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## The Ullmann Reaction. Part I. The Reaction of 2,3-Di-iodonitrobenzene with Copper Bronze

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The reaction of 2,3-di-iodonitrobenzene with copper bronze in dimethylformamide gives 1,5-dinitrobiphenylene, 2,2'-di-iodo-6,6'-dinitrobiphenyl, and 4,5,12,13-tetranitrotetraphenylene. A reaction mechanism is suggested.

CORBETT and HOLT<sup>1</sup> reported that the reaction between copper bronze and 3,4-dibromo-5-nitrotoluene in boiling dimethylformamide gave a 40% yield of a dimethyldinitrobiphenylene. McOmie and his co-workers<sup>2</sup> have since repeated this work and have shown the product to be 3.7-dimethyl-1.5-dinitrobiphenylene. However, despite numerous variations of the reaction conditions their yield of the biphenylene was usually 0-5%.



In the present work the reaction between 2,3-di-iodonitrobenzene (I) and copper bronze in dimethylformamide has been studied and under certain conditions a 43%vield of a dinitrobiphenylene (II) was obtained, other products being a di-iododinitrobiphenyl (III) and a tetranitrotetraphenylene (IV).

The biphenylene (II) was characterised by reduction to an aminonitrobiphenylene which in turn was reduced to a diaminobiphenylene (V). The n.m.r. spectrum of (V) in deuteriodimethyl sulphoxide showed the characteristic pattern for an ABC system in the aromatic region [quartet (B),  $\tau 3.51$ ,  $J_{AB} = 9$  c./sec.,  $J_{BC} =$ 6 c./sec., 2 protons; doublet (C),  $\tau$  3.90,  $J_{BC} = 6$  c./sec., 2 protons; doublet (A),  $\tau$  3.98,  $J_{AB} = 9$  c./sec., 2 protons] indicating that there are only three types of aromatic proton and that these are contained in 1,2,3-trisubstituted benzene rings. Treatment of the diamine



(V) with Raney nickel in ethanol gave 2,3'-diaminobiphenyl showing (II) to be 1,5-dinitrobiphenylene.

The biphenyl (III) also showed the characteristic

<sup>1</sup> J. F. Corbett and P. F. Holt, *J. Chem. Soc.*, 1961, 4261. <sup>2</sup> C. R. Harrison, J. F. W. McOmie, J. B. Searle, J. P. Smith, J. O. Jenkins, and J. W. Smith, *J. Chem. Soc.* (C), 1966, 1769.

n.m.r. spectrum for 1,2,3-trisubstituted benzene rings containing only three types of aromatic proton [two superimposed doublets (A and C),  $\tau 1.74$ ,  $J_{AB}$  and  $J_{BO} =$ 8 c./sec., 4 protons; triplet (B),  $\tau 2.62$ ,  $J_{BO}$  and  $J_{AB} = 8$ c./sec., 2 protons]. This biphenyl can have one of three possible structures (III), (VI), or (VII) of which (VII) can be eliminated because it contains six different protons. Since halogen atoms substituted ortho to a nitro-group are far more reactive towards copper bronze than those substituted meta<sup>3</sup> and since it is known that, under identical conditions, 3-bromo-4-iodo-5-nitrotoluene gives 2,2'-dibromo-4,4'-dimethyl-6,6'-dinitrobiphenyl<sup>1</sup> it is probable that (III) is 2,2'-di-iodo-6,6'-dinitrobiphenyl. This is supported by the n.m.r. data which shows, as would be predicted for (III),  $H_A$  and  $H_0$  together at low field whereas in (VI)  $H_0$  would be expected to appear at a higher field than  $H_{A}$ .

The tetraphenylene (IV) was not very soluble in deuteriochloroform and showed a very weak n.m.r. spectrum. However, two aromatic doublets and a triplet were visible indicating that only three types of aromatic proton are present in the compound. The size of the coupling constants (6-8 c./sec.) suggests that these protons are present in 1,2,3-trisubstituted benzene rings. Total reduction of (IV) gave a tetra-aminotetraphenylene tetrahydrochloride which on treatment with aqueous base gave a tetra-amine. The n.m.r. spectrum of this compound in deuteriodimethyl sulphoxide [quartet (H<sub>B</sub>),  $\tau$  3.59,  $J_{AB} = 7$  c./sec.,  $J_{BC} = 8$  c./sec., 4 protons; doublet (H<sub>c</sub>),  $\tau$  3.88,  $J_{AB} = 8$  c./sec., 4 protons; doublet (H<sub>A</sub>),  $\tau$  4.03,  $J_{AB} = 8$  c./sec., 4 protons] was very similar to that of the diaminobiphenylene (V) and analysis of the spectrum confirms the deductions made from the n.m.r. spectrum of the tetraphenylene (IV).

