120. *The Ullmann Biaryl Synthesis. Part IV.*[1] *The Halogen-transfer.*

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Ullmann condensations of some bromonitro-compounds with iodobenzene, etc., are described. A major side-reaction involving interchange of halogen atoms among the reactants is reported.

THE formation of atypical by-products from Ullmann syntheses of derivatives of 2,4-dinitrobiphenyl by the reaction between derivatives of 1-chloro-2,4-dinitrobenzene and iodobenzene, etc.,[2] is due basically [3] to independent reaction of the aryl iodide with copper. This present communication describes similar condensations with the more reactive 1-bromo-2,4-dinitrobenzene, by use of which it was hoped largely to suppress formation of atypical products. Subsequently other unsymmetrical syntheses were investigated in a study of an unexpected halogen-transfer prominent in some condensations of this nature.

It was initially expected that less of the unsymmetrical product might be formed owing to preferential self-condensation of the reactive nitro-halide to give 2,4,2′,4′-tetranitrobiphenyl. However, satisfactory yields were obtained despite the wide divergence in the relative reactivities towards copper of the individual halides. Moreover, abnormal biaryls similar to those obtained from reactions with the chlorodinitro-analogue were not isolated, and the product was purer.

As shown in the Table, *o*-bromonitrobenzene and methyl *o*-bromobenzoate with iodobenzene give equally good yields of unsymmetrical biaryls. *p*-Bromonitrobenzene and 1-iodonaphthalene gave a very poor yield of 1-*p*-nitrophenylnaphthalene, probably because the *p*-halogen is less reactive.[4]

The simultaneous formation of volatile material, generally of lower boiling point than either of the halides used, was a characteristic of the reactions listed in the Table. This was a sparingly reactive or unreactive halide formed by halogen-transfer between the reactants, *e.g.*, bromobenzene from 1-bromo-2,4-dinitrobenzene and iodobenzene. As shown in the Table, the amount of the transfer varied with the nature and proportions of the reactants, and was less at the lower temperatures. The yield of unsymmetrical biaryl was, however, little influenced by temperature.

Aryl halide (A)	Aryl halide (B)	Ratio, A : B	Reaction temp.	Yield (%) of unsymm. biaryl	Halogen transfer (%)
1,2,4-$C_6H_3Cl(NO_2)_2$	C_6H_5I	1 : 2	190°	25 *	2
,,	*p*-C_6H_4MeI	1 : 1·5	195	25 *	5
,,	*p*-$C_6H_4I{\cdot}OMe$	1 : 1·5	,,	35 *	20
o-$C_6H_4Br{\cdot}NO_2$	C_6H_5I	1 : 1·25	190	60	15
,,	*o*-$C_6H_4I{\cdot}CO_2Me$	,,	175	65	25
,,	α-$C_{10}H_7I$	1 : 1	200	40	30
,,	,,	1 : 1·5	,,	50	40
,,	,,	1 : 2	,,	60	~50
,,	,,	,,	170	55	~30
,,	,,	1 : 1	150	55	~5
p-$C_6H_4Br{\cdot}NO_2$	,,	1 : 1·25	240	5	5
1,2,4-$C_6H_3Br(NO_2)_2$	C_6H_5I	,,	175	60	15
,,	*o*-C_6H_4MeI	,,	,,	55	15
,,	*p*-C_6H_4MeI	,,	,,	50	15
,,	*p*-$C_6H_4I{\cdot}OMe$	,,	,,	55	5
o-$C_6H_4Br{\cdot}CO_2Me$	C_6H_5I	1 : 1·5	190	45	40

* Cf. Part I.

Small quantities of halogen-transfer products have been identified in the reaction

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[1] Part III, preceding paper.

[2] Part I, *J.*, 1960, 566.

[3] Part II, *J.*, 1960, 574.

