

The Copper-promoted Reaction of *o*-Halogenodiarylo-Compounds with Nucleophiles. Part 2.¹ The Copper-promoted Reaction of *o*-Bromodiarylo-Compounds with Diesters of Phosphorous Acid. A Novel Method for the Preparation of Dialkyl Arylphosphonates

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o-Bromodiarylo-compounds react with diethyl phosphite, in the presence of copper(I) iodide and sodium acetate in ethanol, to give the corresponding *o*-diethylphosphonato-diarylo-compounds in good yield. Reaction is facilitated by the presence of an *o*'-donor substituent in the *o*-bromodiarylo-compound. When diethyl phosphite is replaced by diphenyl phosphite the product is again the diethyl phosphonate. The use of diphenyl phosphite in alcohols other than ethanol affords a facile, general method for the preparation of a range of dialkyl phosphonates since the product obtained is the phosphonate ester corresponding to the alcoholic solvent employed.

THE previous paper¹ in this series described the copper-promoted reaction of *o*-bromodiarylo and related compounds with trialkyl phosphites under mild conditions to give the corresponding dialkyl phosphonates. These replacements showed sensitivity to steric effects of substituents in the aryl nucleus carrying the bromine atom, but responded relatively feebly to their polar effects. They were facilitated by *o*'-donor functions and, in this case, depending upon choice of catalyst and solvent, were in competition with reductive substitution and biaryl coupling.

The present investigation was undertaken as a logical extension of what may be regarded as a copper-promoted Michaelis-Arbuzov² reaction to the Michaelis-Becker³ variant of that reaction. Dialkyl phosphites exist⁴ mainly in the phosphoryl form [(RO)₂POH \rightleftharpoons (RO)₂P(O)H] and are therefore unreactive in the Michaelis-Arbuzov reaction. The anions, however, which are readily available^{3b} as sodium salts, or which may be generated *in situ* from the neutral compounds and tertiary amines, react readily with alkyl halides to give high yields of the dialkyl alkylphosphonate [(RO)₂P=O Na⁺ + R'-Hal \rightarrow R'P(O)(OR)₂ + NaHal]. As in the Michaelis-Arbuzov reaction aromatic halides are quite inert⁵ and the Michaelis-Becker reaction cannot be used to prepare dialkyl arylphosphonates. We now report the preparation of *o*-dialkylphosphonodiarylo-compounds by the copper-promoted reaction of *o*-halogenodiarylo-compounds with dialkyl phosphites, and the extension of this reaction to diphenyl phosphite.

EXPERIMENTAL

¹H N.m.r. spectra were recorded on a Hitachi-Perkin-Elmer R-24A spectrometer at 60 MHz or a Varian HA-100 spectrometer at 100 MHz, using tetramethylsilane as internal standard, and mass spectra were recorded with an A.E.I. MS90 spectrometer. Thin layer chromatography was carried out on Eastman Chromagram Sheets 13181 (silica gel) using cyclohexane-chloroform (1:1), nitromethane-toluene (7:93), and ethyl acetate-light petroleum (3:2) as eluants. G.l.c. spectra were obtained with a Pye-Unicam series 104 Chromatograph, using Celite (100-120 mesh) coated with 10% silicone E301 as stationary phase. Light petroleum refers to the fraction of b.p. 60-80 °C.

Diethyl 3,5-Dinitro-6-[2-acetylamino-4-(NN-diethylamino)-phenylazo]phenylphosphonate (10).—(a) A stirred mixture

