Reaction of Simple Arenes with $FSO_3H \cdot SbF_5/SO_2$: One-Pot Synthesis of Aromatic Sulfoxides. Mechanistic Aspects and Synthetic Utility†

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In a simple one-pot reaction, mono-, di-, tri-, and polyalkylbenzenes, isomeric alkylhalobenzenes, and fluoro-, (trifluoromethyl)-, and 1,3,5-trifluorobenzene were converted to their corresponding diaryl sulfoxides with $FSO_3H \cdot SbF_5$ (1:1) (magic acid)/SO_2. Dependency of the yields on the acidity (H_0) and the arene structure was demonstrated. Reduction of the formed sulfoxide was also observed as a minor pathway to give diaryl sulfide. The reduction is superacid-catalyzed, and protonated sulfoxides are the key intermediates en route to sulfides. Protonation of several functionalized diaryl sulfoxides was also studied in magic acid/SO_2 under stable ion conditions. Unlike the parent diphenyl sulfoxide, which is S-protonated, alkyl-, fluoro-, and trifluoromethyl-substituted diaryl sulfoxides O-protonate to give long-lived sulfoxonium ions. The proposed mechanism for the arene/superacid/SO_2 system involves sulfination of the arenium ions, O-protonation of the resulting sulfinic acid, dehydration of the oxonium ion "$ArSO^+$" and arylation. In the absence of SO_2, the fluorosulfonation, ionization, arylation path becomes dominant. The scope of the reaction is sufficiently broad to be synthetically useful. The methodology is also applicable to unsymmetrical (mixed) diaryl sulfoxides.

Introduction

Pioneering work by Olah et al. led to generation and detailed studies of a great variety of stable arenium ions in superacid media.[1,2] Whereas low temperature protonation of benzene, fluorobenzene, and fluorotoluenes with $HF \cdot SbF_5$ or $FSO_3H \cdot SbF_5$ in SO_2ClF cleanly furnishes the arenium ions, addition of SO_2 as cosolvent leads to rapid formation of protonated sulfinic acid.[3-5] Its formation was explained either by nucleophilic attack of SO_2 on the arenium ion or by electrophilic attack of the SO_2–SbF_5 complex (a potent sulfinating agent) on the arene itself, with SO_2 promoting arenium ion deprotonation.[5] Ring sulfination was also observed by Winstein et al.[6] when studying O-protonated aromatic alcohols in magic acid/SO_2. Synthetic utility of O-protonated sulfinic acids (and the derived $ArSO^+$) in electrophilic chemistry, however, remains basically unexplored.

In our previous work on protosolvated onium ions Me_3S^+, Me_3Se^+, and Me_3Te^+ in superacid media and their alkylation ability toward aromatics,[7] an "unexpected" product, *p*-tolyl sulfoxide, was formed in the reaction of toluene with $FSO_3H \cdot SbF_5/SO_2$. We suggested that it might be formed by a fluorosulfonation, ionization, condensation sequence of toluene itself. Such a process should initially give a sulfone that is presumably reduced in situ to a sulfoxide! In view of the importance of sulfoxides as organic synthons (chirons) in synthesis,[8,9] a high-yield one-pot approach from simple arenes is highly desirable. Sulfoxides are usually synthesized by indirect methods, i.e., oxidation of sulfides, reduction of sulfones, or otherwise from sulfinic acid esters, mixed anhydrides, or sulfines with organometallic reagents.[8] Direct preparation of diaryl sulfoxides from simple arenes remains little explored. Syntheses of diaryl sulfoxides from arenes/$SOCl_2$/$AlCl_3$[8] and from arene/arenesulfinyl chloride/$AlCl_3$[10] are usually limited to substrates with activating substituents and often give low yields.[8] The $ArMgX/SOCl_2$ system is more promising but is limited to symmetrical sulfoxides.[8]

We report herein a detailed study of the arene/magic acid/SO_2 reaction, exploring its mechanism and synthetic scope.

Results and Discussion

When a cold homogeneous solution of $FSO_3H \cdot SbF_5$ (1:1) diluted in SO_2 was added slowly to excess toluene (8-fold) in Freon/SO_2 under nitrogen at dry ice–acetone temperature, an orange-green solution was formed, which on warming to −30 °C became dark blue. The temperature was slowly raised to 0 °C (purple solution). Quenching and workup furnished di-*p*-tolyl sulfoxide in 75% isolated yield, in addition to a minor product (6%), which was identified as the sulfide and confirmed by independent reduction of the sulfoxide ($PhTMS/I_2$)[11] and GC co-injection with the reaction mixture.

The di-*p*-tolyl sulfoxide yield increased still further (95% GC yield; 87% isolated) when we decreased the aromatic to superacid ratio to 2:1 (Figure 1).

To establish the role of superacid, in control experiments, the superacid:arene molar ratio was systematically varied from 0.05 to 0.5; the sulfoxide yield increased from 10–12% to 90%. Reactions that gave the highest yields were those in which initially 1 molar equiv of toluene was added to magic acid/SO_2 (−70 °C). After warming to −30 °C under nitrogen, the second mole of arene was injected into the reaction mixture.

In an independent experiment, the progress of reaction with time was monitored by GC. Cold aliquots were withdrawn and quenched at 20-min intervals for 2 h. Following an induction period (ca. 30 min), di-*p*-tolyl sulfoxide was formed rapidly and selectively in the reac-

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‡ In part.

(1) For comprehensive reviews on monoarenium ions, see: Olah, G. A.; Surya Prakash, G. K.; Sommer, J. In Superacids, Wiley: New York, 1985; pp 99–101. Brouwer, D. M.; Mackor, E. L.; MacLean, C. In Carbonium Ions; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley: New York; Vol. 2, Chapter 20.

(2) For representative examples of diarenium ions, see: Pagni, R. M. *Tetrahedron* **1984**, *40*, 4161.

(3) Olah, G. A.; Kiovsky, T. E. *J. Org. Chem.* **1967**, *89*, 5692.

(4) Olah, G. A.; Kiovsky, T. E. *J. Org. Chem.* **1968**, *90*, 2583.

(5) Olah, G. A.; Schlosberg, R. H.; Kelly, D. P.; Mateescu, G. D. *J. Am. Chem. Soc.* **1970**, *92*, 2546.

(6) Brookhart, M.; Anet, F. A. L.; Winstein, S. *J. Am. Chem. Soc.* **1966**, *88*, 5657.

(7) Laali, K.; Chen, H. Y.; Gerzina, R. J.; *J. Organomet. Chem.* **1988**, *348*, 199.

