The Copper-promoted Reaction of o-Halogenodiarylazo-compounds with Nucleophiles. Part 3.[1] The Copper-promoted Reaction of o-Bromodiarylazo-compounds with Carboxylate Ions. A Novel Method for the Preparation of o-Hydroxydiarylazo-compounds

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o-Bromo-o'-acetylaminodiarylazo-compounds react with potassium acetate in the presence of copper(II) acetate in dipolar aprotic solvents to give the copper(II) complex of the corresponding o-hydroxy-o'-acetylaminodiarylazo-compounds in good yield. The reaction proceeds via the intermediate o-acetoxy-o'-acetylaminodiarylazo-compound which undergoes facile, in situ, copper-promoted hydrolysis. When the diarylazo-compound contains two o-bromine atoms only one is replaced, with a single exception.

In 1931 Delfs and Knoche [2] obtained the copper complex of 2-(2-hydroxynaphthyl-1-azo)phenol-4-sulphonic acid by heating aqueous 1-chloro-2-(2-hydroxynaphthyl-1-azo)benzene-4-sulphonic acid, copper sulphate, sodium hydroxide, and ammonia at 80 °C for 1 h. Since then copper and its compounds have been used to promote the replacement of the halogen atom in o-halogenodiarylazo-compounds by a variety of nucleophiles including alkoxide-,[3,4,5,6] phenoxide-,[3,4,6,7] β-dicarbonyl-,[8] sulphinate-,[3,9] cyanide-,[10] and nitrite-[11] ions, ammonia,[3] and aromatic-,[3,4] and aliphatic-[3,4,12] amines. More recently, o-dialkylphosphonatodiarylazo-compounds have been prepared by the copper-promoted reaction of o-bromodiarylazo-compounds with trialkyl phosphites [13] and dialkyl phosphite anions.[1] We now report the preparation of o-hydroxydiarylazo-compounds by the copper-promoted interaction of o-bromodiarylazo-compounds and carboxylate ions under mild conditions.

As long ago as 1929 Hurtley [14] reported that sodium o-bromobenzoate was completely converted into salicyclic acid in 30 min in boiling, aqueous sodium acetate in the presence of copper(II) acetate, but since that time the use of carboxylate ions as nucleophiles in copper-promoted reactions with aryl halides has received scant attention. o-Nitroaryl halides undergo[15] reductive dehalogenation in molten benzoic acid at 150—200 °C in the presence of copper powder and a similar reaction occurs [16] when aryl halides are heated with copper(I) acetate or benzoate in N-heterocyclic solvents. Under rigorously anhydrous conditions reductive dehalogenation is largely suppressed and good yields of aryl benzoates have been obtained [17] by the interaction of aryl halides and copper(I) benzoate in pyridine or diglyme. More recently, methyl salicylate has been found [18] to be the principal product of a reaction that involves methyl o-iodobenzoate, copper(I) triflate, copper(II) triflate, acetone, and aqueous ammonia.

EXPERIMENTAL

Magnetic measurements were made by the Gouy method. The standard used was HgCO(NCS)₄ and susceptibilities of ligands were calculated from Pascal's constants.[19] I.r. spectra were recorded on a Perkin-Elmer Model 577 Grating

Infrared Spectrophotometer using the standard Nujol mull technique. ¹H N.m.r. spectra were measured 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. Mass spectra were recorded with an A.E.I. MS-90 spectrometer. Thin layer chromatography (t.l.c.) was carried out on Eastman Chromogram sheets 13181 (silica gel) using cyclohexane–chloroform (1 : 1), nitromethane–toluene (7 : 93), and ethyl acetate–light petroleum (3 : 2) as eluants. Evaporations under reduced pressure were carried out with a Büchi Rotavapor. Light petroleum refers to the fraction of b.p. 60—80 °C.

General Procedure for the Preparation of the Copper Complexes (13)—(23) *from the* o-*Bromodiarylazo-compounds* (1)—(12).—A dimethylformamide (DMF) (30 ml) solution of copper(II) acetate (0.01 mol equiv.) was added to a stirred mixture of the o-bromodiarylazo-compound (0.01 mol equiv.) and DMF (100 ml) at room temperature. Potassium acetate (0.03 mol equiv.) was added and the reaction was followed by t.l.c. (if necessary the mixture was heated to achieve complete reaction). When the reaction was adjudged complete the mixture was filtered and methanol (300 ml) was added as drops to the stirred filtrate to effect precipitation of the copper complex. The latter was collected by filtration, washed with methanol, and dried. With the exception of the 2,6-dibromodiarylazo-compounds, which are described below, identical products were obtained when the DMF was replaced by dimethyl sulphoxide (DMSO) and the results of these experiments are summarized in Table 1. When the DMF was replaced by certain other solvents different products were obtained.

Pyridine as solvent. Reaction was incomplete after 24 h at room temperature, but went to completion after 24 h at 90 °C. The mixture was then cooled and filtered to give *tetrapyridine-bis-[2-(3-acetylaminato-4-diethylaminophenylazo)-3,5-dinitrophenoxido]dicopper*(II) (1.0 g, 16%) which crystallized from pyridine as glistening brown prisms (Found: C, 52.5; H, 4.3; Cu, 10.0; N, 17.2. C₅₆H₅₆Cu₂N₁₆O₁₂ requires C, 52.85; H, 4.45; Cu, 10.0; N, 17.6%). Dilution of the filtrate with water gave further material (2.6 g) which crystallized from pyridine to give the same product (identical i.r. spectrum) as glistening brown prisms (Found: C, 53.3; H, 4.3; Cu, 9.7; N, 17.3). An attempt to crystallize (thimble) the product from methanol gave bis-[2-(2-acetylaminato-4-diethylaminophenylazo)-3,5-dinitrophenoxido]dicopper(II) (13) as black needles (Found: C, 45.7; H, 3.8; Cu, 13.3; N, 17.3. See Table 1)