of 3-acetylamino-4-(2-bromo-4,6-dinitrophenylazo)-*NN*-diethylaniline (1) (4.8 g), diethyl phosphite (2.7 g), sodium acetate (2.7 g), copper(I) iodide (1.0 g), and ethanol (200 ml) was refluxed for 30 min, when t.l.c. showed reaction to be complete. The mixture was cooled and poured into water (1 500 ml). After 30 min the precipitated product was filtered off, washed with water, and dried. Crystallisation (thimble) from ethanol gave *diethyl 3,5-dinitro-6-[2-acetylamino-4-(NN-diethylamino)phenylazo]phenylphosphonate* (10) (4.5 g, 84%) as glistening black rods (Found: C, 49.5; H, 5.3; N, 15.4; P, 5.85%; *M*⁺ 536. Calc. for C₂₂H₂₉N₆O₈P: C, 49.25; H, 5.45; N, 15.65; P, 5.8%; δ(CDCl₃) 1.3 (12 H, t, MeCH₂), 2.3 (3 H, s, MeCO), 3.5 (4 H, q, MeCH₂N), 4.1 (4 H, p, MeCH₂O), and 6.2-8.3 (5 H, m, aromatic).

(b)-(d) Similar results were obtained when the sodium acetate was replaced by potassium acetate (2.0 g), triethylamine (2.0 g), or tripropylamine (2.9 g), but in the presence of pyridine (1.6 g) little reaction had occurred after 24 h.

Dimethyl 3,5-Dinitro-6-[2-acetylamino-4-(NN-diethylamino)phenylazo]phenylphosphonate (9).—(a) A stirred mixture of 3-acetylamino-4-(2-bromo-4,6-dinitrophenylazo)-*NN*-diethylaniline (1) (4.8 g), diphenyl phosphite (3.5 g), sodium acetate (2.7 g), copper(I) iodide (1.0 g), and methanol (160 ml) was refluxed for 30 min when t.l.c. showed reaction to be complete. The mixture was cooled and filtered. Crystallisation (thimble) of the residue from methanol gave *dimethyl 3,5-dinitro-6-[2-acetylamino-4-(NN-diethylamino)phenylazo]phenylphosphonate* (9) (4.3 g, 85%) as glistening black rods (Found: C, 47.3; H, 4.9; N, 16.6; P, 6.1%. *M*⁺ 508. Calc. for C₂₀H₂₅N₆O₈P: C, 47.25; H, 4.95; N, 16.55; P, 6.1%); i.r. spectrum identical with that of authentic material.¹ G.l.c. examination of the filtrate confirmed the presence of phenol.

(b) A stirred mixture of diphenyl phosphite (3.5 g), copper(I) iodide (1.0 g), and methanol (160 ml) was refluxed for 30 min when g.l.c. showed no ester exchange to have occurred. Sodium acetate (2.7 g) was added and the mixture was boiled for a further 30 min when, again, g.l.c. showed no ester exchange to have occurred. 3-Acetylamino-4-(2-bromo-4,6-dinitrophenylazo)-*NN*-diethylaniline (1) (4.8 g) was added and after 10 min t.l.c. showed complete conversion of the *o*-bromodiarylo-compound to *dimethyl 3,5-dinitro-6-[2-acetylamino-4-(NN-diethylamino)phenylazo]phenylphosphonate* (9) which was isolated as in the preceding experiment. Its i.r. spectrum was identical with that of authentic material.¹

(c) A stirred mixture of diphenyl 3,5-dinitro-6-[2-acetylamino-4-(*NN*-diethylamino)phenylazo]phenylphosphonate

(16) (3.15 g) and methanol (75 ml) was refluxed for 2 h, when t.l.c. showed complete conversion of the diphenyl to the *dimethyl ester*. The latter was isolated as in (a) and had an i.r. spectrum identical with that of authentic material.

The following methods were employed for the preparation of the dialkyl phosphonates listed in the Table, from the corresponding bromo-compounds.

(a) A stirred mixture of the *o*-bromodiaryloxy-compound (0.01 mol), sodium acetate trihydrate (0.02 mol), copper(I) iodide (0.25 g), and dialkyl phosphite (0.015 mol) in the corresponding alcohol (150 ml) was refluxed until reaction was judged to be complete by t.l.c. The mixture was cooled and poured into water (1 200 ml). After 30 min the precipitated product was filtered off, washed with water, dried, and crystallised (thimble) from methanol.

(b) A stirred mixture of the *o*-bromodiaryloxy-compound (0.01 mol), sodium acetate trihydrate (0.02 mol), copper(I) iodide (0.25 g), and diphenyl phosphite (0.015 mol) in the appropriate alcohol (150 ml) was boiled under reflux until reaction was judged to be complete by t.l.c. The product was then isolated as in (a).

