

## Selective Nitration of Aromatic Substrates: Reaction of Nitrogen Dioxide with Arylthallium(III) Compounds

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A method of selectively nitrating aromatic substrates is described in which nitrogen dioxide displaces a thallium(III) substituent electrophilically. High yields of the *para*-isomer were obtained from alkylbenzenes and a number of other substrates containing *ortho-para*-directing groups. Similar specificity was observed with xylenes but the process proved only partially successful when applied to mesitylene where, it is postulated, steric interaction between the methyl groups and the bulky thallium substituent inhibits the reaction. Thermodynamic control leading to *meta*-isomers proved impossible, a low yield of nitroarenes being obtained, the bulk of which originates by direct attack of nitrogen dioxide on regenerated aromatic substrate. Compounds with side-chains which have been reported to direct the incoming thallium substituent to an *ortho*-site also failed to react and an explanation for this is offered.

THE extensive studies reported by McKillop and his co-workers have aroused considerable interest in recent years in the use of thallium(III) as a synthetic reagent in organic chemistry. One aspect of particular interest is the ability of thallium(III) trifluoroacetate to metallate an aromatic ring. The problems of the toxicity and expense of the reagents are compensated by the high degree of selectivity of the electrophile and by the ease with which the metal substituent can be replaced by other functional groups.<sup>1</sup> Normally, with substrates activated to electrophilic attack, the *para*-arylthallium-

(III) trifluoroacetate is obtained in high yield<sup>2</sup> but, should a substituent containing an oxygen atom be present, the *ortho*-isomer frequently predominates, presumably because co-ordination between thallium and the oxygen results in the electrophile being preferentially 'delivered' to the *ortho*-position.<sup>3</sup> Refluxing the reaction mixture is reported to lead to thermodynamic control and the production of the more stable *meta*-isomer.<sup>3</sup>

Amongst the replacement reactions effected on arylthallium compounds that of iododethallation has been particularly widely applied in studying the isomer distribution of thallation reactions,<sup>2,3</sup> but the selective

<sup>1</sup> A. McKillop and E. C. Taylor, *Chem. in Britain*, 1973, **9**, 4.  
<sup>2</sup> 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.

<sup>3</sup> E. C. Taylor, F. Kienzle, R. L. Robey, A. McKillop, and J. D. Hunt, *J. Amer. Chem. Soc.*, 1971, **93**, 4845.

introduction of thiocyanate,<sup>4</sup> cyanide,<sup>5,6</sup> trifluoroacetate (and thence hydroxy),<sup>5</sup> halogen,<sup>7</sup> deuterium,<sup>8</sup> or aryl<sup>9,10</sup> substituents has been demonstrated. What is not clear, however, is the mechanism of dethallation. Those methods which require irradiation<sup>5,9</sup> presumably involve homolysis of the carbon-metal bond but the mode of cleavage in other systems has not been studied. Since thermodynamic control of the isomer distribution can operate at reflux temperatures,<sup>3</sup> it would seem that electrophilic replacement of the metal substituent is possible. Similarly it is difficult to see how else lead(IV) acetate can effect conversion of an arylthallium(III)

the arylthallium intermediates we investigated this system to see whether selective nitration was feasible.

## RESULTS AND DISCUSSION

As a trial experiment 4-methylphenylthallium(III) trifluoroacetate, prepared by the method of McKillop *et al.*,<sup>2</sup> was suspended in trifluoroacetic acid and nitrogen dioxide bubbled in for 10 min to produce a clear brown solution. After work-up the product was analysed by g.l.c. with the result shown in experiment 1, Table 1. Our expectations were fully realised: nitrotoluenes were

TABLE 1

Products from the reaction of nitrogen dioxide with thalliated toluene in trifluoroacetic acid

