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AROMATIC POLYFLUORO COMPOUNDS—XLII

NITRATION OF SOME POLYFLUORO-ARYL COMPOUNDS CONTAINING FUNCTIONAL GROUPS

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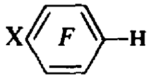
Abstract—Nitration of some derivatives of the tetrafluorobenzenes, polyfluorobiphenyls and tetrafluoro naphthalene are described.

PREVIOUSLY[2] we described the use of a boron trifluoride nitric acid complex as a nitrating agent for simple fluoroaromatic compounds. This present paper describes the use of this reagent for the nitration of aryl fluorides containing functional groups.

In our earlier work nitration of 1,2,4,5-tetrafluorobenzene was shown to occur only in very low yield. Therefore experiments have been carried out to try and improve the yields and also by using suitably substituted compounds to find out whether the low yields in this particular nitration are associated with the *para* orientation of the hydrogen atoms facilitating some decomposition of the molecule.

Nitration of 1,2,4,5-tetrafluorobenzene was achieved in only 18% yield compared with yields of 90–95% for nitration of the isomeric benzenes. No evidence for the formation of *para* benzoquinone was obtained, unlike nitrations previously carried out.[3] Therefore, to study the effect of replacement of one of the H atoms by a group other than fluorine (cf pentafluorobenzene nitrates under the same conditions in 90% yield) a series of compounds of the type  were prepared by standard methods[4] and nitrated. Thus, when X = OMe, OEt,[5] CH_3 or Br, the corresponding nitro compounds were obtained in 47, 62, 42 and 83% yields respectively, when X = CF_3 no nitration was obtained, in accord with classical predictions of the effect of the CF_3-group on nitration *para* to itself.

To determine whether any significance could be attached to the relatively low yields obtained, where possible, a number of isomers of the above compounds were nitrated essentially under the same conditions. Thus 5-bromo-1,2,3,4-tetrafluorobenzene, 1,2,3,4-tetrafluoro-5-iodobenzene and 1,2,3,4-tetrafluoro-5-methylbenzene[6] afforded the corresponding nitro compounds in 84, 79 and 82% yields respectively. In general the yields obtained with other isomers are higher than with *para* by a significant factor. It would therefore seem that some preferential decomposition of *para* isomers is taking place, since use of isomer ratios and rates of reaction obtained for nitration of the corresponding hydrocarbon leads to a prediction that compounds with substituents such as OMe *para* to the hydrogen favour substitution in the *para* position relative to pentafluorobenzene, whereas the opposite result is obtained in terms of isolated yield.

In an attempt to resolve this problem some kinetic studies were attempted using Olah's method[7] bearing in mind the criticism of this by other workers.[8] Thus various mixtures of pentafluorobenzene 1,2,3,4-1,2,3,5- and 1,2,4,5-tetrafluorobenzenes were made up and nitrated at 65°. The results obtained were rather poor since at the low conversions required by the method, side reactions became too significant. Rough calculations suggest that pentafluorobenzene is between 10^{-2} and 10^{-3} times less reactive than 1,2,3,4- and 1,2,3,5-tetrafluorobenzenes which in turn are 10^{-2}–10^{-3} less reactive than benzotrifluoride. 1,2,4,5-tetrafluorobenzene again was anomalous as no reaction took place as detectable by GLC.

As indicated previously,[2] dinitration of the tetrafluoronitrobenzenes proceeds only slowly, as would be expected from a consideration of the deactivating effect of the nitro group. However it was found possible by prolonged heating at 70° to dinitrate 1,2,3,5-tetrafluorobenzene directly in 21% yield, but better, nitration of 2,3,4,6-tetrafluoronitrobenzene yielded the dinitro compound under the same conditions in 60–70% yield. The dinitro compound is extremely susceptible to nucleophilic attack[9] and should be treated with caution since reaction with skin tissue is also rapid and the effects of prolonged exposure of the skin to this dinitro compound are unknown.

Dinitration of 2,3,4,5-tetrafluoronitrobenzene has so far been impossible but a route to the dinitro compound is available by oxidation of the 2,3,4,5-tetrafluoronitraniline.[10] Nitration of 2,3,4,5-tetrafluoroacetanilide proceed rapidly and on hydrolysis afforded the nitraniline free from isomers.

