The Mechanism of Nucleophilic Alkylidene Transfer by Sulfonium and Oxosulfonium Ylides[1]

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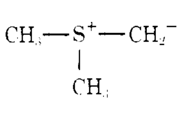
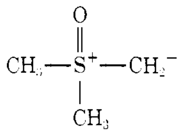
Abstract: Dimethylsulfonium methylide (**1**) is known to react with α,β-unsaturated ketones to yield vinyloxiranes and with cyclohexanones to add methylene across the carbonyl from the axial side. Dimethyloxosulfonium methylide reacts with α,β-unsaturated ketones to produce acylcyclopropanes and with cyclohexanones to add methylene across the carbonyl from the equatorial direction. It has generally been assumed that betaines are intermediates in the nucleophilic methylene transfer reactions of sulfur ylides. The generation of diastereomeric betaine intermediates by methods independent of addition of ylides to carbonyl substrate has led to the conclusion that sulfonium methylides add irreversibly to the carbonyl group, whereas, the addition of oxosulfonium methylides to carbonyl groups is reversible. With **1** the product distribution reflects kinetically controlled betaine formations. In the case of **2**, product distribution is the result of an equilibration among various betaines and the relative rates of collapse of the various betaines to products; in most cases both of these factors favor production of thermodynamically more stable products. *S*-Methyl-*S*-phenylsulfoximine (**10**) was N-methylated with formaldehyde and formic acid to yield *N,S*-dimethyl-*S*-phenylsulfoximine (**11**). Treatment of **10** with *n*-butyllithium in THF gave **12**. Reagent **12** (resolved and racemic versions), (*S*)-*n*-butylsulfinylmethyllithium, and phenylthiomethyllithium were added to benzaldehyde, 4-*tert*-butylcyclohexanone, and/or benzalacetophenone to give adducts which were converted to the corresponding oxosulfonium and sulfonium salts. Treatment of the salts with base resulted in the generation of betaines which collapsed to give cyclopropane or oxirane products.

The complementary behavior of dimethylsulfonium methylide (**1**) and dimethyloxosulfonium methylide (**2**) in their stereo- and regioselectivity is a useful, intriguing, and little understood phenomenon.[2-4] This complementary behavior, which appears to be quite general, can be illustrated by a few examples from the original work of Corey and Chaykovsky (eq 1 and 2).[2]



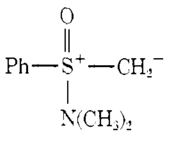
$CH_3-S^+(CH_3)-CH_2^-$

1



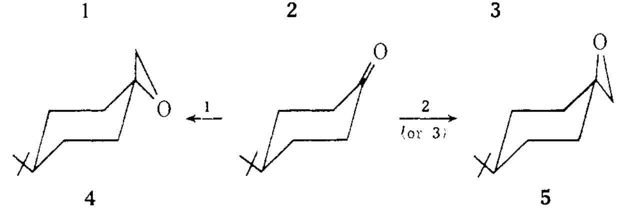
$CH_3-S^+(=O)(CH_3)-CH_2^-$

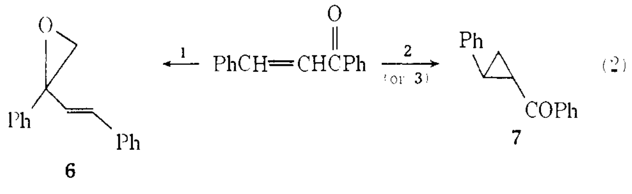
2



$Ph-S^+(=O)(N(CH_3)_2)-CH_2^-$

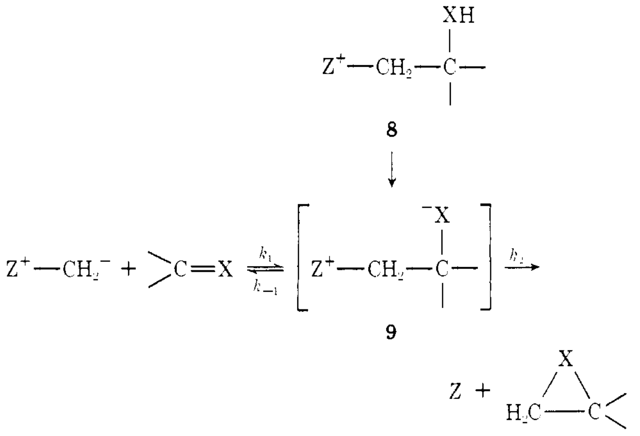
3





Although a zwitterionic intermediate (**9**) has been generally assumed, the reversibility of its formation or even its existence has remained speculative. We felt that pertinent evidence bearing on the general problem of the mechanism of nucleophilic alkylidene group transfer by sulfur ylides would be made available by the independent generation of the proposed intermediates (see Scheme I).[5] A straightforward procedure for the purpose appeared to be the treatment of the conjugate acids **8** of the betaines **9** with base.[6]

Scheme I



Z = dimethyl sulfide, dimethyl sulfoxide, *N,N*-dimethylbenzenesulfinamide, etc.

Results and Discussion

(Dimethylamino)phenyloxosulfonium methylide (**3**)[7,8] has been shown to be of similar stability and reactivity

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[1] Part XLVIII in the series "Chemistry of Sulfoxides and Related Compounds." We gratefully acknowledge support by the National Science Foundation (GP 19623).

[2] E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1353 (1965).

[3] For a review of sulfonium ylide chemistry, see A. W. Johnson, "Ylid Chemistry," Academic Press, New York, N. Y., 1966, Chapter 9.

[4] (a) R. S. Bly, C. M. Dubose, and G. M. Konizer, *J. Org. Chem.*, **33**, 2188 (1968); (b) C. E. Cook, R. C. Corley, and M. E. Wall, *Tetrahedron Lett.*, 891 (1965); (c) R. G. Carlson and N. S. Behn, *J. Org. Chem.*, **32**, 1363 (1967); (d) C. E. Cook, R. C. Corley, and M. E. Wall, *ibid.*, **33**, 2791 (1968).

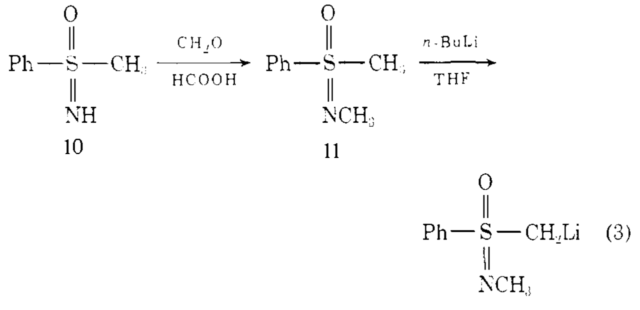
[5] For a preliminary report, see C. R. Johnson and C. W. Schroeck, *J. Amer. Chem. Soc.*, **93**, 5303 (1971).

[6] For other previous examples of generation of betaines by this method, see (a) M. Yashimini and M. J. Hatch, *ibid.*, **89**, 5831 (1967); (b) T. Durst, R. Viau, and M. R. McCloy, *ibid.*, **93**, 3077 (1971); (c) T. Durst, R. Viau, R. Van Den Elzen, and C. H. Nguyen, *Chem. Commun.*, 1334 (1971); (d) J. M. Townsound and K. B. Sharpless, *Tetrahedron Lett.*, 3313 (1972).

[7] C. R. Johnson, E. R. Janiga, and M. Haake, *J. Amer. Chem. Soc.*, **90**, 3890 (1968).

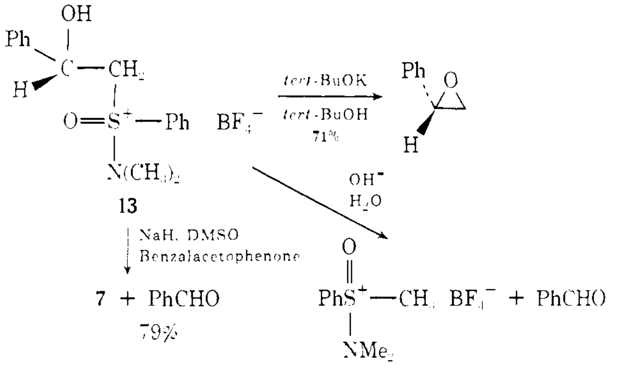
[8] C. R. Johnson, M. Haake, and C. W. Schroeck, *ibid.*, **92**, 6594 (1970).

to methylide **2** (eq 1 and 2); oxosulfonium betaine intermediates derived from **3** should behave in like fashion to those derived from **2**. An independent generation of the former was considered to be a more feasible undertaking. The reagent developed for this purpose was *N*-methylphenylsulfonimidoylmethyllithium (**12**) (eq 3). A chiral version of this reagent was obtained beginning with the resolution of **10** with 10-camphorsulfonic acid. It was found that sulfoximine **10** could be cleanly N-methylated under Eschweiler–Clark conditions.



