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The Role of SET in the Deprotection of (Thio)ketals under Photosensitization by π-Acceptors*

Elisa Fasani, Mauro Freccero, Mariella Mella, and Angelo Albini
Dip.Chimica Organica, Universita', v.Taramelli 17, 27100 Pavia, Italy

Abstract. Efficient deprotection of 2-methyl-2-*tert*-butyl-1,3-dithiolane and of the corresponding oxathiolane to give the ketone is obtained by photosensitization by a catalytic amount of aromatic nitriles (benzenetetracarbonitrile, TCB, and anthracenedicarbonitrile, DCA, the latter only in the presence of biphenyl) or of heterocyclic salts (triphenylpyrylium tetrafluoborate, TPPT, and methylacridinium perchlorate, MAP), in oxygen saturated solutions. The reaction involves SET to the excited π-acceptor and interception of the substrate radical cation either by oxygen (in the case of the heterocyclics) or by the superoxide anion (in the case of the nitriles). Triplet chloranil (Chl) acts both as oxidant and as proton acceptor, and thus deprotection is accompanied by formation of a stoichiometric amount of the hydroquinone $ChlH_2$. The corresponding dioxolane is a weaker donor: SET occurs only with photoexcited TCB and causes C-C bond fragmentation, not deprotection. The other π-acceptors photosensitize the deprotection of the dioxolane, but in this case they act as Lewis acids (Chl gives a trimer under this condition). This method is unsatisfactory with protected aldehydes. The different reactivity of the radical cations of thioketals and of ketals and the scope of this deprotection method are discussed. © 1997, Elsevier Science Ltd. All rights reserved.

The design of easily and selectively removed protecting groups is a constant aim in organic chemistry, due to the importance of the protecting-deprotecting procedure in synthesis.[1] Photochemical reactions operate under peculiarly mild conditions and deprotection methods based on such reactions have been developed.[2] Most of these are based on the incorporation of a o-nitrobenzyl group in the protecting moiety.[2] This makes the group photoremovable through a reaction initiated by (triplet state) intramolecular benzylic hydrogen abstraction by the nitro group. A potentially more general issue is devising photochemical reactions as an alternative to thermal methods for removing unmodified protecting groups. This is a less followed path, however, and has led to no general method.

As far as the carbonyl group is concerned, some photochemical methods related to the usual protection via (thio)acetalisation have been reported. These include on one hand the intramolecular reaction of nitrobenzyl substituted acetals[3] and on the other one intramolecular triplet attack by benzophenone on unmodified thioketals.[4] Furthermore, several recent reports have pointed that a convenient deprotection of acetals and thioacetals is obtained by using mild oxidants, such as of π-electron acceptors, as well as metal complexes.[5-8] Related redox reactions can be electrochemically [9,10] or photochemically[11,12] induced. However, some doubts have been raised about the path followed (e.g. do the acceptor used really operate via a SET path or as Lewis acids),[7,8] and the scope of this approach cannot be evaluated with the sparse data available. Photoinduced SET is a powerful method, since excited states are both stronger oxidant and stronger reductants than their ground state counterpart, and application of this method for a synthetic purpose has been demonstrated.[13-15]

* Dedicated to prof. Paolo Grunanger on occasion of his 70th birthday

Thus, photochemically inducing SET to a weak acceptor (one which would not act in this role in the ground state) is an appealing variation for oxidative deprotection methods, in view of the mild conditions involved. This has prompted us to test systematically this method for the deprotection of unmodified (thio)acetals.

RESULTS

In order to establish the significance of the method we investigated the deprotection of simple 1,3-dithiolane, -oxathiolane and -dioxolane derivatives in a polar solvent such as acetonitrile in the presence of various derivatives known as strong electron acceptors in the excited state. Most experiments were carried out with the 2-methyl-2-*tert*-butyl derivatives **1**, **2**, and **3**. As for the acceptors, these were 2,3,5,6-tetrachloro-1,4-benzoquinone (chloranil, Chl), 1,2,4,5-benzenetetracarbonitrile (TCB), 9,10-anthracenedicarbonitrile (DCA), 2,4,6-triphenylpyrylium tetrafluoborate (TPPT), an 10-methylacridinium perchlorate (MAP). These compounds were carefully purified (see Experimental), with particular attention to the presence of acidic contaminants.

Solutions of the substrates and the acceptors were irradiated in the near uv (lamps centered at 320 nm for TCB, and at 360 nm for the other ones) after purging with either argon or oxygen. Chemical conversion of the substrates, sensitizer consumption, and change in the acidity of the solution were monitored at convenient intervals. Table 1 gathers the results obtained in a homogeneous series of experiments with 1×10^{-2} M substrates. In most cases experiments with 1×10^{-1} M solutions were also carried out and gave essentially the same results.

As one can see, the substrates were largely converted after some hours of irradiation (light was absorbed only by the sensitizer). The main characteristics of the observed reactions were as follows (see Scheme 1).

Scheme 1

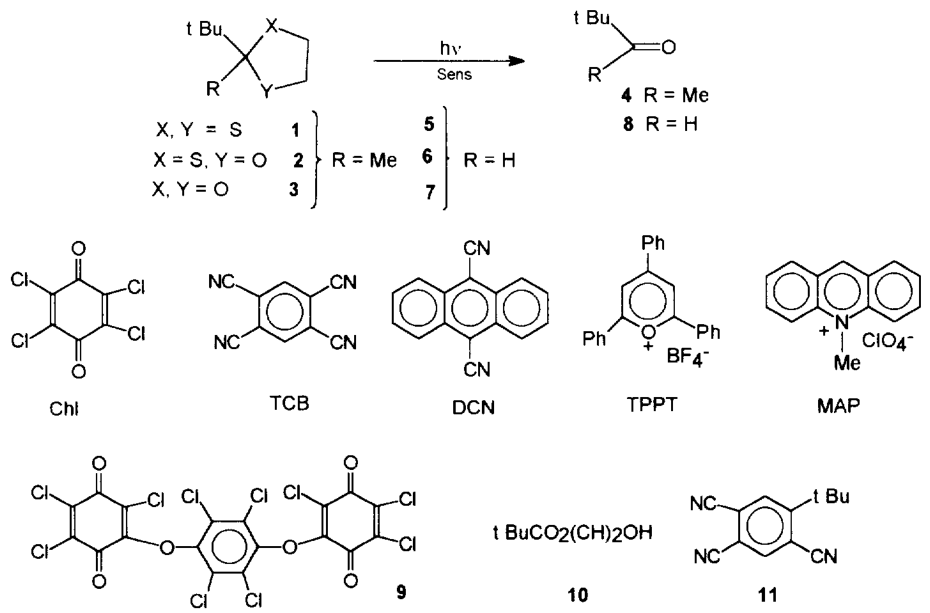

Table 1. Photosensitized Deprotection of the (Thio)ketals **1** to **3** ($1\mathrm{x}10^{-2}$ M).[a]

