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Multiple-Photon Chemistry in the Benzophenone Photoreduction during Laser-Jet Photolysis: Effect of Alcohol Solvent on Cross-Coupling *versus* Hydrogen Abstraction of the Electronically Excited Hydroxydiphenylmethyl Radical

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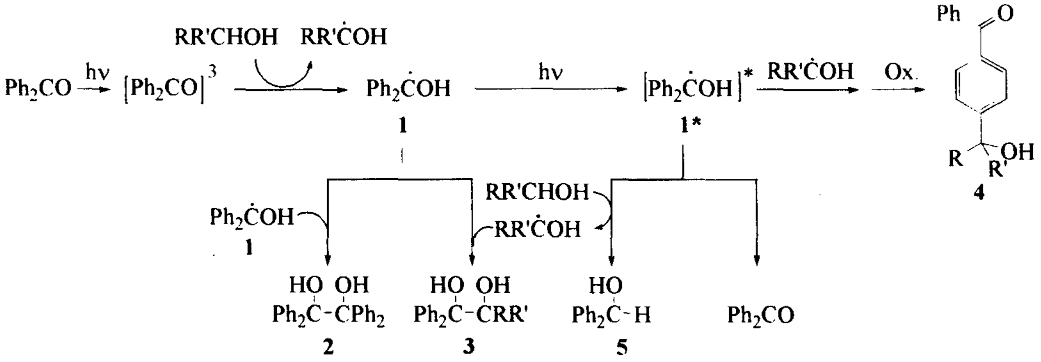
Abstract: The ground state of the hydroxydiphenylmethyl radical (**1**) leads to benzpinacol (**2**) through *head-to-head* coupling and the diols **3** as cross-coupling product. In contrast, under the high-intensity conditions of the laser-jet photolysis, the excited radical **1*** couples in the *para* position to afford the benzophenone derivatives **4** (*head-to-tail* coupling) (higher spin density at the *para* position / AM1 calculations). The major two-photon product is benzhydrol (**5**). The pronounced increase in hydrogen atom abstraction from MeOH to *i*PrOH by **1*** is explained in terms of the greater electrophilic character of the electronically excited radical **1*** *versus* its ground state. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

One of the best investigated photochemical systems is the photoreduction of triplet benzophenone with isopropanol.[1] The electronically excited benzophenone abstracts a hydrogen atom from the solvent to generate a pair of hydroxydiphenylmethyl **1** and the solvent-derived radicals (Scheme 1, left branch), as established by EPR spectroscopy. Subsequently, the ground-state hydroxydiphenylmethyl radical (**1**) may dimerize to benzpinacol (**2**) and cross-couple with the solvent-derived hydroxyalkyl radicals to the mixed pinacol **3** (Scheme 1).



Scheme 1. Reactions of the ground-state and electronically excited hydroxydiphenylmethyl radical (**1**)

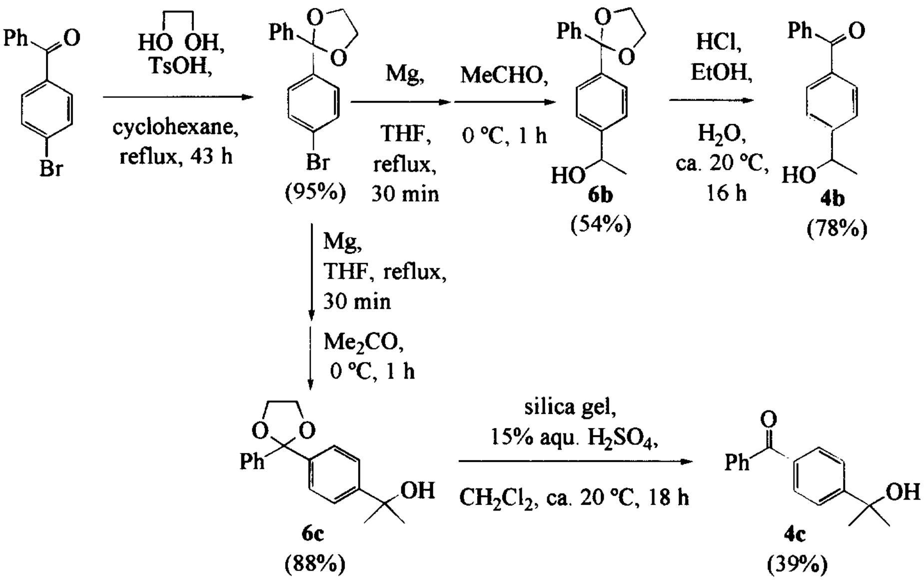
Earlier investigations on the conventional photochemistry of benzophenone in various hydrogen-donating alcohols have shown that isopropanol possesses special attributes in that, as established by Weiner,[2] an efficient cage effect was proposed to operate due to effective hydrogen bonding.[3] However, in another study[4] it was found that in isopropanol the benzpinacol (**2**) was the main product, while in methanol and ethanol the mixed pinacols **3** dominated.[4] Steric factors rather than cage effects were held responsible.[4]

