

A New Biaryl Synthesis Illustrating a Connection between the Ullmann Biaryl Synthesis and Copper-catalysed Decarboxylation

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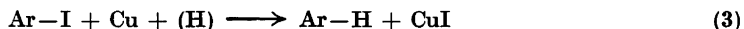
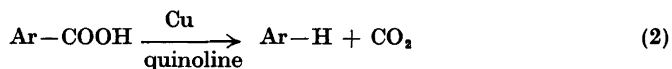
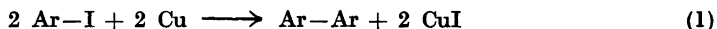
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o-Nitrobenzoic acid with copper(I)oxide in boiling quinoline in the presence of iodobenzene derivatives loses carbon dioxide and gives 2-nitrobiphenyls in fair yields.

The relations of this reaction to the Ullmann biaryl synthesis are discussed.

Copper and copper(I) compounds are important reactants and catalysts in organic chemistry. Very recently copper-promoted organic reactions were reviewed by Bacon and Hill.¹ A comprehensive review of the Ullmann biaryl synthesis by Fanta has also appeared recently.²

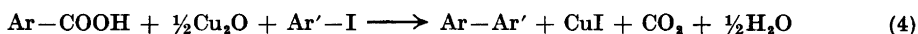
There are indications of a close relation between the Ullmann biaryl synthesis (1) and copper-catalysed decarboxylation of aromatic acids (2). Thus, addition of carboxylic acids¹ to Ullmann reaction mixtures favours reductive dehalogenation (3), which is an important side reaction in the Ullmann biaryl synthesis. The carboxylic acid loses carbon dioxide in this reaction, but little is known about the fate of the rest of the acid molecule.



In the course of work on copper-promoted aromatic reactions (*cf.* Refs. 3, 4) it seemed plausible to assume that the Ullmann biaryl synthesis and copper-catalysed decarboxylation proceed *via* a common intermediate. If this were the case, new synthetic possibilities would open up. It would also be possible to attack the problem of the mechanism of the Ullmann biaryl synthesis in new ways.

The decarboxylation of some benzoic acids in the presence of copper(I)oxide in boiling quinoline was followed by measurement of the carbon dioxide evolution. Fast decarboxylation was observed for *ortho*-substituted acids. *o*-Nitrobenzoic acid was especially rapidly decarboxylated; the reaction was complete within a few minutes. Appreciable amounts of water were formed during the reactions. Benzoic anhydrides also gave carbon dioxide under these conditions. The anhydrides with copper(I)oxide initially evolved carbon dioxide faster than the acids; often the stoichiometric amount was not produced, however.

The fast decarboxylation of *o*-nitrobenzoic acid recalls the particular usefulness of *o*-halogenonitrobenzenes in the Ullmann biaryl synthesis² and seemed to be a further indication of the relations between these reactions. Preparative experiments were undertaken to trap the presumed intermediate of the decarboxylation. *o*-Nitrobenzoic acid was decarboxylated in boiling quinoline in the presence of stoichiometric amounts of copper(I)oxide and *o*-iodoanisole, *p*-iodoanisole, or iodobenzene. After a few minutes the stoichiometric amount of carbon dioxide had been given off. The rate of CO₂ evolution was not affected by the presence of iodoarenes. Water was also formed in the reaction. When ether was added to the reaction mixtures a crystalline complex of copper(I)iodide and quinoline separated and could be collected. 2-Methoxy-2'-nitrobiphenyl, 2-methoxy-4'-nitrobiphenyl, and 2-nitrobiphenyl, respectively, could then be isolated in yields of the order of 50–30 %. No appreciable amounts of symmetrical biphenyls were observed. This reaction seems to open a new route to 2-nitrobiphenyls (4, Ar = *o*-nitrophenyl).



The yields are somewhat lower than the best obtained in unsymmetrical Ullmann couplings of *o*-bromonitrobenzene (*cf.* Ref. 2). On the other hand the isolation of the products is more straightforward, since symmetrical biaryls do not seem to interfere. The main side reaction is the "normal" formation of nitrobenzene. Some reductive dehalogenation also seems to take place.

The reaction seems to be applicable also to other easily decarboxylated acids. 2,4-Dinitrobenzoic acid and iodobenzene thus give 2,4-dinitrobiphenyl (*ca.* 15 %) and also some 2,6-dinitrobiphenyl (*ca.* 5 %) together with *m*-dinitrobenzene.

o-Nitrobenzoic anhydride was used instead of the acid in some experiments, the aim being to suppress the formation of nitrobenzene by decreasing the amount of easily available protons. However, the yields of biaryls were not higher with this reagent. The carbon dioxide evolution in these experiments was rapid, but in general amounted to only 80–90 % of the theoretical yield.

For acids which are not so rapidly decarboxylated other reactions seem to predominate. Thus for benzoic acid (or anhydride) the rate of decarboxylation is low and the carboxylate anion [or copper(I)benzoate] apparently reacts with, *e.g.*, *p*-iodoanisole to give *p*-methoxyphenyl benzoate (*cf.* Forrest⁵).

In the present decarboxylations quinoline has generally been used as solvent. Quinoline (or some other base) seems to be necessary for the decar-

boxylation of the less readily decarboxylated acids. However, decarboxylation and coupling of *o*-nitrobenzoic acid has also been effected in sulpholane.