Experiment no.	Starting material(s)	Length of reflux before nitration (h)	Nitrotoluenes (%)	Ratio of nitrotoluenes ( <i>o</i> : <i>m</i> : <i>p</i> )	Other products (%)
1	4-MeC <sub>6</sub> H <sub>4</sub> ·Ti(O <sub>2</sub> CCF <sub>3</sub> ) <sub>2</sub>	<i>a</i>	97	3·2 : 1·8 : 95·0	
2		2	64	11·1 : 2·4 : 86·5	PhCH <sub>3</sub> (trace)
3		8	50	35·3 : 11·0 : 53·7	PhCH <sub>3</sub> (1)
4		24	36	45·1 : 17·2 : 37·7	PhCH <sub>3</sub> (2) <sup>b</sup>
5		48	24	50·7 : 6·0 : 43·3	PhCH <sub>3</sub> (2), PhCHO, PhCH <sub>2</sub> ·O <sub>2</sub> CCF <sub>3</sub> , MeC <sub>6</sub> H <sub>4</sub> CHO, 4-MeC <sub>6</sub> H <sub>4</sub> OH, MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> Ph
6	PhCH <sub>3</sub> + Ti(O <sub>2</sub> CCF <sub>3</sub> ) <sub>2</sub>	<i>a</i>	98	10·9 : 2·0 : 87·2	
7		24	48	43·0 : 18·2 : 38·8	PhCH <sub>3</sub> (3) <sup>b</sup>

<sup>a</sup> No reflux before nitration. <sup>b</sup> Other products present in small amounts but not identified.

carboxylate into an aryl trifluoroacetate other than by electrophilic plumbodethallation.<sup>5,\*</sup>

The major problem after nitrating an alkylbenzene is to separate the mixture of *ortho*- and *para*-isomers obtained. The use of a thallation-nitrodethallation system could, therefore, have important synthetic applications providing that a means of effecting the last stage of the sequence can be devised. One of the more usual methods of electrophilic nitration, nitric acid in acetic anhydride, is not satisfactory. Rather than displacing the thallium substituent the electrophile enters one of the free positions in the aromatic ring.<sup>14</sup> However, nitrosodethallation is possible by using nitrosyl chloride generated *in situ*.<sup>15</sup> We have recently described the use of nitrogen dioxide in trifluoroacetic acid for the direct nitration of arenes<sup>16</sup> and since the use of this medium should obviate the need to isolate

\* *p*-Halogenophenyl-lead(IV) trifluoroacetates have been identified as intermediates in this process<sup>11</sup> whilst it is believed that other aryl-lead analogues are too labile at room temperature to be detected.<sup>12,13</sup>

<sup>4</sup> E. C. Taylor, F. Kienzle, and A. McKillop, *Synthesis*, 1972, 38; S. Uemura, S. Uchida, M. Okano, and K. Ichikawa, *Bull. Chem. Soc. Japan*, 1973, **46**, 3254.

<sup>5</sup> E. C. Taylor, H. W. Altland, R. H. Danforth, G. McGillivray, and A. McKillop, *J. Amer. Chem. Soc.*, 1970, **92**, 3520.

<sup>6</sup> S. Uemura, Y. Ikeda, and K. Ichikawa, *Tetrahedron*, 1972, **28**, 3025.

<sup>7</sup> S. Uemura, Y. Ikeda, and K. Ichikawa, *Tetrahedron*, 1972, **28**, 5499.

<sup>8</sup> R. B. Herbert, *Tetrahedron Letters*, 1973, 1375.

<sup>9</sup> E. C. Taylor, F. Kienzle, and A. McKillop, *J. Amer. Chem. Soc.*, 1970, **92**, 6088.

produced in almost quantitative yield with the *para*-isomer predominating. The small amounts of the other two isomers may be indicative of thermodynamic equilibrium between the arylthallium compounds being slowly established at room temperature, but it is more likely to reflect *ortho*- and *meta*-impurities in the starting material. Microanalysis, n.m.r. spectroscopy, and melting point determination<sup>2</sup> do not provide any criterion of purity.

That the isomer distribution can be changed by refluxing the solution before passing in nitrogen dioxide is demonstrated by experiments 2–5. The proportions of *ortho*- and *meta*-isomers are increased but even after 24 h under reflux *meta*-substitution did not predominate, in contrast to what has been reported in the iododethallation of other alkylbenzenes.<sup>3</sup> It can be seen, however, that the overall yield declines steadily with time and that eventually the proportion of *meta*-isomer

<sup>10</sup> S. Uemura, Y. Ikeda, and K. Ichikawa, *Chem. Comm.*, 1971, 390.

<sup>11</sup> J. R. Kalman, J. T. Pinhey, and S. Sternhell, *Tetrahedron Letters*, 1972, 5369.

<sup>12</sup> R. O. C. Norman, C. B. Thomas, and J. S. Willson, *J. Chem. Soc. (B)*, 1971, 518.

