# Desulfination of Allylic Sulfinic Acids: Characterization of a Retro-Ene Transition State

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Allylic sulfinic acids have been prepared by cleavage of trialkyltin allylic sulfinates with trifluoroacetic acid (TFA). Allylsulfinic acid prepared in this way could be trapped as the sodium salt or observed by NMR and UV spectroscopy to undergo spontaneous decomposition to propene and sulfur dioxide at ambient temperatures. The corresponding reaction of 1-methylprop-2-enylsulfinic acid was regiospecific, yielding (*E*)- and (*Z*)-2-butene (*E*:*Z* = 82:18). Acidolysis of *E*/*Z* mixtures of trimethyltin 5-methylcyclohex-2-enylsulfinate with [$^2$H]-TFA followed by desulfination indicated that the latter process proceeded with $\gamma$-*syn* deuterium migration, consistent with a concerted, retro-ene mechanism. A detailed kinetic investigation of allylsulfinic acid desulfination supported this conclusion. This reaction obeyed a first order rate law ($k_{297K}$ = (5.5 ± 0.1) × $10^{-4}$ $s^{-1}$ in toluene) with a large, negative activation entropy ($\Delta S^{\ddagger}$ = −146 ± 17 J $K^{-1}$). The rate of desulfination was essentially independent of solvent. The volume profile ($\Delta V^{\ddagger}$ = −5.5 ± 1.0 $cm^3$ $mol^{-1}$, $\Delta V$ = 15 ± 5 $cm^3$ $mol^{-1}$) is comparable to that of a retro Diels–Alder reaction and taken together with the above evidence and a relatively small deuterium kinetic isotope effect ($k_H/k_D$ = 2.5 ± 0.1) strongly supports a concerted desulfination, proceeding via a relatively compact, early transition state.

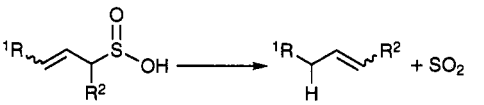
## Introduction

The thermal desulfination of allylic sulfinic acids is a synthetically useful procedure for the regio- and stereospecific synthesis of alkenes. Desulfination occurs readily at ambient temperatures and proceeds with allylic transposition of the double bond (Scheme 1).[1]

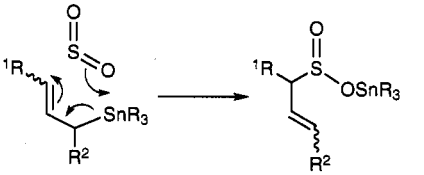
Allylic sulfinic acids are generally unstable,[1] formed only as transient intermediates in a variety of transformations including the sulfur dioxide isomerization of alkenes,[2] the hydrolysis of sulfinimides,[3–5] reduction of $\beta$-ketosulfones,[6] and the oxidation of allylic thiols.[7] The latter has been utilized for the allylic rearrangement of a double bond with concomitant, stereospecific introduction of the fused ring junction in a synthesis of *cis*- and *trans*-hydrindanones.[7]

While a retro-ene mechanism has been proposed for the thermal decomposition of allylic sulfinic acids, the instability of the substrate has precluded a definitive and detailed mechanistic investigation. We have recently communicated that allylic sulfinic acids can be conveniently prepared from allylic stannanes and desulfination monitored by NMR or UV spectroscopy.[8,9]

**Scheme 1**




**Scheme 2**




## Results

**Synthesis of Allylic Sulfinic Acids and Sodium Salt.** Triorganotin allylsulfinates are rapidly and quantitatively formed by bubbling sulfur dioxide through a solution of the allylic stannane. When performed in a relatively nonpolar solvent (chloroform or dichloromethane), the insertion reaction is regio- and stereospecific, proceeding via a concerted, metallo-ene cycloaddition (Scheme 2).[10]

Treatment of allyltributylstannane with sulfur dioxide in this way provided tributyltin allylsulfinate. Addition of 1 equiv of trifluoroacetic acid (TFA) to the tin sulfinate in chloroform immediately yielded tributyltin trifluoroacetate and allylsulfinic acid as determined by $^1$H and $^{13}$C NMR spectroscopy. Subsequent spectra indicated the relatively slow decomposition of the latter to propene. Addition of 0.5 equiv of TFA to tributyltin allylsulfinate provided only one set signals in the $^1$H and $^{13}$C NMR spectra prior to decomposition. These signals were of intermediate chemical shift between starting materials and products, suggesting a rapidly established equilibrium.

