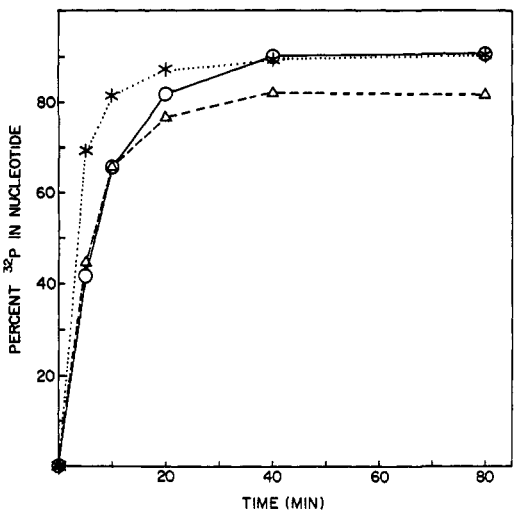

Figure 1. ^{32}P incorporation in the γ phosphate, of ATP (○—○), ϵATP (**1**) (*···*), and ϵCTP (**2c**) (△---△), in the presence of 3-phosphoglyceric acid, glyceraldehyde-3-phosphate dehydrogenase, 3-phosphoglycerate kinase, and $K_2H^{32}PO_4$.

the standard procedure of coupling the reaction to glyceraldehyde-3-phosphate dehydrogenase (muscle).[6] The analogs ϵATP and ϵCTP replaced ATP in this system with K_m equal to 3.7 and 0.85, respectively, while under identical conditions the K_m observed for ATP was 0.57. The V_{max} values for ϵATP and ϵCTP were equal to 46 and 37% of that of ATP. Under the same conditions[7] CTP did not show any activity, which is in agreement with the finding of Adam.[8,9]

If $^{32}PO_4^{3-}$ is added and NADH omitted from the 3-phosphoglycerate system, the net result is equilibration of the γ (terminal) phosphate in the nucleoside triphosphate with the inorganic phosphate. Using conditions similar to known procedures for preparing [γ-^{32}P]ATP,[10] [γ-^{32}P]ϵATP and [γ-^{32}P]ϵCTP were prepared. The nucleoside triphosphate (5 m*M*) was mixed with $K_2H^{32}PO_4$ (0.2 m*M*) in a reaction buffered at pH 8.1 with Tris-HCl (50 m*M*) and containing $MgCl_2$ (6.25 m*M*), dithiothreitol (1.25 m*M*), 3-phosphoglyceric acid (1 m*M*), glyceraldehyde-3-phosphate dehydrogenase (100 μg/ml), and 3-phosphoglycerate kinase (10 μg/ml). The incorporation of ^{32}P into triphosphate was assayed by chromatography of the reaction mixture on polyethylenimine thin layers (Polygram, Brinkmann Instruments) which were developed with 1 *M* LiCl.[11,12] Radioactivities on the chromatograms were measured on a strip scanner (Packard No. 7201). The per cent of the total phosphate incorporated into the triphosphate *vs.* reaction time is plotted in Figure 1. The ϵATP reached equilibrium most rapidly, even though it phosphorylates 3-phosphoglyceric acid most slowly. Apparently the rate of approach to equilibrium in this complex system is determined by factors other than the phosphorylation rate of 3-phosphoglyceric acid. Traces of the corresponding nucleotide diphosphates formed in the enzymatic reaction showed no incorporation of ^{32}P.

The introduction of the second ring on the cytidine portion of CTP gives the new molecule a spatial outline and binding areas roughly similar to those of the corresponding adenine nucleotide. This relationship is shown by the overlay in formula **3**, in which anti conformations are assumed with respect to the ribosyl phosphate unit, indicated schematically. The same conclusion is supported by preliminary results obtained with ϵCDP *vs.* ADP as substrates for pyruvate kinase. Under the conditions employed,[3d] ϵCDP showed activity comparable to ADP, while CDP was considerably less active.[13]

In terms of utility, the availability of γ-^{32}P triphosphates greatly facilitates the enzymatic study of these coenzyme analogs, especially in reactions where phosphate or pyrophosphate is donated to an acceptor. Work along these lines is in progress.

