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Deacetalization by Photoinduced Electron Transfer with a Pyrylium Salt: Effect of Limiting the Amounts of Water, Oxygen and Sensitizer

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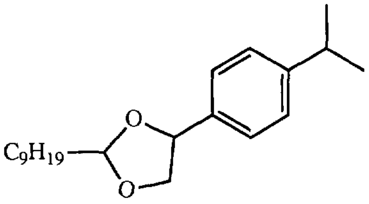
Abstract: The photodeacetalization of 4-(*p*-isopropylphenyl)-2-nonyl-1,3-dioxolane **1** using 2,4,6-triphenylpyrylium tetrafluoroborate (TPT) as sensitizer has been studied to explore the possibility of achieving a slow sunlight-controlled release of polymer-bound carbonyl functionalized semiochemicals. This reaction has been found to produce mainly *n*-decanal and *p*-isopropylbenzaldehyde, together with lower amounts of the corresponding acids. The degree of conversion and the product distribution depended on the presence of water or oxygen and the amount of photosensitizer. The results are justified through generation of the radical cation $\mathbf{1}^{+\cdot}$, followed by ring opening and trapping of the radical/cationic sites by oxygen or water. The delocalized 1,3-radical cations **III** and the ozonides **IV** appear to be involved as key intermediates. Formation of *n*-nonanal as a minor product is explained through cleavage of the C_2-nonyl bond of $\mathbf{1}^{+\cdot}$.

INTRODUCTION

The use of cyclic acetals as carbonyl protecting groups is a well-established methodology, which has been successfully applied to the synthesis of many natural and non-natural organic compounds with complex structures.[1] In general, the deprotection step is based on a simple Brönsted or Lewis acid-catalyzed hydrolytic cleavage of the acetal moiety. This can be a limiting drawback when the synthetic target contains further acid-labile functional groups. An alternative approach has made use of the photoinduced electron transfer (PET) concept, with 2,4,6-triphenylpyrylium tetrafluoroborate (TPT) as photosensitizer.[2-6]

Several acetals have been converted into the corresponding aldehydes or ketones by photolysis with long wavelength light ($\lambda > 400$ nm) in the presence of TPT; however the operating mechanism is not sufficiently understood. In the present work, we have undertaken a systematic examination of the PET-mediated cleavage of the 1,3-dioxolane **1** using TPT as photosensitizer, under a variety of conditions, trying to establish the effect of limiting the amounts of water, oxygen and TPT on the degree of conversion and the product selectivity. On the other hand, the introduction of a *p*-isopropylphenyl substituent at position 4 of the heterocyclic ring was expected to facilitate monitoring of the transformations undergone by the C_4-C_5 fragment, which in the unsubstituted compounds might give rise to highly volatile undetectable products. In the case of **1**, product analysis should reveal the presence of such C_4-C_5 derived products, thus providing a further insight into the reaction mechanism.



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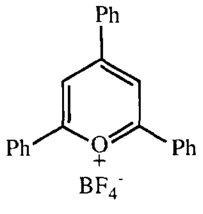


TPT

From the applied point of view, the dioxolane **1** was chosen as model compound to explore the possibility of achieving a slow sunlight-controlled release of polymer-bound carbonyl functionalized semiochemicals.[7] In this context, the synthetic route employed to obtain **1** starting from cumene (see Experimental) can be in principle extended to the functionalization of pending phenyl groups in a polystyrenic backbone.

RESULTS AND DISCUSSION

The required dioxolane **1** was prepared by the following sequence of reactions: a) Friedel-Crafts acylation of cumene with choroacetyl chloride, b) reduction of the obtained aryl ketone with sodium borohydride, c) basic hydrolysis of the resulting chlorohydrine to the corresponding glycol and d) final acetalization with *n*-decanal.

A series of PET-experiments were performed with solutions of **1** and TPT in methylene choride, using the Pyrex-filtered light of a 400 W mercury lamp. Under these conditions, the only absorbing species was the pyrylium salt acting as photosensitizer. Control experiments showed that no reaction occurred when **1** was irradiated in the absence of TPT or when the solutions of **1** and TPT were left in the dark. The results are given in Table 1. In all cases, *n*-decanal and *p*-isopropylbenzaldehyde, together with the respective carboxylic acids were obtained. Their yields depended on the reaction conditions.

