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REDUCTION OF THE 1-(4-THIOMETHYLPHENYL)-2,2,2-TRIFLUOROETHYL CARBOCATION BY SODIUM SULFITE

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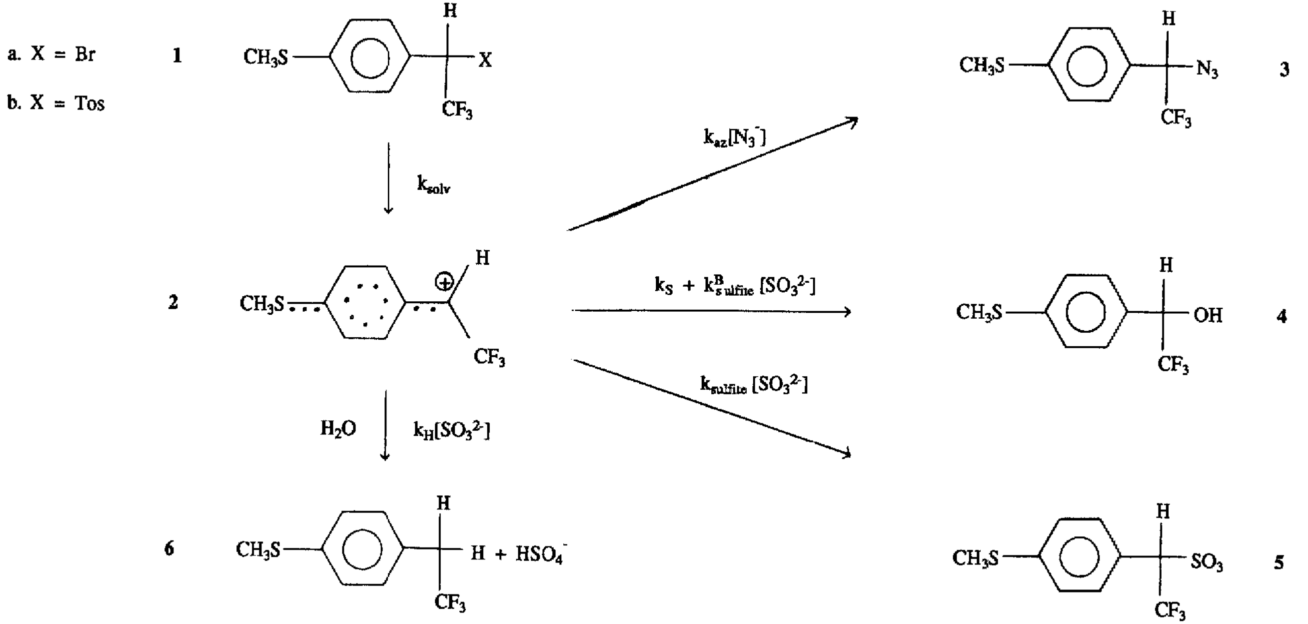
Abstract: The rate of the reaction of sodium sulfite with 1-(4-thiomethylphenyl)-2,2,2-trifluoroethyl bromide in 20% acetonitrile in water is kinetically zero-order in sulfite anion and at 0.27 M SO_3^{2-} the reaction gives a 0.67:0.15:0.18 ratio of the C-1 sulfite adduct, the water adduct and the novel reduction product 1-(4-thiomethylphenyl)-2,2,2-trifluoroethane, respectively.

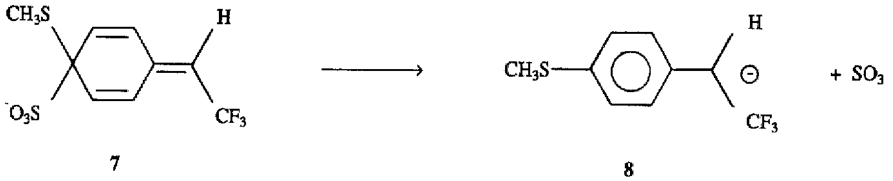
Recent studies of nucleophilic substitution reactions at ring-substituted ($\sigma^+ \le -0.32$) 1-phenyl-2,2,2-trifluoroethyl bromides, mesylates and tosylates have shown that solvent, N_3^-, I^-, Br^-, and amines add to the benzylic carbon of the 1-phenyl-2,2,2-trifluoroethyl carbocation reaction intermediate.[1] I report here that in largely aqueous solvents SO_3^{2-} reduces the 1-(4-thiomethylphenyl)-2,2,2-trifluoroethyl carbocation to the alkane **6** (Scheme).[2] This result is surprising, because an electron pair is not normally transferred from sulfite to a carbocation, but rather, forms a bond with carbon. The most recent work on substitution reactions at ring-substituted phenyltrifluoroethyl derivatives has concentrated on measuring the α-CF_3 substituent effect on the stability of the carbocation reaction intermediates.[1] This communication shows that inductive destabilization of the carbocation reaction intermediates may also dramatically affect the products of their reactions with added nucleophiles.

