The Reaction of Tetramethyl-1,3-cyclobutanedione with Triphenylphosphinemethylene[1]

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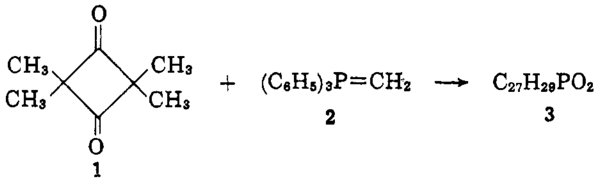
When tetramethyl-1,3-cyclobutanedione (**1**) is treated with triphenylphosphinemethylene (**2**), the unusual adduct **3** having a dipole moment of 6.96 D. is obtained. By spectral (infrared, ultraviolet, and n.m.r.) and chemical studies, this adduct has been characterized as triphenylphosphine-2,2,4-trimethyl-3-oxovalerylmethylene. Compound **3** readily reacts with HCl to give 3,3,5-trimethyl-2,4-dioxohexyltriphenylphosphonium chloride (**5**). Upon treating the latter compound with aqueous sodium carbonate the adduct **3** is recovered (97%). Hydrolysis of compound **3** leads to triphenylphosphine oxide and 3,3,5-trimethylhexane-2,4-dione (isolated as a mono-2,4-DNP) which was identical with an authentic sample prepared in low yield by acylating 2,4-dimethyl-3-pentanone with acetyl chloride.

In connection with other studies,[2] we treated tetramethyl-1,3-cyclobutanedione (**1**) with triphenylphosphinemethylene (**2**). A stable white crystalline adduct ($C_{27}H_{29}PO_2$) was obtained which was unaffected by prolonged heating either in tetrahydrofuran or in 1,2-dimethoxyethane. Since little has been done in the way of isolating and characterizing the intermediates in the Wittig reaction, further characterization of this adduct appeared worthwhile.

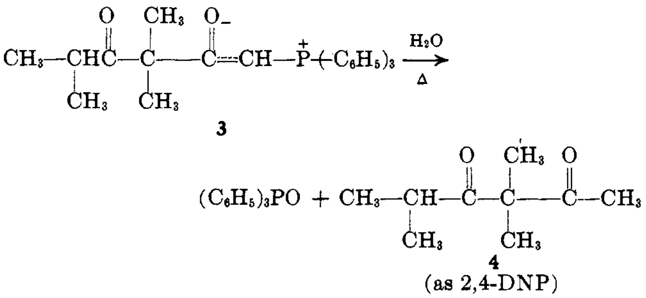


The infrared spectrum shows the presence of two carbonyl bands at 5.83 and 6.53 μ. The long wave length of the former band suggested that ring opening had occurred,[3] whereas the extremely long wave length of the latter band suggested the presence of substantial charge separation in the molecule. This latter conclusion was confirmed by the dipole moment which was found to be 6.96 D. in benzene solution.

The ^1H n.m.r. spectrum (see Experimental) indicates the presence of 15 aromatic hydrogens, an isopropyl group, and two equivalent methyl groups and suggests the presence of a single hydrogen next to phosphorus (doublet with $J = 25$ c.p.s.). The ^{31}P n.m.r. spectrum consists of a broad signal (width at half-height of 100 c.p.s.) at -16.0 p.p.m. from 85% H_3PO_4. The ultraviolet spectrum of the adduct **3**, $\lambda_{\max}^{\mathrm{EtOH}}$ 225 mμ (sh, ϵ 25,300), 266 (6360), 273 (6150), and 293 (5950), bears a marked resemblance to that of triphenylphosphinacetylmethylene.[4]

On the basis of the above physical data, the structure of triphenylphosphine-2,2,4-trimethyl-3-oxovalerylmethylene was assigned to the adduct **3**. This conclusion has been unequivocally confirmed by chemical studies.

Hydrolysis of the adduct in 1:1 water–ethanol for 12.7 days at reflux temperature gave triphenylphosphine oxide (97%) and 3,3,5-trimethylhexane-2,4,-dione (**4**, 86%) isolated as its mono-2,4-dinitrophenylhydrazone. The latter derivative was identical with the 2,4-dinitrophenylhydrazone of a sample of the dione **4** prepared in low yield by acylating 2,4-dimethyl-3-pentanone with acetyl chloride. For steric reasons the mono-2,4-DNP derivative is believed to be that arising from condensation at the 2-position.



