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Chemistry

Comparison of the nitration of polyfluoronitrobenzenes by nitronium salts in superacidic and aprotic media: Activation of the nitronium ion by protosolvation

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ABSTRACT **The reactivity of nitronium tetrafluoroborate in the nitration of deactivated di- and trifluoronitrobenzenes is enhanced in superacidic trifluoromethanesulfonic (triflic) acid compared with aprotic methylene chloride and sulfolane solutions. The enhanced reactivity is discussed in terms of better solubility and higher dissociation of the nitronium salts, as well as protosolvation of NO_2^+ by superacids.**

The nitration of aromatic systems by nitronium salts in aprotic organic solvents has been extensively studied (1–8; for review see ref. 9). Whereas activated π-donor aromatic systems are efficiently nitrated by nitronium salts at ambient or lower temperatures, the presence of several deactivating substituents, such as fluoro and nitro groups, reduces the π-donor ability of the substrate to an extent that electrophilic nitration of such aromatics by nitronium salts under mild conditions is increasingly difficult.

Although polyfluorobenzenes can be nitrated by fuming nitric acid/sulfuric acid or nitric acid/boron trifluoride mixtures (10–12), nitronium tetrafluoroborate in sulfolane nitrates polyfluorobenzenes in only very low yield (12). Enhancement of the reactivity of nitronium salts in the nitration of deactivated aromatics in protic superacids such as fluorosulfonic acid (FSO_3H) and trifluoromethanesulfonic acid [CF_3SO_3H, triflic acid (TfOH)] was observed previously by Olah and Lin (13, 14) and by Coon *et al.* (15), respectively. When $NO_2^+TfO^-$ is formed *in situ* by reaction of TfOH with HNO_3, it mononitrates toluene at −60°C and dinitration is nearly quantitative at 0°C (15). In refluxing fluorosulfonic acid, $NO_2^+BF_4^-$ nitrates dinitrobenzene to 1,3,5-trinitrobenzene, a reaction that is not achieved in aprotic solvents. Furthermore, Olah *et al.* (16, 17) showed that σ-donor alkanes, including even methane, which show limited or no reactivity toward nitronium salts in aprotic solvents, are nitrated, albeit in low yield, in superacid solutions.

In the present paper we report the nitration of highly deactivated polyfluoronitro aromatic systems in TfOH. The corresponding reactions between these aromatic systems and $NO_2^+BF_4^-$ in aprotic solvents were studied for comparison.

EXPERIMENTAL PROCEDURES

All chemicals were obtained from Aldrich and all solvents were dried by literature methods. GC analyses were performed with a quartz silica column (DB-1). GC–MS analyses were carried out on a Finnigan Mat Incos 50 instrument coupled to a Varian model 3700 gas chromatograph. NMR spectra were recorded on a Varian VXR 200 spectrometer from samples in C^2HCl_3 solution with Me_4Si and $CFCl_3$ as internal standards. Melting points were measured on a Mettler FP1 apparatus and are uncorrected.

Nitration in Methylene Chloride. In a typical experiment, to a slurry of nitronium salt (1.38 mmol) in dry CH_2Cl_2 (20 ml) was added the aromatic (1.2 mmol) diluted in CH_2Cl_2 (5 ml) under a dry nitrogen atmosphere at room temperature. The heterogeneous mixture was sonicated for 30 min and an aliquot was withdrawn for GC analysis. The mixture was then refluxed for 2–3 hr. After cooling to room temperature, the reaction mixture was poured into ice/bicarbonate and extracted with CH_2Cl_2. The organic phase was separated and dried ($MgSO_4$) prior to GC–MS analysis.

Nitration in Sulfolane. In a typical experiment, the aromatic (6 mmol) was added to a stirred suspension of $NO_2^+BF_4^-$ (7.5 mmol) in sulfolane (5 ml) at room temperature under dry nitrogen. The reaction mixture was heated as required and then worked up and analyzed as described above.

