Photochemistry of o-Allylphenol. Identification of the Minor Products and New Mechanistic Proposals

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Received August 11, 1992

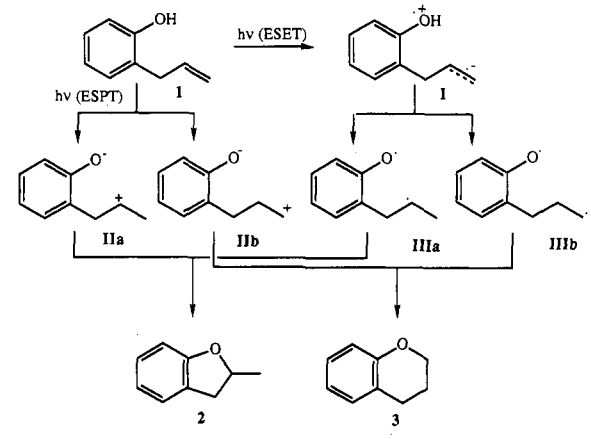
The photochemistry of o-allylphenol (1) in cyclohexane has been reinvestigated. Besides the previously reported cyclic ethers 2 and 3, seven additional minor photoproducts have been detected. Spectroscopic methods, coupled with independent synthesis, have allowed their identification as 2-methylbenzofuran (5), o-propylphenol (8), the epoxide 4, the dihydroxy compound 9, the cyclohexyl ether 6, o-(cyclohexylmethyl)phenol (10), and the dimer 7. Their formation is rationalized through new mechanistic pathways, which involve initial intermolecular electron and/or proton transfer between two molecules of o-allylphenol, as well as di-π-methane rearrangement. Key intermediates appear to be radical V, carbenium ion IX, and carbene XI. This is supported by photolysis of o-allylphenyl acetate (11), which leads to the formation of a radical pair, followed by in cage recombination to the photo-Fries products 12 and 13 or, alternatively, diffusion of the radicals out of the solvent cage to afford the minor products 2, 5, and 6, identical to those obtained by photolysis of 1.

Introduction

The photocyclization of o-allylphenol and related compounds to products with dihydrobenzofuran and/or dihydrobenzopyran structures has been known since 1967.[1] In the last 25 years this reaction has attracted considerable attention, as evidenced by the number of reports appearing in the chemical literature on this topic.[2] However, there is some controversy concerning its mechanistic aspects. The reaction was initially thought to proceed through excited-state proton transfer (ESPT) from the phenolic group to the double bond;[1a,2d] by contrast, later rationalizations have assumed that the key step in this process is intramolecular excited-state electron transfer (ESET) from the phenolic moiety to the olefin (Scheme I).[3] This mechanistic question still remains open, although a very recent work on the photocyclization of vicinal allylnaphthols[2f] has provided evidence to substantiate the ESPT mechanism.

Be this as it may, both mechanisms explain the observed preferential formation of five-membered ring products in view of the the higher stability of the secondary carbenium ion or radical intermediates as precursors. In this context, it would be helpful to conduct a careful product study to check the validity of the accepted mechanistic pathways. In the course of our work on the synthetic applications of the photo-Fries rearrangements[4] we have examined the photochemistry of o-allylphenyl acetate (11). The results led us to reinvestigate the photolysis of o-allylphenol. Besides the reported photocyclization to 2 and 3 we detected several minor photoproducts, whose structures

Scheme I



were assigned by GC/MS and unambiguously confirmed by independent synthesis. The formation of these products cannot be accounted for in terms of the currently accepted mechanisms and requires revision.

Results and Discussion

Photolysis of o-allylphenol was performed in oxygen-saturated cyclohexane solution (ca. 10^{-2} M) during 4 h. A control was run under argon. Analysis of the photolysates by GC revealed that the major photoproduct ws the five-membered ring cyclic ether 2 (yield: 21%), accompanied by minor amounts (3%) of the regioisomer 3. A substantial part of starting material (62%) remained unreacted. In addition, on careful examination of the chromatograms seven additional photoproducts (4–10) were detected in low amounts (less than 1%). Under argon, product 4 was not detected. Although from the preparative point of view these minor products are not significant, we thought that elucidation of their structures might shed new light on the existing mechanistic uncertainties in this process. Therefore, the photolysates were submitted to GC/MS analysis in order to obtain tentative structures on the basis of the m/z values of the molecular ions and the observed fragmentation patterns. Confirmation of the structures was done in all cases by comparison with available

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0022-3263/93/1958-3304$04.00/0

authentic samples or unambiguous synthesis by using well-established procedures.