(8) Drabowicz, J.; Kielbasinski, P.; Mikolajczyk, M. In The Chemistry of Sulfones and Sulfoxides; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; Wiley: New York, 1988; Chapter 8.

(9) Madesclaire, M. *Tetrahedron* **1988**, *44*, 6537.

(10) Olah, G. A.; Nishimura, J. *J. Org. Chem.* **1974**, *39*, 1203.

(11) Olah, G. A.; Balaram Gupta, B. G.; Narang, S. C. *Synthesis* **1977**, 533.

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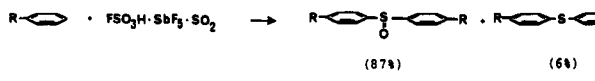


Figure 1. One-pot synthesis of diaryl sulfoxides in magic acid/SO_2.

tion, whereas the sulfide appeared at a much slower rate (qualitatively) after longer reaction times when the sulfoxide concentration had reached close to maximum, suggesting that the sulfide is formed from sulfoxide by in situ reduction!

We then explored the reaction of *p*-toluenesulfinic acid with magic acid/toluene *without* SO_2. The sulfinic acid was generated from its sodium salt by reaction with 1 molar equiv of magic acid and was protonated with an additional equivalent of the superacid in Freon. Reaction with toluene (1 equiv) gave a mixture of di-*p*-tolyl sulfoxide (77%) and di-*p*-tolyl sulfide (23%).

Probing the Reduction. In a control experiment, di-*p*-tolyl sulfoxide was reacted with a 10-fold excess of magic acid in SO_2 at dry ice/acetone temperature. The solution was allowed to warm up gently to 0 °C and then quenched and extracted. GC analysis of the reaction mixture showed a 75% yield of the sulfide and 25% unreacted sulfoxide.

In another experiment, di-*p*-tolyl sulfoxide was allowed to react with *p*-toluenesulfinic acid (generated in situ from the sodium salt with 1 equiv of FSO_3H·SbF_5 (1:1). GC analysis of the reaction mixture following workup showed that only traces of sulfide were formed. Di-*p*-tolyl sulfoxide was also reacted with *p*-toluenesulfinic acid, which was generated in situ from its sodium salt and FSO_3H (1 equiv), to ensure that the presence of SbF_5 did not affect these observations. Again, only traces of sulfide were detected. In a control experiment, reduction by SO_2 itself was also ruled out.

We concluded that di-*p*-tolyl sulfoxide reduction was promoted by the superacid and that reduction by toluenesulfinic acid to form di-*p*-tolyl sulfide and toluenesulfonic acid was unimportant.

Whereas a wide variety of methods are available for sulfoxide → sulfide conversion,[9,12a] reduction in a "highly oxidizing" superacid medium appears unconventional.[12b] We studied low temperature reactions of several functionalized sulfoxides with magic acid/SO_2 under stable ion conditions to establish the potential role of protonated sulfoxides in the reduction step.

Protonation Studies on Functionalized Diaryl Sulfoxides. Aliphatic sulfoxides are protonated on sulfur in superacid media and the S–H signal is observed at 5–7 ppm.[13] With parent diphenyl sulfoxide, protonation is accompanied by ring sulfonation. Ring sulfonation can be avoided by protonation in HF·SbF_5, where a sulfur-protonated onium ion (SH^+ at 5.03 ppm) is observed.[13]

We found that unlike the parent diphenyl sulfoxide, substituted diaryl sulfoxides are O-protonated in magic acid/SO_2. Moreover, the presence of substituents prevents ring sulfonation at low temperature.

Di-*p*-tolyl Sulfoxide 1. Addition of a cold solution of magic acid/SO_2 to di-*p*-tolyl sulfoxide in SO_2 at dry ice–acetone temperature gave a deep-blue solution, the ^1H NMR spectrum of which (−65 °C) showed two diagnostic singlets at 8.97 and 8.92 ppm in a 70:30 ratio indicative of an O-protonated sulfoxonium ion existing in two conformations,[14] in addition to a deshielded aromatic AB system [7.80 ($\Delta\delta$ = 0.30) and 7.53 ppm ($\Delta\delta$ = 0.29)] and a slightly deshielded methyl singlet at 2.42 ppm. The observed chemical shifts for the S–OH protons are close to those of O-protonated sulfinic acids.[15] The ^{13}C NMR of the ion showed a methyl resonance at 22.5 ppm and four aromatic signals at 116 (C_1) 133, 132 (C_2 and C_3), and 147 (C_4). The observed shielding at C_1 and deshielding at C_4 are indicative of π electron delocalization into the sulfoxonium ion ($p\pi$–$d\pi$ overlap) and reflect enhanced C–S double-bond character of the ion.[16]

When the NMR tube was stored at −20 °C and quenched after 24 h, GC analysis showed intact di-*p*-tolyl sulfoxide (54%), di-*p*-tolyl sulfide (25%), as well as two isomeric di-*p*-tolyl sulfonyl fluorides (26%) (ring fluorosulfonation); ^{19}F NMR of the reaction mixture showed a single peak at +39 ppm ascribed to SO_2F group.

Bis(3-(trifluoromethyl)phenyl) Sulfoxide (2). Low-temperature protonation of **2** gave a light-brown solution, the ^1H NMR spectrum of which showed a deshielded aromatic pattern (complex) between 7.9 and 8.55 ppm and two low-field singlets (two conformation)[17] for the S–OH^+ at 12.53 and 12.67 ppm in 42:58 ratio. Increasing the temperature (−20 °C) and prolonged storage (24 h) of the ion solution led to sulfide formation (40%, GC).

Bis(4-fluorophenyl) Sulfoxide (3). **3** was similarly O-protonated in magic acid/SO_2 (yellow-green ion solution) with the S–OH^+ signal appearing as a sharp singlet at 8.92 ppm (a single conformation)[18] and a downfield-shifted aromatic pair of doublet of doublets [7.88 ($\Delta\delta$ = 0.24) and 7.44 ppm ($\Delta\delta$ = 0.29)]. The ^{13}C NMR of the ion showed four signals at 136 (CF), 122, 121 (C_2 and C_3), and 118 (C_1). The observed shielding at C_1 and C_4 is attributed to fluorine back-donation ($n\pi$–$p\pi$–$d\pi$ conjugation); the latter is supported by a low temperature ^{19}F NMR spectrum showing a shift from −107 in the precursor to −78 ppm in the ion, viz. a 29 ppm deshielding at fluorine, which is close to F(para) deshielding observed by Olah and Mo[19] for the *p*-fluorobenzoyl cation (35.2 ppm). Increasing temperature and prolonged reaction times promoted sulfide formation. Thus when the ion solution was stored at −20 °C for 24 h, the ^{19}F NMR spectrum of the crude reaction mixture showed four singlets at −117 (sulfide; 60%), −107 (sulfoxide; 15%), −103 (20%), and −98 ppm (5%).