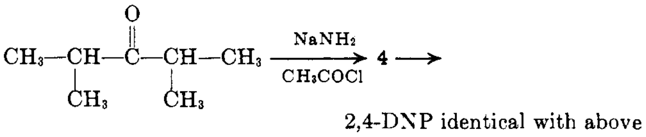
$$CH_3-\underset{CH_3}{CH}-\overset{O}{\overset{\|}{C}}-\underset{CH_3}{\overset{CH_3}{C}}-\overset{O^-}{\overset{|}{C}}{=}CH-\overset{+}{P}(C_6H_5)_3 \xrightarrow[\Delta]{H_2O}$$

3

$$(C_6H_5)_3PO + CH_3-\underset{CH_3}{CH}-\overset{O}{\overset{\|}{C}}-\underset{CH_3}{\overset{CH_3}{C}}-\overset{O}{\overset{\|}{C}}-CH_3$$

4

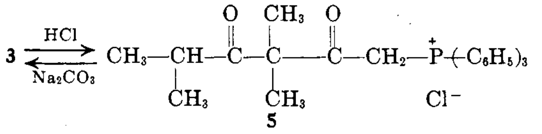
(as 2,4-DNP)



$$CH_3-\underset{CH_3}{CH}-\overset{O}{\overset{\|}{C}}-\underset{CH_3}{CH}-CH_3 \xrightarrow[CH_3COCl]{NaNH_2} 4 \longrightarrow$$

2,4-DNP identical with above

Upon treating a methanolic solution of the adduct **3** with an equivalent of hydrochloric acid, 3,3,5-trimethyl-2,4-dioxohexyltriphenylphosphonium chloride (**5**) was obtained (97%). By shaking the latter compound with aqueous sodium carbonate the original adduct **3** was recovered (97%).



$$3 \underset{Na_2CO_3}{\overset{HCl}{\rightleftarrows}} CH_3-\underset{CH_3}{CH}-\overset{O}{\overset{\|}{C}}-\underset{CH_3}{\overset{CH_3}{C}}-\overset{O}{\overset{\|}{C}}-CH_2-\overset{+}{P}(C_6H_5)_3 \quad Cl^-$$

5

This result can be rationalized by the mechanistic path shown in Scheme I.

Nucleophilic attack of triphenylphosphinemethylene[5] leads to the intermediate **6** of the type which is commonly believed to be involved in the Wittig reaction.[6-8] The formation of the resonance stabilized enolate anion **7** by ring opening of **6** effectively competes with the normal course of the Wittig reaction. Abstraction of a proton from the carbon atom α to the triphenylphos-

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[1] Presented in part at the 146th National Meeting of the American Chemical Society, Denver, Colo., Jan., 1964, Abstracts, p. 22C.

[2] E. A. LaLancette and R. E. Benson, *J. Am. Chem. Soc.*, **83**, 4867 (1961).

[3] J. D. Roberts and W. F. Gorham, *ibid.*, **74**, 2278 (1952).

[4] F. Ramirez and S. Dershowitz, *J. Org. Chem.*, **22**, 41 (1957); $\lambda_{\max}^{\mathrm{EtOH}}$ 268 mμ (ϵ 6600), 275 (6500), and 288 (5700).

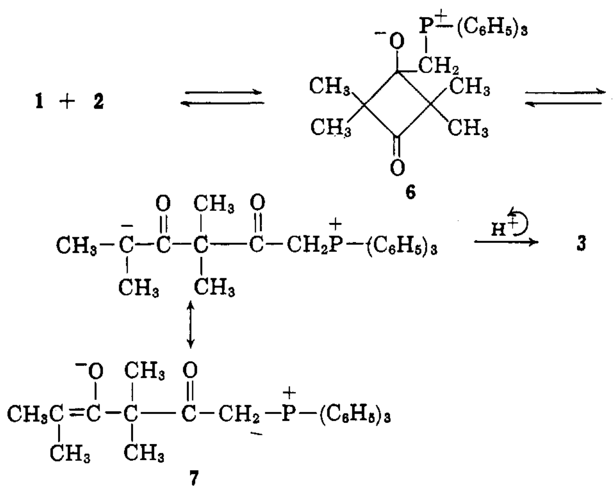
[5] That ylides are nucleophilic reagents follows from their reactions with various reagents, *e.g.*, α-bromo ketones [H. J. Bestman, F. Seng, and H. Schulz, *Ber.*, **96**, 465 (1963)], epoxides, esters, acid halides, alkyl halides, etc. For leading references see S. Trippett, *Quart. Rev.* (London), **17**, 406 (1963).

[6] G. Wittig and U. Schöllkopf, *Ber.*, **87**, 1318 (1954).

[7] A. W. Johnson and R. B. LaCount, *Tetrahedron*, **9**, 130 (1960).

[8] A. J. Speziale and D. E. Bissing, *J. Am. Chem. Soc.*, **85**, 3878 (1963).

Scheme I



phonium group in **7** then leads to the observed adduct **3**. This result constitutes the first example of ring opening of a ketone under Wittig reaction conditions.

