coupling in **2b** attests to their cis geometry. Correspondingly, trans configurations were assigned to **3a** and **3b** on the basis of a vicinal coupling of 6.5 Hz observed for both (Figure 1).

The stereochemistry of each product was deduced utilizing long-range anisotropic shielding and deshielding effects. The results of this self-consistent correlation are depicted in Figure 1. Appropriate nuclear Overhauser effect experiments were also performed to verify the assignments. Although a pure sample of **2b** was not obtained, pmr data obtained on mixtures enriched with **2b** are consistent with the cis structure advanced.

The efficiency with which the acetylenic function participates as the migrating moiety in the rearrangement is intriguing. Relative migratory aptitudes for sp and sp^2 centers cannot be inferred from the fact that PhC≡C migrates to the exclusion of PhCH=CH since the alternate and undetected rearrangement path available for **1a** and **1b** would consist of cyclization with ultimate incorporation of the sp-hybridized atoms 4 and 5 into a cyclopropene ring, which may be inherently less favorable than the observed process involving inclusion of the sp^2 centers 1 and 2 into a cyclopropane ring.

The stereochemical outcome also represents a novel feature of the di-π-methane rearrangement observed for **1a** and **1b**. Such stereospecificity is assumed to be associated with a high degree of concertedness for the bond cleavage and bond formation processes required for atom reorganization of the di-π-methane type. The photorearrangement of **1b** may be formulated as a 4q system as proposed by Woodward and Hoffmann[8] in which a single bond (3–4) adds to a π bond (1–2), *i.e.*, a $[{}_{\pi}2_a + {}_{\sigma}2_a]$ cycloaddition. The results of the analysis using all of the $[{}_{\pi}2_s + {}_{\sigma}2_s]$ and $[{}_{\pi}2_a + {}_{\sigma}2_a]$ combinations of orbitals and two nearly isoenergetic conformations of **1b** confirm that all four possible stereochemically distinct π-cyclopropanes **2a**, **2b**, **3a**, and **3b** may be formed through symmetry-allowed photochemical routes. Presumably additional structural and/or electronic factors determine the lowest energy pathways leading to the preferred products observed.

Neglect of the acetylenic orbitals is at best qualitative since a second π bond is apparently required for facile rearrangement to occur. While there are reported examples of related rearrangements in which a hydrogen or alkyl group migrates, efficiencies of such reactions are lower than that observed for **1a** and **1b**.[9,10] It is noteworthy, however, that overall predictions based upon analysis of the reaction as a $[{}_{\pi}2 + {}_{\sigma}2 + {}_{\pi}2]$ cycloaddition are identical with those reached above.[11]

(8) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1970, p 97.

(9) (a) G. W. Griffin, A. F. Marcantonio, H, Kristinsson, R. C. Petterson, and C. S, Irving, *Tetrahedron Lett.*, 2951 (1965); (b) H. Kristinsson and G, W. Griffin, *J. Amer. Chem. Soc.*, **88**, 378 (1966); (c) W. W. Kwie, B. A. Shoulders, and P. D. Gardner, *J. Amer. Chem. Soc.*, **84**, 2268 (1962); (d) H. E. Zimmerman, R. G. Lewis, J. J. McCullough, A. Padwa, S. W. Staley, and M. Semmelhack, *J. Amer. Chem. Soc.*, **88**, 1965 (1966); (e) O. L. Chapman, T. A. Rettig, A. A. Griswold, A. I. Dutton, and P. Fitton, *Tetrahedron Lett.*, 2049 (1963).

(10) The role of this second π bond has recently been evaluated and it was concluded that the di-π-methane rearrangement is best described as a $[{}_{\sigma}2_a + {}_{\sigma}2_a + {}_{\pi}2_a]$ process: H. E. Zimmerman and R. D. Little, *J. Amer. Chem. Soc.*, **94**, 8256 (1972).

(11) Analysis of this photoconversion as a $4n + 2$ system from the Zimmerman Möbius-Hückel perspective leads to equivalent results: H. E. Zimmerman, *J. Amer. Chem. Soc.*, **88**, 1564, 1566 (1966); *Accounts Chem. Res.*, **4**, 272 (1971).

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Conversion of Ketones to Epoxides *via* β-Hydroxy Sulfides[1]

Sir:

Nucleophilic alkylidene transfer from a sulfur ylide to a carbonyl group is the standard method for achieving the conversion of an aldehyde or ketone to an oxirane.[2] Such reactions are quite general, but in some instances the reactions fail. The two most prevalent reasons for failure are (1) enolization of the substrate[3] and (2) steric hindrance.[4] It appeared to us that one might be able to circumvent these difficulties by use of a simple multistep sequence for the transformation, the first step of which would employ a reagent of amplified nucleophilicity. The model reagent which we chose for this purpose was phenylthiomethyllithium, which is readily prepared by reaction of *n*-butyllithium and thioanisole in the presence of 1,4-diazabicyclo[2.2.2]octane (Dabco).[5] This reagent readily adds to aldehydes and ketones to yield β-hydroxy sulfides[5,6] which, in turn, can be transformed to oxiranes by alkylation at sulfur followed by treatment with base (Scheme I). Note that the intermediate betaine generated by this method[7] is identical with that which would be produced by addition of an alkylphenylsulfonium methylide to the carbonyl compound.