Bis(2,4-dimethylphenyl) Sulfoxide (4). Low temperature protonation of **4** with magic acid/SO_2 gave a light-brown solution, the ^1H NMR spectrum of which exhibited the S–OH^+ signal at 10.01 ppm, close to H_3O^+.[20] The aromatic and methyl protons were at 7.40 (s, $\Delta\delta$ =

(12) (a) Groosert, J. S. In *The Chemistry of Sulfones and Sulfoxides*; Patai, S., Rappoport Z., Sterling, C. J. M., Eds.; Wiley: New York, 1988; Chapter 20. (b) In a recent paper, the SO_3/thiol system was used for reduction of methionine sulfoxide to sulfide in protected peptides, see: Futahi, S.; Yagami, T.; Taike, T.; Akita, T.; Kitagawa, K. *J. Chem. Soc., Perkin Trans 1.* **1990**, 653.

(13) Olah, G. A.; Ku, A. T.; Olah, J. A. *J. Org. Chem.* **1970**, *35*, 3904.

(14) (a) The origin of two conformations is thought to be the near orthogonal relationship of the phenyl rings with respect to the CSC plane. [See: Hargittai, I. In *The Chemistry of Sulfones and Sulfoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; Wiley: New York, 1988; Chapter 2]. (b) We obtained a CSC angle of 112.6° by performing structure minimization (MMX) on **1**.

(15) Olah, G. A.; Ku, A. T.; Olah, J. A. *J. Org. Chem.* **1970**, *35*, 3908.

(16) The positive charge at sulfur contracts the 3d orbital and facilitates $p\pi$–$d\pi$ overlap (see ref 10). The near orthogonal CSC plane in **1** suggests that extended conjugation involving S=OH^+ is not feasible.

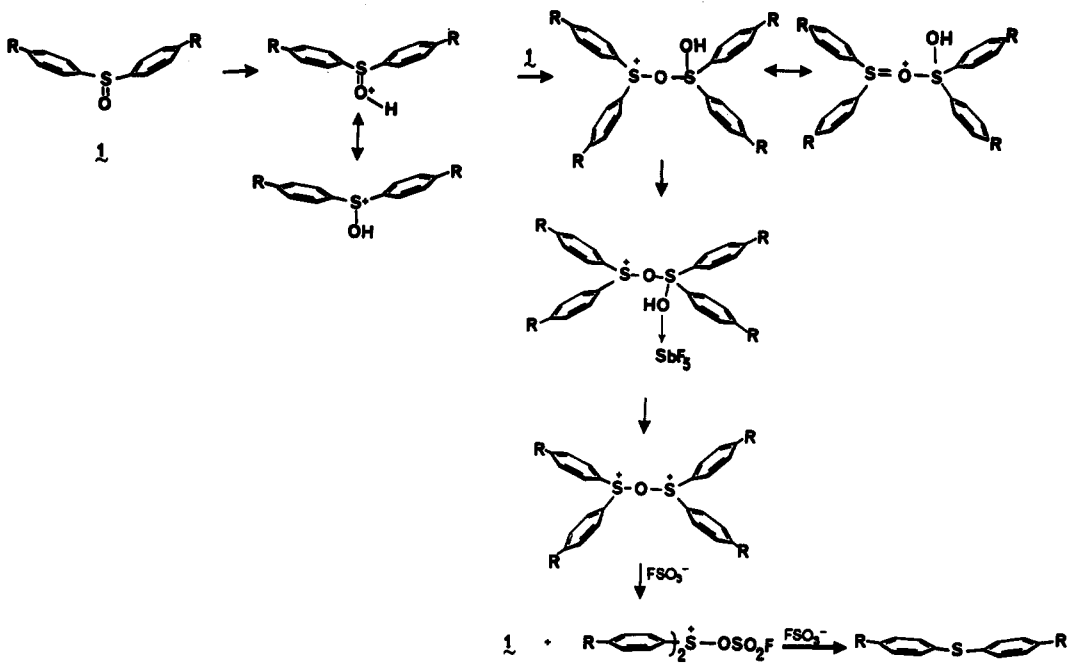
(17) The calculated CSC angle in the minimized structure for **2** is 102.8°.

(18) Although the minimized structure of **3** shows a CSC angle of 105.2°, only one conformation is detectable in the NMR spectrum. We believe this is indicative of a larger difference in stability of the two conformations. MO calculations will be needed to quantify such apparent relative stability differences.

(19) Olah, G. A.; Mo, Y. K. *J. Org. Chem.* **1973**, *38*, 2682.

(20) The calculated CSC angles in the minimized structure for **4** is 105.7°. As the SOH^+ peak is barely visible as a separate signal from H_3O^+, the presence of a second (superimposed) conformation for this ion cannot be excluded.

Scheme I. Suggested Reduction Mechanism



0.41), 7.28, 6.60 (pair of doublets), 2.45, and 2.40 ppm, respectively. The ^{13}C NMR spectrum showed two methyls and six aromatic signals at 21, 24, 117, 130, 131, 134, 141.5, and 147 ppm. The observed deshielding at methyl and shielding at C_1 (117 ppm) are once again taken as evidence for $p\pi$–$d\pi$ overlap and the enhanced CS double bond character of the ion.

Bis(2,4,6-trifluorophenyl) Sulfoxide (5) and Bis(2,4-diethylphenyl) Sulfoxide (6). 5 was found to be protonated on sulfur not on oxygen. A yellow solution was obtained upon low temperature reaction with the superacid/SO_2, the ^1H NMR spectrum of which showed a deshielded triplet for the ring hydrogens at 7.05 ppm [$\Delta\delta$ = 0.20] and a multiplet at 7.20 ppm ascribed to S–H^+. The sulfoxonium ion of 6 was not stable; *m*-diethylbenzenium ion[21] and protonated sulfinic acid were observed instead.

Reduction Mechanism. We found that under stable ion conditions the sulfoxide → sulfide conversion in the superacid via the sulfoxonium ions is a general process, establishing the importance of in situ formed sulfoxonium ions in the arene/magic acid/SO_2 system and their key role in the reduction step.

A similar chemistry was also observed in the more acidic superacid system $HF{\cdot}SbF_5$ (1:1)/SO_2; the blue sulfoxonium ion of 1 was briefly allowed to warm up to ca. −5 °C, whereby it turned dark brown. Quenching and GC analysis furnished the sulfide (90%), together with a new product having a retention time in between sulfide and sulfoxide (10%), and no unreacted sulfoxide remained.