Table 1. TPT-Photosensitized Deacetalization of Dioxolane **1**

Entry	TPT (%)[a]	H_2O[b]	O_2	**1**(%)[c]	R^2CHO (%)[d]	R^4CHO (%)[d]	R^2COOH (%)[d]	R^4COOH (%)[d]
1	20	0.1 ml	+	--	48	48	16	19
2	20	--	+	--	47	27	24	17
3	20	e	+	31	50	12	15	2
4	20	0.1 ml	-	54	35	26	3	2
5	5	--	+	16	32	20	26	14

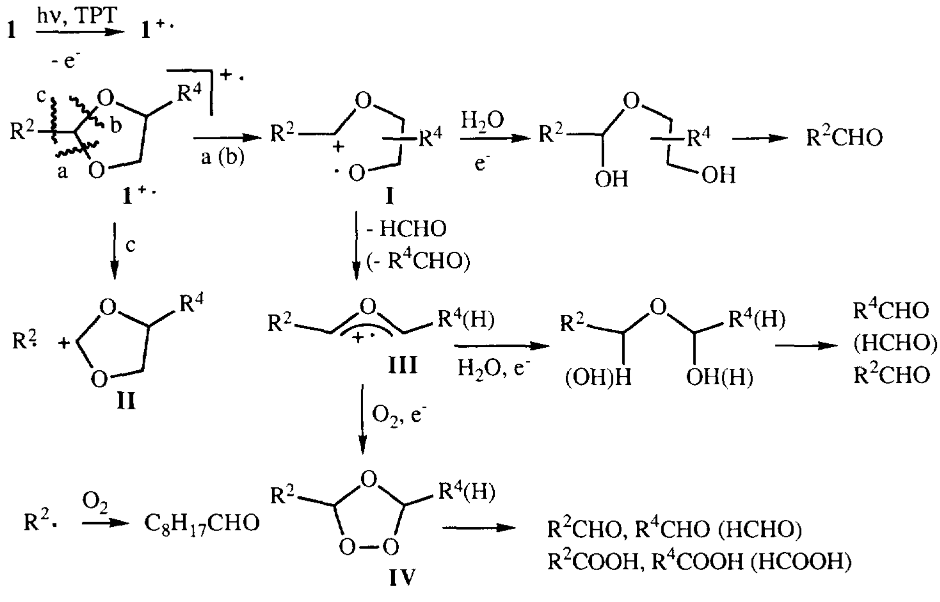
[a] Molar ratio TPT/**1**, in percentage. [b] Amount of water added to the distilled solvent. [c] Recovered dioxolane. [d] $R^2 = n$-C_9H_{19}, $R^4 = p$-$C_3H_7C_6H_4$. [e] Dry solvent was used.

Previously, a 1:2 molar ratio acetal/sensitizer was used,[2] based on the fact that anodic oxidation of the analogous thioacetals leading to the corresponding carbonyl compounds consumes 2 F per mol of thioacetal.[8] Table 1 clearly shows that hydrolysis of the dioxolane **1** proceeded to a considerable extent in the presence of much lower amounts of photosensitizer (20 or even 5 %). Thus, TPT is acting in a catalytic way.

A second point of interest is the role of water. When its content was drastically reduced (entry 3), the conversion decreased in a significant way and the yield of aromatic aldehyde as well as the accompanying acid were markedly lower.

Finally, the presence of oxygen was also found to enhance the process. Thus, when argon was bubbled prior to and during irradiation (entry 4) a considerable amount of the starting material remained unreacted. The two aldehydes were still obtained, but formation of the acids was almost completely prevented.