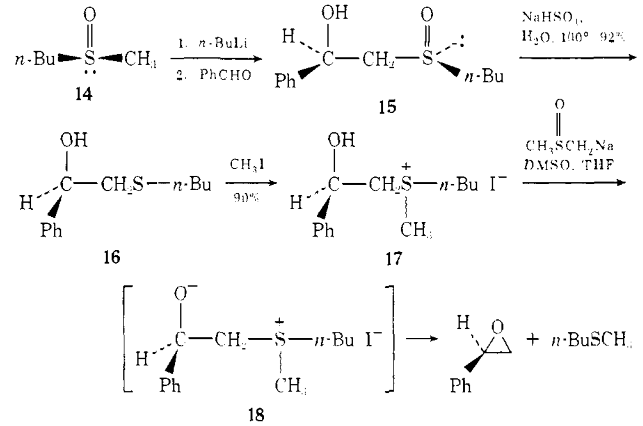
The reaction of (*S*)-**12** with benzaldehyde gave a mixture of diastereomers from which one was obtained pure by recrystallization. Methylation of the pure diastereomer with trimethyloxonium fluoroborate gave **13**. Treatment of **13** with potassium *tert*-butoxide–*tert*-butyl alcohol gave (−)-(*S*)-styrene oxide (71%), $[\alpha]^{25}$D −1.46°, of 22% optical purity. This value of optical purity is the same order of magnitude that would be expected from the direct reaction of optically pure ylide **3** and benzaldehyde,[9] which suggests that the betaine from **13** is in equilibrium with **3** and benzaldehyde. This suspicion was confirmed by generating the betaine in the presence of 1 equiv of a more reactive ylide substrate, *trans*-benzalacetophenone; an 80% yield of cyclopropane **7** was observed by vpc analysis of the reaction mixture. The ylide **3** was also trapped by protonation; the betaine conjugate acid **13**, when dissolved in aqueous sodium carbonate, was quantitatively converted to benzaldehyde and (dimethylamino)methylphenyloxosulfonium fluoroborate (Scheme II).

Scheme II



(+)-(*S*)-*n*-Butyl methyl sulfoxide (**14**)[10] was treated with *n*-butyllithium and the resulting anion added to benzaldehyde to produce a mixture of diastereomeric β-hydroxy sulfoxides. Diastereomer **15** was obtained pure by fractional crystallization. The β-hydroxyl sulfide **16** was obtained by reduction of the sulfoxide **15** with sodium hydrogen sulfite.[11] Iodide **17** was produced and, as a mixture of diastereomers, was treated with dimsyl sodium in DMSO. The resulting *n*-butyl methyl sulfide and styrene oxide were separated by fractional distillation. The styrene oxide had [α]D +32°, representing an optical purity of 90.3%. In this case, collapse of betaine **18** to products was much faster than fragmentation to benzaldehyde and *n*-butylmethylsulfonium methylide (Scheme III).

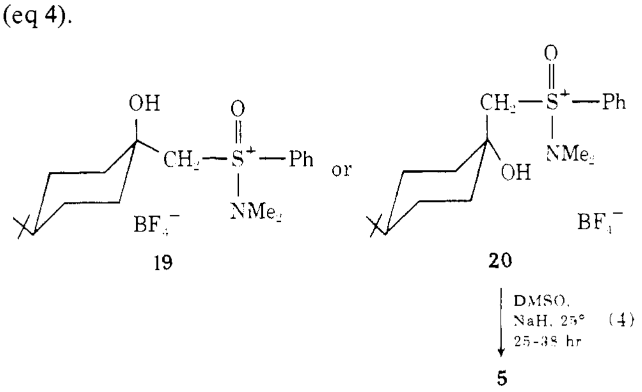
Scheme III



The above results clearly implicate betaine intermediates in nucleophilic methylene transfer reactions of sulfonium ylides to carbonyl groups and lead to the conclusion that the initial attack of an oxosulfonium ylide (*e.g.*, **2** and **3**) at a carbonyl site is "reversible" (Scheme I, $k_{-1} \geq k_2$), whereas attack by a simple sulfonium ylide (*e.g.*, **1**) is "irreversible" ($k_{-1} \ll k_2$).[12] Since oxosulfonium ylides are known to be more stable than sulfonium ylides, it is not surprising that the oxosulfonium ylides are better "leaving groups."

In the examples which we will now discuss we have continued to use the technique of an independent betaine synthesis, but the cases are more complex and revealing, in that the various betaines can lead to diastereomeric or structurally isomeric products.

Reagent **12** was added to 4-*tert*-butylcyclohexanone in ether to give a mixture of diastereomers (45–48% axial; 30–33% equatorial addition) which were separated by fractional recrystallization and methylated to give **19** and **20**. Treatment of either **19** or **20** with base resulted in the exclusive formation of the *Z* oxirane **5** (eq 4).



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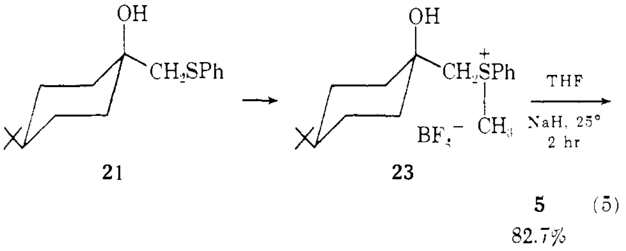
[9] C. R. Johnson and C. W. Schroeck, *J. Amer. Chem. Soc.*, **95**, 7418 (1973).

[10] J. P. Lockard, C. W. Schroeck, and C. R. Johnson, *Synthesis*, in press.

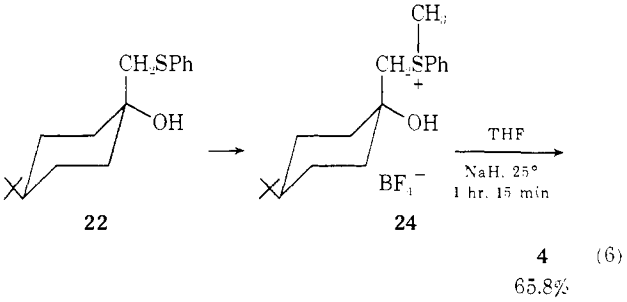
[11] C. R. Johnson, C. C. Bacon, and J. J. Rigau, *J. Org. Chem.*, **37**, 919 (1972).

[12] For discussions of how reversibility of betaine formation might affect product stereochemistry, see ref 4a,b and A. W. Johnson, V. J. Hruby, and J. L. Williams, *J. Amer. Chem. Soc.*, **86**, 918 (1964).

Reaction of 4-*tert*-butylcyclohexanone with phenylthiomethyllithium (prepared by treatment of thioanisole with *n*-butyllithium in the presence of 1,4-diazabicyclo[2.2.2]octane)[13] provided diastereomers **21** and **22** in the ratio of 4:1. After separation by fractional recrystallization from *n*-hexane, the individual diastereomers were alkylated with trimethyloxonium fluoroborate to provide salts **23** and **24**. Treatment of **23** and **24** with base resulted in the conversion to the corresponding *Z* and *E* epoxides (eq 5 and 6).

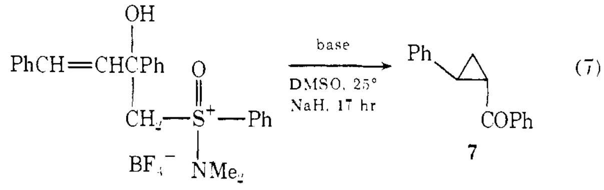


21 **23** **5** (5) 82.7%



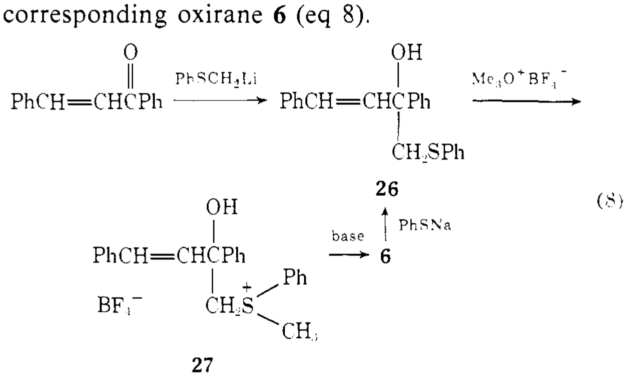
22 **24** **4** (6) 65.8%

Reaction of a twofold excess reagent of **12** with benzalacetophenone in THF gave the 1,2-addition product. This adduct was prone to revert to benzalacetophenone, but with care salt **25** could be prepared. Reaction of salt **25** with base resulted in the formation of cyclopropane **7** (74.3%) plus some benzalacetophenone (12.9%) but no oxirane **6** (eq 7).