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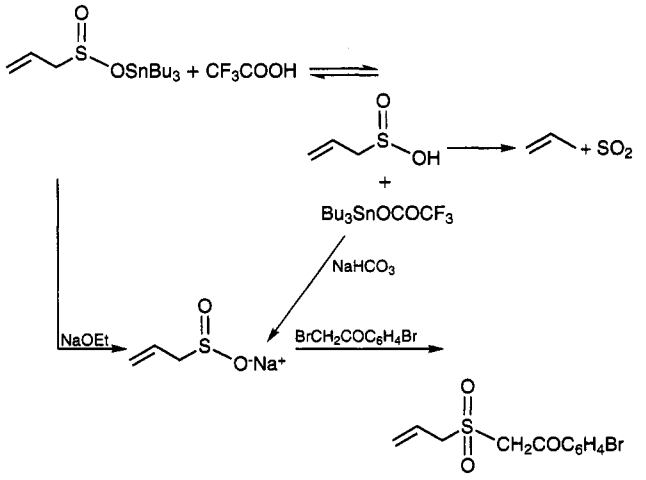
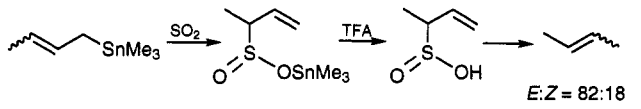
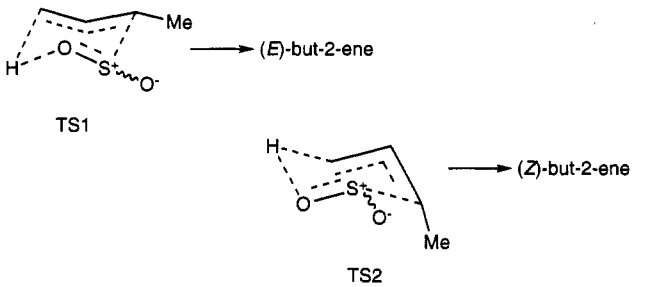
**Scheme 3**




**Scheme 4**




**Scheme 5**



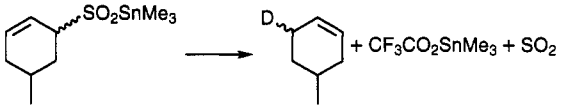

Quenching with 1 equiv of aqueous sodium bicarbonate immediately after acidolysis with 0.97 equiv of TFA provided sodium allylsulfinate in 78% isolated yield (Scheme 3). Alternatively, the sodium salt could be prepared directly from tributyltin allylsulfinate by treatment with an ethanolic solution of sodium hydroxide. The sodium salt was converted to allyl *p*-bromophenacyl sulfone for complete characterization.

**The Regio- and Stereochemistry of Rearrangement.** But-2-enyltrimethylstannane underwent sulfur dioxide insertion to yield trimethyltin 1-methylprop-2-enylsulfinate. Acidification with TFA in chloroform generated the branched sulfinic acid which subsequently underwent desulfination regiospecifically to yield but-2-ene ($E/Z$ = 4.5) (Scheme 4).

This moderate excess of the $E$ isomer can be explained by a mechanism involving the concerted transition states TS1 and TS2 with TS1 of a slightly lower energy (Scheme 5). More conclusive stereochemical information, however, was obtained by employing the configurationally defined, trimethyltin 5-methylcyclohex-2-enylsulfinate (Scheme 6).

