Anomalous Photochemical Addition of Methanol to 6-Methoxydifurocoumarone

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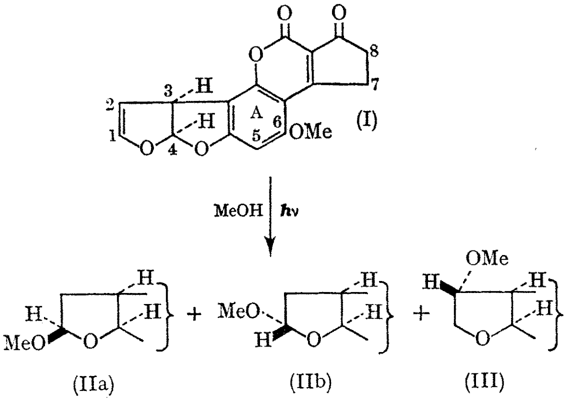
U.V. IRRADIATION of 6-methoxydifurocoumarone (I)[1] in methanol produces two isomeric 2-hydro-1,6-dimethoxydifurocoumarones (IIa) and (IIb) and 1-hydro-2,6-dimethoxydifurocoumarone (III). The formation of (IIa) and (IIb) is not entirely unexpected, since photochemical protic solvent addition to double bonds, as in cyclohexene and larger-ring homologues and conjugated double bonds, has been reported to proceed in the Markovnikov direction similar to the addition reaction in the ground state.[2] The production of (III), the anti-Markovnikov product, is unprecedented. Although cyclopentenes undergo radical reduction and dimerization instead of protolytic addition,[2a,b] and coumarin yields photocycloaddition dimers,[3] neither of these reactions was detected in the photolysis of (I).



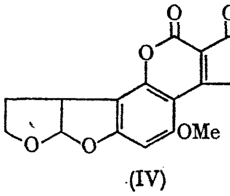
The methanolic solution of (I) ($3{\cdot}2 \times 10^{-3}$ M) was irradiated under nitrogen with RPR 3500 Å lamps in a Pyrex flask. The photoproducts, (IIa)[4] {24%; m.p. 220—223°; $[\alpha]_D$(CHCl$_3$) $-550°$}, (IIb) {30%; m.p. 260—262°; $[\alpha]_D$(CHCl$_3$) $-430°$}, and (III) {38%; m.p. 245—247°; $[\alpha]_D$(CHCl$_3$) $-360°$}, were separated by a silica gel column eluted with a chloroform–methanol mixture. All three compounds analysed for $C_{18}H_{16}O_7$,[†] equivalent to the addition of CH_3OH to (I). The u.v. maxima of these products are identical (363 nm.) with that of the parent compound (I), indicating that the addition of the solvent had not affected the conjugated chromophore. I.r. spectra support the same conclusions, since the 1760 and 1685 cm.$^{-1}$ conjugated lactone and carbonyl bands of the starting material are also present in the three products. It was therefore concluded that the addition occurred at the isolated double bond.

[†] Satisfactory elemental and/or mass spectroscopic analyses were obtained for the three photoproducts. We thank Mr. D. Black and Miss G. Secor for performing these analyses.

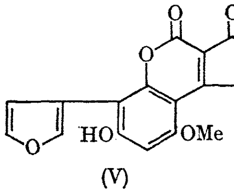
The direction of addition was established by n.m.r. spectroscopy.[4] The appearance of relatively undeshielded methylenic protons at (C-2) absorption in both (IIa) and (IIb) (δ 2·36 and 2·37 multiplets, respectively) suggested that the addition reaction proceeded according to the expected Markovnikov fashion. Structure (IIa) was assigned to the 1-methoxy-isomer with the higher shielded (δ 3·25) aliphatic O–CH_3. Since the β-oriented methoxy-group (IIa) is situated near the top of the aromatic ring A, it is expected that diamagnetic anisotropy from the π-electrons places the β-methoxy-group at a higher field relative to the α-isomer (IIb). The remainder of the protons in (IIa) and (IIb) absorb at positions similar to the ones in 1,2-dihydro-6-methoxy-difurocoumarone (IV). Although the multiplicity of H-1 in (IIa) and (IIb) is different, configurational assignment based on this type of data is not always reliable.[5]

