

Selective Iodination of Phenols in the *ortho*-Position

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Treatment of a phenol with thallium(I) acetate and iodine allows selective *ortho*-iodination.

DURING an investigation of the use of thallium(I) carboxylates in the Prevost reaction,¹ we observed that treatment of *o*-allylphenol (1) with thallium(I) acetate-iodine gave 2-allyl-6-iodophenol (2) as the only identifiable product. The method appeared to offer a convenient alternative to the mercury(II)-iodine² and silver(I) acetate-iodine³ procedures for iodination of activated aryl compounds, and to provide a method for selective *ortho*-substitution. In order to determine whether *ortho*-substitution was a general phenomenon, the reactions with some other phenols have been examined.

Iodination of *o*-cresol with *ca.* 1 mol. equiv. each of thallium(I) acetate and iodine in 'wet' acetic acid † at 20 °C for 48 h gave 2-iodo-6-methylphenol (3) and, as a minor product, 2,4-di-iodo-6-methylphenol (4).⁴ No *para*-monoiodinated cresol was obtained, indicating that the di-iodo-cresol was formed by further iodination of 2-iodo-6-methylphenol. In contrast, iodination of *o*-cresol in the absence of thallium(I) acetate gave 4-iodo-2-methylphenol (5) and 2,4-di-iodo-6-methylphenol (4), but only a low yield of 2-iodo-6-methylphenol.

Iodination of *m*-cresol, which has two positions *ortho* to the phenolic group, gave only one monoiodinated derivative, which from comparison of observed chemical shifts (δ 6.53, 6.86, and 7.54) with those calculated⁵ for the two possible products (6) (δ 6.34, 6.44, and 7.44) and (7) (δ 6.33, 6.34, and 7.35) was identified as 2-iodo-5-methylphenol (6). Although chemical shift additivity parameters are likely to be unreliable for highly substituted benzenes, a second product was tentatively identified as 2,6-di-iodo-3-methylphenol (8) by the same means. The n.m.r. spectrum of the crude product from iodination indicated the formation of a small amount of 2,4,6-tri-iodo-5-methylphenol (9).

Iodination of phenol gave mainly 2-iodophenol (10),⁶ but also appreciable amounts of 2,6-di-iodophenol (11).⁷ However, with higher iodine-to-phenol ratios, di- (12) and tri-iodo- (13) derivatives⁶ were formed in which iodination had occurred in the *para*-position.

In the case of *p*-cresol, with a blocked *para*-position,

† Glacial acetic acid which has not been rigorously dried; iodination in dry acetic acid gave a complex mixture including acetylation products.

¹ R. C. Cambie, R. C. Hayward, J. L. Roberts, and P. S. Rutledge, *J.C.S. Perkin I*, 1974, 1858.

² M. Stefanovic, Lj. Krstic, and S. Mladenovic, *Tetrahedron Letters*, 1971, 3311; A. Hillman-Elies, G. Hillmann, and U. Schiedt, *Z. Naturforsch.*, 1953, **8**, 436.

³ W. G. Dauben and H. Tilles, *J. Amer. Chem. Soc.*, 1950, **72**, 3185; D. Popa, E. Schwenk, and E. Klinsberg, *ibid.*, p. 2623.

⁴ K. T. Potts, *J. Chem. Soc.*, 1953, 3711.

⁵ L. M. Jackman and S. Sternhell, 'Applications of N.M.R. Spectroscopy in Organic Chemistry,' 2nd edn., Pergamon, Oxford, 1969, p. 202.

equal amounts of 2-iodo-4-methyl- (14) and 2,6-di-iodo-4-methyl-phenol (15)⁴ were obtained, along with *ca.* 50% of starting material. However, use of a two-fold excess of reagents gave the same products in a similar ratio with only a trace of starting material. Iodination of the diterpenoids methyl 12-hydroxy podocarpa-8,11,13-trien-19-oate (16) and totara-8,11,13-trien-13-ol (19), each with a blocked *para*-position and in the latter case with a but-tressed phenolic group, gave moderate yields of the *ortho*-iodinated products (17)⁸ and (20). Attempted extension of the method to anisole gave only a low yield of *p*-iodoanisole, and no reaction was observed with methyl 12-methoxy podocarpa-8,11,13-trien-19-oate (18) or with toluene [cf. reaction with thallium(III) trifluoroacetate⁹].