Our former investigations on the laser-jet photochemistry of benzophenone in hydrogen-donating solvents revealed transformations of the electronically excited hydroxydiphenylmethyl radical (**1**).[5] Thus, in ethanol as hydrogen-donating solvent, besides the one-photon products benzpinacol (**2**) and diol **3b** (Scheme 1, right branch), benzhydrol (**5**) and the *para*-coupling product **4b** figure as two-photon products. Addition of free radicals at the *para* position of aromatic rings, as postulated for the formation of **4b**, is also known for other cases.[6] A particular example is the photoreduction of xanthone in ethanol,[7] in which also *para*-coupling was observed as two-photon product but not xanthol.

In view of the earlier studies[4] on the photoreduction of benzophenone as a function of the hydrogen-donating propensity of the solvent under conventional low-intensity conditions, it was of photomechanistic interest to explore such solvent effects on the two-photon process under high-intensity irradiation. Presently we report our laser-jet results on the chemistry of the electronically excited hydroxydiphenylmethyl radical (**1***) in methanol, ethanol, and isopropanol.

RESULTS AND DISCUSSION

The synthesis of the alcohol **4a** was performed according to reported procedures[8] by employing a Friedel-Crafts reaction of toluene with benzoyl chloride, bromination, and hydrolysis. Authentic samples of the products **4b** and **4c** were synthesized as shown in Scheme 2. Protection of the keto group,[9] Grignard reaction with acetaldehyde or acetone and deprotection under acidic conditions[5b,10] gave the desired alcohols **4b** and **4c**.

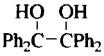
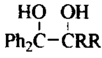
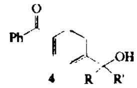
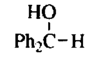


Scheme 2. Synthesis of the cross-coupling products **4b** and **4c**

The product data of the conventional and laser-jet photolyses are presented in Table 1. In the conventional photolysis of benzophenone in methanol, ethanol, and isopropanol (entries 1, 3, 5), the diols **2** and **3** were formed as the main products. Additionally, very small amounts of benzhydrol (**5**) and the *para*-coupling products **4** were detected. The product distribution differs in the three solvents (Table 1), but no definitive trend is evident. For example, the main product in methanol and ethanol is the mixed diol **3**, whereas in isopropanol mainly the dimer **2** was formed. A regular variation is observed in the yields of the trace products **4** and **5** in that from methanol to isopropanol the relative amounts of *para*-coupling product **4** increases and the amount of benzhydrol (**5**) decreases.