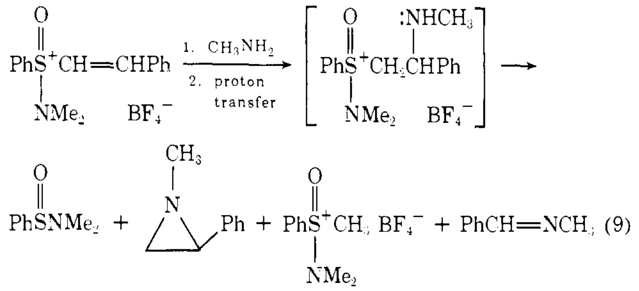
25 **7** (7)

Reaction of phenylthiomethyllithium with benzalacetophenone resulted largely in the production of the 1,2-adduct **26**; this same material was prepared by the addition of sodium thiophenoxide to oxirane **6**. Reaction of **26** with trimethyloxonium fluoroborate and treatment of the resulting salt **27** with base afforded the corresponding oxirane **6** (eq 8).



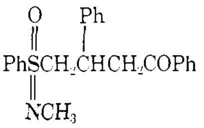
26 **27** (8)

All of the results quoted above show a consistent pattern of irreversible betaine formation between a carbonyl group and a sulfonium methylide and reversible betaine formation between a carbonyl group and an oxosulfonium methylide. From the results illustrated in eq 9 we can conclude that betaine formation resulting from oxosulfonium methylide addition to an imine may also be reversible.[14] If addition of a sulfonium methylide to a carbonyl group is an "irreversible" process, it is probably reasonable to assume that if the same reagent were to add to an electrophilic carbon–carbon double bond, collapse of the betaine to products would be much faster than reversion to starting materials. We will now examine data bearing on the "reversibility" of oxosulfonium methylide addition to electrophilic olefins.



(9)

The chiral reagent (*S*)-**12** added in the conjugate manner to *trans*-benzalacetophenone in dimethylformamide to yield, after neutralization, a mixture of diastereomers **28**. Recall that when **12** was added to the



$$\mathrm{Ph\overset{\overset{O}{\|}}{\underset{\underset{NCH_3}{\|}}{S}}CH_2\overset{\overset{Ph}{|}}{C}HCH_2COPh}$$

28

same substrate in THF, the 1,2-addition product was obtained. Apparently, 1,2 addition is kinetically favored, whereas 1,4 addition is thermodynamically favored. After separation on a silica gel column the diastereomeric adducts were methylated with trimethyloxonium fluoroborate to give **29** and **30**, the conjugate acids of the two diastereomeric betaines expected from chiral ylide **3** and benzalacetophenone. Betaine **31**, generated by treatment of **29** with potassium *tert*-butoxide-*tert*-butyl alcohol, collapsed to give optically pure (+)-(1*S*,2*S*)-*trans*-1-benzoyl-2-phenylcyclopropane (**32**), $[\alpha]^{25}\mathrm{D}$ +393°, in 91% yield. Treatment of **30** in a similar manner resulted in a 93% yield of the enantiomeric cyclopropane, $[\alpha]^{25}\mathrm{D}$ −387°. These results indicate that under the conditions specified, collapse of betaines such as **31** to products is much faster than reversion to ylide and olefin.

Ylide **3** reacts with dimethyl maleate in DMSO or THF to give only *trans*-dimethyl 1,2-cyclopropanedicarboxylate. In a reaction of **3** with a molar excess of dimethyl maleate in DMSO, the excess olefin was found to be half-isomerized to dimethyl fumarate. Little isomerization took place when the experiment was performed in THF. These results indicate that under certain structural and solvent conditions oxosulfonium methylide addition to electrophilic olefins may

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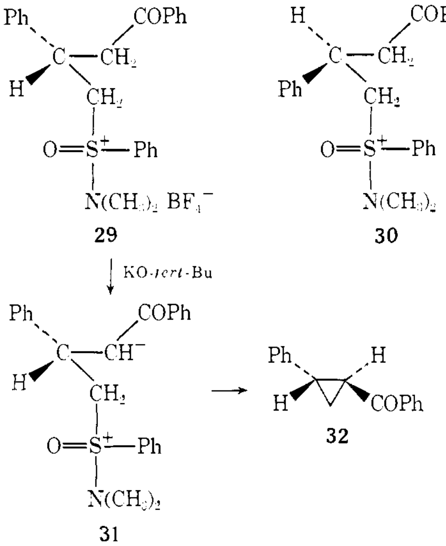
[13] E. J. Corey and D. Seebach, *J. Org. Chem.*, **31**, 4097 (1966).

[14] C. R. Johnson and J. P. Lockard, *Tetrahedron Lett.*, 4589 (1971).



29

30

31

32

be reversible. The experiments conducted in THF point to the fact that the intermediate betaine has sufficient lifetime to allow rotation about a single bond.

Conclusions

Betaines are intermediates in the nucleophilic alkylidene transfer reactions of sulfur ylides.[15] Depending on the structure of the ylide and the substrate, diastereomeric or structurally isomeric betaines may result from the addition of the ylide to the substrate; collapse of these betaines can result in a distribution of products. Scheme IV illustrates the situation when two betaines are involved.[16]

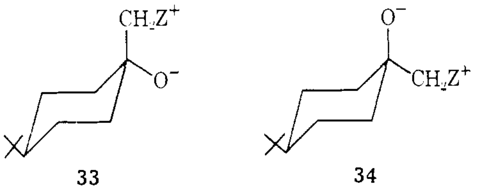
Scheme IV

$$\begin{tikzcd} & {[B]} \arrow[r, "k_2"] \arrow[dl, shift left, "k_{-1}"] & P \\ Y + S \arrow[ur, shift left, "k_1"] \arrow[dr, shift right, "k_1'"'] & & \\ & {[B']} \arrow[r, "k_2'"] \arrow[ul, shift right, "k'_{-1}"'] & P' \end{tikzcd}$$

Y = ylide, S = substrate, B = betaine, P = products

If $k_2 \gg k_{-1}$ and $k_2' \gg k_{-1}$,[16] then the ratio of products (P/P′) will be k_1/k_1'; the product distribution will reflect kinetically controlled betaine production. This is the case in the reactions of simple sulfonium methylides (*e.g.*, eq 1 and 2). The apparent kinetically favored mode of addition of **1** to unencumbered cyclohexanones is axial, whereas 1,2 addition is favored with α,β-unsaturated ketones.

If $k_2 \ll k_{-1}$ and $k_2' \ll k_{-1}$,[16] then P/P′ will be $K_1k_2/K_1'k_2'$ (where $K_1 = k_1/k_{-1}$, etc.). In such a situation the product distribution will be controlled by the position of the prior equilibrium among betaines as well as the ratio of the rate constants of the product producing steps (k_2/k_2'). Such is the case with oxosulfonium methylides **2** and **3**. In the reaction of **2** or **3** to 4-*tert*-butylcyclohexanone initial axial addition may be favored but, if so, is readily reversible. The equilibrium between betaines **33** and **34** would surely favor **34** (eq 10). Moreover, collapse of **33** to product epoxide

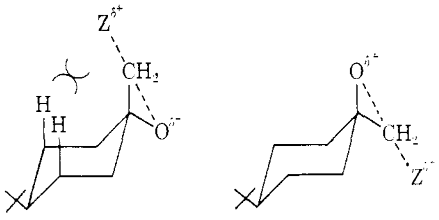


33

34

(10)

should be faster than collapse of **33**, *cf.* transition states **35** and **36**.[17] In this specific case, the equilibrium between the diastereomeric betaines and the relative rates of collapse to products both favor the production of the *Z* epoxide, which is the only product observed.

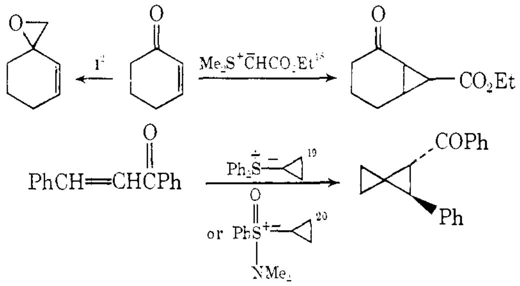


35

36

In the case of α,β-unsaturated ketones the data cited are permissive for kinetically favored, but reversible, 1,2 addition (carbonyl) of oxosulfonium methylides. The thermodynamically favored 1,4 addition ultimately results in the observed cyclopropane products.

Why do substituted methylides exhibit selectivity different than methylides (*e.g.*, eq 11 and 12)? In the first instance, substitution of a carboethoxy group on the methylene dramatically increases ylide stability and, consequently, reversion of any kinetically favored betaine to ylide and substrate is enhanced. (As in the case of oxosulfonium ylides, the carbonyl stabilized ylides are better "leaving groups.") In the second example, the production of a cyclopropane (rather than a vinyloxirane), by the reaction of a sulfonium ylide and an α,β-unsaturated carbonyl compound, can be attributed to a hampering of the collapse of the initially formed 1,2 adduct to vinyloxirane. This collapse involves an SN2 reaction on a cyclopropyl group and is apparently slow enough to lose out in competition with reversion of the betaine to starting ylide and substrate.[19] Here again, reversibility of initial betaine formation accounts for the production of cyclopropane.