Iodination of the activated substrate *NN*-dimethylaniline was also investigated. Treatment with iodine and thallium(I) acetate gave 4-iodo-*NN*-dimethylaniline (21),¹⁰ but the reaction was complicated by oxidation of the starting material. 4,4'-Methylenebis-*(NN)*-dimethylaniline (24) was also isolated, and Methyl Violet cation was recognised by its characteristic violet colour in aqueous solution. Isolation of the dye was not attempted, but Bergmann and Shahak¹¹ have reported the isolation of its crystalline trifluoroacetate from the analogous reaction with silver(I) trifluoroacetate-iodine. Ghosal and Dutta¹² have studied the oxidation of *NN*-dimethylaniline by iodine in dichloromethane. Their reported colour changes corresponded with those observed in acetic acid during the present work. However, although they report formation of *NNN'N'*-tetramethylbenzidine (25) as a major product, none of this compound was isolated or observed in the crude product from the reaction with thallium(I) acetate-iodine. Similar reactions occurred when *N*-methylaniline was treated with thallium(I) acetate-iodine, but in the case of aniline the products were 4-iodoaniline (22)⁴ and 2,4-di-iodoaniline (23),⁴ compounds which are also obtained in the absence of thallium(I) acetate.

Since iodination of phenols with iodine in acetic acid gives mainly *para*-substitution it must compete with the thallium(I) acetate-iodine reaction in this solvent. An

⁶ 'Handbook of Chemistry and Physics,' ed. R. C. Weast and S. M. Selby, 48th edn., The Chemical Rubber Co., Ohio, 1967.

⁷ J. L. Roark and W. B. Smith, *J. Phys. Chem.*, 1969, **73**, 1043.

⁸ J. W. A. Findley and A. B. Turner, *J. Chem. Soc. (C)*, 1971, 547.

⁹ A. McKillop, J. D. Hunt, M. J. Zelesko, J. S. Fowler, E. C. Taylor, G. McGillivray, and F. Kienzle, *J. Amer. Chem. Soc.*, 1971, **93**, 4841; E. C. Taylor, F. Kienzle, R. L. Robey, A. McKillop, and J. D. Hunt, *ibid.*, p. 4845.

¹⁰ H. P. Crocker and B. Jones, *J. Chem. Soc.*, 1959, 1808.

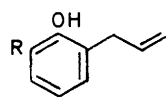
¹¹ E. D. Bergmann and I. Shahak, *J. Chem. Soc.*, 1959, 1418.

¹² S. Ghosal and S. K. Dutta, *Indian J. Chem.*, 1968, **6**, 301.

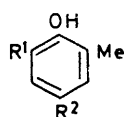
alternative solvent was therefore sought in which competitive reactions would be eliminated so that the *ortho*-directing effect of the thallium(I) acetate would be more pronounced. This was found with dichloromethane, in which *ortho*-substitution still occurred but in which no iodination was observed if thallium(I) acetate was absent. Use of dichloromethane resulted in increased solubility of iodine and facilitated the work-up procedure, since neutralisation of acetic acid was no longer necessary. A

yl (26), and only a trace of 2-iodo-6-methylphenol. No benefit was gained by using dichloromethane in place of acetic acid in the iodination of aniline other than that of easier work-up: the same products were obtained in similar ratios both in the presence and in the absence of thallium(I) acetate.

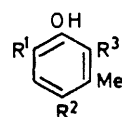
In earlier work,¹ significant differences were observed in the behaviour of thallium(I) carboxylates and silver(I) carboxylates towards alkenes in the presence of iodine.



