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2+2 PHOTOCYCLOADDITION TO A CARBON NITROGEN DOUBLE BOND I. 3-ETHOXYISOINDOLONE

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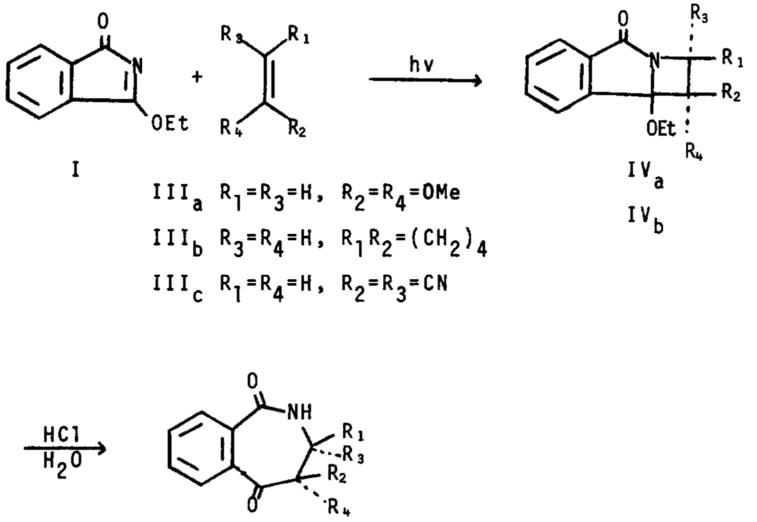
Although 2+2 photocycloadditions of olefins to carbon-oxygen[1] and carbon-carbon[2] double bonds are common, synthetically useful reactions, similar cycloadditions to the carbon-nitrogen double bond are to our knowledge non-existent in the chemical literature.[3] In search of this possibly useful reaction we have investigated photoreactions of olefins with cyclic molecules containing carbonyl and imino ether functional groups in conjugation. This chromophore was selected because it structurally resembles the α,β-unsaturated ketone which when cyclic often undergoes facile photocycloaddition of olefins.[2]

We report here the photochemical reactivity of 3-ethoxyisoindolone (I) with three olefins in the photocycloaddition reaction: an electron rich olefin (1,1-dimethoxyethylene), an electron neutral olefin (cyclohexene), and an electron poor olefin (fumaronitrile).[8]

Irradiation of a mixture of 2.0 g of I[10] and 4.0 g of 1,1-dimethoxyethylene in 125 ml of dry t-butyl alcohol with a 450 watt mercury lamp in a Pyrex immersion well resulted in complete destruction of starting material in 15 min. Upon rotary evaporation of the solvent and excess dimethoxyethylene a crystalline product was obtained (total isolated yield after recrystallization from Skelly solve B, 50%). The photoproduct was identified as the product of regiospecific cycloaddition of 1,1-dimethoxyethylene to the carbon-nitrogen double bond. The nmr spectrum shown in Table I is also consistent with the assigned structure. We note as others have[12] that the azetidine methylene protons are deshielded to an unusual extent. The mass spectrum includes a parent ion at m/e 263 (21% of base) and fragment ions at m/e 235 (9%, $M-C_2H_4$), 234 (53%, $M-C_2H_5$), and 88 (base, 1,1-dimethoxyethylene radical cation).[13]



I

III$_a$ $R_1=R_3=H$, $R_2=R_4=OMe$

III$_b$ $R_3=R_4=H$, $R_1R_2=(CH_2)_4$

III$_c$ $R_1=R_4=H$, $R_2=R_3=CN$

IV$_a$

IV$_b$

V$_a$

V$_b$

Stirring of the photocycloadduct in 3N hydrochloric acid at room temperature for 24 hours resulted in complete destruction of IVa. The product of hydrolysis was obtained in 76% yield after recrystallization from acetonitrile and assigned structure Va, 3,4-benzo-6,7-dihydro-6,6-dimethoxy-1H-azepine-2,5-dione. The nmr spectrum of Va (Table I) provides unambiguous evidence for the regiochemistry of the photocycloaddition. The methylene protons of Va appear as a doublet coupled to the amide proton. Exchange with deuterium oxide results in collapse of this absorption to a singlet. The methylene protons for the product of hydrolysis of a cycloadduct with the opposite regiochemistry would have appeared as a singlet. The infrared spectrum is also consistent with the assigned structure with bands at 3.07, 5.88, 5.99, and 6.14 μ. Like the photocycloadduct, the benzoazepinedione (Va) exhibits a base peak in the mass spectrum at m/e 88 assigned as the dimethoxyethylene radical cation. A weak parent ion is observed at m/e 235 (0.2% of base).

Table I

Nmr Data[a]

Compound	ethoxyl	R_1	R_2	R_3	R_4	aromatic	N-H
IV_a	3H, 1.18 t[b] 1H, 3.2 c 1H, 3.45 c	1H,4.04 d J=10	3H,3.17 s	1H, 3.86 d J=10	3H,3.45 s	4H,7.3- 7.95 m	...
IV_b	3H, 1.18 t[b] 1H, 2.97 c 1H, 3.37 c	8H, 1.1-2.5m		1H, 4.05 q J=8.5	1H,2.53- 2.84 m	4H,7.3- 8.1 m	...
V_a	...	1H,3.46 d J=6.5	3H,3.28 s	1H, 3.45 d J=6.5	3H,3.28 s	4H,7.3- 7.9 m	1H, 8.3 b
V_b	...	8H, 1.1-2.35 m		1H, 4.1- 4.4 m	1H,2.35- 2.8 m	4H,7.4- 8.1 m	1H, 6.8 b

[a] The spectra of IV_a and IV_b were measured at 100 MHz in $DCCl_3$; the spectra of V_a and V_b at 60 MHz ^{a}in DMSO-d_6; resonance positions are given as δ values relative to internal TMS; J values are given in Hz; b=broad singlet, d=doublet, c=complex, m=multiplet, s=singlet, t=triplet.