Diphenyl 3,5-Dinitro-2-[2-acetylamino-4-(NN-diethylamino)phenylazo]phenylphosphonate (16) (with P. A. Mack).—A mixture of 3-acetylamino-4-(2-bromo-4,6-dinitrophenylazo)-*NN*-diethylaniline (1) (4.8 g), diphenyl phosphite (4.7 g), triethylamine (4.0 g), copper(I) iodide (1.0 g), and acetone (120 ml) was stirred at room temperature for 30 min, when t.l.c. showed reaction to be effectively complete. Water (2 l) was added, the mixture was stirred overnight and the *product* (4.4 g, 69.5%) was filtered off, washed with water, and dried. Crystallisation from ethyl acetate–light petroleum gave glistening black prisms (Found: C, 57.1; H, 4.5; N, 13.6; P, 4.8. $C_{30}H_{29}N_6O_8P$ requires C, 56.95; H, 4.6; N, 13.3; P, 4.9%).

Copper(I) Diethyl Phosphite.—A mixture of copper(II) acetate (16 g), diethyl phosphite (44.15 g), and ethanol (200 ml) was stirred at room temperature under nitrogen for 7 h and filtered. The microcrystalline product (14.5 g, 90%) (Found: C, 23.95; H, 4.7; Cu, 31.5; P, 15.65. Calc. for $C_4H_{10}CuO_3P$: C, 23.95; H, 5.0; Cu, 31.7; P, 15.45%) was filtered off, washed exhaustively with ethanol, and dried over phosphorus pentoxide.

Reaction of 3-Acetylamino-4-(2-bromo-4,6-dinitrophenylazo)-NN-diethylaniline (1) with Copper(I) Diethyl Phosphite.—A stirred mixture of 3-acetylamino-4-(2-bromo-4,6-dinitrophenylazo)-*NN*-diethylaniline (1) (4.8 g), copper(I) diethyl phosphite (2.2 g), and dry ethanol (200 ml) was heated to 50 °C under nitrogen. After 1 h t.l.c. showed reaction to be complete, and the sole coloured products to be diethyl 3,5-dinitro-6-[2-acetylamino-4-(*NN*-diethylamino)phenylazo]phenylphosphonate (10) and 3-acetylamino-4-{2-[3,5-dinitro-2-(2-acetylamino-4-*NN*-diethylaminophenylazo)phenyl]-4,6-dinitrophenylazo}-*NN*-diethylaniline (24). The mixture was cooled to room temperature and filtered. Crystallisation (thimble) of the residue from ethanol gave 3-acetylamino-4-{2-[3,5-dinitro-2-(2-acetylamino-4-*NN*-diethylaminophenylazo)phenyl]-4,6-dinitrophenylazo}-*NN*-diethylaniline (24) (1.6 g, 40%) as glistening black rods (Found: C, 54.3; H, 4.8; N, 20.9%. M^+ 798. Calc. for $C_{36}H_{38}N_{12}O_{10}$: C, 54.15; H, 4.8; N, 21.05%). The filtrate was poured into water (500 ml) and the mixture was stirred for 1 h. Filtration gave diethyl 3,5-dinitro-6-[2-acetylamino-4-(*NN*-diethylamino)phenylazo]phenylphosphonate (10) (1.7 g, 32%) which crystallised (thimble) from

methanol as glistening black rods (Found: C, 49.3; H, 5.6; N, 15.4; P, 6.1%; M^+ 536).

