

Nitration of Strongly Deactivated Aromatics with Superacidic Mixed Nitric–Triflatoboric Acid ($\text{HNO}_3/2\text{CF}_3\text{SO}_3\text{H}-\text{B}(\text{O}_3\text{SCF}_3)_3$)^{1a}

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The nitration of various deactivated arenes (including methanesulfonyl-, nitro-, and polyhalobenzenes) was carried out in good yield with mixed nitric–triflatoboric superacid. For example pentafluorobenzene gave pentafluoronitrobenzene in 99% yield, nitrobenzene to *m*-dinitrobenzene in 92% selectivity with 85% overall yield, and methyl phenyl sulfone gave only the *m*-nitro isomer in 78% isolated yield. Thus the new nitrating system gives high regioselectivity and yields under generally mild reaction conditions. The reagent system is compatible with many functional groups of arenes.

Introduction

Electrophilic nitration of arenes is one of the most studied organic reactions. Many nitrating agents (HNO_3 , NO_2Cl , N_2O_5 , RONO_2) with varied Lewis or Bronsted acid catalysts have been used.^{1b–3}

Especially effective for the nitration of many deactivated arenes are stable nitronium salts ($\text{NO}_2^+\text{MX}_{n+1}^-$). The linear NO_2^+ cation is considered a highly polarizable electrophile, but itself does not contain an empty atomic orbital on the nitrogen or a low-lying LUMO. Its activity can be further enhanced by protosolvation resulting in the limiting case in the formation of the superelectrophilic protonnitronium dication, $[\text{NO}_2\text{H}]^{2+}$.⁹ It is the bent protonnitronium $[\text{NO}_2\text{H}]^{2+}$ dication (or protosolvated NO_2^+) which is actually responsible for the nitration of highly deactivated arenes in strong acid solutions. $[\text{NO}_2\text{H}]^{2+}$ was found to be an energy minimum at both HF/6-31G* and MP2/6-31G* levels of *ab initio* calculations¹⁰ and was recently even directly observed by Schwartz *et al.* in the gas phase by mass spectrometry.¹¹

The nitrating ability of nitronium salts was previously found to be significantly enhanced by FSO_3H ¹² or $\text{CF}_3\text{SO}_3\text{H}$.^{13,14} Use of even stronger conjugate superacids such as $\text{HF}-\text{SbF}_5$, $\text{FSO}_3\text{H}-\text{SbF}_5$, or $\text{CF}_3\text{SO}_3\text{H}-\text{SbF}_5$ was,

however, limited because SbF_5 is also a strong oxidizing agent incompatible with many functional groups.

Nitric acid is the most widely used nitrating agent, being a convenient source for the nitronium ion.² Its superacidic activation is not just due to its ready ionization to NO_2^+ (Scheme 1, step A), but NO_2^+ can be protosolvated (or *de facto* protonated) to the gitonion dication, NO_2H^{2+} (step B).^{2,9,13,14}

Triflic acid ($\text{CF}_3\text{SO}_3\text{H}$) is one of the strongest Bronsted acids ($H_0 = -14.1$) ionizing nitric acid to nitronium triflate. The $\text{HNO}_3-\text{CF}_3\text{SO}_3\text{H}$ system was found to be a convenient nitrating agent for a number of arenes, including moderately deactivated ones.^{13,14} To explore enhanced activation of the system, we considered that as the acidity of $\text{CF}_3\text{SO}_3\text{H}$ can be increased by the addition of suitable Lewis acids, resulting in conjugate superacids,^{15a} and increasing the acidity should accordingly affect both equilibrium A and B (Scheme 1) and lead to enhanced nitrating ability.

Addition of BCl_3 to $\text{CF}_3\text{SO}_3\text{H}$ (1:5 molar ratio) produces in a very simple procedure triflatoboric acid ($2\text{CF}_3\text{SO}_3\text{H}-\text{B}(\text{OSO}_2\text{CF}_3)_3$), a very powerful superacid ($H_0 = -20.5$).^{15a} Its acidity greatly exceeds that of $\text{CF}_3\text{SO}_3\text{H}$ itself and approaches that of $\text{CF}_3\text{SO}_3\text{H}-\text{SbF}_5$, one of the strongest superacids known. At the same time, $2\text{CF}_3\text{SO}_3\text{H}-\text{B}(\text{O}_3\text{SCF}_3)_3$ was found to be miscible with most aromatics and does not oxidatively affect arenes with various functional groups (as SbF_5 and other strongly oxidizing superacids tend to). We report now our studies of the highly efficient electrophilic nitration of various deactivated arenes by the superacidic $\text{HNO}_3/2\text{CF}_3\text{SO}_3\text{H}-\text{B}(\text{O}_3\text{SCF}_3)_3$ system in which nitronium triflatoborate ($\text{NO}_2^+\text{B}(\text{O}_3\text{SCF}_3)_4^-$) is the active nitrating agent with further protolytic activation by the acid system.^{15b}

