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Update on novel synthetic approaches towards the construction of carbazole nuclei: a review

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The carbazole scaffold is a significant entity in organic compounds due to its variety of biological and synthetic applications. Traditionally, carbazole skeletons have been synthesized either *via* the Grabe–Ullman method, Clemo–Perkin method or Tauber method. With the passage of time, these methods have been modified and explored to accomplish the synthesis of target compounds. These methods include hydroarylations, C–H activations, annulations and cyclization reactions mediated by a variety of catalysts to construct carbazole-based compounds. This brief review article intends to provide recent updates on important methodological developments reported for the synthesis of carbazole nuclei covering 2019–2023.

Introduction

The chemistry of heterocycles is a fundamental part of organic compounds.[1] Drug design and development is responsible for a wide variety of heterocyclic compounds that have been discovered and exploited in the area of drug synthesis,[2] synthetic polymers,[3] fluorescent probes,[4] agrochemicals,[5] veterinary products,[6] dyes[7] *etc.* A large number of heterocyclic compounds occur naturally having algal, fungal, or plant sources of origin, whose synthesis can be carried out *via* a number of strategies.[8,9] These heterocycles may possess oxygen, nitrogen, or sulfur in their cyclic structure.[10,11] The presence of a heteroatom influences a substantial change in the properties of the respective compounds making them biologically active[12] and medicinally important.[13] The heterocycles containing one or more nitrogen in their structures have a significant place in the synthetic field.[14] Some of the nitrogen-containing drugs are presented in Fig. 1 which include lisinopril[15] (anti-hypertensive) **1**, cephalexin[16] **2** and (+)-penicillin V potassium salt[17] **4** (anti-biotic), enalapril[18] (treat heart failure and diabetes) **3**, Atorvastatin[19] (decrease cholesterol level) **5** and Sumatriptan[20] (treat migraine) **6**.

Carbazole is an important part of significant nitrogen-containing heterocycles. It consists of a tricyclic core with two fused benzene rings on either side of the pyrrole ring (Fig. 2).[21] This heterocyclic moiety accounts for a number of industrial, and biological properties. Carbazoles belong to the class of indoles and represent privileged scaffolds in biological and non-biological systems by exhibiting a wide spectrum of applications in different fields. It exhibits a number of biological activities[22,23] *i.e.*, anti-microbial,[24] anti-cancerous,[25] anti-inflammatory,[26] anti-viral,[27] neuroprotective[28] and anti-oxidative.[29] Among industrial applications, carbazole scaffold has found potential applications in fluorescent probes,[30] bioimaging devices,[31] organic semiconductors[32] and polymers[33,34] *etc.*

Carbazole embodies a vast variety of plant-based natural compounds, harbored with profound pharmaceutical properties.[35,36] It is widespread in a number of naturally occurring compounds such as alkaloids.[37] The Rutaceae family is found to be the source of carbazoles among many other naturally occurring sources.[38] Cancer has been the leading cause of death among mankind. The discovery of multiple etiologies along with their treatments goes side by side. Various naturally occurring compounds have been found active against cancer-causing agents *i.e.*, oncogens. The carbazole derivatives have emerged to find anti-cancerous activities against such oncogens, *i.e.*, ellipticine **11**,[39] a promising anti-tumor drug. Carvedilol **13**,[40] a vasodilator and effective anti-oxidant has been found to be operative in the treatment of heart failure. Along with the compounds as mentioned above, the structures of some of the bioactive carbazoles[38–43] are presented as follows (Fig. 3).

A lot of research has been conducted in the past for the synthesis of N-heterocycles[44,45] including carbazoles.[46–48] The synthesis of carbazole scaffold has been achieved *via* alternative strategies.[49–54] These strategies involved electrocyclic reactions, cycloaddition reactions, annulations and insertion reactions. This review article covers the latest updates on the methodological development of carbazole skeleton reported since 2019. The division of content has been focused on the process involved in the construction of carbazole nuclei. The synthesis

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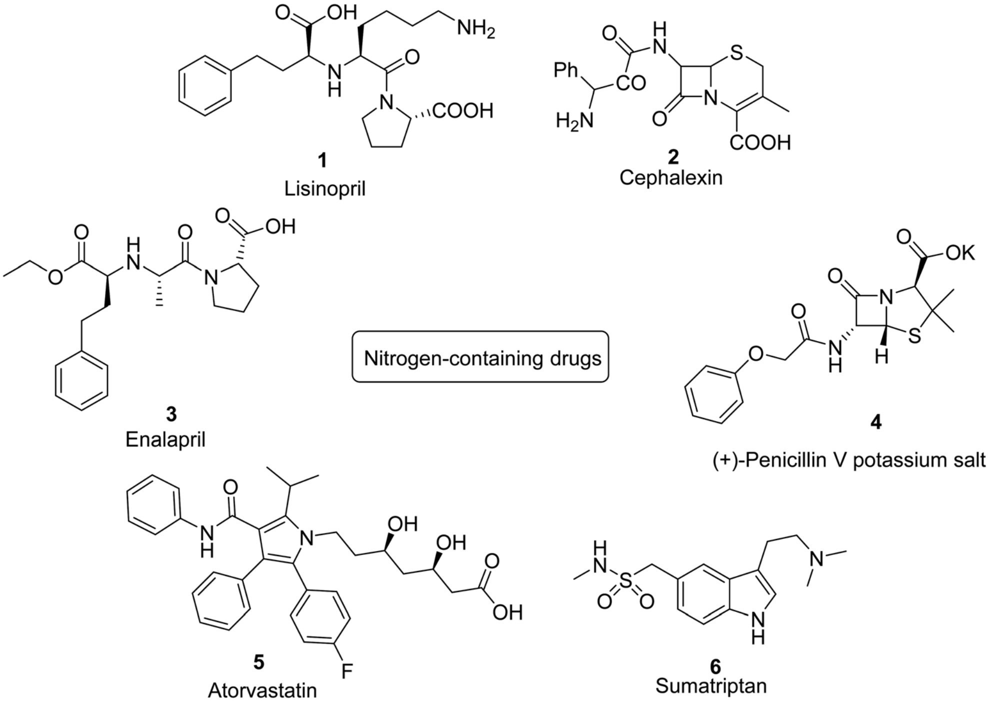


Fig. 1 N-Heterocyclic drugs and their structures.

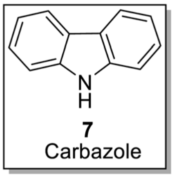


Fig. 2 The structure of [9*H*-carbazole].

of carbazole skeleton has been achieved *via* a number of strategies which have been explained under specific classifications as follows.

Synthesis of carbazole nucleus

Hydroarylation reactions for the synthesis of carbazoles

Transition metals are widely employed as catalysts in the field of organic synthesis.[55] Hydroarylation reactions are considered efficient owing to economically appealing, mild conditions and high-bond forming efficacy.[56] Palladium-catalyzed hydroarylation for carbazole synthesis was proposed by Martin *et al.* in 2021, for which $Pd(PPh_3)_2Cl_2$ was employed as a catalyst with CuI acting as a co-catalyst and triethylamine as a solvent at 40 ° C to accomplish the target compounds.[57] A chemo- and regioselective synthesis of 2- iodo-1-aryl-9*H*-carbazoles was achieved by employing different substrates leading towards a diverse series of three types of products. The Pd-catalysis was performed by reaction of aryl iodides **15**, 2-iodo thiophenes **18** and 3-iodo-indole carbaldehydes **21** with substituted iodo alkynols **14** to furnish respective carbazoles **16**, **19** and **22** in moderate yields (Scheme 1). The feasible mechanistic pathway for this reaction included the synthesis of Sonogashira adduct **A** from alkynols **14** and aryl iodide under palladium catalysis. In the next step, palladium salt coordinated with alkyne moiety to form complex **B** which underwent 5-*endo-dig* carbopalladation to generate pallada-spirocyclopentene intermediate **C**. Next, iodotetrahidrocarbazolium specie **D** was produced *via* 1,2-alkyl migration which was proceeded by 1,4-iodonium migration to give 2-iodo 1-aryl-4,9-dihydro-3*H*-carbazol-4-ols **E**. In the final step, 2-iodocarbazoles were produced after dehydration (Scheme 2).[57] The key attributes of this reaction are the selectivity induced by Pd-catalyst and the functionalization of the aryl iodide group by employing the Suzuki reaction to furnish a variety of compounds. In the subsequent year, Jatoth *et al.* accomplished the synthesis of N-heterocycles fused with carbazole by employing TFA-mediated, metal-free, green, one-pot hydroarylation protocol.[58] The reaction of 3-ethynyl-2-chloro substituted quinoxalin **27** and 5-ethynyl-4-chloro substituted pyrimidines **25** with indole derivatives **24** in the presence of trifluoroacetic acid at room temperature for 60 min furnished N-heterocycle fused substituted carbazoles **26** and **28** in 65–68 and 63–71% respective yields comprising of twelve and two examples each. This methodology features short reaction time, wide substrate scope, facile conditions and good yields of products (Scheme 3).