(11)

(12)

Experimental Section[21]

(+)-(*S*)-*N*,*S*-Dimethyl-*S*-phenylsulfoximine (11). A 0.775-g (5.00 mmol) sample of (+)-*S*-methyl-*S*-phenylsulfoximine,[9] $[\alpha]_D$ +35.6°

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[15] B. M. Trost and M. J. Bogdanowicz (*ibid.*, 887 (1972)) have suggested that sulfurane intermediates are involved in sulfur ylide reactions.

[16] In many cases more than two betaines may be involved; the situation then becomes more complex, but the basic principles governing product distribution will remain the same. In our discussion we are considering only the two extremes, *i.e.*, when $k_2 \gg k_{-1}$ and $k_2 \ll k_{-1}$. Intermediate cases where $k_2 \sim k_{-1}$ could also obtain.

[17] It has been shown that collapse of betaines of this type results in inversion of the carbon atom (ref 6d).

[18] G. B. Payne, *J. Org. Chem.*, 32, 3351 (1967).

[19] B. M. Trost and M. J. Bogdanowicz, *J. Amer. Chem. Soc.*, 93, 3773 (1971).

[20] C. R. Johnson, G. F. Katekar, R. F. Huxol, and E. R. Janiga, *ibid.*, 93, 3771 (1971).

[21] See preceding paper (ref 9) for general details.

(*c* 0.97, acetone) (97.5% optically pure), was heated with 8 ml of 37% aqueous formaldehyde and 40 ml of 98% formic acid on a steam bath in an open flask.[22] After 48 hr, the mixture was poured into an evaporating dish and heated on a steam bath to an oil. The almost colorless material was dissolved in 30 ml of 2 *M* sulfuric acid and extracted with methylene chloride. The aqueous layer was neutralized with solid sodium carbonate. Methylene chloride extraction, drying ($MgSO_4$), and removal of the solvent *in vacuo* gave a nearly colorless oil (0.780 g, 92%), $[\alpha]_{\mathrm{D}}$ +177.4° (*c* 1.16, acetone). A sample of **11** prepared by methylation of optically pure **10** with 1 equiv of trimethyloxonium fluoroborate had $[\alpha]^{25}_{\mathrm{D}}$ +183.2° (*c* 1.7, acetone). The ir and nmr spectra were identical with those of a pure authentic racemic[8] sample of **11**.

***N*-Methyl-*S*-(3-benzoyl-2-phenylpropyl)-*S*-phenylsulfoximines (28).** A solution of 2.5 g (0.0148 mol) of (+)-*N,S*-dimethyl-*S*-phenylsulfoximine (**11**), $[\alpha]_{\mathrm{D}}$ +183.2° (*c* 1.7, acetone), in 20 ml of ether (distilled from sodium) was cooled to 0° under nitrogen. Then 0.0145 mol of *n*-butyllithium (1.6 *M* in hexane) was added over 2 min with good stirring, giving a white homogeneous suspension. After 5 min at 0°, a solution of 2.5 g (0.0120 mol) of *trans*-benzalacetophenone in 8 ml of dimethylformamide (distilled from BaO) was added all at once, and the reaction was allowed to warm up at 25°. The nitrogen flow was increased allowing the ether to evaporate and the reaction to become concentrated in dimethylformamide. After 4 hr (a longer time period may be advantageous), the mixture was diluted with 250 ml of ether and water and washed several times to remove the dimethylformamide. After evaporation of the ethereal layer, the residue was dissolved in 200 ml of chloroform and washed with 75 ml of 3 *M* sulfuric acid to remove the unreacted sulfoximine starting material. The chloroform solution was then washed with 75 ml of 10% sodium hydroxide, dried ($MgSO_4$), and evaporated, yielding a viscous amber liquid. Tlc analysis (silica gel, ether) showed *trans*-benzalacetophenone plus two spots near the bottom of the plate. Chromatography on a 2 ft × 1.5 in. silica gel column with dry ether gave benzalacetophenone and 0.539 g (10.5%) of the faster moving sulfoximine adduct (**28**) with good separation (*ca.* 1.5 l.). Changing to (50:50) ether–methylene chloride yielded 2.317 g (52%) of the slower moving adduct (**28**). Both diastereomers were shown to be pure by tlc analysis; their ir and nmr spectra were nearly identical. Both remained as amber, viscous liquids.

(−)-(2*S*,*SS*)-(Dimethylamino)(3-benzoyl-2-phenylpropyl)phenyloxosulfonium Fluoroborate (30). To a solution of 0.796 g (0.0021 mol) of the slower moving diastereomer **28** in 30 ml of methylene chloride was added 0.315 g (0.0021 mol) of trimethyloxonium fluoroborate. This mixture was allowed to stir in a 20° water bath for 30 min. The clear solution was then diluted with 30 ml of methylene chloride and washed with two 20-ml portions of water. After drying over magnesium sulfate, the solvent was evaporated giving a crystalline solid. Recrystallization twice from methylene chloride–ether yielded 0.68 g (67%) of a white solid: mp 124–125° dec; $[\alpha]_{\mathrm{D}}$ −4.6° (*c* 1.0, acetone); ir (Nujol) 745, 960, 1050 (s), 1220, 1680 cm^{-1}.

Anal. Calcd for $C_{24}H_{26}BF_4NO_2S$: C, 60.13; H, 5.47. Found: C, 60.03; H, 5.56.

(−)-(2*R*,*SS*)-(Dimethylamino)(3-benzoyl-2-phenylpropyl)phenyloxosulfonium fluoroborate (29) was prepared from the faster moving diastereomer **28** by the same method as that described for the synthesis of **30**. After two recrystallizations from methylene chloride–ether, there was obtained a 39% yield of a light brown solid: mp 98–101°; $[\alpha]_{\mathrm{D}}$ −27.4° (*c* 1.0, acetone); ir (Nujol) 693, 730, 758, 850, 955, 1050 (s), 1220, 1680 cm^{-1}. This infrared spectrum was similar to that of **30** but had a few striking differences below 900 cm^{-1}.

Anal. Calcd for $C_{24}H_{26}BF_4NO_2S$: C, 60.13; H, 5.47. Found: C, 58.70; H, 5.55.

(−)-(1*R*,2*R*)-*trans*-1-Benzoyl-2-phenylcyclopropane. To a suspension of 0.479 g (1.00 mmol) of the fluoroborate **30** in 6 ml of *tert*-butyl alcohol (distilled from potassium *tert*-butoxide) was added 1.16 ml (1.02 mmol) of a 0.88 *M* solution of potassium *tert*-butoxide in *tert*-butyl alcohol. The mixture became nearly clear almost immediately; a fine white suspension (potassium fluoroborate) remained until the work-up. After 1 hr at 25°, the mixture was poured into ether and washed with water. The ethereal solution was dried over magnesium sulfate and evaporated. Chromatography on a short column of silica gel with 90:10 ether–pentane gave 0.206 g (93%) of the cyclopropane as an off-white solid: mp 66–70°; $[\alpha]_{\mathrm{D}}$ −387° (*c* 1.02, acetone) [lit.[9] +390.5° (*c* 1.0, acetone), mp 70–71°]; spectral properties were identical with those of an authentic sample. Further elution with ether gave a 69% yield of *N,N*-dimethylbenzenesulfinamide.

(+)-(1*S*,2*S*)-*trans*-1-Benzoyl-2-phenylcyclopropane (32) was prepared from **29** by the same method used to generate the levorotatory isomer from **30** described above. A 91% yield of an off-white solid was obtained: mp 66–70°; $[\alpha]_{\mathrm{D}}$ +393.5° (*c* 1.0, acetone).

(*SS*,2*S*)-*N*-Methyl-*S*-(2-hydroxy-2-phenylethyl)-*S*-phenylsulfoximine. A solution of 1.69 g (0.0100 mol) of (+)-*N,S*-dimethyl-*S*-phenylsulfoximine, $[\alpha]_{\mathrm{D}}$ +183.2° (*c* 1.7, acetone), in 30 ml of dry ether (distilled from sodium) was cooled to 0° under nitrogen. To this solution was added 6.1 ml (0.0100 mol) of 1.65 *M* *n*-butyllithium over 2 min. After 5 min, 1.06 g (0.0100 mol) of benzaldehyde in a small amount of ether was added all at once to the white suspension of sulfoximine anion. The mixture became clear after 5 min and then began to cloud up again; it was allowed to warm to 25°. After 30 min, the mixture was poured into saturated ammonium chloride solution. The ethereal layer was separated and the aqueous layer extracted with methylene chloride. The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure yielding 2.65 g (96%) of a colorless viscous liquid. Analysis by tlc (alumina, ether–ethyl acetate) showed two products and a trace of starting material **11**. The infrared spectrum was consistent with the expected structures. The nmr spectrum showed the ratio of isomers to be 40:60. This ratio was easily determined from the integration of the methine protons of the two structures. Each appears as a clean doublet of doublets, one at δ 5.53, the other at 4.93.

