

## Copper-catalysed Substitution of Aryl Halides by Potassium Phthalimide: an Extension of the Gabriel Reaction

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**Summary** Conversion into phthalimido-compounds is effected by copper-catalysed substitution reactions, in boiling dimethylacetamide, between potassium phthalimide and a wide range of aryl bromides and iodides, thus providing a useful preparative route to aromatic amines.

NUCLEOPHILIC substitution between potassium phthalimide and alkyl halides (the Gabriel reaction)<sup>1</sup> is valued for its wide applicability, irrespective of other functional groups in the halide molecule. Aryl halides are stated to show very little response to this type of reaction, but there are some indications in the literature that it may be stimulated by copper catalysis.<sup>1</sup> Ferrocenyl halides react with copper(II) phthalimide.<sup>2</sup> We have found that under suitable conditions copper catalysis is quite widely effective for reactions between potassium phthalimide and aryl bromides or iodides, though not chlorides. This process provides a useful route to primary aromatic amines *via* their phthaloyl derivatives:  $\text{ArHal} \rightarrow \text{ArN}(\text{CO})_2\text{C}_6\text{H}_4 \rightarrow \text{ArNH}_2$ . Analogously, copper-catalysed conversion of aryl halides into phenols, *via* alkyl ethers, has been described.<sup>3</sup> The scope and limitations so far found for production of the phthalimido-compounds are summarised as follows:

(a) The preferred catalyst is cuprous iodide or bromide, in a homogeneous reaction system, which is conveniently

obtained by using boiling dimethylacetamide as the medium. Rate of reaction increases with copper(I) concentration.

(b) The resulting nucleophilic substitution suffers little or no competition from the reductive type of substitution ( $\text{ArHal} \rightarrow \text{ArH}$ ) which often complicates copper-catalysed reactions of aryl halides with other nucleophiles.<sup>4</sup> Decarboxylation was encountered as a side-reaction of halenoacids.

(c) Ring substituents X, in a series of halides  $\text{C}_6\text{H}_4\text{XBr}$ , exhibited a polar effect in the expected direction for nucleophilic aromatic substitution, but the differences in reaction rates were very much smaller than are customarily found in uncatalysed nucleophilic substitutions of aryl halides. Under standard catalytic conditions, yields of phthalimido-compounds ranged from ~95% to ~35%, the highest figures being achieved when X was a strongly electron-attracting group (*e.g.*,  $\text{NO}_2$ , CN) and the lowest figures resulting when X was strongly electron-repelling (*e.g.*,  $\text{NH}_2$ , OH).

(d) The operation of a marked steric effect was apparent from comparison of yields given by isomeric halides (*o*-, *m*-, and *p*- $\text{C}_6\text{H}_4\text{XBr}$ ) and from the observed failure of reaction in the case of polycyclic halides containing halogen *ortho* to a point of ring juncture.

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<sup>1</sup> Reviewed by M. S. Gibson and R. W. Bradshaw, *Angew. Chem. Intern. Edn.*, 1968, 7, 919.

<sup>2</sup> A. N. Nesmeyanov, *Pure and Appl. Chem.*, 1968, 17, 211.

<sup>3</sup> R. G. R. Bacon and S. C. Rennison, *J. Chem. Soc. (C)*, 1969, 312.

<sup>4</sup> R. G. R. Bacon and O. J. Stewart, *J. Chem. Soc. (C)*, 1969, 301.