Annulation reactions for the synthesis of carbazoles

Annulation reactions are widely employed for the synthesis of functionalized carbazoles. These include [4 + 2] annulation, benzannulation, cascade annulation *etc.*[59,60] Among these, the [4 + 2] annulation is deliberated to be the most productive

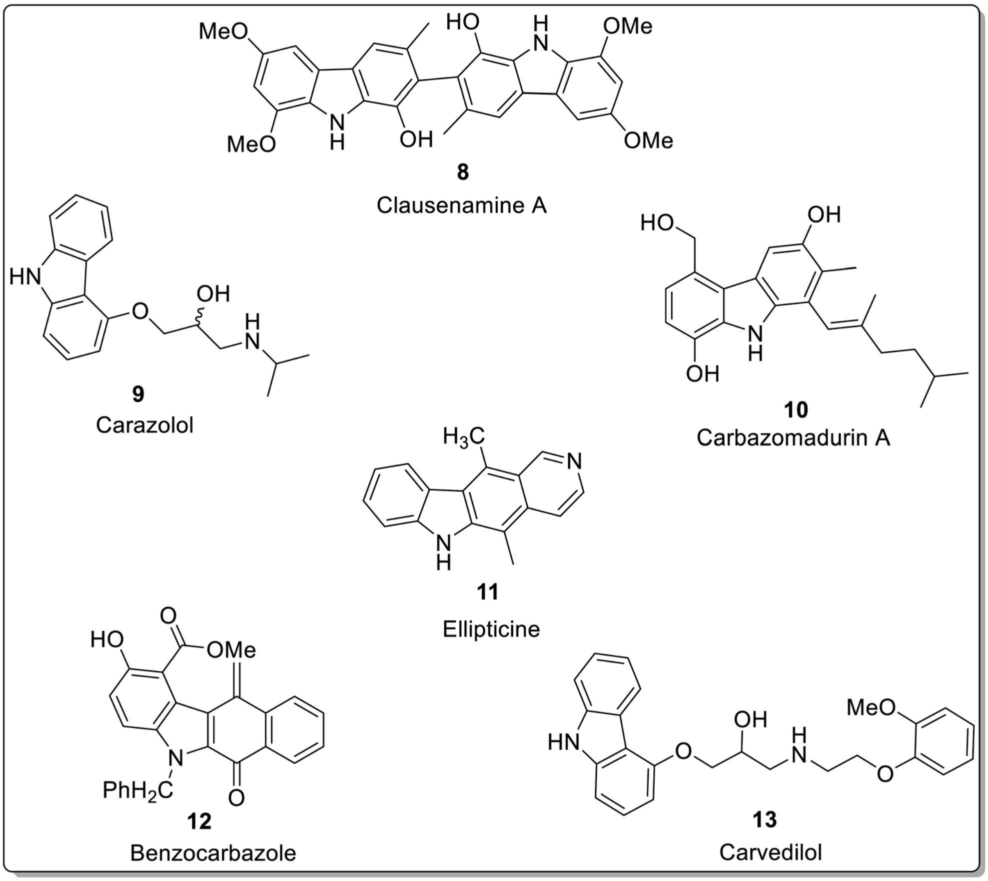
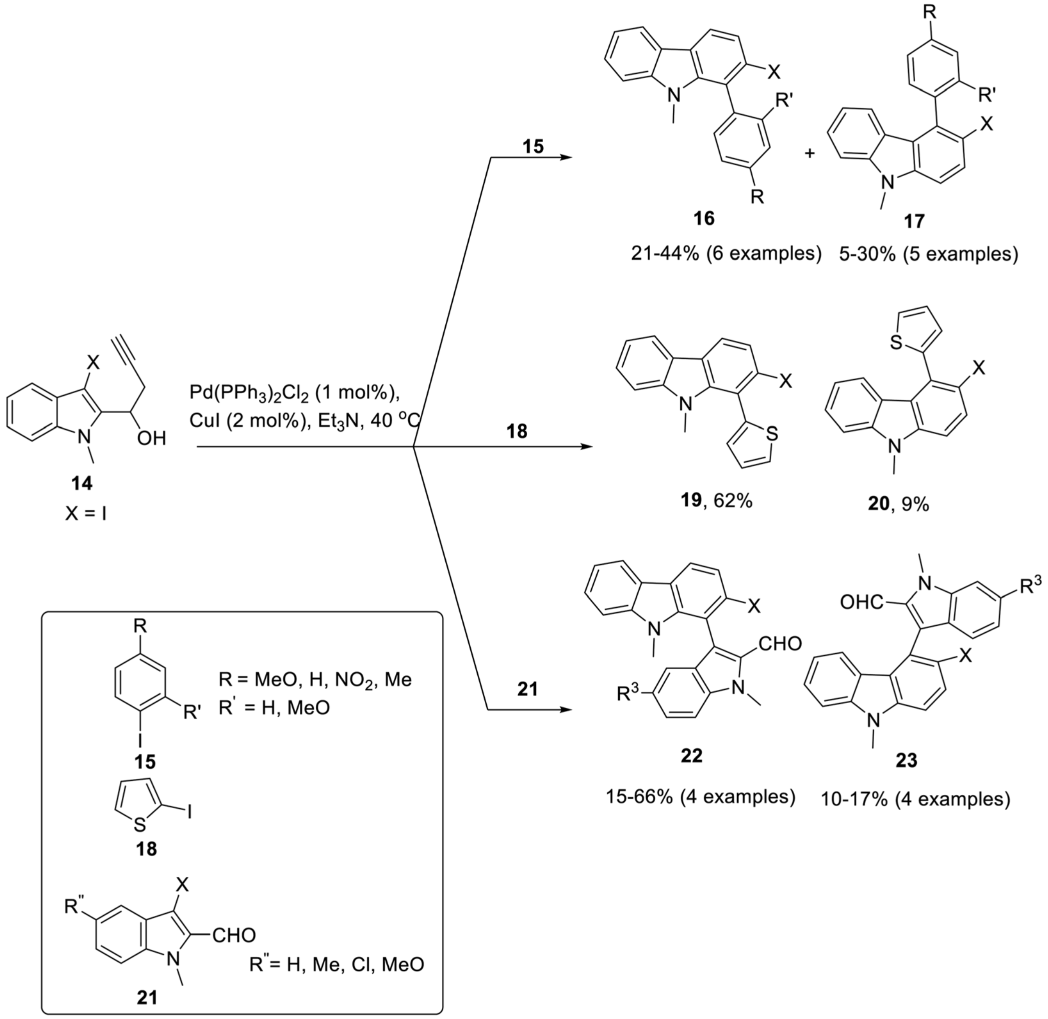


Fig. 3 Structures of carbazole containing natural compounds.

protocol for indole-to-carbazole synthesis. El-Harairy *et al.* in 2019 employed a [4 + 2] annulation protocol based on a Brønsted acid having imidazolium-based ionic liquid with sulfone moiety in butyl acetate to achieve the task.[61] The efficiency of this catalytic system was checked by employing it for the conversion reactions of different indoles. For [4 + 2] annulation, 2 molecules of *N*-methylindole **30** were made to react with 2,5-dihydro-2,5-dimethoxyfuran **29** in the presence of butyl acetate as a solvent and 10 mol% of ionic liquid **31** as a ligand to afford 70–92% of target compounds **32**. Some important features of this methodology included the reusability and effectiveness of ionic liquid in obtaining better selectivity and yields (Scheme 4). The imidazolium-based ionic liquid breaks the stereotype of using toxic and hazardous solvents for the synthesis of organic compounds and introduces a more selective, high-yielding and recoverable green catalytic solvent system with butyl acetate. Another Brønsted acid-catalyzed pinacol rearrangement for the synthesis of functionalized carbazoles from α-(3-indolyl) ketones *via* cascade annulation (one-pot) was reported by Kundu *et al.* in the similar year.[62] The targeted compounds were obtained by reacting 2-alkenyl indole **33** and substituted aldehydes **34** in the presence of 20 mol% of *para*-toluenesulfonic acid (PTSA·H_2O) as a catalyzing agent in toluene as a solvent at 120 °C leading towards the synthesis of functionalized carbazoles **35**. The functionalized carbazoles **35** could further *N*-methylated in the presence of methyl iodide and dimethyl sulfoxide providing carbazole derivatives **35a** in 44–67% yields (Scheme 5). The mechanistic details for the synthesis functionalized carbazole **35** involved the synthesis of indolyl diol **A** which underwent pinacol-type rearrangement to give α-(3-indolyl) ketone **B**. Next, desired carbazole **35** was synthesized *via* tandem cyclization and aromatization of subsequent intermediates (Scheme 6).[62] The catalyst employed for this methodology is commercially available and inexpensive making it a feasible and convenient methodology.

