The chemistry of small-ring compounds. Part 51. Electron-transfer-initiated oxidation of some cyclopropylidene compounds[≠]

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Abstract. Cyclopropylidene compounds of type 1 are found to quench the fluorescence of 9,10dicyanoanthracene (DCA). Nevertheless photo-oxygenation, in the presence of DCA, leads under no circumstances to dioxetanes but (in ethanol) to a methoxy hydroperoxide 5, as tentatively shown in Scheme 2. This hydroperoxide undergoes acid rearrangement either to a lactone or to a cyclobutanone, depending on the reaction conditions (Scheme 3).

Introduction

In a recent publication¹, we reported that an oxaketone of type 2 is formed upon ozonisation of cyclopropylidene compounds with the general structure 1. Yields depend upon the nature of the substituents R and upon the reaction conditions^{1,2}.

$$\bigvee_{R}^{R} \xrightarrow{O_{3}} \bigcup_{0}^{N} (25-65\%)$$

An oxaketone 2 can, in principle, be formed by rearrangement of an appropriate dioxetane (3), a possible intermediate during ozonisation; the strength of the O-O bond in 3 is known to be relatively low³ and might well trigger rearrangement to 2:



We therefore considered ozone-independent approaches towards dioxetanes of type 3. These are in principle obtainable from β -halo hydroperoxides^{4,5,6} but this approach is impractical for cyclopropyl derivatives since the required precursors are only accessible with difficulty and the stability of the cyclopropane moiety is questionable under these reaction conditions^{7,8,9}.

The reaction of singlet oxygen with cyclopropylidene compounds 1 not having abstractable allylic hydrogen to prevent the ene reaction¹⁰ is also unsuitable, since previous work has shown¹¹ that, instead of dioxetanes, substituted cyclobutanones and lactones are formed.

We therefore attempted photo-oxygenation initiated by electron transfer to 9,10-dicyanoanthracene** (DCA), a procedure developed by, among others, *Foote* et al.¹² and *Schaap* et al.¹³, which is also applicable to other cyanosubstituted anthracenes¹⁴. The method appears to work only in the case of electron-rich substrates (possessing a low oxidation potential). This is a logical consequence of the mechanism briefly outlined below, involving formation of an exciplex between DCA and olefin.



Scheme 1. Cyclopropylidene–DCA exciplex and its reactivity towards oxygen.

As shown in Scheme 1, exciplex formation and its dissociation into a radical anion and (especially) radical cation are vital steps in the over-all oxidation process^{12,13,15,16}.

Results

To ascertain the feasibility of the method, three cyclopropylidene compounds (**1a-c**) were first of all tested for their ability to quench the fluorescence of DCA. The results are

^{*} Taken from the Ph.D. Thesis of A. Hofland, University of Amsterdam, 1985.

^{**} Chem. Abstr. name: 9,10-anthracenedicarbonitrile.

Substrate	Solvent	$\begin{matrix} k_{\mathbf{q}} \cdot \mathbf{\tau} \\ (\mathbf{M}^{-1}) \end{matrix}$	$\frac{\tau \cdot 10^9}{(s)}$	$l_{q} \cdot 10^{-9}$ (M ⁻¹ · s ⁻¹)	IP _{vert} (eV)
) Ia	CH ₃ OH c-C ₆ H ₁₂ CH ₃ CN	95.7 0.7 99.0	a a,b 15.3°	 6.47	8.42 8.42 8.42
	CH3CN	120.0	15.3°	7.84	8.18
lc	CH3CN	7.4	15.3°	0.48	8.93

Table I DCA-quenching rates and ionisation potentials of some cyclopropylidene compounds.

