

THALLIUM IN ORGANIC SYNTHESIS. VIII. PREPARATION
OF AROMATIC BROMIDES (1,2)

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Electrophilic substitution of benzenoid compounds represents one of the most exhaustively studied aspects of organic chemistry, both mechanistically and synthetically. Within this context, there are three principal experimental procedures available for the bromination of aromatic compounds. These comprise treatment of the aromatic substrate with (a) molecular bromine (as such, or generated in situ); (b) molecular bromine in the presence of a Lewis acid catalyst; or (c) a "positive" bromine reagent (3). These three techniques, together with a number of somewhat more circuitous procedures such as the Sandmeyer reaction, constitute the most important currently available synthetic routes to aromatic bromides.

We wish to report a new, simple, general procedure for the preparation of aromatic bromides, using thallium(III) acetate (4) and molecular bromine.

Addition of a solution of bromine in carbon tetrachloride to a suspension of thallium(III) acetate in carbon tetrachloride containing an aromatic substrate results in the instantaneous discharge of the red colour of the bromine. The reaction mixture develops brilliant, intense colours varying from yellow to blue. (These colours persist throughout the reaction and are only discharged during the work-up procedure.) The reaction mixture is heated under reflux for 0.5-1 hr, the precipitated inorganic thallium salts removed by filtration and the organic extract washed with sodium bicarbonate solution. The crude aromatic bromide obtained on removal of the solvent is purified by standard techniques. Typical conversions are given in Table 1.

TABLE 1

<u>Aromatic Substrate</u>	<u>Product</u>	<u>Yield, %^{a, b}</u>
Benzene	Bromobenzene	83
Anisole	4-Bromoanisole	91
Fluorobenzene ^c	4-Bromofluorobenzene	70
1,2-Dimethylbenzene	1,2-Dimethyl-4-bromobenzene	85
Biphenyl	4-Bromobiphenyl	93
2-Nitrobiphenyl	2-Nitro-4'-bromobiphenyl	70
4-Methoxybenzaldehyde	3-Bromo-4-methoxybenzaldehyde	66
Methyl 3-methoxybenzoate	Methyl 3-methoxy-4-bromobenzoate	93
1-Methylnaphthalene	1-Methyl-4-bromonaphthalene	84
2-Nitroanisole	2-Nitro-4-bromoanisole	90
Fluorene	2-Bromofluorene	96
Anthracene	9-Bromoanthracene	91
p-Terphenyl	4-Bromo-p-terphenyl	80
Biphenylene	2-Bromobiphenylene	88

^aCalculated on pure recrystallised or redistilled material. All products were >98% pure as isolated, as determined by vpc. ^bNo attempt was made to optimise yields. ^cExcess of the aromatic halide was used as solvent.

As can be seen from Table 1, the present procedure is particularly suitable for the preparation of aromatic bromides from sensitive substrates such as anthracene, biphenylene and fluorene. Under ordinary electrophilic substitution conditions, bromine has a deleterious effect on these three compounds, leading to complex reactions; special techniques are therefore required for the preparation of 9-bromoanthracene, (5) 2-bromobiphenylene (6) and 2-bromofluorene (7). Apart from the experimental simplicity of the reaction, however, the most important advantage of the thallium(III) acetate-bromine method is the remarkable specificity shown by the reagent during the electrophilic substitut-

ion process. In contrast to the vast majority of electrophilic halogenation reactions, application of the above technique to substituted benzenoid compounds results in the formation of a single pure monobromo isomer.

Preliminary kinetic investigations of the mechanism of this substitution process have so far failed to account for this unusual specificity. We have, however, been able to establish that neither a free radical species nor a "positive" halogen reagent such as acetyl hypobromite is involved in the reaction, and that intermediates of the type $\text{ArTl}(\text{OCOCH}_3)_2$ are not formed and subsequently brominated (8). Substitution apparently proceeds via formation of a bromine-thallium(III) acetate-aromatic substrate complex, the exact nature of which is currently under investigation (9).

References

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8. We have been able to show that, under our reaction conditions, compounds of the type $\text{ArTl}(\text{OCOCH}_3)_2$ are not formed to any appreciable extent (for the preparation of such compounds under other conditions, see (a) A.N. Nesmeyanov and R.A. Sokolik, Methods of Elemento-Organic Chemistry. Vol. I. The Organic Compounds of Boron, Aluminium, Gallium, Indium, and Thallium, North Holland Publishing Company, Amsterdam, 1967; (b) A. McKillop, J.S.

Fowler, M.J. Zelesko, J.D. Hunt, E.C. Taylor and G. McGillivray, in preparation). Furthermore, we have found that bromination of compounds of the type $\text{ArTl}(\text{OCOR})_2$ (prepared independently) under the above conditions leads principally to poly-bromination products.

9. The reactions of chlorine and iodine with aromatic compounds in the presence of thallium(III) acetate have also been investigated in detail. Aromatic chlorides and iodides are indeed formed in high yield, but unlike the situation pertaining with bromine, isomeric mixtures of monohalogenated products are obtained (A. McKillop, R.A. Raphael and E.C. Taylor, unpublished results). This procedure thus offers little advantage over existing methods for the preparation of aromatic chlorides and iodides.