

Decarboxylative Couplings of 2,6-Dinitrobenzoic Acid

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Decarboxylative coupling of 2,6-dinitrobenzoic acid with iodobenzene derivatives using copper(I) oxide in quinoline solution gives 2,6-dinitrobiphenyls in fair yields. When 2,6-dimethoxyiodobenzene is used 2,6-dimethoxy-2',4'-dinitrobiphenyl is formed together with the expected 2,6-dimethoxy-2',6'-dinitrobiphenyl. The reactions are compared with the coupling of *m*-dinitrobenzene and iodoarenes.

2,6-Dinitrobiphenyls can readily be prepared by reaction of *m*-dinitrobenzene with iodobenzene derivatives and copper(I) oxide in quinoline.^{1,2} Decarboxylative couplings of 2-nitrobenzoic acid with iodobenzenes using copper(I) oxide in quinoline give 2-nitrobiphenyls, whereas 2,4-dinitrobenzoic acid with iodobenzene gives 2,4-dinitrobiphenyl and some 2,6-dinitrobiphenyl.³

The present communication concerns the decarboxylative coupling of 2,6-dinitrobenzoic acid with iodobenzene derivatives, a reaction which should also yield 2,6-dinitrobiphenyls. However, the "normal" decarboxylation product of 2,6-dinitrobenzoic acid, *m*-dinitrobenzene, also reacts with iodobenzenes as described above to give the same 2,6-dinitrobiphenyls.

The results with 2,6-dinitrobenzoic acid should therefore be compared to those obtained with *m*-dinitrobenzene. Since the decarboxylation is a rapid process and coupling of *m*-dinitrobenzene often relatively slow, an extrapolation to short reaction times should ideally allow a comparison of the reactions. Experimental difficulties hamper such a procedure. The present work is a compromise in an attempt to observe major differences between the two reactions. The figures refer to reaction times of *ca.* 30 min, whereas generally the carbon dioxide evolution had ceased after *ca.* 15 min.

Decarboxylative coupling of 2,6-dinitrobenzoic acid with iodobenzene gave the following yields of 2,6-dinitrobiphenyl at the stated temperatures: 14 % at 180°, 48 % at 200°, and 50 % at 238°. The yields were thus better than those for the direct coupling of *m*-dinitrobenzene and iodobenzene (15 % after 2 h at 220° or 41 % after 2 h at 238°).^{1,2} The results also compare favorably with the couplings of 2-nitrobenzoic and 2,4-dinitrobenzoic acids with iodobenzene.³ The coupling of 2,6-dinitrobenzoic acid with *p*-iodomethoxybenzene gave 4-methoxy-2,6-dinitrobiphenyl (31 % at 238°), that is, about

the same result as in the coupling of *m*-dinitrobenzene and *p*-iodomethoxybenzene (28 % after 0.5 h at 238°).

Preliminary experiments show that when *o*-iodonitrobenzene, *o*-bromonitrobenzene, or methyl *o*-iodobenzoate is used, unsymmetric biphenyls are formed only in low yields and are accompanied by symmetric biphenyls corresponding to the halogenobenzenes. The reaction with activated halogenobenzenes thus seems unimportant from a preparative point of view.

The reaction between 2,6-dinitrobenzoic acid and 2,6-dimethoxyiodobenzene gave practically the same result as that for *m*-dinitrobenzene, namely 45 % 2,6-dimethoxy-2',6'-dinitrobiphenyl and 5 % 2,6-dimethoxy-2',4'-dinitrobiphenyl. Here the coupling reaction of *m*-dinitrobenzene is also very rapid² and the reaction times were the same.

From earlier work, 2,4-dinitrobenzoic acid on reaction with iodobenzene is known to give 16 % 2,4- and 4 % 2,6-dinitrobiphenyl.³ It was now found that its decarboxylative coupling with 2,6-dimethoxyiodobenzene gave 45 % 2,6-dimethoxy-2',4'-dinitrobiphenyl and 10 % 2,6-dimethoxy-2',6'-dinitrobiphenyl. Thus the proportions of products were inverted from those of the 2,6-dinitrobenzoic acid experiment and the total yield of biphenyls was higher.