The 2,6-dinitrobiphenyl obtained in the experiment with 2,4-dinitrobenzoic acid is presumably formed *via m*-dinitrobenzene (*cf.* Forrest⁵). This type of reaction is presently being explored.⁶

The possibility that the 2-nitrobiphenyls are formed similarly *via* nitrobenzene was checked in experiments where nitrobenzene, *o*-iodoanisole and copper(I)oxide were boiled in quinoline. There was little reaction within 30 min. After 10 h, however, 2-methoxy-2'-nitrobiphenyl could be isolated in ca 6 % yield. This indicates that the coupling reactions with *o*-nitrobenzoic acid take place mainly between the iodoarene and the intermediate formed during decarboxylation of *o*-nitrobenzoic acid.

The present reaction seems to be a useful alternative to the Ullmann reaction for the preparation of certain unsymmetrical biaryls.

Available evidence on the mechanism of the Ullmann biaryl synthesis indicates that the reaction proceeds stepwise.¹⁻⁵ A primary reaction between copper and (preferably an activated) halogenoarene seems to give an intermediate, which may then react with a second molecule of halogenoarene to give a biaryl.

Little is known about the mechanism of copper-catalysed decarboxylation. The thermal decarboxylation of picolinic and quinaldic acids has been investigated by Hammick *et al.*⁷⁻⁹ In these cases stabilised anions were apparently formed which could react with carbonyl compounds and even with some nitroarenes to give, *e.g.*, 2-pyridylarenes.

The present results indicate that the Ullmann biaryl synthesis and copper-catalysed decarboxylation proceed *via* a common intermediate.

EXPERIMENTAL

Quantitative decarboxylations

A reaction flask (100 ml) was fitted with a gas inlet tube reaching the bottom and a reflux condenser. The latter was connected to an absorption train consisting of (a) a U-tube with activated charcoal, (b) a U-tube containing anhydrous magnesium perchlorate, (c) a three-way valve connected to (d) tubes for carbon dioxide absorption (Ascarite and magnesium perchlorate).

The flask was charged with quinoline (25 ml), carboxylic acid (0.01 mole) or anhydride (0.005 mole), and copper(I)oxide (0–0.005 mole). The apparatus was swept with dry oxygen-free nitrogen and was placed in a salt bath, the temperature of which was kept at 240°. The Ascarite tubes were weighed at regular intervals, in the beginning of the experiments every fifth minute.

Water was given off during the decarboxylations of the acids.

In several experiments iodoarenes (0.01 mole) were included in the decarboxylation mixture. The rate of carbon dioxide evolution was not affected and biaryls could be isolated from the reaction mixtures.

Thus *o*-nitrobenzoic anhydride and *p*-iodoanisole (0.005 mole Cu₂O) afforded a 32 % yield of crude 2-methoxy-4'-nitrobiphenyl, recrystallised from methanol, m.p. 61–64° (lit.⁵ m.p. 61–62°).

Preparations

A mixture of the carboxylic acid (0.06 mole), the iodoarene (0.05 mole) and copper(I) oxide (0.04 mole) in quinoline (25 ml) in a 250 ml flask equipped with a reflux condenser was heated in a salt bath kept at 240° until carbon dioxide evolution ceased. The reaction mixture was cooled and ether (ca. 200 ml) was added. The yellow quinoline complex of copper(I)iodide was filtered off and washed with ether. The filtrate was extracted with hydrochloric acid (2 M). The ether was washed with water, dried and evaporated. The residue was distilled.

o-Nitrobenzoic acid and *o*-iodoanisole. A vigorous reaction occurred which ceased after ca. 15 min. Distillation gave low-boiling material (ca. 6 g, mainly nitrobenzene) and a fraction b.p. 120–145°/0.1 mm. The latter fraction (ca. 6 g) solidified and on recrystallisation from methanol gave 2-methoxy-2'-nitrobiphenyl (5.1 g, 50 %, m.p. 80–83°) (lit.¹⁰ m.p. 82°). The product was identical with the unsymmetrical biphenyl obtained by Ullmann coupling of *o*-bromonitrobenzene and *o*-iodoanisole (IR).

o-Nitrobenzoic acid and iodobenzene. A vigorous reaction occurred which ceased after 15 min. Distillation gave low-boiling material (ca. 13 g) and a fraction b.p. ca. 130–145°/0.1 mm (4 g). The latter fraction was fairly homogeneous (gas chromatography) and was left with methanol at ca. –10°. A crystalline material deposited slowly (1 g, m.p. 25–33°). The ultraviolet spectrum agrees with that given for 2-nitrobiphenyl¹¹ (lit.⁵ m.p. 37°). The yield of crystalline product was 10 %, but can probably be improved to ca. 30 %.

2,4-Dinitrobenzoic acid and iodobenzene. A vigorous reaction occurred which ceased after ca. 15 min. Distillation gave crude *m*-dinitrobenzene, b.p. 100–125°/0.1 mm, m.p. 75–87° (3 g) and a heterogeneous fraction, b.p. 130–150°/0.1 mm (5 g). Trituration of the latter with methanol gave the sparingly soluble *2,6*-dinitrobiphenyl (0.5 g) which was recrystallised from ethyl acetate, m.p. 187–190° (lit. m.p.⁵ 189–190°). The mother liquors gave crude *2,4*-dinitrobiphenyl (2 g) which was recrystallised from cyclohexane, m.p. 107–110° (lit.⁵ m.p. 110°). The infrared spectra were consistent with the proposed structures.

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