[4] Davey and Latter, *J.*, 1948, 264.

residues of two reported condensations of *o*-bromonitrobenzene with iodides.[5] Longo and Pirona [5] considered the mechanism of this side-reaction to be involved in an unspecified way with dehalogenation of the bromonitro-compound. In the described reaction with α-iodonaphthalene, however, nitrobenzene was not formed to any extent with α-bromonaphthalene. Moreover, it is evident, by computation of the yields of unsymmetrical biaryl and halogen-transfer product under optimum transfer conditions, that the exchange mechanism did not affect the yield of normal condensation product provided sufficient excess of iodide was present to compensate for loss of reactive halide. It seems clear that the halogen-transfer cannot function at temperatures below those at which the halide to be transformed is capable of independent reaction with copper. Thus α-iodonaphthalene was progressively less readily attacked by the metal below 200°. At 150°, at which halogen transfer in the reaction with *o*-bromonitrobenzene almost ceased, the halide was practically unaffected by copper.

Isomers of the individual halogen-transfer products were not formed. For example, oxidation of the bromotoluene obtained from *o*-iodotoluene by this means, or hydrolysis of methyl bromobenzoate formed from methyl *o*-iodobenzoate, afforded *o*-bromobenzoic acid free from isomeric material in each case.

EXPERIMENTAL

For general instructions see Parts I and II.

General Procedure.—The technique for Ullmann condensations outlined in Part I was adhered to. The time required for the addition of copper, however, in reactions involving the highly reactive bromonitro-compounds frequently exceeded that required for the chloronitro-analogues, particularly when low-temperature condensations were carried out.

Ullmann Reactions of 1-*Chloro*-2,4-*dinitrobenzene.*—(a) *With iodobenzene.* After removal of chloroform from the organic product of reaction of the chlorodinitro-compound (50 g.), iodobenzene (100 g., 2 mol.), and copper (50 g.) as described in Part I, the residue was evaporated at 100°/50 mm. and volatile material (10 g.) condensed in a cold trap. Refractionation of the colourless oil at atmospheric pressure gave a middle fraction (4 g.), b. p. 120—135°. Redistillation afforded a small fraction (1·25 g.), b. p. 125—130°, which appeared to be crude chlorobenzene. Nitration of this material by standard methods furnished 1-chloro-2,4-dinitrobenzene (1·1 g.), m. p. and mixed m. p. 50—51° (from 90% methanol) (Found: N, 13·6; Cl, 17·1. Calc. for $C_6H_3O_4N_2Cl$: N, 13·8; Cl, 17·5%).

(b) *With* p-*iodotoluene.* Redistillation of the most volatile fraction (30 g.) from the reaction of the chlorodinitrobenzene (50 g.), *p*-iodotoluene (81 g.), and copper (50 g.) afforded an oil (11·5 g.), b. p. <70°/3 mm. Redistillation at atmospheric pressure gave *p*-chlorotoluene (1·5 g.), b. p. 170—172° (Found: Cl, 27·5. Calc. for C_7H_7Cl: Cl, 28·0%). Subsequently the temperature of the distillate rose steadily to 205°. This material was not further investigated.

(c) *With* p-*iodoanisole.* Reaction, as in (b), with *p*-iodoanisole (87 g.), gave a volatile fraction (10 g.), b. p. <70°/0·4 mm. Redistillation gave *p*-chloroanisole (7·5 g.), b. p. 195—197° (Found: C, 58·4; H, 5·1; Cl, 24·5. Calc. for C_7H_7OCl: C, 58·9; H, 4·9; Cl, 24·9%).

Ullmann Reactions of o-*Bromonitrobenzene.*—(a) *With iodobenzene.* The halogenonitro-compound (20 g.), iodobenzene (25 g.), and copper (20 g.) at 190—195° (3·5 hr.) gave (1) a mobile liquid (4·75 g.), b. p. <130°/30 mm., (2) a pale yellow viscous oil (12·8 g.), b. p. 118—120°/0·2 mm., and (3) a clear red viscous oil (5 g.), b. p. 155—165°/0·2 mm. A small dark residue (0·5 g.) was discarded. Fraction (1), on redistillation, afforded bromobenzene (2 g.), b. p. 157—160° (Found: Br, 51·3. Calc. for C_6H_5Br: Br, 51·0%). Fraction (2) crystallised slowly from aqueous methanol at 0° in pale yellow needles of 2-nitrobiphenyl (11·6 g.), m. p. and mixed m. p. 37° (Found: N, 7·1. Calc. for $C_{12}H_9O_2N$: N, 7·0%). Fraction (3) furnished pale yellow needles (from methanol) of 2,2′-dinitrobiphenyl (3·5 g.), m. p. 126—127°.

