1173. *Some Applications of the Wittig Reaction in the Biphenyl Series*

By D. Muriel Hall and Biravana Prakobsantisukh

Wittig reaction between biphenyl-2,2′-dialdehyde and methoxycarbonylmethylenebiphenylphosphorane gives 2,2′-di-(2-methoxycarbonylvinyl)biphenyl. 2,2′-Bis(triphenylphosphoniomethyl)biphenyl dibromide and its 6-nitro-derivative have been prepared; the diphosphorane from the former compound reacts with benzaldehyde to give 2,2′-di-α-styrylbiphenyl.

The reaction between an alkylidenephosphorane and a carbonyl compound to give an olefin has been widely used as a synthetic tool since its discovery by Wittig and Schöllkopf.[1] We report here some preliminary studies on the applicability of this reaction to the synthesis of 2,2′-disubstituted biphenyl derivatives.

For this purpose the biphenyl structure may be associated initially with either the carbonyl groups or the phosphorane. In the former category, biphenyl-2,2′-dialdehyde

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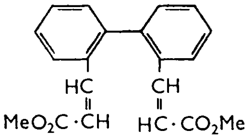
[1] G. Wittig and U. Schöllkopf, *Chem. Ber.*, 1954, **87**, 1318; G. Wittig and W. Haag, *ibid.*, 1955, **88**, 1654.

was found to react satisfactorily with the stable phosphorane [2] (I) to give the ester (II), which could readily be hydrogenated to the known [3] bispropionic ester (III).

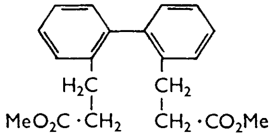
Stable phosphoranes such as (I) are known to lead predominantly to the *trans*-isomer,[4,5] at least in the absence of certain catalysts.[6] Both the ester (II) and the corresponding acid showed medium to strong bands in the infrared * (at 974 and 978 cm.$^{-1}$, respectively), typical [7] of *trans*-HC=CH; this band appears at 978 cm.$^{-1}$ in *trans*-cinnamic acid. The out-of-plane =CH deformation band [7] of *cis*-HC=CH•CH_2R, found at 830 cm.$^{-1}$ in *cis*-cinnamic acid itself, was absent; the ester and acid thus have the *trans,trans*-configuration.

$Ph_3P = CH\cdot CO_2Me$

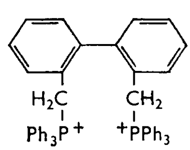
(I)



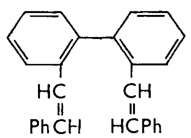
(II)



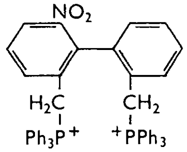
(III)



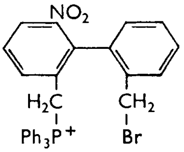
(IV) $2Br^-$



(V)



(VI) $2Br^-$



(VII) Br^-

Biphenyl-2,2′-dialdehyde has been, until recently,[8] a rather inaccessible compound, except in fairly small quantities.[9] As an alternative to the ozonolysis of phenanthrene we investigated a two-stage synthesis from phenanthraquinone which proved to be convenient. Phenanthraquinone was reduced [10] with lithium aluminium hydride, giving *trans*-9,10-dihydro-9,10-dihydroxyphenanthrene, which was oxidised [11] by lead tetra-acetate to the dialdehyde in 73% yield.

It was also intended to use 2,2′-diacetylbiphenyl in reaction with compound (I) but preliminary experiments showed that neither acetophenone nor acetone would react with this phosphorane under conditions normally used for the Wittig reaction. Trippett and Walker,[12] using the ethyl ester, confirmed the non-reactivity of ketones towards phosphoranes of this type, although Fodor and Tömösközi [13] have found that in some cases reaction may be brought about by prolonged heating in a sealed tube. However, in view of our findings with acetophenone, the reaction with the much more sterically hindered 2,2′-diacetylbiphenyl was not attempted.

As an alternative approach to the synthesis of biphenyls with extended carbon chains

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* Relevant spectra will be found in the DMS collection from no. 13,348 onwards.

[2] O. Isler, H. Gutmann, M. Montavon, R. Rüegg, G. Ryser, and P. Zeller, *Helv. Chim. Acta*, 1957, **40**, 1242.

[3] K. Mislow, S. Hyden, and H. Schaefer, *J. Amer. Chem. Soc.*, 1962, **84**, 1449.

