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NEW [4+2]-CYCLOADDITIONS OF IN SITU GENERATED INDOLYL ENOL ETHERS AS HETEROCYCLIC DONOR-ACTIVATED 1,3-DIENES TO CARBAZOLE DERIVATIVES**

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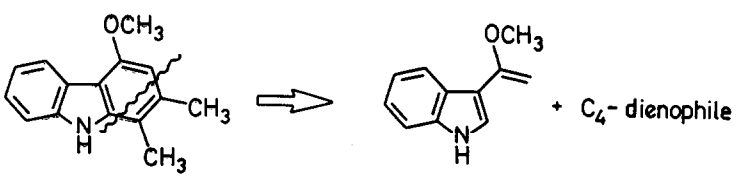
SUMMARY: The ambident alkoxy-indolyl-methylcarbenium ions **1a-c** are deprotonated by NaH to give in situ generated enol ethers which can be easily trapped by a dienophile such as, e.g., dimethyl acetylenedicarboxylate to form the carbazole derivatives **3**, **4**, and I. On reaction with the ethoxy-2-methylindolylcarbenium ion **1d** under the same conditions, a stereoselective Michael-type addition with formation of **6** takes place.

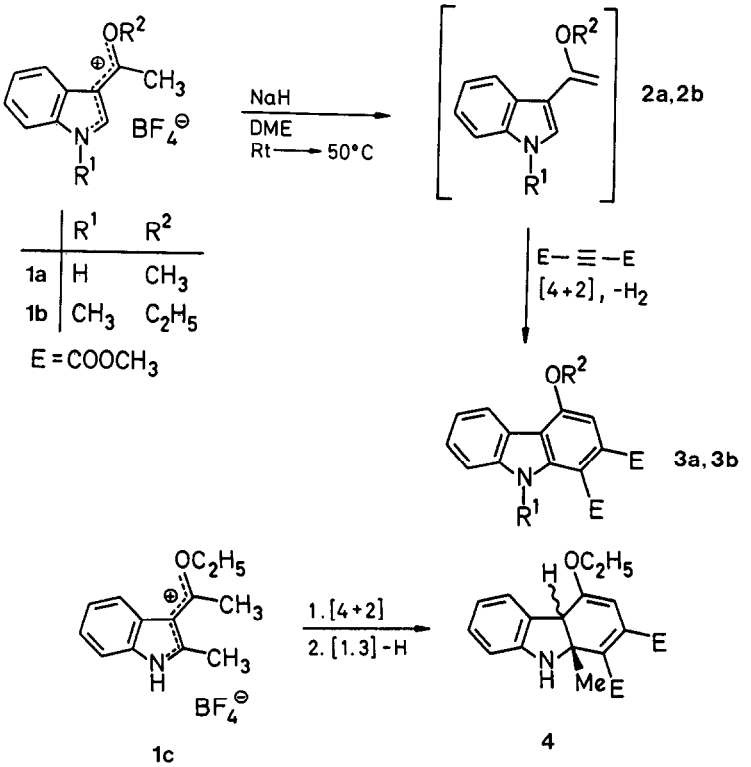
The general interest in the chemistry of carbazoles and structurally related indole derivatives has increased considerably in recent years[1-5] as some of these compounds, both natural products and synthetic compounds, have exhibited pronounced physiological activities. A concept for the preparation of [b]annellated indoles and carbazole alkaloids consists of the [4+2]-cycloaddition to 3-vinylindoles[1-7]. The pronounced enophile reactivity of these compounds is the result of the characteristically high HOMO energy[8]. With the view to a systematic extension of the by no means fully utilized synthetic potential[6] of this type of reaction and to the development of a synthesis of 3-demethoxycarbazomycine I[5] and analogues, we now report on a new variation of this cyclization method.

According to a retrosynthetic analysis, the as yet not synthesized carbazole derivative I, for example, should be accessible from the indolyl enol ether II via a Diels-Alder reaction with a C_4-dienophile as the key step. As intensive studies on the synthesis of isolable II were unsuccessful, we attempted to generate II and its analogues in situ and to trap them with a C_4-dienophile. Preliminary results using these reaction sequences involving cycloadditions with dimethyl acetylenedicarboxylate are described here.