A reaction mechanism compatible with the above observations is depicted in Scheme 1. After generation of the radical cation **1**$^{+\cdot}$ three different types of bond cleavage might in principle take place: a) O_1-C_2, b) O_3-C_2 and c) C_2-R^2. Routes a and b lead to ring opening, with formation of intermediates **I** posessing an oxygen centered radical and a carbocationic center. It is interesting to note that the anodic oxidation of thioacetals is also thought to involve radical cations, which undergo an analogous sulfur-carbon bond cleavage.[8-10] Although acetals are much more difficult to oxidize, it has been reported that some of them undergo electron transfer-mediated deacetalization *via* oxygen-carbon bond cleavage at the radical cation stage.[11-13]



Scheme 1

In the case of the dioxolane **1**, subsequent β-scission of the alkoxy radical **I**[14] would give rise to delocalized 1,3-radical cations **III**, identical to those produced by cleavage of the carbon-carbon bond of oxiranes.[15-18] Trapping of these intermediates by oxygen, followed by decomposition of the resulting ozonides in the conventional manner, explains the isolation of aldehydes and carboxylic acids under aerobic conditions.

Alternatively, nucleophilic trapping of the cationic species **I** and **III** by water would result in the formation of aldehydes, but no acids could be produced in this way. Scheme 1 also explains the requirement of only catalytic amounts of the pyrylium salt, since back electron transfer must occur in the last steps of both routes.

As stated above, cleavage of the C_2-R^2 bond of $\mathbf{1}^{+\cdot}$ (process c) was in principle considered a reasonable possibility. Actually, this cleavage has been observed when the radical cations of acetals are generated in the gas phase (electron impact mass spectrometry) or upon γ-irradiation in freon matrices.[19,20] As a matter of fact, the base peak in the HRMS of **1** was attributed to cation **II** (m/z 191.1077, $C_{12}H_{15}O_2$). However, it was very significant that cleavages a (to give **III**, after loss of formaldehyde: m/z 288.2505, $C_{20}H_{32}O$) and b (to give *p*-isopropylbenzaldehyde: m/z 148.0865, $C_{10}H_{12}O$) were still clearly observable.

In order to check whether cleavage c also occurs in solution, at least to a low extent, the photomixture obtained under the conditions of entry 2 was submitted to GC/MS analysis. The major chromatographic peaks showed good correspondence with the products of Table 1, but in this case minor amounts of *n*-nonanal were also detected. Not even traces of this compound were contaminating the *n*-decanal employed for the synthesis of **1**. Hence, it was considered to be a true reaction product, and its structure was safely assigned by comparison with an authentic sample. The involved mechanistic route is indicated in Scheme 1: C_2-R^2 scission to give **II** plus a nonyl radical, followed by oxygen trapping of the latter.

In summary, PET-mediated deacetalization can be achieved in moderate yields using catalytic amounts of pyrylium salts as photosensitizers. The reaction is enhanced in the presence of both water and oxygen. A plausible mechanism involving radical cations as intermediates has been proposed, and a correlation has been established with the behaviour of similar species in the gas phase. The potential use of this concept to produce a slow sunlight-controlled release of polymer-bound semiochemicals is currently under study.

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EXPERIMENTAL

Melting points are uncorrected and were measured using a Reichert apparatus. Ir spectral data were obtained for liquid film or KBr discs, with a Bio Rad FTS-7 spectrophotometer; the wavenumber values (ν_{max}, cm^{-1}) are indicated only for the most significant bands. ^1H- and ^{13}C-nmr spectra were recorded in $CDCl_3$ with Bruker AC-250, Varian Unity-300 or Varian Unity-400 spectrometers. Chemical shifts are reported as δ values (ppm) using TMS as internal standard. High resolution mass spectra were recorded in a VG AutoSpec spectrometer (Fisons); m/z ratio and relative abundances in percentages (in brackets) are given only for the main peaks. Elemental analyses were determined by " Centro de Investigación y Desarrollo (CSIC) de Barcelona".