Both dimethylsulfonium and dimethyloxosulfonium methylide fail to produce epoxide when allowed to react with deoxybenzoin, presumably because of the ease of enolization of this material by basic reagents. Using the method just described we have been able to convert deoxybenzoin to 2-benzyl-2-phenyloxirane in 79% yield. Utilizing methylthiomethyllithium,[8] a like method applied to the highly hindered 2,2,6,6-tetramethylcyclohexanone resulted in the formation of 4,4,8,8-tetramethyl-1-oxaspiro[2.5]octane in 80% yield. Other examples are summarized in Table I.

(1) Part XLIII in the series "Chemistry of Sulfoxides and Related Compounds."

(2) For a review see A. W. Johnson, "Ylid Chemistry," Academic Press, New York, N. Y., 1966.

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

(4) E. J. Corey and W. Oppolzer, *ibid.*, **86**, 1899 (1964); W. E. Parham and L. J. Czuba, *ibid.*, **90**, 4030 (1968).

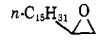
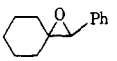
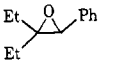
(5) E. J. Corey and D. Seebach, *J. Org. Chem.*, **31**, 4097 (1966).

(6) These same intermediates may be converted to olefins by reductive elimination of their acyl derivatives: R. L. Sowerby and R. M. Coates, *J. Amer. Chem. Soc.*, **94**, 4758 (1972).

(7) For previous examples of generation of betaines by this method see M. Yashimini and M. J. Hatch, *ibid.*, **89**, 5831 (1967); C. R. Johnson and C. W. Schroeck, *ibid.*, **93**, 5303 (1971); T. Durst, R. Viau, and M. R. McCloy, *ibid.*, **93**, 3077 (1971); T. Durst, R. Viau, R. VanDen Elzen, and C. H. Nguyen, *Chem. Commun.*, 1334 (1971); J. M. Townsend and K. B. Sharpless, *Tetrahedron Lett.*, 3313 (1972).

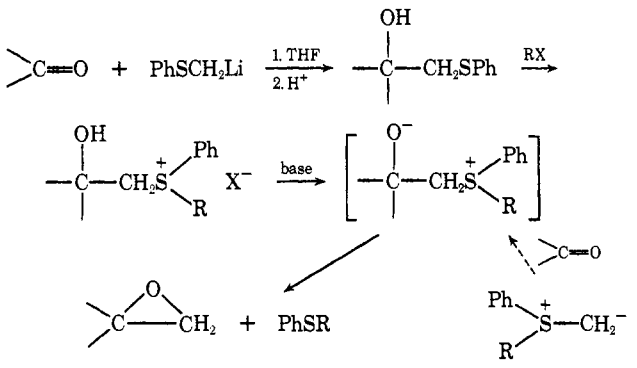
(8) D. J. Peterson, *J. Org. Chem.*, **32**, 1717 (1967).

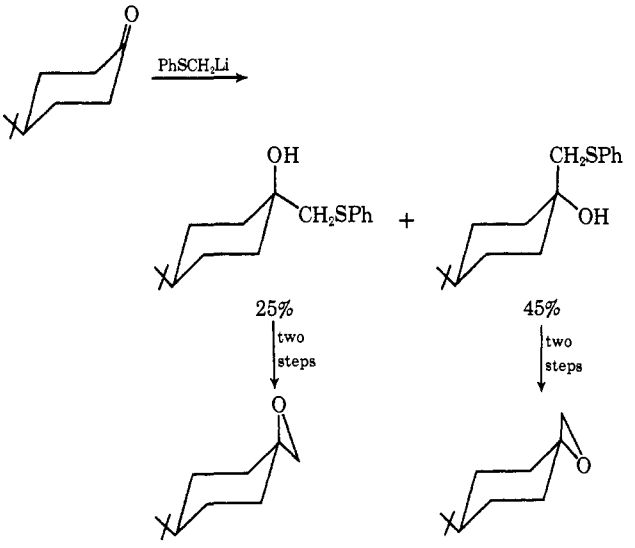
Table I. Oxiranes from Ketones

Ketone	Lithium reagent[a]	Hydroxy sulfide, % isolated	Oxirane	Method[b]	Yield,[c] % isolated
2-Hexadecanone	A	56		D	89
Cyclododecanone	B	65		F	79
Di-*tert*-butyl ketone	A	100		D	86
2,2,6,6-Tetramethylcyclohexanone	A B	91 92		E F	84 87
Benzyl *tert*-butyl ketone	A	90		E	87
Deoxybenzoin	A	88		D	90
1,3-Diphenyl-2-propanone	A	41		D	98
Cyclohexanone	C	81		D	92
3-Pentanone	C	80		D	43[d]