Reactions of 3-Acetylamino-4-(2-bromo-4,6-dinitrophenylazo)-NN-diethylaniline (1) and Diethyl Phosphite in the Presence of Various Copper Salts in Ethanol.—(a) A stirred mixture of copper(II) acetate (2.0 g), diethyl phosphite (2.8 g), and dry ethanol (50 ml) was refluxed under nitrogen for 18 h. During this time the initially blue precipitate rapidly became colourless and, finally, metallic copper was deposited leaving a clear supernatant liquid. 3-Acetylamino-4-(2-bromo-4,6-dinitrophenylazo)-*NN*-diethylaniline (1) (2.4 g) was added and the mixture was boiled under reflux for 30 min when t.l.c. showed complete disappearance of the *o*-bromodiaryloxy-compound and the formation of 3-acetylamino-4-(2,4-dinitrophenylazo)-*NN*-diethylaniline (25) together with a little diethyl 3,5-dinitro-6-[2-acetylamino-4-(*NN*-diethylamino)phenylazo]phenylphosphonate (10). The mixture was filtered while still hot and the residue washed with ethanol. Crystallisation (thimble) from methanol gave 3-acetylamino-4-(2,4-dinitrophenylazo)-*NN*-diethylaniline (25) (1.2 g, 60%) as glistening black needles (Found: C, 53.8; H, 5.1; N, 20.8%. M^+ 400. Calc. for $C_{18}H_{20}N_6O_5$: C, 54.0; H, 5.05; N, 21.0%).

(b) A stirred mixture of copper(II) acetate (2.0 g), diethyl phosphite (2.8 g), and dry ethanol (50 ml) was refluxed for 18 h. The deposited copper powder was then washed exhaustively with dry ethanol by decantation and set stirring with dry ethanol (50 ml). 3-Acetylamino-4-(2-bromo-4,6-dinitrophenylazo)-*NN*-diethylaniline (1) (2.4 g) was added and the mixture was raised to the boil for 1 h when t.l.c. showed complete disappearance of the *o*-bromodiaryloxy-compound and the formation of 3-acetylamino-4-{2-[3,5-dinitro-2-(2-acetylamino-4-*NN*-diethylaminophenylazo)phenyl]-4,6-dinitrophenylazo}-*NN*-diethylaniline (24) together with a trace of 3-acetylamino-4-(2,4-dinitrophenylazo)-*NN*-diethylaniline (25). The mixture was cooled and filtered to obtain the former *product* (1.65 g, 83%) which crystallised (thimble) from ethanol as glistening black rods (Found: C, 54.2; H, 4.8; N, 21.3%).

(c) Copper(II) acetate (2.0 g) was reduced as in the preceding experiment and the well-washed copper powder was set stirring with dry ethanol (50 ml). Diethyl phosphite (2.7 g) and 3-acetylamino-4-(2-bromo-4,6-dinitrophenylazo)-*NN*-diethylaniline (1) (2.4 g) were added and the mixture was raised to the boil. After 1 h t.l.c. showed effectively complete disappearance of the *o*-bromodiaryloxy-compound and the formation of diethyl 3,5-dinitro-6-[2-acetylamino-4-(*NN*-diethylamino)phenylazo]phenylphosphonate (10) and 3-acetylamino-4-(2,4-dinitrophenylazo)-*NN*-diethylaniline (25) in approximately equal amounts, together with a small amount of 3-acetylamino-4-{2-[3,5-dinitro-2-(2-acetylamino-4-*NN*-diethylaminophenylazo)phenyl]-4,6-dinitrophenylazo}-*NN*-diethylaniline (24). The identity of the products was confirmed by comparative t.l.c. in a variety of eluants.

(d) Copper(II) acetate (2.0 g) was reduced as in (b) and the well-washed copper powder was set stirring with dry ethanol (50 ml). Acetic acid (1.2 g) and 3-acetylamino-4-(2-bromo-4,6-dinitrophenylazo)-*NN*-diethylaniline (1) (4.8 g) were added and the mixture was raised to the boil. After 90 min t.l.c. showed effectively complete disappearance of the *o*-bromodiaryloxy-compound and the formation of 3-acetylamino-4-(2,4-dinitrophenylazo)-*NN*-diethylaniline (25) and 3-acetylamino-4-{2-[3,5-dinitro-2-(2-acetylamino-4-*NN*-diethylaminophenylazo)phenyl]-4,6-dinitrophenylazo}-*NN*-diethylaniline (24). The mixture

