Electrophilic Substitution at Saturated Carbon. XXXII. Spectroscopic Observation of Enantiomer Interconversion of 2,2-Dimethyl-1-phenylsulfonylcyclopropyl Anions[1]

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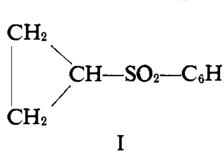
Abstract: The free energies of activation for enantiomer interconversion of the lithium, sodium, and potassium salts generated from metal dimsylates and 2,2-dimethylcyclopropyl phenyl sulfone have been measured in mixtures of dimethyl sulfoxide-d_6 (DMSO-d_6) and tetrahydrofuran-d_8 (THF-d_8) with nuclear magnetic resonance (nmr) spectral techniques. In one-to-one by volume DMSO-d_6–THF-d_8, the lithium salt gave a coalescence temperature (T_c) of +55° and $\Delta F^{\ddagger}$ of 18.0 kcal/mole, whereas the sodium salt gave a T_c of +45° and $\Delta F^{\ddagger}$ of 17.4 kcal/mole. In one-to-two by volume DMSO-d_6–THF-d_8, the sodium salt gave a T_c of +65° and $\Delta F^{\ddagger}$ of 18.5 kcal/mole, and the potassium salt a T_c of +30° and $\Delta F^{\ddagger}$ of 16.6 kcal/mole. The acidities of cyclopropyl phenyl sulfone and isopropyl phenyl sulfone in DMSO–sodium dimsylate were found to be approximately equal by use of nmr techniques.

Carbanions stabilized by certain functional groups centered around second-row elements have exhibited configurational stability when generated by decarboxylation or by proton abstraction with base, and captured by protons donors.[3,4] The most studied of these is the α-sulfonylcarbanion, whose hybridization in open-chain systems is still a subject for controversy.[4,5] The techniques used thus far in study of the symmetry properties of α-sulfonylcarbanions have involved conversion of one optically active compound to a second through the anion as an intermediate.[3] Although the rates of nitrogen inversion of N-sulfonylethylenimines have been measured directly by nmr techniques,[6] sulfonamides which are neutral are poor models for α-sulfonylcarbanions, which possess a formal negative charge.

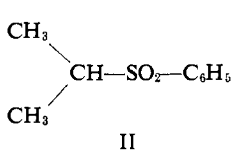
As a preliminary to attempts to study open-chain α-sulfonylcarbanions directly, the present study is concerned with an examination using nmr techniques of the relative acidities, the symmetry properties, and the rates of enantiomer interconversion of phenylsulfonylcyclopropyl anions. Others[7] have prepared the lithium, sodium, and potassium salts of cyclopropyl phenyl sulfone and of isopropyl phenyl sulfone by metalation with phenylmetallics in ether and hydrocarbon solvents. Through deuterium oxide quenching techniques of equilibrium mixtures of the two salts and their conjugate acids, these authors concluded that the two sulfones were of comparable acidity. This conclusion was questioned[8] on the basis that during the quench, proton and deuterium transfers might have occurred between the two carbon acids and their conjugate bases before the deuterium oxide became uniformly distributed throughout the medium.[9] Therefore, the current study was broadened to include a rough determination of the relative acidities of cyclopropyl phenyl sulfone and isopropyl phenyl sulfone with nmr techniques. Such a comparison is relevant to the question of the relative configurational stabilities of the cyclic and open-chain sulfones.

Relative Acidities of Cyclopropyl and Isopropyl Phenyl Sulfones. The nmr spectra[10] of sulfones I and II are recorded in Figure 1. In DMSO, the methylene protons of cyclopropyl phenyl sulfone (I) formed a multiplet between τ 8.70 and 9.19. The multiplet of the methine proton was hidden under the solvent peak, and the aromatic protons appeared as a multiplet between τ 1.75 and 2.3. In the spectrum of the isopropyl phenyl sulfone (II), the methyl protons formed a doublet centered at τ 8.85 with a coupling constant of 7 cps. A symmetrical septet for the methine proton was centered at τ 6.60 (one peak was partly hidden beneath the C^{13} satellite of the solvent), and the aromatic protons formed a multiplet between τ 2.00 and 2.50.



$$\begin{array}{l} CH_2 \\ \vert \quad CH{-}SO_2{-}C_6H_5 \\ CH_2 \end{array}$$

I



$$(CH_3)_2CH{-}SO_2{-}C_6H_5$$

II

A 0.5 *M* solution of sodium dimsylate in DMSO was prepared from sodamide and DMSO, and added to 0.00025 *M* solutions of I and II in DMSO. After about 0.1 equiv of basic solution was added to the cyclopropyl phenyl sulfone solution at 30°, the rate of exchange of the methine proton was sufficiently high so that the methylene protons in the nmr spectrum of the sulfone and its anions gave rise to a single, sharp peak. A similar observation was made for isopropyl phenyl

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(2) Fulbright Visiting Scholar at the University of California at Los Angeles from the Institute of Technology (Politechnika), Lodz, Poland.

(3) For a review, see D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, pp 105–113.

(4) D. J. Cram, R. D. Trepka, and P. St. Janiak, *J. Am. Chem. Soc.*, **88**, 2749 (1966).