From the preparative point of view the use of *m*-dinitrobenzene for the preparation of 2,6-dinitrobiphenyls is generally to be preferred over the decarboxylative coupling of the less readily available 2,6-dinitrobenzoic acid.

In the work on copper-promoted coupling reactions of 2-nitrophenyl and 2,6-dinitrophenyl derivatives we have assumed a common type of intermediate, 2-nitrophenylcopper and 2,6-dinitrophenylcopper, respectively. These may be formed in different ways and may then react, for example, with iodobenzene derivatives to give unsymmetric nitrobiphenyls (*cf.* Ref. 2). So far a direct demonstration of such intermediates is lacking. Work in the thiophene series, however, furnishes analogous examples.^{4,5} In particular, the selective unsymmetric coupling of 2-thienylcopper with iodobenzene is illustrative.⁴

The formation of an organocopper intermediate in the decarboxylation reaction would be analogous to the formation of organomercurials by the decarboxylation of mercury(II) salts of carboxylic acids on heating. For example on heating mercury bis-2,4,6-trinitrobenzoate, bis(2,4,6-trinitrophenyl) mercury is formed.⁷

The dimerisation of arylcopper intermediates to biaryls with the elimination of elemental copper, which may be important in certain other Ullmann type reactions,⁸ does not seem to be important in 2-nitrophenyl or 2,6-dinitrophenyl systems.

There is one notable difference between the decarboxylative couplings and the "direct" couplings which remains to be explored. The rate of CO₂ evolution from the carboxylic acids is practically independent of the presence of iodoarenes and probably determines the rate of the coupling reaction, though other reactions compete, *e.g.* "normal" decarboxylation. The rate of couplings between *m*-dinitrobenzene and iodoarenes on the other hand, seems to depend on the structure of the iodoarene.²

These differences may be used in the further exploration of the reaction mechanisms. Meanwhile the results may be summarised by Fig. 1. Here 2-nitrobenzoic acid couples mainly by the upper route since nitrobenzene reacts

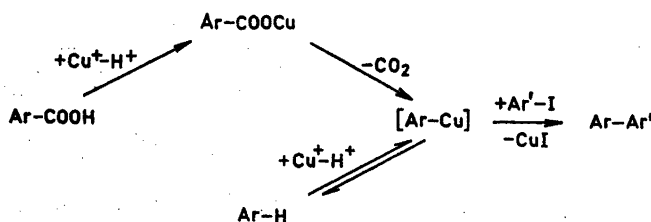


Fig. 1. Schematic representation of reaction paths in decarboxylative coupling assuming arylcopper intermediates. Ar=2-nitrophenyl-, 2,4-dinitrophenyl- or 2,6-dinitrophenyl. The copper species are presumably solvated by the quinoline.

very slowly by the lower path.³ 2,4-Dinitrobenzoic acid couples predominantly by the upper path, the lower furnishing mainly 2,6-dinitrobiphenyls. 2,6-Dinitrobenzoic acid reacts in both ways.

EXPERIMENTAL

The melting points were determined on a Leitz hot stage microscope. For the gas chromatography VPC measurements an Aerograph 204-1B with a hydrogen flame detector was used with 5% SE-30 on Chromosorb W (1.5 m) as stationary phase.

General procedure for decarboxylative coupling. A reaction flask (100 ml) was fitted with a gas inlet tube reaching to 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 U-tube with Ascarite and magnesium perchlorate. The apparatus was swept with dry oxygen-free nitrogen. The flask was charged with quinoline (25 ml), carboxylic acid (0.01 mole), iodobenzene (0.01 mole) and copper(I) oxide (0.005 mole), and was placed in a salt or silicone oil bath which was kept at the desired temperature. A vigorous reaction with gas evolution started immediately and ceased after ca. 15 min. The Ascarite tubes were weighed at short intervals. Over 95% of the theoretical amount of carbon dioxide was found (Fig. 2). The presence of iodobenzenes did not affect the rate of carbon dioxide evolution.