TABLE 1

Copper complexes (13)—(23): experimental and physical data

Copper complex	Reaction conditions Time/h R.T.	Time/h 80 °C	Solvent	Yield (%)	Found (%) C	H	Br	Cu	N	S	Calc. (%) C	H	Br	Cu	N	S	μeff. (B.M.)	ν(C=O) cm⁻¹
(13)	18		DMF	73	45.4	3.9		13.5	17.5		42.25	3.8		13.3	17.5		1.8	1 665br,w
(13)	0.25		DMSO	67	45.1	3.6		13.0	17.3								1.8	1 665br,w
(13)[a]		3	DMF	53	45.5	3.8		13.5	17.2									1 665br,w
(13)[a]	4		DMSO	51	45.0	3.9		13.1	17.6									1 665br,w
(14)		1	DMF	58	42.4	3.4	15.5	11.9	13.5		42.2	3.55	15.6	12.4	13.7		1.8	1 660br,w
(14)		0.25	DMSO	85	42.2	3.7	15.6	12.1	13.5									1 660br,w
(15)		5	DMF	62	47.0	4.3	16.3	13.2	11.4		47.45	4.4	16.65	13.2	11.65		1.75	1 660br,w
(15)		1	DMSO	65	47.4	4.1	16.4	13.0	11.6									1 660br,w
(16)		6	DMSO	28[b]	50.1	4.3		14.9	15.9		49.95	4.4		14.7	16.2		1.8	1 660br,w
(17)		1	DMF	80	42.2	3.5	15.3	12.5	13.5		42.2	3.55	15.6	12.4	13.7		1.8	1 655br,w
(17)		1	DMAC	88	42.5	3.6			13.7									1 655br,w
(17)		1	NMP	89	42.5	3.3			13.4									1 655br,w
(17)		10	Sulpholane	76	42.1	3.5			13.7									1 655br,w
(19)		4	DMF	85	39.2	3.1	28.9	11.5	10.1		39.6	3.3	29.3	11.65	10.25			1 630br,w
(19)		1	DMSO	86	39.2	3.4	29.3	11.5	10.2									1 630br,w
(20)		24	DMF	60	47.5	4.0	16.2	11.4	13.5		47.45	4.4	16.65	13.2	11.65			1 655br,w
(20)		6	DMSO	66	47.6	4.2	16.3	11.4	13.3									1 655br,w
(21)		1	DMF	71	46.3	3.6	16.4	12.6	14.1		46.4	3.7	16.25	12.9	14.25			1 655br,w
(21)	24		DMSO	67	46.7	3.6	16.0	12.7	13.9									1 655br,w
(22)		24	DMF	83	41.7	3.8	14.7	11.1	10.3	5.8	41.9	3.9	14.7	11.65	10.3	5.85		1 660br,w
(22)		6	DMSO	81	41.6	3.7	15.2	11.4	9.9	6.1								1 660br,w
(23)		24	DMF	74	45.9	3.9	15.3	11.9	10.3		45.75	4.05	15.25	12.1	10.7			1 720,s
(23)		4	DMSO	76	45.9	4.1	15.5	11.7	10.7									1 660br,w

[a] Potassium acetate replaced by an equimolar amount of sodium benzoate. [b] Reaction incomplete, much (65%) starting material recovered unchanged.

i.r. spectrum identical with that of authentic material. Crystallization (thimble) of the latter from pyridine gave tetrapyridine–bis-[2-(3-acetylaminato4-diethylaminophenylazo-3,5-dinitrophenoxido]dicopper(II) as glistening brown prisms (Found: C, 52.7; H, 4.4; Cu, 9.9; N, 17 1%; see


(1) – (12)

(13) – (23)
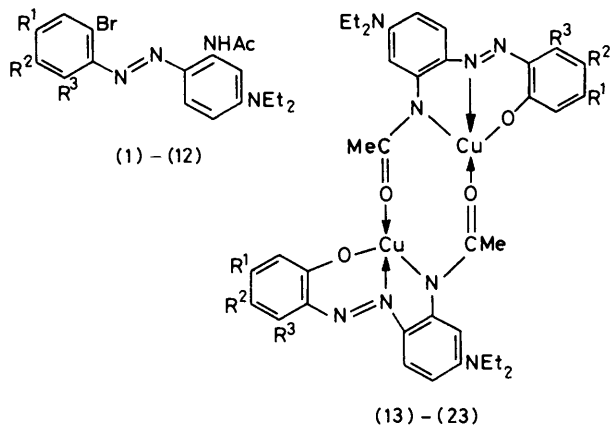
(24) – (34)

| (1), (13), (24) | $R^1 = R^3 = NO_2$, $R^2 = H$ |
(2), (14), (25)	$R^1 = Br$, $R^2 = H$, $R^3 = NO_2$
(3), (15), (26)	$R^1 = Br$, $R^2 = H$, $R^3 = Me$
(4), (16), (27)	$R^1 = R^3 = H$, $R^2 = NO_2$
(5)	$R^1 = R^2 = R^3 = H$
(6), (17), (28)	$R^1 = NO_2$, $R^2 = H$, $R^3 = Br$
(7), (18), (29)	$R^1 = NO_2$, $R^2 = H$, $R^3 = MeO_2C$
(8), (19), (30)	$R^1 = R^3 = Br$, $R^2 = H$
(9), (20), (31)	$R^1 = Me$, $R^2 = H$, $R^3 = Br$
(10), (21), (32)	$R^1 = CN$, $R^2 = H$, $R^3 = Br$
(11), (22), (33)	$R^1 = MeSO_2$, $R^2 = H$, $R^3 = Br$
(12), (23), (34)	$R^1 = MeO_2C$, $R^2 = H$, $R^3 = Br$

above) which, after being heated at 75 °C under reduced pressure over P_4O_{10} for 24 h lost pyridine to give the dicopper(II) (13), i r. spectrum identical with that of authentic material. Demetallization of the tetrapyridine–bis-2[(2-acetylaminato-4-diethylaminophenylazo)-3,5-dinitrophenoxido]dicopper-(II) gave 3-acetylamino-NN-diethyl-4-(2-hydroxy-4,6-dinitrophenylazo)aniline (24) which crystallized (thimble) from methanol as blue-black needles (Found: C, 51.9; H, 4.9; N, 18.3. See Table 2), i.r. spectrum identical with that of authentic material.

