heteroatom bonds in organic chemistry, in order to built natural molecules and bioactives targets containing nitrogen[3].

In the field of transitions metal catalyzed cross-coupling, the "Buchwald-Hartwig reaction" developed in the mid-1990s is now considered the state-of-the-art for the formation of C(sp^2)-N bonds[4,5]. This reaction based on Pd^0-Pd^{II} catalytic system, a bulky phosphine and a base allows the transformation of aromatic and vinylic C(sp^2)-X (X is a halide or pseudo-halide) into C(sp^2)-N in mild conditions for broad range of amines. Nevertheless, this useful and well described method may be narrow because it requires pre-activation of the substrates and tedious synthesis of phosphine ligands.

For a few years, the scientific community explores new strategies in cross-coupling such as direct functionalization by means of C-H bond activation[6-22]. This approach is interesting in terms of step and atom economy since it prevents the pre-activation of the C-H coupling partner. In most instances, the metallated intermediates, pseudo-nucleophilic is associated to an electrophile so as to form the corresponding C-E product (Scheme 1).



Scheme 1: Two ways in C-H activation cross-dehydrogenative coupling.

The emerging challenge is to build new C-N bond between C-nucleophile and *N*-nucleophile. This new trend has to overcome difficulties such as: (1) the C-N bond formation (energically demanding), (2) the pKa (acidity) narrowness on the nitrogen coupling partners, (3) the C-H activation reactivity and selectivity. Despite those challenges, the direct cross-dehydrogenative-amination of inert C(sp^2)-H is possible, by means of C-H activation.

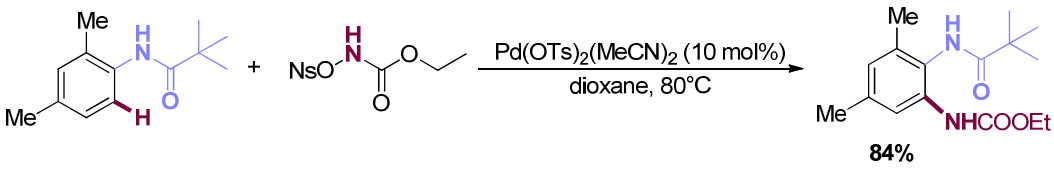
Our goal here is to inventory key reports that have appeared in this field of oxidative amination reactions by C-H activation. We expect that this new type of reactivity will find its place in the organic synthesis toolbox in the coming years such as Ullmann-Goldberg and Buchwald-Hartwig type reactions.

To show the potential of such technology, we will address the evolution of the C-H activation methods reported recently to form C-N bonds, their advantages and their limits. Firstly, we will detail systems that require electrophilic aminating reagents, and then move on to recent direct cross-dehydrogenative-couplings[23,24] amination methods (no pre-activation of either reacting partners). We will present representative examples of each class of reaction.

1.2. Pre-activated or pre-oxidized aminating agents for C-N bond formation reactions.

1.2.1. Usual pre-oxidized aminating agents: if the N-nucleophile is the problem, let us make it an electrophile.

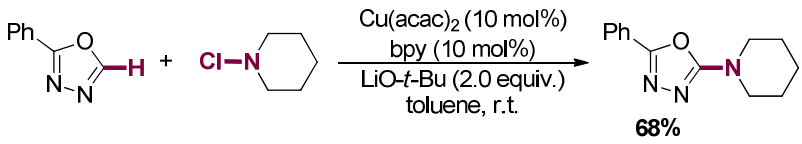
A strategy to form C-N bond from inert C(sp^2)-H and aminating agent is to transform *N*-nucleophile into *N*-electrophile. This straightforward transformation allows the attack of the (pseudo-nucleophilic) C-M metallated intermediate. It has the advantage of providing an "internal oxidant" for the reaction[25], allowing for milder and also more selective reaction conditions. However, the need remains for an extra-synthetic-step of pre-functionalization or pre-oxidation which is not in favour of step and atom economy. Usual pre-functionalizations such as *N*-carboxylates, *N*-tosylates or more often *N*-halides are common for this type of coupling.



Scheme 2: Wing-Yiu Yu's condensation of anilides on *N*-nosyloxycarbamate.

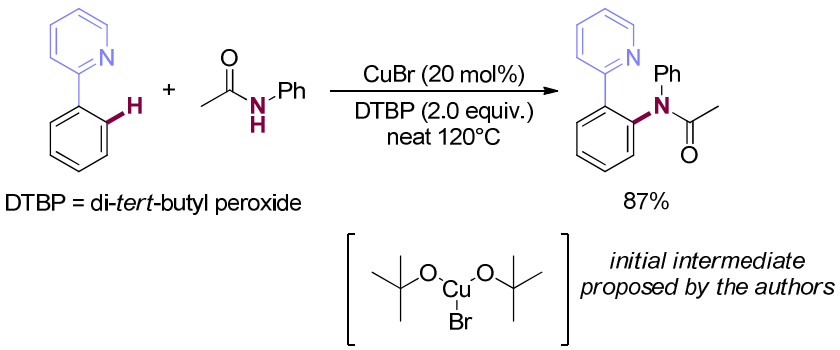
In 2010, Wing-Yiu Yu and his team reported the condensation of anilides on *N*-nosyloxycarbamates with palladium (II) to afford aminoanilines derivatives[26] (Scheme 2). This amination reaction is guided by a chelating directing group in the *ortho*-position. Although the synthesis of starting *N*-nosyloxycarbamates requires two steps, this reaction constitutes a breakthrough to consider for C-N bond formation.

The same year, Miura *et al.* reported an amination reaction catalytic in copper (II). The team condensed 1,2,3-oxadiazole derivatives on chloroamines at room temperature and in presence of base[27-30] (Scheme 3). It is noteworthy that the "labile-acidic" C-H positions in five membered heterocycles rings are particularly suited for couplings with pre-oxidized aminating reagents.



Scheme 3: Miura's condensation of 1,2,3-oxadiazole derivatives on chloroamines.

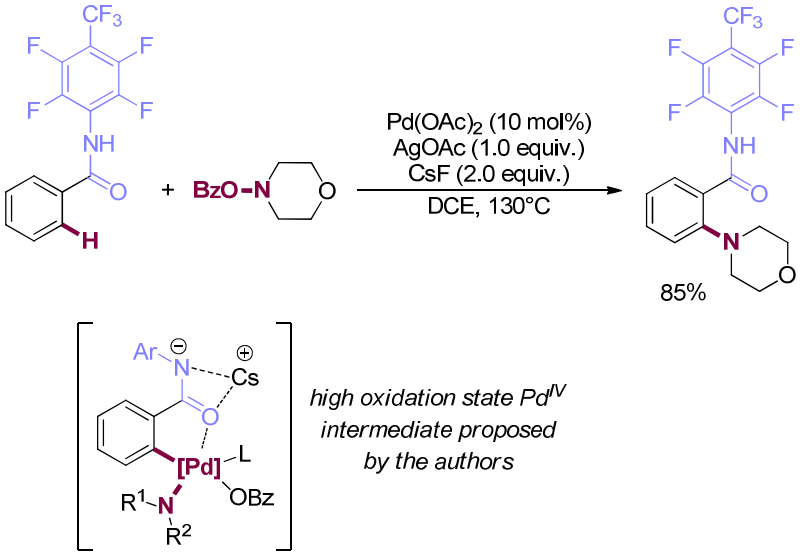
Likewise in 2010, Chao-Jun Li and his co-workers published the coupling between aryl pyridines and acetanilides[31] (Scheme 4). The authors used a copper (I) combined with di-*tert*-butyl peroxide and suggested a Cu^{I}-Cu^{III} catalytic system, in which DTBP would initiate the catalytic cycle by oxidative addition to the copper (I) pre-catalyst.



Scheme 4: Chao-Jun Li's coupling of phenylpyridine with amides.

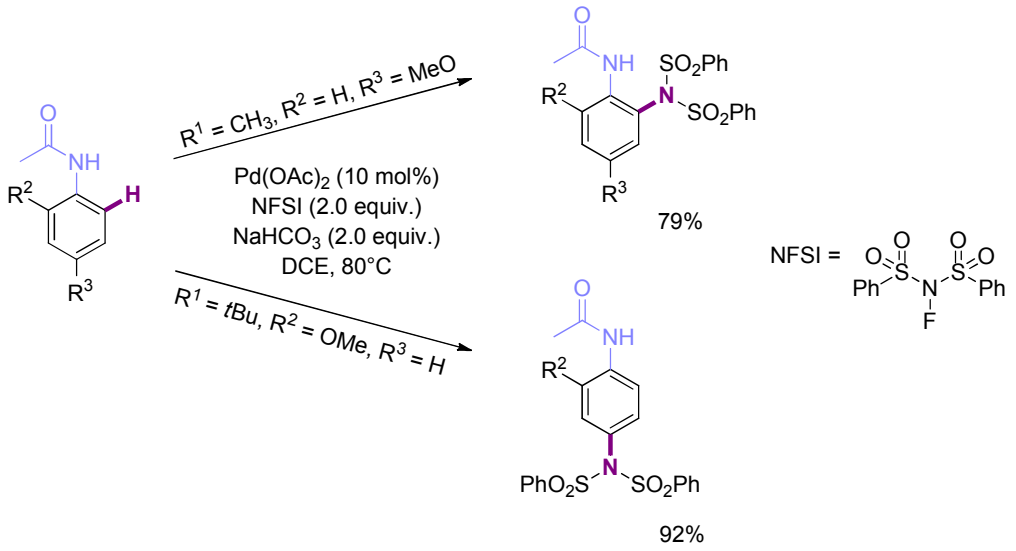
In the light of later examples using electrophilic aminating reagents[32], the *in situ* pre-oxidation of the amide coupling partner cannot be excluded either. Possibly both pathways occur.

In 2011, Jin-Quan Yu reported the condensation of benzamides on *ortho*-benzoyl hydroxylamine with palladium (II) and silver (I) [33]. The preactivation can also be made *in situ*, which avoids an extra pre-synthetic step. The drawback resides in the fact that an exotic fluorinated directing group is required (Scheme 5). Interestingly, the authors proposed a high oxidation state Pd^{IV} intermediate resulting from the oxidative addition of the electrophilic aminating reagent. The reaction would then proceed smoothly to the reductive elimination step, providing high yield *ortho*-amino benzamides.



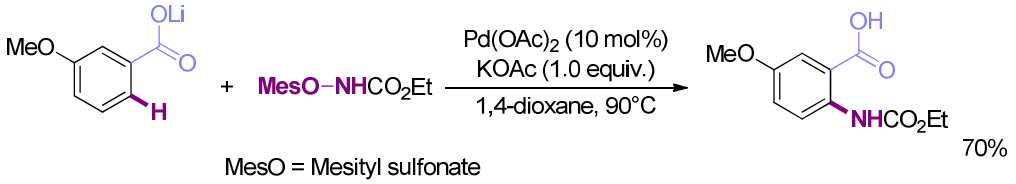
Scheme 5: Jin-Quan Yu's condensation of benzamides on *o*-benzoyl hydroxylamine.

The same year, Qian Zhang explored condensation of electrophilic fluorine based oxidized aminating reagents, with electron-rich acetanilide substrates[34] (Scheme 6). It is noteworthy that in the procedure of Zhang, the *para* position must be blocked so as to permit *ortho* directed C–H functionalization.



Scheme 6: Quian Zhang's fluorinated aminating reagent protocol.

In 2012, Wing-Yiu Yu used carboxylic acid as the directing group and *N*-mesitylsulfonyloxycarbamates as *N*-aminating agent[35] (Scheme 7).

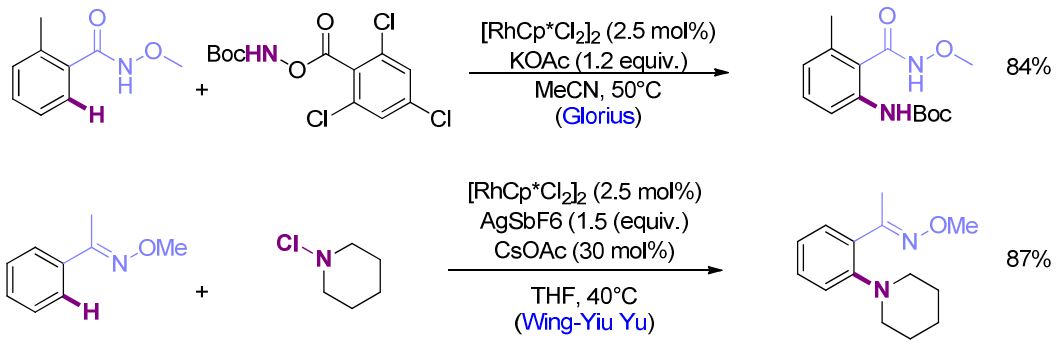


Scheme 7: Wing-Yiu Yu's condensation of carboxylates on *N*-mesitylsulfonyloxycarbamates.

The same year, Glorius and his team published an electrophilic amination reaction based on chloro-amines[36], and in 2013 based on carboxylate-NH-Boc derivatives with a RhCp* catalytic system[37] (Scheme 8).

Independently, Wing-Yiu Yu, reported in 2012 a RhCp* method for the C–H amination of some oxime ethers with secondary chloro-amines[38]. Later in 2013, Wing-Yiu Yu extended his method to include also primary chloro-amines[39] (Scheme 8).

It should be mentioned that Miura's, Chao-Jun Li's, Jin-Quan Yu's and Wing-Yiu Yu's examples (Schemes 3–5 and 8) constitute powerful synthetic methods in the oxidized-aminating reagent category because they present the substantial (optional) advantage of engaging the oxidant separately from the amine coupling partner. Thus, the N–X electrophilic aminating reagent is formed *in situ*. Regarding this specificity, we may consider them as C–N cross-dehydrogenative-couplings.



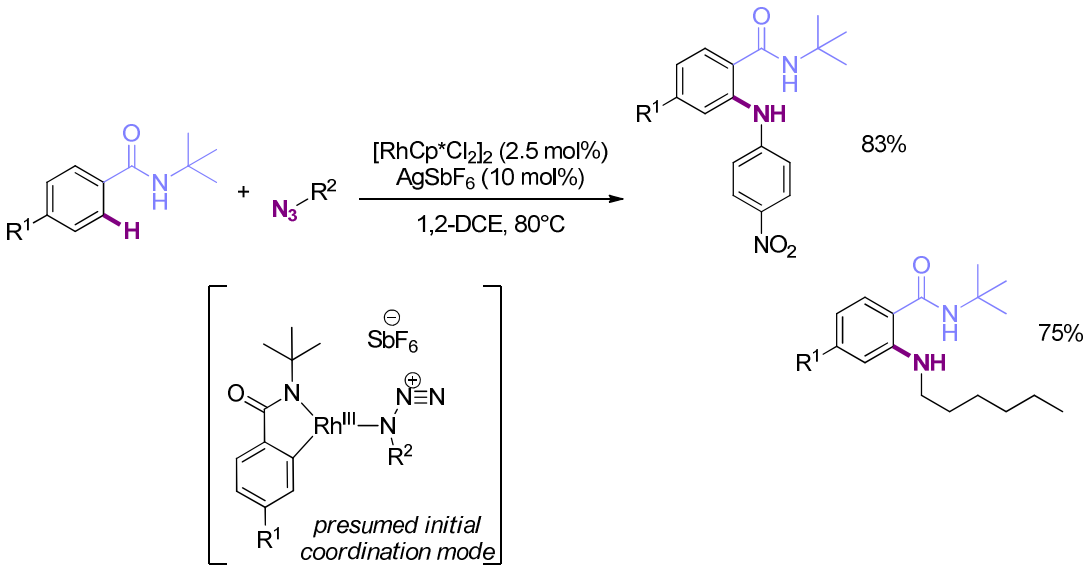
Scheme 8: Glorius's and Wing Yiu Yu's RhCp* oxidative amination reactions.

However, because of the strong/harsh oxidants used, we have classified these reactions as ''electrophilic aminating reagents'', with the previous examples. We acknowledge the arguable character of this classification, particularly in a context in which the mechanisms are not always clearly identified.

1.2.2. Azides as pre-activated aminating agents.

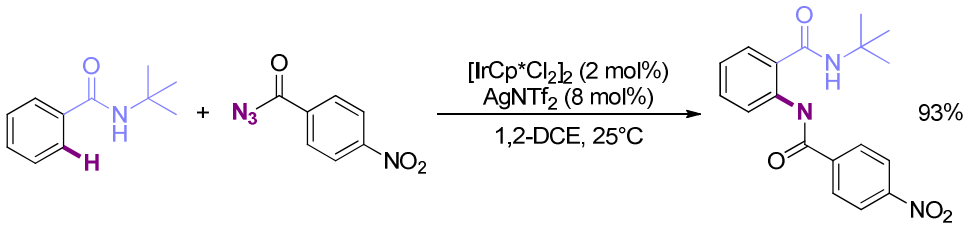
Recently, organic azides were introduced as pre-activated aminating reagents in C–H activation protocols. These building blocks are quite popular since a few years in the field of organic synthesis, as they are ubiquitous and versatile building blocks, for example in the famous ''click'' cyclisation reaction with alkynes[40]. However, the handling, storage and preparation of this type of reagent can be hazardous due to its high reactivity, particularly on a large scale. Ackermann highlighted some recent developments in their preparation[41]. This class of compounds is very reactive in the context of C–H activation. The main advantage is to release only N_2 as a by-product and therefore allows for milder reaction conditions.

However, the modes of action of organic azides can be of multiple sorts, particularly in the coordination spheres of transition metals[42]. In the examples shown here, we will simply consider organic azides as (electrophilic) nitrene precursors, without entering into the mechanistic specificities of each example.



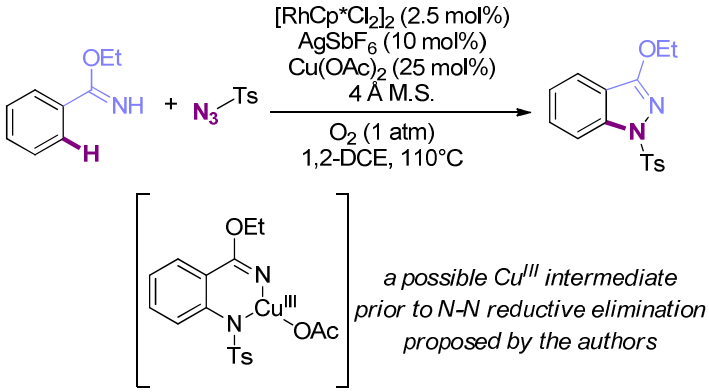
Scheme 9: Sukbok Chang's condensation of aromatic amides on aryl azides.

In 2012, Sukbok Chang and his group were among the first to report the intermolecular condensation of benzamides on sulfonyl azide[43] and aryl azide[44] derivatives with the now well-established cationic $Rh^{III}Cp^*$ catalyst (Scheme 9). This reaction was an important advancement for the intermolecular reactivity of azides, however it is mainly limited to electron poor aryl azides. One year later, Chang *et al.* reported the use of benzyl and alkyl azides as coupling partners[45] (Scheme 9). The team also published on the use of a ruthenium (II) catalytic system, for the coupling of sulfonyl azides[46]. It is assumed that the metallacycle intermediate approaches the azide at the α N atom, liberating N_2 and generating a reactive nitrene intermediate which afterwards inserts into the C–M bond.



Scheme 10: Sukbok Chang's IrCp* method.

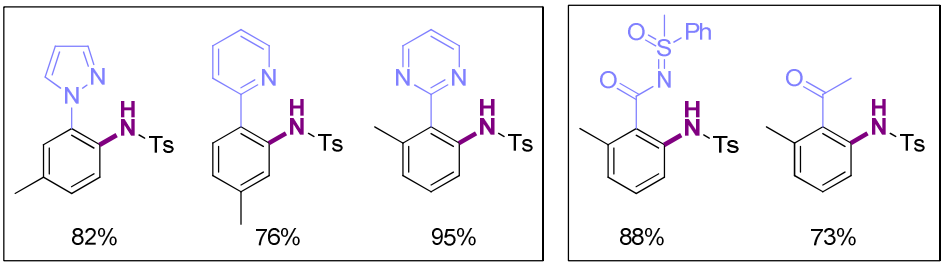
Also in 2013, Chang and co-workers showed that the reaction could be catalyzed by IrCp*, allowing room temperature C–H amination with excellent yields[47] (Scheme 10). The power of azides is well illustrated in the following example: the RhCp* catalysed synthesis of indazoles, reported by Glorius in 2013[48] (Scheme 11).



Scheme 11: Glorius's synthesis of indazoles.

In this case, the electrophilic and oxidizing powers of the azide are such that not only the intermolecular C–N bond is formed, but also an intramolecular N–N bond, a notoriously energetically difficult bond to form by means of catalytic reductive elimination.

In 2013, Ning Jiao also reported a N–N bond forming cyclisation mediated by prior C–H amination with sodium azide using a Pd catalytic system. In the latter case however, an additional very strong oxidant is required in the form of $Ce(SO_4)_2$[49,50].



Ackermann, 2013 **Sahoo and Ning Jiao, 2013**

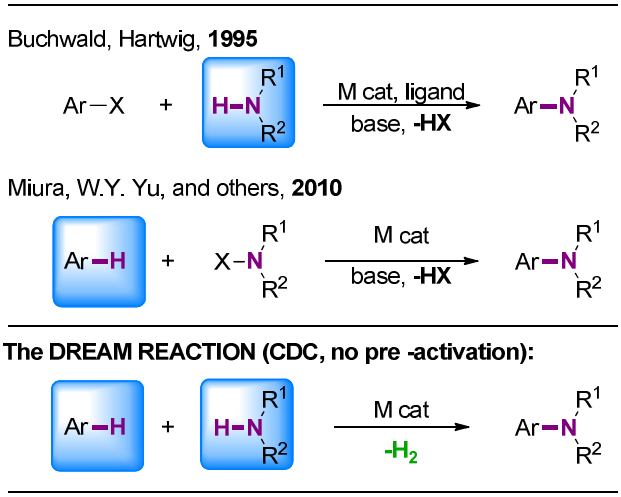
Scheme 12: Condensation of arenes with azides: selected classes of products obtained with Ru catalysed C-H activation.

Many C–H amination reactions were also recently reported with azides using Ru catalytic systems, notably by Ackermann[51], Sahoo[52,53], Ning Jiao[54], and others (Scheme 12).

In summary, pre-oxidized aminating reagents are well suited for C–H activation technologies because of reaction condition compatibility (usually acidic), higher reactivity compared to the corresponding free amines, and because they provide a readily placed internal, highly efficient, oxidizing functionality. Their prior (often tedious) preparation remains a drawback in terms of step and atom economy.

1.3. Cross dehydrogenative couplings (CDCs) for C-N bond formation reactions.

The long awaited (intermolecular) cross dehydrogenative couplings (CDC) for the formation of C–N bonds have remained elusive for a while, although early examples foretold their feasibility. Such a reaction mode is quite attractive because it does not require any pre-activation steps of either C–H or N–H coupling partners (Scheme 13). It only requires an external oxidant in order to scavenge the formal H_2 by-product during the formation of the C–N bond. We speak of formal H_2 by-product for clarity in this redox process, but in reality H_2 is probably not formed in most of the examples described here. The oxidant usually abstracts each hydrogen atom sequentially, from one, then the other coupling partner. Those first examples will be described, commented, compared and analyzed, with a perspective on future frontiers in this field.

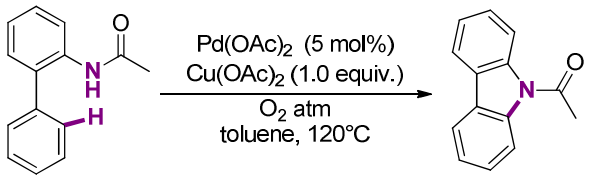


Scheme 13: The cross-dehydrogenative-coupling amination reaction.

1.3.1. Intramolecular C-N bond formation by dehydrogenative coupling.

Although we want to focus on intermolecular CDC amination reactions, it is useful to run through a few early intramolecular examples, in order to understand the emergence of the concept from a historical perspective.

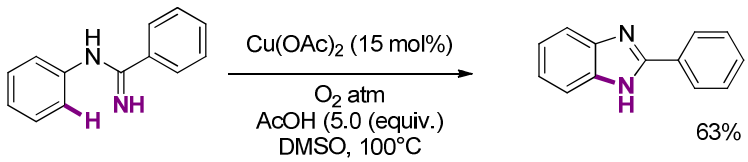
In 2005, Buchwald and his group realized an unprecedented intramolecular CDC with a Pd^{II} based catalytic system, to form acetylated carbazoles[55] (Scheme 14). In this case the reaction is facilitated by the directing group which also serves as a *N*-coupling partner. The cyclising (intramolecular) character of the reaction is also helpful to overcome the high energy barrier of the final C(sp^2)–N reductive elimination step. This was one of the first examples which really validated the concept of CDCs for amination reactions. For these reasons, this early communication truly impacted the field, and convinced many scientists to consider the challenge of CDC aminations seriously.



Scheme 14: Buchwald's CDC for acetylated carbazole formation.

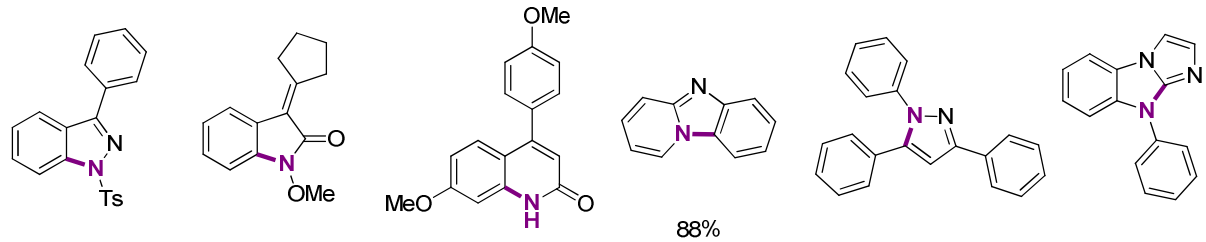
Later in 2008, the same group reported on the formation of benzimidazoles through an unusual C–H, N–H activation cyclisation reaction. This reaction is one of the early Cu^{II} catalyzed examples displaying a C–N bond forming CDC process[56] (Scheme 15).

Although there are arguably more straightforward ways to make benzimidazoles (notably through diamine condensation), this work constituted another clear proof of principle about the feasibility of CDC aminations.



Scheme 15: Buchwald's CDC for the formation of benzimidazole derivatives.

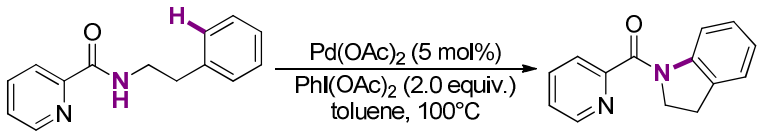
Several other research groups have developed similar intramolecular CDC amination methods based on Pd, Cu, or Ru catalytic systems[57-66]. Some of the typical and original *N*-heterocyclic products that were obtained by applying these technologies are summarized in Scheme 16.



Scheme 16: Non-exhaustive selection of typical N-heterocyclic products obtained by intramolecular CDC amination methods.

More recently Daugulis reported a method to form pyrrolidine, indoline and isoquinoline by double C–H/N–H activation with a Pd^{II} catalytic system and hypervalent iodine as the terminal oxidant. It is noteworthy that the phenyl moiety is quite distant from the amide directing group (Scheme 17), nevertheless the reaction still proceeds smoothly in 80% yield[67].

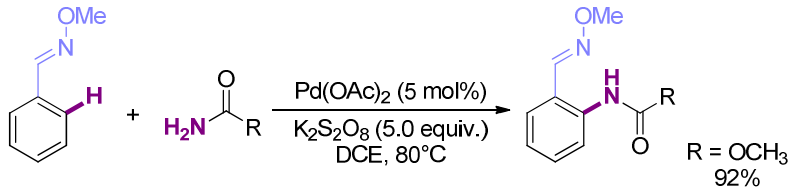
Gong Chen and collaborators also independently reported this reactivity in 2012[68-70]. It should also be noted that hypervalent iodines are strong oxidants. They are in fact so strong that in some cases they mediate C–N bond forming CDCs without a transition metal[71].



Scheme 17: Daugulis's CDC for the cyclization of aryl and alkyl picolinamides.

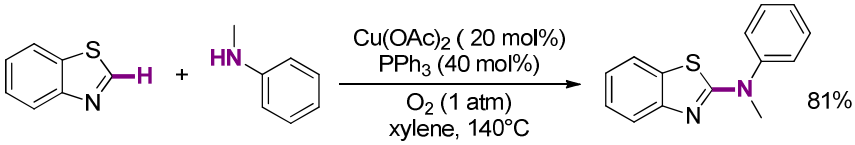
1.3.2. Intermolecular C-N bond formation by cross-dehydrogenative-couplings.

Although rare, more challenging intermolecular CDC reports are starting to appear. In the early cases, we should mention the pioneering work of Wing-Yiu Yu and Chi-Ming Che, who reported in 2006 the direct C–H amidation of some imine derivatives[72] (Scheme 18).



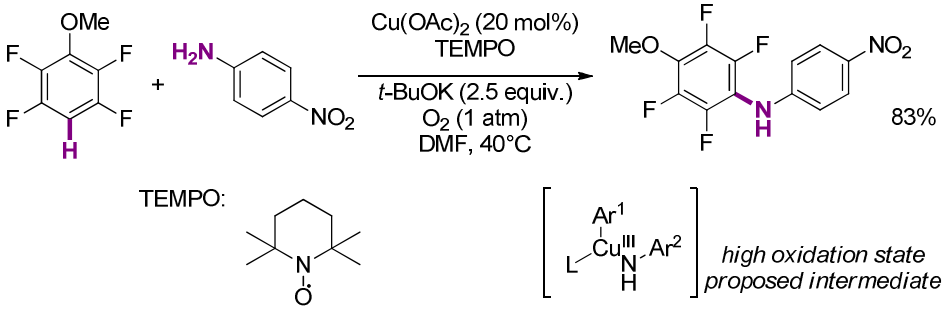
Scheme 18: Yu and Che's early intermolecular CDC of acetamides with imine derivatives.

In 2009, Atsunori Mori also published a reaction of this type, with his azole C–H activation protocol, catalyzed by copper (II) under O_2[73] (Scheme 19).



Scheme 19: Direct azole amination reaction of Mori.

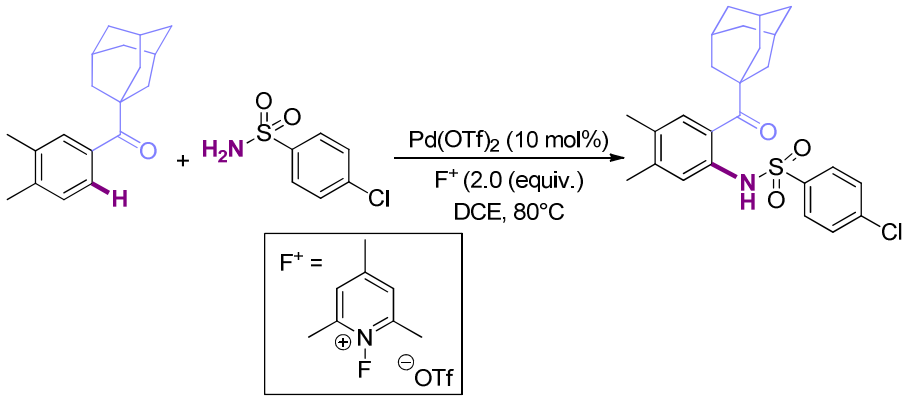
As mentioned above, five-membered heterocyclic rings are particularly suited for C–H bond functionalizations. However this protocol tolerates all sorts of secondary amines, making it a useful synthetic method. The same year, Schreiber also reported a similar reaction, independently of Mori, using pyridine as an additive, for the condensation of amides on five-membered heterocyclic rings[74]. These early methods were elegantly highlighted in 2010 by Armstrong[75] (see references therein). Sukbok Chang also developed an interesting analogous Co catalyzed version of this reaction[76].



Scheme 20: Weiping Su's formation of biarylamines.

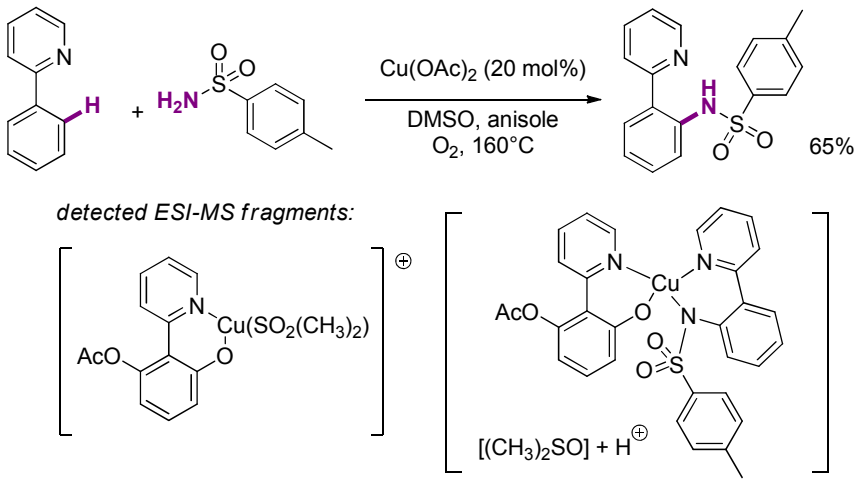
In 2010, Weiping Su and co-workers published a fundamental work on the formation of biarylamine series in the presence of $Cu(OAc)_2$ as catalyst, with TEMPO, a base and under an oxygen atmosphere[77] (Scheme 20). The authors explicitly suggest that the role of the TEMPO co-oxidant, in combination with O_2 , would be to re-oxidize Cu^{II} intermediates to Cu^{III}, thus facilitating the C–N reductive elimination. In this case, this example does not fall into the category of electrophilic aminating reagents (Part 1.2.). This work is therefore among the first to show the plausibility of the concept in an intermolecular fashion, although it presents limited and exotic substrate scope.

Afterwards in 2011, Lei Liu and his team published the condensation of phenone derivatives with sulfonamides. This reaction is limited by a quite special and large directing group. In addition, it requires two equivalents of onerous non atom economical fluoro-oxidant[78] (Scheme 21). Nevertheless, this additional example shows the feasibility of the concept.



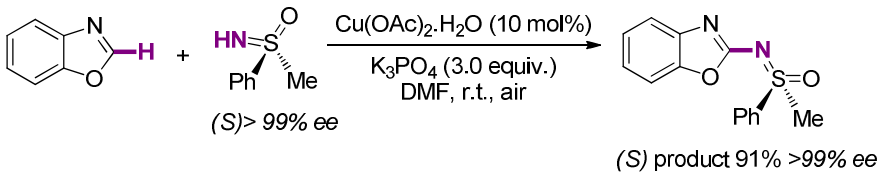
Scheme 21: Lei Liu's CDC of phenones with sulfonamides.

Similarly, in 2011, Nicholas reported the coupling of phenylpyridine with tosylamide[79] (Scheme 22). The authors analysed the reaction mixture by ESI-MS measurements. Two interesting Cu complex ions were detected. The authors attribute the moderate yields to competing hydroxylation and acetoxylation reactions. This reaction had also been reported by Jin-Quan Yu in 2006, using a stoichiometric amount of $Cu(OAc)_2$[80].



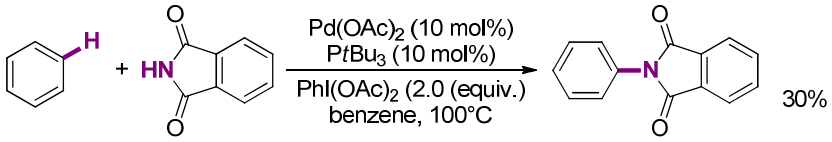
Scheme 22: Nicholas's CDC of phenylpyridine with sulfonamide.

Also in 2011, Bolm and Miura reported the condensation of azoles and polyfluoroarenes on *N*-arylsulfoximines. They showed a nice example where the enantiomeric excess of the substrate is preserved[81] (Scheme 23).



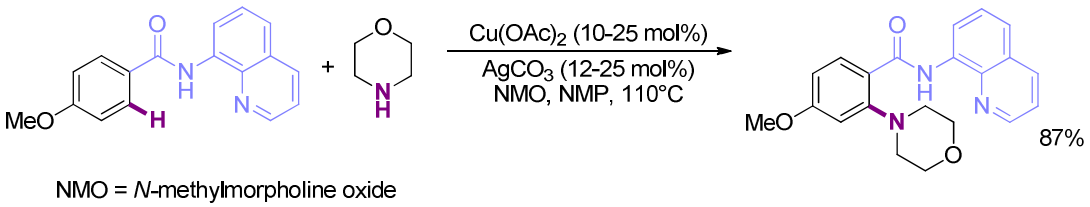
Scheme 23: Bolm and Miura's CDC of azoles with enantiopure N-arylsulfoximines.

In 2013, Hartwig published the coupling of simple arenes and *N*-arylphthalimide. Yields and regio-selectivities are rather limited. Nevertheless, it is noteworthy that the reaction proceeds without a chelate assisting directing group[82] (Scheme 24).



Scheme 24: Hartwig's CDC of arene on *N*-arylphtalimide.

The same year, Daugulis reported the coupling between morpholines and some carboxylic acid derivatives[83] (Scheme 25). The reaction is catalysed by a dual Cu^{II}–Ag^{I} catalytic system. The use and survival of such a basic amine like morpholine under such oxidizing C–H activation conditions is quite remarkable, affording the expected products in excellent yields.



Scheme 25: Daugulis's CDC amination of benzamides with aliphatic amines.

The use of N-methylmorpholine oxide (NMO) as the terminal oxidant is also an unusual but interesting aspect of this reaction.

The wide range of aliphatic amines used as coupling partners and the reasonably simple reaction conditions make this protocol one of the most elegant in this field. Interestingly, the protocol of Daugulis is not too far away from the original conditions of Ullmann, a century earlier. Thus, copper is still a metal of choice to effect the final C–N bond forming reductive elimination, presumably through a copper (III) to Cu (I) process.

1.4. Conclusions and perspectives.

We have collected here a short selection of the literature in the field of CDC C–N bond forming reactions and related reactions. Those examples show the feasibility of direct intermolecular amination without pre-activation or pre-oxidation of both *N*-aminating agent and C-H coupling partner. This novel process is expected to provide useful synthetic routes to built C-N bonds.

Indeed, at least four different metals have already been found as active catalysts, Pd, Cu, Ru, and Co. Rh will probably follow soon, and so will other metals too. The pKa range of the amine coupling partners, a parameter feared to be a barrier in such C–H activation transformations, proved to be managed. From sulfonamides to phthalimides to carbazoles to aliphatic amines, it seems every amine–amide class will find a suitable method to directly aminate C–H bonds in the end. Likewise, on the C–H activation coupling partner side, electron-rich and electron-poor arenes have both been used, with or without a chelate assisting directing group. Interestingly, many of the described examples use simple O_2 as the terminal oxidant. Nevertheless, molecular oxygen has drawbacks, for example in an industrial scaled-up context. In this context, the feasibility of C–N bond forming CDCs that would obviate altogether the need for an oxidant (simply evolving H_2 gas as a by-product) has yet to be explored.

With the above analyzed examples, it seems clear that many more methods describing ‘‘oxidative-Buchwald–Hartwig’’ or ‘‘oxidative-Ullmann–Goldberg’’ type reactivity will appear in the coming years, thus furnishing the organic synthesis toolbox with ready to use, easy, simple and straightforward methods that are often orthogonal or complementary to the classical Buchwald–Hartwig amination reactions.

In the light of these elements, we decided to investigate new cross-dehydrogenative-coupling amination reactions as new topic in our laboratory. Concerned by atom economy and green processes, our objectives were: 1) to obviate pre-activation or pre-oxidation of both C-H coupling partner and *N*-aminating agent. 2) to avoid the use of chelating directing group.

Thus, we studied the reactivity of cyclic secondary amines: carbazole in presence of ruthenium (II) and copper (II). Despite challenging *ortho*-functionalization of those substrates, we were able to built a C-N bond between two carbazoles, allowing selective *ortho*-*N*-carbazolation of carbazole in good yield. For convenience, we named this new class of compounds Lauternazoles. Those results and initial mechanistic experiments will be described chapter II.

In the next chapter, we addressed more challenging hetero-coupling formation. We introduced general diarylamines as C-H coupling partner, and maintained carbazole as aminating agent to form selectively *ortho* C-N functionalization of diarylamines. We developed the ruthenium (II)/ copper (II) catalytic system to perform this reaction under mild conditions (O_2 as terminal oxidant). We highlighted an unusual intramolecular N-H··N interaction in the novel class of compounds: Lauternamines. We suggest that this interaction could be involved in the rate limiting step.

In a third study, we focused our research on ubiquitous phenols. We chose the well-known antipsychotic phenothiazine as *N*-aminating agent to built new C-N bonds. Initially conducted in the presence of transition metals (Ru^{II}/Cu^{II}), this reaction proved to be efficient with the only effect of cumene and O_2. Those components suggested a mechanism initiated by a Hock process, which would form *in situ* peroxo-species as initiator of the reaction. An initial infra-red analysis might point out a strong O-H··N interaction.

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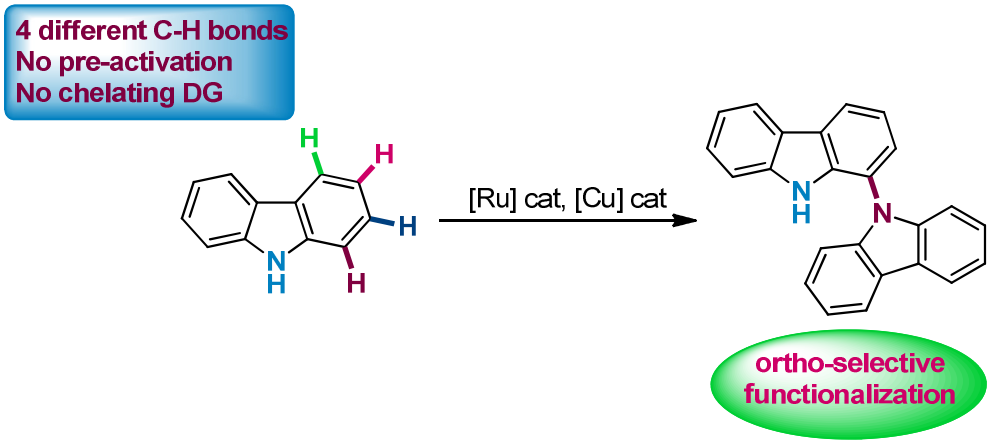
Chapter II.

Toward polynuclear Ru-Cu catalytic dehydrogenative C-N bond formation, on the reactivity of carbazoles.



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2.1. Introduction

Carbazoles are ubiquitous heterocyclic motif in natural products[1]. Mainly found as alkaloids in plants, these structures are widely studied for their biological activities. For instance, girinimbine proved to be an inhibitor of growth and inductor of apoptosis in human hepatocellular carcinoma cells *in vitro*[2]. Carbazoles are also considered as potential drugs against several pathologies such as malaria or HIV [3]. Pfizer commercialized synthetic carprofen under the trade name Rymadyl as a nonsteroidal anti inflammatory drug (Figure 1).

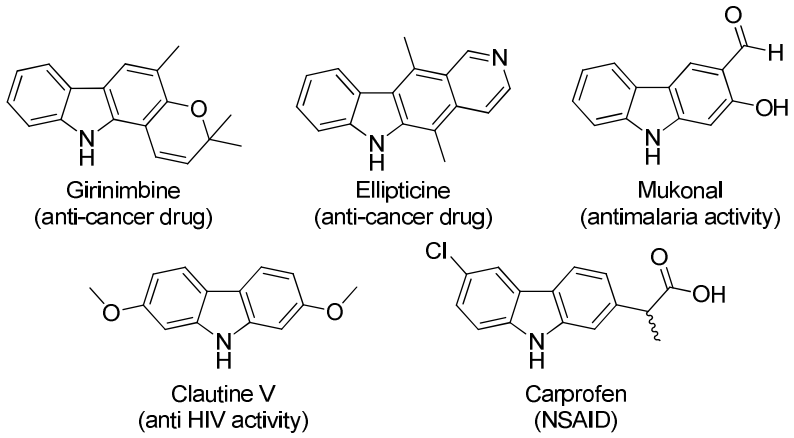
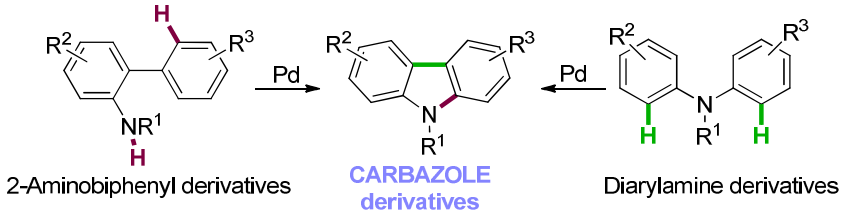


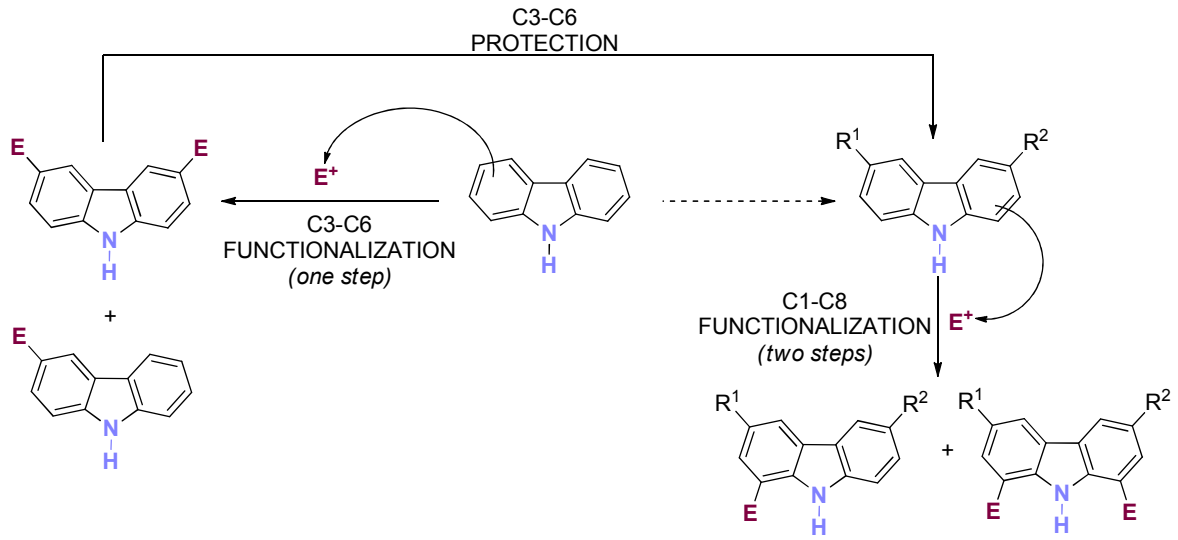
Figure 1: Representative examples of bioactive carbazoles.

Every year, new candidates based on the carbazole structure are discovered and studied for their biological activities[4]. Carbazole derivatives find applications in materials science as luminescent or optoelectronic materials[5]. With eight functionalized positions, combinations are endless. Excluding total synthesis in several steps, the most convenient and versatile methods for carbazole synthesis involve cyclization reactions of 2-aminobiphenyl[6] or diarylamines derivatives[7] (Scheme 1).



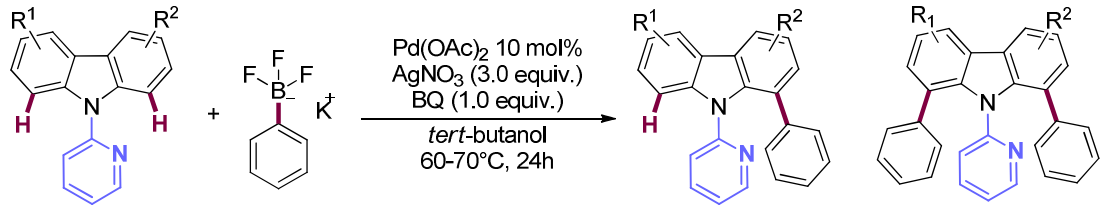
Scheme 1: General strategies for carbazole derivatives synthesis.

However, despite significant progress, limitations remain with regard to the type of substitution that can be accessed. The functionalization of C1 and C8 positions through this pathway is problematic due to steric hindrance close to the reactive site, especially when starting from diarylamines derivatives. Noneless, direct functionalization of C3 and C6 positions can be achieved through electrophilic aromatic substitution (S_EAr) reactions on the carbazole skeleton[8], while less nucleophilic C1 and C8 functionalizations require another strategy (Scheme 2).



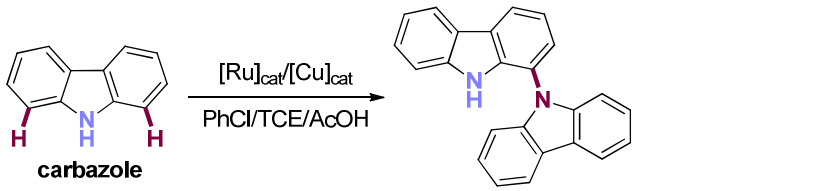
Scheme 2: Synthesis of functionalized carbazoles from carbazole skeleton itself.

Ample evidence of this aspect is the low number of reports describing the *ortho*-functionalization of carbazole which involve several steps: 1) protection of the more nucleophilic *para*-positions, 2) pre-functionalization of *ortho*-position and 3) subsequent introduction of functional group[9] (Scheme 2). Despite important improvement in C-H activation with related nitrogen aromatic systems[10], methods of direct C-H functionalization of carbazole are rare[11]. Moreover, those systems involve the use of chelating directing groups (Scheme 3).



Scheme 3: Chu and Wu's method for direct *ortho*-functionalization.

Considering all these aspects, we decided to investigate new methods to functionalize the *ortho*-position of carbazole with a ruthenium (II) catalyst. This molecule is interesting because it can be used either as C-H coupling partner or as *N*-aminating agent. We immediately observed that carbazole reacts on itself in presence of ruthenium (II) and copper (II) to deliver the corresponding homo- C-N cross-dehydrogenative coupling compound (Scheme 4).



Scheme 4: *Ortho*-condensation of carbazole in presence of ruthenium (II) and copper (II) catalyst.

2.2. Results and discussion.

In search for new cross-coupling with carbazole, we evaluated common C-H activation conditions: ruthenium (II), copper (II), and acetic acid, as described by Ackermann[11], in chlorobenzene. The TLC displays a new spot, less polar, with the same aspect as starting carbazole. After a series of experiments, we obtained the isolated product and performed its analysis. We observed the ability of carbazole to react on itself and form an *ortho*-selective C-N bond in a dehydrogenative fashion. In contrast to previous reports, the reaction was performed without strong chelating directing groups [12] (Scheme 4).

2.2.1. Optimisation.

After the first experiment, only trace quantities of the product were detected by TLC. Therefore, the stoichiometry of each component was adjusted in order to isolate a substantial amount of product. We chose this following procedure as starting point: carbazole (1.0 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (0.5 mol%), $Cu(OAc)_2$ (10 mo%), AcOH (0.5 mL), C_2Cl_4 (2.5 mL), and PhCl (2.5 mL) were united in a screw cap vessel. The reactor was sealed under air. The reaction mixture was heated at 140°C in an oil bath and stirred for 21h. After purification by column chromatography of SiO_2, we obtained 40% isolated yield of the *ortho*-N-functionalized product.

The structure was confirmed by NMR and by X-Ray diffraction analysis (Figure 2). We named the new class of compound Lauternazole for convenience in referencing.

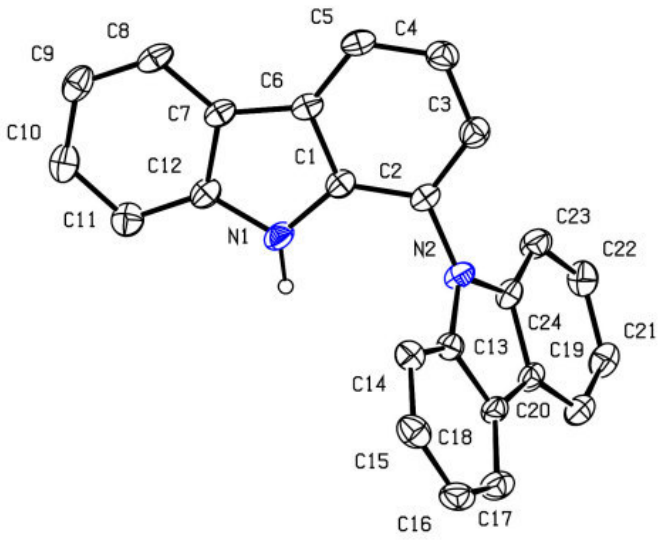


Figure 2: X-Ray structure: **2a** ORTEP view, 30% probability level. Selected torsion angle (deg): C(13)-N(2)-C(2)-C(1) = -69.6(4).

We first optimized qualitatively a part of the reaction parameters. Only probative entries were isolated. We began the optimization by screening solvents, acids and additives.

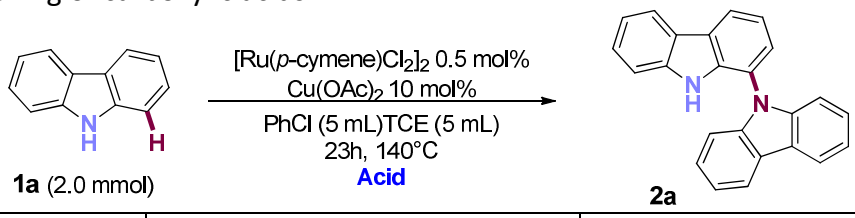
Solvents.

At the early stage of optimization, we used chlorobenzene and tetrachloroethylene as solvents. The study revealed that this solvent mixture is more effective than chlorobenzene and tetrachloroethylene separately. This trend was systematically observed at each stage of the optimization. Common solvents of C-H activation such as 1,4-dioxane[10a-c, 12, 13a] were tested without success. Changing tetrachloroethylene by tetrachloromethane did not give good result. Unfortunately, the yield dropped concomitantly with the formation of by-products. Bromobenzene in replacement of chlorobenzene did not improve the yield. Thus, we chose chlorobenzene and tetrachloroethylene as co-solvent mixture.

Acids.

Carboxylic acids proved to be efficient ligands for C-H activation reactions[13]. The first acid we tried was the cheap and common acetic acid (Table 1) which delivered 40% isolated yield.

Table 1: Screening of carboxylic acids.



1a (2.0 mmol) **2a**

Entry	Acid	Yield
1	*acetic acid*[a]	*40%*
2	succinic acid[b]	trace
3	crotonic acid[b]	trace
4	pivalic acid[b]	27%
5	2,6-dimethylbenzoic acid[b]	5%

Conditions: In a dried Schlenk were introduced carbazole **1a** (2.0 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (0.5 mol%), $Cu(OAc)_2$ (10 mol%), acid ([a]: 1 mL or [b]: 1 g), PhCl (5 mL) and C_2Cl_4 (5 mL). The Schlenk was sealed under air and the mixture was stirred at 140°C for 23h. The crude mixture was purified by a column chromatography of SiO_2.

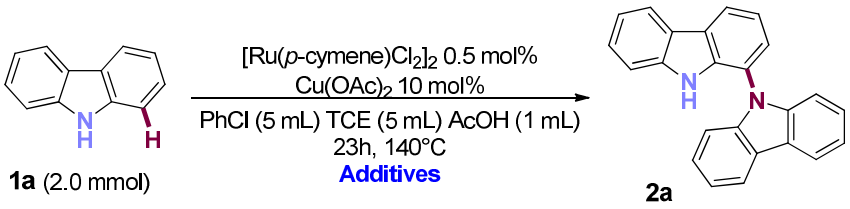
Table 1 points out that acetic acid is the best candidate. By comparison, a bulkier acid such as pivalic acid (Entry 4) decreased performance of the catalytic system with more than 10% loss of yield. Benzoic acid derivatives were not efficient either, giving only 5% isolated yield.

Other double functionalized succinic acid and unsaturated crotonic acid delivered only traces of product. We decided to continue the optimization with acetic acid.

Additives.

In the course of the optimization, we tested a series of additives to unsatisfactory conversion of the starting material (Table 2).

Table 2: Screening of additives.



Nature of additives	Additives	Effect on the reactivity
-Oxidants	-$NaIO_4$, Chloramine T -NFSI, Br_2, CCl_3Br, CCl_4, CBr_4	-Strong decomposition/ Traces of **2a** -Decompostion/ Low yield
-Salts	-$Zn(OAc)_2.(H_2O)x$, -NaOAc, LiCl, KF	-Massive decomposition/Traces of **2a** -Low yield
-Desiccants	-Acetic anhydride, $MgSO_4$, $CaCl_2$, Molecular sieves 4Å	-No product
-Others	-TsOH, malonic acid, TFA	-Decomposition

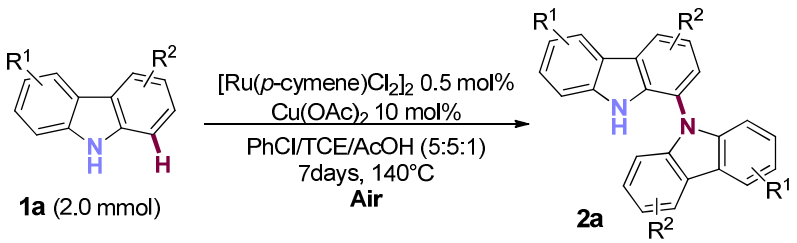
Conditions: In a dried Schlenk were introduced carbazole **1a** (2.0 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (0.5 mol%), $Cu(OAc)_2$ (10 mol%), AcOH (1 mL), PhCl (5 mL) and C_2Cl_4 (5 mL). The Schlenk was sealed under air and the mixture was stirred at 140°C for 23h. Crude mixtures were analyzed by comparing concentration intensities on TLC under UV irradiation for each experiment.

Table 2 demonstrates that each additive was detrimental to the reaction. Indeed, all oxidants showed over reactivity which resulted in strong decomposition. A comparable result was observed with $Zn(OAc)_2.(H_2O)x$ whereas salts such as lithium chloride or potassium fluoride decreased reactivity. Additionally, studying effects of drying agent did not give good results. Unfortunately, all desiccants were non innocent and suppressed all conversion. In the same manner, strong acids were responsible for decomposition. Thus the catalytic system suffered either from over reactivity in presence of additives, or low conversion in their absences.

Others parameters.

It appeared to us that the product formed *in situ* was responsible of a chelate poisoning effect of the catalysts. Thus, the catalytic system, which is efficient at the beginning of the reaction, decreased gradually its activity when concentration of the product increased. Long reaction time was helpful, and seven days of reaction afforded 51% instead of 40% after 23h. Likewise, 14 days of reaction delivered 57% isolated yield.

It is noteworthy that the best oxidant was the oxygen of air. Indeed, a control experiment under inert atmosphere suppressed the reactivity. Moreover, we deducted from further experiments that O_2 is involved at the early stage of the catalytic cycle (See initial mechanistic experiments part).

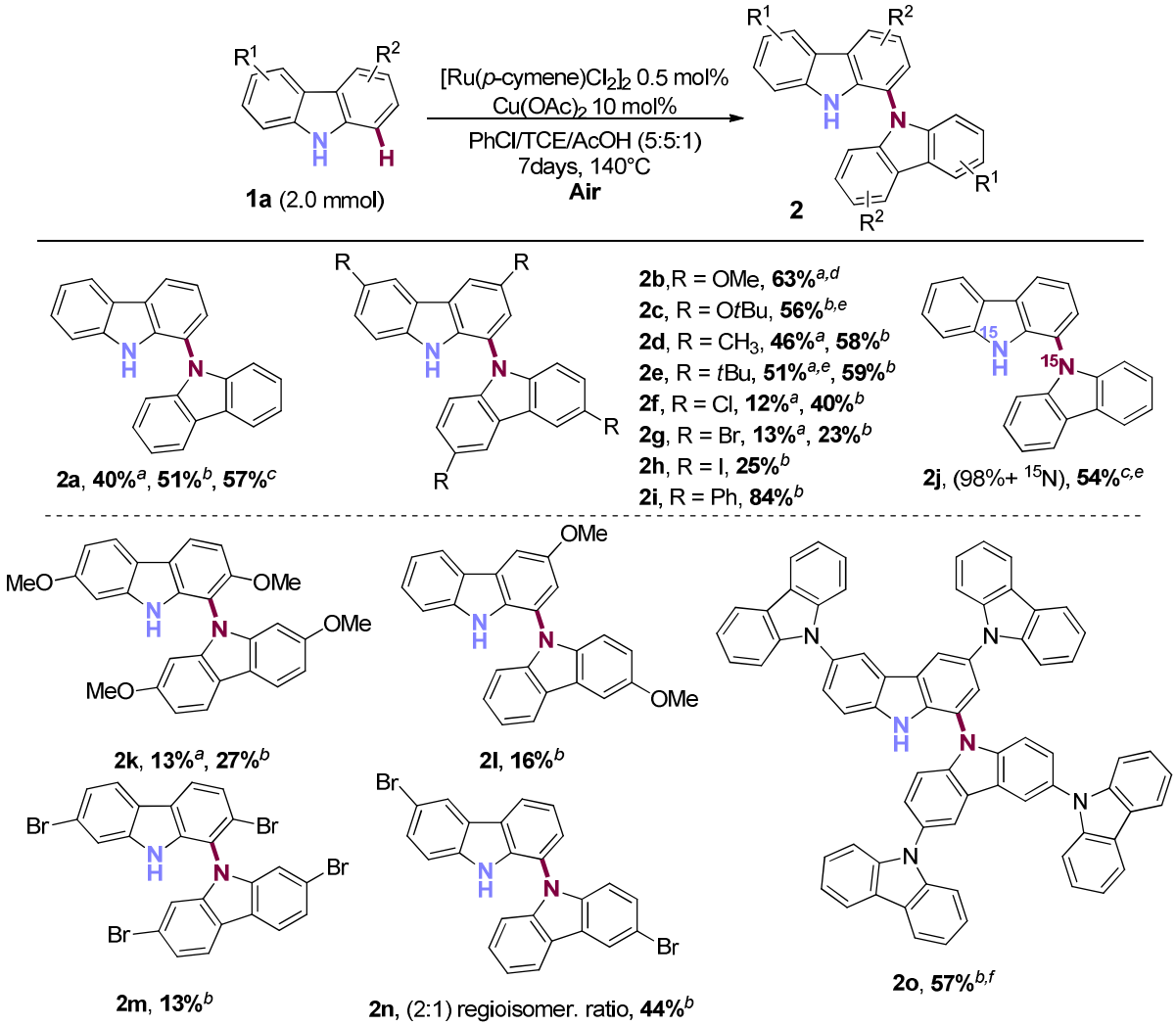


Scheme 5: Final optimized conditions.

The best conditions are describe scheme 5: Carbazole (2.0 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (0.5 mol%), $Cu(OAc)_2$ (10 mol%), C_2Cl_4 (5 mL), PhCl (5 mL), AcOH (1 mL) were assembled in a screw-cap vessel. The reactor was screwed under air and the mixture was stirred at 140°C for 7 days. The crude is directly purified on a column chromatography of SiO_2.

2.2.2. Scope and limits of the reaction.

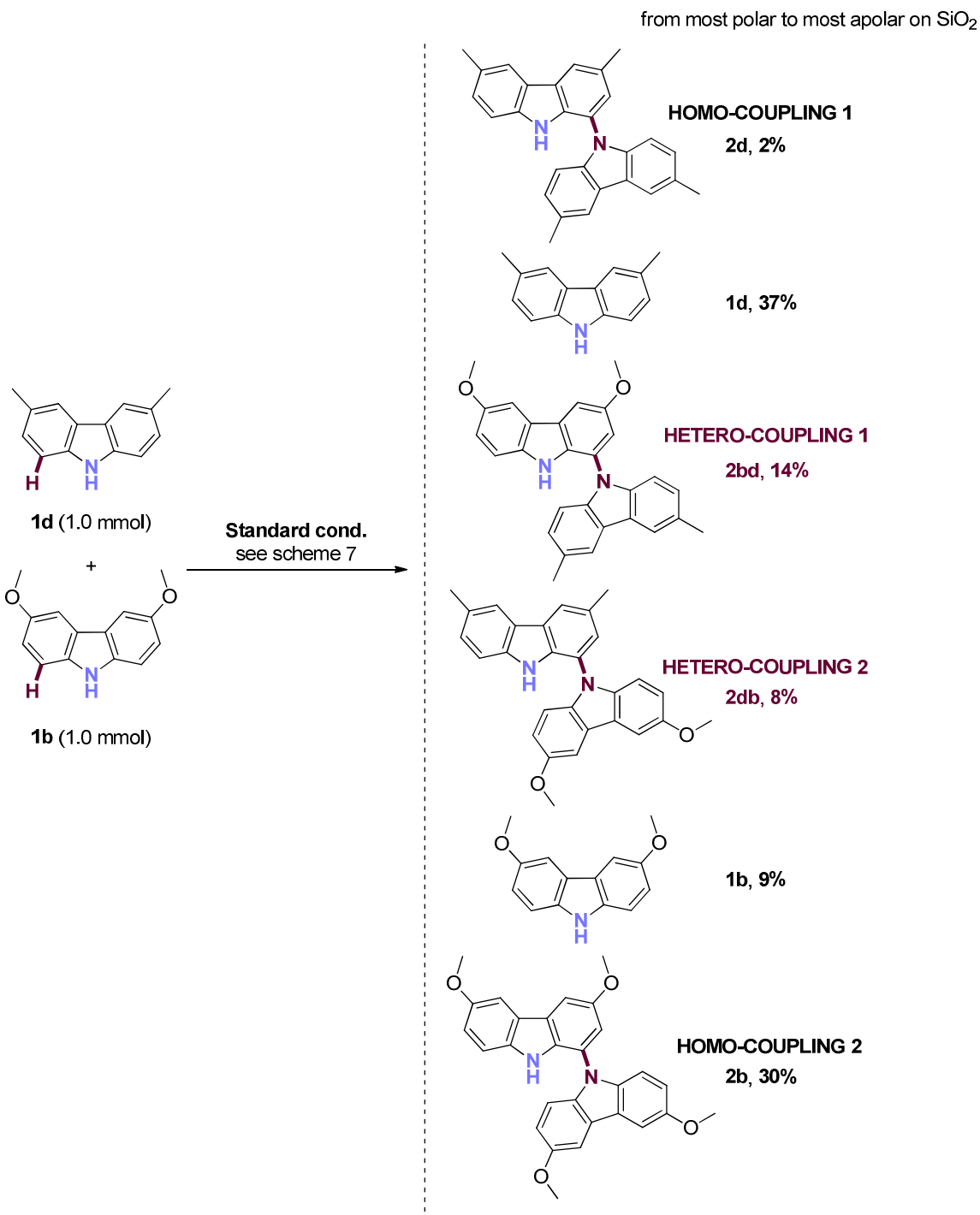
With these conditions, we began to explore the scope and the limits of the reaction. Results will be presented in scheme 6.