Sensitizer (M), Conditions		**1**			**2**			**3**		
		Deprotection (Subst.Conv.)	Converted Sensitizer	Acidity (M) Developed	Deprotection (Subst.Conv.)	Converted Sensitizer	Acidity (M) Developed	Deprotection (Subst.Conv.)	Converted Sensitizer	Acidity (M) Developed
Chl (10^{-2}),	O_2	20(75)	100	$8\mathrm{x}10^{-4}$	95(95)	41	$4\mathrm{x}10^{-5}$	100(100)	5	$1\mathrm{x}10^{-4}$
360 nm, 2h	N_2	10(55)	100	$5\mathrm{x}10^{-4}$	90(90)	100	$6\mathrm{x}10^{-5}$	80(80)	5	$1\mathrm{x}10^{-4}$
TCB ($5\mathrm{x}10^{-3}$)	O_2	60(100)	0	$3\mathrm{x}10^{-3}$	70(70)	0	$9\mathrm{x}10^{-4}$	15(100)	0	$1\mathrm{x}10^{-4}$
320 nm, 1h	N_2	5(10)	0	$1\mathrm{x}10^{-4}$	25(40)	25	$4\mathrm{x}10^{-4}$	0(40)	100	--
DCA ($1\mathrm{x}10^{-4}$)	O_2	80(100)	5	$1\mathrm{x}10^{-3}$	80(100)	10	$6\mathrm{x}10^{-4}$	0(0)	0	--
360 nm, 2h[b]										
TPP ($8\mathrm{x}10^{-5}$)	O_2	90(100)	100	$9\mathrm{x}10^{-4}$	95(100)	100	$8\mathrm{x}10^{-4}$	60(60)	100	$1\mathrm{x}10^{-5}$
360 nm, 3h	N_2	0(0)	0	--	0(0)	0	----	60(60)	100	$1\mathrm{x}10^{-5}$
MAP ($8\mathrm{x}10^{-5}$)	O_2	85(100)	20	$1\mathrm{x}10^{-3}$	95(100)	10	$6\mathrm{x}10^{-4}$	100(100)	20	$1\mathrm{x}10^{-5}$
360 nm, 4h	N_2	5(10)	30	$1\mathrm{x}10^{-5}$	5(10)	40	$3\mathrm{x}10^{-4}$	60(65)	85	$1\mathrm{x}10^{-6}$

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a. Fot the conditions of the experiments, see Experimental. b. In the presence of Biphenyl (0.05 M). No measurable reaction for the same irradiation time when this additive is omitted.

Photosensitization with Chl. Chl was effective only when used in an equimolecular amount with respect to the substrate. Under this condition, sensitized decomposition of **1** to **3** was relatively fast, but the yield of deprotected 3,3-dimethyl-2-butanone (**4**) was different in the various cases. With **1** and **2** Chl was reduced to the corresponding hydroquinone $ChlH_2$ (1:1 molar ratio with reacted substrate in the case of **1** and of **2** in deoxygenated solution, in a lower yield with **2** in oxygen-equilibrated solution). On the other hand, **3** was deprotected with only minor reduction of Chl. Chromatographic separation showed that in this case Chl gave a little $ChlH_2$ and some higher molecular weight products, the main one of which was isolated and identified as the "trimeric" derivative **9** (see Experimental). Ethylene glycol was formed concurrently with the consumption of **3**, but neither 2-mercaptoethanol (from **2**) or ethanedithiol from **1** were detected.

Some increase of the acidity (corresponding to a few percent with respect to the converted Chl, see below) was noticed in all experiments. This was sufficient to cause deprotection of the ketals due to the moisture present in the solvent. As an example when an solution of Chl and dioxolane **3** was irradiated and a partial deprotection was obtained, this continued when the solution was kept in the dark. Also, irradiation of a Chl solution in MeCN led to the development of some acidity and when ketal **3** was added to the preirradiated solution, some hydrolysis took place. Solutions of **1** and **2** and Chl underwent no appreciable change in the dark, while **3** was partly (ca 30%) deprotected overnight when moist (0.1% H_2O) MeCN was used, but not when the solvent had been dried.

Some experiments were carried out also with a protected aldeyde, viz the 2-*tert*-butyl derivatives **5** to **7**. Irradiation for the same time as above led to consistent substrate conversion (40-70%), again with reduction of Chl to $ChlH_2$ in the case of the sulfurated derivatives (**5** and **6**), and to a lesser degree (10%) in the case of **7**. However, in every case the yield of 2,2-dimethylpropanal (**8**) was low ($\leq$20%). In the reaction of the acetal **7** with Chl the main product was the 2-hydroxyethyl ester of pivalic acid (**10**).

For the sake of comparison, further aromatic ketones were used as the sensitizers in the case of **1**. The reaction of this substrate in the presence of benzophenone or trifluoroacetophenone under nitrogen was slow and did not lead to deprotection.

Photosensitization with Aromatic Nitriles. Differently from the Chl case, TCB did not undergo a stoichiometric reaction: the data reported in Table 1 were obtained with half a mole with respect to the substrate, and the sensitizer was consumed in no case under oxygen and only with **3** under nitrogen. The observed reactions were different with sulfur containing or non containing substrates. Thus, both **1** and **2** gave ketone **4** with a reasonable yield. The reaction was fast only in oxygen saturated solutions, while deprotection under nitrogen required a much longer irradiation time, and in that case (not in the presence of oxygen) ethanedithiol and 2-mercaptoethanol were formed. On the other hand, the decomposition of ketal **3** led to some deprotection only in the oxygenated solution containing TCB. Irradiation of nitrogen flushed solutions containing TCB led to the previously reported[16] ipso substitution of the sensitizer to give 5-*tert*-butylbenzene-1,2,4-tricarbonitrile (**11**), not to deprotection.