Preparation of 4-(p-isopropylphenyl)-2-nonyl-1,3-dioxolane 1

Aluminium trichloride (6.87 g, 50 mmol) was added portionwise to a vigorously stirred solution of cumene (3.04 g, 25 mmol) and chloroacetyl chloride (5.0 g, 44.3 mmol) in carbon disulfide (20 ml). The mixture was heated under reflux for 30 min, and poured carefully on ice (20 g) and conc hydrochloric acid (2 ml). After extraction with methylene chloride, the organic layer was washed with dil hydrochloric acid, aqueous sodium bicarbonate and water. Evaporation of the solvent gave *p*-isopropyl-α-chloroacetophenone[21] (4.73 g, 96 %). A solution of sodium borohydride (4.16 g, 0.11 mol) in water (90 ml) was added to ice-water cooled *p*-isopropyl-α-chloroacetophenone (19.67 g, 0.10 mol) in ethanol (180 ml). The mixture was stirred at room temperature and poured slowly onto ice-water (400 ml) and conc hydrochloric acid (45 ml). The solvent was partly evaporated, and the residue extracted with methylene chloride. The organic layer was washed with dil hydrochloric acid, aqueous sodium bicarbonate and water, and dried (Na_2SO_4). Evaporation of the solvent gave 1-(*p*-isopropylphenyl)-2-chloroethanol (19.28 g, 97 %) as a dark oil, which was used without further purification. Ir: 3400 (OH); ^{1}H-nmr: 7.30 and 7.22 (AA'BB', J = 8.2 Hz, 4 H, ArH), 4.86 (dd, J_1 = 8.4 Hz, J_2 = 3.8 Hz, ArC*H*OH), 3.77-3.58 (m, 2 H, CH_2Cl), 2.90 (m, 1 H, ArC*H*Me_2), 2.60 (bs, 1 H, OH), 1.24 (d, J = 6.9 Hz, 6H, 2xCH_3). ^{13}C-nmr: 149.2 (1 C), 137.3 (1 C), 126.8 (2 CH), 126.0 (2 CH), 73.9 (1 CH), 50.8 (1 CH_2), 33.8 (1 CH), 23.9 (2 CH_3).

10 % Aqueous potassium carbonate (390 ml) was added to a solution of 1-(*p*-isopropylphenyl)-2-chloroethanol (39.25 g, 0.197 mol) in ethanol (100 ml). The mixture was heated under reflux for 32 h and then saturated with sodium chloride and extracted with methylene chloride. The organic layer was washed with water and dried. Evaporation of the solvent gave an orange oil, which was washed several times with hot hexane, to give 1-(*p*-isopropylphenyl)-1,2-ethanediol (23.85 g, 67 %) as a white fine dust, mp 93-94.5 °C. Analysis: C 73.34, H 8.86 %; Calcd. for $C_{11}H_{16}O_2$: C 73.30, H 8.95 %. Ir: 3400 (OH); ^{1}H-nmr: 7.30 and 7.19 (AA'BB', J = 8.3 Hz, 4 H, ArH), 4.78 (dd, J_1 = 7.7 Hz, J_2 = 4.0 Hz, ArC*H*OH), 3.75-3.61 (m, 2 H, CH_2OH), 2.89 (m, 1 H, ArC*H*Me_2), 2.58 (bs, 2 H, 2xOH), 1.23 (d, J = 6.9 Hz, 6H, 2xCH_3). ^{13}C-nmr: 148.6 (1 C), 137.9 (1 C), 126.5 (2 CH), 126.1 (2 CH), 74.6 (1 CH), 68.0 (1 CH_2), 33.8 (1 CH), 23.9 (2 CH_3).

