The Mechanism of the Ullmann Diaryl Synthesis.

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New results reported accord with the free-radical mechanism proposed by Rapson and Shuttleworth for this synthesis.

In the reaction of iodobenzene with copper in the presence of an excess of ethyl benzoate it was shown by Rapson and Shuttleworth (*Nature*, 1941, **147**, 675) that, apart from the expected diphenyl, small amounts of ethyl diphenyl-2- and -4-carboxylate had been formed. These had been converted into, and identified as, fluorenone and diphenyl-4-carboxylic acid respectively, the amounts isolated corresponding to 0·6 and 0·2% of the iodobenzene used (Shuttleworth, Thesis, Univ. of Cape Town). It was considered that the result provided evidence for the participation of free radicals in the Ullmann reaction. Fanta (*Chem. Rev.*, 1946, **38**, 139) preferred a mechanism consisting of nucleophilic attack at the carbon–halogen bond by copper with formation of an activated complex at the metal surface, and interaction of the activated complex and a second molecule of the aromatic halide. Bell and Morgan (*J.*, 1954, 1716), however, supported the free-radical mechanism as it is difficult to imagine the existence of a transition complex in the formation of sterically crowded diaryls from 2 : 6-disubstituted halogenobenzenes.

In order to decide whether the intermediate is an aryl radical or a carbanion, Ullmann syntheses were performed with three halogenonitrobenzenes in the presence of an excess of either resorcinol or catechol. Phenols, being acidic, readily give up a proton to carbanions, *i.e.*, their presence in the Ullmann reaction should lead to dehalogenation if carbanions are involved. Resorcinol and catechol would be expected to be about equally effective in this, resorcinol possibly a little more so than catechol, as their dissociation constants are

$3{\cdot}6 \times 10^{-10}$ and $3{\cdot}3 \times 10^{-10}$ at 18° respectively (Landolt–Börnstein, 5th Edn., 1923, Vol. II, pp. 1147, 1139). However, if the mechanism is homolytic, the presence of phenols would again lead to dehalogenation, but catechol would favour the formation of the dehalogenated product more than resorcinol, because, for example, catechol is far more efficient as an antioxidant than resorcinol (cf. Egloff, Morrell, Lowry, and Dryer, *Ind. Eng. Chem.*, 1932, **24**, 1375) and Fieser (*J. Amer. Chem. Soc.*, 1930, **52**, 5204) found the " critical oxidation potential " of resorcinol and catechol to be 1·043 and 0·742 v respectively at 25°.

The important fact established by this investigation is that the Ullmann reaction of *o*- and *p*-iodonitrobenzene and of *o*-bromonitrobenzene carried out in an excess of catechol yielded more of the dehalogenated product (nitrobenzene) than when performed in an excess of resorcinol (cf. Table). This supports a free-radical mechanism for the Ullmann diaryl synthesis as proposed by Rapson and Shuttleworth (*loc. cit.*). That radicals are involved must now be accepted as highly probable, even if it cannot be regarded as rigorously proved.

That dehalogenation has been observed in Ullmann reactions carried out in the presence of tetrahydronaphthalene (Hardacre and Perkin, *J.*, 1929, 180; Lesslie and Turner, *J.*, 1932, 281) can be understood on the basis of a radical mechanism, but Smith (*J. Amer. Chem. Soc.*, 1949, **71**, 2855) and Smith and Campanaro (*ibid.*, 1953, **75**, 3602) found that copper in the presence of benzoic acid is an effective dehalogenating agent for aromatic halogenonitro-compounds. If a radical mechanism were operative, benzoate radicals should be formed and these would decompose with evolution of carbon dioxide (cf. Waters, " The Chemistry of Free Radicals," Oxford Univ. Press, 2nd Edn., 1948, p. 166). Copper and benzoic acid when heated together for 20 min. at 201—208° did not give off carbon dioxide, but in the presence of *o*-iodonitrobenzene 2·6% of carbon dioxide (calc. on the weight of *o*-iodonitrobenzene employed) was obtained. In spite of the difficulties in interpreting heterogeneous reactions this result also points to a radical mechanism.

Addition	Temp.	Yield (%) of dinitrodiphenyl		Yield (%) of tribromoaniline	Increase (%) in insoluble matter
		crude	recryst.		
		o-*Iodonitrobenzene.*			
None	200—220°	88	82	*	*
Resorcinol	200—210	43	37	28	97
Catechol	200—210	40	29	49	102
		p-Iodonitrobenzene.			
None	190—210	144	*	*	38
None	210—220	91	32	*	88
None	240—260	78	*	*	98
None	254—287	97	*	*	101
Resorcinol	240—250	0	*	13	68
Catechol	225—237	0	*	38	121
		o-*Bromonitrobenzene.*			
None	210—220	96	85	0	84
Resorcinol	210—215	0	*	35	94
Catechol	205—216	4	2	66	111

Reaction time: 20 min. after the gradual addition of copper bronze had been completed.
* Not determined.

