Wittig Cyclization and Base-Induced Elimination in the Reactions of Some ω-Benzoylalkyltriphenylphosphonium Salts[1]

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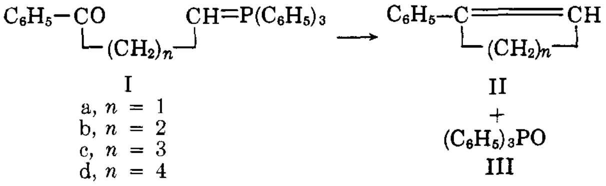
The reactions of four ω-benzoylalkyltriphenylphosphonium salts with organolithium reagents have been studied. An internal Wittig reaction leading to the formation of 1-phenylcyclohexene is observed with the 5-benzoylpentyl salt, but only β-elimination of triphenylphosphine is observed in the reactions of the 1-phenylcyclobutene precursor. The β-elimination of triphenylphosphine from phosphonium salts also has been observed in reactions of two 2-benzoylethyl salts. The study indicates that the formation of cyclopentenes and cyclohexenes constitutes a lower limit on Wittig cyclization reactions.

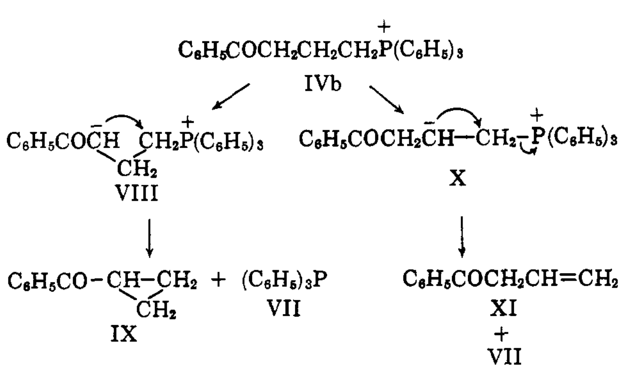
The intermolecular Wittig reaction between a bisphosphorane and a dicarbonyl compound has been utilized in a number of instances for the synthesis of medium and large ring cycloalkenes,[2] but relatively few studies of the simpler intramolecular cyclizations of ω-oxoalkylphosphoranes have been carried out.[3] Two studies of the reactions of the simplest models, ω-benzoylalkyltriphenylphosphoranes (I), have been reported. Bieber and Eisman have shown that Ic, formed by the action of sodium ethoxide on the corresponding phosphonium salt (IVc), undergoes intramolecular cyclization to yield 1-phenylcyclopentene (IIc) and triphenylphosphine oxide (III).[4] A different reaction course was observed with Ia which underwent intermolecular reaction (cyclodimerization) with the formation of 1,4-diphenylcyclohexadiene (V) rather than the cyclopropene (IIa).[5] Since the formation of a dimeric product in the latter reaction indicated the internal Wittig reaction to be subject to ring size limitations, the reactions of Ib and Id (cyclobutene and cyclohexene precursors) have been examined.



1-Phenylcyclohexene (IId) was prepared by treating a suspension of (5-benzoylpentyl)triphenylphosphonium iodide (IVd) in benzene with *n*-butyllithium and refluxing the resulting phosphorane (Id) solution for 13 hr. IId was isolated in 9.6% yield; reaction residues were shown to contain III and IVd.

In the reactions of Ib, neither the expected cycloalkene, 1-phenylcyclobutene (IIb), nor the cyclic diene, 1,5-diphenylcyclooctadiene-1,5 (VI), was detected as a product. The formation of VI might be anticipated by a cyclodimerization process analogous to the formation of V. Treatment of IVb, (3-benzoylpropyl)triphenylphosphonium chloride, with phenyllithium led to the isolation of triphenylphosphine (VII), III, biphenyl, and polymeric material. The use of *n*-butyllithium as base for the generation of Ib led to the isolation of VII (25%), III, unchanged IVb, and polymeric material. Since biphenyl was not isolated in the latter reaction, it is assumed that it was formed during the preparation of phenyllithium. A sample of the latter reaction mixture was examined by g.l.c. and shown to contain no detectable amount of IIb by comparison with the g.l.c. behavior of an authentic sample[6] of IIb.