The key role of the sulfoxonium ion in reduction was also supported by a control experiment in which 1 suspended in Freon-113 was reacted with SbF_5 alone in Freon, initially at −35 °C, and then the temperature was briefly raised to ca. −5 °C before quenching. GC analysis of the crude reaction mixture (yellow-brown) showed that 78% of the sulfoxide remained unreacted and that only 2–3% of the sulfide was formed. An oxidation product (di-*p*-tolyl sulfone) was not present; instead a new product (identical with that formed in the HF/SbF_5 reaction) was formed (19%).[22]

Di-*p*-tolyl sulfoxide 1 was also protonated with half a molar equivalent of the superacid in SO_2 solvent, to mimic the toluene/magic acid/SO_2 reaction more closely. The ^1H NMR spectrum of the deep-blue solution exhibited a single sharp peak at 9.05 ppm in addition to a deshielded aromatic AB and a single methyl peak. Tiny peaks due to residual FSO_3H and H_3O^+ were also present. The integrals confirmed that the 9.05 ppm peak accounted for a single proton in a dimeric structure (two sulfoxide units). The line widths and integrals ruled out an exchange equilibrium between protonated and nonprotonated sulfoxide.

In a control experiment, the sample was allowed to warm up to −10 °C for a few minutes and was cooled back to −70 °C. Irreversible formation of a small aromatic AB and a methyl was observed upfield from the main tolyl absorptions, in addition to a small broad peak at 5.3 ppm, which could be ascribed to a protonated sulfide.[23] The original spectrum is assigned to a dimeric sulfonium ion formed by nucleophilic attack of *p*-tolyl sulfoxide on protonated sulfoxonium ion (Scheme I). As only traces of excess superacid are available, formation of a sulfonium–oxonium dication by OH protonation is not feasible. The downfield position of the OH may, however, be explained by a combination of substantial oxonium ion character of the ion and OH complexation with SbF_5 to give a donor–acceptor complex. The following sequence of events may be proposed to account for the observed reduction at higher temperatures; heterolysis of the S–OH bond gives a disulfonium ether salt.[24a] Nucleophilic attack on S^+ by the

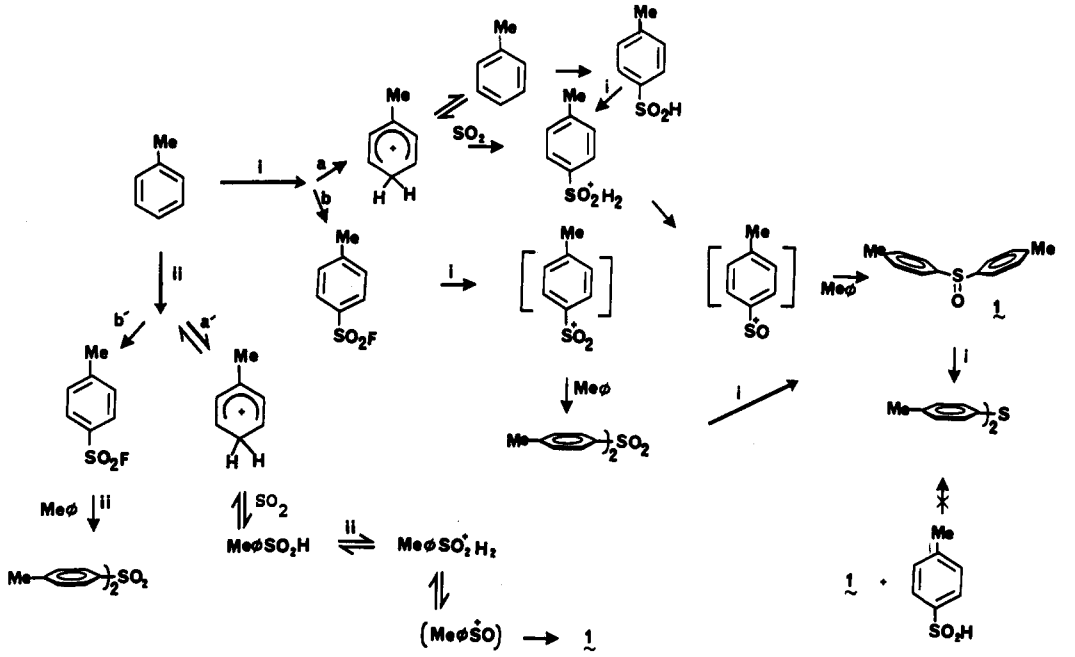
(21) Olah, G. A.; Spear, R. J.; Messina, G.; Westerman, P. W. *J. Am. Chem. Soc.* **1975**, *97*, 4051.

(22) Preliminary work shows that the new minor product is ditolylsulfur difluoride.

(23) Olah, G. A.; White, A. M.; O'Brien, D. H. *Chem. Rev.* **1970**, *70*, 561.

(24) (a) Dication ether salts of general structure >C^+–O–$^+$C< and >P^+–O–$^+$P< have been isolated via reaction of ketones, ureas, Ph_3PO, and HMPA with triflic anhydride, see: Stang, P. J.; Maas, G.; Smith, D. L.; McClosky, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 4838. Maas, G.; Stang, P. J. *J. Org. Chem.* **1983**, *48*, 3038. Gramstad, T.; Husebye, S.; Saebo, J. *Tetrahedron Lett.* **1983**, *24*, 3919. Aaberg, A.; Gramstad, T.; Husebye, S. *Tetrahedron Lett.* **1979**, 2263. (b) The >S^+–O–$^+$S< $2OTf^-$ (or >S^+–OTf^-OTf) analogue is also known (Hendrickson, J. B.; Schwartzman, S. M. *Tetrahedron Lett.* **1975**, 277). Both >P^+–O–$^+$P< and the sulfur analogue oxidize nucleophiles, see: Hendrickson, J. B.; Hussain, M. S. *J. Org. Chem.* **1989**, *54*, 1144.

Scheme II. Reaction Mechanism[a]



[a] (i) $FSO_3H.SbF_5$ (1:1); (ii) FSO_3H; (a, a') SO_2 solvent; (b, b') Freon solvent.

gegenion gives tolyl sulfonium fluorosulfate, regenerating *p*-tolyl sulfoxide.[24b] "Nucleophilic" removal of the fluorosulfate group (presumably by the gegenion) leads to the sulfide [with bis(fluorosulfonyl) peroxide as a possible initial oxidation product],[25] whereas attack on sulfur regenerates more sulfoxide.