Similar experiments with DCA (<1/100th of the substrate, the intense absorption of this photosensitizer in the near uv made it possible to use it in a low amount) gave only a partial deprotection after several hours irradiation in oxygen- (not in nitrogen-) flushed solutions. When biphenyl (0.05 M) was added to the DCA solution, however, compounds **1** and **2** were efficiently deprotected (only in oxygen saturated solutions). Both TCB and DCA were not consumed in these cases. Compound **3** was unaffected upon irradiation with DCA under the above condition. In all of the cases some acidity was developed in oxygen saturated, but much less in oxygen-free, solutions. Again, deprotection was not satisfactory with the protected aldehyde derivatives **5** to **7**.

Photosensitization with TPPT and MAP. Both sensitizers were effective at low concentration (<1/100th of the substrate for the data reported in the Table 1). Deprotection of the derivatives **1** to **3** occurred in a satisfactory way with both sensitizers under conditions where oxygen was employed (except for the **3**/MAP case), and was accompanied by a small development of acidity and partial or total sensitizer consumption. Under deoxygenated conditions, deprotection was slower. Thus, in the case of **2**, TPPT sensitized deprotection required 20 h (rather than 3 h) under deoxygenated conditions, and in this case the ketone was formed along with an equimolecular amount of 2-mercaptoethanol. Compound **3** was deprotected by TPPT with liberation of equimolecular ethyleneglycol both in nitrogen- and in oxygen-flushed solutions.

With MAP, both **1** and **2** were deprotected efficiently under oxygen with minimal sensitizer decomposition, while deprotection was slower and sensitizer decomposition faster under nitrogen.

Complementary Experiments. The absorption spectrum of the sensitizers showed no change upon addition of the above substrates. TCB, DCA, TPPT, and MAP were strongly fluorescent in solution. Compounds **1** and **2** quenched the emission of all the sensitizers, whereas **3** was a quencher only with TCB (see Table 2).

Irradiation of an oxygen-equilibrated solution of **1** in acetonitrile containing Rose Bengal (350-650 nm) under otherwise similar conditions gave the ketone **4** in a moderate yield, accompanied by other decomposition products.

DISCUSSION

The conditions of the experiments were primarily aimed to obtain evidence about the mechanism(s) of the reactions of (thio)ketals photoinduced by π-acceptors, and thus to evaluate the scope and the synthetic utility of carbonyl derivatives deprotection by this method. The presently used sensitizers are weak acceptors in the ground state. Competitive thermal reactions were either negligible or (in the case of **3** with Chl) much slower than the photoinduced reaction. The presently considered sensitizers are no Lewis acids in the ground state (except for the case of Chl, which at any rate is weaker than other acceptors previously considered in the literature, such as dichlorodicyanobenzoquinone)[7] and no mineral acids are present at the beginning of the experiment. A polar solvent, acetonitrile, was chosen in order to facilitate electron transfer, supposed to be the key step of the procedure, and to avoid complications arising from in cage radical ion *pair* reactions, which are likely intemediates in less polar solvents. The only nucleophile present was water (0.1% in the solvent).

The chemical results presented in Table 1 and the fluorescence quenching data and redox potentials[24-30] reported in Table 2 can be rationalized by admitting that different mechanisms are operative in different cases, depending on the interaction occurring with the excited sensitizer and on the reactivity of the primarily formed intermediates.

Mechanism of the Photosensitization. Electronic excitation makes redox processes much easier. SET from the considered substrates (D) to the photoexcited sensitizer is feasible when ΔG_{et} evaluated according to Weller equation (eq.1)[17] is negative.

$$\Delta G_{et} = E_{ox}(D) - E_{red}(S) + E_{exc} \qquad (1)$$

Table 2. Redox Potential and Photophysical Parameters for the Photosensitization of (Thio)ketals **1** to **3**.[a]

Sensitizer,	**1**, E_{ox} 1.6			**2**, E_{ox}, 1.6			**3**, E_{ox}2.8		
$[E_{red}(S), E_{red}(S) + E_{exc}]$	ΔG_{et}	K_{SV}	$k_q x10^{10}$	ΔG_{et}	K_{SV}	$k_q x10^{10}$	ΔG_{et}	K_{SV}	$k_q x10^{10}$
V vs SCE	eV	M^{-1}	$M^{-1}s^{-1}$	eV	M^{-1}	$M^{-1}s^{-1}$	eV	M^{-1}	$M^{-1}s^{-1}$
TCB [-0.65, 3.2][b]	-1.6	150	1.5	-1.6	150	1.5	-0.4	85	0.8
DCA [-0.89, 2.0][b,c]	-0.4	200	1.1	-0.4	95	0.5	0.8	<1	
Chl [0.0, 2.7][d]	-1.1		0.5	-1.1		0.5	0.1		0.0001
TPPT [-0.39, 2.5][b]	-0.9	90	2	-0.9	90	2	0.3	<1	
MAP [-0.44, 2.3][b]	-0.7	510	1.6	-0.7	480	1.5	0.5	<1	

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a. Parameters used: E_{ox} (**1**), ref. 10, 11; (**2**), taken equal to that of **1**, in view of the fact that the IP are very similar, see ref. 24; (**3**) evaluated from the IP, ref. 25, via the Miller equation, ref. 26. E_{red} and E_{exc} of the sensitizers: TCB, DCA, Chl, TPPT, ref. 13, 27; MAP, ref. 28. Fluorescence lifetime: TCB, 10.1 ns, ref 29, DCA, 19.6 ns, ref.27, TPPT, 4.2 ns, ref. 30, MAP, 31 ns, ref. 28. b. Referred to the singlet excited state. c. In the photoreaction the BP is added as "cosensitizer" (E_{ox} 1.8 V). In this case the actual oxidant of the thioketals is $BP^{+\cdot}$. d.Referred to the triplet state.