Since neither IIb nor VI was detected in the reactions of Ib, it appears that polymerization of Ib and elimination of VII from IVb are the major reactions. Elimination of triphenylphosphine from IVb could occur by either of two processes: intramolecular displacement of VII from the inner salt VIII to yield a cyclopropane derivative (IX),[7] or simple β-elimination from the inner salt (X) to yield 3-butenophenone (XI). The inner salts VIII and X could be formed by either the direct attack of base on IVb or by equilibration processes between Ib and IVb. A g.l.c. analysis of the products from the reaction of IVb showed the absence of any detectable amount of VIII,[8] indicating that the probable major process is β-elimination. XI may rearrange to the more stable α,β-unsaturated isomer,[9] crotonophenone (XII), in the strongly basic reaction mixture; neither XI nor XII was detected as reaction product, but might be anticipated to undergo polymerization. Intermolecular reaction of Ib would account for the formation of III and would lead to a polyolefin.



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[2] For a summary of leading references, see C. E. Griffin and J. A. Peters, *J. Org. Chem.*, **28**, 1715 (1963); C. E. Griffin, K. R. Martin, and B. E. Douglas, *ibid.*, **27**, 1627 (1962).

[3] Other intramolecular Wittig cyclizations are reported by H. J. Bestmann and O. Kratzer, *Angew. Chem. Intern. Ed. Engl.*, **1**, 511 (1962); G. Markl, *ibid.*, **1**, 511 (1962); H. O. House and H. Babad, *J. Org. Chem.*, **28**, 90 (1963).

[4] T. I. Bieber and E. H. Eisman, *ibid.*, **27**, 678 (1962).

[5] C. E. Griffin and G. Witschard, *ibid.*, **27**, 3334 (1962).

[6] A. Burger and R. Bennet, *J. Med. Pharm. Chem.*, **2**, 687 (1960).

[7] The formation of mesityl 2-phenylcyclopropyl ketone by a similar internal displacement of VII from an intermediate analogous to VIII formed in the reaction of methylenetriphenylphosphorane and benzalacetomesitylene has been reported; *cf.* J. P. Freeman, *Chem. Ind.* (London), 1254 (1959).

[8] We are indebted to Dr. J. B. Plumb for carrying out this analysis.

[9] The rearrangement of XI to XII has been demonstrated by R. M. Horowitz and T. A. Geissman [*J. Am. Chem. Soc.*, **72**, 1518 (1950)].

A number of simple β-eliminations of VII from phosphonium salts have been reported previously[10]; in these examples, activation of the β-proton toward the attack of base has been provided by the direct or vinylogous attachment of phosphonium,[10a,d] cyano,[10b] carbethoxy,[10c] carboxylate,[10e] and acyl[10f] groups at the β-carbon. In the β-elimination of VII from IVb, the β-proton is not subject to conventional activation since the β-substituent (in IVb) is a phenacyl group. Thus, the present case represents an example of β-elimination in a salt possessing a minimal degree of activation. Cleavage of phosphonium salts lacking β-proton activation is well-known and follows a different course; the action of hydroxide[11a] and alkoxide[11b] ions on these salts has been shown to produce III and alkanes. In these cleavages, attack of base occurs on the phosphorus atom to yield intermediates which subsequently fragment to III. In the reactions under consideration in this study, attack by base (phenyl- or butyllithium) on phosphorus would not be energetically favorable and abstraction of a β-proton with elimination of VII in analogy to Hofmann eliminations would be feasible.