General extraction procedure. The reaction was usually run at 180 - ca. 240° for 0.5 h. When the mixture had cooled, ether was added and the mixture stirred. The yellow crystalline complex of copper iodide and quinoline was filtered off and washed with ether. The filtrate was extracted with 2 M hydrochloric acid to remove the remaining quinoline, washed with water, dried, and the ether evaporated.

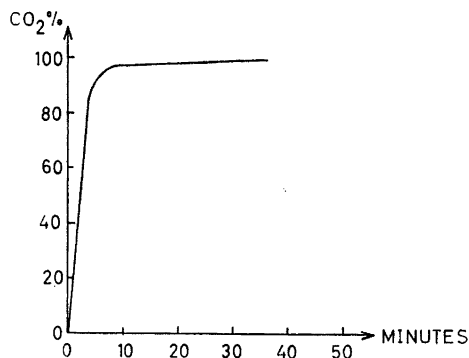


Fig. 2. Carbon dioxide evolution in the decarboxylative coupling of 2,6-dinitrobenzoic acid with *p*-iodoanisole and copper(I) oxide (0.01 mole scale) at 230°.

2,6-Dinitrobiphenyl. 2,6-Dinitrobenzoic acid, iodobenzene, copper(I) oxide and quinoline were reacted at 180° for 0.5 h. Distillation of the evaporation residue gave a low-boiling material (mainly iodobenzene and *m*-dinitrobenzene) and a fraction b.p. 160–220°/0.15 mm. Recrystallisation from ethyl acetate gave pure 2,6-dinitrobiphenyl, m.p. 187–189° (Forrest⁸ reported m.p. 189–190°), 0.34 g, 14 %.

When the reaction was run at 200° for 0.6 h distillation gave 1.17 g of 2,6-dinitrobiphenyl. The same reaction at *ca.* 238° (refluxing solution) gave 1.25 g (50 %) of 2,6-dinitrobiphenyl.

4-Methoxy-2',6'-dinitrobiphenyl, 238°, 0.5 h. 2,6-Dinitrobenzoic acid, *p*-iodoanisole, copper(I) oxide and quinoline. Distillation gave a low-boiling material (mainly *p*-iodoanisole and *m*-dinitrobenzene) and a fraction boiling 170–230°/0.20 mm. Recrystallisation from ethyl acetate gave yellow crystals of 4-methoxy-2',6'-dinitrobiphenyl, m.p. 117–119° (Forrest⁸ reported m.p. 119–120°) 0.85 g (31 %).

2,6-Dimethoxy-2',6'-dinitrobiphenyl and 2,6-dimethoxy-2',4'-dinitrophenyl, 238°, 0.5 h. 2,6-Dinitrobenzoic acid, 2,6-dimethoxyiodobenzene, copper(I) oxide, and quinoline. VPC analysis of the evaporation residue showed two peaks in the range where biphenyls could be expected. Separation of the evaporation residue on a silica gel column with cyclohexane/benzene mixtures, gave: 2,6-dimethoxy-2',6'-dinitrobiphenyl, m.p. 198–199° (1.36 g, 45 %) and 2,6-dimethoxy-2',4'-dinitrobiphenyl, m.p. 159–161° (0.15 g, 5 %). Mixed melting points with authentic 2,6-dimethoxy-2',6'-dinitrobiphenyl and 2,6-dimethoxy-2',4'-dinitrobiphenyl,² respectively, showed no depression.

2,4-Dinitrobenzoic acid, 2,6-dimethoxyiodobenzene, copper(I) oxide, and quinoline were reacted at 238° for 0.5 h. VPC analysis of the evaporation residue showed two peaks corresponding to 2,6-dimethoxy-2',6'-dinitrobiphenyl and 2,6-dimethoxy-2',4'-dinitrobiphenyl. Separation on a silica gel column with cyclohexane/benzene gave: 2,6-dimethoxy-2',6'-dinitrobiphenyl, m.p. 198–199° (0.3 g, 10 %) and 2,6-dimethoxy-2',4'-dinitrobiphenyl, m.p. 159–160° (1.35 g, 45 %).

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