

SYNTHETIC DERIVATIVES OF AROMATIC CARBAZOLE RING**Ajit Nangare^{*1}, Gaurav S. Lodha², Amit N. Chavan² and Mukund G. Matkar³**

¹Asst. Prof. Department of Pharmaceutical Chemistry, Dr. Vithalrao Vikhe Patil Foundation's College of Pharmacy, Vilad Ghat, Ahmednagar, (MS), India, 414111.

²Department of Pharmaceutics, Padmashri Dr. Vithalrao Vikhe Patil Foundation's College of Pharmacy, Vilad Ghat, Ahmednagar, (MS), India, 414111.

³Dr. Vithalrao Vikhe Patil Foundation's College of Pharmacy, Vilad Ghat, Ahmednagar, (MS), India, 414111.

Article Received on
07 Nov. 2018,

Revised on 28 Nov. 2018,
Accepted on 19 Dec. 2018

DOI: 10.20959/wjpr20191-13712

Corresponding Author*Ajit Nangare**

Asst Prof Department of
Pharmaceutical Chemistry,
Dr. Vithalrao Vikhe Patil
Foundation's College of
Pharmacy, Vilad Ghat,
Ahmednagar, (MS), India,
414111.

ABSTRACT

In the recent past 15 years, The Carbazole derivatives have been covering a big part of study because of the synthetic possibility, unusual chemical actions, their biological actions and different application in the pharmaceutical formulations. In this review article, we have given all possible different synthesis routes of Carbazole and its derivatives with its various biological activities. This article covers the synthesis of Carbazole from 2001 to 2009 of all types of reported activity. The literature points out that compounds contain Carbazole ring having a wide range of beneficial uses that comprise of antibacterial and anticancer activity. The purpose of this review is to give an overview of the special property of Carbazole.

KEYWORDS: Carbazole, Antibacterial, Anticancer, Antitumor, Antiepileptic.

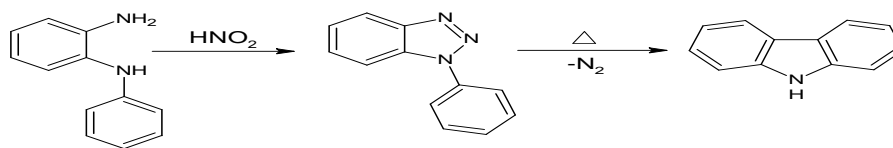
INTRODUCTION

Carbazole is a heterocyclic aromatic compound. It has a tricyclic organic compound consisting of double six-membered benzene ring attached to one side of the five-membered ring containing nitrogen. They are very useful in medicinal chemistry for research areas. Carbazoles have various pharmacological actions like antimicrobial, analgesics, anti-inflammatory, anticonvulsant, antitumor, antioxidant, antiepileptic, etc which shows the potency of given carbazole ring.

SYNTHESIS OF CARBAZOLE

1st Method

In the primary step, an *N*-phenyl-1,2-diaminobenzene (*N*-phenyl-*o*-phenylenediamine) is converted into a diazonium salt which gives 1,2,3-triazole.^[1,2]



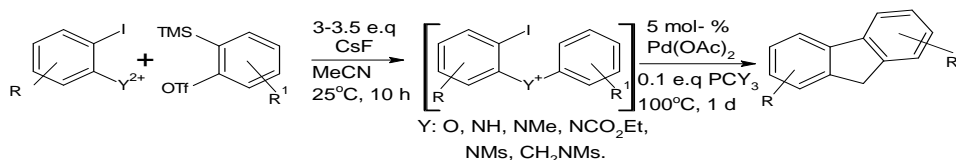
2nd Method

Initially, condensation of phenylhydrazine with cyclohexanone to form an imine. The second step is hydrochloric acid-catalyzed rearrangement reaction. In one modification, both steps are rolled into one by carrying out the reaction in acetic acid.^[5] In the third step, this compound is oxidized by red lead to carbazole itself. It is also known as Borsche–Drechsel reaction.^[3,4]



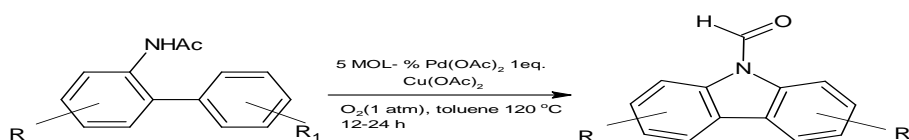
3rd Method

In a primary step for synthesis was by reacting *o*-iodoanilines with silylaryl triflates in an occurrence of CSF to obtain *o*-arylated. In 2nd step, cyclization has been done with the help of Pd catalyst to get Carbazole.^[5]