The product with the shortest retention time had a molecular ion peak of 132 amu and corresponds, therefore, to a dehydrogenated photoproduct of *o*-allylphenol. Its MS was identical to that of commercial 2-methylbenzofuran (**5**).

The second product was identified as 2-propylphenol (**8**), the hydrogenated analogue of **1**, on the basis of its superimposable MS (M^+, 136) to that of purchased **8**.

The third minor photoproduct (obtained only under oxygen) possesses a molecular ion peak at *m/z* 150 and was assigned as the epoxide of *o*-allylphenol (**4**).[5] This was confirmed by treatment of **1** with *m*-chloroperbenzoic acid, whereby the epoxide **4** was obtained with identical GC retention time and MS fragmentation pattern. IR and ^1H NMR spectral data of the synthesized sample were also in agreement with the proposed structure.

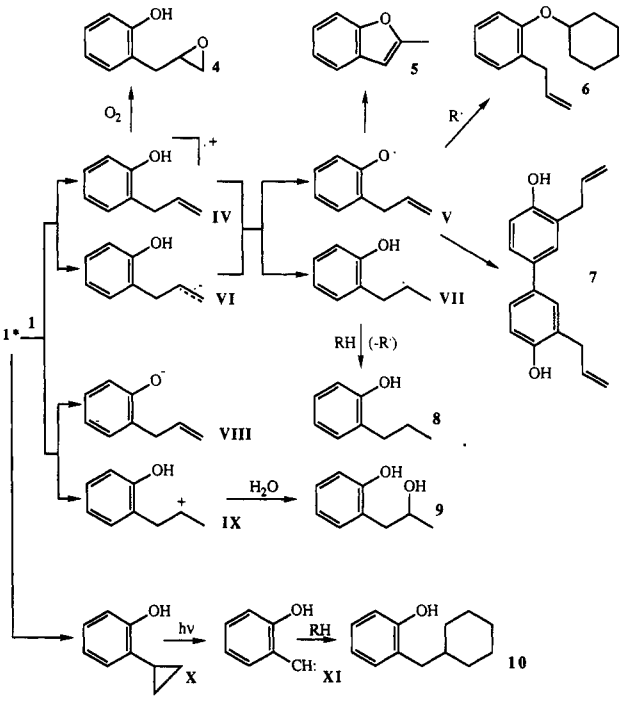
The fourth product exhibited a structure compatible with the MS of the dihydroxy derivative **9** (M^+: *m/z* 152), formally derived from hydration of the olefin moiety of **1**. This photoproduct had not been previously described. We decided to prepare **9** by oxymercuriation–demercuriation of **1**, a reaction reported to give the cyclic ether **2** as the only product.[6] In spite of this precedent, the dihydroxy derivative **9** was indeed obtained in good yield, with **2** as byproduct. The retention times and MS of isolated **9** matched those of the photoproduct. Also, the IR and ^1H NMR spectra are in support of the structural assignment. We were unable to obtain an analytical sample of **9** (probably due to partial dehydration), but treatment with acetyl chloride produced the corresponding diacetate **14**, which gave satisfactory combustion analysis.

The fifth product had a molecular ion of 216 amu and corresponds, therefore, to cyclohexane incorporation. Accordingly, the base peak corresponded to an *m/z* value of 134 (*o*-allylphenol). Among the possible isomeric structures, and most plausible from the mechanistic point of view was the previously unknown cyclohexyl ether **6**. This compound was independently synthesized by reaction of allylphenol with cyclohexyl chloride in the presence of silver nitrate. A comparison of the GC retention times and MS fragmentation patterns confirmed the structure proposed for the photoproduct. Full IR and ^1H NMR spectral data, as well as combustion analysis, completed identification of **6**.

The next product detected by GC/MS was thought to be *o*-(cyclohexylmethyl)phenol (**10**) on the basis of its molecular ion (M^+: *m/z* 190) and the presence of characteristic fragment ions with *m/z* 108 (*o*-methylphenol, base peak) and 107 (*o*-quinone methide). The synthesis of this photoproduct was accomplished from phenol and cyclohexanecarboxylic acid in three steps: esterification, Fries rearrangement, and subsequent Clemmensen reduction of the intermediate hydroxy ketone. This authentic product was identical to that obtained upon irradiation of **1** (GC retention times and MS). Since it is unknown, its identification was completed by combustion analysis, IR and ^1H NMR spectroscopy.

