Thallium in Organic Synthesis. 45. Synthesis of Aromatic Fluorides[1]

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Many useful procedures have been described for the direct monochlorination, -bromination, and -iodination of aromatic compounds;[2–4] there is, however, no general, practical method available for controlled monofluorination. Procedures based on the use of reagents such as elemental fluorine,[5–9] interhalogen halides,[6,10,11] high-valency metal fluorides,[6,12] or xenon difluoride[13,14] are often difficult and dangerous to carry out, usually require specialized apparatus, and usually give complex mixtures of products. Electrolytic methods are equally unattractive.[6,15] The only two generally useful methods for the introduction of fluorine into an aromatic nucleus are nucleophilic displacement of activated halogen and alkoxy groups[16,17] and the Balz–Schiemann reaction.[18–20]

Arylthallium(III) compounds of the type $\mathrm{ArTlX_2}$ are attractive and versatile intermediates for the regiospecific synthesis of a wide range of functionalized aromatic compounds,[21–24] including chlorides,[25] bromides,[25,26] and iodides.[25,27] We now describe the preparation of aromatic fluorides from arylthallium(III) difluorides which are readily available in excellent yield by the simple, two-step procedure summarized in eq 1.[28]

$$\mathrm{ArH} \xrightarrow{\mathrm{TTFA}} \mathrm{ArTl(OCOCF_3)_2} \xrightarrow{\mathrm{KF}} \mathrm{ArTlF_2} \tag{1}$$

We began our investigation by briefly examining the thermal and photochemical stability of arylthallium(III) difluorides. Certain $\mathrm{ArTlX_2}$ compounds are known to decompose thermally as outlined in eq 2;

$$\begin{gathered}\mathrm{ArTlX_2} \xrightarrow{\Delta} \mathrm{ArX} + \mathrm{TlX} \\ \mathrm{X} = \mathrm{I, Br, CN, SCN}\end{gathered} \tag{2}$$

the temperatures necessary, however, vary from approximately 0 °C for X = I to 228 °C for X = CN.[29] Arylthallium(III) difluorides slowly decompose when heated above 200 °C giving the corresponding hydrocarbons in modest yields; pyrolysis of 4-ethylphenylthallium(III) difluoride at 250–300 °C, for example, gave ethylbenzene (41%) as the only identifiable product. The photolysis of other arylthallium(III) compounds yields aryl nitriles,[22,30] aryl thiocyanates,[31] and biphenyls.[32] However, photolysis of phenylthallium(III) difluoride in aqueous potassium fluoride solution at 253.7 nm did not yield fluorobenzene, and phenylthallium(III) difluoride was recovered unchanged. Neither approach was studied further.

We then examined methods for the preparation of arylthallium(III) bis(tetrafluoroborates), $\mathrm{ArTl(BF_4)_2}$, in the expectation that these compounds would decompose in the desired manner, but at moderate temperatures. There are three obvious methods for the preparation of arylthallium(III) bis(tetrafluoroborates): (a) direct thallation of aromatic compounds with $\mathrm{Tl(BF_4)_3}$; (b) treatment of arylthallium(III) bis(trifluoroacetates) with sodium tetrafluoroborate; and (c) reaction of arylthallium(III) difluorides with boron trifluoride. We have been unable to investigate method a thus far as all attempts to prepare the requisite thallating reagent failed.

Table I. Preparation of Aromatic Fluorides

$$\mathrm{ArH} \xrightarrow{\mathrm{TTFA}} \mathrm{ArTl(OCOCF_3)_2} \xrightarrow{\mathrm{KF}} \mathrm{ArTlF_2} \xrightarrow{\mathrm{BF_3}} \mathrm{ArF}$$

Ar	Yield, %[a]	Bp, °C
4-$\mathrm{CH_3C_6H_4}$	50	115–120
4-$\mathrm{C_2H_5C_6H_4}$	48	140–141
2,4-$\mathrm{(CH_3)_2C_6H_3}$	67	140–147
2,5-$\mathrm{(CH_3)_2C_6H_3}$	54	140–147
2,4,6-$\mathrm{(CH_3)_3C_6H_2}$	71	72–80 (32 mm)
4-$\mathrm{C_6H_5C_6H_4}$	45	mp 59–61

[a] Overall yield from ArH to ArF; all yields refer to isolated, distilled, or recrystallized material. No attempt was made to optimize yields.