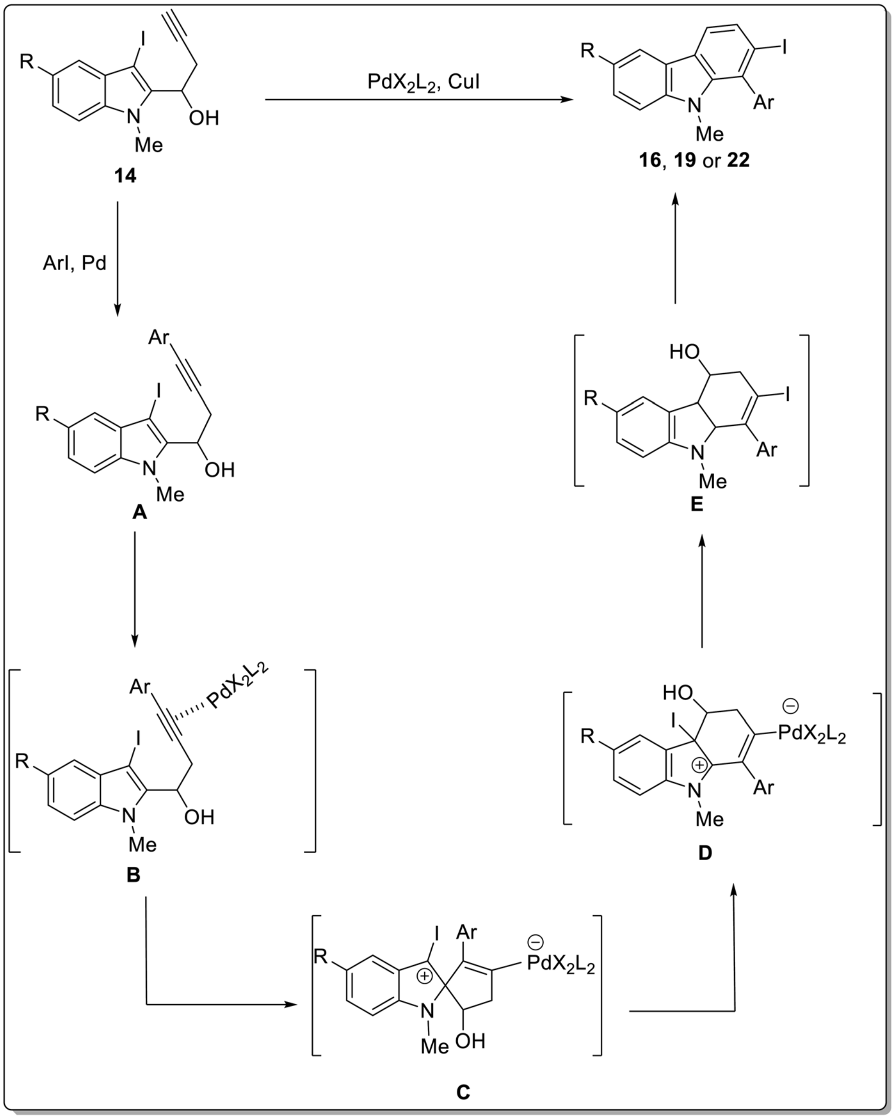
The benzannulation reactions are used widely to access functionalized and naturally occurring carbazoles. The Scheme 7 presents the synthesis of 4-hydroxy carbazoles **38** from nitroindoles **36a** *via* a metal-free benzannulation with alkylidene azalactones **37**, reported by Cao *et al.* in 2021.[63] The *N*-Ts-3-nitroindole **36a** on conjugate vinylogous addition to azalactone **37** in the presence of 2 equivalents of base and 1 : 2 solvent ratio of THF/hexane at 40 °C furnished 4-hydroxy carbazole derivatives **38** in 20–92% yield. The mechanistic details implied the synthesis of dienolate **A** *via* deprotonation of azalactone **37** by K_2CO_3 which gave nitronate intermediate **B** by reacting with 3-nitroindole **36a**. Next, indoline-fused compound **C** was produced from intermediate **B** *via* intramolecular cyclization. The compound **C** eliminated a molecule of nitrous acid to generate indole-fused compound **D** which produced



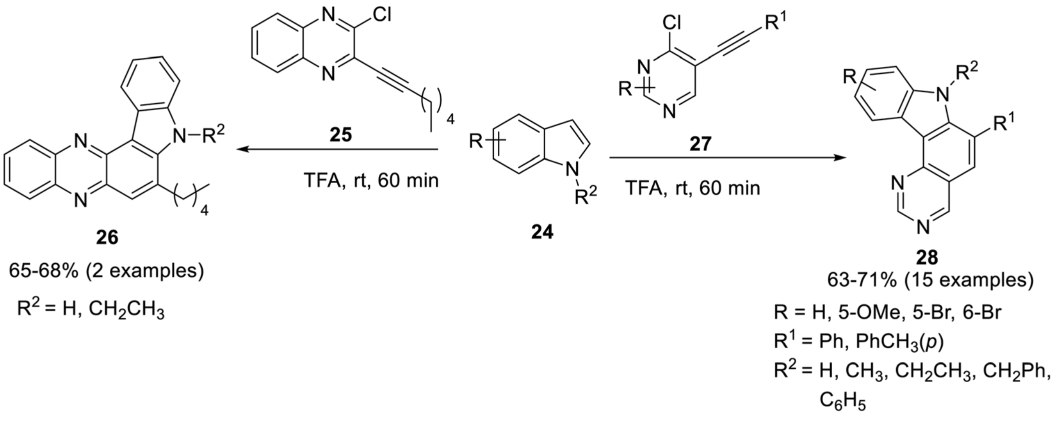
Scheme 1 Pd-catalyzed hydroarylation for synthesis of 2-iodo-1-aryl-9*H*-carbazoles.

potassium carbazol-4-olate **E** followed by acidification to give carbazole derivative **38** (Scheme 8).[63] The azalactone tolerated a wide variety of substrates possessing facile and scalable methodology. Karan *et al.* employed a triple cascade one pot benzannulation protocol and provided a back-to-front approach for synthesizing carbazole nuclei **40** from indole 2-carboxaldehyde **36b** and substituted boronic acids **39**.[64] The one-pot procedure consisted of allylation followed by *E*-2 elimination mediated with triethylamine and 6π-electro cyclization to furnish carbazoles **40** in 49–74% yield range (Scheme 7). The mechanistic details for the synthesis of carbazole **40** inferred the reaction between indole 2-carboxaldehyde **36b** and substituted boronic acids **39** to give allylic alcohol **A**. The next step involved mesylation of allylic alcohol **A** along with triethyl amine assisted elimination to give conjugated alkene **C**. In the final step, carbazoles **40** are produced *via* 6π-electrocyclization and aromatization of alkene **C** (Scheme 9).[64] The developed procedure provided a scalable pathway for the synthesis of carbazole-based natural products *i.e.*, glycozolinol and glycozoline. Another one-pot, metal-free and base-catalyzed synthesis was reported by Singh *et al.* for the synthesis of carbazole-based natural products from carbazole **41**.[65] The synthesized natural products are calothrixin B **41a**, staurosporine **41b** and carbazomycin A **41c** (Fig. 4).

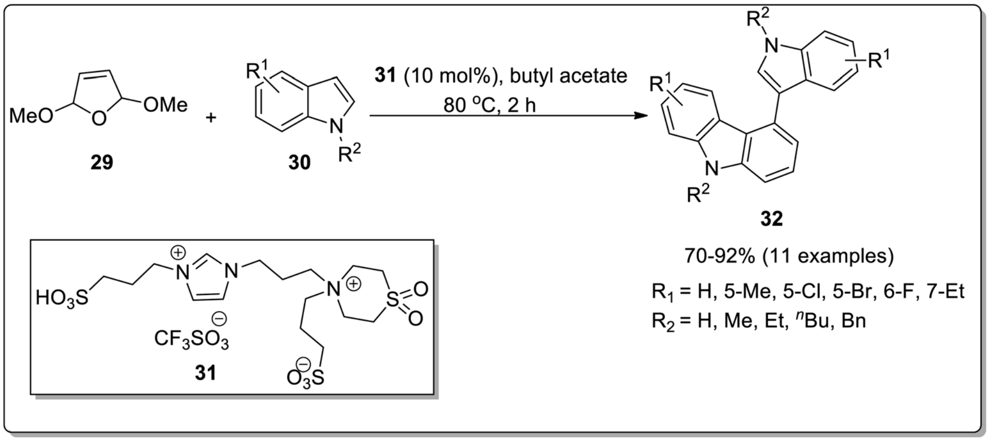
Intramolecular reactions are regioselective, efficient and can be highly versatile. The synthesis of carbazoles has been achieved by various intramolecular cyclization strategies, which might involve serendipitous discovery sometimes.[66] Kumar *et al.* reported the synthesis of tetracyclic carbazoles *via* an intramolecular benzannulation of alkyne-tethered indoles catalyzed with rhodium acetate in the presence of an oxidant and solvent.[67] The reaction conditions were optimized by screening different catalysts and solvents by altering their concentration. The intramolecular benzannulation of ethyl 3-(indol-3-yl)acrylate tethered with alkyne **42** was performed by employing 5 mol% of rhodium acetate, 2 mol% of copper bromide in dimethyl acetate to obtain the annulated product **43**. This methodology has been reported to be atom-economical, feasible and substrate-scalable (Scheme 10). The plausible mechanism for the synthesis of carbazole derivative **43** involved the oxidative addition of Rh(III) to bromocompound **42a** to give intermediate **A**. Next, rhodacycle **B** was produced by



Scheme 2 Mechanistic details for the synthesis of iodocarbazoles **16**, **19** and **22**.[57]



Scheme 3 One-pot hydroarylation for carbazole synthesis.