Acknowledgment. This work was supported by Research Grants GM-05829 and AM-13488 from the National Institutes of Health, U. S. Public Health Service. We wish to thank Professor Gregorio Weber for providing the necessary facilities for fluorescence determinations, Dr. James L. Robinson for valuable discussions concerning the enzyme kinetics, and Joyce Olszowy Harned for technical assistance. One of us (J. R. B.) held a fellowship from the Consejo Nacional de Investigaciones Científicas y Técnicas (Argentina).

(13) K. M. Plowman and A. R. Krall, *Biochemistry*, 4, 2809 (1965).

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(6) T. Bücher, *Methods Enzymol.*, 1, 415 (1955).

(7) The assay mixtures (1 ml) contained 2 m*M* 3-phosphoglyceric acid; 50 m*M* tetramethylammonium *N*-tris(hydroxymethyl)methyl-2-aminoethanesulfonate buffer, pH 7.5; 20 m*M* $MgCl_2$; 0.2 m*M* NADH; 100 μg/ml of rabbit muscle glyceraldehyde-3-phosphate dehydrogenase, EC 1.2.1.12 (Boehringer-Mannheim), and 0.1 μg/ml of yeast 3-phosphoglycerate kinase, EC 2.7.2.3 (Boehringer-Mannheim); 0.1–1.0 m*M* for ATP and ϵCTP; 0.5–5.0 m*M* for ϵATP.

(8) H. Adam, *Biochem. Z.*, 335, 25 (1961).

(9) For CTP to show activity equivalent to that of ϵCTP at 0.15 m*M*, about 70 times higher concentration of substrate and 20 times more enzyme were required.

(10) I. M. Glynn and J. B. Chappell, *Biochem. J.*, 90, 147 (1964).

(11) K. Randerath and E. Randerath, *J. Chromatogr.*, 16, 111 (1964).

(12) R_f values are: phosphate, 0.49; ATP, 0.08; ϵATP, 0.04; ϵCTP, 0.17.

New Synthetic Methods. Transfer of Chirality from Sulfur to Carbon

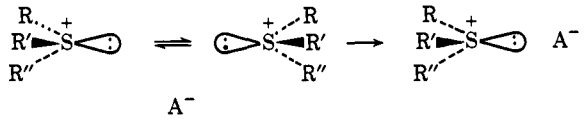
Sir:

The synthesis of enantiomerically pure compounds normally involves the resolution of a racemic mixture at some point in a chemical synthesis with the obvious loss of 50% of the material. The question arises as to whether racemic compounds can be converted 100% into enantiomerically pure substances. We wish to report an approach to this problem.

Sulfonium salts possess the interesting property that although they can be obtained optically active,[1,2] the barrier to inversion is sufficiently low to allow racemization in solution at room temperature or slightly above.[2] Thus, resolution of the salt utilizing an optically active anion such as *l*-malate or dibenzoyl hydrogen tartrate crystallizes one diastereomic salt while retaining the other diastereomer in solution. Racemization of this

(1) K. K. Andersen, *Chem. Commun.*, 1051 (1971).

(2) (a) D. Darwish, S. H. Hui, and R. Tomilson, *J. Amer. Chem. Soc.*, 90, 5631 (1968); (b) R. Scartazzini and K. Mislow, *Tetrahedron Lett.*, 2719 (1967); (c) however, see also K. K. Andersen, M. Cinquini, and N. E. Papanikolaow, *J. Org. Chem.*, 35, 706 (1970).



latter salt followed by resolution effects eventual conversion of the diastereomeric mixture to *only one diastereomer with no loss of material.* If the chirality at sulfur can be transferred to chirality at carbon with a high degree of optical induction, then this method serves as a synthesis of enantiomerically pure substances from racemates.

