Application of Europium(III) Chelate Induced Chemical Shifts to Stereochemical Assignments of Isomeric Perhydrophenalenols

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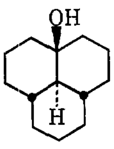
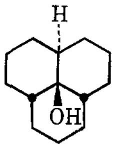
Use of paramagnetic chelates of europium(III) as described by Hinckley[1] and Sanders and Williams[2] to induce large chemical shifts in the nmr spectra of alcohols promises to be an extremely powerful tool for structure determination. In the most favorable instances complex spectra may be reduced to first-order spectra without appreciable loss of resolution thus enabling one to distinguish nonequivalence, multiplicities, and coupling constants directly from the spectrum. Described here is the use of this technique in resolving the signals due to the stereochemically significant protons of *trans,-trans, trans*-perhydro-3a-phenalenol (1)[3] and *cis,cis,-trans*-perhydro-9b-phenalenol (2).[4]



1



2

While there has been considerable recent interest[3-5] in the synthesis and reactions of perhydrophenalenols, assignment of structure and stereochemistry to the various isomers is often difficult owing to the fact that the nmr spectra are relatively uninformative in that they are characterized by broad envelopes between δ 0.5 and 2. Expedients which have been employed include observing whether the compounds exhibit "doublet-like" spectra of the *trans*-decalin type or the "singlet-like" spectra of the *cis*-decalin type. Conversion of the alcohol to a *p*-nitrobenzoate has also been used to induce small chemical shifts (*ca.* 1–2 ppm) in neighboring protons.

At 60 MHz the nmr spectrum of 1 (50 mg, 0.26 mmol) in 0.5 ml of $CDCl_3$ consists of a broad absorption for the carbon-bound protons between 0.5 and 2 ppm from internal TMS. Addition of 135 mg (0.19 mmol) of tris-(dipivalomethanato)europium(III) to the solution produces a spectrum in which the signals due to these protons are spread over a range of 7.5 ppm from δ 2.5 to 10. The most useful signals for assigning a structure are those shown in Figure 1.

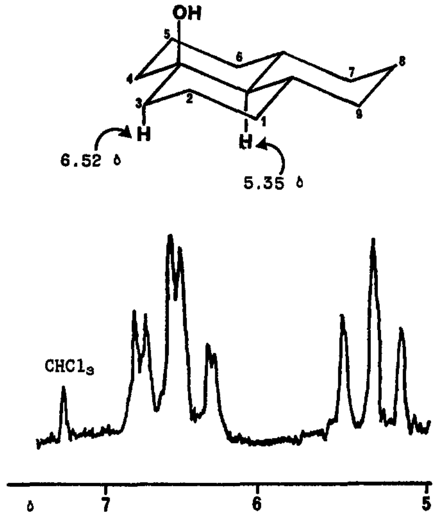


Figure 1.—Portion of the 60-MHz nmr spectrum of 1 in $CDCl_3$ in the presence of $Eu(DPM)_3$.

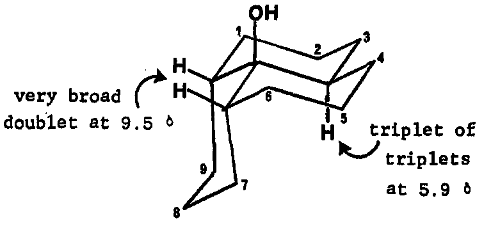
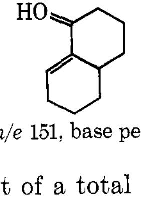


Figure 2.—Assignment of chemical shifts of stereochemically important protons of 2 from 60-MHz nmr spectrum in $CDCl_3$ in the presence of $Eu(DPM)_3$.

Six of the 21 protons bound to carbon in 1 give rise to three sets of two-proton multiplets between δ 8 and 10. These signals are not well resolved and are assigned to the equatorial protons at C-3 and C-4, the axial protons at C-2 and C-5, and the axial protons at C-6a and C-9a in accordance with the principle that the largest paramagnetic shifts should occur at the protons nearest the hydroxyl group.[6] The two-proton signal at δ 6.52 may be assigned as shown in Figure 1 to the axial protons at C-3 and C-4 which appear as a doublet of triplets because the proton at C-3 (or C-4) is coupled equally to the vicinal axial proton at C-2 (or C-5) and to the geminal equatorial proton at C-3 (or C-4) with a coupling constant of 13 Hz, as well as to the vicinal equatorial proton at C-2 (or C-5) with a coupling constant of 3 Hz. The sharp triplet in Figure 1 at δ 5.35 corresponds in area to one proton, and because of its multiplicity it must correspond to unique axial proton at C-9b. The splitting of 12 Hz requires a trans-diaxial orientation of this proton with two equivalent protons and further, since eight other protons in the molecule give signals at lower field in the presence of $Eu(DPM)_3$, it cannot be cis to the hydroxyl group. These observations and the mass spectral data depicted in eq 1 are consistent

$1 \longrightarrow$  (1)

m/e 151, base peak

only with structure 1 out of a total of the ten tertiary perhydrophenalenol isomers.

The type of cleavage shown in eq 1 can occur only

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[1] C. C. Hinckley, *J. Amer. Chem. Soc.*, **91**, 5160 (1969); *J. Org. Chem.*, **35**, 2834 (1970).

[2] J. K. M. Sanders and D. H. Williams, *Chem. Commun.*, 422 (1970).

[3] H. C. Brown and E. Negishi, *J. Amer. Chem. Soc.*, **89**, 5478 (1967).

[4] H. C. Brown and W. C. Dickason, *ibid.*, 91, 1226 (1969); for the analogous system involving fused five-membered rings see J. W. Baum and C. D. Gutsche, *J. Org. Chem.*, **33**, 4312 (1968).

