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Diethyl Isopropyl and Isopropenyl Phosphate via Differently Generated Ketyl Radicals of Acetone Reacting with Diethyl Phosphoric Acid

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Abstract: Photochemically excited acetone reacts in 1,2-dimethoxy ethane with diethyl phosphoric acid to diethyl isopropyl phosphate. The same product is formed by reduction of acetone with magnesium amalgam in benzene in the presence of the same phosphoric acid derivative. Thermal decomposition of tetramethyldioxetane in benzene in the presence of diethyl phosphoric acid appears to yield primarily diethyl isopropenyl phosphate.

INTRODUCTION

It has previously been demonstrated that methyl radicals - generated from the tert-butoxy radical - react with triethyl phosphate to diethyl methyl phosphate.[2] The replacement of ethyl by methyl results apparently from the reaction of the methyl radical with the phosphoryl oxygen what is identical with the reversal of ß scission. Phenyl radicals react obviously in the same way[3] which can be basically formulated by the formation of a tetraalkoxyphosphoranyl radical as the intermediate state (Scheme 1).

$$R^{\bullet} + O{=}P(OR')_3 \longrightarrow ROP^{\bullet}(OR')_3 \longrightarrow ROP(=O)(OR')_2 + R'^{\bullet}$$

Scheme 1.

In this way, phosphoric acid can be brought into organic bonding by a radical reaction which may be important for biological energy metabolism. Of course, the ß scission appears to be not reversible for reasons of energy.[4]

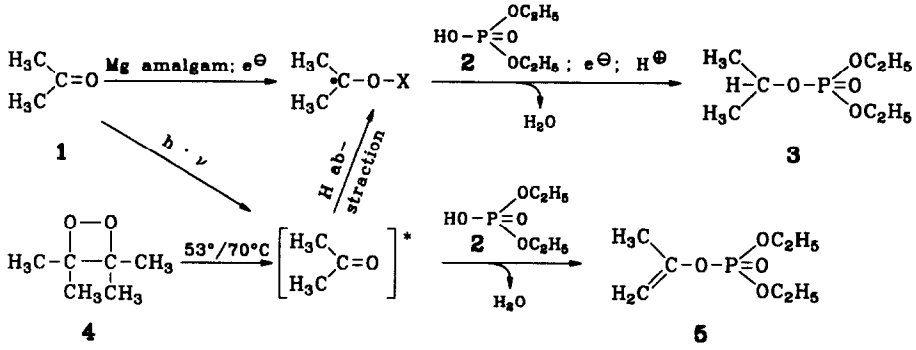
In order to contribute to the elucidation of these contradicting results, we generated carbon radicals of acetone in the presence of diethyl phosphoric acid by different methods and examined whether esters of the

phosphoric acid can be identified. The radical state was generated photochemically, by amalgam reduction, or by thermolysis of tetramethyl dioxetane.[5] The diethyl ester of the phosphoric acid was used because tertiary esters of phosphoric acid - especially its enol esters - are more stable than the corresponding primary esters.[6,7]

RESULTS AND DISCUSSION

Our experiments demonstrate that photochemically excited **1** (Scheme 2) reacts in 1,2-dimethoxy ethane (DME), presumably after hydrogen abstraction, with **2** to diethyl isopropyl phosphate **3**. This reaction product was isolated by fractionation with a Wingler column. The compound **3** is also formed under conditions of pinacol synthesis[8] during reduction of acetone **1** with magnesium amalgam in the presence of **2**. Accordingly, the generated metal ketyl reacts in the same way as the photochemically activated **1** (after H abstraction) with the phosphoric acid derivative.

In the course of thermal decomposition of tetramethyldioxetane **4**, two molecules of **1** are formed. One of these molecules is in the exited triplet state and reaches the ground state under chemiluminescence (Scheme 2).[9] Decomposition of **4** in benzene in the presence of **2** yielded diethyl isopropenyl phosphate **5** which was separated by chromatography on silica gel. This product, however, could not be isolated in pure form.



Scheme 2. Photo reduction: X = H; amalgam reduction: X = $Mg^{\oplus}$.