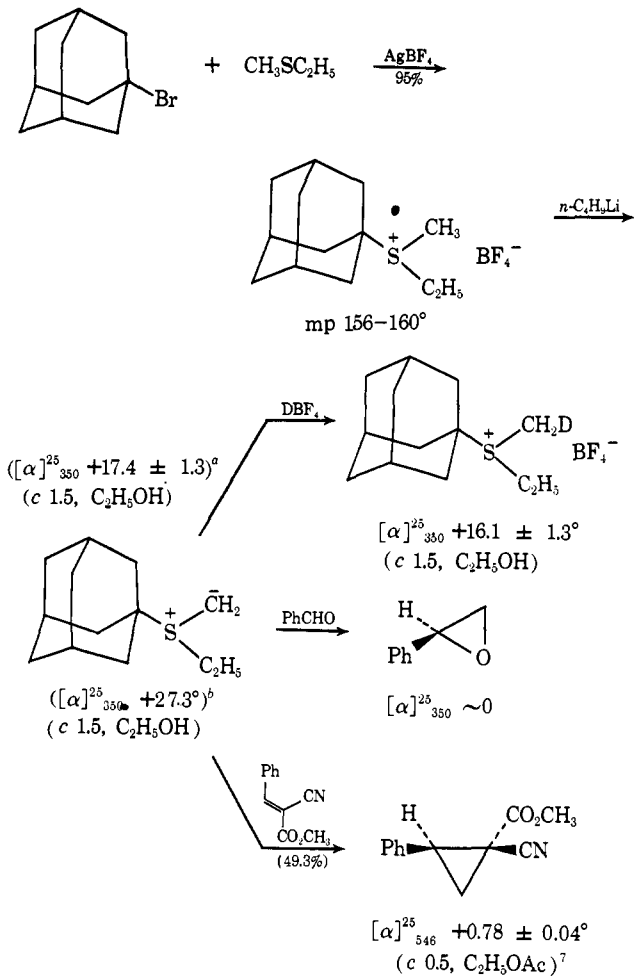
To transfer chirality from sulfur to carbon, we examined the behavior of π sulfuranes (ylides) in three reactions: (1) carbonyl addition, (2) conjugate addition, and (3) [2,3] sigmatropic rearrangement. For the first two reactions, we examined the behavior of adamantylethylsulfonium methylide. The requisite sulfonium salt[3,4] was resolved as its *l*-malate salt (mp 106–109°) by recrystallization from acetone–ether: $[\alpha]^{25}D$ +47.1° (*c* 1.6, methanol). Conversion to the fluoroborate was achieved by treatment with fluoroboric acid at −95° in methylene chloride. Although the rotations of the fluoroborate salt thus obtained varied somewhat, rotations as high as $[\alpha]^{25}_{350}$ +27.3° (*c* 1.5, ethanol) have been obtained.

Base (*n*-butyllithium) treatment of the optically active salt, $[\alpha]^{25}_{350}$ +17.4 ± 1.3° (*c* 1.5, ethanol), in tetrahydrofuran followed by quenching with deuteriofluoroboric acid regenerated starting salt with essentially no loss of optical activity, $[\alpha]^{25}_{350}$ +16.1 ± 1.3° (*c* 1.5, ethanol), and virtually exclusive deuteration at the methyl group (nmr analysis) (Scheme I). *This represents the first demonstration of the maintenance of configuration at sulfur in a simple sulfonium ylide.*[5] The condensations of this ylide led to disappointingly low yields of optical induction.[6,7]

Nevertheless, extension of our studies to the [2,3] sigmatropic rearrangement proved exceptionally exciting. Rearrangement of 1-adamantylallylethylsulfonium fluoroborate, mp 108–110°, under reversible ylide generation conditions generated the desired rearrangement product 1-adamantyl 2-pent-4-enyl sulfide with varying amounts of adamantyl ethyl sulfide and adamantyl allyl sulfide, the ratios being determined by vpc.[8]

