

CROWN-CATION COMPLEX EFFECTS. IX.  
A PHASE TRANSFER CATALYTIC SYNTHESIS OF BROMO- AND IODOARENES

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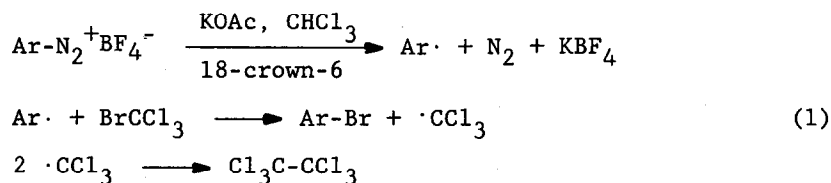
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Ever since Sandmeyer first reported that aryldiazonium halides would undergo cuprous halide catalyzed decomposition to haloarenes, numerous attempts have been made to understand and improve the method.<sup>1</sup> Studies in both areas have met with success, although neither problem appears to be completely resolved. In recent years, the preparation of haloarenes from anilines or other arenes has departed radically from the early approach of Sandmeyer and halogenation methods involving metallation,<sup>2</sup> in situ diazotization,<sup>3</sup> halogen abstraction,<sup>3-7</sup> nucleophilic substitution<sup>8</sup> and "substitutive deamination"<sup>9</sup> have all been developed.

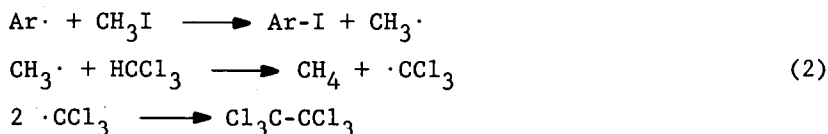
We wish to report that our phase transfer catalytic method for the generation of aryl radicals<sup>10</sup> facilitates the production of diversely substituted aryl bromides and iodides and that good to excellent yields of these halides can routinely be realized at ambient temperature in a short period of time. Furthermore, the stable aryldiazonium tetrafluoroborates are used as starting materials, allowing the reactions to be conducted in complete safety.

The halogenation described herein is carried out in chloroform solution in the presence of a catalytic amount of 18-crown-6 and a moderate excess of halogen source (bromotrichloromethane,<sup>5,6</sup> iodomethane<sup>7</sup> and molecular iodine<sup>11</sup>). The aryl radical displays a high selectivity for Br·<sup>6</sup> and I· rather than H· and Cl·. It is nevertheless the case that some reduction (1-8%) along with small amounts of chlorination (trace-3%) were observed by hydrogen and chlorine atom abstraction, respectively, from the solvent. Except for the 4-methyl compound,<sup>12</sup> it also appears that the nature of the substituent in the aryl radical does not significantly affect the rate or course of reaction. Ortho-substituted aryldiazonium ions also give reduced yields of the desired haloarenes in chloroform solution.

In each of the bromination reactions carried out in chloroform, significant amounts of hexachloroethane<sup>6</sup> were formed (see equation 1). It is noteworthy that in the iodination reactions with iodomethane, some hexachloroethane was formed as a by-product. This material presumably arises by hydrogen atom abstraction



from chloroform by a methyl radical yielding methane and the trichloromethyl radical which then dimerizes (see equation 2). A more economical and convenient



source of iodine atoms is molecular iodine ( $\text{I}_2$ ). Not only is less iodine required (7.5 eq. of  $\text{I}\cdot$  vs approximately 32 eq. of  $\text{MeI}$ ), but one generally observes higher product yields, only trace amounts of chlorinated by-products and smaller amounts of reduction products.

By using tetrahydrofuran<sup>13</sup> instead of chloroform as the cosolvent in the reactions of the aryl radicals with bromotrichloromethane and iodomethane, the chlorinated by-products (including hexachloroethane) can be virtually eliminated. Improved haloarene yields from the 4-methyl- and ortho-substituted aryldiazonium ions have been realized in tetrahydrofuran solution containing 33 vol-% of the halogen source (see Table). We feel this solvent effect is due, at least in part, to the greater ion-solvating power of tetrahydrofuran relative to chloroform.

As noted in previous reports,<sup>8,14</sup> a catalytic amount of 18-crown-6 is necessary to achieve preparatively useful yields in a convenient period of time. Representative procedures are described below.

#### Preparation of 4-Iodoanisole

Potassium acetate (1.20g, 12 mmol) is added in one portion to a stirred colorless mixture of 4-methoxybenzenediazonium tetrafluoroborate (1.33g, 6 mmol) and 18-crown-6 (0.08g, 0.3 mmol) in chloroform (45 ml) and iodomethane (15 ml, 0.25 mol). The mixture becomes yellow after a few minutes. Stirring is continued for two hours, the mixture filtered and the filtrate washed with water and dried over sodium sulfate. The solvent is removed in vacuo and the resulting orange liquid chromatographed on a column of alumina (hexane then ether/hexane) from which is obtained 4-iodoanisole (1.15g, 82%) as a white powder, mp 50-51°C, Lit. mp 51-52°C.