In order to investigate the possible occurrence of β-elimination in structures more favorable toward this process than IVb, the reaction of IVa with bases was reinvestigated; it was reported previously that VII,

$$C_6H_5COCH_2\overset{+}{C}H_2P(C_6H_5)_3$$

IVa

as well as V and III, was detected in the reaction of IVa with phenyllithium.[5] The reaction of IVa with *n*-butyllithium led to the formation of triphenylphosphine (50%) and III (40%). In IVa, β-elimination would be more highly favored than in IVb, since, in the former compound, the β-hydrogen is activated by the benzoyl group. Elimination would lead to the formation of acrylophenone which was not isolated, but the ready polymerization of this compound has been demonstrated.[12]

β-Elimination of VII was demonstrated cleanly in the reaction of phenyllithium and (2-benzoyl-1-phenylethyl)triphenylphosphonium bromide (XIII). Triphenylphosphine (53%) and the elimination product, chalcone (XIV, 48%), were the only products isolated;

$$C_6H_5COCH_2CH(C_6H_5)\overset{+}{P}(C_6H_5)_3 + n\text{-}C_4H_9Li \longrightarrow$$

XIII

$$C_6H_5COCH{=}CHC_6H_5 + VII$$

XIV

no dienes were detected. In the case of XIII, simple cyclization to the cyclopropene and cyclodimerization would be unfavorable processes because of probability and steric factors. The preferred elimination process would be facilitated by the activation of the β-hydrogen by the benzoyl group and the stability of the α,β-unsaturated ketone formed on elimination. No III was detected in this reaction indicating that even the intermolecular Wittig reaction leading to polymer has been suppressed in favor of elimination.

The results of this study indicate that the effective lower limit for Wittig cyclizations of ω-oxoalkylphosphoranes is in the cyclopentene series and that β-elimination of VII can occur readily in phosphonium salts possessing sufficient β-hydrogen activation.

Experimental[13]

(5-Benzoylpentyl)triphenylphosphonium Iodide (IVd).—6-Bromocaproic acid was prepared by the hydrolysis of 6-bromocapronitrile (Columbia Organic Chemicals Co.) with refluxing 48% hydrobromic acid. The acid was isolated in 46% yield by distillation, b.p. 120–130° (1 mm.), lit.[14] b.p. 165–170° (20 mm.). The acid was converted to the corresponding chloride by treatment with excess thionyl chloride at 80° for 1 hr.; distillation gave the product in 92% yield, b.p. 84–90° (2.5 mm.). 6-Bromocaprophenone was prepared by a conventional Friedel–Crafts procedure from the acid chloride, anhydrous benzene, and aluminum chloride with a reaction period of 30 min. The product, isolated in 61% yield by distillation, had b.p. 150–154° (0.7 mm.), lit.[15] b.p. 124° (0.05 mm.). Quaternization was achieved by refluxing a mixture of 16.5 g. (0.063 mole) of triphenylphosphine and 16.0 g. (0.063 mole) of the bromo ketone in 50 ml. of N,N-dimethylformamide for 68 hr.; no solid was formed on cooling. The solvent was removed under reduced pressure and the oily residue was washed with petroleum ether (b.p. 30–60°) and added to 600 ml. of hot aqueous potassium iodide. A viscous oil separated on cooling and was crystallized by the addition of ether to give 21.4 g. (60%) of IVd, m.p. 158–159° (recrystallized from ethanol–ether).

Anal. Calcd. for $C_{30}H_{30}IOP$: C, 63.83; H, 5.36; P, 5.49. Found: C, 63.88, 63.76; H, 5.39, 5.28; P, 5.32, 5.47.

The infrared spectrum of IVd showed bands at 3067 w, 2941 s, 2882 wm, 1669 m, 1585 w, 1433 ms, 1109 s, 994 wm, 746 m, 719 s, and 690 s cm.$^{-1}$.