(5) E. J. Corey and T. H. Lowry, *Tetrahedron Letters*, 793, 803 (1965).

(6) F. A. L. Anet, R. D. Trepka, and D. J. Cram, *J. Am. Chem. Soc.*, **89**, 357 (1967).

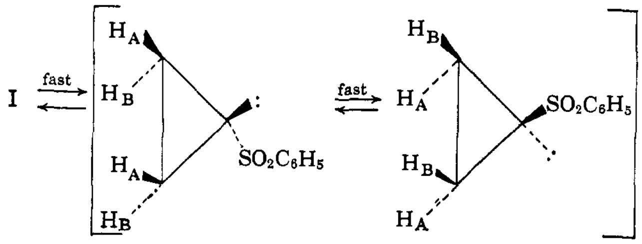
(7) H. E. Zimmerman and B. S. Thyagarajan, *ibid.*, **82**, 2505 (1960).

(8) Reference 3, p 76.

(9) C. D. Ritchie [*J. Am. Chem. Soc.*, **86**, 4488 (1964)] observed that quenching of a mixture of triphenylmethane and dimethyl sulfoxide and their conjugate bases with various deuterium acids led to different relative amounts of deuterated triphenylmethane.

(10) W. E. Truce and L. B. Dale, *J. Org. Chem.*, **26**, 1463 (1961).

sulfone. Clearly, H_A and H_B of the cyclic sulfone anions are exchanging their environments, possibly by the process formulated.



The chemical shift of the methylene protons in the anion of cyclopropyl phenyl sulfone depended on the amount of excess sodium dimsylate present. In the range of 0–1 equiv of excess base, chemical shifts of 29–32 cps were observed (the chemical shifts are all given in cps upfield from the upfield C^{13} satellite of DMSO, which occurs at 84 cps downfield from tetramethylsilane). At 0.5 equiv of added base, the chemical shift was 23.5 cps. The pK_a of DMSO in DMSO is about 31.3,[11] whereas that of dimethyl sulfone in water has been estimated at 23.[12] Other evidence, as well, points to the sulfonyl group being much more acidifying of carbon acids than the sulfinyl group.[13] Very likely, sodium dimsylate reacts essentially quantitatively with the sulfone when the latter is in excess. The small change in chemical shift observed when excess sodium dimsylate was added must be either a medium effect or a common ion effect on ion pair, dissociated ion equilibria. Figure 1 records the nmr spectrum of this solution (and one of the parent acid), and Table I gives the magnitudes of the chemical shifts of the methylene protons as the base concentrations were changed.

Table I. Changes in Chemical Shift with Changes in the Equivalents of Sodium Dimsylate Added to DMSO Solutions of Cyclopropyl Phenyl Sulfone (I)[a]

$NaCH_2SOCH_3$, equiv	Chemical shift,[b] cps
0.1	17.8
0.5	23.5
1.0	28.8
1.25	30.4
1.5	31.2
2.0	32.3

[a] Concentrations are given in Table III in the Experimental Section. [b] Upfield from the upfield C^{13} satellite of DMSO.

The chemical shift of the methyl protons of isopropyl phenyl sulfone anion was 14.5 cps and was independent of the amount of excess sodium dimsylate in the range of 0–0.5 equiv (see Figure 1). This chemical shift is close to that of the sulfone itself (14.5 cps, see Figure 1).

The positions of the peaks for the methyl and methylene protons generated from a 1:1 mixture of sulfones I and II with 0.5 equiv of sodium dimsylate (total sulfone equals 1 equiv) were 14.5 and 23.5 cps, respectively, the same as the chemical shifts for the sulfone–anion equilibria observed for each sulfone taken separately (see Figure 1). Clearly, the relative concentrations of cyclopropyl phenyl sulfone and its anion are not disturbed by the presence of isopropyl phenyl sulfone and its anion. This result indicates that the two sulfones possess about the same acidity, which corroborates the claim of Zimmerman and Thyagarajan.[7]

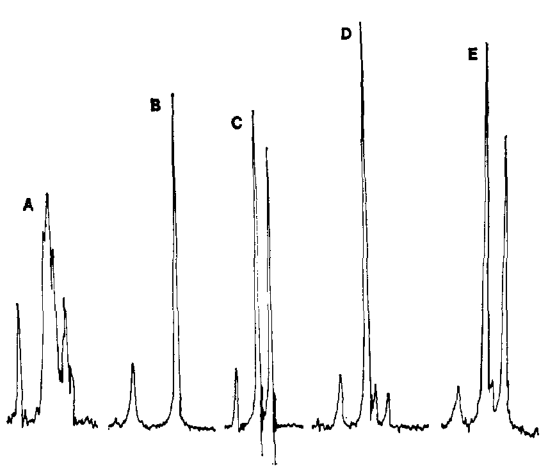
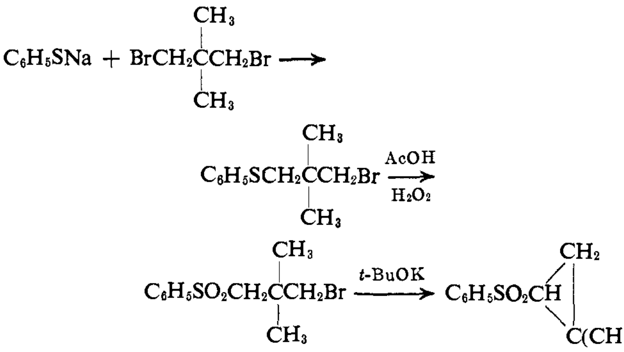


Figure 1. Nmr spectra (DMSO solutions, CH_3 or CH_2 bands only) of cyclopropyl phenyl sulfone: A, no base added; B, 0.5 equiv of base added. Spectra C and D are corresponding spectra of isopropyl phenyl sulfone. Spectrum E is an equimolecular mixture of the two sulfones with 0.5 equiv of base.