[4] S. Trippett, *Quart. Rev.*, 1963, **17**, 406.

[5] L. D. Bergelson and M. M. Shemyakin, *Tetrahedron*, 1963, **19**, 149; A. J. Speziale and D. E. Bissing, *J. Amer. Chem. Soc.*, 1963, **85**, 3878, and references cited therein.

[6] C. Rüchardt, S. Eichler, and P. Panse, *Angew. Chem.*, 1963, **75**, 858.

[7] L. J. Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1958, and references cited therein.

[8] P. S. Bailey and R. E. Erickson, *Org. Synth.*, 1961, **41**, 41; J. O. Hawthorne, E. L. Mihelic, M. S. Morgan, and M. H. Wilt, *J. Org. Chem.*, 1963, **28**, 2831.

[9] W. S. Rapson and R. G. Shuttleworth, *J.*, 1941, 487; R. G. R. Bacon and W. S. Lindsay, *J.*, 1958, 1375.

[10] J. Booth, E. Boyland, and E. E. Turner, *J.*, 1950, 1188.

[11] E. Boyland and G. Wolf, *Biochem. J.*, 1950, **47**, 64. See also R. Criegee, R. Marchand, and H. Wannowius, *Annalen*, 1942, **550**, 99, who similarly oxidised the *cis*-compound.

[12] S. Trippett and D. M. Walker, *J.*, 1961, 1266; *Chem. and Ind.*, 1961, 990.

[13] G. Fodor and I. Tömösközi, *Tetrahedron Letters*, 1961, 579.

in the 2,2'-positions the preparation and reaction of the diphosphorane derived from the phosphonium salt (IV) was investigated. Triphenylphosphine and 2,2'-bisbromomethylbiphenyl reacted in cold benzene to give a mixture of the mono- and di-phosphonium bromides which were difficult to separate. The diphosphonium salt was prepared satisfactorily by prolonged reaction in boiling xylene or by heating the reactants together for a short time at 180° without a solvent. Treatment with n-butyl-lithium gave the diphosphorane which has also been obtained recently by Bestmann, Haberlein, and Kratzer.[14] This reacted with benzaldehyde to give 2,2'-di-α-styrylbiphenyl (V), appearing first in a metastable form, m. p. 121—123°, but later only with m. p. 148—149°.

The *trans,trans*-configuration was assigned to this compound on the basis of its infrared spectrum * which shows a strong band at 965 cm.$^{-1}$ (characteristic of *trans*-HC=CH–) [7,15] and the absence of the many bands which appear in *cis*-stilbene [16,17] but not in *trans*-stilbene.[15] The ultraviolet spectrum has a band at 300 mμ (ε 44,000 in cyclohexane) corresponding to the band of *trans*-stilbene [18] at 295 mμ (ε 29,000 in ethanol); the shortwave band (230 mμ, ε 65,000), which is more characteristic of *cis*-stilbene [18] (224 mμ, ε 24,300) than of *trans*-stilbene (228 mμ, ε 16,400), probably owes its high intensity to overlapping by the strong shortwave biphenyl band.

The above diphosphorane was also treated *in situ* with acetaldehyde but the product was mainly a viscous liquid containing carbonyl and hydroxyl groups and had presumably resulted from a series of aldol condensations induced by traces of butyl-lithium. A very small quantity of an unsaturated hydrocarbon, probably 2,2'-di(prop-1-enyl)biphenyl, was isolated from the mixture.

We were also interested in the stereochemistry of the salt (IV) since it is possible that the $CH_2{\cdot}PPh_3^+$ groups might be large enough to give rise to observable optical activity at low temperatures. However, in some conformations the $^+PPh_3$ group will contribute little or nothing to the energy barrier to racemisation. The contribution of this group to the entropy of activation could therefore be better studied in a compound in which the energy barrier had been raised by the introduction of a third *ortho*-substituent into the biphenyl system.

The diphosphonium salt (VI) was therefore prepared by the interaction of 2,2'-bisbromomethyl-6-nitrobiphenyl [19] and triphenylphosphine. Reaction in boiling xylene gave a mixture of mono- and di-phosphonium salts but heating the reactants in the absence of a solvent [20] gave excellent yields of the diphosphonium salt (VI), provided that the reaction temperature (180°) was higher than the m. p. of the monophosphonium salt and that the reaction time was short (5 min.). The diphosphonium salt was obtained in two different crystalline forms, one a trihydrate (m. p. 212°), the other a dihydrate also solvated with acetone (m. p. 266—268°). The monophosphonium salt was also solvated and was considered to be compound (VII) rather than its structural isomer since the nitro-group will sterically hinder reaction at the methylene group in the other ring, rather than at the one in its own ring. The camphorsulphonate and bromocamphorsulphonate prepared from compound (VI) have shown no evidence of optical resolution but are still under investigation.