Resolution of the racemate as its dibenzoyl hydrogen tartrate salt (mp 127–128°)[9] by recrystallization from methanol–ether, $[\alpha]^{25}_{365}$ −332° (*c* 0.45, ethanol), generated fluoroborate salt with $[\alpha]^{25}_{365}$ +22.2 ± 0.2° (*c* 1.10, ethanol) as described for the ethylmethyl salt. Tretament of this compound with potassium *tert*-butoxide in toluene at −33° for 1 hr generated 48.4% yield of 1-adamantyl 2-pent-4-enyl sulfide with $[\alpha]^{25}_{365}$ −6.86° ± 0.04° (*c* 3.06, chloroform) obtained pure by collection from vpc.[8]

Scheme I. Preparation and Reaction of Optically Active 1-Adamantylethylsulfonium Methylide



[a] Rotation of starting salt for deuterium quench. [b] Rotation of starting salt for epoxidation and cyclopropanation.

To determine the configuration and optical purity of this substance, a correlation with 1-adamantyl 2-pentyl sulfide also available by independent synthesis was made. (*S*)-2-Pentanol, 62.7% optically pure,[10] was converted *via* its tosylate by SN2 displacement to 1-adamantyl 2-pentyl sulfide, $[\alpha]^{25}_{365}$ +7.94 ± 0.6° (*c* 5.35, chloroform).[11] Assuming no racemization and one inversion at carbon (*i.e.*, the displacement step) the sulfide **3** thus obtained was 62.7% optically pure and of the *R* configuration.

Reduction of a sample of **2** of $[\alpha]^{25}_{365}$ −1.20 ± 0.06° (*c* 5.76, chloroform) with diimide gave the same sulfide **3** of $[\alpha]^{25}_{365}$ +2.07 ± 0.09° (*c* 5.00, chloroform) indicating it to be of the *R* configuration and 16.4% optically pure. Utilizing these data, optically pure pentenyl sulfide **2** is calculated to have $[\alpha]^{25}_{365}$ 7.33°. *Thus, the rearrangement proceeds with a minimum of 94% optical induction.* Furthermore, this experiment demonstrates the ability to transfer asymmetry from sulfur to carbon with essentially no loss of optical activity.

(3) For an alternative preparation see ref 2b.

(4) For all new compounds, satisfactory spectral data and elemental compositions have been obtained.

(5) Optically active stabilized ylides have been obtained; see C. R. Johnson and C. W. Schroeck, *J. Amer. Chem. Soc.*, **90**, 6852 (1968); D. Darwish and R. L. Tomilson, *ibid.*, **90**, 5938 (1968).

(6) The low optical yields contrast with the substantial optical yields obtained with the optically active oxosulfonium ylide of Johnson and Schroeck. The differences may be attributed to the higher reactivity of the nonstabilized ylide.

(7) The optical purity of the cyclopropane was determined by comparison with an independently prepared optically active sample; see E. W. Yankee and D. J. Cram, *J. Amer. Chem. Soc.*, **92**, 6329 (1970).