The aromatic derivatives TCB, DCA, TPPT, and MAP are strongly fluorescent, and the involvement of the respective singlet states can be checked by fluorescence quenching. Thus, the excited state reduction potentials, $E_{red}(S^*) = E_{red}(S) + E_{exc}$, reported in Table 2 refer to these states. In the case of Chl, the excited singlet is too short-lived for participating in a bimolecular process, and the $E_{red}(S^*)$ reported refers to the triplet state.

As it appears from Table 2, SET from both the sulphur containing derivatives **1** and **2** is exothermic with all the sensitizers, and indeed these substrates quench the fluorescence of TCB, DCA, TPPT, and MAP at a rate k_d near to the diffusion controlled limit;[31] the different Stern Volmer constants, K_{SV}, reflect the different singlet lifetimes. In the case of DCA, however, the reaction occurs only in the presence of biphenyl (BP), and actually it is the radical cation $BP^{+\cdot}$ which is involved in the SET step (exothermic also in this case, see Table 2, note) from the thioketals (see below, Scheme 2). As for Chl, the fast quenching of the triplet ensures that SET from **1** and **2** is the primary step in this case.

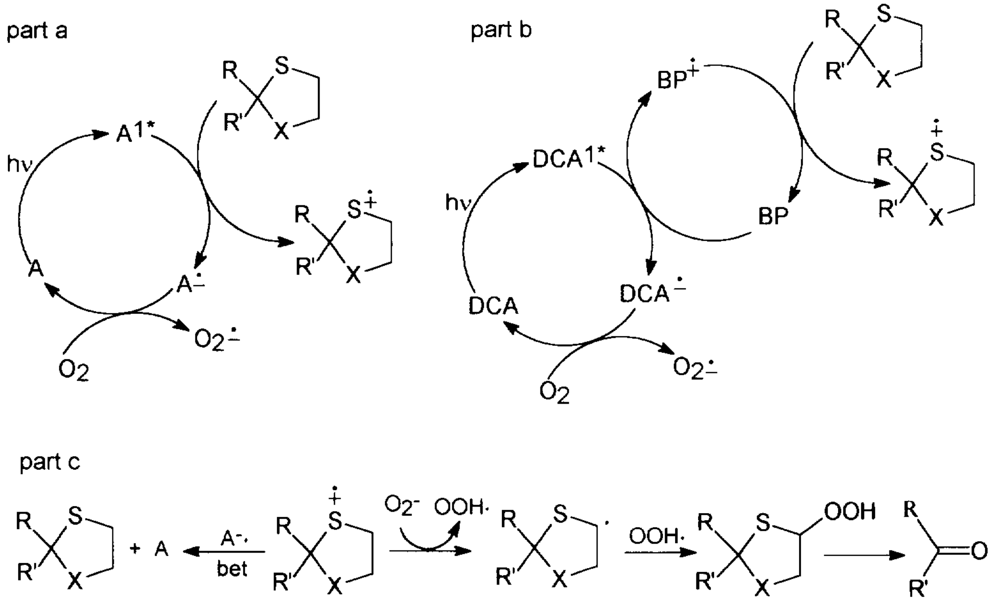
The dioxolane **3** is a much weaker donor. The oxidation potential is not precisely known. The value reported in Table 2 is evaluated from the measured IP. That SET is exothermic with TCB is confirmed by fluorescence quenching. In the other cases, SET is endothermic, and not measurable quenching occurs.

Photosensitized Deprotection of Thioketal 1 and Semithioketal 2. With all the sensitizers, the primary step is photoinduced SET (see Scheme 2). The following behaviour shows important differences, however. A first difference is between chloranil, which is used stoichiometrically both in the presence and the absence of oxygen, and the other cases, where deprotection proceeds efficiently in oxygen-flushed solutions, very slowly or not at all under nitrogen, and requires a catalytic amount of the sensitizer.

In the latter group, the role of oxygen must be clarified. Several mechanisms can be considered for the conversion of the (semi)thioketal radical cation to the ketone taking into account the role of oxygen. Singlet oxygen is a possibility (compare ref.11), since aromatic nitriles are known to sensitize oxygen,[18] and with 0.01 M thioketals some quenching of the sensitizer excited state by oxygen occurs. However, the experiment with Bengalrosa suggests that deprotection through this path is slow and not as clean as the present reaction, and at any rate such a mechanism can not be applied to TPPT, which has been demonstrated to be unable to sensitize oxygen.[19d]

Thus, a reaction of the thioketal radical cation is involved. Two different situations arise according to the sensitizer used. DCA has a more negative reduction potential than dioxygen and TCB close to it. Thus, the superoxide radical anion is formed by secondary electron transfer from the sensitizer radical anions (Scheme 2).[18] Proton transfer from the substrate radical cation to the superoxide anion is a likely path, since this is a Bronsted base in aprotic solvents [the conjugate acid has there pKa =12 (estimated)[19a] vs 4.8 (measured)[19b] in water, see Scheme 2c]. This path is similarity to the chloranil mechanism (Scheme 4); another possibility is reaction with O_2, see Scheme 3. In accord with the mechanism in Scheme 2c is the accelerating effect by BP on the DCA sensitized reaction. A similar effect was noted with other DCA sensitized oxygenations, e.g. in the case of oxirans,[19c] and can similarly be attributed to the prolonged lifetime of the radical cation in the presence of a secondary donor (Scheme 2b), since under this condition energy-wasting back electron transfer to the radical anion is less competitive and there is a better chance for irreversible reaction with $O_2^{-\cdot}$.