Direct Observation of Enantiomer Interconversion of α-Sulfonyl Carbanions. Since the nmr spectra of cyclopropyl phenyl sulfone salts were unsuitable for study of enantiomer interconversion, 2,2-dimethylcyclopropyl phenyl sulfone (III) was examined. This sulfone was prepared by the method formulated.



$$C_6H_5SNa + BrCH_2\overset{CH_3}{\underset{CH_3}{C}}CH_2Br \longrightarrow C_6H_5SCH_2\overset{CH_3}{\underset{CH_3}{C}}CH_2Br \xrightarrow[H_2O_2]{AcOH} C_6H_5SO_2CH_2\overset{CH_3}{\underset{CH_3}{C}}CH_2Br \xrightarrow{t\text{-BuOK}} C_6H_5SO_2CH\langle CH_2, C(CH_3)_2\rangle$$

III

The nmr spectrum of sulfone III in carbon tetrachloride exhibited two sharp singlets for the two methyl groups at τ 8.54 and 8.87 (difference in chemical shift of 20 cps). The methine proton appeared as a quartet distributed between τ 7.67 and 7.97. The sulfone is stable in DMSO solution in the range of 30–120° (nmr spectral criterion).

Solutions of lithium, sodium, and potassium dimsylate-d_5 (*ca.* 0.5 *M*) in DMSO-d_6 were prepared by treatment of DMSO-d_6 with the appropriate amount of metal amide. When 1 equiv of III was added to the lithium dimsylate-d_5 solution and the nmr spectra taken at about 30°, the two methyl groups appeared as a singlet at 13 cps. When cooled to 16° (freezing point of DMSO-d_6), the methyl band of the lithium salt broadened noticeably, but did not resolve. Similarly, a solution of 1

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(11) E. C. Steiner and J. M. Gilbert, *J. Am. Chem. Soc.*, **87**, 382 (1965).

(12) R. G. Pearson and R. L. Dillon, *ibid.*, **75**, 2439 (1953).

(13) (a) D. J. Cram, D. A. Scott, and W. D. Nielsen, *ibid.*, **83**, 3696 (1961); (b) D. J. Cram and S. H. Pine, *ibid.*, **85**, 1096 (1963).

Table II. Coalescence Temperatures, Rates, and Activation Energies for Enantiomer Interconversion of the Lithium, Sodium, and Potassium Salts of 2,2-Dimethylcyclopropyl Phenyl Sulfone (*III*) in DMSO-d_6 Mixtures

Run no.	Metal cation	Metal dimsylate-d_5 concn, *M*	Base and DMSO-d_6, ml	THF-d_8, ml	Wt of III, g	$\Delta\nu$, cps	T_c,[a] °C	At T_c	
								k, sec^{-1}	$\Delta F^{\ddagger}$[b]
1	Li	0.5	0.25	0.25	0.0263	17 ± 1	55	35	18.0
2	Na	0.5	0.25	0.25	0.0263	15.5 ± 1	45	35	17.4
3	Na	0.5	0.125	0.25	0.0132	17 ± 1	65	35	18.5
4	K	0.5	0.125	0.25	0.0132	16 ± 1	30	35	16.6

[a] ± about 4°. [b] Kcal/mole.

equiv of III and of lithium dimsylate-d_5 in a 4:2.5 mixture by volume of DMSO-d_6 and HMPA (hexamethylphosphoramide) exhibited a sharp singlet at 14 cps at 30°, which broadened at ±1° and broadened still further at −14°, but did not resolve before the mixture crystallized.

In mixtures of DMSO-d_6 and THF-d_8 (tetrahydrofuran-d_8) coalescence temperatures (T_5) of the lithium, sodium, and potassium salts of III were reached. Unfortunately, T_c of all three salts could not be determined in the same solvent mixture. The lithium and sodium salts were run in 1:1 (volume) of DMSO-d_6–THF-d$_8$, and the sodium and potassium salts in 1:2 (volume) of DMSO-d_6–THF-d_8. From the differences in chemical shifts of the two methyl groups at temperatures well below T_c ($\Delta\nu$ in cps), the first-order rate constants for enantiomer interconversion for the salts at T_c were calculated by use of eq 1. From the rate constants the free

$$k\,(\text{sec}^{-1}) = \pi\Delta\nu/\sqrt{2} \qquad (1)$$

energies of activation ($\Delta F^{\ddagger}$) for the processes were calculated with eq 2. The concentrations, coalescence tem-

$$\Delta F^{\ddagger} = 2.3RT(\log(kT/h) - \log k) \qquad (2)$$

peratures, rate constants and activation energies are reported in Table II. Figure 2 records the nmr spectra of the methyl groups of the lithium salts of III in 1:1 (volume) DMSO-d_6–THF-d_8 at a series of temperatures. Similar spectra were observed for the sodium and potassium salts.

