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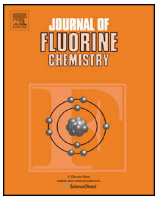

Mono- and dinitration of pentafluorosulfanylbenzenes with $[NO_2][BF_4]$, and substrate selectivity ($PhSF_5$ vs $PhCF_3$ and $PhSF_5$ vs $PhNO_2$) in competitive nitration

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ABSTRACT

$PhSF_5$ **1** reacts with $NO_2^+BF_4^-$/TfOH in CH_2Cl_2 (DCM) at room temperature to give 1-nitro-3-(pentafluorosulfanyl)benzene **2** in near quantitative yield. The dinitro derivative **4** is synthesized from **2** by reaction with $NO_2^+BF_4^-$/TfOH at 70 °C. The p-$MeC_6H_4SF_5$ is mononitrated at room temperature with $NO_2^+BF_4^-$/DCM and dinitrated with $NO_2^+BF_4^-$/TfOH. Substrate selectivity (k_{PhSF_5}/k_{RPh}) in competitive nitration for $PhSF_5/PhCF_3$ and $PhSF_5/PhNO_2$ with $NO_2^+BF_4^-$ in DCM at room temperature was determined at 21.3 and ~1 respectively. Relative stability of the corresponding benzenium ions were gauged by DFT from the isodesmic proton transfer reaction $SF_5{-}C_6H_6^+ + R{-}C_6H_5 \rightarrow SF_5{-}C_6H_5 + R{-}C_6H_6^+$ ($R = CF_3$ and NO_2). These studies indicate that reactivity of $ArSF_5$ in S_EAr is similar to $ArNO_2$.

1. Introduction

Synthesis of SF_5-aromatics continues to be a very active research area and considerable research effort is being directed to the development of methodology to synthesize SF_5-bearing building blocks for elaboration into pharmaceuticals, agrochemicals, and materials [1,2]. Incorporation of SF_5 group(s) imparts favorable physical and chemical characteristics including thermal, hydrolytic, and chemical stability, high density, high electronegativity, and high lipophilicity. Whereas a great majority of the reported methods for the synthesis of SF_5-aromatics begin with nitro-pentafluorosulfanyl benzenes [3–6], access to these compounds has been a major impeding factor to wider synthetic application [7].

The m-nitro and p-nitro derivatives have been accessible via the reaction of isomeric bis(nitrophenyl)disulfides with F_2/N_2 [8] but development of alternative, more practical, methods to elemental fluorination are highly desirable. To that end, Sergeeva and Dolbier [9] reported direct electrophilic nitration of $PhSF_5$ with H_2SO_4/HNO_3/TFA in 87% yield. Preparation of the 3,5-dinitro-SF_5-benzene was disclosed by Umemoto and Chika in a patent [10]. The p-tolyl-SF_5 was dinitrated with HNO_3/fuming H_2SO_4, then side-chain oxidation and decarboxylation furnished the 3,5-dinitro-SF_5-benzene [10].

In continuation of our earlier efforts directed toward the development of new methods for the synthesis of SF_5-aromatics [11] and our long standing interest in aromatic nitration [12] we report an alternative and convenient electrophilic method for the synthesis of the nitro-derivatives by using nitronium salt. Competitive nitration ($PhSF_5$ vs $PhCF_3$ and $PhSF_5$ vs $PhNO_2$) with $NO_2^+BF_4^-$ were also performed to gauge relative reactivity, and relative benzenium ion stabilities were calculated by DFT via isodesmic reactions.

2. Results and discussion

Mechanistic and synthetic aspects of aromatic nitration were extensively studied by Olah et al. over several decades [13]. Experimental and theoretical studies firmly established the concept of protosolvation of the nitronium ion leading to increased reactivity [14,15].

Considering the strongly deactivating effect of SF_5 ($\sigma_p = +0.68$) [1] nitration with the nitronium salt and protosolvation with triflic

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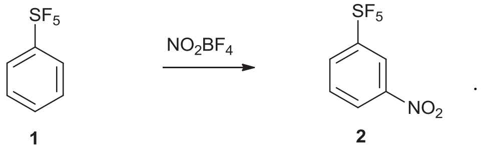
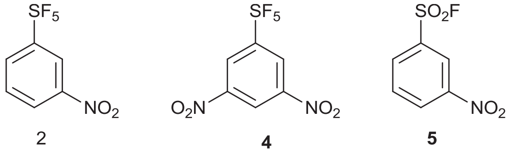
Table 1
Nitration of $PhSF_5$ with nitronium tetrafluoroborate under various conditions.



Solvent	NO_2BF_4	Temp.	Time	**2** (isolated yield, %)[a]
CH_2Cl_2	1.7 eq	rt	1d	61[b]
CH_2Cl_2	1.1 eq	rt	18 h	44[b]
$TfOH/CH_2Cl_2$	1.1 eq	rt	1d	100[c]
TfOH (neat)	1.5 eq	rt	14 h	66[b]
CH_2Cl_2	8.3 eq	then reflux for 3 h		83[c]
TfOH (neat)	15 eq	rt for 4 d; 40 °C for 5 h; 70 °C for 14 h		



(82:9:9 by NMR; before chromatographic isolation)

[a] Isolated yield after SiO_2 column chromatography.
[b] Traces of the *p*-nitro isomer was detected.
[c] Crude product was found to be pure except for a trace of the *p*-nitro isomer.

acid were considered as attractive direct one-pot methods for $ArSF_5$ nitration.