was cooled and filtered, and the residue extracted (thimble) with acetone. The acetone extracts were evaporated on the steam bath, while maintaining constant volume by the addition of ethanol. When crystallisation occurred the mixture was filtered while still hot to obtain 3-acetylamino-4-(2,4-dinitrophenylazo)-NN-diethylaniline (25) (1.6 g, 40%), i.r. and n.m.r. spectra identical with those of authentic material. On cooling the filtrate deposited 3-acetylamino-4-{2-[3,5-dinitro-2-(2-acetylamino-4-NN-diethylaminophenylazo)phenyl]-4,6-dinitrophenylazo}-NN-diethylaniline (24) (1.0 g, 24.5%), i.r. and n.m.r. spectra identical with those of authentic material.

RESULTS

Compound (1) reacts with diethyl phosphite in the presence of sodium acetate and copper(I) iodide in boiling ethanol to give (10) in good yield. The reaction is remarkably clean and neither the Ullman coupling product (24) nor the reductive substitution product (25) are produced in appreciable quantities. The scope of the reaction with

When the diethyl phosphite is replaced by diphenyl phosphite the sole product is the diethyl ester (10). In alcohols other than ethanol, (1) reacts with diphenyl phosphite in the presence of sodium acetate and copper(I) iodide to give the phosphonic acid diester corresponding to the alcoholic solvent employed. This is a remarkably clean and facile reaction, and has been used to prepare the dimethyl (9), diethyl (10), di-n-propyl (11), di-isopropyl (12), di-n-butyl (13), di-n-pentyl (14), and di-n-heptyl (15) esters in good yield from (1). The diphenyl ester (16) can be prepared by the interaction of (1) and diphenyl phosphite in the presence of triethylamine and copper(I) iodide in acetone and readily undergoes transesterification in alcoholic solvents. This supports g.l.c. evidence that reaction of (1) and diphenyl phosphite precedes transesterification in alcoholic solvents.

When (1) is treated with diethyl phosphite and sodium acetate in the presence of copper(II) acetate in dry ethanol, the Ullmann coupling product (24), the reductive substitution product (25), and the diethyl phosphonate (10) are

Dialkyl phosphonates [(9)–(15) and (17)–(23)] prepared from *o*-bromodiarylazo-compounds [(1)–(8)]

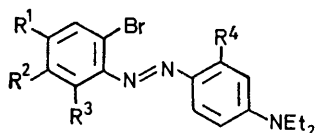
Dialkyl phosphonate	Method	Reaction time h	Analysis (%)										
			Found					Calc.					
			C	H	Br	N	P	C	H	Br	N	P	
(9)	(a)	1	47.5	5.1		16.4	6.2		47.25	4.95		16.55	6.1
(9)	(b)	0.5	47.3	4.9		16.6	6.1						
(10)	(a)	0.5	49.5	5.3		15.4	5.85		49.25	5.45		15.65	5.8
(10)	(b)	0.5	49.1	5.5		15.6	5.9						
(11)	(b)	0.5	49.9	6.2		14.8	5.6		51.05	5.85		14.9	5.5
(12)	(b)	0.5	51.0	6.2		14.6	5.5		51.05	5.85		14.9	5.5
(13)	(b)	0.5	52.9	5.9		14.1	5.1		52.7	6.3		14.2	5.25
(14)	(b)	0.5	54.2	6.7		13.5	5.2		54.2	6.65		13.55	5.0
(15)	(b)	0.5	56.8	6.3		12.3	4.7		56.8	6.55		12.4	4.6
(17)	(a)	1	46.2	5.1	14.2	12.2	5.6		46.3	5.1	14.0	12.3	5.45
(18)	(a)	1	51.1	6.1	14.9	10.2	5.6		51.2	6.0	14.85	9.85	5.75
(19)	(a)	0.2	52.7	6.4	14.3	9.7	5.6		52.9	6.4	14.1	9.85	5.45
(20)	(a)	6	50.3	5.4		14.5	6.6		50.1	5.45		14.6	6.45
(21)	(a)	5	52.4	6.3	16.5	8.7	6.3		52.3	6.05	16.6	8.7	6.4
(22)	(a)	0.25	48.9	5.4		16.9	6.1		48.6	5.5		17.0	6.25
(23)	(a)	18	53.8	6.3		14.0	6.1		53.75	6.15		14.25	6.3