All the reactions described here give only small yields. This is understandable. In these experiments, we have a bimolecular reaction, and one of the reactants has additionally to be in the reactive radical state. The yields, however, are less important, but the principle of the reaction is of interest. Diethyl phosphoric acid reacts with the ketyl radical of acetone to the isopropyl or the isopropenyl ester, respectively. In the course of the reduction of **1** by two one-electron transfer processes, a high-energy intermediate state is obviously passed through which reacts with inorganic phosphate (model: **2**) to the corresponding ester under elimination of water. This high-energy intermediate state is also obtained in the course of decomposition of **4** which obviously proceeds by the biradical mechanism.[10,11] Under these conditions, the formation of **5** is favoured, maybe because benzene is only a weak H donor.[12]

The product obtained by the reaction of excited acetone **1** with the phosphoric acid derivative might be largely dependent upon the rate constant K_H of H abstraction of the solvent.[12] In a weak H donor enol

phosphate **5** is the preferred product, while for good H abstraction the reduced compound **3** is formed. Therefore, in DME (log $K_H \approx 5$ for **1** at room temperature), enol phosphate **5** can be formed, too. During the photochemical reaction, an ethyl transfer between the phosphate molecules under formation of monoethyl phosphoric acid and triethyl phosphate could likewise be observed. The results obtained here could be interpreted in accordance with the initially mentioned experiments[2] as reversal of the ß scission with formation of the phosphoranyl radical as the intermediate product. At present we are investigating the true mechanism of this reaction sequence. The reversal of ß scission becomes explainable by the "Marcus inverted region"[13,14] (increase of the reaction rate with decreasing exoergicity[15] and *vice versa*).

EXPERIMENTAL

General: TLC: cellulose plates (0.1 mm; Merck); HPTLC aluminium sheets (silica gel 60 F_{254}; Merck). CC: silica gel 60 (Merck; 10 g/100 mg substance). All other chemicals (Aldrich and Merck) were of the purest grade commercially available. Solvents were distilled before use. Irradiation: Hg high-pressure diving lamp (150 W; quartz vessel; Heraeus, Hanau). Fractionation: rotating strip column (Wingler, Fritz and Vogt, Normag); 10 theoretical plates. Spectra: ^{1}H-NMR and ^{13}C-NMR: Bruker AM-300 (300.13 and 75.47 MHz, resp.; $CDCl_3$/TMS); ^{31}P-NMR: Bruker AM-250 (101.26 MHz; $CDCl_3/H_3PO_4$ extern.); IR: Perkin-Elmer 297; MS: Varian Mat 311 A (70 eV).

Diethyl phosphoric acid (2). Diethyl chlorophosphate (dist.; 28.9 ml, 0.2 mol) was added dropwise to NaOH (0.4 mol) in water (110 ml) with good cooling (temperature not exceeding 30-40°C). The solution was extracted twice with ether, acidified with H_2SO_4, and evaporated in vacuum (30°C). The free acid was separated with ether from the salt mixture. The ether was washed with a small volume of water, dried ($MgSO_4$), and evaporated (yield 90%). On the cellulose plate [2-PrOH/NH_3(28-30%)/H_2O 8:1:1, by vol]: one blue spot at R_f 0.56 and a very small spot at R_f 0.02 - 0.03 [monoethyl phosphoric acid (MEPA)][6] [$(NH_4)_2MoO_4$; 10 min 75°C; irradiation at 254 nm].[6,7] ^{31}P-NMR: a large signal at $\delta = 0.71$ and a small signal at $\delta = -0.70$ (MEPA; see above).

Diethyl isopropyl phosphate (3) by photochemical excitation of 1 in the presence of 2. A solution of dry **1** (4.2 ml, 57 mmol) and **2** (26.4 g, 171 mmol) in DME (180 ml) was irradiated for 24 h (room temperature; N_2; magnetic stirrer). After neutralisation with KOH (10 mol/l), **2** was separated as diethyl phosphate (DEP), the organic solvent was dried ($MgSO_4$), and evaporated (30°C). The DEP phase was extracted twice with ether, the ether phases were dried ($MgSO_4$), and also evaporated. The combined residues of the organic phases were distilled in vacuum (0.05 mm). Very careful fractionation of approximately six distillates through a Wingler column yielded four fractions. The 4th fraction was pure **3** (44°C; 0.06 mm; 130 mg). TLC: one spot on the cellulose plate at R_f 0.92 (mobile phase, see above), and one spot on the silica gel plate at R_f 0.53 (cyclohexane/ethyl acetate 1:6.5, by vol; detection with $KMnO_4$). ^{1}H-NMR: $\delta = 1.31 - 1.36$ (m, 12H, CH_3), 4.05 - 4.14 (m, 4H, CH_2), 4.60 - 4.69 (m, 1H, C-H). ^{13}C-NMR: $\delta = 15.87$ (d, $^3J_{C\text{-}P} = 6.9$ Hz, O-CH_2-$\underline{C}H_3$), 23.38 (d, $^3J_{C\text{-}P} = 5.2$ Hz, C-$\underline{C}H_3$), 63.19 (d, $^2J_{C\text{-}P} = 5.6$ Hz, O-$\underline{C}H_2$-CH_3), 72.11 (d, $^2J_{C\text{-}P} = 5.7$ Hz, CH). ^{31}P-NMR: $\delta = -1.47$. IR (KBr): 2935 (CH), 1387 (CH_3), 1262 (P=O), 1008 (P-O-CH_2-CH_3). MS: m/z (%) = 195 (3, M^+ - H), 181 (25.3, M^+ - CH_3), 155 [55.4, $(C_2H_5O)_2P(OH)_2$], 110 [90.5, $C_2H_5OP(OH)_2$], 99 [100, $P(OH)_4$], 81 [22.4, $OP(OH)_2$] (see also [16]). Anal. calc. for $C_7H_{17}O_4P$ (196.2): C 42.86, H 8.73, P 15.79; found: C 43.03, H 8.79, P 15.43%.

