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A NOVEL ROUTE TO META-AMINOBENZOTRIFLUORIDE*

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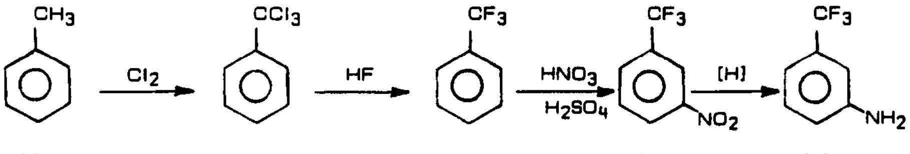
SUMMARY

Product patterns can be altered in reactions of m-nitrobenzotrichloride (VI) with $(AHF)_x \cdot NH_4F$ complex. Side-chain fluorination predominates under 'mild' conditions. In contrast, 'forcing' conditions effected unexpected in-situ fluorination-reduction to give m-aminobenzotrifluoride (V) in high yield (75%) and purity (99.6%). In-situ reduction is probably initiated by a combination of iron from the stainless steel autoclave and trace amounts of moisture. The transformation of (VI) to (V) represents another type of in-situ fluorination-reduction of nitroaromatics, e.g. nitrobenzene (VII) to p-fluoroaniline (VIII). o-Nitrobenzotrichloride (XI) degraded under 'forcing' conditions with $(AHF)_x \cdot NH_4F$.

INTRODUCTION

m-Aminobenzotrifluroide (MABTF) (V) is a valuable intermediate for dyes, germicides, pharmaceuticals and crop protection chemicals [1]. The standard MABTF manufacturing route features a 4-step sequence based on toluene: chlorination; exchange-fluorination; nitration**; and, reduction***.



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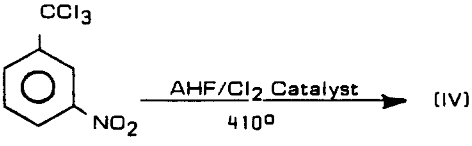
* M. M. Boudakian, U.S. Pat. 4 582 935 (1986).

** Regardless of nitrating agent, ortho- and para-isomers are always formed from nitration of (III).

*** Analytical methods for MABTF (V), and its ortho- and para-isomers, have been published [2].

Alternate approaches to the key MABTF precursor, m-nitrobenzotrifluoride (IV), have been recently published. Vapor phase exchange-fluorination of m-nitrobenzotrichloride (VI)* with AHF gave (IV) as the main product [4].



(VI)

Another route to (IV) featured the 1-step vapor phase reaction of m-nitrotoluene with excess $Cl_2/AHF/CCl_4$ diluent (5). (This process presumably involved in-situ generation of (VI)). Feiring obtained only m-nitrobenzyl fluoride and m-nitrobenzal fluoride from the oxidative fluorination (PbO_2/AHF) of m-nitrotoluene; m-nitrobenzaldehyde was the main product [6,7].

Reactions in AHF·pyridine media have been widely developed by Olah and co-workers [8]. In contrast, reactions with $(AHF)_x \cdot NH_4F$ solvates have been relatively ignored. These stable complexes (x = 1,3,5) significantly reduce AHF vapor pressure [9]. For example, fluorodediazoniation of anilines with $(AHF)_x \cdot NH_4F$ result in higher decomposition temperatures and thereby give higher yields of fluoroaromatics than in AHF alone [10]. $(AHF)_x \cdot NH_4F$ solvates can be considered as effective as Olah's AHF·pyridine system [8] for fluorodediazoniation reactions.

$(AHF)_x \cdot NH_4F$	M.P. (°)
x = 1	126
3	23.2
5	-8.0

Feiring recently applied AHF·pyridine solvates to exchange-fluorination reactions, e.g. conversion of 3,3,3-trichloropropene-1 to give 3,3,3,-trifluoropropene-1 [11]. The present study concerned the related allylic fluorination of m-nitrobenzotrichloride (VI) with $(AHF)_x \cdot NH_4F$ for the expected formation of (IV)**.

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* (VI) has been prepared by nitration of (II) or chlorination (Cl_2O) of m-nitrotoluene [3 a,b].

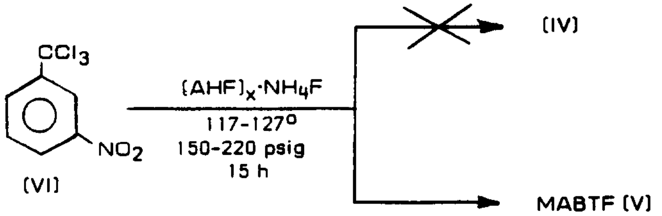
** Other AHF solvates ($NaHF_2$; KF· 7HF; KF·8HF/$SbCl_5$) can effect exchange-fluorination of benzotrichloride, p-chlorobenzotrichloride and xylene hexachloride [12 a,b].