regard to the *o*-bromodiarylazo-compound is broad and is illustrated by the results summarised in the Table. Noteworthy features are: (a) in those cases [(2), (3), (4), and (6)] where the *o*-bromodiarylazo-compound contains two bromine atoms, only the bromine atom *ortho* to the azo-group is replaced by a diethyl phosphonate group; the *p*-bromine atom remains unaffected; (b) the presence of an acetylamino- or an amino-group in the *ortho*-position¹ of the *o*-bromodiarylazo-compound facilitates reaction [(1), (7) *vs.* (5); (3) *vs.* (6)]; (c) polar effects of substituents are markedly different from those anticipated⁶ in uncatalysed nucleophilic replacement reactions [(1), (2), (3), (4), and (8)]; and (d) the replacement reaction is remarkably sensitive to steric effects of substituents in the benzene ring carrying the bromine atom. Those *o*-bromodiarylazo-compounds [(1), (2), (3), and (4)] in which R³ is a group other than hydrogen react much more rapidly than does the comparable unsubstituted compound (8), regardless of the polar nature of the substituent. In these respects the behaviour parallels that¹ with trialkyl phosphites. The reaction proceeds equally well when the sodium acetate is replaced by trialkylamines but is extremely slow in the presence of pyridine. Use of other dialkyl phosphites in the appropriate alcohol gives the corresponding dialkyl phosphonates.

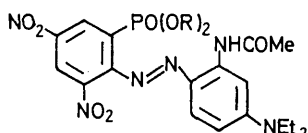
produced in roughly equal proportions. In the absence of sodium acetate the principal product is the dimer (24) together with correspondingly smaller amounts of (10) and (25). This is in marked contrast to the corresponding reaction¹ with triethyl phosphite which gives solely (10) under comparable conditions. In the light of the results of the latter investigation¹ the interaction of copper(II) acetate and diethyl phosphite has been examined. Diethyl phosphite reacts with hydrated copper(II) acetate in dry ethanol at room temperature to give a colourless, crystalline product which analyses correctly for copper(I) diethyl phosphite. The isolated compound reacts with (1) in dry ethanol at 50 °C to give a mixture of the dimer (24) and the diethyl phosphonate (10).

When diethyl phosphite is added to a boiling, dry ethanolic solution of hydrated copper(II) acetate, rapid precipitation of a colourless, crystalline material occurs and on prolonged boiling metallic copper is deposited. Addition of (1) then results in the formation of the reductive substitution product (25), together with a small amount of the diethyl phosphonate (10). In contrast, if the copper is isolated, washed, and suspended in boiling, dry ethanol, addition of (1) results in almost exclusive formation of the dimer (24). In the presence of isolated and washed metallic copper prepared by this method, (1) reacts with diethyl phosphite

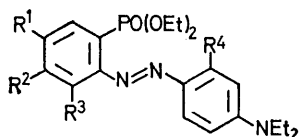
in boiling, dry ethanol to give a mixture of the diethyl phosphonate (10) and the reductive substitution product (25), together with a trace of the dimer (24). The same catalyst promotes the conversion of (1) to a mixture of the dimer (24) and the reductive substitution product (25) in a boiling, dry ethanolic solution of acetic acid.



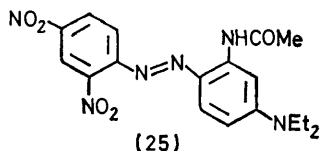
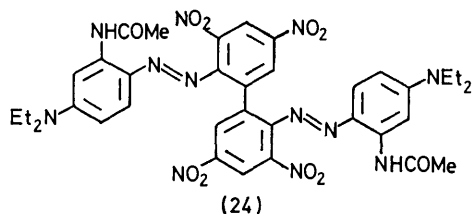
- (1) $R^1 = R^3 = \text{NO}_2$, $R^2 = \text{H}$, $R^4 = \text{NHCOMe}$
 (2) $R^1 = \text{Br}$, $R^2 = \text{H}$, $R^3 = \text{NO}_2$, $R^4 = \text{NHCOMe}$
 (3) $R^1 = \text{Br}$, $R^2 = \text{H}$, $R^3 = \text{Me}$, $R^4 = \text{NHCOMe}$
 (4) $R^1 = \text{Br}$, $R^2 = \text{H}$, $R^3 = \text{Et}$, $R^4 = \text{NHCOMe}$
 (5) $R^1 = R^3 = \text{NO}_2$, $R^2 = R^4 = \text{H}$
 (6) $R^1 = \text{Br}$, $R^3 = \text{Me}$, $R^2 = R^4 = \text{H}$
 (7) $R^1 = R^3 = \text{NO}_2$, $R^2 = \text{H}$, $R^4 = \text{NH}_2$
 (8) $R^1 = R^3 = \text{H}$, $R^2 = \text{NO}_2$, $R^4 = \text{NHCOMe}$



- (9) $R = \text{Me}$ (10) $R = \text{Et}$
 (11) $R = \text{Pr}^n$ (12) $R = \text{Pr}^i$
 (13) $R = \text{Bu}^n$ (14) $R = n\text{-C}_5\text{H}_{11}$
 (15) $R = n\text{-C}_7\text{H}_{15}$ (16) $R = \text{Ph}$



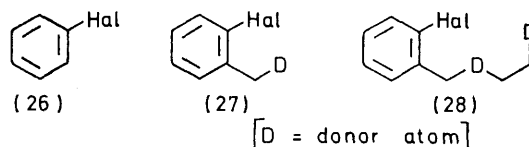
- (17) $R^1 = \text{Br}$, $R^2 = \text{H}$, $R^3 = \text{NO}_2$, $R^4 = \text{NHCOMe}$
 (18) $R^1 = \text{Br}$, $R^2 = \text{H}$, $R^3 = \text{Me}$, $R^4 = \text{NHCOMe}$
 (19) $R^1 = \text{Br}$, $R^2 = \text{H}$, $R^3 = \text{Et}$, $R^4 = \text{NHCOMe}$
 (20) $R^1 = R^3 = \text{NO}_2$, $R^2 = R^4 = \text{H}$
 (21) $R^1 = \text{Br}$, $R^3 = \text{Me}$, $R^2 = R^4 = \text{H}$
 (22) $R^1 = R^3 = \text{NO}_2$, $R^2 = \text{H}$, $R^4 = \text{NH}_2$
 (23) $R^1 = R^3 = \text{H}$, $R^2 = \text{NO}_2$, $R^4 = \text{NHCOMe}$



In view of the effectiveness of copper(I) iodide in promoting the reaction of (1) and diethyl phosphite to give (10), it has been examined as a catalyst for the reaction¹ of (1) with triethyl phosphite. In boiling, dry ethanol little reaction occurred and after 24 h only a small amount of (10) was produced, the bulk of the *o*-bromodiaryldiazo-compound remaining unchanged.

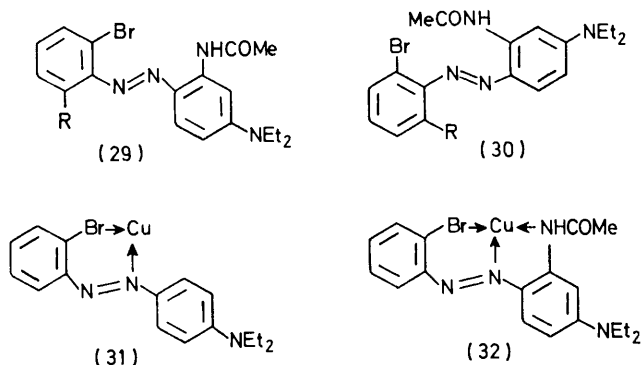
DISCUSSION

In addition to providing a facile method for the preparation of a range of dialkyl arylphosphonates, the interaction of dialkyl phosphites and aryl halides affords a further example of copper-promoted nucleophilic replacement reactions of the latter compounds. The results also serve further¹ to highlight the lack of understanding of the function of the copper in promoting biaryl coupling, nucleophilic substitution, and reductive replacement reactions of aryl halides.