#### Preparation of 4-Bromiodobenzene

Potassium acetate (3.0g, 30.56 mmol) is added in one portion to a stirred violet mixture of 4-bromobenzenediazonium tetrafluoroborate (4.05g, 14.95 mmol), 18-crown-6 (0.20g, 0.76 mmol) and iodine (14.2g, 55.95 mmol) in chloroform (150 ml). The mixture is stirred for 3 hours, filtered and the filtrate washed with 10% aqueous sodium bisulfite (w/w) to remove excess iodine and dried ( $\text{Na}_2\text{SO}_4$ ). The solvent is removed in vacuo and the resulting red solid chromatographed on a short column of alumina (hexane as eluant) yielding 4-bromiodobenzene (3.46g, 82%) as white plates, mp 91-92°C, Lit. mp 92°C.

### Preparation of 4-Bromonitrobenzene

Potassium acetate (1.20g, 12 mmol) is added in one portion to a stirred light yellow mixture of 4-nitrobenzenediazonium tetrafluoroborate (1.42 g, 6 mmol) and 18-crown-6 (0.08g, 0.3 mmol) in chloroform (50 ml) and bromotrichloromethane (10 ml, 0.101 mol). The mixture becomes orange after a few minutes; stirring is continued for two hours and worked up as in the iodomethane reaction. Column chromatography on alumina (hexane then ether/hexane) yields 4-bromonitrobenzene (0.87g, 72%) as a very light yellow powder, mp 125-125.5°C, Lit. mp 125°C.

TABLE

Reactions of  $\text{RARN}_2^+\text{BF}_4^-$  in Chloroform with  
Bromotrichloromethane, Iodomethane and Molecular Iodine<sup>a</sup>

R	% Yield of $\text{RARBr}^b$ using $\text{CBrCl}_3^{c,d}$	% Yield of $\text{RARI}^b$ using $\text{MeI}^{d,e}$	% Yield of $\text{RARI}^f$ using $\text{I}_2^f$
4-MeO	87 (76)	90 (82) <sup>g</sup>	51
3-Me	82	82	93
4-Me	47 [60]	49 [88] <sup>h</sup>	57
3,4-Me <sub>2</sub>	35 [76]	45 [87]	74
4-Br	80 <sup>i,j</sup> [77] <sup>k</sup>	92 [90]	90 <sup>l</sup> (82) <sup>m</sup>
2-Br	43	51 [60]	65
4-Cl	84 <sup>n</sup> [90]	91	91 (83) <sup>o</sup>
3-Cl	88	84	94
2-Cl	43 [70]	46 [57]	77
4-NO <sub>2</sub>	78 (72) <sup>p</sup>	78 (72) <sup>q,r</sup>	80

a) All reactions were carried out at a diazonium ion concentration of 0.1 M at room temperature in the dark under a nitrogen atmosphere. Products were identified by retention times and spectral analyses of samples obtained by preparative GLPC. Yields were determined using a 10' x 0.25" 10% SE-30 on Chromosorb P column utilizing an internal standard and are corrected for detector response. Yields in parentheses are for isolated compounds of >99% purity; b) Yields given in brackets were obtained using 33 vol-% haloalkane in tetrahydrofuran; c) 13.3 vol-%  $\text{CBrCl}_3$  was used. In the isolation reactions, 16.7 vol-% was employed; d) Reasonable yields of products can be obtained by using less haloalkane, but more reduction occurs. Addition of more haloalkane did not significantly alter the yield of the aryl halide; e) 25 vol-% MeI was used in the 4-methoxy and 4-nitro cases and 20 vol-% in all others; f) 3.75 equivalents of molecular iodine used in all cases examined; g) mp 50-51°C, lit. mp 51-52°C, F. Reverdin, Chem. Ber., 29, 997 (1896); h) mp 34-34.5°C, lit. mp 34-35°C, F. C. Whitmore and M. A. Thorpe, J. Amer. Chem. Soc., 55, 782 (1933); i) mp 87.5-89°C, lit. mp 89°C, R. Schiff, Justus Liebigs Ann. Chem., 223, 247 (1884); j) The hexafluorophosphate salt gave a comparable yield; k) Without 18-crown-6 present, the yield was 32%; l) Use of 2.5 equivalents molecular iodine gives approximately the same yield of 4-bromiodobenzene and slightly more bromobenzene; m) mp 91-92°C, lit. mp 92°C, F. D. Chattaway, F. L. Garton and G. D. Parkes, J. Chem. Soc., 125, 1980 (1924); n) mp 66-67°C, lit. mp 67°C, W. Korner, Gazz. Chim. Ital., 4, 305 (1874); o) mp 54-55°C, lit. mp 56-57°C, F. Beilstein and A. Kurbatow, Justus Liebigs Ann. Chem., 176, 27 (1875); p) mp 125-125.5°C, lit. mp 125°C, C. K. Ingold, J. Chem. Soc., 127, 513 (1925); q) 95% pure by GLPC analysis; r) mp 169-171°C, lit. mp 172°C, H. A. Mayes and E. E. Turner, J. Chem. Soc., 500 (1929).

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