For reduction in HF/SbF_5 similar mechanistic steps are proposed; nucleophilic attack by fluoride ion on dication ether salt leads to ditolylsulfonium fluoride and the sulfoxide. A second nucleophilic attack by F^- results in the sulfide and fluorine (oxidation product), whereas F^- quenching of the sulfoxonium ion could result in a *gem*-difluoro derivative.[22]

Arene/Superacid Reaction in the Absence of SO_2. Reaction of toluene with magic acid (2:1) in the absence of SO_2 (Freon solvent) gave a mixture of di-*p*-tolyl sulfone and di-*p*-tolyl sulfoxide in a 54:46 ratio (GC). The identity of the sulfone was confirmed by independent synthesis (oxidation of authentic sulfoxide[26] and GC coinjection).

For comparison, low-temperature reaction of an authentic sample of *p*-toluenesulfonyl fluoride with toluene (1 equiv) in magic acid was also examined. The substrate was first reacted with the superacid in Freon at dry ice–acetone temperature and then slowly added to cold toluene/Freon. The reaction progress was monitored by GC analysis. The sulfone was rapidly formed (no induction period) and the amount increased, whereas the sulfoxide appeared later and increased slowly. The final reaction mixture consisted of 70% sulfone and 30% sulfoxide, e.g., a very similar product mixture to those of toluene/magic acid (2:1)/Freon system.

Thus in the absence of SO_2, aryl sulfone formation is a dominant process, but sulfoxide is also formed.

Influence of H_0. The reaction of toluene with the less acidic superacid FSO_3H was also investigated with and without SO_2 in Freon solvent. In the presence of SO_2, *p*-tolyl sulfone and sulfoxide were formed in a ca. 1:1 ratio (GC) but in much lower yields (7.3 and 7.2%) compared to an identical reaction in magic acid. In addition, two isomeric toluenesulfonyl fluorides were detected (4.4% total).[27]

Thus lowering the acidity led to a substantial decrease in sulfoxide in favor of sulfone.

In the absence of SO_2, except for a reduction in yield, the arene/FSO_3H system gave a product mixture quite similar to that of arene/magic acid/Freon, viz. sulfone:sulfoxide 7:3 (GC).

Reaction Mechanism. Our experimental data and control experiments are compatible with the following mechanistic scenario (Scheme II): Low temperature protonation of toluene in magic acid/SO_2 gives an arenium ion (path a), which reacts with SO_2 to give a protonated sulfinic acid. Dehydration of the oxonium ion gives a "sulfinyl cation"; nucleophilic attack by arene furnishes the sulfoxide, which is in situ protonated. Arenesulfinic acid may also be formed by electrophilic sulfination of the arene itself with SO_2/SbF_5, as pointed out by Olah et al.[5]

A long-lived arylsulfinyl cation has not been observed under stable ion conditions. High substrate selectivity (K_T/K_B) and predominant para substitution observed in aromatic sulfinylation are strongly indicative of a weakly electrophilic onium ion.[10] In SO_2 solvent, arenium ion sulfination is the dominant pathway and the fluorosulfonation, ionization, arylation sequence (Path b), which leads to a sulfone, is not competitive.

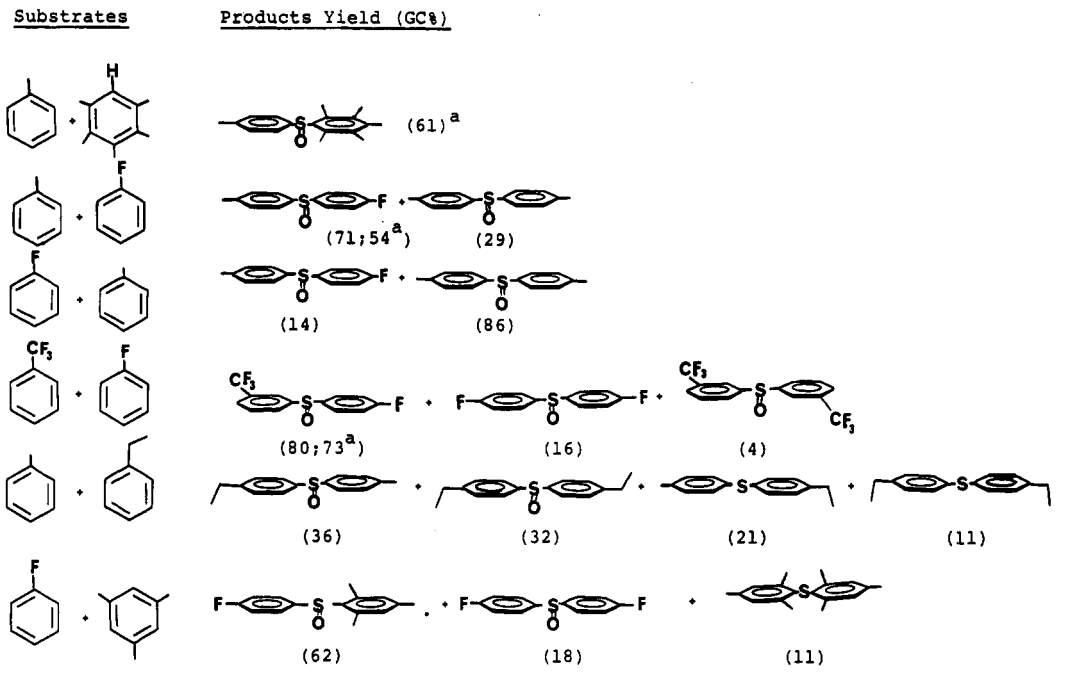
In the absence of SO_2, only path b is viable, which leads to the sulfone. The sulfoxide formed in the arene/magic acid/Freon system must, therefore, arise from sulfone reduction. As diaryl sulfones were shown by Olah et al.[13] to be O-protonated in superacid media, the sulfone → sulfoxide reduction must, in all probability, go through a diaryl sulfonium cation.

(25) (a) For a review of sulfonyl peroxides, see: Hoffman, R. V. In *The chemistry of Peroxides*; Patai, S., Ed.; Wiley: New York, 1983; Chapter 9. (b) For oxidation of anhydrides, see: Swern, D. In *Organic Peroxides*; Swern, D., Ed.; Wiley: New York, 1970; Vol. 1, Chapter 6.

(26) MCPBA was used as oxidant to prepare the authentic sulfone.

(27) Ambient reaction of aromatic compounds with FSO_3H was reported to give arenesulfonic acid, arenesulfonyl fluorides, and diaryl sulfone [Steinkoff, W. *J. Prakt. Chem.* **1927**, *117*(2), 1].