Nitration in TfOH. In a typical reaction $NO_2^+BF_4^-$ (7.5 mmol) was charged into a dry reaction tube under nitrogen. TfOH (≈3 ml) was added with cooling at dry ice/acetone temperature. The temperature was allowed to rise during vigorous vortex mixing. At 35–40°C BF_3 was evolved. Following BF_3 evolution, the tube was cooled and the aromatic (6 mmol) was added. The solution was heated as required and worked up as above. Compounds **2**, **5**, and **9** were purified by recrystallization (CH_2Cl_2/pentane): **2** [m.p. 76°C (lit., 75–76°C)]; ^1H NMR 7.33 ppm (1H, t, J_{H-F} = 9.8 Hz, 3-H), 8.96 (1H, t, J_{H-F} = 7.5 Hz, 5-H); ^{19}F NMR −101.1 ppm (s, 2,4-F); *m/z* 204 (M^+, 43%); **5** [m.p. 72°C (lit., 71–72°C)]; ^1H NMR 8.81 ppm (t d, J_{H-F} = 9.1 and 2.2 Hz); ^{19}F NMR −124.9 ppm (2F, m, 1,2-F), −147.0 (1F, m, 2-F); *m/z* 222 (M^+, 100%); **9** [m.p. 53°C (lit., 52–53°C)]; ^1H NMR 7.16 ppm (t d, J_{H-F} = 9.0 and 2.2 Hz); ^{19}F NMR −107.0 ppm (2F, d, J_{H-F} = 9.0 Hz, 1,5-F), −121.8 (1F, s, 3-F); *m/z* 222 (M^+, 100%).

RESULTS AND DISCUSSION

Nitrations of 2,4-difluoronitrobenzene, **1**; 2,3,4-trifluoronitrobenzene, **4**; and 1,3,5-trifluorobenzene, **7**, with $NO_2^+BF_4^-$ in both CH_2Cl_2 and sulfolane solutions were studied. Compound **1** was not nitrated at room temperature in CH_2Cl_2, but on refluxing for 2 hr a 30% yield of the dinitro product **2** was shown by GC–MS. In sulfolane, **1** was not nitrated after heating at 70°C for 2 hr. Compound **4** was not nitrated after refluxing in CH_2Cl_2 or after heating in sulfolane at 70°C for 2 hr. Compound **7** was mononitrated to **8** in 90% yield on refluxing in CH_2Cl_2, but no further nitration occurred. In sulfolane the nitration of **7** to **8** was not observed. The low reactivity of deactivated aromatics with $NO_2^+BF_4^-$ in sulfolane solution was not unexpected (12). These results show that nitration of these aromatic systems in aprotic solvents is very limited.

Subsequently we studied a series of nitration reactions in TfOH solution. Compound **1** was nitrated to **2** in 34% isolated

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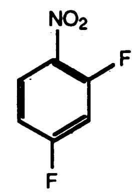
Abbreviation: TfOH, triflic acid (trifluoromethanesulfonic acid).
†On summer leave from Kent State University.



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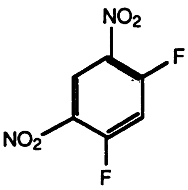

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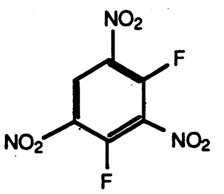

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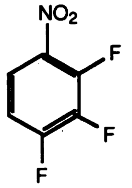

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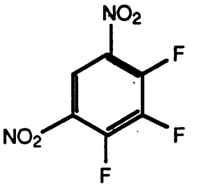

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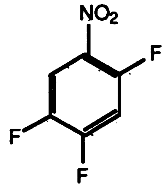

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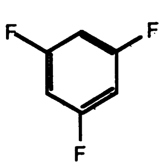

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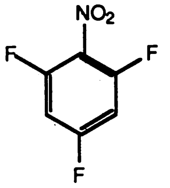

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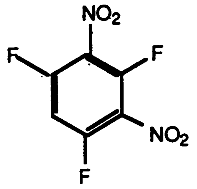

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yield, after heating at 70°C for 2 hr. Similarly, **4** gave **5** in 65% isolated yield, and **7** gave the dinitrated product **9** in 29% isolated yield on reaction with two equivalents of $NO_2^+BF_4^-$. No attempts to obtain the trinitrated products under more vigorous conditions were made.

Interestingly, **6** was not nitrated under conditions identical to those used to nitrate its isomer **4**. A consideration of the resonance structures of the corresponding σ complexes leading to **5** and 2,4,5-trifluoro-1,3-dinitrobenzene shows that whereas in both cases positive charge is located adjacent to two fluorine-substituted and one unsubstituted ring position, the σ complex leading to **5** is additionally mesomerically stabilized by a para fluorine atom. Our results are collated in Table 1.

2,4-Dinitrofluorobenzene was not nitrated after heating at 120°C overnight, and pentafluorobenzene was nitrated to pentafluoronitrobenzene in only 5% isolated yield.

In a control experiment, $NO_2^+TfO^-$, formed by reaction of $NO_2^+BF_4^-$ with TfOH, was isolated. Nitration of **1** was then studied with isolated $NO_2^+TfO^-$ in CH_2Cl_2 solvent. No reactivity enhancement was observed as compared to aprotic nitration with $NO_2^+BF_4^-$ in CH_2Cl_2. The nature of the counter ion thus has no major effect on the reactivity.