α-*Picoline as solvent.* Little reaction was apparent after 24 h at room temperature, but complete disappearance of the starting material occurred within 24 h at 90 °C when, in addition to the principal product which remained on the baseline, t.l.c. showed the presence of a coloured product having the same R_F value as that of 3-acetylamino-NN-diethyl-4-(2,4-dinitrophenylazo)aniline (36) in a variety of eluants. After being cooled to room tempreature the mixture was filtered and the residue was washed with ethanol to give the dicopper(II) (13)(2.3 g, 48%) as black microneedles (Found: C, 45.2; H, 3.8; Cu, 13.7; N, 17.2%; see above), i.r. spectrum identical with that of authentic material. Dilution of the filtrate with water gave the NN-diethylani-

line (36) (0.5 g, 12.5%) which crystallized (thimble) from ethanol as black microneedles (Found: C, 54.2; H, 4.8; N, 21.5. Calc. for $C_{18}H_{19}N_6O_5$: C, 54.1; H, 4.8; N, 21.05%), i.r. spectrum identical with that of authentic material.[13] In an attempt to prepare an α-picoline-containing complex analogous to that obtained with pyridine a sample of the dicopper(II) complex (13) was crystallized (thimble) from α-picoline. The product, which was collected by filtration, washed with cyclohexane, and dried (room temperature) proved to be unchanged starting material (Found: C, 45.1; H, 3.7; Cu, 13.0; N, 17.0%; see above), i.r. spectrum identical with that of authentic material.
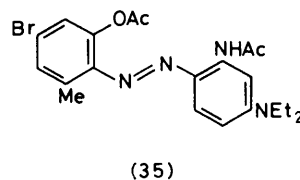

(35)
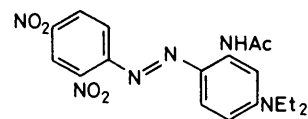
(36)

2,6-*Lutidine as solvent.* Again little or no reaction was detected after 24 h at room temperature, but effectively complete disappearance of the starting material occurred within 10 h at 85 °C when, in addition to the principal product which remained on the baseline, t.l.c. showed the presence of a coloured product having the same R_F value as that of the NN-diethylaniline (36) in a variety of eluants. Work-up of the cooled reaction mixture as in the preceding experiment gave the dicopper(II) complex (13) (2.2 g, 46%) (Found: C, 45.1; H, 3.5; Cu, 13.2; N, 17.5%; see above) and the NN-diethylaniline (36) (0.9 g, 22.5%) (Found: C, 53.8; H, 4.9; N, 21.3%; see above). Both products had i.r. spectra identical with those of authentic samples.

Ethanol as solvent. Reaction was effectively complete after 18 h at the boil, after which the mixture was filtered while still hot. Extraction (thimble) of the residue with boiling methanol until the extracts were no longer coloured left the dicopper(II) complex (13) (1.2 g, 25%) (Found: C, 45.1; H, 3.6; Cu, 13.6; N, 17.9%; see above), i.r. spectrum identical with that of authentic material. The methanol extracts were cooled to deposit the NN-diethylaniline (36) (0.5 g, 12.5%) which crystallized (thimble) from methanol as black microneedles (Found: C, 54.15; H, 5.0; N, 20.9%; see above), i.r. spectrum identical with that of authentic material. After being cooled to room temperature the original filtrate was filtered to obtain 3-acetylamino-4-(2-ethoxy-4,6-dinitrophenylazo)-NN-diethylaniline (37) (2.4 g, 54%) which crystallized (thimble) from ethanol as black rods (Found: C, 54.1; H, 5.6; N, 19.2. $C_{20}H_{24}N_6O_6$ requires C, 54.05; H, 5.45; N, 18.9%); δ(CDCl$_3$) 1.3 (6 H, t, $MeCH_2N$), 1.5 (3 H, t, $MeCH_2O$), 2.25 (3 H, s, AcO), 3.5 (4 H, q, MeCH_2N), 4.3 (2 H, q, MeCH_2O), and 6.3—8.7 (5 H, m, Ar-H).

Tetra-γ-picoline–Bis-[2-(2-acetylaminato-4-diethylamino-phenylazo)-3,5-dinitrophenoxido]dicopper(II).—The dicopper-(II) complex (13) (1.0 g) was extracted (thimble) into boiling (25 mmHg) γ-picoline (20 ml). After the mixture had been cooled, cyclohexane was added as drops to the stirred solution until crystallization commenced. The mixture was left overnight and the product (1.1 g, 79%) (Found: C, 54.4; H, 5.2; Cu, 9.45; N, 17.1. $C_{60}H_{64}Cu_2N_{16}O_{12}$ requires C, 54.25; H, 4.85; Cu, 9.55; N, 16.9%) was collected by filtration, washed with cyclohexane, and dried (room temperature).

(37)

(38)

(39)

(40)

(41)

(42)

D = Donor atom

(43)
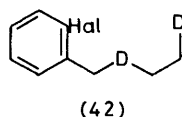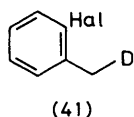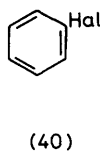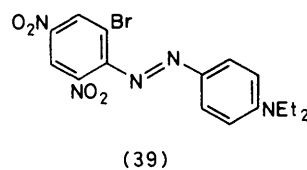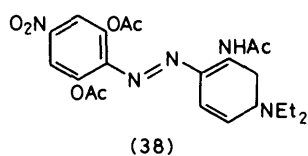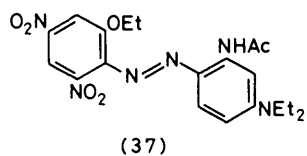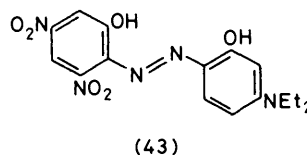
Bis-[2-(3-*acetylaminato-4-diethylaminophenylazo*)-5-*bromo*-3-*nitrophenoxido*]*dicopper*(II) (14).—A dimethylformamide (DMF) (10 ml) solution of copper(II) acetate (0.25 g) was added to a stirred DMF (15 ml) solution of 3-acetyl-amino-4-(4-bromo-2-hydroxy-6-nitrophenylazo)-*NN*-diethylaniline (25) (0.5 g) and the mixture was stirred at room temperature for 15 h. The product (0.5 g, 88%) (Found: C, 42.3; H, 3.5; Br, 15.8; Cu, 12.3; N, 13.5. See Table 1) was collected by filtration and washed with methanol. Its i.r. spectrum was identical with that of authentic material.