Scheme III. Synthesis of Mixed Sulfoxides[a]



[a] Isolated yield.

In the lower acidity superacid FSO_3H/SO_2, arenium ion (or arene) sulfination (path a') becomes competitive with ring fluorosulfonation because (a) the arenium ion is less fully protonated, hence *nucleophilic* attack by SO_2 is less effective, or (b) SO_2 is not as effective as SO_2/SbF_5 for *electrophilic* sulfination of the arene itself in equilibrium. Hence, sulfone and sulfoxide are formed in nearly equal amounts. The crucial sulfinic acid protonation step is likely to be an equilibrium in the lower H_0 superacid, which could also contribute to lowering sulfoxide yield.

Synthetic Scope. The reaction was tested for a variety of arene substrates (Table I) to determine the synthetic scope and limitations of our one-pot synthesis.

Both steric and electronic factors appear to be important. Whereas near quantitative yields were obtained with toluene, fluorobenzene, ethylbenzene, and α,α,α-trifluorotoluene, the yields decreased with *m*-xylene, *m*-diethylbenzene, and mesitylene. 1,3,5-Trifluorobenzene gave a better conversion than pentamethylbenzene. Electronically, alkyl substituents in the ortho/para positions increase benzenium ion stability relative to halogen substituent, and hence retard reaction with SO_2. Sterically, when in the meta position, both alkyl and halo groups increase the degree of crowding in the transition state for arenium ion sulfination and the subsequent arylation step.

Halotoluenes. Low temperature protonation studies with isomeric fluorotoluenes showed that fluorine takes preference over a methyl in directing the position of protonation. With *o*- and *m*-fluorotoluenes the arenium ion of protonation para to fluorine is exclusively observed.[3,4] Aprotic sulfonation of halotoluenes also showed the same trends; with 2-fluoro- and 3-fluorotoluene, we obtained 95% of the 5-sulfonic acid and 90% of the 6-sulfonic acid, respectively.[27] 2-Chloro- and 3-chlorotoluene gave 70% of the 5-sulfonic acid and 79% of the 6-sulfonic acid, respectively.[28] In agreement with protonation and sulfonation data, reaction of 2-fluoro- and 3-fluorotoluene and 2-chlorotoluene with magic acid/SO_2 gave only the sulfoxide derived from initial sulfination para to F and Cl (just one methyl absorption in the NMR). With 3-fluorotoluene, traces of sulfone and sulfonyl fluorides were present (GC) and with 2-chlorotoluene ca. 5% of the sulfide was detected (GC). 3-Chlorotoluene, on the other hand, gave a mixture of three symmetrical (isomeric) diaryl sulfoxides (three different methyls in the ^1H and ^{13}C NMR spectra). The isomer distribution was calculated from the relative integrals in the proton spectrum as 50% (6-ArSO), 35% (4-ArSO), and 15% (5-ArSO).

Synthesis of Unsymmetrical (Mixed) Sulfoxides. The "arylsulfinyl cation" generated in situ by addition of 1 molar equiv of the arene to magic acid/SO_2 in Freon solvent may also be arylated with a different arene injected into the cold reaction mixture, to give mixed sulfoxides. We found that the order of addition controlled the ratio of the symmetrical to mixed sulfoxides. For example, addition of fluorobenzene to the arenium ion of toluene in SO_2 gave a 71% yield of the desired mixed sulfoxide, whereas reverse addition gave an 86% yield of tolyl sulfoxide and only 14% of the unsymmetrical product (Scheme III). Representative examples are included in Table I.

Polycyclic Aromatics. Extension to polycyclic arenes was briefly explored with 1-methylnaphthalene (1-MN), 2-methylnaphthalene (2-MN), and 1-chloronaphthalene (1-ClN) as substrates.

Under stable ion conditions in magic acid/SO_2ClF, 1-MN and 2-MN are exclusively protonated at the 4 and 1 positions, respectively.[29] 1-ClN is predominantly protonated at the 4 position (90%).

Whereas 1-MN reacted with 2 equiv of the superacid in SO_2 to give a mixture of sulfoxide and sulfone (^1H NMR), extensive tar and polymeric materials were formed. Similar observations were made with 2-MN and 1-ClN. The reactions were subsequently carried out in FSO_3H/SO_2 to

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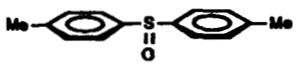
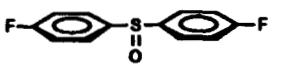
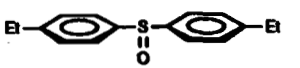
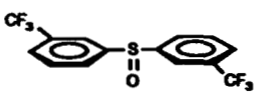
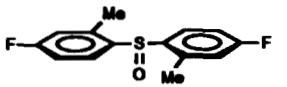
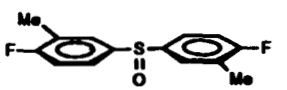
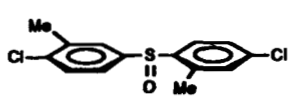
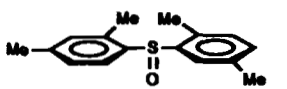
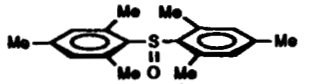
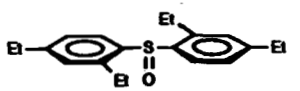
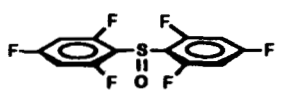
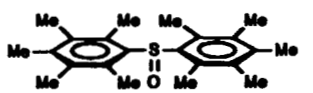
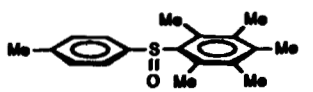
Table I. Spectral Data for Diaryl Sulfoxides[a]

