148. The Reaction of Singlet Oxygen with Adamantylideneadamantane Mediated by Rose Bengal

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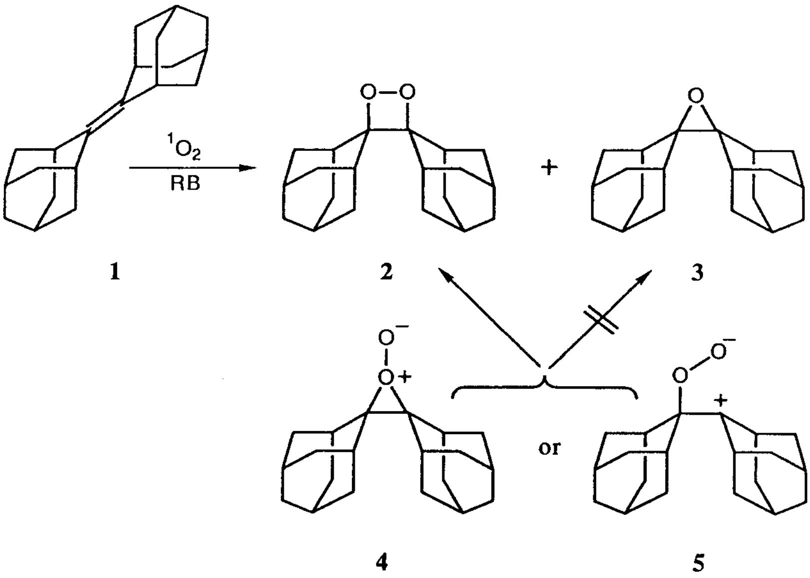
The photo-oxygenation of adamantylideneadamantane (**1**) on siliceous supports using admixed granules of ion-exchange resin fixed to methylene blue (MB) and rose bengal (RB) gave exclusively the corresponding dioxetane derivative **2** for the former sensitizer, while the latter gave **2** and traces of the epoxide **3**. RB and the charge-transfer complex produced from *N*-ethylcarbazole and 2,4,5,6-tetranitrofluoren-9-one both reacted with chemically generated singlet oxygen to give superoxide radical anion. Trapping of the latter with 5,5-dimethyl-1-pyrroline 1-oxide gave an adduct exhibiting a characteristic ESR spectrum. The treatment of **1** in MeOH with 30% aqueous H_2O_2 for 22 h at 60° gave **3** in 100% yield. Repetition of this experiment in the presence of 2,6-di(*tert*-butyl)-*p*-cresol caused no significant change. These results indicate that singlet oxygen reacts with **1**, in the presence of RB, by two different processes. The first leads to dioxetane formation. The second process involves conversion of singlet oxygen by RB to superoxide radical anion which subsequently gives H_2O_2 so producing epoxide **3** from **1**.

Introduction. – Adamantylideneadamantane (**1**) when exposed to singlet oxygen in solution gives almost exclusively dioxetane derivative **2** accompanied by small varying



Scheme

amounts of epoxide **3** [1] *(Scheme)*. This result has provoked controversy [2] concerning the origin of the epoxide which is thought to arise from the perepoxide **4** or the zwitterionic peroxide **5**, the presumed precursor to the dioxetane. In certain instances when electrophilic agents are present, such as aryl sulfoxides, **4** or **5** can be intercepted and reduced to epoxide **3** [3]. However, we have deduced that dioxetane **2** is the *bona fide* product of the reaction of **1** with singlet oxygen, whereas epoxide **3** is the consequence of an incidental, parasitic reaction involving radicals. A variety of agents and conditions can stimulate this latter reaction, even making it the dominant course. Of particular interest is the arcane role of xanthene dyes exemplified by erythrosin and rose bengal (RB) [4] [5]. Used as addends they have a remarkable effect. The RB-sensitized photo-oxygenation of **1** in acetone and the thermal decomposition of 1,4-dihydro-1,4-dimethyl-naphthalene 1,4-endoperoxide (DMNP) in the presence of **1** and RB acetone are essentially the same, producing the expected dioxetane **2**, but also substantial amounts of epoxide **3**. Greater quantities of RB produce correspondingly greater amounts of epoxide, making it the major product. We have suggested that the dimeric form of RB in solution behaves as a charge-transfer complex and interacts with singlet oxygen to produce superoxide radical ion which decays to H_2O_2 thereby causing epoxidation [4]. We now investigate the validity of these suggestions by undertaking appropriate chemical and spectroscopic tests. The photo-oxygenation of **1** in the solid phase should permit the influence of solvent and sensitizer to be elucidated. Evidence for superoxide radical anion will be sought by spin trapping with 5,5-dimethyl-1-pyrroline 1-oxide (DMPO) and examination of the adduct by ESR spectroscopy. Lastly, the action of H_2O_2 on **1** will be studied.