Scheme 6: Substrates Scope of the reaction. [a] Reaction time: 23h. [b] 7 days. [c] 14 days. [d] Entry **2b**: No yield improvement beyond 23h. [e] 1 mmol scale. [f] 0.65 mmol scale.

The reaction tolerates efficiently EDG such as methoxy groups **1b** which affords 63% isolated yield after only 23h. Lauternazoles **2d** and **2e** obtained respectively from 3,6-dimethylcarbazole and 3,6-di-*tert*-butylcarbazole were isolated in good yield (60%) after 7 days. EWG such as halides are less favorable since we obtained corresponding products (entries **2f**-**h**, **2m**-**n**) between 13 and 44% isolated yield. Surprisingly, mono-functionalized 3-methoxycarbazole delivered only one single product which is in favor of the most enriched ring of the carbazole **2i**. The mono-brominated carbazole **1n** provided a 2:1 regioisomeric ratio also in favor of the most electro-enriched cycle of the carbazole.

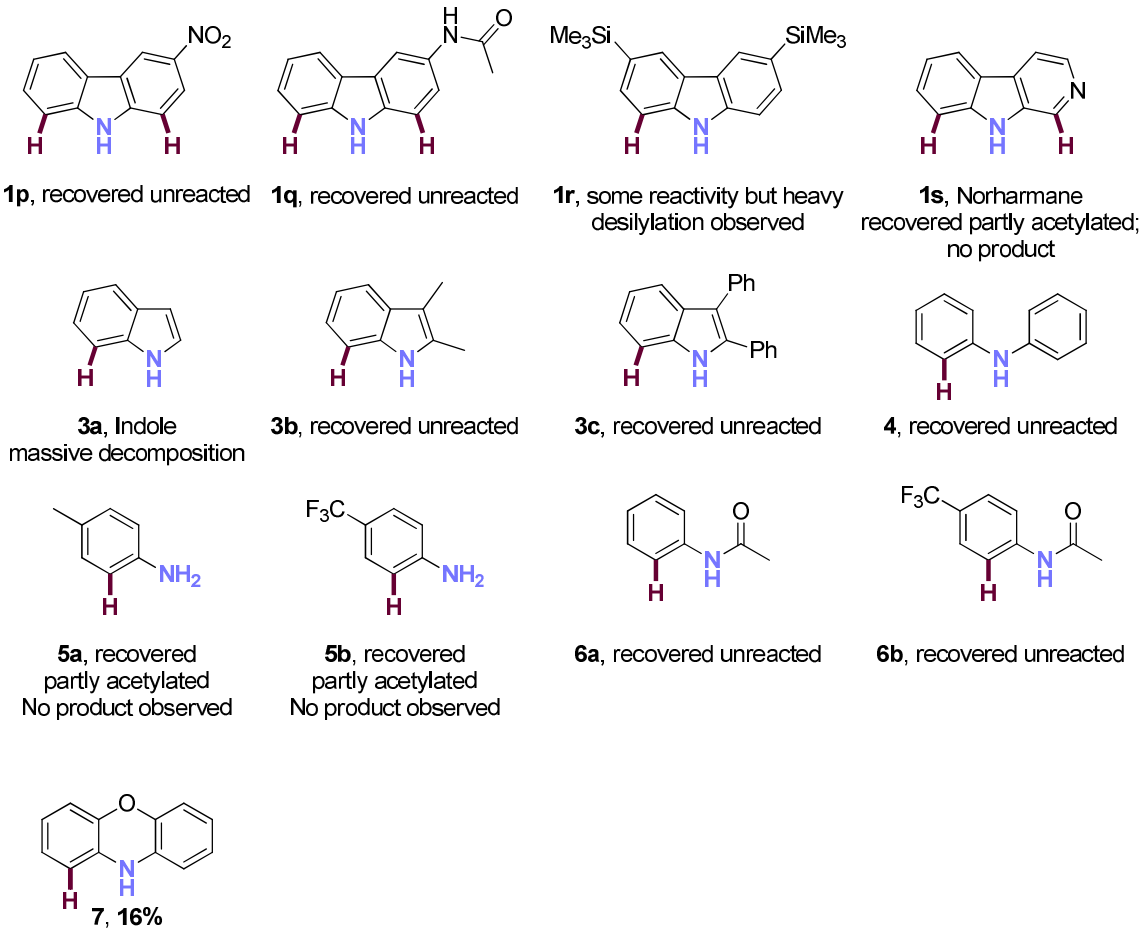
In order to induce formation of hetero-coupling product, we carried out the reaction with 3,6-dimethoxycarbazole **1b** and 3,6-dimethylcarbazole **1d**, because of their good reactivity, “unbiaised” electronic-steric similarity, acceptable polarity difference (for purification) and their easy detectable functional group by NMR. Results are detailed scheme 7.



Scheme 7: Hetero-coupling formation and relative yields of all components.

Interestingly, **1b** is more reactive than **1d** with only 9% unreacted starting material against 37% for **1d**. We assume that methoxy group makes the molecule better C-H coupling partner and better *N*-aminating agent since the major lauternazole is the homo-coupling product of **1b**. The overall yield of coupling product is 54%.

In contrast to substrates **1a** to **1o**, similar structural candidates did not afford expected results. (Scheme 8).

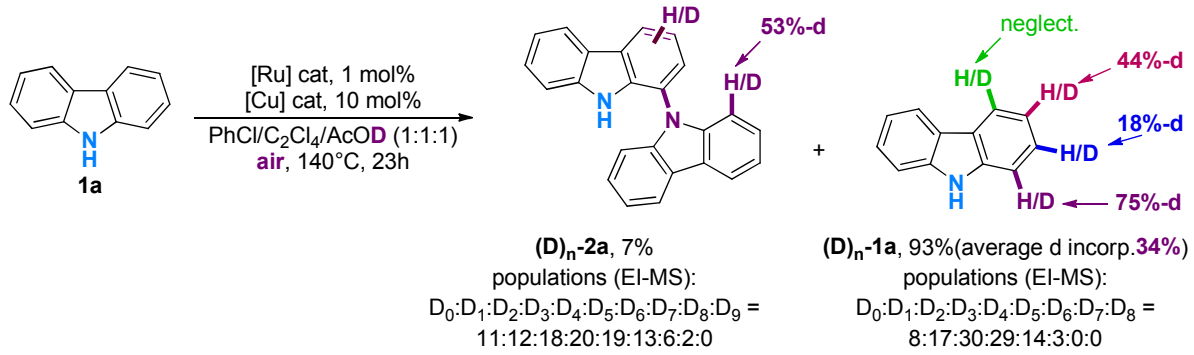


Scheme 8: Limits of the substrate scope: Screening of *N*-aminating agents and results.

Scheme 8 shows the limits of the reactivity. For instance, 3-nitrocarbazole **1p** or 3-acetamidecarbazole **1q**, were recovered unreacted. This result could be explained by the chelate poisoning effect of polar functional groups. For the same reason, acetanilides **6a**-**b**, did not afford the expected products. Aniline substrates **5a**-**b,** recovered partially acetylated could suffer of pKa incompatibility. Interestingly, the phenoxazine afford promising 16% isolated yield of the desired *ortho*-N-functionalized product.

2.2.3. Initial mechanistic experiments.

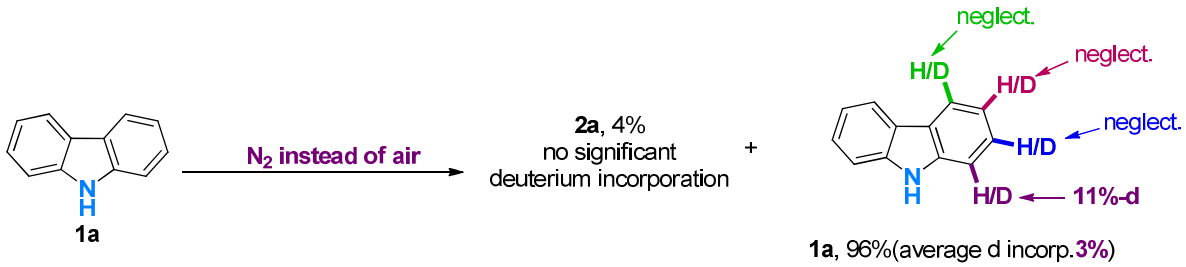
In order to shed some light on the reaction mechanism, we performed a series of isotopic and kinetic experiments. Thus, we carried out the reaction with carbazole **1a,** using our standard conditions with an excess of deuterium-labeled acetic acid (AcOD-d1) (Scheme 9).



Scheme 9: Deuterium scrambling **experiment 1**. Conditions: : In a dried Schlenk were introduced carbazole **1a** (2.0 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (0.5 mol%), Cu(OAc)$_2$ (10 mol%), AcO**D**-d1 (5 mL), PhCl (5 mL) and C_2Cl_4 (5 mL). The Schlenk was sealed under air and the mixture was stirred at 140°C for 23h. The crude mixture was purified by a column chromatography of SiO_2.

The result of this first deuterium scrambling experiment was surprising. Interestingly, the unreacted carbazole was recovered with an impressive deuterium grade not only at C1 (75%), but also at C2 (18%) and C3 positions (44%), despite the fact that C2 and C3 functionalization were never observed. This result may indicate the catalyst approaches the carbazole from the top, through coordination to its electron-rich π-aromatic system. This coordination mode could explain C-H activation of C1, C2 and C3 positions. The reversibility of this step suggests the C-H activation is not the rate limiting step.

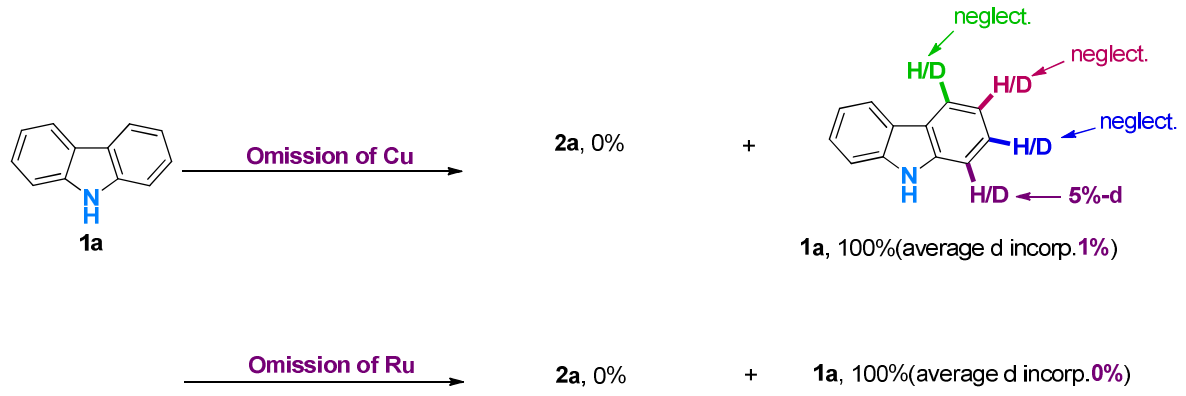
In a second experiment, we tested the influence of oxygen by following deuterium incorporation under inert atmosphere (Scheme 10).



Scheme 10: Deuterium scrambling **experiment 2**. Conditions: In a dried Schlenk were introduced carbazole **1a** (2.0 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (0.5 mol%), $Cu(OAc)_2$ (10 mol%), AcOD-d1 (5 mL), PhCl (5 mL) and C_2Cl_4 (5 mL). The Schlenk was sealed under N_2 and the mixture was stirred at 140°C for 23h. The crude mixture was purified by a column chromatography of SiO_2.

Under inert atmosphere, deuterium incorporation is completely nonexistent. Thereby, oxygen seems to be strongly involved in the step of C-H activation. This **experiment 2** might indicate that oxygen of air behaves not only as oxidant but also as co-catalyst.

In a last **experiment 3**, copper (II) and ruthenium (II) were respectively omitted in order to determine which catalyst is involved in the step of C-H activation (Scheme 11).



Scheme 11: Deuterium scrambling **experiment 3**. Conditions: Experiment 1 without ruthenium (II) or copper (II).

In both cases, no traces of product were detected. We assume therefore that both ruthenium (II) and copper (II) are essential for the formation of the product. Moreover, no significant deuterium incorporation appeared. As a consequence, we concluded Ru (II) and Cu (II) are both required for the C-H activation step.

Those three deuterium scrambling experiments pointed out that C-H activation involved ruthenium (II), copper (II) and oxygen. The fact that C-H activation is reversible may indicate that the C-N reductive elimination is in reality the rate limiting step, an event known to be difficult. We decided to achieve a series of kinetic experiments to gain a better understanding of the C-H activation step.

We performed a set of reactions to determine the initial kinetic orders of ruthenium (II) and copper (II). To estimate ruthenium (II) kinetic order, we carried out the reactions in our standard conditions as a function of ruthenium (II) concentration: 0.5% < [Ru] < 4%. Results are presented figure 3.

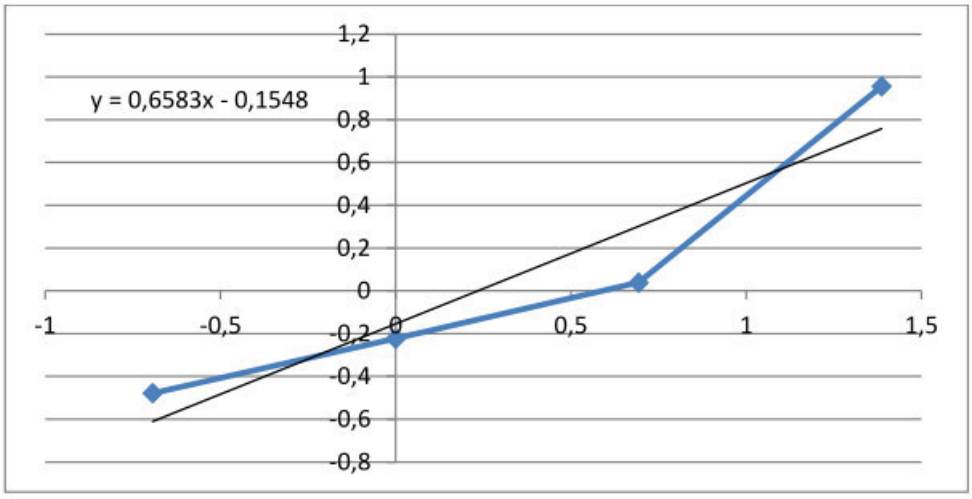


Figure 3: Initial rates (3h): ln (yield) = f (ln ([Ru])) for 0.5% < [Ru] < 4%.

At the initial stage (3h), we calculated ln (yield) = 0.6583 ln ([Ru]) - 0.1548. The reaction is clearly first order in ruthenium (II), although with a slightly broken kinetic order of 0.7 attributable to initial Ru (II) dimer dissociation process (Figure 3).

In the same manner, we began experiments to determine copper (II) kinetic order in our standard conditions. We carried out the reactions as a function of copper (II) concentration: 10% < [Cu] < 4% (Figure 4).

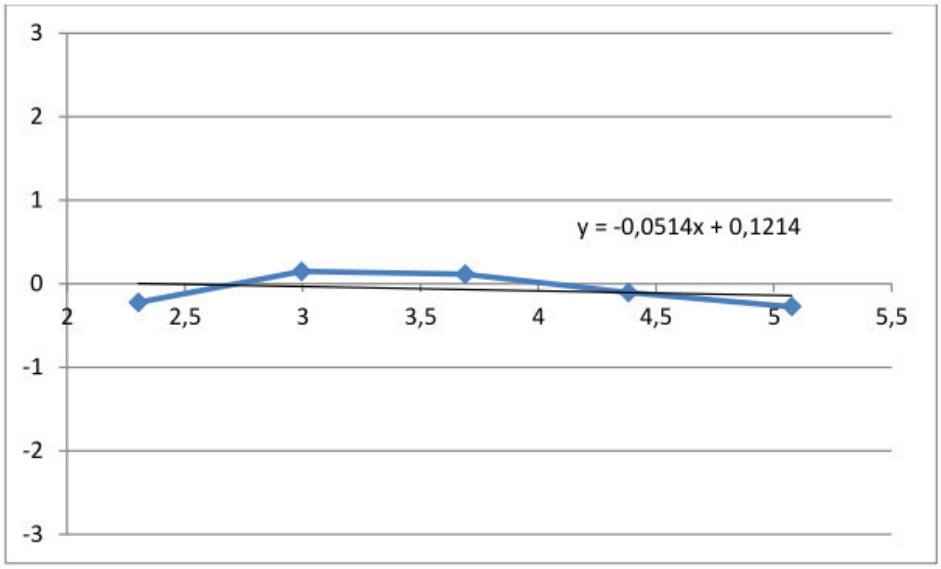


Figure 4: Initial rates (3h): ln (yield) = f (ln ([Cu])) for 10% < [Cu] < 160%.

We calculated: ln (yield) = -0.0514 ln ([Cu]) + 0.1214 (see figure 4). This result was somehow surprising since it indicated the kinetic order of copper (II) was zero. This statement was in contrast with deuterium scrambling experiments which showed the essential role of copper (II). Nevertheless, we established that in our standard conditions, copper (II) was in excess regarding ruthenium (II). Thus, an excess of ruthenium (II) catalyst could betray the kinetic order of copper (II). We carried out the reactions as a function of higher ruthenium (II) concentration: (4% < [Ru] < 16%.). As expected, we obtained a zero kinetic order of ruthenium (II) in otherwise standard conditions (Figure 5).

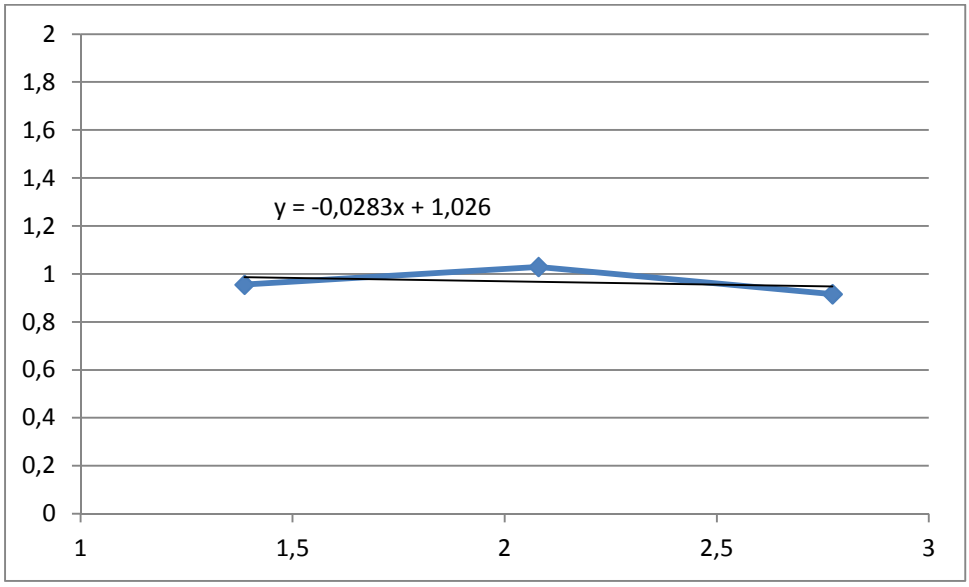


Figure 5: Initial rates (3h): ln (yield) = f (ln ([Ru])) for 4% < [Ru] < 16%.

A new set of experiments was carried out reactions at 16 mol% of ruthenium (II) and as a function of copper (II) concentration: 2.5% < [Cu] < 10% (Figure 6).

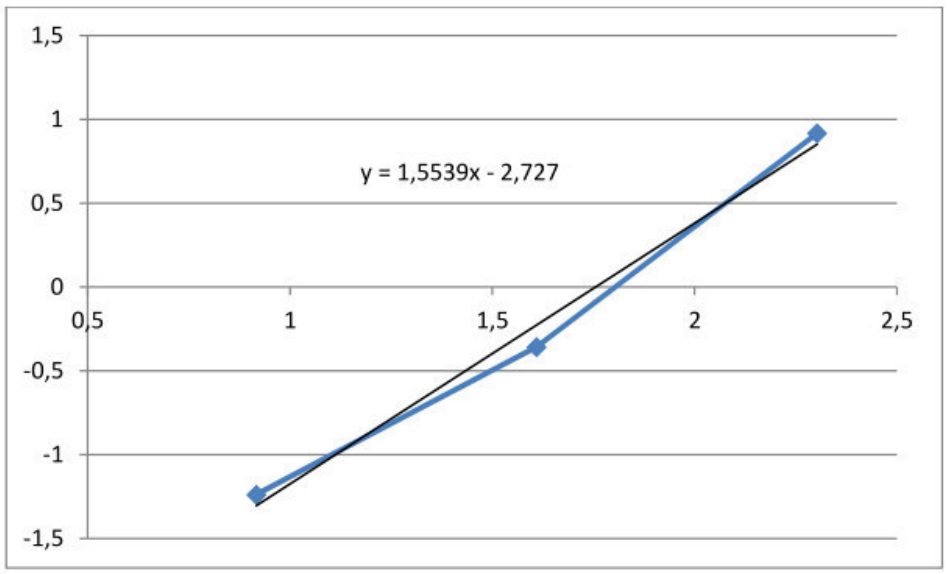


Figure 6: Initial rates (3h): ln (yield) = f (ln ([Cu])) for 2.5% < [Cu] < 10%, [Ru] = 16%, at otherwise standard conditions.

At high ruthenium loading (16 mol%), in which [Ru] > [Cu], we measured a second kinetic order for copper: 1.6 (Figure 6). Thus, we think both ruthenium and copper are involved in the rate limiting step(s). Astonished by this high copper kinetic order, we implemented reactivity-based Job plot experiments with the two variables [Cu] and [Ru] (Figure 6).

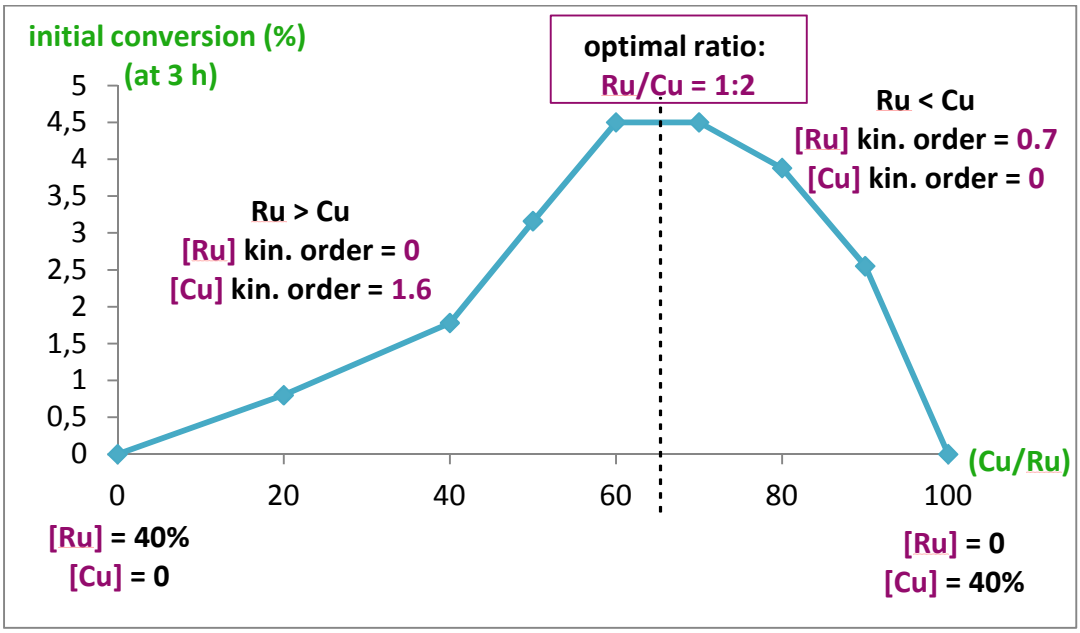
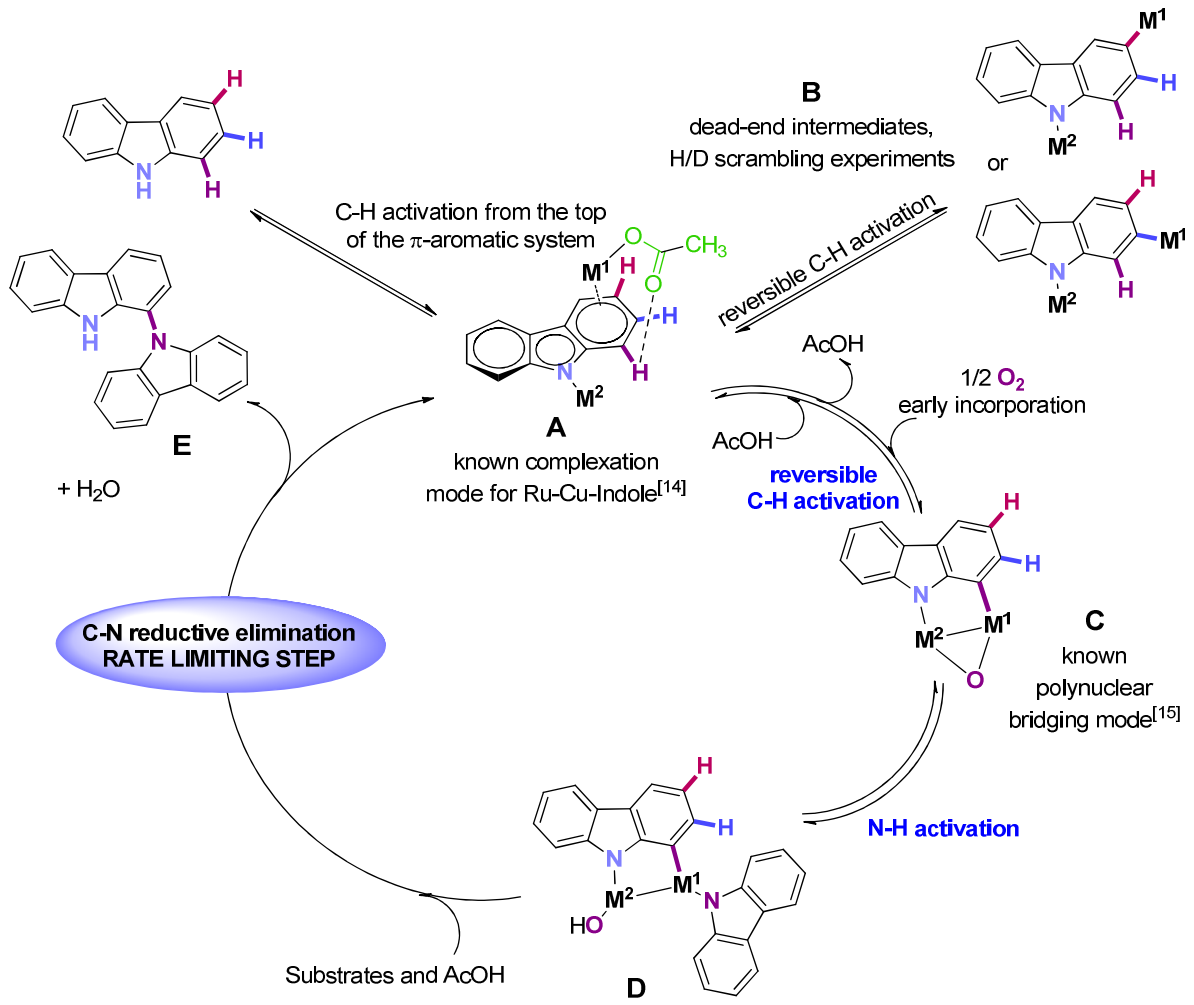


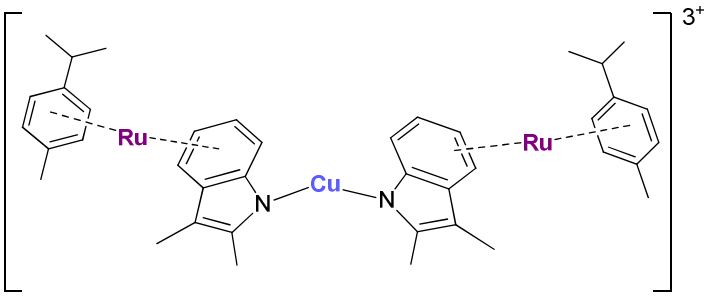
Figure 6: Initial reactivity Job plot. [Cu] + [Ru] = 40 mol%, reaction time: 3h, in otherwise standard conditions.

The highest initial rate was not obtained at the expected ratio [Ru]/[Cu] 1:1 but optimal ratio is one ruthenium center for two copper centers (See figure 6). Therefore with those clues of reactivity, elements of polynuclear coordination mode of Dubois, Murai and Chang, we proposed initial hypothetical mechanism (Scheme 12).

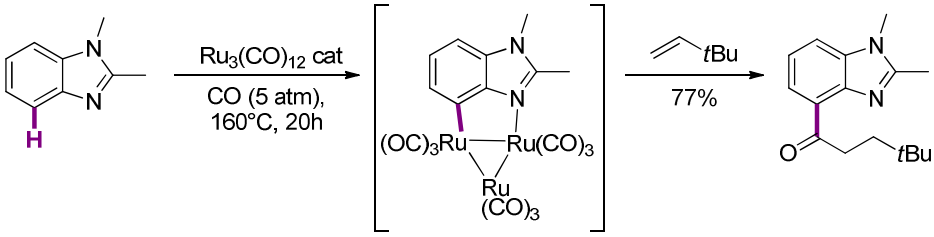


Scheme 12: Proposed initial mechanistic elements.

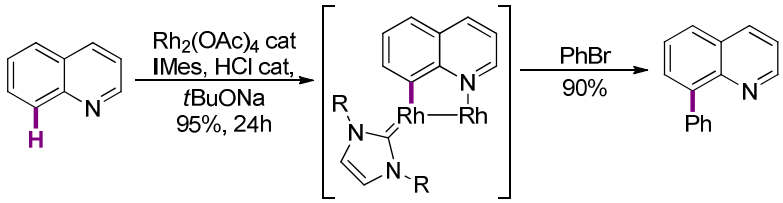
This initial proposed mechanism includes collected data of isotopic and kinetic experiments with additional literature references. According to Dubois, who reported a coordination mode for a Ru-Cu-Indole complex (Scheme 13), we suggest a polynuclear coordination on the carbazole[14]. Dubois describes a ruthenium on the top of the plane, and copper coordinate to the nitrogen atom. When ruthenium and copper are coordinated, reversible C-H activation may occur on C1 (step C), C2 and C3 (step B) positions. According to isotopic experiments (Part 2.2.3.), and Murai and Chang's work (Schemes 14 and 15 respectively) we proposed the incorporation of the oxygen in a polynuclear bridging mode. [15]. The next step is presumably the N-H activation (Step D) followed by the C-N reductive elimination (Step E).



Scheme 13: Polynuclear Ru/Cu/Indole complex of Dubois.



Scheme 14: Polynuclear Ru catalysed C-H activation reaction of some azole derivatives by Murai.



Scheme 15: Polynuclear Rh catalysed C-H activation reaction of quinoline derivatives.

2.3. Conclusion and outlook.

As a conclusion, we successfully performed *ortho*-functionalization of carbazole. This molecule acts either as C-H coupling partner or as *N*-aminating agent under our reaction conditions. We were able to create a C-N bond, which is known to be challenging, without pre-activation of the starting material. Moreover, the reaction is *ortho*-selective even in the absence of chelating directing groups, whereas the selectivity commonly observed with usual S_EAr reactions is *para*-functionalization. The system which consists in cooperative effect of ruthenium (II), copper (II) and oxygen, activates not only the C1-position but also C2 and C3 positions despite the fact that C2 and C3 functionalized products were never observed. Furthermore, we always observed mono-functionalization and therefore a control of the reactivity.

This catalytic system was a first example aiming to build C-N bonds with Ru (II)/Cu (II) catalysts by C-H activation. We expect to improve this method and broaden the scope of such reactions and include substrates such as diarylamines, indoles, phenothiazines, anilines, benzofuranes, phenols,... Further mechanistic studies of the reaction are planned in order to understand the role of the oxygen as potential co-catalyst. We think C-H activation technology will promote the development of new types of cross-couplings in the near future. Thus, we will focus our research on such cross-dehydrogenative-couplings.

2.4. References.

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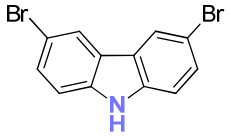
2.5. Experimental part.

2.5.1. General Information.

All reactions were carried out in dried reaction vessels with sealed Teflon screw caps under air, unless otherwise specified. NMR spectra were obtained on Bruker AMX 400 or on Bruker Avance 600 systems using $CDCl_3$, $(CD_3)_2SO$, or C_6D_6 as solvents, with proton and carbon resonances at 400/600 MHz and 101/151 MHz, respectively. Coupling constants (*J)* are quoted in Hz. Flash chromatography was performed on silica gel (40-63 mesh) by standard technique. GC-MS spectra were recorded on an Agilent Technologies 7890A GC-system with an Agilent 5975C VL MSD or an Agilent 5975 inert Mass Selective Detector (EI) and a HP-5MS column (0.25 mm x 30 m, film: 0.25 µm). The major signals are quoted in m/z with the relative intensity in parentheses. The method used starts with the injection temperature T_0 . After holding this temperature for 3 min, the column is heated to temperature T_1 (ramp) and this temperature is held for an additional time t. Method: 50_40: T_0=50°C, T_1=320°C, ramp = 40°C/min; t = 4 min. Substrates **1a, 1e, 1f, 1h, 1j** and **1o** were purchased either from ABCR or TCI, and engaged directly.

2.5.2. Substrates preparation.



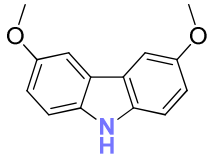
3,6-dibromo-9*H*-carbazole
Chemical Formula: $C_{12}H_7Br_2N$
Exact Mass: 322,89
Molecular Weight: 325,00
m/z: 324.89 (100.0%), 322.89 (51.4%), 326.89 (48.7%), 325.90 (13.1%), 323.90 (6.7%), 327.89 (6.5%)
Elemental Analysis: C, 44.35; H, 2.17; Br, 49.17; N, 4.31

1g. 3,6-dibromocarbazole. Carbazole (**1a,** 120 mmol) is placed in 500 mL round bottom flask, and suspended in 200 mL of a 1:1 mixture of AcOH and EtOH. Br_2 (240 mmol) is diluted in 15 mL AcOH and placed in a dropping funnel. The Br_2 is added dropwise under strong magnetic stirring. The resulting crude is evaporated and recrystallized from toluene five times. 32.8 mmol of **1g** are obtained as a light grey solid.

The toluene layers are reunited, evaporated, and resubmitted to crystallization five times. 20.9 mmol are obtained. A final round of recrystallization cycles yields 8.8 mmol. Overall yield: 52.1%.

^{1}H NMR (600 MHz, $CDCl_3$ / $(CD_3)_2SO$) δ (ppm): 10.52 (s, NH), 7.90 (d, *J* = 2 Hz), 7.27 (dd, ^{3}J = 8.5 Hz, *J* = 2.0 Hz), 7.16 (d, ^{3}J = 8.5 Hz).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$ / $(CD_3)_2SO$) δ (ppm): 138.89 (s, C_{quat}), 128.66 (s, CH), 123.56 (s, C_{quat}), 122.73 (s, CH), 112.62 (s, CH), 111.45 (s, C_{quat}, C-Br).



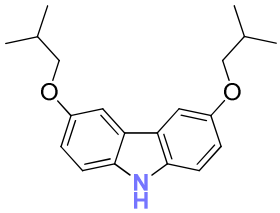
3,6-dimethoxy-9*H*-carbazole
Chemical Formula: $C_{14}H_{13}NO_2$
Exact Mass: 227,09
Molecular Weight: 227,26
m/z: 227.09 (100.0%), 228.10 (15.4%), 229.10 (1.6%)
Elemental Analysis: C, 73.99; H, 5.77; N, 6.16; O, 14.08

1b. 3,6-dimethoxycarbazole. 3,6-dibromocarbazole **1g** (30.8 mmol) and CuI (61.8 mmol) are placed in a Schlenk reactor under N_2 atmosphere. DMF (10 mL) and a solution of MeONa/MeOH (5.4 M, 35 mL) are added. The reactor is sealed under N_2 and heated at 120°C for 20 h. The crude is then directly filtered over a SiO_2 plug in ethyl acetate. The crude is then reduced, and purified over SiO_2 gel column chromatography. (height 370 mm, width 55 mm) in pentane/CH_2Cl_2 = 6/4 (1L), then pentane/ CH_2Cl_2= 1/1 (1L), then pure CH_2 Cl_2 (1L). 61.5% isolated yield (white solid).

Note: the NMR signals of this molecule are very broad, consistent with the literature.

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.1-7.7 (very broad signal, 1H, NH), 7.53 (broad s, 2H), 7.4-7.2 (broad signal, 2H), 7.09 (dd,^{3}J = 8.8 Hz, *J* = 2.3 Hz). 3.97 (s, 6H, CH_3O).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ (ppm): 153.72 (broad s, C_{quat}), 135.32 (broad s, C_{quat}), 123.87 (s, C_{quat}), 115.38 (broad s, CH), 111.69 (broad s, CH), 103.00 (s, CH), 56.22 (s, CH_3O).

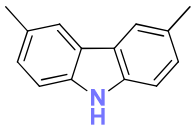


3,6-diisobutoxy-9*H*-carbazole
Chemical Formula: $C_{20}H_{25}NO_2$
Exact Mass: 311,19
Molecular Weight: 311,42
m/z: 311.19 (100.0%), 312.19 (22.4%), 313.20 (2.3%)
Elemental Analysis: C, 77.14; H, 8.09; N, 4.50; O, 10.28

1c. 3,6-di-(isobutoxy)-carbazole: Note: These are *not* optimized conditions. 3,6-dibromocarbazole **1g** (9.5 mmol), CuI (36.9 mmol) and sodium terbutoxyde (138.5 mmol) are placed in a Schlenk reactor under N_2 atmosphere. DMF (10 mL) and isobutanol (40 mL) are added. The reactor is sealed under N_2 and heated at 140°C for 16 h. The crude is then directly filtered over a SiO_2 plug in ethyl acetate. The crude is then reduced, and purified over SiO_2 gel column chromatography in toluene. 20.0% isolated yield (white solid).

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ (ppm): 10.76 (s, 1H, NH), 7.66 (d, J = 2.7 Hz, 2H), 7.31 (d, ^3J = 8.8 Hz, 2H), 6.97 (dd, ^3J = 8.7 Hz, J = 2.6 Hz, 2H), 3.81 (d, ^3J = 6.6 Hz, 4H), 2.06 (m, 2H), 1.02 (d, J = 6.6 Hz 12 H).

^{13}C {^{1}H} NMR (101 MHz, $(CD_3)_2SO$) δ (ppm): 152.02 (s, C_{quat}), 135.18 (s, C_{quat}), 122.78 (s, C_{quat}), 115.32 (s, CH), 111.52 (s, CH), 103.76 (s, CH), 74.57 (s, CH 2), 27.91 (s, CH), 19.23 (s, CH_3).



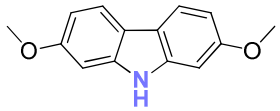
3,6-dimethyl-9*H*-carbazole
Chemical Formula: $C_{14}H_{13}N$
Exact Mass: 195,10
Molecular Weight: 195,26
m/z: 195.10 (100.0%), 196.11 (15.3%), 197.11 (1.1%)
Elemental Analysis: C, 86.12; H, 6.71; N, 7.17

1d. 3,6-dimethylcarbazole. 3,6-dibromocarbazole **1g** (16.3 mmol) is placed in a round bottom flask under N_2 atmosphere. Freshly distilled diethyl ether (200 mL) is added. The mixture is cooled to 0°C. *N*-butyllithium (17.5 mmol) is introduced dropwise. The mixture is stirred at this temperature for 1 h. Trimethylsilyl chloride (17.3 mmol) is added.

The reaction mixture is stirred again for 1 h at room temperature. The suspension is cooled to -78°C. *T*-butyllithium (67.5 mmol) is carefully introduced. After 1 h 30 of stirring at 0°C, methyliodide (82 mmol) is added at -78°C. The suspension is slowly warmed up at room temperature and stirred for the weekend. HCl 1M (50 mL) is added. Layers are separated. Organic phase is washed with HCl 1M (2x50 mL) and distilled water (2x50 mL) then dried over $MgSO_4$. The crude is then reduced, and purified over SiO_2 gel column chromatography in pentane/CH_2Cl_2 = 6/4. 44.6% isolated yield (white solid).

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.87 (broad s, 2H, CH), 7.85 (broad, 1H, NH), 7.35-7.32 (d, *J* = 8.2 Hz, 2H), 7.25 (dd, ^3J = 8.2 Hz, *J* = 1.5 Hz, 2H), 2.56 (s, 6H, CH_3).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ (ppm): 138.19 (s, C_{quat}), 128.62 (s, C_{quat}), 127.13 (s, CH), 123.53 (s, C_{quat}), 120.32 (s, CH), 110.36 (s, CH), 21.59 (s, CH_3).

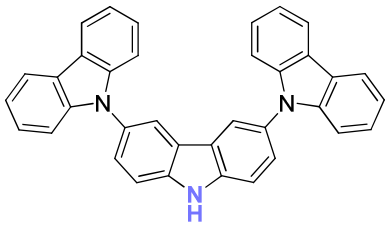


2,7-dimethoxy-9*H*-carbazole
Chemical Formula: $C_{14}H_{13}NO_2$
Exact Mass: 227,09
Molecular Weight: 227,26
m/z: 227.09 (100.0%), 228.10 (15.4%), 229.10 (1.6%)
Elemental Analysis: C, 73.99; H, 5.77; N, 6.16; O, 14.08

1i. 2,7-dimethoxycarbazole. Commercial 2,7-dibromocarbazole (from TCI, 9.2 mmol) and CuI (36.9 mmol) are placed in a Schlenk reactor under N_2 atmosphere. DMF (10 mL) and a solution of MeONa/MeOH (5.4 M, 45 mL) are added. The reactor is sealed under N_2 and heated at 110°C for 20 h. The crude is then directly filtered over a SiO_2 plug in ethyl acetate. The crude is then reduced, and purified over SiO_2 gel column chromatography. (height 320 mm, width 35 mm) in CH_2Cl_2 (5L), 61.1% isolated yield (light pink solid).

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ (ppm): 10.97 (s, 1H, NH), 7.84 (d, 2H, ^3J = 8.4 Hz), 6.94 (d, 2H, *J* = 2.0 Hz), 6.73 (dd, 2H, ^3J = 8.4 Hz, *J* = 2.0 Hz), 3.82 (s, 6H, CH_3).

^{13}C {^{1}H} NMR (101 MHz, $(CD_3)_2SO$) δ (ppm): 157.52 (s, C_{quat}), 140.99 (s, C_{quat}), 119.89 (s, CH), 116.43 (s, C_{quat}), 107.28 (s, CH), 94.62 (s, CH), 55.19 (s, CH_3).

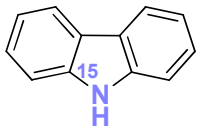


9'*H*-9,3':6',9''-terbenzo[*b*]indole
Chemical Formula: $C_{36}H_{23}N_3$
Exact Mass: 497,19
Molecular Weight: 497,59
m/z: 497.19 (100.0%), 498.19 (40.0%), 499.20 (7.5%)
Elemental Analysis: C, 86.90; H, 4.66; N, 8.44

1k. 2,7-di-(N-dicarbazo)-carbazole. Note: these are *not* optimized conditions. 3,6-dibromocarbazole **1g** (15.4 mmol), carbazole **1a** (153.4 mmol), CuI (61.5 mmol), *N,N*-tetramethylethylenediamine (120 mmol), K_3PO_4 (61.5 mmol) were united in a Schlenk reactor and exposed to 50 mL 1,4-dioxane under inert atmosphere. The reactor was sealed and heated at 135°C for 20 h. The crude is then directly filtered over a SiO_2 plug in ethyl acetate. The crude is then reduced, and purified over SiO_2 gel column chromatography. (height 330 mm, width 55 mm) in pentane/ CH_2Cl_2 = 6/4. This was however insufficient, thus a crystallization by slow evaporation of CH_2Cl_2 afforded the product as a white solid. 4.5% isolated yield.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ (ppm): 11.92 (s, 1H, NH), 8.52 (d, 2H, *J* = 2 Hz), 8.24 (d, 4H, ^3J = 7.6 Hz), 7.86 (d, 2H, ^3J = 8.4 Hz), 7.62 (dd, 2H, ^3J = 8.4 Hz, *J* = 2 Hz), 7.41 (m, 4H), 7.34 (d, 4H, ^3J = 8.4 Hz), 7.26 (m, 4H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CD_3)_2SO$) δ (ppm): 141.20 (s, C_{quat}), 139.67 (s, C_{quat}), 128.12 (s, C_{quat}), 126.05 (s, CH), 125.39 (s, CH), 123.35 (s, C_{quat}), 122.34 (s, C_{quat}), 120.38 (s, CH), 119.96 (s, CH), 119.57 (s, CH), 112.55 (s, CH), 109.66 (s, CH).



Chemical Formula: $C_{12}H_9{}^{15}N$
Exact Mass: 168,07
Molecular Weight: 168,20
m/z: 168.07 (100.0%), 169.07 (13.0%)
Elemental Analysis: C, 85.69; H, 5.39; N, 8.92

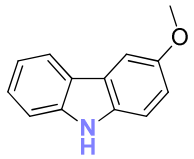
1l.^{15}N-carbazole (^{15}N, 98%+). Note: these are not optimized conditions.^{15}N-aniline (^{15}N, 98%+, commercial from Aldrich, 10.6 mmol) is diluted in 100 mL CH_2Cl_2 together with Et_3N (100 mmol). Acetyl chloride (100 mmol) is added slowly drop wise at r.t. under strong magnetic stirring. The crude is then filtered on a SiO_2 plug in EtOAc and evaporated. The crude is then purified over SiO_2 gel column chromatography (height 400 mm, width 35 mm) in 100% EtOAc, yielding the acetanilide in 93.9% (white solid). Inspired from a protocol from Taillefer et al. [16], the product is then engaged directly with CuI (1 mmol), K_3PO_4 (20 mmol), Dipivaloylmethane (CAS nr: 1118-71-4, 2 mmol), iodobenzene (15 mmol), and exposed to toluene (60 mL) in a Schlenk reactor under inert atmosphere. The reactor is then sealed and exposed to 140°C for 24 h. The crude is then filtered on a SiO_2 plug in EtOAc, and evaporated. The crude is then purified over SiO_2 gel column chromatography (height 450 mm, width 55 mm) in 100% EtOAc, yielding the diphenylacetamide in 55.8 % yield (5.92 mmol, white solid). The compound is then directly engaged in a ring-closing oxidation inspired of a protocol from Yuanjiang Pan et al. [17] The product is united with $Pd(OAc)_2$ (0.89 mmol), Ag_2O (14.8 mmol) in AcOH (30 mL) in a Schlenk reactor under inert atmosphere. The reactor is then sealed and exposed to 140°C under strong magnetic stirring for 36 h. The crude is then filtered on a SiO_2 plug in EtOAc, and evaporated. Two evaporations from toluene allow the removal of AcOH. The residue is then directly treated with $LiAlH_4$ (25 mmol) in 1,4-dioxane (30 mL). Caution is required here because of strongly exothermic reaction. The reaction takes place in a 250 mL round bottom flask equipped with a high condenser. The suspension is slowly and gently heated until boiling, under strong magnetic stirring, and then left to cool down at r.t.. The crude is then quenched drop wise with EtOH, and evaporated thrice with toluene. The crude is then filtered on a SiO_2 plug in CH_2Cl_2, and evaporated.

The crude is then purified over SiO_2 gel column chromatography. (height 420 mm, width 35 mm) in CH_2Cl_2 (100%), yielding 1.35 mmol of ^{15}N-carbazole as a white solid (22.8% over the last step, and 12.7% in overall yield).

The solubility in $CDCl_3$ is poor (hence the high temp. NMR), but this solvent allows easy recovery of the precious compound.

^{1}H NMR (600 MHz, 119 mM in $CDCl_3$, 323 K) δ (ppm): 8.11 (broad d, 2H, J = 7.2 Hz), 7.98 (d, NH, $^1J_{H\text{-}N}$ = 96.0 Hz), 7.45 (broad & tall signal, 4H), 7.27 (very broad signal, 2H).

^{13}C{^{1}H} NMR (151 MHz, 119 mM in $CDCl_3$, 323 K) δ (ppm): 139.62 (d,$^1J_{C\text{-}N}$ = 15.3 Hz, C_{quat}), 125.81 (d, $J_{C\text{-}N}$ = 2.3 Hz, CH), 123.52 (d,$^2J_{C\text{-}N}$ = 4.1 Hz, C_{quat}), 120.28 (s, CH), 119.48 (s, CH), 110.53 (d, $J_{C\text{-}N}$ = 2.3 Hz, CH).

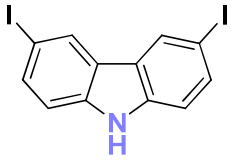


3-methoxy-9*H*-carbazole
Chemical Formula: $C_{13}H_{11}NO$
Exact Mass: 197,08
Molecular Weight: 197,23
m/z: 197.08 (100.0%), 198.09 (14.2%), 199.09 (1.1%)
Elemental Analysis: C, 79.16; H, 5.62; N, 7.10; O, 8.11

1m. 3-methoxycarbazole. 3-bromocarbazole (**1j**) (commercial from TCI, 8.1 mmol) was united with CuI (16.3 mmol) and submitted to DMF (10 mL). A solution of MeONa/MeOH (5.4 M, 25 mL) was added under inert atmosphere in a Schlenk reactor. The reactor was sealed and heated to 120°C for 20 h. The crude is then filtered on a SiO_2 plug in EtOAc, and evaporated. The crude is then purified over SiO_2 gel column chromatography. (height 380 mm, width 35 mm) in pentane/CH_2Cl_2 = 6/4. 61.6% isolated yield (white powder).

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.06 (d, 1H, ^3J = 7.8 Hz), 7.93 (broad s, NH), 7.60 (d, 1H, J = 2.4 Hz), 7.43 (m, 2H), 7.36 (d, 1H, ^3J = 8.8 Hz), 7.25 (m, 1H), 7.10 (dd, 1H, ^3J = 8.8 Hz, J = 2.4 Hz), 3.97 (s, CH 3).

$^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ (ppm): 153.92 (s, C_{quat}), 140.29 (s, C_{quat}), 134.38 (s, C_{quat}), 125.83 (s, CH), 123.80 (s, C_{quat}), 123.37 (s, C_{quat}), 120.28 (s, CH), 119.08 (s, CH), 115.10 (s, CH), 111.33 (s, CH), 110.77 (s, CH), 103.17 (s, CH), 56.11 (s, CH).



3,6-diiodo-9*H*-carbazole
Chemical Formula: $C_{12}H_7I_2N$
Exact Mass: 418,87
Molecular Weight: 419,00
m/z: 418.87 (100.0%), 419.87 (13.1%)
Elemental Analysis: C, 34.40; H, 1.68; I, 60.57; N, 3.34

1n. 3,6-diiodocarbazole. Carbazole (**1a,** 60 mmol) was suspended in AcOH (200 mL), and heated to 100°C. As soon as the temperature is reached, the heating is stopped, and ICl (120 mmol) diluted in AcOH (6 mL) is added dropwise under strong magnetic stirring. At the end of the addition, the crude is carried to 100°C again, and then left to stir at room temperature for 1 h. The crude is evaporated, and recrystallized five times from toluene. The toluene layers are reunited, evaporated, and resubmitted to five successive recrystallizations. Overall yield: 17.6% (white solid).

^{1}H NMR (600 MHz, C_6D_6) δ (ppm): 8.12 (s, 2H), 7.65 (d, ^{3}J = 8.2 Hz, 2H), 6.63 (d, ^{3}J = 8.2 Hz, 2H), 6.48 (broad s, NH).

$^{13}C\{^{1}H\}$ NMR (151 MHz, C_6D_6) δ (ppm): 138.50 (s, C_{quat}), 134.64 (s, CH), 129.59 (s, CH), 124.63 (s, C_{quat}), 112.30 (s, CH), 82.21 (s, C_{quat}, C-I).

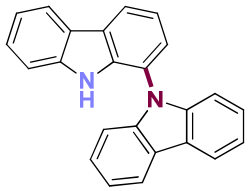
2.5.3. New cross dehydrogenative products.

Standard conditions.

Unless otherwise specified, the substrate (2 mmol scale), $[(p\text{-cymene})RuCl_2]_2$ (0.01 mmol), $Cu(OAc)_2$ (0.2 mmol), PhCl (5 mL), C_2Cl_4 (5 mL), and AcOH (1 mL) are united under air in a 170 mL reactor equipped with Teflon screw cap.

The reactor is then sealed (*tightly)* and exposed to 140°C for 23 h, 7 days, or 14 days. (magnetic stirring set to approx. 500 turns/min). The reactor is then cooled to room temperature and the crude mixture (typically blackish slurry) is directly engaged (unless otherwise specified) on SiO_2 gel column chromatography for purification.

Products characterization.



9*H*-1,9'-bicarbazole
Chemical Formula: $C_{24}H_{16}N_2$
Exact Mass: 332,13
Molecular Weight: 332,40
m/z: 332.13 (100.0%), 333.13 (26.7%), 334.14 (3.3%)
Elemental Analysis: C, 86.72; H, 4.85; N, 8.43

(2a). From carbazole **1a.** Product purified by SiO_2 gel column chromatography (height 430 mm, width 35 mm) in pentane/CH_2Cl_2 = 6/4. (white solid). Reaction time: Isolated yield:

23 h: 40.0%

7 days: 50.5%

14 days: 56.6%

^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ (ppm): 11.04 (s, NH), 8.36 (d, ^3J = 7.7 Hz, 1H), 8.32 (d, ^3J = 7.7 Hz, 2H), 8.26 (d, ^3J = 8.1 Hz, 1H), 7.54 (dd, ^3J = 7.5 Hz, J = 0.9 Hz, 1H), 7.43-7.38 (m, 5H), 7.31 (dd, $^3J \sim ^3J \sim$ 7.2 Hz, 2H), 7.24 (sym. m, lines: 7.258, 7.250, 7.244, 7.243, 7.237, 7.231, 7.229, 7.223, 7.216, 1H), 7.09 (d, ^3J = 8.1 Hz, 2H).

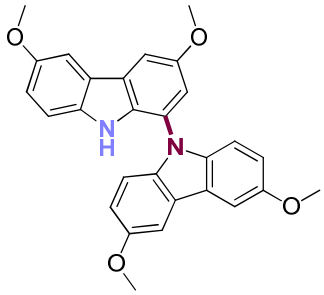
$^{13}C\{^1H\}$ NMR (151 MHz, $(CD_3)_2SO$) δ (ppm): 141.26 (s, C_{quat}), 140.63 (s, C_{quat}), 136.83 (s, C_{quat}), 126.65 (s, CH), 126 .62 (s, CH), 125.57 (s, C_{quat}), 125.20 (s, CH), 123.46 (s, C_{quat}), 123.02 (s, C_{quat}), 121.03 (s, CH), 121.01 (s, CH), 120.94 (s, CH), 120.61 (s, C_{quat}), 120 .29 (s, CH), 119.80 (s, CH), 119.63 (s, CH), 112.07 (s, CH), 110.30 (s, CH).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.25 (d, ^{3}J = 7.8 Hz, 3H), 8.19 (d, ^{3}J = 8.0 Hz, 1H), 7.77 (broad s, NH), 7.64 (dd, ^{3}J = 7.7 Hz, J = 0.9 Hz, 1H), 7.48-7.29 (m, 8H), 7.24 (d, ^{3}J = 8.1 Hz, 2H).

$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 140.70 (s, C_{quat}), 139.35 (s, C_{quat}), 136.03 (s, C_{quat}), 126.52 (s, CH), 126.20 (s, CH), 125.68 (s, C_{quat}), 124.87 (s, CH), 123.55 (s, C_{quat}), 123.42 (s, C_{quat}), 120.63 (s, C_{quat}), 120.58 (s, CH), 120.49 (s, CH), 120.23 (s, CH), 120.16 (s, CH), 120.10 (s, CH), 120.03 (s, CH), 111.0 (s, CH), 110.08 (s, CH).

GC-MS: Rt (50_40): 13.8 min; EI: 333 (26), 332 (100), 331 (31), 330 (40), 329 (8), 166 (16), 165 (16), 164 (6).

EI-HRMS: mass spectrometry: *m/z* calc. 332.1313 $[(C_{24}H_{16}N_2)]^{\bullet+}$, measured 332.1332.



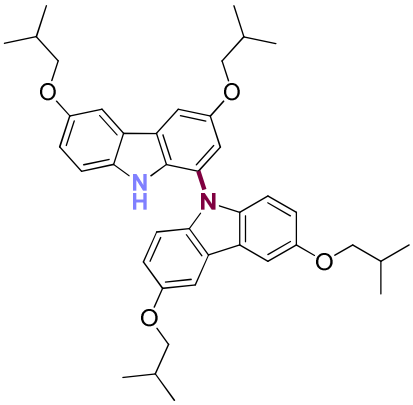
3,3',6,6'-tetramethoxy-9*H*-1,9'-bicarbazole
Chemical Formula: $C_{28}H_{24}N_2O_4$
Exact Mass: 452,17
Molecular Weight: 452,50
m/z: 452.17 (100.0%), 453.18 (30.7%), 454.18 (5.4%)
Elemental Analysis: C, 74.32; H, 5.35; N, 6.19; O, 14.14

(2b). From carbazole **1b.** 23 h reaction time. Product purified by SiO_2 gel column chromatography (height 410 mm, width 55 mm) in CH_2Cl_2 . Isolated yield: 62.6% (light yellow solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.66 (d, J = 2.2 Hz, 2H, possibly including broad NH), 7.61 (d, J = 2.4 Hz, 2H), 7.59 (d, J = 2.4 Hz, 1H), 7.25 (d, J = 2.2 Hz, 1H), 7.19 (d, ^{3}J = 8.8 Hz, 1H), 7.16 (d, ^{3}J = 8.8 Hz, 2H), 7.06 (dd, ^{3}J = 8.8 Hz, J = 2.4 Hz, 1H), 7.02 (dd, ^{3}J = 8.8 Hz, J = 2.4 Hz, 2H), 4.00 (s, 3H, CH_3O), 3.96 (s, 3H, CH_3O), 3.95 (s, 6H, 2 CH_3O).

$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 154.15 (s, C_{quat}), 153.91 (s, C_{quat}), 153.85 (s, C_{quat}), 136.03 (s, C_{quat}), 135.01 (s, C_{quat}), 131.65 (s, C_{quat}), 125.64 (s, C_{quat}), 123.80 (s, C_{quat}), 123.72 (s, C_{quat}), 121.62 (s, C_{quat}), 115.95 (s, CH), 115.26 (s, CH), 113.38 (s, CH), 111.89 (s, CH), 111.04 (s, CH), 103.20 (s, CH), 103.07 (s, CH), 103.03 (s, CH), 56.32 (s, CH_3O), 56.14 (s, CH_3O), 56.12 (s, CH_3O).

EI-HRMS: mass spectrometry: *m/z* calc. 452.1736 $[(C_{28}H_{24}N_2O_4)]^{\bullet+}$, measured 452.1765.



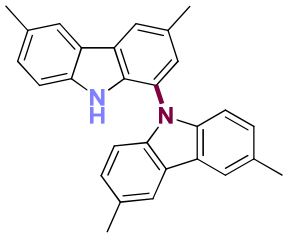
3,3',6,6'-tetraisobutoxy-9*H*-1,9'-bicarbazole
Chemical Formula: $C_{40}H_{48}N_2O_4$
Exact Mass: 620,36
Molecular Weight: 620,82
m/z: 620.36 (100.0%), 621.36 (44.0%), 622.37 (10.3%), 623.37 (1.7%)
Elemental Analysis: C, 77.39; H, 7.79; N, 4.51; O, 10.31

(2c). From carbazole **1c.** Product purified by SiO_2 gel column chromatography in toluene/ethanol = 100/1. Isolated yield: 56.1% (white solid).

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ (ppm): 10.36 (broad s, NH), 7.84 (d, *J* = 2.2 Hz, 1H), 7.82-7.78 (m, 2H) 7.73 (d, *J* = 2.4 Hz, 1H), 7.15 (d, ^{3}J = 8.8 Hz, 1H), 6.97 (d, *J* = 2.2 Hz, 1H), 6.96-6.88 (broad m, 5H), 3.89-3.72 (broad m, 8H), 2.10-1.93 (broad m, 4H), 1.05-0.91 (broad m, 24H).

$^{13}C\{^{1}H\}$ NMR (101 MHz, $(CD_3)_2SO$) δ (ppm): 153.14 (s, C_{quat}), 152.40 (s, C_{quat}), 152.20 (s, C_{quat}), 135.85 (s, C_{quat}), 135.53 (s, C_{quat}), 131.51 (s, C_{quat}), 125.19 (s, C_{quat}), 123.49 (s, C_{quat}), 122.87 (s, C_{quat}), 121.01 (s, C_{quat}), 116.15 (s, CH), 115.61 (s, CH), 113.15 (s, CH), 112.22 (s, CH), 110.62 (s, CH), 104.48 (s, CH), 104.29 (s, CH), 103.91 (s, CH), 74.79 (s, CH_2), 74.70 (s, CH_2), 74.60 (s, CH_2), 27.94 (s, CH), 27.90 (s, CH), 19.24 (s, CH_3), 19.20 (s, CH_3).

EI-HRMS: mass spectrometry: *m/z* calc. 620.3614 $[C_{40}H_{48}N_2O_4]^{\bullet+}$, measured 620.3622.



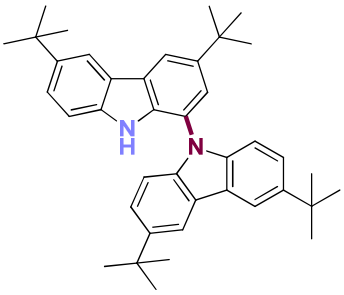
3,3',6,6'-tetramethyl-9*H*-1,9'-bicarbazole
Chemical Formula: $C_{28}H_{24}N_2$
Exact Mass: 388,19
Molecular Weight: 388,50
m/z: 388.19 (100.0%), 389.20 (30.6%), 390.20 (4.5%)
Elemental Analysis: C, 86.56; H, 6.23; N, 7.21

(2d). From carbazole **1d.** Product purified by SiO_2 gel column chromatography pentane/CH_2Cl_2 = 6/4. Isolated yield: 58.0% (white solid).

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.08 (broad s, 2H), 8.06 (broad s, 1H), 8.01 (broad s, 1H), 7.61 (broad s, NH), 7.48 (d, *J* = 0.7 Hz, 1H), 7.29-7.26 (broad m, 3H), 7.18 (d, ^3J = 8.4 Hz, 2H), 7.16 (d, ^3J = 8.1 Hz, 1H), 2.71 (s, 3H, CH_3), 2.66 (s, 6H, 2 CH_3), 2.63 (s, 3H, CH_3).

^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ (ppm): 139.44 (s, C_{quat}), 138.06 (s, C_{quat}), 134.64 (s, C_{quat}), 129.59 (s, C_{quat}), 129.39 (s, C_{quat}), 129.21 (s, C_{quat}), 127.82 (s, CH), 127.47 (s, CH), 125.79 (s, CH), 125.73 (s, C_{quat}), 123.71 (s, C_{quat}), 123.64 (s, C_{quat}), 120.80 (s, C_{quat}), 120.56 (s, CH), 120.11 (s, CH), 110.79 (s, CH), 109.99 (s, CH), 21.65 (s, CH_3), 21.62 (s, CH_3). One CH and one CH_3 line are overlapped.

ESI H.R. mass spectrometry: *m/z* calc. 411.1832 $[(C_{28}H_{24}N_2)Na]^+$, measured 411.1834.