Scheme 2

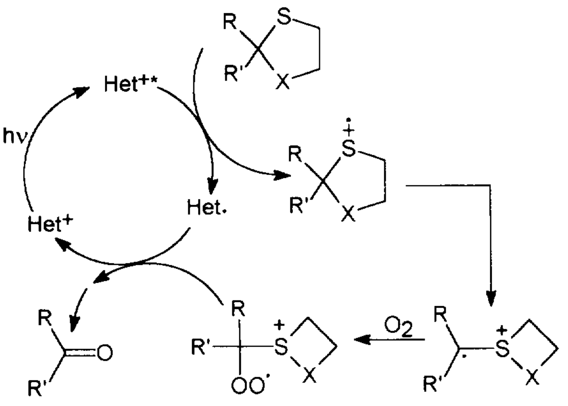


The situation is different with the heterocyclic salts as sensitizers. These compounds are reduced at a potential less negative than dioxygen, thus no secondary electron transfer from O_2 occurs. Indeed, in the case of TPPT it has been proved that the pyranyl radical when generated by electron transfer (from alkenes) forms no superoxide, although it adds (rather slowly) oxygen.[19d] On the other hand, with these cations as the sensitizers, SET involves no charge separation. Therefore diffusion out of cage is faster than with the aromatic nitriles, where a pair of opposedly charged radical ions is formed. Indeed, a relatively slow ($<1 \times 10^{6}$ M^{-1} s^{1}) rate has been measured for the bimolecular back electron transfer between a radical cation (that of adamantylidenadamantane) and the TPPT radical in dichloromethane[19d] (compare with rate constants $>1 \times 10^{9}$ $M^{-1} s^{1}$ measured with the nitriles). The substrate radical cation is thus expected to be much longer lived under this conditions, and reaction with dioxygen, although slower than that with superoxide, becomes significant (a few examples of reactions of radical cations with dioxygen have been reported).[19e]

The chemical reaction may be either hydrogen abstraction from the ring methylene, or, since the electrochemical literature suggests that the radical cations of thioketal undergo fast C-S bond cleavage,[10,11] oxygen addition to the radicalic center in the distonic radical cation arising form ring opening (see Scheme 3), as proposed by Kamata.[11] The latter reaction may be considered also for the cyanoaromatic sensitized reaction, although it appears doubtful that the radical cation is sufficiently long lived in that case.

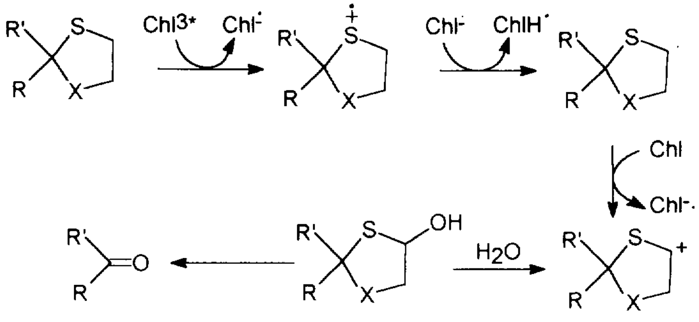
As mentioned above, the sensitizers act catalytically and are either not degraded, as with the aromatic nitriles where the radical anion is reoxidized by oxygen (Scheme 2), or only to a small extent, as with the heterocyclic salts TPPT and MAP. The neutral radicals formed from the sensitizers are mainly reoxidized also in these case (Scheme 3), but some other process (reasonably radicalic coupling)[19f] competes to a degree, since they are wholly or partly consumed at the end of the irradiation.

Scheme 3



Again a different situation arises with chloranil, although electron transfer is the primary step also in this case (see Table 2 for the quenching constants). In the radical anion $Chl^{-\cdot}$ the negative charge is localized on the oxygen some, and this gives to this species, contrary to the case of the radical anions of the aromatic nitriles considered above, a basic character.[20a] Therefore, a proton is transferred from the substrate radical cation to $Chl^{-\cdot}$ (Scheme 4). The resulting α-thio radicals are then oxidized by ground state chloranil (E_{red} 0.0V vs SCE) and the cation adds water (0.1% in acetonitrile) finally yielding the ketone. As it appears from Table 1, this deprotection is quantitative with **2**, while it is much less efficient with **1**, probably due to the occurring of polymerization processes under this condition.

Scheme 4



The oxidation of the intermediate α-thio radical is a key step for deprotection. Other ketones such as trifluoroacetophenone do slowly consume **1**, and the reaction occurring certainly is homolytic hydrogen abstraction. However, this does not lead to deprotection (when oxygen is excluded), since the ground state ketone is not able to oxidize the first formed radicals (E_{red}-1.38V).[20c]

Thus, here Chl acts both as sensitizer and as proton acceptor and it reacts stoichiometrically, not catalytically. The primary SET step and the following α-thio radical oxidation both yield the radical anion $Chl^{-\cdot}$ and this is protonated to yield the phenoxyl radical $ChlH^{\cdot}$. This disproportionates to Chl and $ChlH_2$, and the overall process can be depicted as a two-electron redox reaction with the 1:1 stoichiometry (eq.2).

$$Chl + RR'CSCH_2CH_2S + H_2O + h\nu \rightarrow CHlH_2 + RR'CO \qquad (2)$$

When oxygen is present, $CHlH_2$ is in part reoxidized, and the sensitizer consumption is less than stoichiometric (at least with **2**).

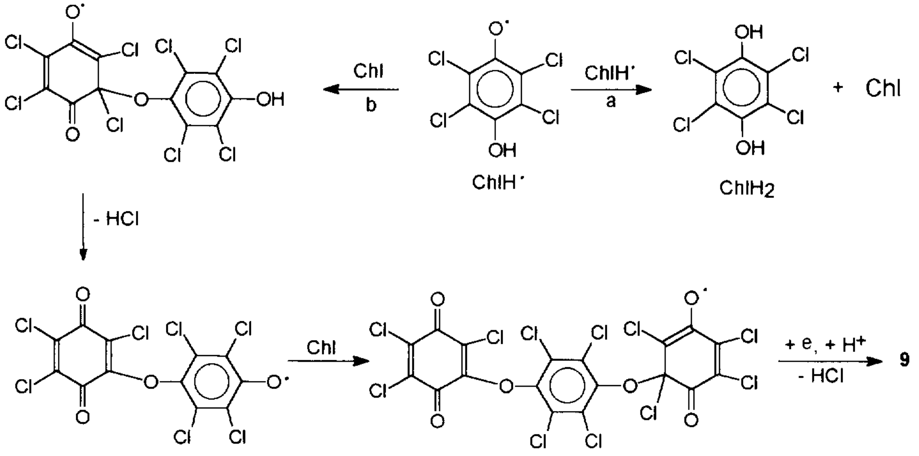
Photosensitized Deprotection of Ketal 3. In this case no SET takes place with DCA, TPP, and MAP. A more or less extensive deprotection occurs, however, with the last two sensitizers as well as with Chl. This is can be imputed to two causes. The first one is the greater acid-sensitivity of these derivatives. As it appears in Table 1, some acidity is liberated upon irradiation, and part of the deprotection may be accounted for as a dark process, as shown by the fact that deprotection continues in an irradiated solution. However, reaction under irradiation is faster than expected with the low acidity level attained, as shown in separate experiments. Thus, part of deprotection may be due to the excited sensitizers acting as a Lewis acid,[22] a mechanism which, as seen above, is unimportant for thioketals , but may have a role with ketals, which are much more sensitive to acid catalyzed hydrolysis. One may notice that a little deprotection takes place also with semithioketals (see Table 1, experiments under deoxygenated conditions) although much less efficiently than in the presence of oxygen.

