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Convenient Synthesis of Dimethyl-1-Aryl-4-Hydroxy-N-Methylcarbazole-2,3-Dicarboxylates via Michael Initiated Ring Closure Methodology

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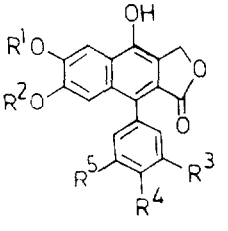
Abstract : A convenient method has been described for the synthesis of dimethyl-1-aryl-4-hydroxy-N-methylcarbazole-2,3-dicarboxylates (**3a-d**) from ethyl N-methyl-2-benzylindole -3-carboxylates (**2a-d**).

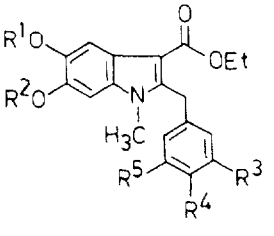
Several carbazole derivatives including ellipticine and olivacine are known to possess anticancer activity[1]. The naphthalenic lignans like (**1a-c**) do not contain nitrogen heterocyclic ring, still possess useful biological activities[2,3]. In view of this numerous methods have been developed for their synthesis[4]. Their indole analogues, however, have not been thoroughly investigated[5].

In this communication, we report the synthesis of carbazoles (**3a-d**) using a Michael initiated ring closure reaction (Scheme 1) similar to that used by Harrowven[6] for the synthesis of naphthalene derivatives.

The donor anion **4** generated from the corresponding ethyl 2-benzyl-N-methylindole-3-carboxylates (**2a-d**) by reaction with LDA in THF at - 78°C, reacted with dimethyl acetylenedicarboxylate to provide the carbazoles (**3a-d**) in 53, 57, 47 and 52% yields respectively. The starting indoles were obtained from appropriate 2-nitrobenzaldehydes using the nitrene approach developed by us[7] for the synthesis of ethyl 2-alkylindole-3-carboxylates.



1



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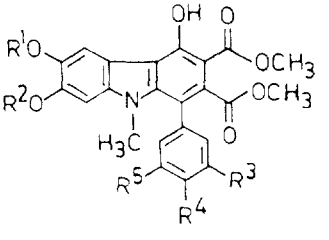
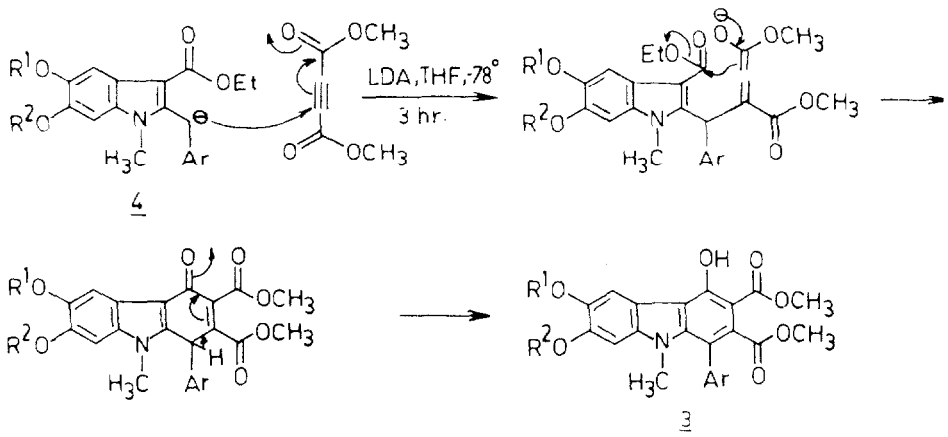


3

1	R^1	R^2	R^3	R^4	R^5
a	$-CH_2-$		H	$-OCH_2O-$	
b	CH_3	CH_3	H	$-OCH_2O-$	
c	$-CH_2-$		OCH_3	OCH_3	OCH_3

2,3	R^1	R^2	R^3	R^4	R^5
a	$-CH_2-$		H	H	H
b	$-CH_2-$		H	$-OCH_2O-$	
c	CH_3	CH_3	H	$-OCH_2O-$	
d	$-CH_2-$		OCH_3	OCH_3	OCH_3



4 3

Scheme 1

All the carbazole derivatives (**3a-d**) gave satisfactory analytical and spectral[8] data.

The work is in progress, by similar methods, for the synthesis of other carbazoles and pyridocarbazoles.

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8. ^{1}H-NMR ($CDCl_3$) data of some selected compounds **3a** : 3.09, s, 3H, -COOMe, 3.43, s, 3H, -NMe, 3.88, s, 3H, -COOMe, 6.02, s, 2H, $-OCH_2O-$, 6.76, s, 1H, ArH, 7.38, s, 5H, Ph-, 7.88, s, 1H, ArH, 12.00, s(exchangeable with D_2O), 1H, -OH. **3b** : 3.21, s, 3H, -COOMe, 3.60, s, 3H, -NMe, 3.88, s, 3H, -COOMe, 6.02, s, 4H, 2 x $-OCH_2O-$, 6.76, s, 1H, ArH, 6.84, s, 3H, 3ArH, 7.88, s, 1H, ArH, 12.00, s(exchangeable with D_2O), 1H, -OH.

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