



Solid Supported Synthesis of Bio-Active N-Alkyl Carbazole Compounds Using Microwaves

H P Narkhede

Smt. P K Kotecha Mahila Mahavidyalaya, Bhusawal, Dist-Jalgaon, (M. S.), **INDIA**

Email: narkhede.hemant@rediffmail.com

Accepted on 26th February 2014

ABSTRACT

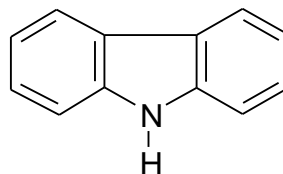
Carbazole readily reacts with alkyl halides after adsorption on solid supports and on irradiation with microwaves to afford the corresponding products in good yields. The method was found to be satisfactory for resolution of pure products, in a shorter time as compared to the conventional method. The additional features of methodology includes very faster reaction, higher yields and purity of the products and ecofriendly approach.

Keywords: Carbazole, Microwave Irradiation, Alkyl halides, Solid Supports.

This work was presented in International Conference on Emerging Trends in Chemical Sciences, Jan.23-25, 2007 at University of Mumbai (M.S.), INDIA, Abstract no. OP- 9, Page 31.

INTRODUCTION

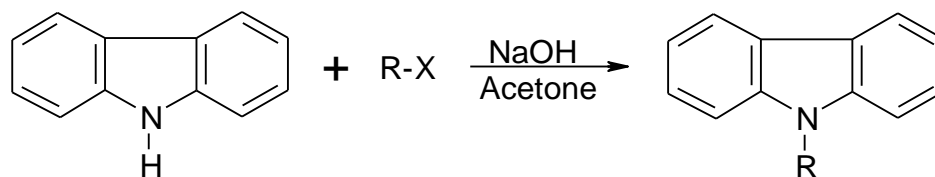
The derivatives of carbazole are well known for their pharmacological activities. Several reports have appeared on synthesis of carbazole derivatives in connection with the search for newer physiologically active compounds. Carbazomycin A and Carbazomycin B have found to be useful antibacterial and antifungal agents[1, 2]. It has been reported that pyridocarbazoles shows marked anticancer and anti- HIV activities[3,4].



Carbazole

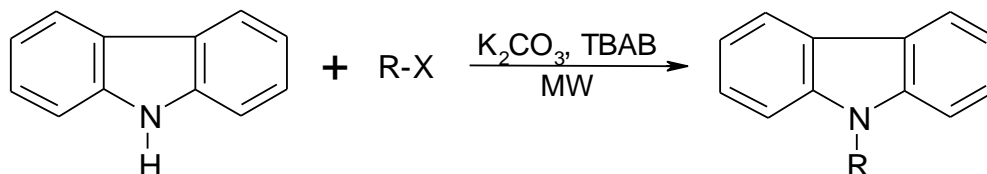
Carbazoles display a range of biological activities making them attractive compounds to synthetic & medicinal chemists [5-8]. The N-alkyl derivatives of carbazole are usually prepared by treating potassium carbazole with alkyl halides or alkyl sulfates[9]. Nearly quantitative yields of N-alkyl & N-acyl derivatives of carbazole may be obtained when a solution of carbazole in acetone or alcohol is treated with alkylating

or acylating agents, respectively in the presence of alkali (Scheme 1a)[10,11]. N-Alkyl carbazoles were also prepared by microwave irradiation using phase transfer catalyst (Scheme 1b)[12].



R=Alkyl or Acyl group

Scheme 1a.



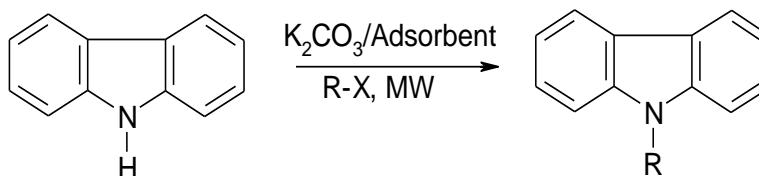
Scheme 1b

In continuation of work on greener alternatives, the emphasis has been given on the development of simple, fast and eco-friendly synthetic approach for derivatization of carbazole.