Reaction of the dione **1** with alkoxides results in an analogous ring opening to give the 2,2,4-trimethyl-3-oxovalerate anion.[9] Similarly, cleavage of the cyclobutadione takes place upon treating **1** with ammonia and amines,[10] hydrazine,[11] alcohols, phenols, and mercaptans,[12] and trialkyl phosphites.[13]

Experimental

Triphenylphosphine-2,2,4-trimethyl-3-oxovalerylmethylene (3).—To a stirred suspension of 12.75 g. (35.7 mmoles) of methyltriphenylphosphonium bromide in 250 ml. of dry tetrahydrofuran there was added in one portion 24.6 ml. (39.4 mmoles) of a 1.60 *M* butyllithium solution in hexane. After stirring at ambient temperature for 3 hr. a solution of 5 g. (35.7 mmoles) of dione **1** in 50 ml. of dry tetrahydrofuran was added over a period of 20 min. The reaction mixture was then heated at reflux temperature for 18.5 hr. and taken to dryness *in vacuo;* the residue was partitioned between 500 ml. of benzene and 100 ml. of water. The organic phase was washed with water (three 250-ml. portions) and saturated sodium chloride solution and dried ($MgSO_4$). Concentration of the filtered solution to approximately 75 ml. and the addition of 410 ml. of petroleum ether (b.p. 30–60°) resulted in the crystallization of 10.1 g. (68%) of triphenylphosphine-2,2,4-trimethyl-3-oxovalerylmethylene (**3**), m.p. 136–137.3°. An analytical sample was obtained by recrystallization from petroleum ether, m.p. 139–140°.

Anal. Calcd. for $C_{27}H_{29}PO_2$: C, 77.85; H, 7.02; P, 7.45; mol. wt., 416.51. Found: C, 77.81; H, 7.15; P, 7.51; mol. wt., 387 (boiling point in ethylene chloride).

Spectral data showed $\lambda_{\max}^{\mathrm{KBr}}$ (μ), 3.24, 3.34, 3.38, and 3.44 (saturated and unsaturated C—H stretching), 5.83 (C=O), 6.32, 6.73, and 6.95 (C_6H_5—P), 6.53 ($>\dot{C}\cdots O$), 7.19 and 7.29 (*gem*-dimethyl); $\lambda_{\max}^{\mathrm{EtOH}}$ mμ (ϵ), 225 (sh, 25,300), 266 (6360), 273 (6150), and 293 (5950); ^{1}H n.m.r. [$CDCl_3$ solution, δ in p.p.m. *vs.* $(CH_3)_4Si$], multiplet at 7.38 (aromatic H), doublet at 3.73 (J = 25 c.p.s., $-\overset{\overset{O}{\|}}{C}\cdots CH-$), septuplet at 3.07 ($J$ = 7 c.p.s., $>CH-$), 1.38 ($CC(CH_3)_2C$), and doublet at 1.0 (J = 7 c.p.s., $(CH_3)_2CH-$).

3,3,5-Trimethyl-2,4-dioxohexyltriphenylphosphonium Chloride (5).—A solution of 1 g. (2.4 mmoles) of adduct **3** in 10 ml. of methanol was treated with 0.2 ml. (2.4 mmoles) of 12 *N* hydrochloric acid. The reaction mixture was stirred for 10 min. at room temperature and the methanol was removed under a stream of nitrogen. The resulting oil was then boiled with benzene whereupon it readily crystallized to give 1.05 g. (97%) of 3,3,5-trimethyl-2,4-dioxohexyltriphenylphosphonium chloride (**5**), m.p. 183.8–184° (dec.).

Anal. Calcd. for $C_{27}H_{30}ClPO_2$: C, 71.58; H, 6.68; P, 6.85. Found: C, 71.43; H, 6.44; P, 7.03.

Spectral data showed $\lambda_{\max}^{\mathrm{Nujol}}$ (μ), 5.83 and 5.91; ^{1}H n.m.r. [$(CD_3)_2SO$ solution, δ in p.p.m. *vs.* $(CH_3)_4Si$], 7.77 (aromatic H), doublet at 6.30 (J = 13 c.p.s.), unresolved multiplet at 3.78 ($>CH-$), 1.45 ($CC(CH_3)_2C$), and doublet at 0.87 (J = 7 c.p.s., $(CH_3)_2CH-$).

Reaction of 3,3,5-Trimethyl-2,4-dioxohexyltriphenylphosphonium Chloride with Base.—A suspension of 0.64 g. (1.42 mmoles) of 3,3,5-trimethyl-2,4-dioxohexyltriphenylphosphonium chloride in a solution of 5 g. of sodium carbonate and 45 ml. of water was shaken at room temperature for 21 hr. The suspended white solid was collected by filtration and washed with water to give 0.57 g. (97%) of triphenylphosphine-2,2,4-trimethyl-3-oxovaleryl methylene (**3**), m.p. 137–138.5°.