EXPERIMENTAL

Reactions were carried out in boiling tubes heated in a metal-bath, the temperatures recorded being internal and uncorrected. The thermometer served as stirrer and no attempt was made to exclude air except in the experiments with benzoic acid. Even at higher temperatures, the exposed part of the boiling tube was sufficient to obviate the need for a condenser. The usual procedure was as follows: the iodonitrobenzene (2 g.) was melted and mixed with resorcinol or catechol (4·4 g., 5 mol.), heated to the stated temperature, and copper bronze (from B.D.H. Ltd.; 2 g.) was added slowly at such a rate as to keep the temperature within the required limits. The reaction was completed by heating for 20 min. The product was cooled and water added. The solid (A) was filtered off and washed with boiling methyl alcohol (10 c.c.). The filtrate and washings were transferred to a distillation flask and, being oily, usually required methyl alcohol (10 c.c.) for rinsing. On distillation, nitrobenzene and possibly some unchanged halogenonitrobenzene were collected in the distillate, which was reduced by heating with tin (2 g.) and hydrochloric acid (30 c.c.) for 3 hr. under reflux. Methyl alcohol was distilled off, then any aniline after the solution had been made alkaline. The yield of aniline was determined by precipitation as tribromoaniline and weighing. The filtrate from which nitrobenzene had been distilled was made alkaline and extracted with ether. The extract, when dried and evaporated, may yield some dinitrodiphenyl. The aqueous layer was acidified and continuously extracted with ether, the extract being evaporated to dryness as a check on the changes undergone by the phenol. The solid (A) was continuously extracted with benzene, the extract on evaporation yielding most of the dinitrodiphenyl formed. The residue, usually copper and copper halide only, was weighed, the increase in weight above 2 g. providing a useful indication of the extent to which reaction had occurred. This increase is recorded in the last column of the Table on the basis of the increase in weight expected if all the halogen had combined with the copper. The yield of crude dinitrodiphenyl recorded in the Table is the total obtained from both the benzene and the ether extract; as this may include unaltered halogenonitrobenzene and substances not volatile in steam, the yield on purification is also given. For *o*-bromonitrobenzene the amount used (1·62 g.) had been proportionally reduced. For experiments without addition, double quantities and the normal, simple procedure were employed.

o-*Iodonitrobenzene.*—When prepared from *o*-nitrobenzenediazonium chloride it was obtained in citron needles, m. p. 51—52° (from methyl alcohol). The reaction was carried out also in the presence of boiling tetralin (5 mol.) for 1 hr. at 200—208°, the yields obtained being crude dinitrodiphenyl 85%, tribromoaniline 11%, increase in insoluble matter 96%. No appreciable reaction occurred between *o*-iodonitrobenzene and catechol at 200—208° during 20 min.

p-*Iodonitrobenzene.*—Preparation from *p*-nitrobenzenediazonium chloride gave almost colourless needles, m. p. 173·5—174·8° (from chlorobenzene–alcohol). At lower temperatures much remains unchanged in the Ullmann reaction as can be seen from the small increase in insoluble matter and the apparently high yield of dinitrodiphenyl. From the complex product formed at higher temperatures, a small amount of a *substance* was obtained forming orange prisms, m. p. 312—312·5° (from chlorobenzene–alcohol) (Found: C, 62·9; H, 3·6; N, 12·5. $C_{12}H_8O_3N_2$ requires C, 63·2; H, 3·5; N, 12·3%). On treating *p*-iodonitrobenzene (2 g.) with catechol (4·4 g.) for 20 min. at 230—241°, no tribromoaniline could be isolated in the usual manner, but a black amorphous powder (2·48 g.) was formed. This contains nitrogen and iodine and is insoluble or only slightly soluble in most solvents, but largely soluble in acetone and completely soluble in pyridine, giving brown solutions. In sulphuric acid it gives a dirty green-blue solution. The substance was not investigated further, but it is formed as a by-product in the Ullmann reaction in the presence of catechol. Similar compounds were formed in small amount in the other reactions in the presence of phenols. In the Ullmann reaction in the presence of resorcinol, more than 33% of *p*-iodonitrobenzene was recovered unchanged. In the reactions in the presence of resorcinol or catechol the figures quoted for the yield of tribromoaniline do not include tribromoaniline derived from unchanged *p*-iodonitrobenzene distilled together with the nitrobenzene.

o-*Bromonitrobenzene.*—For this compound comparison of the weight of tribromoaniline obtained with the amount of bromine required for the bromination (Wild, "Estimation of Organic Compounds," Cambridge Univ. Press, 1953, pp. 89, 180) enables one to determine the proportion of unchanged *o*-bromonitrobenzene present in the nitrobenzene of the steam-distillate. In this manner it was shown that in the straightforward Ullmann reaction the tribromoaniline isolated (2%) was derived from unchanged *o*-bromonitrobenzene, and that in the reactions in the presence of a phenol none of the tribromoaniline had been formed from unaltered starting material. Such a check is impossible in the experiments with iodo-compounds, as iodine is replaced during the reduction and the bromination, but the figures for the increase in insoluble matter are a good indication of the extent to which iodine is removed during the reaction proper.

Nitrobenzene.—Estimation *via* aniline and tribromoaniline gave 90% of the theoretical values. In control experiments it was found that catechol and copper bronze produce aniline from nitrobenzene, more reduction occurring at higher temperatures, but the addition of iodine suppresses the reduction almost entirely.

Reactions in the Presence of Benzoic Acid.—Nitrogen, purified by passage through soda-lime and sulphuric acid, was passed over the surface of the mixture heated in a boiling tube. The gases then passed through a condenser, a liquid-nitrogen trap, calcium chloride, soda-lime (*A*), calcium chloride (*B*), and soda-lime. The mixture was kept at 200—210° (internal) for 20 min. and the passage of gas was continued for a further 20 min. whilst cooling, the liquid nitrogen being removed during the last 10 min. When a mixture of *o*-iodonitrobenzene (2 g.), copper bronze (2 g.), and benzoic acid (" AnalaR "; 4·9 g., 5 mol.) was taken, the increase in weight of (*A*) + (*B*) was 9·3 mg.; there was no increase in weight when a mixture of copper bronze and benzoic acid was heated alone. In the former case, a 75% yield of tribromoaniline was obtained, Smith and Campanaro (*loc. cit.*) recording a 53% yield of nitrobenzene from a similar reaction.

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