

A novel synthesis of α - and β -morpholino enones by electron transfer sensitized photooxidation of 2-morpholinocyclopropanols

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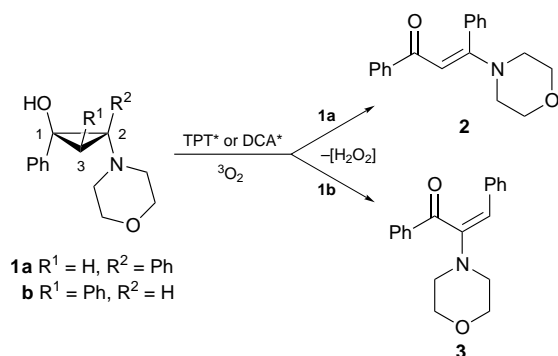
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An electron transfer mechanism is proposed to account for the photooxidation of 2-morpholinocyclopropanols **1** to the amino enone derivatives **2** and **3** in the presence of 9,10-dicyanoanthracene or triphenylpyrylium tetrafluoroborate and triplet oxygen.

Photoinduced electron transfer (ET) *cis*–*trans* isomerization and oxidative ring opening of cyclopropanes have been the subject of numerous investigations.^{1,2} Dioxolane derivatives and, in some cases, hydroperoxides and chalcones are formed by electron transfer photooxidation of aryl substituted cyclopropanes. Several mechanisms involving the superoxide anion radical, a chain reaction with triplet oxygen, or reaction of triplet oxygen with a 1,3-biradical formed by back electron transfer to the cyclopropane cation radical have been discussed.^{3–5} Recently we reported that the irradiation of β -(*N,N*-dialkylamino)propiophenones gives 2-aminocyclopropanols that undergo oxidative ring opening to β -amino enones.^{6a} Due to the electron donor properties of amino groups, 2-morpholino-1,2-diphenylcyclopropanol **1a** and 2-morpholino-1,3-diphenylcyclopropanol **1b** appeared to be excellent candidates for electron transfer studies. They were synthesized by photocyclization⁶ and used as model compounds to investigate the possibility of oxidative ring opening in presence of the photoexcited electron acceptors 9,10-dicyanoanthracene (DCA) or triphenylpyrylium tetrafluoroborate (TPT).

Irradiation ($\lambda_{\text{irr}} > 395$ nm) of aerated solutions of **1a** (2×10^{-4} M) in the presence of catalytic amounts (0.1 equiv.) of DCA in MeCN or TPT in CH_2Cl_2 gave the β -morpholino- β -phenylvinyl phenyl ketone **2** in 36 ($t_{\text{irr}} = 0.5$ min) and 41% ($t_{\text{irr}} = 5.2$ min) yield, respectively. Photolysis of a mixture of **1b** and DCA or TPT under the same conditions gave the α -morpholino chalcone **3** in 28 and 26% yield, respectively (Scheme 1). Continuous irradiation leads to the decomposition of **2** and **3**. The reported yields are the maximum values observed during the photolysis.[†] The formation of **2** and **3** was confirmed by HPLC analysis with authentic reference compounds.[‡]

The oxidation potentials $E(\text{D}/\text{D}^+)$ of **1a** and **1b** together with the ΔG values for photoinduced ET are given in Table 1. The free energy changes (ΔG) for the one-electron transfer process



Scheme 1

Table 1 Oxidation potentials and calculated ΔG values for ET from **1** to ^{1/3}TPT* and ¹DCA*

Compound	$E(\text{D}/\text{D}^+)/\text{V}^{a,b}$	$\Delta G/\text{kcal mol}^{-1}$		
		¹ TPT* ^c	³ TPT* ^c	¹ DCA* ^d
1a	1.44	–25.11	–13.11	–12.27
1b	1.37	–26.72	–14.72	–13.88

^a Pt electrode/SCE, 0.1 M Et₄NClO₄ in MeCN. ^b $E(\text{D}/\text{D}^+) = 1.53$ V. ^c $E(\text{A}^-/\text{A}) = -0.29$ V, $E(^1\text{A}^*) = 65$ kcal mol⁻¹, $E(^3\text{A}^*) = 53$ kcal mol⁻¹ (ref. 13). ^d $E(\text{A}^-/\text{A}) = -0.89$ V, $E(^1\text{A}^*) = 66$ kcal mol⁻¹ (ref. 13).