The reaction with chloranil was studied in some detail. In this case in wet acetonitrile a slow deprotection takes place also in the dark, consistently with the role of Chl of weak Lewis acid in the ground state. The reaction under irradiation is faster and consumes only a few percent of sensitizer, in accordance with the idea of an increased Lewis acidity of the excited sensitizer, and proving that Chl has here a different role than in the reaction with the sulfurated derivatives **1** and **2**, where a stoichiometric amount of Chl is consumed. A little

$ChlH^{\cdot}$ is formed also in this case, but its steady state concentration is low as shown but the difference in the Chl derived products.

Thus, not only the Chl consumption is quite low, but also disproportionation to $ChlH_2$ (Scheme 5, path a) accounts only for a part of the sensitizer reacted, another product being the "trimeric" compound **9**. Formation of this product may explained by trapping of $ChlH^{\cdot}$ by Chl, a reaction which may compete with disproportionation at the low radical steady-state concentration attained in this experiment, and a possible mechanism is outlined in Scheme 5, path b.

Scheme 5



On the other hand, singlet excited TCB is the strongest electron acceptor of the series and the dioxolane is oxidized in this case, as confirmed by fluorescence quenching (see Table 2). We previously studied the dioxolanes - TCB photochemistry in deoxygenated acetonitrile,[16] and found that the radical cation undergoes carbon-carbon bond cleavage to yield an alkyl radical (which is trapped by $TCB^{-\cdot}$ resulting in final ipso substitution on the ring) and a α,α-dioxycation (which adds water to yield the corresponding orthoacid, see Scheme 6, path a). This is the reaction observed here under nitrogen, and TCB is alkylated when irradiated in the presence of the dioxolane **3** to yield **11**. Under oxygen TCB alkylation is precluded, but deprotection to the ketone occurs only as a minor path (see Table 1).

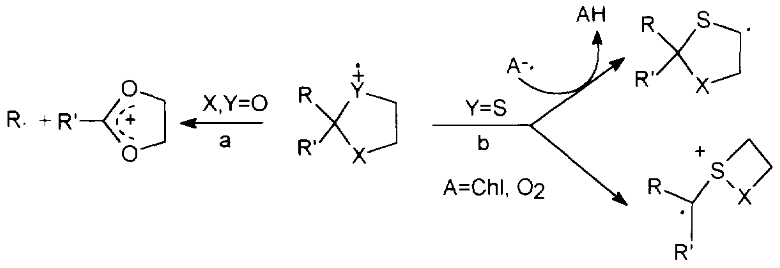
Deprotection of (Thio)acetals 5, 6, and 7. With sulfurated derivatives, the initial steps of the electron transfer mechanism discussed above remain the same. The fact that deprotection occurs here in a worse yield, is due to competitive paths involving the hydrogen atom in position 2, either proton abstraction (by $O_2^{-\cdot}$ or $Chl^{-\cdot}$) or a different reaction with oxygen. Indeed, dithiolan-2-yl radicals are known to have a ylide structure,[21] and to react differently from 2,2-disubstituted derivatives. Interestingly, a clean reaction occurs with Chl and acetal **7**. The first step is hydrogen abstraction from position 2, followed by oxidation by ground state Chl to the cation. Water addition then leads to ring opening yielding the open-chain ester **10**.

Comparison of the Radical Cation Reactions. In many of the reactions reported here the radical cations of the (thio)ketals are the key intermediates. Their formation depends on the feasibility of photoinduced SET (see eq.1) and their fate on the availability of a reaction path fast enough to compete with back electron transfer. The free energy change for the cleavage of a radical ion can be evaluated through the appropriate thermochemical cycle,[15,23a] which leads to eq. 3

$$\Delta G(RX^{+\cdot}) = \Delta G(RX) + F[E_{ox}(X\cdot) - E_{ox}(RX)] \quad (3)$$

Dioxolanes are difficult to oxidize (a strong acceptor such as excited TCB is required). The radical cation $3^{+\cdot}$ has thus a large energy content and C-C bond fragmentation in position 2 (evaluated to be slightly endothermic through eq.3, ca +5 kcal M^{-1})[23b] occurs at a high enough rate to be competitive with back electron transfer. On the other hand, dithiolanes radical cations are strongly stabilized with respect to dioxolanes (E_{ox} is lower by≈1.3 V). As a consequence, C-C fragmentation is strongly endothermic for radical cation $1^{+\cdot}$, while deprotonation from position 4 is only slightly endothermic (ca +5 kcal M^{-1})[23b] and presumably so is C-S bond fragmentation (an easily oxidized thiyl radical is formed). Thus, two reactions can occur, viz deprotonation in the presence of a nucleophile such as $O_2^{-\cdot}$ and $Chl^{-\cdot}$.and, when back electron transfer is sufficiently slow, ring cleavage to give a distonic species (Scheme 6).

Scheme 6



Comparison of the Sensitizers. All the sensitizers considered here act as π-acceptors with sufficiently good donors such as thioketals. Cyanoaromatics yield a radical ion pair, the lifetime of which is severely limited by back electron transfer; and reaction occurs only in the presence of oxygen which is reduced to superoxide by the sensitizer radical anion, and works better in the presence of a "cosensitizer" such as biphenyl (see Scheme 2b). Heterocyclic salts give a radical - radical cation pair; the lack of electrostatic attraction slows down back electron transfer. Thus, reaction of the radical cation with oxygen becomes significant (see Scheme 3). Again differently, Chl gives a nucleophilic radical anion, and the radical cation reacts with this species, not with oxygen (see Scheme 4).