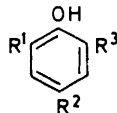
- (1) R = H
(2) R = I



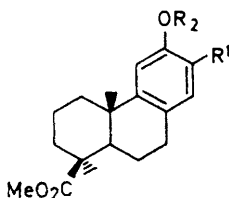
- (3) R¹ = I, R² = H
(4) R¹ = R² = I
(5) R¹ = H, R² = I



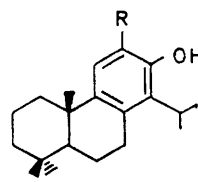
- (6) R¹ = I, R² = R³ = H
(7) R¹ = R³ = H, R² = I
(8) R¹ = R³ = I, R² = H
(9) R¹ = R² = R³ = I



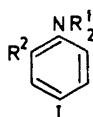
- (10) R¹ = I, R² = R³ = H
(11) R¹ = R³ = I, R² = H
(12) R¹ = R² = I, R³ = H
(13) R¹ = R² = R³ = I
(14) R¹ = I, R² = Me, R³ = H
(15) R¹ = R³ = I, R² = Me



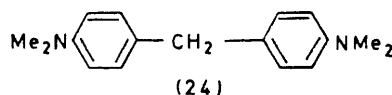
- (16) R¹ = R² = H
(17) R¹ = I, R² = H
(18) R¹ = H, R² = Me



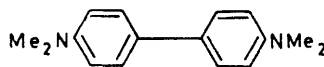
- (19) R = H
(20) R = I



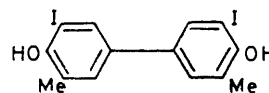
- (21) R¹ = Me, R² = H
(22) R¹ = R² = H
(23) R¹ = H, R² = I



(24)



(25)



(26)

disadvantage was that thallium(I) acetate is less soluble in dichloromethane than in acetic acid. However, if the ratio of thallium(I) acetate to iodine was doubled the yield of 2-iodo-6-methylphenol (3) from *o*-cresol was increased by 14%. On the other hand, doubling the amount of iodine without increasing the amount of thallium(I) acetate drastically reduced conversion into 2-iodo-6-methylphenol, presumably owing to the formation of polyiodides.¹³ Treatment of *o*-cresol with 2 mol. equiv. of iodine and a correspondingly increased amount of thallium(I) acetate gave a compound tentatively identified as 4,4'-dihydroxy-3,3'-di-iodo-5,5'-dimethylbiphen-

In the present study, treatment of *o*-cresol with silver(I) acetate-iodine in acetic acid gave 2-iodo-6-methylphenol (3) and 2,4-di-iodo-6-methylphenol (4) in yields similar to those obtained with thallium(I) acetate-iodine. Likewise, reaction of *o*-cresol with silver(I) acetate-iodine in dichloromethane gave 2-iodo-6-methylphenol and starting material in amounts similar to those obtained with thallium(I) acetate-iodine. It thus appears that iodination with silver(I) acetate-iodine is also regioselective.

The iodination of phenols, in particular substituted

¹³ A. G. Sharpe, *J. Chem. Soc.*, 1952, 2165; M. B. Robin and P. Day, *Adv. Inorg. Chem. Radiochem.*, 1967, 10, 371.

phenols, has not received much attention,* and few successful mono-iodination procedures are recorded. Thus, although the yields from iodinations with thallium(I) acetate-iodine are not quantitative, the method offers a favourable alternative to most preparative-methods, many of which cannot be controlled and which lead to di- and tri-iodinated products only.⁴ In the absence of thallium(I) or silver(I) carboxylates, aryl iodination of phenols probably occurs *via* free or solvated molecular iodine,¹⁸ leading, as expected, to predominantly *para*-substitution. The selectivity of thallium(I) acetate-iodine or silver(I) acetate-iodine substitution can be explained by initial complexing of the reagents¹ or by an initial π -complex of iodine with the aryl ring. In either case further co-ordination between the metal and the oxygen of the phenolic group then occurs such that only *ortho*-attack is possible.

EXPERIMENTAL

General experimental details have been described previously.¹ G.l.c. was carried out with a Varian Aerograph series 1800 instrument [nitrogen as carrier gas and either a $\frac{1}{2}$ in glass column (8 ft) packed with 3% OV-17 on 70-80 mesh Chromosorb W or a $\frac{1}{4}$ in column (12 ft) packed with 7% OV-17 on 70-80 mesh Chromosorb W].