EXPERIMENTAL

Biphenyl-2,2'-dialdehyde.—*trans*-9,10-Dihydro-9,10-dihydroxyphenanthrene [10] was obtained as long needles, m. p. 195—196°. Booth and Boyland [10] obtained it in two forms: needles, m. p. 185—187°, and prisms, m. p. 194°. The dihydrodihydroxyphenanthrene (4·35 g.) was

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* Cf. footnote on previous page.

[14] H. J. Bestmann, H. Haberlein, and O. Kratzer, *Angew. Chem.*, 1964, **76**, 226.

[15] American Petroleum Institute, Research Project No. 44, Infrared Spectral Data, Serial No. 2299.

[16] American Petroleum Institute, Research Project No. 44, Infrared Spectra Data, Serial No. 2298.

[17] M. Oki and H. Kunimoto, *Spectrochim. Acta*, 1963, **19**, 1463.

[18] R. N. Beale and E. M. F. Roe, *J.*, 1953, 2755.

[19] D. M. Hall and T. M. Poole, unpublished work.

[20] Cf. L. Horner and E. Lingnau, *Annalen*, 1955, **591**, 135.

suspended in benzene (125 c.c.) and lead tetra-acetate (9·1 g.) was added to the stirred suspension; stirring was continued at room temperature for 2 hr. Lead diacetate was filtered off and the filtrate was distilled under reduced pressure giving the dialdehyde (3·15 g., 73%), m. p. 56—59°. Crystallisation from dry ether–light petroleum (b. p. 40—60°) gave nearly colourless crystals, m. p. 61—62°.

2,2′-*Di*-(2-*methoxycarbonylvinyl*)*biphenyl* (II).—Methoxycarbonylmethylenetriphenylphosphorane[2] (I), m. p. 170—172° (lit.,[2] 162—163°) (15·9 g., 2 mol.), and biphenyl-2,2′-dialdehyde (5 g., 1 mol.) were heated in dry toluene solution under reflux for 16 hr. After removal of most of the solvent the remaining solution was chromatographed on silica gel, eluting with methanol–toluene (1 : 1), and then on alumina (benzene solution). Fractional crystallisation of the various solids from light petroleum (b. p. 80—100°) and from methanol separated the required ester (5·1 g. crude) from the triphenylphosphine oxide but removal of the last traces of oxide from the ester was accompanied by considerable loss of material. The pure trans,trans-*ester* had m. p. 123—124° (MeOH) (Found: C, 74·2; H, 5·7. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6%). Hydrolysis (ethanolic KOH) gave the acid, m. p. 294—296° (decomp.), from glacial acetic acid (lit.,[21] m. p. 286°) (Found: C, 73·6; H, 5·1. Calc. for $C_{18}H_{14}O_4$: C, 73·5; H, 4·8%). Hydrogenation of the ester in methanol over palladium on charcoal gave 2,2′-di-(2-methoxycarbonylethyl)biphenyl, m. p. 62—63° (hexane) (lit.,[3] 61—62° and 74·5—75·5°).

2,2′-*Bis*(*triphenylphosphoniomethyl*)*biphenyl Dibromide* (IV).—(*a*) *In boiling xylene.* 2,2′-Bisbromomethylbiphenyl[22] (34 g., 1 mol.) and triphenylphosphine (70 g., 2·67 mol.) were dissolved separately in sodium-dried xylene (1200 c.c. in all) and the mixed solutions were heated under reflux, with stirring, for 140 hr. The solid was collected, washed with benzene and light petroleum, and crystallised from ethanol–ethyl acetate, giving the *dibromide dihydrate* (70 g., 78%), m. p. 323—326°, after loss of water between 250 and 300° (Found: C, 66·1; H, 5·1; ionic Br, 17·7; P, 6·8. $C_{50}H_{42}Br_2P_2, 2H_2O$ requires C, 66·7; H, 5·15; Br, 17·7; P, 6·9%) (OH band at 3410 cm.$^{-1}$).