The last photoproduct was a dimer of *o*-allylphenol, as evidenced by the *m/z* value (266) of its molecular peak.

Scheme II



RH = Cyclohexane

For definitive identification, we performed the oxidative coupling of **1** by means of cerium(IV) sulfate. A mixture of dimers was obtained, from which the major component was isolated by column chromatography. Physical data and spectral analyses allowed us to assign this product to the known structure of 4,4′-dihydroxy-3,3′-di(2-propenyl)-biphenyl (**7**).[7] Good correspondence was obtained upon comparison of its GC retention time and MS fragmentation with those of the photodimer.

Our careful product study of the photolysate obtained by irradiation of *o*-allylphenol in cyclohexane solution in the presence of air oxygen has allowed us to identify the seven new photoproducts **4–10**, which went unnoticed in previous work.[1,2] Photoproducts **5–10** were also obtained under argon. More significant, their formation cannot be explained in terms of the two currently accepted mechanisms, i.e., intramolecular excited-state electron transfer and/or proton transfer.

These pathways operate through the intermediates **I–III**, while the new photoproducts reported in this paper appear to require the involvement of other intermediates. For instance, the formation of **9**, **6**, and **10** can be rationalized readily from the carbenium ion **IX**, the radical **V**, and the carbene **XI**. We propose that, in the addition to the previously established intramolecular electron or proton transfers, analogous processes take place intermolecularly for *o*-allylphenol (see Scheme II). Oxygenation of the radical cation **IV** would lead to the epoxide **4**, a process which is well substantiated in the literature.[8] Hydrogenation of the *o*-allylphenol (**1**) to **8** is initiated through acceptance of an electron by the olefin. The following steps from **VI** are self-evident and do not deserve more detailed comments.

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(6) (a) Adams, R., Roman, F. L.; Sperry, W. N. *J. Am. Chem. Soc.* **1922**, *44*, 1781. (b) Mills, L. E.; Adams, R. *J. Am. Chem. Soc.* **1923**, *45*, 1842.

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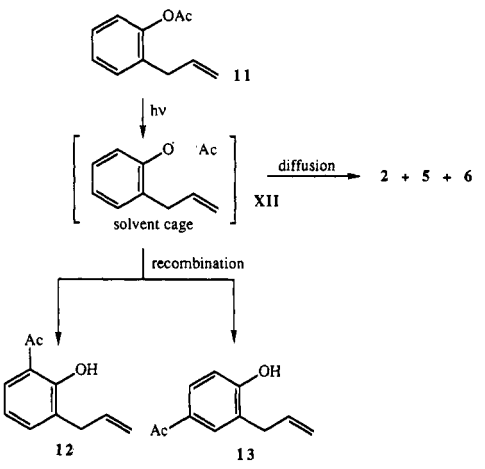
Scheme III



A key intermediate in the photochemistry of **1** is undoubtly the *o*-allylphenoxy radical (**V**). This species undergoes intermolecular radical reactions (C–C coupling to the dimer **7** or O–C coupling to the ther **6**), as well as intramolecular addition to the double bond to give ultimately the benzofuran **5**. Further support in favor of the proposed mechanism is the detection of dicyclohexyl ether in the photomixture, which would arise from coupling of cyclohexyl radical with cyclohexyloxy radical. The latter species is known to intervene when cyclohexyl radical is generated in the presence of oxygen.[9]

As suggested above, the formation of *o*-cyclohexylmethylphenol (**10**) can be best justified as the result of *o*-hydroxyphenyl carbene (**XI**) insertion into a carbon–hydrogen bond of cyclohexane. The di-π-methane rearrangement of **1**, followed by photochemical cleavage of the resulting *o*-cyclopropylphenol (**X**) with extrusion of ethylene, is postulated as possible route to the carbene **XI**. The facts that photolysis of the methyl ether of *o*-allylphenol gives rise to an analogous cyclopropyl derivative[10] and that phenylcyclopropanes are known to undergo photoextrusion of olefins with formation of phenyl carbene[11] constitute literature precedents in support of the proposed mechanistic pathway.