<sup>13</sup> J. R. Campbell, J. R. Kalman, J. T. Pinhey, and S. Sternhell, *Tetrahedron Letters*, 1971, 1763; H. C. Bull, J. R. Kalman, J. T. Pinhey, and S. Sternhell, *ibid.*, 1974, 853, 857.

<sup>14</sup> E. C. Taylor, H. W. Altland, and A. McKillop, in preparation; cited in ref. 1.

<sup>15</sup> E. C. Taylor, R. H. Danforth, and A. McKillop, *J. Org. Chem.*, 1973, **38**, 2088.

<sup>16</sup> R. O. C. Norman, W. J. E. Parr, and C. B. Thomas, *J.C.S. Perkin I*, 1974, 369.

begins to fall as well. We cannot, of course, be certain that, for the tolylthallium(III) trifluoroacetates, the *meta*-isomer is thermodynamically the most stable.

Passing nitrogen dioxide into the thallation mixture without prior isolation of the organometallic intermediate also proved effective (experiment 6). As might be anticipated, the selectivity is somewhat lower but the convenience of not having to isolate the intermediate more than offsets this. Refluxing the mixture before adding nitrogen dioxide produced results similar to those above, a fall in overall yield and an increase in *ortho*- and *meta*-isomers. The reason for the low yields under these conditions is discussed below.

A 'one-pot' experiment using ethylbenzene as the substrate gave a higher positional selectivity than shown by toluene but the total conversion into nitroarene was lower (experiment 8, Table 2). Refluxing the solution

Unfortunately the method of work-up employed is such that most of this compound would be lost on removal of the ether. Other products identified by g.l.c.-mass spectrometry were found in experiments 4 and 5 but none were present in more than *ca.* 0.5% yield. In the ethylbenzene system acetophenone was always produced and, after reflux, a large amount of the arene was recovered. We considered three possibilities for the low yields after reflux.

(i) Nitrodethallation occurs much more slowly for a *meta*-alkylphenylthallium compound than for the *ortho*- and *para*-isomers. The inductive effect of the methyl group would certainly favour the process for the last two compounds. However passing in nitrogen dioxide for 1.25 h instead of the usual 10–15 min made no significant difference to the relative proportions of the isomers nor to the overall yield. As an added check

TABLE 2

Products from the reaction of nitrogen dioxide with thalliated aromatic hydrocarbons in trifluoroacetic acid

Experiment no.	Starting material	Nitroarenes (%)	Ratio of nitroarenes ( <i>o</i> : <i>m</i> : <i>p</i> )	Other products (%)
8	PhEt + Tl(O <sub>2</sub> CCF <sub>3</sub> ) <sub>3</sub>	76	5.3 : 1.7 : 93.0	PhAc (1.7)
9	PhEt + Tl(O <sub>2</sub> CCF <sub>3</sub> ) <sub>3</sub> <sup>a</sup>	3.5	41.6 : 1.7 : 56.6	PhAc (2.3), PhEt (23)
10	4-EtC <sub>6</sub> H <sub>4</sub> ·Tl(O <sub>2</sub> CCF <sub>3</sub> ) <sub>2</sub>	77	0.4 : 0.2 : 99.4	PhAc (0.1)
11	PhEt <sup>b</sup>	11	42.5 : 2.0 : 55.5	PhEt (58)
12	PhPr <sup>i</sup> + Tl(O <sub>2</sub> CCF <sub>3</sub> ) <sub>3</sub>	68	1.6 : 2.1 : 96.3	PhCH <sub>2</sub> Ac (0.3)
13	PhPr <sup>i</sup> + Tl(O <sub>2</sub> CCF <sub>3</sub> ) <sub>3</sub> <sup>a</sup>	4.7	26.1 : 3.6 : 70.3	PhPr <sup>i</sup> (2), PhCH <sub>2</sub> Ac (0.4)
14	PhBu <sup>t</sup> + Tl(O <sub>2</sub> CCF <sub>3</sub> ) <sub>3</sub>	88	1.8 : 3.3 : 94.8	4-Bu <sup>t</sup> C <sub>6</sub> H <sub>4</sub> OH (0.6)
15	PhBu <sup>t</sup> + Tl(O <sub>2</sub> CCF <sub>3</sub> ) <sub>3</sub> <sup>a</sup>	45	6.0 : 25.0 : 69.0	PhBu <sup>t</sup> (7), 4-Bu <sup>t</sup> C <sub>6</sub> H <sub>4</sub> OH (1.5)