(*b*) *Without a solvent.* The dibromo-compound (3·4 g., 1 mol.) and triphenylphosphine (9·0 g., 3·44 mol.) were ground together and then placed in a bath at 290° and well stirred by hand. The mixture became soft but not molten. It was kept at this temperature for 5 min. and then cooled and ground with benzene. The insoluble material was washed with light petroleum and crystallised from ethanol–ethyl actate, giving the bisphosphonium dibromide (6·63 g., 74%), m. p. 324—327°.

The *dipicrate*, prepared in aqueous solution by using sodium picrate, had m. p. 209—210° (from aqueous ethanol) (Found: C, 64·3; H, 4·3; N, 7·6; P, 5·4. $C_{62}H_{46}N_6O_{14}P_2$ requires C, 64·1; H, 4·0; N, 7·2; P, 5·3%). The di-(+)-*camphorsulphonate* was obtained as a trihydrate, m. p. 70°, $[\alpha]^{22}_{5461}$ +21·5° (*c* 0·500 in 96% EtOH) but could not be crystallised (Found: C, 69·2; H, 6·1; P, 4·9; S, 5·1. $C_{70}H_{72}O_8P_2S_2,3H_2O$ requires C, 68·8; H, 6·4; P, 5·1; S, 5·2%).

2,2′-*Di*-α-*styrylbiphenyl* (V).—The bisphosphonium dibromide (13·5 g., 1 mol.) was finely ground and added in small portions to an ethereal solution of n-butyl-lithium (4 mol., made from 0·84 g. of lithium and 5·55 g. of n-butyl chloride) under nitrogen with stirring. When the exothermic reaction was over benzaldehyde (3·2 g., 2 mol.) was added and the mixture then stirred and heated for 2½ hr. The solid complex of triphenylphosphine oxide and lithium bromide was filtered off and washed with ether; solvent was removed from the filtrate and washings and the residue was digested with a little ethanol. The solid obtained was crystallised from hexane (charcoal) and gave 2,2′-di-α-styrylbiphenyl (0·75 g.), m. p. 121—123° (Found: C, 93·9; H, 6·4. $C_{28}H_{22}$ requires C, 93·8; H, 6·2%). The second crop (0·23 g.) had m. p. 119° but on crystallisation from light petroleum (b. p. 60—80°) the m. p. rose to 148—149° (Found: C, 93·4; H, 6·3%); the m. p. of a mixture with first crop was 145—146°. The low melting form was not obtained again (even on seeding solutions) and after 1 month the specimen of the first crop was found to have m. p. 146—147·5°. Yield of crystallised material 22%.

Hydrogenation in ethyl acetate solution over platinum (12 hr. at room temperature) gave 2,2′-*diphenethylbiphenyl* (Found: C, 92·4; H, 7·7. $C_{28}H_{26}$ requires C, 92·8; H, 7·2%), shown by its infrared and ultraviolet spectra to be free from olefinic double bonds ($\lambda_{\text{max.}}$ 300 mμ, ε 2300 in cyclohexane). With a shorter reduction time (5 hr.) hydrogenation was incomplete; with a longer reduction time (21 hr.) hydrogenation of two of the aromatic rings occurred,

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[21] F. Mayer, *Ber.*, 1911, **44**, 2298.

[22] D. M. Hall, M. S. Lesslie, and E. E. Turner, *J.*, 1950, 711.

giving 2,2′-bis-(2-*cyclohexylethyl*)*biphenyl* (Found: C, 88·85; H, 10·1. $C_{28}H_{38}$ requires C, 89·8; H, 10·2%), of which there was insufficient for satisfactory purification.