General Procedure for Aryl Iodinations.—A solution of iodine in either acetic acid (*ca.* 120 ml per g of iodine) or dichloromethane (*ca.* 60 ml per g of iodine) was added slowly to a stirred solution of substrate and thallium(I) acetate, and the mixture was stirred at *ca.* 20 °C for 48 h. Unless otherwise stated, the molar ratios substrate : iodine : thallium(I) acetate were 1 : 1 : 1.2. Precipitated thallium(I) iodide was removed, and when acetic acid was the solvent the filtrate was neutralised with saturated sodium hydrogen carbonate solution (method A) or with 15% sodium hydroxide solution (method B) before extraction with ether. When dichloromethane was the solvent it was partly removed by evaporation and ether was added to the mixture (method C). The ethereal solutions were washed with water, 5% sodium thiosulphate or sodium disulphite solution, and saturated sodium chloride solution, and then dried (Na₂SO₄ or MgSO₄) and evaporated. The product was examined as soon as possible by n.m.r. and t.l.c. (in hexane or hexane-benzene). Product ratios were determined from integration of the aryl methyl peaks for each component in the n.m.r. spectrum of the total product and/or by g.l.c. Compounds are recorded in order of increasing *R_F* value in t.l.c.

Iodinations of *o*-Cresol.—The reactions shown in Table 1 were carried out with *o*-cresol (0.32 g, 3.0 mmol), iodine, and thallium(I) acetate. Products were isolated by preparative t.l.c. and characterised as (i) *o*-cresol; (ii) 4-iodo-2-methylphenol (5), δ 2.20 (3 H, s, ArMe), 6.60 (1 H, d, *J* 7.8 Hz, 6-H), 7.35 (1 H, d, *J* 7.8 Hz, 5-H), and 7.44 (1 H, s, 3-H); (iii) 2, 4-di-iodo-6-methylphenol (4), m.p. 58-61° (lit.,⁴ 67°), δ 2.25 (3 H, s, ArMe), 5.40 (1 H, s, OH), 7.37 (1 H, d, *J* 2 Hz), and 7.75 (1 H, d, *J* 2 Hz, 3-H); (iv) 4,4'-dihydroxy-3,3'-di-

* Reagents used for the iodination of phenols include iodine and potassium iodide in ethylamine,⁴ mercury(II) oxide-iodine,¹⁴ hypochlorous acid and potassium iodide,¹⁵ iodic acid-iodine,¹⁶ sodium phosphate-iodine,¹⁶ and nitrogen iodide.¹⁷

¹⁴ H. Hlasiwetz and P. Weselsky, *Ber.*, 1872, **5**, 380; G. Kone, *Ann. Phys. Chem.*, 1845, **66**, 300; R. L. Taylor, *Chem. News*, 1897, **76**, 22.

iodo-5,5'-dimethylbiphenyl (26), m.p. 168-171°, δ 2.37 (6 H, s, ArMe), 7.21 (2 H, d, *J* 2 Hz, 6- and 6'-H), and 7.61 (2 H,

TABLE 1
Iodination of *o*-cresol

Reactant ratios	Solvent	Time (h)	Work-up method	Product wt (g)	Product ratios				
					(i)	(ii)	(iii)	(iv)	(v)
1 : 1 : 1.2	HOAc	48	A	0.42	2	1	5		
1 : 1 : 0	HOAc	23	A	0.46	9	8	7	1	
1 : 1 : 0		23	C	0.31	1				
1 : 1 : 1.2	CH ₂ Cl ₂	6	C	0.42	11				9
1 : 1 : 1.2		23	C	0.44	1				2
1 : 1 : 1.2		48	C	0.41	1				2
1 : 2 : 1.2		48	C	0.42	3				2
1 : 1 : 2.4		48	C	0.38	1				2.5
1 : 2 : 2.4		23	C	0.51				4	1
1 : 1 : 1.2	HOAc *	23	A	0.63	6 Components				
1 : 1 : 1.2 †	HOAc	23	A	0.35	2	4	4	1	
1 : 1 : 1.2 †	CH ₂ Cl ₂	23	A	0.33	1				1