Results. – The photo-oxygenation of adamantylideneadamantane (**1**), coated on particles of various siliceous supports admixed with granules of sensitizer-bound ion-exchange resin, gave products remarkably similar in composition to those obtained in solution *(Table 1)* [1e]. When methylene blue (MB) was used, only dioxetane **2** was formed *(Table 1, Entries 1–6)*. The yields depended on the intensity and duration of illumination. The weaker Na lamp (*C*; luminosity of 4800 lumens) needed to shine for periods three times longer than the halogen W filament lamp (*A*; 12500 lumens) in order to produce the same effect (*Entries 2* and *5*).

Dioxetane was also the main product when RB was used as sensitizer. Nonetheless, small amounts of epoxide were formed as well *(Entries 7–11)*, which became appreciable, when silica supports were used *(Entry 9)*.

Photo-oxygenation of a mixture of adamantane with **1** left the former entirely unchanged (*Entries 6* and *12*). No adamantan-1-ol, the product expected from the reaction of O_3 with adamantane [6], was formed. Moreover, highly sensitive tests for O_3 (detection of lower limit 0.0001 ppm) carried out on the effluent gases were all negative [7].

Next, the crucial question of whether RB can convert singlet oxygen to superoxide radical antion ($O_2^{\overline{\cdot}}$) was addressed. It is known that $O_2^{\overline{\cdot}}$ can be captured by 5,5-dimethyl-1-pyrroline 1-oxide (DMPO) to yield a spin adduct characterized by the hyperfine couplings $A(^{14}N) = 14.2$ G and $A(^1H) = 11.6$ G [8]. The addition of 1,4-dihydro-1,4-dimethylnaphthalene 1,4-peroxide (DMNP) to a solution of RB and DMPO in the dark produced an ESR spectrum *(Fig.)* entirely consistent with that of the aforementioned superoxide radical-anion adduct. The same experiment carried out in the light furnished an identical spectrum exhibiting the same hyperfine splitting constants, but of increased intensity.

Table 1. *Photo-oxygenation of Adamantylideneadamantane* (**1**) *on Solid Supports*

Entry	Quantity[a]) [mmol]	Support[b])	Sensitizer[c])	Light[d]) source	Cell temp.[e])	Reaction time [h]	Products [%]		Total yield [%]
							2	**6**	
1	0.326	*Florisil*	MB	*A*	36°	24	100	–	74
2	0.210	SiO_2		*A*	36	8	100	–	67
3	0.161	SiO_2		*B*	50	6	100	–	59
4	0.157	*Florisil*		*B*	50	40	100	–	100
5	0.192	*Aerosil*		*C*	28	24	100	–	66
6	0.300[g])	*Florisil*		*A*	36	63	100	–	87
7	0.190	*Aerosil 200*	RB	*A*	10	20	98.6	1.4	50.5
8	0.282	*Florisil*		*A*	36	30	98.0	2.0	95
9	0.181	SiO_2		*B*	50	8	91	9.0	88
10	0.347	SiO_2		*B*	20	20	96	4.0	94
11	0.150	*Aerosil*		*C*	28	28	97	3.0	64
12	0.375[h])	*Florisil*		*B*	20	9	97	3.0	61

[a]) 2% of **1** to support by weight.

[b]) *Florisil* (*Fluka*) is a mixture of SiO_2 and MgO, 100–200 mesh. SiO_2 (*Merck*) 60–230 mesh. *Aerosil* (*Degussa*), 99.9% SiO_2, extra pure, 200 mesh.

[c]) Methylene blue (MB) attached to *Amberlite* ion-exchange resin *IRA* 120 (*Fluka*); rose bengal (RB) fixed on *IRA 401* according to *Williams et al.* [17]. The dried resin was mixed with the support in a ratio of 1:4.

[d]) Irradiation provided by either two *Sylvania FFX* 500-W projector bulbs (*A*), or just one (*B*), or with a *Sylvania SLP* 35-W Na vapor lamp (*C*).

[e]) Temperature controlled by a *Colora* thermostat.

[f]) All products were analyzed by weighing the fractions obtained by column chromatography over *Florisil* or TLC over silica using pentane and pentane/Et_2O as eluents. The fractions so obtained were weighed. Dioxetane **2** was estimated as a mixture of **2** and its cleavage product adamantan-2-one.

