THE FIRST PHOTOCYCLOADDITIONS OF INDOLIZINE

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<u>Abstract:</u> (2-Methyl)indolizine upon photoexcitation is trapped by stilbenes with fluorescence quenching and gives regio- and stereoselectively only the l:l-adducts **3** (**6**) and the l:2-adduct **4** in good yields. The surprising results are rationalized in terms of the well-documented diradical mechanism and quantum chemical data.

Although indolizines are strongly worked upon because of their widespread biological actions¹ and although the photophysical data of indolizine (1) (UV: O/O-transition at 383 nm; fluorescence yield 0.84, fluorescence lifetime 42 nsec, no phosphorescence at 77 K)² appear particularly favourable for photo(cyclo)additions, nothing is reported about such reactions with indolizine nes. We report here on the first examples of photochemical [2+2]-cycloadditions of indolizine (1) and 2-methylindolizine which stand out for their unusual regio- and stereoselectivities.

If indolizine $(1)^3$ is irradiated nearly selectively in benzene⁴ in the presence of excess <u>trans</u>-stilbene (2), only the adducts 3 and 4 are isolated in the ratio of 4.8:1. None of the possible adducts of further [2+2]-, or



of $[4+2]^{-5}$, or of $[8+2]^{-6}$, or of substituting⁷, or of rearranging additions^{7,8} could be detected. There is quenching of the fluorescence with a Stern-Volmer slope of 2.2 [l/mol] in benzene. This gives a quenching constant of 5.2 $\cdot 10^{-7}$ [l/mol \cdot sec] if the above value of the fluorescence lifetime in hexane is assumed.

Upon photolysis in dilute solutions (313 nm, methanol) 3 decomposes to give back 1 and 2 (thereof <u>cis</u>-stilbene and phenanthrene are formed, as has been shown by the UV- and HPLC-analysis). Also in the mass spectra (70 eV,

6155

6156

m/z = 297, 7% M⁺) the [2+2]-cycloreversion is prominent (180, 43%, stilbene⁺ and 117, 100%, indolizine⁺). As the crystals of 3 and 4 did not grow favourably for X-ray crystal structure investigations the precise structures of these compounds had to be determined by comparison with the product of hydrogenation 5 (PtO₂, methanol) and with the 5,6-⁹, 5,8-dihydro-⁹, and 5,6,7,8-tetrahydroindolizines⁹. COSY-2D-experiments with compound 3 (Bruker 250) prove the assignment of the signals. The coupling constants ¹⁰ have been optimized via spectra simulations up to the coincidence of appearances by using the extensive empirical material of Ref.¹¹.

The 2:1-adduct **4** is also obtained by photoaddition of **2** to electronically excited **3** [in benzene, $\lambda \max$ (lg ϵ) = 292(4.05), 307(sh, 3.89), onset of the absorption at 330 nm]. However, the yield is not higher in this experiment (as compared to the one with **1** as the starting material) and there arise considerable amounts of **1** which photoequilibrate with **3** in the presence of **2**. The orientation of the phenyl groups in **4** again is derived from ¹H-NMR spectra.¹⁰

The regioselectivity and the stereospecificity in the formation of 3 are surprising. The reasons for these observations are apparent in the well-established electrostatic and steric effects which operate in diradical mechanisms via singlets, both in the production and in the reactions of short-lived diradicals.^{5,7,11} In particular it is seen that electronically excited 1 is trapped at those centers (5 and 6) which bear the highest sum of charge densities in the first excited singlet state (S_1) according to SCF-CI-calculations (1.23+1.08).¹² Thus, the centers 7 and 8 (1.02+1.13)¹² are clearly disfavoured, even though the steric effects appear almost identical. The stereospecificities are most easily rationalized in terms of geometrically least hindered approaches of 2 towards 1* or 3*, resp., as well as in terms of sterically and electrostatically favoured ring closures of the diradicals.¹³

The operation of these effects is very pronounced. Thus, despite of their lower solubilities and longer wavelength absorptions (as compared to 2), also 4,4'-dichlorostilbene (0.07 molar) and 4,4'-dimethoxystilbene (0.08 molar) are chemically productive quenchers for 1*. Here only the substituted



adducts 6 are isolated (6, R = H, Ar = $4-ClC_6H_4$: 77% at 60% conversion; 6, R = H, Ar = $4-CH_3OC_6H_4$: 45% at 50% conversion).