arene substrate(s)	sulfoxide	yield (GC %) isolated	mp (°C)	^{1}H NMR	^{13}C NMR (^{1}H decoupled)	IR (cm^{-1})
toluene		95 (87)	94–96	2.36 (s), 7.24 (d, J = 7.2), 7.51 (d, J = 7.2)	21.3, 124.93, 129.93, 141.35, 143.0	3060, 2990, 1600, 1510, 1430, 1050
fluorobenzene		100 (55)	oil	7.16 (t, J = 8.7), 7.64 (dd, J = 7.36 and 4.2)	116.6 (d, J_{CF} = 22.2), 127.1 (d, J_{CF} = 8.33), 141.1, 164 (d, J_{CF} = 252)	3040, 2990, 1585, 1470, 1380, 1230, 1040
ethylbenzene		97 (90)	oil	1.22 (q, J = 7.96), 2.6 (t, J = 7.8), 7.24 (d, J = 7.97), 7.137 (d, J = 7.97)	15.4, 28.64, 124.91, 128.75, 131.1, 142.75	3050, 2985, 2925, 1610, 1490, 1410, 1040
(trifluoromethyl)-benzene		81 (55)	44–45	7.5 (d, J = 7.2), 7.62 (t, J = 7.2), 7.80 (m) [7.96 (br s), 7.86 (d), 7.74 (d)][b]	126.65 (q, J_{CF} = 20), 128.51, 129.96, 130.1, 132.94, 133.2, 137, 138.2	3020, 1590, 1445, 1340, 1065
m-fluorotoluene		74 (60)	115–117	2.33 (d, $^5J_{HF}$ = 5), 6.94 (d, J = 8.7), 7.08 (t, J = 7.91), 8.21 (t, J = 7.1)	20.24, 113.20 (d, J_{CF} = 22), 119.53 (d, J_{CF} = 22), 132.68 (d, 9.6), 134.67, 141.17, 165.30 (d, J_{CF} = 255)	3040, 2085, 1590, 1475, 1410, 1231, 1060
o-fluorotoluene		72 (64)	62–63.5	2.30 (d, $^4J_{HF}$ = 18), 7.08 (t, J = 8.7), 7.42 (t, J = 5), 7.48 (d, J = 6.6)	13.5, 115.13 (d, J_{CF} = 24), 126.91, 128 (d, J_{CF} = 22), 129, 141, 163.5 (d, J_{CF} = 250)	3060, 2085, 1585, 1485, 1235, 1045
o-chlorotoluene		69 (66)	77–78	2.40 (s), 7.28 (d, J = 7), 7.42 (d, J = 7), 7.51 (s)	20.14, 123.27, 126.63, 130.0, 131.75, 137.8, 143.57	3050, 2885, 1590, 1470, 1385, 1045
m-xylene		65 (61)	167–169	2.33 (s), 2.35 (s), 6.99 (s), 7.13 (d, J = 7.8), 7.56 (d, J = 7.8)	18.4, 21.1, 126.19, 127.75, 131.55, 136.46, 139.21, 141.24	3060, 2985, 1600, 1445, 1040
mesitylene		48 (26)	198–200	2.2 (s), 2.34 (s), 6.79 (s)	20.64, 21.52, 131.88, 138.42, 138.43, 142.13	3040, 2985, 1590, 1440, 1030
m-diethylbenzene		32 (27)	oil	1.18 (t, J = 5.48), 1.23 (t, J = 5.05), 2.67 (q, J = 7.45), 2.79 (q, J = 7.31), 7.08 (s), 7.16 (d, J = 7.98), 7.57 (d, J = 7.98)	14.88, 15.1, 25.04, 28.57, 126.18, 126.54, 128.48, 131.1, 138.66, 142.52	3085, 2990, 2970, 1600, 1460, 1060
1,3,5-trifluorobenzene		30 (10)	oil	6.85 (J_{HF} = 8.1)	102.7 (t, J_{CF} = 8.1), 132.57 (m), 167.36 (d, J_{CF} = 279), 161.1 (d, J_{CF} = 262.2)	3100, 1610, 1455, 1420, 1225, 1050
pentamethylbenzene		– (15.5)	95–97	2.23 (s), 2.27 (s), 2.57 (s)	16.8, 16.97, 18.8, 127.80, 134.91, 135.29, 142.11	3050, 2985, 2925, 1610, 1490, 1410, 1040
toluene and pentamethylbenzene		– (61)	183–184	2.19 (s), 2.26 (s), 2.36 (s), 2.40 (s), 7.21 (d, J = 7.2), 7.28 (d, J = 7.2)	16.2, 17.3, 21.1, 124.34, 129.38, 134.49, 135.34, 137.64, 139.18, 139.30, 142.1	3050, 2885, 1595, 1450, 1380, 1040

toluene and fluorobenzene		71 (54)	oil	2.29 (s), 7.12 (m), 7.42 (m)	21.18, 116 (d, J_{CF} = 28), 124.8, 126.9 (d, J_{CF} = 8), 129.9, 133, 141, 141.8, 146, 164 (d, J_{CF} = 250)	3020, 2875, 1595, 1490, 1230, 1045
fluorobenzene and trifluoromethylbenzene		80 (73)	oil	7.07 (t, J = 8.1), 7.34 (t, J = 7.03), 7.45 (d, J = 6.38), 7.63 (d, J = 7.6), 7.69 (br, d)	115.23 (d, J_{CF} = 21), 116.53 (d, J_{CF} = 22), 126.8 (d, J_{CF} = 8), 128.16, 129.65, 132.28, 132.40, 132.51, 140.1, 165 (d, J_{CF} = 252)	3080, 1595, 1490, 1440, 1230, 1040

[a] J values are in hertz. [b] Assigned to ring fluorosulfonation product (10–12%):

avoid SbF_5-meditated oxidative side-product formation. Thus, 1-MN reacted to give a 21% isolated yield of the sulfone. The product showed a single deshielded methyl at 2.76 ppm ($\Delta\delta$ = 0.17) and a distinct 1190 cm^{-1} absorption in the IR spectrum. There was no signal in the ^{19}F NMR spectrum, ruling out any sulfonyl fluorides.

Observed absence of sulfoxide with 1-MN may be due to a much higher stability of its arenium ion, which lacks sufficient reactivity toward SO_2 at low temperature. At higher temperatures, ring flurosulfonation, ionization, and arylation paths take over and lead to sulfone.

Surprisingly, 2-MN and 1-ClN did not form sulfones or sulfoxides with FSO_3H/SO_2. The substrates were recovered intact (75–85%) upon quenching and workup.

Experimental Section

The aromatic substrates were the highest purity commercial samples, which were distilled once and stored over molecular sieves. *p*-Toluenesulfinic acid–sodium salt and *p*-toluenesulfonyl fluoride were purchased (Aldrich) and used without further purification. FSO_3H (Allied) and SbF_5 (Aldrich) were freshly distilled in an all-glass distillation unit under dry nitrogen. Anhydrous Freon-113 (Aldrich) and SO_2 (Linde) were used without further purification. Diaryl sulfoxides used for protonation studies were products obtained through this work as described.

The proton and carbon spectra were recorded on a GN-300 wide-bore instrument using a 5-mm switchable probe. ^{19}F NMR data were acquired with a dedicated 5-mm fluorine probe. Low temperature spectra were obtained by precooling the probe, while shimming on acetone-d_6. The sample tube containing the cold ion solution was quickly introduced into the magnet and spun for ca. 5 min prior to data acquisition; CD_2Cl_2 was used as lock and reference. For ^{19}F work, an external $CFCl_3$/acetone-d_6 (1:1) sample provided the lock and reference.