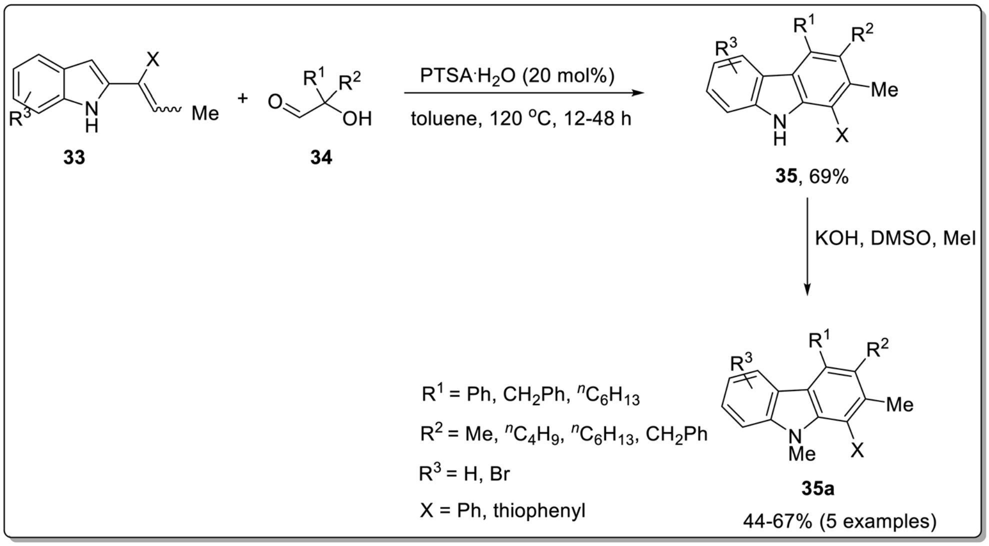
Scheme 4 [4 + 2] Annulation for the synthesis of carbazole.

a concerted metalation deprotonation step followed by 6-membered rhodacycle intermediate **C** synthesis *via* an internal alkyne insertion. In the final step, the target compound was synthesized by reductive elimination of intermediate **C** (Scheme 11).[67] The exploitation of stable bisalkynol **44**, obtained from *N*,*N*-bis(2- bromoallyl)amines, for a gold-catalyzed back-to-front approach to access carbazoles **45** *via* a double benzannulation strategy was proposed by Muñoz-Torres *et al.* in 2021.[68] The reaction proceeded in the presence of 5 mol% of $NaAuCl_4 \cdot 2H_2O$ in DCM which induced double benzannulation to give substituted carbazoles in 60–85% yields (Scheme 12). This useful methodology allows the regioselective synthesis of functionalized carbazoles from readily available starting materials.

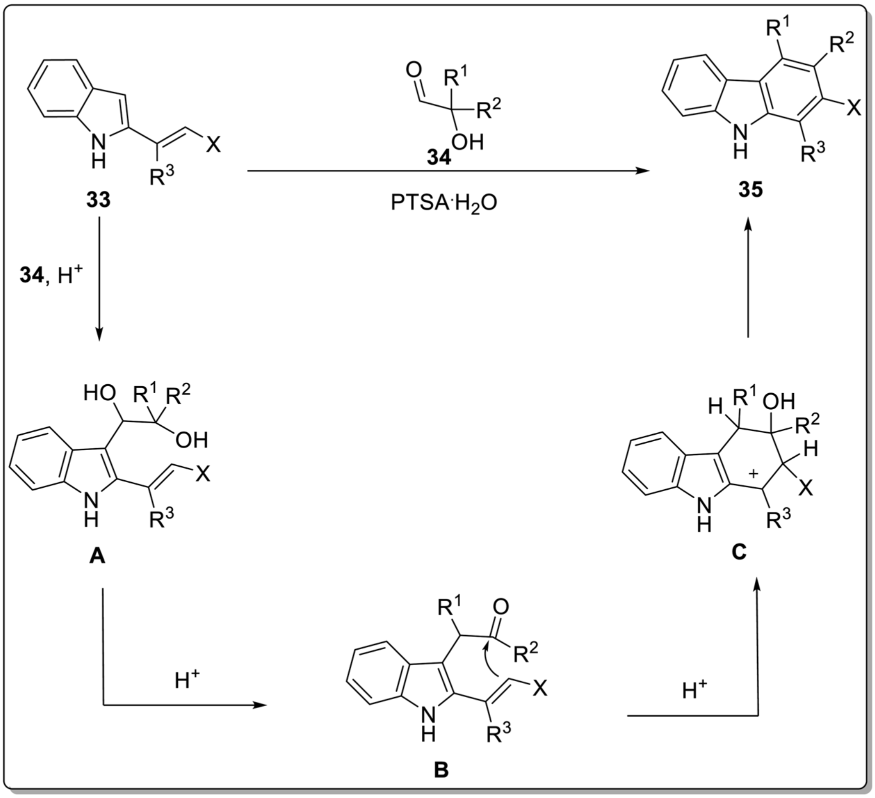
The carbazole and its derivatives have been constructed by various strategies.[69] Despite the difficulty of synthesizing N–H carbazole from N–H indole, a three-component annulation reaction for the carbazole development has been reported by Huang *et al.* in 2021.[70] It involved the reaction between an indole **46**, bromoacetaldehyde dimethyl acetal **47** and 1,3-dicarbonyl compound **48** to furnish carbazole-2-carboxylates **49.** The synthesized carbazole compounds were further substituted by hydrazine and amide to afford biologically active compounds, which were screened and evaluated against different cell lines (Scheme 13).

C–H activation for the synthesis of carbazoles

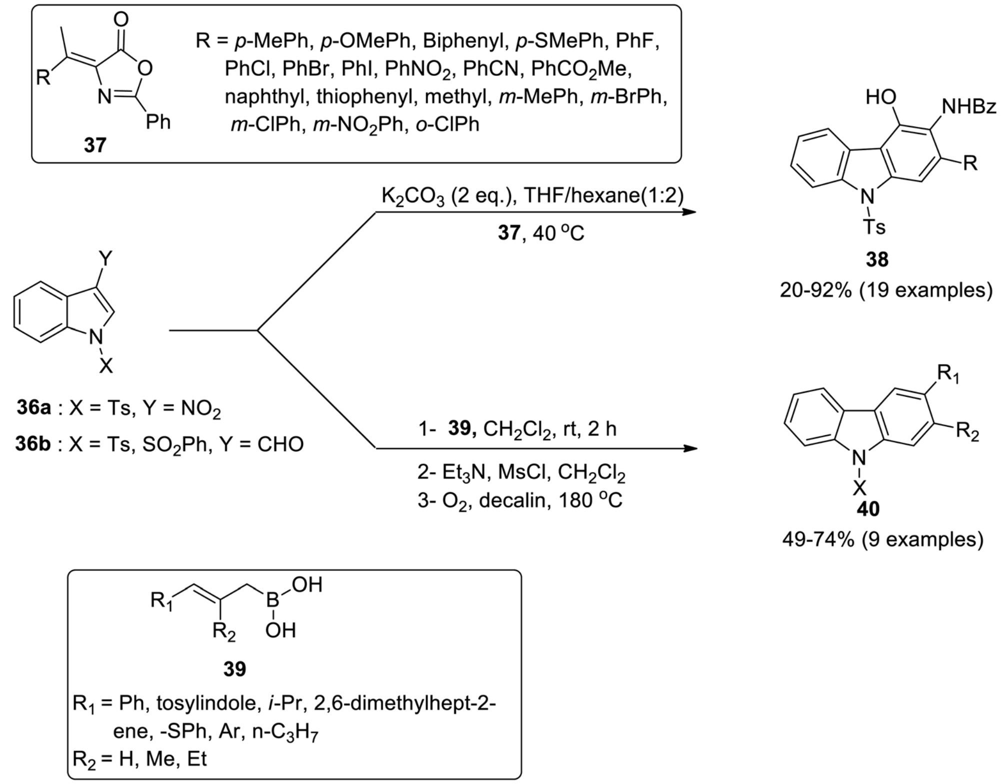
The carbazole nucleus can be constructed *via* C–C, C–N and C–H activation. Among these, C–H activation approach catalyzed with metal salts is considered to be an efficient and mild approach. In that respect, C–H activation *via* intermolecular and intramolecular reactions has been included in this review. Khan *et al.* reported the synthesis of functionalized carbazoles by employing Pd-catalyzed intramolecular C–H activation in 2019.[71] This approach consisted of *N*-arylation by Chan-Lam coupling of boronic acids **53** and *o*-iodoanilines **52** in the



