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THALLIUM IN ORGANIC SYNTHESIS. IX. FACILE THALLATION OF AROMATIC COMPOUNDS WITH THALLIUM(III) TRIFLUOROACETATE (1,2)

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Electrophilic mercuration of aromatic substrates has been the subject of much research since Dimroth (4) first discovered that treatment with mercury(II) compounds resulted in the formation of C-Hg bonds. It is surprising, however, that few other metal salts have been studied in detail with respect to their ability to effect electrophilic metallation. The synthesis of organothallium compounds by direct formation of C-Tl bonds (thallation) appears to be one of the least investigated of such reactions.

The first successful thallation of an aromatic substrate was described by Gilman and Abbott, (5) who obtained di-4-dibenzofurylthallium chloride in 9% yield by treatment of dibenzofuran with thallium(III) chloride at 165°. Glushkova and Kocheshkov (6) have since shown that the reaction of thallium(III) tri-isobutyrate with an excess of benzene or activated aromatic substrate as solvent at 95-115° leads to arylthallium di-isobutyrates. The range of aromatic substrates which can be effectively thallated by this technique, however, is severely limited by the poor electrophilicity of thallium(III) tri-isobutyrate. Furthermore its utility is also restricted by the necessity of using an excess of the aromatic substrate as solvent, and by the moderate yields obtained. Perhaps as a consequence, no synthetic applications of thallation have ever been described.

We report the preparation of thallium(III) trifluoroacetate (TTFA) and its use as a reagent for the thallation of aromatic compounds. TTFA is conveniently prepared by heating under reflux a suspension of thallium(III) oxide (50 g) in 250 ml of trifluoroacetic acid, with stirring, for 96 hrs; the reaction mixture is protected from light. Filtration to remove a small amount of insoluble solid gives a clear, colourless solution of TTFA in TFA (0.88 molar). Solid TTFA, obtained by evaporation of the solvent under reduced pressure, is a colourless, crystalline water-sensitive solid which decomposes without melting above 100°. Both the solution of TTFA in TFA and the solid salt can be stored at room temperature in stoppered flasks protected from light for long periods without appreciable decomposition.

A solution of TTFA in TFA constitutes a powerful reaction mixture for the direct thallation of aromatic compounds (eq. 1). Reaction with substrates

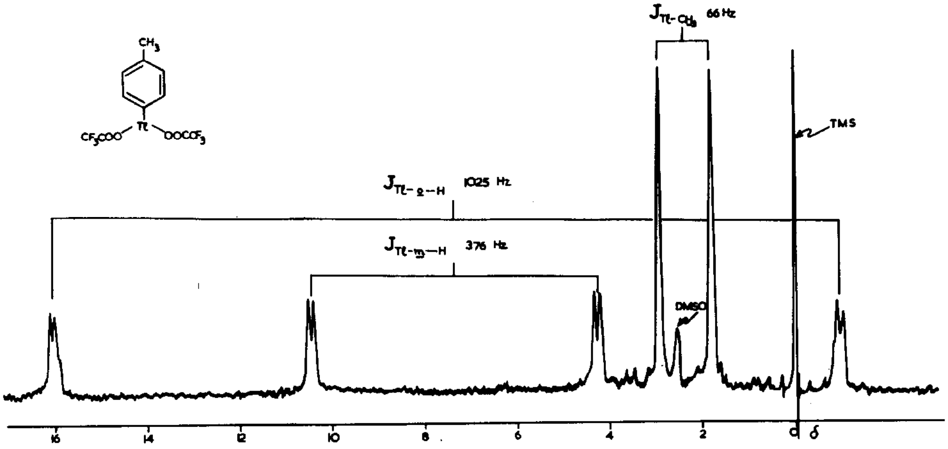
$$\mathrm{Ar{-}H} + \mathrm{Tl(OCOCF_3)_3} \longrightarrow \mathrm{ArTl(OCOCF_3)_2} + \mathrm{CF_3COOH} \qquad \text{(eq. 1)}$$