[b] The ethoxyl protons appear as an ABX_3 pattern; $J_{AX}=J_{BX}$ and J_{AB} are of opposite sign; for IV_a $J_{AX}=J_{BX}=7.1$ and $J_{AB}=9.0$ and for IV_b $J_{AX}=J_{BX}=7.0$ and $J_{AB}=8.8$.

Irradiation of 2.0 g of 3-ethoxyisoindolone in the presence of cyclohexene in t-butyl alcohol solvent resulted in no reaction and 95% recovery of III. When the solvent was changed to methylene chloride, however, the cycloaddition occurred smoothly in less than 30 min. to yield a single cycloadduct assigned structure IV_b (yield 51%). The cis-anti-cis stereochemistry was assigned on the basis of the nmr spectrum (Table I). The methine proton adjacent to nitrogen appears as a quartet with approximately equal coupling to the adjacent methine and methylene protons. This would only be likely for a cis ring juncture. A cycloadduct with the cis-syn-cis configuration would have one or more of the cyclohexane protons in the shielding region of the aromatic ring. Since none of the cyclohexane protons appear to be strongly shielded, the anti configuration was assigned. Like the dimethoxyethylene cycloadduct, hydrolysis of IV_b with dilute hydrochloric acid gave a benzoazepinedione (V_b, quantitative yield).

With the electron poor olefin, fumaronitrile, 3-ethoxyisoindolone shows no photochemical reactivity in the protic solvent, *t*-butyl alcohol, or the aprotic solvent, methylene chloride; however, fumaronitrile is isomerized to maleonitrile. In both media better than 95% of I is recovered after irradiation.

For 2+2 cycloaddition of olefins to the carbon nitrogen double bond of keto imino ethers to be of general utility it should be competitive in systems for which α-cleavage[8] is also possible.

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Footnotes and References

(1) D.R. Arnold, in "Advances in Photochemistry", Vol. 6, W.A. Noyes, Jr., G.S. Hammond and J.N. Pitts, Jr., Eds., John Wiley and Sons, Inc., New York, N.Y., 1966, p. 310.

(2) O.L. Chapman and G. Lenz in "Organic Photochemistry", Vol. 1, O.L. Chapman, Ed., Marcel Dekker, Inc., New York, N.Y., 1967, p. 283; P.E. Eaton, *Acc. Chem. Res.*, *1*, 50 (1968); P. deMayo, *Ibid.*, *4*, 41 (1971); P.G. Bauslaugh, *Synthesis*, *2*, 287 (1970).

(3) A 1,2-diazetidine has been proposed as an unstable intermediate in the photoreaction of N-*p*-dimethylaminobenzylideneaniline.[4] The photodimer of benzaldehyde cyclohexylimine was originally reported to be a 1,2-diazetidine[5] and subsequently shown by Padwa and co-workers to be a reductive dimer, N,N'-dicyclohexyl-1,2-diphenyl-1,2-diaminoethane.[6] A cycloadduct was suggested as a possible intermediate in the photoreaction of N-acetyldiphenylmethylene imine with several olefins.[7]

(4) S. Searles, Jr. and R.A. Clasen, *Tetrahedron Let.*, 1627 (1965).

(5) R.O. Kan and R.L. Furey, *J. Am. Chem. Soc.*, *90*, 1666 (1968).

(6) A. Padwa, W. Bergmark, and D. Pashayan, *Ibid.*, *90*, 4458 (1968).

(7) N. Toshima, S. Asao, K. Takado, and H. Hirai, *Tetrahedron Let.*, 5123 (1970).

(8) Initially 2-ethoxypyrrolin-5-one (II) was examined in the photocycloaddition reaction because of its structural resemblance to 2-cyclopentenones. Irradiation of II in *t*-butyl alcohol in the presence of 1,1-dimethoxyethylene, however, did not yield a photocycloadduct but the product of photochemical α-cleavage followed by rearrangement and solvent incorporation yielding *t*-butyl (ethoxycyclopropyl)carbamate.[9] 3-Ethoxyisoindolone was then selected since α-cleavage would be energetically unfavorable.

(9) T.H. Koch and R.J. Sluski, *Tetrahedron Let.*, 2391 (1970).

(10) 3-Ethoxyisoindolone was prepared by the O-alkylation of the silver salt of phthalimide with ethyl iodide using a procedure analogous to that reported for the synthesis of 2-ethoxypyrrolin-4-one.[11] The isoindolone gives the following spectral absorptions: ir (KBr) 5.68, 5.72, and 6.46 μ; nmr ($DCCl_3$) δ 1.55 (t, J=7Hz, 3H), 4.77 (q, J=7Hz, 2H), 7.42-7.92 ppm (m, 4H); uv λ_{max} (C_6H_{12}) 216 (ε 38,000), 288 (ε 1900), and 298 nm (ε 2100).

(11) S.J. Comstock and H.L. Wheeler, *Am. Chem. J.*, *13*, 522 (1891).

(12) The α-methylene protons of azetidine appear at δ3.54 ppm. O.E. Edwards, G. Fodor, and L. Marion, *Can. J. Chem.*, 44, 13 (1966).

(13) All new molecules gave satisfactory elemental analyses.