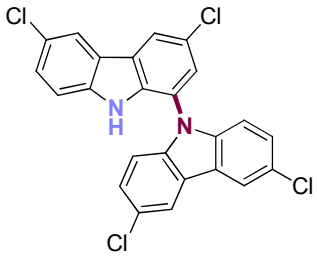
3,3',6,6'-tetra-*tert*-butyl-9*H*-1,9'-bicarbazole
Chemical Formula: $C_{40}H_{48}N_2$
Exact Mass: 556,38
Molecular Weight: 556,82
m/z: 556.38 (100.0%), 557.39 (43.8%), 558.39 (9.4%), 559.39 (1.4%)
Elemental Analysis: C, 86.28; H, 8.69; N, 5.03

(2e). From carbazole **1e.** Product purified by SiO_2 gel column chromatography in pentane/dichloromethane = 3/2. Isolated yield: 58.6% (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.25 (d, *J* = 1.7 Hz, 2H), 8.22 (d, *J* = 1.7 Hz, 1H), 8.19 (d, *J* = 1.7 Hz, 1H), 7.65 (d, *J* = 1.7 Hz, 2H), 7.64 (broad s, NH), 7.51-7.45 (m, 3H), 7.24 (d, ^3J = 8.3 Hz, 1H), 7.16 (d, ^3J = 8.6 Hz, 2H), 1.53 (s, 9H, $C(CH_3)_3$), 1.52 (s, 18H, $C(CH_3)_3$), 1.50 (s, 9H, $C(CH_3)_3$).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 143.36 (s, C_{quat}), 142.90 (s, C_{quat}), 142.80 (s, C_{quat}), 139.14 (s, C_{quat}), 137.82 (s, C_{quat}), 134.23 (s, C_{quat}), 125.37 (s, C_{quat}), 124.16 (s, CH), 123.81 (s, CH), 123.45 (s, C_{quat}), 123.37 (s, C_{quat}), 122.43 (s, C_{quat}), 120.46 (s, C_{quat}), 116.44 (s, CH), 116.36 (s, CH), 115.75 (s, CH), 110.43 (s, CH), 109.52 (s, CH), 34.81 (s, C_{quat}), 34.69 (s, C_{quat}), 32.09 (s, $(CH_3)_3$), 32.04 (s, $(CH_3)_3$).

EI-HRMS: mass spectrometry: *m/z* calc. 556.3817 $[C_{40}H_{48}N_2]^{\bullet+}$, measured 556.3828.



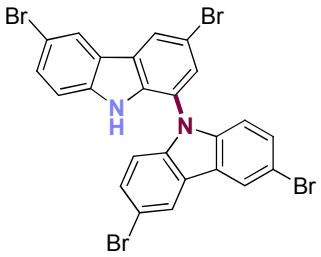
3,3',6,6'-tetrachloro-9*H*-1,9'-bicarbazole
Chemical Formula: $C_{24}H_{12}Cl_4N_2$
Exact Mass: 467,98
Molecular Weight: 470,18
m/z: 469.97 (100.0%), 467.98 (78.2%), 471.97 (48.1%), 470.98 (26.1%), 468.98 (20.4%), 472.97 (12.8%), 473.97 (10.3%), 471.98 (3.3%), 474.97 (2.7%), 469.98 (2.7%), 473.98 (1.6%)
Elemental Analysis: C, 61.31; H, 2.57; Cl, 30.16; N, 5.96

(2f). From carbazole **1f.** Product purified by SiO_2 gel column chromatography (height 420 mm, width 35 mm) in pentane/dichloromethane = 6/4. Isolated yield: 39.8% (white solid).

^{1}H NMR (400 MHz, $CDCl_3$ + $(CD_3)_2SO$) δ (ppm): 10.78 (s, NH), 8.13 (d, 1H, *J* = 1.7 Hz), 8.09 (d, 2H, *J* = 1.7 Hz), 8.02 (broad d, 1H, *J* ~ 1.0 Hz), 7.44 (d, 1H, *J* = 2.0 Hz), 7.33 (dd, 2H, ^3J = 8.6 Hz, *J* = 2.0 Hz), 7.29 (m, 2H), 7.07 (d, 2H,^3J = 8.6 Hz).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$ + $(CD_3)_2SO$) δ (ppm): 139.28 (s, C_{quat}), 138.91 (s, C_{quat}), 135.17 (s, C_{quat}), 126.59 (s, CH), 126.55 (s, CH), 125.45 (s, C_{quat}), 125.17 (s, C_{quat}), 124.59 (s, CH), 124.46 (s, C_{quat}), 123.67 (s, C_{quat}), 123.19 (s, C_{quat}), 122.73 (s, C_{quat}), 120.21 (s, CH), 120.04 (s, C_{quat}), 119.68 (s, CH), 119.62 (s, CH), 112.66 (s, CH), 111.16 (s, CH).

EI-HRMS: mass spectrometry: *m/z* calc. 469.9725 $[(C_{24}H_{12}Cl_4N_2)]$•+, measured 469.9746.



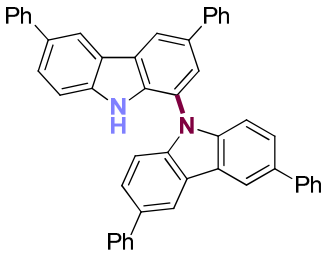
3,3',6,6'-tetrabromo-9*H*-1,9'-bicarbazole
Chemical Formula: $C_{24}H_{12}Br_4N_2$
Exact Mass: 643,77
Molecular Weight: 647,98
m/z: 647.77 (100.0%), 645.77 (68.5%), 649.77 (65.0%), 648.77 (26.7%), 646.77 (18.3%), 651.77 (18.0%), 643.77 (17.6%), 650.77 (16.9%), 644.78 (4.6%), 652.77 (4.1%), 649.78 (3.3%), 647.78 (2.2%)
Elemental Analysis: C, 44.49; H, 1.87; Br, 49.32; N, 4.32

(2g). From carbazole **1g.** Product purified by SiO_2 gel column chromatography (height 460 mm, width 35 mm) in pentane/dichloromethane = 6/4. Isolated yield: 23.3% (white solid).

^{1}H NMR (400 MHz, C_6D_6) δ (ppm): 8.01 (d, *J* = 2.0 Hz, 2H), 7.89 (d, *J* = 2.0 Hz, 1H), 7.88 d, *J* = 2.0 Hz, 1H), 7.31 (dd, ^3J = 8.8 Hz, *J* = 2.0 Hz, 1H), 7.29 (dd, ^3J = 8.8 Hz, *J* = 2.0 Hz, 2H), 7.13 (d, *J* = 2.0 Hz, 1H), 6.53 (broad s, NH), 6.38 (d, ^3J = 8.8 Hz, 2H), 6.33 (d, ^3J = 8.8 Hz, 1H).

^{13}C{^{1}H} NMR (101 MHz, C_6D_6) δ (ppm): 139.53 (s, C_{quat}), 138.19 (s, C_{quat}), 134.89 (s, C_{quat}), 130.18 (s, CH), 130.08 (s, CH), 128.21 (s, CH), 127.95 (s, CH), 126.24 (s, C_{quat}), 124.45 (s, C_{quat}), 124.05 (s, C_{quat}), 123.90 (s, CH), 123.79 (s, CH), 120.78 (s, C_{quat}), 114.05 (s, C_{quat}), 113.59 (s, C_{quat}), 112.90 (s, CH), 112.41 (s, C_{quat}), 111.70 (s, CH).

EI-HRMS: mass spectrometry: *m/z* calc. 647.7693 $[(C_{24}H_{12}Br_4N_2)]^{\bullet+}$, measured 647.7709.



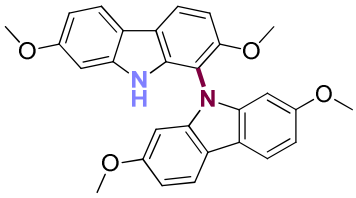
3,3',6,6'-tetraphenyl-9*H*-1,9'-bicarbazole
Chemical Formula: $C_{48}H_{32}N_2$
Exact Mass: 636,26
Molecular Weight: 636,78
m/z: 636.26 (100.0%), 637.26 (52.3%), 638.26 (13.6%), 639.27 (2.2%)
Elemental Analysis: C, 90.54; H, 5.07; N, 4.40

(2h). From carbazole **1h.** Product purified by SiO_2 gel column chromatography (height 460 mm, width 35 mm) in pentane/dichloromethane = 6/4. Isolated yield: 83.5% (white solid).

^{1}H NMR (600 MHz, C_6D_6) δ (ppm): 8.69 (d, *J* = 1.5 Hz, 2H), 8.57 (d, *J* = 1.2 Hz, 1H), 8.51 (d, *J* = 1.8 Hz, 1H), 7.92 (d, *J* = 1.5 Hz, 1H), 7.86-7.85 (m, 4H), 7.80 (dd, ^3J = 8.4 Hz, *J* = 1.2 Hz, 2H), 7.76 (dd, ^3J = 8.4 Hz, *J* = 1.2 Hz, 2H), 7.74 (dd, ^3J = 8.5 Hz, *J* = 1.8 Hz, 2H), 7.72 (dd, ^3J = 8.5 Hz, *J* = 1.8 Hz, 1H), 7.49-7.20 (aromatic area, ~14H), in which: 7.30 (d, ^3J = 8.5 Hz, 2H), 7.19 (broad s. NH), 6.91 (broad d, ^3J = 7.9 Hz, 1H).

^{13}C{^{1}H} NMR (151 MHz, C_6D_6) δ (ppm): 142.12 (s, C_{quat}), 141.13 (s, C_{quat}), 139.49 (s, C_{quat}), 135.92 (s, C_{quat}), 134.52 (s, C_{quat}), 134.46 (s, C_{quat}), 134.12 (s, C_{quat}), 129.02 (s, CH), 129.00 (s, CH), 128.95 (s, CH), 127.62 (s, CH), 127.59 (s, CH), 127.11 (s, CH), 126.87 (s, CH), 126.83 (s, CH), 126.45 (s, CH), 126.38 (s, CH), 124.71 (s, C_{quat}), 124.45 (s, CH), 124.37 (s, C_{quat}), 121.19 (s, C_{quat}), 119.43 (s, CH), 119.30 (s, CH), 118.96 (s, CH), 111.79 (s, CH), 110.82 (s, CH). One CH and three C_{quat} lines are overlapped.

ESI H.R. mass spectrometry: *m/z* calc. 659.2458 $[(C_{48}H_{32}N_2)Na]^+$, measured 659.2449.



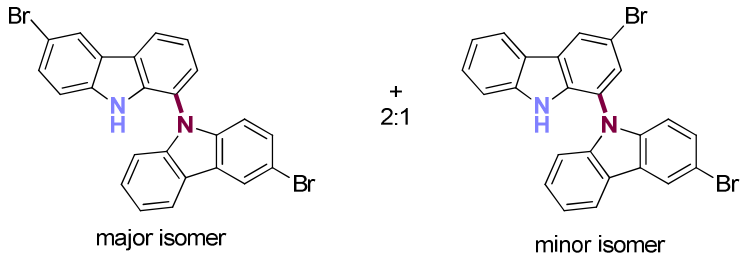
2,2',7,7'-tetramethoxy-9*H*-1,9'-bicarbazole
Chemical Formula: $C_{28}H_{24}N_2O_4$
Exact Mass: 452,17
Molecular Weight: 452,50
m/z: 452.17 (100.0%), 453.18 (30.7%), 454.18 (5.4%)
Elemental Analysis: C, 74.32; H, 5.35; N, 6.19; O, 14.14

(2i). From carbazole **1i.** Product purified by SiO_2 gel column chromatography (height 450 mm, width 55 mm) in toluene/EtOAc = 7/3. Isolated yield: 27.0% (colorless viscous substance which slowly solidifies in vacuum).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.03 (d, 1H, ^3J = 8.5 Hz), 7.96 (d, 2H, ^3J = 8.6 Hz), 7.92 (d, 1H, ^3J = 8.6 Hz), 7.66 (s, NH), 7.07 (d, 1H, ^3J = 8.8 Hz), 6.90 (dd, 2H, ^3J = 8.6 Hz, J = 2.4 Hz), 6.86 (dd, 1H, ^3J = 8.8 Hz, J = 2.4 Hz), 6.67 (d, 1H, J = 2.2 Hz), 6.52 (d, 2H, J = 2.2 Hz), 3.80 (s, 3H, CH_3), 3.79 (s, 3H, CH_3), 3.73 (s, 6H, CH_3).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 158.68 (s, C_{quat}), 158.46 (s, C_{quat}), 154.24 (s, C_{quat}), 142.00 (s, C_{quat}), 141.01 (s, C_{quat}), 138.24 (s, C_{quat}), 120.43 (s, CH), 120.23 (s, CH), 120.04 (s, CH), 119.11 (s, C_{quat}), 117.50 (s, C_{quat}), 117.34 (s, C_{quat}), 108.61 (s, CH), 108.40 (s, CH), 107.99 (s C_{quat}), 105.33 (s, CH), 95.13 (s, CH), 94.60 (s, CH), 56.62 (s, CH_3), 55.69 (s, CH_3), 55.59 (s, CH_3).

EI-HRMS: mass spectrometry: *m/z* calc. 452.1736 [($C_{28}H_{24}N_2O_4$)]•+, measured 452.1746.



Chemical Formula: $C_{24}H_{14}Br_2N_2$
Exact Mass: 487,95
Molecular Weight: 490,19
m/z: 489.95 (100.0%), 487.95 (51.3%), 491.95 (48.8%), 490.95 (26.7%), 488.96 (13.4%), 492.95 (13.1%), 491.96 (3.3%), 489.96 (1.7%), 493.95 (1.7%)
Elemental Analysis: C, 58.81; H, 2.88; Br, 32.60; N, 5.71

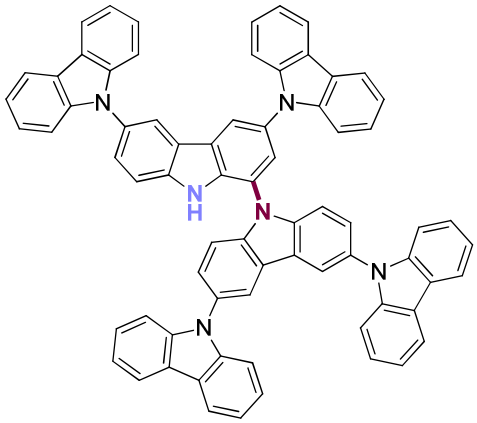
(2j)-mixture of isomers. From carbazole **1j.** Product purified by SiO_2 gel column chromatography (height 400 mm, width 35 mm) in pentane/dichloromethane = 6/4. Isolated yield: 44.1% (white solid, also much more soluble in comparison to **2g,** the tetra-bromo-analogue).

Note for the ^{1}H NMR: because the regio-isomeric ratio is precisely 2:1, the normalized integration (^{1}H) is calibrated for ^{1}H of the minor isomer, for convenience. Identification through HMBC-NMR.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.17 (m, 4H, lines 8.1774, 8.1732, 8.1683, 8.1634, 8.1597, 8.1548), 8.10 (d, 2H, *J* = 1.7 Hz), 7.99 (m, 5H, lines 8.0076, 7.9972, 7.9880, 7.9794, 7.9782, 7.9715, 7.9703), 7.93 (d, 1H, ^3J = 7.8 Hz), 7.55 (s, NH minor), 7.54 (s, NH major), 7.51 (d, 1H, *J* = 1.7 Hz), 7.41 (dd, 2H, ^3J = 7.6 Hz, *J* = 1.0 Hz), 7.32-7.08 (araomatic area, ~15H, lines: 7.3194, 7.3139, 7.3084, 7.3035, 7.2974, 7.2919, 7.2901, 7.2870, 7.2815, 7.2705, 7.2620, 7.2583, 7.2546, 7.2516, 7.2436, 7.2412, 7.2381, 7.2345, 7.2235, 7.2204, 7.1996, 7.1972, 7.1892, 7.1868, 7.1795, 7.1691, 7.1679, 7.1630, 7.1605, 7.1520, 7.1495, 7.1397, 7.1379, 7.1202, 7.1025, 7.1000, 7.0847), 7.06 (d, 1H, ^3J = 8.0 Hz), 7.01 (~t or d+dd, 3H, ^3J ~^3J ~ 7.8 Hz), 6.93 (d, 2H, ^3J = 8.8 Hz), 6.89 (d, 1H, ^3J = 8.6 Hz), 6.87 (d, 2H, ^3J = 8.6 Hz).

$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 140.95 (s, C_{quat}), 140.79 (s, C_{quat}), 139.65 (s, C_{quat}), 139.28 (s, C_{quat}), 139.10 (s, C_{quat}), 137.94 (s, C_{quat}), 136.22 (s, C_{quat}), 134.71 (s, C_{quat}), 129.41 (s, CH), 129.13 (s, CH), 129.01 (s, CH), 127.48 (s, CH), 127.28 (s, CH), 127.21 (s, CH), 127.08 (s, CH), 125.50 (s, CH), 125.44 (s, C_{quat}), 125.35 (s, C_{quat}), 125.17 (s, C_{quat}), 124.83 (s, C_{quat}), 123.44 (s, CH), 123.40 (s, CH), 123.35 (s, CH), 122.66 (s, C_{quat}), 122.58 (s, C_{quat}), 122.40 (s, C_{quat}), 121.12 (s, C_{quat}), 121.02 (s, CH), 120.87 (s, CH), 120.85 (s, CH), 120.83 (s, CH), 120.77 (s, CH), 120.74 (s, CH), 120.66 (s, CH), 120.64 (s, CH), 120.37 (s, C_{quat}), 113.49 (s, C_{quat}), 113.23 (s, C_{quat}), 113.03 (s, C_{quat}), 112.53 (s, CH), 111.93 (s, C_{quat}), 111.53 (s, CH), 111.52 (s, CH), 111.29 (s, CH), 110.28 (s, CH), 110.27 (s, CH). Note: one C_{quat} and one CH lines are overlapped.

EI-HRMS: mass spectrometry: *m/z* calc. 489.9503 $[(C_{24}H_{14}Br_2N_2)]^{\bullet+}$, measured 489.9514.



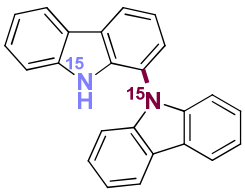
6',6''-di(9*H*-carbazol-9-yl)-9'*H*-9,3':1',9'':3'',9'''-quatercarbazole
Chemical Formula: $C_{72}H_{44}N_6$
Exact Mass: 992,36
Molecular Weight: 993,16
m/z: 992.36 (100.0%), 993.37 (78.4%), 994.37 (30.3%), 995.37 (8.2%), 993.36 (2.2%), 994.36 (1.7%), 996.38 (1.4%)
Elemental Analysis: C, 87.07; H, 4.47; N, 8.46

(2k). From carbazole **1k.** Product purified by SiO_2 gel column chromatography (height 280 mm, width 35 mm) in pentane/dichloromethane = 6/4. Isolated yield: 56.6% (white solid, caution: this compound has a tendency to tail on silica, use short column).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.53 (d, 1H, *J* = 1.7 Hz), 8.43 (m, ~3H, lines: 8.4493, 8.4450, 8.4181), 8.23 (m, ~8H, lines: 8.2558, 8.2360, 8.2281, 8.2165, 8.2091), 8.10 (d, 1H, *J* = 1.7 Hz), 7.76 (dd, 2H, ^{3}J = 8.6 Hz, *J* = 2.0 Hz), 7.73-7.33 (aromatic area, ~29H, lines: 7.7300, 7.7257, 7.7153, 7.6939, 7.6371, 7.6163, 7.5424, 7.5399, 7.5222, 7.5008, 7.4965, 7.4697, 7.4605, 7.4495, 7.4000, 7.3817, 7.3627, 7.3474, 7.3303).

$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 141.77 (s, C_{quat}), 141.73 (s, C_{quat}), 141.67 (s, C_{quat}), 140.28 (s, C_{quat}), 139.17 (s, C_{quat}), 135.78 (s, C_{quat}), 131.26 (s, C_{quat}), 130.92 (s, C_{quat}), 127.32 (s, CH), 128.88 (s, CH), 126.62 (s, C_{quat}), 126.25 (s, CH), 126.06 (s, CH), 124.90 (s, CH), 124.60 (s, C_{quat}), 124.35 (s, C_{quat}), 123.48 (s, C_{quat}), 123.33 (s, C_{quat}), 121.37 (s, C_{quat}), 120.61 (s, CH), 120.47 (s, CH), 120.33 (s, CH), 120.25 (s, CH), 119.95 (s, CH), 112.82 (s, CH), 111.53 (s, CH), 109.67 (s, CH), 109.60 (s, CH). Note: six CH and two C_{quat} lines are overlapped.

ESI H.R. mass spectrometry: *m/z* calc. 1015.3520 $[(C_{72}H_{44}N_6)Na]+$, measured 1015.3495.



Chemical Formula: $C_{24}H_{16}{}^{15}N_2$
Exact Mass: 334,13
Molecular Weight: 334,38
m/z: 334.13 (100.0%), 335.13 (26.1%), 336.13 (3.2%)
Elemental Analysis: C, 86.21; H, 4.82; N, 8.97

(2l). From carbazole **1l,** (two weeks reaction time). Product purified by SiO_2 gel column chromatography (height 420 mm, width 35 mm) in pentane/dichloromethane = 6/4. (white solid). Reaction time: Isolated yield: 54.1% (white solid).

Note: for precise NMR coupling measurements, the compound was analyzed on a 200 MHz, 400 MHz and 600 MHz for comparison. 2D NMR spectra were recorded the 400 MHz. The ^{1}H NMR was definitely sharper on the 600 MHz:

^{1}H NMR (600 MHz, 150 mM in $CDCl_3$) δ (ppm): 8.273 (d, 2H, ^{3}J = 7.7 Hz), 8.267 (d, 1 H, ^{3}J = 7.7 Hz), 8.21 (d, 1H, ^{3}J = 7.7 Hz), 7.76 (d, NH, ^{1}J = 97.6 Hz), 7.65 (dm, 1H, ^{3}J = 7.6 Hz, also J ~ 1.0 Hz), 7.48 (dd, 1H, ^{3}J ~ ^{3}J ~ 7.7 Hz), 7.44 (d+dd, 3H, ^{3}J ~^{3}J ~ 7.7 Hz), 7.38 (ddd, 2H, ^{3}J ~ ^{3}J ~ 7.5 Hz, J ~ 1.0 Hz), 7.33 (ddd, 1H, ^{3}J ~ ^{3}J ~ 7.5 Hz, J ~ 0.7 Hz), 7.29 (d, 1H, ^{3}J = 8.1 Hz), 7.26 (d, 2H, ^{3}J = 8.5 Hz).

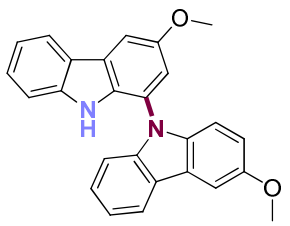
The multiplets in the ^{13}C NMR were best defined on the 200 MHz:

^{13}C{^{1}H} NMR (50 MHz, 150 mM in $CDCl_3$) δ (ppm): 140.72 (d, $^{1}J_{CN}$ = 16.0 Hz, C_{quat}), 139.35 (d, ^{1}J *CN* = 15.5 Hz, C_{quat}), 136.02 (dd, $^{1}J_{CN}$ = 16.4 Hz, $^{2}J_{CN}$ = 1.0 Hz, C_{quat}), 126.56 (d, J = 1.8 Hz, CH), 126.25 (d, J = 1.8 Hz, CH), 125.70 (dd, J = 3.7 Hz, J = 1.4 Hz, C_{quat}), 124.93 (dd, J ~ J ~ 1.5 Hz, CH), 123.58 (d, $^{2}J_{CN}$ = 4.1 Hz, C_{quat}), 123.43 (d, $^{2}J_{CN}$ = 3.7 Hz, C_{quat}), 120.63 (dd, $^{1}J_{CN}$ = 17.3 Hz, $^{2}J_{CN}$ = 0.9 Hz, C_{quat}), 120.63 (d, J = 1.0 Hz, CH), 120.55 (d, J = 1.0 Hz, CH), 120.29 (broad s, CH), 120.21 (s, CH), 120.14 (d, J = 1.8 Hz, CH), 120.06 (s, CH), 111.05 (d, J = 1.8 Hz, CH), 110.14 (d, J = 1.4 Hz, CH).

^{1}H-^{15}N HMBC (^{1}H: 400 MHz, ^{15}N: 41 MHz (corr. 96 Hz), 150 mM in $CDCl_3$) δ (ref.CH_3NO_2, ppm): -291.7 (s, NH).

^{1}H-^{15}N HMBC (^{1}H: 400 MHz, ^{15}N: 41 MHz (corr. 2 Hz), 150 mM in $CDCl_3$) δ (ref. CH_3NO_2, ppm): -276.5 (s, tertiary N), -291.7 (s, NH).

EI-HRMS: mass spectrometry: *m/z* calc. 334.1254 [($C_{24}H_{16}{}^{15}N_2$)] $^{\bullet+}$, measured 334.1264.



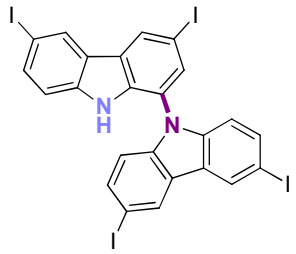
Chemical Formula: $C_{26}H_{20}N_2O_2$
Exact Mass: 392,15
Molecular Weight: 392,45
m/z: 392.15 (100.0%), 393.16 (28.4%), 394.16 (4.3%)
Elemental Analysis: C, 79.57; H, 5.14; N, 7.14; O, 8.15

(2m). From carbazole **1m**. 7 days reaction time. Product purified by SiO_2 gel column chromatography in toluene/ethanol = 100/1. Isolated yield: 16.1% (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.09 (d, ^{3}J = 7.6 Hz, 1H), 8.03 (d, ^{3}J = 7.8 Hz, 1H), 7.62 (d, *J* = 2.2 Hz, 1H), 7.60 (d, *J* = 2.4 Hz, 1H), 7.53 (broad s, NH), 7.36-7.04 (m, 8H), 6.95 (dd, ^{3}J = 8.8 Hz, *J* = 2.4 Hz, 1H), 3.91 (s, 3H, CH_3O), 3.88 (s, 3H, CH_3O).

$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 154.54 (s, C_{quat}), 154.22 (s, C_{quat}), 141.01 (s, C_{quat}), 140.03 (s, C_{quat}), 135.47 (s, C_{quat}), 130.84 (s, C_{quat}), 126.54 (s, CH), 126.24 (s, CH), 125.80 (s, C_{quat}), 124.02 (s, C_{quat}), 123.47 (s, C_{quat}), 123.34 (s, C_{quat}), 121.23 (s, C_{quat}), 120.53 (s, CH), 120.47 (s, CH), 119.85 (s, CH), 119.57 (s, CH), 115.16 (s, CH), 113.32 (s, CH), 111.12 (s, CH), 110.91 (s, CH), 110.27 (s, CH), 103.52 (s, CH), 103.48 (s, CH). 56.35 (s, CH_3), 56.08 (s, CH_3).

EI-HRMS: mass spectrometry: *m/z* calc. 392.1525 $[(C_{26}H_{20}N_2O_2)]^{\bullet+}$, measured 392.1510.



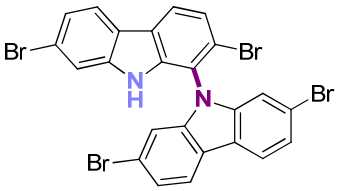
3,3',6,6'-tetraiodo-9*H*-1,9'-bicarbazole
Chemical Formula: $C_{24}H_{12}I_4N_2$
Exact Mass: 835,72
Molecular Weight: 835,98
m/z: 835.72 (100.0%), 836.72 (26.1%), 837.72 (3.4%)
Elemental Analysis: C, 34.48; H, 1.45; I, 60.72; N, 3.35

(2n). From carbazole **1n**. 7 days reaction time. Product purified by SiO_2 gel column chromatography (height 460 mm, width 35 mm) in pentane/CH_2Cl_2 = 6/4. Isolated yield: 24.9% (white solid).

^{1}H NMR (400 MHz, C_6D_6) δ (ppm): 8.17 (d, *J* = 1.7 Hz, 2H), 8.04 (d, *J* = 1.5 Hz, 1H), 8.03 d, *J* = 1.5 Hz, 1H), 7.46 (dd, ^{3}J = 8.8 Hz, *J* = 2.0 Hz, 1H), 7.43 (dd, ^{3}J = 8.8 Hz, *J* = 1.6 Hz, 2H), 7.30 (d, *J* = 1.5 Hz, 1H), 6.47 (broad s, NH), 6.28 (d, ^{3}J = 8.8 Hz, 2H), 6.21 (d, ^{3}J = 8.8 Hz, 1H).

$^{13}C\{^{1}H\}$ NMR (101 MHz, C_6D_6) δ (ppm): 139.73 (s, C_{quat}), 138.38 (s, C_{quat}), 135.68 (s, CH), 135.63 (s, CH), 135.11 (s, C_{quat}), 133.21 (s, CH), 129.91 (s, CH), 129.87 (s, CH), 129.83 (s, CH), 126.65 (s, C_{quat}), 124.86 (s, C_{quat}), 124.43 (s, C_{quat}), 120.92 (s, C_{quat}), 113.28 (s, CH), 112.09 (s, CH), 83.84 (s, C_{quat}, C-I), 83.39 (s, C_{quat}, C-I), 81.76 (s, C_{quat}, C-I).

GC-MS: EI: *m/z* calc. 835.72 $[(C_{24}H_{12}I_4N_2)]^{\bullet+}$, measured 835.70.



2,2',7,7'-tetrabromo-9*H*-1,9'-bicarbazole
Chemical Formula: $C_{24}H_{12}Br_4N_2$
Exact Mass: 643,77
Molecular Weight: 647,98
m/z: 647.77 (100.0%), 645.77 (68.5%), 649.77 (65.0%), 648.77 (26.7%), 646.77 (18.3%), 651.77 (18.0%), 643.77 (17.6%), 650.77 (16.9%), 644.78 (4.6%), 652.77 (4.1%), 649.78 (3.3%), 647.78 (2.2%)
Elemental Analysis: C, 44.49; H, 1.87; Br, 49.32; N, 4.32

(2o). From carbazole **1o**. 7 days reaction time. Product purified by SiO_2 gel column chromatography in pentane/dichloromethane = 3/2. Isolated yield: 12.8% (white solid).

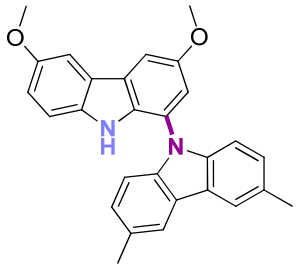
^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ (ppm): 11.45 (s, NH), 8.39 (d, ^3J = 8.6 Hz, 1H), 8.33 (d, ^3J = 8.3 Hz, 2H), 8.25 (d, ^3J = 8.3 Hz, 1H), 7.71 (d, ^3J = 8.3 Hz, 1H), 7.54-7.48 (m, 3H), 7.41 (dd, ^3J = 8.3 Hz, J = 1.7 Hz, 1H), 7.09 (d, J = 1.5 Hz, 2H).

$^{13}C\{^1H\}$ NMR (101 MHz, $(CD_3)_2SO$) δ (ppm): 141.18 (s, C_{quat}), 138.69 (s, C_{quat}), 123.87 (s, C_{quat}), 123.65 (s, CH), 123.41 (s, CH), 122.76 (s, CH), 122.69 (s, CH), 122.58 (s, CH), 121.80 (s, C_{quat}), 121.54 (s, C_{quat}), 120.27 (s, C_{quat}), 119.57 (s, C_{quat}), 119.50 (s, C_{quat}), 119.35 (s, C_{quat}), 117.33 (s, C_{quat}), 114.13 (s, CH), 112.39 (s, CH). One CH line is overlapped.

EI-HRMS: mass spectrometry: *m/z* calc. 643.7734 $[(C_{24}H_{12}Br_4N_2)]^{\bullet+}$, measured 643.7748.

Hetero-coupling: See scheme 7

From 3,6-dimethoxycarbazole **1b** and 3,6-dimethylcarbazole **1d**. Purification: SiO_2 gel column chromatography, pentane/CH_2Cl_2 = 6/4 to pure CH_2Cl_2. There is significantly more **2bd (14%)** than **2db (8%)** and especially more homo-coupling product **2b (30%)** than **2d (2%).** The overall yield of coupling products is 54%. Characterization of **2bd**:



3,6-dimethoxy-3',6'-dimethyl-9*H*-1,9'-bicarbazole
Chemical Formula: $C_{28}H_{24}N_2O_2$
Exact Mass: 420,18
Molecular Weight: 420,50
m/z: 420.18 (100.0%), 421.19 (30.6%), 422.19 (4.9%)
Elemental Analysis: C, 79.98; H, 5.75; N, 6.66; O, 7.61

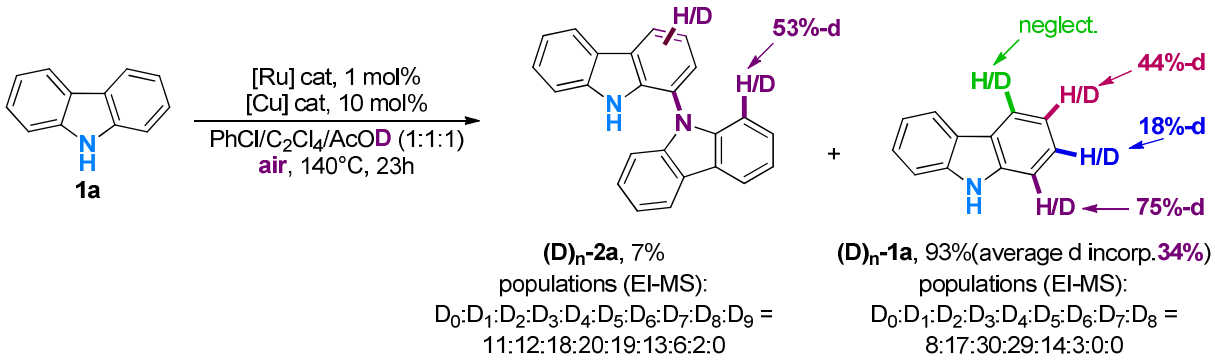
2bd.

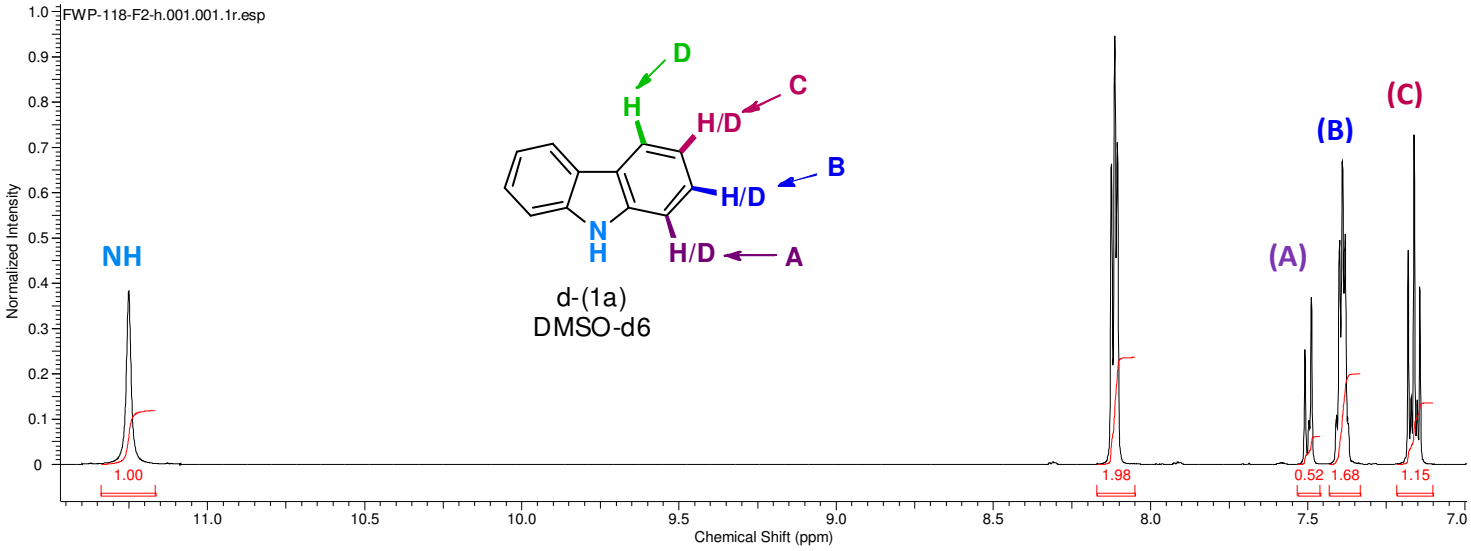
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.98 (broad s, 2H), 7.66 (d, *J* = 2.2 Hz, 1H), 7.59 (d, *J* = 2.4 Hz, 1H), 7.48 (broad s, NH), 7.27 (d, (d, *J* = 2.2 Hz, 1H), 7.22 (dd, , ^{3}J = 8.4 Hz, *J* = 1.2 Hz, 2H), 7.17 (d, ^{3}J = 8.6 Hz, 1H), 7.14 (d, ^{3}J = 8.0 Hz, 2H), 7.06 (dd, ^{3}J = 8.8 Hz, *J* = 2.4 Hz, 1H), 4.00 (s, 3H, CH_3O), 3.97 (s, 3H, CH_3O), 2.58 (s, 6H, 2 CH_3-Ar).

$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ (ppm): 153.91 (s, C_{quat}), 153.86 (s, C_{quat}), 139.00 (s, C_{quat}), 134.96 (s, C_{quat}), 131.64 (s, C_{quat}), 129.39 (s, C_{quat}), 127.33 (s, CH), 125.60 (s, C_{quat}), 123.73 (s, C_{quat}), 123.56 (s, C_{quat}), 121.57 (s, C_{quat}), 120.37 (s, CH), 115.92 (s, CH), 113.40 (s, CH), 111.85 (s, CH), 109.80 (s, CH), 103.11 (s, CH), 103.07 (s, CH), 56.31 (s, CH_3O), 56.14 (s, CH_3O), 21.44 (s, CH_3-Ar).

2.5.4. Isotopic and kinetic experiments.

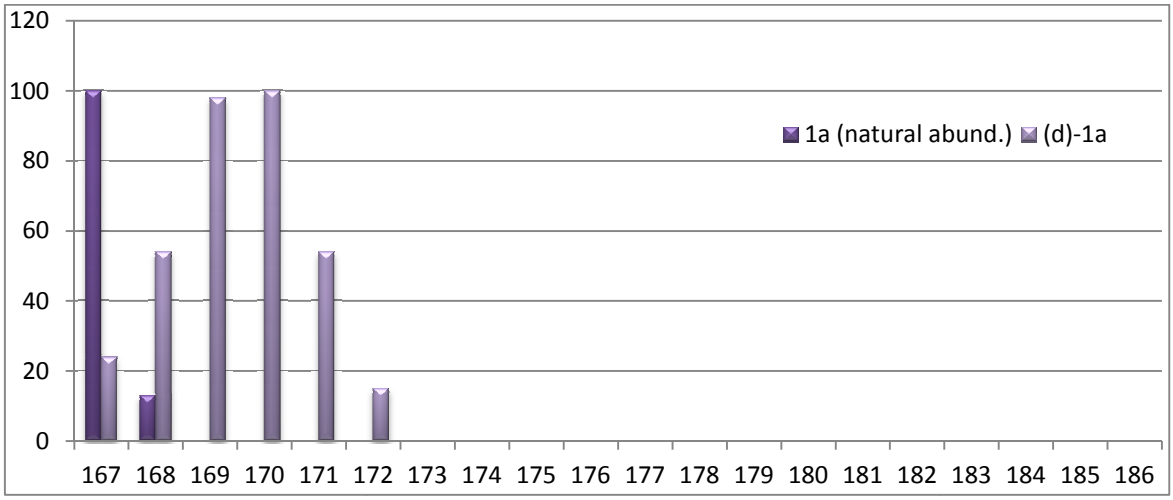
In the first experiment, carbazole **1a** (2 mmol), $[(p\text{-cymene})RuCl_2]_2$ (0.02 mmol), $Cu(OAc)_2$ (0.2 mmol), PhCl (5 mL), C_2Cl_4 (5 mL), and AcO**D** (acetic acid-d_1, **5 mL**) are united under **air** in a 170 mL reactor equipped with Teflon screw cap. The reactor is then sealed (*tightly*) and exposed to 140 °C for 23 h (magnetic stirring set to approx. 500 turns/min). The reactor is then cooled to room temperature and the crude mixture is directly purified by SiO_2 gel column chromatography (height 380 mm, width 35 mm) in pentane/CH_2Cl_2 = 6/4. (white solids). The first fraction consists of the coupling product **(d)-2a** (7% isolated yield) and the second fraction, of the starting material **(d)-1a** (93% isolated yield), both white powders.





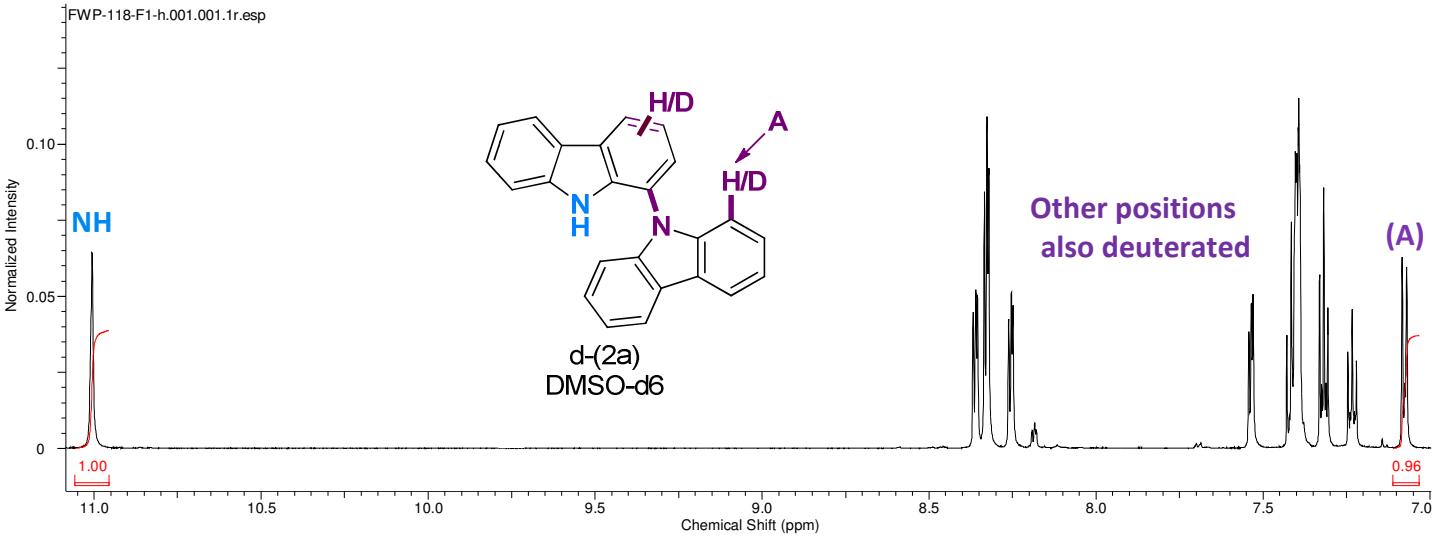
(d)-1a, GC-MS: R_t (50_40): 8.8 min; EI: 172 (15), 171 (54), 170 (100), 169 (98), 168 (54), 167 (24).

Note: **1a (natural abundance)**, GC-MS: R_t (50_40): 8.8 min; EI: 168 (13), 167 (100).

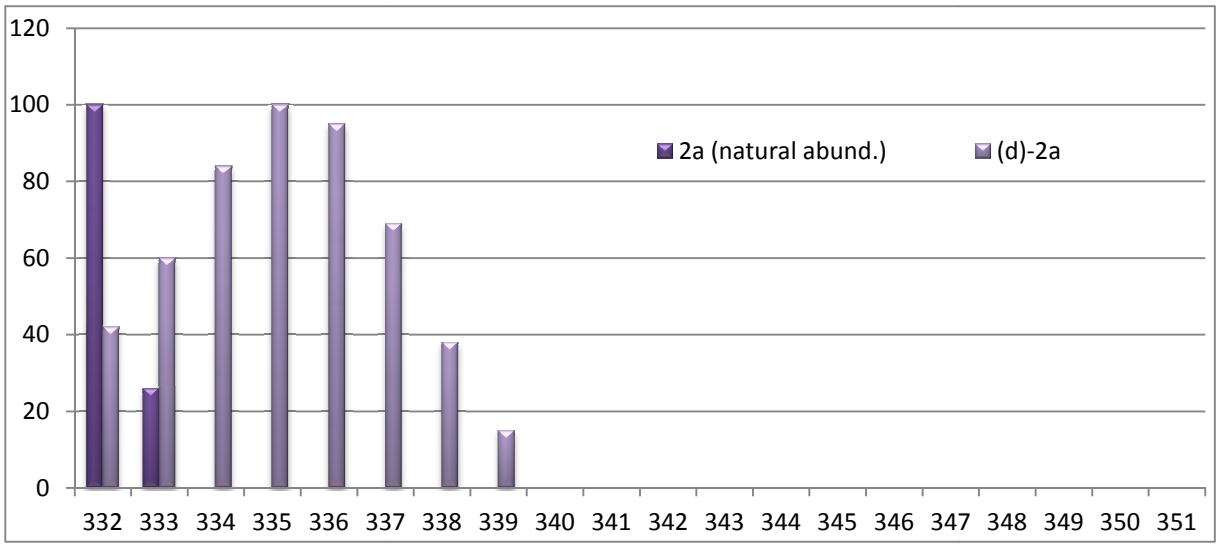


Calculated values (% of total) for populations of **1a**, **(d_1)-1a**, **(d_2)-1a**, **(d_3)-1a**, etc:

D0	7 .9
D1	16 .7
D2	29 .9
D3	28 .9
D4	13 .9
D5	3 .1
D6	-0 .4
D7	0 .1
D8	0 .0



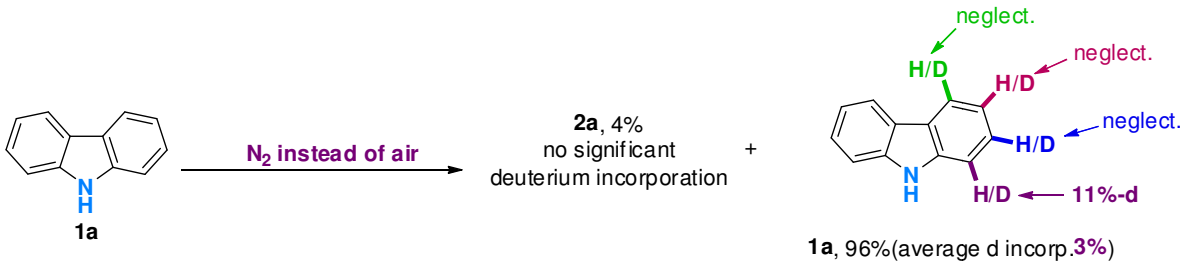
(d)-2a, GC-MS: R_t (50_40): 13.8 min; EI: 339 (15), 338 (38), 337 (69), 336 (95), 335 (100), 334 (84) 333 (60), 332 (42).
Note: **2a (natural abundance)**, GC-MS: R_t (50_40): 13.8 min; EI: 333 (26), 332 (100).



Calculated values (% of total) for populations of **2a**, **(d_1)-2a**, **(d_2)-2a**, **(d_3)-2a**, etc:

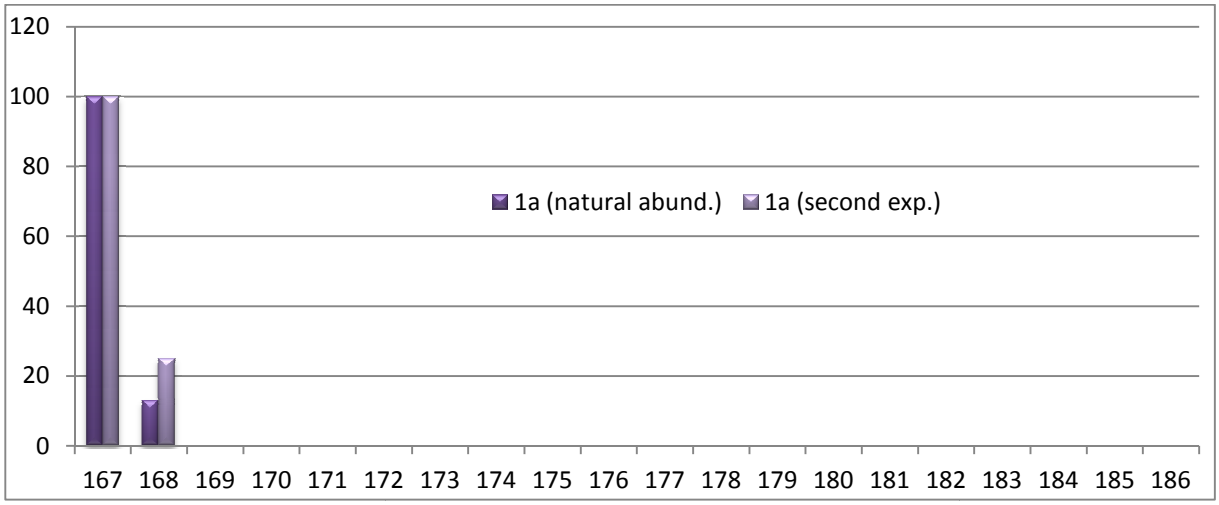
D0	10 .5
D1	12 .3
D2	17 .8
D3	20 .4
D4	18 .5
D5	12 .5
D6	6 .3
D7	2 .1
D8	-0 .6
D9	0 .1
D10	0 .0
D11	0 .0
D12	0 .0
D13	0 .0
D14	0 .0
D15	0 .0

In a second experiment, carbazole **1a** (10 mmol), $[(p\text{-cymene})RuCl_2]_2$ (0.1 mmol), $Cu(OAc)_2$ (1 mmol), carefully degased (with dry N_2 gas) PhCl (25 mL), C_2Cl_4 (25 mL), and AcO**D** (acetic acid-d_1, **10 mL**) are united under **N_2** in a 170 mL reactor equipped with Teflon screw cap. (Note: the scale of this experiment is larger than previously in order to minimize O_2 and H_2O contaminations while operating). The reactor is then sealed (*tightly*) under N_2 atmosphere and exposed to 140 °C for 23 h (magnetic stirring set to approx. 500 turns/min). The reactor is then cooled to room temperature and the crude mixture is directly purified by SiO_2 gel column chromatography (height 380 mm, width 35 mm) in pentane/CH_2Cl_2 = 6/4. (white solids). The first fraction consists of the coupling product **2a** (4% isolated yield) and the second fraction, of the starting material **1a** (96% isolated yield), both white powders.



1a, GC-MS: R_t (50_40): 8.8 min; EI: 168 (25), 167 (100).

Note: **1a (natural abundance)**, GC-MS: R_t (50_40): 8.8 min; EI: 168 (13), 167 (100).



Calculated values (% of total) for populations of **1a**, **(d_1)-1a**, **(d_2)-1a**, **(d_3)-1a**, etc:

D0	90 .4
D1	10 .8
D2	-1 .4
D3	0 .2
D4	0 .0
D5	0 .0
D6	0 .0
D7	0 .0
D8	0 .0

2.5.5. Crystallographic data.

Table 1. Crystal data and structure refinement for 13076ocu.

Identification code	13076ocu	
Empirical formula	C24 H18 N2	
Formula weight	334.40	
Temperature	150(2) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 11.6032(5) Å	α= 90°.
	b = 7.0985(2) Å	β= 118.601(6)°.
	c = 11.9333(6) Å	ɣ = 90°.
Volume	862.95(6) $Å^3$	
Z	2	
Density (calculated)	1.287 Mg/m^3	
Absorption coefficient	0.583 mm^{-1}	
F(000)	352	
Crystal size	0.44 x 0.37 x 0.27 mm^3	
Theta range for data collection	4.22 to 62.70°.	
Index ranges	-13<=h<=12, -8<=k<=8, -12<=l<=13	
Reflections collected	5651	
Independent reflections	2706 [R(int) = 0.0176]	
Completeness to theta = 62.70°	99.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8585 and 0.7835	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2706 / 2 / 239	
Goodness-of-fit on F^2	1.087	
Final R indices [I>2sigma(I)]	R1 = 0.0236, wR2 = 0.0606	
R indices (all data)	R1 = 0.0242, wR2 = 0.0611	
Absolute structure parameter	-0.1(4)	
Extinction coefficient	0.0259(13)	
Largest diff. peak and hole	0.100 and -0.106 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 13076ocu. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1)	2666(1)	3405(2)	-682(1)	31(1)
C(1)	2030(1)	2781(2)	-1962(1)	26(1)
C(2)	2490(1)	3154(2)	-2821(1)	29(1)
C(3)	1857(1)	2378(2)	-4034(1)	33(1)
C(4)	783(1)	1216(2)	-4404(1)	38(1)
C(5)	330(1)	829(2)	-3545(1)	38(1)
C(6)	936(1)	1622(2)	-2341(1)	33(1)
C(7)	3098(1)	5208(2)	-206(1)	24(1)
C(8)	3487(1)	5549(2)	1088(1)	25(1)
C(9)	3903(1)	7317(2)	1617(1)	29(1)
C(10)	3970(1)	8782(2)	886(1)	31(1)
C(11)	3601(1)	8459(2)	-383(1)	29(1)
C(12)	3158(1)	6708(2)	-933(1)	27(1)
N(2)	3452(1)	4040(1)	1867(1)	25(1)
C(13)	4548(1)	3151(2)	2840(1)	24(1)
C(14)	5873(1)	3478(2)	3252(1)	28(1)
C(15)	6770(1)	2398(2)	4257(1)	31(1)
C(16)	6365(1)	1038(2)	4847(1)	33(1)
C(17)	5047(1)	716(2)	4429(1)	30(1)
C(18)	4120(1)	1783(2)	3415(1)	25(1)
C(19)	2701(1)	1848(2)	2766(1)	25(1)
C(20)	1730(1)	870(2)	2900(1)	31(1)
C(21)	432(1)	1333(2)	2120(1)	33(1)
C(22)	77(1)	2746(2)	1194(1)	31(1)
C(23)	1017(1)	3734(2)	1030(1)	30(1)
C(24)	2328(1)	3270(2)	1829(1)	25(1)

Table 3. Bond lengths [Å] and angles [°] for 13076ocu.

N(1)-C(7)	1.3922(17)	C(12)-H(12)	0.9500
N(1)-C(1)	1.4123(16)	N(2)-C(24)	1.3942(16)
N(1)-H(1N)	0.898(9)	N(2)-C(13)	1.3965(16)
C(1)-C(2)	1.3892(18)	C(13)-C(14)	1.3912(17)
C(1)-C(6)	1.3931(19)	C(13)-C(18)	1.4092(18)
C(2)-C(3)	1.3863(18)	C(14)-C(15)	1.3832(19)
C(2)-H(2)	0.9500	C(14)-H(14)	0.9500
C(3)-C(4)	1.379(2)	C(15)-C(16)	1.402(2)
C(3)-H(3)	0.9500	C(15)-H(15)	0.9500
C(4)-C(5)	1.384(2)	C(16)-C(17)	1.3816(19)
C(4)-H(4)	0.9500	C(16)-H(16)	0.9500
C(5)-C(6)	1.381(2)	C(17)-C(18)	1.3960(18)
C(5)-H(5)	0.9500	C(17)-H(17)	0.9500
C(6)-H(6)	0.9500	C(18)-C(19)	1.4469(18)
C(7)-C(12)	1.3955(17)	C(19)-C(20)	1.3955(18)
C(7)-C(8)	1.4076(17)	C(19)-C(24)	1.4116(18)
C(8)-C(9)	1.3840(18)	C(20)-C(21)	1.379(2)
C(8)-N(2)	1.4319(15)	C(20)-H(20)	0.9500
C(9)-C(10)	1.3831(19)	C(21)-C(22)	1.400(2)
C(9)-H(9)	0.9500	C(21)-H(21)	0.9500
C(10)-C(11)	1.3812(19)	C(22)-C(23)	1.3864(19)
C(10)-H(10)	0.9500	C(22)-H(22)	0.9500
C(11)-C(12)	1.3843(18)	C(23)-C(24)	1.3943(18)
C(11)-H(11)	0.9500	C(23)-H(23)	0.9500
C(7)-N(1)-C(1)	128.96(10)	C(1)-C(2)-H(2)	120.1
C(7)-N(1)-H(1N)	114.2(9)	C(4)-C(3)-C(2)	121.18(13)
C(1)-N(1)-H(1N)	111.6(9)	C(4)-C(3)-H(3)	119.4
C(2)-C(1)-C(6)	118.98(11)	C(2)-C(3)-H(3)	119.4
C(2)-C(1)-N(1)	123.45(11)	C(3)-C(4)-C(5)	119.12(13)
C(6)-C(1)-N(1)	117.40(11)	C(3)-C(4)-H(4)	120.4
C(3)-C(2)-C(1)	119.76(12)	C(5)-C(4)-H(4)	120.4
C(3)-C(2)-H(2)	120.1	C(6)-C(5)-C(4)	120.31(13)

C(6)-C(5)-H(5)	119.8	C(13)-C(14)-H(14)	121.3
C(4)-C(5)-H(5)	119.8	C(14)-C(15)-C(16)	121.56(13)
C(5)-C(6)-C(1)	120.64(13)	C(14)-C(15)-H(15)	119.2
C(5)-C(6)-H(6)	119.7	C(16)-C(15)-H(15)	119.2
C(1)-C(6)-H(6)	119.7	C(17)-C(16)-C(15)	120.77(13)
N(1)-C(7)-C(12)	124.31(11)	C(17)-C(16)-H(16)	119.6
N(1)-C(7)-C(8)	117.97(11)	C(15)-C(16)-H(16)	119.6
C(12)-C(7)-C(8)	117.72(11)	C(16)-C(17)-C(18)	118.90(12)
C(9)-C(8)-C(7)	120.99(11)	C(16)-C(17)-H(17)	120.6
C(9)-C(8)-N(2)	119.65(11)	C(18)-C(17)-H(17)	120.6
C(7)-C(8)-N(2)	119.36(10)	C(17)-C(18)-C(13)	119.42(12)
C(10)-C(9)-C(8)	120.48(12)	C(17)-C(18)-C(19)	133.50(11)
C(10)-C(9)-H(9)	119.8	C(13)-C(18)-C(19)	107.08(10)
C(8)-C(9)-H(9)	119.8	C(20)-C(19)-C(24)	119.23(12)
C(11)-C(10)-C(9)	118.98(12)	C(20)-C(19)-C(18)	134.19(12)
C(11)-C(10)-H(10)	120.5	C(24)-C(19)-C(18)	106.58(10)
C(9)-C(10)-H(10)	120.5	C(21)-C(20)-C(19)	119.00(12)
C(10)-C(11)-C(12)	121.26(11)	C(21)-C(20)-H(20)	120.5
C(10)-C(11)-H(11)	119.4	C(19)-C(20)-H(20)	120.5
C(12)-C(11)-H(11)	119.4	C(20)-C(21)-C(22)	121.11(12)
C(11)-C(12)-C(7)	120.55(11)	C(20)-C(21)-H(21)	119.4
C(11)-C(12)-H(12)	119.7	C(22)-C(21)-H(21)	119.4
C(7)-C(12)-H(12)	119.7	C(23)-C(22)-C(21)	121.32(12)
C(24)-N(2)-C(13)	108.41(10)	C(23)-C(22)-H(22)	119.3
C(24)-N(2)-C(8)	126.08(10)	C(21)-C(22)-H(22)	119.3
C(13)-N(2)-C(8)	125.45(10)	C(22)-C(23)-C(24)	117.27(12)
C(14)-C(13)-N(2)	129.14(11)	C(22)-C(23)-H(23)	121.4
C(14)-C(13)-C(18)	122.03(11)	C(24)-C(23)-H(23)	121.4
N(2)-C(13)-C(18)	108.83(10)	N(2)-C(24)-C(23)	128.84(12)
C(15)-C(14)-C(13)	117.32(12)	N(2)-C(24)-C(19)	109.10(10)
C(15)-C(14)-H(14)	121.3	C(23)-C(24)-C(19)	122.06(11)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for 13076ocu. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1)	46(1)	23(1)	24(1)	0(1)	17(1)	-6(1)
C(1)	30(1)	19(1)	24(1)	2(1)	10(1)	5(1)
C(2)	30(1)	25(1)	30(1)	1(1)	14(1)	2(1)
C(3)	42(1)	30(1)	28(1)	2(1)	18(1)	5(1)
C(4)	43(1)	34(1)	26(1)	-3(1)	9(1)	3(1)
C(5)	34(1)	35(1)	37(1)	-5(1)	10(1)	-7(1)
C(6)	37(1)	29(1)	36(1)	-1(1)	19(1)	-3(1)
C(7)	24(1)	24(1)	23(1)	0(1)	11(1)	1(1)
C(8)	25(1)	24(1)	25(1)	4(1)	12(1)	-1(1)
C(9)	33(1)	28(1)	24(1)	-3(1)	12(1)	-2(1)
C(10)	34(1)	23(1)	34(1)	-2(1)	15(1)	-3(1)
C(11)	32(1)	24(1)	33(1)	6(1)	18(1)	3(1)
C(12)	32(1)	25(1)	24(1)	2(1)	14(1)	3(1)
N(2)	28(1)	24(1)	21(1)	3(1)	10(1)	-2(1)
C(13)	31(1)	22(1)	18(1)	-3(1)	12(1)	-1(1)
C(14)	34(1)	27(1)	24(1)	-3(1)	16(1)	-2(1)
C(15)	30(1)	33(1)	27(1)	-4(1)	12(1)	2(1)
C(16)	37(1)	32(1)	26(1)	3(1)	12(1)	8(1)
C(17)	39(1)	26(1)	24(1)	0(1)	16(1)	-1(1)
C(18)	33(1)	22(1)	20(1)	-3(1)	13(1)	-1(1)
C(19)	33(1)	23(1)	20(1)	-4(1)	12(1)	-3(1)
C(20)	40(1)	28(1)	26(1)	-1(1)	17(1)	-6(1)
C(21)	35(1)	35(1)	32(1)	-6(1)	18(1)	-10(1)
C(22)	30(1)	32(1)	30(1)	-6(1)	13(1)	-3(1)
C(23)	34(1)	26(1)	26(1)	-1(1)	13(1)	-1(1)
C(24)	30(1)	24(1)	22(1)	-4(1)	13(1)	-4(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 13076ocu.

	x	y	z	U(eq)
H(2)	3236	3938	-2577	34
H(3)	2169	2650	-4621	40
H(4)	358	688	-5237	45
H(5)	-400	15	-3785	45
H(6)	605	1374	-1766	40
H(9)	4144	7526	2488	35
H(10)	4266	9992	1252	37
H(11)	3651	9457	-888	35
H(12)	2892	6527	-1812	32
H(14)	6151	4405	2858	33
H(15)	7681	2583	4554	37
H(16)	7004	329	5542	40
H(17)	4776	-216	4825	36
H(20)	1961	-101	3519	37
H(21)	-233	683	2213	40
H(22)	-825	3032	667	38
H(23)	776	4689	400	36
H(1N)	2454(14)	2689(19)	-187(12)	30

Table 6. Torsion angles [°] for 13076ocu.