Mono and dinitration of 2*H*,2′*H*-octafluorobiphenyl proceeded rapidly to either the mono or dinitro product in good yield. These two compounds clearly have potential as precursors of some interesting heterocyclic compounds.

Nitration of 1,2,3,4-tetrafluoronaphthalene afforded a compound identified as 1,2,3,4-tetrafluoro-5,7-dinitronaphthalene.

This is the orientation expected on the basis of Wheland type intermediates and it has further been shown that nitration with the usual nitrating mixture of sulphuric/nitric acids affords mainly the 5-nitrocompound[11]. Hexafluorobenzene reacts very slowly with the nitrating mixture to yield a small quantity of tetrafluror-*p*-benzoquinone as well as unreacted starting material.

Thus nitration with the BF_3/HNO_3 complex has been shown to be useful in the preparation of hitherto unattainable compounds.

EXPERIMENTAL

Nitration of 1,2,4,5-*tetrafluoronitrobenzene*. 1,2,4,5-Tetrafluoronitrobenzene (5·0 g) was added to a mixture of sulpholane (30 cc) and fuming nitric acid (2·1 cc) saturated with BF_3. The resulting soln was stirred and heated at 65° for 1–5 hr, when the mixture was cooled and poured onto ice. Steam distillation of the aqueous layer afforded a green oil (1·15 g) which was distilled *in vacuo* to yield 2,3,5,6-tetrafluoronitrobenzene (0·8 g) b.p. 76°/25 mm. (Found: C, 36·9; H, 1·0. $C_6H_4F_4NO_2$ requires: C, 36·9; H, 0·5%).

Nitration of bromo-2,3,5,6-*tetrafluorobenzene*. Bromo-2,3,5,6-tetrafluorobenzene (1·95 g) was added to a mixture of sulpholane (10 cc), fuming HNO_3 (1·5 cc) saturated with BF_3. The mixture was stirred at 65° for 2 hr. Working up as above gave a crystalline solid (2·2 g) sublimation at 80°/25 mm afforded 4-bromo-2,3,5,6-tetrafluoronitrobenzene (1·9, 82%) m.p. 50–51°. (Found: C, 26·3; H, 0·3. $C_6BrF_4NO_2$ requires: C, 26·2; H, 0%). Oxidation of the corresponding aniline with peroxytrifluoroacetic gives the same compound.

Nitration of 2,3,5,6-*tetrafluoroanisole*. The anisole (2·2 g) was added to sulpholane (10 cc) fuming HNO_3 (1·4 cc) saturated with BF_3. After being stirred at 70° for 1·5 hr, the mixture was worked as above to yield a yellow oil (1·5 g) which crystallized on standing to give 2,3,5,6-tetrafluoro-4-nitro anisole m.p. 38–40° cited 39–40°[13] identical with a sample prepared from pentafluoronitrobenzene and sodium methoxide.

Nitration of 2,3,5,6-tetrafluorotoluene. The toluene (2·5 g) was added to sulpholane (10 cc) fuming HNO_3 (1·4 g) saturated with BF_3 at 0°. The mixture was heated to and stirred at 70° for 2·75 hr. Working up as described above followed by distillation of the crude product *in vacuo* gave 2,3,5,6-tetrafluoro-4-nitrotoluene (1·2 g, 4·2%) m.p. 33–34°. (Found: C, 40·0; H, 1·8. $C_7H_3F_4NO_2$ requires: C, 40·2; H, 1·4%).

Di-nitration of 1,2,3,5-tetrafluorobenzene. A mixture of 1,2,3,5-tetrafluorobenzene (6·3 g) sulpholane (20 cc) and fuming HNO_3 (6 cc) saturated with BF_3 was heated at 65° for 7 days. Working up as previously afforded, 1,2,3,5-tetrafluoro-4-nitrobenzene (1·7 g 20%) and tetrafluoro-*m*-dinitrobenzene (2·1 g 21%) b.p. 228–229°. (Found: C, 29·9; H, 0·4. $C_6F_4N_2O_4$ requires: C, 30; H, 0%). The dinitro compound reacts rapidly with the skin and should be treated with caution.