The tetraphenylene (IV) was synthesised by the fusion of the biphenyl (III) with cuprous oxide at 350° and also by the reaction of (III) with copper bronze at 230°. These methods appear to be related to the preparation of tetraphenylene by the reaction of 2,2'-dihalogenobiphenyls with lithium<sup>4</sup> or magnesium<sup>5</sup> although this is the first time copper or cuprous oxide has been used in such a procedure. Since such reactions can give only one tetranitrotetraphenylene then (IV) must be 4,5,12,13-tetranitrotetraphenylene.

The Ullmann reactions were carried out in dimethyl-

<sup>3</sup> N. Kornblum and D. L. Kendall, J. Amer. Chem. Soc., 1952, 74, 5782.

<sup>4</sup> G. Wittig and G. Lehmann, *Ber.*, 1957, **90**, 875. <sup>5</sup> W. S. Rapson and R. G. Shuttleworth, and J. N. van Niekerk, *J. Chem. Soc.*, 1943, 326.

formamide at 152°; in some cases the aryl halide (I) was added slowly to the copper bronze (Method 1; see Experimental section) and in other cases the reverse applied (Method 2). When there is always a large excess of copper bronze in the reaction mixture (Method 1) the yield of the biphenylene (II) is a maximum and the yield of the biphenyl (III) is a minimum. The converse applies when there is always a large excess of aryl halide (I) in the reaction mixture (Method 2) and as the additions are varied between these two extremes there is a gradual transition in the yields of (II) and (III). This result can best be explained in terms of the mechanism shown in the Scheme.

The reaction between 2,3-di-iodonitrobenzene and copper bronze at 152°

Method (see	Method Copper (see bronze			Yields (%)		
Experi-	(g. atoms/	Time of	Biphenvl-		Tetra-	
mental	mole	addition	ene	Biphenvl	phenvlene	
section)	halide)	(hr.)	(II)	(III)	(IV)	
1	3.0	9	43	6	5	
1	3.0	5	38	10	5	
1	3.0	1	<b>43</b>	20	3	
1	$3 \cdot 0$	0	30	33	5	
$^{2}$	$3 \cdot 0$	5	<b>25</b>	46	1	
<b>2</b>	$3 \cdot 0$	9	<b>22</b>	42	5	
3	1.5	1 <u>2</u>	0	75	0	
3	$3 \cdot 0$	$\frac{1}{2}$	0	75	0	
	$(I)  \int Cu  Cu or (VIII) $			(1)	→ (IV) → (II)	

The structure of the intermediate, of which (VIII) is a representation, is unknown but there is mounting evidence to show that this is a copper aryl.<sup>6,7</sup> However, Hashimoto and Nakano,8 in a study of the thermal decomposition of copper aryls, have shown that biaryls are obtained via a radical mechanism. If such a mechanism holds true under Ullmann conditions it would be expected that such a reaction would show evidence of radicals. This is only rarely the case<sup>9</sup> although it must be remembered that this may be a result of the radicals not having much freedom in the system. Bacon and Hill<sup>10</sup> pointed out that it may be unjustified to distinguish between the two intermediates (VIII) because copper aryls may be regarded as a source of aryl radicals and thus both species may be involved in the Ullmann reaction. The following discussion may be applied to

- <sup>8</sup> H. Hashimoto and T. Nakano, J. Org. Chem., 1966, **31**, 891.
  <sup>9</sup> P. E. Fanta, Chem. Rev., 1964, **64**, 627.
  <sup>10</sup> R. G. R. Bacon and H. A. O. Hill, Quart. Rev., 1965, **19**, 95.

either the aryl radical intermediate or the copper aryl intermediate.

The intermediate (VIII) can give both the biphenyl (III) by dimerisation or reaction with aryl halide (I), and the biphenylene (II) via a benzyne intermediate (IX). A benzyne intermediate, which has been postulated to explain the formation of biphenylenes in other Ullmann reactions,<sup>1,2,11</sup> provides the simplest explanation for the formation of the biphenylene (II) since the biphenyl (III) is not converted to (II) under the reaction conditions. Indeed, if the biphenyl (III) could be cyclised to give a biphenylene the product would be 1,8- not 1,5-dinitrobiphenylene. The dependence of the reaction upon the aryl halide concentration can be explained in terms of this mechanism if the rate of formation of the biphenyl (III) is faster than the rate of formation of the benzyne intermediate (IX). Thus, when the intermediate (VIII) is produced using a large excess of aryl halide (I) the production of the biphenyl (III) will be favoured, whereas when very low concentrations of the aryl halide (I) are used the biphenyl formation will be statistically unfavourable and the intermediate (VIII) will exist long enough to permit the slow formation of the benzyne intermediate (IX) which can give the biphenylene (II) by dimerisation.