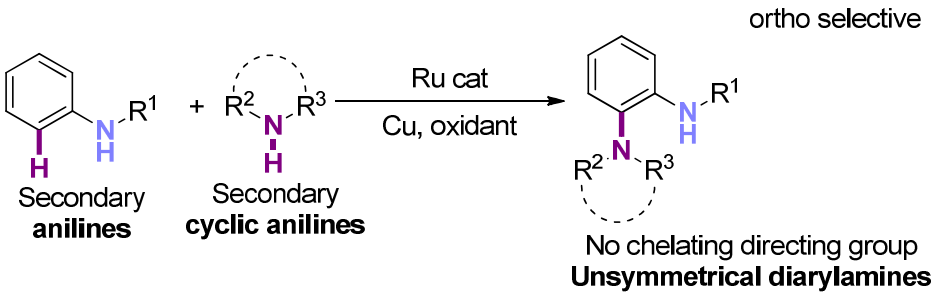
C(7)-N(1)-C(1)-C(2)	50.60(19)
C(7)-N(1)-C(1)-C(6)	-134.07(14)
C(6)-C(1)-C(2)-C(3)	0.20(19)
N(1)-C(1)-C(2)-C(3)	175.46(12)
C(1)-C(2)-C(3)-C(4)	-0.8(2)
C(2)-C(3)-C(4)-C(5)	0.2(2)
C(3)-C(4)-C(5)-C(6)	1.0(2)
C(4)-C(5)-C(6)-C(1)	-1.6(2)
C(2)-C(1)-C(6)-C(5)	1.0(2)
N(1)-C(1)-C(6)-C(5)	-174.52(13)
C(1)-N(1)-C(7)-C(12)	-10.8(2)
C(1)-N(1)-C(7)-C(8)	168.45(12)
N(1)-C(7)-C(8)-C(9)	-178.77(11)
C(12)-C(7)-C(8)-C(9)	0.52(17)
N(1)-C(7)-C(8)-N(2)	1.33(17)
C(12)-C(7)-C(8)-N(2)	-179.38(11)
C(7)-C(8)-C(9)-C(10)	-1.30(19)
N(2)-C(8)-C(9)-C(10)	178.60(11)
C(8)-C(9)-C(10)-C(11)	0.79(19)
C(9)-C(10)-C(11)-C(12)	0.48(19)
C(10)-C(11)-C(12)-C(7)	-1.26(18)
N(1)-C(7)-C(12)-C(11)	179.98(12)
C(8)-C(7)-C(12)-C(11)	0.75(17)
C(9)-C(8)-N(2)-C(24)	106.21(14)
C(7)-C(8)-N(2)-C(24)	-73.89(15)
C(9)-C(8)-N(2)-C(13)	-70.50(16)
C(7)-C(8)-N(2)-C(13)	109.40(13)
C(24)-N(2)-C(13)-C(14)	-178.41(11)
C(8)-N(2)-C(13)-C(14)	-1.22(19)
C(24)-N(2)-C(13)-C(18)	0.87(13)
C(8)-N(2)-C(13)-C(18)	178.06(10)
N(2)-C(13)-C(14)-C(15)	179.30(12)

C(18)-C(13)-C(14)-C(15)	0.10(17)
C(13)-C(14)-C(15)-C(16)	-0.48(19)
C(14)-C(15)-C(16)-C(17)	0.8(2)
C(15)-C(16)-C(17)-C(18)	-0.66(19)
C(16)-C(17)-C(18)-C(13)	0.28(18)
C(16)-C(17)-C(18)-C(19)	-178.57(13)
C(14)-C(13)-C(18)-C(17)	0.00(18)
N(2)-C(13)-C(18)-C(17)	-179.35(10)
C(14)-C(13)-C(18)-C(19)	179.13(10)
N(2)-C(13)-C(18)-C(19)	-0.22(13)
C(17)-C(18)-C(19)-C(20)	-0.5(2)
C(13)-C(18)-C(19)-C(20)	-179.50(13)
C(17)-C(18)-C(19)-C(24)	178.45(13)
C(13)-C(18)-C(19)-C(24)	-0.50(13)
C(24)-C(19)-C(20)-C(21)	-0.65(18)
C(18)-C(19)-C(20)-C(21)	178.25(13)
C(19)-C(20)-C(21)-C(22)	0.74(19)
C(20)-C(21)-C(22)-C(23)	-0.3(2)
C(21)-C(22)-C(23)-C(24)	-0.25(19)
C(13)-N(2)-C(24)-C(23)	178.92(12)
C(8)-N(2)-C(24)-C(23)	1.75(19)
C(13)-N(2)-C(24)-C(19)	-1.20(13)
C(8)-N(2)-C(24)-C(19)	-178.37(10)
C(22)-C(23)-C(24)-N(2)	-179.79(12)
C(22)-C(23)-C(24)-C(19)	0.34(18)
C(20)-C(19)-C(24)-N(2)	-179.78(10)
C(18)-C(19)-C(24)-N(2)	1.04(13)
C(20)-C(19)-C(24)-C(23)	0.11(18)
C(18)-C(19)-C(24)-C(23)	-179.07(11)

Symmetry transformations used to generate equivalent atoms:

Chapter III

Ruthenium catalysed cross dehydrogenative *ortho*-*N*-amination of diarylamines; Versatile access to unsymmetrical diarylamines.



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3.1. Introduction.

As nitrogen containing compounds, anilines such as diarylamines offer a large field of application; these molecules are valuable for industry as dyes, or stabilizer for explosives, synthetic rubbers and propellants[1]. Diarylamine derivatives can also be use in agriculture as biocides[2] or in medicine, as nonsteroidal anti-inflammatory drug (NSAID) to treat pain and inflammatory disorders[3]. (Figure 1)

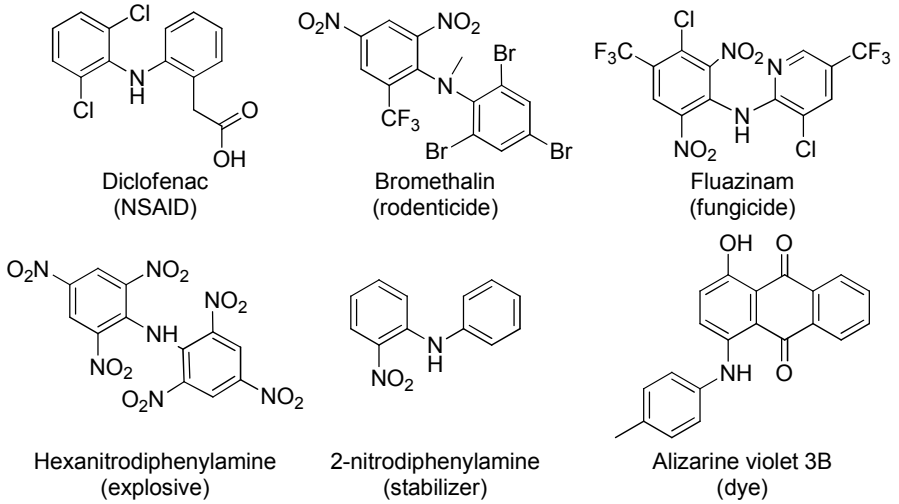
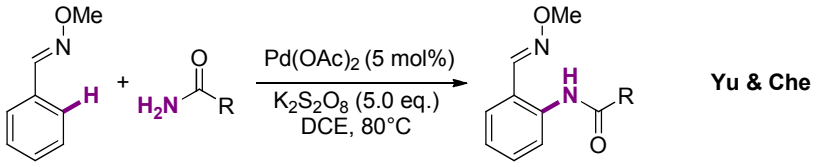


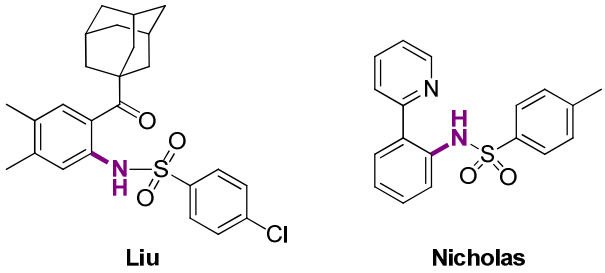
Figure 1: Selected examples of diarylamines and their applicability in medicine and industry.

Despite the fact that the homo-coupling product of diarylamines was never observed in the previously developed conditions (See Chapter II), we expected that an improvement of the ruthenium (II)/copper (II) catalytic system would allow the formation of new hetero-coupling products, based on secondary amines, by C-H activation reaction[5]. Diverse strategies have been developed over the past few years in order to form selective intermolecular C-N bonds by CDC. In 2006, Wing-Yiu Yu and Chi-Ming Che, introduced chelating directing groups for achieving the formation of C-N bond between *N*-amide and imines derivatives with palladium (II). This strategy has the advantage of being truly selective for *ortho*-functionalization (Scheme1).[6]



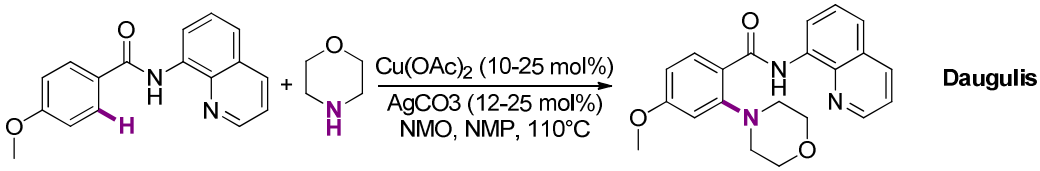
Scheme1: Yu and Che's early C-N bond formation by intermolecular CDC.

In 2011, Lei Liu showed that phenone derivatives were effective in cross-coupling with sulfonamides[7]. The same year, Nicholas chose the phenylpyridine as chelating DG for copper (II) catalyzed amination reaction with tosylamide (Scheme 2). [8]



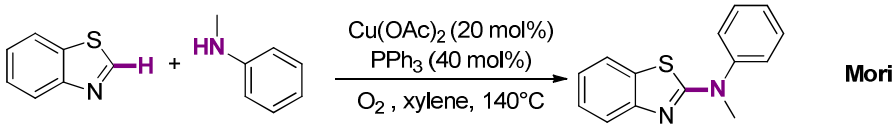
Scheme 2: Liu and Nicholas condensation of sulfonamides.

In 2013, Daugulis introduced the bidentate 8-aminoquinoline chelating DG. Thus, he reported elegant cross-coupling between the morpholine and carboxylic acids derivatives (Scheme 3) [9].



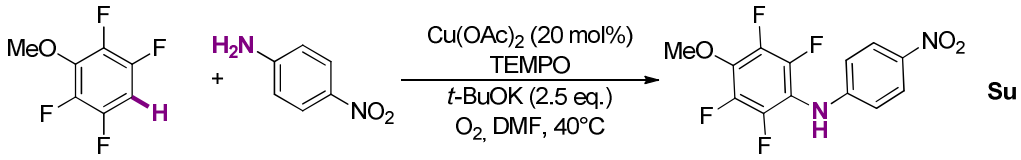
Scheme 3: Daugulis CDC with bidentate chelating DG 8-aminoquinoline.

Another strategy for the development of intermolecular C-N bond formation by CDC without a chelating DG appeared with the work of Atsunori Mori in 2009[10] (Scheme 4). This approach consists in coupling the *N*-aminating agent to a five-membered heterocyclic rings, with one "labile/acidic" C-H position. Those C-H coupling partners are particularly suited for C-H bond functionalizations. Mori reports condensation of aniline derivatives on heterocyclic rings. The same year, Schreiber reported a similar reaction independently [11]. Later on, Bolm and Miura described a similar example with impressive preservation of enantiomeric excess of the substrate [12].



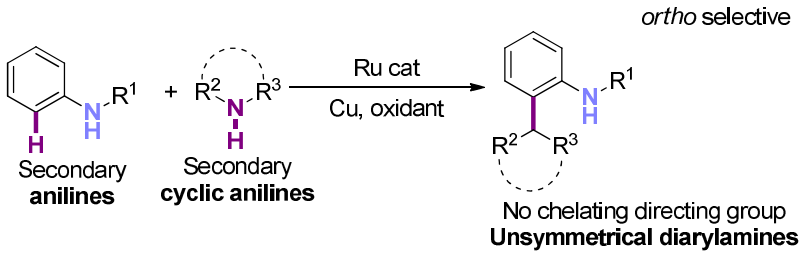
Scheme 4: Mori's direct amination of azoles.

By contrast, Weiping Su designed exotic anisole derivatives for synthesizing diarylamines with copper (II) catalyst and avoid uses of chelating DG (Scheme 5) [13].



Scheme 5: Su's conditions for diphenylamines formation.

With these reports, we assume that hetero-coupling formation could occur also in our reaction conditions. Therefore, we improved the ruthenium (II)/copper (II) catalytic system until being able to implement the hetero-coupling product of diarylamines with cyclic secondary anilines (Scheme 6).



Scheme 6: *N*-amination of secondary anilines by ruthenium catalyst.

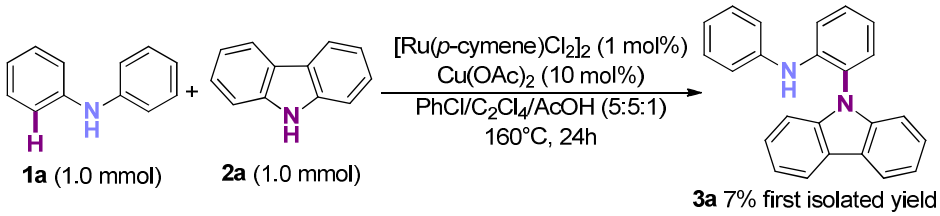
3.2. Results and discussions.

In search for substrates that would allow implementing the formation of new cross-coupling products, we hypothesized diarylamines were prime targets for hetero-coupling reactions. More general and structurally similar to carbazole, we hypothesized a ruthenium catalyst could activate the π-aromatic system on the same manner as with carbazole (See chapter II).

3.2.1. Optimization.

The first time, we engaged carbazoles in combination with diphenylamines according to the previous optimized conditions, a product of dehydrogenative-coupling was detected by GC-MS. The formation of the product was really low and we observed the presence of acetylated carbazoles, acetylated diphenylamines and elements of decomposition. We believed that higher temperature could allow isolating a substantial amount of product for the identification of the product.

Therefore, the reaction was carried out at 160°C in the same conditions: carbazole (1.0 mmol), diphenylamine (1.0 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (1 mol%), Cu(OAc)$_2$ (10 mol%), chlorobenzene (5 mL), C_2Cl_4 (5 mL) and acetic acid (1 mL) united in a sealed screw caps vessel under air were stirred at 160°C for 24h. We were pleased to isolate 7% of the cross-dehydrogenative herero-coupling product **3a** (Scheme 7).The structure was confirmed by X-Ray christallography (Scheme 8).



Scheme 7: First attempt to form cross-dehydrogenative-coupling between carbazole and diphenylamine.

In order to optimize reaction conditions, we studied effects of solvents, acids, the ratio ruthenium/copper, the ratio copper/acid, temperature and time of reaction. Only probative entries were isolated.

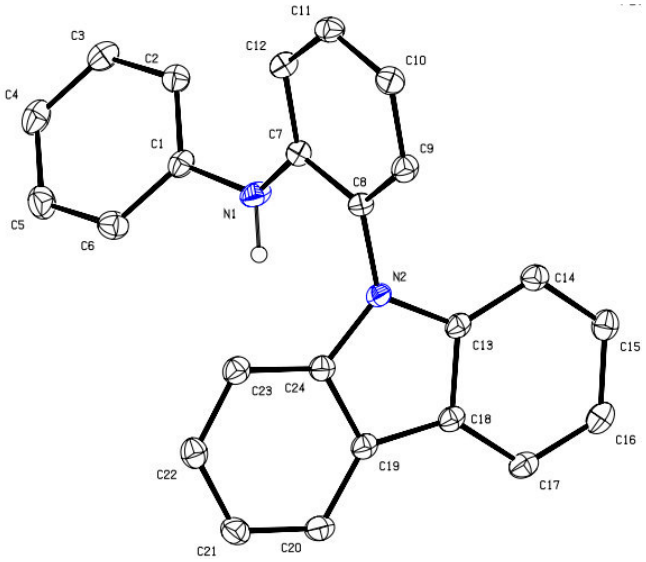


Figure 2: X-Ray structure: **3a** ORTEP view, 30% probability level. Selected torsion angle (deg): C(9)-C(8)-N(2)-C(24) = 106.21(16).

-Solvents

Preliminarily experiments have shown that diarylamines are not stable and decompose a lot in the reaction conditions. We considered that the first step towards the stabilization of secondary amines was to study effects of solvents. Thus, we started screening major classes of solvent. Our catalytic system is composed of two solvents: 1) chlorobenzene, probably necessary to dissolve substrates in the mixture and reach high temperature and 2) tetrachloroethylene, whose role is unclear but essential.

In a first stage, we started to replace chlorobenzene. We observed that polar solvent such as *N*-methyl-pyrrolidone (NMP) used in CDC amination by Daugulis[9], or *N*,*N*-dimethylformamide (DMF) led to massive decomposition in our reaction conditions. 1,4-dioxane often used in C-H activation did not give good result and resulted in poor yield and decomposition (Table1).

Table1: Screening of solvents

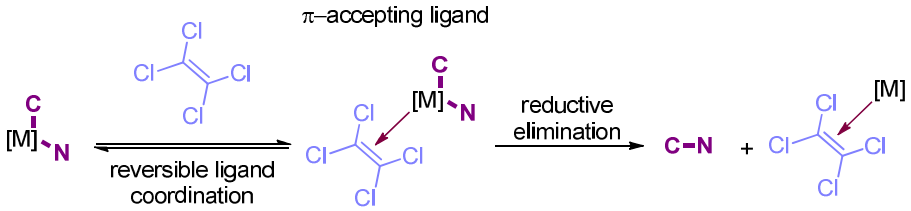
Solvents	NMP, DMF THF, 1,4-dioxane	PhCl, *o*-chlorotoluene, *o*-fluorotoluene, *o*, *m*, *p*-xylene, mesitylene, *p*-cymene, *tert*-butylbenzene	Diphenylether, cumene
Observations	Lot of decomposition Low yields	Low decomposition Modest yields	Low decomposition Good yields

In contrast, aromatic solvents proved to be positive for the system. We observed more stability overall and interesting results with diphenylether and cumene. Surprisingly, *p*-cymene similar to cumene and moreover the π-arene ligand on the ruthenium was less effective than cumene.

In the same manner, tetrachloroethylene was removed and/or replaced by several poly-halogenated solvents. Structurally similar hexachloro-1,3-butadiene or tribromoethylene led to more decomposition and/or gas emission.

Bromoarenes derivatives such as bromobenzene, 1,2,3,4-tetrabromobenzene and hexabromobenzene did not increase the yield and induced more decomposition. Therefore we assumed that tetrachloroethylene was essential component for the stability of the system. Moreover, implementing the reaction without cumene led to substrate solubility issues and consequently low yield. Eventually, the best ratio observed for this mixture was 4:1 C_2Cl_4/cumene.

Although the role of tetrachloroethylene is unclear, control experiments suggest it did not act as co-oxidant. Knochel hypothesized electron-poor olefins could take an important place during the reductive elimination by pulling electron density from the metal and facilitate its reduction to form C-N bonds (Scheme 8) [14]. Additionally, tetrachloroethylene could stabilize starting materials and products at high temperature through π-π interactions and therefore preventing decomposition.



Scheme 8: Knochel's hypothesis on the role of electron poor olefins.

-Ruthenium, copper and acetic acid.

The ruthenium (II) displayed reactivity for the C-N bond formation by CDC in our previous report. Hence, we carried out the reaction in presence of $[Ru(p\text{-cymene})Cl_2]_2$ and $[Ru(Cp^*)Cl]_4$. The ligand *p*-cymene showed more activity than the pentamethylcyclopentadienyl (Cp*) ligand. Finally, we increased from 1% to 5% the amount of ruthenium (II) catalyst.

With the same approach, we considered the role of $Cu(OAc)_2$. Its replacement by Silver(I) oxide or Copper(II) oxide showed promising results whereas strong oxidants such as hypervalent iodine (e.g. (diacetoxyiodo)-benzene), or peroxides (e.g. cumene hydroperoxide or *tert*-butyl-hydroperoxide) led to substantial decomposition. Regarding the price and the efficiency, we chose to maintain copper acetate as oxidant.

Interestingly, acetic acid remained the best carboxylic acid we have tried. For instance, formic acid reacts violently with decomposition. Pivalic acid, used often for C-H activation reactions[15], or hindered pentamethylbenzoic acid, 1-adamantanecarboxylic acid and cyclopropane carboxylic acid were less effective.

Additionally, we observed a correlation between amount of copper and acetic acid. Therefore, we performed a series of experiments in order to define the ideal ratio 2.2 eq./0.5 mL between $Cu(OAc)_2$/ AcOH.

-*Temperature*

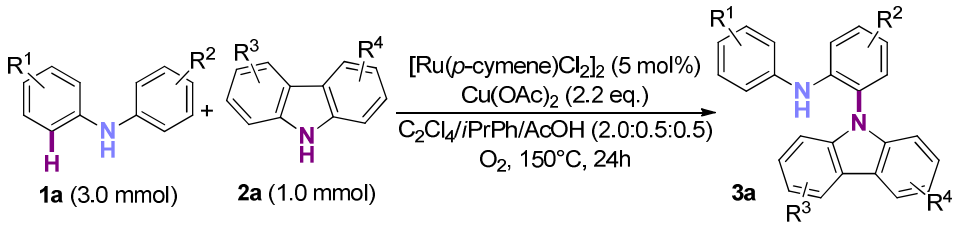
At the beginning of the optimization, we increased the temperature from 140°C to 150°C to prevent formation of Lauternazoles and reach substantial amounts of the hetero-coupling product. In the late stage of the development, we controlled the efficiency of last elements of optimization. Hence, we multiplied by three the amount of diarylamine to offset the strong decomposition of diarylamines. Besides, we flushed our reactor with an atmosphere of oxygen to keep a suitable amount of oxidant, which is partly consumed in the decomposition phase. Finally, we carried out last temperature experiments under these conditions: Carbazole (1.0 mmol), diphenylamine (3.0 mmol), $[Ru(p\text{-cymene})\ Cl_2]_2$ (5 mol%), $Cu(OAc)_2$ (2.2 eq.), C_2Cl_4 (2.5 mL), cumene (0.5 mL), AcOH (0.5 mL) were united in a screw caps vessels and stirred under O_2 for 24h. As shown in table 2 the temperature is critical for the C-N bond formation.

Table 2: Late-stage of temperature optimization.

Temperature (°C)	Isolated yields (%)
140	neglectable
150	64.4[a]
160	62.6
170	57.4
180	51.8[b]

[a] The reaction started in the same conditions but under inert atmosphere provided 39.0% isolated yield. [b] The reaction started in the same conditions under air provided 50.2% isolated yield.

Increasing from 140 to 150°C allowed to reach 64% isolated yield. Interestingly, only 10°C were necessary to surpass the energetic barrier of the known to be difficult C-N bond reductive elimination. The absence of oxygen had negative effect on the reaction outcome since it afforded 1.6 times lower yield. At 180°C, the difference between air and O_2 atmosphere is negligible. Moreover, increase the time of reaction to 3 or 6 days was detrimental to the final yield because of more decomposition.

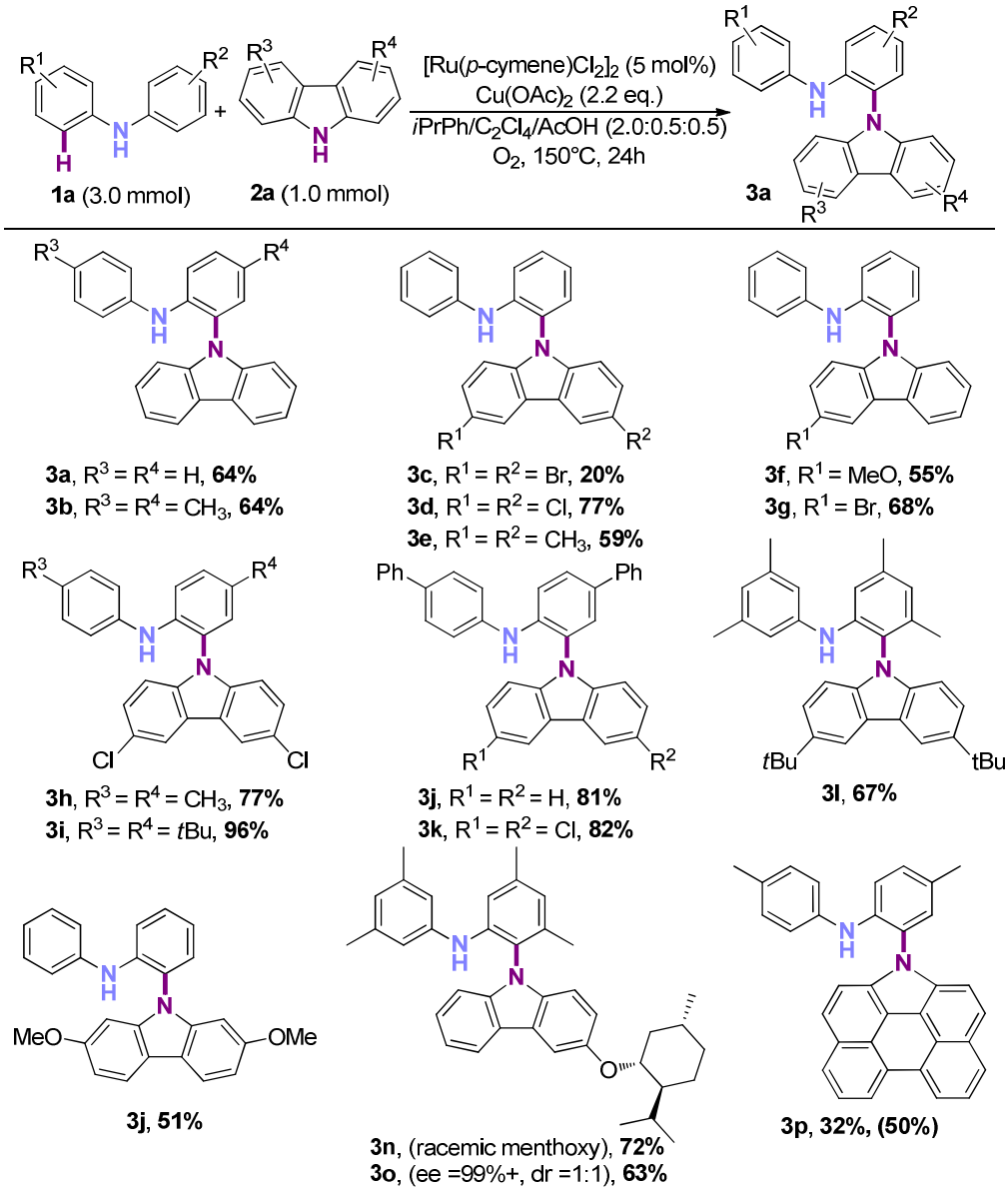


Scheme 9: Final optimized conditions.

The best conditions are described in scheme 9: Carbazole (1.0 mmol), diphenylamine (3.0 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (5 mol%), $Cu(OAc)_2$ (2.2 eq.), C_2Cl_4 (2 mL), cumene (0.5 mL), AcOH (0.5 mL) were assembled in a screw-cap vessel and flushed with O_2. The Schlenk was sealed and the mixture was stirred at 150°C for 24 hours. The crude mixture was treated by 5 mL of acetylacetone (acacH), heated for 1h at 150°C (to release the final Lauternamine from copper). The crude is filtrate over a plug of silica gel and the concentrate is purified on a large column chromatography of SiO_2.

3.2.2. Scope and limits of the reaction.

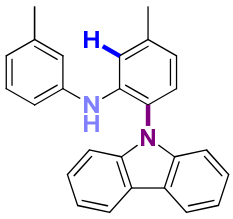
With this optimized conditions in hand, we started to explore electronic and steric effects on the reactivity. The results are presented scheme 10.



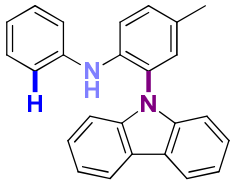
Scheme 10: Substrate scope of the C-N cross dehydrogenative coupling of lauternamines.

The reaction tolerates a number of functional groups including halides such as Br or Cl (**3c**, **3d**, **3g**, **3k**), or electron-rich methoxy (**3f**, **3j**) and menthoxy-group (**3n**, **3o**). Interestingly, 3,6-dichlorocarbazole (**3d**, **3h**, **3i**, **3k**) proved to be an excellent *N*-coupling partner with high yields (77, 77, 96 and 82% isolated yields respectively).

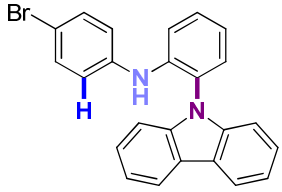
By comparison, 3,6-dibromocarbazole **3c** drops the yield from 77 to 20% with simple diphenylamine. 4,4'-diphenyl diarylamine revealed to be extremely good C-H coupling partner with carbazole **3j** and 3,6-dichlorocarbazole **3k** with 81 and 82% isolated yields respectively. Surprisingly, 3-menthoxycarbazole survived in our conditions and afforded 72 and 63% of the corresponding products **3n** and **3o**. It is noteworthy that sterics do not seem to play a detrimental role. For instance, 1,3,5-dixylylamine afforded products **3l**, **3n**, **3o** in promising yields with 67, 72 and 63% isolated yields respectively. Moreover, introduction on methoxy on C2 and C7 of carbazole still provided 51% of the product. Besides, studying selectivity of this *N*-amination reaction by introduction of intramolecular steric and/or electronic competition on the diarylamines provided encouraging results (Scheme 11).



3q, (5:1) regioisom. ratio, **44%**



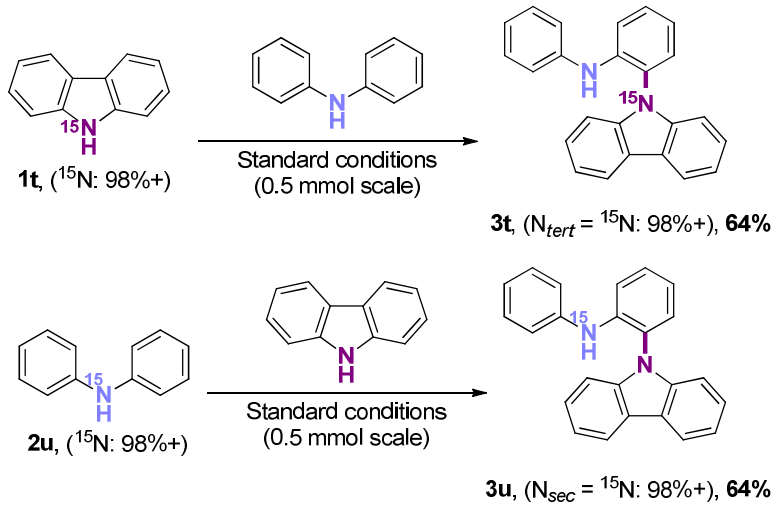
3r, (2:1) regioisom. ratio, **56%**



3s, (1.5:1) regioisom. ratio, **56%**

Scheme 11: Induction of regioselectivity with sterics and electronics.

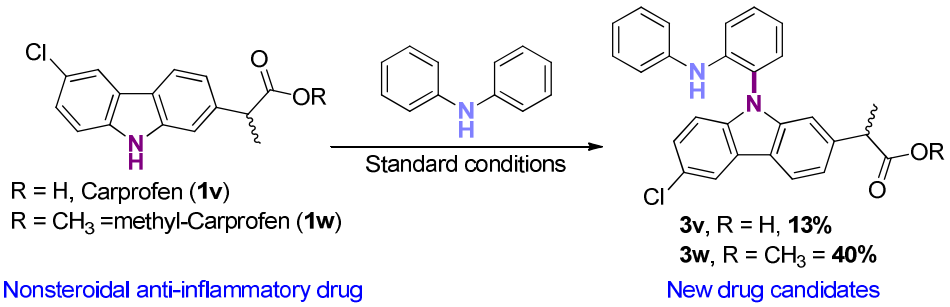
Indeed, we observed that the 3,3'-diphenylamine in cross-coupling with carbazole induced a significant 5:1 regioisomeric ratio for the product **3q** in favor of the less hindered C6 position. Electronics, whether EDG (**3r**) or EWG (**3s**) led to minor effects on the regioselectivity, giving 2:1 and 1.5:1 ratio in favor of the more electron rich phenyl ring.



Scheme 12: Semi labelled ^{14}N-^{15}N hetero-coupling product with regioisotopic control.

This new protocol can be applied on unsymmetrical semi labelled diarylamines **3t** and **3u** from ^{15}N-carbazole and $Ph_2{}^{15}NH$ to access semi labelled ^{14}N-^{15}N hetero-coupling product (Scheme 12).

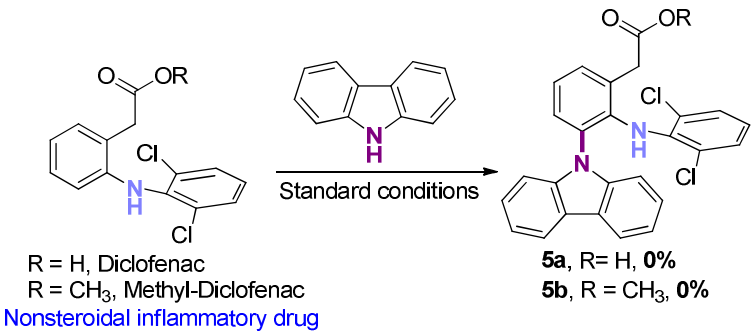
Interestingly, biological active Carprofen, a nonsteroidal anti-inflammatory drug commercialized as a racemate by Pfizer under the name trade name Rimadyl could also be part of the scope. This challenging entry (**3v**) considering the carboxylic acid functionality led to promising 13% isolated yield. The poor yield could be explained by decarboxylative events and substantial decomposition (Scheme 13).



Scheme 13: One pot reaction for new drug candidates.

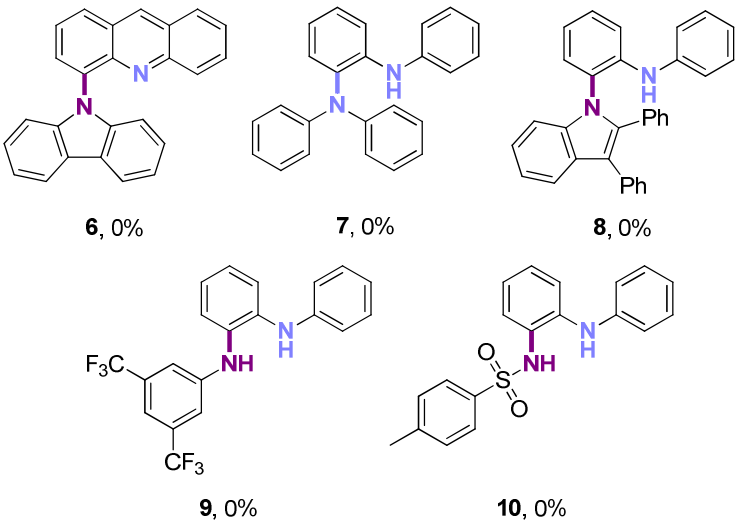
To prevent decarboxylative events, we protected the carboxylic acid by ester functionalization. This strategy was beneficial since it provided 40% isolated yield. This result encouraged us to attempt a second NSAID derived from diphenylamine in our catalytic system. Thus,

Diclofenac and methyl-Diclofenac were tested in coupling with carbazole. Unfortunately, none of the expected products were detected (Scheme 14).



Scheme 14: Negative result of Diclofenac and Methyl-Diclofenac.

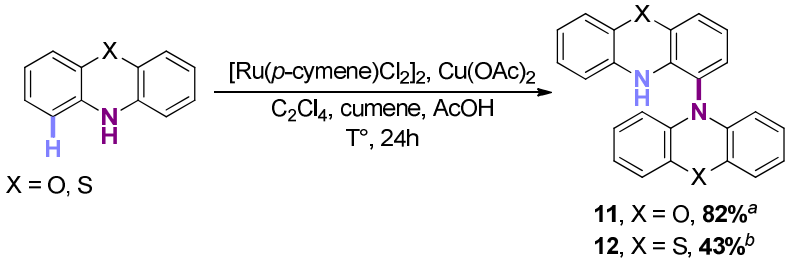
In order to develop the substrate scope, we tried relevant aminating agents and C-H coupling partners (Scheme 15).



Scheme 15: Unsuccessful C-H and N-H coupling partner.

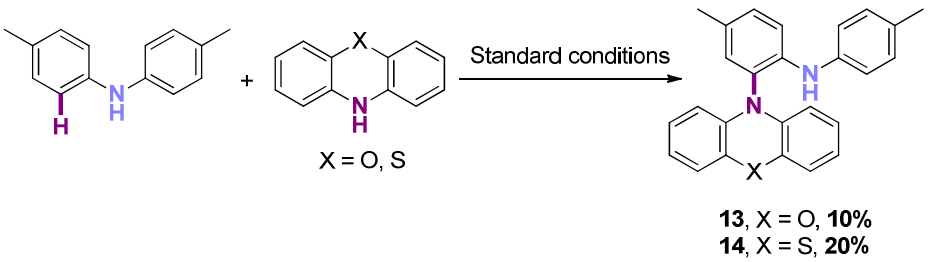
Unfortunately, substrates such as primary anilines did not afford the expected product **9.** (Even with strong EWG to approach pKa of carbazoles). 2,3-diphenylindole, 4-toluenesulfonamide did not allow formation of the expected products **8** and **10**. Moreover, the diphenylamine itself could not be used as *N*-coupling partner (**7**).

Additionally, we set up a reaction with more strained tricyclic phenoxazine (Scheme 16). We observed that this molecule reacts efficiently in the reaction conditions to provide high yield of the homo-coupling product.



Scheme 16: Homo-coupling of phenoxazine and phenothiazine.
[a] Conditions: phenoxazine (1.0 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (0.0125 mmol), $Cu(OAc)_2$ (0.55 mmol), C_2Cl_4 (2 mL), cumene (0.5 mL), AcOH (0.5 mL) at 150°C. [b] Conditions: phenothiazine (2.0 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (0.025 mmol), $Cu(OAc)_2$ (0.25 mmol), C_2Cl_4 (4 mL), cumene (1 mL), AcOH (1 mL) at 130°C.

In the same manner, we obtained the homo-coupling product of the phenothiazine in slightly biased conditions. Unfortunately, the reaction conditions delivered modest yield (43%) even after extensive optimization. We hypothesized that the sulfur contained in the molecule probably interacts strongly with copper and limits kinetics of the reaction. Otherwise, we observed that copper was hard to take off even after acacH treatment.



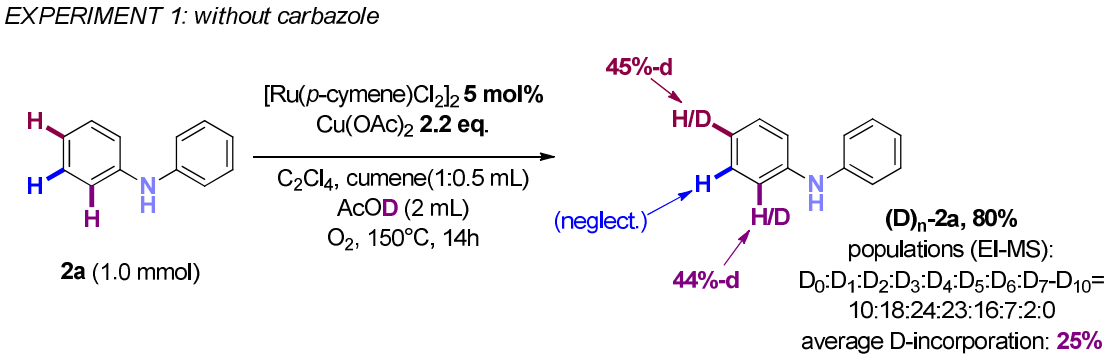
Scheme 17: Hetero-coupling products of phenoxazine and phenothiazine.

Encouraged by these new elements, we carried out reactions with phenoxazine and phenothiazine, in cross-coupling with *p*,*p*'-ditolylamine. Under standard conditions, these combinations did not give satisfactory results (10 and 20% isolated yield respectively) (Scheme 17).

3.2.3. Discussion.

3.2.3.1. Elements of mechanism.

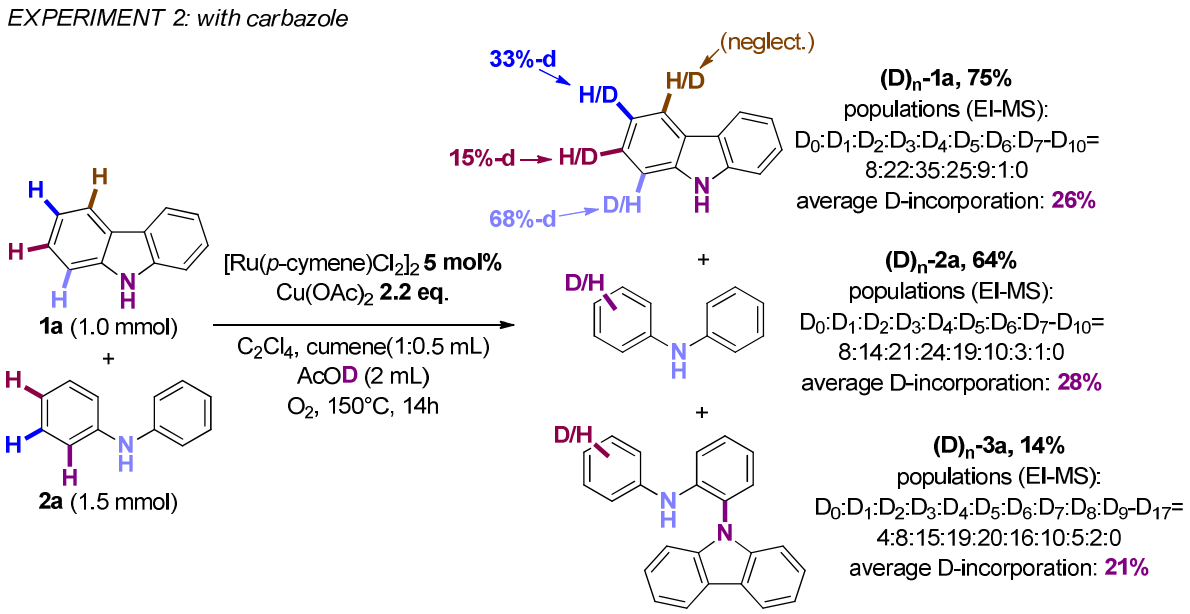
In order to shed some light on the reaction mechanism, we performed H/D scrambling experiments with acetic acid-d1. Deuterium incorporation detailed in schemes 18 and 19 are determined from ^{1}H NMR spectrum and AUP of GC-MS chromatograms. Firstly, we implemented the reaction in absence of carbazole in order to follow deuterium incorporation of the C-H coupling partner. For a better overview, an excess of deuterated acetic acid was engaged in this experiment (Scheme 18).



Scheme 18: H/D scrambling *experiment 1.*

This *experiment 1* displays that C-H activation is not the rate limiting step. Indeed, incorporation in *ortho* (44%-d) and *para*-position (45%-d) of diphenylamine **(D)$_n$-2a** tends to prove that the catalyst approached the starting material by the top of the π-aryl system to C-H activated most nucleophilic positions of the ring reversibly. Interestingly, *para-N*-carbazolation of diarylamines was never observed despite substantial deuterium incorporation.

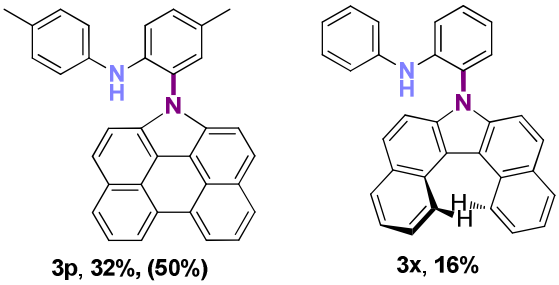
In a second experiment, we carried out the same reaction in presence of carbazole. *Experiment 2* was consistent with *experiment 1* regarding deuterium incorporation of unreacted diphenylamine **(D)$_n$-2a** (25% and 28% average D-incorp. respectively) (Scheme 19). It is interesting to point out that carbazole **(D)$_n$-1a** (*N*-coupling partner) was found with important deuterium incorporation especially *ortho*-position (68% of deuterium). Moreover, incorporation in *meta* and *para*-position of carbazole suggests a coordination of the metal on the top of the π-aryl ring as for homo-coupling of carbazoles (See Chapter II).



Scheme 19: H/D scrambling *experiment 2*.

In the light of these results, we assume C-H activation is not the rate limiting step. In a last control experiment, we engaged *experiment 1* without copper and oxygen in order to compare this new reactivity with our previous investigation on the reactivity of carbazole[4]. We detected significant deuterium incorporation meaning that those components do not proceed at the C-H activation step, but later on the catalytic cycle.

Additionally, it seems that the planarity of the *N*-aminating partner (carbazole) could be helpful for the reactivity. Indeed, 7*H*-dibenzo[*c,g*]carbazole, afforded lower yield of the product **3x** (16%) than the product **3p** of 6*H*-phenanthro[1,10,9,8-*c,d,e,f,g*]carbazole (32%) (Scheme 20).



Scheme 20: Planar versus twisted carbazole.

3.2.3.2. Molecules properties.

Interestingly, products resulting of non-symmetrical carbazoles led to systematic chiral C-N cross-coupling products. For instance, product **3f** showed a good dissociation of the racemate on the chiral analytical HPLC (OD-H column, figure 2).

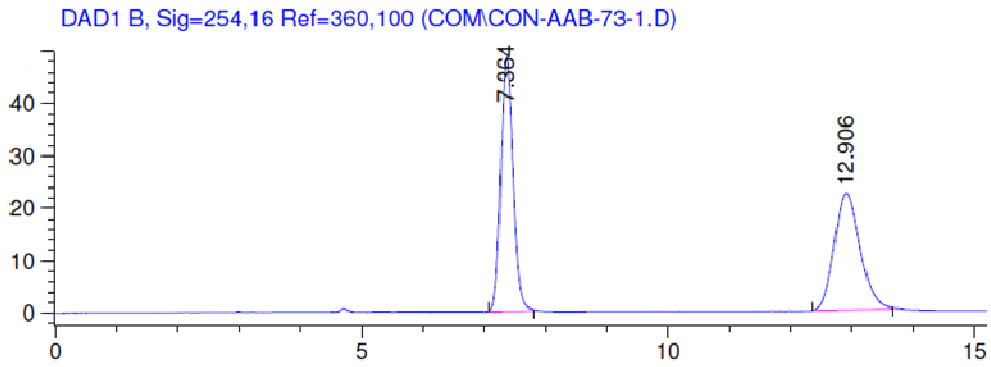


Figure 2: OD-H HPLC profile of **3f**, flow: 1mL/min in hexane-*i*PrOH (97:3), detection 254 nm, vertical axis in mAU, horizontal axis in minutes (t = 7.36 min, 50.8% of integration, first enantiomer, t = 12.91 min, 49.2% of integration second enantiomer).

This result suggested an element of chirality in the cross-coupling product. Thus, we suspect an intermolecular N-H··N interaction which may induce a C-N_{tert} axis of chirality (Figure 3).

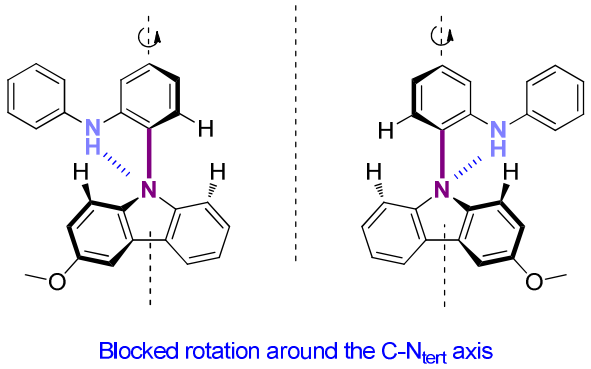


Figure 3: Two isomers of product **3f** around C-N_{tert} axis.

In the same manner, the product **3o** (resulting from the carbazole functionalized by enantiopure menthoxy unit) afforded 63% isolated yield of a 1:1 diastereomeric mixture (AD-H column, figure 4 A). The racemic version of menthoxy unit on the carbazole was characterized as two diastereomeric products. The second diastereomer displays the two peaks of two enantiomers (Figure 4 B).

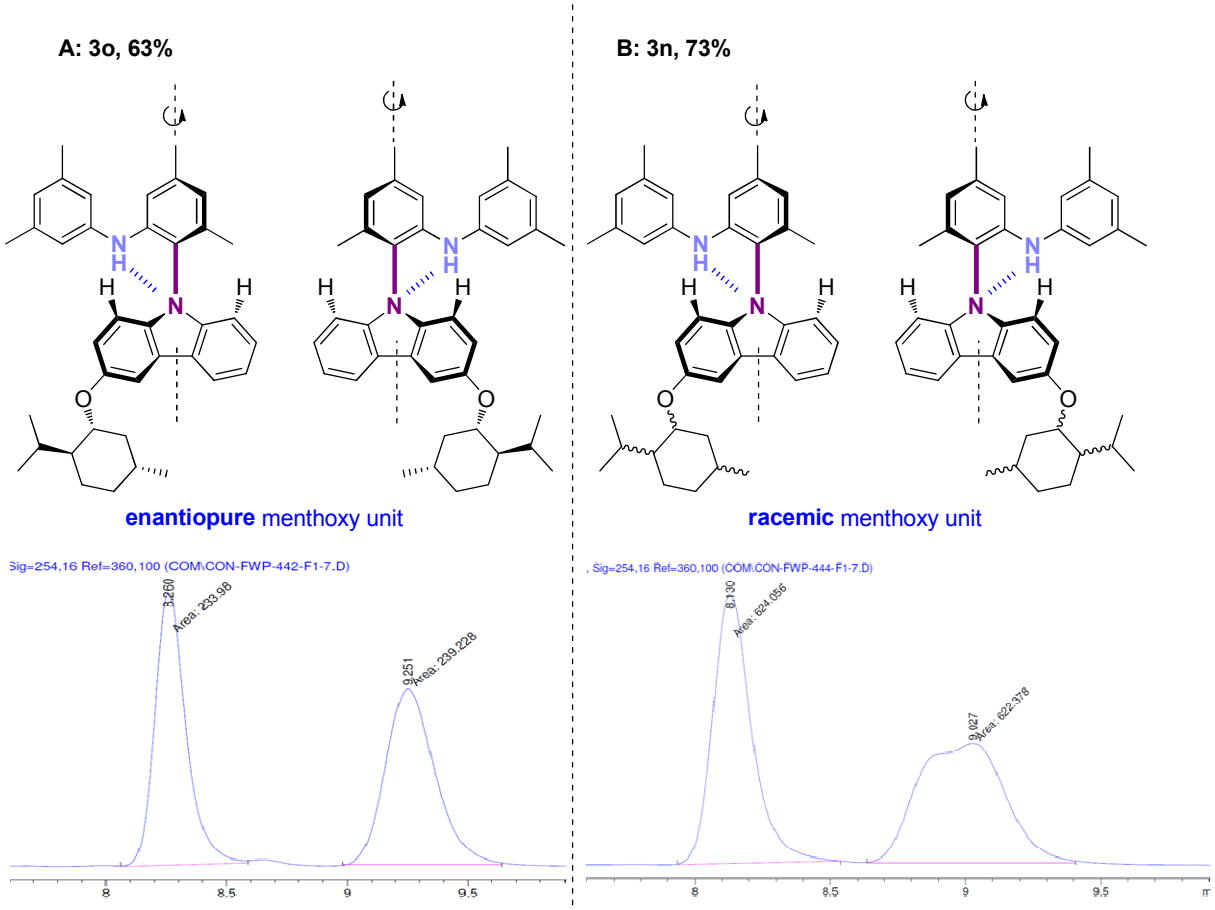


Figure 4: **A**: AD-H HPLC profile of (enantiopure)-**3o**, retention times: 8.26 min (first diastereomer), 9.25 (second diastereomer). **B**: AD-H HPLC profile of (racemic)-**3n**, retention times: 8.1-8.3 min (two enantiomers of first diastereomer), 8.85 min (first enantiomer of second diastereomer), 9.03 min (second enantiomer of second diastereomer).

Product **3v** could be characterized by ^{1}H NMR as two diastereomers. The presence of splitted signals notably N-H (two singlets) and methyl group (two doublets) supports this conclusion (Figure 5).

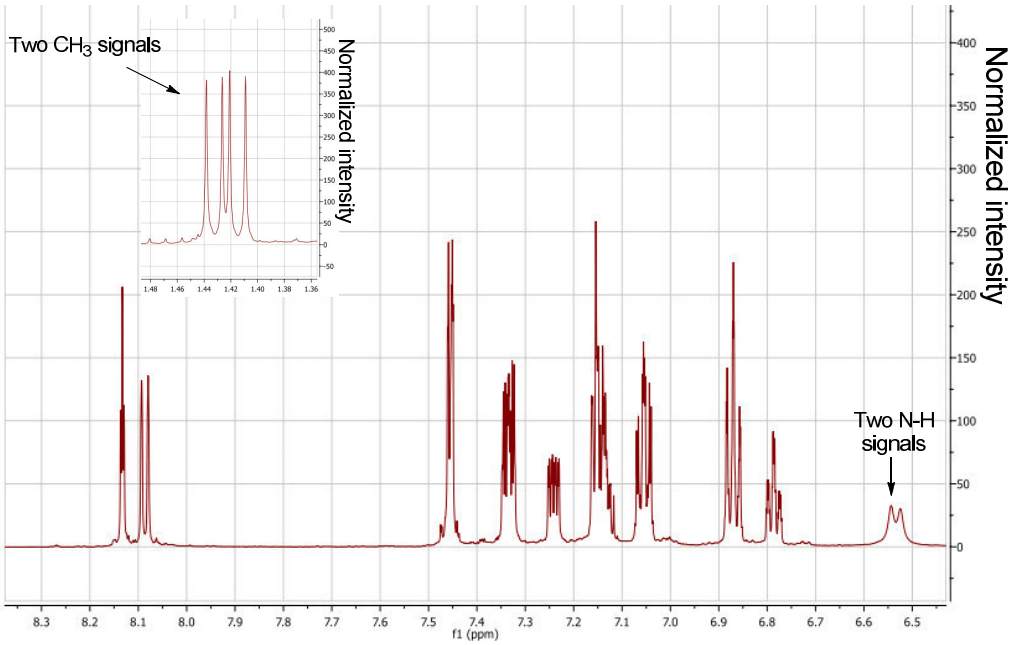


Figure 5: ^{1}H NMR (600 MHz, DMSO-d_6) at 130°C of **3v** δ (ppm): 6.55 ppm (NH), 1.43 (CH_3 split as two doublets).

In order to obtain the temperature of inversion over the C-N_{tert} rotational axis, a temperature gradient was tested for this molecule **3v**. Unfortunately thermal decomposition occurred before inversion (Figure 6)

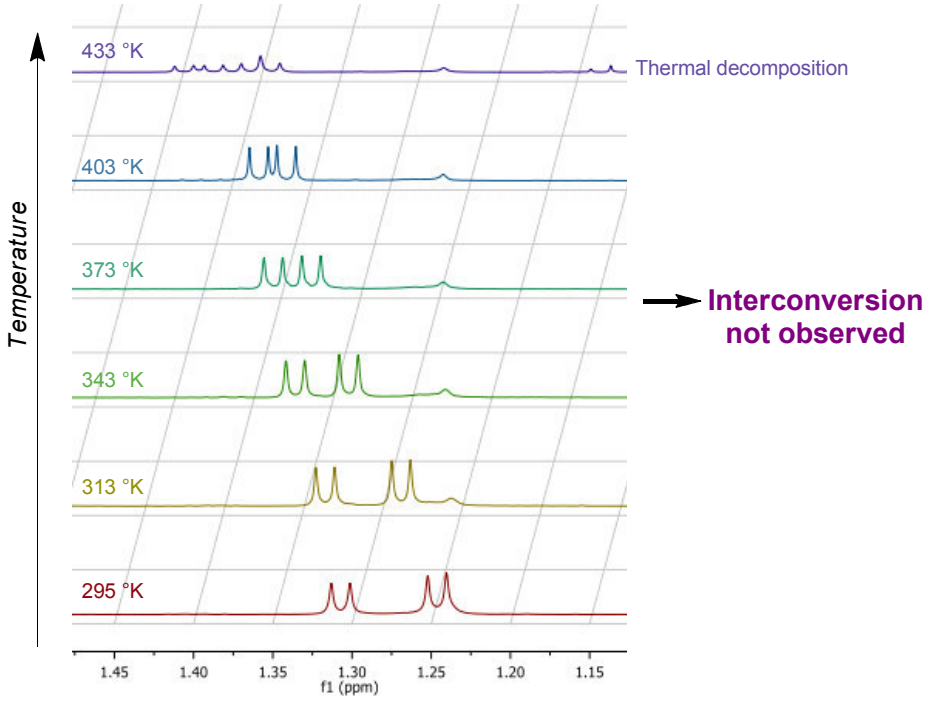
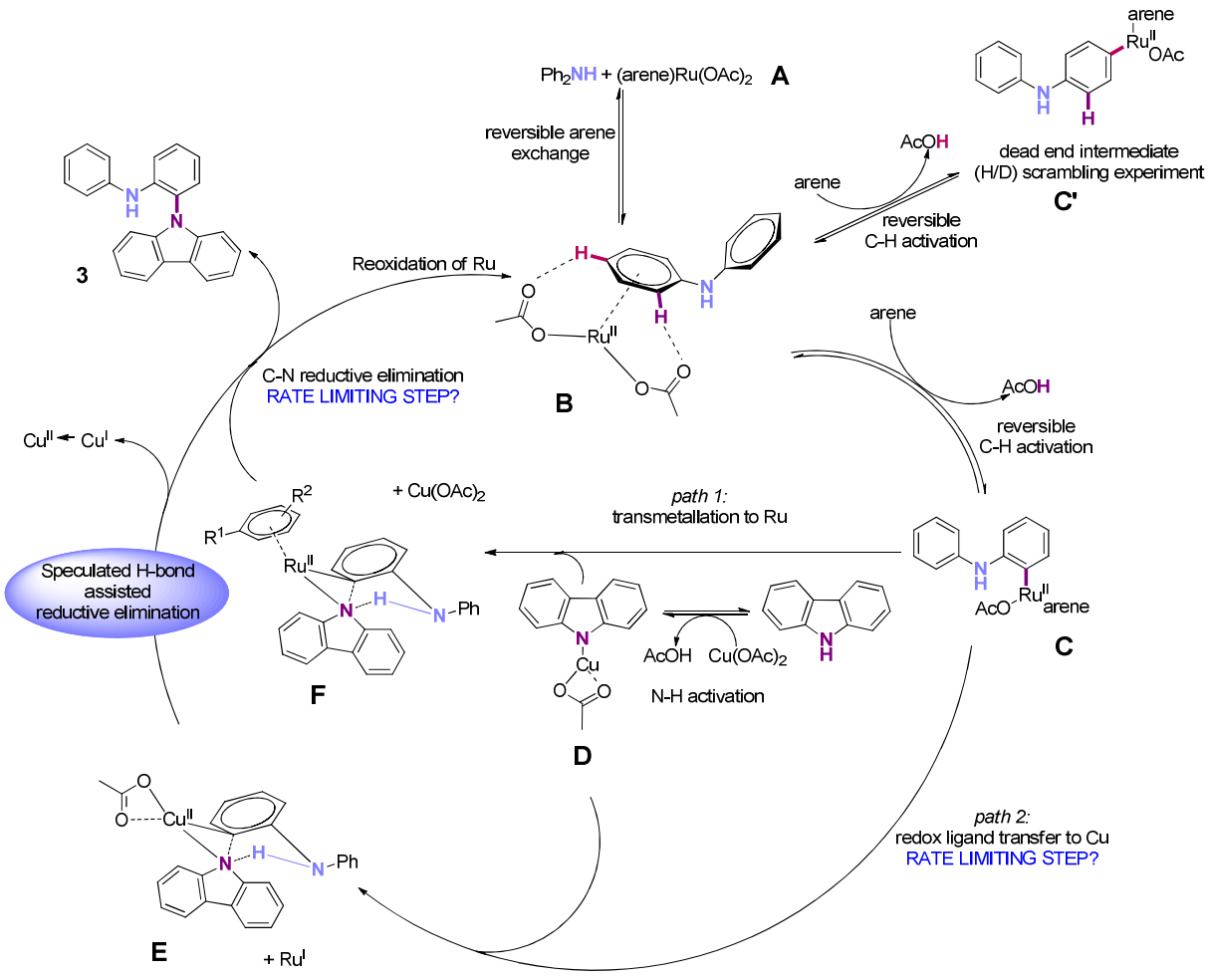


Figure 6: ^{1}H NMR spectrum of **3v** methyl signal at different temperature.

We considered also N_{sec} atom of the lauternamines as plausible center of chirality if slow and/or hindered pyramidal inversion occurred. To control this hypothesis, we submitted a sample with product resulting from a symmetric carbazole (entry **3a**). The analysis of the product on chiral analytical HPLC (OD-H column) disproved this hypothesis showing no racemate separation.

3.2.3.3. Hypothetical mechanism.

Based on first elements of reactivity we proposed an initial reaction mechanism. As mentioned in the H/D scrambling experiments part, only the ruthenium (II) is responsible for the C-H activation step of the diphenylamines (Steps **A** to **C** - Scheme 20).



Scheme 20: Hypothetical mechanism for the cross-dehydrogenative amination of diarylamines.

Thus, the ruthenium coordinated to the π-aryl system of diarylamines could C-H activate most nucleophilic *ortho* and *para* position of the molecule (Step **B** – Scheme 20). Simultaneously, azaphile copper might be involved in the N-H activation, and then the transmetallation of carbazole. (Step **D** – Scheme 20). The intra-molecular N-H··N interaction, inspired us for two scenarios where this hydrogen bond could have significant role in the C-N reductive elimination. The carbazole **D** may be transmetalated to the ruthenium to form a six membered ring **F**, or on the contrary, ruthenium intermediate **C** could transmetalate its ligand to form similar six membered cycle **E** with copper. Regarding their respective oxidation state, **E** and **F** are speculative. The following step (reductive elimination) could be assisted by the intramolecular hydrogen-bond since only *ortho*-functionalized product **3a** is release. We assume tetrachloroethylene might also participate to the C-N bond reductive elimination thanks to its electro-withdrawing abilities (See optimization). We suggest two possible rate limiting step namely transmetalation (**C** to **E** – Scheme 20) and/or C-N reductive elimination (**E** and **F** to **3** – Scheme 20). Further studies are planned to prove or disprove this mechanism.

3.3. Conclusions and outlooks.

In summury we developed an intermolecular cross-dehydrogenative coupling between carbazole and diarylamines. We reported this *ortho*-selective reaction without any help of chelating directing group, nor pre-functionalized or pre-oxidized substrates. We synthesized a library of new molecules: Lauternamines which present chiral properties with asymmetric carbazoles.

In the near future, we plan to study more deeply the mechanism of the reaction and elucidate effect of the Hydrogen-bond on the reactivity. We are interested in developing an enantioselective version of the reaction to access directly chiral molecules. This class of compounds could also be tested as ligand on asymmetric catalysis. We would like to investigate the effect of functional group (EWG or EDG) on the strength of Hydrogen bond.

3.4. References.

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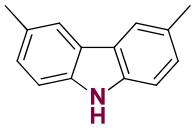
3.5. Experimental part.

3.5.1. General information.

All reactions were carried out in dried reaction vessels with sealed Teflon screw caps under oxygen, unless otherwise specified. NMR spectra were obtained on *Bruker AMX* 400 or on *Bruker Avance* 600 systems using $CDCl_3$, $(CD_3)_2SO$, or C_6D_6 as solvents, with proton and carbon resonances at 400/600 Hz and 101/151 MHz, respectively. Coupling constants (*J*) are quoted in Hz. Flash chromatography was performed on silica gel (40-63 mesh) by standard technique. GC-MS spectra were recorded on a *Bruker 436-GC/SCION SQ Premium* EI, 230 V. The major signals are quoted in *m/z* with the relative intensity in parentheses. The method used starts with the injection temperature T_0. After holding this temperature for 3 min, the column is heated to temperature T_1 (ramp) and this temperature is held for an additional time t. Method: 50_40: T_0 = 50 °C, T_1 = 320 °C, ramp = 40 °C/min; t = 5 min. Some substrates were purchased either from Sigma Aldrich, Acros or TCI, and engaged directly. Other substrates were prepared according to literature and/or home-made procedures.

3.5.2. Substrates preparation.



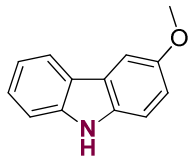
3,6-dimethyl-9*H*-carbazole
Chemical Formula: $C_{14}H_{13}N$
Exact Mass: 195,10
Molecular Weight: 195,26
m/z: 195.10 (100.0%), 196.11 (15.3%), 197.11 (1.1%)
Elemental Analysis: C, 86.12; H, 6.71; N, 7.17

3,6-dimethylcarbazole 1e: 3,6-dibromocarbazole (16.3 mmol) is placed in a round bottom flask under N_2 atmosphere. Freshly distilled diethyl ether (200 mL) is added. The mixture is cooled to 0°C. *N*-butyllithium (17.5 mmol) is introduced dropwise. The mixture is stirred at this temperature for 1h. Trimethylsilyl chloride (17.3 mmol) is added. The reaction mixture is stirred again for 1h at room temperature. The suspension is cooled to -78°C. *T-butyl*lithium (67.5 mmol) is carefully introduced. After 1.5h of stirring at 0°C, methyl iodide (82 mmol) is added at -78°C.

The suspension is slowly warmed up at room temperature and stirred for the weekend. HCl 1M (50 mL) is added. Layers are separated. The organic phase is washed with HCl 1M (2x50 mL) and distilled water (2x50 mL) then dried over $MgSO_4$. The crude is then reduced, and purified over SiO_2 gel column chromatography in pentane/CH_2Cl_2 (6:4). 45% isolated yield (white solid).

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.87 (broad s, 2H), 7.85 (broad, 1H, N*H*), 7.35-7.32 (d, *J* = 8.2 Hz, 2H), 7.25 (dd, ^3J = 8.2 Hz, *J* = 1.5 Hz, 2H), 2.56 (s, 6H, CH_3).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ (ppm): 138.19 (s, C_{quat}), 128.62 (s, C_{quat}), 127.13 (s, CH), 123.53 (s, C_{quat}), 120.32 (s, CH), 110.36 (s, CH), 21.59 (s, CH_3).

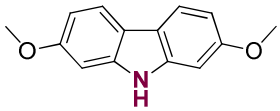


3-methoxy-9*H*-carbazole
Chemical Formula: $C_{13}H_{11}NO$
Exact Mass: 197,08
Molecular Weight: 197,23
m/z: 197.08 (100.0%), 198.09 (14.2%), 199.09 (1.1%)
Elemental Analysis: C, 79.16; H, 5.62; N, 7.10; O, 8.11

3-methoxycarbazole 1f: 3-bromocarbazole (commercial from TCI, 8.1 mmol) was united with CuI (16.3 mmol) and submitted to DMF (10 mL). A solution of MeONa/MeOH (5.4 M, 25 mL) was added under inert atmosphere in a Schlenk reactor. The reactor was sealed and heated to 120°C for 20h. The crude is then filtered on a SiO_2 plug in EtOAc, and evaporated. The crude is then purified over SiO_2 gel column chromatography. (height 380 mm, width 35 mm) in pentane/CH_2Cl_2 (6:4). 62% isolated yield (white powder).

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.06 (d, 1H, ^3J = 7.8 Hz), 7.93 (broad s, N*H*), 7.60 (d, 1H, *J* = 2.4 Hz), 7.43 (m, 2H), 7.36 (d, 1H, ^3J = 8.8 Hz), 7.25 (m, 1H), 7.10 (dd, 1H, ^3J = 8.8 Hz, *J* = 2.4 Hz), 3.97 (s, CH_3).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ (ppm): 153.92 (s, C_{quat}), 140.29 (s, C_{quat}), 134.38 (s, C_{quat}), 125.83 (s, CH), 123.80 (s, C_{quat}), 123.37 (s, C_{quat}), 120.28 (s, CH), 119.08 (s, CH), 115.10 (s, CH), 111.33 (s, CH), 110.77 (s, CH), 103.17 (s, CH), 56.11 (s, CH_3).

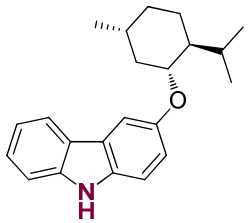


2,7-dimethoxy-9*H*-carbazole
Chemical Formula: $C_{14}H_{13}NO_2$
Exact Mass: 227,09
Molecular Weight: 227,26
m/z: 227.09 (100.0%), 228.10 (15.4%), 229.10 (1.6%)
Elemental Analysis: C, 73.99; H, 5.77; N, 6.16; O, 14.08

2,7-dimethoxycarbazole: Commercial 2,7-dibromocarbazole (from TCI, 9.2 mmol) and CuI (36.9 mmol) are placed in a Schlenk reactor under N_2 atmosphere. DMF (10 mL) and a solution of MeONa/MeOH (5.4 M, 45 mL) are added. The reactor is sealed under N_2 and heated at 110°C for 20h. The crude is then directly filtered over a SiO_2 plug in ethyl acetate. The crude is then reduced, and purified over SiO_2 gel column chromatography. (height 320 mm, width 35 mm) in CH_2Cl_2 (5 L), 61% isolated yield (light pink solid).

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ (ppm): 10.97 (s, 1H, N*H*), 7.84 (d, 2H, ^3J = 8.4 Hz), 6.94 (d, 2H, J = 2.0 Hz), 6.73 (dd, 2H, ^3J = 8.4 Hz, J = 2.0 Hz), 3.82 (s, 6H, CH_3).

^{13}C {^{1}H} NMR (101 MHz, $(CD_3)_2SO$) δ (ppm): 157.52 (s, C_{quat}), 140.99 (s, C_{quat}), 119.89 (s, CH), 116.43 (s, C_{quat}), 107.28 (s, CH), 94.62 (s, CH), 55.19 (s, CH_3).



3-(((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)oxy)-9*H*-carbazole
Chemical Formula: $C_{22}H_{27}NO$
Exact Mass: 321,21
Molecular Weight: 321,46
m/z: 321.21 (100.0%), 322.21 (24.2%), 323.22 (2.8%)
Elemental Analysis: C, 82.20; H, 8.47; N, 4.36; O, 4.98

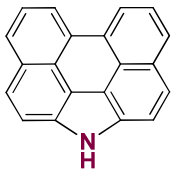
3-menthoxycarbazole: 3-bromocarbazole (commercial from TCI, 5.0 mmol) and (-) menthol (50 mmol) were united with CuI (10.0 mmol), 2,2,6,6-tetramethyl-3,5-heptanedione (20.0 mmol), K_3PO_4 (10 mmol) and cumene (10 mL) under inert atmosphere in a Schlenk reactor. The reactor was sealed and heated to 170°C for 48h. The crude is then filtered on a SiO_2 plug in CH_2Cl_2, and evaporated.

The crude is then purified over SiO_2 gel column chromatography in hexane/CH_2Cl_2 (6:4) and in a second time in hexane/EtOAc. 17% isolated yield (white powder).

^{1}H NMR (400 MHz, C_6D_6): δ (ppm):8.01 (d, *J* = 8.3 Hz, 1H), 7.91 (m, 1H), 7.44-7.40 (m, 1H), 7.36-7.33 (m, 1H), 7.14-7.12 (m, 1H), 7.06-7.04 (m, 1H), 6.55 (broad s, N*H*), 4.25-4.19 (m, 1H), 2.75-2.67 (m, 1H), 2.44-2.39 (m, 1H), 1.77-0.83 (aliphatic area; 1.09 (d, *J* = 7.0 Hz, 3H), 1.01 (d, *J* = 7.0 Hz, 3H), 0.88 (d, *J* = 6.5 Hz, 3H)).

^{13}C {^{1}H} NMR (101 MHz, C_6D_6): δ (ppm): 152.74 (s, C_{quat}) 140.50 (s, C_{quat}), 134.78 (s, C_{quat}), 125.65 (s, CH), 124.22 (s, C_{quat}), 123.53 (s, C_{quat}), 120.48 (s, CH), 119.00 (s, CH), 117.38 (s, CH), 111.29 (s, CH), 110.66 (s, CH), 106.90 (s, CH), 79.04 (s, CH), 48.58 (s, CH), 40.74 (s, CH_2), 34.64 (s, CH_2), 31.37 (s, CH), 26.24 (s, CH), 23.80 (s, CH_2), 22.11 (s, CH_3), 20.88 (s, CH_3), 16.67 (s, CH_3).

EI-HRMS: mass spectrometry: *m/z* calc. 321.2093 $[C_{22}H_{27}NO]^{\bullet+}$, measured 321.2089.



1*H*-phenanthro[1,10,9,8-*cdefg*]carbazole
Chemical Formula: $C_{20}H_{11}N$
Exact Mass: 265,09
Molecular Weight: 265,31
m/z: 265.09 (100.0%), 266.09 (22.0%), 267.10 (2.3%)
Elemental Analysis: C, 90.54; H, 4.18; N, 5.28

1-Nitroperylene

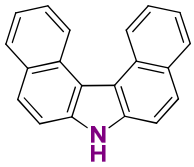
To a 50°C solution of perylene (19.8 mmol) in 200 mL of 1,4-dioxane is added a mixture of 6 mL of water and 4.0 mL of nitric acid (d 1.5). The resulting solution is stirred at 60°C for 35 min, and then poured into 2.0 L of water. The resulting mixture is filtered and washed with 200 mL of water. The red solid is purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (3/2). 7% isolated yield (red solid)

6H-phenanthro[1,10,9,8-c,d,e,f,g]carbazole

A mixture of 1-nitroperylene (1.3 mmol) and 10 mL of triethylphosphite is stirred at 160°C under nitrogen for 3h. The reaction mixture is cooled to room temperature, filtered and washed with pentane. The crude product is purified by column chromatography on silica gel using CH_2Cl_2 as an eluent. 84% isolated yield (light yellow solid).

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm): 12.19 (s, 1 H, N*H*), 8.76 (d, *J* = 7.3 Hz, 2H), 8.19 (d, *J* = 8.0 Hz, 2H), 7.98 (d, *J* = 8.8 Hz, 2H), 7.93 (d, *J* = 8.8 Hz, 2H), 7.82 (t, *J* = 7.8 Hz, 2H).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6): δ (ppm): 130.61 (s, C_{quat}), 129.70 (s, C_{quat}), 128.29 (s, C_{quat}), 125.06 (s, CH), 124.59 (s, CH), 124.21 (s, C_{quat}), 123.56 (s, CH), 120.82 (s, CH), 116.94 (s, C_{quat}), 115.56 (s, CH).

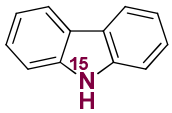


7*H*-dibenzo[*c*,*g*]carbazole
Chemical Formula: $C_{20}H_{13}N$
Exact Mass: 267,10
Molecular Weight: 267,32
m/z: 267.10 (100.0%), 268.11 (21.8%), 269.11 (2.3%)
Elemental Analysis: C, 89.86; H, 4.90; N, 5.24

7H-dibenzo[c,g]carbazole 1x: In a dried Schlenk were introduced binaphtylamine (7.0 mmol) and 6 mL of HCl_{aq} (12M) in 55 mL of dioxane. The mixture was stirred under nitrogen for 65h. The reaction was neutralized with $NaHCO_3$, extracted with DCM, then dried over $MgSO_4$. The crude is then reduced, and purified over SiO_2 gel column chromatography in pentane/CH_2Cl_2 (1:3). 66% isolated yield (beige solid).

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm): 9.26 (d, 2H, *J* = 8.5 Hz), 8.51 (broad s, NH), 8.07 (˜d, 2H, *J* = 8.0 Hz), 7.85 (d, 2H, *J* = 8.6 Hz), 7.73 (dt, 2H, *J* = 1.2 Hz, *J* = 7.0 Hz), 7.58-7.53 (m, 4H).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6): δ (ppm): 136.17 (s, C_{quat}), 130.00 (s, C_{quat}), 129.25 (s, CH), 126.85 (s, CH), 125.52 (s, CH), 125.23 (s, CH), 123.36 (s, CH), 117.67 (s, C_{quat}), 112.65 (s, CH).



Chemical Formula: $C_{12}H_9{}^{15}N$
Exact Mass: 168,07
Molecular Weight: 168,20
m/z: 168.07 (100.0%), 169.07 (13.0%)
Elemental Analysis: C, 85.69; H, 5.39; N, 8.92

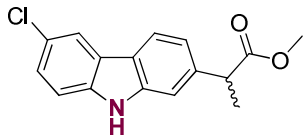
^{15}N carbazole (^{15}N, 98%+) 1t: Note: these are not optimised conditions. ^{15}N-aniline (^{15}N, 98%+, commercial from Aldrich, 10.6 mmol) is diluted in 100 mL CH_2Cl_2 together with Et_3N (100 mmol). Acetylchloride (100 mmol) is added slowly drop wise at r.t. under strong magnetic stirring. The crude is then filtered on a SiO_2 plug in EtOAc and evaporated. The crude is then purified over SiO_2 gel column chromatography (height 400 mm, width 35 mm) in 100% EtOAc, yielding the acetanilide in 93.9% (white solid). Inspired from a protocol from Taillefer et al., [15] the product is then engaged directly with CuI (1 mmol), K_3PO_4 (20 mmol), Dipivaloylmethane (CAS nr: 1118-71-4, 2 mmol), iodobenzene (15 mmol), and exposed to toluene (60 mL) in a Schlenk reactor under inert atmosphere. The reactor is then sealed and exposed to 140°C for 24h. The crude is then filtered on a SiO_2 plug in EtOAc, and evaporated. The crude is then purified over SiO_2 gel column chromatography (height 450 mm, width 55 mm) in 100% EtOAc, yielding the diphenylacetamide-^{15}N in 55.8% yield (5.92 mmol, white solid). The compound is then directly engaged in a ring-closing oxidation inspired of a protocol from Yuanjiang Pan *et al.* [16] The product is united with $Pd(OAc)_2$ (0.89 mmol), Ag_2O (14.8 mmol) in AcOH (30 mL) in a Schlenk reactor under inert atmosphere. The reactor is then sealed and exposed to 140 °C under strong magnetic stirring for 36 h. The crude is then filtered on a SiO_2 plug in EtOAc, and evaporated. Two evaporations from toluene allow the removal of AcOH. The residue is then directly treated with $LiAlH_4$ (25 mmol) in 1,4-dioxane (30 mL). Caution is required here because of strongly exothermic reaction. The reaction takes place in a 250 mL round bottom flask equipped with a high condenser. The suspension is slowly and gently heated until boiling, under strong magnetic stirring, and then left to cool down at r.t.. The crude is then quenched drop wise with EtOH, and evaporated thrice with toluene. The crude is then filtered on a SiO_2 plug in CH_2Cl_2, and evaporated.

The crude is then purified over SiO_2 gel column chromatography. (height 420 mm, width 35 mm) in CH_2Cl_2 (100%), yielding 1.35 mmol of ^{15}N-carbazole as a white solid (23% over the last step, and 13% in overall yield).

The solubility in $CDCl_3$ is poor (hence the high temp. NMR), but this solvent allows easy recovery of the precious compound.

^{1}H NMR (600 MHz, 119 mM in $CDCl_3$, 323 K) δ (ppm): 8.11 (broad d, 2H, J = 7.2 Hz), 7.98 (d, NH, $^1J_{H\text{-}N}$ = 96.0 Hz), 7.45 (broad & tall signal, 4H), 7.27 (very broad signal, 2H).

^{13}C {^{1}H} NMR (151 MHz, 119 mM in $CDCl_3$, 323 K) δ (ppm): 139.62 (d, $^1J_{C\text{-}N}$ = 15.3 Hz, C_{quat}), 125.81 (d, $J_{C\text{-}N}$ = 2.3 Hz, CH), 123.52 (d, $^2J_{C\text{-}N}$ = 4.1 Hz, C_{quat}), 120.28 (s, CH), 119.48 (s, CH), 110.53 (d, $J_{C\text{-}N}$ = 2.3 Hz, CH).

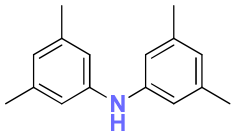


methyl 2-(6-chloro-9*H*-carbazol-2-yl)propanoate
Chemical Formula: $C_{16}H_{14}ClNO_2$
Exact Mass: 287,07
Molecular Weight: 287,74
m/z: 287.07 (100.0%), 289.07 (32.0%), 288.07 (17.7%), 290.07 (5.7%), 289.08 (1.9%)
Elemental Analysis: C, 66.79; H, 4.90; Cl, 12.32; N, 4.87; O, 11.12

Carprofenmethylester: Carprofen (1.5 mmol) and *p*-toluenesulfonic acid (0.75 mmol) were dissolved in methanol (30 mL) and stirred for 1h under reflux. The solvent was evaporated and the product was purified by SiO_2 gel column chromatography Hexane/CH_2Cl_2 (3:7). 99% isolated yield (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.11 (broad s, NH), 7.98 (d, 1H, J = 1.4 Hz), 7.94 (d, 1H, , ^3J = 8.0 Hz), 7.39 – 7.28 (m, 3H), 7.18 (dd, 1H, ^3J = 8.2 Hz, J = 1.4 Hz), 3.89 (q, 1H, ^3J = 7.2 Hz), 3.68 (s, COO**CH$_3$**), 1.59 (d, CH**CH$_3$**, ^3J = 7.2 Hz).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 174.56 (s, C_{quat}, **C**OOMe), 139.39 (s, Cquat), 138.33 (s, C_{quat}), 137.08 (s, C_{quat}), 124.83 (s, CH), 123.95 (s, C_{quat}), 123.29 (s, C_{quat}), 120.64 (s, C_{quat}), 119.60 (s, CH), 118.93 (s, CH), 118.61 (s, CH), 110.46 (s, CH), 108.42 (s, CH), 50.71 (s, COO**C**H$_3$), 44.30 (s, CH, benzylic position), 17.32 (s, CH_3).

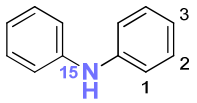


bis(3,5-dimethylphenyl)amine
Chemical Formula: $C_{16}H_{19}N$
Exact Mass: 225,15
Molecular Weight: 225,33
m/z: 225.15 (100.0%), 226.16 (17.5%), 227.16 (1.4%)
Elemental Analysis: C, 85.28; H, 8.50; N, 6.22

1,3,5-dixylyamine 2l: Commercial 1,3,5-xylylamine (40 mmol) and Et_3N (80 mmol) are diluted in 100 mL CH_2Cl_2, and acetylchloride (80 mmol) is then cautiously added drop wise. After 1 hour stirring at r.t., the crude is filtered over a plug of SiO_2 in CH_2Cl_2. The organic solvent is then evaporated, and the crude is crushed in boiling toluene, and filtered hot (removal of salt residues). The resulting clear hot toluene layers are left to cool down for 24 hours yielding, after crystallization and filtration, 1,3,5- xilylacetamide in 99% isolated yield (white crystalline material). 20 mmol of that material is then united with CuI (2 mmol), K_3PO_4 (40 mmol), Dipivaloylmethane (CAS nr: 1118-71-4, 4 mmol), Commercial 1,3,5-iodoxylene (30 mmol), toluene (50 mL), and the reactor is then sealed for 48 hours at 150°C (Taillefer's procedure). [15] The crude is then cooled down to r.t., filtered over a SiO_2 plug in ethyl acetate, and evaporated. The crude is then directly united with KOH (20 g), H_2O (20 mL) and ^{i}PrOH (20 mL), and heated in a sealed reactor at 160°C for 3 days. After cooling at r.t., the crude is directly extracted thrice in CH_2Cl_2. TLC analysis shows good but incomplete hydrolysis. The product is nevertheless purified over SiO_2 gel column chromatography. (height 360 mm, width 55 mm) in hexane/CH_2Cl_2 (7:3), yielding 7.37 mmol of 1,3,5-dixylylamine (37% isolated yield, light yellow & clear sticky oil, "like honey").

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.63 (s, 4H), 6.51 (s, 2H), 2.20 (s, 12H).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 143.19 (s, C_{quat}), 139.01 (s, C_{quat}), 122.80 (s, CH), 115.79 (s, CH), 21.43 (s, CH_3).



Chemical Formula: $C_{12}H_{11}{}^{15}N$
Exact Mass: 170,09
Molecular Weight: 170,22
m/z: 170.09 (100.0%), 171.09 (13.1%)
Elemental Analysis: C, 84.67; H, 6.51; N, 8.81

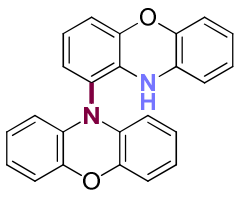
^{15}N-diphenylamine (^{15}N, 98%+) 2u: The diphenylacetamide-^{15}N obtained as intermediate in the synthesis of **1c** (6.79 mmol), is united with KOH (15 g), H_2O (20 mL), ^{i}PrOH (20 mL), sealed in a closed reactor and heated at 160 °C for 48 hours. After cooling at r.t., the crude was directly extracted thrice with CH_2Cl_2. The organic were united, evaporated, and purified over a SiO_2 plug in CH_2Cl_2. 6.63 mmol of ^{15}N-diphenylamine (^{15}N, 98%+) were obtained (98% isolated yield), as a white shiny solid.

^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 7.18 (~dd, 2H, ^{3}J ~ ^{3}J ~ 8 Hz, H^2), 6.98 (~d, 2H, ^{3}J ~ 8.2 Hz, H^1), 6.84 (~t, 1H, ^{3}J ~ 7.3 Hz, H^1), 5.58 (very broad d, $^{1}J_{HN}$ = 44 Hz, NH).

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.33 (~dd, 2H, ^{3}J ~ ^{3}J ~ 8 Hz, H^2), 7.14 (~d, 2H, ^{3}J ~ 8.2 Hz, H^1), 7.00 (~t, 1H, ^{3}J ~ 7.3 Hz, H^1), 5.75 (broad s, NH).

^{13}C {^{1}H} NMR (151 MHz, $CDCl_3$) δ (ppm): 143.14 (d, $^{1}J_{C\text{-}N}$ = 15.3 Hz, C_{quat}), 129.41 (d, $^{3}J_{C\text{-}N}$ = 1.5 Hz, CH, C^2), 121.05 (s, CH, C^3), 117.86 (d, $^{2}J_{C\text{-}N}$ = 2.3 Hz, CH, C^1).

3.5.3. New Homo-coupling products.



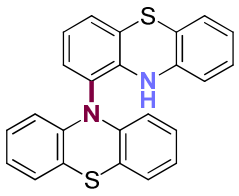
10*H*-1,10'-biphenoxazine
Chemical Formula: $C_{24}H_{16}N_2O_2$
Exact Mass: 364,12
Molecular Weight: 364,40
m/z: 364.12 (100.0%), 365.12 (26.7%), 366.13 (3.7%)
Elemental Analysis: C, 79.11; H, 4.43; N, 7.69; O, 8.78

14a. The phenoxazine (1.0 mmol), [(*p*-cymene)$RuCl_2$]$_2$ (0.0125 mmol), $Cu(OAc)_2$ (0.55 mmol), C_2Cl_4 (2 mL), cumene (0.500 mL) and AcOH (0.125 mL) are united under air in a small 70 mL reactor equipped with Teflon screw cap. The reactor is sealed (tightly) and exposed to 150°C for 24h. (magnetic stirring set to approx. 600 turns/min). The reactor is then cooled to room temperature and the crude mixture is directly purified by SiO_2 gel column chromatography pentane/ CH_2Cl_2 (3:2). 82% isolated yield (white solid).

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm): 8.20 (s, 1H, NH), 6.77-6.73 (m, 2H), 6.73-6.63 (m, 10H), 6.61- 6.57 (m, 1H), 6.01-5.98 (m, 2H).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6): δ (ppm): 144.34 (s, C_{quat}), 143.61 (s, C_{quat}), 142.61 (s, C_{quat}), 132.67 (s, C_{quat}), 132.05 (s, C_{quat}), 131.31 (s, C_{quat}), 124.94 (s, CH), 123.93 (s, CH), 123.66 (s, CH), 121.82 (s, C_{quat}), 121.41 (s, CH), 121.36 (s, CH), 120.94 (s, CH), 115.12 (s, CH), 115.09 (s, CH), 114.96 (s, CH), 114.03 (s, CH), 112.81 (s, CH).

EI-HRMS: mass spectrometry: *m/z* calc. 364.1212 $[C_{24}H_{16}N_2O_2]^{\bullet+}$, measured 364.1198.



10*H*-1,10'-biphenothiazine
Chemical Formula: $C_{24}H_{16}N_2S_2$
Exact Mass: 396,08
Molecular Weight: 396,53
m/z: 396.08 (100.0%), 397.08 (26.1%), 398.07 (9.1%), 398.08 (3.8%), 399.07 (2.5%), 397.07 (2.3%)
Elemental Analysis: C, 72.70; H, 4.07; N, 7.06; S, 16.17

14b. The phenothiazine (2.0 mmol), [(*p*-cymene)$RuCl_2$]$_2$ (0.025 mmol), $Cu(OAc)_2$ (0.25 mmol), C_2Cl_4 (4 mL), cumene (1 mL) and AcOH (0.250 mL) are united under air in a 170 mL reactor equipped with Teflon screw cap. The reactor is sealed (tightly) and exposed to 130°C for 24h. (magnetic stirring set to approx. 600 turns/min). The reactor is then cooled to room temperature and the crude mixture is directly purified by SiO_2 gel column chromatography pentane/CH_2Cl_2 (4:1). 43% isolated yield (white solid).

^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm): 8.05 (s, 1H, NH), 7.16 (dd, ^3J = 7.6 Hz, J = 1.4 Hz, 1H), 7.09 (dd, ^3J = 7.9 Hz, J = 1.5 Hz, 1H), 7.02-6.77 (m, 11H), 6.09 (dd, ^3J = 8.2 Hz, J = 1.1 Hz, 2H).

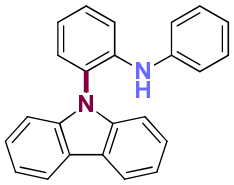
^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6): δ (ppm): 141.93 (s, C_{quat}), 141.45 (s, C_{quat}), 141.08 (s, C_{quat}), 129.56 (s, CH), 127.57 (s, CH), 127.35 (s, CH), 126.91 (s, CH), 126.24 (s, CH), 126.16 (s, C_{quat}), 126.14 (s, CH), 123.58 (s, CH), 122.64 (s, CH), 122.55 (s, CH), 119.40 (s, C_{quat}), 119.27 (s, C_{quat}), 117.26 (s, C_{quat}), 116.01 (s, CH), 115.39 (s, CH).

EI-HRMS: mass spectrometry: *m/z* calc. 396.0755 $[C_{24}H_{16}N_2S_2]^{\bullet+}$, measured 396.0750.

3.5.4. New hetero-coupling products.

Standard conditions: Unless otherwise specified, the carbazole (1 mmol scale), and the diarylamine (3 mmol), [(*p*-cymene)$RuCl_2$]$_2$ (0.05 mmol), $Cu(OAc)_2$ (2.2 mmol), C_2Cl_4 (2 mL), cumene (0.5 mL) and AcOH (0.5 mL) are united under air in a 170 mL reactor equipped with Teflon screw cap. The reactor is then flushed with oxygen atmosphere (1-3 min.), then sealed (tightly) and exposed to 150°C for 24h. (magnetic stirring set to approx. 600 turns/min). The reactor is then cooled to room temperature and the mixture (typically blackish slurry) is treated with 5 mL acetylacetone (acacH) and heated at 150°C for 1h.

The crude is directly engaged (unless otherwise specified) on SiO_2 gel column chromatography for purification. The expected cross-coupling products are generally the most apolar/nonpolar species of their respective reaction mixture, with R_f typically comprised between 0.5 and 0.9 in the given solvent systems.



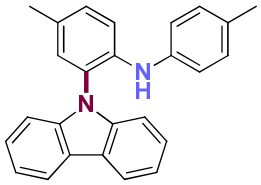
2-(9*H*-carbazol-9-yl)-*N*-phenylaniline
Chemical Formula: $C_{24}H_{18}N_2$
Exact Mass: 334,15
Molecular Weight: 334,41
m/z: 334.15 (100.0%), 335.15 (26.2%), 336.15 (3.4%)
Elemental Analysis: C, 86.20; H, 5.43; N, 8.38

3a. From carbazole and diphenylamine. The reactor is then cooled to room temperature and the crude mixture is directly purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (7:3). 64% isolated yield (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.06 (d, ^3J = 7.8 Hz, 2H), 7.42 (dd, ^3J = 8.3 Hz, J = 1.3 Hz, 1H), 7.33- 7.18 (aromatic area, 6H), 7.14-7.09 (aromatic area, 4H), 6.93-6.89 (aromatic area, 3H), 6.84 (~dd, $^3J \sim {}^3J \sim$ 7.5 Hz, 1H), 5.36 (broad s, NH).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 141.54 (s, C_{quat}), 141.44 (s, C_{quat}), 140.90 (s, C_{quat}), 129.86 (s, CH), 129.37 (s, CH), 129.32 (s, CH), 126.26 (s, CH), 124.41 (s, C_{quat}), 123.64 (s, C_{quat}), 122.55 (s, CH), 120.45 (s, CH), 120.36 (s, CH), 120.29 (s, CH), 120.18 (s, CH), 115.83 (s, CH), 110.20 (s, CH).

ESI-HRMS: mass spectrometry: *m/z* calc. 357.1362 $[(C_{24}H_{18}N_2)Na]^+$, measured 357.1364.



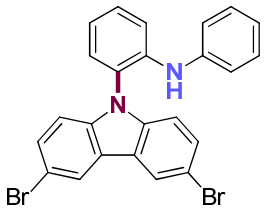
2-(9*H*-carbazol-9-yl)-4-methyl-*N*-(*p*-tolyl)aniline
Chemical Formula: $C_{26}H_{22}N_2$
Exact Mass: 362,18
Molecular Weight: 362,47
m/z: 362.18 (100.0%), 363.18 (29.1%), 364.19 (3.9%)
Elemental Analysis: C, 86.15; H, 6.12; N, 7.73

3b. From carbazole and 4,4'-ditolylamine. The reactor is then cooled to room temperature and the crude mixture is directly purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (7:3). 64% isolated yield (white sticky solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.04 (d, ^3J = 7.8 Hz, 2H), 7.31-7.25 (aromatic area, 3H), 7.19-7.12 (aromatic area, 4H), 7.06 (dd, ^3J = 8.3 Hz, J = 2.0 Hz, 1H), 7.01 (d, J = 1.8 Hz, 1H), 6.90 (broad d, ^3J = 8.3 Hz, 2H), 6.78 (broad d, ^3J = 8.3 Hz, 2H), 4.94 (very broad NH), 2.21 (s, 3H, CH_3), 2.14 (s, 3H, CH_3).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 141.01 (s, C_{quat}), 139.51 (s, C_{quat}), 139.38 (s, C_{quat}), 131.79 (s, C_{quat}), 130.00 (s, CH), 129.83 (s, CH), 129.60 (s, C_{quat}), 126.21 (s, CH), 124.20 (s, C_{quat}), 123.60 (s, C_{quat}), 120.41 (s, CH), 120.07 (s, CH), 115.96 (s, CH), 110.27 (s, CH), 20.77 (s, CH_3), 20.49 (s, CH_3). Two CH lines are overlapped.

EI-HRMS: mass spectrometry: *m/z* calc. 362.1783 $[C_{26}H_{22}N_2]^{\bullet+}$, measured 362.1779.



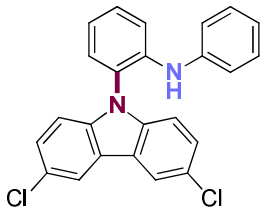
2-(3,6-dibromo-9*H*-carbazol-9-yl)-*N*-phenylaniline
Chemical Formula: $C_{24}H_{16}Br_2N_2$
Exact Mass: 489,97
Molecular Weight: 492,21
m/z: 491.97 (100.0%), 489.97 (50.5%), 493.96 (47.8%), 492.97 (25.7%), 490.97 (13.6%), 494.97 (12.5%), 493.97 (3.4%), 495.97 (1.6%)
Elemental Analysis: C, 58.56; H, 3.28; Br, 32.47; N, 5.69

3c From 3,6-dibromo-carbazole and diphenylamine. The crude is filtered on a SiO_2 plug in CH_2Cl_2, and evaporated. Product is purified by SiO_2 gel column chromatography pentane/CH_2Cl_2 (8:2) and a second time with pentane/CH_2Cl_2 (9:1). 20% Isolated yield (yellow solid).

^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 8.52 (d, *J* = 2.0 Hz, 2H), 7.52 (d, *J* = 2.0 Hz, 1H), 7.50 (d, *J* = 2.0 Hz, 1H), 7.50 (broad s, NH), 7.47 (dd, ^3J = 8.2 Hz, *J* = 1.2 Hz, 1H), 7.45 – 7.41 (m, 1H), 7.32 (dd, ^3J = 7.8 Hz, *J* = 1.3 Hz, 1H), 7.12 (s, 1H), 7.11 (s, 1H), 7.10 – 7.05 (m, 3H), 6.93 (d, ^3J = 7.7 Hz, 2H), 6.77 (t, ^3J = 7.3 Hz, 1H).

^{13}C {^{1}H} NMR (151 MHz, DMSO-d_6) δ (ppm): 141.60 (s, C_{quat}), 139.87 (s, C_{quat}), 138.54 (s, C_{quat}), 128.51 (s, CH), 128.24 (s, CH), 128.02 (s, CH), 127.81 (s, CH), 123.73 (s, C_{quat}), 123.08 (s, CH), 122.40 (s, C_{quat}), 119.93 (s, CH), 119.55 (s, CH), 117.60 (s, CH), 117.14 (s, CH), 111.24 (s, CH), 110.88 (s, C_{quat}).

ESI-HRMS: mass spectrometry: *m/z* calc. 514.9552 $[(C_{24}H_{16}Br_2N_2)Na]^+$, measured 514.9544.



2-(3,6-dichloro-9*H*-carbazol-9-yl)-*N*-phenylaniline
Chemical Formula: $C_{24}H_{16}Cl_2N_2$
Exact Mass: 402,07
Molecular Weight: 403,30
m/z: 402.07 (100.0%), 404.07 (64.1%), 403.07 (26.7%), 405.07 (16.7%), 406.06 (10.2%), 404.08 (3.3%), 407.07 (2.7%), 406.07 (2.2%)
Elemental Analysis: C, 71.47; H, 4.00; Cl, 17.58; N, 6.95

3d. From 3,6-dichloro-carbazole and diphenylamine. The crude is filtered on a SiO_2 plug in CH_2Cl_2, and evaporated. Product is purified by SiO_2 gel column chromatography toluene/hexane (8:3). 77% Isolated yield (white solid).

^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 8.38 (d, *J* = 2.1 Hz, 2H), 7.51 (s, 1H), 7.48 (dd, ^3J = 8.3 Hz, *J* = 1.0 Hz, 1H), 7.45 – 7.41 (m, 1H), 7.40 (dd, ^3J = 8.7 Hz, *J* = 2.1 Hz, 2H), 7.31 (dd, ^3J = 7.8 Hz, *J* = 1.3 Hz, 1H), 7.16 (d, ^3J = 8.7 Hz, 2H), 7.10 – 7.04 (m, 3H), 6.93 (d, ^3J = 7.7 Hz, 2H), 6.77 (m, 1H).

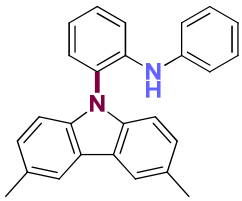
^{13}C {^{1}H} NMR (151 MHz, DMSO-d_6) δ (ppm): 142.20 (s, C_{quat}), 140.45 (s, C_{quat}), 138.99 (s, C_{quat}), 129.05 (s, CH), 128.83 (s, CH), 128.39 (s, CH), 125.98 (s, CH), 124.42 (s, C_{quat}), 123.79 (s, C_{quat}), 123.18 (s, C_{quat}), 120.52 (s, CH), 120.12 (s, CH), 120.00 (s, CH), 118.24 (s, CH), 117.71 (s, CH), 111.40 (s, CH).

or

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.06 (d, *J* = 1.8 Hz, 2H), 7.50 (dd, ^3J = 8.3 Hz, *J* = 1.3 Hz, 1H), 7.43 – 7.36 (m, 3H), 7.28 (dd, ^3J = 7.8 Hz, *J* = 1.5 Hz, 1H), 7.23 (m, 2H), 7.15 (d, ^3J = 8.7 Hz, 2H), 7.04 (m, 1H), 7.02 – 6.96 (m, 3H), 5.29 (broad s, NH).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 139.72 (s, C_{quat}), 139.38 (s, C_{quat}), 137.91 (s, C_{quat}), 128.11 (s, CH), 127.82 (s, CH), 127.63 (s, CH), 125.28 (s, CH), 124.29 (s, C_{quat}), 121.94 (s, C_{quat}), 121.73 (s, C_{quat}), 121.08 (s, CH), 118.70 (s, CH), 118.58 (s, CH), 118.54 (s, CH), 114.37 (s, CH), 109.60 (s, CH).

EI-HRMS: mass spectrometry: *m/z* calc. 402.0691 $[C_{24}H_{16}Cl_2N_2]^{\bullet+}$, measured 402.0683.



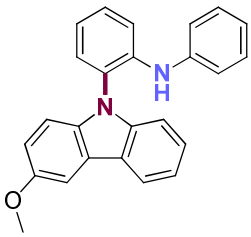
2-(3,6-dimethyl-9*H*-carbazol-9-yl)-*N*-phenylaniline
Chemical Formula: $C_{26}H_{22}N_2$
Exact Mass: 362,18
Molecular Weight: 362,47
m/z: 362.18 (100.0%), 363.18 (29.1%), 364.19 (3.9%)
Elemental Analysis: C, 86.15; H, 6.12; N, 7.73

3e. From 3,6-dimethylcarbazole and diphenylamine. Product purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (4:1). 59% isolated yield (white solid).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.83 (m, 2H), 7.43 (dd, ^3J = 8.3 Hz, J = 1.3 Hz, 1H), 7.28 (m, 1H), 7.21 (dd, ^3J = 7.8 Hz, J = 1.5 Hz, 1H), 7.16-7.11 (m, 4H), 7.01 (d, ^3J = 8.3 Hz, 2H), 7.95-7.85 (m, 4H), 5.40 (broad s, NH), 2.46 (s, CH_3).

^{13}C {1H} NMR (101 MHz, $CDCl_3$): δ (ppm): 141.52 (s, C_{quat}), 141.44 (s, C_{quat}), 139.39 (s, C_{quat}), 129.71 (s, CH), 129.28 (s, C_{quat}), 129.27 (s, CH), 129.06 (s, CH), 127.33 (s, CH), 124.80 (s, C_{quat}), 123.61 (s, C_{quat}), 122.40 (s, CH), 120.28 (s, CH), 120.25 (s, CH), 120.16 (s, CH), 115.63 (s, CH), 109.81 (s, CH), 21.44 (s, CH_3).

EI-HRMS: mass spectrometry: *m/z* calc. 362.1783 $[C_{26}H_{22}N_2]^{\bullet+}$, measured 362.1780.



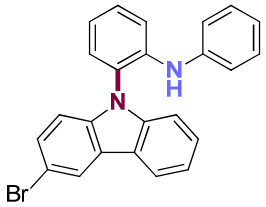
2-(3-methoxy-9*H*-carbazol-9-yl)-*N*-phenylaniline
Chemical Formula: $C_{25}H_{20}N_2O$
Exact Mass: 364,16
Molecular Weight: 364,44
m/z: 364.16 (100.0%), 365.16 (27.3%), 366.16 (3.9%)
Elemental Analysis: C, 82.39; H, 5.53; N, 7.69; O, 4.39

3f. From 3-methoxy-carbazole and diphenylamine. The crude is filtered on a SiO_2 plug in CH_2Cl_2, and evaporated. Product is purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (8:3). 55% isolated yield (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.18 (d, ^{3}J = 7.5 Hz, 1H), 7.77 (d, J = 2.4 Hz, 1H), 7.50 (dd, ^{3}J = 8.2 Hz, 1.3 Hz, 1H), 7.40 (dd, ^{3}J = 7.2 Hz, J = 1.4 Hz, 1H), 7.38 (s, NH), 7.33 (m, 1H), 7.28 (dd, ^{3}J = 7.8 Hz, J = 1.5 Hz, 1H), 7.22 – 7.16 (m, 1H), 7.16 – 7.03 (m, 5H), 7.02 – 6.94 (m, 3H), 6.77 (tt, ^{3}J = 7.3 Hz, J = 1.0 Hz, 1H), 3.85 (s, 3H, CH_3).

^{13}C {1H} NMR (101 MHz, DMSO-d_6) δ (ppm): 152.69 (s, C_{quat}), 141.66 (s, C_{quat}), 139.70 (s, C_{quat}), 139.46 (s, C_{quat}), 134.01 (s, C_{quat}), 127.84 (s, CH), 127.56 (s, CH), 127.48 (s, CH), 125.04 (s, C_{quat}), 124.49 (s, CH), 122.37 (s, C_{quat}), 121.91 (s, C_{quat}), 119.67 (s, CH), 119.07 (s, CH), 118.93 (s, CH), 117.78 (s, CH), 117.29 (s, CH), 116.48 (s, CH), 113.26 (s, CH), 109.47 (s, CH), 108.82 (s, CH), 102.04 (s, CH), 53.99 (s, CH_3).

EI-HRMS: mass spectrometry: *m/z* calc. 364.1576 $[C_{25}H_{20}N_2O]^{\bullet+}$, measured 364.1587.



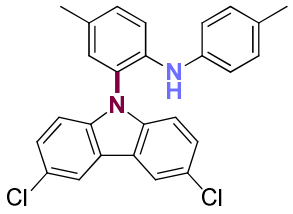
2-(3-bromo-9*H*-carbazol-9-yl)-*N*-phenylaniline
Chemical Formula: $C_{24}H_{17}BrN_2$
Exact Mass: 412,06
Molecular Weight: 413,31
m/z: 414.06 (100.0%), 412.06 (99.3%), 413.06 (26.0%), 415.06 (25.3%), 416.06 (3.3%)
Elemental Analysis: C, 69.74; H, 4.15; Br, 19.33; N, 6.78

3g. From 3-bromo-carbazole and diphenylamine. The crude is filtered on a SiO_2 plug in CH_2Cl_2, and evaporated. Product is purified by SiO_2 gel column chromatography pentane/CH_2Cl_2 (7:3). 68% Isolated yield (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.27 (d, J = 1.7 Hz, 1H), 8.11 (d, ^{3}J = 8.5 Hz, 1H), 7.49 (m, 2H), 7.46 – 7.42 (m, 1H), 7.42 – 7.36 (m, 1H), 7.34 – 7.29 (m, 2H), 7.25 – 7.20 (m, 3H), 7.11 (d, ^{3}J = 8.6 Hz, 1H), 7.03 (dd, ^{3}J = 7.7 Hz, J = 1.4 Hz, 1H), 6.99 (m, 3H), 5.36 (broad s, NH).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 139.77 (s, C_{quat}), 139.54 (s, C_{quat}), 139.49 (s, C_{quat}), 137.78 (s, C_{quat}), 127.93 (s, CH), 127.87 (s, CH), 127.58 (s, CH), 127.14 (s, CH), 125.20 (s, CH), 123.52 (s, C_{quat}), 122.08 (s, C_{quat}), 121.40 (s, CH), 120.92 (s, CH), 120.75 (s, C_{quat}), 118.80 (s, CH), 118.75 (s, CH), 118.56 (s, CH), 114.15 (s, CH), 111.15 (s, C_{quat}), 109.80 (s, CH), 108.50 (s, CH). One CH line is overlapped.

EI-HRMS: mass spectrometry: *m/z* calc. 412.0575 $[C_{24}H_{17}BrN_2]^{\bullet+}$, measured 412.0575.



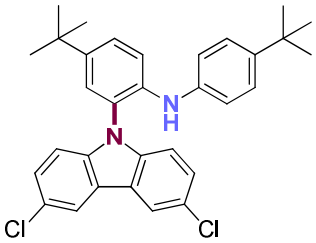
2-(3,6-dichloro-9*H*-carbazol-9-yl)-4-methyl-*N*-(*p*-tolyl)aniline
Chemical Formula: $C_{26}H_{20}Cl_2N_2$
Exact Mass: 430,10
Molecular Weight: 431,36
m/z: 430.10 (100.0%), 432.10 (64.1%), 431.10 (28.9%), 433.10 (18.2%), 434.09 (10.2%), 432.11 (3.9%), 435.10 (2.9%), 434.10 (2.6%)
Elemental Analysis: C, 72.39; H, 4.67; Cl, 16.44; N, 6.49

3h. From 3,6-dichloro-carbazole and 4,4'-ditolylamine. Product purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (4:1). 77% isolated yield (white solid).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.96 (d, *J* = 1.8 Hz, 2H), 7.30 (d, *J* = 2.0 Hz, 1H), 7.27 (d, *J* = 2.0 Hz, 1H), 7.25 (d, *J* = 8.3 Hz, 1H), 7.15-7.03 (m, 3H), 7.01-6.91 (m, 3H), 6.81-6.76 (m, 2H), 4.99 (broad s, NH), 2.25 (s, CH_3), 2.18 (s, CH_3).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$): δ (ppm): 139.67 (s, C_{quat}), 139.29 (s, C_{quat}), 138.97 (s, C_{quat}), 132.13 (s, C_{quat}), 130.47 (s, CH), 129.89 (s, C_{quat}), 129.87 (s, CH), 129.65 (s, CH), 126.96 (s, CH), 125.90 (s, C_{quat}), 123.64 (s, C_{quat}), 123.29 (s, C_{quat}), 120.36 (s, CH), 120.27 (s, CH), 116.33 (s, CH), 111.53 (s, CH), 20.73 (s, CH_3), 20.43 (s, CH_3).

ESI-HRMS: mass spectrometry: *m/z* calc. 453.0896 $[(C_{26}H_{20}Cl_2N_2)Na]^{+}$, measured 453.0901.



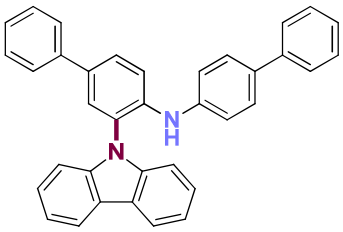
4-(*tert*-butyl)-*N*-(4-(*tert*-butyl)phenyl)-2-(3,6-dichloro-9*H*-carbazol-9-yl)aniline
Chemical Formula: $C_{32}H_{32}Cl_2N_2$
Exact Mass: 514,19
Molecular Weight: 515,52
m/z: 514.19 (100.0%), 516.19 (64.2%), 515.20 (35.0%), 517.19 (22.6%), 518.19 (10.4%), 516.20 (5.9%), 518.20 (3.8%), 519.19 (3.6%)
Elemental Analysis: C, 74.55; H, 6.26; Cl, 13.75; N, 5.43

3i. From 3,6-dichloro-carbazole and bis(4-tert-butylphenyl)amine. The crude is filtered on a SiO_2 plug in CH_2Cl_2, and evaporated. Product is purified by SiO_2 gel column chromatography pentane/toluene (8:2). 96% isolated yield (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.36 (d, *J* = 2.0 Hz, 2H), 7.47 – 7.35 (m, 4H), 7.27 (d, *J* = 2.0 Hz, 2H), 7.14 (d, ^3J = 8.7 Hz, 2H), 7.04 (d, ^3J = 8,7 Hz, 2H), 6.80 (d, ^3J = 8.6 Hz, 2H), 1.27 (s, CCH_3, 9H), 1.18 (s, CCH_3, 9H).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ 141.96 (s, C_{quat}), 141.33 (s, C_{quat}), 138.80 (s, C_{quat}), 138.09 (s, C_{quat}), 137.25 (s, C_{quat}), 125.09 (s, CH), 124.89 (s, CH), 124.24 (s, CH), 123.97 (s, CH), 122.78 (s, C_{quat}), 122.63 (s, C_{quat}), 122.21 (s, C_{quat}), 119.04 (s, CH), 116.87 (s, CH), 116.53 (s, CH), 110.54 (s, CH), 32.10 (s, C_{quat}, **C**CH_3), 31.82 (s, C_{quat}, **C**CH_3), 29.36 (s, C**C**H_3), 29.27 (s, C**C**H_3).

ESI-HRMS: mass spectrometry: *m/z* calc. 537.1835 $[(C_{32}H_{32}Cl_2N_2)Na]^+$, measured 537.1833.



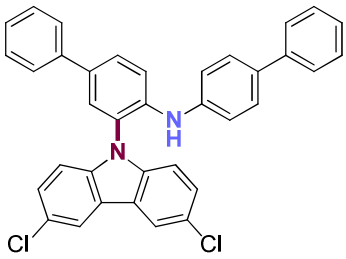
N-([1,1'-biphenyl]-4-yl)-3-(9*H*-carbazol-9-yl)-[1,1'-biphenyl]-4-amine
Chemical Formula: $C_{36}H_{26}N_2$
Exact Mass: 486,21
Molecular Weight: 486,61
m/z: 486.21 (100.0%), 487.21 (39.7%), 488.22 (7.5%)
Elemental Analysis: C, 88.86; H, 5.39; N, 5.76

3j. From carbazole and 4,4'diphenyl-diphenylamine.The reactor is then cooled to room temperature and the crude mixture is directly purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (7:3). 81% isolated yield (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.07 (broad d (possibly with second order), ^3J ~ 7.2 Hz, 2H), 7.56- 7.16 (aromatic area, ~ 21H), 6.98 (broad d (possibly with second order), ^3J ~ 8.6 Hz, 2H), 5.49 (broad s, NH).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 140.92 (s, C_{quat}), 140.67 (s, C_{quat}), 140.63 (s, C_{quat}), 140.37 (s, C_{quat}), 139.86 (s, C_{quat}), 135.36 (s, C_{quat}), 133.56 (s, C_{quat}), 128.94 (s, CH), 128.82 (s, CH), 128.19 (s, CH), 127.98 (s, CH), 127.83 (s, CH), 127.02 (s, CH), 126.91 (s, CH), 126.68 (s, CH), 126.46 (s, CH), 126.40 (s, CH), 125.03 (s, C_{quat}), 123.75 (s, C_{quat}), 120.55 (s, CH), 120.35 (s, CH), 120.32 (s, CH), 116.47 (s, CH), 110.29 (s, CH).

ESI-HRMS: mass spectrometry: *m/z* calc. 509.1988 $[(C_{36}H_{26}N_2)Na]^+$, measured 509.1980.



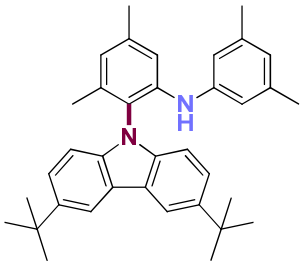
N-([1,1'-biphenyl]-4-yl)-3-(3,6-dichloro-9*H*-carbazol-9-yl)-[1,1'-biphenyl]-4-amine
Chemical Formula: $C_{36}H_{24}Cl_2N_2$
Exact Mass: 554,13
Molecular Weight: 555,50
m/z: 554.13 (100.0%), 556.13 (64.2%), 555.14 (39.2%), 557.13 (25.5%), 558.13 (10.4%), 556.14 (7.5%), 558.14 (4.8%), 559.13 (4.0%)
Elemental Analysis: C, 77.84; H, 4.35; Cl, 12.76; N, 5.04

3k. From 3,6-dichloro-carbazole and 4,4'diphenyl-diphenylamine. The crude is filtered on a SiO_2 plug in CH_2Cl_2, and evaporated. Product is purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (7:3). 82% isolated yield (yellow solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 8.41 (d, *J* = 2.1 Hz, 2H), 7.80 (m, 2H), 7.67 – 7.61 (m, 4H), 7.54 (d, ^3J = 7.3 Hz, 2H), 7.43 – 7.38 (m, 8H), 7.32 – 7.24 (m, 4H), 7.06 (d, ^3J = 8.6 Hz, 2H).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 140.46 (s, C_{quat}), 138.46 (s, C_{quat}), 138.34 (s, C_{quat}), 137.49 (s, C_{quat}), 137.33 (s, C_{quat}), 131.40 (s, C_{quat}), 130.83 (s, C_{quat}), 127.40 (s, CH), 127.29 (s, CH), 125.98 (s, CH), 125.51 (s, CH), 125.00 (s, CH), 124.94 (s, CH), 124.50 (s, CH), 124.32 (s, CH), 123.83 (s, C_{quat}), 122.75 (s, C_{quat}), 122.17 (s, C_{quat}), 118.88 (s, CH), 117.75 (s, CH), 116.92 (s, CH), 110.39 (s, CH). Two CH lines are overlapped.

ESI-HRMS: mass spectrometry: *m/z* calc. 577.1209 $[(C_{36}H_{24}Cl_2N_2)Na]^+$, measured 577.1197.



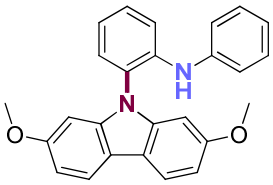
2-(3,6-di-*tert*-butyl-9*H*-carbazol-9-yl)-*N*-(3,5-dimethylphenyl)-3,5-dimethylaniline
Chemical Formula: $C_{36}H_{42}N_2$
Exact Mass: 502,33
Molecular Weight: 502,73
m/z: 502.33 (100.0%), 503.34 (39.4%), 504.34 (7.8%)
Elemental Analysis: C, 86.01; H, 8.42; N, 5.57

3l. From 3,6 di-*tert*-butylcarbazole and 1,3,5-dixylylamine.The reactor is then cooled to room temperature and the crude mixture is directly purified by SiO_2 gel column chromatography hexane/toluene (9:1). Difficult purification, two columns were necessary. 67% isolated yield (sticky colourless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.06 (d, *J* = 1.6 Hz, 2H), 7.31 (dd, ^3J = 8.5 Hz, *J* = 1.9 Hz, 2H), 7.02 (s, 1H), 6.90 (d, ^3J = 8.5 Hz, 2H), 6.56 (s, 1H), 6.49 (s, 2H), 6.45 (s, 1H), 5.16 (s, NH), 2.25 (s, 3H, CH_3), 2.08 (s, 6H, CH_3), 1.61 (s, 3H, CH_3), 1.35 (s, 18H, ^{t}Bu).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 142.72 (s, C_{quat}), 142.52 (s, C_{quat}), 141.81 (s, C_{quat}), 138.97 (s, C_{quat}), 138.85 (s, C_{quat}), 138.72 (s, C_{quat}), 124.15 (s, CH), 123.95 (s, CH), 123.31 (s, C_{quat}), 122.31 (s, CH), 120.55 (s, C_{quat}), 118.58 (s, CH), 116.39 (s, CH), 113.37 (s, CH), 109.34 (s, CH), 34.84 (s, C_{quat}), 32.19 (s, CH3, ^{t}Bu), 21.83 (s, CH_3), 21.39 (s, CH_3), 17.69 (s, CH_3). One C_{quat} line is overlapped.

EI-HRMS: mass spectrometry: *m/z* calc. 502.3348 $[C_{36}H_{42}N_2]^{\bullet+}$, measured 502.3343.



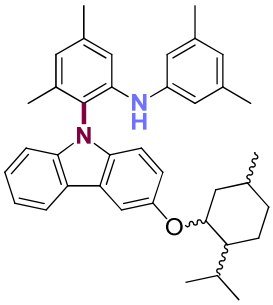
2-(2,7-dimethoxy-9*H*-carbazol-9-yl)-*N*-phenylaniline
Chemical Formula: $C_{26}H_{22}N_2O_2$
Exact Mass: 394,17
Molecular Weight: 394,47
m/z: 394.17 (100.0%), 395.17 (29.2%), 396.17 (4.4%)
Elemental Analysis: C, 79.16; H, 5.62; N, 7.10; O, 8.11

3m. From 2,7-dimethoxy-carbazole and diphenylamine. The reactor is then cooled to room temperature and the crude mixture is directly purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (1:1). Difficult purification, two columns were necessary. 51% isolated yield (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.81 (d, ^3J = 8.6 Hz, 2H), 7.46 (dd, ^3J = 8.3 Hz, J = 1.3 Hz, 1H), 7.31 (m, ^3J = 7.3 Hz and also J = 1.5 Hz, 1H), 7.26 (dd, ^3J = 7.9 Hz, J = 1.5 Hz, 1H), 7.14 (second ordered m, 2H), 6.98- 6.94 (aromatic area, 3H), 6.87 (broad dd, or t, $^3J \sim {}^3J$ = 7.4 Hz, 1H), 6.79 (dd, ^3J = 8.5 Hz, J = 2.4 Hz, 2H), 6.56 (d, J = 2.4 Hz, 2H), 5.39 (s, NH), 3.66 (s, 6H, CH_3).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 158.49 (s, C_{quat}), 142.14 (s, C_{quat}), 141.69 (s, C_{quat}), 141.11 (s, C_{quat}), 129.65 (s, CH), 129.36 (s, CH), 129.28 (s, CH), 124.65 (s, C_{quat}), 122.39 (s, CH), 120.61 (s, CH), 120.21 (s, CH), 119.74 (s, CH), 117.49 (s, C_{quat}), 116.62 (s, CH), 108.86 (s, CH), 94.38 (s, CH), 55.66 (s, CH_3).

EI-HRMS: mass spectrometry: *m/z* calc. 394.1681 $[C_{26}H_{22}N_2O_2]^{\bullet+}$, measured 394.1678.



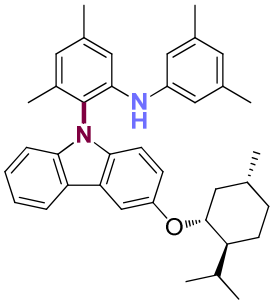
N-(3,5-dimethylphenyl)-2-(3-((2-isopropyl-5-methylcyclohexyl)oxy)-9*H*-carbazol-9-yl)-3,5-dimethylaniline
Chemical Formula: $C_{38}H_{44}N_2O$
Exact Mass: 544,35
Molecular Weight: 544,77
m/z: 544.35 (100.0%), 545.35 (41.6%), 546.35 (9.0%), 547.36 (1.1%)
Elemental Analysis: C, 83.78; H, 8.14; N, 5.14; O, 2.94

3n. From racemic 3-menthoxy-carbazole and 1,3,5-dixylylamine. The reactor is then cooled to room temperature, the crude filtered over SiO_2 plug in ethyl acetate, evaporated, and the residue purified by SiO_2 gel column chromatography in hexane/ethyl acetate (95:5). Difficult purification, two columns were necessary. 72% isolated yield (white solid) 1:1 diastereomeric mixture.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.03 (broad d, ^3J = 7.7 Hz, 1H, both dias), 7.57 (broad s, 1H, both dias), 7.29 (~dd, ^3J ~ ^3J ~ 7.6 Hz, 1H, both dias), 7.19-6.91 (aromatic area), 6.62-6.42 (aromatic area, 5H, both dias), 5.24 (broad s, NH of one dia), 5.16 (broad s, NH of the other dia), 4.01 (ddd, $^3J_{trans}$ ~ $^3J_{trans}$ ~ 10.3 Hz, $^3J_{cis}$ = 3.8 Hz, 1H, both dias), 2.33-0.78 (aliphatic area), in which: 2.28 (s, 3H, CH_3, both dias), 2.13 (s, 6H, CH_3, both dias), 1.65 (s, 1*CH_3 of one dia), 1.64 (s, 1*CH_3 of other dia), 0.90 (d, ^3J = 6.9 Hz, 3H, CH_3, both dias), 0.85 (d, ^3J = 6.5 Hz, 3H, CH_3, both dias), 0.80 (d, ^3J = 6.9 Hz, 1*CH_3 of one dia), 0.79 (d, ^3J = 6.9 Hz, 1*CH_3 of other dia).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 152.74 (s, C_{quat}), 142.40 (s, C_{quat}), 142.38 (s, C_{quat}), 141.61 (s, C_{quat}), 141.60 (s, C_{quat}), 140.95 (s, C_{quat}), 139.08 (s, C_{quat}), 138.84 (s, C_{quat}), 138.64 (s, C_{quat}), 138.62 (s, C_{quat}), 135.45 (s, C_{quat}), 126.13 (s, CH), 124.14 (s, CH), 123.81 (s, C_{quat}), 123.79 (s, C_{quat}), 123.21 (s, C_{quat}), 123.20 (s, C_{quat}), 122.29 (s, CH), 122.27 (s, CH), 120.40 (s, CH), 120.16 (s, C_{quat}), 119.42 (s, CH), 118.45 (s, CH), 117.44 (s, CH), 117.39 (s, CH), 113.29 (s, CH), 110.47 (s, CH), 110.43 (s, CH), 109.89 (s, CH), 107.07 (s, CH), 107.06 (s, CH), 79.21 (s, CH-O, one dia), 79.18 (s, CH-O, other dia), 48.34 (s, CH or CH_3), 40.58 (s, CH_2), 34.64 (s, CH_2), 31.51 (s, CH or CH_3), 26.01 (s, CH or CH_3), 23.63 (s, CH_2), 22.25 (s, CH or CH_3), 21.74 (s, CH or CH_3), 21.31 (s, CH or CH_3), 20.99 (s, CH or CH_3), 20.98 (s, CH or CH_3), 17.52 (s, CH or CH_3), 17.51 (s, CH or CH_3), 16.60 (s, CH or CH_3). One C_{quat} line could be overlapped.

ESI-HRMS: mass spectrometry: *m/z* calc. 567.3346 $[(C_{38}H_{44}N_2O)Na]^+$, measured 567.3340, *m/z* calc. 545.3527 $[(C_{38}H_{44}N_2O)H]^+$, measured 545.3517.



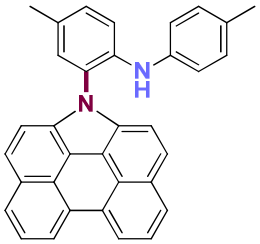
N-(3,5-dimethylphenyl)-2-(3-(((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)oxy)-9*H*-carbazol-9-yl)-3,5-dimethylaniline
Chemical Formula: $C_{38}H_{44}N_2O$
Exact Mass: 544,35
Molecular Weight: 544,77
m/z: 544.35 (100.0%), 545.35 (41.6%), 546.35 (9.0%), 547.36 (1.1%)
Elemental Analysis: C, 83.78; H, 8.14; N, 5.14; O, 2.94

3o. From natural (enantiopure) 3-menthoxy-carbazole and 1,3,5-dixylylamine. The reactor is then cooled to room temperature, the crude filtered over SiO_2 plug in ethyl acetate, evaporated, and the residue purified by SiO_2 gel column chromatography in hexane/ethyl acetate (95:5). Difficult purification, two columns were necessary. 63% Isolated yield (white solid), in the form a 1:1 diastereomeric mixture.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.03 (broad d, ^{3}J = 7.7 Hz, 1H, both dias), 7.57 (broad s, 1H, both dias), 7.29 (~dd, $^{3}J \sim {}^{3}J \sim$ 7.6 Hz, 1H, both dias), 7.19-6.91 (aromatic area), 6.62-6.42 (aromatic area, 5H, both dias), 5.24 (broad s, NH of one dia), 5.16 (broad s, NH of the other dia), 4.01 (ddd, $^{3}J_{trans} \sim {}^{3}J_{trans} \sim$ 10.3 Hz, $^{3}J_{cis}$ = 3.8 Hz, 1H, both dias), 2.33-0.78 (aliphatic area), in which: 2.28 (s, 3H, CH_3, both dias), 2.13 (s, 6H, CH_3, both dias), 1.65 (s, 1*CH_3 of one dia), 1.64 (s, 1*CH_3 of other dia), 0.90 (d, ^{3}J = 6.9 Hz, 3H, CH_3, both dias), 0.85 (d, ^{3}J = 6.5 Hz, 3H, CH_3, both dias), 0.80 (d, ^{3}J = 6.9 Hz, 1*CH_3 of one dia), 0.79 (d, ^{3}J = 6.9 Hz, 1*CH_3 of other dia).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 152.74 (s, C_{quat}), 142.40 (s, C_{quat}), 142.38 (s, C_{quat}), 141.61 (s, C_{quat}), 141.60 (s, C_{quat}), 140.95 (s, C_{quat}), 139.08 (s, C_{quat}), 138.84 (s, C_{quat}), 138.64 (s, C_{quat}), 138.62 (s, C_{quat}), 135.45 (s, C_{quat}), 126.13 (s, CH), 124.14 (s, CH), 123.81 (s, C_{quat}), 123.79 (s, C_{quat}), 123.21 (s, C_{quat}), 123.20 (s, C_{quat}), 122.29 (s, CH), 122.27 (s, CH), 120.40 (s, CH), 120.16 (s, C_{quat}), 119.42 (s, CH), 118.45 (s, CH), 117.44 (s, CH), 117.39 (s, CH), 113.29 (s, CH), 110.47 (s, CH), 110.43 (s, CH), 109.89 (s, CH), 107.07 (s, CH), 107.06 (s, CH), 79.21 (s, CH-O, one dia), 79.18 (s, CH-O, other dia), 48.34 (s, CH or CH_3), 40.58 (s, CH_2), 34.64 (s, CH_2), 31.51 (s, CH or CH_3), 26.01 (s, CH or CH_3), 23.63 (s, CH_2), 22.25 (s, CH or CH_3), 21.74 (s, CH or CH_3), 21.31 (s, CH or CH_3), 20.99 (s, CH or CH_3), 20.98 (s, CH or CH_3), 17.52 (s, CH or CH_3), 17.51 (s, CH or CH_3), 16.60 (s, CH or CH_3). One C_{quat} line could be overlapped.

ESI-HRMS: mass spectrometry: *m/z* calc. 567.3346 $[(C_{38}H_{44}N_2O)Na]^+$, measured 567.3340, *m/z* calc. 545.3527 $[(C_{38}H_{44}N_2O)H]^+$, measured 545.3517.



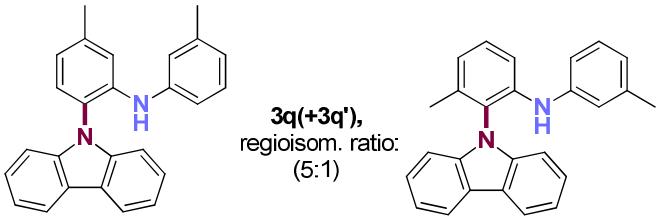
4-methyl-2-(1*H*-phenanthro[1,10,9,8-*cdefg*]carbazol-1-yl)-*N*-(*p*-tolyl)aniline
Chemical Formula: $C_{34}H_{24}N_2$
Exact Mass: 460,19
Molecular Weight: 460,57
m/z: 460.19 (100.0%), 461.20 (37.0%), 462.20 (6.7%)
Elemental Analysis: C, 88.67; H, 5.25; N, 6.08

3p. From perycarbazole and 4,4'-ditolylamine. Product purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (3:2) and in a second time in hexane/CH_2Cl_2 (2:1). 32% isolated yield (bright orange solid). (NMR yield: 50%, but product very difficult to purify).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.55 (d, *J* = 7.5 Hz, 2H), 8.02 (d, *J* = 8.0 Hz, 2H) 7.80-7.60 (m, 6H), 7.36 (d, *J* = 8.3 Hz, 1H), 7.28 (m, 1H), 7.15-7.12 (m, 1H), 6.93 (d, *J* = 8.3 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 5.34 (broad s, NH), 2.31 (s, CH_3), 2.17 (s, CH_3).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$): δ (ppm): 139.42 (s, C_{quat}), 137.97 (s, C_{quat}), 132.39 (s, C_{quat}), 131.54 (s, C_{quat}), 130.58 (s, C_{quat}), 129.86 (s, CH), 129.76 (s, C_{quat}), 129.43 (s, CH), 129.35 (s, C_{quat}), 129.09 (s, CH), 126.26 (s, C_{quat}), 125.27 (s, CH), 125.11 (s, CH), 124.88 (s, C_{quat}), 124.29 (s, CH), 120.96 (s, CH), 119.74 (s, CH), 118.48 (s, C_{quat}), 116.61 (s, CH), 114.43 (s, CH), 20.72 (s, CH_3), 20.58 (s, CH).

ESI-HRMS: mass spectrometry: *m/z* calc. 483.1832 $[(C_{34}H_{24}N_2)Na]^+$, measured 483.1829.



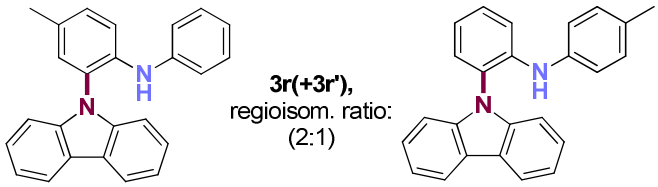
Chemical Formula: $C_{26}H_{22}N_2$
Exact Mass: 362,18
Molecular Weight: 362,47
m/z: 362.18 (100.0%), 363.18 (29.1%), 364.19 (3.9%)
Elemental Analysis: C, 86.15; H, 6.12; N, 7.73

3q (**3q'**). From carbazole and 3,3'-ditolylamine. Product purified by SiO_2 gel column chromatography hexane/toluene (4:1). 44% isolated yield (white solid).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.09 (dm, ^3J = 7.8 Hz, 2H minor), 8.07 (dm, ^3J = 7.8 Hz, 2H major), 7.35- 6.98 (aromatic area, ~ 14H), 5.26 (s, NH major), 5.22 (s, NH minor), 2.33 (s, CH_3 major), 2.17 (s, CH_3 major), 2.15 (s, CH_3 minor), 1.69 (s, CH_3 minor).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$): δ (ppm): 141.55 (s, C_{quat}), 141.43 (s, C_{quat}), 141.30 (s, C_{quat}), 141.03 (s, C_{quat}), 140.22 (s, C_{quat}), 139.44 (s, C_{quat}), 139.21 (s, C_{quat}), 139.11 (s, C_{quat}), 139.07 (s, C_{quat}), 129.50 (s, CH), 129.28 (s, CH), 129.05 (s, CH), 128.99 (s, CH), 126.30 (s, CH), 126.15 (s, CH), 123.52 (s, C_{quat}), 123.28 (s, CH), 121.74 (s, C_{quat}), 121.51 (s, CH), 121.35 (s, CH), 121.21 (s, CH), 121.03 (s, CH), 120.51 (s, CH), 120.36 (s, CH), 120.05 (s, CH), 120.05 (s, CH), 119.99 (s, CH), 117.59 (s, CH), 117.39 (s, CH), 116.24 (s, CH), 112.90 (s, CH), 110.18 (s, CH), 109.82 (s, CH), 21.77 (s, CH3), 21.42 (s, CH3), 21.39 (s, CH3), 17.61 (s, CH3).

EI-HRMS: mass spectrometry: *m/z* calc. 362.1783 $[C_{26}H_{22}N_2]^{\bullet+}$, measured 362.1786.



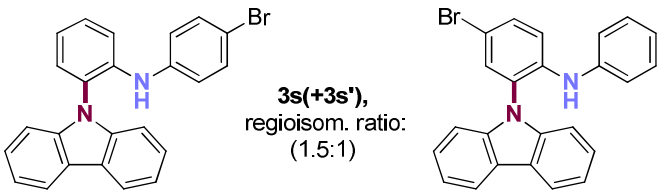
Chemical Formula: $C_{25}H_{20}N_2$
Exact Mass: 348,16
Molecular Weight: 348,44
m/z: 348.16 (100.0%), 349.17 (27.3%), 350.17 (3.6%)
Elemental Analysis: C, 86.17; H, 5.79; N, 8.04

3r (3r'). From carbazole and 4-methyl-diphenylamine. The reactor is then cooled to room temperature and the crude mixture is directly purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (7:3). Difficult purification, two columns were necessary. 56% isolated yield (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.06 (broad d, ^3J = 7.7 Hz, 2H of minor), 8.05 (broad d, ^3J = 7.6 Hz, 2H of major), 7.35 (d, ^3J = 8.3 Hz, 2H of minor or 1H of major), 7.33-7.03 (aromatic area), 6.93 (broad d, ^3J = 8.1 Hz, 2H of minor or 1H of major), 6.88-6.77 (aromatic area), 5.26 (s, NH of minor), 5.25 (s, NH of major), 2.23 (s, CH_3 of major), 2.16 (s, CH_3 of minor).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 142.28 (s, C_{quat}), 142.15 (s, C_{quat}), 140.98 (s, C_{quat}), 140.92 (s, C_{quat}), 138.72 (s, C_{quat}), 138.68 (s, C_{quat}), 132.53 (s, C_{quat}), 130.35 (s, C_{quat}), 130.07 (s, CH), 129.97 (s, CH), 129.88 (s, CH), 129.79 (s, CH), 129.41 (s, CH), 129.28 (s, CH), 126.24 (s, CH), 126.22 (s, CH), 124.86 (s, C_{quat}), 123.81 (s, C_{quat}), 123.62 (s, C_{quat}), 123.61 (s, C_{quat}), 121.84 (s, CH), 121.35 (s, CH), 120.43 (s, CH), 120.14 (s, CH), 120.10 (s, CH), 119.65 (s, CH), 119.35 (s, CH), 116.75 (s, CH), 115.16 (s, CH), 110.26 (s, CH), 110.23 (s, CH), 20.82 (s, CH_3 of minor), 20.54 (s, CH_3 of major). One CH line is overlapped.

ESI-HRMS: mass spectrometry: *m/z* calc. 371.1519 $[(C_{25}H_{20}N_2)Na]^+$, measured 371.1517.



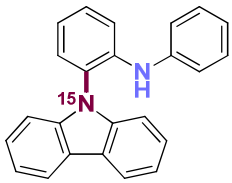
Chemical Formula: $C_{24}H_{17}BrN_2$
Exact Mass: 412,06
Molecular Weight: 413,31
m/z: 414.06 (100.0%), 412.06 (99.3%), 413.06 (26.0%), 415.06 (25.3%), 416.06 (3.3%)
Elemental Analysis: C, 69.74; H, 4.15; Br, 19.33; N, 6.78

3s (3s'). From carbazole and 4-bromo-diphenylamine. The crude is filtered on a SiO_2 plug in CH_2Cl_2, and evaporated. Product is purified by SiO_2 gel column chromatography pentane/toluene (8:3). 56% Isolated yield (white solid).

^{1}H NMR (600 MHz, DMSO-d_6) δ (ppm): 8.20 (d, *J* = 5.0 Hz, 2H), 8.18 (d, *J* = 5.1 Hz, 2H), 7.65 (broad s, NH, major), 7.59 (broad s, NH, minor), 7.56 (dd, ^3J = 8.9 Hz, *J* = 2.4 Hz, 1H, minor), 7.52 (d, ^3J = 8.2 Hz, 1H, major), 7.46 - 7.42 (m, 2H), 7.40 – 7.31 (m, 4H), 7.27 – 7.17 (m, 7H), 7.15 – 7.12(m, 4H), 7.02 (d, ^3J = 8.1 Hz, 2H, minor), 6.90 (d, ^3J = 8.7 Hz, 2H, major), 6.82 (t, ^3J = 7.3 Hz, 1H, minor).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 139.31 (s, C_{quat}), 139.14 (s, C_{quat}), 139.11 (s, C_{quat}), 139.07 (s, C_{quat}), 139.02 (s, C_{quat}), 138.88 (s, C_{quat}), 130.69 (s, CH), 130.52 (s, CH), 130.47 (s, CH), 128.20 (s, CH), 127.68 (s, CH), 127.65 (s, CH), 124.64 (s, CH), 124.49 (s, CH), 123.63 (s, C_{quat}), 123.14 (s, C_{quat}), 121.96 (s, C_{quat}), 121.83 (s, C_{quat}), 121.39 (s, CH), 119.61 (s, CH), 119.20 (s, CH), 119.01 (s, CH), 118.72 (s, CH), 118.65 (s, CH), 118.44 (s, CH), 114.98 (s, CH), 114.47 (s, CH), 112.62 (s, C_{quat}), 108.91 (s, C_{quat}), 108.20 (s, CH), 108.18 (s, CH).

EI-HRMS: mass spectrometry: *m/z* calc. 412.0575 $[C_{24}H_{17}BrN_2]^{\bullet+}$, measured 412.0570.



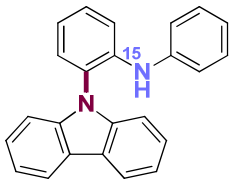
Chemical Formula: $C_{24}H_{18}N^{15}N$
Exact Mass: 335,14
Molecular Weight: 335,41
m/z: 335.14 (100.0%), 336.15 (26.2%), 337.15 (3.3%)
Elemental Analysis: C, 85.94; H, 5.41; N, 8.65

3t. From carbazole-^{15}N (^{15}N-98%+) and diphenylamine. The reactor is then cooled to room temperature and the crude mixture is directly purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (7:3). 64% isolated yield (white solid).

^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 8.05 (d, ^3J = 7.6 Hz, 2H), 7.41 (broad d, ^3J = 8.2 Hz, 1H), 7.34- 6.80 (aromatic area, 14H), 5.32 (broad s, NH).

^{13}C {^{1}H} NMR (50 MHz, $CDCl_3$) δ (ppm): 141.60 (d, J_{CN} = 1.5 Hz, C_{quat}), 141.48 (s, C_{quat}), 140.92 (d, $^1J_{CN}$ = 15.4 Hz, C_{quat}), 129.87 (d, J_{CN} = 2.2 Hz, CH), 129.38 (s, CH), 129.32 (s, CH), 126.26 (d, J_{CN} = 1.5 Hz, CH), 124.45 (d, $^1J_{CN}$ = 16.1 Hz, C_{quat}), 123.66 (d, J_{CN} = 3.7 Hz, C_{quat}), 122.57 (s, CH), 120.45 (d, J_{CN} = 1.5 Hz, CH), 120.39 (s, CH), 120.31 (d, J_{CN} = 2.2 Hz, CH), 120.18 (s, CH), 115.86 (d, J_{CN} = 1.5 Hz, CH), 110.20 (d, J_{CN} = 2.2 Hz, CH).

EI-HRMS: mass spectrometry: *m/z* calc. 335.1440 $[C_{26}H_{22}N_{15}N]^{\bullet+}$, measured 335.1439.



Chemical Formula: $C_{24}H_{18}N^{15}N$
Exact Mass: 335,14
Molecular Weight: 335,41
m/z: 335.14 (100.0%), 336.15 (26.2%), 337.15 (3.3%)
Elemental Analysis: C, 85.94; H, 5.41; N, 8.65

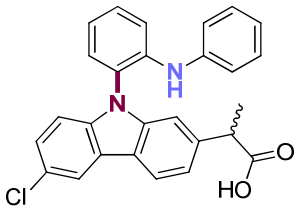
3u. From carbazole and diphenylamine-^{15}N (^{15}N-98%+). The reactor is then cooled to room temperature and the crude mixture is directly purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (7:3). 64% isolated yield (white solid).

^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm): 8.07 (d, ^3J = 7.6 Hz, 2H), 7.43 (broad d, ^3J = 8.2 Hz, 1H), 7.36- 6.82 (aromatic area, 14H), 5.05 (very broad s, NH).

^{13}C {^{1}H} NMR (50 MHz, $CDCl_3$) δ (ppm): 141.57 (d, $^1J_{CN}$ = 16.1 Hz, C_{quat}), 141.46 (d, $^1J_{CN}$ = 15.4 Hz, C_{quat}), 140.92 (s, C_{quat}), 129.86 (s, CH), 129.39 (d, J_{CN} = 1.5 Hz, CH), 129.32 (d, J_{CN} = 2.2 Hz, CH), 126.25 (s, CH), 124.43 (d, J_{CN} = 1.5 Hz, C_{quat}), 123.65 (s, C_{quat}), 122.56 (s, CH), 120.45 (s, CH), 120.40 (s, CH), 120.32 (d, J_{CN} = 2.9 Hz, CH), 120.18 (s, CH), 115.84 (d, J_{CN} = 1.8 Hz, CH), 110.21 (s, CH).

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.22 (d, ^3J = 7.6 Hz, 2H), 7.58 (broad d, ^3J = 8.3 Hz, 1H), 7.48- 7.26 (aromatic area, 10H), 7.08-7.05 (aromatic area, 3H), 7.01 (~t, ^3J = 7.6 Hz, 1H), 5.51 (d, $^1J_{HN}$ = 89.1 Hz, NH).

EI-HRMS: mass spectrometry: *m/z* calc. 335.1440 $[C_{26}H_{22}N^{15}N]^{\bullet+}$, measured 335.1436.



2-(6-chloro-9-(2-(phenylamino)phenyl)-9*H*-carbazol-2-yl)propanoic acid
Chemical Formula: $C_{27}H_{21}ClN_2O_2$
Exact Mass: 440,13
Molecular Weight: 440,92
m/z: 440.13 (100.0%), 442.13 (32.6%), 441.13 (30.0%), 443.13 (9.5%), 442.14 (4.2%), 444.13 (1.5%)
Elemental Analysis: C, 73.55; H, 4.80; Cl, 8.04; N, 6.35; O, 7.26

3v. From racemic carprofen and diphenylamine. The reactor is then cooled to room temperature and the crude mixture is directly purified by SiO_2 gel column chromatography hexane/ethyl acetate (1:1). Difficult purification, two columns were necessary. 13% Isolated yield (sticky lightly golden solid).

Note: The ^{1}H NMR profile is better defined on the *Bruker 600*. ^{13}C experiments were measured on both *Bruker 600* and *400*. The high temperature experiments were carried out on the *Bruker 600*.

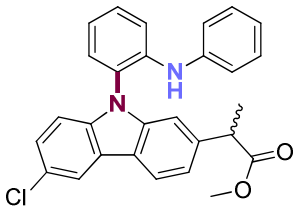
^{1}H NMR (600 MHz, DMSO-d_6, 298 K): δ (ppm): 8.26 (d, *J* = 2.1 Hz, 1H of one dia), 8.25 (d, *J* = 2.1 Hz, 1H of other dia), 8.17 (d, ^{3}J = 7.9 Hz, 1H of one dia), 8.16 (d, ^{3}J = 7.9 Hz, 1H of other dia), 7.47 (large second ordered m, lines: 7.5154, 7.5134, 7.5017, 7.4993, 7.4875, 7.4856, 7.4792, 7.4597, 7.4528, 7.4509, 7.4410, 7.4386, 7.4269, 7.4249, 3H of both dias), 7.36-7.32 (aromatic area, 2H of both dias), 7.19 (~dt, ^{3}J = 7.9 Hz, *J* ~ 1.8 Hz, 1H of both dias), 7.16-7.07 (aromatic area, 5H of both dias), 6.95 (second order m, lines: 6.9653, 6.9634, 6.9580, 6.9560, 6.9511, 6.9497, 6.9438, 6.9423, 2H of both dias), 6.76 (~t or ~dd*second ordered m, ^{3}J ~ ^{3}J ~ 7.4 Hz, 1H of both dias), 3.75 (q, ^{3}J = 7.1 Hz, 1H, benzylic position of one dia), 3.72 (q, ^{3}J = 7.1 Hz, 1H, benzylic position of other dia), 1.31 (d, ^{3}J = 7.1 Hz, CH_3 of one dia), 1.25 (d, ^{3}J = 7.1 Hz, CH_3 of other dia).

Note: at high temperature, for example 403 K, signals of the product shift slightly. Notably, the two diastereomeric NH signals become visible at 6.54 and 6.52 ppm, see spectra.

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6, 298 K): δ (ppm): 175.42 (s, C_{quat}t, COOH of one dia), 175.39 (s, C_{quat}, COOH of the other dia), 142.69 (s, C_{quat}), 142.67 (s, C_{quat}), 141.06 (s, C_{quat}), 140.92 (s, C_{quat}), 140.68 (s, C_{quat}), 140.57 (s, C_{quat}), 140.45 (s, C_{quat}), 140.36 (s, C_{quat}), 138.99 (s, C_{quat}), 138.82 (s, C_{quat}), 129.15 (s, CH), 129.12 (s, CH), 128.72 (s, CH), 125.46 (s, C_{quat}), 125.31 (s, CH), 125.28 (s, CH), 124.42 (s, C_{quat}), 124.39 (s, C_{quat}), 123.88 (s, C_{quat}), 121.09 (s, CH), 121.05 (s, CH), 121.02 (s, C_{quat}), 120.70 (s, CH), 120.60 (s, CH), 120.37 (s, CH), 120.33 (s, CH), 120.11 (s, CH), 119.70 (s, CH), 119.35 (s, CH), 119.14 (s, CH), 119.12 (s, CH), 117.94 (s, CH), 117.79 (s, CH), 111.56 (s, CH), 111.50 (s, CH), 109.32 (s, CH), 108.86 (s, CH), 45.36 (s, CH, benzylic position of one dia), 45.23 (s, CH, benzylic position of the other dia), 19.14 (s, CH_3 of one dia), 18.72 (s, CH_3 of the other dia).

3 C_{quat} lines and 4 CH lines are overlapped, thus 43 lines were found out of expected 50, which is pretty good for two such similar diastereomers.

ESI-HRMS: mass spectrometry: *m/z* calc. 463.1184 $[(C_{27}H_{21}ClN_2O_2)Na]^+$, measured 463.1177.



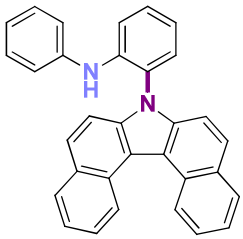
methyl 2-(6-chloro-9-(2-(phenylamino)phenyl)-9*H*-carbazol-2-yl)propanoate
Chemical Formula: $C_{28}H_{23}ClN_2O_2$
Exact Mass: 454,14
Molecular Weight: 454,95
m/z: 454.14 (100.0%), 456.14 (32.0%), 455.15 (30.6%), 457.15 (10.4%), 456.15 (5.2%), 458.15 (1.6%)
Elemental Analysis: C, 73.92; H, 5.10; Cl, 7.79; N, 6.16; O, 7.03

3w. From Carprofenmethylester (methyl 2-(6-chloro-9H-carbazol-2-yl)propanoate) and diphenylamine. The crude is filtered on a SiO_2 plug in CH_2Cl_2, and evaporated. Product is purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (3:7). 40% isolated yield (beige solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.09 (d, *J* = 1.9 Hz, 1H of one dia), 8.05 (d, ^{3}J = 8.1 Hz, 1H of other dia), 7.53 (d, ^{3}J = 8.3 Hz, 1H of one dia), 7.44 – 7.38 (m, 1H of one dia), 7.37 – 7.30 (m, 2H of both dias), 7.29 – 7.20 (m, 3H of both dias), 7.17 – 7.12 (m, 2H of both dias), 7.08 – 6.93 (m, 4H of both dias), 5.35 (s, NH of both dias), 3.81 (m, ^{3}J = 7.2 Hz, 1H, benzylic position of both dias), 3.60 (s, CH_3 of one dia), 3.57 (s, CH_3 of other dia), 1.50 (d, ^{3}J = 7.2 Hz, CH_3 of one dia), 1.48 (d, ^{3}J = 7.2 Hz, CH_3 of other dia).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm) 173.49 (s, C_{quat}, **C**OOMe of one dia), 173.44 (s, C_{quat}, **C**OOMe of other dia), 139.75 (s, C_{quat}), 139.68 (s, C_{quat}), 139.64 (s, C_{quat}), 139.63 (s, C_{quat}), 139.54 (s, C_{quat}), 139.51 (s, C_{quat}), 138.26 (s, C_{quat}), 138.09 (s, C_{quat}), 137.72 (s, C_{quat}), 137.70 (s, C_{quat}), 127.94 (s, CH), 127.92 (s, CH), 127.89 (s, CH), 127.69 (s, CH), 127.68 (s, CH), 124.54 (s, CH), 124.11 (s, C_{quat}), 122.83 (s, C_{quat}), 122.26 (s, C_{quat}), 120.95 (s, CH), 120.15 (s, C_{quat}), 120.12 (s, C_{quat}), 119.14 (s, CH), 119.10 (s, CH), 118.87 (s, CH), 118.51 (s, CH), 118.50 (s, CH),118.47 (s, CH), 118.45 (s, CH), 118.39 (s, CH), 114.61 (s, CH), 114.58 (s, CH), 109.35 (s, CH), 107.58 (s, CH), 107.44 (s, CH), 49.87 (s, COO**C**H_3 of one dia), 49.85 (s, COO**C**H_3 of other dia), 43.70 (s, CH, benzylic position of one dia), 43.58 (s, CH, benzylic position of other dia), 16.70 (s, CH3, of one dia), 16.22 (s, CH_3, of other dia).

ESI-HRMS: mass spectrometry: *m/z* calc. 477.1341 $[(C_{28}H_{23}ClN_2O_2)Na]^{+}$, measured 477.1322.

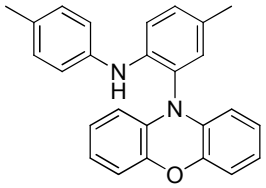


2-(7*H*-dibenzo[*c*,*g*]carbazol-7-yl)-*N*-phenylaniline
Chemical Formula: $C_{32}H_{22}N_2$
Exact Mass: 434,18
Molecular Weight: 434,53
m/z: 434.18 (100.0%), 435.18 (35.6%), 436.19 (5.9%)
Elemental Analysis: C, 88.45; H, 5.10; N, 6.45

3x. From 7H-dibenzo[c,g]carbazole and diphenylamine. The crude is filtered on a SiO_2 plug in CH_2Cl_2, and evaporated. Product is purified by SiO_2 gel column chromatography hexane/CH_2Cl_2 (13:7). 16% isolated yield (yellow solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.28 (d, 2H, *J* = 8.5 Hz), 8.05 (dt, 2H, *J* = 1.0 Hz, *J* = 8.1 Hz), 7.86 (d, 2H, *J* = 8.8 Hz), 7.75-7.71 (m, 2H), 7.57-7.53 (m, 3H), 7.49-7.46 (m, 3H), 7.39 (dd, 1H, *J* = 1.5 Hz, ^3J = 7.8 Hz), 7.21-7.17 (m, 2H), 7.08(dt, 1H, *J* = 1.4 Hz, ^3J = 7.6 Hz), 6.99-6.92 (m, 3H), 5.30 (very broad s, NH).

^{13}C {^{1}H} NMR (50 MHz, $CDCl_3$) δ (ppm): 141.96 (s, C_{quat}), 141.08 (s, C_{quat}), 137.80 (s, C_{quat}), 130.42 (s, CH), 130.34 (s, C_{quat}), 129.98 (s, CH), 129.28 (s, CH), 129.25 (s, CH), 129.13 (s, C_{quat}), 127.17 (s, CH), 125.62 (s, CH), 125.26 (s, CH), 123.59 (s, CH), 122.79 (s, CH), 120.62 (s, CH), 120.24 (s, CH), 118.02 (s, C_{quat}), 115.77 (s, CH), 111.81 (s, CH).

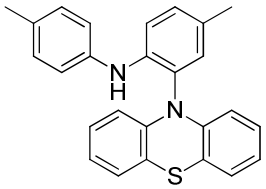


4-methyl-2-(10*H*-phenoxazin-10-yl)-*N*-(*p*-tolyl)aniline
Chemical Formula: $C_{26}H_{22}N_2O$
Exact Mass: 378,17
Molecular Weight: 378,47
m/z: 378.17 (100.0%), 379.18 (28.4%), 380.18 (4.1%)
Elemental Analysis: C, 82.51; H, 5.86; N, 7.40; O, 4.23

13. From phenoxazine and ditolylamine. The crude is filtered on a SiO_2 plug in CH_2Cl_2, and evaporated. Product is purified by SiO_2 gel column chromatography hexane/toluene (4:1). 11% isolated yield (white solid).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.19 (m, 1H), 7.04-6.90 (m, 6H), 6.64-6.57 (m, 6H), 6.00-5.98 (m, 2H), 5.79 (very broad, NH), 2.21 (s, 6H, CH_3).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$): δ (ppm):144.22 (s, C_{quat}), 141.07 (s, C_{quat}), 139.36 (s, C_{quat}), 133.12 (s, C_{quat}), 131.99 (s, C_{quat}), 131.11 (s, CH), 130.49 (s, C_{quat}), 130.10 (s, CH), 129.82 (s, CH), 125.20 (s, C_{quat}), 123.64 (s, CH), 121.72 (s, CH), 120.85 (s, CH), 115.53 (s, CH), 115.52 (s, CH), 113.49 (s, CH), 20.75 (s, CH_3), 20.44 (s, CH_3).



Chemical Formula: $C_{26}H_{22}N_2S$
Exact Mass: 394,15
Molecular Weight: 394,53
m/z: 394.15 (100.0%), 395.15 (29.7%), 396.15 (5.0%), 396.16 (3.9%), 397.15 (1.3%)
Elemental Analysis: C, 79.15; H, 5.62; N, 7.10; S, 8.13

14. From phenothiazine and ditolylamine. The crude is filtered on a SiO_2 plug in CH_2Cl_2, and evaporated. Product is purified by SiO_2 gel column chromatography hexane/toluene (4:1). 24% isolated yield (white solid).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 7.24 (d, *J* = 8.3 Hz, 1H), 7.09-6.72 (m, 12H), 6.32-6.31 (m, 2H), 5.95 (very broad s, NH), 2.26 (s, 3H, CH_3), 2.20 (s, 3H, CH_3).

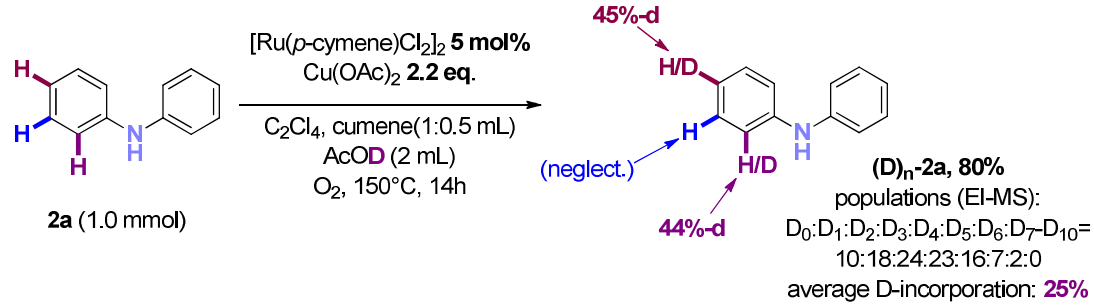
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$): δ (ppm):143.05 (s, C_{quat}), 139.34 (s, C_{quat}), 132.37 (s, C_{quat}), 131.87 (s, C_{quat}), 129.97 (s, CH), 129.77 (s, CH), 129.72 (s, C_{quat}), 127.53 (s, CH), 127.30 (s, CH), 126.78 (s, CH), 122.88 (s, C_{quat}), 122.85 (s, CH), 120.68 (s, CH), 116.31 (s, CH), 115.68 (s, CH), 115.63 (s, CH), 20.74 (s, CH_3), 20.54 (s, CH_3).

3.5.5. Isotopic experiments.

H/D scrambling experiment 1

In the first experiment, diphenylamine **2a** (1 mmol), [(*p*-cymene)$RuCl_2$]$_2$ (0.05 mmol), $Cu(OAc)_2$ (2.2 mmol), cumene (0.5 mL), C_2Cl_4 (1 mL), and AcO**D** (acetic acid-d_1, 2 mL) are united in a 170 mL reactor equipped with Teflon screw cap and flushed with **O_2**. The reactor is then sealed (*tightly*) and exposed to 150 °C for 14 h (magnetic stirring set to approx. 500 turns/min). The reactor is then cooled to room temperature. Acetylacetone (AcacH, 5 mL) is added to the reaction mixture and exposed to 150 °C for 1 h. Filtration over SiO_2 gel affords the crude mixture, which is purified by SiO_2 gel chromatography (height 380 mm, width 35 mm) in pentane/CH_2Cl_2 (7:3). 80% isolated yield (white solid).

EXPERIMENT 1: without carbazole



Scheme 21: H/D scrambling experiment 1.

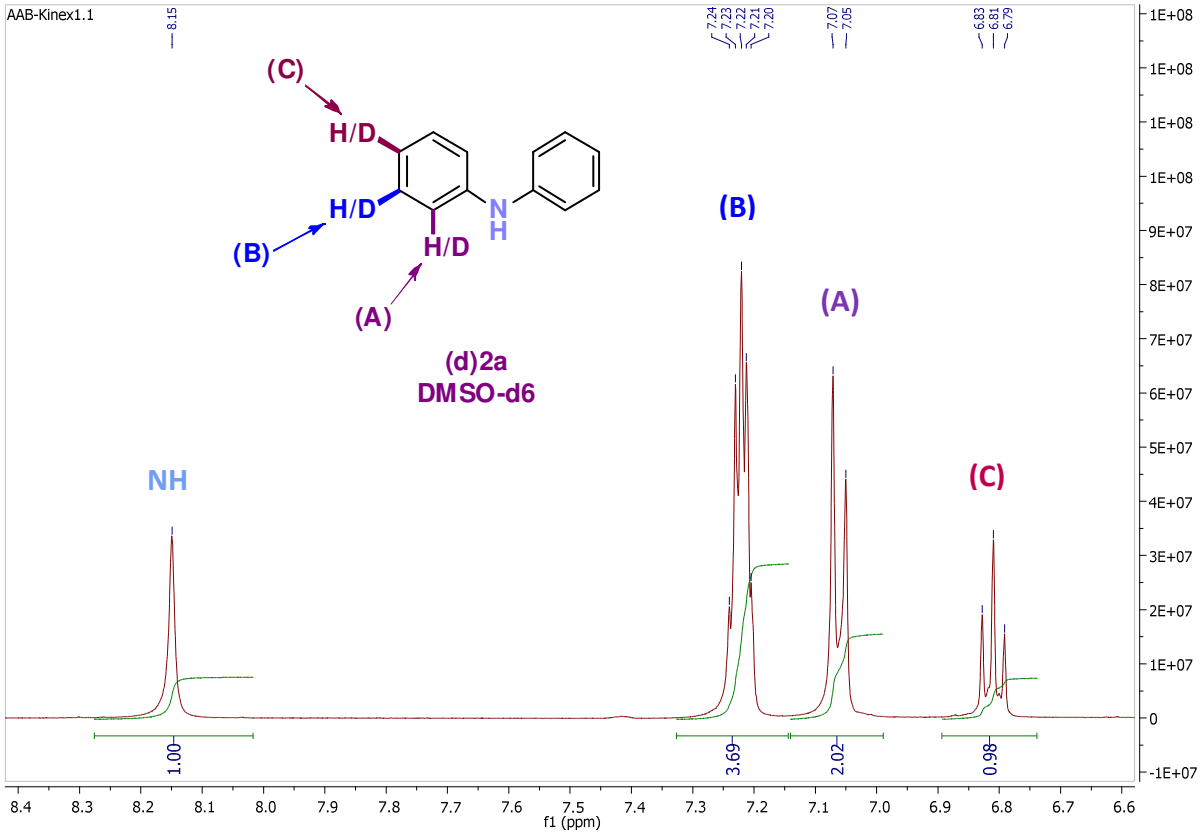


Figure 7: ^{1}H NMR profile of **(d)-2a.**

(d)-2a, GC-MS: R_t: 5.8 min; EI: 176 (1.8), 175 (10.5), 174 (35.4), 173 (72.9), 172 (100.0), 171(98.1), 170 (72.4), 169 (39.0).

Note: **2a (natural abundance)**, GC-MS: R_t: 5.8 min; EI: 170 (13.3), 169 (100.0).

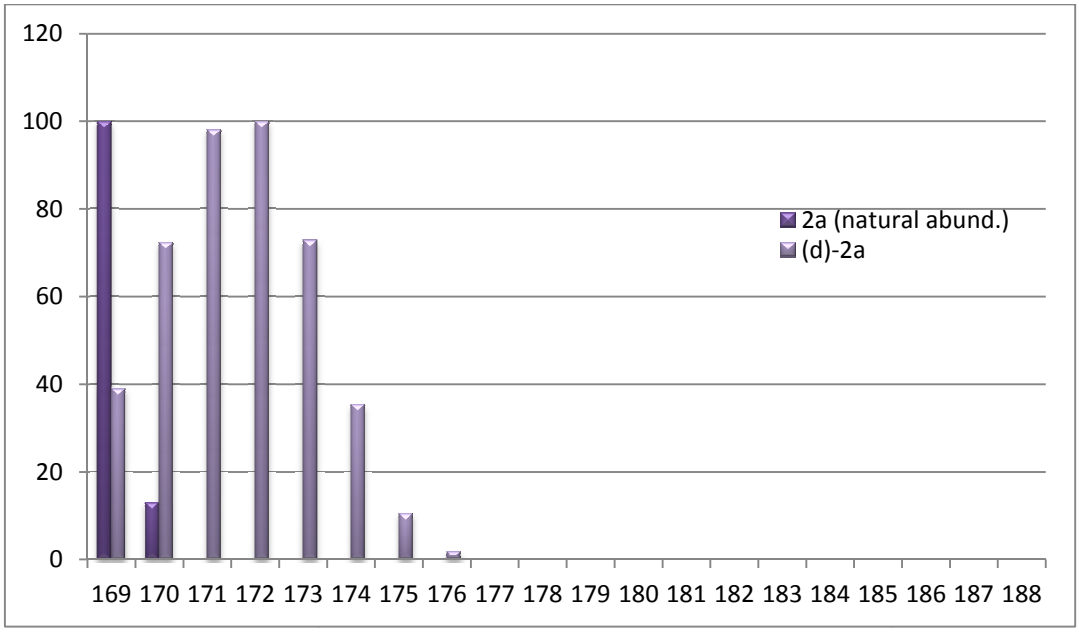


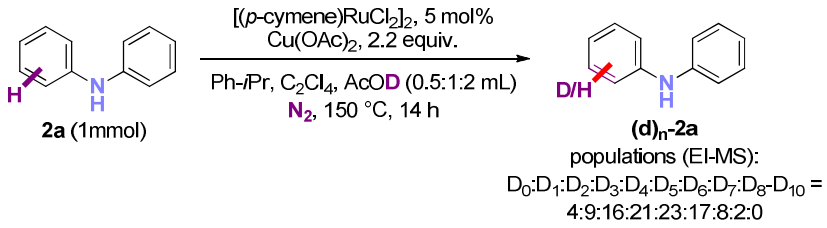
Figure 8: EI profile of (d)-2a.

Calculated values (% of total) for populations of **2a**, **(d1)-2a**, **(d2)-2a**, **(d3)-2a**, etc:

D0	10.2
D1	17.7
D2	23.5
D3	23.2
D4	16.1
D5	7.2
D6	1.8
D7	0.2
D8	0.0
D9	0.0
D10	0.0

H/D scrambling experiment under N_2

In a second experiment, diphenylamine **2a** (1 mmol), $[(p\text{-cymene})RuCl_2]_2$ (0.05 mmol), $Cu(OAc)_2$ (2.2 mmol), cumene (0.5 mL), C_2Cl_4 (1 mL), and AcO**D** (acetic acid-d_1, 2 mL) are united under **N_2** in a 170 mL reactor equipped with Teflon screw cap The reactor is then sealed (*tightly*) and exposed to 150 °C for 14 h (magnetic stirring set to approx. 500 turns/min). The reactor is then cooled to room temperature. Acetylacetone (5 mL) is added under **N_2** to the reaction mixture and exposed to 150 °C for 1 h. Filtration over SiO_2 gel affords the crude mixture, which is analyzed by GC-MS.



Scheme 22: H/ scrambling experiment under N_2.

(d)-2a, GC-MS: R_t: 5.8 min; EI: 177 (1.9) 176 (11.5), 175 (39.8), 174 (77.6), 173 (100.0), 172 (91.5), 171 (65.7), 170 (36.3), 169 (15.3).

Note: **2a (natural abundance)**, GC-MS: R_t: 5.8 min; EI: 170 (13.3), 169 (100.0).

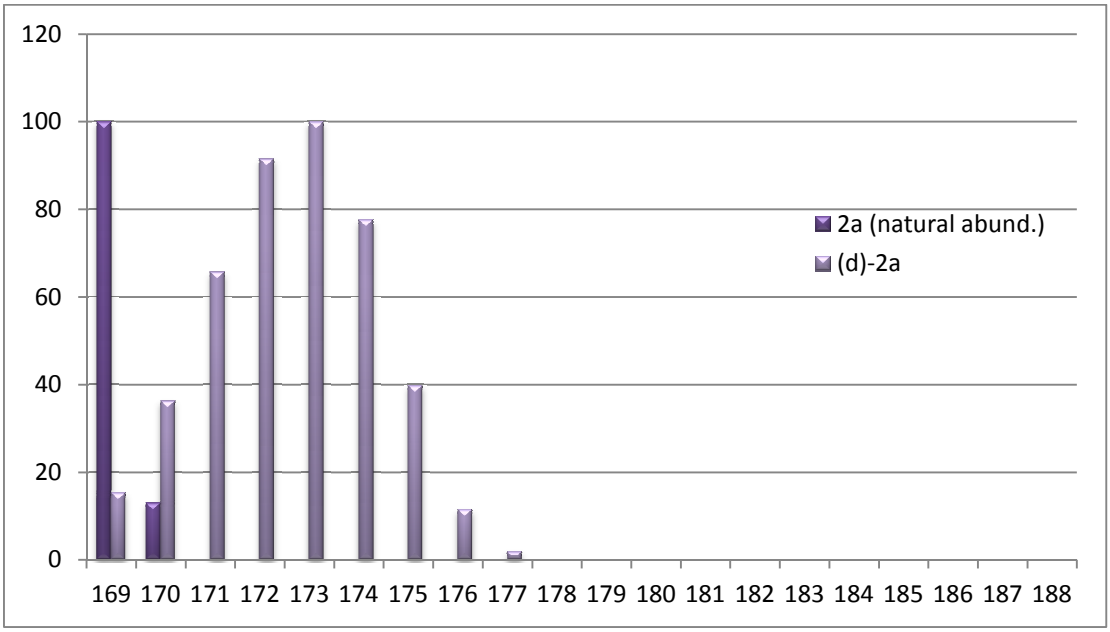


Figure 9: EI profile of (d)-2a after H/D scrambling experiment under N_2.

Calculated values (% of total) for populations of **2a**, **(d1)-2a**, **(d2)-2a**, **(d3)-2a**, etc:

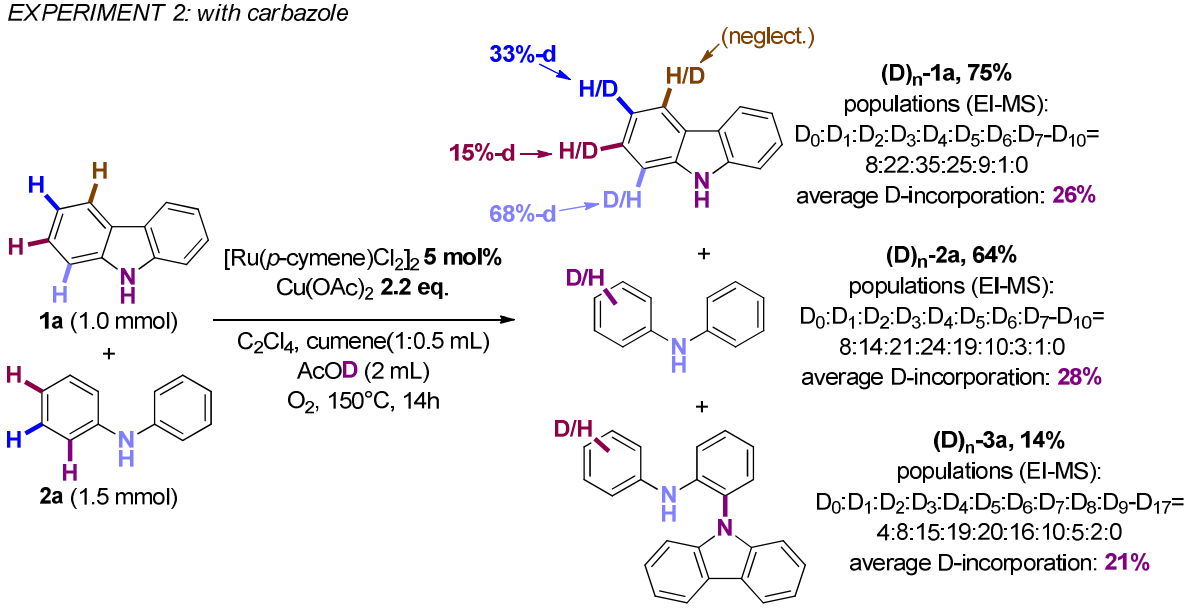
D0	3.9
D1	8.8
D2	15.7
D3	21.5
D4	22.9
D5	17.0
D6	8.0
D7	1.9
D8	0.2
D9	0.0
D10	0.0

H/D scrambling experiment 2.

In a third experiment, diphenylamine **2a** (1 mmol), carbazole **1a** (0.5 mmol) [(*p*-cymene)$RuCl_2$]$_2$ (0.05 mmol), $Cu(OAc)_2$ (2.2 mmol), cumene (0.5 mL), C_2Cl_4 (1 mL), and AcO**D** (acetic acid-d_1, 2 mL) are united in a 170 mL reactor equipped with Teflon screw cap and flushed with **O_2**.

The reactor is then sealed (*tightly*) and exposed to 150 °C for 24 h (magnetic stirring set to approx. 500 turns/min). The reactor is then cooled to room temperature. Acetylacetone (5 mL) is added to the reaction mixture and exposed to 150 °C for 1 h. Filtration over SiO_2 gel affords the crude mixture, which is analyzed by GC-MS.

EXPERIMENT 2: with carbazole



Scheme 22: H/ scrambling experiment 2.

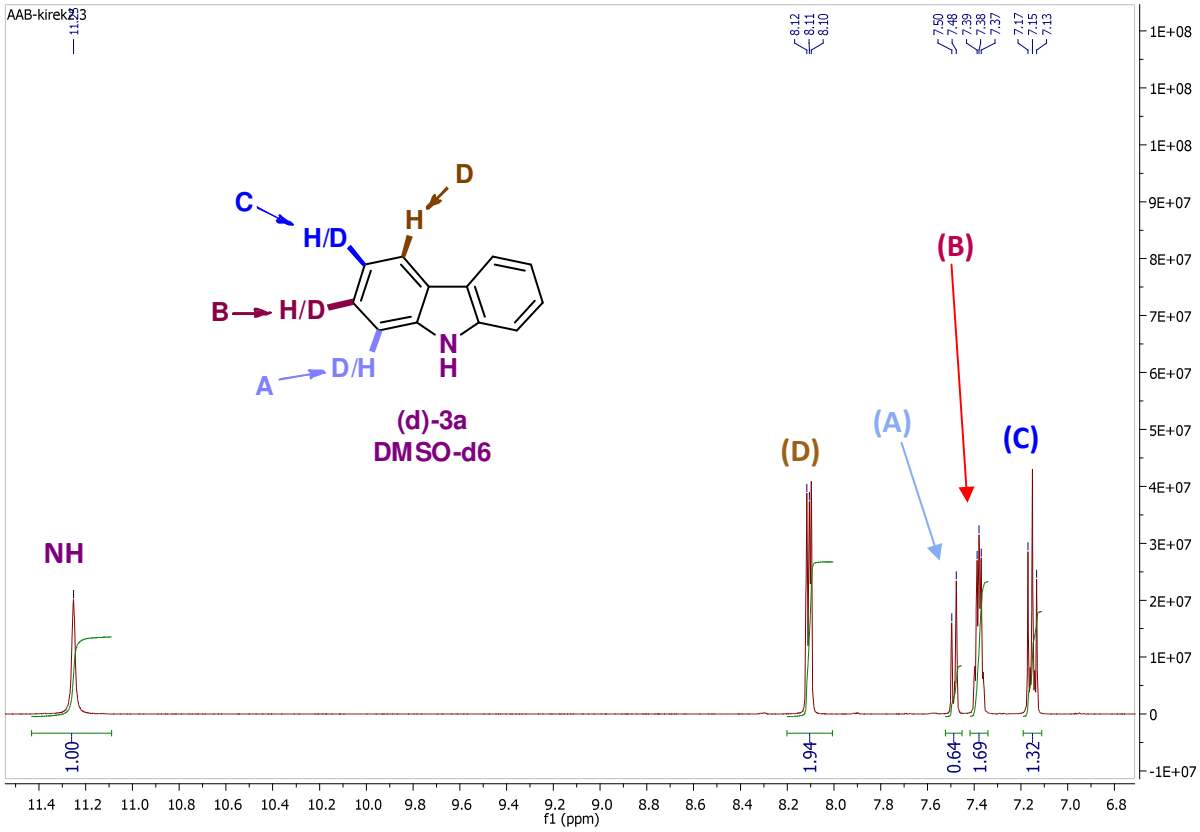


Figure 10: ^{1}H NMR profile of (d)-2a after H/D scrambling experiment 2.

(d)-2a, GC-MS: R_t: 5.8 min; EI: 177 (0.4) 176 (3.3), 175 (17.1), 174 (47.9), 173 (84.1), 172 (100.0), 171 (87.2), 170 (57.8), 169 (28.5).

Note: **2a (natural abundance)**, GC-MS: R_t: 5.8 min; EI: 170 (13.3), 169 (100.0).

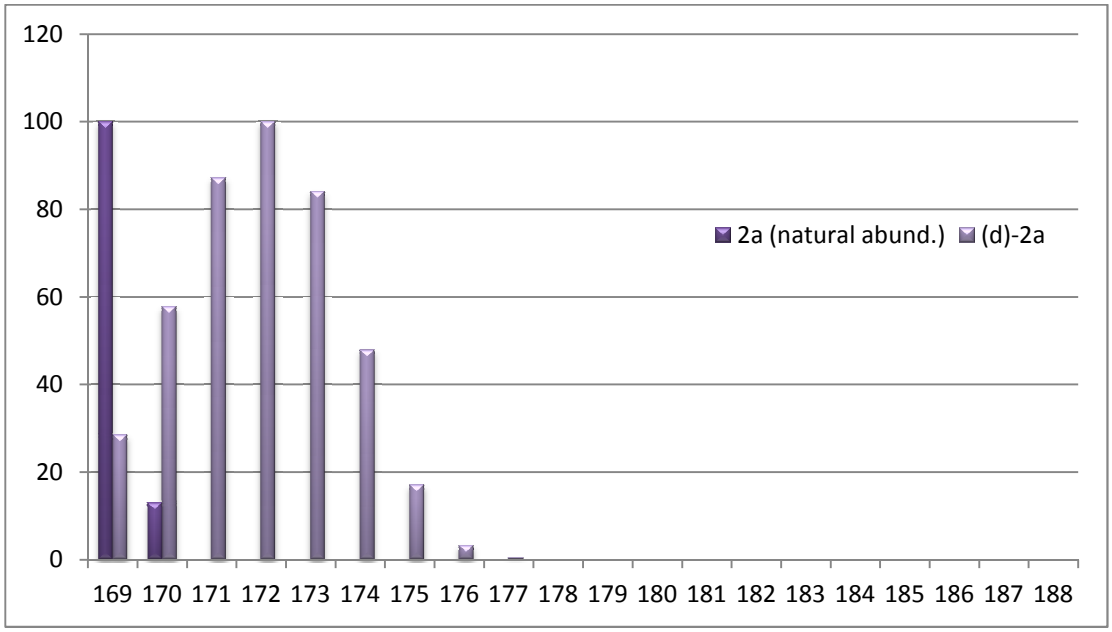


Figure 11: EI profile of (d)-2a after H/D scrambling experiment 2.

Calculated values (% of total) for populations of **2a**, **(d1)-2a**, **(d2)-2a**, **(d3)-2a**, etc:

D0	7,6
D1	14,3
D2	21,3
D3	23,7
D4	19,2
D5	10,2
D6	3,2
D7	0,5
D8	0,0
D9	0,0
D10	0,0

(d)-1a, GC-MS: R_t: 6.4 min; EI: 175 (0.1) 174 (0.2), 173 (1.0), 172 (6.7), 171 (31.3), 170 (78.4), 169 (100.0), 168 (62.1), 167 (20.3).

Note: **1a (natural abundance)**, GC-MS: R_t: 6.4 min; EI: 168 (13.1), 167 (100.0).

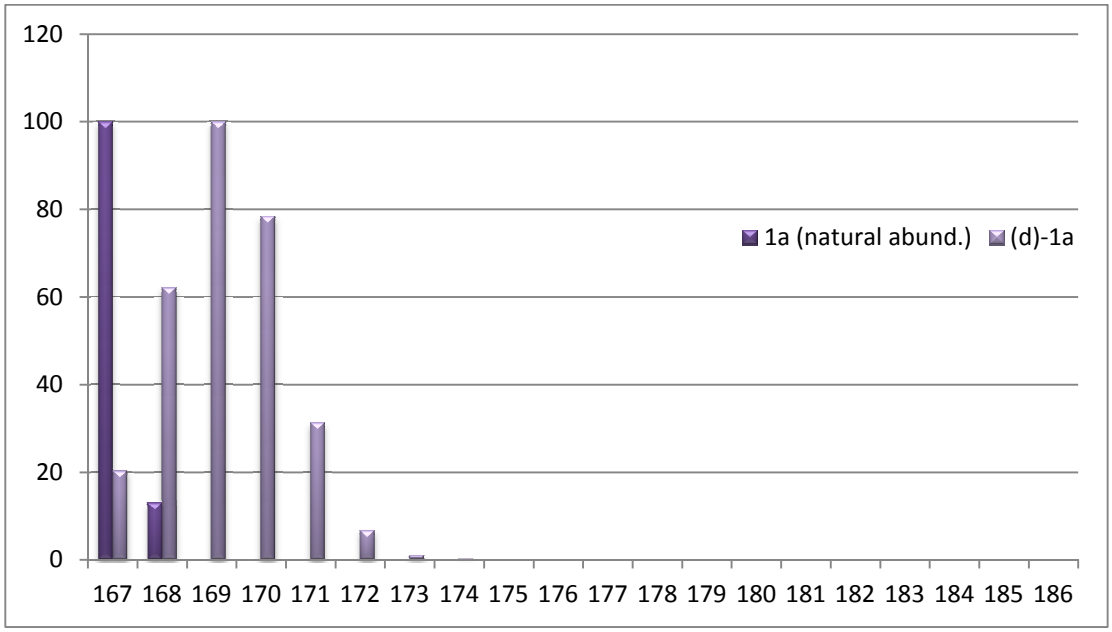


Figure 12: EI profile of (d)-1a after H/ scrambling experiment 2.

Calculated values (% of total) for populations of **1a**, **(d1)-1a**, **(d2)-1a**, **(d3)-1a**, etc:

D0	7,6
D1	22,4
D2	34,7
D3	25,0
D4	8,5
D5	1,4
D6	0,2
D7	0,1
D8	0,0

(d)-3a, GC-MS: R_t: 8.9 min; EI: 345 (0.5) 344 (0.8), 343 (3.5), 342 (13.1), 341 (30.7), 340 (56.9), 339 (85.4), 338 (100.0), 337 (90.9), 336 (67.0), 335 (36.8), 334 (16.8).

Note: **3a (natural abundance)**, GC-MS: R_t: 8.9 min; EI: 336 (3.4), 335 (26.2), 334 (100.0).

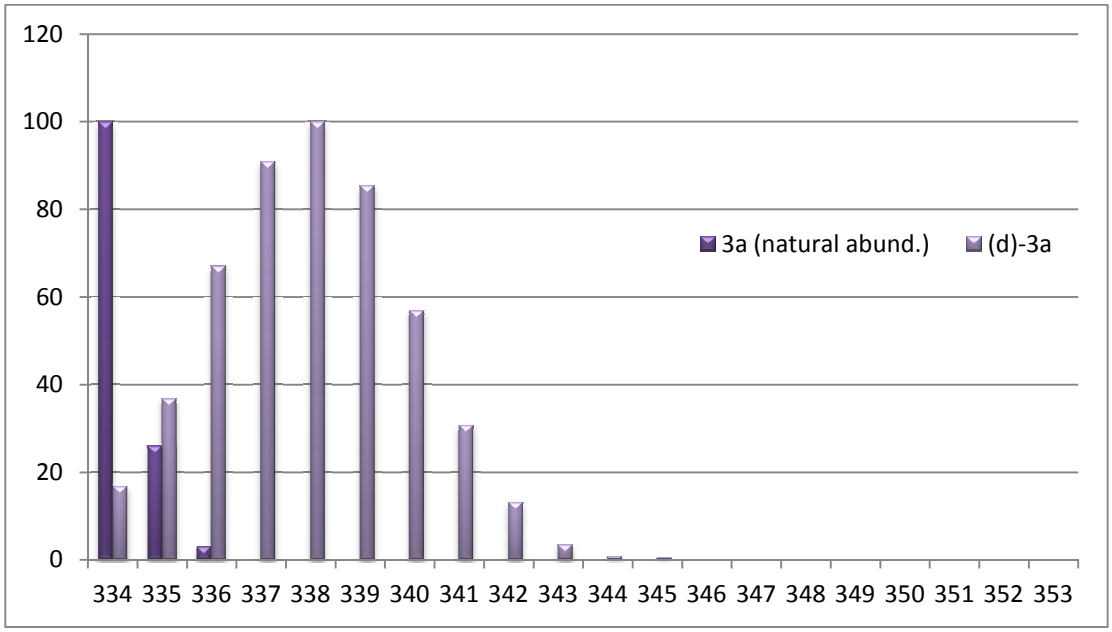


Figure 13: EI profile of (d)-3a after H/D scrambling experiment 2.

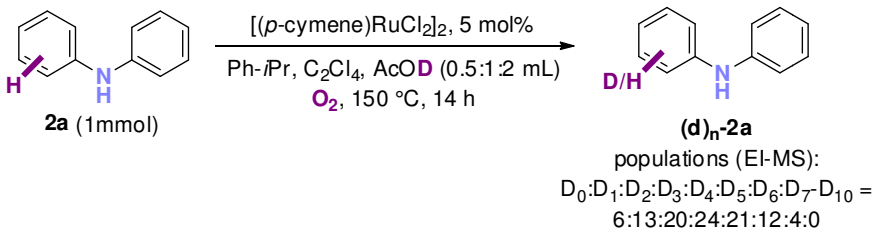
Calculated values (% of total) for populations of **3a**, **(d1)-3a**, **(d2)-3a**, **(d3)-3a**, etc:

D0	4,3	**D9**	0,3
D1	8,3	**D10**	0,1
D2	14,9	**D11**	0,1
D3	19,2	**D12**	0,0
D4	20,2	**D13**	0,0
D5	16,1	**D14**	0,0
D6	9,8	**D15**	0,0
D7	4,8	**D16**	0,0
D8	1,8	**D17**	0,0

H/D scrambling experiment without $Cu(OAc)_2$.

In a forth experiment, diphenylamine **2a** (1 mmol), [(*p*-cymene)$RuCl_2]_2$ (0.05 mmol), cumene (0.5 mL), C_2Cl_4 (1 mL), and AcO**D** (acetic acid-d_1, 2 mL) are united in a 170 mL reactor equipped with Teflon screw cap and flushed with **O_2**. The reactor is then sealed (*tightly*) and exposed to 150 °C for 14 h (magnetic stirring set to approx. 500 turns/min).

The reactor is then cooled to room temperature. Filtration over SiO_2 gel affords the crude mixture, which is analyzed by GC-MS.



2a (1mmol)

$(d)_n$-2a
populations (EI-MS):
D_0:D_1:D_2:D_3:D_4:D_5:D_6:D_7-D_{10} =
6:13:20:24:21:12:4:0

Scheme 23: H/D scrambling experiment without $Cu(OAc)_2$.

(d)-2a, GC-MS: R_t: 5.8 min; EI: 176 (3.0), 175 (20.4), 174 (57.6), 173 (92.5), 172 (100.0), 171 (81.3), 170 (51.4), 169 (23.7).

Note: **2a (natural abundance)**, GC-MS: R_t: 5.8 min; EI: 170 (13.3), 169 (100.0).

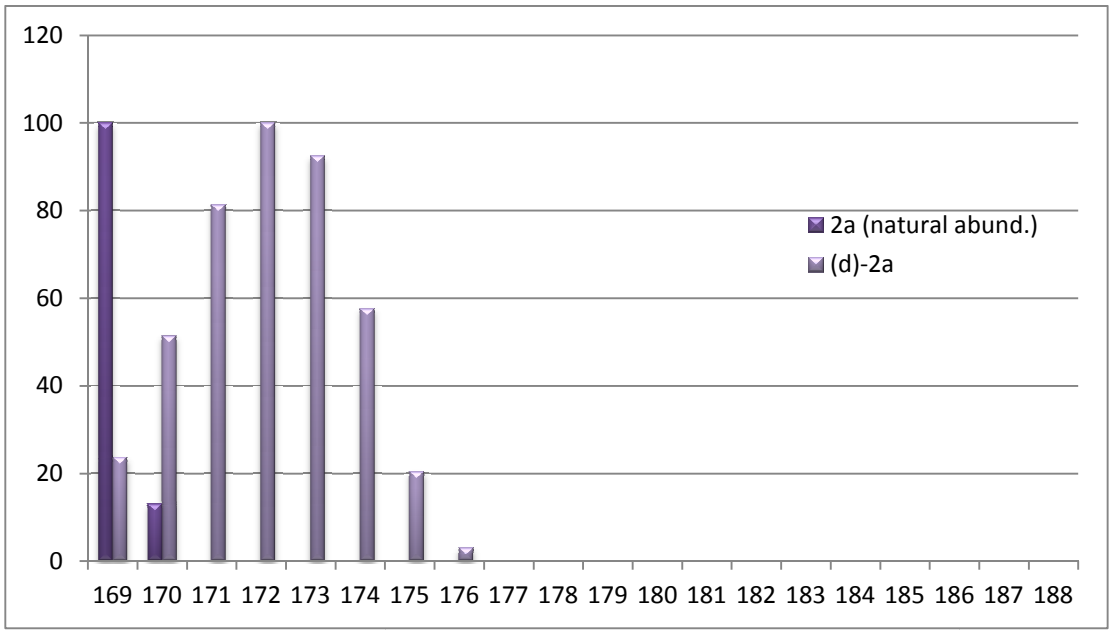


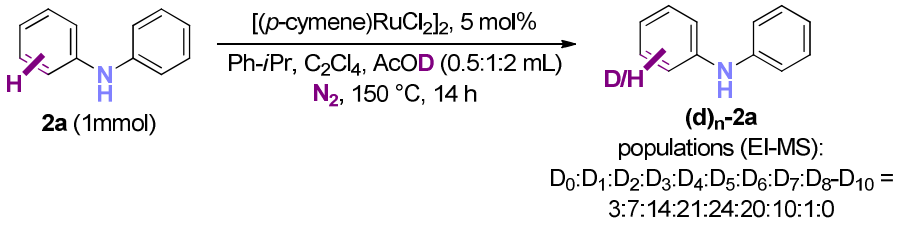
Figure 14: EI profile of (d)-2a after H/D scrambling experiment without $Cu(OAc)_2$.

Calculated values (% of total) for populations of **2a**, **(d1)-2a**, **(d2)-2a**, **(d3)-2a**, etc:

D0	6.2
D1	12.7
D2	19.7
D3	23.7
D4	21.2
D5	12.4
D6	3.8
D7	0.3
D8	0.0
D9	0.0
D10	0.0

H/D scrambling experiment without Cu(OAc)$_2$ under N$_2$.

In a fifth experiment, diphenylamine **2a** (1 mmol), [(*p*-cymene)RuCl$_2$]$_2$ (0.05 mmol), cumene (0.5 mL), C_2Cl_4 (1 mL), and AcO**D** (acetic acid-d$_1$, 2 mL) are united in a 170 mL reactor equipped with Teflon screw cap and flushed with **N_2**. The reactor is then sealed (*tightly*) and exposed to 150 °C for 14 h (magnetic stirring set to approx. 500 turns/min). The reactor is then cooled to room temperature. Filtration over SiO_2 gel affords the crude mixture, which is analyzed by GC-MS.



Scheme 24: H/D scrambling experiment without Cu(OAc)$_2$ under N$_2$.

(d)-2a, GC-MS: R_t: 5.8 min; EI: 177 (0.8), 176 (7.7), 175 (45.8), 174 (86.6), 173 (100.0), 172 (83.5), 171 (57.3), 170 (29.3), 169 (10.7).

Note: **2a (natural abundance)**, GC-MS: R_t: 5.8 min; EI: 170 (13.3), 169 (100.0).

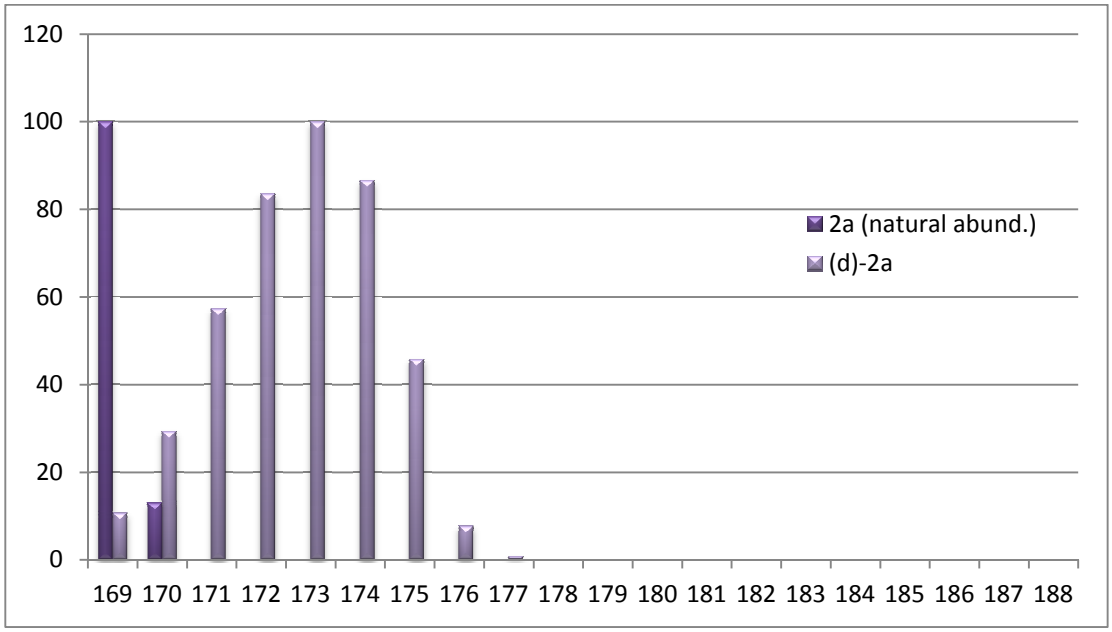


Figure 15: EI profile of (d)-2a after H/D scrambling experiment without $Cu(OAc)_2$ under N_2.

Calculated values (% of total) for populations of **2a**, **(d1)-2a**, **(d2)-2a**, **(d3)-2a**, etc:

D0	2.9
D1	7.5
D2	14.4
D3	20.5
D4	24.1
D5	20.1
D6	9.7
D7	0.8
D8	0.1
D9	0.0
D10	0.0

3.5.6. Crystallographic data (See figure 3).

Table 1. Crystal data and structure refinement for 13076ocu.

Identification code	13076ocu	
Empirical formula	C24 H18 N2	
Formula weight	334.40	
Temperature	150(2) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 11.6032(5) Å	α= 90°.
	b = 7.0985(2) Å	β= 118.601(6)°.
	c = 11.9333(6) Å	ɣ = 90°.
Volume	862.95(6) $Å^3$	
Z	2	
Density (calculated)	1.287 Mg/m^3	
Absorption coefficient	0.583 mm^{-1}	
F(000)	352	
Crystal size	0.44 x 0.37 x 0.27 mm^3	
Theta range for data collection	4.22 to 62.70°.	
Index ranges	-13<=h<=12, -8<=k<=8, -12<=l<=13	
Reflections collected	5651	
Independent reflections	2706 [R(int) = 0.0176]	
Completeness to theta = 62.70°	99.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8585 and 0.7835	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2706 / 2 / 239	
Goodness-of-fit on F^2	1.087	
Final R indices [I>2sigma(I)]	R1 = 0.0236, wR2 = 0.0606	
R indices (all data)	R1 = 0.0242, wR2 = 0.0611	
Absolute structure parameter	-0.1(4)	
Extinction coefficient	0.0259(13)	
Largest diff. peak and hole	0.100 and -0.106 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 13076ocu. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1)	2666(1)	3405(2)	-682(1)	31(1)
C(1)	2030(1)	2781(2)	-1962(1)	26(1)
C(2)	2490(1)	3154(2)	-2821(1)	29(1)
C(3)	1857(1)	2378(2)	-4034(1)	33(1)
C(4)	783(1)	1216(2)	-4404(1)	38(1)
C(5)	330(1)	829(2)	-3545(1)	38(1)
C(6)	936(1)	1622(2)	-2341(1)	33(1)
C(7)	3098(1)	5208(2)	-206(1)	24(1)
C(8)	3487(1)	5549(2)	1088(1)	25(1)
C(9)	3903(1)	7317(2)	1617(1)	29(1)
C(10)	3970(1)	8782(2)	886(1)	31(1)
C(11)	3601(1)	8459(2)	-383(1)	29(1)
C(12)	3158(1)	6708(2)	-933(1)	27(1)
N(2)	3452(1)	4040(1)	1867(1)	25(1)
C(13)	4548(1)	3151(2)	2840(1)	24(1)
C(14)	5873(1)	3478(2)	3252(1)	28(1)
C(15)	6770(1)	2398(2)	4257(1)	31(1)
C(16)	6365(1)	1038(2)	4847(1)	33(1)
C(17)	5047(1)	716(2)	4429(1)	30(1)
C(18)	4120(1)	1783(2)	3415(1)	25(1)
C(19)	2701(1)	1848(2)	2766(1)	25(1)
C(20)	1730(1)	870(2)	2900(1)	31(1)
C(21)	432(1)	1333(2)	2120(1)	33(1)
C(22)	77(1)	2746(2)	1194(1)	31(1)
C(23)	1017(1)	3734(2)	1030(1)	30(1)
C(24)	2328(1)	3270(2)	1829(1)	25(1)

Table 3. Bond lengths [Å] and angles [°] for 13076ocu.