General Method for the Preparation of the 2-*Hydroxydiaryl-azo-compounds* (24)—(34) *from the Copper Complexes* (13)—(23).—Hydrochloric acid (60 ml of 2M) was added as drops to a stirred mixture of the copper complex (1.0 g) and DMF (20 ml). The mixture was stirred overnight at room

temperature whereupon the 2-hydroxydiarylazo-compound was collected by filtration, washed with (i) 2M hydrochloric acid, (ii) water until acid-free, and (iii) methanol, and then crystallized (thimble) from the latter solvent. The results of these experiments are summarized in Table 2.

4-(2-*Acetoxy*-4-*bromo*-6-*methylphenylazo*)-3-*acetylamino-NN-diethylaniline* (35).—A mixture of copper(II) acetate (2.1 g) and DMSO (130 ml) was stirred at room temperature for 30 min whereupon 3-acetylamino-4-(2,4-dibromo-6-methylphenylazo)-*NN*-diethylaniline (3) (4.8 g) was added. After a further 30 min potassium acetate (3.0 g) was added, the mixture was stirred for 1 h at room temperature, and filtered. Water (100 ml) was added as drops to the stirred filtrate during 30 min and, after a further hour, the mixture was filtered to obtain the crude product (3.2 g, 70%). The latter was dissolved in a mixture of ethyl acetate and light petroleum (50 ml, 1 : 3), alumina (0.5 g) was added, and the mixture was filtered. With time the filtrate deposited the product which was recovered by filtration and was then crystallized from methanol as *orange plates* (Found: C, 54.7; H, 5.4; Br, 16.9; N, 11.9. $C_{21}H_{25}BrN_4O_3$, M^+ 461, requires C, 54.65; H, 5.5; Br, 17.35; N, 12.15%); δ(CDCl₃) 1.25 (6 H, t, MeCH_2), 2.15 (3 H, s, AcO), 2.25 (3 H, s, *Ac*NH), 2.4 (3 H, s, *Me*-aryl), 3.45 (4 H, q, MeCH_2), and 6.25—8.1 (5 H, m, aromatic); ν (Nujol) 1 763 (ester C=O) and 1 693 cm⁻¹ (amide C=O).

Bis-[2-(2-*acetylaminato*-4-*dimethylaminophenylazo*)-5-*bromo*-3-*methylphenoxido*]*dicopper*(II) (15).—A stirred mixture of the *NN*-diethylaniline (35) (3.0 g), copper(II) acetate (1.4 g), sodium acetate trihydrate (2.7 g), and DMSO (85 ml) was heated to 50 °C for 18 h whereupon reaction was adjudged to be complete by t.l.c. Methanol (300 ml) was added as drops to the cooled mixture during 45 min and, after a further 2 h, the mixture was filtered. The residue was washed with methanol, water, and finally again with methanol to obtain the product (2.0 g, 64%) as fine rubine hairs (Found: C, 47.3; H, 4.4; Br, 16.85; Cu, 13.1; N, 11.9%. See Table 1), i.r. spectrum identical with that of authentic material.

Reaction of 3-*Acetylamino*-4-(2,6-*dibromo*-4-*nitrophenyl-azo*)-NN-*diethylaniline* (6) *with Potassium Acetate*.—(*a*) A mixture of the *NN*-diethylaniline (6) (5.1 g), copper(II) acetate (2.0 g), potassium acetate (3.0 g), and DMF (100 ml) was stirred at room temperature and the reaction was monitored by t.l.c. After 18 h the mixture contained some unchanged starting material, a product with a lower R_F value than that of the starting material, and a product which

TABLE 2

o-Hydroxydiarylazo-compounds (24)—(34): physical data

Compound	Found (%)					Calc. (%)					ν(C=O)/ cm⁻¹
	C	H	Br	N	S	C	H	Br	N	S	
(24) a	51.8	4.7		19.0		51.9	4.85		18.5		1 695s,s
(24) b	51.9	4.8		18.4							1 695s,s
(25) a	48.2	4.4	17.7	15.4		48.0	4.45	17.75	15.55		1 692s,s
(26) a	54.4	5.6	19.1	13.2		54.4	5.5	19.05	13.2		1 687s,s
(27) b	58.5	5.3		18.7		58.35	5.45		18.9		1 690s,s
(28) a	48.1	4.4	17.7	15.2		48.0	4.45	17.75	15.55		1 685s,s
(30) a	44.7	4.2	33.3	11.3		44.65	4.15	33.05	11.55		1 685s,s
(30) b	44.6	4.2	33.2	11.5							1 685s,s
(31) a	54.4	5.3	19.1	13.0		54.4	5.5	19.05	13.35		1 681s,s
(32) a	53.4	4.8	18.7	16.0		53.0	4.7	18.6	16.25		1 685s,s
(33) a	47.4	4.75	16.9	11.5	6.5	47.2	4.85	16.55	11.6	6.6	1 687s,s
(34) a	51.6	5.1	17.2	12.0		51.85	5.0	17.25	12.1		1 720s,s 1 682s,s

a Ex copper complex prepared in DMF.   *b Ex* copper complex prepared in DMSO.

remained on the baseline of the chromatogram. The mixture was then heated to 60 °C for 1 h after which all the starting material had disappeared, only a trace of the mobile product was detectable, and the principal product was that which remained on the baseline of the chromatogram. The mixture was filtered, methanol (300 ml) was added as drops to the stirred filtrate over 45 min and after a further 3 h, the mixture was filtered to obtain bis-[2-(2-acetylaminato-4-dimethylaminophenylazo)-3-bromo-5-nitrophenoxido]dicopper-(II) (17) (4.1 g, 80%) as black prisms (Found: C, 42.2; H, 3.5; Br, 15.3; Cu, 12.5; N, 13.5. $C_{36}H_{36}Br_2Cu_2N_{10}O_8$ requires C, 42.4; H, 3.55; Br, 15.6; Cu, 12.4; N, 13.7%).