Method b was unsuccessful; arylthallium(III) bis(trifluoroacetates) do not undergo ligand exchange effectively when treated with aqueous ethanolic solutions of sodium tetrafluoroborate. Investigation of method c, however, led to the development of a convenient procedure for the direct conversion of certain arylthallium(III) difluorides into the corresponding aromatic fluorides.

Passage of boron trifluoride through a cold, stirred suspension of the arylthallium(III) difluoride in either petroleum ether or cyclohexane followed by warming of the reaction mixture gave the aromatic fluoride directly; experimental data for a number of conversions are listed in Table I. The yields of aromatic fluorides prepared by this simple, three-step procedure are moderate and roughly comparable to those reported for the preparation of the same compounds from aryl amines by the Balz–Schiemann reaction. The latter process, while more complicated, is more general than the arylthallium(III) difluoride route which is limited to aromatic substrates which contain neither powerful electron-withdrawing groups nor oxygen or amino substituents. Arylthallium(III) difluorides which do contain such substituent groups give negligibly low yields of aryl fluorides. It should be noted, however, that the arylthallium(III) difluoride route avoids the use of aryl amines and their nitro precursors, many of which are potent carcinogens.

We have not studied the mechanism of the reaction between arylthallium(III) difluorides and boron trifluoride, but formation and subsequent decomposition of arylthallium(III) bis(tetrafluoroborates) is a reasonable hypothesis. Many inorganic fluorides react readily with boron trifluoride to give tetrafluoroborate salts,[33] and arylthallium(III) difluorides, which are known to be ionic,[28] would be expected to react analogously.

Experimental Section

General Procedure for the Preparation of Aromatic Fluorides. Dry, finely powdered arylthallium(III) difluoride (0.05 mol)[28] was added to 150 ml of reagent-grade cyclohexane contained in a 500 ml, three-necked Morton flask fitted with a gas inlet tube, a reflux condenser protected by a drying tube, and a mechanical stirrer with a bearing. The mixture was stirred vigorously and cooled in an ice bath, and boron trifluoride gas was bubbled through the suspension for 1 h (effluent boron trifluoride was trapped in dilute ammonium hydroxide). The boron trifluoride inlet was then removed, and the mixture was heated under reflux for 2 h. The cooled reaction mixture was filtered to remove insoluble salts and the filter cake washed with cyclohexane. Solvent was removed by careful distillation at atmospheric pressure through a 30 × 1.5 cm Vigreux column and the residual oil or solid distilled or recrystallized; experimental data are given in Table I.

Registry No.—ArH (Ar = 4-$\mathrm{CH_3C_6H_4}$), 108-88-3; ArH (Ar = 4-$\mathrm{C_2H_5C_6H_4}$), 100-41-4; ArH (Ar = 2,4-$\mathrm{(CH_3)_2C_6H_3}$), 108-38-3; ArH (Ar = 2,5-$\mathrm{(CH_3)_2C_6H_3}$), 106-42-3; ArH (Ar = 2,4,6-$\mathrm{(CH_3)_3C_6H_2}$), 108-67-8; ArH (Ar = 4-$\mathrm{C_6H_5C_6H_4}$), 92-52-4; $\mathrm{ArTlF_2}$ (Ar = 4-$\mathrm{CH_3C_6H_4}$), 60705-27-3; $\mathrm{ArTlF_2}$ (Ar = 4-$\mathrm{C_2H_5C_6H_4}$), 60705-28-4; $\mathrm{ArTlF_2}$ (Ar =

$2,4\text{-}(CH_3)_2C_6H_3$), 27675-05-4; $ArTlF_2$ (Ar = $2,5\text{-}(CH_3)_2C_6H_3$), 29396-64-3; $ArTlF_2$ (Ar = $2,4,6\text{-}(CH_3)_3C_6H_2$), 27675-11-2; $ArTlF_2$ (Ar = $4\text{-}C_6H_5C_6H_4$), 60705-29-5; ArF (Ar = $4\text{-}CH_3C_6H_4$), 352-32-9; ArF (Ar = $4\text{-}C_2H_5C_6H_4$), 459-47-2; ArF (Ar = $2,4\text{-}(CH_3)_2C_6H_3$), 452-65-3; ArF (Ar = $2,5\text{-}(CH_3)_2C_6H_3$), 696-01-5; ArF (Ar = $2,4,6\text{-}(CH_3)_3C_6H_2$), 392-69-8; ArF (Ar = $4\text{-}C_6H_5C_6H_4$), 324-74-3.

