Notiz / Note

Paterno-Büchi Reaction of 2-Morpholinoacrylonitrile with Benzil

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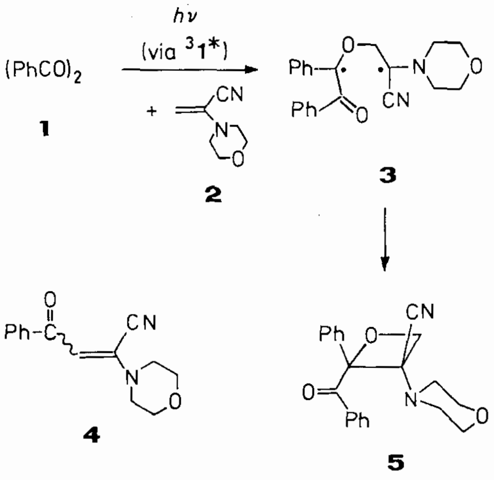
In the lowest excited triplet state, benzil (**1**) adds highly regio- and stereoselectively to the olefin 2-morpholinoacrylonitrile (**2**) to form solely the oxetane **5**.

The special stabilization of radicals attributed to captodative substitution[1] has stimulated the investigation of various cycloadditions of captodatively substituted alkenes, especially of α-aminoacrylonitriles, to electronically excited aldehydes or ketones. 1-Acetonaphthone as well as (but less efficiently) 1-naphthophenone and 1- or 2-naphthaldehyde tend to undergo 1,4-addition[2-8] and (ocassionally) 1,2-addition[2,3,5]. Benzophenone, which efficiently sensitizes the head-to-head dimerization of 2-aminoacrylonitrile[9], forms an oxetane with 2-morpholinoacrylonitrile (**2**) in low yield and also induces the formation of two different dimers of that olefin[10]. For the head-to-head [2 + 2] dimer of **2**, formed by photosensitation by 2-acetonaphthone[3,10], the *trans* configuration has recently been unambiguously established by X-ray crystallography[11]. In this paper we report on the smooth oxetane formation[12] of **2** with electronically excited benzil (**1**).

Argon-purged solutions of benzil (**1**), when flashed with a 7-ns excimer laser pulse at 308 nm[13], show transient absorptions at 480 nm (in benzene) or 460 and 485 nm (in methanol), which are attributed to the lowest excited triplet state of benzil[14], 10 ns (the fivefold of the reported lifetime of the lowest excited singlet[15]) after excitation.

The spectrum in the absence of added **2** and an intensity-normalized spectrum in the presence of added **2** have the same appearance, which means that on the ns time scale neither a diradical nor any other species originating from excited **1** and **2** can be observed. Rate constants for quenching of excited **1** by **2** can be extracted from Stern-Volmer plots relating the decay of triplet-triplet absorption of **1** with the concentration of added **2**; the values are $2.7 \times 10^7\ \mathrm{M^{-1}\,s^{-1}}$ for benzene and $2.4 \times 10^8\ \mathrm{M^{-1}\,s^{-1}}$, respectively, for methanol as solvent. The transient is not quenched by methyl viologen in methanol[16], which supports the conclusion that this transient is not a diradical but the n,π* triplet of benzil.

For product formation studies, benzene solutions of **1** and **2** (0.07 M in either reactant) have been irradiated for one to several hours with a 125-W high-pressure mercury arc through Duran glass ($\lambda \geq 280$ nm). Alternatively, acetonitrile or 2-methyl-2-propanol can be used as solvents without any significant changes. Optimal yields (54%) of a single regio- and stereoisomer **5** out of the a priori possible four oxetanes have been obtained after irradiation for one hour, the yield of **5** drops drastically, however, upon prolonged irradiation. At the same time, small amounts ($\leq 5\%$) of minor byproducts are generated such as benzoin and 3-benzoyl-2-morpholinoacrylonitrile (**4**). The latter compound probably originates from the addition of benzoyl radicals (formed by either symmetric photocleavage of benzil[14] or secondary photolysis of **5**) to **2**.



The 300-MHz ^{1}H-NMR spectrum of **5** shows an AB pattern with $\delta_A = 4.82$ and $\delta_B = 4.66$, the average chemical shift ($\delta = 4.74$) and the observed coupling constant of which ($|J_{AB}| = 6.14$ Hz) are normal for an α-CH$_2$ group in oxetanes[17]. This demonstrates **5** to be a head-to-head adduct[12]. The *cis* orientation of the morpholino and benzoyl groups in **3** is derived from a NOE signal intensity difference determination[18]. For this to be conclusive, the overlapping signals for the aryl protons (from $\delta = 7.32$ to 7.87) have to be assigned. From these, the isolated 2H-signal centered at $\delta = 7.86$ is certainly due to the benzoyl *ortho*-hydrogen atoms[17]. Irradiation into this signal enhances the intensity of the multiplets at $\delta = 7.57$ and 7.37, thus both signals are likely to be due to benzoyl

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protons as well. Irradiation into the signal centered at δ = 2.53 assigned to the equatorial[19] protons flanking the morpholino nitrogen enhances the signal intensity at δ = 7.57, pointing to a spatial proximity of the morpholino and benzoyl groups.