Hydrolysis of Triphenylphosphine-2,2,4-trimethyl-3-oxovaleryl methylene.—A mixture of 2 g. (4.8 mmoles) of adduct **3**, 100 ml. of ethanol, and 100 ml. of water was heated at reflux temperature for 12.7 days. The reaction mixture was then distilled until the column head temperature rose to 98°. The solid which separated in the distillation pot was collected by filtration and washed with water to give 1.29 g. (97%) of triphenylphosphine oxide, m.p. 149–151.5°. The filtrate and washings were combined with the distillate and treated with a solution of 0.8 g. of 2,4-dinitrophenylhydrazine, 4 ml. of concentrated sulfuric acid, and 6 ml. of water. The resulting solution was warmed for 10 min. and allowed to crystallize to give a total of 1.33 g. (86%) of the mono-2,4-dinitrophenylhydrazone derivative of 3,3,5-trimethylhexane-2,4-dione. An analytical sample was obtained by recrystallization from ethanol, m.p. 145–146°.

Anal. Calcd. for $C_{15}H_{20}N_4O_5$: C, 53.56; H, 5.99; N, 16.67. Found: C, 53.35; H, 6.02; N, 17.08.

Spectral data indicated ^{1}H n.m.r. [$CDCl_3$ solution, δ in p.p.m. *vs.* $(CH_3)_4Si$], 11.21 (NH), 9.20 (isolated aromatic H), weak-strong-strong-weak AB pattern at 8.40 and 8.10 (J = 10 c.p.s., adjacent aromatic H), a septuplet at 3.14 (J = 7 c.p.s., $>CH-$ 2.07 ($-C(=N)CH_3$), 1.53 ($CC(CH_3)_2C$), and a doublet at 1.13 (J = 7 c.p.s., $(CH_3)_2CH-$).

3,3,5-Trimethylhexane-2,4-dione (4).—A mixture of sodamide (from 0.16 g.-atom of sodium) in 110 ml. of ether and 20 g. (0.175 mole) of 2,4-dimethyl-3-pentanone was heated at reflux temperature for 3 hr. The reaction mixture was then cooled to 0°, and a solution of 12.55 g. (0.16 mole) of acetyl chloride in 25 ml. of ether was added as quickly as the exothermic reaction permitted. The reaction mixture was then heated on a steam bath for 2 hr., the product partitioned between ether and water, the aqueous phase extracted once with ether, and the combined ether phases dried ($MgSO_4$). The ether was removed from the filtered solution, and the residue was distilled through an 18-in. spinning-band column. After the recovery of 9 g. of 2,4-dimethyl-3-pentanone, an intermediate fraction of 1.56 g. (6%) of impure 3,3,5-trimethylhexane-2,4-dione was collected, b.p. about 42° (3 mm.), and purified *via* g.l.c. at 125° [25% 1,2,3-tris(2-cyanoethoxy)propane on 60–80-mesh Gas Chrom P].

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.19; H, 10.31. Found: C, 69.19; H, 10.35.

Spectral data indicated ^{1}H n.m.r. [neat, δ in p.p.m. *vs.* $(CH_3)_4Si$], septuplet at 2.95 (J = 7 c.p.s., $>CH-$), 2.10 ($-C(=O)CH_3$), 1.35 ($CC(CH_3)_2C$), and 1.02 (J = 7 c.p.s., $(CH_3)_2CH-$).

A 2,4-dinitrophenylhydrazone derivative prepared in the usual manner had m.p. 145.4–146.2° after recrystallization from ethanol.

Anal. Calcd. for $C_{15}H_{20}N_4O_5$: C, 53.56; H, 5.99; N, 16.67. Found: C, 53.49; H, 5.93; N, 16.54.

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(10) (a) R. H. Hasek, E. U. Elam, and J. C. Martin, *ibid.*, **26**, 4340 (1961); (b) W. Leimgruber and M. Creighton, 146th National Meeting of the American Chemical Society, Denver, Colo., Jan., 1964, Abstracts, p. 37C.

(11) "Tetramethyl-1,3-cyclobutanedione, 2,2,4,4-Tetramethylcyclobutanediol, Properties, Reactions," Eastman Chemical Products, Inc., Technical Data Report No. TDR-N-110, 1960.

(12) R. H. Hasek, E. U. Elam, J. C. Martin, and R. G. Nations, *J. Org. Chem.*, **26**, 700 (1961).

(13) W. G. Bentrude and E. R. Witt, *J. Am. Chem. Soc.*, **85**, 2522 (1963).