^a No data concerning the lifetime of excited DCA for this solvent are available. ^b Although reported by *Foote* et al.¹⁸, no exciplex fluorescence can be detected in cyclohexane in our case. ^c Refs. 19 and 20.

summarized in Table I. All quenchings followed the Stern-Volmer equation¹⁷ from which quenching constants were determined whenever possible.

$$I_0/I_q = 1 + k_q \cdot \tau \cdot [Q]$$

In this table, the vertical ionization potentials, as determined by photo-electron spectroscopy, are also presented, since these play an important rôle in the exciplex formation. It can be seen that the lower the IP, the higher the quenching efficiency; this is already indicative of electron-transfer



Fig. 1. Electron-transfer quenching rate versus ΔG^* using the formula according to Rehm and Weller (drawn line). The experimental k_q data for quenching of DCA by three olefins have been fitted to this line (+) in order to estimate ΔG^* values for these processes.

quenching. The free-energy change ΔG^* in kcal/mol for this reaction is given by:

 $\Delta G^* = 23.06 \cdot (E_{D/D^+} - E_{A/A^-} - e_{o/a\varepsilon}^2 - \Delta E_{0,0}),$

- where: E_{D/D^+} is the oxidation potential of the donor (in Volts);
 - $E_{A/A^{-}}$ is the reduction potential of the acceptor DCA (-0.98 Volts rel. to SCE in CH₃CN);
 - $\Delta E_{o,o}$ is the energy of the singlet excited state of the acceptor (2.89 eV for DCA);
 - $e_{o/a\epsilon}^2$ is the *Coulomb* stabilization of the radical ion pair which is quite small (about 0.06 eV) in solvents with a high dielectric constant such as CH₃CN($\epsilon = 37.5$).

With the help of the relation between k_q and ΔG^* , described by *Rehm* and *Weller* (see Fig. 1), we can thus estimate oxidation potentials for **1a-c**. These are in good agreement with the vertical ionization potentials, namely 1.80 V, 1.75 V and 2.01 V (versus SCE in CH₃CN) for **1a**, **1b** and **1c**, respectively.

It should be noted that, according to the *Rehm* and *Weller* plot of $k_q vs \Delta G^*$, the reaction between excited DCA and the "butterfly" substrate 1,1'-bicyclopropylidene 1c must be slightly endothermic.

The DCA quenching by **1a-1c** renders our synthetic scheme for dioxetanes **3** at least feasible as far as the primary electron transfer is concerned. The next step (Scheme 1) involves dissociation of the exciplex into polar species which should strongly depend upon the polarity of the solvent. For many reactions, acetonitrile has proved to be the solvent of choice in DCA-sensitized photo-oxidations¹⁷. However, despite the observation of fluorescence quenching for substrates **1a-c**, no photo-oxidation was found in this solvent even after 20 h of irradiation.

Bearing in mind that the solvent separation of a tight ion pair such as 4 can be enhanced by the use of a protic solvent, we employed methanol. In this case, the uptake of one equivalent of oxygen was observed (gas burette) and the substrate 1 was completely consumed. NMR and IR suggested the structure of the oxidation product to be that of the methoxy hydroperoxide 5:

It should be noted that, in the reaction with 1a, the addition of a small amount of DABCO (1,4-diazabicyclo[3.3.0]octane) is essential to prevent formation of singlet oxygen which attacks substrates containing active allylic hydrogen^{10,11}. DABCO was omitted in reactions with **1b** and **1c**. Methoxy hydroperoxides similar to **5** have also been found by *Mattes* et al.¹⁴ in the 2,6,9,10-tetracyanoanthracene (TCA) sensitized photo-oxidation of 1,1-dimethylindene in methanol.

An important observation is that no products are formed when the reaction is carried out in the absence of oxygen (under Argon). Since methanol is also essential (vide supra), we consider the transition state to involve the tight ion pair 4 (Scheme 1), in close association with oxygen and methanol. It was also considered that the process of methanol addition could be reversible. Reversible oxygen addition, however, seems less likely due to the C-O bond strength. Details of a more precise transition state are still lacking; for a tentative picture we refer to the work of one of the authors $(AH)^2$. This is based on the assumption that, in the first instance, the role of the oxygen is merely to change the spin state of the excited radical ion pair [DCA^{-•} 4^{+•}]* from singlet to triplet. It can be argued that the triplet state needs a longer time to return to the ground state and is therefore more available for solvent separation. Combination of methanol with the cation radical within the triplet leads to methoxy hydroperoxide 5 as depicted in Scheme 2. This would explain the observed low quantum yield as well as the necessary presence of both oxygen and methanol.