References and Notes

(1) (a) For the previous paper in this series, see E. C. Taylor, C.-S. Chiang, A. McKillop, and J. F. White, *J. Am. Chem. Soc.*, **98**, 6750 (1976). (b) We are indebted to the National Science Foundation (Grant MPS72-00427) and to Eli Lilly & Co. for support of this work. We also wish to express our gratitude to Dr. F. Scheidl and his staff at Hoffmann-La Roche, Inc., for the microanalysis of organothallium compounds.

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Highly Strained Ring Systems. Hydrolysis of Tricyclo[4.1.0.0^{2,7}]hept-3-yl Derivatives. Evidence for Participation of Bicyclo[1.1.0]butane Ring

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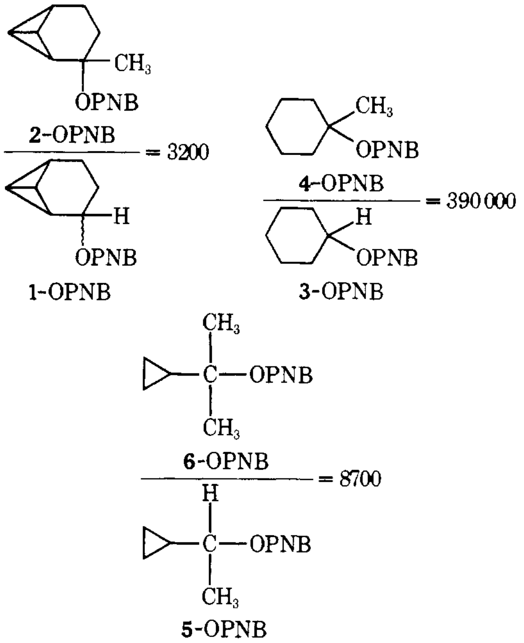
Preparation and studies of strained ring compounds have long intrigued organic chemists. Especially bicyclo[1.1.0]butane, which has the highest strain energy in bicyclic ring systems, has provided many interesting aspects as regards relationships between strain energy and reactivity.[1] However, only a few solvolytic studies with bicyclo[1.1.0]butane derivatives have been reported.[2] Thus, we synthesized tricyclo[4.1.0.0^{2,7}]hept-3-yl and 3-methyltricyclo[4.1.0.0^{2,7}]hept-3-yl p-nitrobenzoates (1-OPNB and 2-OPNB, respectively), and investigated their solvolytic reactivity in order to determine whether the tricyclo[4.1.0.0^{2,7}]hept-3-yl carbonium ion is a nonclassical ion by bicyclobutane ring participation or a classical ion associated with a relief of its ring strain.

Synthesis of the parent tricyclic ketone was carried out as described in the literature.[3] Treatment of this ketone with sodium borohydride or methyllithium gave alcohol 1-OH or 2-OH, wihch was converted to its corresponding p-nitrobenzoate 1-OPNB (mp 92.0–93.0 °C) or 2-OPNB (mp 79.5–80.5 °C) in the usual fashion.

The hydrolysis rates of 1-OPNB and 2-OPNB were measured in aqueous acetone mixtures by titrating the liberated p-nitrobenzoic acid displaying nice first-order behavior. The kinetic data are summarized in Table I with literature values for related compounds.

The p-nitrobenzoate (1-OPNB) undergoes hydrolysis at a rate 5×10^7 times faster than does cyclohexyl p-nitrobenzoate (3-OPNB), while the rate of 1-OPNB is essentially the same as that of methylcyclopropylcarbinyl p-nitrobenzoate (5-OPNB). It has been suggested that an α-CH_3/H rate ratio in solvolysis reaction of a charge-delocalized system would decrease when compared to that of a charge-localized system.[4] Thus a rate ratio of 2-OPNB/1-OPNB was compared to that of 4-OPNB/3-OPNB (a charge-localized system), as well as that of 6-OPNB/5-OPNB (a charge-delocalized system). As seen in Table I, the rate ratio of 2-OPNB/1-OPNB exhibits approximately the same as that of 6-OPNB/5-OPNB within a factor of 3, whereas it is about 100 times less than that of 4-OPNB/3-OPNB. Consequently, these findings suggest that the importance factor underlying the solvolytic reactivity of 1-OPNB is stabilization of its transition state by assisting in charge delocalization rather than by a relief of angle strain.



Hydrolysis of 1-OPNB gives rise to *anti*-7-norbornenol (7-OH) as an only alcoholic product (89%, GLC analysis).