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A GENERAL SYNTHETIC METHOD OF 1,2-DIHYDROCYCLOBUTA[c]-COUMARIN AND ITS 1-SUBSTITUTED DERIVATIVES[1]

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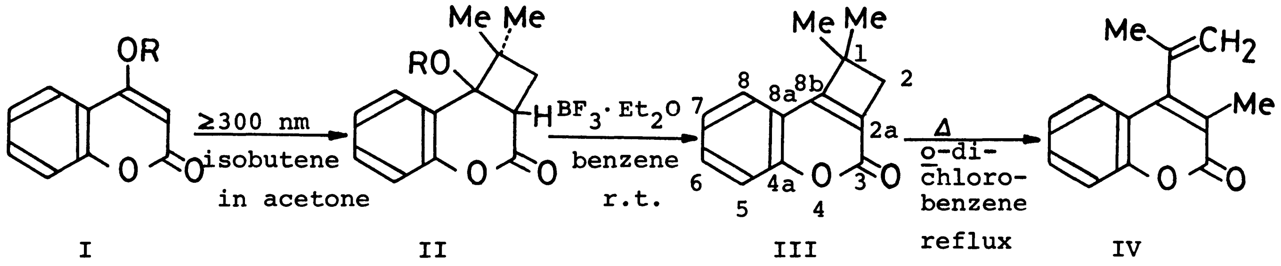
4-Methoxycoumarin reacts photochemically with ethylene and its substituted derivatives to form 8b-methoxy-1,2,2a,8b-tetrahydrocyclobuta[c]coumarin and its 1-substituted derivatives, which in turn eliminate methanol by boron trifluoride etherate in benzene to give the corresponding 1,2-dihydrocyclobuta[c]coumarins in high overall yields.

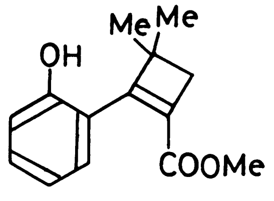
We have recently shown that intermolecular 2+2 cycloaddition of heterocyclic enone compounds having an alkoxy function at the β-position, namely 4-methoxy-2-pyridone[2] and -quinolone[3], with olefins can be effected photochemically and the resulted adducts can be transformed to 1,2-dihydrocyclobuta[c]-pyridin- and -quinolin-3(4H)ones by treatment with sodium methoxide in methanol. In an extension for our synthetic study of cyclobutene fused heterocycles, we applied this method to the synthesis of title compounds starting from 4-alkoxy- and 4-acyloxycoumarins. Though the 2+2 adducts[4] were obtained in high yields, these adducts merely gave the ring-opened hydroxy esters by the action of sodium methoxide in methanol and hence, no desired compound was obtained. However, use of boron trifluoride etherate in benzene for the elimination of methanol or acetic acid from the adducts was found to give the desired compounds. Thus, we now have established a general synthetic route for 1,2-dihydrocyclobuta[c]coumarins and this paper describes these results in some detail.

A solution of 4-methoxycoumarin (Ia) in acetone in the presence of a large excess of isobutene was irradiated at ≥ 300 nm (Toshiba 400P high pressure mercury lamp, Pyrex filter) until disappearance of the starting coumarin. Evaporation of the solvent followed by silica gel column chromatography gave the cycloadduct (IIa,