When the biphenyl (III) was cyclised by heating with cuprous oxide alone or with copper bronze, with or without solvent, the tetraphenylene (IV) was found in 4-20%yield. The same reaction may be responsible for the formation of the tetraphenylene (IV) in yields of up to 5% in the reaction of aryl halide (I) with copper bronze in dimethylformamide. The production of the tetraphenylene (IV) is unexpected because 2,2'-di-iodobiphenyls usully react with cuprous oxide,<sup>12,13</sup> or copper bronze,<sup>14</sup> to give biphenylenes. However, it should be noted that the nitro-substituents in the tetraphenylene (IV) are relatively strain free because the aromatic rings in (IV) are held at about  $75^{\circ}$  to each other, whereas in the planar, 1,8-dinitrobiphenylene the same groups would be expected to be under considerable steric strain.

2,3-Di-iodonitrobenzene (I) reacts with copper bronze without solvent at 150-160° (Method 3) to give the biphenyl (III) only; the yield (75%) is independent of the proportion of starting metal (1.5-3 g. atoms). The high yield of (III) is to be expected because the reaction fulfils the condition for preferential biphenyl formation discussed earlier, *i.e.*, very high aryl halide concentration. The absence of the tetraphenylene (IV) and the insensitivity of the reaction towards an excess of copper bronze is probably the result of the stability of the biphenyl (III) towards copper under the reaction conditions. It was found that (III) only reacts with copper in the absence of solvent at above  $230^{\circ}$ . There is no ready explanation for the absence of the biphenylene (II) although it seems that the solvent must play an

<sup>11</sup> E. R. Ward and B. D. Pearson, J. Chem. Soc., 1961, 515.

- W. C. Lothrop, J. Amer. Chem. Soc., 1941, 63, 1187.
   W. Baker, M. P. V. Boarland, and J. F. W. McOmie, J. Chem. Soc., 1954, 1476.
  - 14 J. C. Salfield and E. Baume, Tetrahedron Letters, 1966, 3365.

<sup>&</sup>lt;sup>6</sup> A. H. Lewin and T. Cohen, *Tetrahedron Letters*, 1965, 4531. <sup>7</sup> N. Nilsson, *Tetrahedron Letters*, 1966, 679.

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important role in reactions carried out in dimethylformamide.

## EXPERIMENTAL

Dimethylformamide was dried over barium oxide and redistilled under nitrogen, copper bronze (B.D.H.) was dried at 100° and all Ullmann reactions were carried out under nitrogen.

2-Iodo-6-nitroaniline.-2,3-Dinitroiodobenzene<sup>15</sup> (20 g.) in ethanol (150 ml.) and aqueous ammonia (26 ml., d 0.88) was heated in an autoclave at 140° for 2 hr. Evaporation of the solvent and the addition of a little water gave deep red needles of the nitro-amine, 16.5 g. (92%), m. p. 103-105° (lit.,<sup>16</sup> m. p. 108°).

2,3-Di-iodonitrobenzene.-2-Iodo-6-nitroaniline (20 g.) in glacial acetic acid (200 ml.) was added, with stirring, to sodium nitrite (6 g.) in concentrated sulphuric acid (80 ml.) keeping the temperature below 20°. The resulting solution was added to potassium iodide (20.5 g.) in water (200 ml.) at 50°. Decomposition of the complex was rapid and was brought to completion by heating the mixture on a steambath for  $\frac{1}{2}$  hr. The mixture was diluted with cold water and the product was extracted with ether, the ether extract was washed with 5% aqueous sodium metabisulphite and with water, and dried (Na<sub>2</sub>SO<sub>4</sub>). After removal of the solvent the 2,3-di-iodonitrobenzene crystallised from methanol as lustrous brown needles (22 g., 78%), m. p. 122-124° (lit.,<sup>17</sup> m. p. 110·2°).