Results and Discussion

Results of nitration of deactivated arenes with 1:1 $\text{HNO}_3/2\text{CF}_3\text{SO}_3\text{H}-\text{B}(\text{O}_3\text{SCF}_3)_3$ system are summarized in Scheme 2 and Table 1. The data indicate a highly active

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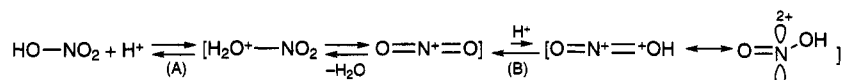
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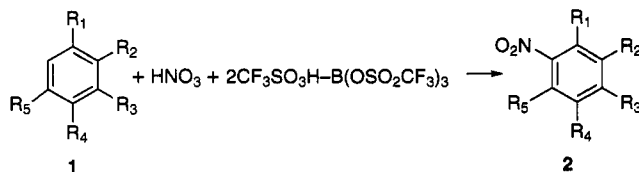
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(15) (a) Olah, G. A.; Sommer, J.; Prakash, G. K. S. *Superacids*; Wiley-Interscience: New York, 1985. (b) $2\text{CF}_3\text{SO}_3\text{H}/\text{B}(\text{OSO}_2\text{CF}_3)_3$ is the minimum optimized ratio for the reaction to take place. Although stoichiometrically only $\text{NO}_2^+\text{B}(\text{OSO}_2\text{CF}_3)_4^-$ and H_3O^+ are produced, as pointed out by a referee, a slight excess of acid is sufficient to result in protosolvated nitronium ion in small concentration which is the *de facto* nitrating species. Further, as the reaction proceeds more protons are generated.

Scheme 1



Scheme 2



1	2	R ₁	R ₂	R ₃	R ₄	R ₅
a	a	F	F	H	F	H
b	b	F	F	F	H	F
c	note 1	F	F	H	F	F
d	d	Cl	Cl	H	Cl	Cl
e	e	Cl	Cl	Cl	Cl	Cl
f	f	F	F	F	F	F
g	g	H	NO ₂	H	H	H
h	h	H	SO ₂ CH ₃	H	H	H
i	i	H	CF ₃	H	CF ₃	H
j	j	CF ₃	H	H	CF ₃	H
k	k	H	NH ₃ ⁺ OTf ⁻	H	H	H
l	l	F	SO ₂ CH ₃	F	H	F
m	m	F	NO ₂	F	H	F
n	n	F	F	F	NO ₂	H
o	o	F	F	H	NO ₂	F
p	p	F	F	F	H	F
q	q	F	F	F	NO ₂	F
r	r	F	CHO	H	H	H

¹2,5-Difluoro-1,4-benzoquinone was formed.

Table 1. Nitration of Deactivated Aromatics

arene	mole ratio arene:HNO ₃ : acid	T (°C)	time (h)	product	yield ^a (%)
1a	0.9:1.0:1.0	20	3	2a ¹⁸	83 ^b
1b	0.9:1.0:1.0	20	3	2b ¹⁹	89 ^b
1c	0.8:1.0:1.0	20	0.5	i	
1d	0.5:1.0:1.0	20	7	2d ²⁰	84 ^c
1e	0.8:1.0:1.0	20	5	2e ²¹	80 ^c
1f	0.8:1.0:1.0	20	3	2f ²²	99 ^a
1g	1.0:1.0:1.0	20	3	2g ^{h,23}	85 ^b
1h	0.8:1.0:1.0	20	3	2h ²⁴	78 ^b
1i	0.8:1.0:1.0	20	20	2i ^{d,25}	53 ^a
1j	1.0:1.0:1.0	20	20	2j ²⁵	14 ^a
1k	0.8:1.0:1.0	20	3	2k ²⁶	67 ^b
1l	0.35:1.0:1.0	20	4	2l ²⁷	96 (78) ^b
1m	0.5:1.0:1.0	20	4	2m ²⁸	75 (56) ^b
1n	0.5:1.0:1.0	65	6	2n ²⁹	96 ^b
1o	0.5:1.0:1.0	90	5	2o ^j	4 ^a
1p	0.9:1.0:1.0	20	3	2p ²⁰	89
1q	0.25:1.0:1.0	100	6	2q ³⁰	83 ^a
1r	0.9:1.0:1.0	20	3	2r ³¹	52 ^a