Also in the laser-jet photolyses of benzophenone (entries 2, 4, 6) the diols **2** and **3** are the major products, but in contrast to the conventional irradiations (entries 1, 3, 5), the sum of the diols **2** and **3** is significantly less

Table 1. Product Data of the Conventional (Low Intensity) and Laser-Jet (High Intensity) Photolyses of Benzophenone in Methanol, Ethanol, and Isopropanol

entry	solvent	photolysis mode	conversion [%][a]	mb [%][a]	product distribution [%][a,b]			
					 $Ph_2C(OH)-C(OH)Ph_2$ **2**	 $Ph_2C(OH)-C(OH)RR'$ **3**	 **4**	 $Ph_2C(OH)-H$ **5**
1	MeOH	conv.[c]	75	64	38	56[d]	0[d]	6
2	MeOH	LJ[e,f]	11	100	39	40[d]	4[d]	17
3	EtOH	conv.[g]	78	68	27	67[h]	2[h]	4
4	EtOH	LJ[e,i]	28	86	17	52[h]	7[h]	24
5	*i*PrOH	conv.[j]	85	44	60	33[k]	5[k]	2
6	*i*PrOH	LJ[e,l]	10	93	51	11[k]	8[k]	30

[a] Conversion, mass balance (mb) and product distribution by HPLC analysis, error ± 5% of stated value; [b] normalized to 100%; [c] 3.4 W MLUV (333-, 351- and 364-nm argon laser lines), 1 min; [d] R = R′= H, (..**a**); [e] MLUV, 0.8 mL/min, Ar atmosphere; [f] 3.4 W, 1 cycle; [g] 3.5 W MLUV, 1 min; [h] R = H, R′= Me, (..**b**); [i] 3.5 W, 1 cycle; [j] 3.6 W MLUV, 30 s; [k] R = R′= Me, (..**c**); [l] 3.6 W MLUV, 1 cycle.

and decreases in the order *i*PrOH < EtOH < MeOH. This decrease in the sum of the diols **2** and **3** is compensated by a corresponding increase in the benzhydrol (**5**), which augments in the order *i*PrOH > EtOH > MeOH (entries 2, 4, 6). A similar trend is also displayed in the *para*-coupling product **4** (entries 2, 4, 6), but it is less pronounced.

On comparison of the product distribution of the laser-jet photolyses with those of the conventional photolyses (Table 1) one notes that in the laser-jet experiments the amounts of benzpinacol (**2**) and diol **3** become smaller, while more of the *para*-coupling products **4** and benzhydrol (**5**) are formed. This fact confirms that the products **4** and **5** are formed in a two-photon process from the excited radical **1*** (Scheme 1, right-hand branch).

The increasing amount of two-photon products in the sequence *i*PrOH > EtOH > MeOH follows the hydrogen-donating ability *i*PrOH > EtOH > MeOH. This order is documented by the quenching rate constants (k_q) of triplet-excited benzophenone through intermolecular hydrogen transfer, which are 7.5×10^6, 1.9×10^6 and 0.21×10^6 $s^{-1}M^{-1}$ for *i*PrOH, EtOH and MeOH.[11] Consequently, the steady-state concentration of hydroxydiphenylmethyl radicals is highest in *i*PrOH, its photochemical excitation under the laser-jet conditions more probable and, hence, the two-photon products **4** and **5** are formed more efficiently. In addition, as suggested in the low-intensity study with isopropanol,[4] the transient radical **1** may be more persistent in the order *i*PrOH > EtOH > MeOH, so that the probability for a further excitation augments.

As observed previously already for ethanol[5b] in the laser-jet photolysis, the electronically excited radical **1*** leads to notably more *para* product **4** through cross-coupling than under low-intensity irradiations (Table 1). Moreover, the amount of *para*-coupling increases again in the order *i*PrOH > EtOH > MeOH. First of all, in view of the remarkable lifetime (3.9 ns)[12] of the electronically excited radical **1***, such a bimolecular coupling seems to be feasible. Additionally our AM1 calculations[5b] show that in the ground state **1** the highest spin density is located on the carbon atom bearing the hydroxy group, while in the excited state **1*** the highest spin density is on the *para* position. Thus, in the ground state of radical **1** *head-to-head* coupling to the diols **3** is expected to be preferred, while in the electronically excited state **1*** *head-to-tail* coupling to the ketones **4** should dominate, as observed (Table 1).