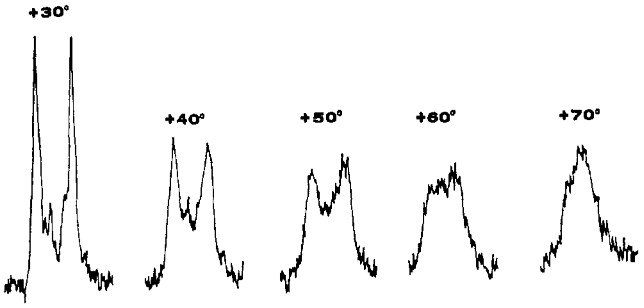

Figure 2. Nmr spectra (methyl bands only) of the Li salt of 2,2-dimethylcyclopropyl phenyl sulfone in THF–DMSO (1:1) at various temperatures. The separation of the two methyl bands at 30° is 16 cps.

Discussion

The similarity in pK_a's of the cyclopropyl and isopropyl systems (I and II) indicates the lack of additivity of the s character acidifying effect of the cyclopropane ring, and the combined inductive and d orbital acidifying effects of the sulfone group in sulfone I.[7] On the MSAD pK_a scale,[14] cyclopropane protons are about 5 pK_a units more acidic than the secondary protons of propane. From the estimated pK_a of dimethyl sulfone of 23[12] and the effects of the two methyl groups (pK_a increasing by about four units)[14] and the phenyl group (pK_a decreasing by one unit), the pK_a of isopropyl phenyl sulfone is estimated as being about 26, whereas that of the secondary hydrogen of propane is estimated at 44. Thus, the phenylsulfonyl group has a potential acidifying power of about 18 pK_a units. If the two effects were additive, III would have a pK_a of about 21. Clearly, the orbital requirements for acidifying the proton by increased s character, by inductive effect, and by d orbital overlap effects are somewhat incompatible. Possibly, the electron pair of the cyclopropyl anion occupies an orbital close to being completely s, and s–d overlap is less stabilizing than sp^3–d or p–d overlap. On the other hand, the inductive effect is accommodated by increased p character in the σ bond which transmits the effect,[15] and, therefore, the s character acidifying effect and the inductive effect should strengthen one another. Apparently, the cancellation of s character and d orbital effects in I costs the system almost 20% of the total potential acidifying power of the substituents.

The observation of coalescence of the nmr bands due to the methyl groups of the lithium, sodium, and potassium salts of 2,2-dimethylcyclopropyl phenyl sulfone indicates that at T_c the two methyl groups are exchanging environments because of rapid equilibration between enantiomeric forms. The free energies of activation for enantiomer interconversion change by only a few kcal/mole in passing from the lithium to the sodium to the potassium salts (see Table II). In previous work,[16a] neohexyllithium, dineohexylmagnesium, and dineohexylzinc in ether were found to undergo α-methylene group inversion with activation energies of 15, 20, and 26 kcal, respectively. Changes in the metal resulted in much larger changes in activation energies than were observed with changes of the metal in this study. Furthermore, 2,2-dimethylcyclopropylmagnesium bromide in ether proved to be configurationally stable on the nmr time scale up to 175°.[16b]

These facts suggested[16] that the former work involved organometallic compounds which in ether contained carbon–metal bonds with covalent character which varied from metal to metal. Inversion involved ionization of these bonds. The present work involves conjugate bases of a much stronger acid, metals less prone

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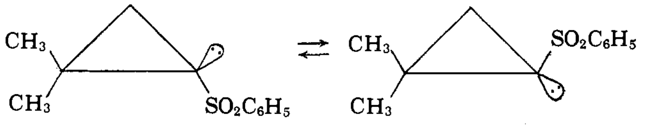
(14) Reference 3, p 19.

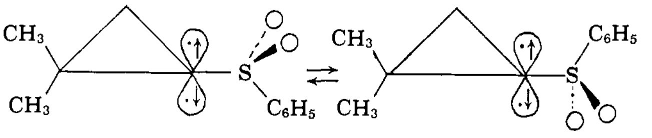
(15) Reference 3, p 56.

(16) (a) M. Witanowski and J. D. Roberts, *J. Am. Chem. Soc.*, 88, 737 (1966); (b) M. E. Howden and J. D. Roberts, private communication.

to form covalent bonds, and a much more polar medium. The fact that all three salts gave somewhat different activation energies for enantiomer interconversion (Table II) indicates that free anions were not involved, whereas the closeness of the activation energies indicates that covalent bonds were not involved. Thus, it seems highly likely that metal carbanide ion pairs were the species under observation. Possibly, ion-pair dissociation was involved in the enantiomer interconversion process. This hypothesis is consistent with the observed decrease in rate for the sodium salt of III when the solvent was changed from 1:1 to 1:2 DMSO–THF. Two explanations exist for the observed enantiometer interconversion of the anion of III. In the first, the anion is presumed pyramidal, and inversion is the observed process. In the second, the bonds to the anion are presumed to lie in a plane, and the observed process is one of rotation. These two possibilities are formulated.



inversion



rotation

Although no experimental evidence favors one explanation over the other, the pyramidal anion and the inversion mechanism of enantiometer interconversion is much preferred for several reasons. The strain of the cyclopropane ring is lower with the pyramidal anion than with the planar anion. Charge separation in the ion pairs would be greater with the planar than with the pyramidal anion. The rotation mechanism for enantiomer interconversion places a strict conformational requirement on the anion, whereas available experimental evidence[17] suggests lack of a conformational preference when the charge of the anion occupies a p orbital.