* Dried redistilled solvent. Solvolysis of the product with methanolic potassium hydroxide for 2 h gave a mixture similar to those formed by iodination with 'wet' acetic acid. † Reaction with silver(I) acetate.

d, *J* 2 Hz, 2- and 2'-H), *m/e* 466 (*M*⁺) and 338 (*M* - I, *m*^{*} 245); and (v) 2-iodo-6-methylphenol (3), orange oil, δ 2.32 (3 H, s, ArMe), 5.30 (1 H, s, OH), 6.57 (1 H, M of AMX, *J* 7.8 Hz, 4-H), 7.10 (1 H, d, showing further splitting, *J* 7.8 Hz, 5-H), and 7.51 (1 H, dd, *J* 7.8 and 1.5 Hz, 3-H).

Iodination of *m*-Cresol.—The reactions shown in Table 2

TABLE 2
Iodination of *m*-cresol

Solvent	Time (h)	Work-up method	Product wt (g)	Products (%)			
				(i)	(ii)	(iii)	(iv)
HOAc	48	A	0.55	38	47	12	5
CH ₂ Cl ₂	24	C	0.45	30	50	12	8
CH ₂ Cl ₂	48	C	0.52	35	38	13	10

were carried out with *m*-cresol (0.32 g, 3.0 mmol), iodine, and thallium(I) acetate. Products were isolated by preparative t.l.c. and characterised as (i) *m*-cresol; (ii) 2-iodo-5-methylphenol (6), an oil, δ 2.30 (3 H, s, ArMe), 5.30 (1 H, s, OH), 6.53 (1 H, dd, *J* 7.8 and 2 Hz, 4-H), 6.86 (1 H, d, *J* 2 Hz, 6-H), and 7.54 (1 H, d, *J* 7.8 Hz, 3-H); (iii) 2,6-di-iodo-3-methylphenol (8), δ 2.44 (3 H, s, ArMe), 5.85 (1 H, s,

TABLE 3
Iodination of phenol

Reactant ratios	Solvent	Work-up method	Product wt (g)	Product ratios				
				(i)	(ii)	(iii)	(iv)	(v)
1 : 1 : 1.2	HOAc	A	0.47	4	5			1
1 : 2 : 2.4	HOAc	A	0.81		2		1	
1 : 3 : 3.6	HOAc	A	1.07			2	25	2
1 : 1 : 1.2	CH ₂ Cl ₂	C	0.41	1	3			2

OH), 6.57 (1 H, d, *J* 7.8 Hz, 4-H), and 7.54 (1 H, d, *J* 7.8 Hz, 5-H); and (iv) 2,4,6-tri-iodo-3-methylphenol (9), δ 2.38 (3 H, s, ArMe), 5.92 (1 H, s, OH), and 8.0 (1 H, s, 5-H).

Iodination of Phenol.—The reactions shown in Table 3

¹⁵ B. Klimentko, *Z. phys. Chem.*, 1897, **23**, 552, 588; W. Bray, *ibid.*, 1906, **54**, 463.

¹⁶ V. Cofman, *J. Chem. Soc.*, 1919, 1040.

¹⁷ T. Selivanov, *Ber.*, 1894, **27**, 1012.

¹⁸ E. Grovenstein and N. S. Arahamian, *J. Amer. Chem. Soc.*, 1962, **84**, 212; A. R. Butler, *J. Chem. Educ.*, 1971, **48**, 508.

were carried out with phenol (0.28 g, 3.0 mmol), iodine, and thallium(I) acetate for 20 h. Products were isolated by preparative t.l.c. and characterised as (i) phenol; (ii) 2-iodophenol (10), m.p. 42–43° (lit.,⁶ 43°), δ 4.90br (1 H, s, OH), and 6.5–8.0 (4 H, m, ArH) (cf. ref. 7); (iii) 2,4-di-iodophenol (12), m.p. 70–71° (lit.,⁶ 72–73°), δ 5.40br (1 H, s, OH), 6.80 (1 H, d, J 8.8 Hz, 6-H), 7.53 (1 H, dd, J 8.8 and 1.8 Hz, 5-H), and 7.98 (1 H, d, J 1.8 Hz, 3-H); (iv) 2,4,6-tri-iodophenol (13), m.p. 161° (lit.,⁶ 156–158°), δ 5.81 (1 H, s, OH), and 8.0 (2 H, s, 3- and 5-H); and (v) 2,6-di-iodophenol (11), m.p. 65.5–67.5° (lit.,⁷ 68°), δ 5.78br (1 H, s, OH), 6.42 (1 H, t, J 7.8 Hz, 4-H), and 7.72 (2 H, d, J 7.8 Hz, 3- and 5-H).

Iodination of *p*-Cresol.—*p*-Cresol (0.32 g, 3.0 mmol) was treated with iodine and thallium(I) acetate in acetic acid. Work-up by method A gave an orange oil (0.61 g) which was separated by preparative t.l.c. into (i) *p*-cresol (48%); (ii) 2-iodo-4-methylphenol (14) (26%), δ 2.27 (3 H, s, ArMe), 5.23 (1 H, s, OH), 6.87 (1 H, d, J 8 Hz, 6-H), 7.08 (1 H, dd, J 8 and 2 Hz, 5-H), and 7.52 (1 H, d, J 2 Hz, 3-H); and (iii) 2,6-di-iodo-4-methylphenol (15) (26%), needles (from ether), m.p. 59–59.5° (lit.,⁴ 60°), δ 2.24 (3 H, s, ArMe), 5.61 (1 H, s, OH), and 7.53 (2 H, s, 3- and 5-H). Repetition with substrate: iodine: thallium(I) acetate ratios of 1:2:2.4 and work-up by method B gave a mixture which was shown by g.l.c. to contain (i) *p*-cresol (2%); (ii) 2-iodo-4-methylphenol (46%); and (iii) 2,6-di-iodo-4-methylphenol (52%).

Iodination of Methyl 12-Hydroxypodocarpa-8,11,13-trien-19-oate.—Methyl podocarpate (0.29 g, 1.0 mmol) was treated with iodine and thallium(I) acetate in acetic acid and the mixture was heated at ca. 50 °C for 2 h. Work-up by method A gave an orange oil (0.40 g) which was separated by preparative t.l.c. (chloroform) to give starting material (trace) and methyl 12-hydroxy-13-iodopodocarpa-8,11,13-trien-19-oate (17), which crystallised from chloroform-pentane as cream needles (0.25 g, 61%), m.p. 170–173° (lit.,⁸ 174–175°), ν_{\max} 3 510 (OH) and 1 718 cm⁻¹ (CO₂Me), δ 1.03 (3 H, s, 10-Me), 1.30 (3 H, s, 4-Me), 1.20–2.87 (11 H, m, CH₂), 3.63 (3 H, s, CO₂Me), 5.07 (1 H, s, OH), 6.80 (1 H, s, 11-H), and 7.16 (1 H, s, 14-H); acetate, m.p. 182.5–183° (lit.,⁸ 183–184°).

Iodination of Totara-8,11,13-trien-13-ol.—Totarol (0.41 g, 1.6 mmol) was treated with iodine and thallium(I) acetate in acetic acid and the mixture was worked up by method A to give an orange oil (0.56 g) which was chromatographed on silica gel. Elution with benzene gave 12-iodototara-8,11,13-trien-13-ol (20), which crystallised from ethyl acetate as irregular crystals (70%), m.p. 143–144° (Found: C, 58.2; H, 7.0; I, 30.9. C₂₀H₂₉IO requires C, 58.3; H, 7.1; I, 30.8%), $[\alpha]_D^{20} + 57.9^\circ$ (c 0.85), ν_{\max} 3 520 cm⁻¹ (OH), δ 0.92 and 0.94 (6 H, 4-Me₂), 1.16 (3 H, s, 10-Me), 1.31 (6 H, d, J 7 Hz, 15-Me₂), 5.09 (1 H, s, OH), and 7.43 (1 H, s, 11-H).

