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# Facile Synthesis Of Biologically Active Carbazole Derivatives Using Polymer-Supported Carbazolyl Anion #

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**ABSTRACT**

Facile synthesis of biologically active N-alkyl and N-acyl carbazole derivatives under mild conditions is described. The compounds were synthesized by reacting polymer-supported carbazolyl anion with alkyl and acyl chlorides, respectively. Furthermore, dimeric products containing alkylene and diketo alkylene bridges were also achieved by reacting polymer-supported carbazolyl anion with α,ω-dibromoalkanes and acid dichlorides, respectively. 

**KEYWORDS**

Carbazole;
Polymer-supported reactions;
Alkylation;
Acylation;
Dimers.

## INTRODUCTION

Carbazoles display a range of biological activities making them attractive compounds to synthetic and medicinal chemists[1-4]. As a result, in the past two decades numerous carbazole alkaloids and synthetic analogues, many of them possessing useful pharmacological properties, have been studied. A strong interest in this area by chemists and biologists reflected due to the intriguing structural features and promising biological activities exhibited by many carbazole compounds. The explosive growth of carbazole chemistry is emphasized by the large number of monographs, accounts, and reviews[5-8].

Several methods have been reported for alkylation and acylation of carbazole[9-12], however, these conventional methods have drawbacks such as lower yields, high temperature conditions, longer reaction time and formation of by products. The synthesis of dimmers[10-16] requires several hours and isolation and purification result in lower yields. In continuation of our work on structural modification of biologically

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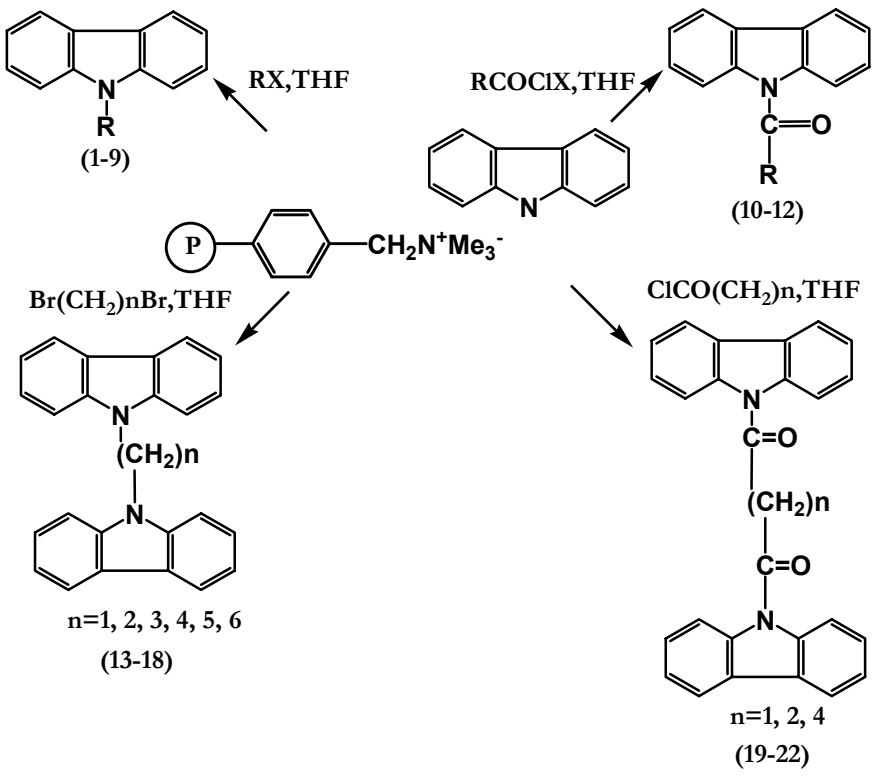


SCHEME 1

active compounds[17-19], we report herein facile synthesis of N-alkyl, N-acyl and dimeric carbazoles using polymer-supported carbazolyl anion.

Amberlite IRA-400(chloride form) resin was used to support carbazolyl anion. The alkyl halides, acid chlorides, α,ω-dibromoalkanes and acid dichlorides were added to the carbazolyl anion-supported resin in THF and mixture was stirred until the reaction was completed (SCHEME 1). In general all reactions with acid chlorides were found to be faster than that with alkyl halides. Isolation of pure products by simple filtration and evaporation of solvent is an important feature of this rapid method. The method is also inexpensive as the resin could be used repeatedly and regenerated to its initial activity by treatment with dil. HCl solution. We have developed a simple and convenient method for the N-alkylation and N-acylation of carbazole that occurs remarkably fast under mild conditions with higher yields.