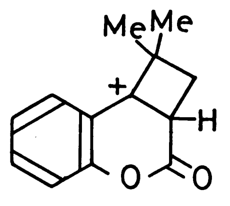
	R
a	Me
b	Ac



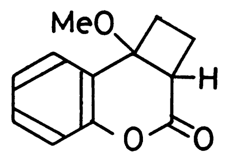
mp 95-95.5°) in 92% yield as a sole product. The gross structural feature of the adduct was deduced from similarity of its UV [λ_{max}^{MeOH} nm: 263 (sh), 270, and 277] and IR spectra [ν_{max}^{KBr} cm^{-1}: 1760 and 1240] with those of 3,4-dihydrocoumarin. The final confirmation of the structure of IIa was provided from PMR spectrum [$\delta(CDCl_3)$: 0.82 s (3H), 1.36 s (3H), 1.56 t (H_2), 2.10 t ($H_{2'}$) and 3.41 t (H_{2a}) with $J_{H_2-H_{2'}} = J_{H_2-H_{2a}} = J_{H_{2'}-2a}$ =10.5 Hz] in which the appearance of 2a-proton signal as a triplet centered at δ 3.41 indicated the head-to-tail structure. Treatment of IIa with sodium methoxide in methanol gave only the ring-opened hydroxy ester (V, mp 86.5-87°).[5] Action of concd. sulfuric acid to IIa in methanol at reflux afforded the desired product (III) in 46% yield, together with 51% of the same ester. Since the same mixture was obtained either from IIa or V by the same acid treatment, it is clear that an equilibrium is existed between these two products under these conditions. In order to avoid the undesirable ring-opening reaction in the course of methanol elimination reaction of IIa, we examined the use of a variety of Lewis acids in an aprotic solvent. As a result, it was found that the action of boron trifluoride etherate to IIa in benzene at room temperature led to the selective formation (89%) of 1,1-dimethyl-1,2-dihydrocyclobuta[c]coumarin (III, mp 97-98°). The structure of the cyclobutene (III) was determined from its PMR spectrum [δ ($CDCl_3$): 1.55 s (6H) and 2.92 s (2H)] as well as its conversion to 4-isopropenyl-3-methylcoumarin (IV, mp 73-73.5°) by refluxing in o-dichlorobenzene.[6] The 2+2 photochemical addition to isobutene and subsequent elimination of acetic acid from the adduct (IIb, mp 128-129°, 90%) to III also proceeded, when 4-acetoxycoumarin (Ib) was used as the starting material. However, the adduct[7] obtained from Ia and acrylonitrile did not eliminate methanol even in refluxed benzene containing boron trifluoride etherate, and was recovered unchanged. It seems reasonable to assume that the elimination of methanol or acetic acid from IIa or IIb proceeded



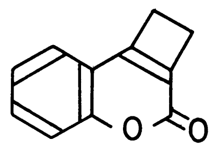
V



VI



VII



VIII

via the carbonium ion intermediate (**VI**). This novel boron trifluoride catalized methanol elimination reaction was successfully applied to the cycloadducts[3] obtained from 4-methoxy-2-quinolone with electron rich olefins and led in all cases to the corresponding 1,2-dihydrocyclobuta[c]quinolin-3(4H)ones in nearly quantitative yields.

In order to demonstrate generality of this two step procedure for the preparation of 1,2-dihydrocyclobuta[c]coumarins, the synthesis of the parent compound was carried out. The cycloadduct (**VII**, mp 56-56.5°, 80%) obtained in the first step gave, upon treatment with boron trifluoride etherate in benzene, 1,2-dihydrocyclobuta[c]coumarin (**VIII**, mp 145-146.5°) in a quantitative yield.

At present, our efforts are focussed on the examination of physical and spectroscopical properties, as well as chemical properties (e.g., their utility in organic synthesis as the heterocyclic analogues of benzocyclobutene[8]) of now readily available 1,2-dihydrocyclobuta[c]coumarins.[9]

REFERENCES AND NOTES

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3) C. Kaneko and T. Naito, Chem. Pharm. Bull., 27, 2254 (1979). See also, C. Kaneko, T. Naito, and M. Somei, JCS Chem. Comm., 1979, 804.

4) Coumarin derivatives have been reported to form photodimers[a] and inter-[b] and intramolecular alkene cycloaddition products[c] on both direct and sensitized irradiation. a) G.S. Hammond, C.A. Stout, and A.A. Lamola, J. Am. Chem. Soc., 86, 3103 (1964); b) D.J. Haywood, R.G. Hunt, C.J. Potter, and S.T. Reid, JCS Perkin I, 1977, 2458; c) D.J. Haywood and S.T. Reid, Tet. Lett., 1979, 2637.

5) Satisfactory analyses and spectra have been obtained for all new compounds.

6) For related intramolecular rearrangement reactions, see: T. Kametani, M. Tsubuki, Y. Shiratori, Y. Kato, H. Nemoto, M. Ihara, K. Fukumoto, F. Sato, and H. Inoue, J. Org. Chem., 42, 2672 (1977); C. Kaneko, T. Naito, and M. Ito, Tet. Lett., 21, 1645 (1980).

7) Obtained as a mixture of diastereoisomers.

8) Benzocyclobutenes have been effectively utilized as starting materials for the synthesis of polycyclic ring systems, see: W. Oppolzer, Synthesis, 1978, 793; T. Kametani and K. Fukumoto, Heterocycles, 3, 29 (1975).

9) The first synthesis of 1,2-dihydrocyclobuta[c]coumarin derivative was reported by Reid *et al.*[4b] Thus, the acetate derived from the cyclobutane adduct formed from 4-hydroxycoumarin and cyclohexene was pyrolyzed at about 200° to give the cyclobutene derivative (1,2-tetramethylene-1,2-dihydrocyclobuta[c]coumarin) and two other products derived therefrom.

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