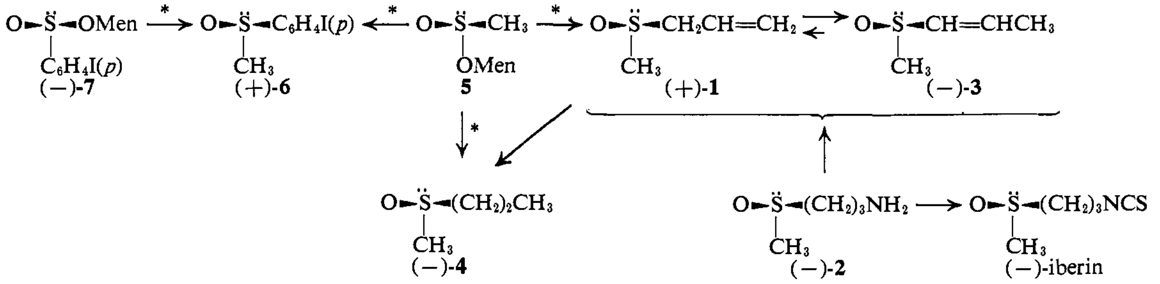
The Absolute Configuration of Methyl Allyl Sulfoxide. Stereochemistry of the Grignard Synthesis of Optically Active Sulfoxides[1]

Sir:

The claim[2] that (−)-methyl allyl sulfoxide (**1**) is produced in the Hofmann degradation of (−)-3-methylsulfinylpropylamine (**2**) has in turn led to the conclusion[3] that (−)-**1** has the (*R*) configuration. We now report (a) that the Hofmann degradation of **2** in fact yields a mixture of (+)-**1** and (−)-methyl propenyl sulfoxide (**3**), with the latter predominating and imposing its sign on the mixture, and (b) that (*R*)-(+)-**1** is a relay compound in a sequence of transformations which provides *rigorous* evidence for the previously unproven, albeit reasonable, assumption that the Andersen synthesis of optically active sulfoxides[4] proceeds with inversion of configuration[4,5] at sulfur (Chart I; Men = (−)-menthyl).

Chart I



The (*R*) configuration of (−)-iberin has been established by X-ray analysis of the thiourea derivative obtained from reaction with (*R*)-1-phenylethylamine;[3] conversion[6] of (−)-**2** into (−)-iberin establishes the (*R*) configuration of the former. Hofmann elimination of the trimethylammonium hydroxide derivative of (−)-**2** in our hands afforded a product ($[\alpha]_{\mathrm{D}}$ −142° (ethanol), lit.[2] $[\alpha]_{\mathrm{D}}$ −158° (ethanol)) whose pmr spectrum appeared as a superposition of two nicely separated sets of signals, A and B. Set A, identical with the 60-MHz pmr spectrum of racemic **1** prepared by sodium metaperiodate oxidation of methyl allyl sulfide, consisted of a singlet at τ 7.42 (S-methyl), two broad singlets at τ 6.57 and 6.45 (S-methylene), and a multiplet centered at τ 4.45 (vinyl); the relative integrated intensities of the S-methylene and vinyl signals were 2 and 3. Set B, corresponding to constitution **3** of as yet unspecified *cis/trans* geometry, consisted of a multiplet centered at τ 8.07 (C-methyl), a singlet at τ 7.44 (S-methyl), and a multiplet centered at τ 3.61 (vinyl); the relative integrated intensities of the C-methyl and vinyl signals were 3 and 2. The product of the Hofmann degradation of **2** stood thus revealed as a mixture of **1** and **3**. Both compounds necessarily have the (*R*) configuration. The composition of the mixture (20 ± 1% of **1** and 80 ± 1% of **3**) was determined by weighted comparison of the relative integrated intensities of the two vinyl multiplets at τ 4.45 and 3.61 and independently confirmed by weighted comparison of the C-methyl and S-methylene signals with the combined S-methyl signals.

A mixture of diastereomeric (−)-menthyl methanesulfinates, presumably enriched in the (*R*) epimer (**5**),[7] of 32.4% diastereomeric purity,[8] gave (−)-methyl *n*-propyl sulfoxide (**4**), $[\alpha]_{\mathrm{D}}$ −42° (ethanol), on treatment with *n*-propylmagnesium bromide, and (+)-**1**, $[\alpha]_{\mathrm{D}}$ + 4.9° (ethanol), on treatment with allylmagnesium bromide. When this sample of (+)-**1** was heated with tetramethylammonium hydroxide, in simulation of the conditions encountered in the Hofmann elimination of **2**, a product was obtained, $[\alpha]_{\mathrm{D}}$ −45° (ethanol), whose composition was 20 ± 1% of **1** and 80 ± 1% of **3** by nmr. This result is in agreement with studies[9] of the base-catalyzed equilibration of **1**. Reduction of (+)-**1** with diimide afforded (−)-**4** ($[\alpha]_{\mathrm{D}}$ −35° (ethanol)). The (*R*) configuration is thus established for (+)-**1** and (−)-**4**.