Further experimental evidence for the proposed photochemistry of **1** was obtained from photolysis experiments carried out with the acetate of *o*-allylphenol (**11**).[12] The major photoproduct was in this case the *o*-hydroxy ketone **12**,[2d] which arises from photo-Fries rearrangement of the phenyl ester moiety. A smaller amount of the para isomer **13**[2d] was also obtained. Again, a careful analysis by GC/MS allowed us to detect three minor photoproducts (ca. 1%). Their structures were assigned as those corresponding to products **2**, **5**, and **6** by comparison with the authentic materials obtained in the photolysis of *o*-allylphenol.

It is well established that photo-Fries rearrangement of aryl esters takes place through homolysis of the carbonyl–oxygen bond to afford solvent-caged acyl–aryloxy radical pairs (Scheme III).[4] Radical recombination at the ortho or para carbons of the ring leads to the rearranged hydroxy ketones. This model also explains formation of the detected minor products: diffusion of the allylphenoxy radical (**V**) out of the solvent cage gives rise to the statistically free radical, identical to the species generated in the photolysis of *o*-allylphenol. The steps which lead from this radical to the photoproducts have been already discussed.

Experimental Section

Melting points are uncorrected IR spectra were obtained in CCl_4 solutions; ν_{max} (cm^{-1}) is given only for the main bands. ^1H NMR spectra were measured in CCl_4 with a 60-MHz instrument; chemical shifts are reported in δ (ppm), using TMS as internal standard. Mass spectra were obtained under electron impact; the ratios m/z and the relative intensities are reported. Combustion analyses were performed at the Instituto de Química Bio-Orgánica of the CSIC in Barcelona. Isolation and purification were done by flash column chromatography on silica gel Merck 60 (0.040–0.063 mm), by conventional column chromatography on silica gel Merck 60 (0.063–0.200 mm), or by preparative layer chromatography on silica gel Merck 60 PF_{254}, using hexane or dichloromethane as eluent.

Irradiation Procedure. Solutions of 1.00 g of *o*-allylphenol (**1**) or its acetate **11** in cyclohexane (400 mL) were irradiated for 6 h with a 125-W medium-pressure mercury lamp inside a quartz immersion well, under continuous magnetic stirring. After evaporation of the solvent, the photomixtures were analyzed by GC/MS. Upon irradiation of **1**, photoproducts **4**–**10** were detected in low amounts (less than 1%, relative ratios 1/1/5/2/5/3/1). The major photoproducts **2**, **3**, **12**, and **13** were isolated by means of flash column chromatography (hexane). The structures of the minor photoproducts were assigned by comparison of their GC retention times and mass spectral data with those of authentic samples. Compounds **5** and **8** were commercially available (Aldrich Catalog Nos. 22434-O and P 5360-8), while compounds **4**[5] and **7**[7] were obtained by standard methods. Alternative syntheses were designed for the new compounds **6**, **9** and **10** (see below).

Preparation of *o*-(2-Hydroxypropyl)phenol (9). *o*-Allylphenol (6.70 g, 50.0 mmol) was added to a solution of mercuric acetate (6.00 g, 50.0 mmol) in 100 mL of water/tetrahydrofuran (1:1 vol/vol). The reaction mixture was stirred at room temperature for 1 h. Then, 50 mL of NaOH (3 M) and subsequently a solution of $NaBH_4$ (1.00 g, 25.0 mmol) in 50 mL of NaOH (3 M) were added. The reaction was stirred for 3 h at 25 °C. After the mercury layer and the aqueous alkaline phase was separated, the organic layer was retained. The aqueous phase was extracted with ether. The organic layer was combined with the ether extract and evaporated. The residue (5.30 g) was submitted to column chromatography (dichloromethane), yielding unreacted *o*-allylphenol (2.44 g, 46%), 2-methyl-2,3-dihydrobenzofuran (**2**) (0.58 g, 11%) and the desired dihydroxy compound **9** (2.27 g, 43%). Oil. IR: 3600–3200 (br, OH). ^1H NMR: 7.1 (m, 4H, Ar*H*), 6.1 (br s, 2H, O*H*), 4.2 (m, 1H, C*H*), 2.8 (d, J = 5 Hz, 2H, CH_2), 1.2 (d, J = 6 Hz, 3H, CH_3). MS: 152 (M^+, 25), 108 (100), 107 (56), 77 (33), 45 (18). To achieve a satisfactory combustion analysis, the diacetate **14** was prepared by adding acetyl chloride (1.4 mL, 19.6 mmol) to a solution of **9** (1.00 g, 6.57 mmol) in dichloromethane (25 mL) containing potassium carbonate (2.00 g). The reaction mixture was stirred during 3 h. Filtration and evaporation of the solvent gave **14** in quantitative yield. An analytical sample was obtained by preparative layer chromatography (dichloromethane). Oil. Anal. C, 66.21; H, 6.91 (Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.82). IR: 1760 and 1730 (C=O, ester); ^1H NMR: 7.2 (m, 4H, Ar*H*), 5.2 (m, 1H, C*H*), 2.8 (dd+dd, J_{gem} = 14 Hz, J_{vic} = 6 Hz, 2H, CH_2), 2.4 (s, 3H, ArOCOCH_3), 2.0 (s, 3H, CHOCOCH_3), 1.2 (d, J = 7 Hz, 3H, CHCH_3). MS: 236 (M^+, 1), 194 (1), 176 (17), 134 (100), 119 (20), 107 (35), 43 (79).

