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SOLID SUPPORTED SYNTHESIS OF BIO-ACTIVE DIMERIC ALKYLENE AND DIKETOALKYLENE 9H-CARBAZOLE COMPOUNDS VIA GREENER METHODOLOGY

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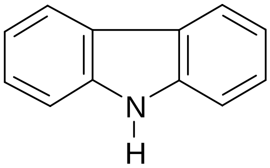
ABSTRACT

9H-carbazole readily reacts with dibromoalkane/acid di chloride after adsorption on solid supports and 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 include very faster and solvent free reaction, easy work-up, higher yields and purity of the products and thus ecofriendly approach.

Key words: Solid support, Microwave, Bioactive, 9H-carbazole.

INTRODUCTION

The derivatives of 9H-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].



9H-carbazole

9H-carbazole display a range of biological activities making them attractive compounds to synthetic & medicinal chemists[5-8]. The N-alkyl derivatives of 9H-carbazole

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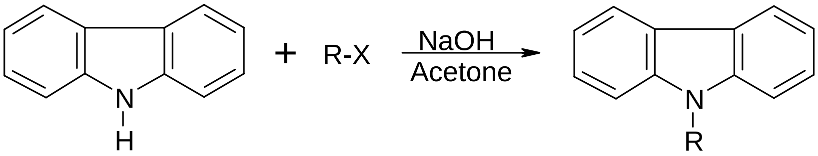
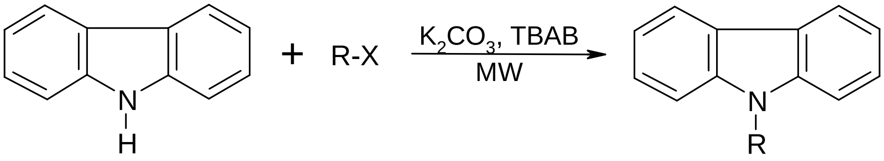
are usually prepared by treating potassium carbazole with alkyl halides or alkyl sulfates.[9] Nearly quantitative yields of N-alkyl & N-acyl derivatives of 9H-carbazole may be obtained when a solution of 9H-carbazole in acetone or alcohol is treated with alkylating or acylating agents, respectively in the presence of alkali (**Scheme 1**)[10,11]. N-Alkyl carbazoles were also prepared by microwave irradiation using phase transfer catalyst **(Scheme 2)**[12].



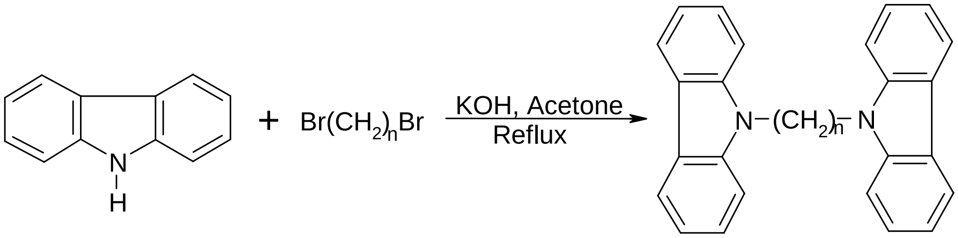
R=Alkyl or Acyl group

Scheme 1



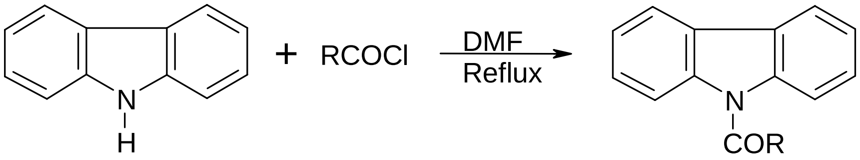
Scheme 2

N,N'alkylenedicarbazoles have been prepared by reaction with α, ω-dibromoalkanes **(Scheme 3)**.[10,11,13,14]



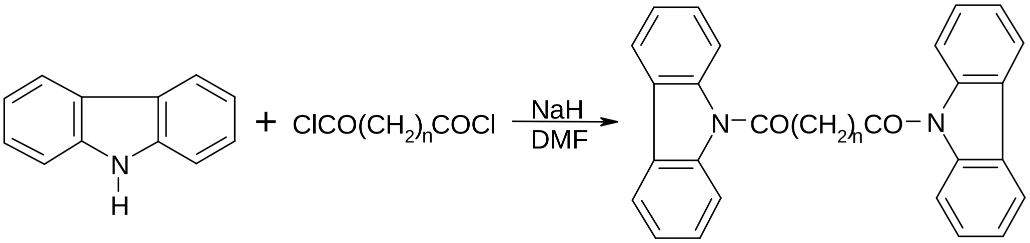
Scheme 3

Treatment of 9H-carbazole magnesium halides with benzoyl chloride and with acetyl chloride results in formation of the corresponding N-acylcarbazoles[15,16]. The 9-acyl carbazole have been prepared through the action of acyl halides or anhydrides on carbazole[17] **(Scheme 4)**.