GC analyses were performed with an HP 5890A instrument using a 5-m HP methylsilicone gum capillary column.

IR spectra were recorded on a Perkin-Elmer Model 1310 spectrophotometer.

General Procedure for Sulfoxide Synthesis. In a typical experiment, toluene (0.92 g, 0.01 mol) was diluted with 25 mL of Freon-113 and cooled to −78 °C under nitrogen. A clear solution of magic acid (3.168 g, 0.01 mol) was diluted with 5 mL of SO_2 at dry ice–acetone temperature (vortex). The superacid was slowly added to the aromatic and the solution slowly warmed to −30 °C. To the latter was dropwise added (via a precooled syringe or pipet) a second molar equivalent of the arene diluted in Freon. The mixture was slowly allowed to reach 0 °C. Stirring was continued for ca. 1.5 h under a nitrogen atmosphere, following which the reaction mixture was carefully quenched (ice/bicarbonate), extracted (CH_2Cl_2), dried ($MgSO_4$), and separated. The crude mixture was concentrated and analyzed by GC prior to crystallization [CH_2Cl_2/hexane (1:1), ethyl acetate or hot methanol]. In the GC monitoring experiments, ca. 2 mL of cold aliquots were withdrawn from the reaction mixture at 0 °C, at 20-min intervals for a total of 2 h. The aliquots were quenched and worked up as before.

The procedure for mixed sulfoxide synthesis was as above, except that a different arene (1 equiv) diluted in Freon solvent was injected into arene/superacid (1:1)/SO_2 at −30 °C.

Di-*p*-tolyl Sulfoxide Reaction with Magic Acid. To a clear solution of magic acid (0.5 mL) diluted in SO_2 (2 mL) was added a solution of di-*p*-tolyl sulfoxide (30 mg) in SO_2 (0.5 mL) at dry ice/acetone temperature under a nitrogen atmosphere. The solution was slowly warmed to 0 °C over a period of 90 min, then quenched, extracted, and analyzed by GC.

Di-*p*-tolyl Sulfoxide Reaction with Toluenesulfinic Acid. Di-*p*-tolyl sulfoxide (30 mg) dissolved in SO_2 (2 mL) was added to a cold solution of toluenesulfinic acid (100 mg; generated from the sodium salt and 1 equiv of magic acid) diluted in SO_2 (1 mL). The temperature was slowly increased to 0 °C over a 90-min period. The mixture was quenched, extracted, and subjected to GC analysis.

Stable Ion Generation. To the diaryl sulfoxide substrate (40–60 mg) charged into a 10-mm NMR tube and diluted with

0.5 mL of SO_2 was slowly added a clear, homogeneous solution of magic acid (1 mL) in SO_2 (ca. 1 mL) at dry ice-acetone temperature with efficient vortex mixing. A cold aliquot was withdrawn with a precooled pipet (SO_2) and transferred into a 5-mm NMR tube under nitrogen, to which ca. 5 drops of cold CD_2Cl_2 had been added (vortex). NMR spectra were recorded at -65 °C.

Molecular Modeling. MMX force field energy calculations on the sulfoxide substrates were carried out by using the PCMODEL program (Serene Software). Good convergence was achieved after 100 iterations. The CSC angles were obtained directly from the minimized structures.

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Solvolysis Rates and β-Deuterium Secondary Kinetic Isotope Effects of Some Tertiary and Secondary Alk-5-enyl Derivatives. Evidence for π-Participation

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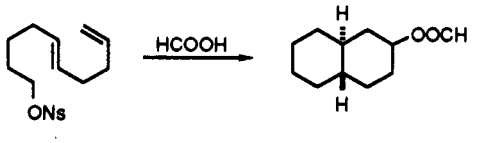
Tertiary 1,1-dimethylalk-5-enyl chlorides solvolyze in 80% v/v ethanol with no or moderate rate enhancements attributable to π-participation. However, secondary β-deuterium kinetic isotope effects (KIE, two deuterated methyl groups) are significantly reduced (k_H/k_D = 1.22-1.57) relative to the saturated analogues (k_H/k_D = 1.80), indicating participation of the double bond. Secondary 1-methylalk-5-enyl tosylates show the same trends, i.e., no or very moderate rate enhancements but reduced β-deuterium secondary KIE relative to the saturated analogue.

Introduction

Biomimetic cationic polycyclizations have been extensively investigated.[1,2] A great deal of fascinating synthetic work has been reported. It was demonstrated that (poly)cyclic products are obtained from mono-, di-, and polyolefinic substrates with a variety of leaving groups in reactions that proceed by way of carbocation intermediates; under appropriate conditions rings may be produced with high stereoselectivity or stereospecificity from epoxides, acetals, or sulfonate esters. For example, the formolysis of 5,9-decadienyl *p*-nitrobenzenesulfonate proceeds with bicyclization to yield decalin products stereospecifically.[3] From the *E* isomer only the *trans*-decalin ester is formed while the *Z* isomer gives exclusively the *cis*-decalin derivative.



The cyclization mechanism is, however, not well understood; it is not certain whether the final product arises by way of formation of an initial carbenium ion intermediate, which then cyclizes in a stepwise manner through discrete partially cyclized intermediates, whether only the formation of the first ring is concerted with the departure of the leaving group, or whether the whole polycyclization process is concerted. Concerted processes inevitably involve π-participation, i.e., one or more double bonds would be involved in the rate-determining formation of the carbocation. The usual method for detecting such participation involves the comparison of reaction rates. Unfortunately, kinetic data reported in the literature are scarce. We therefore initiated an investigation involving measurements of solvolysis rates of pertinent substrates. As a first step, we set out to detect simple π-participation, i.e., to investigate the reactivity of olefinic substrates containing only one CC double bond at the 5-position.[4,5]

For biomimetic cationic monocyclization, the reported rate data are not without ambiguity. Bartlett[6] and Trahanovsky[7] demonstrated that the solvolysis of 5-hexenyl *p*-nitrobenzenesulfonate proceeds with a slight rate enhancement relative to the saturated analogue and produces some cyclohexyl and methylcyclopentyl derivatives. Van Tamelen[8] reported that the acid-catalyzed epoxide ring opening of 1 proceeds with extensive cyclization and at a rate much faster than that of its saturated analogue. In our previous work we extensively examined solvolysis rates of a series of benzylic chlorides 2 and their saturated analogues.[9] Although the observed rate enhancements due

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