

THALLIUM IN ORGANIC SYNTHESIS. X. A ONE-STEP SYNTHESIS
OF ARYL IODIDES (1,2)

Alexander McKillop, J.S. Fowler, M.J. Zelesko, J.D. Hunt

School of Chemical Sciences, University of East Anglia, Norwich, England

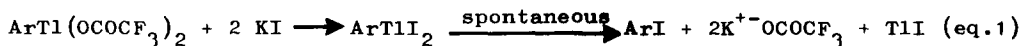
Edward C. Taylor and G. McGillivray (3)

Department of Chemistry, Princeton University, Princeton, N.J., U.S.A.

(Received in UK 2 May 1969; accepted for publication 21 May 1969)

We report a simple, one-step synthesis of aromatic iodides which utilizes the in situ formation of arylthallium di-trifluoroacetate intermediates, is effective with a wide range of aromatic substrates, and proceeds in high yield in aqueous solution at room temperature.

A previous paper (2) has described the synthesis of thallic trifluoroacetate (TTFA) and its utilization for direct thallation of aromatic substrates. We have found that treatment of the resulting arylthallium di-trifluoroacetates with aqueous potassium iodide at room temperature results in rapid precipitation of thallium(I) iodide and formation of the corresponding aromatic iodides in high yield (eq. 1). The overall process of thallation followed by treatment



with iodide ion thus constitutes an extremely simple synthesis of aromatic iodides (4,5).

Three general methods are recommended for effecting this conversion:

Method A To a solution of an aromatic compound in the TTFA/TFA mixture, which has been allowed to stand, or has been heated, until thallation is complete, is added an aqueous solution of potassium iodide. Thus, mesitylene (0.86 g, 0.0072 mole) was added to 10 ml of TTFA in TFA (0.0088 mole) and the reaction mixture allowed to stand at room temperature for 1 hr. A solution of 8.3 g (0.05 mole) of potassium iodide in 25 ml of water was then added, the

mixture stirred at room temperature for 15 min, ca.1g of sodium metabisulfite added, and the mixture stirred until the colour changed from blue-black to yellow. The reaction mixture was made basic with aqueous sodium hydroxide and extracted with ether. The dried (Na_2SO_4) extracts were evaporated and the residue distilled under reduced pressure to give 1.66 g (94%) of pure iodomesitylene as a colourless solid, mp 29-30°.

Method B The intermediate arylthallium di-trifluoroacetate may be isolated from the thallation mixture either directly by filtration or by dilution of the mixture with ether and 1,2-dichloroethane followed by evaporation under reduced pressure to remove solvents and excess TFA. An aqueous suspension of the arylthallium di-trifluoroacetate is then treated at room temperature with aqueous potassium iodide and the reaction mixture worked up as in Method A. Thus, heating a solution of benzoic acid and TTFA/TFA for 24 hrs at 70° followed by cooling and filtration gave o-carboxyphenylthallium di-trifluoroacetate, mp 247-248°, in 79% yield. Treatment of an aqueous suspension of this compound with potassium iodide at room temperature gave o-iodobenzoic acid, mp 163°, in 96% yield.

Method C For acid sensitive substrates, it is advantageous to use solid TTFA in acetonitrile solution for the thallation step. Addition of aqueous potassium iodide and subsequent work-up are carried out as described above in Method A. In this manner, 2-methylthiophene is converted to 2-methyl-5-iodothiophene in 98% yield.

Representative syntheses of aromatic iodides by Methods A, B and C are summarized in Table 1.

TABLE 1

Substrate	Synthesis of Aromatic Iodides <u>via</u> Thallation		Aromatic Iodide			
	Thallation Conditions ^a		Method	Yield %	Product Distribution (%) ^b	
	Temp, °C	Time hrs			<u>o</u>	<u>m</u>
Benzene	22	16	A	96	Iodobenzene	
			B ^a	90		

TABLE 1 continued

Substrate	Thallation Conditions ^a		Aromatic Iodide				
	Temp °C	Time hrs	Method	Yield %	Product Distribution (%) ^b		
					<u>o</u>	<u>m</u>	<u>p</u>
Fluorobenzene	22	16	A	70	11		89
Chlorobenzene	73	0.5	A	80	23		77
<u>o</u> -Xylene	22	0.3	A	72	4-Iodo- <u>o</u> -xylene		
			B	98			
<u>m</u> -Xylene	22	0.8	A	100	4-Iodo- <u>m</u> -xylene		
<u>p</u> -Xylene	22	1.25	A	91	2-Iodo- <u>p</u> -xylene		
Anisole	22	0.25	A	75	17		83
Mesitylene	22	1	A	94	Iodomesitylene		
Benzoic acid	73	21	A	76	95		5 ^c
			B	96	100		
o,m,p -Trifluoro-toluene	73	98	A	54	3	81	16
Thiophene	22	0.25	C	82	2-Iodothiophene ^d		
2-Methylthiophene	22	0.25	C	98	2-Methyl-5-iodothiophene		
2-Chlorothiophene	22	1	C	98	2-Chloro-5-iodothiophene		
<u>p</u> -t-Butyltoluene	22	4.5	A	94	2-Iodo-4- <u>t</u> -butyltoluene		
<u>o</u> -Nitroanisole	73	19	A	94	2-Nitro-4-iodoanisole		
<u>p</u> -Nitroanisole	73	22.5	A	90	2-Iodo-4-nitroanisole		

^a When the intermediate arylthallium di-trifluoroacetate is to be isolated, a slight molar excess of the aromatic substrate should be used, since isolation of the product is complicated by the presence of unreacted TFA. ^b Determined by comparison of glc retention times and/or infrared spectra with authentic samples. In some cases (e.g., anisole) the product distribution was determined by integration of the methyl region of the 100 MHz nmr spectrum (expanded to 100 Hz). ^c Product distribution determined by methylation of the product with diazomethane and analysis of the resulting methyl esters by glc and 100 MHz nmr spectroscopy. ^d an unidentified, high-boiling compound constituted ~9% of the crude product.

References

1. We gratefully acknowledge the financial support of this work by the Smith Kline and French Laboratories, Philadelphia, Pa.
2. A. McKillop, J.S. Fowler, M.J. Zelesko, J.D. Hunt, E.C. Taylor and G. McGillivray, Tetrahedron Letters, previous communication.
3. On leave from the University of South Africa; a grant from the Ernest Oppenheimer Memorial Trust and a travel grant from the C.S.I.S. (South Africa) are gratefully acknowledged.
4. It has been reported (F. Challenger and B. Parker, J. Chem. Soc., 1462 (1931); F. Challenger and O.V. Richards, ibid., 405 (1934)) that treatment of phenylthallium di-chloride, -bromide, -cyanide, etc. with potassium iodide gave some iodobenzene, but neither conditions nor yields were specified. No synthetic utility was either evident or implied, and the inaccessibility of ArTlX_2 compounds precluded investigation of this observation as a general synthetic route to aromatic iodides.
5. The ease with which the C-Tl bond is cleaved in the conversion of ArTlX_2 to ArX appears to be a function of X; iodine lies at the most reactive end of the spectrum (cf. the instability of TlI_3 : F.A. Cotton and G. Wilkinson, Advanced Inorganic Chemistry, Interscience Publishers, New York, N.Y., 1966, p. 440).