405. The Use, in Wittig Reactions, of Phosphonium Salts and Phosphobetaines containing a Basic Group.

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Quaternary phosphonium salts and phosphobetaines containing the *p*-dimethylaminophenyl group have been prepared and used in the Wittig olefin synthesis. The solubility of the resulting phosphine oxide in dilute acid facilitates the isolation of the resulting olefin.

ONE of the chief technical difficulties associated with the Wittig olefin synthesis is separation of the olefin from the accompanying phosphine oxide. When a phosphonium halide is used in ether with an alkyl- or aryl-lithium as base, most of the phosphine oxide can be removed as an insoluble complex with lithium halide, but in other solvents, *e.g.*, tetrahydrofuran, this is not possible. The problem becomes particularly acute when stable Wittig reagents such as formylmethylenetriphenylphosphorane are used.[1] A way of overcoming the difficulty appeared to be the incorporation in the phosphonium salt or phosphobetaine of a basic group which would allow ready separation of the resulting phosphine oxide by extraction into dilute acid. Such phosphonium salts and phosphobetaines have now been prepared and used in Wittig reactions with the expected benefits in the ease of isolation of the resulting olefins.

p-Dimethylaminophenyldiphenylphosphine was prepared by the action of phenylmagnesium bromide on *p*-dimethylaminophenyldichlorophosphine. Michaelis and Schenk [2] reported that, although this phosphine reacted vigorously with alkyl and benzyl halides, the resulting salts were not crystalline. This is true of the methiodide, but in general the salts with other alkyl and with benzyl halides are crystalline. The benzylphosphonium bromide with butyl-lithium and fluorenone gave benzylidenefluorene (75%). The phosphobetaines $p\text{-Me}_2\text{N}{\cdot}\text{C}_6\text{H}_4{\cdot}\text{PPh}_2\text{:CH}{\cdot}\text{COR}$ (I; R = H, Me, OEt, or Ph) were also prepared and used in Wittig reactions with aldehydes, the ease of isolation of the products being particularly striking (see Experimental section). The phosphonium salt from chloroacetaldehyde was exceptional in showing no infrared carbonyl absorption below 6·1 μ; this may mean that the salt is really an ammonium-phosphobetaine (the phosphobetaines show their carbonyl absorption [3] at 6·1 μ), but attempts to use it directly in Wittig reactions were unsuccessful. The aldehyde-betaine (I; R = H) with 2,7-dimethylocta-2,6-dien-4-yne-1,8-dial gave only 12% of the required C_{12}-dial, a yield comparable with that obtained by use of formylmethylenetriphenylphosphorane followed by counter-current distribution.[3] The low yields are not due to further reaction of the product with the betaines, as the C_{12}-dial does not react with phosphobetaines.

The non-crystalline methiodide from *p*-dimethylaminophenyldiphenylphosphine gave,

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[1] Trippett and Walker, *Chem. and Ind.*, 1960, 202.

[2] Michaelis and Schenk, *Ber.*, 1888, **21**, 1497; *Annalen*, 1890, **260**, 1.

[3] Trippett and Walker, *J.*, 1961, 1266.

on alkaline hydrolysis, 82% of (*p*-dimethylaminophenyl)methylphenylphosphine oxide and is therefore substantially pure, but it could not be used successfully in Wittig reactions. Reduction of this phosphine oxide with lithium aluminium hydride gave (*p*-dimethylaminophenyl)methylphenylphosphine, which gave a crystalline methiodide. With butyllithium in tetrahydrofuran this methiodide gave a clear yellow solution which, on addition of *p*-nitrobenzophenone, became black: none of the expected olefin could be isolated. A similar failure in the use of a phosphonium iodide in a Wittig reaction has been reported,[4] but in that case—methylenetriphenylphosphorane and cyclopentanone—the reaction was normal when the bromide was used; in our case, use of the methobromide was equally unsuccessful, the clear yellow solution of phosphorane again becoming black on addition of *p*-nitrobenzophenone. This failure must be due to the nitro-group, for a similar reaction with benzophenone gave 1,1-diphenylethylene in 85% yield. Nitro-groups have not previously been found to interfere with Wittig reactions.

p-Dimethylaminophenyldichlorophosphine with methylmagnesium iodide gave *p*-dimethylaminophenyldimethylphosphine. The salts from this and benzyl bromide and phenacyl bromide were prepared and used in Wittig reactions. The phosphorane prepared from the methiodide again failed to react normally with *p*-nitrobenzophenone.