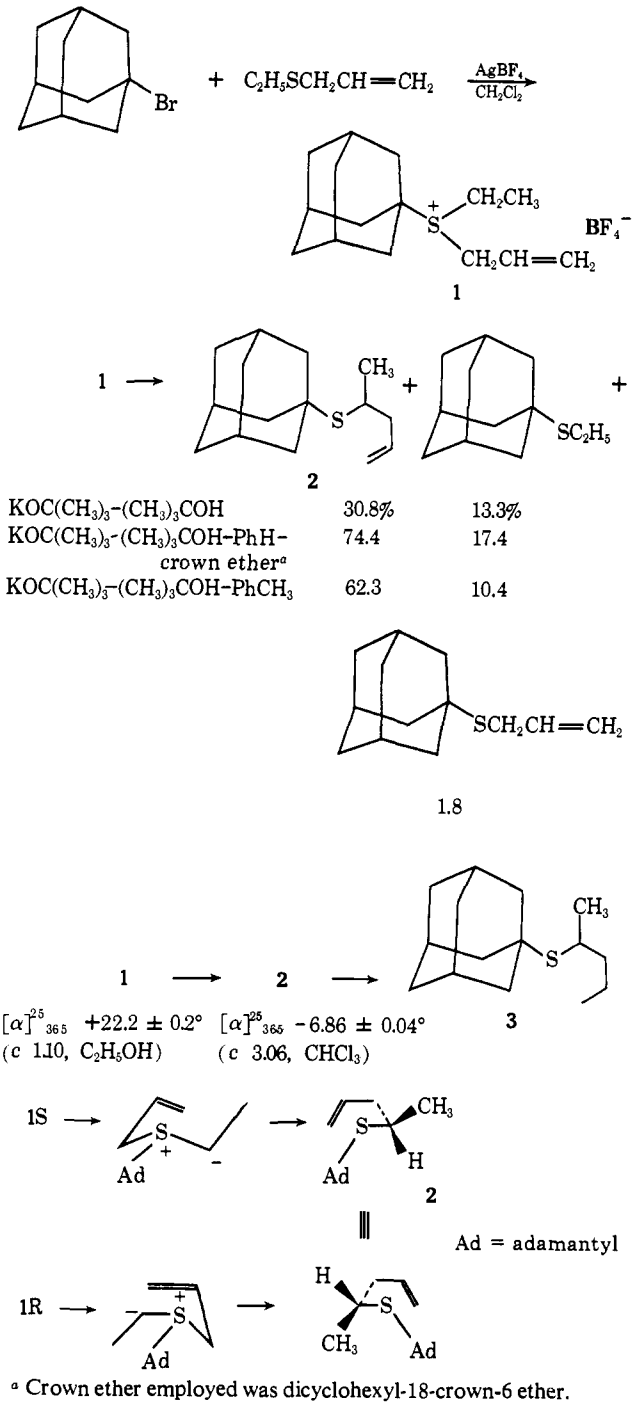
(8) A 1.5-m 10% Carbowax on Chromosorb W column at 178° was employed.

(9) The melting point listed refers to a sample of salt with $[\alpha]^{25}_{350}$ −334° (*c* 0.4, ethanol).

(10) R. H. Pickard and W. J. Kenyon, *J. Chem. Soc.*, 45 (1911).

(11) To minimize optical fractionation no purification of the tosylate was performed. The entire crude material was directly reacted with sodium adamantyl thiolate and the final product isolated by collection of the entire peak from a vpc column.[8] Necessary controls demonstrate lack of racemization on vpc.

Scheme II. Preparation and [2,3] Sigmatropic Rearrangement of Optically Active Ylide



[a] Crown ether employed was dicyclohexyl-18-crown-6 ether.

A brief discussion of the mechanism of the [2,3] sigmatropic rearrangement is in order.[12-14] Obviously, the faithful translation of optical activity from sulfur to carbon supports the concerted nature of the rearrangement. Assuming the folded envelope conformation, obtention of the *R* enantiomer of sulfide requires the conformations depicted in Scheme II for the *R* and *S* configurations of π sulfurane. Of the possible reactive conformations of the *S* enantiomer, the one depicted minimizes nonbonded interactions, whereas the one depicted for the *R* enantiomer maximizes the nonbonded interactions. On this basis the *S* configuration may be assigned to the starting salt. The observation of such high optical induction for the [2,3] sigmatropic rearrangement has important implications in relation to the formation of presqualene and its monoterpene analog chrysanthemol.[15,16]

Acknowledgment. We wish to thank the National Institutes of Health and the National Science Foundation for their generous support of our program.

(12) J. E. Baldwin and R. E. Hackler, *J. Amer. Chem. Soc.*, 91, (1969); R. W. C. Cose, A. M. Davies, W. D. Ollis, C. S. Smith, and I. O. Sutherland, *Chem. Commun.*, 293 (1969).