All of the following data were obtained for reaction of ca. 0.05 mM substrate in 20% acetonitrile in water at a constant ionic strength of 0.8 ($NaClO_4$). The mechanism in the Scheme is proposed to explain the results of rate and product studies for the reaction of **1** in the presence of Na_2SO_3 and/or NaN_3. Formation of the azide adduct **3** from **1a** and **1b** is by an S_N1 mechanism through the very unstable carbocation intermediate **2**.[1b,c] The rate constant ratio k_{az}/k_s for **2** partitioning between reaction with azide and solvent (calculated from the ratio of the concentrations of the azide and water adducts) is 210 M^{-1}.[3] This gives $k_s \cong 2 \times 10^7 s^{-1}$, assuming a value of 5×10^9 $M^{-1}s^{-1}$ for the diffusion-limited rate constant k_{az}.[1b,4]

The product yields for the reaction of **1a** in the presence of 0.27 M sodium sulfite are: C-1 adduct **5**, 67%;[5] hydride adduct **6**, 18%;[2] and water adduct **4**, 15%. There is strong evidence that both of the products of the sulfite reaction are produced by SO_3^{2-} capture of the carbocation intermediate **2**. (1) The same product concentration ratio **6**:**4** is obtained for the reaction of **1a** and **1b** with Na_2SO_3. The observation of leaving-group independent product


a. X = Br
b. X = Tos
1
2
3
4
5
6
CH₃S
H
X
CF₃
OH
N₃
SO₃
H + HSO₄⁻
k_solv
k_az[N₃⁻]
k_S + k^B_sulfite [SO₃²⁻]
k_sulfite [SO₃²⁻]
H₂O
k_H[SO₃²⁻]

Scheme


7
8
CH₃S
⁻O₃S
H
CF₃
+ SO₃

ratios is evidence that **6** and **4** are formed by partitioning of the intermediate **2**, rather than by reaction of sulfite dianion with a species which contains the leaving group. (2) The observed first-order rate constant for **1a** reaction decreases from $5.7 \times 10^{-4} s^{-1}$ to $2.8 \times 10^{-4} s^{-1}$ as the [Na_2SO_3] is increased from 0.0 M to 0.27 M.[6] This is consistent with an S_N1 reaction mechanism and a modest depression of the rate constant k_{solv} for **2** formation due to a specific Na_2SO_3 salt effect. (3) There is up to a 66% yield of the azide adduct **3**, and the same proportional *decrease* in the yields of the adducts **4**, **5** and **6** from the reaction of **1b**, as [NaN_3] is increased from 0.0 to 0.11 M at a constant concentration of 0.23 M Na_2SO_3. This result shows that all of the reaction products, including the reduction product **6**, are formed by reactions with the carbocation intermediate **2**. It is inconsistent with **6** formation by the direct reaction between sulfite and **1b**. For this reaction the yield of **6** would have remained constant with increasing [NaN_3], because azide anion trapping of **2** can not affect the yield of a product from a step that occurs prior to **2** formation.