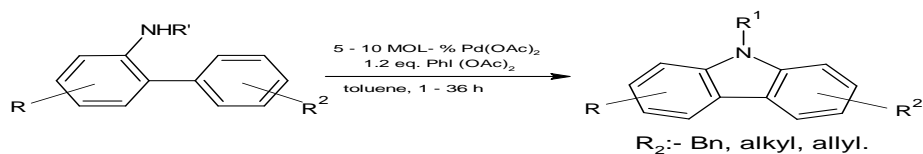
4th Method

In this synthesis, the palladium is catalyzed tandem which was directed to C-H functionalization and amide arylation which provides the series of Carbazole.^[6]

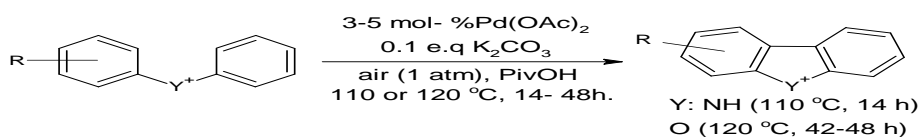
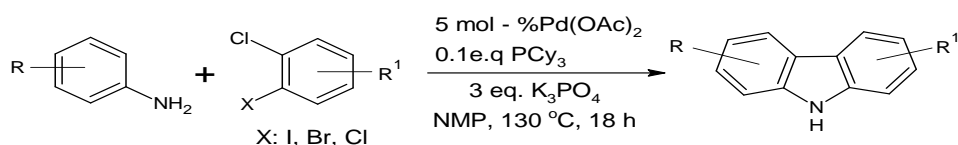


5th Method

In the extremely mild conditions, the Pd (II)-catalyzed C-H bond amination reaction operate by following procedure good yield of Carbazole have been got.^[7]

**6th Method**

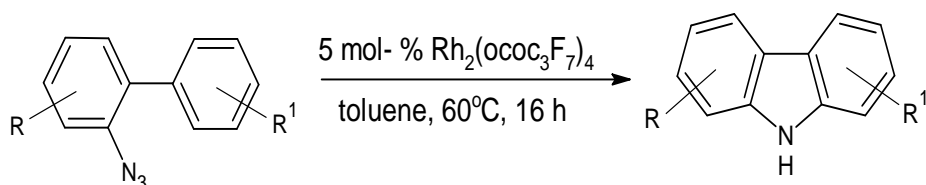
In presence of a pivalic acid as a reaction solvent, the intramolecular palladium(II)-catalyzed oxidative carbon-carbon bond formation has happened. Instead of acetic acid, results in broader substrate scope, greater reproducibility, and higher yields.^[8]

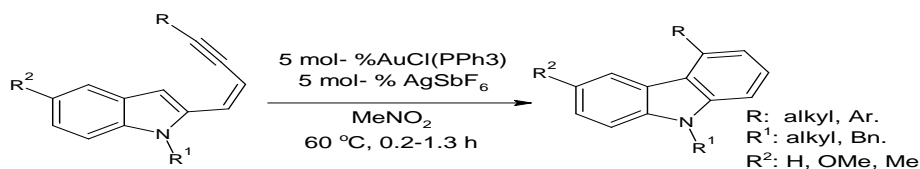
**7th Method**

In a palladium- catalyzed reaction sequence having of an intermolecular amination and an intramolecular direct arylation A palladium-catalyzed reaction sequence consists of an intermolecular amination and an intramolecular direct arylation enable deeply selective synthesis of functionalized indoles or carbazoles.^[9]

8th Method

By using $\text{Rh}_2(\text{OCOC}_7\text{H}_{15})_4$ or $\text{Rh}_2(\text{OCOC}_3\text{F}_7)_4$ as catalysts at 60°C various carbazole derivatives has been synthesis.^[10]

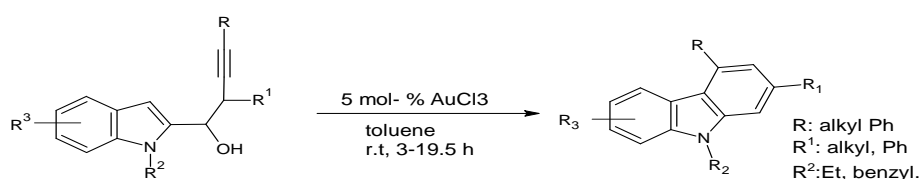


9th Method

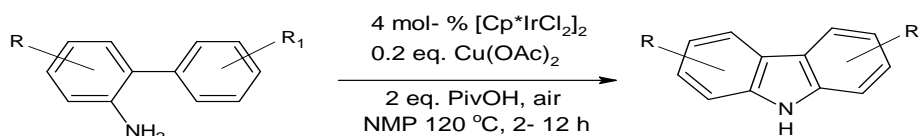
A gold(I)-catalyzed intramolecular hydroarylation of (*Z*)-2-(ethynyl)indoles gives carbazoles in good yield in presence of *N*-alkyl indoles-2-carboxaldehydes with propargylaldehydes.^[11]