In all three alcohols, substantially more benzhydrol (**5**) is formed in the laser-jet compared to the conventional photolyses; furthermore, the yield increases from 17% in methanol to 30% in isopropanol (Table 1). At the relatively high steady-state concentrations of the hydroxydiphenylmethyl radical **1**, which is expected to follow the order *i*PrOH > EtOH > MeOH under the high-intensity conditions of the laser-jet photolysis, it is tempting to propose that disproportionation of two ground-state radicals **1** is the course of action to produce benzhydrol (**5**) and benzophenone. However, this mechanistic route is questionable[5b] because it is difficult to rationalize how an increase in concentration should influence the reaction mode and selectivity of an intermediate. Besides, one should have detected proportionally higher amounts of benzhydrol (**5**) compared to the dimerization to benzpinacol (**2**) also in the conventional photolyses. More definitive, in the laser-jet modus the highest yield of benzhydrol (**5**) is observed in isopropanol, while the low-intensity irradiation affords more in methanol. Clearly, these observed trends cannot be reconcilized in terms of disproportionation of two ground-state radicals **1** into benzhydrol (**5**) and benzophenone.

Consequently, the high-intensity product benzhydrol (**5**) must be linked with the electronically excited radical **1***, generated through two-photon chemistry, namely hydrogen abstraction from the alcohol solvent (Scheme 1, right-hand branch). This process is not feasible for the ground-state radical **1** since such hydrogen abstraction is endothermic, ca. 7 kcal/mol estimated for ethanol. The higher reactivity of the excited hydroxydiphenylmethyl radical **1*** has already been documented in trapping experiments with methyl methacrylate, in which **1*** reacts about 10^5 times faster than the ground state.[13]

As already stated, AM1 calculations[5a] suggest that the distribution of the spin densities differs in the ground state (**1**) and the excited state (**1***) of the hydroxydiphenylmethyl radical. In the ground state, the highest spin density is located on the carbon atom with the hydroxy group, in the excited state **1*** it is delocalized into the aromatic rings and is concentrated mainly in the *para* position. Thus, the spin density on the hydroxy-bearing carbon atom is reduced and compared to its ground state, the excited radical **1*** is expected to be more electrophilic. This carbenium ion-like character on the α carbon atom makes the electronically excited radical **1*** more reactive and promotes hydrogen abstraction from alcohols to afford benzhydrol (**5**). Since the nucleophilicity of the alcohol as hydrogen atom donor towards electrophilic radicals increases with the degree of methylation, one should expect that the formation of benzhydrol (**5**) also increases in the order *i*PrOH > EtOH > MeOH, as observed (Table 1).

In summary, our solvent effects in the photoreduction of benzophenone in the hydrogen atom-donating alcohols methanol, ethanol and isopropanol have disclosed for the first time the electrophilic character of the electronically excited hydroxydiphenylmethyl radical **1***, generated under the high intensities of the laser-jet photolysis. Not only is the excited radical **1*** expectedly more reactive than its ground state and effects H abstraction, but it is sensitive towards the nucleophilicity of the hydrogen donor, as confirmed by the increased yield of benzhydrol (**5**) product in the order *i*PrOH > EtOH > MeOH. Through product studies, the laser-jet technique provides a valuable mechanistic tool to explore the photochemistry of transient radicals in solution.

EXPERIMENTAL SECTION

Materials and General Aspects. Benzophenone was recrystallized twice from ethanol before use. Benzhydrol (**5**) is commercially available and was used without further purification. All solutions were degassed by purging with a slow stream of dry argon gas for 20 min before irradiation. For column chromatography, silica gel (32 - 63 mm mesh) was used in a substrate : adsorbent ratio of 1 : 100. The HPLC analyses were carried out on a Waters analytical system (Waters 510 pumps, Waters 486 tunable absorbance detector, Maxima 820 software) or on a Kontron analytical system (LC T-414 pumps, Uvicon 720 LC spectrometer and Anacomp 220 integrator or Kontron HPLC detector 430 and DS450-MT2 software), equipped with an RP-18 reversed-phase column (Knauer Eurospher 100-C18, 5 mm). As eluent, a 65 : 35 solvent mixture of MeOH and water was used or a gradient [55 : 45 MeOH : water (7 min), in 18 min to 100% MeOH (30 min) or 62 : 38 MeOH : water (25 min), in 20 min to 100% MeOH (5 min)] with a solvent flow rate of 0.5 mL/min. The detection wavelength was 215 nm and 1,2-dicyanobenzene the internal standard. NMR spectra were recorded on a Bruker AC 200 or a Bruker AC 250 spectrometer and the IR spectra on a Perkin-Elmer 1420 spectrophotometer.