A similar preparation of **5** (29% diastereomerically pure[8]) afforded (+)-methyl *p*-iodophenyl sulfoxide (**6**), $[\alpha]_{\mathrm{D}}$ +29° (ethanol), on treatment with *p*-iodophenylmagnesium iodide. Since (−)-**4** and (+)-**6** are generated from the same precursor, it follows that (+)-**6** has the (*R*) configuration regardless of whether the Grignard reaction proceeds with retention or with inversion of configuration, *i.e.*, regardless of the configuration of **5**, provided only that the Grignard reactions leading to **1**, **4**, and **6** all have the *same* stereochemical consequence.

Reaction of diasteromerically pure (−)-menthyl (−)-*p*-iodobenzenesulfinate (**7**), $[\alpha]_{\mathrm{D}}$ −146° (acetone), with methylmagnesium iodide yielded (+)-**6**, $[\alpha]_{\mathrm{D}}$ +99° (ethanol). Since the absolute configuration of (−)-**7** is known by X-ray analysis[10] to be (*S*) at sulfur, it follows that the Grignard displacement reaction (−)-(*S*)-**7** → (+)-(*R*)-**6** proceeds with inversion of configuration; it also follows that **5** has the (*R*) configuration. The inversion mechanism has thus been *rigorously* established as a consequence of having compounds of unambiguously determined configuration, *i.e.*, (−)-iberin and (−)-**7**, linked by a chain of trans-

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[1] This work was supported by the National Science Foundation under Grant No. GP-3375 and by the Air Force Office of Scientific Research under Grant No. AF-AFOSR-1188-67.

[2] P. Karrer, N. J. Antia, and R. Schwyzer, *Helv. Chim. Acta*, **34**, 1392 (1951).

[3] K. K. Cheung, A. Kjaer, and G. A. Sim, *Chem. Commun.*, 100 (1965).

[4] K. K. Andersen, *Tetrahedron Letters*, 93 (1962).

[5] K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, **87**, 1958 (1965).

[6] P. Karrer, E. Scheitlin, and H. Siegrist, *Helv. Chim. Acta*, **33**, 1237 (1950).

[7] K. K. Andersen, *J. Org. Chem.*, **29**, 1953 (1964); M. M. Green, Ph.D. Dissertation, Princeton University, 1965.

[8] Calibration by conversion to methyl *p*-tolyl sulfoxide; *cf.* M. M. Green, M. Axelrod, and K. Mislow, *J. Am Chem. Soc.*, **88**, 861 (1966).

[9] D. E. O'Connor and W. I. Lyness, *ibid.*, **86**, 3840 (1964).

[10] E. B. Fleischer, M. Axelrod, M. Green, and K. Mislow, *ibid.*, **86**, 3395 (1964).

formations containing *an odd number of Grignard displacement steps* (asterisked in Chart I).

The optical stability[11] and rotatory dispersion characteristics[5] of **1** are under investigation.

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(11) D. R. Rayner, E. G. Miller, P. Bickart, A. J. Gordon, and K. Mislow, *J. Am. Chem. Soc.*, **88**, 3138 (1966).

(12) National Aeronautics and Space Administration Fellow, 1965–1967.

(13) National Aeronautics and Space Administration Fellow, 1964–1966.

(14) Public Health Service Postdoctoral Fellow, 1966–1967.

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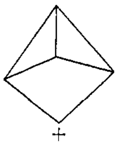
The Degenerate 9-Homocubyl Cation

Sir:

Intriguing rearrangement processes are possible whereby individual atoms and bonds become interchanged, but only lead to products of the same gross structure as that of the starting materials. Such transformations can only be followed by special techniques, as the loss of optical activity, the dispersal of an isotopic label, or the observation of equivalency by nmr. The most interesting of these degenerate rearrangements are those capable of mixing *all* atoms of a given kind completely. Bullvalene is the best known organic molecule of this type: every Cope rearrangement returns to bullvalene and at temperatures somewhat above ambient all H and all C atoms become equivalent on the nmr time scale.[1]

Carbonium ions are particularly prone toward rearrangement, and it is expected that further degenerate examples might be found within this class of species. At room temperature the nmr spectrum of the 2-norbornyl cation shows but a single proton resonance, indicating the time-average equivalence of all 11 hydrogens present.[2] This equivalence is not achieved simply, from a mechanistic viewpoint. Three types of rearrangements are necessary, Wagner–Meerwein, 6,2-(6,1-) hydride shifts, and 3,2-hydride shifts. Each of these lead from one 2-norbornyl cation to another, but all three processes are needed to achieve the observed equivalence.