As expected, also the more electron-rich 2-methylindolizine photoadds 2 regioselectively and stereospecifically to give a single adduct 6 (R =

 CH_3 , Ar = Ph: 60%). On the contrary, 2-phenyl- and 1,3-diacetyl-indolizine upon photoexcitation do not form adducts with 2 in detectable quantities.

The experimental results show that indolizines may be used for photocycloadditions, even though the quenching constant of 1* with 2 is far below the diffusion limit. They are the basis for further practical uses, theoretical investigations, and photophysical measurements.

Typical procedure:

A solution of 1.0 g (8.5 mmoles) of 1 and 15 g (83 mmoles) of 2 in 300 ml of benzene is irradiated with a high-pressure mercury lamp (Hanau TQ 718, 500 W) through a bandpass filter (Wertheimer UVW 55, $\lambda = 310 - 410$ nm) under argon at 20 - 25°C for 5 hours. Following the evaporation of the solvent the largest part of excess 2 is separated out by crystallization from methanol and the mother liquor separated by chromatography (200 g Si0₂-40, benzene/<u>n</u>-hexane = 1/4). One obtains 1.20 g (48%) of 3 with m.p. 111°C (from toluene/<u>n</u>-hexane = 1/5), 425 mg (10%) of 4 with m.p. 193°C (from diethyl ether), and 50 mg of recovered 1.

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- 10. RACCOON (P.F. Schatz, program IB 003, project SERAPHIM); 250 MHz, $CDC1_3$, **d** [ppm], \exists [Hz]. **3**: **d** = 7.42-7.11(10 H); 6.50-6.48(3-H); 6.41(8-H, \exists =10.5; 1.8); 6.11-6.08(2-H); 6.07-6.05(1-H); 5.21(7-H, \exists =10.5;2.8); 4.63(5-H, \exists = 8.3;8.2); 4.20(9-H, \exists =10.4;8.3); 3.93(10-H, \exists =10.4;8.2); 3.845(6-H, \exists =8.2; 8.2;2.8;1.8). 4: **d** = 7.39-7.05(20 H); 6.63-6.61(3-H); 5.95-5.92(2-H); 4.89 -4.87(1-H); 4.61(5-H, \exists =9.0;8.3); 3.81(10-H, \exists =11.3;8.3); 3.76(8-H, \exists =7.5; 7.5); 3.675(12-H, \exists =10.5;7.5); 3.67(6-H, \exists =11.3;9.0; <0.5); 3.41(11-H, \exists = 10.5;10.0); 3.29(9-H, \exists =8.3;8.3); 2.68(7-H, \exists =10.0;7.5;<0.5). 5: **d** = 7.42-7.16(10 H); 6.44-6.43(1-H); 6.10-6.08(2-H); 5.85-5.84(3-H); 4.55-4.47(5-H); 3.97-3.87(9-H;10-H); 3.26-3.15(6-H,m, \exists =7.0); 2.79(8-H, \exists =-15.6;4.0;4.0); 2.55(8'-H, \exists =-15.6;12.2;4.0); 1.76(7'-H, \exists =-13.2;7.0;4.0;4.0); 1.64(7-H, \exists =-13.2;12.2;4.0;<0.5).
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- 13. 4-Membered rings ([2+2]-adduct) will close faster than 5-([8+2]-adduct) and 6-membered ones ([4+2]-adduct) for steric reasons; CNDO-(QCPE No. 240, J.D. Bowden, G.S. Owen, and E. Raaen, program IB 1406, project SERAPHIM) and MNDO-calculations (QCPE No. 353, W. Thiel, K.E. Gilbert, and J.J. Gajewski) using STRPI/MMPMI-geometries (QCPE No. 395, R.M. Jarret, M. Saunders, K.E. Gilbert, and J.J. Gajewski, Version 1) reveal considerable charge density differences between the reacting centers of the (ground state) diradical which is formed by single-bond formation of 2 and 1* at its center 5.

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