Usefulness of this Photodeprotection Method. In the case of ketals, photosensitization occurs via acid (or Lewis acid) catalysis and appears to have no advantage over thermal methods. On the other hand with thioketals and semithioketals, photosensitization is a useful deprotection procedure, e.g. with TPPT or DCA/biphenyl, and MAP where near-UV and visible light can be used (and thus competitive excitation of the substrate is avoided, even if this contains unsaturations). These sensitizers suffer only a limited decomposition under this condition and this, together with the catalytic amount used, is also a positive factor. The deprotection has some mechanistic analogy with methods based on electrochemistry and on chemical oxidation, with the advantage that it occurs conveniently in neat organic solvents, and the addition of conducting or reacting salts is not required.

Conclusions. The present work has been carried out with simple aliphatic substrates. The results highlight the difference in the chemical reactivity between the radical cations of dioxolanes on one hand and oxathiolanes and dithiolanes on the other one. This photoinduced deprotection procedures operates on commonly used protected derivatives rather than requiring the elaboration of new protecting groups. Evaluation of the synthetic potential must await tests, although the easier oxidation of the thioketal moiety with respect to most chemical functionalities is promising. In view of the simple experimental set-up, the mild conditions, and the absence of the toxic reagents required in thermal oxidations, the method could be considered among standard procedures.

EXPERIMENTAL

The (thio)ketals were prepared according to published procedures. TCB was a commercial sample. Chl was purified by alumina chromatography and sublimation, and TPPT by recrystallization. DCA and MAP were prepared as described and purified by recrystallization. Product **11** had been previously reported.[16] Acid concentration in acetonitrile was established with a pHmeter versus a scale based on dilute HCl solutions. The acidity measured in a solution of purified Chl was 1×10^{-5} M, in the other cases $<5\times10^{-7}$ M.

Photodeprotection Experiments. Aliquots (5 mL) of a solution of the (thio)ketal (1×10^{-2}M) and the sensitizer (molarity, see Table 1) in a Pyrex tube were flushed with nitrogen or oxygen for 10 min, serum capped and irradiated by means of a multilamp apparatus fitted with 6 15W phosphor coated lamps (center of emission 320 or 360 nm). The reaction course was monitored by GC and HPLC.

Larger scale experiments were carried out on 1×10^{-1} or 1×10^{-2} M (thio)ketal solutions (100 mL) in an immersion well apparatus by irradiation with a 125 W medium pressure mercury arc through Pyrex. Under this conditions irradiation (3 h) of Chl/**3** (both 1×10^{-2} M) led to the consumption of 34% Chl. The gummy residue from the evaporation of the solution was chromatographed on silica gel eluting with a cyclohexane-benzene 8:2 mixture and gave (besides unreacted Chl) 15 mg (6%) $ChlH_2$ and 12 mg (5%) product **9**.

9, mp>250°C, Analysis: found: C, 32.0%; calculated for $C_{18}Cl_{10}O_6$: C, 32.4%; ^{13}C nmr ($CDCl_3$) δ 125.28, 125.29, 138.3, 140.9, 146.7, 150.2, 170.4, 170.9; ir (KBr) 1682, 1575, 1166 cm^{-1}; mass spectrum 662 (M^+, the expected pattern for a Cl_{10} derivative is observed)

Photophysical Experiments. Fluorescence quenching was measured by means of an Aminco Bowman MPF spectrofluorimeter. Quenching of Chl triplet was measured by flash photolysis using an apparatus previously described.[32]

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REFERENCES

1. Greene, T.W.; Wuts, P.G.M. *Protective Groups in Organic Synthesis*; Wiley: New York, 1991
2. Pillai, V.R.N., *Org.Photochem.* **1987**, *9*, 225. Pillai, V.R.N., *Synthesis* **1980**, 1
3. Hebert, J.; Gravel, D. *Can.J.Chem.* **1974**, *52*, 187. Gravel, D.; Hebert, J.; Thoraval, D. *Can.J.Chem.* **1983**,

61, 400

4. Takahashi, T.; Nakamura, C.Y.; Satoh, J.Y. *J.Chem.Soc., Chem.Commun.* **1977**, 680

5. Oikawa, Y.; Tanaka, T.; Horita, K. *Tetrahedron Lett.* **1984**, *25*, 5393. Schmittel, M.; Levis, M. *Synlett.* **1996**, 315

6. Tanemura, K.; Suzuki, T. Horaguchi, T. *J.Chem.Soc., Chem.Commun.* **1992**, 979

7. Oku, A.; Kinugasa, M.; Kamada, T. *Chem. Lett.* **1993**, 165. Zhang, Z.; Magnusson, G. *J.Org.Chem.* **1996**, *61*, 2394

8. Tanemura, K.; Suzuchi, T.; Horaguchi, T. *Bull.Chem.Soc.Jpn.* **1994**, *67*, 290. Tanemura, K.; Dohya, H.; Imamura, M.; Suzuki, T.; Horaguchi, T. *J.Chem.Soc., Perkin Trans.1* **1996**, 453

9. Masui, M.; Kawaguchi, T.; Ozaki, S. *J.Chem.Soc., Chem.Commun.* **1985**, 1484. Noyori, R.; Kurimoto, I. *J.Chem.Soc., Chem.Commun.* **1986**, 1425

10. Gourcy, J.; Martingly, P.; Simonet, J.; Jeminet, G. *Tetrahedron* **1981**, *37*, 1495. Platen, M.; Steckhan, E. *Chem. Ber.* **1984**, *117*, 1679

11. Kamata, M.; Kato, Y.; Hasegawa, E. *Tetrahedron Lett.* **1991**, *32*, 4349. Kamata, M.; Sato, M.; Hasegawa, E. *Tetrahedron Lett.* **1992**, *33*, 5085. Kamata, M.; Murakami, Y.; Tamagawa, Y.; Kato, M.; Hasegawa, E. *Tetrahedron* **1994**, *50*, 12821

12. Garcia, H.; Iborra, S.; Miranda, M. A.; Primo, J. *New J.Chem.* **1989**, *13*, 805. Yan, B.Z.; Zhang, Z.G.; Yuan, H.C.; Wang, L.C.; Xu, J.H. *J.Chem.Soc., Perkin Trans.2* **1994**, 2545