MATERIALS AND METHODS

Carbazole, Microwave Irradiation, Alkyl halides, Solid Supports such as silica gel, alumina fly ash.

Present Work: As a part of developing environmentally benign new methodologies for the synthesis of biologically active compounds[17, 18-20], we report herein facile synthesis of N-alkyl, N-acylcarbazole using microwave assisted reactions. The present work includes solid state alkylation and acylation of carbazole derivatives using commercial solid supports such as silica gel and alumina with the addition of newer support fly ash. Carbazole was adsorbed on silica gel / alumina / fly ash and by using aqueous sodium carbonate and alkyl halides, acid chlorides and irradiated under MW to give the desired products (Scheme 1c).



Scheme 1c

- a) R = CH₃, b) R = CH₂CH₃, c) R = CH₂CH₂CH₃ d) R = CH(CH₃)₂ e) R = CH₂(CH₂)₂CH₃
f) R = CH₂CH(CH₃)₂, g) R = CH₂CH=CH₂

Experimental: All chemicals were of analytical grade (s. d. fines Chem. Ltd., Mumbai, INDIA) and THF was freshly distilled before use. Microwave oven (model OM9918C, 2450 MHz, 900 W) was used to carry out the reactions. The fly ash was collected from Thermal Power Plant, Deepnagar, Bhusawal, Dist. Jalgaon, (M.S.), INDIA and used as such for the reactions. Silica gel and alumina were of synthetic grade (s. d. fine Chem. Ltd., Mumbai, INDIA). The reactions were monitored by silica gel TLC using

chloroform: acetone (7:3) or n-hexane: chloroform (7:3). Melting points were determined by open capillary method and are uncorrected.

Synthesis of N-alkyl Carbazole (1a-g): Carbazole (10mmol), aqueous potassium carbonate (5 mL, 1.5 N) and adsorbent (1.5 g) were mixed thoroughly and irradiated in microwave oven till complete removal of water. To this dried content, alkyl halide (10 mmoles) was added and again irradiated in microwave oven at power level 30 at pulse of 30 sec. for 1 - 5 min. After completion of reaction (monitored by TLC), the contents were cooled and extracted with THF (2 x 20 mL). The extract was dried with anhydrous sodium sulphate, filtered and removal of the solvent afforded the products **1a-g**.

RESULTS AND DISCUSSION

Carbazole derivatives: Synthesis of Carbazole derivatives and physical properties are presented in table 1 and spectral data in table 2.

Table 1. Synthesis of Carbazole derivatives and physical properties

Compd. No.	Irradiation Time in min	Solid support, Yield (%)			mp (^o C)	lit. ²⁰ mp (^o C)
		Silica gel	Alumina	Fly-ash		
1a	2	84	89	88	91	91
1b	2	80	78	80	69	69
1c	3	86	86	86	49	49-50
1d	2.5	88	90	90	123	123
1e	4	89	91	89	58	58
1f	3.5	86	89	88	52	52
1g	4.5	80	81	80	55	54-55

Solid-supported reagents are easily removed from reaction contents by filtration. Excess reagents can be used to drive reactions to completion without introducing difficulties in purification. Recycling of recovered reagents is economical, environmentally-sound, and efficient. Toxic, explosive, and noxious reagents are often more safely handled when contained on solid support.

Table 2. Spectral data of Carbazole derivatives

Compd. No.	IR (ν , cm^{-1})	¹ H NMR (δ , ppm)
1a	3060,2850,1630,1500, 1450,1205,800,750	3.66 (s, 3H, NCH ₃); 7.20-8.11 (m, 8H, Ar-H)
1b	3060,2850,1630,1500, 1450,1205,800,750	1.35 (t, 3H, CH ₃); 4.27 (s, 2H, NCH ₂); 7.20-8.10 (m, 8H, Ar-H)

1e	3045,2930,2860,1625, 1485,1325,1215,755	0.92 (t, 3H, CH ₃); 1.32 (m, 2H, CH ₂); 1.80 (m, 2H, CH ₂); 4.29 (t, 2H, NCH ₂); 7.17-8.15 (m, 8H, Ar-H)
1g	3060,2981,2940,1600, 1496,1268,997,933, 756	4.90 (d, 2H, NCH ₂); 5.10 (d, 2H, CH ₂ =); 5.80 (m, 1H, CH=); 7.18-8.12 (m, 8H, Ar-H)

Characterization: The synthesized carbazole compounds were characterized by their physical constants, comparative TLC and spectroscopic (¹H NMR and IR) techniques. The spectral data of the synthesized compounds were found to be satisfactory with reported data.