Preparation of *o*-Allylphenyl Cyclohexyl Ether (6). Cyclohexyl chloride (1.76 g, 14.9 mmol) and silver nitrate (2.58 g) were added to *o*-allylphenol (2.00 g, 14.9 mmol). The resulting mixture was stirred for 4 h at room temperature and then filtered.

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The filtrate was purified by column chromatography (hexane), giving the ether **6** (0.2 g, 6%) as the only identifiable product. Most of the starting *o*-allylphenol (80%) was recovered unchanged. The reaction was not optimized, since the amount of **6** obtained was enough to perform its complete characterization. An analytical sample was obtained by preparative layer chromatography (hexane). Oil. Anal. C, 83.27; H, 9.43 (Calcd for $C_{15}H_{20}O$: C, 83.28; H, 9.32). ^{1}H NMR: 7.0 (m, 4H, Ar*H*), 6.5–5.7 (m, 1H, C*H*=CH_2), 5.3–4.8 (m, 2H, CH=CH_2), 4.5 (m, 1H, OC*H*), 3.4 (d, J = 7 Hz, 2H, CH_2), 1.6 (m, 10H, (CH_2)$_5$). MS: 216 (M^+, 15), 134 (100), 133 (24), 119 (31), 55 (20).

Preparation of *o*-(Cyclohexylmethyl)phenol (10). Cyclohexanecarboxyl chloride (6.56 g, 44.0 mmol) was added to a solution of phenol (4.13 g, 44.0 mmol) in 50 mL of benzene, in the presence of magnesium (2.00 g, 80.0 mmol). The reaction mixture was refluxed for 3 h, filtered, washed with 10% NaOH and then with water, dried (Na_2SO_4), and concentrated in vacuo to afford phenyl cyclohexanecarboxylate (**15**)[13] (8.10 g, 90%). Three g of $AlCl_3$ was added to 3.00 g (14.7 mmol) of the ester **15**. The reaction mixture was maintained at 150 °C for 3 h and then poured onto a cold aqueous solution of HCl (20%). The resulting suspension was extracted with ether, and the extract was evaporated, affording an oily residue, which was purified by column chromatography (dichloromethane). This led to the obtention of cyclohexyl 2-hydroxyphenyl ketone (**16**)[14] (2.10 g, 70%). Eight g of zinc was added to a solution of mercuric chloride (1.00 g) in 20 mL of HCl (0.6 M). After the liquid layer was separated, 18 mL of HCl (8 M), 1.00 g of the ketone **16**, and 6 mL of toluene were consecutively added to the remaining solid. The reaction mixture was refluxed for 3 h, and then 15 mL of water was added. Extraction with ether, followed by evaporation of the solvent, gave a residue which was purified by column chromatography (dichloromethane), affording 0.65 g of *o*-(cyclohexylmethyl)phenol (**10**) (yield: 70%). An analytical sample was obtained by recrystallization from petroleum ether. Mp: 60–61 °C. Anal. C, 82.26; H, 9.60 (Calcd for $C_{13}H_{18}O$: C, 82.05; H, 9.53). IR: 3500–3200 (OH). ^{1}H NMR: 7.0 (m, 4H, Ar*H*), 5.1 (br s, 1H, O*H*), 2.5 (d, J = 6 Hz, 2H, CH_2), 2.0–0.7 (m, 11H, C_6H_{11}). MS: 190 (M^+, 15), 108 (100), 107 (45), 83 (13), 77 (15).

Acknowledgment. Financial support by the DGICYT (Grant PB-88 0494) is gratefully acknowledged. We also thank Mr. Manuel Adelantado for his excellent technical assistance in the mass spectral measurements.

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