[5] F. A. Carey and H. S. Tremper, *ibid.*, **36**, 758 (1971).

[6] P. V. Demarco, T. K. Elzey, R. B. Lewis, and E. Wenkert, *J. Amer. Chem. Soc.*, **92**, 5734, 5737 (1970); G. H. Wahl, Jr., and M. R. Peterson, Jr., *Chem. Commun.*, 1167 (1970).

when the hydroxyl group is at C-3a, -6a, or -9a.[7] The base peak for **2** is at *m/e* 176 corresponding to loss of H_2O from the molecular ion.

The nmr spectrum of **2** (0.31 mmol) in 0.5 ml of $CDCl_3$ containing 0.21 mmol of $Eu(DPM)_3$ was completely consistent with the structure proposed by Brown.[3] Here, as in **1**, considerable simplification of the spectrum results from the near equality of the geminal and trans-diaxial coupling constants. The lowest field signal (δ 9.5) is a very broad doublet assigned to the protons at C-6a and C-9a, consistent with the 1,2-cis relationship of these protons to the complexed hydroxyl and the expected large (13 Hz) coupling to the axial proton at C-7 (or C-9) with smaller gauche couplings to both protons at C-6 (or C-1) and the equatorial proton at C-7 (or C-9).

The signals from the axial protons at C-1 and C-6 appear as a broadened triplet at δ 8.6, and the signals from the axial protons at C-3 and C-4 appear as a quartet of doublets at δ 7.4. The unique axial proton at C-3a gives rise to a triplet of triplets at δ 5.9 resulting from coupling to the two equivalent axial protons at C-3 and C-4 (J = 13 Hz) and to two equivalent equatorial protons at C-3 and C-4 (J = 3 Hz).

It seems reasonable that the stereochemistry of all perhydrophenalenols, as well as related systems, should be capable of being determined by use of $Eu(DPM)_3$ induced chemical shifts in conjunction with mass spectrometry.

Experimental Section

Nmr spectra were determined on a Hitachi Perkin-Elmer R-20 spectrometer at 30°. Mass spectra were measured on a Hitachi Perkin-Elmer RMU-6E instrument using an ionizing potential of 70 eV and an unheated inlet.

Compound **1** was prepared as described previously,[5] while **2** was provided by W. C. Dickason and H. C. Brown of Purdue University.

Registry No.—**1,** 27390-92-7; **2,** 16664-34-9.

Acknowledgment.—Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work. Thanks are also given to Professor Donald Hunt for a gift of $Eu(DPM)_3$ and to Professor H. C. Brown and Dr. W. C. Dickason for a sample of **2** and numerous helpful comments.

[7] H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, p 107.

Differences in Stability, Gas–Liquid Chromatographic Retention Times, and Esterification Rates for the Diastereoisomers of 2,3-Dimethylsuccinic Acid and Its Esters

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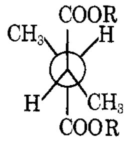
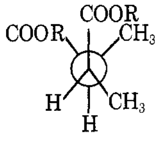
This report is concerned with the differences that are observed in certain properties of diastereoisomers of 2,3-dimethylsuccinic acid, and its esters, which arise from conformational factors. Equilibrium studies of the acid diastereoisomers have been previously reported;[1] however, the analysis of the diastereoisomers by gas–liquid chromatography, as used in this study, should be superior to the previously used analytical method of mixture melting points.

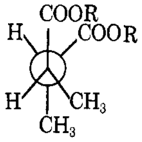
It has been pointed out[2] that, if only steric interactions are considered to be present in the diastereoisomers of 2,3-dimethylsuccinic acid, conformer MA would be predicted to be the most stable configuration. That the equilibrium of such a system is not influenced by entropy differences of the meso and racemic forms (they are essentially equivalent entropywise) has been noted.[3]



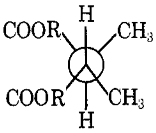
MA



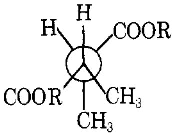
MB



MC



RA



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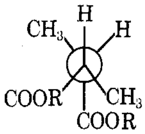

RC

It has been reported[4] that the meso isomer, as predicted, was experimentally determined to be more stable than the racemate and this result has been generally cited[2,5] as an example of diastereoisomer equilibrium. However, Eberson[1] more recently found that the racemate was somewhat more stable and explained this by assuming a stabilizing effect due to intermolecular hydrogen bonding in the racemate conformer RC. Cason and Schmitz[6] postulated cyclic hydrogen-bonded structures for both the meso and racemic forms to explain somewhat similar reported stabilities. The present study finds the racemate–meso ratio of acids at equilibrium in 5 *N* hydrochloric acid to be about 2:1 (Table I) which would favor Eberson's conclusion. The finding of Paolillo and Temussi,[7] using nmr, that the racemate in water consists mainly of the RA conformer rather than the RC one does not affect Eberson's general conclusions.

TABLE I

RESULTS OF THE EQUILIBRIUM EXPERIMENTS

Equilibrium mixture	—% of the diastereoisomers— Meso	Racemate
Acids	32.4	67.6
Methyl esters	49.5	50.5
Isopropyl esters	74.4	25.6

Since the increased stability of the acid racemate can be attributed to formation of intramolecular hydrogen bonds, which are not formed in the diesters, it was rea-

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[1] L. Eberson, *Acta Chem. Scand.*, **13**, 203 (1959).

[2] D. R. Barton and R. C. Cookson, *Quart. Rev.*, **10**, 44 (1956).

[3] L. I. Peterson, *J. Amer. Chem. Soc.*, **89**, 2677 (1967).

[4] R. P. Linstead and M. Whalley, *J. