SYNTHESIS OF CARBAZOLES AND DERIVATIVES FROM ALLENES

DOI: http://dx.medra.org/10.17374/targets.2022.25.409

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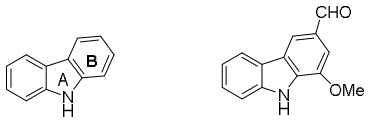
Abstract. *Carbazole heterocycles are ubiquitous in nature, and frequent motifs in materials such as polymers, dyes and light emitted devices. Among the wide variety of strategies towards the synthesis of carbazoles, the allene-based methodology represents one of the most recurring and promising recent approaches. Transition metal-catalyzed cyclization reactions of indole-tethered allenes easily provide the carbazole skeleton through short reaction sequences and under mild reaction conditions. Also, intermolecular cycloadditions between allenes and indoles have been employed for the preparation of carbazole systems. Novel methodologies, mechanistic investigations, and the synthesis of naturally occurring molecules and non-natural analogous have been recently presented by different authors, stating the indole-allene approach to carbazoles as one of the most fascinating and straightforward synthesis of heterocyclic cores.*

Contents

1. Introduction

Despite the carbazole nucleus **1** was first isolated from the distillation of the coal tar about 150 years ago,[1] the biggest attention to this kind of molecules started after the discovery of the pharmaceutical properties of Murrayanine **2**, a 4-formyl decorated carbazole found in *Murraya Koenigii* plant in 1965 (Scheme 1).[2] Since then, great effort has been made regarding the isolation and characterization of novel carbazole alkaloids from natural sources, along with the laboratory synthesis of both natural and non-natural structures in the search of new pharmacological features.[3-8] Besides the biological activities exhibited from the carbazole family, intriguing photo-physical properties of carbazole-based materials have also been reported in polymeric and organic light-emitted devices,[9-11] synthetic dyes,[12] or conductive polymers,[13-14] giving the carbazole motif a prominent place in organic synthesis.



1 Carbazole skeleton **2** Murrayanine

Scheme 1. The carbazole skeleton and Murrayanine alkaloid.

The synthesis of the carbazole skeleton has been accomplished through one of the main following strategies: (a) synthesis of the B ring from indole derivatives, or (b) synthesis of the A ring from bis-aryl starting materials. Route (a) normally comprises metal-catalyzed coupling reactions of indoles with

unsaturated moieties such as alkynes or alkenes, cycloadditions, or electrophilic cyclizations.[15] On the other hand, the most common transformations based on route (b) are nitrene insertions, metal-catalyzed aminations, and modifications of indole synthesis methodologies such as the Fischer or the Plieninger indolization.[16-18]

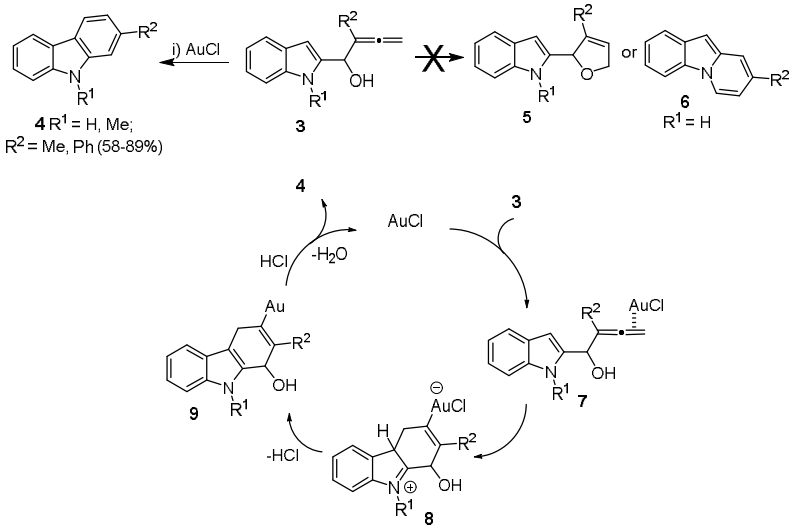
Apart from the most classical approaches, during the last years different authors have developed an interesting range of methodologies for the synthesis of carbazoles from indoles based on allene chemistry. The electrophilic nature of the allene moiety in the presence of a metal salt facilitates the nucleophilic addition of the indole unit providing several routes to build the B ring. In addition, cycloadditions and electrocyclizations of allenes and indole rings have been described providing the carbazole skeleton.[19] Moreover, the indole-allene strategy has emerged as a versatile tool to generate dihydrocarbazole molecules (DHC), tetrahydrocarbazole analogues (THC) and β-carboline derivatives, recurring motifs in organic synthesis, materials and medicinal chemistry.[20-34]

This chapter presents a critic overview about the synthesis of both naturally occurring and synthetic carbazoles and derivatives using indole rings and allenes as key reactants. Most significant examples are detailed and organized according to the transition metal employed as catalyst. Gold and gold/silver catalysis will be first discussed, followed by the reported examples using platinum and palladium catalysis. We will also contemplate a final section compiling rare examples based in alternative metals and metal-free methodologies for the synthesis of carbazoles and derivatives.

2. Synthesis of carbazoles and derivatives by transition metal catalysis

2.1. Gold and silver catalysis

Gold complexes, specially Au(I) salts, have shown great activity in promoting carbocyclization processes from allene and indolylallene systems. In our research group, we have studied the mechanistic facets of this transformation and the structural diversity that can be achieved. Thus, indole-tethered allenols **3,** which may exhibit three possible reaction sites providing the corresponding carbo-, oxy-, or aza-cyclisation products **4**, **5** and **6**, respectively, exclusively yielded the carbazole structure **4** (Scheme 2).

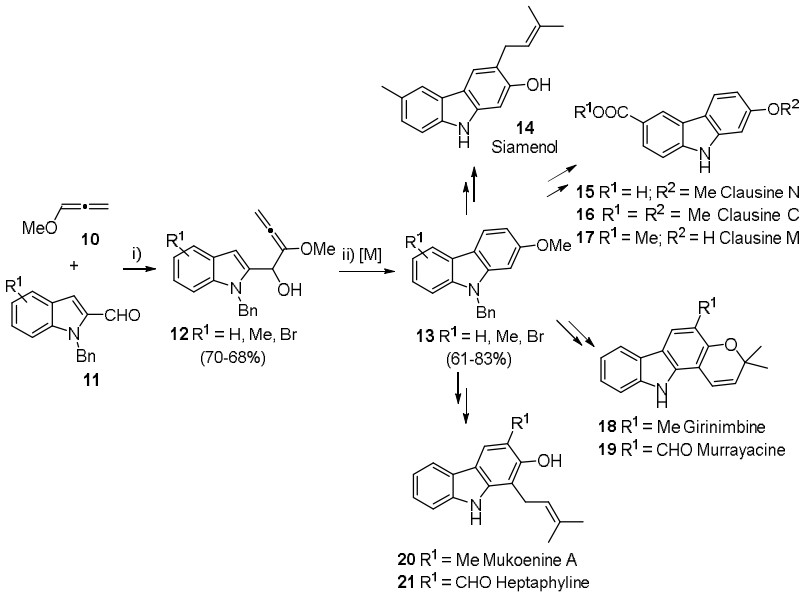


Scheme 2. Carbazole synthesis through Au-catalyzed carbocyclization of indole-tethered allenes.

The methodology was applied for both methyl- and sterically hindered phenyl-substituted allenols **3**, leading to carbazoles **4** with good yields. The reaction mechanism was proposed to start with coordination of terminal allenic bond to the metal leading to intermediate **7**, followed by a *6-endo* carbometallation reaction

to give the zwitterionic vinyl gold intermediate **8**. Then, loss of HCl would lead to the neutral complex **9**, and dehydration and protonolysis steps eventually furnish carbazoles **4**, with catalyst regeneration (Scheme 2, bottom).[35]

Ma and co-workers have extended the gold-mediated synthesis of carbazoles to terminal-substituted allenes, yielding densely functionalized carbazoles through a 1,2-shift rearrangement in gold carbene intermediates.[36] Also, the synthesis of a family of naturally occuring carbazoles have been reported, including a gold-catalyzed carbocyclization process as the key step of the route. Thus, treatment of methoxypropadiene **10** with *n*BuLi and indole-2-carbaldehydes **11** led to indole-tethered allenols **12** (Scheme 3). Carbocyclization of compounds **12** under gold-catalyzed conditions followed by spontaneous dehydratation provided 2-methoxy-3-methylcarbazoles **13** in high yields. Carbazoles **13** were further employed as precursors for the synthesis of a family of natural products such as Siamenol **14** or the Clausine family drugs **15**-**17**, both commonly used in traditional medicine and exhibiting interesting anti-HIV activities. Also, alternative routes gave access to Girinimbine **18**, Murrayacine **19**, or Mukoenine-type structures **20**, **21**, showing cytotoxic activity against a wide variety of cell lines.[37]

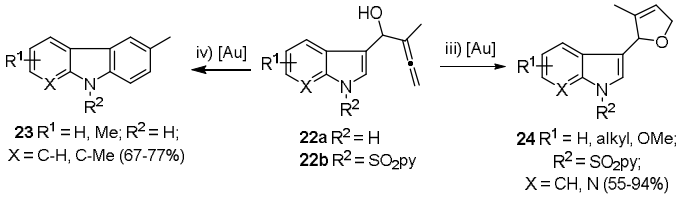


Scheme 3. Synthesis of naturally occurring carbazole alkaloids through gold-catalyzed carbocyclization of indolylallenes.

In order to improve the substitution pattern in final carbazoles, indole rings **22** bearing an allenol substituent at the 3-position have also been investigated in our laboratories. In this case, the route requiered the use of protecting groups at the N1 position prior to the synthesis of the allene moiety and further deprotection before carbocyclization may take place. Then, treatment of allenols **22** with Gagosz's catalyst provided the expected carbazoles **23** with good yields and under mild reaction conditions. Noteworthy, deactivated indoles **22b** was fully converted into the dihydrofuran derivatives **24** under otherwise similar reaction conditions (Scheme 4).[38]

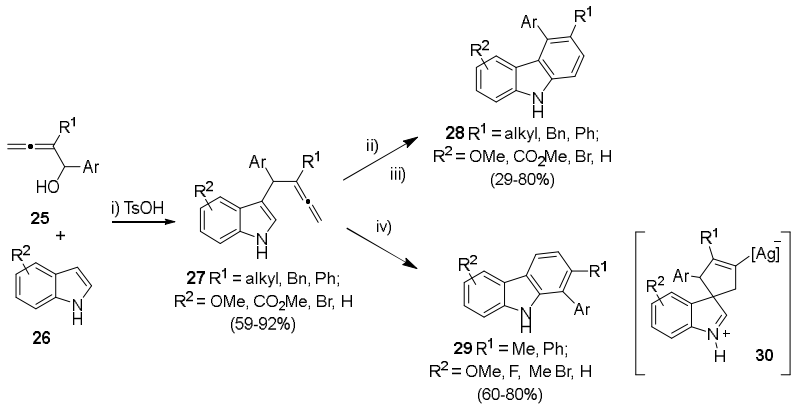
Allenyl C3-linked indole analogous **27**, prepared from reaction of allenols **25** and indole **26** under acidic conditions, are also able to evolve to the corresponding carbazole molecules **28** and **29** using two different strategies. In one hand, gold-catalyzed 6-*endo* carbocyclization of **27** using silver complexes as counterions generated the corresponding dihydrocarbazole, wich is subsequently oxidized under DDQ conditions to yield fully aromatic carbazole system **28** (Scheme 5, top).[39] On the other hand, we have discovered a straighforward procedure based on silver nanoparticles (AgNPs) and high temperatures to

access the target molecules **29** in one step. Noteworthy, carbazoles **29** exhibited improved yields and a different substitution pattern. In light of these results, a divergent reaction mechanism should be operating in both transformations, pointing to spirocyclic species **30** as key intermediates when AgNPs are employed (Scheme 5, bottom).[40]



iii) **22** (1 equiv.), $[(Ph_3P)AuNTf_2]$ (5 mol%), DCE, rt. iv) **22** (1 equiv.), $[(Ph_3P)AuNTf_2]$ (5 mol%), Toluene, rt.

Scheme 4. Synthesis of carbazoles through gold-catalyzed carbocyclization of oxyallenyl C3-linked indoles.



i) **25** (1 equiv.), **26** (1.5 equiv.), TsOH (5 mol%), DCE, rt. ii) **27** (1 equiv.), $AuCl(PPh_3)$ (5 mol%), $AgBF_4$ (5 mol%), DCE, 0 °C. iii) DDQ (1.2 equiv.), DMF, rt. iv) **27** (1 equiv.), $AgNP{\cdot}SiO_2$ (1% weight), DCE, 150 °C.

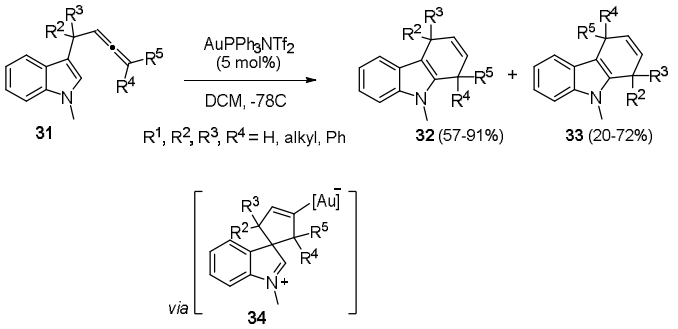
Scheme 5. Synthesis of carbazoles through gold- and silver-catalyzed cyclization of C3-allenylindoles.

Cationic gold species have been reported to promote the synthesis of DHCs **32** and **33** from allenylindoles **31**. In this case, a reaction mechanism where C3 *vs* C2 indole nucleophilicity compete should be operating, yielding a mixture of carbocyclization products **32** and rearrangement products **33** trough spirocyclic intermediates **34** (Scheme 6).[41]

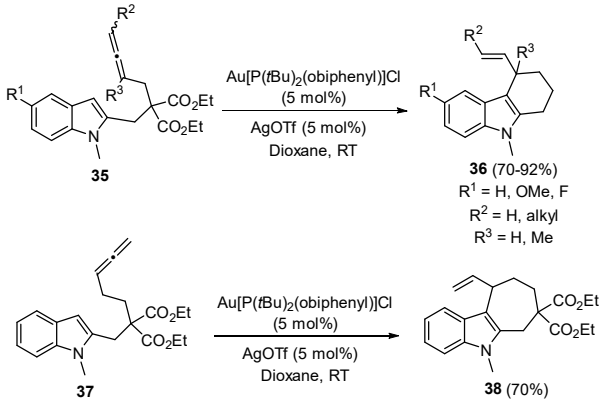
The THC skeleton can be obtained following an alternative strategy, based on a change on the indole-allene connectivity. Thus, the nucleophilic addition of the C3 indole position could be directed towards the proximal allenic carbon, generating the saturated six-membered ring in the THC skeleton. Widenhoefer and co-workers described the first intramolecular nucleophilic addition of this kind, using C2-indolylallenes **35** for the synthesis of THCs **36**.[42] Also, 7-memebered rings in structures **38** were synthesized through a less common 7-*exo*-*trig* process, starting from allenylindole **37** bearing a four-carbon chain link (Scheme 7). The same group developed the enantioselective version using BIPHEP ligands and providing the THC molecules in up to 92% ee.[43]

Although the main part of the allene-based carbocyclization reactions generating carbazole-type molecules take place intramolecularly, some examples of intermolecular reactions between allenes and indoles can be found. Recent reports from Rossi and co-workers described the formal [4+2] cycloaddition of

indoles and allenamides building the THC motif. Thus, addition of the indole **39** to the allene moiety in allenamides **40** through the C3 position would lead to vinyl-metal intermediate **42**, which is proposed to evolve to THC **41** through a cyclization step (Scheme 8a).[44] More recently, the enantiomeric version of this transformation provided optically pure THCs exhibiting up to 97% ee.[45] Also, alternative C3-tethered alkenyl indoles **43** were submitted to gold catalysis in the presence of allenamide **44** to yield adducts **45.** The reaction is described to proceed through a similar mechanistic pathway, and enantioenriched final THCs **45** were obtained in good to excellent yields and up to 99% ee (Scheme 8b). In a parallel work, Zhang research group studied the [3+2] *vs* [2+2] competition in similar substrates.[46]

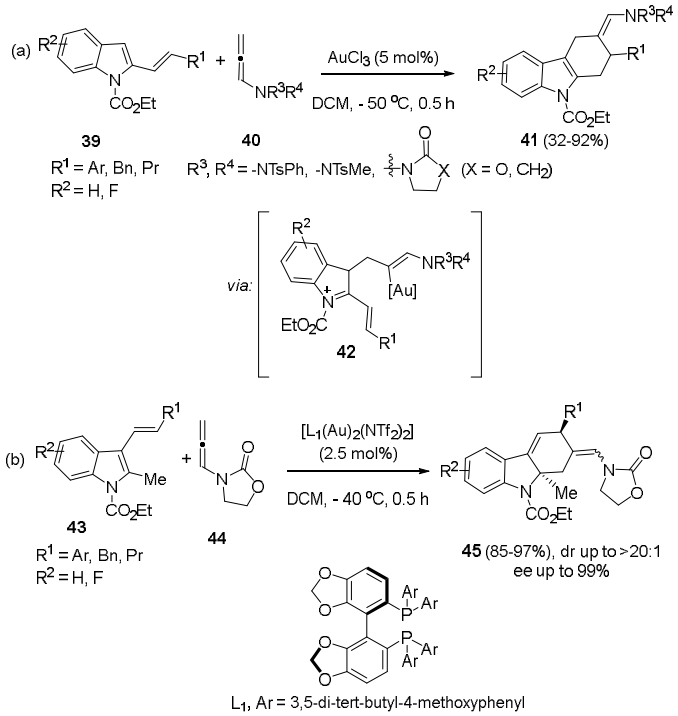


Scheme 6. Synthesis of DHCs through gold-catalyzed carbocyclization of C3-allenylindoles.



Scheme 7. Synthesis of THCs and related systems through gold-catalyzed carbocyclization of C2-allenylindoles.

The β-carboline motif can be also obtained using the gold-catalyzed indole-allene cycloaddition, showing the great versatility that gold complexes exhibit in catalyzing carbocyclization processes. For example, carbocyclization of tryptamine-derived allenamides **46** provided substituted tetrahydrocarbolines **47** in excellent yields. Moreover, the use of enantioenriched phosphine PC-PHOS as chiral ligand allowed the preparation of carbolines **47** exhibiting high enantioselectivities (Scheme 9, reaction a). In order to prove the synthetic utility of the methodology, the authors applied the above-mentioned catalytic system to the desymmetrative cyclization of allenamides **46a**, providing tetrahydrocarbolines **47a** in excellent yields and high enantioselectivities (Scheme 9, reaction b). In addition, three naturally occurring systems were obtained in gram-scale manner taking advantage of this transformation. (*R*)-Desbromoarborescidine A, C, and (*R*)-deplancheine were accessed from tetrahydrocarboline **46b** in 26, 68 and 57% yield, respectively (Scheme 9, reaction c).[47]

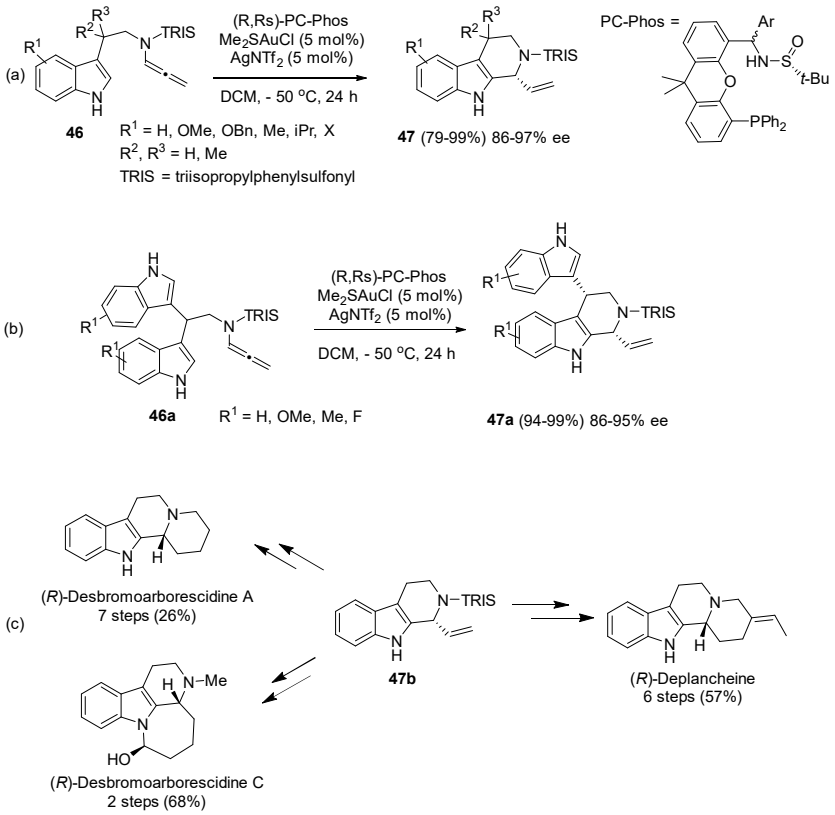


Scheme 8. Synthesis of THCs and related systems through intermolecular allenamide-indole cycloaddition.

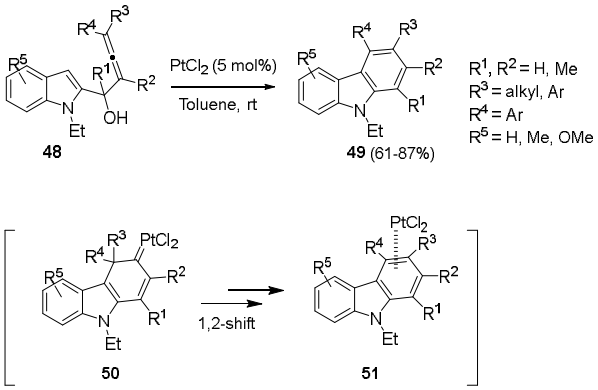
2.2. Platinum catalysis

Despite the similar reactivity gold and platinum catalysts may display, some reports have shown intriguing differences, mainly related to divergent mechanistic pathways.[48] In the context of the carbazole preparation from indolylallenes, Ma and collaborators have reported several platinum-mediated synthesis of carbazoles, including naturally occurring structures.[49] Opposite to the final protodemetallation step shown in the gold-catalyzed cycle (**9** to **4** in Scheme 2), the authors proposed a platinum carbene species **50** as the most plausible key intermediates to account for the observed final structures **49**. Thus, a 1,2-shift rearrangement from intermediate **50** followed by dehydrogenation would lead to the coordination species **51**, providing the highly decorated and fully aromatic carbazole skeletons **49**. Interestingly, the platinum carbene strategy allows the use of allenes **48** showing double terminal substitution (Scheme 10).[50-52]

Taking advantage of the facility of platinum species to evolve through carbene intermediates, Alonso and Muñoz devised a tandem methodology to prepare functionalized THCs **53** and **54** from C3-linked allenylindoles **52** (Scheme 11).[53,54] The reaction mechanism proposed involves carbocyclization followed by addition of an external nucleophile onto the platinum carbene intermediate **55**. The reaction proceeded with good to excellent yields using both C- and N-based nucleophiles (**56** and **57**, respectively), unraveling a divergent regioselectivity. Thus, while C-based nucleophiles exclusively provided isomers **53**, the use of azoles **57** as *N*-nucleophiles favored the formation of isomers **54** as major compounds because of the direct attack of the azole onto the metal carbene **55**. In addition, when indoles are used as external nucleophiles, structures **53** simultaneously show the THC and the bis(indolyl)methane motifs, also a recurring topic in organic chemistry and natural products. Noteworthy, the best results were obtained when Au(I) and Pt(II) salts were used as catalytic pair, generating *in situ* bimetallic particles acting as heterogeneous catalyst, in equilibrium with soluble bimetallic clusters as homogeneous counterparts.



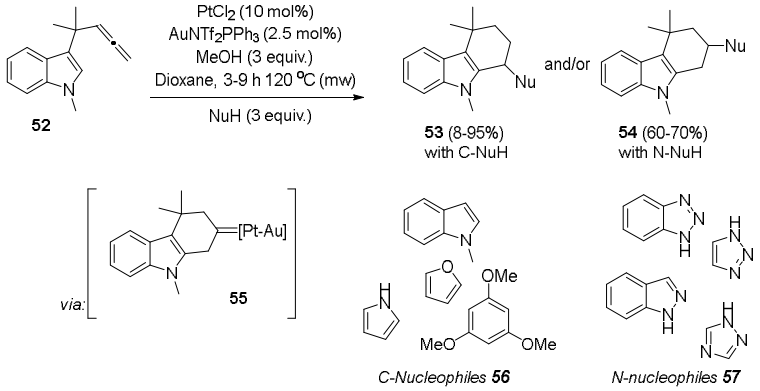
Scheme 9. Synthesis of tetrahydrocarboline skeletons through gold-catalyzed cyclization of allenamides.



Scheme 10. Pt-catalyzed synthesis of carbazoles *via* metal carbene intermediates.

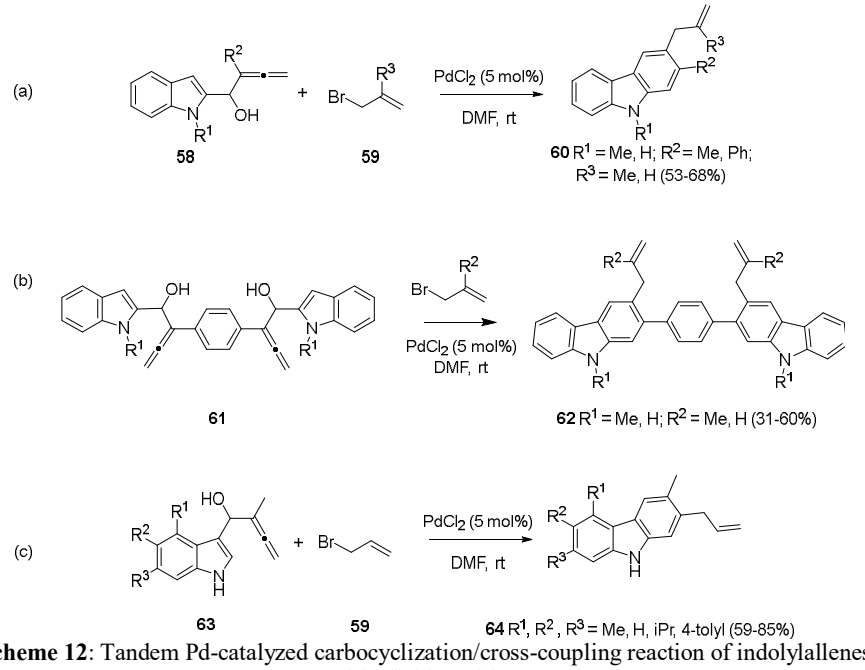
2.3. Palladium catalysis

Besides the ability of many transition metal species to promote the carbocyclization of indolylallenes directed to the carbazole synthesis, palladium complexes are also able to catalyze tandem processes through cross-coupling reaction yielding substituted carbazole structures.



Scheme 11. Tandem Au/Pt-catalyzed carbocyclization/nucleophilic addition with indolylallenes and nucleophiles.

In our research group, we have investigated palladium-catalyzed tandem reactions and the mechanistic features behind the synthesis of biologically attractive carbazoles. Thus, taking advantage of the improved π-coordinating nature of palladium ions, a tandem process including carbocyclization step followed by cross-coupling reaction of allenols **58** with allyl bromides **59** was developed (Scheme 12, reaction a).

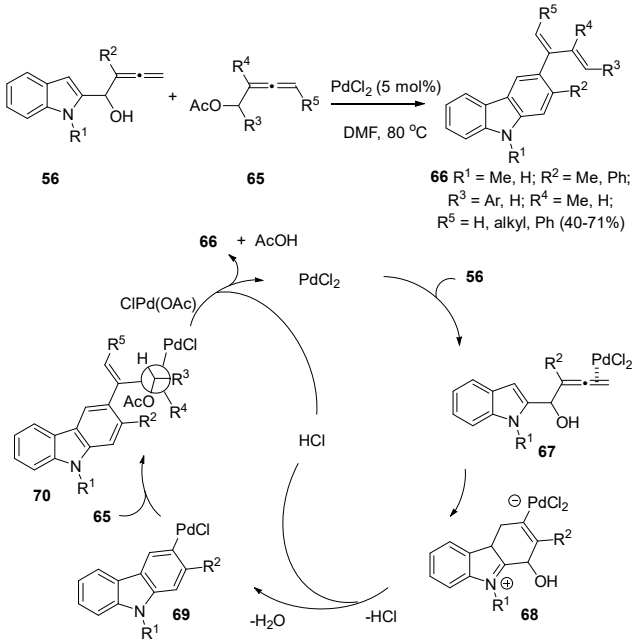


Scheme 12: Tandem Pd-catalyzed carbocyclization/cross-coupling reaction of indolylallenes with allyl bromides.

Carbazoles **60** bearing different allyl substituents at 3-position were synthesised in good yields and with complete regioselectivity.[55] The methodology was also successfully applied to the synthesis of allyl-substituted bis-carbazoles **62** from bis-indolylallenes **61** with fair yields (Scheme 12, reaction b). In a different approach, C3-linked allenylindoles **63** were investigated under similar reaction conditions

providing 2-allylsubstituted carbazoles **64** using $PdCl_2$ as metal source, and tolerating diverse substitution on the indole ring (Scheme 12, reaction c).[56]

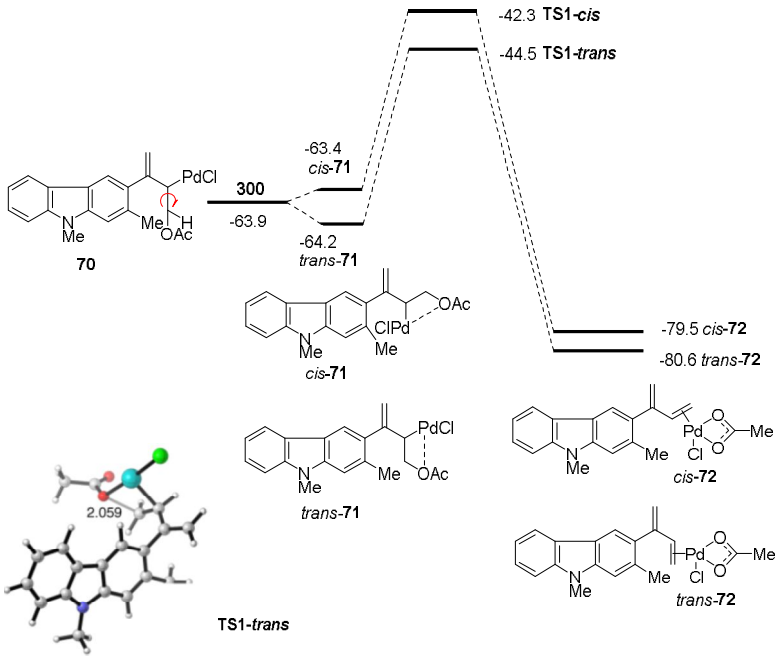
Alternatively, the cross-coupling reaction was performed in the presence of a second allenic unit **65**, giving access to carbazoles **66** bearing the pharmacologically attractive 3-(buta-1,3-dienyl) motif.[57] The scope of the methodology was extended to a wide number of differently substituted allenols **65**, yielding carbazoles **66** with moderate to good yields (Scheme 13). Interestingly, the transformation took place in a complete chemo- regio- and stereoselective manner, as no oxycyclization products were observed,[59] and only *E*-butadienyl isomers were obtained. In addition, this report constituted the first cross-coupling reaction of two allenic moieties incorporating a carbocyclization step. The most plausible mechanistic pathway would start from coordination of the terminal allenic double bond to the palladium center to give complex **67**, followed by *6-endo* carbopalladation yielding alkenyl metal species **68**. Loss of HCl and dehydration would provide palladacarbazole **69**. Then, cross-coupling reaction towards at the central allenic carbon of the acetyl-protected allenol **65** would lead to intermediate **70**. Observed butadienyl carbazoles **66** could be eventually obtained by deacetoxy-palladation of intermediates **70**, regenerating the catalytic species after the extrusion of AcOH.[58]



Scheme 13. Tandem Pd-catalyzed carbocyclization/cross-coupling reaction of indolylallenes with acetyl-protected allenols.

In order to get full understanding of the noteworthy chemo-, regio- and stereoselectivity displayed on this transformation, we performed DFT calculations revealing a computed carbocyclization reaction profile from allenols **56** notably favoured in comparison to the oxycyclization process. This result supports the chemoselectivity observed in the first step of the tandem reaction towards the generation of the carbazole structure in compounds **66**. Moreover, the complete stereoselectivity observed in the diene generation can be explained considering the computed results for the depalladation step (Scheme 14). Free rotation along the C-C single bond in intermediate **70** could lead to both *cis*-**71** or the more stable *trans*-**71** intermediate. Demetallation step is calculated to proceed through a lower energy barrier from *trans*-**71** complex, yielding the also more favoured *trans*-**72** coordination adduct. Thus, the more plausible reaction pathway is the

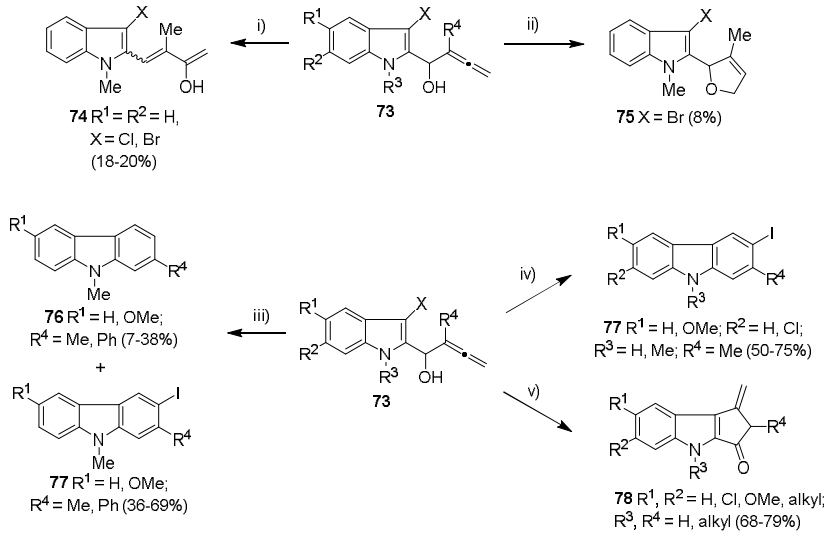
kinetically and thermodynamically controlled *trans*-deacetoxypalladation process through transition state **TS1-*trans***.



Scheme 14. DFT computed reaction profile for deacetoxypalladation step in carbocyclization/cross-coupling reaction of indolylallenes. Relative free energies are given in Kcal mol^{-1}.

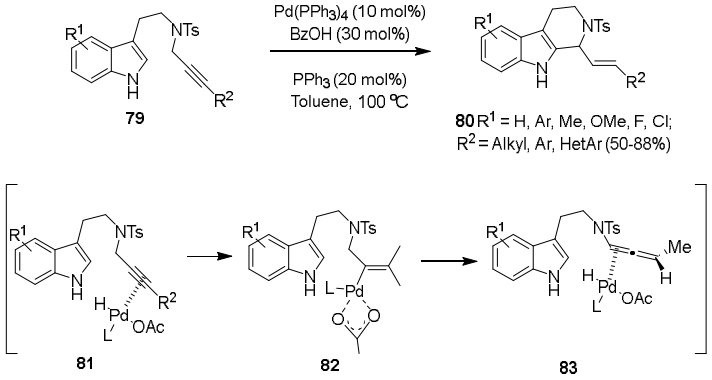
Related 3-halo-(indol-2-yl)-α-allenols **73** exhibited a complex reactivity pattern, showing divergent behavior depending on the halide substitution at the indole 3-position. While 3-chloro- and 3-bromo-indoles reacted with gold salts to yield dienes **74** *via* a 1,3-hydroxyl migration in complex reaction mixtures (Scheme 15, top left), palladium catalysis only provided dihydrofuran systems **75** in low yields when 3-bromo-(indol-2-yl)-α-allenols **73** were employed (Scheme 15, top right). More interestingly, a different and dual behavior has been observed with 3-iodoindole derivatives **73** in the presence of palladium salts. Thus, the reaction of **73** under the bimetallic pair $Pd(PPh_3)_2Cl_2$/CuI yielded iodocarbazoles **77** as the sole reaction products in good yields, through an unprecedented 1,3-intramolecular migration of iodine.[60] On the other hand, the presence of a base in the reaction media under otherwise similar experimental conditions, allowed a switch in the reaction pathway, yielding cyclopentenones **78** through an intramolecular Heck-type process (Scheme 15, bottom, right).[61] Gold catalysis from iodo-derivatives **73** led to mixtures of carbazoles **76** and the above mentioned iodo-carbazoles **77** (Scheme 15, bottom, left).

The Maestri research group has reported a palladium-based alternative to the synthesis of tetrahydro-β-carbolines described in Scheme 9. In this approach, readily available propargyl triptamines **79** undergo a palladium hydride-mediated isomerization to the corresponding allenamides **83**, key intermediates in the proposed reaction pathway. Initial coordination of the platinum hydride complex would generate intermediate **81**. Then, insertion of the metal hydride onto the proximal allenic double bond providing alkenyl palladium system **82**, followed by C-H indole activation and reductive elimination would explain the formation of the observed tetrahydrocarbolines **80**. Interestingly, Maestri's approach is based on the use of palladium salts and carboxylic acid as co-catalysts, performing a multiple role along the catalytic cycle, acting as a hydride source, metal ligand, and as activating agent in the indole C-H insertion (Scheme 16).[62]



i) **73** (1 equiv.), $(Ph_3P)AuNTf_2$ (5 mol%), DCE, rt. ii) **73** (1 equiv.), $[(Ph_3P)_2PdCl_2]$ (5 mol%), DMF, rt. iii) **73** (1 equiv.), $(Ph_3P)AuNTf_2$ (5 mol%), DCE, rt. iv) **73** (1 equiv.), $[(Ph_3P)_2PdCl_2]$ (5 mol%), CuI (5 mol%), DMF, 70 °C. v) **73** (1 equiv.), $Pd(PPh_3)_2Cl_2$ (5 mol%), CuI (5 mol%), TEA, 70 °C.

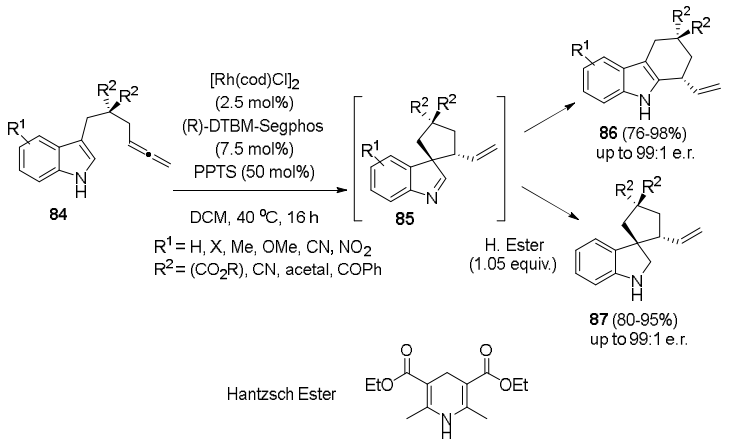
Scheme 15. Divergent reactivity on 3-halo-(indol-2-yl)-allenols under metal catalysis.



Scheme 16. Palladium-mediated synthesis of tetrahydro-β-carbolines.

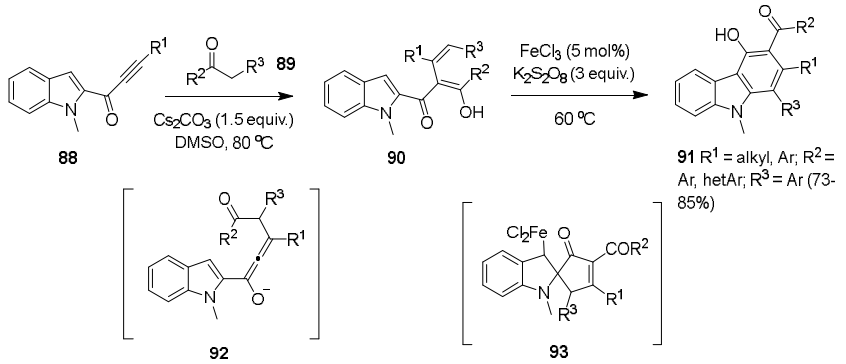
2.4. Other metals

Although the synthesis of carbazole-type structures using allenes and transition metal catalysts is mainly limited to coinage metals and palladium complexes, we can find a few examples in the literature describing this transformation supported by other metallic species. In one of those rare examples, Breit and collaborators have recently reported the enantioselective reaction of indole-tethered allenes **84** in the presence of rhodium salts to give the THC core **86.** The reaction is proposed to undergo through spirocycle **85** as key intermediate, obtained from the attack of the most nucleophilic position C3 of the indole ring to the proximal allenic carbon. Further rearrangement through a C-C single bond shift would provide the observed structures **86** (Scheme 17, top).[63] In a parallel work, the same authors reported that intermediate **85** can also be trapped *in situ* with Hantzsch ester as reductant to give functionalized vinyl spiroindoles **87**, also supporting the mechanistic pathway proposed for the synthesis of carbazole-type molecules **86** (Scheme 17, bottom).[64]



Scheme 17. Rh-based carbocyclization of indole-tethered allenes.

Li and co-workers have recently described an intricate reaction mechanism for the synthesis of densely decorated carbazoles. Indole-tethered alkynones **88** reacted in the presence of a base and carbonyls **89** through allenic intermediates **92** to provide substituted indoles **90**. Then, iron salts promoted the synthesis of carbazoles **91** under oxidative conditions through spirocycles **93**. The authors have reported a one-pot methodology for this transformation, starting from alkyne derivatives **88** and building a wide family of carbazoles **91** in good yields, also exhibiting a high functional group tolerance (Scheme 18).[65]



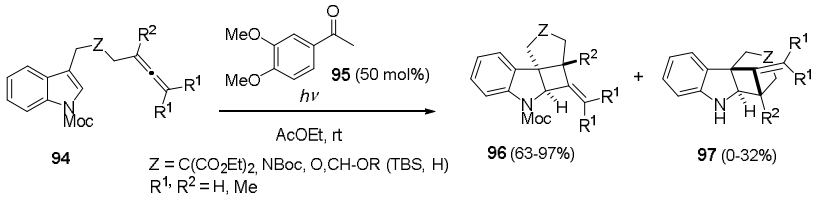
Scheme 18. Fe-based synthesis of functionalized carbazoles.

3. Metal-free methodologies

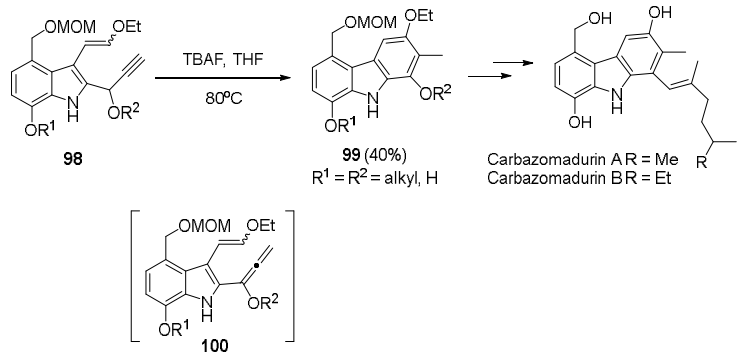
Although uncommon, the synthesis of carbazoles in the absence of a metal catalyst has provided a couple of interesting results in the fields of mechanistic investigations and total synthesis. One of those infrequent metal-free approaches for the generation of carbazole-type molecules has been presented by Ohkuma and Arai. In this work, photo-induced [2+2] intramolecular cycloaddition between the distal allenic bond and the indole double bond in substrates **94** using ketone **95** as photo-inductor led to a mixture of compounds **96** (parallel cycloaddition) and **97** (crossed cycloaddition). In any case, the carbazole-containing structures **97** were obtained as minor isomers (Scheme 19).[66] Importantly, products **96** were the sole isomers observed from similar starting materials under metal-catalysed conditions, as it has been reported by Voituriez and collaborators in a later work.[67]

In a different approach, thermally induced [2+2+2] cycloaddition of propargylic indoles **98** has been employed for the synthesis of carbazoles **99**. The transformation proceeded through the 2-allenyl

intermediate **100**, *in situ* generated from **98** in the presence of a base. Carbazoles **99** were further used as precursors in the total synthesis of Carbazomadurin A and B, two neuronal cell-protecting alkaloids (Scheme 20).[68]



Scheme 19. Photochemical cycloaddition of indole-tethered allenes.



Scheme 20. Synthesis of carbazoles through thermally allene-alkene cycloaddition.

4. Conclusions

The biological importance of carbazole alkaloids, along with the increasing use of these structures in organic materials, has motivated the organic chemists to develop a growing number of synthetic methodologies oriented to these molecular motifs. In this regard, the last decades have witnessed the occurrence of more sophisticated strategies beyond the classical approaches, in order to get a more diverse and interesting pattern of substitution around the heterocyclic core, and more efficient and atom economic procedures. Among those methodologies, the formation of the ring B from reaction of conveniently substituted indoles and allenes has emerged as one of the most powerful tools to build the carbazole skeleton. This strategy has provided several advantages: on one hand, the use of inexpensive and readily available indole rings as starting materials has facilitated a quick access to the tricyclic core. On the other hand, the electrophilic nature of the allene moiety in the presence of transition metals perfectly complements the strong nucleophilic character of the indole ring, promoting ring-closing processes. In addition, transition metal catalysis allows the use of milder reaction conditions, improves the functional group tolerance and also provides a greener alternative for the preparation of the carbazole skeleton.

Notwithstanding the great effort that has been done to date towards the synthesis of carbazole-type molecules, the continuous necessity of improved structures showing higher activities, more useful applications, and the interest on developing novel methodologies, will certainly result in more results in the future in this field. The extensive use of precious metals and palladium salts in allene carbocyclization reactions, as previously described, has left the door open to the implementation of alternative strategies based on different metals such as Fe, Ni, Mn, or Cu, providing more economic and sustainable approaches. In addition, the use of photo-assisted methodologies remains unexplored regarding the allene-based synthesis of carbazoles. The application of novel strategies, such as the bimetallic hybrid catalysis, will keep attratting the attention of the research community towards this important class of the heterocyclic compounds.

Acknowledgements

This work was supported in part by AEI (MICIU) and FEDER (Project PGC2018-095025-B-I00).

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