Diethyl isopropyl phosphate (3) by reduction of 1 with Mg amalgam in the presence of 2. A solution of $HgCl_2$ (recryst.; 4.1 g, 15.1 mmol) in **1** (dry; 23 ml, 312 mmol) was dropped in 5 min to a suspension of magnesium powder (up to 50 mesh; dry; 3.6 g, 148 mmol) in benzene (dry; 45 ml) (room temperature; magnetic stirrer). After the start of the vigorous reaction (temperature rises to 67°C; note 1), a solution of **2** (17.4 g, 113 mmol) in **1** (15 ml, 203 mmol) was slowly added dropwise (ca. 30 min). One minute after the last drop, the reaction was stopped by ice cooling. The amalgam and the partially formed Mg pinacolate were separated by centrifugation, and washed twice with benzene. The combined organic phases were evaporated (30°C), the residue was extracted with ether, and let stand at -20°C for 2 h. After centrifugation, the ether phase was evaporated, and the residue extracted exhaustively with n-hexane. The hexane phase was evaporated to dryness.

The residues of 6 preparations (colourless oil) were distilled in vacuum (0.05 mm) with a Vigreux column (20 cm). Careful fractionation of the distillate with the Wingler column yielded approximately 200 mg of pure **3** (44°C; 0.06 mm; note 2). The analytical data of this product agreed with the data of the product formed by photochemical excitation of **1**.

Note 1: This vigorous reaction is essential for the generation of the ketyl radical, and consequently for the binding of **2**. The dryness of all reactants is very important. If the reaction does not proceed within 5 min, short heating is necessary.

Note 2: The separation of **3** from pinacol is difficult. Very careful fractionation is necessary.

Diethyl isopropenyl phosphate (5) by thermal decomposition of 4 in the presence of 2. Tetramethyl dioxetane **4** was prepared in small amounts (500 mg; 4.3 mmol) using the method of Kopecky et al..[17,18] The yellow crystals (116 mg, 1 mmol) were dissolved in benzene (10 ml). After addition of **2** (770 mg, 5 mmol), the compound **4** was decomposed under nitrogen at 53°C (2h) and 70°C (1h).[18,5] After cooling at room temperature, the excess of **2** was separated by cautious neutralisation with KOH (10 and 1 mol/l), and the DEP phase was extracted twice with ether. Both benzene and ether phases were washed with a small portion of water, dried ($MgSO_4$), and evaporated in vacuum (30°C). The residues of 4 preparations were chromatographed (silica gel column, n-hexane/THF/MeOH 7:1.5:1.5, by vol). - Comparison of the spectra of the yielded colourless oil (about 160 mg) with the spectra of **5** prepared by the Perkow reaction (reaction of chloroacetone with triethyl phosphite[19]) demonstrated a mixture of **5** and **3**, too difficult to separate. Therefore, **5** obtained by decomposition of **4** could not be purified completely on a silica gel column. The formation of **5**, however, was confirmed by NMR spectra: ^{1}H-NMR: δ = 4.51 and 4.77 (2s, 2H, $=CH_2$). ^{13}C-NMR: δ = 151.1 (d, $^3J_{C\text{-}P}$ = 8.4 Hz, quaternary C). ^{31}P-NMR: δ = -6.44.

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