<sup>a</sup> Solution refluxed for 24 h before nitrogen dioxide was passed in. <sup>b</sup> No thallium(III) trifluoroacetate employed.

for 24 h before nitration resulted in a minimal yield of ethylnitrobenzenes and, once again, a very small amount of the *meta*-isomer. Isolating the arylthallium compound and then nitrating gave almost exclusively *p*-ethylnitrobenzene in good yield. The greater selectivity in this latter experiment compared with experiment 1 is more apparent than real. Whereas *p*-tolylthallium(III) trifluoroacetate precipitates from trifluoroacetic acid within minutes of mixing the reagents, and can be easily filtered off and washed, the *p*-ethyl compound is extremely soluble. The only way to isolate it was to remove all the solvent and then to transfer the resultant solid to a Büchner funnel using a minimum quantity of dichloroethane. Even so the amount of recovered material was low (*ca.* 17%) but it was probably much purer than the analogue from toluene. This problem of isolation was even more serious with some of the alkylbenzenes studied later and eventually attempts to isolate the organometallic compounds were abandoned. The only arenes besides toluene to precipitate the thalliated species were *o*- and *m*-xylene.

The question of the fate of the rest of the starting material remains. In experiments 1 and 5 no other products were detected by g.l.c. However, in the other experiments in Table 1 extra volatile compounds were present. The most important of these is toluene.

we subjected a product from experiment 7 to McKillop's iododethallation procedure<sup>2</sup> without nitrating it. None of our g.l.c. columns were of sufficient resolution to enable the isomer ratio of the iodotoluenes to be determined but the total yield of these compounds (41%) was in agreement with the yield of nitrotoluenes obtained in experiment 7.

(ii) Direct nitration of the aromatic ring can occur without displacement of the thallium substituent (*cf.* ref. 14). The deactivating effect of the nitro-group might then substantially reduce the rate of nitrodethallation. Any arylthallium compound remaining, if it were not lost in work-up, would be too involatile to be detected by g.l.c. We therefore subjected a reaction product from experiment 8 to the iododethallation procedure<sup>2</sup> which is apparently successful even in the presence of electron-withdrawing substituents.<sup>2,3,14</sup> No 1-ethyl-4-iodo-2-nitrobenzene was obtained nor were there any other peaks in this region of the g.l.c. trace. We conclude therefore that the thallium group is removed completely on nitration.

(iii) Alkylbenzenes can react with thallium(III) in other ways than by metallation. The continual regeneration of the alkylbenzene during the thermodynamic equilibration process will greatly increase the likelihood of its being consumed in these alternative

processes thus leading to much lower yields of nitroarenes after reflux. In the case of ethylbenzene, where the accountability under kinetic control suggests the competitive process(es) would have to proceed at a rate comparable to metallation, almost no arylthallium compound survives heating.

In many of its reactions thallium(III) is intermediate in its properties between mercury(II) and lead(IV).<sup>17,18</sup> With lead(IV) it has been demonstrated that electron transfer processes can compete with metallation of the aromatic ring.<sup>12,19</sup> Whilst there have been no reports of products derived by electron transfer in thallium(III) systems, radical cations have been detected by e.s.r. spectroscopy at low temperatures when thallium(III) trifluoroacetate is added to neat alkylbenzenes and can even be formed under conditions similar to ours with certain substrates.<sup>20</sup> An alkylbenzene radical cation would be expected either to lose a proton from the side-chain giving ultimately a benzyl cation or to undergo nucleophilic attack at a ring position<sup>19,21</sup> with, in trifluoroacetic acid, competition occurring between acid and surplus arene for the electron-deficient radical cation. In the case of toluene reaction with the acid predominates but, if xylenes are used, biaryls are the major product.

The by-products obtained from toluene could be derived from radical cations but they are not present in sufficient yield to suggest that radical cation formation is ever a significant competitor to metallation. Interestingly, on mixing an arene with a solution of the oxidant a colour characteristic of the particular arene is immediately formed and then disappears within a few minutes. We are tempted to suggest that this is due to the transient radical cation or some species derived therefrom, though Kochi has attributed the colour to a charge transfer species.<sup>20</sup> It is difficult to see in what other way thallium(III) and an aromatic hydrocarbon can interact though, for reasons suggested later, we suspect that a hydrogen atom in a benzylic position could be implicated.