The material was dissolved in cyclohexane and white crystals formed upon standing for a long period (0.263 g, mp 95–98°). A second crop (0.202 g) was obtained upon cooling to 0°. The two crops of crystals were combined and recrystallized from hexane, giving a white solid (*ca.* 0.4 g), mp 99–100°. It was found by tlc to be the pure faster moving isomer: $[\alpha]_{\mathrm{D}}$ +43.3° (*c* 1.0, acetone); nmr ($CDCl_3$) δ 8.1–7.5 (m, 5, Ph–S), 7.25 (s, 5, PhCH), 6.50 (s, 1, OH), 4.90 (d-d, 1, CH), 3.60–2.90 (m, 2, CH_2), 2.72 (s, 3, N–CH_3). The configuration assignments were based on the reductive cleavage of the carbon–sulfur bond with dissolving aluminum to give (+)-(*S*)-1-phenylethanol.[23]

Anal. Calcd for $C_{15}H_{17}NO_2S$: C, 65.42; H, 6.22. Found: C, 65.56; H, 6.34.

(+)-(*SS*,2*S*)-(Dimethylamino)(2-hydroxy-2-phenylethyl)phenyloxosulfonium Fluoroborate (13). To a solution of 0.550 g (2.00 mmol) of the above sulfoximine in 20 ml of methylene chloride was added 0.296 g (2.00 mmol) of trimethyloxonium fluoroborate. After 30 min at 25°, the clear solution was washed with 15 ml of water. The aqueous washings were extracted several times with methylene chloride. The combined solutions were dried over magnesium sulfate and evaporated, giving a viscous liquid. After standing under dry ether for an extended period, the material crystallized. The ether was decanted away, and the solid was recrystallized from methylene chloride–ether yielding 0.555 g (74%) of a white solid: mp 115–117° (with a little softening at 110°); $[\alpha]_{\mathrm{D}}$ +45.1° (*c* 1.0, acetone). The spectral properties of this material were identical with those of an analyzed racemic sample, mp 138–139.5°.

(−)-Styrene Oxide. Reaction of (+)-13 with Potassium *tert*-Butoxide. A solution of 0.377 g (1.00 mmol) of (+)-**13** was treated with 1.02 mmol of potassium *tert*-butoxide in *tert*-butyl alcohol. After chromatography, 0.085 g (71%) of styrene oxide was obtained, $[\alpha]_{\mathrm{D}}$ −1.46° (*c* 4.7, acetone), identified by comparative spectra. Optical data for an authentic sample:[24] $[\alpha]_{\mathrm{D}}$ +35.17° (neat); $[\alpha]_{\mathrm{D}}$ +6.64° (*c* 4.9, acetone) [lit.[25] $[\alpha]_{\mathrm{D}}$ +34.2° (neat) highest reported]. Assuming the authentic sample to be 100% optically pure, this reaction went with 22% retention of optical purity.

(−)-(*SS*,2*S*)-*n*-Butyl (2-Hydroxy-2-phenylethyl) Sulfoxide (15). A solution of 1.20 g (0.010 mol) of (+)-*n*-butyl methyl sulfoxide (**14**),[10] $[\alpha]_{\mathrm{D}}$ +111.7° (*c* 1.02, isooctane), in 50 ml of dry ether (distilled from sodium) was cooled to −78° under nitrogen; the sulfoxide crystallized. To this solid white mass was added 0.011 mol of *n*-butyllithium (6.7 ml, 1.65 *M* in hexane). The mixture was

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[22] For other examples of N-alkylation of sulfoximines by this procedure, see T. R. Williams, R. E. Booms, and D. J. Cram, *J. Amer. Chem. Soc.*, **93**, 7338 (1971); H. Schmidbaur and G. Kammer, *Chem. Ber.*, 104, 3234 (1971).

[23] C. W. Schroeck and C. R. Johnson, *J. Amer. Chem. Soc.*, **93**, 5305 (1971).

[24] G. A. Dutra, Ph.D. Dissertation, Wayne State University, 1972.

[25] D. J. Pasto, C. C. Cumbo, and J. Fraser, *J. Amer. Chem. Soc.*, **88**, 2194 (1966).

allowed to warm slightly to break up the solid and then was cooled to −78°.[26] The mixture was still opaque but was stirring well. After 10 min, 1.17 g (0.011 mol) of benzaldehyde was added all at once in a small amount of ether, and the mixture was allowed to warm up to 0° for 5 min. The mixture was poured into ammonium chloride solution, and the ether layer was separated. The aqueous layer was extracted well with chloroform. The solution was dried over sodium sulfate and evaporated giving a viscous liquid. A white crystalline solid was obtained from ether–pentane (*ca.* 50:50) at 25°. The material (a mixture of isomers) was recrystallized from the same solvents to a constant melting point and optical rotation yielding 0.322 g (14%) of white solid **15**: mp 113.5–114.5°; $[\alpha]_D$ −60.3° (*c* 0.921, acetone); ir ($CHCl_3$) 690, 916 (w), 1010 (s), 3300 cm^{-1}; nmr ($CDCl_3$) δ 7.5–7.2 (m, 5, Ph), 5.45–5.10 (d-d, 1, C*H*–OH), 5.0 (s, 1, OH), 3.1–2.4 (m, 4, CH_2–SO–CH_2), 2.0–1.1 (m, 4, CH_2–CH_2–CH_3), 1.1–0.7 (m, 3, CH_2CH_3).

The liquors were concentrated and redissolved in pentane with only a small amount of ether. Upon cooling to 0°, the diastereomer of **15** was obtained (1.27 g) for a total yield of 70%, mp 51–54° (cloudy). A sample obtained similarly from a previous run had the following properties: mp 53–55°; $[\alpha]_D$ +54.0° (*c* 1.0, acetone); its ir (melt) and nmr were nearly identical with the spectra of the higher melting isomer (**15**) described above.

(−)-(*S*)-2-(*n*-Butylthio)-1-phenylethanol (16). A 0.308-g (1.36 mmol) sample of the sulfoxide (**15**) was heated on a steam bath in 50 ml of saturated aqueous sodium bisulfite solution.[11] After 8 hr, tlc analysis (silica gel, ether) of the solution still showed a small amount of sulfoxide, so 5 ml of methanol was added to aid the solubility. The mixture was refluxed for 4 hr and then extracted with several portions of pentane. The organic solution was dried over sodium sulfate and evaporated under reduced pressure to a constant weight. A 0.262-g (92%) yield of the sulfide was obtained as a colorless liquid: $[\alpha]_D$ −29.4° (*c* 1.10, acetone); ir (neat) 698, 914 (w), 1055, 3400 cm^{-1}; nmr ($CDCl_3$) δ 7.35 (s, 5, Ph), 4.83–4.53 (d-d, 1, C*H*OH), 3.3 (broad s, 1, OH), 2.9–2.3 (m, 4, CH_2–S–CH_2), 1.8–1.1 (m, 4, CH_2–CH_2CH_3), 1.1–0.7 (m, 3, CH_2CH_3). The material was pure by tlc analysis.

(2*S*)-*n*-Butyl(2-hydroxy-2-phenylethyl)sulfonium Iodide (17). A 0.247-g (1.18 mmol) sample of the sulfide **16** was dissolved in 4 ml of methyl iodide, and the mixture was allowed to stand at 25° for 24 hr. The product salt crystallized out of the methyl iodide and the solution became yellow. Ether was added slowly to a volume of 75 ml to more completely precipitate the salt, and the mixture was cooled to 0° overnight. After filtering and washing with fresh cold ether, a 0.372-g (90%) yield of a white solid was obtained: mp 95.5–97.5°; ir (Nujol) 704, 742, 778, 1060, 3270 cm^{-1}; nmr ($CDCl_3$) δ 7.8–7.2 (m, 5, Ph–), 6.8–6.4 (m, 1, C*H*OH), 4.8 (broad s, 1, OH), 4.5–3.4 (m, 4, CH_2–S(CH_3)–CH_2), 3.28 and 3.13 (2 s, 3, S–CH_3), 2.1–1.2 (m, 4, –CH_2–CH_2–CH_3), 1.2–0.7 (m, 3, CH_2–CH_3).