(b) The preceding experiment was repeated using DMSO (100 ml) in place of DMF. After 30 min at room temperature t.l.c. showed complete disappearance of the starting material, two coloured products with lower R_F values than that of the starting material, and a heavy, coloured spot on the baseline of the chromatogram. After a further hour t.l.c. showed the presence of only the latter material and the mixture was filtered. Methanol (300 ml) was added as drops to the stirred filtrate during 45 min and, after a further 3 h, the mixture was filtered to obtain the product (3.3 g) as blue hair-like crystals {Found: C, 46.6; H, 3.9; Br, 4.8; Cu, 12.7; N, 14.1%; the dicopper(II) complex (17), $C_{36}H_{36}Br_2Cu_2N_{10}O_8$. requires C. 42.2; H, 3.55; Br, 15.6; Cu, 12.4; N, 13.7%; bis-[3-acetoxy-2-(2-acetylaminato-4-dimethylaminophenylazo)phenoxido]dicopper(II) (18) $C_{40}H_{42}Cu_2N_{10}O_{12}$ requires C, 48.9; H, 4.3; Cu, 12.95, N, 14.25%}; v(Nujol) 1 770ss (ester C=O) and 1 660br, w cm^{-1} (amide C=O).

A mixture of the crude product (3.0 g), DMF (25 ml), and hydrochloric acid (150 ml of 2M) was stirred overnight at room temperature and filtered. After being washed with hydrochloric acid (20 ml of 2M), water until acid-free, and, finally, methanol, the demetallized product (2.7 g) was crystallized (thimble) from methanol as fine black hairs. T.l.c. showed it to be a mixture of two coloured compounds, one of which had the same R_F value as authentic 3-acetyl-amino-4-(6-bromo-2-hydroxy-4-nitrophenylazo)-NN-diethylaniline (28) in a variety of eluants. The two components were separated by preparative t.l.c. to obtain 3-acetylamino-4-(6-bromo-2-hydroxy-4-nitrophenylazo)-NN-diethylaniline (28) M^+ 449, i.r. spectrum identical with that of authentic material, and 4-(6-acetoxy-2-hydroxy-4-nitrophenylazo)-3-acetylamino-NN-diethylaniline (29), M^+ 429, fragmentation pattern consistent with this structure, v (Nujol) 1 773ss (ester C=O) and 1 685ss cm^{-1} (amide C=O).

RESULTS

In the presence of copper(II) acetate, compound (1) reacts with potassium acetate in DMSO at room temperature to give a highly crystalline copper complex, demetallization of which gives compound (24). Analytical results on the copper complex, which is also produced when compound (24) reacts with copper(II) acetate, are in good agreement with a constitution comprising one atom of copper and one molecule of compound (24). Since the latter is only a tridentate ligand the complex probably exists as a binuclear species in order to satisfy the co-ordination requirements of the copper(II) atom. The complex is uncharged and shows normal magnetic properties, which precludes monatomic bridging [20] between the two copper atoms, and [20] the dimeric structure (13) is favoured. Support for this is provided by the bathochromic shift [21] of the carbonyl

stretching frequency (v 1 665 br,w cm^{-1}) in the complex compared with that (v 1 695ss cm^{-1}) in the free ligand.

The copper complex (13) is interesting on several counts: it is the first recorded [22] example of a metal complex dyestuff based on the o-hydroxy-o'-acetylaminodiarylazo-system in which the acetyl amino-group functions as a bidentate donor, and a proton has been lost from the acetyl-amino-group.

The reaction is solvent sensitive and compound (1) reacts with potassium acetate in the presence of copper(II) acetate in pyridine to give a complex having 1 : 1 : 2 stoicheiometry in copper, doubly deprotonated compound (24), and pyridine. The same product is obtained by crystallization of complex (13) from pyridine. I.r. spectra indicate that the complex is a carbonyl-bridged dimer, but on available evidence it is not possible to state with certainty whether the pyridine molecules are bound to the copper to give a 6-co-ordinate species or are present as solvent of crystallization. In either event the pyridine is loosely held since crystallization of the complex from methanol or even heating it under reduced pressure gives complex (13). However, since a comparable complex can be prepared from γ-picoline, but not from the sterically hindered α-picoline or 2,6-lutidine the former appears more likely. In the two latter solvents compound (1) reacts with potassium acetate in the presence of copper(II) acetate to give a mixture of compounds (13) and (36). Reductive substitution is not uncommon in copper-promoted reactions of aryl halides and is usually associated [18,23—25] with the presence of hydrogen donors in the reaction mixture. In the instances described herein the hydrogen source is believed [26] to be the α-methyl groups in the α-picoline and 2,6-lutidine, respectively. In ethanol the principal product of the reaction is compound (37), but complex (13) and compound (36) are also produced in significant quantities.