There is a 2.2-fold increase in the yield of the water adduct relative to the azide adduct as [Na_2SO_3] is increased from 0 to 0.27 M at 5.3 mM [NaN_3]. This result is consistent with a sulfite-catalyzed pathway for the formation of the water adduct.[7,8] This pathway ($k_B[SO_3^{2-}]$, Scheme) may involve general-base catalysis by the sulfite dianion of water addition to **2**,[7] and/or the formation of the O-sulfite nucleophile adduct followed by its breakdown to give the alcohol.[8]

It may be necessary to expand the mechanism in the Scheme in order to account for all of the experimental results. The product concentration ratio **6**:**5** = $k_H/k_{sulfite}$ for the reaction of **1b** increases from 1.0:6.0 to 1.0:3.6 as [Na_2SO_3] is increased from 0.053 M to 0.27 M. Similarly, when **1b** reaction is carried out at a constant [N_3^-] (5.3 mM) the product rate constant ratio k_{az}/k_H decreases from 56 to 20 as [Na_2SO_3] is increased from 0.053 to 0.27 M. These changes are explained most simply by specific salt effects on one or more of the rate constants for **2** capture. However, they may point to a more complex mechanism for **6** formation in which the observed second-order rate constant k_H increases with increasing [Na_2SO_3]. This would occur if the overall velocity for **6** formation were proportional to $[SO_3^{2-}]^2$.

The competitive formation of the nucleophile adduct **5** and reduction product **6** from the carbocation **2** arises from *the partitioning of an electron pair at the sulfite dianion between covalent bond formation* ($k_{sulfite}$) *and electron transfer* (k_H) to **2**. While the reduction reaction is unusual, it is strongly favored by electrostatics. The driving force for the transfer of two electrons from sulfite to C-α of **2** is the change in the charge-dipole interactions between C-α and the electron-withdrawing CF_3 group - from strongly destabilizing at **2** to strongly stabilizing at **8** - associated with the change in charge at C-α from +1 to -1.

There are at least two plausible mechanisms for the conversion of **2** to **6**. (1) The reduction might occur by a two-step process in which the electron pair from the sulfite dianion is added to the C-4 ring position to give the covalent adduct **7**, and then abandoned by elimination of SO_3 to give the carbanion **8**, which is protonated by solvent. A related aromatic substitution reaction at a carbocation destabilized by two CF_3 groups is a step in the proposed mechanism for the formation of CH_3CH_2O-$ArC(CF_3)_2$-OCH_2CH_3 from the reaction of CH_3O-$ArC(CF_3)_2$-Tos in ethanol.[9] (2) The reduction of **2** may occur by two single electron transfers. If the electrons are transferred from different sulfite dianions, then the net velocity for the formation of the reduction product might depend on $[SO_3^{2-}]^2$. This is a possible explanation for the changing k_{az}/k_H and $k_H/k_{sulfite}$ values noted above. Further work is needed to determine the mechanism for electron transfer from sulfite dianion to the carbocation **2**.

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2. The products of the reaction of sulfite with **1a** were purified for spectral analysis by preparative HPLC over a reverse base octadecylsilane column, eluting with methanol/water. It is assumed that sulfate dianion is a reaction product; however, no attempt was made to identify SO_4^{2-} in the presence of a >>1,000 fold excess of SO_3^{2-}. The product **6** was identified by comparison with **6** synthesized chemically by catalytic hydrogenation of **1b**.[10] Samples of **6** obtained from chemical synthesis, and the reaction of sulfite with **1a** were shown to be the same compound by UV, NMR and mass spectroscopy. UV spectrum (water) λ_{max} 254; ^{1}H NMR ($CDCl_3$) δ 2.49 (s, 3, CH_3), 3.33 (q, J = 11 Hz, 2, CH_2), 7.23 (m, 4, C_6H_4); exact mass spectrum calcd. for $C_9H_9F_3S$ 206.0377, found 206.0378.

3. The products of these reactions were separated by HPLC, detected by their absorbance at 254 nm, and the product concentration ratios determined directly from the ratios of peak areas, with the assumption that the adducts have the same extinction coefficient at 254 nm (this assumption was shown to hold for **3**, **4**, and **6**). The rate constant ratios for partitioning of **2** were calculated from the product ratio and the ratio of the concentrations of the two nucleophiles. These methods and calculations are described in greater detail elsewhere.[1d,4]

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5. The sulfite adduct was purified by preparative HPLC. UV spectrum (water) λ_{max} 259; ^{1}H NMR (acetone d_6) δ 2.49 (s, 3, CH_3), 4.53 (q, J = 10 Hz, 1, CH), 7.54, 7.21 (A_2B_2, J = 8 Hz, 4, C_6H_4).

6. The reaction of **1a** was followed by monitoring the absorbance decrease at 280 nm.

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