The Ullmann Reactions.-Method 1. Copper bronze (see Table) and dimethylformamide (50 ml.) were stirred and heated in a vapour bath of dimethylformamide. 2,3-Di-iodonitrobenzene (5 g.) in dimethylformamide (25 ml.) was added using a pharmaceutical perfusor (B. Braun Apparatebau, Melsungen) over the time shown in the Table. The mixture was stirred and heated for 1 hr. after the addition was complete.

Method 2. 2,3-Di-iodonitrobenzene (5 g.) in dimethylformamide (75 ml.) was stirred and heated in a vapour bath of dimethylformamide. Copper bronze (see Table) was added in small regulated portions over the time shown in the Table. The mixture was stirred and heated for 1 hr. after the addition was complete.

Method 3. 2,3-Di-iodonitrobenzene (5 g.) was heated in a vapour bath of dimethylformamide. Copper bronze (see Table) was added at such a rate that the temperature did not rise above  $160^{\circ}$  ( $\frac{1}{2}$  hr.). The mixture was heated and stirred for  $\frac{1}{2}$  hr. after the addition was complete.

The reaction mixtures from Methods 1 and 2 were poured into large excesses of ice-cold water and the precipitated solids were filtered off using a filter aid. In all three methods the solid products were extracted with boiling acetone (250 ml., Soxhlet, 24 hr.). The extract was reduced to 20 ml. by evaporation and cooled to give bright yellow needles of 1,5-dinitrobiphenylene, m. p. 272-274° [Found: C, 59.6; H, 2.5; N, 11.8%; M (mass spectroscopy), 242. C<sub>12</sub>H<sub>6</sub>N<sub>2</sub>O<sub>4</sub> requires C, 59.5; H, 2.5; N, 11.6%; M, 242].

The mother-liquors, after the removal of solvent, were chromatographed on alumina  $(30 \times 2 \text{ cm.})$  using benzene as eluent. An initial yellow band gave a pale yellow solid which crystallised as pale yellow prisms of 2,2'-di-iodo-6,6'-dinitrobiphenyl, m. p. 152-153° (Found: C, 29.1; H, 1.4; N, 5.8. C<sub>12</sub>H<sub>6</sub>I<sub>2</sub>N<sub>2</sub>O<sub>4</sub> requires C, 29.05; H, 1.2; N. 5.65%).

A second yellow band gave an orange solid which crystallised from benzene-light petroleum (b. p. 40-60°) as bright orange needles, m. p. 231-232° (solvent of crystallisation lost 200-220°). Sublimation at 185°/15 mm. gave 4,5,12,13-tetranitrotetraphenylene, m. p. 231-232° free from solvent of crystallisation [Found: C, 59.5; H, 2.5; N, 11.5%; M (mass spectroscopy),  $485 \pm 1$ .  $C_{24}H_{12}N_4O_8$ requires C, 59.5; H, 2.5; N, 11.6%; M, 484].

1-Amino-5-nitrobiphenylene.---1,5-Dinitrobiphenylene (1.5 g.), sodium sulphide (3 g.), ethanol (150 ml.), and water (15 ml.) were heated under reflux for  $\frac{1}{2}$  hr. The bright red solution was diluted with water and the precipitate, after the removal of unchanged starting material by hot filtration, crystallised from methanol to give bright red needles of 1-amino-5-nitrobiphenylene (0.7 g., 53%), m. p. 186-188° (Found: C, 67.7; H, 3.8; N, 13.4. C<sub>12</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub> requires C, 67.9; H, 3.8; N, 13.2%).

1,5-Diaminobiphenylene.---1-Amino-5-nitrobiphenylene (0.42 g.), stannous chloride (2.6 g.), ethanol (9 ml.), and concentrated hydrochloric acid (15 ml.) were heated under reflux for 1 hr. The mixture was made alkaline with aqueous potassium hydroxide and the free base was extracted with methylene dichloride. The extract was washed with water and dried  $(K_2CO_3)$  and the solvent removed by evaporation. Crystallisation of the solid residue from methanol gave pale yellow needles of 1,5-diaminobiphenylene (0.3 g., 84%), m. p. 233-235° (Found: C, 78.8; H, 5.4; N, 15.6. C<sub>12</sub>H<sub>10</sub>N<sub>2</sub> requires C, 79.1; H, 5.5; N, 15.4%).

2,3-Diacetamidobiphenyl from 1,5-Diaminobiphenylene.-1,5-Diaminobiphenylene (0.1 g.), ethanol (15 ml.), and Raney nickel (0.2 g.) were heated under reflux for 1 hr. The catalyst was filtered off and the solvent was removed by evaporation. Thin-layer chromatography of the residual red oil on Whatman's Silica Gel 41, developing with benzene-8% methanol, gave a chromatogram which on treatment with iodine vapour showed one intense yellow spot. The position and colour of this spot was not altered by the addition of an authentic sample of 2,3'-diaminobiphenyl to the sample under test.