RESULTS AND DISCUSSION

Reactions of Meta-Nitrobenzotrichloride (VI)

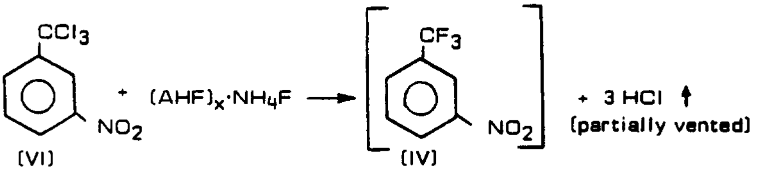
(a) In-Situ Fluorination-Reduction

The reaction of (VI) with $(AHF)_x \cdot NH_4F$ under 'forcing' conditions (high temperatures/long reaction times in a ss autoclave) resulted in unexpected in-situ fluorination-reduction to give MABTF (V) in high yield (75%) and purity (99.6%). None of the exclusively fluorinated product (IV) was found..



In contrast, Klauke *et al.* observe only fluorination from the lower chlorinated homolog of (VI), m-nitrobenzal chloride, and AHF (70-115°/145-336 psig/ 3.5 h/ss autoclave) to give m-nitrobenzal fluoride [13].

The reduction phase of the transformation of (VI) to (V) may be due to release of iron from the ss reactor wall* **, incompletely vented HCl (or NH_4Cl/NH_4F***) as a proton source and *wet* ammonium fluoride. Commercial ammonium bifluoride was found to contain 0.6 wt % water (corresponding to 1/10 molar ratio of H_2O/(VI)) which could be sufficient to initiate reduction. Water subsequently formed could then be recycled for completion of the reduction sequence.



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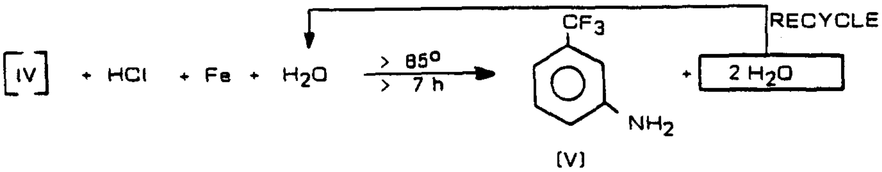
* "Wet" reduction of m-nitrobenzotrifluoride (IV) to MABTF (V) by Fe/H_2O in the presence of proton sources such as HCl is well known [14 a,b].

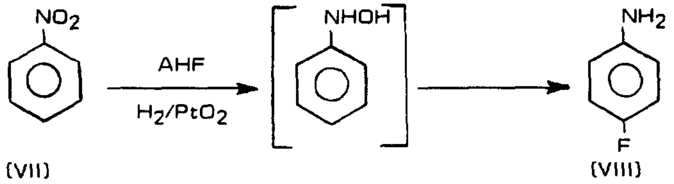
** Presence of H_2O in $NH_4F \cdot HF$ might release Fe from the ss reactor wall. For example, Fe released from a ss autoclave was "sufficient" to catalyze the AHF/benzotrichloride reaction [15].

*** $NH_4F \cdot (HF)_x + HCl \rightleftharpoons NH_4Cl \cdot (HF)_x + \uparrow$



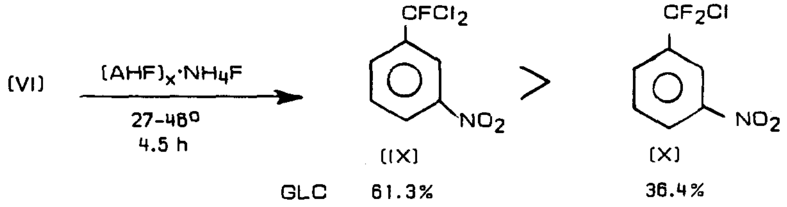
Hydrolytic stability of (IV) and (V) in the above mixture was also surprising since Simons *et al*. effected facile hydrolysis of benzotrifluoride (III) to benzoic acid with aqueous HF at 100° [16].