Different isomeric ratios of the $Z$ and $E$ diastereomers of trimethyltin 5-methylcyclohex-2-enylsulfinate were reacted with both 1.0 and 2.0 equiv of [$^2$H]-TFA in dichloromethane or chloroform. The relative proportions of $Z$ and $E$ 5-deuterio-3-methylcyclohexene were determined by integration of the $^2$H NMR spectrum of the corresponding dibromides.[11] Desulfination was stereospecific at both concentrations of [$^2$H]-TFA (within experimental error) with *syn* deuterium substitution.

**Scheme 6**




| *E:Z* | 1.0 equiv of TFA-*d* | *E:Z* |
|---|---|---|
| 68:32 | | 67:33 |
| 67:33 | | 63:37 |
| 45:55 | | 46:54 |
| 42:58 | | 38:62 |
| | 2.0 equiv of TFA-*d* | |
| 67:33 | | 67:33 |
| 41:59 | | 40:60 |

TFA-*d* = $CF_3CO_2D$

**Table 1. Solvent Dependance of Desulfination of Allylsulfinic Acid**

| solvent | relative rate |
|---|---|
| toluene | 1.00 |
| dichloromethane | 0.96 |
| acetone | 1.05 |

**Table 2. Decomposition of Allylsulfinic Acid at 28.0 °C**

| bar | $k_{rel}$ | bar | $k_{rel}$ |
|---|---|---|---|
| 10 | 1.00 | 750 | 1.13 |
| 100 | 1.02 | 1000 | 1.28 |
| 500 | 1.10 | | |

**The Kinetics of Desulfination.** The decomposition of allylsulfinic acid (generated *in situ* by acidolysis of the tributyltin sulfinate with TFA) to propene and sulfur dioxide could be conveniently and accurately monitored by $^1$H NMR or UV spectroscopy or by measuring the change in density throughout the course of the reaction. First-order desulfination was observed to at least 4 half-lives by all three techniques at stoichiometries up to 1.0 equiv of TFA. A rate constant of $(5.5 \pm 0.1) \times 10^{-4}$ s$^{-1}$ in toluene at 297 K was obtained with good agreement between the methods used. This value was essentially solvent independent (Table 1).

Variable temperature NMR spectroscopy over the range −20 to +35 °C in toluene as solvent was used to obtain the activation parameters of $\Delta H^{\ddagger} = 48 \pm 4$ kJ mol$^{-1}$ and $\Delta S^{\ddagger} = -146 \pm 17$ J K$^{-1}$ for desulfination. A deuterium kinetic isotope effect of 2.5 ± 0.1 at 297 K was determined by cleavage of tributyltin allylsulfinate with [$^2$H]-TFA in toluene and monitoring of desulfination by $^1$H NMR spectroscopy.

At greater than 1.0 equiv of TFA, the rate of desulfination was too fast to measure by conventional techniques, suggesting a second, presumably acid-catalyzed mode of decomposition.

**A Volume Profile for Desulfination.** An activation volume was determined for the thermal decomposition of allylsulfinic acid (prepared *in situ*) in dichloromethane by monitoring the appearance of $SO_2$ (320 nm) at 28.0 °C and elevated pressures. Two or three experiments were performed at each pressure, and each obeyed a first-order rate law to at least 4 half-lives (Table 2).

The plot of ln $k$ against pressure (Figure 1) was linear within experimental error. An activation volume of −5.5 ± 1.0 cm$^3$ mol$^{-1}$ was calculated according to the equation $\Delta V^{\ddagger} = -RT \cdot d/dp(\ln k)$.

(11) Kitching W., Wickham, G.; Young, D. J. *Organometallics* **1988**, *7*, 1187.