One complication to studying nitrodehallation is that nitrogen dioxide will react directly with any residual arene.<sup>16</sup> However, this latter process is relatively slow compared with the former. The result of passing nitrogen dioxide into a solution of ethylbenzene for 15 min is given in experiment 11 where only a fraction of the hydrocarbon is nitrated and the isomer distribution is very similar to that of experiment 9. It is probable therefore that most, if not all, the nitro-products in this latter experiment arise from the hydrocarbon rather than the organometallic intermediate.

\* The small amount of benzyl methyl ketone produced probably results from the oxidation of a trace of  $\alpha$ -methylstyrene.<sup>22</sup>

<sup>17</sup> R. J. Ouellette, in 'Oxidation in Organic Chemistry,' part B, ed. W. S. Trahanovsky, Academic Press, New York, 1973, ch. 3.

<sup>18</sup> H.-J. Kabbe, *Annalen*, 1962, **656**, 204; A. Lethbridge, R. O. C. Norman, and C. B. Thomas, *J.C.S. Perkin I*, 1974, 1929; A. Lethbridge, R. O. C. Norman, W. J. E. Parr, and C. B. Thomas, *ibid.*, submitted for publication.

Similarly, after heating, some of the nitrotoluenes probably arise directly from toluene. This competitive route to nitroarenes following reflux will be in part responsible for the discrepancy between our isomer distribution and that reported earlier<sup>3</sup> under thermodynamically controlled conditions.

The results from the substitution of two more alkylbenzenes are also included in Table 2. Compared with ethylbenzene, cumene gives a somewhat lower yield of nitrated products and prolonged heating leads to the destruction of the majority of the arylthallium(III) carboxylates.\* However, *t*-butylbenzene is more closely analogous to toluene with the reflux treatment leading to a substantial yield of the *meta*-nitro-derivative. These facts are consistent with competitive removal of the thallium(III) in some way other than by metallation, ethylbenzene and cumene reacting more effectively than toluene and *t*-butylbenzene. The only reaction we can envisage which might fit the sequence cumene > ethylbenzene > toluene ~ *t*-butylbenzene is one involving loss of a hydrogen atom from the benzylic position, the stability of the resultant radicals falling in this order; *t*-butylbenzene would, of course, be precluded from reacting in this way. Despite the large numbers of investigations on thallium(III) oxidations during recent years,<sup>1,17</sup> there are no reports of the oxidant effecting simple radical reactions, though Kochi's results<sup>20</sup> suggest that thallium(II) could have a discrete existence. In addition a simple one-electron process would be expected to give benzylic products but, except for the minor products in experiment 7, none were detected and we have no grounds for suggesting that a benzylic thallium compound, too involatile for g.l.c. detection and stable to nitrogen dioxide, is formed.

The selectivity of polysubstituted alkylbenzenes was also briefly examined. *p*-Xylene gave an 83% yield of 1,4-dimethyl-2-nitrobenzene and *m*-xylene too produced a single isomer, 1,3-dimethyl-4-nitrobenzene (90%), suggesting that it is extremely difficult for the bulky electrophile to enter between two methyl groups. Treatment of *o*-xylene gave predominantly 1,2-dimethyl-4-nitrobenzene (84%) together with a small amount (4%) of the 3-nitro-isomer. However, mesitylene behaves less satisfactorily: the usual procedure led to a 27% yield of nitromesitylene. Thallation would be expected to be slow due to steric interaction between adjacent methyl substituents and the incoming thallium group but a longer reaction time (56 h) only reduced the yield of nitromesitylene to 14%. Neither bimesityl nor 2,3',4,5',6-pentamethyldiphenylmethane, the products of radical cation generation from mesitylene,<sup>19,21</sup> could be detected. The only other volatile products present (in

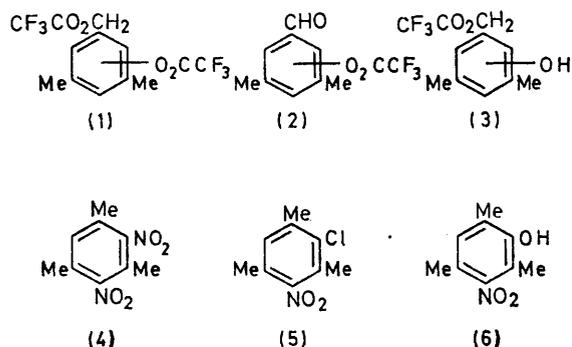
<sup>19</sup> R. O. C. Norman and C. B. Thomas, *J. Chem. Soc. (B)*, 1970, 421; R. O. C. Norman, C. B. Thomas, and J. S. Willson, *J.C.S. Perkin I*, 1973, 325.