The residual oil was triturated with two drops of acetic anhydride to give a yellow solid. Crystallisation from benzene gave colourless needles which had the same m. p., mixed m. p., and i.r. spectrum as an authentic sample of 2,3'-diacetamidobiphenyl.

 $2,3'\text{-}Diacetamidobiphenyl.--2,3'\text{-}Diaminobiphenyl}$ was prepared from 2,3'-dinitrobiphenyl by the method of Case and Idelson.18 Trituration with acetic anhydride gave 2,3'-diacetamidobiphenyl which crystallised as needles from benzene, m. p. 185-187° (Found: C, 71.5; H, 6.1; N, 10.4.  $C_{18}H_{16}N_2O_2$  requires C, 71.7; H, 6.0; N, 10.4%).

4,5,12,13-Tetranitrotetraphenylene.-(a) Copper bronze (0.32 g.) was added over 15 min. to 2,2'-di-iodo-6,6'-dinitrobiphenyl (1 g.) preheated at 230°. The mixture was stirred for a further 2 hr. at this temperature and then for 2 hr. at 180° when it was cooled and extracted with acetone (250 ml. Soxhlet, 24 hr.). The solvent was removed by evaporation and the residual solid was dissolved in benzene (25 ml.). Chromatography upon alumina using benzene as gave 4,5,12,13-tetranitrotetraphenylene which eluent

<sup>&</sup>lt;sup>15</sup> D. L. Vivian, J. Org. Chem., 1956, 21, 1188.
<sup>16</sup> R. S. Kapil, J. Chem. Soc., 1959, 4127.

G. Korner and A. Contardi, Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat., 1906, [5], 15, II, 579.
 F. H. Case and A. Idelson, J. Org. Chem., 1962, 27, 4651.

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crystallised from chloroform as bright orange needles (0.1 g., 20%), m. p.  $231-232^{\circ}$ .

(b) 2,2'-Di-iodo-6,6'-dinitrobiphenyl (1 g.), copper bronze (0.26 g.), and dimethylformamide (25 ml.) were stirred and heated under reflux for 15 hr. The products were extracted as in the previous Ullmann reactions and chromatography on alumina gave starting material (0.8 g.) and 4,5,12,13-tetranitrotetraphenylene (0.025 g., 5%), m. p. 231-232°.

(c) 2,2'-Di-iodo-6,6'-dinitrobiphenyl (0.5 g.) and cuprous oxide (5 g.) were ground together and heated at  $100^{\circ}/$ 14 mm. for  $\frac{1}{2}$  hr. The mixture was then heated at  $340-360^{\circ}$ until no more solid sublimed from the reaction vessel ( $\frac{1}{4}$  hr.). The sublimate was dissolved in benzene (5 ml.) and chromatography on alumina gave starting materal (0.03 g.) and 4,5,12,13-tetranitrotetraphenylene (0.01 g., 4%), m. p. 231-232°.

The products obtained in (a)—(c) had the same m. p., mixed m. p., and i.r. spectrum as the 4,5,12,13-tetranitrotetraphenylene isolated from the reaction of 2,3-diiodonitrobenzene and copper.

4,5,12,13-Tetra-aminotetraphenylene Tetrahydrochloride.---4,5,12,13-Tetranitrotetraphenylene (0.2 g.), stannous chloride, (1·1 g.), ethanol (4 ml.), and concentrated hydrochloric acid (6·3 ml.) were heated under reflux for 3 hr. The solution was diluted with an equal volume of water and the precipitate was crystallised from very dilute hydrochloric acid, giving needles of the *tetrahydrochloride* (0·16 g., 79%), which decomposed above 175° (Found: C, 56·2; H, 4·9; N, 11·25.  $C_{24}H_{24}N_4Cl_4$  requires C, 56·5; H, 4·75; N, 11·0%).

The tetrachloride (0.16 g.) was shaken with an excess of 10% aqueous sodium hydroxide solution for  $\frac{1}{2}$  hr. The free amine was extracted with methylene dichloride, and the extract was washed with water and dried (K<sub>2</sub>CO<sub>3</sub>). The solvent was removed by evaporation and crystallisation of the residue from benzene-light petroleum (b. p. 40-60°) gave the tetra-amine as a deep yellow powder, (0.1 g., 67%), m. p. 164-165°.

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