Nitration of $PhSF_5$ **1** with nitronium tetrafluoroborate was carried out under heterogeneous conditions in DCM at room temperature and after 1 day 1-nitro-3-(pentafluorosulfanyl)benzene **2** was obtained in 61% yield (Table 1). A small amount of 1-nitro-4-(pentafluorosulfanyl)benzene **3** was detected in the product mixture by ^1H NMR analysis. Nitration with 1.1 equiv. of NO_2BF_4 in TfOH/DCM resulted in near quantitative conversion to **2**, whereas nitration in neat TfOH at room temperature gave **2** in 66% yield. Both **1** and **2** were found to be stable in TfOH (no side reactions).

The use of excess NO_2BF_4 in DCM without TfOH resulted only in **2**, and refluxing in DCM after 3 h showed just a trace of the dinitro-derivative **4**. Increasing the temperature to 70 °C gave a mixture of **2**, **4**, and **5** in 82:9:9 ratio by ^1H NMR (Table 1).

Nitration of **2** in TfOH at 70 °C after 14 days (Scheme 1) gave a mixture of **4**, **6**, and **5** (Scheme 1) in 85:10:5 ratio by ^1H NMR. Silica gel column chromatographic separation afforded pure **4** in 17% yield, **6** in 2% yield, and **5** in 1% yield.

Surprisingly, nitration of the mono-nitro derivative **2** with $NO_2^+BF_4^-$ in $CH_2Cl–CH_2Cl$ (DCE) as solvent under reflux or in TfOH/DCE at 70 °C were unsuccessful and **2** was recovered (Table S1 in supplementary information).

Nitration of 1-methyl-4-(pentafluorosulfanyl)benzene **7** with NO_2BF_4 in DCM at room temperature gave the mononitro derivative 1-methyl-2-nitro-4-(pentafluorosulfanyl)benzene **8** in 89% yield (Table 2). Use of excess amounts of NO_2BF_4 in DCE as solvent at 70 °C did not lead to dinitration and the mononitrated product **8** was obtained in 89% yield.

Heating in neat TfOH at 70 °C with excess nitronium tetrafluoroborate furnished the desired 2-methyl-1,3-dinitro-5-(pentafluorosulfanyl)benzene **9**, along with 5-(fluorosulfonyl)-2-methyl-1,3-dinitrobenzene **10**, and 1-(fluorosulfonyl)-4-methylbenzene **11** in 77:19:4 ratio by ^1H NMR. Silica gel column chromatography purification afforded pure **9** in 47% isolated yield and 5-(fluorosulfonyl)-2-methyl-1,3-dinitrobenzene **10** in 18% yield.

3. Substrate selectivity in competitive nitration

The $–SF_5$, $–NO_2$, and $–CF_3$ groups represent the extreme examples of deactivating *meta* directing substitutents in S_EAr chemistry (σ_m and σ_p are 0.61 and 0.68 for SF_5, 0.71 and 0.78 for NO_2, and 0.43 and 0.54 for CF_3) [16].

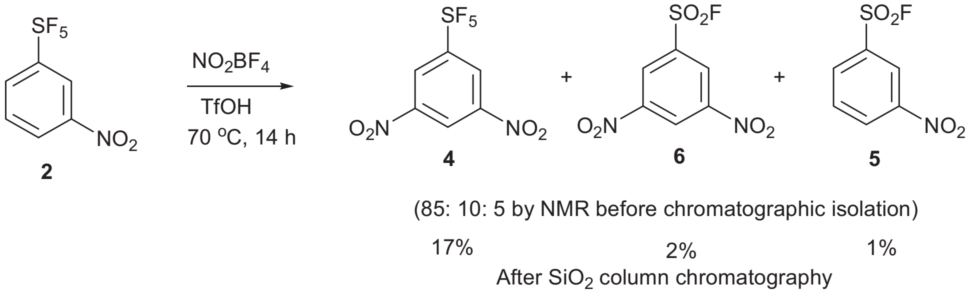
In the context of the present nitration study it was relevant to measure substrate selectivity for $PhSF_5$ vs $PhNO_2$ and $PhSF_5$ versus $PhCF_3$.

Nitronium tetrafluoroborate was added to 1:1 mixture of substrates in DCM, and after 8 h mixing at room temperature an aliquot was withdrawn, diluted with $CDCl_3$ and examined directly by NMR. Substrate selectivity was derived based on the ratio of the corresponding nitro-products (Tables 3 and 4).

In competitive nitration of $PhSF_5$ vs $PhCF_3$ (Table 3) the $C_6H_5SF_5/NO_2–C_6H_4–SF_5$ ratio was 87:13 whereas $PhCF_3/NO_2–C_6H_4–CF_3$ was 5:95, consistent with stronger deactivating effect of the SF_5 substituent, leading to a ratio of nitration rate constants $k_{PhCF_3}/k_{PhSF_5} = 21.3$. After 1 day, the $PhCF_3$ was completely nitrated.

In competitive nitration of $PhSF_5$ vs $PhNO_2$ after 7 h the $C_6H_5–SF_5/SF_5–C_6H_4(NO_2)$ and $PhNO_2/C_6H_4(NO_2)_2$ ratios were about equal (97:3) and after 1 day the ratios were 87:13 and 91:9. The data suggests a $k_{PhNO_3}/k_{PhSF_5} = {\sim}1$ showing similar deactivating effects.

Focusing on benzenium ion stabilities, and as an extension of the substrate selectivity measurements, relative energies of the *meta* protonated benzenium ions were calculated from the isodesmic reactions (Eq. (1)) with R = H, NO_2 and CF_3 by the DFT method at various levels and by incorporating solvent effect (PCM) (supplementary information).



Scheme 1. Dinitration of $PhSF_5$ with nitronium tetrafluoroborate in TfOH.