[g]) 0.321 mmol of adamantane was admixed with **1**. No trace of adamantan-1-ol was detected.

[h]) 0.380 mmol of adamantane admixed. Same result as in g.

Figure. *ESR spectrum obtained by mixing solutions of DMPO and RB in 2-methoxyethanol with an aqueous solution of DMNP*

Essentially the same ESR spectrum could be reproduced by mixing solutions containing either *N*-ethylcarbazole (EC) and 2,4,5,7-tetranitrofluoren-9-one (TENF) in a 1:1 ratio or fluorene (F) and TENF (1:1 ratio) with DMPO and DMNP.

On the contrary, mixing solutions of EC, DMPO and DMNP, or F/DMPO and DMNP, or TENF, DMPO and DMNP gave no ESR spectra. Furthermore, mixing F/TENF with DMPO also gave no ESR signal. On the other hand, an EC/TENF mixture did produce a weak spectrum with DMPO, but the observed hyperfine coupling constants, $A(^{14}N) = 15$ G and $A(^{1}H) = 22.5$ G, were not in accord with the superoxide adduct.

As a further check, solutions of DMPO and DMNP, a degassed solution of RB in the dark and in the light, and finally a solution of **1**, DMPO and DMNP were all mixed and investigated in turn. None gave rise to any ESR signal.

Lastly, the behavior of **1** towards the supposed epoxidizing species H_2O_2, was examined. Simple treatment of **1** with 30% aqueous H_2O_2 gave only epoxide **3** *(Table 2)*. In acetone solution at 30°, longer exposure times resulted in increased amounts of epoxide *(Entry 1)*. At higher temperatures (60°) better yields were obtained *(Entry 2)*. Epoxidation was significantly more efficient in MeOH solution (*Entries 2* and *3*); a 100% yield being obtained at 60° after 36 h exposure *(Entry 2)*. The addition of a radical scavenger [9], 2,6-di(*tert*-butyl)-*p*-cresol (DTBPC), to the reaction mixture was without effect *(Entry 3)*. Other typical olefins, such as cyclohexene, were inert *(Entry 4)* to H_2O_2, while styrene gave polymers under the same conditions *(Entry 5)*.

Table 2. *Oxidation of Adamantylideneadamantane* (**1**) *with Aqueous* H_2O_2 (30%)

Entry	Olefin ([mg])	H_2O_2 30% [ml]	Solvent ([ml])	Temp. [°C]	Time [h]	Products [%]		
						2	**3**	**1**
1	**1** (5)	1	Me_2CO (4)	30	2	–	traces	98
					4	–	10%	90
					9	–	20	80
					24	–	50	50
2	**1** (6)	–	MeOH (5)	60	4	–	20	80
					23	–	90	10
					36	–	100	0
3	**1** (6) + DTBPC (100)	1	MeOH (10)	60	22	–	70	30
4	Cyclohexene	2	MeOH (5)	60	48	no reaction		
5	Styrene (250)	2	MeOH (5)	60	36	polymers		
	Styrene (10)	1	MeOH (5)		24	polymers		

Discussion. – The disparity of product composition obtained in the solid phase using MB and RB, although slight, is significant. The intermediacy of the perepoxide or zwitterionic peroxide as a precursor to the dioxetane is real, but cannot be responsible for epoxide in the present case. In both the MB- and RB-sensitized reactions, intermediates **4** or **5** will undoubtedly be implicated, consequently epoxide arising therefrom should be formed to the same extent. When MB is used, none is formed, and even RB only leads to a minor amount, while dioxetane is formed exclusively and predominantly respectively.

It has been suggested [10] that the perepoxide **4** could react with singlet oxygen to give epoxide and O_3 by oxygen transfer. All attempts to detect O_3 by chemical trapping with adamantane in the reaction mixture or in the effluent gases proved negative. Moreover, if this mechanism were valid, it would be difficult to understand why it would operate for RB, even to a minor extent, but not at all for MB. Consequently, this pathway can be discounted.

The small amount of epoxide formed by RB-sensitized heterogeneous photo-oxygenation probably arises by contamination. Immobilized RB could produce superoxide which, with moisture, would decompose to H_2O_2, the supposed epoxidant, as superoxide itself is ineffective [1e]. We, therefore, believe that traces of H_2O_2, rather than any gaseous species, are transferred by physical contact between the two sets of particles.

In fact, H_2O_2 is confirmed to be an efficient epoxidizing agent for **1**, which turns out to be chemoselective, since conventional olefins do not react. The process probably entails the electrophilic addition of H_2O_2 to the double bond in a process akin to ionic bromination [11] as the radical scavenger DTBPC is without effect.

In the present instance, the decomposition of superoxide radical anion to H_2O_2 can only be surmised. Nonetheless, traces of H_2O would readily produce hydroperoxy radicals which would rapidly disproportionate to O_2 and H_2O_2 [12].

It is not generally appreciated that RB, although extensively studied, is often impure. Even when purified, it presents a complicated structure liable to change in different environments [13]. We originally postulated that RB in the ground state partly dimerizes in solution to form a charge-transfer complex which donates a single electron to singlet oxygen to give superoxide radical anion [4]. Certainly, a superoxide radical anion is formed as attested by the DMPO spin-trapped adduct. Moreover, it is seen here that genuine charge-transfer complexes, EC/TENF and F/TENF, also react with chemically generated singlet oxygen to afford the same DMPO adduct. It cannot be concluded from these two pieces of evidence that RB is a charge-transfer complex, but only that it behaves as such towards singlet oxygen. In fact, RB, as a xanthene dye, may be a sufficiently good electron donor in the monomeric state to be able, like *N,N,N',N'*-tetramethylbenzene-1,4-diamine [14], to reduce singlet oxygen, not only in solution, but also when immobilized in the heterogeneous phase.

The spin-trapping experiments are significant in providing the first evidence for the production of superoxide from RB in the ground state and charge-transfer complexes. In this connection, it is worth noting that superoxide radical anion has been reported to be generated from the interaction of triplet oxygen and illuminated RB bound to polymer and in solution [15]. However, it may well be that in this case and others [16], a dark reaction is responsible for the production of superoxide and H_2O_2.

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Experimental Part

General. TLC: silica gel *60 F254 Merck* (eluent pentane/Et_2O 9:1). Prep. layer chromatography: silica gel *60 F254* (thickness 2 mm, eluents, pentane and pentane/Et_2O 9:1). All solvents were of anal. grade (*Merck*).

Materials. Adamantylideneadamantane (2-(tricyclo[3.3.1.1^{3,7}]decylidene)tricyclo[3.3.1.1^{3,7}]decane; **1**; m.p. 178°) and 1,4-dihydro-1,4-dimethylnaphthalene-1,4-peroxide (DMNP) were prepared and purified according to published procedures [18] [19]. Rose bengal (RB, *Fluka, purum*) was purified by column chromatography over *Florisil* (*Fluka*, acetone/Et_2O 2:1). Methylene blue (MB, *Fluka, puriss.*) and H_2O_2 (30%; *Fluka, purum p.a.*) were used as received. Fluorene (*F, Fluka*), *N*-ethylcarbazole (EC, *EGA*), and 2,4,5,7-tetranitrofluoren-9-one (TENF, *Aldrich*) were purified by recrystallization. 5,5-Dimethyl-1-pyrroline 1-oxide (DMPO, *Aldrich*) was carefully purified with activated charcoal and stored as an aq. soln. (10% by weight).

Photo-oxygenation of **1** *on Solid Supports.* The experiment consists of the irradiation of a stirred mixture of the olefin **1** absorbed on particles of siliceous support admixed with particles of the appropriate amberlite resin to which the sensitizer methylene blue (MB) or rose bengal (RB) is bound. A 2% ethereal soln. of **1** was added to the support. By evaporation of solvent the different supports became coated with **1**. Information on the reaction conditions are given in *Table 1*. The two sets of particles (support and resin) were cooled and jumbled in an O_2 stream in a glass apparatus which was ordinarily used for irradiation in soln. [20].

Attempted Detection of O_3. The method was based on the chemiluminescent reaction of O_3 with rhodamine B, which affords a sensitivity to at least 0.001 ppm [7].

Oxidation of **1** *with 30% Aq.* H_2O_2. To a soln. of **1** in MeOH or acetone [19] was added 30% aq. H_2O_2 (1 ml). The turbid soln. was stirred slowly in a sealed flask in the dark at 30% or heated under reflux for the time indicated (*Table 2*). The product composition was assayed by TLC over silica.

Spin Trapping. Experiments were performed by adding an aq. soln. of freshly purified DMPO (80 ml) to a soln. of the reactants in 2-methoxyethanol (80 ml) [6]. The final concentrations of the various reactants were RB: 4 mM, **1**: 10 mM, DMNP: 60 mM, TENF: 10 mM, F: 10 mM, EC: 10 mM, F: 10 mM. To generate singlet oxygen, solid DMNP (10 mg), freshly purified by chromatography over silica gel, was added to the soln. of reactants. The resulting soln. (80 ml) was then transferred to a flat quartz ESR cell. ESR spectra were obtained by using a *Varian E-9* spectrometer (X-band, 100-kHz field modulation) which was equipped with a *Jeol* cylindrical cavity resonator allowing direct irradiation of the sample.

REFERENCES

[1] a) A. P. Schaap, G. R. Faler, *J. Am. Chem. Soc.* **1973,** *95,* 3381; b) P. D. Bartlett, M. S. Ho, *ibid.* **1974,** *96,* 627; c) B. D. Bartlett, *Chem. Rev.* **1976,** 149; d) C. W. Jefford, A. F. Boschung, *Tetrahedron Lett.* **1976,** 4471; e) C. W. Jefford, A. F. Boschung, *Helv. Chim. Acta* **1977,** *60,* 2673.

[2] A. P. Schaap, K. A. Zaklika, in 'Singlet Oxygen', Eds. H. H. Wasserman and R. W. Murray, Academic Press, New York, 1979, Chapt. 6; A. A. Frimer, *Chem. Rev.* **1979,** *96,* 359.

[3] A. P. Schaap, S. G. Recher, G. R. Faler, S. R. Villasenor, *J. Am. Chem. Soc.* **1983,** *105,* 1691.

[4] C. W. Jefford, M. Jimenez Estrada, G. Barchietto, *Tetrahedron* **1987,** *43,* 1737.

[5] C. W. Jefford, W. Knöpfel, L. C. Smith, S. Kohmoto, K. A. Almqvist, M. Jimenez Estrada, G. Barchietto, 'Oxygen and Oxyradicals in Chemistry and Biology', Eds. M. A. J. Rodgers and E. L. Powers, Academic Press, New York, 1981, p. 397.

[6] Z. Cohen, E. Keinan, Y. Mazur, T. H. Varkony, *J. Org. Chem.* **1975,** *40,* 2141.

[7] F. Celardin, M. Marcantonatos, *Anal. Chim. Acta* **1973,** *67,* 225; b) J. A. Hodgeson, K. J. Krost, A. E. O'Keefe, R. K. Stevens, *Anal. Chem.* **1970,** *42,* 1795.

[8] G. R. Buettner, L. W. Oberley, *Biochem. Biophys. Res. Commun.* **1978,** *83,* 69; W. Damerau, *Z. Chem.* **1983,** *23,* 62.

[9] K. U. Ingold, *Chem. Rev.* **1961,** *61,* 563.

[10] M. J. S. Dewar, A. C. Griffin, W. Thiel, I. J. Turchi, *J. Am. Chem. Soc.* **1975,** *97,* 4439.

[11] J. Strating, J. W. Wieringa, H. Wynberg, *Chem. Commun.* **1969,** 907; J. H. Wieringa, J. Strating, H. Wynberg, *Tetrahedron Lett.* **1970,** 4579.

[12] a) J. Wilshire, D. T. Sawyer, *Acc. Chem. Res.* **1979,** *12,* 105; b) D. T. Sawyer, M. J. Gibian, *Tetrahedron* **1979,** *35,* 1471.

[13] a) J. J. M. Lamberts, D. C. Neckers, *J. Am. Chem. Soc.* **1983,** *105,* 7465; b) J. J. M. Lamberts, D. C. Neckers, *Z. Naturforsch., B* **1984,** *39,* 474.

[14] I. Saito, T. Matsuura, K. Inoue, *J. Am. Chem. Soc.* **1983,** *105,* 3200.

[15] V. S. Srinivasan, D. Podolski, N. J. Westrick, D. C. Neckers, *J. Am. Chem. Soc.* **1978,** *100,* 6513.

[16] M. Roncel, J. A. Navarro, M. A. De la Rosa, *J. Photochem. Photobiol. A* **1988,** *45,* 341.

[17] J. R. Williams, G. Orton, L. R. Unger, *Tetrahedron Lett.* **1973,** 4603.

[18] J. E. McMurry, M. P. Fleming, *J. Org. Chem.* **1976,** *41,* 896.

[19] H. H. Wasserman, D. L. Larsen, *J. Chem. Soc., Chem. Commun.* **1972,** 253.

[20] C. W. Jefford, A. F. Boschung, *Helv. Chim. Acta* **1974,** *57,* 2242.