An examination of open-chain α-sulfonylcarbanions through use of nmr techniques is in progress.

Experimental Section

Melting points were determined with the Fisher-Johns melting point apparatus and are uncorrected. The nmr spectra were obtained with an A-60 analytical nmr spectrometer with variable-temperature controller V-6040 manufactured by Varian Associates, Palo Alto, Calif. The thin-walled nmr tubes were closed tightly with rubber stoppers.

In the preliminary experiments it was learned that DMSO solutions of carbanions are very sensitive to atmospheric oxygen and moisture. For example, exposure of the nmr tubes to the atmosphere for a few seconds and then shaking their contents caused considerable changes in the nmr spectra. All preparations of samples for nmr studies (including weighings) were performed in a drybox (Dri-Lab HE-43 inert atmosphere chamber and Dri-Train HE-93 purification train manufactured by Vacuum/Atmospheres Corp., Los Angeles, Calif.).

Solvents. Dimethyl sulfoxide (J. T. Baker Chemical Co.) was kept for 2 days over active molecular sieves (dried overnight in an electric furnace at 570°F) and then distilled at about 0.1 mm. The DMSO was stored over molecular sieves and under nitrogen. Hexamethylphosphoramide (a gift from DuPont Organic Chemical Dept.) was purified by distillation through a small Vigreux column at 86° (1 mm). Tetrahydrofuran was refluxed over calcium hydride for 5 hr and then distilled. A fraction with bp 65.5–66° was collected and stored under nitrogen in a paraffin-sealed flask. Tetrahydrofuran-d_8 was obtained from Merck Sharp and Dohme of Canada, Ltd., Montreal, Canada. Dimethyl sulfoxide-d_6 (98.6% deuterated) was prepared locally by W. K. Kollmeyer by a procedure to be reported in a future paper of this series.

Metal Amides. Lithium amide (95% pure) was obtained from K and K Laboratories, Inc., Plainview, N. Y. Sodium amide (90%) was purchased as a suspension in paraffin oil from Matheson Coleman and Bell. Potassium amide was prepared by dissolving metallic potassium in liquid ammonia in the presence of a catalytic amount of ferric sulfate.[18] Potassium (4.5 g) cut in small pieces was dissolved in 100 ml of liquid ammonia. Before introducing the potassium and liquifying the ammonia gas, the flask was carefully dried, evacuated, and filled with dry nitrogen. Ammonia gas was dried by passing over solid potassium hydroxide (column 40 cm long). The liquid ammonia solution was filtered through sintered glass filter and evaporated through a U tube with mercury. The remaining white powder (3.55 g, assumed purity 95% potassium amide) was stored in a tightly closed flask.

Preparation of Lithium, Sodium, and Potassium Dimsylate Solutions. The amide was placed in a 25-ml, two-necked flask with a magnetic stirring bar sealed in glass. This operation was carried out in a drybox. The flask was removed from the drybox and dimethyl sulfoxide injected by use of a syringe through a rubber cap. The mixture was stirred at room temperature, and the ammonia gas evolved was removed continuously by means of a connection to an oil pump. The time required for completion of the reaction was: 3 min for potassium amide (0.0362 g), 45 min for sodium amide (0.0269 g), and 90 min for lithium amide (0.0152 g). Dimethyl sulfoxide (5 ml) was used in every case. In the preparation of lithium and sodium dimsylates, a small amount of undissolved powder remained. Before use, the solutions were filtered in a drybox using a sintered glass filter and a rubber bulb. The solutions were clear, colorless, or pale yellow, slightly viscous liquids. Generally, before every series of experiments, fresh solutions of dimsylate were prepared, but they are stable for at least several days when stored in an efficient drybox.

The solutions of dimsylate-d_5 were prepared similarly from 0.0151 g (0.000625 mole) of lithium amide, 0.0268 g (0.000625 mole) of sodium amide, 0.0362 g of potassium amide (0.000625 mole), and 1.25 ml of DMSO-d_6 in each case.

Purification of Cyclopropyl Phenyl Sulfone (I). The crude product, a viscous, brownish oil (12.2 g prepared as previously[7,10]), was purified by fractional distillation under high vacuum with the use of a short Vigreux column. The fraction boiling at 100–102° (0.01 mm) was collected as a pale yellow, viscous oil (9.63 g), which solidified after standing, mp 34–35° [lit. bp 128–130° (0.01 mm), mp 35–36°;[7] and bp 130–135° (0.5 mm), mp 36–37.5°[10]]. The sample applied to a thin-layer chromatograph with ether–pentane (1:1) as elution solvent gave a single spot after development with iodine vapor.

In carbon tetrachloride, the nmr spectrum of I exhibited three complex multiplets for the aromatic, methine, and methylene protons: τ 2.35–2.90, 7.69–8.17, and 8.95–9.50, respectively.