13. Fox, M.A.; Chanon, M. Photoinduced Electron Transfer, Elsevier, Amstderdam: 1988

14. Mattes, S.L.; Farid, S. *Org.Photochem.* **1983**, *6*, 233

15. Albini, A.; Mella, M.; Freccero, M. *Tetrahedron* **1994**, *50*, 575. Saeva, F.D. *Top.Curr.Chem.* **1991**, *156*, 59

16. Mella, M.; Fasani, E.; Albini, A. *J.Org.Chem.* **1992**, *57*, 3051

17. Rehm, D.; Weller, A. *Isr.J.Chem.* **1970**, *8*, 259

18. Steichen, D.S.; Foote, C.S. *J.Am.Chem.Soc.* **1981**, *103*, 1855. Araki, Y.; Dobrowolski, D.C.; Goyne, T.E.; Hanson, D.C.; Jiang, Z.Q.; Lee, K.J.; Foote, C.S. *J.Am.Chem.Soc.* **1984**, *106*, 4570. Tsuchya, M.; Ebbesen, T.W.; Nishimura, Y.; Sakuragi, H.; Tokumaru, K. *Chem.Lett.* **1987**, 2121. Albini, A.; Spreti, S. *Gazz.Chim.Ital.* **1985**, *115*, 227

19a. Chin, D.H.; Chiericato, G.; Nanni, E.J.; Sawyer, D.T. *J.Am.Chem.Soc.* **1982**, *104*, 1296 b. Sawyer, D.T.; Valentine, J.S. *Acc.Chem.Res.* **1981**, *14*, 393. c. Schaap, A.P.; Lopez, L.; Gagnon, S.D. *J.Am.Chem.Soc.* **1983**, *105*, 663.. d. Akaba, R.; Sakuragi, H.; Tokumaru, K. *J.Chem.Soc., Perkin Trans 2*, **1991**, 291. e. Lopez, L. *Top.Curr.Chem.* **1990**, *156*, 117. f. Fukuzumi, K.; Tanii, K.; Ishikawa, M.; Tanaka, T. *J.Chem.Soc., Perkin Trans.2* **1989**, 1801

20a. Direct measurements of the basicity are not available. A pKa value of -1.9 in water has been estimated, ref. 20b, and the value in an aprotic solvent is certainly largely positive. b. Baciocchi, E.; Del Giacco, T.; Elisei, F.; Ioele, M. *J.Org.Chem.* **1995**, *60*, 7974. c. Wagner, P.J.; Truman, R.J.; Puchalski, A.E.; Wake, R. *J.Am.Chem.Soc.* **1986**, *108*, 7727

21. Bonifacic, M.; Asmus, K.D. *J.Org.Chem.* **1986**, *51*, 1216

22. For an analogy see: Hashimoto, S.; Kurimoto, I.; Fujii, Y.; Noyori, R. *J.Am.Chem.Soc.* **1985**, *107*, 1427. Noyori, R.; Kurimoto, I. *J.Chem.Soc., Chem. Commun.* **1986**, 1425

23a. Wayner, D.D.M.; Dannenberg, J.J.; Griller, D. *Chem.Phys.Lett.* **1986**, *131*, 189. b. Evaluated BDE for $3^{+\cdot}$ deprotonation in 4 BDE = 92 - 23.06 (3.0 + 1.87) =-20.3 kcal M^{-1}, for fragmentation of the t-butyl radical

BDE = 82 - 23.06 (3.0 + 0.35) = +4.7 kcal M^{-1}, see ref.15 and 23a; notice that with a non nucleophilic radical anion ($TCB^{-\cdot}$) and a non nucleophilic solvent like MeCN only C-C bond fragmentation takes place, in accordance with previous experience (ref.15) showing that deprotonation of radical cations is a slower than other fragmentation under such conditions. In the case of $1^{+\cdot}$ for the deprotonation in 4 one can evaluate the BDE = 85 - 23.06 (1.6 + 1.87) = +5 kcal M^{-1}, while fragmentation of the t-butyl radical is by far too endothermic, BDE = 80 - 23.06 (1.6 + 0.8) = +25 kcal M^{-1}. The 4-C-H bond energy is taken as 85 kcal M^{-1} since it is reported that in aprotic solvents, this is close to the S-H BDE, ref. 23c,d; the Eox of the 2-dithiolanyl radical is estimated as -0.8 V by modification of that of the 2-dioxolanyl radical, see above. c. Inbar, S.; Linschitz, H.; Cohen, S.G. *J.Am.Chem.Soc.* **1982**, *104*, 1679. d. Fine, D.H.; Westmore, J.B. *Can.J.Chem.* **1970**, *48*, 395

24. Gleiter, R.; Hoffmann, H.; Irngartinger, H.; Nixdorf, M. *Chem. Ber.* **1994**, *127*, 2215
25. Sweigart, D.A.; Turner, D.W. *J.Am.Chem.Soc.* **1972**, *94*, 5599
26. Miller, L. *J.Org.Chem.* **1972**, *37*, 916
27. Kavarnos, G.J.; Turro, N.J. *Chem.Rev.* **1986**, *86*, 401
28. Fukuzumi, S.; Kuroda, S.; Taroka, T. *J.Chem.Soc., Chem.Commun.* **1986**, 1553. Poulos, A.T.; Hammond, G.S.; Burton, M.E. *Photochem.Photobiol.* **1981**, *34*, 169. Gebert, H.; Regenstein, W.; Bendig, J.; Kreysig, D. *Z.Phys.Chem.(Leipzig)* **1982**, *263*, 65. Bendig. J.; Kreysig, D.; Gebert, H.; Regenstein, W. *J.prakt.Chem.* **1979**, *321*, 420
29. Mella, M.; d'Alessandro, N.; Freccero, M.; Albini, A. *J.Chem.Soc., Perkin Trans. 2* **1993**, 515
30. Wintgens, V.; Kossanyi, J.; Sinalty, M. *Bull.Chem.Soc.Fr.* **1983**, II, 115
31. Photoinduced SET from thioethers to aromatic nitriles has been previously documented. Beecroft, R.A.; Davidson, R.S.; Goodwin, B.; Pratt, J.E. *Tetrahedron* **1984**, *40*, 4487
32. Mella, M.; Freccero, M.; Albini, A. *Tetrahedron* **1996**, *52*, 5549

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