(b) *With methyl* o-*iodobenzoate.* *o*-Bromonitrobenzene (20·2 g.), the iodo-ester (32·7 g.), and copper (19 g.) reacted at 175° for 3·5 hr. Fractionation of the products gave a colourless liquid (8·5 g.), b. p. 85—95°/0·5 mm., and methyl 2′-nitrobiphenyl-2-carboxylate (17 g.), b. p. 160—170°/0·5 mm. Redistillation of the lower-boiling liquid yielded a fraction (5·25 g.), b. p.

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[5] Longo and Pirona, *Gazzetta*, 1947, **77**, 117.

245—250°, which on hydrolysis with dilute aqueous alkali afforded *o*-bromobenzoic acid (4·5 g.), m. p. and mixed m. p. 147—148° (Found: Br, 40·0. Calc. for $C_7H_5O_2Br$: Br, 39·8%).

(c) *With α-iodonaphthalene.* (1) Equimolar amounts. α-Iodonaphthalene (76·2 g.) and *o*-bromonitrobenzene (60·4 g.) were treated with copper (50 g.) at 200° for 4·5 hr. Fractional distillation of the organic products yielded a mobile liquid (24 g.), b. p. 70—85°/0·2 mm., and a red viscous oil (53 g.), b. p. 150—165°/0·1 mm. A dark red residue (7 g.) was discarded. Redistillation of the more volatile fraction afforded naphthalene (1·5 g.), b. p. 220—225°, and α-bromonaphthalene (19·2 g.), b. p. 275—280° (Found: C, 57·9; H, 3·6; Br, 38·1. Calc. for $C_{10}H_7Br$: C, 58·0; H, 3·4; Br, 38·6%). The viscous oil furnished prismatic needles of 1-*o*-nitrophenylnaphthalene (32 g.), m. p. 90—92° (lit., 89°) after 3 crystallisations from methanol.

The same reactants (¼ scale) at 145—150° for 7 hr. afforded a pale yellow oil (8 g.), b. p. 100—110°/0·5 mm., then a viscous red oil (13 g.), b. p. 177—182°/0·8 mm. There was no distillation residue. The lower-boiling fraction was added to warm methanol (100 ml.) containing picric acid (10 g.). On cooling, the halogenonaphthalene picrates separated in fine yellow needles which, after decomposition with dilute aqueous ammonia, gave an oil (4·3 g.), b. p. 157—162°/15 mm., d_4^{20} 1·69 (Found: C, 50·5; H, 3·2; I, 46·0. Calc. for $C_{10}H_7I$: C, 47·2; H, 2·8; I, 50·0%). The methanolic mother-liquors, after removal of solvent and excess of picric acid, afforded unchanged *o*-bromonitrobenzene (3·7 g.). The main product crystallised from methanol (50 ml.) giving, in a single operation, 1-*o*-nitrophenylnaphthalene (9·8 g.), m. p. 93—94° (Found: N, 5·6. Calc. for $C_{16}H_{11}O_2N$: N, 5·6%).

Under the same conditions, $<10\%$ of the iodide alone underwent reaction with copper (based on recovery of halide and weight increase of inorganic material).

(2) With 1·5 mol. of α-iodonaphthalene. The iodide (76·2 g.), *o*-bromonitrobenzene (40·3 g.), and copper bronze (50 g.) at 200° (4·5 hr.) gave naphthalene (1 g.), α-bromonaphthalene (16·6 g.), and the unsymmetrical biaryl (24·2 g.), m. p. 90—92°.

(3) With 2 mol. of α-iodonaphthalene. The iodide (76·2 g.), with *o*-bromonitrobenzene (30·2 g.) and copper (50 g.) at 200° (4·5 hr.) yielded volatile material (28 g.), 75—95°/0·4 mm., α-bromonaphthalene (17 g.) (Found: Br, 38·3%), and the nitro-hydrocarbon (22·2 g.), m. p. 90—92° (after 3 crystallisations from methanol).