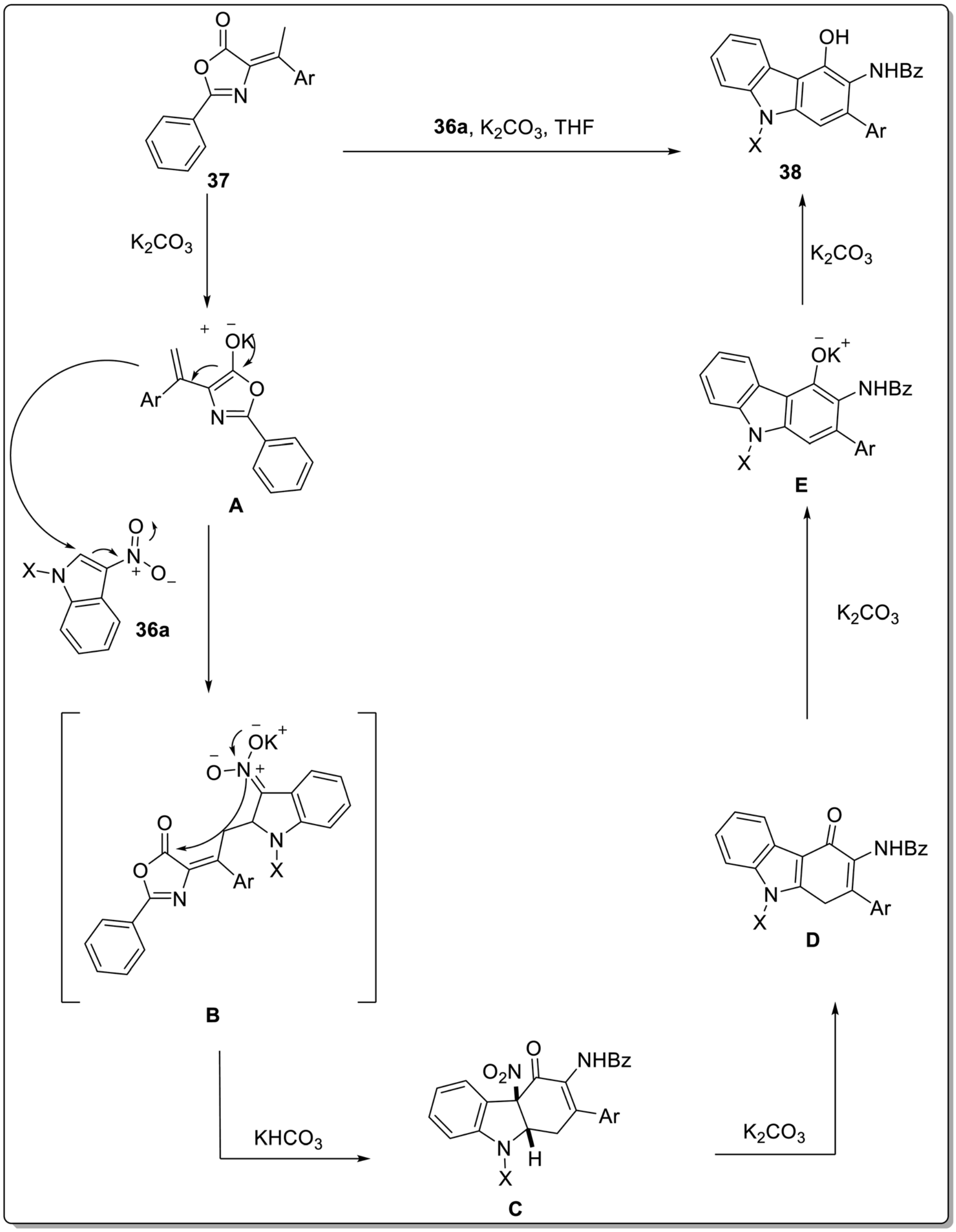
Scheme 5 One-pot cascade annulation reaction for synthesis of carbazole nucleus.



Scheme 6 Mechanistic details for the synthesis of functionalized carbazole 35.[62]



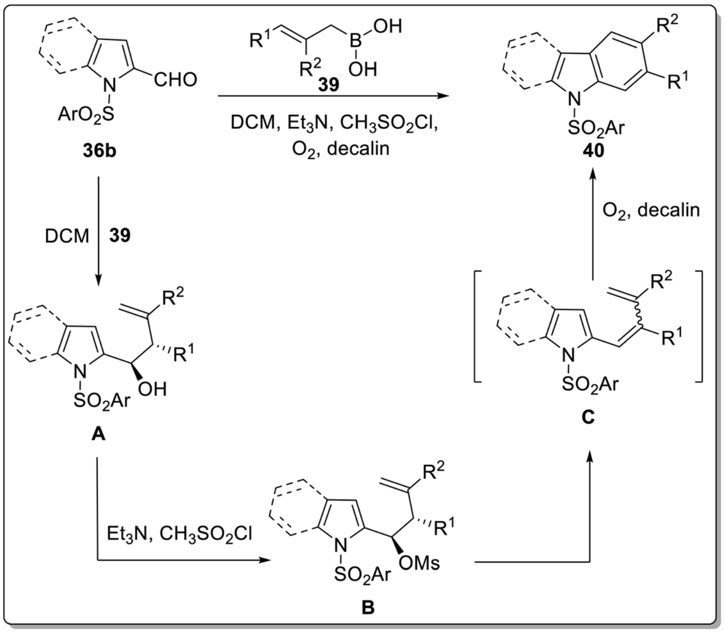
Scheme 7 Synthesis of 4-hydroxy carbazole 38 and substituted carbazoles 40.



Scheme 8 Mechanistic details for the synthesis of carbazole derivative **38**.[63]

presence of 10 mol% of $Cu(OAc)_2$, 1.2 equivalents of DBU as a base and decanoic acid as a solvent to give 2-iodo-*N*-phenyl aniline **54.** The second step involved 5 mol% of palladium catalyst and 6 equivalents of DBU-mediated C–H activation of 2-iodo-*N*-phenyl aniline **54** in toluene under a nitrogen atmosphere to furnish carbazoles **55a** in the 41–93% yield range. Alam *et al.* proposed a similar methodology with modified conditions including less catalyst loading of DBU(2 equiv.) in DMF and alteration with microwave irradiation for the synthesis of substituted carbazoles **55b** in 20–95% yields.[72] The Pd-catalyzed strategy was also amenable for the synthesis of 1-hydroxy carbazoles under aerobic conditions (Scheme 14). The plausible mechanism proposed for the synthesis of carbazoles **55a** and **55b** took place in four steps which involved the synthesis of pallado σ-complex **A** by *in situ* generated Pd(0) species *via* oxidative addition. Next, σ-bond metathesis gave intermediate **B** constituting C–H activation step followed by DBU-assisted deprotonation to furnish 6-membered palladacycle **C**. The final step consisted of reductive elimination to generate carbazole **55a** and **55b** (Scheme 15). Microwave irradiation led to the synthesis of products in better yields with less amount of base and solvent in a short reaction time.

Another class of carbazole *i.e.*, indolocarbazole has found significant value in the organic field.[73] Intramolecular C–H activation methodology to access carbazole skeleton has also been reported by Youn *et al.* (2019)[74] and Martinez-Lara *et al.*



Scheme 9 Mechanistic details for the synthesis of carbazole derivative **40**.[64]

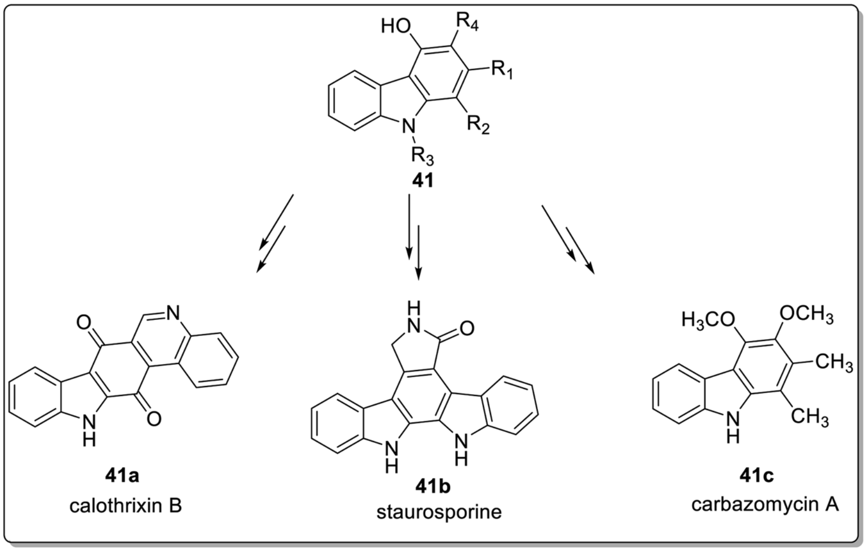
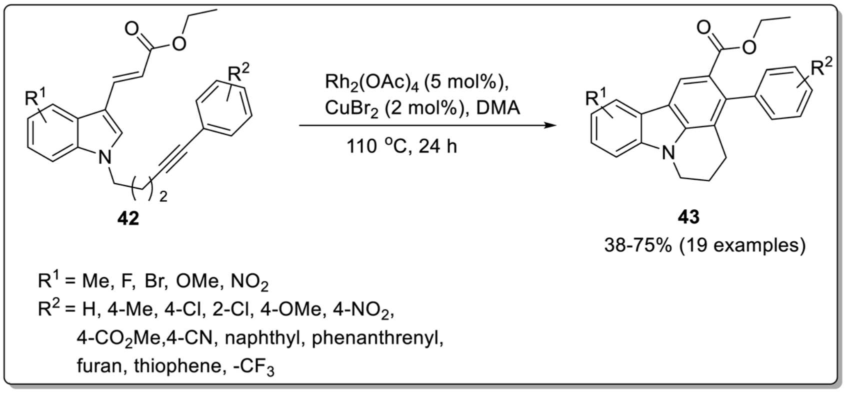
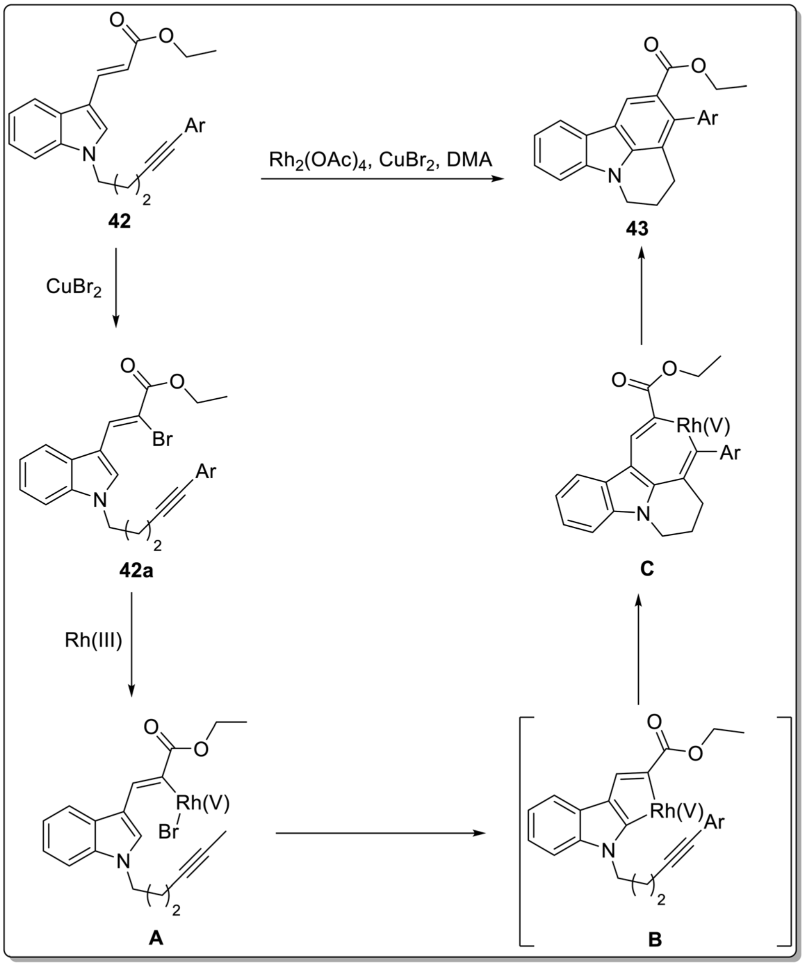