I II

The ambident cations **1**, first described by us[9], seemed to be synthetically attractive starting materials for the realization of this concept. Compounds **1a-c** can indeed be deprotonated by NaH in DME and the enol ethers **2** thus generated in situ can be trapped easily with dimethyl acetylenedicarboxylate to give the cycloadducts **3a,b** (11 and 6%) and **4** (cis/trans 4:1 by ^{1}H-NMR spectroscopic measurements, 28%, reaction conditions: DME, 20-50 °C, 30 min, nitrogen atmosphere; separation by flash chromatography: silica gel, petroleum ether/ethyl acetate)[10]. Whereas product formation in the cycloadditions with **1a,b** is governed by the driving force of the indolization via a dehydrogenation step, the reaction with **1c**, as expected, is terminated at the stage **4** as a result of a blockage of the indolization step. The primarily formed cycloadduct from the cycloaddition with **1c** is stabilized by a non-stereospecific [1,3]-H shift with formation of an annellated 1,3-cyclohexadiene structure. The carbazole **3a** represents a synthetically attractive precursor (COOMe ⟶ Me) for the total synthesis of 3-demethoxycarbazomycine I[11]. For this purpose, **3a** is hydrolyzed (KOH/MeOH) to the dicarboxylic acid and then reduced to I with $HSiCl_3$ according to a known procedure[11] (1. $HSiCl_3$/MeCN, $(n\text{-}Pr)_3N$; 2. KOH/MeOH).

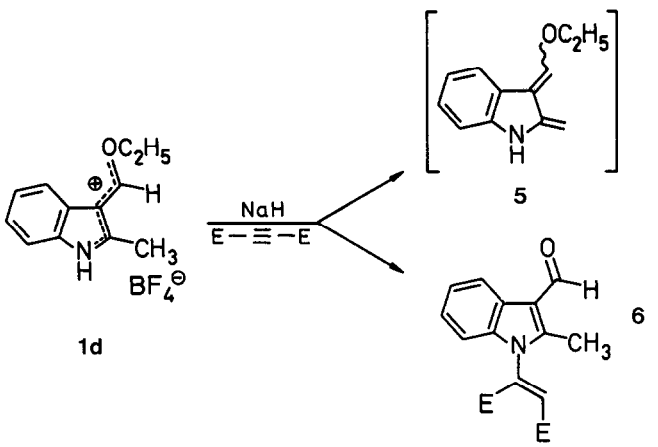


	R^1	R^2
1a	H	CH_3
1b	CH_3	C_2H_5

E = $COOCH_3$

With regard to this methodology, suitable alkoxy-indolylcarbenium ions could also be employed for the in situ generation of synthetically attractive indolo[2,3]quinodimethanes as 4^π-components[12]. For example, the cation **1d**, which could form **5** via deprotonation, might be considered as a suitable pre-

cursor. However, even on multiple variations of the reaction conditions and in the presence of radical inhibitors, this concept could not be realized. Instead of formation of the expected 2,3-dimethoxycarbonylcarbazole derivative[12], only a stereoselective Michael-type reaction with formation of **6** (11%, flash chromatography) in addition to a dealkylation of the cation **1d**[9] (formation of 2-methylindole-3-carboxaldehyde) and polymerization occurred[13].



The constitutions of I, **3**, and **6** as well as the configurations of **4** and **6** given above have been unequivocally confirmed by elemental analysis, mass spectrometry, and ^{1}H-NMR spectroscopy (selective decoupling and NOE measurements)[10].

Preliminary experiments using this new "in situ vinylindole variation" have shown that reactions with other dienophiles (e.g. maleic anhydride, N-phenylmaleimide) can also be realized. A systematic investigation of the synthetic potential of this type of reaction for the preparation of further new carbazole derivatives is now in progress in our laboratory.

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8. The HOMO energy of 1'-donor-activated 3-vinylindoles is in the range 6.9 to 7.2 eV (PE spectroscopy, R. Gleiter, University of Heidelberg, Heidelberg, FRG); J. Schmidt Burnier, W.L. Jorgensen, J. Org. Chem. **48**, 3923 (1983) (CAMEO method).
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