[a] A, $PhSCH_2Li$(Dabco) in THF; B, CH_3SCH_2Li(TMEDA) in hexane; C, PhSCHLiPh in THF. [b] D, β-hydroxy sulfide was alkylated with trimethyloxonium fluoroborate in methylene chloride followed by treatment of the solution with 0.5 *N* NaOH; E, trimethyloxonium fluoroborate in nitromethane, followed by treatment of the salt in methanol with 1.3 equiv of K_2CO_3 in methanol. [c] For conversion of β-hydroxy sulfide to oxirane. [d] The corresponding ketone, 4-phenyl-3-hexanone (21%), and olefin, 2-ethyl-1-phenylbutene (15%), were also isolated.

Scheme I





The overall yields are remarkably high and point to the fact that this sequence may be worthy of consideration even in those cases where a one-step ylide reagent would work. Neither thioanisole nor dimethyl sulfide presents any difficulty in separation from the oxiranes.

Diastereomeric epoxides are often very difficult to impossible to separate, at least on a preparative scale. This is not usually true of more polar diastereomeric alcohols. Using the present three-step method, resolution of the diastereomers may be achieved at the more convenient β-hydroxy sulfide stage.[9]

The lithio derivative of benzyl phenyl sulfide was added to cyclohexanone; the adduct thus produced was converted to 2-phenyl-1-oxaspiro[2.5]octane in 75% overall yield. It is pertinent to note that this product could not be obtained by reaction of diphenylsulfonium benzylide and cyclohexanone.[10] The method cannot accommodate wide structural variation of the transfer group; higher alkyl aryl sulfides undergo ortho nuclear metalation by *n*-butyllithium.[11] This limitation could doubtlessly be circumvented by development of effective methods of producing the necessary α-lithio derivatives.

When the transition state for collapse of the intermediate betaine to oxirane is crowded, other reaction pathways begin to compete. Benzophenone was allowed to react with α-lithiobenzyl phenyl sulfide and the adduct was methylated with trimethyloxonium fluoroborate followed by treatment with aqueous base.

(9) The reaction of dimethylsulfonium methylide with 4-*tert*-butylcyclohexanone gives a mixture of the (*E*)- and (*Z*)-epoxides (17:83) (ref 3).

(10) See ref 2, p 333.

(11) H. Gilman and F. J. Webb, *J. Amer. Chem. Soc.*, **71**, 4062 (1949).

The products were benzhydryl phenyl ketone (29%), presumably from rearrangement of the expected epoxide, and triphenylethylene (31%). The olefin may result from an elimination reaction initiated by attack of hydroxide at the sulfonium site, formation of a methylide, or formation of a cyclic sulfurane.

In a typical experimental procedure the ketone was added to a solution of 1.1 equiv of phenylthiomethyllithium (Dabco) in THF. The reaction times were varied from 2 hr to overnight depending on the reactivity of the ketone. The β-hydroxy sulfides, usually purified by chromatography on silica gel, were treated with a slight excess of trimethyloxonium fluoroborate in methylene chloride until most of the oxonium salt had been consumed (homogeneous solution). Excess 0.5 *N* aqueous sodium hydroxide was added and the two phases were efficiently stirred together overnight. The epoxides thus produced were purified by distillation or by chromatography on silica gel.

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Asymmetric Deuteration at the α Carbon of L-Aspartic Acid *via* the Template Action of a Dissymmetric Cobalt(III) Complex

Sir:

Stereospecific deuterium labeling of amino acids can be achieved enzymatically as for example with glutamate–oxaloacetate transaminase (aspartate aminotransferase) and glutamate–pyruvate aminotransferase (alanine aminotransferase) which have been used, respectively, to selectively deuterate aspartic acid[1] and glutamic acid[2] at the α carbon. As would be expected the deuteration proceeds with retention of configuration due to the asymmetry of the enzyme active site.