Nitration of 2,3,4,6-tetrafluoro-nitrobenzene. The nitrobenzene (12·9 g) was added to a mixture of sulpholane (30 cc) and fuming HNO_3 (20 cc) saturated with BF_3 at 0°. The mixture was heated to 70° and maintained at this temp for 7 days. Working up as previously gave a mixture of starting material (2%) and the dinitro compound (98%). Separation by preparative scale GLC afforded pure tetrafluoro-1,3-dinitrobenzene (10·9 g) identical to the sample described above.

Nitration of 2,2′-H-octafluorobiphenyl. (a) The biphenyl (2·5 g) was added to a mixture of sulpholane (12 cc) and fuming HNO_3 (0·7 cc) saturated with BF_3. The mixture was heated at 65° for 5 hr. Working up as above afforded 2*H*-2′ nitro octafluorobiphenyl (2·7 g) m.p. 52–53°. (Found: C, 42; H, 0·4. $C_{12}HF_8NO_2$ requires: C, 42; H, 0·3%). (b). The biphenyl (3·3 g) was added to a mixture of sulpholane (20cc) and fuming HNO_3 (4 cc) saturated with BF_3. The soln was stirred at 65° for 4 hr. Separation of described above gave 2,2′ dinitro octafluorobiphenyl (3·2) m.p. 119–120 (from petrol b.p. 60/80) identical with an authentic sample prepared by the Ullman reaction of 2-bromo-3,4,5,6-tetrafluoronitrobenzene.[14]

Nitration of 1,2,3,4-tetrafluoro-5-iodobenzene. The iodobenzene (6·0 g) was added to a mixture of sulpholane (20 cc) and fuming HNO_3 (2·5 cc) saturated with BF_3. The mixture was heated at 60° for 2·5 hr. Working up as above yielded 2,3,4,5-tetrafluoro-6-iodonitrobenzene (3·5 g) b.p. 122°/28 mm. (Found: C, 22·5; H, 0·2. $C_6F_4INO_2$ requires: C, 22·4; H, 0%).

Nitration of 2,3,4,5-tetrafluoroacetanilide. The anilide (1·0 g) was heated at 65° for 2 hr with a mixture of sulpholane (20 cc) and fuming HNO_3 (2 cc) saturated with BF_3. Working up as above afforded 2,3,4,5-tetrafluoro-6-nitroacetanilide (0·8 g) hydrolysis for 1 hr with 50% H_2SO_4 afforded 2-amino-3,4,5,6-tetrafluoronitrobenzene (0·4 g) m.p. 43°.[10]

Nitration of 1,2,3,4-tetrafluoro-naphthalene. The naphthalene (1·85 g) was heated at 65° for 1 hr with a mixture of sulpholane (20 cc) and fuming HNO_3 (2 cc) saturated with BF_3. The mixture was poured onto ice and extracted with ether (3 × 25 cc). The combined dried ($MgSO_4$) extracts were distilled to leave a red residue which was chromatographed on an alumina column (22″ × 1¼″) using CCl_4/benzene as eluant. The first band (0·01 g) had an IR spectrum similar to 1,2,3,4-tetrafluoro-5-nitronaphthalene[11] the major eluate a pale yellow solid (0·6 g) was recrystallized from petrol (b.p. 60/80°) to yield 1,2,3,4-tetrafluoro-5,7-dinitronaphthalene m.p. 132–133°. (Found: C, 41·6; H, 0·9. $C_{10}H_2F_4N_2O_4$ requires: C, 41·4; H, 0·7%). The PMR spectrum showed two protons not inconsistent with the structure.

Reaction of hexafluorobenzene with the nitrating complex. Hexafluorobenzene (11·4 g) was added to a mixture of sulpholane (20 cc) and fuming HNO_3 (4 cc) saturated with BF_3. The mixture was heated at 70° for 5 days. A white solid formed after 1 day which sublimed from the solution to the flask walls analysis of this solid showed it to be wholly inorganic. Working up of the liquid portion as above afforded unchanged hexafluorobenzene and a pale yellow solid (0·6 g) shown by comparison with an authentic sample to be tetrafluoro-1,4-benzoquinone.

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