APPLICATIONS

Microwave chemistry has opened up several new avenues in organic synthesis. Many reactions that previously were not possible, or resulted in a low yield, can now often be performed quickly, safely and efficiently in a few minutes. In summary, MAOS has changed the world of organic chemistry and drug discovery, and it would be wise to embrace this new technology or be left lagging behind with conventional heating methodologies .

CONCLUSIONS

MW methodology in chemical synthesis produces clean, high performance reactions in minimum time. It leads to clear improvements and simplifications of procedure compared with conventional methods. Microwave assisted solventless, alkylation, acylation and dimerization of Carbazole . Very faster reaction, higher yields, easy work-up, purity of the products and thus ecofriendly approach .Silica gel, alumina and fly ash are used as a solid support . Importantly, fly ash was found to be new solid support for organic reactions in dry media as efficient as commercial ones such silica gel and alumina.

REFERENCES

- [1] D N Chowdary, S K Basak and B P Das, *Curr.Sci.*, **1978**, 47, 490-491.
- [2] K.Sakano, K. Ishimaru and S.Nakamura, *J. Antibiot*, **1980**, 33, 683-690.
- [3] U. Pindur, *Chimia*, **1990**, 44, 406-412.
- [4] H J Knolker and K R Reddy, *Chem. Rev.*, **2002**, 102, 4303 -4427.
- [5] J.Leonard, *J. Nat. Prod. Rep.*, **1999**, 16, 319.
- [6] D. P Chakraborty, *In the Alkaloids, Chemistry and Pharmacology, Vol. 44*, **1993**, G. A. Cordell Ed., Academic Press, Inc., Chapt. 4, 257-364.
- [7] H. J Knolker, K. R Reddy, *Chem. Rev.*, **2002**, 102 (11), 4303.
- [8] G. W.Gribble, *Synlett*, **1991**, 289.
- [9] H.Nishi, H. Kohno and T.Kano, *Bull. Chem. Soc. Jpn.*, **1981**, 54, 1897.
- [10] L. J Kricka, A Ledwith, *J. Chem. Soc. Perkin Trans.* **1972**, 1, 2292.
- [11] J Heller, Hewett, *W.A.Makromol. Chem.*, **1964**, 73, 48.
- [12] D. Bogdal, J. Pielichowski and K. Jaskot, *Synth. Commun*, **1997**, 27(9), 1553.
- [13] B. M Vittimberga, M. L.Herz, *J. Org. Chem.*, **1970**, 35(11), 3694.
- [14] N.Chandrika, T.H. Suresha Kumara, Gopalpur Nagendrappa, P. R .Chetana, H.B.V. Sowmya, S.K. Rashmi, R.Dileep, C. Sandeep, *Journal of Applicable Chemistry* **2013**, 2 (6) , 1535-1542.

- [15] Shaik Khadar Yazdan, K. Renuka Sowjanya, K. Sai Avinash and M. Ratna Kumari, *Journal of Applicable Chemistry*, **2013**, 2 (6), 1679-1682.
- [16] ASG Prasad, G.Venkata Rao and Mandava V. Basaveswara Rao, *Journal of Applicable Chemistry*, **2012**, 1.
- [17] H. P Narkhede., U. B.More, D. S.Dalal, N. S.Pawar, D. H. More and P. P.Mahulikar, *Synth. Commun.* **2007**, 37(4), 575-579.
- [18] P. P Kumbhar (Mahulikar), U. R Kapadi, D. G.Hundiwale, S. B Attarde, P. M Dewang and N. S. Pawar, *Org. Prep. Proc. Int.*, **2000**, 32 (6), 600.
- [19] N. S Pawar, D. S. Dalal, S. R. Shimpi and P. P. Mahulikar, *Eur. J. Pharm. Sci.*, **2004** , 21, 115.