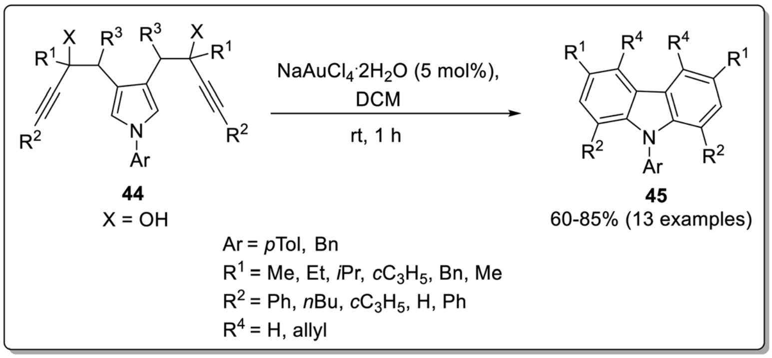
Fig. 4 Structure of carbazole derivative **41** and natural products (calothrixin B **41a**, staurosporine **41b** and carbazomycin A **41c**) obtained by it.



Scheme 10 Rhodium catalyzed intramolecular benzannulation for synthesis of carbazole.



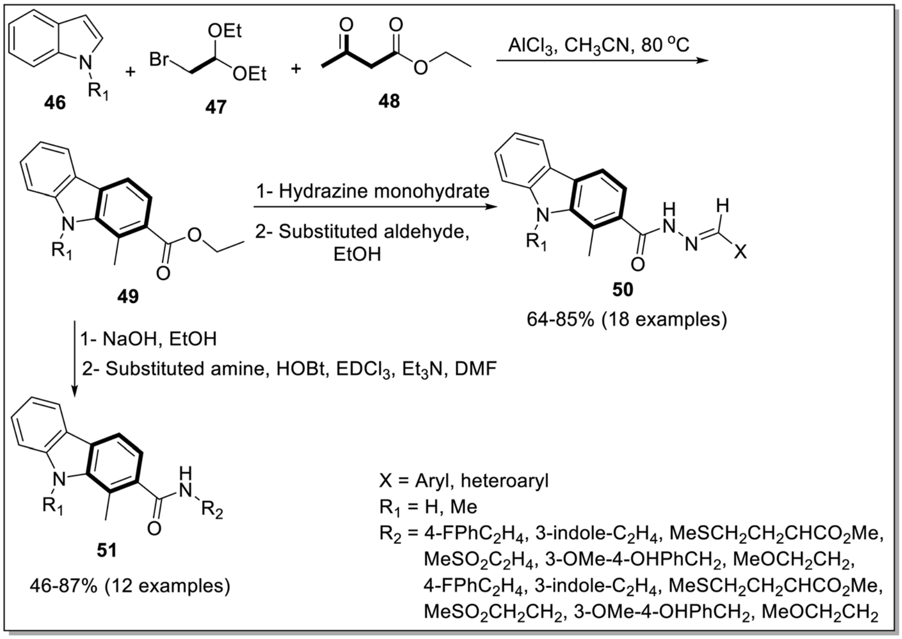
Scheme 11 Mechanistic details for the synthesis of carbazole derivative **43**.[67]



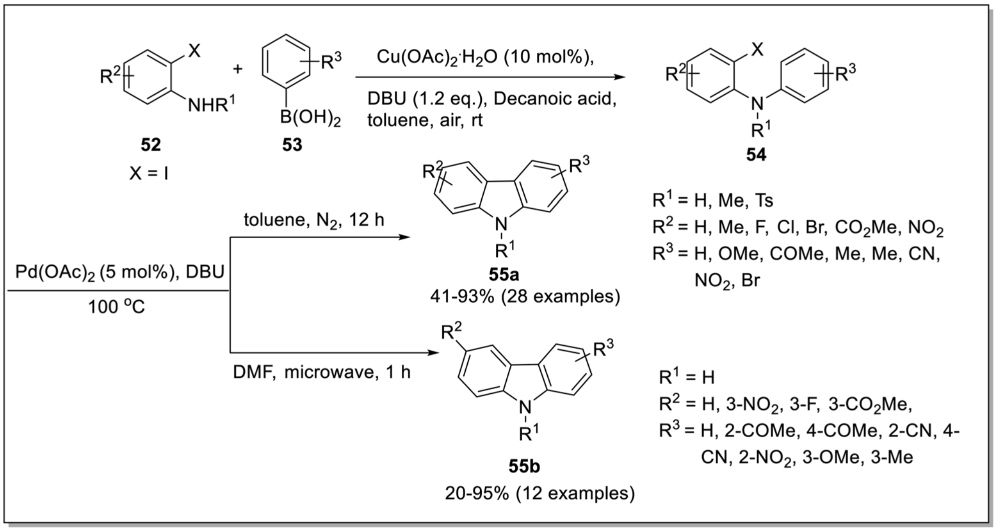
Ar = *p*Tol, Bn
R^1 = Me, Et, *i*Pr, *c*C_3H_5, Bn, Me
R^2 = Ph, *n*Bu, *c*C_3H_5, H, Ph
R^4 = H, allyl

Scheme 12 Gold-catalyzed double benzannulation for synthesis of carbazole **45**.

(2021).[75] The palladium-catalyzed C–H activation, reported by Youn *et al.* exploited *N*-Ts-2-aminobiaryl derivatives **56** as starting compounds. Hydroxy carbazole **58** was furnished in the presence of 5 mol% Pd$(OAc)_2$, bathocuproine **57** as a ligand, sodium acetate as an additive and oxygen as an oxidant (Scheme 16). The methodology acquired by Martinez-Lara *et al.* explored the synthesis of indolocarbazoles *via* gold and molybdenum catalyzed reaction.[47] The synthesis commenced with the construction of alpha-indol-3-yl alkyl propargylic alcohol **60** from bis-indolyl ketone **59** by Pd-catalysis. The indolo (2,3-*c*) carbazoles **61** were afforded by regioselective gold-catalyzed cyclization causing 1,2-alkyl migration followed by dioxomolybdenum-mediated Cadogan reductive cyclization reaction to furnish 64–85% yields (Scheme 17). The gold catalysis can also induce 1,2-alkenyl migration which will provide



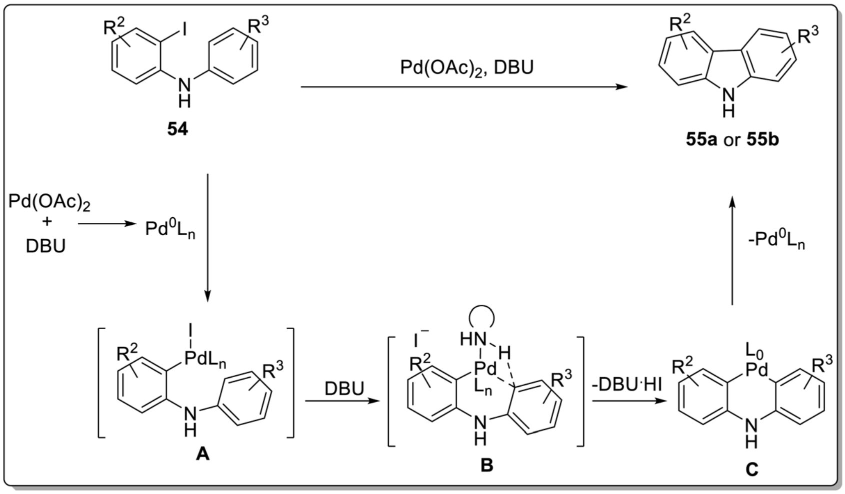
Scheme 13 $AlCl_3$-mediated annulation for the synthesis of carbazoles **49** and its derivatives.