Many of the products have been reported in the literature as indicated by the reference, their authenticity confirmed by comparison with the literature results. ^a GC determined yield. ^b Isolated yield. ^c Solid starting material is poorly soluble in the reaction media. ^d C₆H₄(COOH)₂ was formed as byproduct. ^e Mixture of two isomers, higher ratio of *meta* isomer. ^f Total yield combining rearranged (33%) plus normal nitration product. ^g Remainder is 2,3,4,6-tetrafluorobenzene. ^h 2:6:100 isomer ratio. ⁱ 2,5-Difluoro-1,4-benzoquinone was formed in 74% yield. ^j Isolated in only 4% yield and authenticity determined by only GC-MS.

reagent system whose nitrating ability is higher than that of previously studied systems such as NO₂⁺BF₄⁻/CF₃SO₃H,¹⁴ NO₂O₃SCF₃/CF₃SO₃H,¹⁶ and HNO₃/CF₃SO₃H.¹³

It is considered that in superacidic triflatoboric acid, nitric acid is ionized to nitronium tetratriflatoborate [NO₂⁺B(O₃SCF₃)₄⁻] which then can be further protosolvated by the superacid. Isomeric 1,2,4-, 1,2,3-, and 1,3,5-trifluorobenzenes were readily nitrated at room temperature. In contrast with NO₂⁺BF₄⁻/CF₃SO₃H, 1,3,5-trifluorobenzene could be nitrated only in refluxing methylene chloride and was not nitrated in sulfolane solution.¹⁴ 1,2,3,5-Tetrafluorobenzene and even pentafluorobenzene were nitrated at room temperature in the present system with excellent yield. On the other hand, the NO₂⁺BF₄⁻/CF₃SO₃H system did not nitrate C₆F₅H either at room or at more elevated temperatures. HNO₃/BF₃ in sulfolane was reported¹⁸ to nitrate perfluorobenzenes only upon prolonged heating. 1,2,4,5-Tetrachloro- and pentachlorobenzenes were also readily nitrated in the present system at room temperature, *albeit* in lower yields, probably due to the limited solubility of the starting materials.

It is interesting to note that in the reaction of 1,2,4,5-tetrafluorobenzene oxidative quinone formation took place (see Table 1). It was the only case where such oxidation was observed; the corresponding 1,2,4,5-tetrachlorobenzene, on the other hand, underwent normal nitration.

Beside its high nitrating ability of strongly deactivated arenes under mild reaction conditions, the HNO₃/2CF₃SO₃H-B(OSO₂CF₃)₃ system also demonstrated high regioselectivity. Nitrobenzene reacted cleanly to give *m*-dinitrobenzene as the major isomeric product (92.3%) in 85% overall yield. Methyl phenyl sulfone gave only the *m*-nitro isomer. Nitration of 1,2,4-trifluorobenzene gave only one product, 2,4,5-trifluoronitrobenzene. Its formation indicated back-donation by two fluorine atoms in the *ortho* and *para* positions in stabilizing the σ -intermediate. No isomeric 2,3,6-trifluoronitrobenzene was formed. 1,3-Bis(trifluoromethyl)benzene was selectively nitrated at the 5-position. However, CF₃ groups were not

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stable in the acid system, and the reaction was complicated by their competing hydrolysis to carboxylic acids. 1,4-Bis(trifluoromethyl)benzene, having only *ortho* positions available for attack, was remarkably resistant to nitration.

Nitration of other highly deactivated arenes was also selective. Only 1,2,3-trifluoro-4,6-dinitrobenzene was obtained upon nitration of 1,2,3-trifluoro-4-nitrobenzene, indicative of stabilization of the intermediate σ -complex by the *o*- and *p*-fluorine atoms. Polyfluoronitrobenzenes as well as polyfluorophenyl methyl sulfones were also nitrated. Nitration of di- and trifluoronitrobenzenes was earlier reported with the $\text{HNO}_3\text{-CF}_3\text{SO}_3\text{H}$ system.¹⁴ $\text{NO}_2^+\text{BF}_4^-/\text{CF}_3\text{SO}_3\text{H}$ required heating at 70 °C in order to obtain moderate yields. In contrast, 2,4,6-trifluoronitrobenzene and 2,4,6-trifluorophenyl methyl sulfone was nitrated with the $\text{HNO}_3/2\text{CF}_3\text{SO}_3\text{H-B}(\text{OSO}_2\text{CF}_3)_3$ at room temperature with good yields (see Table 1). 2,4,6-Trifluoronitrobenzene was most readily nitrated¹⁴ because mesomeric back-donation by all three fluorine atoms helped stabilize the intermediate σ -complex. Isomeric trifluoronitrobenzenes, however, displayed a wide range of reactivity. Whereas 2,4,6-trifluoronitrobenzene reacted at room temperature, 2,3,4-trifluoronitrobenzene, in which the σ -complex was mesomerically stabilized by only two fluorine atoms, required more elevated temperatures although the yield of the nitro product is excellent (see Table 1). On the other hand, 2,4,5-trifluoronitrobenzene was left practically unchanged even after prolonged treatment at higher temperatures. Moreover, attempts to nitrate 1,3-dinitrobenzene even with an 8-fold excess of triflatoboric acid at 90 °C, for 10 h were unsuccessful. However, nitration of tetrafluoronitrobenzene was readily achieved. Whereas 2,4,5-trifluoronitrobenzene was resistant to nitration even at higher temperatures, 2,3,4,6-tetrafluorobenzene was successfully nitrated to 2,4,5,6-trifluoro-1,3-dinitrobenzene in excellent yield (see Table 1). This result further underlines the role of *n*-donation by the *o*- and *p*-fluorine, which can overcome the inductive *meta*-fluorine deactivation of the aromatic ring.