4-(1-Hydroxyethyl)benzophenone (4b) was synthesized according to literature.[5b]

Diols 2 and 3. Benzpinacol (**2**) and the known unsymmetrical pinacols 1,1-diphenylethane-1,2-diol (**3a**), 1,1-diphenylpropane-1,2-diol (**3b**), and 2-methyl-1,1-diphenylpropane-1,2-diol (**3c**) were isolated from irradiated solutions of benzophenone in methanol, ethanol, and isopropanol and identified by their ^{1}H and ^{13}C NMR spectra.

4-Hydroxymethylbenzophenone (4a). Friedel-Crafts reaction of toluene with benzoyl chloride led to 4-methylbenzophenone. Bromination of the latter gave 4-bromomethylbenzophenone and subsequent hydrolysis the ketone **4a**, all conducted according to reported procedures.[8]

2-[4-(1-Hydroxyethyl)phenyl]-2-phenyl-1,3-dioxolane (6b). A solution of 3.06 g (10.0 mmol) of 2-(4-bromophenyl)-2-phenyl-1,3-dioxolane[9] and 2.18 g (20.0 mmol) of ethyl bromide in 10 mL of dry THF was added to 850 mg (35.0 mmol) of magnesium turnings in 2 mL of dry THF. The resulting Grignard solution was kept under reflux for 30 min, cooled to 0 °C and 6.00 mL (4.68 g, 106 mmol) of acetaldehyde were added carefully. The mixture was stirred for 1 h at 0 °C, afterwards it was allowed to warm up during 1 h to room temperature (ca. 20 °C) and poured onto 60 g of crushed ice and 60 mL of a saturated ammonium chloride solution were added. The aqueous solution was extracted twice with 180 mL of methyl *tert*-butyl ether and the combined organic phases were washed once each with 120 mL of a saturated $NaHSO_3$ solution, a saturated $NaHCO_3$ solution, and water. After drying over Na_2SO_4, the solvent was removed at 40 °C/20 Torr to yield 3.10 g of an yellow oil. Silica gel chromatography [2 : 1 petroleum ether (30-50) : ethyl acetate as eluent, R_f = 0.6] of 1.00 g of the crude product led to 491 mg (54%) of the dioxolane **6b** as colorless powder, m. p. 58 - 58.5 °C. IR (KBr): ν = 3290 cm^{-1} (OH), 2950 (CH), 2860 (CH).- ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.44 (d, J = 6 Hz, 3H, CH_3), 2.27 (br. s, 1H, OH), 4.06 (m, 4H, CH_2), 4.83 (q, J = 6 Hz, 1H, CH), 7.26 - 7.37 (m, 5H, aromatic H), 7.46 - 7.55 (m, 4H, aromatic H).- ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 25.3 (q, CH_3), 65.1 (t, CH_2), 70.4 (d, CH), 109.6 (s, OCO), 125.5 (d), 126.4 (d), 126.6 (d), 128.3 (d), 128.4 (d), 141.6 (s), 142.3 (s), 145.9 (s). $C_{17}H_{18}O_3$ (270.3): calcd. C 75.53, H 6.71, found C 75.49, H 6.47.