Scheme 4

The N-acyl dimmers have been prepared by reacting 9H-carbazole with acid dichlorides[18] (**Scheme 5**).



Scheme 5

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 9H-carbazole.

Present work

As a part of developing environmentally benign new methodologies for the synthesis of biologically active compounds[19,15,16], we report herein facile synthesis of N-alkyl, N-acyl and dimericcarbazoles using microwave assisted reactions. The present work includes solid state alkylation and acylation of 9H-carbazole derivatives using commercial solid supports such as silica gel and alumina with the addition of newer support fly ash. 9H-carbazole was adsorbed on silica gel/alumina/fly ash and by using aqueous sodium carbonate and α,ω-dibromoalkanes and irradiated under MW to give the desired products (**Scheme 6**).

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

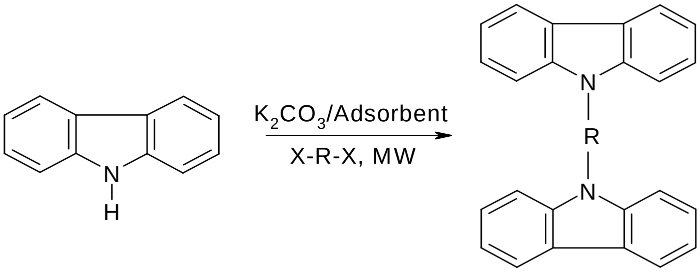
Plant, Deepnagar, Bhusawal, Dist. Jalgaon, (M.S.), INDIA and used as such for the reactions. Silica gel and alumina were of synthetic grade (s. d. fine Chem. Ltd., Mumbai, INDIA).The reactions were monitored by silica gel TLC using chloroform: acetone (7:3) or n-hexane: chloroform (7:3). Melting points were determined by open capillary method and are uncorrected.

Synthesis of dimeric 9H-carbazole products (1a-c)

The dimeric alkylene and diketoalkylene products of 9H-carbazole were prepared with α,ω-dibromoalkane (5 mmoles) using above procedure, to afford **(1a-c)** (**Scheme 6**).

Synthesis of dimeric 9H-carbazole products (1d-g)

The dimeric alkylene and diketoalkylene products of 9H-carbazole were prepared with α,ω-dibromoalkane (5 mmoles) and diacid chloride (5 mmoles) using above procedure, to afford **(1d-g)**, respectively (**Scheme 6**).



Scheme 6

(a) R = $-CH_2CH_2-$, X = Br
(b) R = $-CH_2CH_2CH_2-$, X = Br
(c) R = $-CH_2(CH_2)_2CH_2-$X = Br
(d) R = -COCO-, X = Cl
(e) R = $-COCH_2CO-$, X= Cl
(f) R = $-CO(CH_2)_2CO-$, X = Cl
(g) R = $-CO(CH_2)_4CO-$, X = Cl

Characterization

The synthesized 9H-carbazole compounds were characterized by their physical constants, comparative TLC and spectroscopic (^{1}H NMR and IR) techniques. The spectral data of the synthesized compounds were found to be satisfactory with reported data.

Table 1: 9H-carbazole derivatives

Compd. No.	Irradiation Time in min	Solid support, yield (%)			m.p. (°C)	Lit. m.p. (°C)
		Silica gel	Alumina	Fly-ash		
1a	3	81	82	81	304	304-305
1b	3.5	80	88	86	185	185-186
1c	4	85	87	86	209	208-209
1d	0.5	94	95	95	189	189-190
1e	0.75	86	88	86	158	158
1f	1	88	89	89	210	210-211
1g	2.	89	92	90	196	195-197

Table 2: Elemental analysis data for compounds 1a-g and ^{1}H NMR

Compd.	Elemental analysis data (Found)			^{1}H NMR ($CDCl_3$)
	C	H	N	(δ)
1a	86.63 (86.52)	5.59 (5.74)	7.77 (7.81)	1.53 (s, 4H, NCH_2CH_2N); 7.06-8.09 (m, 8H, Ar-H)
1b	86.60 (86.43)	5.59 (5.68)	7.48 (7.32)	- -
1c	86.52 (86.44)	6.23 (6.40)	7.21 (7.33)	- -
1d	80.40 (80.23)	4.15 (4.35)	7.21 (7.38)	7.14-8.09 (m, 8H, Ar-H)
1e	80.58 (80.70)	4.51 (4.38)	6.96 (7.18)	- -
1f	75.94 (76.12)	4.84 (4.67)	6.72 (6.89)	- -
1g	81.06 (87.24)	5.44 (5.27)	6.30 (6.55)	- -

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