The same reactants, at 170° (6·5 hr.), gave a volatile fraction (36 g.), b. p. 150—180°/25 mm., d_4^{20} 1·65, and the unsymmetrical biaryl (20·3 g.), m. p. 92—93° [after a single crystallisation from methanol of the appropriate fraction (28·5 g.), b. p. 155—160°/0·1 mm.]. There was no distillation residue. Attempted separation of the mixed halogenonaphthalenes by distillation proved unsatisfactory. No fore-run of naphthalene, however, was obtained. Approximate estimation of the mixture by calculation from the specific gravities of α-bromonaphthalene and its iodo-analogue indicated *ca.* 70% of the iodide.

Reaction between p-*Bromonitrobenzene and α-Iodonaphthalene.*—The bromonitro-compound (20 g.), α-iodonaphthalene (31·7 g.), and copper (20 g.) reacted at 240—245° for 6 hr. Fractionation gave (1) a yellow oil (15 g.), b. p. 95—115°/0·4 mm., which solidified, (2) a red viscous oil containing suspended crystals (9 g.), b. p. 175—195°/0·5 mm., and a dark residue (6 g.) which was discarded. Fraction (1) afforded unchanged bromonitrobenzene (7·5 g.) on crystallisation from methanol. The mother-liquors were refluxed for 4 hr. with concentrated hydrochloric acid (25 ml. in 50 ml. of water) and granulated zinc (10 g.), then poured into water (500 ml.). The neutral material was extracted with light petroleum. Removal of the solvent followed by distillation furnished naphthalene (2 g.) and an oil (1·5 g.), b. p. 270—280°. Crystallisation of the picrate of this material from methanol gave yellow needles of α-bromonaphthalene picrate (2·15 g.), m. p. 133° (Found: C, 44·3; H, 2·2; N, 9·4; Br, 17·7. Calc. for $C_{16}H_{10}O_7N_3Br$: C, 43·9; H, 2·3; N, 9·6; Br, 18·3%). Fraction (2) was refluxed in methanol (150 ml.) until the red oil had dissolved, then the solution was cooled and filtered from insoluble 1,1′-binaphthyl (3 g.), m. p. 155—156°. Concentration of the mother-liquors to half-bulk yielded a further quantity of the same hydrocarbon (1·5 g.). The residue, after removal of solvent, was chromatographed on alumina in benzene–light petroleum (1 : 2), affording successively 1,1′-binaphthyl (1 g.) and, on elution with benzene–light petroleum (2 : 1), pale greenish-yellow needles (from methanol) of 1-p-*nitrophenylnaphthalene* (1·4 g.), m. p. 132° (Found: C, 77·3; H, 4·6; N, 5·3. $C_{16}H_{11}O_2N$ requires C, 77·1; H, 4·4; N, 5·6%).

Ullmann Reactions of 1-*Bromo*-2,4-*dinitrobenzene.*—(a) *With iodobenzene.* The bromonitro-compound (100 g.), iodobenzene (103 g.), and copper (75 g.) reacted at 190° (4 hr.) affording 2,4-dinitrobiphenyl (52 g.), m. p. 110° (from benzene–light petroleum). The mother-liquors were evaporated, then the residue was distilled *in vacuo*, to give (1) a volatile fraction (9 g.), b. p. <110°/15 mm., (2) crude 2,4-dinitrobiphenyl (17 g.), b. p. 170—185°/0·5 mm., and (3) a dark residue (10·5 g.) which was not further examined. Fraction (1) yielded bromobenzene (7·3 g.), b. p. 157—160° (Found: Br, 51·2. Calc. for C_6H_5Br: Br, 51·0%). Crystallisation of fraction (2) from methanol or benzene–light petroleum gave a further quantity of the unsymmetrical biaryl (9·5 g.).