Acid-catalyzed decomposition of methoxy hydroperoxide 5

Attempted purification of 5 by means of column chromatography under acidic conditions leads to a cyclobutanone derivative 6 and a substituted lactone 7:



The ratio of 6 to 7 is dependent upon the conditions under which the decomposition takes place. When 5 is treated with dry *p*-toluenesulphonic acid in 10% H₂O₂ in diethyl ether, the yield of lactone 7 is quantitative, whereas 6 turns out to be the only product when the medium is a 1/1 mixture of water and acetonitrile. Considering the ease with which the *Baeyer-Villiger* oxidation of cyclobutanone derivatives takes place²¹, the following mechanism is proposed for the acid-catalyzed decomposition of 5.

The key step in this mechanism is the ring enlargement of the cyclopropyl carbocation 8 to cyclobutyl cation 9, stabilised by the methoxy group, a process well-known in small-ring chemistry⁸.



Scheme 2. Tentative reaction path for the formation of 5a.



Scheme 3. Acid-catalysed decomposition of methoxy hydroperoxides $5a [R, R = (CH_2)_5]$ and 5b (R, R = adamantylidene).

Compound	R,Rª	IR	¹ H NMR
5a b OCH ₃ R	(CH ₂)5	3050 (w) 2960 (s) 2850 (s) 1450 (m) 1420 (m) 1250 (s)	0.75 (s, 4H), 1.25–1.85 (m, 10H), 3.45 (s, 3H), 7.80 (br. s, 1H).
но 5b ^ь	Ad ^a	3065 (w) 2980 (s) 2950 (s) 2850 (s) 1450 (m) 1260 (s)	0.95 (s, 4H), 1.25–2.30 (m, 14H), 3.40 (s, 3H), 8.00 (br. s, 1H).
6a P R	(CH ₂)5	2940 (s) 2860 (s) 1760 (s)	1.80 (t, J 8.0, 2H), 2.95 (t, J 8.0, 2H), 1.2–1.8 (m, 10H).
60 ^R	Adª	2920 (s) 2860 (m) 1755 (s)	1.80 (t, J 8.0, 2H), 2.78 (t, J 8.0, 2H), 1.2–2.1 (m, 14H).
7a O R R	(CH ₂)5	2940 (s) 2860 (s) 1725 (s) 950 (s)	2.00 (t, J 7.5, 2H), 2.58 (t, J 7.5, 2H), 1.25–1.90 (m, 10H).
7b	Adª	2920 (s) 2860 (m) 1720 (s) 910 (s)	2.15 (t, J 7.5, 2H), 2.58 (t, J 7.5, 2H), 1.25–2.30 (m, 14H).

Table II Spectroscopic properties of methoxy hydroperoxides 5a and 5b, cyclobutanone derivatives 6a and 6b and lactones 7a and 7b.

Experimental

Instruments (general)

100-MHz ¹H NMR spectra were recorded on a Varian XL-100/12 spectrometer; double resonance was applied whenever coupling of signals was suspected. The appropriate coupling constants were measured directly from the spectra. The samples were dissolved in $CDCl_3$, except where indicated otherwise. The chemical shifts are given in ppm (δ), relative to TMS as internal standard.

The infrared spectra were recorded on a Perkin-Elmer 289 apparatus. Samples were dissolved in either CHCl₃ or CDCl₃. Fluorescence measurements were taken on a Spec Fluorolog instrument.

Photo-electron spectra were recorded on a Perkin-Elmer PS 18 spectrometer equipped with a Helectros Development He(I)/He(II) hollow cathode source. The spectra were obtained at room temperature using argon and xenon as internal calibrants.

Synthesis of the cyclopropylidene compounds 1a-c

The olefins 1a and 1b were prepared by a *Wittig* reaction according to *Utimoto* et al.²². Illustrative is the synthesis of cyclopropylidene-cyclohexane 1a:

A sodium hydride dispersion in mineral oil (11.5 g, 0.24 mole of NaH) was placed in a dry three-necked flash and washed with 2×250 ml of pentane to remove the mineral oil. Dry THF (200 ml, distilled from sodium/benzophenone) was distilled directly into the flask under nitrogen. (3-Bromopropyl)phosphonium bromide (46.4 g, 0.10 mole), dried over molecular sieves in vacuo for 16 h at 75°C, was then added. The mixture was brought to reflux temperature and 0.5 ml of dry ethanol was added to initiate the reaction. After 4 h, the solution had become intensely vellow and evolution of hydrogen gas could no longer be detected. Cyclohexanone (8.8 g, 9.3 ml, 0.09 mole) was added carefully. After 16 h under reflux, some extra sodium hydride was added to remove the last traces of ylid. The THF was evaporated under reduced pressure and the residue was taken up in hexane. After filtration, the hexane was evaporated, again under reduced pressure. The crude reaction mixture was first purified by column chromatography (basic aluminium oxide/hexane), after which 1a was further purified by distillation (85°C, 80 mm Hg) and by preparative GLC prior to use.

1a: ¹H NMR: 0.95–1.05 (4H, q, J_{allyl} 1.5), 1.35–1.70 (6H, m), 2.0–2.3 (4H, m). IR (v in cm⁻¹, liq. cap.): 3060 (m), 2980 (s), 1930 (s), 2860 (m), 2840 (m), 1785 (w).

Cyclopropylideneadamantane 1b was finally purified by means of sublimation (60° C, 10^{-2} mm Hg). Its spectroscopic properties are as follows:

1b: ¹H NMR: 0.95 (s, 4H), 1.7-2.0 (m, 12H), 2.9 (br. s, 2H). IR (ν in cm⁻¹): 3050 (m), 2910 (s), 2580 (s), 1780 (w), 1450 (w). 1,1'-Bicyclopropylidene **1c** was synthesized using an entirely different route which is described in refs. 2 and 23. Its spectral properties are:

1c: ¹H NMR: 1.16 (s). IR (v in cm^{-1}): 3080 (w), 1405 (m). In Raman, a C=C absorption at 1830 cm^{-1} is observed.

Photo-oxidation of 1a and 1b and attempted photo-oxidation of 1c in methanol

The reaction vessel (a screwhead 10 ml tube), filled with 3 ml of dry methanol, 1.0 mmole of the olefin, 15 mg of 9,10-dicyanoan-thracene (DCA) and, in the case of 1a, 50 mg of 1,4-diazabicylo-octane, was suspended in a silver-coated Dewar vessel, filled with a filter solution of 20 g/1 NaNO₂ (low cut-off, lowest passing Hg lines 408 nm and 436 nm; DCA has four strong absorptions of $\varepsilon \sim 10^4$ in the region 350-425 nm).

A water-cooled Hanau TQ 150, 50 W high-pressure mercury lamp was placed in the Dewar at about 5 cm distance from the reaction vessel. The reaction vessel was attached to a vibro-mixer to ensure efficient dispersion of the oxygen, the uptake of which was monitored by a gas burette. The uptake was shown to be first order in the olefin ($k \sim 1.4 \times 10^{-4} \text{ s}^{-1}$ for **1a** and $k \sim 1.6 \times 10^{-4} \text{ s}^{-1}$ for **1b**). Control experiments showed a dependence upon the amount of DCA added. After 16 h, the crude reaction mixture was purified by means of reversed-phase liquid chromatography (silylated silica gel/methanol), p = 0.5 atm). The spectral data of the methoxy hydroperoxides **5a,b** thus obtained are given in Table II.

Upon treatment of an NMR sample of these methoxy hydroperoxides with a minute amount (10 mg) of *p*-toluenesulphonic acid, cyclobutanones **6a** and **6b** and lactones **7a** and **7b** were the only products (Table II). The spectral data of the lactones were confirmed by *Baeyer-Villiger* oxidation of the corresponding ketones with *m*-chloroperbenzoic acid in methylene chloride/buffer solution (pH 8.7).

Acknowledgements

Thanks are due to Prof. J. W. Verhoeven for fruitful theoretical discussions and to Prof. A. de Meijere and Dr. D. Kaufmann for their warm hospitality to one of us (AH), thus catalysing the synthesis of 1,1'-bicyclopropylidenes. We also acknowledge the help of Mr. R. Andrea in recording photoelectron spectra and Mr. H. J. van Ramesdonk for fluorescence measurements.

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