1-Phenylcyclohexene. (IId).—A suspension of 18.8 g. (0.033 mole) of IVd in 190 ml. of anhydrous benzene was treated with a solution of 0.033 mole of *n*-butyllithium in hexane; the reaction mixture was refluxed for 13 hr., allowed to cool, and quenched with 50 ml. of water. The organic layer was dried over sodium sulfate, concentrated on a steam bath, and distilled to give 0.50 g. (9.6%) of IId, b.p. 90.5–93.5° (1.5 mm.), lit.[16] b.p. 126–128° (16 mm.). The observed ultraviolet and infrared spectra of IId agreed with the values reported by Mixer and Young.[17] A brown solid which separated during the course of the reaction was shown to consist of III and unchanged IVd by examination of its infrared spectrum.

(3-Benzoylpropyl)triphenylphosphonium Chloride (IVb).—A mixture of 100 g. (0.55 mole) of γ-chlorobutyrophenone, 158 g. of triphenylphosphine, and 200 ml. of toluene was refluxed for 15 hr. After cooling, the solvent was removed under reduced pressure and the red residue was crystallized by trituration with a small amount of acetone to give 80 g. (33%) of IVb, m.p. 184.5–186° (recrystallized from acetone–petroleum ether).

Anal. Calcd. for $C_{28}H_{26}ClOP$: C, 75.59; H, 5.89; P, 6.96; Cl, 7.97. Found: C, 73.76, 73.57; H, 6.01, 6.16; P, 6.82; Cl, 7.74, 7.79.

The infrared spectrum of IVb had bands at 3030 w, 2899 m, 1678 s, 1600 m, 1486 wm, 1437 s, 1404 w, 1369 m, 1297 w, 1206 wm, 1136 w, 1109 s, 1026 w, 996 m, 980–973 w, 945 w, 752 ms, 722 s, and 690 s cm.$^{-1}$.

Reaction of (3-Benzoylpropyl)triphenylphosphonium Chloride (IVb) with Base.—A mixture of 4.44 g. (0.01 mole) of IVb and 0.012 mole of *n*-butyllithium in 500 ml. of benzene was refluxed for 20 hr., cooled, and quenched with water. The organic layer was separated and concentrated on a steam bath. The residue

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(10) (a) G. Wittig, H. Eggers, and P. Duffner, *Ann.*, **619**, 10 (1958); (b) H. Hoffmann, *Chem. Ber.*, **94**, 1331 (1961); (c) A. Aksnes, *Acta Chem. Scand.*, **15**, 438 (1961); (d) J. A. Ford, Jr., and C. V. Wilson, *J. Org. Chem.*, **26**, 1433 (1961); (e) D. B. Denney and L. C. Smith, *ibid.*, **27**, 3404 (1962); (f) H. J. Bestmann, F. Seng, and J. Schulz, *Chem. Ber.*, **96**, 465 (1963).

(11) (a) M. Zanger, C. A. Vander Werf, and W. E. McEwen, *J. Am. Chem. Soc.*, **81**, 3806 (1959); (b) M. Grayson and P. T. Keough, *ibid.*, **82**, 3919 (1960).

(12) J. F. Norris and H. B. Couch, *ibid.*, **42**, 2329 (1920).

(13) All melting points are uncorrected; microanalyses were performed by Galbraith Laboratories. Infrared spectra were recorded on Perkin-Elmer Model 21 and Beckman IR-8 spectrophotometers, and ultraviolet spectra were recorded on a Cary Model 14 spectrophotometer.

(14) C. S. Marvel, D. W. MacCorquodale, F. E. Kendall, and W. A. Lazier, *J. Am. Chem. Soc.*, **46**, 2838 (1924).

(15) G. C. Coker, British Patent 830,519; *Chem. Abstr.*, **54**, 18,567 (1960).

(16) C. C. Price and J. V. Karabinos, *J. Am. Chem. Soc.*, **62**, 1160 (1940).