(+)-(*R*)-Styrene Oxide. Treatment of β-Hydroxysulfonium Salt 17 with Dimsyl Sodium. A solution of 0.352 g (1.0 mmol) of the sulfonium iodide (**17**) in 1 ml of dry dimethyl sulfoxide (distilled from CaH) and 2 ml of dry tetrahydrofuran (distilled from sodium) was cooled to −10° (ice–salt) under nitrogen. Then 1 ml of freshly prepared 1 *M* methylsulfinyl methide solution[27] was added over 1 min. The mixture was allowed to warm up to 20° over 1 hr. After an additional 20 min at 20–25°, the mixture was poured into water and the solution was extracted well with ether. The ether solution was washed twice with water and dried over sodium carbonate. The solvent was boiled away at atmospheric pressure, and the slightly yellow liquid was evaporatively distilled twice at 1 mm. The styrene oxide was collected on a water-cooled coldfinger condenser as a colorless liquid (0.069 g, 58%): $[\alpha]_D$ +32.0° (*c* 1.06, *dl*-styrene oxide), identical in all respects with an authentic optically active sample, prepared[24] from (−)-(*R*)-mandelic acid;[28] $[\alpha]_D$ +35.17° (neat), +35.44° (*c* 0.96, *dl*-styrene oxide) [lit.[25] $[\alpha]_D$ +34.2° (neat) (highest reported)]. The *n*-butyl methyl sulfide, collected in a Dry Ice trap, was identical with an authentic sample. Both products were pure by vpc analysis.

(*Z*)- and (*E*)-(4-*tert*-Butyl-1-hydroxy-cyclohexylmethyl)-*N*-methyl-*S*-phenylsulfoximine. To a magnetically stirred solution of 12.20 g (0.072 mol) of *N*,*S*-dimethyl-*S*-phenylsulfoximine in 100 ml of anhydrous ether at −78° and under nitrogen was added 42.0 ml (0.070 mol) of 1.67 *M* *n*-butyllithium in hexane. The solution was warmed to 25°, and 10.72 g (0.070 mol) of solid 4-*tert*-butylcyclohexanone was added. After 2 hr, the solution was quenched in 400 ml of water. The phases were separated, and the aqueous portion was extracted with ether. The combined ether fractions were extracted with 0.5 *M* aqueous H_2SO_4 and then with water. The ethereal solution was dried ($MgSO_4$), and the solvent was removed to give a white solid. Fractional recrystallization from *n*-hexane gave: (a) 7.08 g (31.5%) of (*Z*)-*S*-(4-*tert*-butyl-1-hydroxycyclohexylmethyl)-*N*-methyl-*S*-phenylsulfoximine; mp 147.5–148.5°; ir (KBr) 3300 (m, OH), 2960(s), 2870 (shoulder), 1460 (m), 1440 (s), 1430 (m), 1360 (w), 1230 (s), 1150 (s), 1135 (s), 1100 (s), 1075 (m), 1015 (m), 980 (m), 930 (w), 875 (s), 850 (s), 830 (w), 780 (s), 755 (s), 725 (m), 695 (m), 685 (m) cm^{-1}; nmr ($CDCl_3$) δ 8.13–7.90 (m, 2), 7.83–7.43 (m, 3), 6.25 (broad s, 1, O*H*), 3.41 (d, 1, J = 14 Hz, *H*CHS), 2.97 (d, 1, J = 14 Hz, HC*H*S), 2.67 (s, 1, N–CH_3), 2.00–0.96 (m, 9, cyclohexyl protons), 0.90 (s, 9, C(CH_3)$_3$); and (b) 10.87 g (48.4%) of (*E*)-*S*-(4-*tert*-butyl-1-hydroxycyclohexylmethyl)-*N*-methyl-*S*-phenylsulfoximine; mp 117–118°; ir (KBr) 3280 (m, OH), 2940 (s), 2860 (shoulder), 1440 (s), 1390 (w), 1360 (m), 1220 (s), 1190 (m), 1045 (s), 1130 (shoulder), 1100 (w), 1080 (m), 1058 (s), 987 (m), 924 (w), 872 (s), 840 (s), 780 (s), 752 (s), 720 (w), 697 (w), 685 (w) cm^{-1}; nmr ($CDCl_3$) δ 8.05–7.83 (m, 2), 7.77–7.48 (m, 3), 6.75 (broad s, 1, O*H*), 3.45 (d, 1, J = 14 Hz, *H*CHS), 3.28 (d, J = 14 Hz, HC*H*S), 2.65 (s, 1, NCH_3), 2.00–0.95 (m, 9, cyclohexyl protons), 0.85 (s, 9, C(CH_3)$_3$).

Reduction of Above Adducts to 4-*tert*-Butyl-1-methylcyclohexanols. To a solution of 0.203 g (0.63 mmol) to (*Z*)-*S*-(4-*tert*-butyl-1-hydroxycyclohexylmethyl)-*N*-methyl-*S*-phenylsulfoximine in 50 ml of a 90% THF–10% water mixture was added 0.374 g (10.5 mmol) of freshly amalgamated aluminum foil. The mixture was refluxed for 2.5 hr and then stirred at 25° overnight. The reduction mixture was filtered, and the inorganic residue was washed copiously with THF. The solvent was removed *in vacuo*, and the residue was dissolved in 100 ml of ether. The ethereal solution was extracted with several portions of 1 *M* aqueous potassium hydroxide (to remove thiophenol) and dried ($MgSO_4$); the solvent was removed *in vacuo*. A glpc of the residue showed that it contained (*Z*)-4-*tert*-butyl-1-methylcyclohexanol but none of the *E* isomer. Column chromatography on silica gel using benzene as the eluent gave 0.038 g (35.7%) of the *Z* alcohol: mp 67–69° (lit.[21] 70.5–71°); ir (KBr) and nmr ($CDCl_3$) were identical with those of an available sample.

In a similar experiment, 0.575 g (1.78 mmol) of the *E* isomer gave, after sublimation, 0.078 g (25.9%) of (*E*)-4-*tert*-butyl-1-methylcyclohexanol: mp 96–97° (lit.[29] 97.5–98°); ir (KBr) and nmr ($CDCl_3$) were identical with those of an available sample. A glpc of the crude reaction mixture showed that none of the *Z* isomer was present. Also, 0.079 g (13.7%) of starting material was recovered.

(*E*)-(4-*tert*-Butyl-1-hydroxycyclohexylmethyl)dimethylaminophenyloxosulfonium Fluoroborate (20). To a solution of 0.353 g (1.09 mmol) of (*E*)-*S*-(4-*tert*-butyl-1-hydroxycyclohexylmethyl)-*N*-methyl-*S*-phenylsulfoximine in 20 ml of dry dichloromethane at 25° was added 0.162 g (1.09 mmol) of trimethyloxonium fluoroborate. The mixture was stirred for 15 hr before 20 ml of water was added. The phases were separated, and the water phase was extracted with two 10-ml portions of dichloromethane. The combined fractions were dried ($MgSO_4$), and the solvent was removed by rotary evaporation at 25° to give an oil. Pumping under high vacuum (0.05 mm) for 1 hr gave 0.455 g (97.8%) of **20** as a noncrystalline, white solid: ir (KBr) 3500 (m, OH), 3030 (w), 2920 (s), 2850 (shoulder), 1460 (shoulder), 1440 (m), 1380 (w), 1360 (w), 1260 (m), 1195 (w), 1060 (s), 935 (m), 840 (w), 750 (s), 710 (m), 680 (m) cm^{-1}; nmr ($CDCl_3$) δ 8.33–8.13 (m, 2), 8.03–7.65 (m, 3), 4.65 (d, 1, J = 14 Hz, *H*CHS), 4.35 (d, 1, J = 14 Hz, HC*H*S), 3.20 (shoulder, 1, O*H*), 3.14 (s, 6, N(CH_3)$_2$), 2.4–1 (m, 11.3), 0.84 (s, 9.3, C(CH_3)$_3$). All attempts to crystallize **20** failed.

(*Z*)-(4-*tert*-Butyl-1-hydroxycyclohexylmethyl)dimethylaminophenyloxosulfonium Fluoroborate (19). By a method similar to that described above for **20**, 1.468 g (4.55 mmol) of the *Z* sulfoximine gave 1.876 g (97%) of **19** as a noncrystalline, white solid.

Reaction of 19 and 20 with NaH in DMSO. To a magnetically stirred suspension of 5.18 mmol of NaH (0.219 g of a 56.8% dispersion in mineral oil, washed with three portions of *n*-hexane), in 25 ml of dry DMSO at 25° and under nitrogen, was added 2.039 g (4.80 mmol) of solid **20**. Hydrogen was evolved rapidly for 10 min, and

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[26] For repetition of this procedure we recommend the use of THF instead of ether and lithium diethylamide as base.

[27] E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1345 (1965).

[28] I. Tomoskozi, *Tetrahedron*, **19**, 1969 (1963).