Reaction of 2,2′-*Bisbromomethyl*-6-*nitrobiphenyl with Triphenylphosphine*.—(*a*) *In xylene*. 2,2′-Bisbromomethyl-6-nitrobiphenyl[19] (2 g., 1 mol.) and triphenylphosphine (4 g., 2·9 mol.) were dissolved separately in dry xylene (100 c.c. in all) and the mixture heated at 140° for 10 hr. The precipitate was collected, washed well with xylene, and crystallised from ethanol–ether; two crystalline fractions and much brown gum were obtained. Recrystallisation of the first crop from acetone gave 0·54 g. (10%) of 6-*nitro*-2,2′-*bis*(*triphenylphosphoniomethyl*)*biphenyl dibromide* (V), m. p. 266—268°, solvated with water and acetone (Found: C, 63·3; H, 5·0; Br, 16·4; P, 6·0. $C_{50}H_{41}Br_2NO_2P_2,2H_2O,(CH_3)_2CO$ requires C, 63·4; H, 5·1; Br, 15·9; P, 6·2%) (OH band at 3400 cm.$^{-1}$, C=O band at 1701 cm.$^{-1}$). Recrystallisation of the second crop from acetone gave the *monophosphonium bromide* (0·7 g., 19%) [probably (VII)], m. p. 157—160°, also solvated with water and acetone [Found: C, 58·5; H, 4·3; Br, 23·4; P, 4·0. $2C_{32}H_{26}Br_2NO_2P,H_2O,(CH_3)_2CO$ requires C, 58·7; H, 4·4; Br, 23·3; P, 4·5%] (OH band at 3348 cm.$^{-1}$, C=O band at 1704 cm.$^{-1}$, and C–Br band at 610 cm.$^{-1}$).

In another preparation in which the salt was crystallised repeatedly from ethanol–ethyl acetate but not from acetone, the diphosphonium salt was obtained as a *trihydrate*, m. p. 212° (Found: C, 62·2; H, 5·0; Br, 16·5; P, 6·2. $C_{50}H_{41}Br_2NO_2P_2,3H_2O$ requires C, 62·3; H, 4·9; Br, 16·6; P, 6·4%) (OH peak at 3400 cm.$^{-1}$). Subsequent recrystallisation from acetone gave the other solvated form, b. p. 266—268°.

(*b*) *Without solvent*. The dibromo-compound (2·5 g.) and triphenylphosphine (6 g., 3·5 mol.) were ground together and the mixture was placed in a bath preheated to 190°. The melt was stirred and soon set to a hard mass. After 5 min. it was cooled, ground with xylene, and collected (6·5 g.), m. p. 190°. Crystallisation from acetone gave the solvated dibromide, m. p. 256—258° (4·4 g., 68%), raised to 265—266° on recrystallisation.

Other 6-*Nitro*-2,2′-*bis*(*triphenylphosphoniomethyl*)*biphenyl Salts*.—The *dipicrate*, obtained from the dibromide and sodium picrate, crystallised from ethanol in yellow needles, m. p. 135—136° (decomp.) (Found: C, 61·7; H, 4·2; N, 8·2; P, 4·8. $C_{62}H_{45}N_7O_{16}P_2$ requires C, 61·7; H, 3·8; N, 8·1; P, 5·1%).

The *dicamphorsulphonate* was prepared in aqueous ethanol and crystallised from acetone–ether. It had m. p. 170—172° and $[\alpha]_{5461}^{22}$ +21·0° (*c* 1·00 in 96% EtOH), unchanged by recrystallisation from this and other solvents or by warming to 100° (Found: C, 67·2; H, 6·2; P, 4·8; S, 5·1. $C_{70}H_{71}NO_{10}P_2S_2,2H_2O$ requires C, 67·3; H, 6·1; P, 5·0, S, 5·1%) (OH band at 3433 cm.$^{-1}$).

Treatment of the dicamphorsulphonate in aqueous ethanol with aqueous potassium iodide gave the *di-iodide*, m. p. 280—282° (from ethanol) (Found: C, 58·3; H, 4·25; I, 25·6; P, 6·0. $C_{50}H_{41}I_2NO_2P_2,H_2O$ requires C, 58·8; H, 4·2; I, 24·8; P, 6·1%) (OH bands at 3646 and 3410 cm.$^{-1}$).

The *di-α-bromocamphor-π-sulphonate* was crystallised from ethyl acetate and had m. p. 168° (decomp.), $[\alpha]_{5461}^{18\cdot6}$ +48·0° (*c* 1·00 in 96% EtOH), unchanged by heating the solution in a sealed tube at 100° for 3 hr. (Found: C, 58·6; H, 5·4; Br, 11·3; P, 4·55; S, 4·55. $C_{70}H_{69}Br_2NO_{10}P_2S_2,3H_2O$ requires C, 59·0; H, 5·3; Br, 11·2; P, 4·35; S, 4·5%). (OH band at 3393 cm.$^{-1}$.)

Spectra.—Ultraviolet absorption spectra were measured on a Unicam S.P. 500 spectrophotometer. Infrared spectra were measured on a Grubb–Parsons GS 2A double-beam recording spectrophotometer.

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