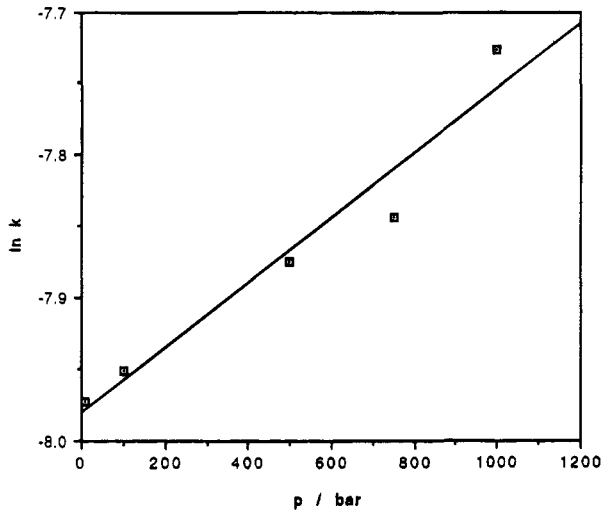



**Figure 1.** Plot of ln($k$) against pressure.

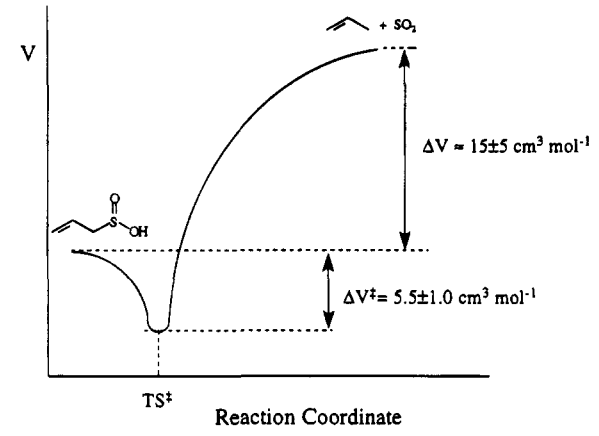
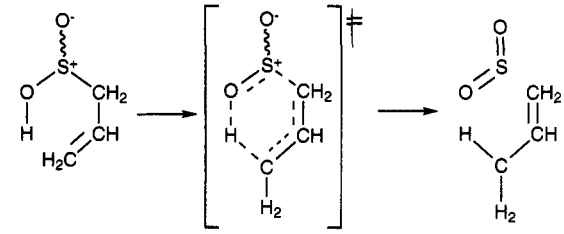



**Figure 2.** Volume profile for desulfination.

The instability of allylsulfinic acid precluded the possibility of calculating the change in volume for this reaction from the partial molar volumes of the reactants and products. It was possible, however, to monitor the change in density throughout the course of the reaction and then extrapolate to $t = 0$, thereby obtaining the initial density. The final density measurement was taken at 5 half-lives, and a reaction volume of 15 ± 5 cm$^3$ mol$^{-1}$ could be calculated. This relatively large uncertainty persisted despite a large number of experiments and appears to be due to the necessity for extrapolation to $t = 0$ and a slight deviation from first-order decomposition, noticeable after approximately 3 half-lives. While this deviation had little effect on the calculation of the rate constant (which was in good agreement with that measured by NMR and UV spectroscopy) it did provide uncertainty in the final density measurement. This deviation appeared to be due to a slow decomposition of one of the other reaction components (either tributyltin trifluoroacetate or residual tributyltin allylsulfinate).

Despite the uncertainty in this value, the fact of a positive reaction volume together with a negative activation volume indicates a reaction volume profile (Figure 2) comparable to that of a retro Diels–Alder reaction.[12]

**Scheme 7**



## Discussion

The observations of first-order reaction kinetics and highly stereoselective $\gamma$-*syn* substitution strongly support a retro-ene mechanism for the thermal desulfination of allylic sulfinic acids (Scheme 7). The large, negative entropy of activation is consistent with a rigid, cyclic transition state which the relative independence of reaction rate on solvent indicates is nonpolar.

The value of −5.5 cm$^3$ mol$^{-1}$ for the activation volume is not what would be intuitively expected, since bond breaking involves a volume increase (of the order of +10 cm$^3$ mol$^{-1}$) and so is normally retarded by elevated pressure.[12] This volume contraction could indicate either charge development (with associated electrorestriction of solvent) or an "early" (reactant like), rigid transition state. The minimal effect of solvent on rate supports the latter interpretation. The relatively small deuterium kinetic isotope effect of 2.5 is also consistent with an unsymmetrical transition state.

The reaction volume of 15 ± 5 cm$^3$ mol$^{-1}$ is in the range expected for a dissociation of a neutral molecule into two neutral fragments.[13] Overall, the volume profile is comparable to that for a retro Diels–Alder reaction ($\Delta V^{\ddagger}$ = −1.0 to −3.4 cm$^3$ mol$^{-1}$, $\Delta V$ = +28.7 cm$^3$ mol$^{-1}$) for which volume and other kinetic and thermodynamic data has been employed to support a concerted process with an early transition state.[12] The operation of secondary orbital interactions has been invoked as a possible explanation for the slight acceleration of the latter dissociative reaction by pressure. This explanation would appear, however, to be unsuitable in this instance.

The reverse reaction (addition of sulfur dioxide to an allylic moiety) is a synthetically useful procedure for the allylic transposition of double bonds but is difficult to study because the equilibrium overwhelmingly favors starting material in most instances.[1] The present study suggests (by virtue of microscopic reversibility) that this reaction should also proceed *via* a concerted (i.e., "ene") mechanism with a late transition state rather than the multistep process proposed previously.[2] This reaction should be substantially accelerated and thermodynamically favored by elevated pressures.

Finally, we have also observed a much faster, acid-catalyzed pathway for the decomposition of allylic sulfinic acids. This reaction is also highly stereoselective with $\gamma$-*syn* substitution which can be rationalized by a retro-ene desulfination of a protonated sulfinic acid intermediate (Scheme 8).

## Experimental Section

**Materials.** Allyltributylstannane was purchased from Aldrich and used without further purification. All other allylic stannanes were prepared from the corresponding allylic

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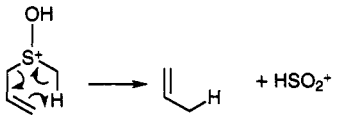
**Scheme 8**




chloride and trimethyltin lithium as previously described.[14,15] Trialkyltin allylic sulfinates were prepared from the corresponding allylic stannane and sulfur dioxide as previously described.[11,15]

**Sodium Allylsulfinate.** (A) Tributyltin allylsulfinate (1.0 g, 2.53 mmol) in dry dichloromethane (10 mL) was added to a flame-dried round-bottomed flask. To the stirred solution was added TFA (1.298 M, 1.90 mL, 2.47 mmol). An aqueous solution of sodium bicarbonate (0.259 M, 9.48 mL, 2.46 mmol) was immediately added and the resulting solution stirred at room temperature for 10 min. Further water (10 mL) was added and the aqueous layer separated and washed with dichloromethane (2 × 10 mL). The aqueous layer was evaporated to dryness *in vacuo* to yield sodium allylsulfinate as a white powder (254 mg, 78%). $^1$H NMR ($D_2O$): $\delta$ 5.57–5.88 (m, 1H); 5.06–5.25 (m, 2H); 3.00 (d, $J$ = 7.6 Hz, 2H). $^{13}$C NMR ($D_2O$): $\delta$ 130.1, 123.5, 67.6. Repeated attempts at combustion analysis failed to give satisfactory results; therefore, the salt was derivatized with *p*-bromophenacyl bromide to yield the corresponding sulfone.

(B) Tributyltin allylsulfinate (5.0 g, 12.65 mmol) in dry dichloromethane (15 mL) was added to a flame-dried round-bottomed flask. To the stirred solution was added a solution of sodium (0.291 g, 12.65 mmol) dissolved in dry ethanol (10 mL). The resulting solution was stirred at room temperature for 3 h and the white precipitate filtered, washed with dichloromethane, and dried *in vacuo* to yield sodium allylsulfinate (1.52 g, 94%) which was spectroscopically identical to that produced in procedure A.