<sup>20</sup> I. H. Elson and J. K. Kochi, *J. Amer. Chem. Soc.*, 1973, **95**, 5060.

<sup>21</sup> R. O. C. Norman, C. B. Thomas, and P. J. Ward, *J.C.S. Perkin I*, 1973, 2914.

<sup>22</sup> A. McKillop, J. D. Hunt, F. Kienzle, E. Bigham, and E. C. Taylor, *J. Amer. Chem. Soc.*, 1973, **95**, 3635.

yields <2%) were tentatively identified, on the basis of their g.l.c.-mass spectra, as the trifluoroacetates (1)–(3), dinitromesitylene (4), and chloronitromesitylene (5).<sup>\*</sup> Differential thermal mass spectrometry of a base extract of the crude product showed nitromesityl (6)



and a lesser quantity of a nitroxyleneol to be formed as well.

We next examined aromatic substrates other than alkylbenzenes (Table 3). Anisole was converted into

TABLE 3

Products from the reaction of nitrogen dioxide with some thalliated aromatic substrates in trifluoroacetic acid

Substrate	Mono-nitroarene (%)	<i>o</i> : <i>m</i> : <i>p</i> Ratio	Other products (%)
PhOMe	69	21 : 0 : 79	
PhOMe <sup>a</sup>	77	7 : 0 : 93	
PhPh	50	11 : 0 : 89	4,4'-Dinitro-biphenyl
PhCl	57	33 : — : 67 <sup>b</sup>	PhCl ( <i>ca.</i> 15)
PhBr	46	38 : — : 62 <sup>b</sup>	PhBr ( <i>ca.</i> 12)

<sup>a</sup> At  $-20^\circ$ . <sup>b</sup> It proved impossible to resolve completely *m*-halogenonitrobenzene from the *p*-isomer: mass spectrometry suggested that the amount of the *meta*-compound was negligible.

nitroanisoles, the yield and the selectivity being markedly better at low temperatures (*cf.* ref. 2). Biphenyl showed a high specificity but the synthetic utility of the method is reduced by the co-formation of 4,4'-dinitro-biphenyl. There will, of course, be no steric constraint to the introduction of another thallium group into the second aromatic ring and even if the original substituent is electron-withdrawing † the electrophile preferentially attacks the 2'- and 4'-positions.<sup>23</sup>

\* The origin of the chlorine is not clear but it may be similar to that in some lead(IV) oxidations.<sup>19</sup>

† It has been claimed that a  $\text{Ti}(\text{O}_2\text{CCF}_3)_2$  substituent is electron-withdrawing on the grounds that reaction of *p*-ethylphenylthallium(III) trifluoroacetate with nitric acid in acetic anhydride leads to 4-ethyl-3-nitrophenylthallium(III) trifluoroacetate.<sup>14</sup> However, ignoring any steric interaction which might be important in this system, this result only proves that the  $\text{Ti}(\text{O}_2\text{CCF}_3)_2$  group is less electron-donating than an ethyl group. We found that the reaction of benzene with 2 equiv. thallium(III) trifluoroacetate followed by treatment with nitrogen dioxide resulted in the formation solely of nitrobenzene (69% yield), suggesting that monothallation deactivates the aromatic ring sufficiently to inhibit substitution by a second thallium group.

The two halogenobenzenes investigated behave somewhat anomalously: residual aromatic substrate was present irrespective of whether an excess of thallium(III) or a longer reaction time were employed. This suggests that an equilibrium is established between reactants and the organometallic intermediate. The selectivities too were unexpected: a disproportionately high yield of the *ortho*-isomer was obtained, in agreement with the results reported in other systems.<sup>2</sup> The isomer-distribution is similar to that resulting from direct nitration of the halogenobenzenes<sup>16,24</sup> but the extent of conversion is far too high to result, in other than small part, from this route. It would appear that, in comparison with other substituents, the halogen atom favours the electrophile entering the *ortho*-position but prior complexation of the thallium atom to the halogen after the manner of oxygenated side-chains<sup>3</sup> seems unlikely particularly since anisole, which might be expected to favour this sort of interaction, behaves normally.