Photoproduct (III) was shown to be a positional isomer of (IIa) and (IIb) by n.m.r. spectroscopy. The appearance of two nonequivalent *O*-methylenic protons (at C-1) at δ 3·70 and 4·19 with geminal couplings of 3 and 11 Hz. indicates that the OCH_3 was added to C-2. The α-configuration is tentatively assigned on the basis that the OCH_3 absorption of δ 3·54 is at a lower field than the expected value of δ 3·3—3·4.[6]

Because of insufficient starting material, no attempt has been made to elucidate the mechanism of this reaction. It is assumed, however, that since the photoreaction was carried out in a Pyrex flask in which the light energy (82 kcal. at 3500 Å) is insufficient to cleave the OH bond in methanol (100 kcal./mole)[7] or to excite the nonconjugated enolic double bond, the initial step must involve the excitation of the carbonyl function (either the lactonic and/or the ketonic carbonyl). Because the starting material and the three products possess the same sign of rotation and similar o.r.d. curves and since an optically inactive intermediate such as (V) which allows the direct excitation of the C-1 double bond is not likely, one may further conclude that the photo-addition must be a self-sensitized one. Whether the energy transfer occurs in triplet or singlet state is not certain. Triplet–triplet energy transfer is usually favoured because of the relatively longer lifetime of the triplet state; however, a singlet–singlet transfer cannot be excluded, especially in an intramolecular process.



(IV)



(V)

Although it has been argued that photochemical polar addition to cyclopentene was not possible because of severe strain in the orthogonally oriented π^* intermediate,[8] the addition of methanol to 2,3-dihydrofuran is permissible probably because the participation of the nonbonding electrons of the oxygen exerts a stabilizing effect on the excited intermediate. The mechanism of this unexpected photochemical reaction and the extent of participation by the ether-oxygen is being investigated with simpler and more accessible starting materials.

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[1] Formerly known as aflatoxin B_1. The nomenclature for linear difuro-containing mould metabolites of *Aspergillus* species has been put forward by A. C. Waiss, jun., M. Wiley, D. R. Black, and R. E. Lundin, *Tetrahedron Letters*, 1968, 3207.

[2] (a) P. J. Kropp and H. J. Krauss, *J. Org. Chem.*, 1967, **32**, 3222; (b) P. J. Kropp, *J. Amer. Chem. Soc.*, 1966, **88**, 4091; (c) J. A. Marshall and R. D. Carrol, *ibid.*, p. 4092; (d) B. J. Ramey and P. D. Gardner, *ibid.*, 1967, **89**, 3949; (e) C. C. Leznoff and G. Just, *Canad. J Chem.*, 1964, **42**, 2801.

[3] G. S. Hammond, C. A. Stout, and A. A. Lamola, *J. Amer. Chem. Soc.*, 1964, **86**, 3103 and references therein.

[4] An acid-catalysed methanol adduct to (I) was reported recently (M. F. Dutton and J. G. Heathcote, *Chem. and Ind.*, 1968, 418. We have found this to be identical with (IIa) and we observed signals due to small amounts of (IIb) in the n.m.r. spectrum of our crude reaction product.

[5] L. H. Zalkow and M. Ghosal, *Chem. Comm.*, 1967, 922.

[6] L. D. Hall, *Adv. Carbohydrate Chem.*, 1964, **19**, 51.

[7] J. G. Calvert and J. N. Pitts, "Photochemistry." Wiley, New York, 1967, p. 824.

[8] P. J. Kropp, *J. Amer. Chem. Soc.*, 1967, **89**, 3650; P. J. Kropp and H. J. Krauss, *ibid.*, p. 5199.