Isopropyl Phenyl Sulfone (II). The isopropyl phenyl sulfide was obtained by a method described in the literature.[7] From 16.5 g (0.15 mole) of thiophenol and 18.45 g (0.15 mole) of 2-bromopropane, 18.57 g (81%) of isopropyl phenyl sulfide was obtained, bp 52° (2 mm), $n^{25}\text{D}$ 1.5433 [lit.[7] bp 83° (10 mm), $n^{25}\text{D}$ 1.5439].

The sulfide was oxidized to the sulfone with a mixture of acetic acid–perhydrol. To a solution of 15.2 g (0.1 mole) of the sulfide in 35 ml of glacial acetic acid, was added, dropwise, a 30% solution of hydrogen peroxide (23 g) and acetic acid (30 ml). The temperature of the exothermic reaction was kept below +40° by external cooling with an ice–water bath. After the exothermic reaction stopped, the mixture was warmed for 2 hr to +50°, then poured into 200 ml of water, and extracted four times with 60-ml portions of hexane–benzene (1:1). The extracts were washed first with a solution of sodium thiosulfate and then with water and dried over sodium sulfate. After removing the solvent under low vacuum, the residual oil was distilled under higher vacuum, bp 85–90° (0.02 mm), and yielded 10.24 g, $n^{25}\text{D}$ 1.5533.

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[17] Reference 3, p 80.

[18] C. R. Hauser, P. S. Skell, R. D. Bright, and W. B. Renfrow, *J. Am. Chem. Soc.*, **69**, 589 (1947).

Table III. Solutions Employed for Equilibration Experiments

Wt of sulfones				DMSO, ml	Solution $NaCH_2SO_2CH_3$ in DMSO, ml[a]	Equiv base per equiv sulfone	Total vol, ml
I		II					
g	mole	g	mole				
0.0461	0.00025	...	...	0.4	0.25	0.5	0.65
...	...	0.0456	0.00025	0.4	0.25	0.5	0.65
0.0461	0.00025	0.0456	0.00025	0.15	0.50	0.5	0.65
...	...	0.0456	0.00025	0.15	0.50	1.0	0.65
...	...	0.0456	0.00025	...	0.62	1.2	0.62
...	...	0.0456	0.00025	...	0.75	1.5	0.75
...	...	0.0456	0.00025	...	1.00	2.0	1.00

[a] 0.0025 *M*.

This product was a mixture of sulfoxide and sulfone (nmr and thin layer chromatography), and was oxidized again in acetic acid (30 ml) containing 15 ml of hydrogen peroxide (30%) overnight at 50°. After isolation (see above), the fraction boiling at 100–102° (0.13 mm) was collected, yield 10 g (54%), $n^{26}D$ 1.5305 [lit.[7] bp 112–113° (0.30 mm), $n^{25}D$ 1.5302]. In the nmr spectrum of isopropyl phenyl sulfone in carbon tetrachloride, aromatic protons produced a multiplet at τ 2.22–2.55, the methine proton appeared as a symmetrical septet centered at τ 6.95, and the methyl protons gave a doublet centered at τ 8.79.

1,3-Dibromo-2,2-dimethylpropane. The substance was prepared as before.[19] From 215 g of 2,2-dimethyl-1,3-propanediol and 562.4 g of phosphorus tribromide (Matheson Coleman and Bell, practical grade), 150 g (31.5%) of 2,2-dimethyl-1-3-dibromopropane was obtained, bp 75° (12 mm), $n^{26}D$ 1.5015 [lit. bp 84° (28 mm), $n^{20}D$ 1.5050;[19a] bp 68° (9 mm), $n^{20}D$ 1.5050[19b]]. In the nmr spectrum of the substance, two singlets appeared at τ 6.58 and 8.82, due to the methylene and methyl protons, respectively (relative areas 4 and 6).

3-Bromo-2,2-dimethylpropyl Phenyl Sulfide. In a three-necked 500-ml, round-bottomed flask equipped with mechanical stirrer, reflux condenser, and dropping funnel, were placed 4 g (0.1 mole) of sodium hydroxide and 11.0 g (0.1 mole) of thiophenol in 40 ml of alcohol. The mixture was heated on a steam bath and stirred until all the sodium hydroxide had dissolved. The 2,2-dimethyl-1,3-dibromopropane (92 g, 0.4 mole) in 50 ml of dioxane was added at once, and the reaction mixture was heated on a steam bath and stirred for 14 hr. A white precipitate of salt was formed. The reaction mixture was poured into 1 l. of water and ice, and an oily lower layer separated. The water layer was extracted three times with pentane (300 ml), and the pentane extracts were used to dissolve the oil and then were dried. The pentane was removed under vacuum and the residue distilled at about 30 mm. Dioxane and unreacted 2,2-dimethyl-1,3-dibromopropane were distilled at bp 31–84° (12 mm). The residue was distilled under oil pump vacuum, and a fraction (18.3 g, 71%) boiling at 128–137° (2 mm) was collected. In the flask remained a very viscous, brown oil (probably for the most part disubstituted product) which was discarded. The crude sulfide was redistilled, and 16.84 g of product with bp 132–134° (2 mm), $n^{26}D$ 1.5714 was collected. This product probably contained a small amount of disubstituted compound. An attempt to remove this by column chromatography on silica gel was unsuccessful. On thin-layer chromatographic plates, only a single spot was detected (solvents: pentane, pentane–ether (95:5), and cyclohexane).