Our attempts to *ortho*-nitrate suitable substrates were unsuccessful. Methyl benzoate was recovered in 77% yield after 48 h thalliation followed by nitration, and some methanol was detected. Presumably hydrolysis occurs to a limited extent either in the supposedly anhydrous solvent or during work-up. A trace (<0.2%) of a methyl nitrobenzoate was obtained but its retention time and its mass spectrum were consistent with the *meta*- rather than the *ortho*-compound.

Nor did benzyl alcohol, whose side-chain should cause negligible deactivation of the aromatic ring to electrophilic substitution, behave as expected. Three peaks, in addition to starting material, were detected by g.l.c., the most abundant of which was benzyl trifluoroacetate ‡ (42%). Benzaldehyde (1.9%) and a trace of an unidentified product were also present. None of the nitrobenzyl alcohols were produced. We were able to demonstrate that a product was obtained, by using the iodination procedure, whose g.l.c.-mass spectrum was consistent with its being an iodobenzyl alcohol (major ions at *m/e* 234, 128, 127, 107, 79, and 77) but in the absence of authentic samples we could not confirm which isomer it was nor measure its yield. Benzyl trifluoroacetate (4%), benzaldehyde (0.8%), and residual benzyl alcohol (17%) were also present. We suspect that it may be the trifluoroacetate rather than the alcohol which is thalliated initially, the iodobenzyl alcohol being generated on work-up.

Reactions with benzyl methyl ether and with methyl phenethyl ether were even less successful: not only was there no residual starting material but volatile products were almost non-existent. From the former, benzyl alcohol, benzyl trifluoroacetate, methyl benzoate, benzaldehyde, and methyl *o*-nitrobenzyl ether were formed,

‡ A control experiment showed that dissolving benzyl alcohol in trifluoroacetic acid for 10 min resulted, after work-up, in a mixture of benzyl trifluoroacetate (34%) and the alcohol (38%) and that some of the latter arose from hydrolysis during work-up.

<sup>23</sup> Y. Mizuno and O. Simamura, *J. Chem. Soc.*, 1958, 3875.

<sup>24</sup> M. L. Bird and C. K. Ingold, *J. Chem. Soc.*, 1938, 918.

but none of them exceeded 0.2% in yield. From methyl phenethyl ether the crude product gave no g.l.c. peaks but a white solid, apparently inorganic, slowly precipitated out.

We believe that this failure of *ortho*-orientation to occur under our conditions stems from the fact that the thallium(III) is preferentially delivered to the *ortho*-position through initial co-ordination to an oxygen atom in the side-chain<sup>3</sup> and that this interaction persists in the thalliated intermediate making it harder to displace the metal substituent with an electrophile. This problem must be unimportant under the conditions for iodination. In support of this a solid, isolated from thalliation of benzyl methyl ether, was shown unambiguously by n.m.r. spectroscopy to contain a metal substituent adjacent to the methoxymethyl group. However, on treatment with nitrogen dioxide, it failed to yield any methyl nitrobenzyl ether. (Interestingly the n.m.r. spectrum showed the metal atom to couple not only to the aromatic but also to the benzylic protons.)

We thus have a useful method for selectively nitrating aromatic substrates. In comparison with other syntheses involving thalliation, it suffers from the drawbacks that *ortho*-orientation appears not to be practical and that the conditions necessary to effect *meta*-orientation are such that only a low conversion can be achieved. Nevertheless, the method possesses considerable potential for the synthesis of some nitro(alkyl)-benzenes and related compounds.

#### EXPERIMENTAL

<sup>1</sup>H N.m.r. spectra were measured for solutions in deuteriochloroform on a Perkin-Elmer R 10 or a Varian A60A 60 MHz spectrometer. G.l.c. was carried out on a Pye 104 instrument using 6 ft ×  $\frac{1}{4}$  in columns packed with 10% diethylene glycol adipate (DEGA), 10% Carbowax 20 M, or 10% Apiezon L, each coated on Celite. For quantitative work the DEGA and Carbowax columns were employed with an internal standard. A hydrogen flame ionisation detector gave a linear response, the relationship between the quantity of a material injected and its peak area being established by the analysis of synthetic mixtures. Preparative g.l.c. was on a Pye 105 instrument using a 6 ft ×  $\frac{3}{8}$  in 10% DEGA column. Mass spectrometry was on an A.E.I. MS12 spectrometer coupled *via* a stainless steel capillary to a gas chromatograph. M.p.s were taken on a Kofler micro-hot stage.