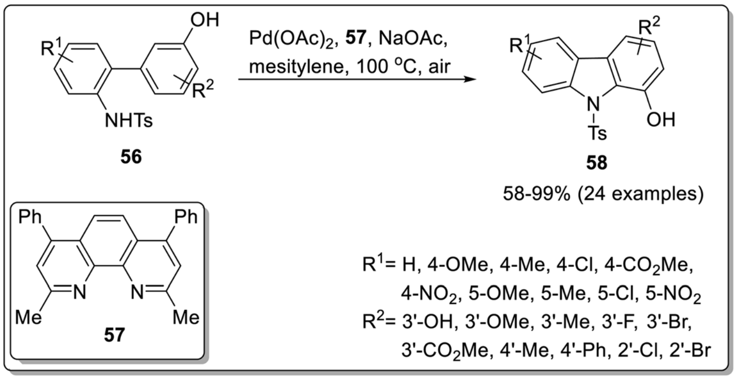
Scheme 14 Pd-catalyzed and microwave-assisted synthesis of carbazole *via* C–H activation.

indolo (3,2-α) carbazoles in the presence of toluene as a solvent making it a regioselective catalyst.

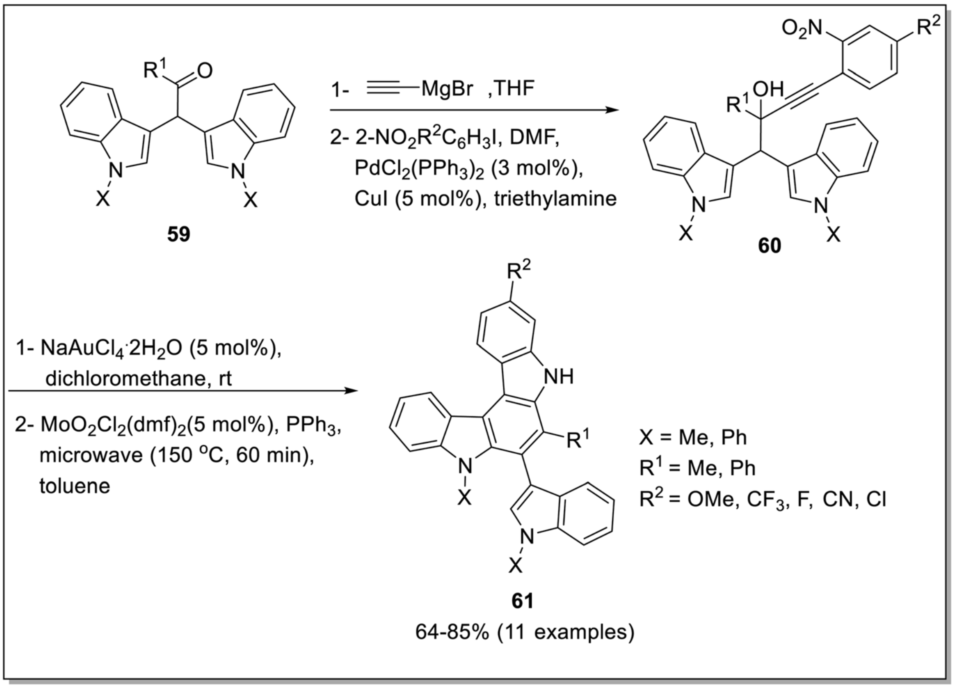
Min *et al.* reported an intermolecular rhodium catalyzed C–H activation protocol for the synthesis of C2-formylated nucleus of carbazole.[76] The tandem cross-coupling reaction between indolyl nitrones **62** and 2-methylidene cyclic carbonates **63** was proceeded in the presence of 5 mol% of rhodium catalyst, a combination of $CuF_2{\cdot}MgSO_4$ as an additive and toluene as solvent at 120 °C for 12 h to give target compounds **64** in 10–71% yields (Scheme 18). The mechanism of reaction involves C–H activation of rhodium catalyst as the first step followed by migratory insertion of cyclic carbonates. The next step involved β-*O*-elimination for the removal of carbon dioxide and exo [3 + 2] cycloaddition reaction and oxidation to give bridged heterocycle. Further, aromatization and formylation provided targeted carbazole. The proposed mechanism implied the synthesis of intermediate **A** *via* C–H activation step between [Rh(III) $Cp^*(MeCN)_3(SbF_6)_2$] and indolyl nitrone **62.** Next, cyclic carbonate **63** and intermediate **A** coordinated to give intermediate **B** which underwent migratory insertion to give eight-membered O–Rh(III)–C complex **C.** The complex **C** generated intermediate **D** by β-*O*-elimination. Further, bridged heterocycle **E** was afforded *via* exotype [3 + 2] cycloaddition step. The aromatization of bridged heterocycle **E** was succeeded by



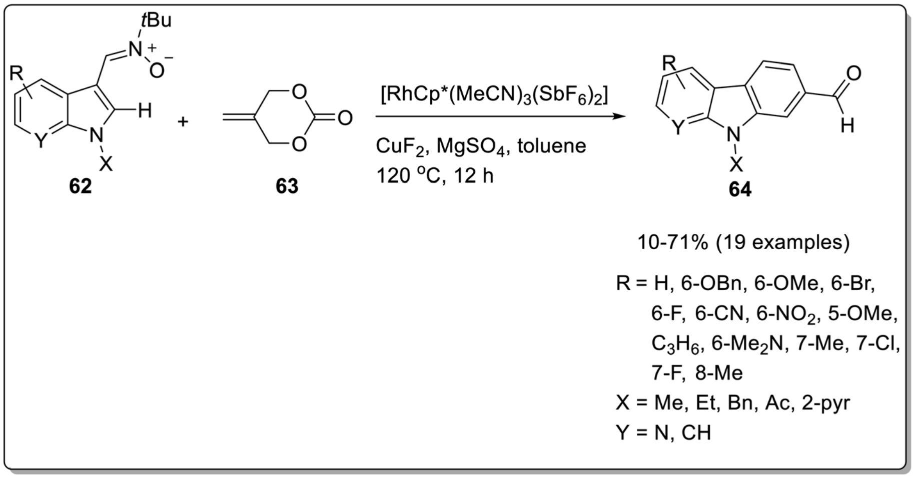
Scheme 15 Mechanistic details for the synthesis of carbazoles **55a** and **55b**.[71,72]



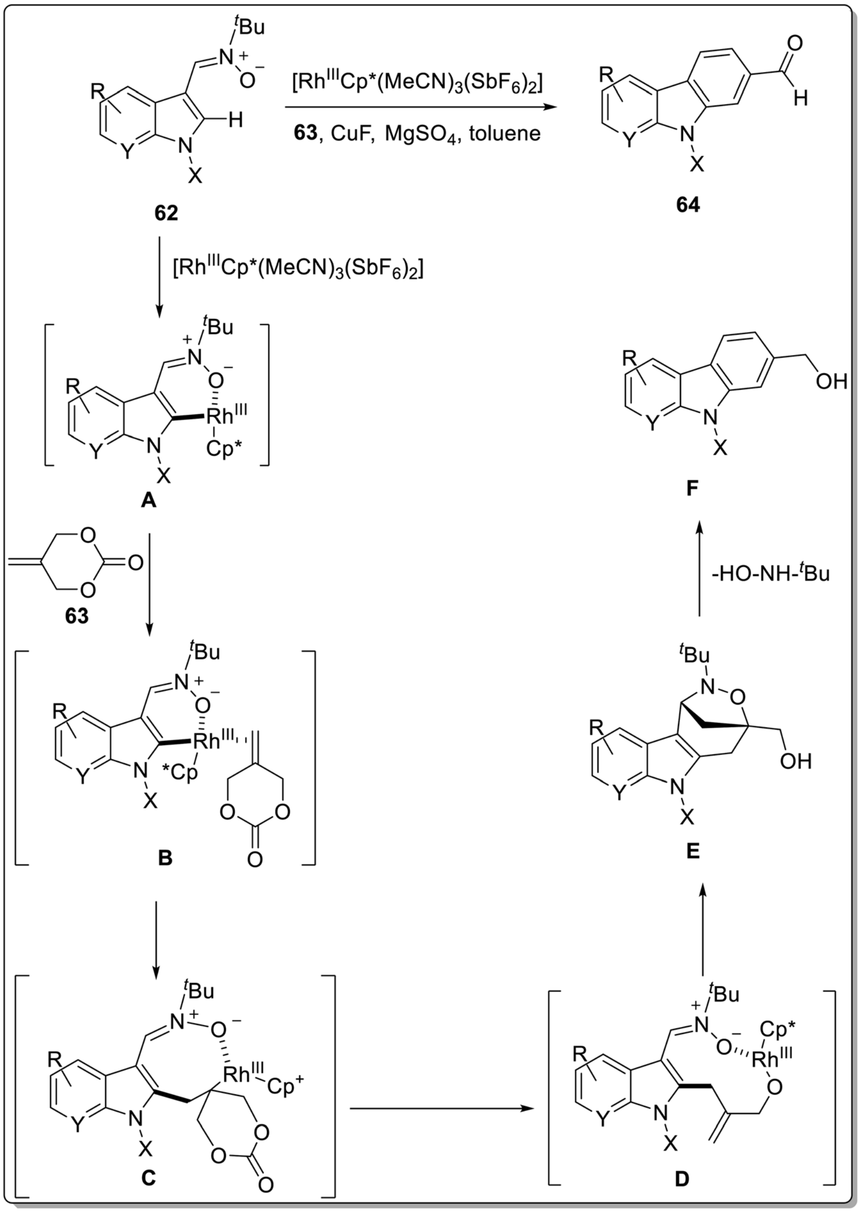
Scheme 16 Pd-catalyzed C–H amidation for synthesis of 1-hydroxy carbazoles.