Anal. Calcd for $C_{11}H_{15}BrS$: C, 50.96; H, 5.83; S, 12.48. Found: C, 51.55; H, 5.84; S, 13.16.

The nmr spectrum of the sulfide in carbon tetrachloride showed a broad multiplet in the aromatic region at τ 2.5–2.9 (relative area 5), a singlet at 8.90 (relative area 6) for two methyl groups, and two singlets at 6.62 (relative area 2) and 7.00 (relative area 2) for the two methylene groups.

3-Bromo-2,2-dimethylpropyl Phenyl Sulfone. In a three-necked, round-bottomed flask equipped with mechanical stirrer, condenser, thermometer, and dropping funnel, were placed 207.8 g of 3-bromo-2,2-dimethylpropane phenyl sulfide and 550 ml of glacial acetic acid. The solution was stirred, and 244 ml of 30% hydrogen peroxide was added slowly. The reaction was exothermic, and the temperature rose to 80°. The flask was placed in an ice–water bath. After about half of the hydrogen peroxide had been added, the temperature decreased to 35°. The flask was heated with an electric heating mantle to 75° for 16 hr. The reaction mixture was poured into 5 l. of water with ice, and the lower oily layer separated. The water layer was extracted five times with benzene, and the extracts were combined with the oil. The resulting benzene solution was washed with a saturated solution of sodium bicarbonate and then with water and dried. After the solvent was evaporated under vacuum, there remained 232.8 g (8%) of sulfone.

Anal. Calcd for $C_{11}H_{15}BrO_2S$: C, 45.40; H, 5.18. Found: C, 45.57; H, 5.27.

The nmr spectrum of this sulfone in carbon tetrachloride exhibited an absorption for 5 aromatic protons as a multiplet at τ 1.9–2.5, 6 protons as a single at 8.68 (*gem*-dimethyl protons), and two singlets arising from the methylene protons at 6.38 (2 protons) and 6.90 (2 protons).

2,2-Dimethyl-1-phenylsulfonylcyclopropane (III). Sodium *t*-butoxide in *t*-butyl alcohol was prepared from 19.32 g (0.84 g-atom) of sodium cut into small pieces and 420 ml of the alcohol. The reaction was completed by heating and stirring for 4 hr and then leaving for 8 hr. A stream of dry nitrogen was passed through the flask, and 203.7 g (0.7 mole) of 3-bromo-2,2-dimethylpropyl phenyl sulfide was added. The reaction was exothermic, and the flask was cooled for a while with a water bath and then warmed to 90° for 6 hr with stirring. After cooling, the brownish reaction mixture was poured into 3 l. of cold water, and an oil separated. The water layer was extracted three times with benzene. After removing the solvent under vacuum, the oily residue crystallized at 0°. The crude product was crystallized from pentane. The weight of the first crop of white crystals was 94.5 g, mp 47–48°. By concentration the mother liquors gave additional crops weighing 19.5 g, total yield 124.50 g (87%).

Anal. Calcd for $C_{11}H_{14}O_2S$: C, 62.82; H, 6.71. Found: C, 63.01; H, 6.74.

In the nmr spectrum in carbon tetrachloride, five aromatic protons appeared as a multiplet at τ 1.84–2.47 (relative area 5), the methine proton as a quartet at 7.67–7.97 (relative area 1), the methylene protons as a multiplet at 9.19 and partly hidden under two sharp singlets from methyl groups at 8.54 and 8.87.

Experiments to Show that DMSO, THF, and Sulfones Were Water Free. A few minute crystals of triphenylmethane were dissolved in DMSO (0.4 ml). After addition of one drop of a solution of sodium dimsylate, the solution turned red. Addition of a few drops of solutions of sulfone I or II caused the red color to disappear leaving a yellow solution. Also, a few minute crystals of (4-biphenyl)chrysofluorene were dissolved in DMSO (0.4 ml).[20] After adding the first drop of a solution of sodium dimsylate, the solution turned red. The color did not disappear after adding solutions of sulfone I or II. The same experiment was repeated with the same results in the DMSO–THF solutions.

Solutions of Carbanions for Nmr Measurements. A sample of sulfone was weighed in an nmr tube (drybox atmosphere); DMSO was added by use of a syringe, and the sulfone dissolved. Sodium dimsylate solution was added by use of a small syringe, and the tube was shaken. A temporary light green color appeared, which soon turned pale yellow. The tube was tightly closed with

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[19] (a) F. C. Whitmore, A. H. Popkin, H. J. Bernstein, and J. P. Wilkins, *J. Am. Chem. Soc.*, **63**, 124 (1941); (b) R. W. Shortridge, R. A. Craig, K. W. Greenlee, J. M. Derfer, and C. E. Board, *ibid.*, 70, 946 (1948).

[20] W. Dilthey, *J. Prakt. Chem.*, **109**, 319 (1925).

a rubber stopper and taken out of the drybox. Usually after several hours, the color darkened, but no differences in the nmr spectra were observed. Small amounts of dimsylate solutions were measured by counting the number of drops added (one drop = *ca.* 0.008 ml).