A solution of 1-(*p*-isopropylphenyl)-1,2-ethanediol (0.81 g, 4.5 mmol), *n*-decanal (0.50 g, 3.0 mmol) and *p*-toluenesulfonic acid (15 mg) in dry benzene (40 ml) was heated under reflux for 1 h, with continuous azeotropic removal of water in a Dean-Stark apparatus. The solution was washed with aqueous sodium bicarbonate and brine, and dried. Evaporation of the solvent gave a colourless oil, which was filtered through a short column of silica gel to obtain a 1:1 diastereoisomeric mixture of *4-(p-isopropylphenyl)-2-nonyl-1,3-dioxolane 1* (0.90 g, 94 %). Analysis: C 79.16, H 10.59 %; Calcd. for $C_{21}H_{34}O_2$: C 79.19, H 10.76 %. HRMS: 318.2570 (1), 317.2485 (2), 288.2505 (1), 272.2505 (2), 245.1914 (2), 229.1937 (2), 191.1077 (100), 148.0865 (4), 121.0653 (97). Column chromatography with hexane as eluant allowed isolation of the *trans* isomer. ^{1}H-nmr: 7.26 and 7.20 (AA'BB', J = 8.3 Hz, 4 H, ArH), 5.22 (t, J = 4.8 Hz, 1H, C_2-H), 5.00 (dd, J_1 = 8.0 Hz, J_2 = 6.4 Hz, 1H, C_4-H), 4.36 (dd, J_1 = 8.4 Hz, J_2 = 6.4 Hz, 1H, C_5-H), 3.70 (t, J = 8.2 Hz, 1H, C_5-H), 2.89 (m, 1 H, ArC*H*Me_2), 1.74-1.69 (m, 2 H, C_2-H_2), 1.52-1.41 (m, 2 H, C_2-C-CH_2), 1.40-1.20 (m, 18 H, 6xCH_2 + 2xCH_3), 0.87 (t, J = 6.7 Hz, 3 H, CH_2C*H_3*). NOE experiments: on irradiation at δ 1.72, NOE is observed at δ 5.22, 5.00 and 4.36; on irradiation at δ 5.00, NOE is observed at δ 7.23, 4.36 and 1.72; on irradiation at d 5.22 NOE is observed at δ 7.23, 3.70 and 1.72.^{13}C-nmr: 148.7 (1 C), 137.1 (1 C), 126.6 (2 CH), 126.1 (2 CH), 105.7 (CH), 77.4 (1 CH), 72.5 (1 CH_2), 34.4 (1 CH_2), 33.8 (1 CH), 31.9-24.0 (6 CH_2), 23.9 (2 CH_3), 22.6 (CH_2), 14.1 (CH_3). Further elution gave the *cis* isomer. ^{1}H-nmr: 7.29 and 7.20 (AA'BB', J = 8.2 Hz, 4 H, ArH), 5.06 (t, J = 4.8 Hz, 1H, C_2-H), 4.96 (t, J = 6.8 Hz, 1H, C_4-H), 4.15 (t, J = 7.2 Hz, 1H, C_5-H), 3.74 (dd, J_1 = 7.9 Hz, J_2 = 6.8 Hz, 1H, C_5-H), 2.89 (m, 1 H, ArC*H*Me_2), 1.83-1.74 (m, 2 H, C_2-H_2), 1.55-1.20 (m, 20 H, 7xCH_2 + 2xCH_3), 0.87 (m, 3 H, CH_3). NOE experiments: on irradiation at δ 4.15, NOE is observed at δ 4.96 and 3.74.

General Irradiation Procedure

A stirred solution of the dioxolane **1** (0.251 g, 0.79 mmol) and TPT (0.066 g, 0.17 mmol) in methylene chloride (125 ml) was placed in a Pyrex cylindrical flask provided with cooling system and irradiated for 4 h with two 400 W medium pressure mercury lamps. The solution was extracted with 1 M sodium hydroxide (3 x 33 ml). The organic layer was washed with brine and dried. The solvent was evaporated, and the residue filtered through a short silica gel column with hexane as eluant. Evaporation of the solvent gave a yellow oil, whose ^{1}H-nmr spectrum allowed identification of *n*-decanal and *p*-isopropylbenzaldehyde as main components of the mixture. The aqueous layer was acidified with conc hydrochloric acid under cooling and extracted with ethyl acetate. The solvent was dried and evaporated to give a dark solid material, whose ^{1}H-nmr spectrum allowed identification of decanoic acid and *p*-isopropylbenzoic acid.

In one case the solvent was carefully dried, while in other experiments water (0.1 ml) was added to the reaction mixture. Eventually, argon was bubbled through the solution prior to and during irradiation.

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