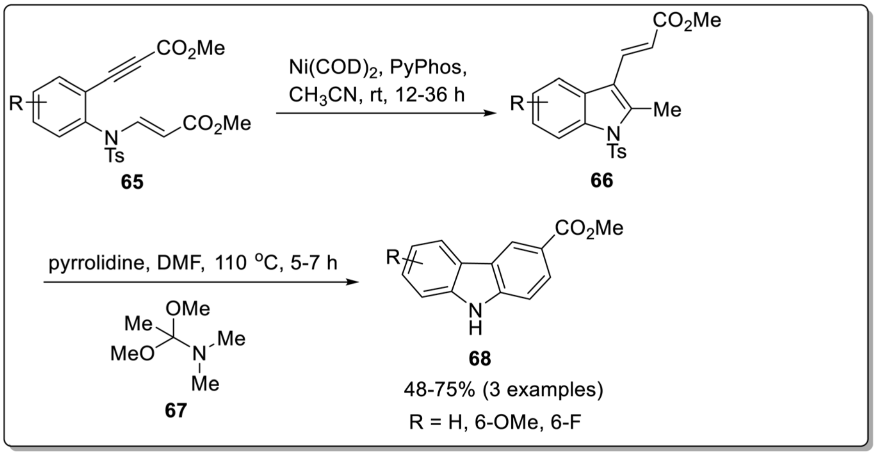
Scheme 17 Synthesis of carbazole *via* Au- and Mo-catalysis.



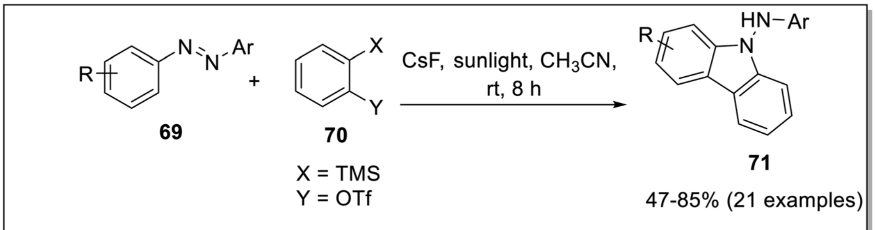
Scheme 18 Rh-catalyzed synthesis of carbazoles.



Scheme 19 Mechanistic details for the synthesis of carbazoles **64**.[76]



Scheme 20 Ni-catalyzed carboamination for the synthesis of carbazoles derivatives.



R = H, 3-Me, 3-Et, 3-^{t}Bu, 3-^{i}Pr, 3-MeO, 3-Br, 3-Cl, 1-Me, 1-F, 2-Me, 4-Me, 1,2-Me,1,3-Me, 1-Me,3-Br, 3-CN, 1-Et

Ar = Ph, Tolyl, 4-EtPh, 4-^{t}BuPh, 4-*i*PrPh, 4-OMePh, 4-BrPh, 4-ClPh, 2-MePh, 2-FPh, 3-MePh, 2,3-MePh, 2,4-MePh, 2-Me,4-BrPh, 2,6-MePh, 2,4,6-MePh, 2-CO_2EtPh, 4-FPh, diphenyl

Scheme 21 Sunlight-mediated [3 + 2] cycloaddition for carbazole synthesis.

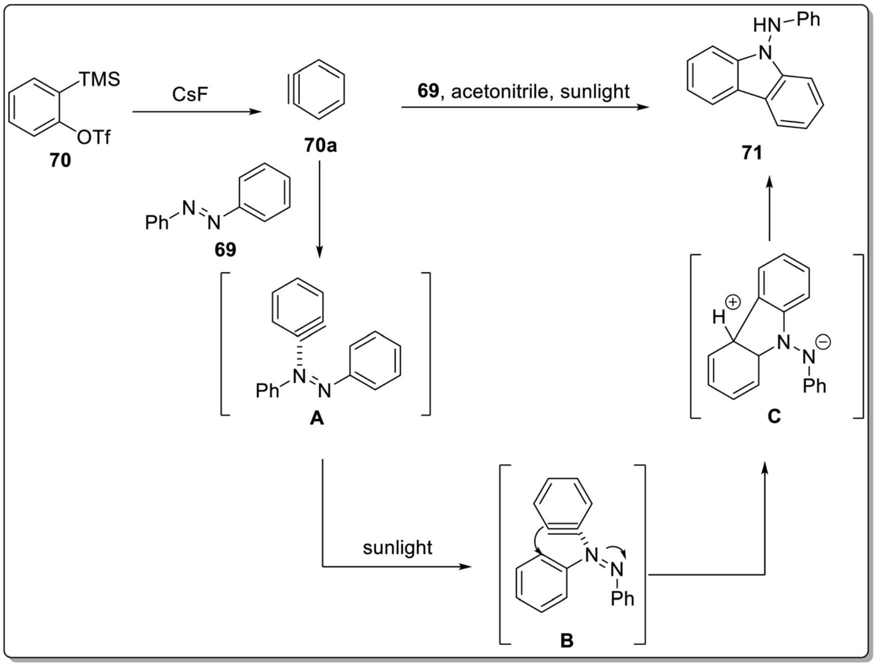
aerobic oxidation to furnish C2-formylated carbazole **64** (Scheme 19).[76]

Synthesis of carbazole *via* carboamination

2-Alkynyl anilines have been utilized for the synthesis of indoles *via* annulation reaction catalyzed by transition metals.[77] But these reactions have certain drawbacks, including low substrate scalability and high temperature requirements.[78] Thus, to overcome these shortcomings, Tambe *et al.* reported an alternative methodology, namely, trans carboamination for synthesizing functionalized indoles catalyzed by nickel complex and applied it to synthesize carbazoles.[79] The method consisted of propynyl anilino acrylate **65** undergoing carboamination in the presence of Ni(COD)$_2$ as a catalyst, PyPhos as ligand and CH_3CN as a solvent in the reaction mixture to afford functionalized indoles **66** which were cyclized in the presence of pyrrolidine and DMF to furnish carbazoles **68** with a yield range of 48–75% (Scheme 20). The salient features of this methodology included efficient synthetic access to multifunctionalized indoles which could be converted to important N-heterocycles *via* one step process.

Synthesis of carbazoles *via* [3 + 2] cycloaddition

In 2021, Zhang *et al.* aimed at the construction of carbazole skeleton **71** by [3 + 2] cycloaddition reaction between azobenzenes **69** and arynes **70** catalyzed by sunlight.[80] The cycloaddition was performed in the presence of CsF in CH_3CN mediated by sunlight (Scheme 21). The important features of this reaction include good compatibility of functional groups and catalyst-free conditions. The mechanism consisted of the synthesis of benzyne **70a** by treating compound **70** with CsF. Next, intermediate **A** was synthesized by interaction of benzyne **70a** and azobenzene **69.** The intermediate **A** underwent rotation mediated by sunlight to produce intermediate **B** followed by intramolecular cyclization to furnish five-membered intermediate **C.** The final step involved aromatization facilitated by water molecules to generate target compound **71** (Scheme 22).



Scheme 22 Mechanistic details for the synthesis of carbazoles **71**.[80]

Conclusion

To conclude the updates provided in the article, the carbazole skeleton has been reported to be constructed *via* allylation, annulation, C–H activation, transition-metal catalyzed as well as under metal-free and sunlight mediated methodologies. These involve either oxidative cyclization of biphenyls with an *ortho* nitrogen, metal-catalyzed indole cyclization or a step-by-step synthesis of carbazole starting from phenyl systems. These strategies have been applied to wide substrate scope which includes pyrimidine derivatives, bisalkynyls, substituted biaryls, indolyl nitrones, alkyne anilinoacrylates, and azobenzenes. The employment of these methods has aided in the synthesis of carbazole-based significant natural products and derivatives employed in pharmacological and industrial areas. Additionally, there are certain drawbacks in the reported methodologies as well which include the use of expensive catalysts, harsh chemicals, toxic solvents and extensive energy resources. These can be overcome by employing cost-effective resources and reagents to reduce the harmful impacts. To add further, there's still room left for improvement to this significant research area for introducing more environment-friendly and benign methods to carry out the required synthesis.

Conflicts of interest

There are no conflicts to declare.

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