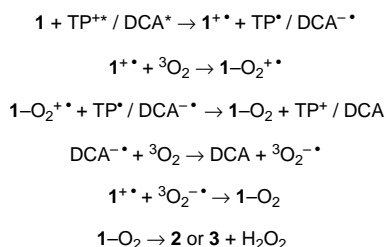
from the cyclopropane derivatives to photoexcited ¹TPT* or ¹DCA* were estimated by application of the Rehm–Weller equation [eqn. (1)].⁸ The Coulombic term ($e^2/\epsilon a$) was neglected

$$\Delta G = E(\text{D}/\text{D}^+) - E(\text{A}^-/\text{A}) - E(\text{A}^*) - e^2/\epsilon a \quad (1)$$

due to the lack of charge separation in case of TPT and the small estimated value of 0.06 eV⁹ in MeCN for DCA as photosensitizer. Involvement of ³TPT* in photoinduced ET processes, especially at low donor concentrations (*ca.* 10⁻⁴ M), has been reported and cannot be ruled out in the case of **1**.^{10,11}

Fluorescence quenching experiments of ¹TPT* by **1a** and **1b** (0.4×10^{-3} – 6×10^{-3} M) were performed in aerated CH_2Cl_2 solutions. § The fluorescence was quenched at almost diffusion controlled rates (**1a**: $k_q = 2.1 \times 10^{10}$ M⁻¹ s⁻¹; **1b**: $k_q = 2.0 \times 10^{10}$ M⁻¹ s⁻¹), calculated from the slopes of the Stern–Volmer plots (**1a**: $k_q\tau = 61$ M⁻¹; **1b**: $k_q\tau = 58$ M⁻¹) and a singlet lifetime of TPT of 2.9 ns.¹² As expected, the formation of **2** in the DCA-sensitized photolysis of **1a** was completely quenched by the addition of an equimolar amount of triethylamine, whose oxidation potential [$E(\text{D}/\text{D}^+) = 0.76$ V, SCE, MeCN]¹³ is lower than that of **1a**. The DCA anion radical was detected by EPR measurements in the DCA-sensitized photoreaction of **1a** and **1b** in oxygen free MeCN. ¶ No signals could be detected for the cation radical of **1**. The formation of the DCA anion radical was also observed by DCA-sensitized photolysis of the β -amino enone **2**.

The values of the oxidation potentials of **1** (Table 1) are lower than those of the *trans* and *cis* isomers of 1,2-diphenylcyclopropane, [$E(\text{D}/\text{D}^+) = 1.51$ and 1.75 V]. || Even though the measured oxidation potentials of **1a,b** are unexpectedly high compared to those for tertiary amines [*N*-methylmorpholine: $E(\text{D}/\text{D}^+) = 1.1$ V, Ag/AgCl, MeCN]⁹ for reasons that are not clear, they reflect the good electron donor ability of **1**. The negative ΔG values for single electron transfer from **1a** and **1b** to ^{1/3}TPT* and ¹DCA*, the fluorescence quenching of ¹TPT* at a diffusion controlled rate and the detection of DCA^{-•} by EPR spectroscopy strongly suggest that the formation of the radical cation of **1** by photoinduced ET is the primary process in the photooxidation of **1**. The cation radical of **1** could undergo reaction with triplet oxygen to give **1**–O₂^{•+}. Back ET gives **1**–O₂ or the ground state reactants. Hydroperoxides formed from **1**–O₂ by internal hydrogen transfer are assumed to be intermediates which form **2** or **3** by elimination of hydrogen peroxide. In contrast to TPT, the DCA-sensitized photooxida-

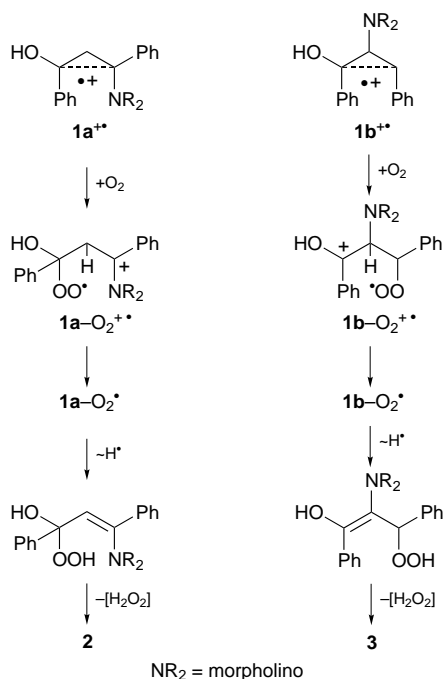


Scheme 2

tion could lead to the formation of a superoxide anion radical by reaction of triplet oxygen with DCA^{-*} and would provide a second pathway to generate $1-\text{O}_2^{**}$.¹⁰ A simplified mechanism for photoinduced ET oxidation of **1** is summarized in Scheme 2.