N(1)-C(7)	1.3922(17)	C(12)-H(12)	0.9500
N(1)-C(1)	1.4123(16)	N(2)-C(24)	1.3942(16)
N(1)-H(1N)	0.898(9)	N(2)-C(13)	1.3965(16)
C(1)-C(2)	1.3892(18)	C(13)-C(14)	1.3912(17)
C(1)-C(6)	1.3931(19)	C(13)-C(18)	1.4092(18)
C(2)-C(3)	1.3863(18)	C(14)-C(15)	1.3832(19)
C(2)-H(2)	0.9500	C(14)-H(14)	0.9500
C(3)-C(4)	1.379(2)	C(15)-C(16)	1.402(2)
C(3)-H(3)	0.9500	C(15)-H(15)	0.9500
C(4)-C(5)	1.384(2)	C(16)-C(17)	1.3816(19)
C(4)-H(4)	0.9500	C(16)-H(16)	0.9500
C(5)-C(6)	1.381(2)	C(17)-C(18)	1.3960(18)
C(5)-H(5)	0.9500	C(17)-H(17)	0.9500
C(6)-H(6)	0.9500	C(18)-C(19)	1.4469(18)
C(7)-C(12)	1.3955(17)	C(19)-C(20)	1.3955(18)
C(7)-C(8)	1.4076(17)	C(19)-C(24)	1.4116(18)
C(8)-C(9)	1.3840(18)	C(20)-C(21)	1.379(2)
C(8)-N(2)	1.4319(15)	C(20)-H(20)	0.9500
C(9)-C(10)	1.3831(19)	C(21)-C(22)	1.400(2)
C(9)-H(9)	0.9500	C(21)-H(21)	0.9500
C(10)-C(11)	1.3812(19)	C(22)-C(23)	1.3864(19)
C(10)-H(10)	0.9500	C(22)-H(22)	0.9500
C(11)-C(12)	1.3843(18)	C(23)-C(24)	1.3943(18)
C(11)-H(11)	0.9500	C(23)-H(23)	0.9500

C(7)-N(1)-C(1)	128.96(10)	C(4)-C(3)-H(3)	119.4
C(7)-N(1)-H(1N)	114.2(9)	C(2)-C(3)-H(3)	119.4
C(1)-N(1)-H(1N)	111.6(9)	C(3)-C(4)-C(5)	119.12(13)
C(2)-C(1)-C(6)	118.98(11)	C(3)-C(4)-H(4)	120.4
C(2)-C(1)-N(1)	123.45(11)	C(5)-C(4)-H(4)	120.4
C(6)-C(1)-N(1)	117.40(11)	C(6)-C(5)-C(4)	120.31(13)
C(3)-C(2)-C(1)	119.76(12)	C(6)-C(5)-H(5)	119.8
C(3)-C(2)-H(2)	120.1	C(4)-C(5)-H(5)	119.8
C(1)-C(2)-H(2)	120.1	C(5)-C(6)-C(1)	120.64(13)
C(4)-C(3)-C(2)	121.18(13)	C(5)-C(6)-H(6)	119.7

C(1)-C(6)-H(6)	119.7	C(14)-C(15)-H(15)	119.2
N(1)-C(7)-C(12)	124.31(11)	C(16)-C(15)-H(15)	119.2
N(1)-C(7)-C(8)	117.97(11)	C(17)-C(16)-C(15)	120.77(13)
C(12)-C(7)-C(8)	117.72(11)	C(17)-C(16)-H(16)	119.6
C(9)-C(8)-C(7)	120.99(11)	C(15)-C(16)-H(16)	119.6
C(9)-C(8)-N(2)	119.65(11)	C(16)-C(17)-C(18)	118.90(12)
C(7)-C(8)-N(2)	119.36(10)	C(16)-C(17)-H(17)	120.6
C(10)-C(9)-C(8)	120.48(12)	C(18)-C(17)-H(17)	120.6
C(10)-C(9)-H(9)	119.8	C(17)-C(18)-C(13)	119.42(12)
C(8)-C(9)-H(9)	119.8	C(17)-C(18)-C(19)	133.50(11)
C(11)-C(10)-C(9)	118.98(12)	C(13)-C(18)-C(19)	107.08(10)
C(11)-C(10)-H(10)	120.5	C(20)-C(19)-C(24)	119.23(12)
C(9)-C(10)-H(10)	120.5	C(20)-C(19)-C(18)	134.19(12)
C(10)-C(11)-C(12)	121.26(11)	C(24)-C(19)-C(18)	106.58(10)
C(10)-C(11)-H(11)	119.4	C(21)-C(20)-C(19)	119.00(12)
C(12)-C(11)-H(11)	119.4	C(21)-C(20)-H(20)	120.5
C(11)-C(12)-C(7)	120.55(11)	C(19)-C(20)-H(20)	120.5
C(11)-C(12)-H(12)	119.7	C(20)-C(21)-C(22)	121.11(12)
C(7)-C(12)-H(12)	119.7	C(20)-C(21)-H(21)	119.4
C(24)-N(2)-C(13)	108.41(10)	C(22)-C(21)-H(21)	119.4
C(24)-N(2)-C(8)	126.08(10)	C(23)-C(22)-C(21)	121.32(12)
C(13)-N(2)-C(8)	125.45(10)	C(23)-C(22)-H(22)	119.3
C(14)-C(13)-N(2)	129.14(11)	C(21)-C(22)-H(22)	119.3
C(14)-C(13)-C(18)	122.03(11)	C(22)-C(23)-C(24)	117.27(12)
N(2)-C(13)-C(18)	108.83(10)	C(22)-C(23)-H(23)	121.4
C(15)-C(14)-C(13)	117.32(12)	C(24)-C(23)-H(23)	121.4
C(15)-C(14)-H(14)	121.3	N(2)-C(24)-C(23)	128.84(12)
C(13)-C(14)-H(14)	121.3	N(2)-C(24)-C(19)	109.10(10)
C(14)-C(15)-C(16)	121.56(13)	C(23)-C(24)-C(19)	122.06(11)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for 13076ocu. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1)	46(1)	23(1)	24(1)	0(1)	17(1)	-6(1)
C(1)	30(1)	19(1)	24(1)	2(1)	10(1)	5(1)
C(2)	30(1)	25(1)	30(1)	1(1)	14(1)	2(1)
C(3)	42(1)	30(1)	28(1)	2(1)	18(1)	5(1)
C(4)	43(1)	34(1)	26(1)	-3(1)	9(1)	3(1)
C(5)	34(1)	35(1)	37(1)	-5(1)	10(1)	-7(1)
C(6)	37(1)	29(1)	36(1)	-1(1)	19(1)	-3(1)
C(7)	24(1)	24(1)	23(1)	0(1)	11(1)	1(1)
C(8)	25(1)	24(1)	25(1)	4(1)	12(1)	-1(1)
C(9)	33(1)	28(1)	24(1)	-3(1)	12(1)	-2(1)
C(10)	34(1)	23(1)	34(1)	-2(1)	15(1)	-3(1)
C(11)	32(1)	24(1)	33(1)	6(1)	18(1)	3(1)
C(12)	32(1)	25(1)	24(1)	2(1)	14(1)	3(1)
N(2)	28(1)	24(1)	21(1)	3(1)	10(1)	-2(1)
C(13)	31(1)	22(1)	18(1)	-3(1)	12(1)	-1(1)
C(14)	34(1)	27(1)	24(1)	-3(1)	16(1)	-2(1)
C(15)	30(1)	33(1)	27(1)	-4(1)	12(1)	2(1)
C(16)	37(1)	32(1)	26(1)	3(1)	12(1)	8(1)
C(17)	39(1)	26(1)	24(1)	0(1)	16(1)	-1(1)
C(18)	33(1)	22(1)	20(1)	-3(1)	13(1)	-1(1)
C(19)	33(1)	23(1)	20(1)	-4(1)	12(1)	-3(1)
C(20)	40(1)	28(1)	26(1)	-1(1)	17(1)	-6(1)
C(21)	35(1)	35(1)	32(1)	-6(1)	18(1)	-10(1)
C(22)	30(1)	32(1)	30(1)	-6(1)	13(1)	-3(1)
C(23)	34(1)	26(1)	26(1)	-1(1)	13(1)	-1(1)
C(24)	30(1)	24(1)	22(1)	-4(1)	13(1)	-4(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 13076ocu.

	x	y	z	U(eq)
H(2)	3236	3938	-2577	34
H(3)	2169	2650	-4621	40
H(4)	358	688	-5237	45
H(5)	-400	15	-3785	45
H(6)	605	1374	-1766	40
H(9)	4144	7526	2488	35
H(10)	4266	9992	1252	37
H(11)	3651	9457	-888	35
H(12)	2892	6527	-1812	32
H(14)	6151	4405	2858	33
H(15)	7681	2583	4554	37
H(16)	7004	329	5542	40
H(17)	4776	-216	4825	36
H(20)	1961	-101	3519	37
H(21)	-233	683	2213	40
H(22)	-825	3032	667	38
H(23)	776	4689	400	36
H(1N)	2454(14)	2689(19)	-187(12)	30

Table 6. Torsion angles [°] for 13076ocu.

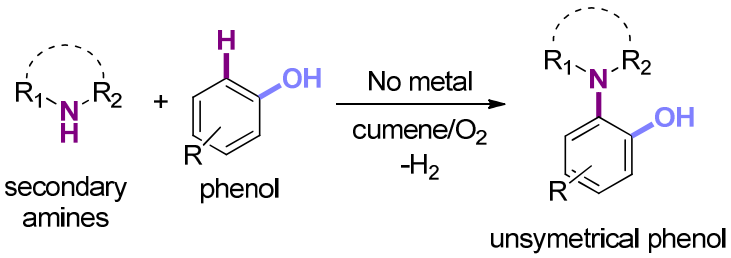
C(7)-N(1)-C(1)-C(2)	50.60(19)
C(7)-N(1)-C(1)-C(6)	-134.07(14)
C(6)-C(1)-C(2)-C(3)	0.20(19)
N(1)-C(1)-C(2)-C(3)	175.46(12)
C(1)-C(2)-C(3)-C(4)	-0.8(2)
C(2)-C(3)-C(4)-C(5)	0.2(2)
C(3)-C(4)-C(5)-C(6)	1.0(2)
C(4)-C(5)-C(6)-C(1)	-1.6(2)
C(2)-C(1)-C(6)-C(5)	1.0(2)
N(1)-C(1)-C(6)-C(5)	-174.52(13)
C(1)-N(1)-C(7)-C(12)	-10.8(2)
C(1)-N(1)-C(7)-C(8)	168.45(12)
N(1)-C(7)-C(8)-C(9)	-178.77(11)
C(12)-C(7)-C(8)-C(9)	0.52(17)
N(1)-C(7)-C(8)-N(2)	1.33(17)
C(12)-C(7)-C(8)-N(2)	-179.38(11)
C(7)-C(8)-C(9)-C(10)	-1.30(19)
N(2)-C(8)-C(9)-C(10)	178.60(11)
C(8)-C(9)-C(10)-C(11)	0.79(19)
C(9)-C(10)-C(11)-C(12)	0.48(19)
C(10)-C(11)-C(12)-C(7)	-1.26(18)
N(1)-C(7)-C(12)-C(11)	179.98(12)
C(8)-C(7)-C(12)-C(11)	0.75(17)
C(9)-C(8)-N(2)-C(24)	106.21(14)
C(7)-C(8)-N(2)-C(24)	-73.89(15)
C(9)-C(8)-N(2)-C(13)	-70.50(16)
C(7)-C(8)-N(2)-C(13)	109.40(13)
C(24)-N(2)-C(13)-C(14)	-178.41(11)
C(8)-N(2)-C(13)-C(14)	-1.22(19)
C(24)-N(2)-C(13)-C(18)	0.87(13)
C(8)-N(2)-C(13)-C(18)	178.06(10)
N(2)-C(13)-C(14)-C(15)	179.30(12)
C(18)-C(13)-C(14)-C(15)	0.10(17)
C(13)-C(14)-C(15)-C(16)	-0.48(19)
C(14)-C(15)-C(16)-C(17)	0.8(2)

C(15)-C(16)-C(17)-C(18)	-0.66(19)
C(16)-C(17)-C(18)-C(13)	0.28(18)
C(16)-C(17)-C(18)-C(19)	-178.57(13)
C(14)-C(13)-C(18)-C(17)	0.00(18)
N(2)-C(13)-C(18)-C(17)	-179.35(10)
C(14)-C(13)-C(18)-C(19)	179.13(10)
N(2)-C(13)-C(18)-C(19)	-0.22(13)
C(17)-C(18)-C(19)-C(20)	-0.5(2)
C(13)-C(18)-C(19)-C(20)	-179.50(13)
C(17)-C(18)-C(19)-C(24)	178.45(13)
C(13)-C(18)-C(19)-C(24)	-0.50(13)
C(24)-C(19)-C(20)-C(21)	-0.65(18)
C(18)-C(19)-C(20)-C(21)	178.25(13)
C(19)-C(20)-C(21)-C(22)	0.74(19)
C(20)-C(21)-C(22)-C(23)	-0.3(2)
C(21)-C(22)-C(23)-C(24)	-0.25(19)
C(13)-N(2)-C(24)-C(23)	178.92(12)
C(8)-N(2)-C(24)-C(23)	1.75(19)
C(13)-N(2)-C(24)-C(19)	-1.20(13)
C(8)-N(2)-C(24)-C(19)	-178.37(10)
C(22)-C(23)-C(24)-N(2)	-179.79(12)
C(22)-C(23)-C(24)-C(19)	0.34(18)
C(20)-C(19)-C(24)-N(2)	-179.78(10)
C(18)-C(19)-C(24)-N(2)	1.04(13)
C(20)-C(19)-C(24)-C(23)	0.11(18)
C(18)-C(19)-C(24)-C(23)	-179.07(11)

Symmetry transformations used to generate equivalent atoms:

Chapter IV

O_2 mediated dehydrogenative amination of phenols.



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4.1. Introduction.

Phenols are valuable structural motifs in organic syntheses. [1a] Examples such as adrenaline, used in medicine, or vanillin used as flavor or fragrance show a wide range of applications (Figure 1). Cheap and easily accessible, phenols are ubiquitous building blocks to design elaborated molecules for cosmetics and medicine, as well as plastics and related material. In this context, efficient methods for post-functionalizing phenols are of high interest.

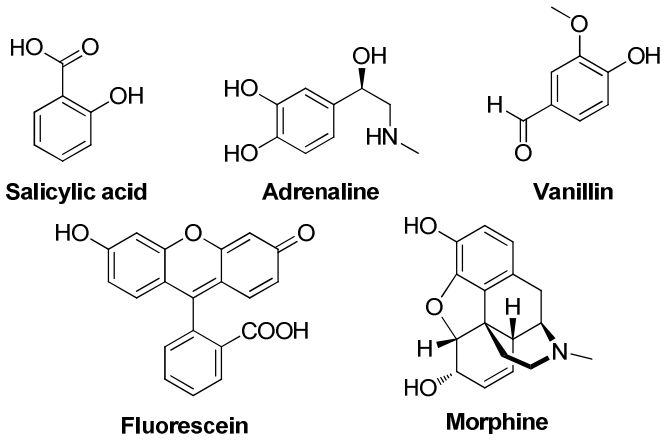
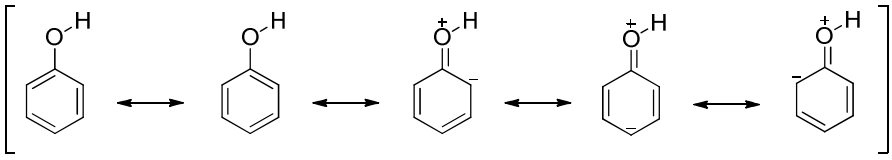


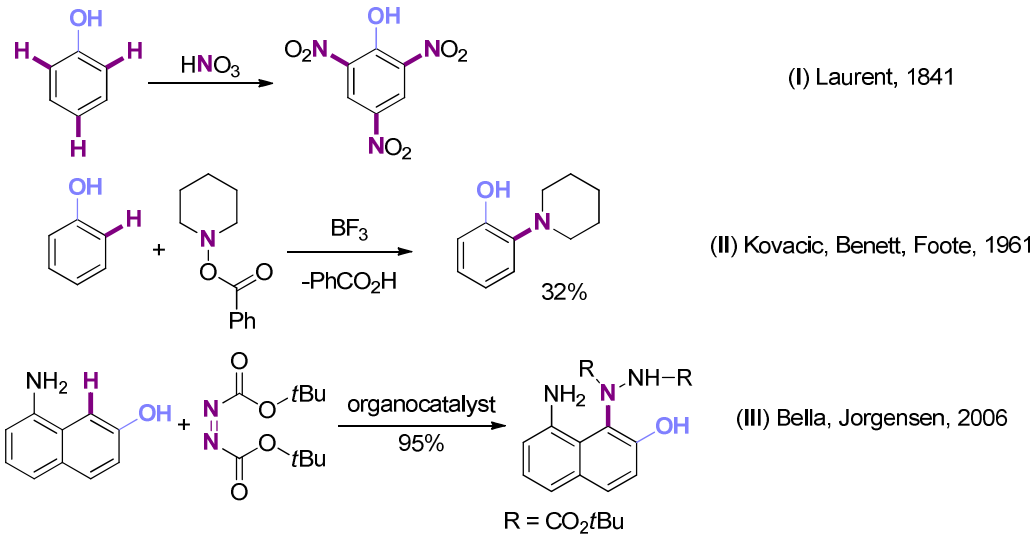
Figure 1: Well-known examples of phenols widely used in medicine and industry.

In term of reactivity, *ortho*- and *para*-positions of phenols are known to be readily accessible by electrophilic aromatic substitution (S_EAr).[1a] Indeed, the electro-donating nature of hydroxyl group on the benzene ring render C2, C4 and C6 positions more nucleophile by resonance (Scheme 1). For instance, alkylation and alcylation by Charles Friedel and James Crafts[2] are efficient pathways to build Carbon-Carbon bonds in one step. Indeed, their invention based on the nucleophilicity of electro-enriched arenes coupled with an electrophile partner allows efficient introduction of functional groups on arenes. Although the post-functionalization of phenols by S_EAr reactions is well described in the literature, it is mostly to create Carbon-Carbon bonds. [1]



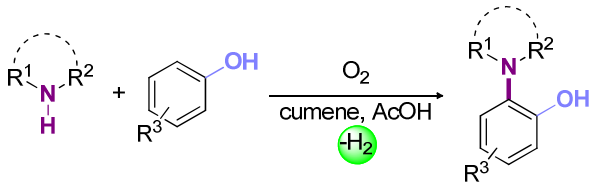
Scheme1: Mesomeric stabilisation of phenol

In 1841, Auguste Laurent was a pioneer to create C-N bonds on phenol, forming picric acid [3] by nitration of the molecule (S_EAr) more than thirty years before Friedel and Crafts (Scheme 2 (I)). Excluding work of Kovacic, Benett and Foote in 1961 (Scheme 2 (II)), where they describe *ortho*-functionalization of phenol by piperidine[4], and recent work of Bella and Jørgensen in 2006 with their exotic aminating agent[5] (Scheme 2 (III)) very few description of metal-free direct amination reaction on phenol are reported.



Scheme 2: Previous methods for direct amination of phenol.

A recurrent problem of such a reaction resides in the fact that the aromatic ring and the nitrogen atom are electron rich, making them both nucleophilic and thus, not inclined to condense on oneother. To create a C-N bond, the aromatic ring or the nitrogen atom must reverse its electronic nature to restore a nucleophile-electrophile connection. This is probably a reason why metal free amination descriptions are rare[6]. However, Antonchick and other research groups surpassed this problem by introduction of hypervalent iodine. [7] Mechanisms of such catalysts are still controversial since coordination of iodine is hard to predict and control. Nevertheless, we found a pathway to create a C-N bond between electro-enriched arenes and an aminating agent in a dehydrogenative fashion without transition metal, halides or elaborated organocatalyst (Scheme 3).



Scheme 3: This work: Dehydrogenative condensation of phenols on secondary amines.

4.2. Results and discussions.

In line with dehydrogenative amination reactions previously developed in the laboratory[8], we decided to focus our research on a new amination reaction for arenes without chelating directing group. We discovered that phenothiazine were particularly reactive in coupling with phenols. As expected, when we initiated the project, we obtained a product of cross-dehydrogenative coupling selectively in *ortho*-position with ruthenium catalyst. We optimized parameters of the reaction and acknowledge that metal catalysts were not critical for the C-N bond formation. Thus we were able to build a new C-N bond between phenol and phenothiazine in metal free, halide free and organocatalyst free conditions.

4.2.1. Optimization.

In an initial stage, we engaged in reaction 4-*tert*-butylphenol (1.0 mmol), phenothiazine (1.5 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (5 mol%), $Cu(OAc)_2$ (2.2 eq), AcOH (0.5 mL), cumene (0.5 mL), and C_2Cl_2 (2.5 mL). All components were united in a screw cap vessel under O_2. The mixture was strirred at 150°C for 24h. The analysis of the crude by GC-MS showed phenothiazine was converted and partly acetylated (m/z = 241.1 at 7.105 min) while two peaks corresponding to a heterocoupling product (m/z = 346.9 at 8.492 min) and acetylated heterocoupling product (m/z = 388.9 at 8.555 min) appeared (Figure 2). To identify the nature of the coupling, we purified the product (30% isolated yield) by column chromatography of SiO_2. NMR and XRD analysis (Figure 3) confirmed the *ortho*-N-amination of phenol.

We optimized a part of reaction parameters qualitatively. Only probative entries were isolated and reported (Table 1).

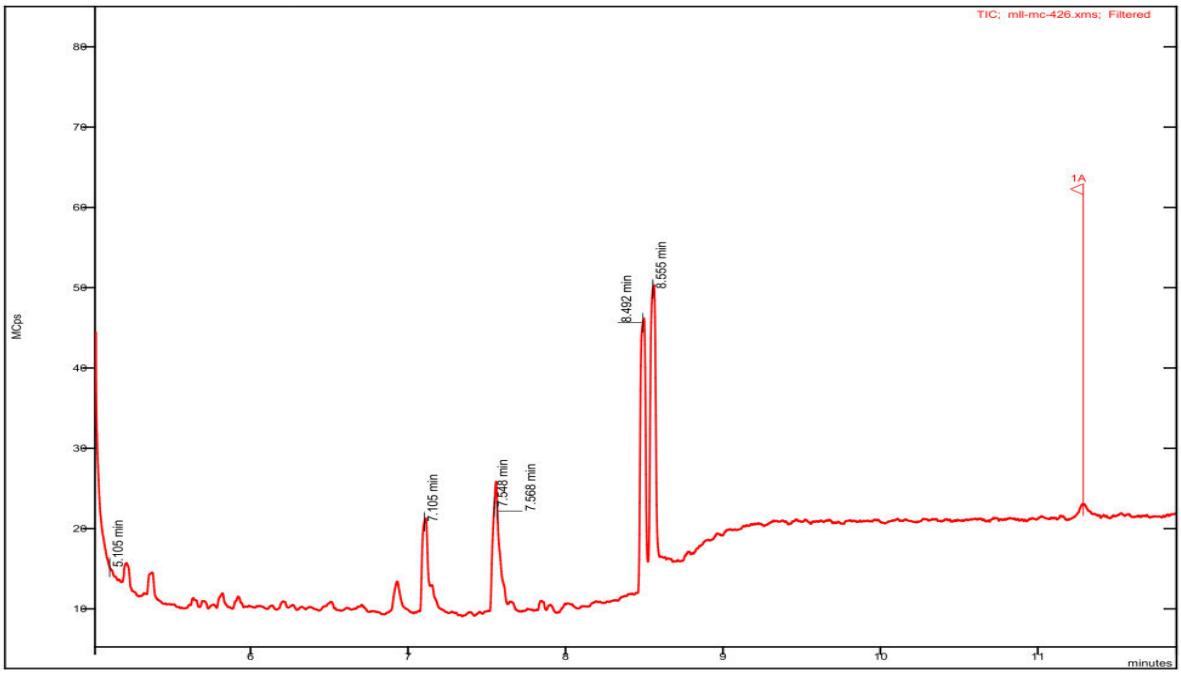


Figure 2: GC profile for entry 0; New peak of product m/z = 346.9 at 8.492 min. (Peak of residual acetylated phenothiazine at 7.105 min m/z = 241.1 and peak of acetylated product at 8.555 min m/z = 388.9).

In order to avoid the formation of the homo-coupling product of the phenothiazine (broad peak at 11.28 min, m/z = 395.9 (Figure2)), we started by reversing the limiting reagent. We obtained an improvement of the reactivity and 70% isolated yield (Entry 4 (Table 1)). In a second step, we evaluated the effect of temperature. Lowering it to 90°C decreased the yield to 22% (Entry 1 (Table 1)). According to TLC and GCMS profile, we observed a systematic conversion of phenothiazine regardless of temperature. This statement could be explained by formation of instable phenothiazine-metal intermediates unable to reach the energetic barrier necessary for the formation of the carbon-nitrogen bond at low temperature. In presence of metallic species, 130°C was found to be the best temperature.

Control experiments confirmed that norbornadiene was more effective than *p*-cymene as ligand for ruthenium, giving us the possibility to divide by two the amount of ruthenium species.

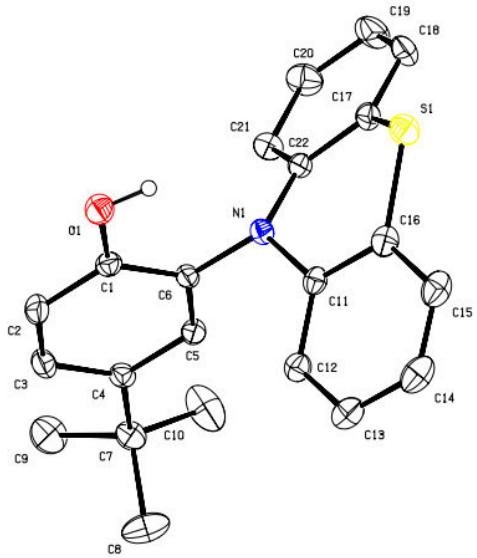
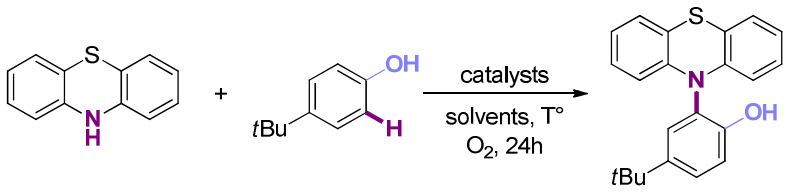


Figure 3: X-Ray structure: **3a** ORTEP view, 30% probability level). Selected torsion angle (deg): C(11)-N(1)-C(6)-C(5) = 96.56(17).

Quantities of copper were divided by two at the early stage of optimization because of sticky effect in sulfur containing molecules. Surprisingly, control experiment without copper afforded 63% isolated yield of the product (Entry 4 (Table 1)). More remarkably, the reaction carried out without copper and without ruthenium still provided 38% of the desired product. Therefore, all reactions were systematically carried out in new vessels, with new stirring bars and new caps.

Tetrachloroethylene, cumene, acetic acid and oxygen were removed and/or substituted to have a critical overview of essential components. Removing C_2Cl_4 was crucial for the reaction, giving 59% isolated yield. The replacement of cumene by chlorobenzene, or nitrogen instead of oxygen atmosphere completely shut off formation of the product. According to TLC, acetic acid seems to stabilize the system along with less decomposition. Finally, the oil bath was head up to 150°C to observe higher yields (Table 1-Entry 7).

Table 1: Optimization of the reaction conditions. [a]



1a **2a** **3a**

Entry	Catalysts	Solvents	Temperature	Isolated yield
1	$[Ru(norbornadiene)Cl_2]_n$ $Cu(OAc)_2$ [b]	C_2Cl_4/cumene AcOH	90°C	22%
2	$[Ru(norbornadiene)Cl_2]_n$ $Cu(OAc)_2$ [b]	C_2Cl_4/cumene AcOH	110°C	19%
3	$[Ru(norbornadiene)Cl_2]_n$ $Cu(OAc)_2$	C_2Cl_4/cumene AcOH	130°C	77%
4	$[Ru(p\text{-cymene})Cl_2]_2$ $Cu(OAc)_2$ [c]	C_2Cl_4/cumene AcOH	150°C	70%
4	$[Ru(norbornadiene)Cl_2]_n$	C_2Cl_4/cumene AcOH	130°C	63%
5		C_2Cl_4/cumene AcOH	130°C	38%
6		cumene [d] AcOH	130°C	59%
7		cumene [d] AcOH	150°C	63%

[a] Reactions conditions: 1.0 mmol **1a**, 3.0 mmol **2a**, 5mol% [Ru], 1.0 eq [Cu], 2.0 mL C_2Cl_2, 0.5 mL cumene, 0.5 mL AcOH, O_2, 24h. [b] 0.2 eq [Cu] (yields similar with 1.0 eq of [Cu] according to TLC and GCMS profile). [c] 2.2 eq [Cu]. [d] 2.5 mL cumene.

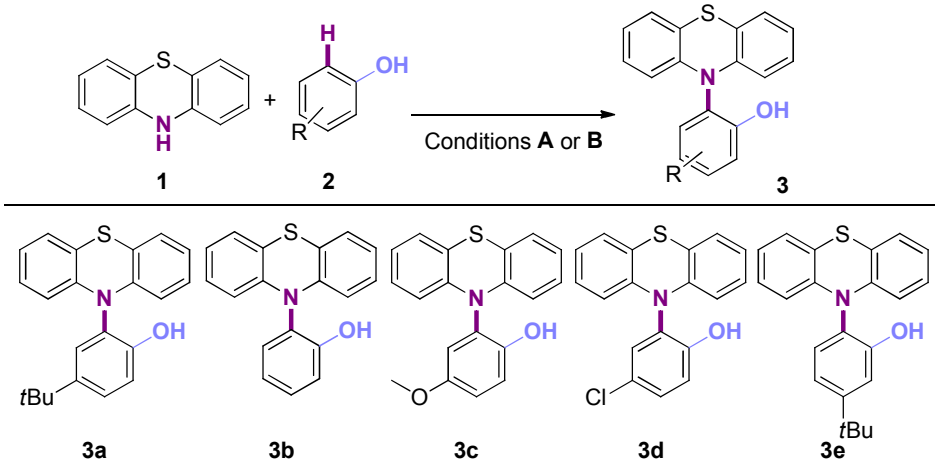
After an optimization period, we defined the best conditions as follows: phenothiazine 1.0 mmol, 4-*tert*-butylphenol (3.0 mmol), cumene (2.5 mL), and AcOH (0.5 mL) were united in a screw caps vessel, flushed with O_2 and transferred in a 150°C oil bath for 24h. The crude was filtered on a plug of silica gel with DCM. The product was purified by a column chromatography of SiO_2 giving 63% isolated yield.

We were able to engage more reactive phenoxazine as well in this reaction conditions by decreasing the temperature to 130°C.

4.2.2. Scope and limits of the reaction.

In the course of the optimization, we investigated substituent effects on phenols. Despite the fact that we studied a metal free reaction, we found interesting results with metal species. Confrontation of results are presented Table 2.

Table 2: Yields comparison between metal catalyzed reaction and metal free reaction.

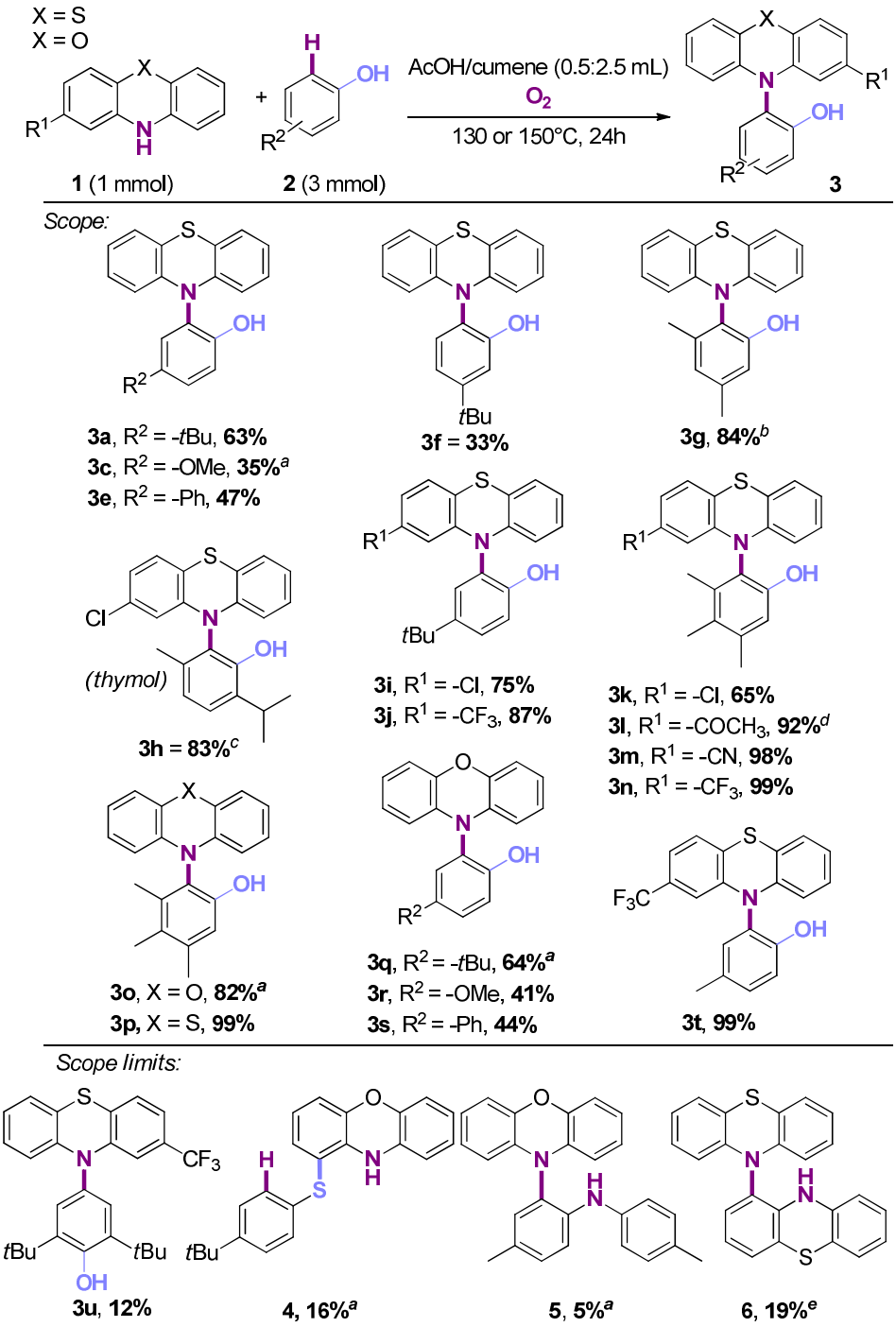


	3a	3b	3c	3d	3e
Conditions **A**:	77%	21%	35%	51%	48%
Conditions **B**:	63%	—	35%[a]	—	33%

Conditions **A**: 1.0 mmol **1**, 3.0 mmol **2**, 5mol% $[Ru(norbornadiene)Cl_2]_n$, 1.0 eq $Cu(OAc)_2$, 2.0 mL C_2Cl_4, 0.5 mL cumene, 0.5 mL AcOH, were united in a Schlenk and flushed with O_2. The reaction was stirred at 130°C for 24h.
Conditions **B**: 1.0 mmol **1**, 3.0 mmol **2**], 2.5 mL cumene, 0.5 mL AcOH, were united in a Schlenk and flushed with O_2. The reaction was stirred at 150°C for 24h.
[a] Reaction performed at 130°C.

This table shows addition of metal gave higher yields compared to metal free conditions, notably with *tert*-butylphenol (**3a** and **3e**). Electro-withdrawing groups such as chlorine afforded 51% isolated yield in presence of ruthenium and copper (**3d**) whereas only traces were observed in metal free conditions. In contrast, more electron-rich methoxy provided same result with or without metallic species (**3c**). This trend could be explained by instability and decomposition of 4-methoxyphenol and the resulting product (**3c**) in these reaction conditions.

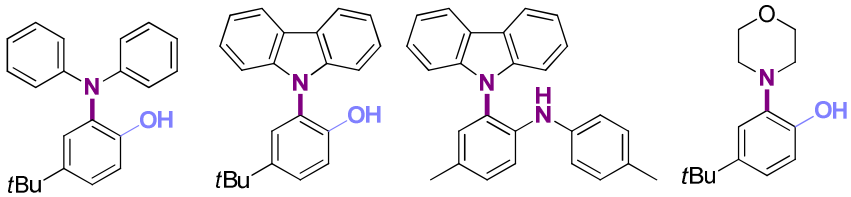
Considering the cost of metals and the differences in term of yields, we chose to continue the scope of the reaction in metal free conditions. With these conditions in hand, we explored the scope of this new protocol (Scheme 4).



Scheme 4: Substrates scope and limits of the reaction. [a] Reaction performed at 130°C. [b] 62:38 ratio ortho/para. [c] 37:63 ratio ortho/para. [d] Reaction performed at 170 °C. [e] 2 mmol scale, 130 °C.

Interestingly, the reaction tolerates a number of functional groups, including acetyl (**3l**) and nitrile (**3m)** providing 92 and 98% isolated yields respectively. Electro-enriched phenols combined with electron-poor phenothiazines (**3l-3n**, **3p**, **3t**) were particularly efficient affording yields above 92%. In contrast, electro withdrawing groups on phenol such as phenyl (**3e** and **3s**) were less effective. Indeed, the yields did not go beyond 50%. Thymol, compound known to be a strong antimicrobiological agent was engaged in the reaction conditions, giving a good global yield (**3h** with 83%) for 4:6 *ortho* to *para* selectivity. On the contrary, a ratio 6:4 *ortho/para* is observed when we engaged 3,5-dimethylphenol **2g**. Steric hindrance of isopropyl in the thymol could explain this exchange of *o*:*p* ratio.

Electron rich products such as diphenylamine are suspected of multi-functionalization, a recurrent problem of S_EAr reaction. We noticed as well that overly reactive phenols, such as 2,6-di-*tert*-butylphenol (Entry **3u**) or 4-*tert*-butylthiophenol (Entry **4**), which tend to yield competing C-C homocoupling product were detrimental to the reaction. Interestingly, we obtained an unexpected result on the coupling reaction between 4-*tert*-butylthiophenol and phenoxazine (Entry **4**). The phenothiazine inverted its reactivity being the C-H coupling partner to form the C-S bond instead of C-N bond (Scheme 4).



7, (0%) **8, (0%)** **9, (0%)** **10, (0%)**

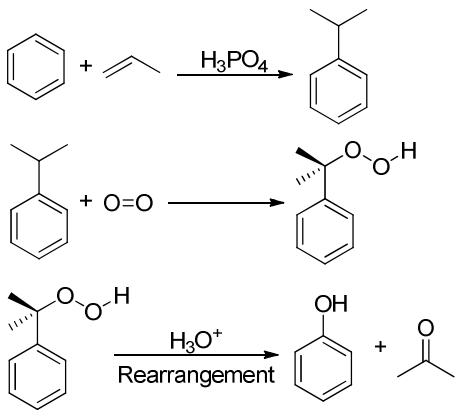
Scheme 5: Unsuccessful substrate scope.

In order to develop the substrate scope of *N*-coupling partner, we engaged couples as carbazole/4-*tert*-butylphenol (**8**) and carbazole/di-tolylamine (**9**) with intention to form new C-N bonds (Scheme 5). Interestingly, the reactivity of carbazole, which refered as a good aminating agent in our previous reports, became inexistent without metallic species. In the same manner, di-arylamines coupled with phenol (**7**) did not afford expected amino-phenol. These unsuccessful examples could indicate that the strained cyclic geometry of phenothiazines and phenoxazines is crucial for the reactivity to occur. Indeed, the butterfly shaped structure may facilitate the oxidation step during the reaction, or account as higher electrophile once it is oxidized, and render easier the approach of the nucleophile. Studies comparing bond dissociation energy (BDE) of secondary aromatic amines point out a particular low BDE for phenothiazines and phenoxazines comparing to diarylamines[9].

4.2.3. Discussion.

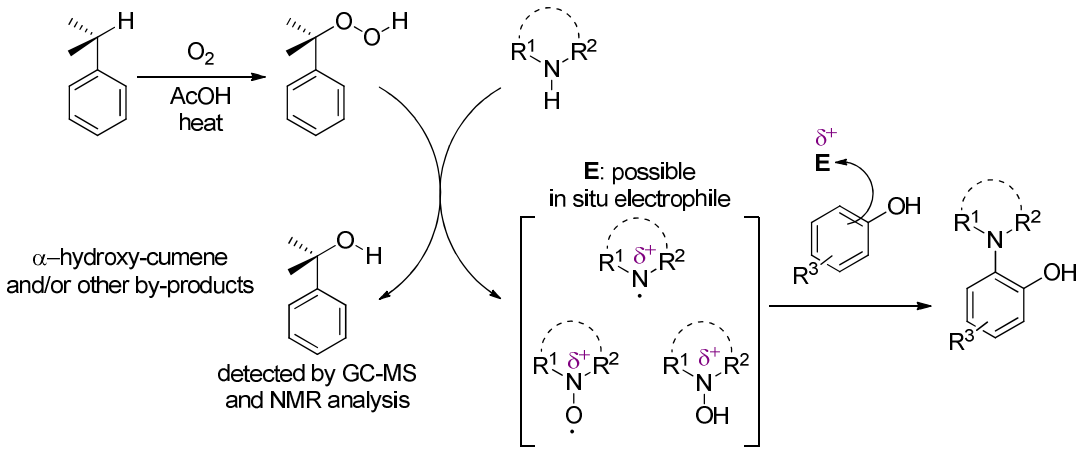
4.2.3.1. Elements of mechanism.

In the course of the optimization, we studied the role of solvents in the reaction. Interestingly, changing cumene to chlorobenzene decreased significantly the formation of the product. We suspected that the benzylic position, particularly suitable for radicals is crucial for the initiation of the reactivity. The cumene process[10], which affords phenol and acetone from cumene and propylene, could describe the first steps of the mechanism (Scheme 6).



Scheme 6: Reaction scheme of industrial Hock process for phenol and acetone synthesis.

In this scenario, cumene could be oxidized by O_2, a step facilitated by acetic acid. Stable α-peroxo-species might be transferred to the nitrogen of the phenothiazines. This oxidation step could be sufficient to reverse the philicity of amines. Simultaneously, phenol, known to be a good nucleophile for S_EAr reaction could attack the newly formed *N*-electrophile and afford the coupling product. Our hypothesis is supported by a detection of α-hydroxy-cumene in several GC-MS samples but also by NMR analysis. We suggest a mechanism such as described scheme 7.

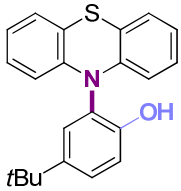
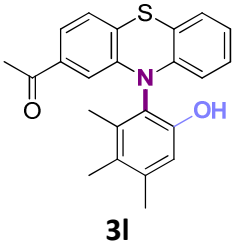


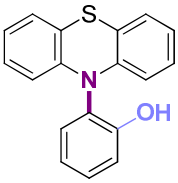
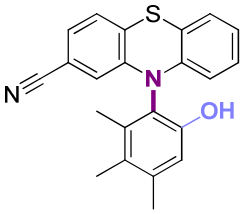
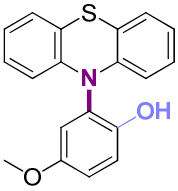
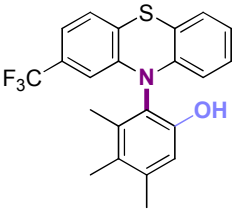
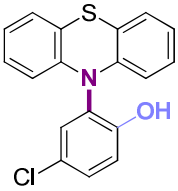
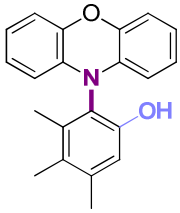
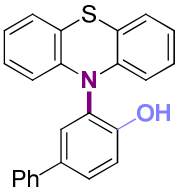
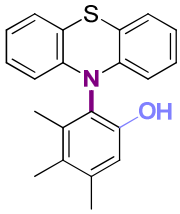
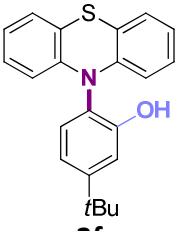
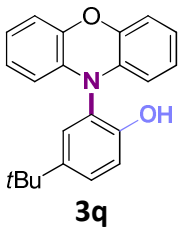
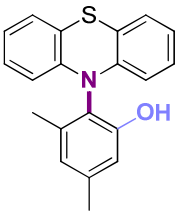
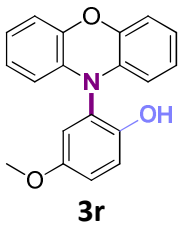
Scheme 7: Hypothetical mechanism for the dehydrogenative amination of phenol.

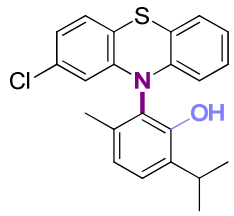
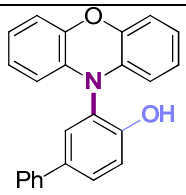
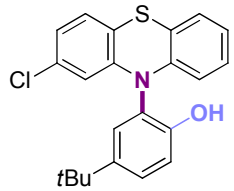
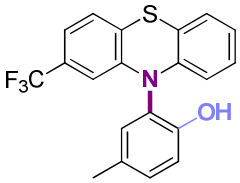
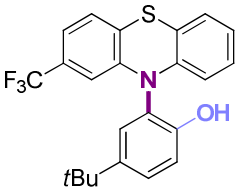
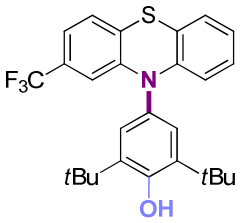
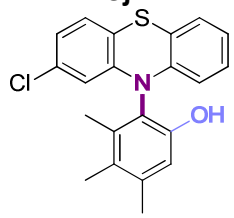
4.2.3.2. On the strength of Hydrogen bond.

With this new class of compounds in hand, we decided to performed IR analysis for each compounds (**3a**-**3u**) in order to evaluate the strength of the suspected intramolecular hydrogen bond. Results are presented table 3.

Table 3: Vibration frequency evolution of O-H bond with electronic effects.

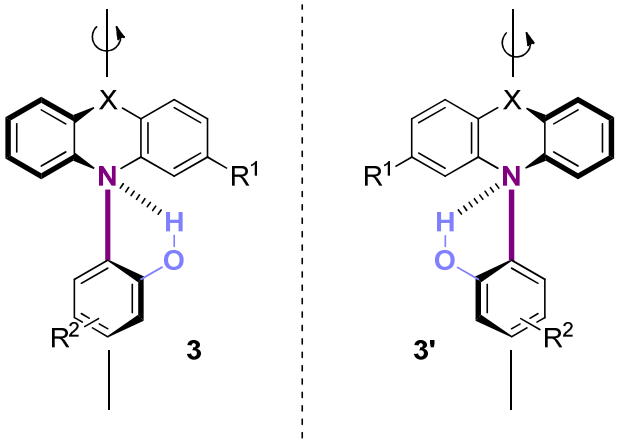
Product	**ν** (cm^{-1})	**Product**	**ν** (cm^{-1})
 **3a**	3401	 **3l**	3313

Product	**v** (cm^{-1})	Product	**v** (cm^{-1})
 **3b**	3458	 **3m**	3362
 **3c**	3379	 **3n**	3499
 **3d**	3376	 **3o**	3459
 **3e**	3383	 **3p**	3448
 **3f**	3539	 **3q**	3445
 **3g**	*Ortho*: 3479 *Para*: 3572	 **3r**	3449

Product	**v** (cm^{-1})	Product	**v** (cm^{-1})
 **3h**	*Ortho*: 3481 *Para*: 3526	 **3s**	3409
 **3i**	3361	 **3t**	3449
 **3j**	3412	 **3u**	3624
 **3k**	3474	ArOH	3600-3650

The theoretical IR value of O-H stretching vibration is typically 3600-3650 cm^{-1} for phenols. Surprisingly, the large O-H bond vibration frequency is in the range of 3300-3550 cm-1 in the case of the *ortho*-functionalized products. By comparison, the *para*-functionalized product **3u** showed a high 3624 cm^{-1} value for the O-H stretching bond corresponding to the theoretical value. Likewise, we obtained a difference of 100 cm^{-1} between the *ortho*- and *para*-**3g** products. (Only 50 cm^{-1} were observed between the *ortho*- and *para*-**3h** products. Nevertheless, we consider this example as biased because of probable chlorine interaction).

With these results, we postulate the probable existence of intramolecular hydrogen bond O-H···N. Indeed, these lower vibration frequency values in presence of *ortho*-*N*-substituents could be explained by a non-covalent bond which rendered the molecule more rigid. In theory, EWG on the phenol coupled with EDG on the phenothiazine would give best results. If we consider unbiased molecules such as the product based on *p*-chlorophenol **3d** or *p*-phenylphenol **3e**, we obtained lowest values: 3376 and 3383 respectively. Further studies will be undertaken to confirm this hypothesis. To demonstrate the presence of such an interaction, we are currently working on the synthesis and isolation of a potential chiral product based on unsymmetrical phenothiazine. Collecting this data would allow solving the chirality presented scheme 8.



Scheme 8: Expected isolable diastereomers products.

4.3. Conclusion and outlooks.

In summary, we have developed a system of metal free amination of phenols. This protocol based on exclusive organic O_2 activation is expected to change the way nitrogen reactivity is apprehended in C-N bond forming reactions. This dehydrogenative amination reaction respects our objectives since it does not require chelating directing group or an additional step of pre-activation or pre-oxidation of starting materials. We plan to develop new cross-coupling amination reactions based on that concept. We expect to reach better selectivity by the addition of transition metals. The next obvious challenge will be to further expand the scope of *N*-aminating agents.

We are currently preparing chiral products to prove the existence of this intramolecular interaction. The strength of this intramolecular N··H-O interaction will be studied more deeply. Finally, we would like to test this new class of compounds as potential new class of ligands in asymmetric catalysis.

4.4. References.

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4.5. Experimental section.

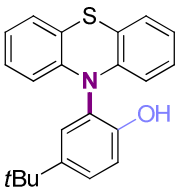
4.5.1. General Information.

All reactions were carried out in dried reaction vessels with **sealed** Teflon screw caps under **oxygen**, unless otherwise specified. NMR spectra were obtained on Bruker AMX 400 or on Bruker Avance 600 systems using $CDCl_3$, $(CD_3)_2SO$, or C_6D_6 as solvents, with proton and carbon resonances at 400/600 MHz and 101/151 MHz, respectively. Coupling constants (*J*) are quoted in Hz. Flash chromatography was performed on silica gel (40-63 mesh) by standard technique. GC-MS spectra were recorded on a Bruker 436-GC/SCION SQ Premium EI, 230 V, The major signals are quoted in m/z with the relative intensity in parentheses. The method used starts with the injection temperature T0. After holding this temperature for 3 min, the column is heated to temperature T1 (ramp) and this temperature is held for an additional time t. Method: 50_40: T0 = 50 °C, T1 = 320 °C, ramp = 40 °C/min; t = 5 min. Substrates were purchased either from Sigma Aldrich, Acros, TCI, or ABCR. Product **6** was already characterized by us in a previous report.[8a]

4.5.2. Methods.

Standard conditions: Unless otherwise specified, the phenothiazine or phenoxazine (1 mmol scale), and the phenol (3 mmol), cumene (2.5 mL) and AcOH (0.5 mL) are united under air in a 170 mL reactor equipped with Teflon screw cap. The reactor is then flushed with oxygen atmosphere (1-2 min.), then sealed (tightly) and exposed to 130 (phenoxazine) or 150°C (phenothiazine) for 24 h. (magnetic stirring set to approx. 700 turns/min). The reactor is then cooled to room temperature. The crude is directly engaged (unless otherwise specified) on SiO_2 gel column chromatography for purification. The expected cross-coupling products are generally the most apolar species of their respective reaction mixture, with Rf typically comprised between 0.3 and 0.7 in the given solvent systems.

4.5.3. Product Characterization.



Chemical Formula: $C_{22}H_{21}NOS$
Exact Mass: 347,13
Molecular Weight: 347,47
m/z: 347.13 (100.0%), 348.14 (24.1%), 349.13 (4.6%), 349.14 (3.2%), 348.13 (1.2%), 350.13 (1.1%)
Elemental Analysis: C, 76.04; H, 6.09; N, 4.03; O, 4.60; S, 9.23

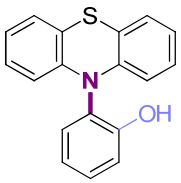
3a. From phenothiazine and 4-*tert*-butylphenol. The reactor is cooled to room temperature and the crude mixture is filtrated with dichloromethane over a plug of silica gel. The concentrate is purified by SiO_2 gel column chromatography hexane/ethyl acetate (17:3). Isolated yield: 63% (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.74 (s, OH), 7.39 (dd, 1H, ^3J = 8.4 Hz, J = 2.4 Hz), 7.15 (d, 1H, J = 2.4 Hz), 7.06 (d, 1H, ^3J = 8.8 Hz), 6.99 (dd, 2H, ^3J = 7.6 Hz, J = 1.6 Hz), 6.91 (~td, 2H, ^3J = 7.8 Hz, J = 1.5 Hz), 6.80 (~td, 2H, ^3J = 7.5 Hz, J = 1.1 Hz), 6.05 (dd, 2H, ^3J = 8.0 Hz, J = 1.2 Hz), 1.25 (s, 9H, *t*Bu).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 153.02 (s, C_{quat}), 143.68 (s, C_{quat}), 143.00 (s, C_{quat}), 127.40 (s, CH), 127.24 (s, CH), 126.85 (s, CH), 126.17 (s, CH), 125.66 (s, C_{quat}), 122.09 (s, CH), 118.35 (s, C_{quat}), 116.65 (s, CH), 115.33 (s, CH), 33.82 (s, C_{quat}), 31.29 (s, *t*Bu).

IR (neat, cm^{-1}): v: 3401 (broad), 3189 (broad), 3060, 2960, 2866, 1587, 1572, 1503, 1461, 1443, 1364, 1345, 1308, 1285, 1238, 1216, 1172, 1158, 1044, 967, 925, 820, 729.

EI-HRMS: mass spectrometry: m/z calc. 347.1344 $[C_{22}H_{21}NOS]^{\bullet+}$, measured 347.1375.



Chemical Formula: $C_{18}H_{13}NOS$
Exact Mass: 291,07
Molecular Weight: 291,37
m/z: 291.07 (100.0%), 292.08 (19.7%), 293.07 (4.7%), 293.08 (2.0%), 292.07 (1.2%)
Elemental Analysis: C, 74.20; H, 4.50; N, 4.81; O, 5.49; S, 11.01

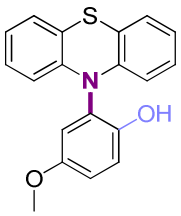
3b. METAL CATALYZED. From phenothiazine and phenol. 1.0 mmol of phenothiazine, 3.0 mmol of phenol, 5mol% $[Ru(norbornadiene)Cl_2]_n$, 1.0 eq $Cu(OAc)_2$, 2.0 mL C_2Cl_2, 0.5 mL cumene, 0.5 mL AcOH, were united in a Schlenk and flushed with O_2. The reaction was stirred at 130°C for 24h.. The reactor is cooled to room temperature and the crude mixture is filtrated with dichloromethane over a plug of silica gel. The concentrate is purified by SiO_2 gel column chromatography hexane/ethyl acetate (4:1). Isolated yield: 21% (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.95 (s, OH), 7.38 (dt, 1H, *J* = 1.6 Hz, ^3J = 7.7 Hz), 7.22 (dd, 1H, *J* = 1.6 Hz, ^3J = 7.7 Hz), 7.14 (dd, 1H, *J* = 1.2 Hz, ^3J = 8.2 Hz), 7.03-6.97 (m, 3H), 6.88 (dt, 2H, *J* = 1.6 Hz, ^3J = 7.8 Hz), 6.79 (dt, 2H, *J* = 1.2 Hz, ^3J = 7.4 Hz), 6.04 (dd, 2H, *J* = 1.0 Hz, ^3J = 8.2 Hz).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 155.55 (s, C_{quat}), 142.76 (s, C_{quat}), 131.33 (s, CH), 130.24 (s, CH), 127.19 (s, CH), 126.40 (s, C_{quat}), 126.16 (s, CH), 122.13 (s, CH), 121.01 (s, CH), 118.24 (s, C_{quat}), 117.24 (s, CH), 115.26 (s, CH).

IR (neat, cm^{-1}): v: 3458 (broad), 3415 (broad), 3208 (broad), 3063, 2923, 2853, 1587, 1569, 1491, 1460, 1441, 1340, 1307, 1292, 1264, 1229, 1210, 1171, 1147, 1102, 1032, 966, 945, 931, 850, 817, 752.

EI-HRMS: mass spectrometry: m/z calc. 291.0718 $[C_{18}H_{13}NOS]^{\bullet+}$, measured 291.0743.



Chemical Formula: $C_{19}H_{15}NO_2S$
Exact Mass: 321,08
Molecular Weight: 321,39
m/z: 321.08 (100.0%), 322.09 (20.8%), 323.08 (4.6%), 323.09 (2.6%), 322.08 (1.2%)
Elemental Analysis: C, 71.00; H, 4.70; N, 4.36; O, 9.96; S, 9.98

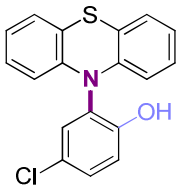
3c. From phenothiazine and 4-methoxyphenol. Reaction temperature: 130°C. The reactor is cooled to room temperature and the crude mixture is filtrated with dichloromethane over a plug of silica gel. The concentrate is purified by SiO_2 gel column chromatography hexane/DCM (1:1) and a second time with hexane/ethyl acetate (4:1). Isolated yield: 35% (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.47 (s, OH), 7.07 (d, 1H, ^3J = 9.2 Hz), 7.00-6.97 (m, 3H), 6.93-6.88 (m, 2H), 6.81-6.78 (m, 3H), 6.09 (dd, 2H, ^3J = 8.0 Hz, J = 1.0 Hz), 3.70 (s, 3H, OCH_3).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 153.46 (s, C_{quat}), 149.23 (s, C_{quat}), 142.62 (s, C_{quat}), 127.23 (s, CH), 126.38 (s, C_{quat}), 126.13 (s, CH), 122.16 (s, CH), 118.19 (s, C_{quat}), 117.74 (s, CH), 116.17 (s, CH), 115.32 (s, CH), 115.30 (s, CH), 55.48 (s, OCH_3).

IR (neat, cm^{-1}): v: 3379 (broad), 3199 (broad), 2954, 2929, 2833, 1621, 1590, 1569, 1497, 1461, 1438, 1345, 1308, 1281, 1235, 1217, 1154, 1104, 1076, 1036, 975, 966, 929, 920, 849, 810, 781, 743, 736, 720.

EI-HRMS: mass spectrometry: m/z calc. 321.0823 $[C_{19}H_{15}NO_2S]^{\bullet+}$, measured 321.0848.



Chemical Formula: $C_{18}H_{12}ClNOS$
Exact Mass: 325,03
Molecular Weight: 325,81
m/z: 325.03 (100.0%), 327.03 (36.6%), 326.04 (19.6%), 328.03 (7.5%), 327.04 (2.2%), 329.03 (1.6%), 326.03 (1.2%)
Elemental Analysis: C, 66.36; H, 3.71; Cl, 10.88; N, 4.30; O, 4.91; S, 9.84

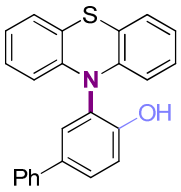
3d. METAL CATALYSED. From phenothiazine and 4-chlorophenol. 1.0 mmol of phenothiazine, 3.0 mmol of 4-chlorophenol, 5mol% $[Ru(norbornadiene)Cl_2]_n$, 1.0 eq $Cu(OAc)_2$, 2.0 mL C_2Cl_2, 0.5 mL cumene, 0.5 mL AcOH, were united in a Schlenk and flushed with O_2. The reaction was stirred at 130°C for 24h.. The reactor is cooled to room temperature and the crude mixture is filtrated with dichloromethane over a plug of silica gel. The concentrate is purified by SiO_2 gel column chromatography hexane/ethyl acetate (9:1). Isolated yield: 51% (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.31 (s, OH), 7.44 (dd, 1H, *J* = 2.7 Hz, *J* = 8.8 Hz), 7.35 (d, 1H, *J* = 2.6 Hz), 7.16 (d, 1H, *J* = 8.8 Hz), 7.00 (dd, 2H, *J* = 1.5 Hz, ^3J = 7.5 Hz), 6.92 (~t, 2H, ^3J = 7.8 Hz), 6.81 (~t, 2H, ^3J = 7.4 Hz), 6.06 (dd, 2H, *J* = 0.9 Hz, *J* = 8.2 Hz).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 154.85 (s, C_{quat}), 142.28 (s, C_{quat}), 131.10 (s, CH), 130.19 (s, CH), 127.56 (s, C_{quat}), 127.31 (s, CH), 126.26 (s, CH), 123.43 (s, C_{quat}), 122.41 (s, CH), 118.71 (s, CH), 118.40 (s, C_{quat}), 115.21 (s, CH).

IR (neat, cm^{-1}): v: 3376 (broad), 3129 (broad), 3062 (broad), 2924, 2853, 1887 (small), 1766 (small), 1587, 1573, 1482, 1462, 1440, 1338, 1306, 1298, 1279, 1210, 1167, 1088, 1041, 1010, 954, 924, 872, 845, 819, 737, 712, 659, 683.

EI-HRMS: mass spectrometry: m/z calc. 325.0328 ^{35}Cl 327.0305 ^{37}Cl $[C_{18}H_{12}ClNOS]^{\bullet+}$, measured 325.0338 ^{35}Cl 327.0305 ^{37}Cl.



Chemical Formula: $C_{24}H_{17}NOS$
Exact Mass: 367,10
Molecular Weight: 367,46
m/z: 367.10 (100.0%), 368.11 (26.2%), 369.10 (4.6%), 369.11 (3.7%), 370.10 (1.2%), 368.10 (1.2%)
Elemental Analysis: C, 78.45; H, 4.66; N, 3.81; O, 4.35; S, 8.73

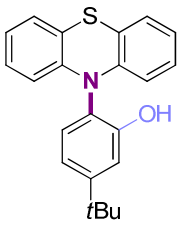
3e. From phenothiazine and 4-phenylphenol. The reactor is cooled to room temperature and the crude mixture is filtrated with dichloromethane over a plug of silica gel. The concentrate is purified by SiO_2 gel column chromatography hexane/ethyl acetate (17:3). Isolated yield: 47% (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.16 (s, OH), 7.74 (dd, 1H, ^3J = 8.4 Hz, J = 2.0 Hz), 7.65 (d, 2H, ^3J = 7.2 Hz), 7.55 (d, 1H, J = 2.4 Hz), 7.40 (t, 2H, ^3J = 7.6 Hz), 7.28 (t, 1H, ^3J = 7.2 Hz), 7.24 (d, 1H, ^3J = 8.4 Hz), 7.00 (dd, 2H, ^3J = 7.2 Hz, J = 0.8 Hz), 6.92 (~t, 2H, ^3J = 7.7 Hz), 6.81 (~t, 2H, ^3J = 7.4 Hz), 6.14 (d, 2H, ^3J = 8.0 Hz).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 155.15 (s, C_{quat}), 142.74 (s, C_{quat}), 138.85 (s, C_{quat}), 133.09 (s, C_{quat}), 129.19 (s, CH), 128.86 (s, CH), 128.29 (s, CH), 127.28 (s, CH), 126.83 (s, CH), 126.20 (s, CH), 125.98 (s, CH), 122.20 (s, CH), 118.32 (s, C_{quat}), 117.83 (s, CH), 115.34 (s, CH). One C_{quat} is overlapped.

IR (neat, cm^{-1}): v: 3383 (broad), 3220 (broad), 3062, 3032, 1589, 1574, 1509, 1484, 1459, 1442, 1313, 1296, 1283, 1271, 1232, 1205, 1162, 1111, 1077, 1042, 926, 910, 826, 748, 695.

EI-HRMS: mass spectrometry: m/z calc. 367.1031 $[C_{24}H_{17}NOS]^{\bullet+}$, measured 367.1056.



Chemical Formula: $C_{22}H_{21}NOS$
Exact Mass: 347,13
Molecular Weight: 347,47
m/z: 347.13 (100.0%), 348.14 (24.1%), 349.13 (4.6%), 349.14 (3.2%), 348.13 (1.2%), 350.13 (1.1%)
Elemental Analysis: C, 76.04; H, 6.09; N, 4.03; O, 4.60; S, 9.23

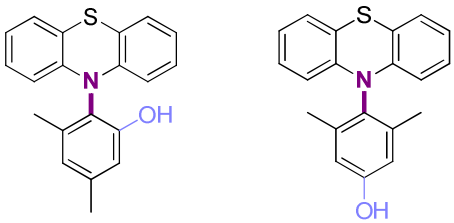
3f. From phenothiazine and 3-*tert*-butylphenol. The reactor is cooled to room temperature and the crude mixture is filtrated with dichloromethane over a plug of silica gel. The concentrate is purified by SiO_2 gel column chromatography hexane/ethyl acetate (17:3). Isolated yield: 33% (yellow sticky foam).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.94 (s, OH), 7.14 (d, *J* = 2.1 Hz, 1H), 7.11 (d, ^3J = 8.1 Hz, 1H), 7.03 (dd, 1H, ^3J = 8.2 Hz, *J* = 2.2 Hz), 6.97 (dd, 2H, ^3J = 7.6 Hz, *J* = 1.6 Hz), 6.88 (~td, ^3J = 7.8 Hz, *J* = 1.5 Hz, 2H), 6.78 (~td, ^3J = 7.4 Hz, *J* = 1.1 Hz, 2H), 6.03 (dd, 2H, ^3J = 8.2 Hz, *J* = 1.0 Hz), 1.31 (s, 9H, *t*Bu).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 154.76 (s, C_{quat}), 153.10 (s, C_{quat}), 142.89 (s, C_{quat}), 130.55 (s, CH), 127.18 (s, CH), 126.18 (s, CH), 123.64 (s, C_{quat}), 122.16 (s, CH), 118.22 (s, C_{quat}), 118.01 (s, CH), 115.24 (s, CH), 113.97 (s, CH), 34.42 (s, C_{quat}), 31.06 (s, CH_3, *t*Bu).