It has been known for some time that certain amino acid and peptide cobalt(III) chelates will undergo deuteration at the α carbon of a glycine or glycine-like chelate ring.[3-5] It was thought that if the deuteration were carried out employing a dissymmetric template such as a resolved *cis*-$Co(en)_2L_2^n$ complex, deuteration with (partial) retention of configuration might be observed. We have previously demonstrated that the diastereomers of $Co(en)_2$(L-aa)$^{2+}$ (aa = aspartate and glutamate chelated through the five-membered ring containing the α carbon as illustrated in Figure 1) will

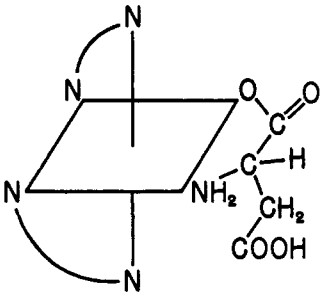

Figure 1. Aspartic acid chelated through the five-membered ring.

selectively deuterate at the α carbon to give the 2-^{2}H amino acids.[4] We have now shown that the deuteration proceeds with at least 77 ± 2% retention of configuration for the aspartic acid complex.

Aspartatobis(ethylenediamine)cobalt(III) perchlorate (1.34 g, 3.00 mmol) was dissolved in 10 ml of deuterium oxide. A mixture of the Na_2CO_3 (0.1 g) and $NaHCO_3$ (0.1 g) was added to bring the pD of the solution to *ca.* 9.5. The solution was allowed to stand at 35° until the pmr signal (a triplet) of the methine proton of the coordinated aspartic acid, Figure 1, was no longer detectable (3 days).[4] The solution was then added to 50 ml of 0.1 *N* HCl, and a solution of 2 g of $NaBH_4$ in 15 ml water was added dropwise until a pH of 7 was attained. The black precipitate was immediately removed by filtration using Celite Filter Aid and washed with a small amount of water. The combined filtrate was diluted to 100 ml with water and loaded on a Bio-Rad AG-1-X4 anion-exchange column (50–100 mesh, 165 mequiv capacity) at a rate of 2–3 ml/min. After rinsing with 1.5 l. of distilled water, the eluting solution was changed to 0.1 *N* HCl. Beginning 25 ml before the eluent became acidic, 150 ml of solution was collected and evaporated to dryness.

A quantitative amino acid analysis (Beckman 121C automatic amino acid analyzer) showed that the sample consisted of 0.12 g (0.9 mmol) of aspartic acid, a 30% yield based on the original amount of complex taken for deuteration (product is retained by the filtrate after reduction). From this information and comparison of the ORD curves obtained for the sample and a standard sample of L-aspartic acid, the aspartic acid obtained from the deuterated $Co(en)_2$(L-asp)$^{2+}$ was found to consist of 79% L and 21% D isomer. A repeat of the deuteration and isolation yielded 75% L and 25% D. The ORD and CD data were obtained with a JASCO Model ORD/UV-5 with CD attachment. The CD spectra were also recorded on a Cary Model 61 recording spectropolarimeter.[6] The pmr spectra were recorded on a Varian A-60 spectrometer with sodium 2,2-dimethyl-2-silapentane-5-sulfonate (TMS*) employed as an external standard.

Figure 2 summarizes the circular dichroism (CD) spectra obtained before and after deuteration of Λ-$Co(en)_2$(L-Asp)$^{2+}$.[7] If complete retention of configura-

(1) T. B. Dougherty, V. R. Williams, and E. S. Younathan, *Biochemistry*, **11**, 2493 (1972), and references therein.
(2) D. J. Whelan and G. J. Long, *Aust. J. Chem.*, **22**, 1779 (1969).
(3) (a) D. H. Busch and D. H. Williams, *J. Amer. Chem. Soc.*, **87**, 4644 (1965); (b) J. B. Terrill and C. N. Reilley, *Inorg. Chem.*, **5**, 1988 (1966); (c) J. L. Sudmeier and G. Occupati, *ibid.*, **7**, 2524 (1968); (d) P. F. Coleman, J. I. Legg, and J. Steele, *ibid.*, **9**, 937 (1970); (e) A. Y. Girgis and J. I. Legg, *J. Amer. Chem. Soc.*, **94**, 8420 (1972).
(4) J. I. Legg, and J. Steele, *Inorg. Chem.*, **10**, 2177 (1971).
(5) D. A. Buckingham, L. G. Marzilli, and A. M. Sargeson, *J. Amer. Chem. Soc.*, **89**, 5133 (1967).
(6) Although the analytical data obtained for the isomers agreed with previously obtained data, the Δε of the CD maxima were not identical (ref 4). Therefore, the spectra of the isomers used in this study were recorded on a Cary 61 and found to be in agreement with the spectra obtained with the JASCO. We are grateful to Professor B. L. Vallee of the Harvard Medical School for the use of the Cary 61.
(7) The absolute configurations of these complexes have been tentatively assigned, ref 4. However, the reasoning presented here is independent of these assignments. The IUPAC nomenclature, *Inorg. Chem.*, **9**, 1 (1970), is used.