In conclusion, mixed nitric-triflatoboric superacid $\text{HNO}_3/2\text{CF}_3\text{SO}_3\text{H-B}(\text{OSO}_2\text{CF}_3)_3$ is an efficient, powerful new nitrating reagent for electron deficient aromatics under mild conditions.

Experimental Section

All aromatics were obtained from Aldrich and were used without additional purification. Triflic acid was from 3M Industrial Chemical Product Division. GC analyses were

performed using a quartz silica column (DB-1). GC-MS analyses were carried out using a Hewlett-Packard 5971 series mass selective detector coupled to a Hewlett-Packard 5980 series gas chromatograph. NMR spectra were recorded at 200 MHz in CDCl_3 solution with Me_4Si (^1H and ^{13}C) and CFCl_3 (^{19}F) as internal chemical shift standards. Melting points were measured on a Mel-Temp II apparatus and are uncorrected.

Identification of products was based on their GC and GC-MS analyses and comparison of the spectroscopic data with those reported in the literature and authentic samples. The spectroscopic and high-resolution mass spectroscopic data on the unknown compound **2l** and **2r** are given in the refs 27 and 31. Their proton spectra are included in the supporting information.

Preparation of Triflatoboric Acid ($2\text{CF}_3\text{SO}_3\text{H-B}(\text{O}_3\text{SCF}_3)_3$).¹⁴ BCl_3 (6.5 g, 55 mmol) was condensed (bp = 12.5 °C) at -78 °C into a Schlenk flask under dry nitrogen atmosphere. The flask was brought to -25 °C using CCl_4 /dry ice bath. Dropwise addition of $\text{CF}_3\text{SO}_3\text{H}$ was started under vigorous stirring. The first portion of $\text{CF}_3\text{SO}_3\text{H}$ (15 mL) was added carefully over a period of 1 h to prevent too intensive HCl evolution and BCl_3 loss. After HCl evolution had practically stopped, the remaining 9.5 mL of $\text{CF}_3\text{SO}_3\text{H}$ was added over a period of 15 min. The homogeneous mixture was allowed to warm to 0 °C and stirred for 3 h. During this period dry nitrogen gas was passed through the mixture to drive out any dissolved HCl. A 42.3 g (55 mmol) yield of $2\text{CF}_3\text{SO}_3\text{H-B}(\text{OSO}_2\text{CF}_3)_3$ was obtained which was stored in a freezer.

Typical Nitration Procedure. Nitric acid (90%) was dehydrated by distillation from 30% oleum (2 molar equiv excess) at reduced pressure. HNO_3 (0.15 g, 2.4 mmol) was mixed with 1 mL (1.8 g, 2.4 mmol) of $2\text{CF}_3\text{SO}_3\text{H-B}(\text{OSO}_2\text{CF}_3)_3$ under dry nitrogen in a three-necked round-bottom flask. The nitronium salt ($\text{NO}_2^+\text{B}(\text{O}_3\text{SCF}_3)_4^-$) partially precipitated as a white solid. Without isolation, the calculated amount of arene was then added while the mixture was vigorously stirred (for the reaction time and temperature, see Table 1). Subsequently, the reaction mixture was quenched with ice water and extracted by CHCl_3 (3 \times 20 mL), and the combined chloroform extracts were washed carefully with a 5% aqueous sodium bicarbonate solution. The CHCl_3 extract, dried over MgSO_4 , was evaporated to give crude nitro products. The crude products were further purified by distillation or recrystallization.

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Supporting Information Available: ^1H NMR spectra of **2l** (Figure 1) and **2r** (Figure 2) (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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