The results of treatment of a variety of o-bromo-o'-acetylaminodiarylazo-compounds with potassium acetate in a number of dipolar aprotic solvents in the presence of copper(II) acetate are summarized in Table 1. Several features are noteworthy. (a) In those cases where the diarylazo-compound contains two bromine atoms in ortho- and para-positions with respect to the azo-group [compounds (2), (3), and (8)] only the bromine atom in the ortho-position is replaced by a hydroxy-group; the p-bromine atom is unaffected. (b) In those instances where the diarylazo-compound contains two bromine atoms ortho to the azo-group [compounds (6) and (8)—(12)] only one bromine atom is replaced by a hydroxy-group; the other remains intact. The single exception to this is the formation of a mixture of complexes (17) and (18) when compound (6) reacts with potassium acetate in DMSO in the presence of copper(II) acetate. In the solvents DMF, dimethylacetamide (DMAC), N-methylpyrrolidone (NMP), and sulpholane, the complex (17) is the sole product. (c) Polar effects of substituents are markedly different from those anticipated [27] in uncatalyzed nucleophilic replacement reactions. (d) The replacement reaction is sensitive to the steric effect of substituents in the benzene ring that carries the bromine atom. Those compounds [(1)—(3), (6), and (8)—(12)] in which R^3 is a group other than hydrogen react more readily than do those [(4) and (5)] in which R^3 is hydrogen, irrespective of the polar nature of the substituents. This is particularly noticeable in the case of compound (5) which fails to react under the conditions employed in this work. It is also noteworthy

that the acetylamino-group in the *ortho*-position is necessary for the reaction to proceed. Thus compound (39) failed to undergo any reaction when heated with potassium acetate and copper(II) acetate in DMF at 60 °C for 18 h.

o-Bromodiarylazo-compounds are particularly convenient compounds with which to work since their intense colour makes it easy to follow reactions by t.l.c. In the present case the conversion of the *o*-bromo-*o'*-acetylaminodiaryl-azo-compound into the copper complex of the corresponding *o*-hydroxy-*o'*-acetylaminodiarylazo-compound clearly proceeds *via* an intermediate species. This was isolated in the case of compound (3) and proved to be compound (35). The latter compound readily underwent conversion into complex (15) on treatment with copper(II) acetate in DMSO. Significantly only one intermediate species was detected when compound (6) was treated with potassium acetate in the presence of copper(II) acetate in DMF, DMAC, NMP, and sulpholane, whilst an additional intermediate was observed when the reaction was carried out in DMSO. Although these compounds have not been isolated they are assumed, reasonably, to be compounds (7) and (38), respectively.

DISCUSSION

In previous papers [1,13] in this series aryl halides have been 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 (40); 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 it being involved in the formation of a six-membered chelate ring (41); 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 it being involved in the formation of an annelated copper chelate complex in which the halogen is part of a six-membered chelate ring (42). The classification was based on the reactivity of bromine atoms representative of the three types towards copper-promoted nucleophilic substitution and, at least in part, holds good for the present results. Thus, under the mild conditions employed throughout the present work the *p*-bromine atoms in compounds (2), (3), and (8) (Type I aryl halides) are uniformly inert. Surprisingly, in the light of earlier work [1,13] the *o*-bromine atom in compound (39) (Type II aryl halide) also failed to undergo substitution under the present conditions. However, under more severe conditions compound (39) reacts [28] with potassium acetate in DMSO in the presence of copper(II) acetate to give the copper complex of compound (43). With the single exception of that in compound (5) the *o*-bromine atoms in the Type III aryl halides [(1)—(12)] undergo substitution more or less readily under the present conditions.

It is, therefore, tempting to rationalize the overall reaction in terms of a mechanism such as that outlined in Scheme 1. Enhancement of the reactivity of the *o*-bromodiarylazo-compound when R is a group other than hydrogen, irrespective of its polar character, leads to the inference that structure (45) is more favourable for this reaction than is structure (44). This is in firm agreement

with earlier, similar observations.[1,13] Nucleophilic attack by carboxylate ion is facilitated by polarization of the carbon–bromine bond resulting from the formation of an annelated copper(II) complex of partial structure (46). The intermediate formation of the *o*-acetoxy-*o*-acetyl-aminodiarylazo-compound (35) has been demonstrated
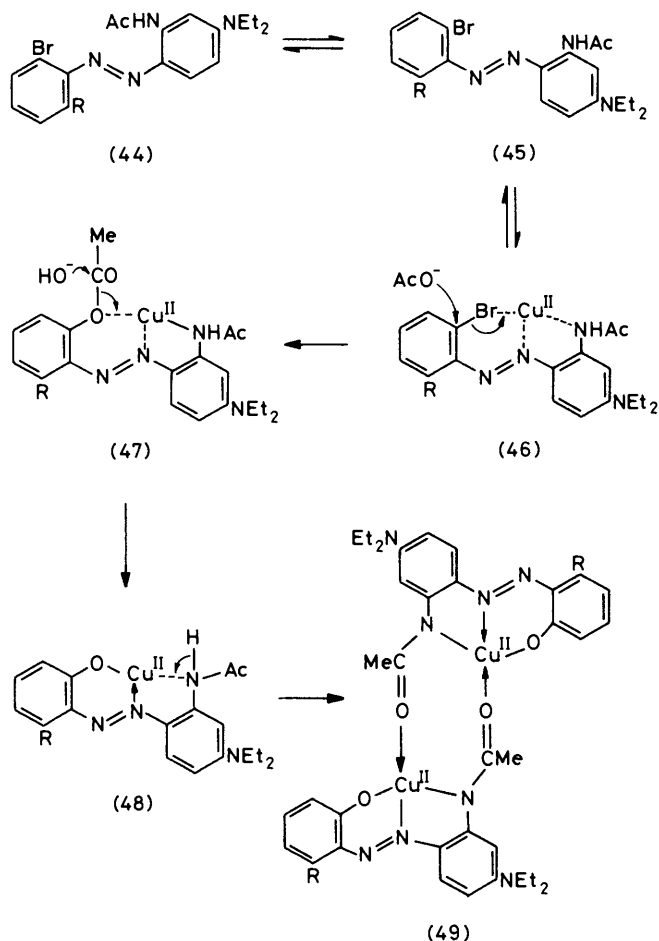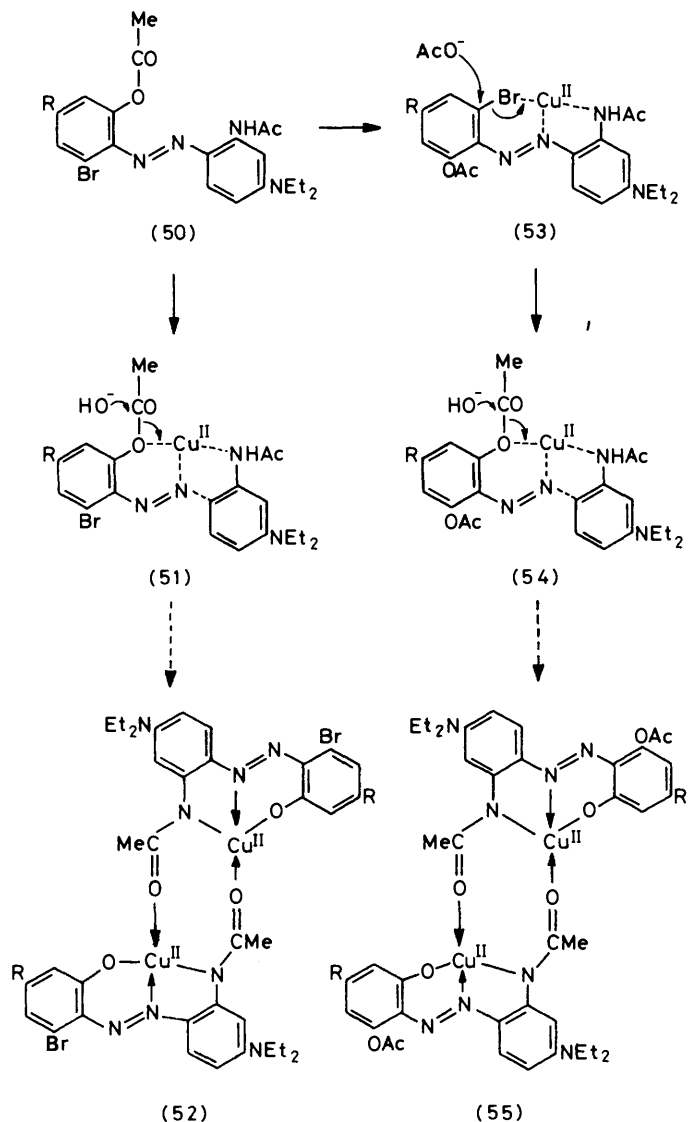