The conversion of (VI) to (V) represents another type of *in-situ* fluorination-reduction of nitroaromatics. An earlier example (for *ring-fluorinated* aromatics) was the single-step transformation of nitrobenzene (VII) via N-phenylhydroxylamine to *p*-fluoroaniline (VIII) with AHF/H_2 [17].



(b) Fluorination

Cross-over from *in-situ* fluorination-reduction to exclusively fluorination occurred at more moderate conditions. While (VI) was inert to AHF (18°), mono- and difluorination ((IX) > (X)) was effected with $(AHF)_x \cdot NH_4F$ at 27-46°. At higher temperatures (80-5°/135 psig/7 h), difluorination predominated to give > 80% yield of (X).

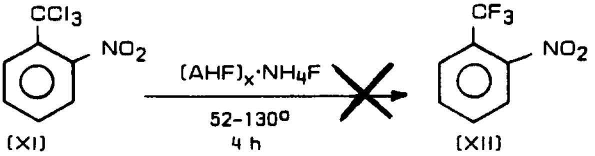


Fluorination of Ortho-Nitrobenzotrichloride (XI)

Reactions of o-nitrobenzotrichloride (XI) with fluorinating agents are virtually unknown. A vague patent example claimed that o-nitrobenzotrifluoride (XII) was formed from (XI) and SbF_3 in unspecified amounts [18]. However, attempts to confirm this experiment (twice) gave only tars and carbonaceous solids*.

Numerous examples have been reported on the side-chain fluorination (AHF) of ortho-trichloromethylaromatics, o-$CCl_3C_6H_4$-X: X = Cl [20]; $N(CO)_2C_6H_4$ [21]; CN [22]; $CHCl_2$ [23]; $\mathrm{O}\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{Y}$ (Y = halogen, OR, C_6H_5) [24]; NCO**; and, $\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{Cl}$ [27].

Attempts to fluorinate (XI) with AHF were unsuccessful. (XI) was inert to AHF (14-18°) or $(AHF)_x \cdot NH_4F$ (25-51°); degradation occurred at higher temperatures (52-130°).



Similar resinification was noted by Klauke *et al.* with o-nitrobenzal chloride and AHF [13].

EXPERIMENTAL

CAUTION: Hydrogen fluoride is extremely corrosive to human tissue, contact resulting in painful slow-healing burns. Laboratory work with HF should be conducted only in an efficient hood with operator wearing full face shield and protective clothing.

m-Aminobenzotrifluoride (V) via In-Situ Fluorination-Reduction of m-Nitrobenzotrichloride (VI)

(a) Absence of Organic Solvent

m-Nitrobenzotrichloride (VI) (0.20 Mol, 48.1 g; GLC, 100%), ammonium bifluoride (1.0 Mol, 57.1 g; Harshaw; 0.6 wt % H_2O, 0.019 Mol) and AHF (7.5 Mol, 150 g; Matheson;

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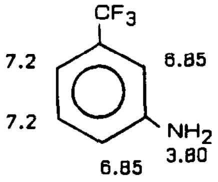
* (XI) is thermally unstable and degrades upon distilling at 150°/atm. press.; distillation of (XI) can be effected at reduced pressures (100°) [19].

** 2-(Trifluoromethyl)phenyl carbamic fluoride formed in-situ is hydrolyzed to o-aminobenzotrifluoride [25]. Rearrangement can also occur to give 2-(N-trifluoromethylamino)benzoylfluoride [26].

H_2O specification, 300-400 ppm) were heated in a 1-liter Parr Type 316 stainless steel stirred autoclave. (The transfer operations were conducted with rigid exclusion of moisture). The sealed reactor was pressurized four times each with N_2 (110 psig) and then vented. By-product HCl was periodically vented into a caustic scrubber.

Stage	Temp. (°)	Press. (psig)	Time (h)	HCl (Mol)
A	46-75	40-150	3	0.306
B	79-96	50-105	7	0.122
C	101-127	60-120	4	None

The reactants were neutralized (15% aqueous ammonia), extracted with CH_2Cl_2 and concentrated to give a liquid (20.1 g; 0.125 Mol; 62.5% yield of (V)); GLC (SF-96), 98.5%; n^{25}_{D} 1.4798 (reported [1] for (V), n^{20}_{D} 1.4788). Product structure for (V) was confirmed by mass spectroscopy and NMR assay. (Addition of $Eu(fod)_3$ resulted in almost first order spectra giving one singlet, two doublets and one triplet).