(17) R. Y. Mixer and W. G. Young, *ibid.*, **78**, 3379 (1956).

was dissolved in benzene and chromatographed on a 40-cm. Florisil column; elution with benzene led to the isolation of VII (25%), III (26%), and a brown oil which was shown to contain unchanged IVb. The organic layer from a similar reaction was examined by quantitative g.l.c.[18] and no peaks corresponding to either IIb or phenyl cyclopropyl ketone (IX) were observed; an unidentified peak with a retention time of 22 min. was the only peak observed. Under the conditions employed, authentic samples of IIb and IX had retention times of 48 and 27 min., respectively.

When this reaction was carried out with phenyllithium as base, but under otherwise identical conditions, the only materials isolated were biphenyl and unchanged IVb.

Reaction of (2-Benzoylethyl)triphenylphosphonium Bromide (IVa) with *n*-Butyllithium.—The reaction of IVa (0.011 mole) and *n*-butyllithium (0.015 mole) was carried out in the same manner as in the preceding experiment. Chromatographic separation on a Florisil column led to the isolation of VII (50%) by elution with benzene and III (40%) and IVa (5%) by elution with acetone.

(2-Benzoyl-1-phenylethyl)triphenylphosphonium Bromide (XIII).—A mixture of 60 g. (0.208 mole) of β-bromo-β-phenylpropiophenone, prepared by the method of Kashiwagi,[19] 54.4 g. (0.208 mole) of triphenylphosphine, and 200 ml. of anhydrous benzene was refluxed for 3 hr. On cooling two layers formed; the viscous orange layer was heated on a steam bath with 200 ml. of acetone. XIII (87 g., 76%) was obtained when the solution was cooled; XIII was recrystallized from acetone and melted at 149.5–151.0°.

Anal. Calcd. for $C_{33}H_{28}BrOP$: C, 71.86; H, 5.12. Found: C, 71.42, 71.61; H, 5.39, 5.24.

The infrared absorption spectrum of XIII had bands at 1678 m, 1600 w, 1449 w, 1437 ms, 1325 w, 1212 ms, 1190 w, 1106 s, 996 w, 976 w, 917 w, 750 s, 727 s, 702 ms, and 690 ms cm.$^{-1}$.

Reaction of (2-Benzoyl-1-phenylethyl)triphenylphosphonium Bromide (XIII) with Phenyllithium.—A mixture of 11.0 g. (0.02 mole) of XIII, 0.025 mole of phenyllithium, and 1.3 l. of anhydrous toluene was refluxed for 24 hr., cooled, and concentrated under reduced pressure to a volume of 15 ml. The residue was chromatographed on a 60-cm. neutral alumina column; elution with petroleum ether gave 2.78 g. (53%) of VII and elution with ethyl acetate gave 2.00 g. (48%) of chalcone (XIV). No other materials could be isolated from the column. The infrared spectrum of the residue indicated the presence of XIII, but gave no indication of III. XIV was identified by mixture melting point and infrared spectra comparisons with an authentic sample.

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[18] Gas-liquid chromatography was carried out on an F and M Model 500 gas chromatograph using a 21-ft. Apiezon L column (16.9% on Chromosorb W, 110-120 mesh) at a column temperature of 200°, an injection port temperature of 245°, and a flow rate of 24.3 ml./min. (helium).

[19] H. Kashiwagi, *Bull. Soc. Chem. Japan*, **26**, 355 (1953).

The Preparation of Olefins by Pyrolysis of Carbalkoxyphosphonium Salts[1,2]

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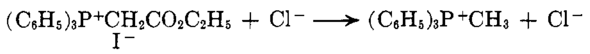
It has been found that phosphonium salts, $R_3P^+CH_2CO_2R'X^-$, decompose at convenient rates at temperatures between 130 and 225°. The products of these decompositions are carbon dioxide, $R_3P^+CH_3\ X^-$, and an olefin derived from R'. Salts have been prepared and decomposed where R' is a primary, secondary, or tertiary alkyl group. In most cases it was possible to isolate pure terminal olefins from decomposition of salts, R' = 1°. Where isomer formation was possible, *i.e.*, R' = 2°, 3°, the ratio of isomers was determined in many cases. A definite tendency to form the thermodynamically most stable olefins was noted. Olefins from several systems were found to be those arising from carbonium ion rearrangements.