2-[4-(1-Hydroxy-1-methylethyl)phenyl]-2-phenyl-1,3-dioxolane (6c). A solution of 3.06 g (10.0 mmol) of 2-(4-bromophenyl)-2-phenyl-1,3-dioxolane[9] and 2.18 g (20.0 mmol) of ethyl bromide in 10 mL of dry THF was added to 850 mg (35.0 mmol) of magnesium turnings in 2 mL of dry THF. The resulting Grignard solution was kept under reflux for 30 min, cooled to 0 °C and 6.00 mL (4.74 g, 81.6 mmol) of acetone were added carefully. The mixture was stirred for 1 h at 0 °C, afterwards it was allowed to warm up during 1 h to room temperature (ca. 20 °C), poured onto 60 g of crushed ice, and 60 mL of a saturated ammonium chloride solution were added. The aqueous solution was extracted twice with 180 mL of methyl *tert*-butyl ether and the combined organic phases were washed once each with 120 mL of a saturated $NaHSO_3$ solution, a saturated $NaHCO_3$ solution, and water. After drying over Na_2SO_4, the solvent was removed at 40 °C/20 Torr to yield 3.34 g of an yellow solid. Silica gel chromatography [2 : 1 petroleum ether (30-50) : ethyl acetate as eluent, R_f = 0.5] of 1.00 g of the crude product led to 753 mg (88%) of the dioxolane **6c** as colorless powder, m. p. 83 - 83.5 °C. IR (KBr): ν = 3320 cm^{-1} (OH), 2950 (CH), 2900 (CH), 2860 (CH).- ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.55 (s, 6H, CH_3), 4.07 (m, 4H, CH_2), 7.27 - 7.58 (m, 9H, aromatic H), the OH proton is not resolved.- ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 31.6 (q, CH_3), 64.8 (t, CH_2), 72.4 (s, COH), 109.3 (s, OCO), 124.2 (d), 125.9 (d), 126.1 (d), 128.0 (d), 128.1 (d), 140.5 (s), 142.0 (s), 148.8 (s). $C_{18}H_{20}O_3$ (284.4): calcd. C 76.02, H 7.09, found C 75.73, H 7.36.

4-(1-Hydroxy-1-methylethyl)benzophenone (4c). To a suspension of 6.00 g of silica gel in 15 mL of CH_2Cl_2 were added 0.6 mL of H_2SO_4 (15%),[10] followed by 473 mg (1.66 mmol) of 2-[4-(1-hydroxy-1-methylethyl)phenyl]-2-phenyl-1,3-dioxolane (**6c**) in 1 mL of CH_2Cl_2. The mixture was stirred for 18 h at room temperature (ca. 20 °C) and neutralized with 500 mg of solid $NaHCO_3$. After an additional 5 min, the solid material was removed by filtration, the filter cake was washed with CH_2Cl_2, and the solvent was removed from the combined filtrates at 40 °C/20 Torr to yield 227 mg (57%) of an yellow oil. Silica gel chromatography [2 : 1 petroleum ether (30-50) : ethyl acetate as the eluent, $R_f = 0.5$] of 357 mg of the crude product led to 242 mg (39%) of the known alcohol **4c**[4] as colorless powder, m. p. 89 - 89.5 °C. ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 1.61$ (s, 6H, CH_3), 7.41 - 7.64 (m, 5H, aromatic H), 7.72 - 7.82 (m, 4H, aromatic H).

Conventional Laser Irradiations. The irradiations were carried out in Schlenk tubes at the 333-, 351-, and 363-nm lines of a Coherent INNOVA 100 argon ion laser supplied with UV optics. The beam was widened with a quartz lens (f = 50 mm) to a size of ca. 1 cm in diameter and the 2.5-mL samples were irradiated under an argon gas atmosphere for the time stated in Table 1.

Laser-Jet Irradiations. The experimental setup, as described in detail in recent publications,[14] was employed. The beam of the argon ion laser was focused by means of a quartz lens (f = 80 mm) onto a free-falling liquid jet of the photolysis solution. The free-falling liquid jet was maintained by means of a Bischoff 2200 HPLC pump, by forcing the substrate solution through a 100-mm capillary. The irradiation chamber was kept under a positive argon gas pressure and the substrate solution was passed once through the focal region of the laser beam.

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