(b) Presence of CH_2Cl_2 Solvent

A mixture consisting of (VI) (0.14 Mol, 33.5 g; GLC, 94.6%), ammonium bifluoride (0.7 Mol, 40.0 g; 0.6 wt % H_2O, 0.013 Mol), CH_2Cl_2 (150 ml) and AHF (5.25 Mol, 105 g) was heated in three stages.

Stage	Temp. (°)	Press. (psig)	Time (h)
A	68-95	90-160	2.5
B	68-101	90-118	6.5
C	103-117	190-220	6.5

Additional AHF [5.25 Mol, 105 g] was transferred prior to Stage C. A total of 0.232 Mol HCl was collected. The reactants were neutralized (15% aqueous ammonia), steam-distilled and concentrated to give 16.0 g of (V) (75% yield, when corrected for 94.6% assay of (VI)); GLC, 99.6%; n_D^{23} 1.4778.

Fluorination of m-Nitrobenzotrichloride (VI)

(a) Autoclave Conditions

Only fluorinated products were formed from (VI) (0.14 Mol, 33.6 g; GLC, 100%), ammonium bifluoride (0.07 Mol, 40.0 g; 0.6 wt % H_2O, 0.013 Mol), CH_2Cl_2 (150 ml) and AHF (5.25 Mol, 105 g) under 'moderate' conditions: 80-85°; 7 h; 135 psig. The reactants were neutralized (15% aqueous ammonia), steam distilled* and concentrated to give a liquid (24.2 g). Mass spectral and GLC (SF-96: 120-250° at 8°/min) revealed three components: m-$CF_3C_6H_4NO_2$ (IV) (6.79 min; 4.0%); m-$CF_2ClC_6H_4NO_2$ (10.44 min; 90.6%); and, m-$CFCl_2C_6H_4NO_2$ (13.43 min; 3.8%).

(b) Atmospheric Pressure Conditions

No exchange-fluorination (absence of HCl evolution) occurred when (1) (0.2 Mol, 48.1 g; GLC, 100%) and AHF (5 Mol, 100 g) were heated at 18° (4 h) in a 2-liter 304 stainless steel reaction flask (SGA Scientific).

Ammonium bifluoride (1.0 Mol, 57.1 g; 0.17 wt % H_2O, 0.0053 Mol) and AHF (2.5 Mol, 50 g) were added to the above reactants and heated at 27-46° (4.5 h). The mixture was neutralized (5% aqueous ammonia), extracted with CH_2Cl_2 and concentrated to give a liquid (33.0 g). Mass spectroscopy and GLC disclosed two main components: m-$CF_2ClC_6H_4NO_2$ (36.38%); m-$CFCl_2C_6H_4NO_2$ (61.34%).

Attempted Fluorination of o-Nitrobenzotrichloride (XI)**

(a) Hydrogen Fluoride Media

1. Atmospheric Pressure Conditions - (XI) (0.2 Mol, 48.1 g; GLC, 97.7%) was inert (no HCl) to AHF (5 Mol, 100 g) when stirred in a ss reactor at 14° (2 h). While

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* Swarts also noted similar hydrolytic stability of (X) (prepared by nitration of $C_6H_5CF_2Cl$) [28].

** (XI) is a minor product from the nitration of benzotrichloride [3a]. More recent methods to (XI) are based on the chlorination of o-nitrobenzyl chloride [29].

ammonium bifluoride (1 Mol, 57.1 g; H_2O, 0.17 wt %, 0.0053 Mol) and additional AHF (1 Mol, 20 g) increased the temperature to 25-51° (3 h), negligible HCl evolution (0.032 Mol) was again noted.

2. Pressure Fluorination Conditions - (XI) (0.2 Mol, 48.1 g; GLC, 97.7%), AHF (7 Mol, 140 g), ammonium bifluoride (1 Mol, 57.1 g; H_2O, 0.17 wt %, 0.0053 Mol) and CH_2Cl_2 (75 ml) were heated in a 1-liter ss autoclave from 52 to 130° (4 h/170 psig). Negligible HCl evolution (0.024 Mol) was noted. The reactants were neutralized (15% aqueous ammonia), CH_2Cl_2 (300 ml) added and the carbonaceous solids (26 g, corresponding to 54.1% of (XI)) filtered. Concentration of the CH_2Cl_2 layer gave primarily tars.

(b) Antimony Trifluoride

(XI) (0.05 Mol, 8.94 g; GLC, 97.7%) and antimony trifluoride (0.20 Mol, 35.8 g; Fisher A-854) were heated gradually (0.75 h) to 62° with agitation. An exotherm occurred (temperature rose to 115° within 5 min) to give tars and carbonaceous solids.

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