**Materials.**—Thallium(III) trifluoroacetate (Emanuel), trifluoroacetic acid (Fisons laboratory reagent), and nitrogen dioxide (Matheson) were used without further purification.

\* This was found to be generally true of those substrates for which all three isomers were available. The correction factors of isomers were in any case very similar.

† The gas inlet tube must not be fitted with a glass frit, since a white solid which will block the frit precipitates out during the nitration. This precipitate is believed to be a nitronium salt: on treatment with a drop of water it dissolves with evolution of nitrogen dioxide.

Most of the aromatic substrates were at hand within this Department and many of the nitro-products were available either commercially or from previous studies.<sup>25</sup> In a few cases authentic samples of *meta*-isomers could not be obtained; these were assigned on the basis of g.l.c.–mass spectrometry and expected retention time, and correction factors were assumed intermediate between those of the *ortho*- and *para*-isomers.\* Methyl phenethyl ether<sup>26</sup> and 1-ethyl-4-iodo-2-nitrobenzene<sup>27</sup> were prepared by standard methods.

*t*-Butylbenzene was nitrated by the method of Shine and Chamness.<sup>28</sup> The resultant mixture of *t*-butylnitrobenzenes was distilled and from the distillate were separated by preparative g.l.c., *o*-*t*-butylnitrobenzene, b.p. 119–120° at 13 mmHg (lit.,<sup>29</sup> 114.5° at 10 mmHg), and *p*-*t*-butylnitrobenzene, b.p. 112–114° at 2 mmHg (lit.,<sup>28</sup> 133° at 10 mmHg).

**Thalliation.**—The method employed for thalliation was based on that of McKillop *et al.*<sup>2</sup> To a solution of thallium(III) trifluoroacetate (0.00186 mol) in trifluoroacetic acid (2.5 ml) was added an equivalent amount of the aromatic substrate in trifluoroacetic acid (2.5 ml) and the mixture stirred at room temperature for the appropriate period of time (usually 1 h). In some cases the arylthallium product separated out but usually it remained in solution: it was isolated in a few instances. That derived from toluene was filtered off and washed several times with small quantities of 1,2-dichloroethane and dried: *p*-tolylthallium(III) trifluoroacetate had m.p. 165–185° (decomp.) (lit.,<sup>2</sup> 174–190°). Soluble organometallic compounds were isolated by removal of the solvent followed by a rapid washing out of the reaction vessel with a minimum of 1,2-dichloroethane. Of these only 2-methoxymethylphenylthallium(III) trifluoroacetate was fully characterised. This had m.p. 92–94° (decomp.) (lit.,<sup>2</sup> 160–163°);  $\tau$  (CF<sub>3</sub>CO<sub>2</sub>H) 2.39 (m,  $J_{\text{TH}}$  ca. 460 Hz, 3- and 5-H), 2.48 (dt,  $J'_{\text{TH}}$  141,  $J''$  7 Hz, 4-H), 2.65 (dd,  $J'''_{\text{TH}}$  554,  $J''''$  8 Hz, 6-H), 5.20 (d,  $J''''_{\text{TH}}$  115 Hz, CH<sub>2</sub>), and 6.20 (s, OCH<sub>3</sub>).

In experiments designed to test thermodynamic control the crude thalliation mixture, after stirring at room temperature for 1 h, was refluxed for the requisite length of time.

**Nitration.**—Nitrogen dioxide was bubbled through the solution obtained on thalliation usually for 15 min.† The solution was poured into water, and the ether extracts were washed with sodium carbonate solution and dried (MgSO<sub>4</sub>). The solvent was removed and the product analysed by g.l.c.–mass spectrometry. In a few instances previously isolated arylthallium compounds were employed. Then the arylthallium compound (0.00186 mol) was dissolved or suspended in trifluoroacetic acid (5 ml) and treated as above.

**Iodination.**—The iodination procedure employed was method A of McKillop *et al.*<sup>2</sup>

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<sup>27</sup> A. Kövendi and M. Kircz, *Chem. Ber.*, 1964, **97**, 1896.

<sup>28</sup> H. J. Shine and J. T. Chamness, *J. Org. Chem.*, 1967, **32**, 901.

<sup>29</sup> 'Heilbron's Dictionary of Organic Compounds,' Eyre and Spottiswoode, London, 1965.