which are activated towards electrophilic substitution is <u>generally complete within a few minutes at room temperature</u>. Thallation of mildly deactivated substrates such as the halobenzenes requires longer reaction times at room temperature, or 30 minutes at reflux temperature (73°), and deactivated substrates such as benzoic acid and α,α,α-trifluorotoluene are thallated after 21 and 98 hrs reflux respectively. For acid-sensitive substrates (e.g. thiophenes), solid TTFA in acetonitrile are the conditions of choice. In the majority of examples studied, the arylthallium di-trifluoroacetates formed crystallize from the reaction mixture and are isolated by simple filtration. They are stable, colourless, crystalline solids which, in general, are soluble in methanol, ethanol, glyme, acetonitrile, tetrahydrofuran and DMSO. Most were analytically pure as isolated. Representative $\mathrm{ArTl(OCOCF_3)_2}$ compounds formed were (Ar, % yield, mp °C) (7): C_6H_5, 96, 184-189; <u>p</u>-$CH_3C_6H_4$-, 75, 205-208; 3,4-$(CH_3)_2C_6H_3$-, 79, 184-190; 2,4,6-$(CH_3)_3C_6H_2$-, 94, 155-157; <u>o</u>-$COOHC_6H_4$-, 79, 247-248; <u>p</u>-ClC_6H_4-, 85, 159; 2-thienyl-, 82, 194-196.

Only a small amount of <u>ortho</u> substituted products was observed with those substrates with <u>ortho</u>-<u>para</u> directing substituents; the overwhelming preference for <u>para</u> substitution may be associated with the steric bulk of thallium. It is noteworthy that benzoic acid gave 95% <u>ortho</u> substitution. Metallation <u>ortho</u>

to an aromatic carboxyl group is not without precedent (8), but the percentage of *ortho* substitution in the present case is most unusual. We suggest that thallation of benzoic acid occurs by initial formation of a mixed thallium(III) salt $\left[C_6H_5COOTl(OCOCF_3)_2\right]$ followed by *intra*molecular delivery of thallium to the *ortho* position.

Nmr studies on $RTlX_2$ compounds have shown (9) that, in benzene and substituted benzenes, Tl-H coupling constants are ~130 times greater than the corresponding H-H coupling constants. As a consequence, examination of the well-defined nmr spectra of the arylthallium di-trifluoroacetates proved to be an invaluable aid to structural elucidation, and unequivocally established the position of thallation (confirmed by subsequent iodination with aqueous potassium iodide (10)). *p*-Tolylthallium di-trifluoroacetate, for example, showed (Figure 1) two symmetrical *ortho* protons ($J_{Tl-\underline{o}-H}$1025 Hz) and two symmetrical *meta* protons ($J_{Tl-\underline{m}-H}$376 Hz); splitting of the methyl group (66 Hz) was in agreement with the predicted value (9).



NMR SPECTRUM OF *p*-TOLYLTHALLIUM DI-TRIFLUOROACETATE IN DMSO-d_6 SOLUTION AT 60 MHz

Treatment of aqueous ethanol solutions of $ArTl(OCOCF_3)_2$ compounds with inorganic anions provides a wide range of $ArTlX_2$ compounds, which are effective intermediates for the formation of substituted aromatic compounds (ArX) by subsequent cleavage of the C-Tl bond. These reactions will be described in subsequent papers (10). TTFA, as the reagent of choice for the preparation of these highly versatile and reactive intermediate arylthallium compounds, makes possible for the first time their practical utilization in organic synthesis.

References

1. We gratefully acknowledge the financial support of this work by the Smith Kline and French Laboratories, Philadelphia, Pa.
2. Part VIII: A.McKillop, D. Bromley and E.C.Taylor, Tetrahedron Letters, in press.
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. O. Dimroth, Ber., 32, 758 (1899).
5. H. Gilman and R.K. Abbott, Jr., J. Amer. Chem. Soc., 65, 122 (1943).
6. (a) V.P. Glushkova and K.A. Kocheshkov, Izvest. Akad. Nauk SSSR, Otd.Khim. Nauk, Eng. Trans., 1211 (1957); (b) A.N. Nesmeyanov and A. Sokolik, Methods of Elemento-Organic Chemistry. Vol. 1. The Organic Compounds of Boron, Aluminium, Gallium, Indium and Thallium, North Holland Publishing Company, Amsterdam, 1967, pp. 571-574.
7. It should be noted that melting points of these compounds should not be used as a reliable criterion of purity, since they vary erratically according to the rate of heating, amount of sample, degree of compactness and crystal size.
8. L.G. Makarova and A.N. Nesmeyanov, Methods of Elemento-Organic Chemistry. Vol. 4. The Organic Compounds of Mercury, North Holland Publishing Company, Amsterdam, 1967, pp. 105-107.
9. J.P. Maher and D. F. Evans, J. Chem. Soc., 637 (1965).
10. For the use of arylthallium di-trifluoroacetates as intermediates in the synthesis of aryl iodides, see A. McKillop, J.S. Fowler, M.J. Zelesko, J.D. Hunt, E.C. Taylor and G. McGillivray, Tetrahedron Letters, following communication.