## EXPERIMENTAL

All chemicals used were of analytical grade. THF, chloroform, n-hexane and acetone were distilled before use. Commercial Amberlite IRA-400(chloride form) resin was activated by treatment with dilute HCl solution before use. Melting points are uncorrected.

### General procedure for supporting carbazolyl anion on amberlite IRA-400

The potassium salt of carbazole was prepared by the fusion of carbazole(25g, 145mmoles) and potassium hydroxide(8.5g, 155mmoles) at 260$^0$C[13]. Then it was dissolved in a mixture of acetone and water(2:8). The activated Amberlite IRA-400(chloride form) (100g) was packed on a column(2cm diameter and 45cm length) and was eluted slowly dropwise(1.5ml/min) with the solution of potassium carbazole. Thereafter, the resin was washed with distilled water until complete removal of chloride ions and excess of carbazolyl anion. It was then washed with ethanol followed by acetone and dried in vacuo at 50$^0$C for 4 hr. The exchange capacity of carbazolyl anion supported resin was determined by passing aqueous 1N KCl(100ml) solution through supported resin(1g) packed in a column. The carbazolyl anion in the eluent was titrated against 0.01N HCl using methyl orange as indicator. The exchange capacity

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of the supported resin was found to be 1.2mmole carbazolyl anion per gram of dry resin.

**Synthesis of N-alkyl (1-9) and N-acyl (10-12)carbazoles**

A mixture of carbazolyl anion supported Amberlite IRA-400(chloride form) resin(10g, 12mmoles) and alkyl halide(s) (12mmoles) or acid chloride(s) (12mmoles) in THF(25ml) was stirred for 10-45min or 10-25min depending on the reactivity of the alkyl halide(s) or acid chloride(s), respectively. The progress of the reaction was monitored by TLC (chloroform:acetone, 7:3 or n-hexane: chloroform, 7:3). Then the resin was filtered off and washed with THF(3×5 ml). The filtrate was dried over sodium sulphate or with calcium chloride and removal of the solvent afforded the N-alkyl carbazole(1-9) or N-acyl(10-12) carbazoles, respectively as listed in the TABLE 1.

**TABLE 1: Carbazole derivatives**

| Compd. No. | Substituents R or n | Yield (%) | m.p. [Lit.][20] ($^0$C) |
|---|---|---|---|
| Parent | H | -- | 246 [246] |
| 1 | $CH_3$ | 94 | 91 [91] |
| 2 | $CH_3CH_2$ | 94 | 69 [69] |
| 3 | $CH_3CH_2CH_2$ | 93 | 49 [49-50] |
| 4 | $(CH_3)_2CH$ | 90 | 123 [123] |
| 5 | $CH_3(CH_2)_2CH_2$ | 91 | 58 [58] |
| 6 | $(CH_3)_2CHCH_2$ | 89 | 52 [52] |
| 7 | $CH_2$=$CHCH_2$ | 89 | 55 [54-55] |
| 8 | $C_6H_5CH_2$ | 94 | 120 [119-120] |
| 9 | $HOOCCH_2$ | 90 | 212 [212-213] |
| 10 | $CH_3CO$ | 95 | 77 [77.2] |
| 11 | $CH_3CH_2CO$ | 94 | 112 [112] |
| 12 | $C_6H_5CO$ | 97 | 98 [98.5] |
| 13 | n = 1 | 90 | 307dec.[307dec.] |
| 14 | n = 2 | 91 | 304 [304-305] |
| 15 | n = 3 | 88 | 185 [185-186] |
| 16 | n = 4 | 89 | 209 [208-209] |
| 17 | n = 5 | 90 | 184 [184] |
| 18 | n = 6 | 87 | 126 [125-127] |
| 19 | n = 0 | 96 | 189 [189-190] |
| 20 | n = 1 | 93 | 158 [158] |
| 21 | n = 2 | 92 | 210 [210-211] |
| 22 | n = 4 | 95 | 196 [195-197] |

**Synthesis of carbazole dimers (13-18 and 19-22)**

Dimeric products containing alkylene bridge(13-18) and diketo alkylene bridge(19-22) were synthesized by reacting 20g(24mmoles) of carbazolyl anion supported resin with 12mmoles of α,ω-dibromoalkane(s) and acid dichloride(s), respectively and reactions were monitored by TLC as described in above procedure.

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