Iodination of Anisole.—Anisole (1.3 g, 5.0 mmol) was treated with iodine and thallium(I) acetate in acetic acid for 48 h and the mixture was worked up by method B to give a yellow oil (0.18 g). Preparative t.l.c. gave anisole (34%) and 4-iodoanisole (66%), m.p. 48–50.5° (lit.,¹⁹ 51–52°). The n.m.r. spectrum was identical with that recorded.²⁰

The yield was not improved by refluxing the mixture for 6 h, or by using method A in the work-up.

Iodination of *NN*-Dimethylaniline.—*NN*-Dimethylaniline (0.73 g, 6.0 mmol) was treated with iodine and thallium(I) acetate in acetic acid. A blue-purple solution was obtained from which the colour (Methyl Violet) was extracted into the aqueous phase during work-up by method A. The product (0.87 g) was separated by preparative t.l.c. (benzene-hexane) into (i) 4,4'-methylenebis-*NN*-dimethylaniline (24), δ 2.90 (12 H, s, NMe), 3.83 (2 H, s, CH₂), 6.70 (4 H, d, 3-, 3', 5-, and 5'-H), and 7.33 (4 H, d, 2-, 2', 6-, and 6'-H); (ii) an unstable green oil which rapidly turned purple (Methyl Violet); and (iii) 4-iodo-*NN*-dimethylaniline (21), which crystallised from methanol as fine plates, m.p. 77° (lit.,¹⁰ 79°), δ 2.97 (6 H, s, Me), 6.51 (2 H, d, J 9.5 Hz, 3- and 5-H), and 7.50 (2 H, d, J 9.5 Hz, 2- and 6-H) (cf. ref. 20). The ratio of (iii) to (i) was 5:2. Both fractions gradually turned purple when left in ether solution.

Iodination of *N*-Methylaniline.—*N*-Methylaniline (0.64 g, 6.0 mmol) was treated with iodine and thallium(I) acetate in acetic acid for 50 h. The aqueous phase turned purple during the extraction into ether. Work-up by method A gave a mixture of at least five components (t.l.c.). The n.m.r. spectrum showed that the major product was *p*-iodo-*N*-methylaniline: δ 2.83 (3 H, s, Me), 3.23 (1 H, s, $W_{\frac{1}{2}}$ 4 Hz, NH), 6.40 (2 H, d, J 9 Hz, 3- and 5-H), and 7.46 (2 H, d, J 9 Hz, 2- and 6-H). Attempted isolation of other components resulted in their decomposition.

TABLE 4
Iodination of aniline

Reactant ratios	Solvent	Time (h)	Work-up method	Product wt (g)	Products (%)		
					(i)	(ii)	(iii)
1:1:1.2	HOAc	17	A	0.85	10	82	8
1:1:1.2		48	A	1.12	2	90	7
1:1:1.2		60	A	1.02		85	15
1:1:0	CH ₂ Cl ₂	23	B	0.98	6	84	10
1:1:1.2		48	C	0.89	10	67	22
1:1:1.2		48	C	0.94	12	75	13

Iodination of Aniline.—The reactions shown in Table 4 were carried out with aniline (0.47 g, 5.0 mmol), iodine, and thallium(I) acetate. Products were isolated by preparative t.l.c. and characterised as (i) aniline; (ii) 4-iodoaniline, m.p. 59–62° (lit.,⁶ 62–63°), δ 3.36br (2 H, s, NH₂), 6.45 (2 H, d, J 9 Hz, 2- and 6-H), and 7.41 (2 H, d, J 9 Hz, 3- and 5-H); and (iii) 2,4-di-iodoaniline, m.p. 91–94° (lit.,⁶ 95–96°), δ 4.07br (2 H, s, NH₂), 6.50 (1 H, d, J 9 Hz, 6-H), 7.37 (1 H, dd, J 9 and 2 Hz, 5-H), and 7.90 (1 H, d, J 2 Hz, 3-H).

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