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One Pot Synthesis of 4-Hydroxy-3-Substituted Carbazoles via Sulfoxide Stabilised Carbanion

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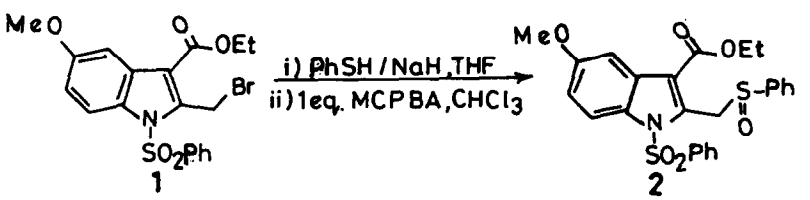
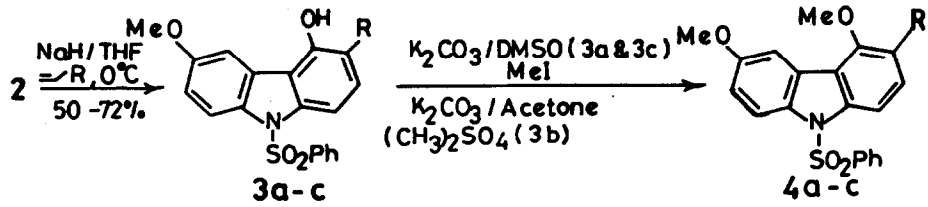
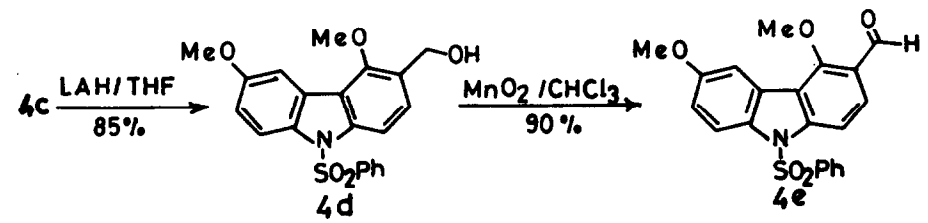
Abstract : A convenient method for the synthesis of 4-hydroxy-3-substitutedcarbazoles (Potential intermediate for pyridocarbazole alkaloids) from ethyl 5-methoxy-2-phenylsulfinylmethyl-1-phenylsulfonylindole-3-carboxylate is reported.

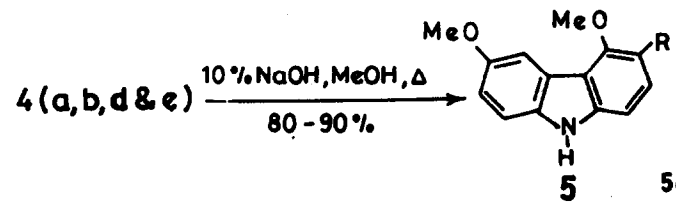
Many annelation methods based on the Michael addition followed by intramolecular cyclisation have been reported[1]. However a similar approach to carbazoles from indole was unknown till recently. In continuation of our attempts to synthesize 'C' ring oxygenated pyridocarbazole alkaloids and also prompted by a recent report[2] on the synthesis of dimethyl-1-aryl-4-hydroxy-N-methylcarbazole-2,3-dicarboxylates, we report here a facile synthesis of 4-hydroxy-3-substituted carbazoles from the bidentate synthon **2** by a Michael addition promoted annelation strategy involving a sulfoxide stabilised carbanion at indole-2-position.



Treatment of the bromo compound 1 with thiophenol in NaH/THF gave the sulfide 1a (mp 94°,EtOH) which on oxidation with 1 eq. of MCPBA gave the sulfoxide 2 (mp 94°,MeOH) in an overall yield of 85%. The reaction of sulfoxide 2 with Michael acceptors in NaH/THF led to the hydroxycarbazoles (3a-c) in 50-72% yields with concurrent loss of phenylsulfoxide unit.







5a (mp 162-164°, MeOH)
5b (mp > 350°, $CHCl_3$)
5d (mp 172- 174°, $CHCl_3$)
5e (mp 124-126°, MeOH)

R=	a	b	c	d	e
3	$COCH_3$	CN	CO_2Et	-	-
4	$COCH_3$	CN	CO_2Et	CH_2OH	CHO
5	$COCH_3$	CN	-	CH_2OH	CHO

The hydroxy carbazoles 3a and 3c were methylated with MeI/K_2CO_3 in DMSO. In the case of 3b methylation was carried out with dimethyl sulfate/K_2CO_3 in boiling acetone.The carbazole 4c was reduced to alcohol (85% mp152-154°, MeOH) using LAH without cleaving the N-phenylsulfonyl group, which on oxidation with active MnO_2 gave the 4,6-dimethoxy-N-phenylsulfonylcarbazole-3-aldehyde 4e (90% mp 184-186°, MeOH).

All these compounds (4a, b, d and e) were treated with 10% sodium hydroxide in boiling methanol to give the N-freecarbazoles 5. Moody et al have used[3] similar carbazoles to synthesize Murrayafoline A, and Murrayaquinone A' type of alkaloids.

All these carbazole derivatives gave satisfactory spectral data[4].

Further work is in progress to use these carbazoles to synthesize pyridocarbazole alkaloids oxygenated in C-and/or D-ring.

Typical experimental procedure for 3a-c

To a solution of ethyl 5-methoxy-2-phenylsulfinylmethyl-1-phenylsulfonylindole-3-carboxylate 2 (497mg, 1 mmol) in dry THF (10 ml) under N_2, sodium hydride was added (48 mg, 1mmol) and stirred at 0°C for 15 min. Then one equivalent of Michael acceptor dissolved in dry THF (5 ml) was slowly added. After stirring for 3h at 0°C, the reaction mixture was quenched with saturated solution of NH_4Cl (10 ml) and extracted with chloroform (3 x 10 ml). The solvent was removed from the dried (Na_2SO_4) extract and the orange residue was recrystallised from methanol. 3a (mp 194°, MeOH), 3b (mp 184-186°, benzene-petrol), 3c (mp 160-162°, MeOH), 4a (mp 134-136°,MeOH), 4b (mp 174-176°, MeOH), 4c (mp 110-112°, MeOH).

Acknowledgement :

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(b) Martin,T.; Moody,C.J. J.Chem.Soc., Perkin Trans.I. **1988**, 241-246.
4. H^1-nmr($CDCl_3$) data of some selected compounds.
2 δ 1.6,t,3H,-$CO_2CH_2\underline{CH_3}$, 4.05,s.3H,-OCH_3, 5.3, d(J=15Hz), 1H, -$C\underline{H}_AH_BSOph$, 5.6, d(J=15Hz), 1H, -$CH_A\underline{H}_BSOph$, 7.1-8.3,m, 13H, ArH.
4a δ 2.62,s,3H,-$COCH_3$, 3.78,s,3H, -OCH_3, 3.85,s, 3H, -OCH_3, 7-8.2,m, 10H, ArH
4b δ 1.3-1.5,t,3H, - $CO_2CH_2\underline{CH_3}$, 3.85, s, 3H, -OCH_3, 4.05, s, 3H, -OCH_3, 4.3-4.6, q, 2H, - $CO_2\underline{CH_2}CH_3$, 7.1-8.3, m, 10H, ArH
4e δ 3.8, s, 3H,- OCH_3, 4.1, s, 3H,- OCH_3,7.05-9.1, m, 10H, ArH, 11.5, s, 1H,- C$\underline{H}$O.

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