[29] C. H. DePuy and R. W. King, *J. Amer. Chem. Soc.*, **83**, 2743 (1961).

the solution turned brownish yellow. After 24 hr, the solution was quenched in 400 ml of water, and the resulting mixture was extracted with four 200-ml portions of pentane. The combined pentane fractions were dried (Na_2SO_4), and the solvent was distilled from the reaction products. The last traces of solvent were removed under aspirator vacuum to give a clear liquid. An nmr (CCl_4) of this showed it to be a mixture of the *Z* oxirane **5** and *N,N*-dimethylphenylsulfinamide. None of the *E* isomer **4** was detected. Rapid column chromatography on silica gel (eluted with an 80% pentane–20% ether mixture) gave 0.574 g (71.3%) of **5** as a clear, colorless liquid: nmr (CCl_4) δ 2.46 (s, 2, oxirane, CH_2), 2.03–1.00 (m, 9), 0.92 (s, 9, $C(CH_3)_3$). Also, 0.039 g (5.3%) of 4-*tert*-butylcyclohexanone was obtained from the column.

In a similar experiment, 2.010 g (4.73 mmol) of **19** gave 0.590 g (74.3%) of the *Z* oxirane **5** and 0.033 g (4.6%) of 4-*tert*-butylcyclohexanone. Again, an nmr (CCl_4) of the crude reaction mixture indicated that none of the *E* oxirane **4** was produced.

4-*tert*-Butyl-1-(phenylthiomethyl)cyclohexanols (21 and 22). To a mechanically stirred solution of 9.095 g (0.0734 mol) of thioanisole and 8.481 g (0.0757 mol) of 1,4-diazabicyclo[2.2.2]octane, in 400 ml of dry THF at 0° and under nitrogen, was added 44.4 ml (0.0710 mol) of 1.60 *M* *n*-butyllithium in hexane.[19] After 1 hr, 10.270 g (0.0667 mol) of solid 4-*tert*-butylcyclohexanone was added, and the solution was stirred at 0° for 1 hr and then at 25° for 2 hr before being quenched in 1 l. of water. The resulting mixture was extracted with dichloromethane. The combined fractions were extracted with 0.5 *N* aqueous HCl and dried ($MgSO_4$), and the solvent was removed *in vacuo* to give an off-white solid. An nmr ($CDCl_3$) showed this to be composed largely of a 1 : 4 mixture of the (*Z*)- and (*E*)-β-hydroxysulfides **22** and **21**, respectively. Fractional recrystallization from pentane gave: (a) 2.125 g (11.4%) of **22** as a white solid; mp 120–121°; nmr ($CDCl_3$) δ 7.63–7.16 (m, 5), 3.23 (s, 1, CH_2S), 2.42 (broad s, 1, O*H*), 2.10–0.90 (m, 9), 0.85 (s, 8.7, $C(CH_3)_3$); and (b) 6.974 g (37.6%) of **21** as a white solid; mp 71–73°; nmr ($CDCl_3$) δ 7.60–7.10 (m, 5), 3.08 (s, 1, CH_2S), 1.98 (s, 1, O*H*), 1.93–0.97 (m, 8.8), 0.85 (s, 9, $C(CH_3)_3$).

Reductions of 21 and 22 to 4-*tert*-Butyl-1-methylcyclohexanols. A mixture of 0.260 g (0.94 mmol) of **22** and ~1 g of Raney nickel (W2) in 100 ml of absolute ethanol was refluxed for 21 hr and then was filtered. The solvent was removed *in vacuo* to give a white solid. This was dissolved in 50 ml of dichloromethane, the solution was filtered, and the solvent was removed *in vacuo* to give 0.133 g (83.5%) of (*E*)-4-*tert*-butyl-1-methylcyclohexanol: mp 96–98° (lit.[29] 97.5–98°); ir (KBr) and nmr ($CDCl_3$) were identical with those of an available sample.

By a similar procedure 0.518 g (1.87 mmol) of **21** gave 0.262 g (82.7%) of (*Z*)-4-*tert*-butyl-1-methylcyclohexanol.

(4-*tert*-Butyl-1-hydroxycyclohexylmethyl)methylphenylsulfonium Fluoroborate (23 and 24). A mixture of 1.030 g (3.71 mmol) of **21** and 0.572 g (3.86 mmol) of trimethyloxonium fluoroborate in 40 ml of dry dichloromethane at 25° was stirred for 2 hr and then was quenched in 100 ml of water. The organic and aqueous phases were separated, and the water portion was extracted once with dichloromethane. The fractions were combined, and the solvent was removed *in vacuo* (below 25°). Recrystallization of the resulting residue from dichloromethane–ether gave 1.254 g (89.1%) of **23** as a white solid: mp 147–148° dec; nmr ($CDCl_3$) δ 8.17–7.88 (m, 2), 7.83–7.52 (m, 3), 4.19 (d, 1, *J* = 14 Hz, *H*CHS), 3.62 (d, 1, *J* = 14 Hz, HC*H*S), 3.37 (s, 3, CH_3S), 3.20 (s, 1, O*H*), 2.20–0.80 (m, 18, $C(CH_3)_3$ and cyclohexyl protons).

By a similar procedure, 1.579 g (5.68 mmol) of **22** gave 2.124 g (98.4%) of **24**. All attempts to crystallize **24** failed, and it was obtained as a noncrystalline, white solid: nmr ($CDCl_3$) δ 8.23–7.97 (m, 2), 7.90–7.53 (m, 3), 4.12 (d, 1, *J* = 14 Hz, *H*CHS), 3.82 (s, 1, *J* = 14 Hz, HC*H*S), 3.87–3.40 (1, O*H*), 3.37 (s, 3, CH_3S), 2.30–0.80 (m, 18, $C(CH_3)_3$ and cyclohexyl protons).

Reaction of 23 with Sodium Hydride in THF. To a magnetically stirred suspension of 3.30 mmol of sodium hydride (0.139 g of a 56.8% dispersion in mineral oil, washed with three portions of *n*-hexane), in 100 ml of dry THF at 0° and under nitrogen, was added 1.231 g of solid **23**. After 0.5 hr, the mixture was warmed to 25°, stirred for an additional 1.5 hr, and then quenched in 500 ml of water. The aqueous mixture was extracted with pentane, the combined pentane fractions were dried (Na_2SO_4), and the solvent was removed by distillation. An nmr (CCl_4) of the colorless liquid residue showed it to be a mixture of the *Z* oxirane **5** and thioanisole. None of the *E* isomer of **4** was detected. Column chromatography on silica gel, with pentane–ether as the eluent, gave 0.345 g (86%) of thioanisole and 0.450 g (82.7%) of **5**. The ir (neat) and nmr (CCl_4) of each of these products were identical with those of authentic samples.

Reaction of 24 with Sodium Hydride in THF. Following a procedure similar to that given above for **23**, *E* oxirane **4** was obtained from **24**. Column chromtography of the reaction mixture on silica gel with pentane–ether as eluent gave thioanisole and **4** (66%) as a clear, colorless liquid.

***trans*-1,3-Diphenyl-3-hydroxy-4-thiophenoxy-1-butene (26).** *trans*-Benzalacetophenone (2.035 g, .78 mol) was converted to the oxirane **6**,[2] *in situ*. Then, 21.2 mmol of sodium thiophenoxide in 30 ml of dry DMSO was added, and the solution was stirred for 0.5 hr before being quenched in 1 l. of water. The aqueous mixture was extracted with dichloromethane, the combined extracts were dried ($MgSO_4$), and the solvent was removed *in vacuo* to give a light yellow oil. Column chromatography on silica gel (gradiently eluted with pentane–ether) afforded 2.549 g (78.5%) of **26** as a clear, viscous oil: ir (neat) 3480 (broad, OH), 3065 (shoulder), 3050 (m), 3020 (m), 2920 (w), 1595 (m), 1490 (s), 1478 (s), 1445 (s), 1435 (s), 1335 (m), 1300 (w), 1165 (m), 1155 (w), 1085 (w), 1065 (m), 1022 (m), 1000 (w), 970 (s), 745 (s), 695 (s) cm^{-1}; nmr ($CDCl_3$) δ 7.70–7.10 (m, 15, aromatic protons), 6.83 (d, 1, *J* = 16 Hz, vinyl proton), 6.44 (d, 1, *J* = 16 Hz, vinyl proton), 3.60 (s, 2, CH_2S), 3.30 (s, 1, O*H*).

Reaction of (*trans*-2,4-Diphenyl-2-hydroxy-3-butenyl)methylphenylsulfonium Fluoroborate (27) in Dichloromethane with 0.5 *M* Aqueous NaOH. By stirring a mixture of 1.030 g (3.10 mmol) of **26** and 0.490 g (3.31 mmol) of trimethyloxonium fluoroborate in 30 ml of dichloromethane at 5° for 2 hr salt **37** was generated. Then, 30 ml of 0.5 *M* aqueous NaOH was added, and the mixture was stirred at 0–5° for 13 hr. The water and dichloromethane phases were separated, and the aqueous portion was extracted with 20 ml of dichloromethane. The combined fractions were dried (K_2CO_3), and the solvent was removed *in vacuo* (below 25°) to give 1.062 g of a light yellow liquid. An nmr (CCl_4) showed this to be a 1 : 1 mixture of **6** and thioanisole with a trace (~4%) of **26** present. Both nmr and ir showed that neither the cyclopropane **7** nor benzalacetophenone was present.