SCHEME 1

in the conversion of compound (3) into complex (15). In the complex of partial structure (47), co-ordination of the ester group with the copper ion considerably enhances the electrophilic character of the acyl carbon atom and consequently the ester group is readily hydrolyzed, probably by water present in the solvent. The metal ion is necessary for the facile hydrolysis to occur, since compound (35) is recovered unchanged from hot DMSO solution. Involvement of the acyl oxygen atom of the ester group in co-ordination to the copper rather than the more usual [29] carbonyl oxygen has been postulated in comparable copper-promoted hydrolyses of 8-acetoxyquino-line [30] and β-alkoxycarbonylethyl salicylaldimines.[31] A similar mechanism might be expected to result in hydrolysis of the *o'*-acetylamino-group in compounds (48) or (49) and the metal ion-promoted hydrolysis of chelating amides is well known.[32] However, the effect of metal ions on the rate of hydrolysis of chelated amides is

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surprisingly small compared with their effect on the rate of hydrolysis of esters.[33] The loss of a proton from the co-ordinated amide group in partial structure (48) has considerable precedent [34] in the peptide field.

The behaviour of those diarylazo-compounds that contain two o-bromine atoms [compounds (6) and (8— 12)] in their copper-promoted reactions with acetoxy-ions is in marked contrast to that in their copper-

(50) (53)

(51) (54)

(52) (55)

SCHEME 2

promoted reactions with other nucleophiles, e.g. cyanide,[10] nitrite,[11] sulphinate,[3,9] and dialkylphosphite [1] ions, trialkylphosphites,[13] etc. In the latter cases both o-bromine atoms undergo nucleophilic replacement whereas in the former only one of the o-bromine atoms is replaced. The single exception to this occurred in the reaction of compound (6) in DMSO when a mixture of the products in which one [complex (17)] and both bromine atoms [complex (18)] were replaced was obtained. Significantly,

in the latter product one of the bromine atoms was replaced by an acetoxy-group. In dipolar aprotic solvents other than DMSO only one bromine atom was replaced, giving complex (17). This may be seen as providing support for the rationale outlined in Scheme 1. Thus, two reaction routes (Scheme 2) are open to the product (50) resulting from the replacement of one o-bromine atom by an acetoxy-group. The first of these is identical with that in Scheme 1, viz. copper-promoted hydrolysis (51) of the acetoxy-group followed by proton loss from the amide group to give the stable copper complex (52). The o-bromine atom in this product is no longer capable of involvement in an activated intermediate such as complex (46) and no further reaction occurs. In the alternative route, nucleophilic replacement of the bromine atom by an acetoxy-group is promoted by the formation of an annelated copper complex (53) as in Scheme 1. Subsequent copper-promoted hydrolysis (54) then leads to the stable copper complex (55). The o-acetoxy-group in this product is no longer capable of involvement in an intermediate such as complex (47) and is not hydrolyzed under the conditions employed. Why the latter route is restricted to only example (6) of the various o,o-dibromodiarylazo-compounds examined and is followed only in DMSO is not clear.

Attempts to isolate copper(II) complexes of o-bromo- and o-acetoxy-o'-acetylaminodiarylazo-compounds from the various media in which the reactions were carried out have, so far, been unsuccessful. This does not, of course, preclude the intervention of transient complexes such as (46), (47), (51), (53), and (54), but present evidence, although strongly supportive, does not unequivocally justify this conclusion.

Copper-promoted nucleophilic substitution reactions of aryl halides are frequently accompanied by reductive replacement and biaryl coupling and in these respects the present reaction is singularly clean. No evidence of biaryl coupling has been obtained and reductive replacement has been observed only in a limited number of solvents (ethanol, α-picoline, and 2,6-lutidine). The implications of this will be discussed in future papers. The formation of compound (37) when compound (1) is treated with potassium acetate in the presence of copper-(II) acetate in ethanol is ascribed to the greater nucleophilicity [35] of the ethoxide ion than the acetate ion, although the former is likely to be present only in very low concentration.