(13) For an oxygen analog see J. E. Baldwin and J. E. Patrick, *J. Amer. Chem. Soc.*, 93, 3556 (1971); V. Rautenstrauch, *Chem. Commun.*, 4 (1970). For transfer of chirality from nitrogen to carbon in a Stevens rearrangement, see R. K. Hill and T. H. Chan, *J. Amer. Chem. Soc.*, 88, 866 (1966).

(14) For a nitrogen analog see R. W. Jemison and W. D. Ollis, *Chem. Commun.*, 294 (1969); S. Mageswaran, W. D. Ollis, I. O. Sutherland, and Y. Thebtaranonth, *ibid.*, 1494 (1971).

(15) B. M. Trost, P. Conway, and J. Stanton, *ibid.*, 1639 (1971).

(16) For leading references see R. M. Coates and W. H. Robinson, *J. Amer. Chem. Soc.*, 94, 5920 (1972); C. D. Poulter, O. J. Muscio, C. J. Spillner, and R. G. Goodfellow, *ibid.*, 94, 5921 (1972).

(17) Recipient of Camille and Henry Dreyfus Teacher-Scholar Award.

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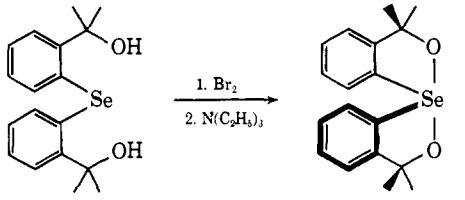
Organoselenium Stereochemistry. Configurational Stability of Dialkoxydiarylselenium Compounds

Sir:

We wish to report the synthesis and characterization of several new cyclic chiral dialkoxydiarylselenuranes,[1,2] and some results of a study of their configurational stability, including the first example of the separation of diastereomers differing in configuration at tetracoordinate selenium.

The reaction of dimethyl 2,2′-selenodibenzoate[4c] (**1**) with methyllithium gave the tertiary glycol **2**[7a] which could be cyclized to the spiroselenurane **3**[1b,7a] by treatment of the corresponding selenide dibromide with triethylamine. Compound **3** was assigned the indicated structure on the basis of the following evidence:



2, mp 106° **3**, mp 123° dec

(1) (a) We use the name "selenurane" (in analogy with sulfurane) for tetrasubstituted selenium(IV) compounds. The name selenane, used by J. I. Musher,[3a] is not acceptable since it is the established systematic name for selenacyclohexane. (b) The *Chemical Abstracts* name for **3** is 3,3,3′,3′-tetramethyl-1,1′-spirobi[3*H*-2,1-benzooxaselenole].

(2) Dialkoxyselenuranes,[4a] diacyloxyselenuranes,[4b,c] and related sulfur compounds[5,6] have been reported.

(3) For a discussion of bonding in high-valent metalloid compounds, see: (a) J. I. Musher, *Ann. N. Y. Acad. Sci.*, 192, 52 (1972); (b) J. I. Musher, *Angew. Chem., Int. Ed. Engl.*, 8, 54 (1969).

(4) (a) R. Paetzold and U. Lindner, *Z. Anorg. Allg. Chem.*, 350, 295 (1967); (b) D. G. Foster, *Recl. Trav. Chim. Pays-Bas*, 54, 447 (1935); (c) R. Lesser and R. Weiss, *Chem. Ber.*, 47, 2510 (1914).

(5) (a) R. J. Arhart and J. C. Martin, *J. Amer. Chem. Soc.*, 94, 4997 (1972); (b) E. F. Perozzi and J. C. Martin, *ibid.*, 94, 5519 (1972).

(6) I. Kapovits and A. Kalman, *Chem. Commun.*, 649 (1971).

(7) (a) Elemental analysis, nmr spectra (CCl_4), and infrared spectra were consistent with the structures assigned. (b) High temperature nmr spectra were measured using hexachlorobutadiene as solvent.