10th method

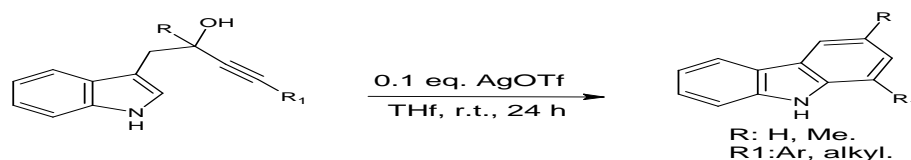
At 25⁰c. temperature, by Action of toluene, incyclization's of 1-(indol-2-yl)-3-alkyn-1-ols AuCl₃-catalisation occurs.^[12]

**11th Method**

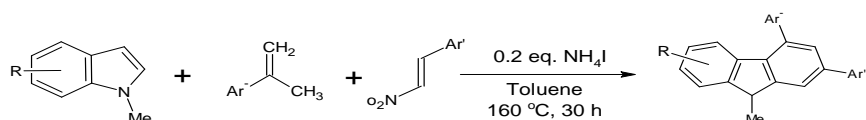
By dehydrogenative cyclization of 2-aminobiphenyls with iridium catalyst continue in existence of copper as co-catalyst and air as an oxidant to gives N-H carbazoles.^[13]

**12th Method**

At room temperature, using Ag(I), indole-tethered propargyl alcohol gives more yield of carbazoles.^[14]

**13th Method**

At room temperature, for the synthesis of the iodocarbazoles by iodocyclization with aromatization and immigration in less time.^[15]



The reaction gives good yield through formal [2 + 2 + 2] annulation of indoles, ketones, and gives the number of carbazoles.^[16]

CONCLUSION

Carbazole is a Six-member ring which provides Therapeutic properties like anticancer activity; antimicrobial activity etc. in given review gives Possible All Methods of Synthesis of carbazole Compound.

REFERENCES

1. Carl Graebe; Fritz Ullmann. "Ueber eine Neue Carbazolsynthese". Justus Liebigs Ann. Chem. (in German), 1896; 291(1): 16–17.
2. O. Bremer. "Über die Bedeutung der Graebe-Ulmannschen Carbazolsynthese und deren Übertragung auf N-substituierte Pyridino-triazole". Justus Liebigs Ann. Chem. (in German), 1934; 514(1): 279–291.
3. W. Borsche. "Ueber Tetra- und Hexahydrocarbazolverbindungen und eine neue Carbazolsynthese. (Mitarbeiter von A. Witte and W. Bothe.)". Justus Liebigs Ann. Chem. (in German), 1908; 359(1–2): 49–80.
4. E. Drechsel "Ueber Elektrolyse des Phenols mit Wechselströmen". J. prakt. Chem. (in German), 1888; 38(1): 65–74.
5. Z. Liu, R. C. Larock, Org. Lett., 2004; 6: 3739-3741.
6. W. C. P. Tsang, N. Zheng, S. L. Buchwald, J. Am. Chem. Soc., 2005; 127: 14560-14561.
7. J. A. Jordan-Hore, C. C. C. Johansson, M. Gulias, E. M. Beck, M. J. Gaunt, J. Am. Chem. Soc., 2008; 130: 16184-16186.
8. B. Liégault, D. Lee, M. P. Huestis, D. R. Stuart, K. Fagnou, J. Org. Chem., 2008; 73: 5022-5028.
9. L. Ackermann, A. Althammer, P. Mayer, Synthesis, 2009; 3493-3503.
10. B. J. Stokes, B. Jovanović, H. Dong, K. J. Richert, R. D. Riell, T. G. Driver, J. Org. Chem., 2009; 74: 3225-3228.
11. C. Praveen, P. T. Perumal, Synlett, 2011; 268-272.
12. Y. Qiu, W. Kong, C. Fu, S. Ma, Org. Lett., 2012; 14: 6198-6201.

13. C. Suzuki, K. Hirano, T. Satoh, M. Miura, *Org. Lett.*, 2015; 17: 1597-1600.
14. . M. J. James, R. E. Clubley, K. Y. The palate, T. J. Procter, A. C. Wyton, P. O'Brien, R. J. K. Taylor, W. P. Unsworth, *Org. Lett.*, 2015; 17: 4372-4375.
15. J. Wang, H.-T. Zhu, Y.-F. Qiu, Y. Niu, S. Chen, Y.-X. Li, X.-Y. Liu, X.-M. Liang, *Org. Lett.*, 2015; 17: 3186-3189.
16. S. Chen, Y. Li, P. Ni, H. Huang, G.-J. Deng, *Org. Lett.*, 2016; 18: 5384-5387.