Possible pathways for the formation of **2** and **3** by reaction of the cation radicals of **1a** and **1b** with oxygen are given in Scheme 3. Obviously, the regioselectivity of ring opening is determined by the position of the phenyl groups. C(1)–C(3) ring cleavage of **1b** excludes resonance stabilization of the radical cation by the electron releasing morpholino group. However, the almost bisected conformation of the C(3)-phenyl group and the cyclopropane ring of **1b** should allow a strong interaction between their orbitals, in contrast to the morpholino group, which is the better electron donor but is arranged in a perpendicular fashion.^{6a**}

High quantum yields for consumption of **1a** in the presence of TPT^* (8×10^{-5} M) in CH_2Cl_2 were found.^{††} The values show considerable dependence on the concentration of the donor **1a** and amount to 11 ($[\mathbf{1a}] = 4.1 \times 10^{-4}$ M), 20 ($[\mathbf{1a}] = 6.0 \times 10^{-4}$ M) and 27 ($[\mathbf{1a}] = 1.6 \times 10^{-3}$ M). The high values indicate that a chain reaction occurs with generation of $\mathbf{1a}^{**}$ by hole transfer from $\mathbf{1a}-\text{O}_2^{**}$ to **1a**. Quantum yields > 1 were reported for ET sensitized oxygenations and ring opening of several cyclopropanol derivatives and small strained ring systems.^{3,16} An alternative pathway for the photooxidation could involve singlet oxygen generated by energy transfer from photoexcited TPT and DCA. However, the cyclopropanol **1a** was completely recovered after photolysis ($\lambda_{\text{irr}} > 395$ nm) in MeCN in the



Scheme 3

presence of Methylene Blue as photosensitizer for singlet oxygen.

In summary, the novel synthesis of α - and β -morpholinones by DCA- or TPT-sensitized photooxidation of 2-morpholinocyclopropanols described herein increases the synthetic utility of the photochemical reactivity of cyclopropane derivatives.

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Footnotes and References

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† Consumption of **1** > 85%; **2** and **3** are formed in the *E* configuration, assigned from $\lambda_{\text{max}} = 350$ (**2**) and 282 nm (**3**); **2** and **3** were isolated by column chromatography from irradiations in CH_2Cl_2 of **1a** or **1b** (4×10^{-3} M) in the presence of TPT (4×10^{-4} M) and identified by their NMR spectra.

‡ Reference compounds **2** and **3** were prepared according to literature procedures (ref. 7).

§ $[\text{TPT}] = 3.6 \times 10^{-5}$ M in CH_2Cl_2 , excitation at 410 nm, fluorescence intensity measured at 460 nm.

¶ Hyperfine coupling constants for DCA^{-*} at 245 K generated by > 395 nm irradiation of **1** (5×10^{-3} M) and DCA (2×10^{-3} M) in MeCN recorded on a X Band Spectrometer Bruker ER 220D: **1a**/DCA, 0.238, 0.132, 0.114 mT; **1b**/DCA, 0.242, 0.125, 0.111 mT; cf. ref. (14).

|| Oxidation potentials (Ag/AgNO_3 , MeCN) from ref. (1), 0.34 V added for SCE as reference electrode.

** It should be noted that formation of **2** and **3** indicates the cleavage of the respective longest cyclopropane bond of **1a**, C(1)–C(2) = 1.54, C(1)–C(3) = 1.51, C(2)–C(3) = 1.50 Å and of **1b**, C(1)–C(3) = 1.52, C(1)–C(2) = 1.50, C(2)–C(3) = 1.49 Å, see X-ray structures of **1a** and **1b** in ref. 6(a).

†† Consumption of **1a** < 10%; $\lambda_{\text{irr}} = 405$ nm by combination of a band pass filter WG 305 and a metall interference filter UV-SKIF 405 nm (Carl Zeiss Jena); actinometer potassium ferri oxalate (ref. 15).

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