EXPERIMENTAL

p-*Dimethylaminophenyldiphenylphosphine*.—To a stirred solution of phenylmagnesium bromide, prepared from magnesium (13·6 g.) and bromobenzene (93 g.) in ether (250 ml.), cooled in ice–salt, was added *p*-dimethylaminophenyldichlorophosphine (42 g.) in ether (250 ml.) during 2 hr. The solution was stirred at room temperature for 1 hr. and cooled in ice, and saturated aqueous ammonium chloride (300 ml.) was added. The resulting precipitate was extracted into benzene (1·5 l.), the extract dried and evaporated to low bulk and ethanol (50 ml.) added. Crystallisation gave *p*-dimethylaminophenyldiphenylphosphine (42 g.), m. p. 152—153°.

Quaternisation with the following halides gave the corresponding phosphonium halides. *Ethyl bromide*, m. p. (from acetone–light petroleum) 193—194° (Found: C, 63·9; H, 6·1; N, 3·2. $C_{22}H_{25}BrNP$ requires C, 63·7; H, 6·1; N, 3·4%); *allyl bromide*, m. p. (from water) 232—234° (Found: C, 64·8; H, 5·85; N, 3·2. $C_{23}H_{25}BrNP$ requires C, 64·8; H, 5·9; N, 3·3%); *benzyl bromide*, m. p. (from chloroform–ethyl acetate) 227—228° (Found: N, 2·8. $C_{27}H_{27}BrNP$ requires N, 2·95%); *acetonyl chloride*, m. p. (from chloroform–ethyl acetate) 204—206° (Found: N, 3·5. $C_{23}H_{25}ClNOP$ requires N, 3·5%); *formylmethyl chloride*, m. p. (from chloroform–ethyl acetate) 172—173° (Found: N, 3·5. $C_{22}H_{23}ClNOP$ requires N, 3·65%); *ethoxycarbonylmethyl bromide*, m. p. 84—87° (Found: C, 58·7; H, 5·85; N, 2·7. $C_{24}H_{27}BrNO_2P,H_2O$ requires C, 58·7; H, 5·9; N, 2·75%). The salts from phenacyl bromide, chloroacetamide, and bromoacetamide were not crystalline.

Reaction of Benzylidene-(p-*dimethylaminophenyl*)*diphenylphosphorane with Fluorenone*.—To a stirred suspension of benzyl-(*p*-dimethylaminophenyl)diphenylphosphonium bromide (4·8 g.) in ether (100 ml.), ethereal 1·3N-butyl-lithium (8·5 ml.) was added, followed after 10 min. by fluorenone (1·85 g.) in ether (25 ml.). The resulting suspension was set aside at room temperature for 18 hr., then washed with dilute hydrochloric acid and with water, dried, and evaporated. Crystallisation of the residue from ethanol gave 9-benzylidenefluorene (75%), m. p. 72—74°, undepressed on mixture with an authentic sample of m. p. 74—75°.

A similar reaction with benzyl-(*p*-dimethylaminophenyl)dimethylphosphonium bromide gave a 78% yield of benzylidenefluorene.

Acetonylidene-(p-*dimethylaminophenyl*)*diphenylphosphorane*.—Acetonyl-(*p*-dimethylaminophenyl)diphenylphosphonium chloride (4·5 g.) was dissolved in water (100 ml.) at 0°, and the solution was made alkaline to phenolphthalein with dilute sodium hydroxide, and extracted with chloroform. The extract was dried and evaporated. Crystallisation of the residue from ethyl acetate gave the *phosphorane*, m. p. 176—177° (Found: N, 4·1. $C_{23}H_{24}NOP$ requires N, 3·9%).

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[4] Collins and Hammond, *J. Org. Chem.*, 1960, **25**, 1435.

A solution of this phosphorane (2·5 g.) and benzaldehyde (0·75 g.) in benzene (50 ml.) was refluxed for 7 hr., cooled, and washed with dilute hydrochloric acid (3 times) and with water. Evaporation, and crystallisation of the residue from light petroleum (b. p. 40—60°) at 0°, gave benzylideneacetone (78%), m. p. 40—41° (lit., m. p. 42°).

Formylmethylene - (p - dimethylaminophenyl)diphenylphosphorane.—Formylmethyl - (*p* - dimethylaminophenyl)diphenylphosphonium chloride was dissolved in ethanol, triethylamine (1·1 mol.) added, and the solution diluted with much water and extracted with benzene. The extract was dried and evaporated to give the *phosphorane*, m. p. (from acetone) 210—211° (Found: C, 75·9; H, 6·5; N, 4·1. $C_{22}H_{22}NOP$ requires C, 76·1; H, 6·65; N, 4·0%).

A solution of this phosphorane (1·5 g.) and 2,7-dimethylocta-2,6-dien-4-yne-1,8-dial (0·32 g.) in benzene (30 ml.) was refluxed for 19 hr., cooled, washed with dilute hydrochloric acid and with water, dried, and evaporated. Crystallisation of the residue from aqueous methanol gave 4,9-dimethyldodeca-2,4,8,10-tetraen-6-yne-1,12-dial (12%), m. p. and mixed m. p. 161—162°. A similar reaction with benzaldehyde gave cinnamaldehyde, isolated as the 2,4-dinitrophenylhydrazone (58%), m. p. and mixed m. p. 252—253°.