**Allyl *p*-Bromophenacyl Sulfone.** *p*-Bromophenacyl bromide (434 mg, 1.56 mmol) was added to a stirred suspension of sodium allylsulfinate (200 mg, 1.56 mmol) in methanol (10 mL). The solution was stirred at room temperature for 5 h, the methanol removed *in vacuo*, and the resulting solid redissolved in dichloromethane (10 mL). The dichloromethane solution was washed with water (2 × 10 mL) and dried ($Na_2SO_4$) and the solvent removed. The resulting solid was recrystallized from ethanol to yield allyl *p*-bromophenacyl sulfone as pale yellow needles (434 mg, 92%). Mp: 128–130 °C. IR (KBr): 1680 (s), 1320 (s), 1140 (s) cm$^{-1}$. $^1$H NMR: $\delta$ 7.79 (dd, $J$ = 8.6, 2.2 Hz, 2H); 7.59 (d, $J$ = 8.5 Hz, 2H); 6.03–5.79 (m, 1H); 5.55 (d, $J$ = 12.5 Hz, 1H); 5.49 (d, $J$ = 5.6 Hz, 1H); 4.52 (s, 2H); 3.94 (d, $J$ = 7.4 Hz, 2H). $^{13}$C NMR: $\delta$ 168.4, 134.5, 132.2, 130.5, 130.1, 125.9, 124.4, 58.0, 57.2. Anal. Calcd for $C_{11}H_{11}SO_3Br$: C, 43.6; H, 3.7; S, 10.6; Br, 26.4. Found: C, 43.9; H, 3.7; S, 10.6; Br, 27.7.

**Regio- and Stereochemical Study.** Trimethyltin 1-methylprop-2-enylsulfinate (ca. 100 mg) was dissolved in deuteriochloroform (0.75 mL) and TFA (1.0 equiv) added dropwise with agitation at room temperature. $^1$H and $^{13}$C NMR spectra were acquired and indicated quantitative conversion to the corresponding alkene and trimethyltin trifluoroacetate. The reactions of *E*/*Z* mixtures of trimethyltin 5-methylcyclohex-2-enylsulfinate with [$^2$H]-TFA were performed in nondeuterated solvents. Determination of the relative proportions of (*Z*)- and (*E*)-5-deuterio-3-methylcyclohexene required conversion to the corresponding dibromides (by careful addition of bromine at 0 °C) and integration of the $^2$H NMR spectrum.[11]

**Kinetic Measurements. (A) By 1H NMR Spectroscopy.** Tributyltin allylsulfinate (0.1 g, 0.25 mmol) was dissolved in deuterated solvent (0.75 mL) in an NMR tube. TFA (17.5 $\mu$L, 0.23 mmol) was added *via* syringe with agitation and the time noted. The sample was then inserted into the temperature-equilibrated NMR spectrometer and $^1$H spectra collected at intervals of 1 min. The rate of decomposition of allylsulfinic acid was determined by integration of the doublet at $\delta$ 3.09 relative to the residual H resonances in toluene between $\delta$ 7.09 and 6.98.

$^1$H NMR: $\delta$ 5.45–5.75 (m, 1H, $-CH=$), 5.00–5.20 (m, 2H, $=CH_2$), 3.09 (d, $J$ = 7.3 Hz, 2H, $-CH_2-$).

**(B) By UV Spectrophotometry.** To 4.0 mL of a 4.86 × $10^{-2}$ M dichloromethane solution of tributyltin allylsulfinate was added 0.5 mL of a 3.24 × $10^{-1}$ M dichloromethane solution of TFA (0.83 equiv). The solution was thoroughly mixed with a syringe and transferred into a 1 cm spectrophotometer cell (Spectrocil) capped with a mercury seal to allow pressure equalization.[16] The cell was placed in a thermostated, high-pressure pressure vessel fitted with sapphire windows which was mounted inside the spectrometer. The vessel was filled with ethanol as the pressure-transmitting medium and pressure applied with a hand pump. Progress of the reaction was monitored by observing the appearance of $SO_2$ at 320 nm.

**(C) By Densitometry.** Dichloromethane solutions of tributyltin allylsulfinate and TFA (0.11 to 0.83 equiv) were mixed to produce concentrations of allylsulfinic acid beween 0.01 and 0.1 M. The change in density with time was determined using a thermostated (25.00 °C), Parr high-precision density meter. Different stoichiometries and concentrations of TFA had no observable effect on the first-order rate constant for decomposition.

**Acknowledgment.** The authors gratefully acknowledge the Australian Department of Industry, Science and Technology for financial support of this collaboration.

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