More elegant conceptually is the degeneracy which might be achieved in the homolog ions of regular polyhedra, *e.g.*, the homotetrahedryl cation I,[3] the homocubyl cation II, and the homododecahedryl cation III.[4] In these three systems only one kind of rearrangement process—a simple 1,2-C,C shift—should not only produce eventual equivalence of all H and all C atoms in each of these ions, but should also permit the positional exchange of all C–H units in a manner similar to that of bullvalene.[1] Were each of the C–H units somehow to be uniquely identified, a vast number of different arrangements would be possible in each of the three ions: homotetrahedryl (I) $5!/2 = 60$; homocubyl (II) $9!/2 = 181{,}440$; and homododecahedryl (III) $21!/2 = 2.56 \times 10^{19}$.



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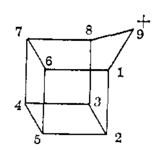
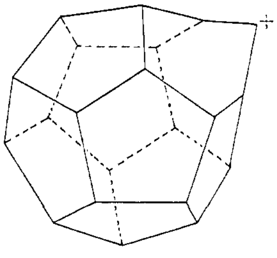


II

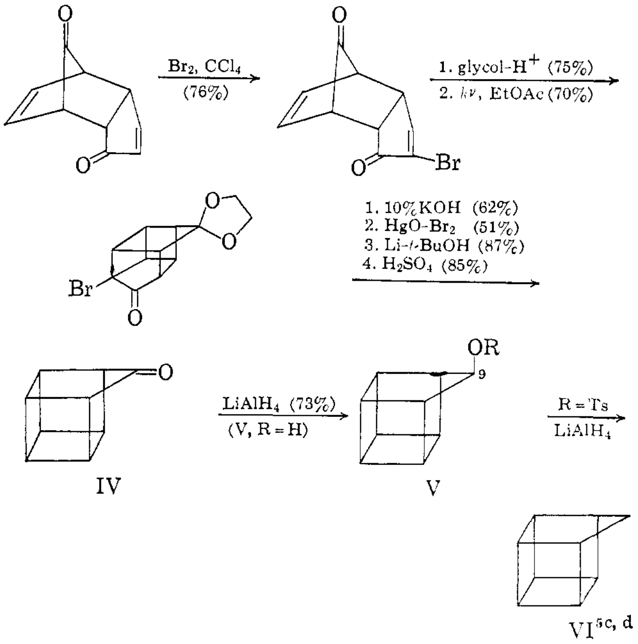


III

We report here the preliminary results of a study of one of these ions, the 9-homocubyl cation (II), which demonstrate that the predicted degeneracy can be achieved under solvolytic conditions.

A number of synthetic approaches to the homocubane (pentacyclo[4.3.0.0^{2,5}.0^{3,8}.0^{4,7}]nonane) ring systen have been described.[5] The desired starting material, 9-homocubyl tosylate (V, R = Ts), mp 73–73.5°, was prepared by a sequence similar to that of Eaton and Cole[5a,c] and summarized in Chart I. The nmr spectra of all compounds were entirely consistent with the structures assigned and with expectation based on previous findings.[5] In particular, 9-homocubanol (V, R = H), mp 157°, and its tosylate, acetate, and formate derivatives all gave similar basic three-peak spectra, integrating for one (C*H*OR; δ = 4–5 ppm), two ($\delta \sim$ 3.5–3.7 ppm), and six protons ($\delta \sim$ 3.2–3.3 ppm).

Chart I



The kinetic acetolysis of V (R = Ts) was carried out in unbuffered media. Despite darkening of the solution at longer reaction times, indicative, perhaps, of

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(1) W. von E. Doering and W. Roth, *Tetrahedron*, **19**, 715 (1963); J. F. M. Oth, R. Merényi, G. Engel, and G. Schröder, *Tetrahedron Letters*, 3377 (1966); G. Schröder, J. F. M. Oth, and R. Merényi, *Angew. Chem. Intern. Ed. Engl.*, **4**, 752 (1965).

(2) P. von R. Schleyer, W. E. Watts, R. C. Fort, Jr., M. B. Comisarow, and G. A. Olah, *J. Am. Chem. Soc.*, **86**, 5679 (1964); M. Saunders, P. von R. Schleyer, and G. A. Olah, *ibid.*, **86**, 5680 (1964); F. R. Jensen and B. H. Beck, *Tetrahedron Letters*, 4287 (1966).

(3) S. Masamune, K. Fukumoto, Y. Yasunari, and D. Darwish, *ibid.*, 193 (1966).

(4) For an approach to dodecahedrane, see R. B. Woodward, T. Fukunaga, and R. C. Kelly, *J. Am. Chem. Soc.*, **86**, 3162 (1964).

(5) (a) P. E. Eaton and T. W. Cole, Jr., *ibid.*, **86**, 962, 3157 (1964); (b) K. V. Scherer, Jr., R. S. Lunt, III, and G. A. Ungefug, *Tetrahedron Letters*, 1199 (1965); (c) G. L. Dunn, V. J. DiPasquo, and J. R. E. Hoover, *ibid.*, 3737 (1966); (d) W. G. Dauben and D. L. Whalen, *ibid.*, 3743 (1966); (e) C. G. Chin, H. W. Cuts, and S. Masamune, *Chem. Commun.*, 880 (1966).