IR (neat, cm^{-1}): v: 3539, 3494, 3062, 2958, 2864, 1574, 1506, 1481, 1459, 1443, 1437, 1394, 1363, 1297, 1269, 1256, 1234, 1198, 1172, 1124, 1093, 1072, 1041, 945, 914, 901, 884, 831, 815, 729, 659.

EI-HRMS: mass spectrometry: m/z calc. 347.1344 $[C_{22}H_{21}NOS]^{\bullet+}$, measured 347.1359.



Chemical Formula: $C_{20}H_{17}NOS$
Exact Mass: 319,10
Molecular Weight: 319,42
m/z: 319.10 (100.0%), 320.11 (21.9%), 321.10 (4.6%), 321.11 (2.7%), 320.10 (1.2%)
Elemental Analysis: C, 75.20; H, 5.36; N, 4.39; O, 5.01; S, 10.04

3g. From phenothiazine and 3,5-dimethylphenol. The reactor is cooled to room temperature and the crude mixture is filtrated with dichloromethane over a plug of silica gel. The concentrate is purified by SiO_2 gel column chromatography hexane/ethyl acetate (17:3). Isolated yield: 84%.

Ortho-functionalized product: 52% isolated yield (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.67 (s, OH), 6.94 (dd, 2H, ^3J = 7.4 Hz, J = 1.0 Hz), 6.86 (~td, 2H, ^3J = 7.8 Hz, J = 1.2 Hz), 6.77-6.72 (m, 4H), 6.00 (d, 2H, ^3J = 8.0 Hz), 2.28 (s, CH_3), 2.07 (s, CH_3).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 155.72 (s, C_{quat}), 142.19 (s, C_{quat}), 139.36 (s, C_{quat}), 138.00 (s, C_{quat}), 127.75 (s, CH), 126.53 (s, CH), 123.24 (s, C_{quat}), 123.09 (s, CH), 122.49 (s, CH), 118.59 (s, C_{quat}), 115.44 (s, CH), 115.17 (s, CH), 21.42 (s, CH_3), 17.41 (s, CH_3).

IR (neat, cm^{-1}): v: 3479 (broad), 2920 (broad), 1619, 1571, 1499, 1460, 1441, 1334, 1311, 1247, 1206, 1156, 1042, 968, 928, 840, 738.

EI-HRMS: mass spectrometry: m/z calc. 319.1031 $[C_{20}H_{17}NOS]^{\bullet+}$, measured 319.1035.

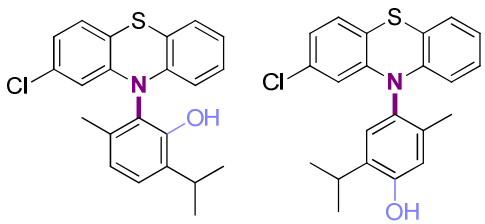
Para-functionalized product: 32% isolated yield (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.62 (s, OH), 6.92 (d, 2H, ^3J = 6.8 Hz), 6.85 (~t, 2H, ^3J = 7.4 Hz), 6.75 (~t, 2H, ^3J = 7.2 Hz), 6.72 (s, 2H), 5.85 (d, 2H, ^3J = 8.0 Hz), 2.02 (s, 2*CH_3).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 156.98 (s, C_{quat}), 141.12 (s, C_{quat}), 138.42 (s, C_{quat}), 127.98 (s, C_{quat}), 127.55 (s, CH), 126.25 (s, CH), 122.18 (s, CH), 117.28 (s, C_{quat}), 115.97 (s, CH), 113.75 (s, CH), 17.53 (s, CH_3).

IR (neat, cm^{-1}): v: 3572, 1595, 1459, 1436, 1312, 1243, 1182, 1144, 1031, 853, 747.

EI-HRMS: mass spectrometry: m/z calc. 319.1031 $[C_{20}H_{17}NOS]^{\bullet+}$, measured 319.1036.



Chemical Formula: $C_{22}H_{20}ClNOS$
Exact Mass: 381,10
Molecular Weight: 381,92
m/z: 381.10 (100.0%), 383.09 (36.5%), 382.10 (24.1%), 384.10 (7.8%), 383.10 (3.2%), 385.09 (1.5%), 384.09 (1.5%), 382.09 (1.2%), 385.10 (1.1%)
Elemental Analysis: C, 69.19; H, 5.28; Cl, 9.28; N, 3.67; O, 4.19; S, 8.40

3h. From 2-chlorophenothiazine and thymol. The reactor is cooled to room temperature and the crude mixture is filtrated with dichloromethane over a plug of silica gel. The concentrate is purified by SiO_2 gel column chromatography hexane/ethyl acetate (17:3) then a second time with hexane/DCM (3:1). Isolated yield: 83%.

Ortho-functionalized product: 31% (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.12 (s, OH), 7.24 (d, 1H, ^{3}J = 7.6 Hz), 6.96 (d, 1H, ^{3}J = 8.2 Hz), 7.56 (dd, 1H, ^{3}J = 7.6 Hz, J = 1.5 Hz), 6.93-6.86 (m, 2H), 6.82-6.78 (m, 2H), 5.92 (dd, 1H, ^{3}J = 8.0 Hz, J = 1.2 Hz), 5.82 (d, 1H, J = 2.0 Hz), 3.31 (septuplet, 1H, ^{3}J = 6.8 Hz), 2.10 (s, 3H, CH_3), 1.23 (d, 1*CH_3, ^{3}J = 6.8 Hz), 1.21 (d, 1*CH_3, ^{3}J = 6.8 Hz).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 152.43 (s, C_{quat}), 142.79 (s, C_{quat}), 140.54 (s, C_{quat}), 134.23 (s, C_{quat}), 133.99 (s, C_{quat}), 131.48 (s, C_{quat}), 127.55 (s, CH), 127.21 (s, CH), 126.18 (s, CH), 126.12 (s, CH), 125.18 (s, C_{quat}), 122.73 (s, CH), 122.08 (s, CH), 121.54 (s, CH), 118.14 (s, C_{quat}), 117.61 (s, C_{quat}), 115.02 (s, CH), 114.03 (s, CH), 26.24 (s, CH), 22.74 (s, CH_3), 22.46 (s, CH_3), 16.85 (s, CH_3).

IR (neat, cm^{-1}): v: 3481 (broad), 3058, 2963, 2925, 2869, 1611, 1590, 1566, 1499, 1483, 1455, 1438, 1424, 1393, 1345, 1285, 1266, 1239, 1192, 1168, 1145, 1127, 1104, 1081, 1067, 1043, 978, 952, 942, 851, 817, 801, 778, 745, 713, 670.

ESI H.R. mass spectrometry: m/z calc. 381.0954 $[C_{22}H_{20}ClNOS]^{\bullet+}$, measured 381.0970.

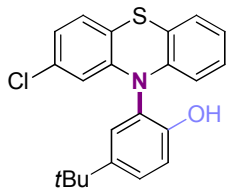
Para-functionalized product: 52% (yellow sticky solid)

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.75 (s, OH), 7.02-6.98 (m, 3H), 6.93-6.89 (m, 2H), 6.85-6.80 (m, 2H), 5.99 (dd, 1H, *J* = 8.4 Hz, *J* = 1.2 Hz), 5.88 (d, 1H, *J* = 2.4 Hz), 3.21 (septuplet, 1H, ^{3}J = 6.8 Hz), 1.98 (s, CH_3), 1.16 (d, 6H, ^{3}J = 7.2 Hz).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 154.58 (s, C_{quat}), 144.23 (s, C_{quat}), 141.98 (s, C_{quat}), 135.00 (s, C_{quat}), 134.81 (s, C_{quat}), 131.70 (s, C_{quat}), 128.54 (s, C_{quat}), 127.75 (s, CH), 127.64 (s, CH), 127.56 (s, CH), 126.43 (s, CH), 122.81 (s, CH), 121.64 (s, CH), 117.99 (s, CH), 117.61 (s, C_{quat}), 117.06 (s, C_{quat}), 115.08 (s, CH), 114.01 (s, CH), 26.28 (s, CH), 23.39 (s, CH_3), 16.78 (s, CH_3).

IR (neat, cm^{-1}): v: 3526 (broad), 3425 (broad), 3059, 2960, 2924, 2868, 1616, 1591, 1565, 1508, 1460, 1439, 1411, 1392, 1341, 1293, 1236, 1160, 1126, 1100, 1041, 953, 909, 851, 797, 742.

ESI H.R. mass spectrometry: m/z calc. 381.0954 $[C_{22}H_{20}ClNOS]^{\bullet+}$, measured 381.0950.



Chemical Formula: $C_{22}H_{20}ClNOS$
Exact Mass: 381,10
Molecular Weight: 381,92
m/z: 381.10 (100.0%), 383.09 (36.5%), 382.10 (24.1%), 384.10 (7.8%), 383.10 (3.2%), 385.09 (1.5%), 384.09 (1.5%), 382.09 (1.2%), 385.10 (1.1%)
Elemental Analysis: C, 69.19; H, 5.28; Cl, 9.28; N, 3.67; O, 4.19; S, 8.40

3i. From 2-chlorophenothiazine and 4-*tert*-butylphenol. The reactor is cooled to room temperature and the crude mixture is filtrated with dichloromethane over a plug of silica gel.

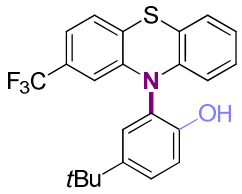
The concentrate is purified by SiO_2 gel column chromatography hexane/DCM (2:3). Isolated yield: 75% (white foam).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.89 (s, OH), 7.44 (dd, 1H, ^3J = 8.4 Hz, J = 2.4 Hz), 7.19 (d, 1H, J = 2.4 Hz), 7.09 (d, 1H, ^3J = 8.4 Hz), 7.05-7.01 (m, 2H), 6.96-6.91 (m, 1H), 6.88-6.82 (m, 2H), 6.05 (dd, 1H, ^3J = 8.0 Hz, J = 0.4 Hz), 5.98 (d, 1H, J = 2.0 Hz), 1.26 (s, 9H, *t*Bu)

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 152.78 (s, C_{quat}), 144.38 (s, C_{quat}), 144.01 (s, C_{quat}), 142.31 (s, C_{quat}), 131.67 (s, C_{quat}), 127.59 (s, CH), 127.52 (s, CH), 127.35 (s, CH), 127.26 (s, CH), 126.38 (s, CH), 125.14 (s, C_{quat}), 122.81(s, CH), 121.68 (s, CH), 118.14 (s, C_{quat}), 117.67 (s, C_{quat}), 116.86 (s, CH), 115.72 (s, CH), 114.73 (s, CH), 33.94 (s, C_{quat}), 31.31 (s, *t*Bu).

IR (neat, cm^{-1}): v: 3361, 3172, 2963, 1591, 1567, 1504, 1459, 1439, 1392, 1363, 1312, 1300, 1285, 1238, 1220, 1159, 1126, 1106, 1039, 968, 944, 851, 831, 819, 803, 783, 748.

EI-HRMS: mass spectrometry: m/z calc. 381.0954 $[C_{22}H_{20}ClNOS]^{\bullet+}$, measured 381.1005.



Chemical Formula: $C_{23}H_{20}F_3NOS$
Exact Mass: 415,12
Molecular Weight: 415,47
m/z: 415.12 (100.0%), 416.13 (25.1%), 417.12 (4.8%), 417.13 (3.2%), 416.12 (1.2%), 418.12 (1.1%)
Elemental Analysis: C, 66.49; H, 4.85; F, 13.72; N, 3.37; O, 3.85; S, 7.72

3j. From 2-trifluorophenothiazine and 4-*tert*-butylphenol. The reactor is cooled to room temperature and the crude mixture is filtrated with dichloromethane over a plug of silica gel. The concentrate is purified by SiO_2 gel column chromatography hexane/ethyl acetate (18:2 to 17:3). Isolated yield: 87% (yellow sticky foam).

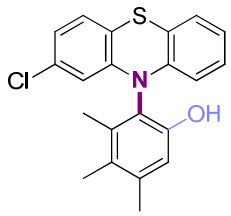
^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.91 (s, OH), 7.43 (dd, 1H, ^3J = 8.4 Hz, J = 2.4 Hz), 7.22-7.20 (m, 2H), 7.11-7.09 (m, 2H), 7.02 (dd, 1H, ^3J = 7.6 Hz, J = 1.2 Hz), 6.95 (~td, 1H, ^3J = 7.8 Hz, J = 1.5 Hz), 6.80 (~td, 1H, ^3J = 7.3 Hz, J = 0.8 Hz), 6.20 (s, 1H), 6.05 (d, 1H, ^3J = 8.0 Hz), 1.25 (s, 9H, *t*Bu).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 152.69 (s, C_{quat}), 143.97 (s, C_{quat}), 143.52 (s, C_{quat}), 142.12 (s, C_{quat}), 127.77 (s, CH), 127.75 (q, ^{2}J = 31.9 Hz, C_{quat}), 127.37 (s, CH), 127.29 (s, CH), 126.96 (s, CH), 126.36 (s, CH), 124.84 (s, C_{quat}), 124.16 (s, C_{quat}), 123.87 (q, ^{1}J = 273.5 Hz, C_{quat}), 122.90 (s, CH), 118.50 (q, ^{3}J = 3.6 Hz, CH), 117.37 (s, C_{quat}), 116.85 (s, CH), 115.68 (s, CH), 110.70 (q, ^{3}J = 4.6 Hz, CH), 33.86 (s, C_{quat}), 31.20 (s, *t*Bu).

^{19}F NMR (376.5 MHz, DMSO-d_6) δ (ppm): -61.80 (s, CF_3).

IR (neat, cm^{-1}): v: 3412 (broad), 2962, 2907, 2870, 1602, 1570, 1507, 1467, 1442, 1411, 1365, 1326, 1286, 1272, 1236, 1212, 1197, 1164, 1102, 1086, 1041, 970, 948, 875, 818, 745, 733.

EI-HRMS: mass spectrometry: m/z calc. 415.1218 $[C_{23}H_{20}F_3NOS]^{\bullet+}$, measured 415.1219.



Chemical Formula: $C_{21}H_{18}ClNOS$
Exact Mass: 367,08
Molecular Weight: 367,89
m/z: 367.08 (100.0%), 369.08 (37.0%), 368.08 (23.9%), 370.08 (8.6%), 369.09 (2.5%), 371.07 (1.5%), 371.08 (1.1%)
Elemental Analysis: C, 68.56; H, 4.93; Cl, 9.64; N, 3.81; O, 4.35; S, 8.72

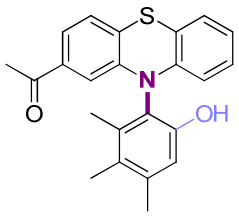
3k. From 2-chloro-phenothiazine and 3,4,5-trimethylphenol. The crude mixture is purified by SiO_2 gel column chromatography hexane/Ethyl Acetate (9:1). Isolated yield: 65% (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.56 (s, OH), 6.99 (d, ^{3}J = 8.3 Hz, 1H), 6.98 (dd, ^{3}J = 7.6 Hz, *J* = 1.5 Hz, 1H), 6.89 (~td, ^{3}J = 7.8 Hz, *J* = 1.6 Hz, 1H), 6.84-6.78 (aromatic area, 3H), 5.99 (dd, ^{3}J = 8.2 Hz, *J* = 0.8 Hz, 1H), 5.92 (d, *J* = 2.2 Hz, 1H), 2.27 (s, CH_3), 2.11 (s, CH_3), 2.10 (s, CH_3).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 152.42 (s, C_{quat}), 143.50 (s, C_{quat}), 141.29 (s, C_{quat}), 137.82 (s, C_{quat}), 135.55 (s, C_{quat}), 131.65 (s, C_{quat}), 127.53 (s, CH), 127.34 (s, CH), 126.95 (s, C_{quat}), 126.21 (s, CH), 122.70 (s, CH), 122.48 (s, C_{quat}), 121.51 (s, CH), 117.98 (s, C_{quat}), 117.47 (s, C_{quat}), 115.51 (s, CH), 115.39 (s, CH), 114.29 (s, CH), 20.55 (s, CH_3), 15.25 (s, CH_3), 14.05 (s, CH_3).

IR (neat, cm^{-1}): ν: 3474 (broad), 3312 (broad), 3058, 2921, 2855, 1583, 1566, 1464, 1437, 1393, 1337, 1301, 1287, 1234, 1211, 1172, 1126, 1107, 1071, 1041, 1000, 951, 901, 850, 795, 769, 744, 706, 670.

EI-HRMS: mass spectrometry: *m/z* calc. 367.0798 $[C_{21}H_{18}ClNOS]^{\bullet+}$, measured 367.0812.



Chemical Formula: $C_{23}H_{21}NO_2S$
Exact Mass: 375,13
Molecular Weight: 375,48
m/z: 375.13 (100.0%), 376.13 (26.1%), 377.13 (5.2%), 377.14 (3.0%), 378.13 (1.2%)
Elemental Analysis: C, 73.57; H, 5.64; N, 3.73; O, 8.52; S, 8.54

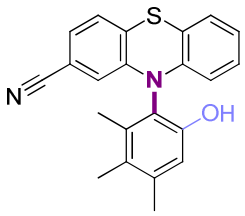
3l. From 2-acetylphenothiazine and 3,4,5-trimethylphenol. The reactor is cooled to room temperature and the crude mixture is filtrated with dichloromethane over a plug of silica gel. The concentrate is purified by SiO_2 gel column chromatography hexane/ethyl acetate (18:2 to 15:5). Isolated yield: 92% (yellow foam).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.48 (s, OH), 7.40 (dd, 1H, *J* = 8.0 Hz, *J* = 1.6 Hz), 7.10 (d, 1H, *J* = 8.0 Hz), 6.97 (dd, 1H, *J* = 7.6 Hz, *J* = 1.6 Hz), 6.89-6.85 (m, 1H), 6.79-6.76 (m, 2H), 6.50 (d, 1H, *J* = 1.6 Hz), 5.94 (dd, 1H, *J* = 8.0 Hz, *J* = 1.0 Hz), 2.36 (s, 3H), 2.28 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 196.77 (s, C_{quat}), 152.61 (s, C_{quat}), 142.14 (s, C_{quat}), 141.46 (s, C_{quat}), 137.58 (s, C_{quat}), 135.84 (s, C_{quat}), 135.56 (s, C_{quat}), 127.74 (s, CH), 126.76 (s, C_{quat}), 126.16 (s, CH), 126.00 (s, CH), 125.57 (s, C_{quat}), 123.26 (s, CH), 122.65 (s, C_{quat}), 122.38 (s, CH), 117.23 (s, C_{quat}), 115.51 (s, CH), 115.27 (s, CH), 112.66 (s, CH), 26.37 (s, CH_3), 20.56 (s, CH_3), 15.27 (s, CH_3), 14.08 (s, CH_3).

IR (neat, cm^{-1}): v: 3313 (broad), 3061, 2919, 1654 (carbonyl), 1587, 1557, 1465, 1440, 1404, 1356, 1332, 1300, 1237, 1162, 1129, 1110, 1072, 1041, 995, 934, 880, 852, 805, 773, 748.

EI-HRMS: mass spectrometry: m/z calc. 375.1293 $[C_{23}H_{21}NO_2S]^{\bullet+}$, measured 375.1318.



Chemical Formula: $C_{22}H_{18}N_2OS$
Exact Mass: 358,11
Molecular Weight: 358,46
m/z: 358.11 (100.0%), 359.12 (24.0%), 360.11 (4.7%), 360.12 (3.2%), 359.11 (1.5%), 361.11 (1.1%)
Elemental Analysis: C, 73.71; H, 5.06; N, 7.82; O, 4.46; S, 8.95

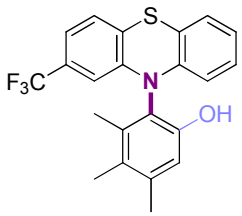
3m. From 2-cyano-phenothiazine and 3,4,5-trimethylphenol. The crude mixture is purified by SiO_2 gel column chromatography hexane/Ethyl Acetate (8:2). Isolated yield: 98% (bright yellow solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.61 (s, OH), 7.19 (dd, ^{3}J = 7.9 Hz, J = 1.4 Hz, 1H), 7.16 (d, ^{3}J = 7.9 Hz, 1H), 6.98 (dd, ^{3}J = 7.4 Hz, J = 1.4 Hz, 1H), 6.92 (~td, ^{3}J = 7.8 Hz, J = 1.5 Hz, 1H), 6.82 (m, 2H), 6.06 (d, J = 1.1 Hz, 1H), 5.96 (d, ^{3}J = 7.5 Hz, 1H), 2.28 (s, CH_3), 2.11 (s, 6H, 2*CH_3).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 152.26 (s, C_{quat}), 142.65 (s, C_{quat}), 140.86 (s, C_{quat}), 138.05 (s, C_{quat}), 135.54 (s, C_{quat}), 127.97 (s, CH), 127.10 (s, CH), 126.31 (s, CH), 126.06 (s, C_{quat}), 125.59 (s, CH), 122.99 (s, CH), 122.00 (s, C_{quat}), 118.72 (s, C_{quat}), 117.02 (s, C_{quat}), 116.21 (s, CH), 115.69 (s, CH), 115.42 (s, CH), 109.47 (s, C_{quat}), 20.57 (s, CH_3), 15.26 (s, CH_3), 14.02 (s, CH_3). One C_{quat} line is overlapped.

IR (neat, cm^{-1}): v: 3362 (large broad), 2916, 2857, 2231 (medium sharp, nitrile), 1589, 1555, 1492, 1460, 1439, 1419, 1399, 1333, 1300, 1265, 1240, 1127, 1108, 1071, 1062, 1042, 998, 985, 936, 862, 847, 810, 801, 774, 745, 713.

EI-HRMS: mass spectrometry: *m/z* calc. 358.1140 $[C_{22}H_{18}N_2OS]^{\bullet+}$, measured 358.1149.



Chemical Formula: $C_{22}H_{18}F_3NOS$
Exact Mass: 401,11
Molecular Weight: 401,44
m/z: 401.11 (100.0%), 402.11 (24.8%), 403.10 (4.5%), 403.11 (3.2%), 404.11 (1.2%)
Elemental Analysis: C, 65.82; H, 4.52; F, 14.20; N, 3.49; O, 3.99; S, 7.99

3n. From 2-trifluoromethylphenothiazine and 3,4,5-trimethylphenol. The crude mixture is purified by SiO_2 gel column chromatography hexane/Ethyl Acetate (9:1). Isolated yield: 99% (white to light yellow, foamy to crispy solid).

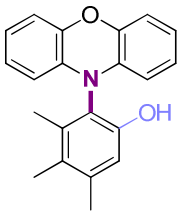
^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.62 (s, OH), 7.19 (d, ^3J = 7.8 Hz, 1H), 7.09 (d, ^3J = 7.8 Hz, 1H), 7.00 (d, ^3J = 7.3 Hz, 1H), 6.90 (~t, ^3J = 7.6 Hz, 1H), 6.82 (m, 2H), 6.16 (s, 1H), 5.98 (d, ^3J = 8.0 Hz, 1H), 2.27 (s, CH_3), 2.12 (s, CH_3), 2.10 (s, CH_3).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 152.52 (s, C_{quat}), 142.78 (s, C_{quat}), 141.32 (s, C_{quat}), 137.94 (s, C_{quat}), 135.49 (s, C_{quat}), 127.83 (q, ^2J = 31.0 Hz, CF_3-C_{quat}), 127.80 (s, CH), 126.95 (s, C_{quat}), 126.91 (s, CH), 126.30 (s, CH), 124.20 (~q, ^4J = 1.5 Hz, C_{quat}), 123. 90 (q, ^1J = 272.6 Hz, C_{quat}, CF_3), 122.90 (s, CH), 122.28 (s, C_{quat}), 118.48 (q, ^3J = 3.6 Hz, CH), 117.50 (s, C_{quat}), 115.48 (s, CH), 115.44 (s, CH), 110.41 (q, ^3J = 3.6 Hz, CH), 20.54 (s, CH_3), 15.23 (s, CH_3), 14.01 (s, CH_3).

^{19}F NMR (376.5 MHz, DMSO-d_6) δ (ppm): -61.62 (s, CF_3).

IR (neat, cm^{-1}): v: 3499 (small broad), 3419 (small broad), 2921, 1604, 1588, 1570, 1496, 1469, 1441, 1411, 1325, 1303, 1246, 1210, 1164, 1143, 1119, 1085, 1040, 1001, 955, 904, 872, 814, 775, 744, 674.

EI-HRMS: mass spectrometry: *m/z* calc. 401.1061 $[C_{22}H_{18}F_3NOS]^{\bullet+}$, measured 401.1068.



Chemical Formula: $C_{21}H_{19}NO_2$
Exact Mass: 317,14
Molecular Weight: 317,38
m/z: 317.14 (100.0%), 318.14 (23.1%), 319.15 (2.9%)
Elemental Analysis: C, 79.47; H, 6.03; N, 4.41; O, 10.08

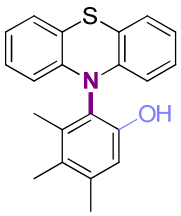
3o. From phenoxazine and 3,4,5-trimethylphenol. The crude mixture is purified firstly by three sets of double crystallization from toluene. The remaining organic layers are purified by SiO_2 gel column chromatography hexane/Ethyl Acetate (9:1). Isolated yield: 82% (colorless to light yellow crystals).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.32 (s, OH), 6.75 (s, 1H), 6.66-6.56 (aromatic area, 6H), 5.70 (second order system, lines: 5.7185, 5.7160, 5.7059, 5.6984, 5.6953, 5.6896, 5.6827, 5.6740, 5.6702, 2H), 2.25 (s, CH_3), 2.10 (s, CH_3), 2.03 (s, CH_3).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 152.08 (s, C_{quat}), 143.25 (s, C_{quat}), 137.54 (s, C_{quat}), 136.83 (s, C_{quat}), 132.80 (s, C_{quat}), 126.42 (s, C_{quat}), 123.68 (s, CH), 120.79 (s, CH), 119.85 (s, C_{quat}), 115.84 (s, CH), 114.91 (s, CH), 112.12 (s, CH), 20.45 (s, CH_3), 15.09 (s, CH_3), 14.13 (s, CH_3).

IR (neat, cm^{-1}): v: 3459, 3441, 3415, 2917, 1631, 1589, 1484, 1464, 1419, 1386, 1373, 1334, 1292, 1269, 1194, 1186, 1148, 1123, 1089, 1040, 997, 921, 904, 871, 862, 850, 805, 761, 739, 711, 682.

EI-HRMS: mass spectrometry: *m/z* calc. 317.1416 $[C_{21}H_{19}NO_2]^{\bullet+}$, measured 317.1437.



Chemical Formula: $C_{21}H_{19}NOS$
Exact Mass: 333,12
Molecular Weight: 333,45
m/z: 333.12 (100.0%), 334.12 (23.9%), 335.11 (4.5%), 335.13 (2.5%), 336.12 (1.1%)
Elemental Analysis: C, 75.64; H, 5.74; N, 4.20; O, 4.80; S, 9.62

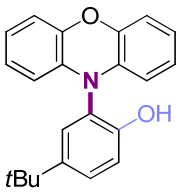
3p. From phenothiazine and 3,4,5-trimethylphenol. The reactor is cooled to room temperature and the crude mixture is filtrated with dichloromethane over a plug of silica gel. The concentrate is purified by SiO_2 gel column chromatography hexane/ethyl acetate (18:2 to 15:5). Isolated yield: 99% (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.40 (s, OH), 6.94 (dd, 2H, ^3J = 7.2.Hz, J = 1.6 Hz), 6.86 (dd, 1H, ^3J = 8.3 Hz, J = 1.8 Hz), 6.84 (dd, 1H, ^3J = 7.3 Hz, J = 1.8 Hz), 6.78 (s, 1H), 6.75 (td, 2H, ^3J = 7.3 Hz, J = 1.2 Hz), 5.97 (dd, 2H, ^3J = 8.0 Hz, J = 1.2 Hz), 2.25 (s, 3H, CH_3), 2.09 (s, 6H, CH_3).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 152.62 (s, C_{quat}), 142.00 (s, C_{quat}), 137.27 (s, C_{quat}), 135.82 (s, C_{quat}), 127.26 (s, CH), 126.64 (s, C_{quat}), 126.03 (s, CH), 123.04 (s, C_{quat}), 121.98 (s, CH), 118.11 (s, C_{quat}), 115.45 (s, CH), 114.97 (s, CH), 20.51 (s, CH_3), 15.24 (s, CH_3), 14.16 (s, CH_3).

IR (neat, cm^{-1}): v: 3448 (bs), 3290 (bs), 3054 (bs), 2920, 2856, 1595, 1579, 1463, 1442, 1434, 1374, 1336, 1300, 1236, 1210, 1172, 1126, 1106, 1073, 1041, 917, 860, 780, 748.

IE-GCMS: *m/z* calc. $[C_{21}H_{19}NOS]^{\bullet+}$: 333.1 (100%), 334.4 (22.7), 335.1 (4.5), measured: 331.1 (100%), 334.1 (24.1), 335.1 (7.3).



Chemical Formula: $C_{22}H_{21}NO_2$
Exact Mass: 331,16
Molecular Weight: 331,41
m/z: 331.16 (100.0%), 332.16 (24.1%), 333.16 (3.2%)
Elemental Analysis: C, 79.73; H, 6.39; N, 4.23; O, 9.66

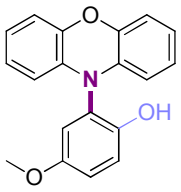
3q. From phenoxazine and 4-*t*Butyl-phenol. The crude mixture is purified by SiO_2 gel column chromatography hexane/Ethyl Acetate (9:1). Isolated yield: 64% (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.63 (s, OH), 7.37 (dd, ^3J = 8.5 Hz, J = 2.4 Hz, 1H), 7.18 (d, J = 2.4 Hz, 1H), 7.04 (d, ^3J = 8.5 Hz, 1H), 6.70-6.59 (aromatic area, 6H), 5.81 (second order system, lines: 5.8345, 5.8226, 5.8163, 5.8069, 5.8038, 5.7994, 5.7881, 2H), 1.26 (s, 9H, *t*Bu).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 152.51 (s, C_{quat}), 143.43 (s, C_{quat}), 143.33 (s, C_{quat}), 133.56 (s, C_{quat}), 127.85 (s, CH), 126.72 (s, CH), 123.58 (s, CH), 122.87 (s, C_{quat}), 120.83 (s, CH), 117.19 (s, CH), 114.91 (s, CH), 112.63 (s, CH), 33.82 (s, C_{quat}), 31.27 (s, 3*CH_3).

IR (neat, cm^{-1}): v: 3445, 2957, 1591, 1506, 1486, 1460, 1323, 1293, 1274, 1247, 1214, 1185, 1161, 1129, 1046, 835, 823, 746, 733, 713, 695.

EI-HRMS: mass spectrometry: *m/z* calc. 331.1572 $[C_{21}H_{21}NO_2]^{\bullet+}$, measured 331.1585.



Chemical Formula: $C_{19}H_{15}NO_3$
Exact Mass: 305,11
Molecular Weight: 305,33
m/z: 305.11 (100.0%), 306.11 (20.8%), 307.11 (2.8%)
Elemental Analysis: C, 74.74; H, 4.95; N, 4.59; O, 15.72

3r. From phenoxazine and 4-methoxyphenol. The reactor is cooled to room temperature and the crude mixture is filtrate with dichloromethane over a plug of silica gel.

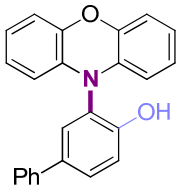
The concentrate is purified by SiO_2 gel column chromatography hexane/ethyl acetate (17:3). Isolated yield 41% (yellow solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.37 (s, OH), 7.05 (d, 1H, ^3J = 8.8 Hz), 6.96 (dd, 1H, ^3J = 8.8 Hz, J = 2.8 Hz), 6.83 (d, 1H, J = 2.8 Hz), 6.66 (m, 6H), 5.87 (m, 2H), 3.70 (s, 3H, OCH_3).

^{13}C NMR (101 MHz, DMSO-d_6) δ (ppm): 153.25 (s, C_{quat}), 148.82 (s, C_{quat}), 143.26 (s, C_{quat}), 133.30 (s, C_{quat}), 123.68 (s, C_{quat}), 123.58 (s, CH), 120.94 (s, CH), 118.27 (s, CH), 116.14 (s, CH), 115.69 (s, CH), 114.92 (s, CH), 112.80 (s, CH), 55.50 (s, OCH_3).

IR (neat, cm^{-1}): v: 3449, 3059 (broad small signal), 2934 (bss), 2843 (ss), 1591, 1483, 1464, 1448, 1329, 1293, 1277, 1249, 1228, 1200, 1172, 1145, 1122, 1087, 1033, 973, 924, 864, 840, 821, 795.

ESI H.R. mass spectrometry: m/z calc. 305.1052 $[C_{19}H_{15}NO_3]^{\cdot+}$, measured 305.1057.



Chemical Formula: $C_{24}H_{17}NO_2$
Exact Mass: 351,13
Molecular Weight: 351,40
m/z: 351.13 (100.0%), 352.13 (26.2%), 353.13 (3.8%)
Elemental Analysis: C, 82.03; H, 4.88; N, 3.99; O, 9.11

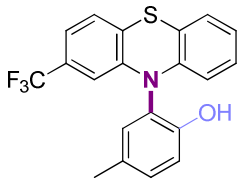
3s. MII-504 From phenothiazine and *p*-phenylphenol. The crude mixture is purified by SiO_2 gel column chromatography hexane/Ethyl Acetate (9:1). Isolated yield: 99% (white to light yellow, foamy to crispy solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.05 (s, OH), 7.71 (dd,1H, ^3J = 8.4 Hz, J = 2.4 Hz), 7.65 (d, 2H, ^3J = 7.6 Hz), 7.58 (d, 1H, J = 2.4 Hz), 7.41 (t, 2H, ^3J = 7.6 Hz), 7.29 (t, 1H, ^3J = 7.6 Hz), 7.20 (d, 1H, J = 8.4 Hz), 6.67, (m, 6H), 5.91 (m, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ (ppm): 154.77 (s, C_{quat}), 143.31 (s, C_{quat}), 138.88 (s, C_{quat}), 133.39 (s, C_{quat}), 132.88 (s, C_{quat}), 129.58 (s, CH), 128.83 (s, CH), 128.22 (s, CH), 126.81 (s, CH), 125.96 (s, CH), 124.12(s, C_{quat}), 123.64 (s, CH), 121.00 (s, CH), 118.31 (s, CH), 114.98 (s, CH), 112.80 (s, CH).

IR (neat, cm^{-1}): v: 3409, 3033 (small signal), 1745 (broad small signal), 1590, 1512, 1475, 1464, 1410, 1330, 1292, 1270, 1240, 1200, 1177, 1153, 1127, 1094, 1077, 1044, 915, 887, 861, 844, 758, 747, 731, 694.

EI-HRMS: mass spectrometry: *m/z* calc. 351.1259 $[C_{21}H_{21}NO_2]^{\bullet+}$, measured 351.1248.



Chemical Formula: $C_{20}H_{14}F_3NOS$
Exact Mass: 373,07
Molecular Weight: 373,39
m/z: 373.07 (100.0%), 374.08 (21.8%), 375.07 (4.5%), 375.08 (2.7%), 374.07 (1.2%)
Elemental Analysis: C, 64.33; H, 3.78; F, 15.26; N, 3.75; O, 4.28; S, 8.59

3t. From 2-trifluoromethylphenothiazine and paracresol. The crude mixture is purified by SiO_2 gel column chromatography hexane/Ethyl Acetate (9:1). Isolated yield: 99% (white to light yellow, foamy to crispy solid).

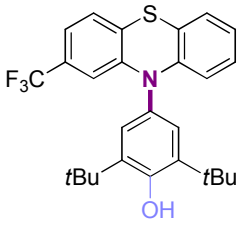
^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 9.92 (s, OH), 7.22 (dd, ^3J = 8.3 Hz, J = 2.0 Hz, 1H), 7.21 (d, ^3J = 7.8 Hz, 1H), 7.12-7.07 (m, 3H), 7.02 (dd, ^3J = 7.6 Hz, J = 1.5 Hz, 1H), 6.93 (~td, ^3J = 7.8 Hz, J = 1.6 Hz, 1H), 6.84 (~td, ^3J = 7.4 Hz, J = 1.1 Hz, 1H), 6.25 (d, J = 1.4 Hz, 1H), 6.08 (dd, ^3J = 8.3 Hz, J = 1.0 Hz, 1H), 2.25 (s, CH_3).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 153.00 (s, C_{quat}), 143.34 (s, C_{quat}), 142.06 (s, C_{quat}), 131.21 (s, CH), 130.84 (s, CH), 130.31 (s, C_{quat}), 127.79 (q, ^2J = 31.9 Hz, CF_3-C_{quat}), 127.70 (s, CH), 126.93 (s, CH), 126.32 (s, CH), 125.21 (s, C_{quat}), 124.23 (s, C_{quat}), 123.89 (q, ^1J = 272.6 Hz, C_{quat}, CF_3), 122.90 (s, CH), 118.52 (q, ^3J = 3.6 Hz, CH), 117.47 (s, C_{quat}), 117.02 (s, CH), 115.82 (s, CH), 110.78 (q, ^3J = 4.6 Hz, CH), 19.79 (s, CH_3).

^{19}F NMR (376.5 MHz, DMSO-d_6) δ (ppm): -61.70 (s, CF_3).

IR (neat, cm^{-1}): v: 3449, 2927, 1593, 1572, 1505, 1469, 1440, 1408, 1386, 1326, 1306, 1282, 1260, 1230, 1214, 1161, 1113, 1086, 1043, 970, 953, 942, 923, 867, 813, 797, 770, 742, 717, 657.

EI-HRMS: mass spectrometry: *m/z* calc. 373.0748 $[C_{20}H_{14}F_3NOS]^{\bullet+}$, measured 373.0751.



Chemical Formula: $C_{27}H_{28}F_3NOS$
Exact Mass: 471,18
Molecular Weight: 471,58
m/z: 471.18 (100.0%), 472.19 (29.6%), 473.19 (4.7%), 473.18 (4.6%), 474.18 (1.3%), 472.18 (1.2%)
Elemental Analysis: C, 68.77; H, 5.98; F, 12.09; N, 2.97; O, 3.39; S, 6.80

3u. From 2-trifluoromethylphenothiazine and 2,4-*tert*-butylphenol. The reactor is cooled to room temperature and the crude mixture is filtrated with dichloromethane over a plug of silica gel. The concentrate is purified by SiO_2 gel column chromatography hexane/ethyl acetate (17:3). Isolated yield: 12% (white solid).

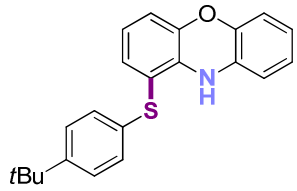
^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.49 (broad s, OH), 7.23 (d, 1H, ^3J = 8.0 Hz), 7.12 (dd, 1H, ^3J = 8.0 Hz, J = 0.8 Hz), 7.08 (s, 2H), 7.06 (dd, 1H, ^3J = 7.6 Hz, J = 1.5 Hz), 6.97 (~td, ^3J = 7.3 Hz, J = 1.5 Hz, 1H), 6.87 (~td, ^3J = 7.3 Hz, J = 1.0 Hz, 1H), 6.27 (d, 1H, J = 1.6 Hz), 6.15 (dd, 1H, ^3J = 8.4 Hz, J = 0.8 Hz), 1.40 (s, 18H, *t*Bu).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 154.00 (s, C_{quat}), 144.81 (s, C_{quat}), 143.36 (s, C_{quat}), 142.43 (s, C_{quat}), 130.89 (s, C_{quat}), 127.87 (s, CH), 127.64 (q, ^2J = 31.9 Hz, C_{quat}-CF_3), 127.24 (s, CH), 126.63 (s, CH), 126.06 (s, CH), 124.27 (s, C_{quat}), 123.79 (q, ^1J = 273.5 Hz, C_{quat}, CF_3), 123.05 (s, CH), 118.68 (q, ^3J = 3.6 Hz, CH), 117.59 (s, C_{quat}), 115.85 (s, CH), 110.67 (q, ^3J = 3.6 Hz, CH), 34.80 (s, C_{quat}), 30.22 (s, *t*Bu).

^{19}F NMR (376.5 MHz, DMSO-d_6) δ (ppm): -62.86 (s, CF_3).

IR (neat, cm^{-1}): v: 3624, 3066, 2966 (broad), 2923 (broad), 2872 (broad), 1588, 1567, 1467, 1428, 1409, 1361, 1322, 1227, 1159, 1141, 1090, 1043, 995, 956, 875, 813, 773, 785, 717, 656.

EI-HRMS: mass spectrometry: m/z calc. 471.1844 $[C_{27}H_{28}F_3NOS]^{\bullet+}$, measured 471.1861.



Chemical Formula: $C_{22}H_{21}NOS$
Exact Mass: 347,13
Molecular Weight: 347,47
m/z: 347.13 (100.0%), 348.14 (24.1%), 349.13 (4.6%), 349.14 (3.2%), 348.13 (1.2%), 350.13 (1.1%)
Elemental Analysis: C, 76.04; H, 6.09; N, 4.03; O, 4.60; S, 9.23

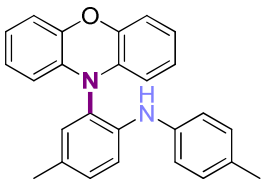
4. From phenoxazine and 4-*t*Butyl-thiophenol. The crude mixture is purified by SiO_2 gel column chromatography hexane/Ethyl Acetate (98:2). Isolated yield: 16% (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.91 (s, NH, satellites: ~0.4% integration, d, $^1J_{1H\text{-}15N}$ = 94.2 Hz), 7.35 (half of AA'BB' pattern, lines: 7.3706, 7.3643, 7.3593, 7.3480, 7.3430, 7.3367, 2H), 7.12 (other half of AA'BB' pattern, lines: 7.1454, 7.1391, 7.1341, 7.1228, 7.1178, 7.1115, 2H), 6.89 (dd, ^3J = 7.8 Hz, J = 1.5 Hz, 1H), 6.86 (~dd, ^3J = 7.5 Hz, J = 1.2 Hz, 1H), 6.74-6.69 (aromatic area, 2H), 6.64-6.59 (aromatic area, 3H), 1.24 (s, 3*CH_3).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 148.73 (s, C_{quat}), 143.41 (s, C_{quat}), 142.63 (s, C_{quat}), 134.69 (s, C_{quat}), 132.61 (s, C_{quat}), 131.22 (s, C_{quat}), 131.10 (s, CH), 127.31 (s, CH), 126.21 (s, CH), 123.86 (s, CH), 121.25 (s, CH), 120.59 (s, CH), 116.26 (s, CH), 114.77 (s, CH), 114.76 (s, CH), 114.53 (s, C_{quat}), 34.13 (s, C_{quat}), 30.96 (s, 3*CH_3).

IR (neat, cm^{-1}): v: 3383, 3058, 2961, 2923, 2865, 1586, 1571, 1490, 1459, 1398, 1362, 1285, 1274, 1245, 1214, 1197, 1179, 1152, 1117, 1106, 1078, 1062, 1030, 1011, 951, 922, 854, 835, 820, 774, 748, 721.

EI-HRMS: mass spectrometry: *m/z* calc. 347.1344 $[C_{22}H_{21}NOS]^{\bullet+}$, measured 347.1348.



Chemical Formula: $C_{26}H_{22}N_2O$
Exact Mass: 378,17
Molecular Weight: 378,47
m/z: 378.17 (100.0%), 379.18 (28.4%), 380.18 (4.1%)
Elemental Analysis: C, 82.51; H, 5.86; N, 7.40; O, 4.23

5. From phenoxazine and 4-*t*Butyl-thiophenol. The crude mixture is purified by SiO_2 gel column chromatography hexane/toluene (8:2). Isolated yield: 5% (white solid).

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.61 (s, NH, satellites: ~0.4% integration, d, $^1J_{1H\text{-}15N}$ = 90.4 Hz), 7.23 (d, ^3J = 8.4 Hz, 1H), 7.13 (dd, ^3J = 8.5 Hz, J = 1.8 Hz, 1H), 7.05-6.98 (aromatic area, 5H), 6.68-6.65 (aromatic area, 2H), 6.62 (second order pattern, lines: 6.6424, 6.6392, 6.6311, 6.6242, 6.6210, 6.6179, 6.6148, 6.6079, 6.5991, 6.5966, 4H), 5.91 (second order pattern, lines: 5.9292, 5.9198, 5.9117, 5.9092, 5.9029, 5.8960, 5.8872, 5.8841, 2H), 2.24 (s, CH_3), 2.21 (s, CH_3).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ (ppm): 143.69 (s, C_{quat}), 141.07 (s, C_{quat}), 140.17 (s, C_{quat}), 133.15 (s, C_{quat}), 130.74 (s, CH), 129.96 (s, CH), 129.89 (s, C_{quat}), 129.66 (s, C_{quat}), 129.34 (s, CH), 125.11 (s, C_{quat}), 123.44 (s, CH), 120.99 (s, CH), 119.83 (s, CH), 116.28 (s, CH), 114.87 (s, CH), 112.95 (s, CH), 20.29 (s, CH_3), 19.90 (s, CH_3).

IR (neat, cm^{-1}): v: 3377, 2917, 2846, 1607, 1590, 1512, 1485, 1460, 1444, 1330, 1315, 1292, 1272, 1236, 1210, 1151, 1131, 1106, 1044, 823, 811, 798, 769, 736, 696, 659.

EI-HRMS: mass spectrometry: *m/z* calc. 378.1732 $[C_{26}H_{22}N_2O]^{\bullet+}$, measured 378.1742.

4.5.4. Crystallographic data (See figure 3).

Table 1. Crystal data and structure refinement for 14087o.

Identification code	shelx	
Empirical formula	C22 H21 N O S	
Formula weight	347.46	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 11.4015(5) Å	α= 90°.
	b = 9.0993(3) Å	β= 97.929(4)°.
	c = 17.8329(8) Å	ɣ = 90°.
Volume	1832.40(13) $Å^3$	
Z	4	
Density (calculated)	1.259 Mg/m^3	
Absorption coefficient	0.186 mm^{-1}	
F(000)	736	
Crystal size	0.200 x 0.120 x 0.100 mm^3	
Theta range for data collection	2.725 to 28.499°.	
Index ranges	-15<=h<=14, -12<=k<=12, -19<=l<=23	
Reflections collected	9382	
Independent reflections	4628 [R(int) = 0.0305]	
Completeness to theta = 25.242°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.93713	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4628 / 0 / 233	
Goodness-of-fit on F^2	1.019	
Final R indices [I>2sigma(I)]	R1 = 0.0479, wR2 = 0.0980	
R indices (all data)	R1 = 0.0760, wR2 = 0.1114	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.249 and -0.303 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 14087o. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	9865(1)	1535(1)	2012(1)	38(1)
C(1)	9347(1)	2848(2)	1794(1)	27(1)
C(2)	9938(2)	3816(2)	1373(1)	34(1)
C(3)	9419(2)	5132(2)	1127(1)	33(1)
C(4)	8299(1)	5547(2)	1292(1)	27(1)
C(7)	7720(2)	7008(2)	1026(1)	35(1)
C(8)	8177(2)	8210(2)	1592(1)	61(1)
C(9)	8033(2)	7443(2)	250(1)	55(1)
C(10)	6373(2)	6920(3)	957(2)	65(1)
C(5)	7748(1)	4585(2)	1735(1)	27(1)
C(6)	8253(1)	3244(2)	1982(1)	24(1)
N(1)	7678(1)	2254(1)	2447(1)	25(1)
C(11)	7839(1)	2577(2)	3238(1)	26(1)
C(12)	8455(1)	3818(2)	3524(1)	31(1)
C(13)	8644(2)	4089(2)	4294(1)	39(1)
C(14)	8194(2)	3151(2)	4791(1)	46(1)
C(15)	7561(2)	1927(2)	4516(1)	43(1)
C(16)	7398(2)	1613(2)	3745(1)	34(1)
S(1)	6721(1)	-53(1)	3424(1)	41(1)
C(17)	6073(2)	505(2)	2515(1)	32(1)
C(18)	5049(2)	-206(2)	2185(1)	43(1)
C(19)	4575(2)	90(2)	1447(1)	49(1)
C(20)	5112(2)	1103(2)	1039(1)	45(1)
C(21)	6125(2)	1840(2)	1364(1)	33(1)
C(22)	6616(1)	1549(2)	2107(1)	27(1)

Table 3. Bond lengths [Å] and angles [°] for 14087o.

O(1)-C(1)	1.365(2)	N(1)-C(11)	1.428(2)
O(1)-H(1)	0.84(2)	N(1)-C(22)	1.430(2)
C(1)-C(6)	1.383(2)	C(11)-C(12)	1.390(2)
C(1)-C(2)	1.390(2)	C(11)-C(16)	1.401(2)
C(2)-C(3)	1.381(2)	C(12)-C(13)	1.384(2)
C(2)-H(2)	0.9500	C(12)-H(12)	0.9500
C(3)-C(4)	1.401(2)	C(13)-C(14)	1.379(3)
C(3)-H(3)	0.9500	C(13)-H(13)	0.9500
C(4)-C(5)	1.387(2)	C(14)-C(15)	1.380(3)
C(4)-C(7)	1.531(2)	C(14)-H(14)	0.9500
C(7)-C(10)	1.525(3)	C(15)-C(16)	1.392(2)
C(7)-C(9)	1.527(3)	C(15)-H(15)	0.9500
C(7)-C(8)	1.530(3)	C(16)-S(1)	1.7601(19)
C(8)-H(8A)	0.9800	S(1)-C(17)	1.7608(18)
C(8)-H(8B)	0.9800	C(17)-C(22)	1.392(2)
C(8)-H(8C)	0.9800	C(17)-C(18)	1.393(3)
C(9)-H(9A)	0.9800	C(18)-C(19)	1.377(3)
C(9)-H(9B)	0.9800	C(18)-H(18)	0.9500
C(9)-H(9C)	0.9800	C(19)-C(20)	1.371(3)
C(10)-H(10A)	0.9800	C(19)-H(19)	0.9500
C(10)-H(10B)	0.9800	C(20)-C(21)	1.390(2)
C(10)-H(10C)	0.9800	C(20)-H(20)	0.9500
C(5)-C(6)	1.394(2)	C(21)-C(22)	1.391(2)
C(5)-H(5)	0.9500	C(21)-H(21)	0.9500
C(6)-N(1)	1.4409(19)		

C(1)-O(1)-H(1)	107.7(15)	C(2)-C(3)-H(3)	119.0
O(1)-C(1)-C(6)	121.92(15)	C(4)-C(3)-H(3)	119.0
O(1)-C(1)-C(2)	118.99(15)	C(5)-C(4)-C(3)	116.60(15)
C(6)-C(1)-C(2)	119.08(15)	C(5)-C(4)-C(7)	120.99(15)
C(3)-C(2)-C(1)	120.21(15)	C(3)-C(4)-C(7)	122.38(15)
C(3)-C(2)-H(2)	119.9	C(10)-C(7)-C(9)	107.42(16)
C(1)-C(2)-H(2)	119.9	C(10)-C(7)-C(8)	109.79(18)
C(2)-C(3)-C(4)	121.97(15)	C(9)-C(7)-C(8)	108.13(17)

C(10)-C(7)-C(4)	111.46(15)	C(13)-C(12)-H(12)	119.7
C(9)-C(7)-C(4)	111.16(16)	C(11)-C(12)-H(12)	119.7
C(8)-C(7)-C(4)	108.82(14)	C(14)-C(13)-C(12)	120.45(18)
C(7)-C(8)-H(8A)	109.5	C(14)-C(13)-H(13)	119.8
C(7)-C(8)-H(8B)	109.5	C(12)-C(13)-H(13)	119.8
H(8A)-C(8)-H(8B)	109.5	C(13)-C(14)-C(15)	119.62(17)
C(7)-C(8)-H(8C)	109.5	C(13)-C(14)-H(14)	120.2
H(8A)-C(8)-H(8C)	109.5	C(15)-C(14)-H(14)	120.2
H(8B)-C(8)-H(8C)	109.5	C(14)-C(15)-C(16)	120.60(18)
C(7)-C(9)-H(9A)	109.5	C(14)-C(15)-H(15)	119.7
C(7)-C(9)-H(9B)	109.5	C(16)-C(15)-H(15)	119.7
H(9A)-C(9)-H(9B)	109.5	C(15)-C(16)-C(11)	119.86(17)
C(7)-C(9)-H(9C)	109.5	C(15)-C(16)-S(1)	119.36(14)
H(9A)-C(9)-H(9C)	109.5	C(11)-C(16)-S(1)	120.66(13)
H(9B)-C(9)-H(9C)	109.5	C(16)-S(1)-C(17)	99.21(8)
C(7)-C(10)-H(10A)	109.5	C(22)-C(17)-C(18)	120.16(17)
C(7)-C(10)-H(10B)	109.5	C(22)-C(17)-S(1)	121.20(13)
H(10A)-C(10)-H(10B)	109.5	C(18)-C(17)-S(1)	118.44(14)
C(7)-C(10)-H(10C)	109.5	C(19)-C(18)-C(17)	120.61(17)
H(10A)-C(10)-H(10C)	109.5	C(19)-C(18)-H(18)	119.7
H(10B)-C(10)-H(10C)	109.5	C(17)-C(18)-H(18)	119.7
C(4)-C(5)-C(6)	122.17(15)	C(20)-C(19)-C(18)	119.52(18)
C(4)-C(5)-H(5)	118.9	C(20)-C(19)-H(19)	120.2
C(6)-C(5)-H(5)	118.9	C(18)-C(19)-H(19)	120.2
C(1)-C(6)-C(5)	119.91(14)	C(19)-C(20)-C(21)	120.64(18)
C(1)-C(6)-N(1)	118.21(14)	C(19)-C(20)-H(20)	119.7
C(5)-C(6)-N(1)	121.87(14)	C(21)-C(20)-H(20)	119.7
C(11)-N(1)-C(22)	119.78(13)	C(20)-C(21)-C(22)	120.45(17)
C(11)-N(1)-C(6)	115.67(13)	C(20)-C(21)-H(21)	119.8
C(22)-N(1)-C(6)	117.58(12)	C(22)-C(21)-H(21)	119.8
C(12)-C(11)-C(16)	118.73(15)	C(21)-C(22)-C(17)	118.61(15)
C(12)-C(11)-N(1)	121.24(15)	C(21)-C(22)-N(1)	121.61(14)
C(16)-C(11)-N(1)	120.02(15)	C(17)-C(22)-N(1)	119.75(15)
C(13)-C(12)-C(11)	120.69(17)		

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$x 10^3)for 14087o. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	34(1)	31(1)	49(1)	3(1)	11(1)	6(1)
C(1)	27(1)	27(1)	28(1)	-4(1)	2(1)	0(1)
C(2)	26(1)	41(1)	37(1)	-3(1)	11(1)	-2(1)
C(3)	32(1)	36(1)	32(1)	3(1)	9(1)	-7(1)
C(4)	30(1)	28(1)	24(1)	-1(1)	2(1)	-5(1)
C(7)	37(1)	31(1)	35(1)	7(1)	2(1)	0(1)
C(8)	79(2)	36(1)	61(2)	-11(1)	-9(1)	17(1)
C(9)	72(2)	45(1)	49(1)	18(1)	12(1)	2(1)
C(10)	39(1)	59(2)	95(2)	40(1)	6(1)	10(1)
C(5)	26(1)	29(1)	27(1)	-2(1)	6(1)	0(1)
C(6)	26(1)	25(1)	22(1)	-1(1)	4(1)	-5(1)
N(1)	24(1)	27(1)	24(1)	2(1)	4(1)	-2(1)
C(11)	25(1)	29(1)	26(1)	2(1)	5(1)	7(1)
C(12)	27(1)	35(1)	31(1)	0(1)	3(1)	3(1)
C(13)	35(1)	45(1)	34(1)	-7(1)	-2(1)	8(1)
C(14)	55(1)	56(1)	25(1)	-1(1)	1(1)	16(1)
C(15)	56(1)	45(1)	29(1)	10(1)	12(1)	12(1)
C(16)	36(1)	33(1)	32(1)	6(1)	8(1)	8(1)
S(1)	53(1)	31(1)	41(1)	10(1)	15(1)	0(1)
C(17)	31(1)	29(1)	39(1)	0(1)	13(1)	1(1)
C(18)	34(1)	38(1)	61(1)	-2(1)	19(1)	-11(1)
C(19)	30(1)	52(1)	65(1)	-7(1)	1(1)	-14(1)
C(20)	37(1)	47(1)	49(1)	-3(1)	-6(1)	-4(1)
C(21)	32(1)	31(1)	35(1)	1(1)	2(1)	-3(1)
C(22)	24(1)	24(1)	34(1)	-2(1)	7(1)	1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 14087o.

	x	y	z	U(eq)
H(2)	10701	3571	1255	41
H(3)	9834	5777	837	39
H(8A)	7849	9161	1410	91
H(8B)	9043	8247	1643	91
H(8C)	7931	7991	2085	91
H(9A)	7801	6653	-114	82
H(9B)	8889	7608	287	82
H(9C)	7612	8347	79	82
H(10A)	6087	6123	609	97
H(10B)	6028	7853	760	97
H(10C)	6139	6727	1456	97
H(5)	7001	4847	1875	32
H(12)	8750	4489	3186	37
H(13)	9088	4927	4483	47
H(14)	8318	3347	5319	55
H(15)	7234	1293	4856	51
H(18)	4675	-902	2470	52
H(19)	3880	-405	1223	59
H(20)	4790	1303	529	55
H(21)	6483	2548	1077	40
H(1)	9410(20)	1090(20)	2271(13)	54(7)

Table 6. Torsion angles [°] for 14087o.

O(1)-C(1)-C(2)-C(3)	178.09(15)
C(6)-C(1)-C(2)-C(3)	-2.1(2)
C(1)-C(2)-C(3)-C(4)	0.5(3)
C(2)-C(3)-C(4)-C(5)	1.7(2)
C(2)-C(3)-C(4)-C(7)	179.63(16)
C(5)-C(4)-C(7)-C(10)	-27.7(2)
C(3)-C(4)-C(7)-C(10)	154.48(18)
C(5)-C(4)-C(7)-C(9)	-147.53(17)
C(3)-C(4)-C(7)-C(9)	34.7(2)
C(5)-C(4)-C(7)-C(8)	93.5(2)
C(3)-C(4)-C(7)-C(8)	-84.3(2)
C(3)-C(4)-C(5)-C(6)	-2.4(2)
C(7)-C(4)-C(5)-C(6)	179.67(14)
O(1)-C(1)-C(6)-C(5)	-178.76(14)
C(2)-C(1)-C(6)-C(5)	1.4(2)
O(1)-C(1)-C(6)-N(1)	2.5(2)
C(2)-C(1)-C(6)-N(1)	-177.32(14)
C(4)-C(5)-C(6)-C(1)	0.9(2)
C(4)-C(5)-C(6)-N(1)	179.55(14)
C(1)-C(6)-N(1)-C(11)	96.56(17)
C(5)-C(6)-N(1)-C(11)	-82.12(18)
C(1)-C(6)-N(1)-C(22)	-112.67(16)
C(5)-C(6)-N(1)-C(22)	68.64(19)
C(22)-N(1)-C(11)-C(12)	-146.52(15)
C(6)-N(1)-C(11)-C(12)	3.6(2)
C(22)-N(1)-C(11)-C(16)	35.1(2)
C(6)-N(1)-C(11)-C(16)	-174.77(14)
C(16)-C(11)-C(12)-C(13)	0.9(2)
N(1)-C(11)-C(12)-C(13)	-177.50(15)
C(11)-C(12)-C(13)-C(14)	-1.9(3)
C(12)-C(13)-C(14)-C(15)	0.7(3)
C(13)-C(14)-C(15)-C(16)	1.5(3)
C(14)-C(15)-C(16)-C(11)	-2.5(3)
C(14)-C(15)-C(16)-S(1)	173.48(15)

C(12)-C(11)-C(16)-C(15)	1.3(2)
N(1)-C(11)-C(16)-C(15)	179.71(15)
C(12)-C(11)-C(16)-S(1)	-174.63(12)
N(1)-C(11)-C(16)-S(1)	3.7(2)
C(15)-C(16)-S(1)-C(17)	151.20(15)
C(11)-C(16)-S(1)-C(17)	-32.81(16)
C(16)-S(1)-C(17)-C(22)	33.16(16)
C(16)-S(1)-C(17)-C(18)	-151.96(15)
C(22)-C(17)-C(18)-C(19)	1.3(3)
S(1)-C(17)-C(18)-C(19)	-173.64(16)
C(17)-C(18)-C(19)-C(20)	-0.5(3)
C(18)-C(19)-C(20)-C(21)	-0.5(3)
C(19)-C(20)-C(21)-C(22)	0.7(3)
C(20)-C(21)-C(22)-C(17)	0.0(3)
C(20)-C(21)-C(22)-N(1)	177.87(16)
C(18)-C(17)-C(22)-C(21)	-1.0(3)
S(1)-C(17)-C(22)-C(21)	173.77(13)
C(18)-C(17)-C(22)-N(1)	-178.92(16)
S(1)-C(17)-C(22)-N(1)	-4.1(2)
C(11)-N(1)-C(22)-C(21)	147.23(15)
C(6)-N(1)-C(22)-C(21)	-2.3(2)
C(11)-N(1)-C(22)-C(17)	-34.9(2)
C(6)-N(1)-C(22)-C(17)	175.53(14)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for 14087o [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...N(1)	0.84(2)	2.30(2)	2.7886(18)	117.0(18)
C(12)-H(12)...O(1)#1	0.95	2.50	3.346(2)	148.6

Symmetry transformations used to generate equivalent atoms:
#1 -x+2,y+1/2,-z+1/2

General conclusion.

To conclude on these three years of research, we successfully performed the formation of carbon-nitrogen bonds for some classes of amines with a ruthenium (II)/ copper (II) catalytic systems, but also without metallic catalysis.

We were able to form new classes of products derived from carbazoles, diarylamines, phenothiazines, phenoxazines and phenols (Figure 1).

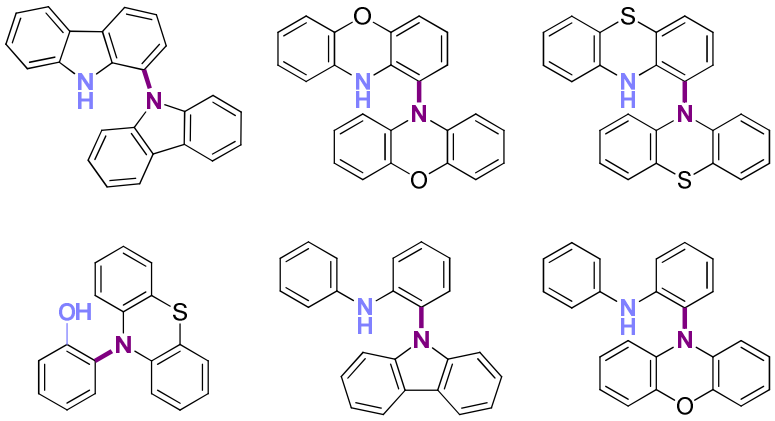


Figure 1: Newly formed C-N bond during those three years.

We realized our objectives by using starting materials without prior pre-activation or pre-oxidation, and without chelating directing group to avoid an extra-step of preparation and in our concern for atom economic cross-coupling reactions. Thus, all our cross-coupling reactions were dehydrogenative.

The study of deuterium incorporation in our reaction conditions (for the formation of Lauternazoles and Lauternamines), and some literature reports gave us initial mechanistic keys for each system and the possibility to suggest a mechanism.

Finally, we pointed out an intramolecular interaction which led to unprecedented chirality in our final products. The chiral HPLC showed the formation of two enantiomers and/or diastereomers.

In the near future, we expect to prove the existence of this interaction by NMR, IR and XRD analysis.

Studies to test these amino-amines and amino-phenols products as ligands are planned to have an overview of their activity in enantioselective catalysis.

In terms of C-N bond formation, we planned to improve the catalytic system with the aim of including general anilines or indoles as *N*-aminating agents. The current carboxylate ligand probably needs to be changed to carry out such basic reactions in good conditions.

Regarding chiral products, we would like to change ligands of the reaction (*p*-cymene and acetate) in order to develop an enantioselective reaction and obtain separately enantiomers.

Finally, we hope that the last catalytic system, inspired from the Hock process, will be used and develop as a new substrate activation mode and allow better selectivity and broader substrate scope.

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2009 **Bachelor of Science - Major in Chemistry**
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2008 **Second year degree of Biology and Biochemistry**
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2006-2007 First year of Pharmaceutical Science
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PUBLICATIONS

"Toward polynuclear Ru-Cu catalytic dehydrogenative C-N bond formation, on the reactivity of carbazoles"
Louillat, M.-L. ; Patureau, F. W. *Org. Lett.* **2013**, *15*, 164.

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Jones, A. W.; **Louillat-Habermeyer, M.-L.**; Patureau, F. W.*, Adv. Synth. Catal.* **2015**, DOI: 10.1002/adsc.201401136.