(b) *With* o-*iodotoluene*. The bromonitro-compound (45 g.), *o*-iodotoluene (49·5 g.), and copper (34 g.) at 175° (3·5 hr.) yielded a mixture of halogenotoluenes (13 g.), b. p. <140°/25 mm., and a pale red viscous oil (32 g.), b. p. 180—185°/0·5 mm., which crystallised from methanol in yellow needles of 2'-*methyl*-2,4-*dinitrobiphenyl* (26 g.), m. p. 88° (Found: C, 60·6; H, 3·9; N, 10·8. $C_{13}H_{10}O_4N_2$ requires C, 60·5; H, 3·9; N, 10·9%). Redistillation of the first fraction furnished *o*-bromotoluene (4·5 g.), b. p. 180—182° (Found: Br, 46·7. Calc. for C_7H_7Br: Br, 46·8%), followed by a mixture of *o*-bromo- and *o*-iodo-toluene (8 g.), b. p. 183—208°, which was not further investigated.

Oxidation of the *o*-bromotoluene obtained from the halogen transfer by Bigelow's technique [6] afforded *o*-bromobenzoic acid free from isomeric material.

(c) *With* p-*iodotoluene*. A reaction similar to (b) with *p*-iodotoluene furnished 4'-methyl-2,4-dinitrobiphenyl (24·3 g.), m. p. 87—88°, on crystallisation of the crude material (30 g.), b. p. 170—180°/0·3 mm., from methanol. Refractionation (twice) of the crude mixed halogenotoluenes (15 g.), b. p. <140°/30 mm., gave *p*-bromotoluene (4·5 g.), b. p. 185—190° (Found: Br, 46·7%), followed by mixed *p*-bromo- and *p*-iodo-toluene (8·5 g.), b. p. 195—210°.

(d) *With* p-*iodoanisole*. 1-Bromo-2,4-dinitrobenzene (50 g.), *p*-iodoanisole (59 g.), and copper (37 g.) at 175° (3·5 hr.) gave a fore-run (15 g.), b. p. 50—80°/0·3 mm., then crude 4'-methoxy-2,4-dinitrobiphenyl as an orange viscous oil (34·5 g.), b. p. 190—205°/0·3 mm. Crystallisation of the latter from methanol afforded yellow needles of the pure biaryl (31 g.), m. p. 94—95°. The fore-run was cooled to 0°, then the oil (4·5 g.) was decanted from crystallised *p*-iodoanisole (10 g.) and refractionated to give, after a small low-boiling fraction, *p*-bromoanisole (1·5 g.), b. p. 212—216° (Found: Br, 42·3. Calc. for C_7H_7OBr: Br, 42·8%).

Reaction of Methyl o-*Bromobenzoate with Iodobenzene*.—The iodide (13·3 g.), methyl *o*-bromobenzoate (9 g.), and copper (11 g.) reacted at 195—200° for 5·5 hr. Fractional distillation of the organic material yielded (1) a volatile fore-run (4·5 g.), b. p. <140°/100 mm., (2) a fraction (1·5 g.), b. p. 60—100°/0·8 mm., which partly solidified (it was not further examined), (3) crude methyl biphenyl-2-carboxylate (4·8 g.), b. p. 120—130°/0·8 mm., and (4) methyl biphenate (1·8 g.), b. p. 245—255°/0·8 mm. Redistillation of fraction (1) at atmospheric pressure gave bromobenzene (2·8 g.), b. p. 156—158° (Found: Br, 50·7. Calc. for C_6H_5Br: Br, 51·0%). Hydrolysis of fraction (3) with 5% methanolic potassium hydroxide (50 ml.) gave biphenyl-2-carboxylic acid (3·7 g.), m. p. 113° (from benzene–light petroleum) (lit., 113—114°) (Found: C, 78·5; H, 5·1. Calc. for $C_{13}H_{10}O_2$: C, 78·8; H, 5·1%). Crystallisation of fraction (4) from methanol furnished colourless needles of methyl biphenate (0·8 g.), m. p. 73°.

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[*Received, April 28th*, 1959.]

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[6] Bigelow, *J. Amer. Chem. Soc.*, 1922, **44**, 2015.