The work described here provides a novel, facile method for the preparation of o-hydroxy-o'-acetylaminodiarylazo-compounds, otherwise very difficult to obtain, and serves to cast some light on the role of copper in reactions of this type. However, many problems remain outstanding in the field of copper catalysis and elucidation of these awaits the outcome of continuing studies

REFERENCES

[1] Part 2, N. Hall and R. Price, *J. Chem. Soc., Perkin Trans. 1*, 1979, 2873.

[2] D. Delfs and R. Knoche, 1933, DRP 571,859.

[3] D. Delfs, 1938, DRP 658,841.

[4] B. I. Stepanov, M. I. Salivon, W. F. Lagidse, and L. A. Dedukina, *Zh. Obshch. Khim.*, 1958, **28**, 1915.

[5] B. I. Stepanov and M. A. Andreeva, *Zh. Obshch. Khim.*, 1958, **28**, 2490; 1958, **28**, 2966; *Zh. Org. Khim.*, 1966, **2**, 2214; 1969, **5**, 140.

[6] B. I. Stepanov, *Zh. Obshch. Khim.*, 1958, **28**, 2678; 1960, **30**, 2008; N. A. Rozanel'skaya and B. I. Stepanov, *ibid.*, 1961, **31**, 758; B. I. Stepanov, I. I. Vorob'eva, and M. A. Andreeva, *ibid.*, 1962, **32**, 3281; M. A. Andreeva, N. N. Vorozhtov, N. I. Krizhechkovskaya, B. I. Stepanov, and G. G. Yakobson, *ibid.*, 1963, **33**, 988.

[7] B. I. Stephanov, L. A. Dedukina, and T. T. Strashnova, *Zh. Obshch. Khim.*, 1958, **28**, 1921.

[8] B. I. Stepanov, S. V. Mikheeva, and M. A. Andreeva, *Zh. Obshch. Khim.*, 1970, **40**, 2292.

[9] G.B. 1,281,735, Sandoz, 1972.

[10] G.B. 1,226,950, I.C.I., 1971.

[11] G.B. 1,125,683, Bayer, 1968; G.B. 1,184,825, Cassella, 1970.

[12] T. A. Liss and D. Baer, *Inorg. Chem.*, 1969, **8**, 1328.

[13] N. Hall and R. Price, *J. Chem. Soc., Perkin Trans. 1*, 1979, 2634.

[14] W. R. H. Hurtley, *J. Chem. Soc.*, 1929, 1870.

[15] W. T. Smith, *J. Am. Chem. Soc.*, 1949, **71**, 2855; W. T. Smith and L. Campanaro, *ibid.*, 1953, **75**, 3602.

[16] R. G. R. Bacon and H. A. O. Hill, *J. Chem. Soc.*, 1964, 1112.

[17] T. Cohen and A. Lewin, *J. Am. Chem. Soc.*, 1966, **88**, 4521.

[18] T. Cohen and I. Cristea, *J. Org. Chem.*, 1975, **40**, 3649.

[19] B. N. Figgis and J. Lewis, ' Modern Co-ordination Chemistry,' eds. J. Lewis and L. Wilkins, Interscience, New York, 1966, p. 415.

[20] M. Kato, H. B. Jonassen, and J. C. Fanning, *Chem. Rev.*, 1964, **64**, 99; G. A. Barclay, C. M. Harris, B. F. Hoskins, and E. Kokot, *Proc. Chem. Soc.*, 1961, 264; C. M. Harris, E. Kokot, S. L. Lenzer, and T. M. Lockyer, *Chem. Ind. (London)*, 1962, 651; G. A. Barclay, and B. F. Hoskins, *J. Chem. Soc.*, 1965, 1979; M. Kishita, Y. Muto, and M. Kubo, *Austr. J. Chem.*, 1957, **10**, 386; M. Kishita, Y. Muto, and M. Kubo, *Naturwissenschaften*, 1957, **44**, 372.

[21] M. Kishita, Y. Muto, and M. Kubo, *Naturwissenschaften*, 1957, **44**, 612; *Austr. J. Chem.*, 1958, **11**, 309; M. Kishita and M. Kubo, *Bull. Chem. Soc. Jpn.*, 1962, **35**, 1241; M. Kubo, Y. Kuroda, M. Kishita, and Y. Muto, *Austr. J. Chem.*, 1963, **16**, 7.

[22] R. Price in ' The Chemistry of Synthetic Dyes,' ed. K. Venkataraman, Academic Press, New York and London, 1970, p. 303.

[23] R. G. R. Bacon and H. A. O. Hill, *Quart. Rev.*, 1965, **19**, 95.

[24] T. Cohen and I. Cristea, *J. Am. Chem. Soc.*, 1976, **98**, 748.

[25] G. van Koten, J. T. B. H. Jastrzebski, and J. G. Noltes, *Tetrahedron Lett.*, 1976, 233; G. van Koten and J. G. Noltes, *J. Organomet. Chem.*, 1875, **84**, 129; 1975, **85**, 105.

[26] R. Price, *Dyes and Pigments*, 1981, **2**, 11, and refs. therein.

[27] J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, 1951, **49**, 273.

[28] R. Price, unpublished result.

[29] M. Lappert, *J. Chem. Soc.*, 1961, 817.

[30] C. R. Wasmuth and H. Freiser, *Talanta*, 1962, **9**, 1059.

[31] R. P. Houghton and D. J. Pointer, *J. Chem. Soc.*, 1965, 4214.

[32] L. Meriwether and F. H. Westheimer, *J. Am. Chem. Soc.*, 1956, **78**, 5119; J. P. Collman and D. A. Buckingham, *ibid.*, 1963, **85**, 3039.

[33] Q. Fernando, *Adv. Inorg. Chem. Radiochem.*, 1965, **7**, 185.

[34] W. L. Koltun, M. Fried, and F. R. N. Gurd, *J. Am. Chem. Soc.*, 1959, **81**, 301; 1960, **82**, 233; R. B. Martin, M. Chamberlain, and J. T. Edsall, *ibid.*, 1960, **82**, 459.

[35] J. O. Edwards and R. G. Pearson, *J. Am. Chem. Soc.*, 1961, **84**, 16.