Ethoxycarbonylmethylene-(p-dimethylaminophenyl)diphenylphosphorane.—A solution of ethoxycarbonylmethyl-(*p*-dimethylaminophenyl)diphenylphosphonium bromide (1 g.) in ethanol (15 ml.) at 0° was made alkaline to phenolphthalein with dilute sodium hydroxide solution, diluted with ice-water, and rapidly extracted with chloroform. The extract was dried and evaporated, and the residue crystallised from ethyl acetate–light petroleum to give the *ester-phosphorane* (0·8 g.), m. p. 141—142° (Found: C, 73·9; H, 6·65; N, 3·55. $C_{24}H_{26}NO_2P$ requires C, 73·7; H, 6·65; N, 3·6%).

A solution of this phosphorane (2·3 g.) and benzaldehyde (0·6 g.) in benzene (50 ml.) was refluxed for 18 hr., cooled, washed with dilute hydrochloric acid and with water, dried, and evaporated. The residue, after hydrolysis with alcoholic 2N-sodium hydroxide for 0·5 hr., gave, on acidification, cinnamic acid (0·7 g.), m. p. and mixed m. p. 132—133°.

(p-Dimethylaminophenyl)dimethylphenylphosphonium Bromide.—Finely powdered (*p*-dimethylaminophenyl)methylphenylphosphine oxide (14 g.) was added in 15 min. to a stirred solution of lithium aluminium hydride (6 g.) in dibutyl ether (150 ml.) heated on a water-bath. Heating was continued for 18 hr., the suspension was cooled, methanol (30 ml.) was added, and solvents were removed under reduced pressure. Distillation of the residue gave *(p-dimethylaminophenyl)methylphenylphosphine* (8 g.), b. p. 175—176°/0·15 mm. The *methiodide* had m. p. (from chloroform–benzene) 234—235° (Found: C, 49·8; H, 5·6; N, 3·9. $C_{16}H_{21}INP$ requires C, 49·9; H, 5·45; N, 3·65%). The *methobromide* had m. p. (from chloroform–benzene) 252—253° (Found: C, 56·65; H, 6·3; N, 3·95. $C_{16}H_{21}BrNP$ requires C, 56·7; H, 6·2; N, 4·15%).

A suspension of the methobromide (3·8 g.) in tetrahydrofuran (150 ml.) was treated with ethereal 1·15N-butyl-lithium (11 ml.) and stirred at room temperature for 1 hr. Benzophenone (2·25 g.) in ether (25 ml.) was added and the resulting white suspension refluxed overnight. Solvent was then removed and the residue shaken with ether and dilute hydrochloric acid. The ether extract was washed with water, dried, and evaporated, and the residue distilled to give 1,1-diphenylethylene (1·9 g.), b. p. 140—141°/14 mm.

(p-Dimethylaminophenyl)dimethylphosphine. To a stirred solution of methylmagnesium iodide, prepared from magnesium (11·2 g.) and methyl iodide (63 g.) in ether (250 ml.), cooled in ice-salt, *p*-dimethylaminophenyldichlorophosphine (34 g.) in ether (200 ml.) was added during 2 hr. The solution was set aside at room temperature for 1 hr., then cooled, and saturated aqueous ammonium chloride (600 ml.) added. The ethereal layer was dried and evaporated, and the residue distilled to give (*p*-dimethylaminophenyl)dimethylphosphine (19·5 g.), b. p. 86—88°/0·2 mm.

Treatment of the phosphine in benzene with benzyl bromide gave the *phosphonium bromide*, m. p. (from water) 217—219° (Found: C, 58·1; H, 6·3; N, 3·8. $C_{17}H_{23}BrNP$ requires C, 57·9; H, 6·5; N, 4·0%). Similar treatment with phenacyl bromide gave the *phenacylphosphonium bromide*, m. p. (from ethanol) 249—250° (decomp.) (Found: C, 57·3; H, 6·0; N, 3·5. $C_{18}H_{23}BrNOP$ requires C, 56·8; H, 6·0; N, 3·7%). With aqueous alkali at 0°, this gave *benzoylmethylene-(p-dimethylaminophenyl)dimethylphosphorane*, m. p. (from benzene–light petroleum) 136—137° (Found: N, 4·8. $C_{18}H_{22}NOP$ requires N, 4·7%).

A solution of this phosphorane (3·0 g.) and benzaldehyde (1·06 g.) in benzene (50 ml.) was refluxed for 12 hr., cooled, and washed with dilute hydrochloric acid and with water.

Evaporation, and crystallisation of the residue from aqueous ethanol, gave benzylideneacetophenone (76%), m. p. 58·5—59·5°.

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