Table 1. Nitration of fluoronitrobenzenes with $NO_2^+BF_4^-$ in aprotic CH_2Cl_2, sulfolane, and superacidic TfOH solution

Substrate	Solvent	Temp.	Time, hr	Product	Yield, % (GC)
1	CH_2Cl_2	RT	2	2	0
	CH_2Cl_2	Reflux	2	2	30
	Sulfolane	70°C	2	2	0
	TfOH	70°C	2	2	34*
4	CH_2Cl_2	Reflux	4	5	0
	Sulfolane	70°C	2	5	0
	TfOH	70°C	2	5	65*
7	CH_2Cl_2	Reflux	4	8	90
	CH_2Cl_2	Reflux	4	9	0
	Sulfolane	70°C	2	8	0
	TfOH	70°C	2	9	29*

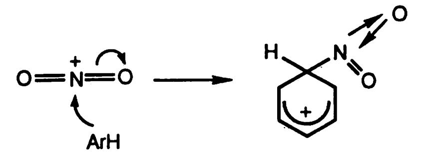
*Isolated yield.

In the course of our study we found that $NO_2^+SbF_6^-$ is not soluble in TfOH, indicating that there is no exchange of the counter ion (in accordance that HF-SbF_5 is a stronger acid than TfOH).

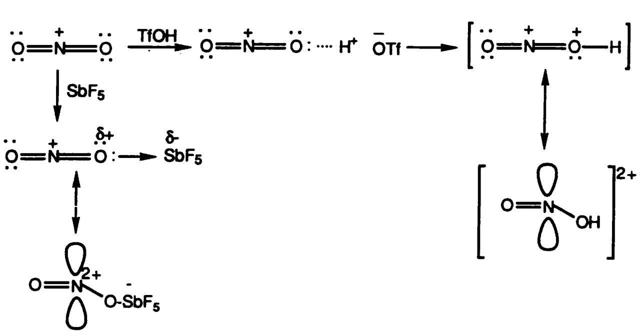
$NO_2^+BF_4^-$ and $NO_2^+SbF_6^-$ are insoluble in TfOH·SbF_5 (1:1) superacid system. This is also indicative that in SbF_5-containing superacids bearing bulky (oligomeric) gegenions such as $SbF_5(TfO)^-$ and $Sb_2F_{10}(TfO)^-$ (18, 19), the nitronium salts are not solvated sufficiently on steric grounds. As a consequence, these superacids also show no enhancement of activity. For example, nitration of **1** with TfOH·SbF_5 (1:1) in Freon 113 solvent gave only a 15% yield of **2**.

When SbF_5 was added to a solution of $NO_2^+TfO^-$ in TfOH, the nitronium salt remained soluble although some turbidity was observed. In all probability SbF_5 complexes with TfOH. At low SbF_5 concentration the contribution of the complexed gegenions to the overall superacid acidity is rather small, as also found for FSO_3H·SbF_5 system (20). Thus $NO_2^+X^-$ where $X = [SbF_5(TfO)]^-$ should be insignificant, as these ions would be insoluble in TfOH, as shown by our experiments.

The increased reactivity of the nitronium ion in superacid solution can be rationalized in terms of its protosolvation (21). In its ground state, the linear nitronium ion lacks a suitable low-lying LUMO (lowest unoccupied molecular orbital) to overlap with the matching HOMO (highest occupied molecular orbital) of the nucleophile, in this case the aromatic ring. Despite the presence of a formal positive charge at nitrogen, there is no vacant *p* orbital at nitrogen. Nucleophilic attack by π-donor aromatic systems causes π polarization of the nitronium ion and the subsequent bending of the linear ion leads to a bonding interaction. However, with highly deactivated aromatic systems such π polarization by nucleophilic assistance is not as likely.



Activation of nitronium may be achieved by protonation (protosolvation) of an oxygen lone pair in a protic superacid solvent or by complexation with a Lewis superacid such as SbF_5. Complexation weakens the N–O π-bond character, leading to partial electron deficiency at the nitrogen *p* orbital and bending of the nitronium ion, which lowers the activation barrier for bonding interaction with π or σ donors.



We have recently found that at the 6-31G*, 6-31G**, and MP2/6-31G** levels of theory the protonitronium dication NO_2H^{2+} is an energy minimum (for a recent review of onium dications, see ref. 21). In earlier studies this was not the case (22).

Nitration of deactivated polyfluoronitrobenzenes with nitronium salts in superacidic TfOH in contrast to similar nitration in aprotic CH_2Cl_2 indicates better solubility and protosolvolytic activation of the nitronium ion in the superacidic medium.

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