Because of the general availability of alcohols, methods for their conversion to olefins have been the subject of constant investigation. In particular, mild methods have been sought. Pyrolytic decomposition of esters and xanthates has often been used.[5]

It is the purpose of this report to present a new and synthetically useful pyrolytic method for the conversion of an alcohol to an olefin. This work received its stimulus from the casual observations of Michaelis and Gimborn[6a] and Piaux.[6b] Michaelis and Gimborn found that triphenylcarbethoxymethylphosphonium chloride (I) slowly decomposes on heating at 100° to give triphenylmethylphosphonium chloride. They speculated, and quite reasonably so, that ethylene and carbon dioxide were the other products. Piaux found that



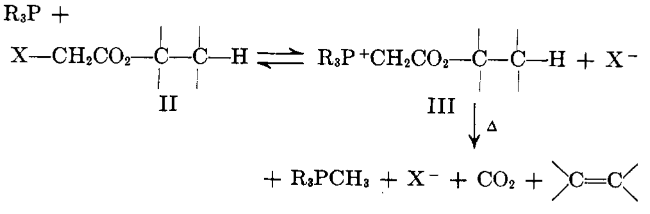
$$\underset{I^-}{(C_6H_5)_3P^+CH_2CO_2C_2H_5} + Cl^- \longrightarrow (C_6H_5)_3P^+CH_3 + Cl^-$$

heating phenyldimethylcarbethoxymethylammonium iodide yielded phenyltrimethylammonium iodide.

The initial phase of this investigation was directed at establishing the course of decomposition of salts of this type. Having found that olefins were formed, the later work has been directed towards extending the reaction to systems which would establish its generality and limitations. The results of these experiments are now being reported.[7] Consideration of mechanism and related matters, in particular the solvolysis of these salts, will be discussed in a subsequent report.

Results and Discussion

It has been found that a wide variety of α-halo esters (II)[8] react with tributyl or triphenylphosphine to give salts (III). Heating of these salts at temperatures between 130 and 225° leads to decomposition with



$$R_3P + X{-}CH_2CO_2{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}H \rightleftharpoons R_3P^+CH_2CO_2{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}H + X^-$$

II III

$$\xrightarrow{\Delta} + R_3PCH_3 + X^- + CO_2 + \rangle C{=}C\langle$$

$R = C_4H_9, C_6H_5;\ X = Br, Cl$

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[2] A preliminary account appeared in *J. Am. Chem. Soc.*, **83**, 3336 (1961).

[3] Rutgers Research Council Faculty Fellow, 1963-1964.

[4] National Science Foundation Cooperative Graduate Fellow in Chemistry, 1960-1961.

[5] C. H. DePuy and R. W. King, *Chem. Rev.*, **60**, 431 (1960).

[6] (a) A. Michaelis and V. Gimborn, *Ber.*, **27**, 272 (1894); (b) L. Piaux, *Compt. rend.*, **190**, 645 (1930).

[7] For some interesting olefin-forming pyrolytic decompositions of phosphorus-containing compounds, see H. E. Baumgarten and R. E. Allen, *J. Org. Chem.*, **26**, 1533 (1961); W. J. Bailey, W. M. Muir, and F. Marktscheffel, *ibid.*, **28**, 2150 (1963).

[8] In general, α-bromoacetates were used. These were prepared in high yield by esterification with α-bromoacetic acid or, in the case of acid-sensitive alcohols, α-bromoacetyl bromide was used.