In the previous paper¹ in this series aryl halides were divided into three classes: Type I, those in which the halogen does not occupy a potentially chelating position relative to any donor groups which may be present in the molecule (26); Type II, those in which the halogen is so located relative to one donor group in the molecule that, in principle, the possibility exists of its being involved in the formation of a six-membered chelate ring (27); and Type III, those in which the halogen is so located relative to two donor groups in the molecule that, formally, the possibility exists of its being involved in the formation of an annelated copper chelate complex in which the halogen is part of a six-membered chelate ring (28). The classification was based on the reactivity of bromine atoms representative of the three types in diaryldiazo-compounds and holds good for the present results. Thus, under the mild conditions employed throughout the present work the *p*-bromine atoms in (2), (3), (4), and (6) (Type I aryl halides) are uniformly inert. The *o*-bromine atoms in (5) and (6) (Type II aryl halides) undergo nucleophilic substitution but no reductive replacement or biaryl coupling has been observed. All three reactions occur with (1), (2),⁷ (3),⁷ (4), and (7) (Type III aryl halides) and nucleophilic substitution by diethyl phosphite proceeds more rapidly than in the corresponding Type II *o*-bromodiaryldiazo-compounds. A notable exception is (8) which reacts only slowly with diethyl phosphite. This result is in keeping with the observation¹ that those Type III *o*-bromodiaryldiazo-compounds having a substituent other than hydrogen in the 6-position react more readily than do those in which the 6-position is occupied by hydrogen. Since the polar character of the 6-substituent had little influence this was seen as a steric effect, and the inference was drawn

that structure (29) is more favourable for reaction to occur than structure (30). This led to consideration of the possibility that activation of the bromine atoms in Types II and III *o*-bromodiarylazo-compounds was the result of polarisation of the carbon-bromine bond arising from copper complex formation [(31) and (32)]. However, no complexes of this type were isolated and no



firm conclusions could be drawn regarding their involvement or otherwise. The same is true of the present work.

The favoured conditions for the preparation¹ of *o*-diethylphosphonatodiarylazo-compounds from *o*-bromodiarylazo-compounds and triethyl phosphite involve the use of copper(II) acetate in dry ethanol. These conditions cannot be employed with diethyl phosphite since the latter rapidly reduces the copper(II) acetate, with liberation of acetic acid, and biaryl coupling and reductive replacement reactions intervene. These results serve further to illustrate the very facile biaryl coupling of (1) in the presence of copper powder in boiling ethanol, and the diversion of this reaction to reductive replacement in the presence of protic acids. None of the proposed mechanisms summarised in the previous paper¹ in this series offers a satisfactory explanation for these reactions, or why they should be restricted to Type III aryl halides.

Copper(I) iodide promotes the present reaction very

efficiently but is ineffective in the corresponding reaction¹ employing triethyl phosphite. Triethyl phosphite is a good ligand and readily forms complexes⁸ with copper(I) iodide. Significantly, iodo(triethyl phosphite)-copper(I) fails to react with (1) in boiling, dry ethanol to any appreciable extent. This raises further questions; for example, does the co-ordinated triethyl phosphite no longer function as a nucleophile, or is the copper inaccessible to the aryl halide? Neither of these situations can arise with diethyl phosphite and reasons can be seen why, for example, copper(II) acetate fails satisfactorily to promote reaction between diethyl phosphite and aryl halides. What is not clear is why copper(I) iodide is so effective in this case, and why it must be used in near-stoichiometric quantities. Any attempt to provide answers to the many questions relating to the function of copper in promoting nucleophilic substitution, biaryl coupling, and reductive replacement of aryl halides on the basis of the present results would be pure speculation and serve little useful purpose. Elucidation of these problems must await the results of continuing studies.

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