The measurements of the nmr spectra usually were made about 0.5 hr after preparing the sample. In cases where a small amount of base was used (*ca.* five to ten drops, 0.1–0.2 equiv) after 2–3 hr at 30°, the spectra changed considerably. Probably the small amount of dimsylate deteriorated, possibly by penetration of oxygen.

Solutions for Equilibration of Cyclopropyl Phenyl Sulfone (I) and Isopropyl Phenyl Sulfone (II) and Their Respective Anions. Table III records the weights and volumes employed for the nmr spectra of I and II and their respective anions. The solutions were prepared employing the precautions mentioned in the last section. The solution of sodium dimsylate was prepared from 0.1073 g of sodamide (90%) and 5 ml of DMSO (0.5 *M*).

Stereospecific Introduction of Azide Functions into Organic Molecules[1a,b]

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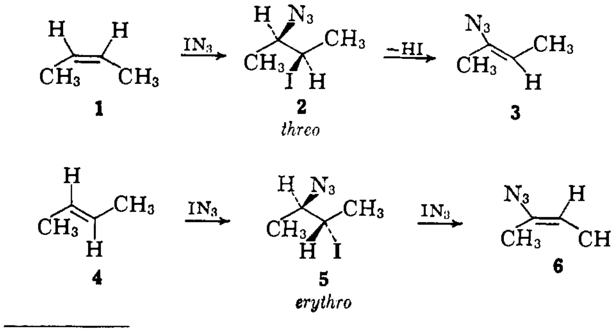
Abstract: Iodine azide prepared *in situ* by the reaction of sodium azide and iodine monochloride in acetonitrile has been shown to add in good yield and in a highly stereospecific manner to a variety of unsaturated systems. Thus, cyclohexene and 2-cholestene produce the *trans* and the *trans*-diaxial adduct, respectively; straight-chain *cis* and *trans* olefins give respectively the *threo* and *erythro* adducts; terminal olefins form adducts where the azido function is at the 2 position; and conjugated olefins such as 1,2-dihydronaphthalene lead to products with the azido function occupying the benzylic position. Tolane and 1,3-cyclooctadiene yield one-to-one adducts; conjugated ketones and esters give adducts where the azido function occupies the β position; and isonitriles give iodotetrazoles. Possible mechanisms for these reactions are discussed.

In our studies on the use of pseudohalogens as a method of stereospecific synthesis of organic nitrogen compounds,[2] we were led to the consideration that α,β-iodo azides may be formed by the addition of the pseudohalogen iodine azide (IN_3). Organic azides are of considerable use in organic synthesis. A new useful synthesis of azides would be of value since the only known general route to aliphatic azides involves nucleophilic displacement of groups such as halides and tosylates. Such reactions often are accompanied by elimination, rearrangement, and introduction of undesirable stereochemistry.

Iodine azide was first synthesized and isolated by Hantsch[3] in 1900 by stirring an aqueous suspension of silver azide in ether with iodine. From this suspension he was able to isolate highly explosive yellow crystals of iodine azide. This method was found unsuitable for the generation of IN_3 as applicable in the synthesis of α,β-iodo azides. Thus, when an olefin was added to the slurry of IN_3 formed as described by Hantsch, only black intractable oils that showed both hydroxyl and azido absorption in the infrared resulted. These findings were not too surprising since it is known that IN_3 slowly decomposes in the presence of water.

We have found that when iodine monochloride is added to a cold stirred slurry of sodium azide in acetonitrile, the dark color of iodine monochloride is replaced with the yellow-orange color of, presumably, IN_3. Although iodine azide has never been isolated from these solutions, its presence can be inferred. If the inorganic salts are filtered and an olefin is added to the clear yellow-orange solution, a high yield of an α,β-iodo azide can be obtained. Since sodium azide is essentially insoluble in acetonitrile, these results are incompatible with azide ion attacking a cation derived from iodine monochloride but are completely consistent with the existence of IN_3 in solution.

We have observed that the addition of IN_3 is highly stereospecific. The iodo azide adducts of *cis*- and *trans*-2-butene possess the *threo*- and *erythro*-2-azido-3-iodobutane structures **2** and **5**, respectively. Although the stereochemistry of these adducts is not obvious directly from their physical data, except that these isomers are formed cleanly and uncontaminated with each other, insight can be gained from a *trans* elimination of hydrogen iodide to form in both cases the vinyl azides.[4] It would be expected that the azido group, because of a magnetic anisotropic effect, would deshield a *cis* hydrogen and cause a downfield shift with respect to a *trans*



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(1) (a) Stereochemistry. XXIII. For paper XXII see A. Hassner, P. Catsoulacos, and E. G. Nash, *Tetrahedron Letters*, 489 (1967). (b) A preliminary report of part of this work has appeared: A. Hassner and L. A. Levy, *J. Am. Chem. Soc.*, 87, 4203 (1965). (c) National Aeronautics and Space Administration predoctoral fellow.

(2) See A. Hassner, M. Lorber, and C. H. Heathcock, *J. Org. Chem.*, 32, 540 (967), and preceeding papers.

(3) A. Hantsch, *Ber.*, 33, 524 (1900).

(4) The synthetic utility of α,β-iodo azides in general will be reported in a following paper.