Since singlet-excited **1** has a high (0.92) intersystem crossing efficiency[15,20], reactions starting from the lowest excited triplet of **1** are most likely. Although the ns-flash experiments have not revealed any other intermediates than triplet-excited **1**, it is conceivable that the highly regio- and stereoselective formation of **5** is due to the intermediacy of a stabilized triplet diradical **3** which is sufficiently long-lived to reach a *minimally hindered cisoid conformation* prior to intersystem crossing and ring closure.

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Experimental

Apparatus and methodology for the laser flash experiments were entirely the same as described before[13]. Solutions probed for transients were prepared by using spectrograde solvents and adjusted to an optical density of 1.0 at 308 nm. – Melting points (uncorrected): Kofler micro-hot stage apparatus. – Elemental analyses: Carlo Erba 1106 CHN-analyzer. – IR: Perkin Elmer spectrometer 283. – 300-MHz ^{1}H and 75-MHz ^{13}C NMR: Bruker WM 300, TMS as internal standard. – MS (70 eV, EI mode, temp. of inlet system given): MAT 311 A.

Irradiation of Benzil (**1**) *in Solution in the Presence of* **2**: A solution of 1.049 g (4.99 mmol) of **1** and 0.691 g (5.00 mmol) of 2-morpholinoacrylonitrile[21] (**2**, m.p. 61 °C, from pentane) in 70 ml of benzene was purged with a stream of purified argon for 30 min prior to and during the 1-h irradiation with a 125-W high-pressure mercury burner through a water-jacketed Duran immersion well (λ ⩾ 280 nm). The residue obtained upon concentration of the solution was subjected to preparative layer chromatography using glass plates 48 cm wide and 20 cm high covered with a 1 mm thick layer of air-dry slurry-applied silica gel Merck PF_{254}. Two successive developments using petroleum ether (b.p. range 60–90 °C)/ethyl acetate (5:1) were needed. From a zone with R_f = 0.53 0.328 g of **1** was recovered, thus 0.721 g (3.43 mmol) had been converted. Starting material **2** could not be recovered from the chromatograms.

rel-(2S,3R)-2-Benzoyl-3-morpholino-2-phenyloxetane-3-carbonitrile (**5**): The main intense zone at R_f = 0.20 gave 585 mg (49%, based on converted **1**), m.p. 136 °C (from ethanol). – IR (KBr): ṽ = 2220 cm^{-1} (CN), 1680 (C=O). – ^{1}H NMR (CDCl$_3$): δ = 2.39 [mc, 2H, N(CH$_{ax}$)$_2$], 2.53 [mc, 2H, N(CH$_{eq}$)$_2$], 3.50 [mc, 2H, O(CH$_{ax}$)$_2$], 3.46 [mc, 2H, O(CH$_{eq}$)$_2$], AB (δ_A = 4.82, δ_B = 4.66, $|J_{AB}|$ = 6.14 Hz), 7.32–7.54 (several m, 6H, aromatic H), 7.57 (mc, 2H, benzoyl-H), 7.86 (mc, 2H, benzoyl-H). – NOE: see main part. – ^{13}C NMR (CDCl$_3$): δ = 47.7 (NCH$_2$); 65.9 (OCH$_2$); 67.3 (C-3); 72.3 (C-4); 96.6 (C-2); 116.2 (CN); 126.4, 128.2, 128.4, 129.3, 130.1, 133.0, 133.1, 133.7 (all aromatic C); 195.6 (C=O). – MS (70 eV, 124 °C): *m/z* (%) = 321 (0.2) [M$^+$ – HCN], 210 (3), 191 (0.4), 178 (2), 165 (0.4), 152 (0.5), 138 (14) [represents **2**], 105 (100) [PhCO], 77 (53), 69 (15), 51 (16).

$C_{21}H_{20}N_2O_3$ (348.4)
Calcd. C 72.39 H 5.79 N 8.04
Found C 72.44, 72.34 H 5.74, 5.71 N 8.08, 8.02

In addition, numerous weak zones were observed in similar experiments but after longer irradiation times (5 h). The material migrating at R_f = 0.39 was identified as benzoin, m.p. 133 °C, by comparison with an authentic sample.

E-(or Z)-3-Benzoyl-2-morpholinoacrylonitrile (**4**): From a zone at R_f ≈ 0.05 a mixture was isolated, which upon repeated preparative layer chromatography using the same solvent as before but three sucessive developments, gave 45 mg (5% based on converted **1**), m.p. 144–146 °C (from methanol). – IR (KBr): ṽ = 2235 cm^{-1} (weak, CN), 1629 and 1586 (medium), 1559 (intense). – ^{1}H NMR (CDCl$_3$): δ = 3.50 [mc, 4H, N(CH$_2$)$_2$], 3.82 [mc, 4H, O(CH$_2$)$_2$], 6.41 (s, 1H), three mc at 7.45 (2H), 7.53 (1H) and 7.90 (2H) for benzoyl H. – MS (70 eV, 139 °C): *m/z* (%) = 242 (55) [M$^+$], 225 (14), 185 (18), 137 (64), 105 (91), 91 (92), 86 (58), 77 (100).

$C_{14}H_{14}N_2O_2$ (242.3) Calcd. C 69.40 H 5.83 N 11.56
Found C 69.15 H 5.83 N 11.50

CAS Registry Numbers

1: 134-81-6 / **2**: 5807-03-4 / **4**: 138901-53-8 / **5**: 138901-54-9

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