***S*-(*trans*-2,4-Diphenyl-2-hydroxy-3-butenyl)-*N*-methyl-*S*-phenylsulfoximine.** To a solution of 1.70 g (10.0 mmol) of *N,S*-dimethyl-*S*-phenylsulfoximine, in 100 ml of dry THF at −65° and under nitrogen, was added 5 ml (10.0 mmol) of 2.0 *M* *n*-butyllithium in hexane. After 5 min, the solution was warmed to 0°, and 1.03 g (4.95 mmol) of *trans*-benzalacetophenone in 10 ml of THF was added. The solution was stirred for 2.5 hr at 0° and then quenched in 500 ml of water. The aqueous mixture was extracted with dichloromethane. The combined fractions were quickly extracted with two portions of 1 *M* aqueous H_2SO_4 and then with an aqueous $NaHCO_3$ solution. The organic phase was dried ($MgSO_4$), and the solvent was removed on the rotary evaporator below room temperature to give a pale yellow oil. Drying under high vacuum (0.05 mm, 1 hr) gave 1.846 g (98.9%) of diastereomeric products as a pale yellow, noncrystalline solid: nmr (CCl_4) δ 7.93–7.06 (m, 16, aromatic and O*H* protons), 6.90, 6.83, 6.57, and 6.07 (four doublets, 1.96, *J* = 16 Hz, vinyl protons of diastereomers), 3.63 and 3.58 (two singlets, 1.96, CH_2S protons of diastereomers), 2.62 and 2.60 (two overlapping singlets, 3, diastereomeric NCH_3). Neither *trans*-benzalacetophenone nor 1,4-addition product **20** were detected by nmr: ir (CCl_4) 3155 (broad, OH), 3050 (w), 3030 (m), 3000 (m), 2940 (m), 2910 (shoulder), 2890 (m), 2845 (m), 2780 (m), 1610 (shoulder), 1600 (m), 1580 (w), 1482 (m), 1444 (s), 1242 (s), 1145 (s), 1105 (m), 1071 (s), 1060 (m), 970 (m), 960 (m), 870 (m), 675 (s) cm^{-1}. A very weak peak at 1690 cm^{-1} (C=O) indicated that a trace amount of the 1,4-addition product **20** was present.

Reaction of (Dimethylamino)(*trans*-2,4-diphenyl-2-hydroxy-3-butenyl)phenyloxosulfonium Fluoroborate (25) with Aqueous Base. The sulfonium salt **25** was generated *in situ* by stirring a mixture of 0.449 g (1.119 mmol) of **19** and 0.190 g (1.28 mmol) of trimethyloxonium fluoroborate in 20 ml of dichloromethane at 0–15° for 3 hr. Then, 20 ml of dichloromethane and 40 ml of 0.5 *M* aqueous NaOH were added, and the mixture was stirred at 25° for 36 hr. The phases were separated, and the aqueous portion was extracted once with dichloromethane. The combined organic fractions were dried (K_2CO_3), and the solvent was removed *in vacuo* to give 0.429 g of a yellow oil. An nmr (CCl_4) indicated that this was largely a mixture of *trans*-1-benzoyl-2-phenylcyclopropane (**7**), *N,N*-dimethylbenzenesulfinamide, *trans*-benzalacetophenone, and a small amount of the precursor sulfoximine. None of the oxirane **6** was detected. Column chromatography on silica gel (gradiently eluted with pentane–dichloromethane) gave 0.119 g (44.9%) of **7**, 0.058 g (23.3%) of *trans*-benzalacetophenone, and 0.093 g of an oil which was shown by nmr (CCl_4) to be a 1:1 mixture of the β-hydroxysulfoximine (14.7%) and phenyl methyl sulfone.[7] Each product was identified by comparative nmr and/or ir with available samples.

Reaction of 25 with NaH in DMSO. The salt **25** (3.60 mmol) was generated (see above) in 30 ml of dichloromethane at 0–10° for 3.5 hr. The solvent was removed *in vacuo* (below 25°) at the aspirator and then under high vacuum (0.05 nm) to give a white, noncrystalline solid. This was dissolved in 10 ml of dry DMSO, and the solution was added to a magnetically stirred suspension of 3.72 mmol of NaH (0.157 g of a 57% dispersion in mineral oil, washed with several portions of pentane) in 5 ml of DMSO under nitrogen and at 25°. After 17 hr, 100 ml of pentane was added, and the mixture was quenched in 200 ml of water. The phases were separated, and the aqueous portion was extracted several times with pentane. The combined pentane fractions were dried (K_2CO_3), and the solvent was removed *in vacuo* at room temperature. A nmr (CCl_4) of the crude reaction mixture showed that none of the oxirane **7** was present. Column chromatography on silica gel (gradiently eluted with pentane–dichloromethane) gave 0.553 g (74.3%) of *trans*-1-benzoyl-2-phenylcyclopropane (**7**), 0.096 g (12.9%) of *trans*-benzalacetophenone, and 0.2864 g (47.1%) of *N*,*N*-dimethylbenzenesulfinamide.

Reaction of 25 with NaH in THF. A THF solution of **25** was treated with sodium hydride, and the mixture was stirred for 12.5 hr before being worked up as described above. From an nmr (CCl_4) of the crude reaction mixture, it was found to be composed of cyclopropane **7**, *trans*-benzalacetophenone, and THF polymer. None of the oxirane **6** or starting β-hydroxysulfoximine was present. The mixture was not separated into its components.

Treatment of *trans*-Benzalacetophenone with (Dimethylamino)methylphenyloxosulfonium Fluoroborate (3) in Dichloromethane and in the Presence of 0.5 *M* Aqueous NaOH. To a solution of 1.154 g (5.55 mmol) of *trans*-benzalacetophenone and 1.554 g (5.73 mmol) of **24**, in 75 ml of dichloromethane at 25°, was added 75 ml of 0.5 *M* aqueous NaOH. The mixture was stirred for 20.5 hr. The water and dichloromethane phases were separated, and the water portion was extracted with dichloromethane. The combined organic fractions were dried (K_2CO_3), and the solvent was removed *in vacuo* to give a pale yellow oil. Column chromatography on silica gel (eluted with 80% pentane–20% dichloromethane) gave 0.897 g (72.8%) of *trans*-1-benzoyl-2-phenylcyclopropane (mp 40–44°, lit.[8] mp 45–48°) and 0.192 g (∼16%) of benzalacetophenone containing a small amount of methyl phenyl sulfone as an impurity. Each product was identified by comparative ir and nmr.

Stereochemistry of α-Halo Sulfoxides. II. Interdependent Stereochemistry at Sulfur and α-Carbon in the α-Halogenation of Sulfoxides[1]

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Abstract: α-Halogenation of alkyl aryl and dialkyl sulfoxides by electrophilic halogenating reagents follows two different stereochemical processes which involve either double retention or double inversion at sulfur and carbon. When the α carbon is a chiral or prochiral center, optically active sulfoxides afford only one of the two possible diastereomeric α-halo sulfoxides, whose optical purity and chirality depend on the nature of the substrate and the reaction conditions. Possible mechanisms of these reactions, involving stereospecific migration of the halogen from sulfur to the α carbon in a halooxosulfonium salt intermediate, are discussed. Reductive dehalogenation of α-halo sulfoxides and α-halo sulfones with zinc and sodium sulfite usually proceeds with inversion of configuration at carbon.

Conversion of methyl aryl sulfoxides into chloromethyl and bromomethyl derivatives by electrophilic halogenating reagents in pyridine is accompanied by retention of configuration at the sulfur atom, but this same reaction proceeds with inversion in the presence of a molar excess of silver(I) nitrate.[1] Both processes are highly stereoselective, and the most relevant feature is that they occur seemingly without any substitution of ligands at the chiral center. This has been explained assuming that the formation of the new sulfur–halogen bond in the halooxosulfonium salt intermediate is followed by breaking of the same bond according to two different mechanisms of retention or inversion.[1]

Preliminary results[2] indicated a close relationship between the stereochemical courses at sulfur and α carbon when the latter is a chiral or prochiral center.

In this paper we report the results of the study of the stereochemical processes at sulfur and carbon and of the factors by which they are affected.

Results

Alkyl *p*-Tolyl Sulfoxides. When in alkyl *p*-tolyl sulfoxide **1** the methyl group is replaced by the ethyl or isopropyl group, α-halogenation is accompanied by inversion of sign of optical rotation (Table I).

The sign of the Cotton effect, attributed[3,4] to the n–π* transition of the sulfinyl group, in compounds **2** and **3**, is opposite to that of products **5a,b** and **6a,b**. This, together with the reduction with zinc and methanol of (−)-bromo derivatives, **5b** and **6b** to the (−)-sulfoxides **2** and **3**, enantiomeric to the starting ones,

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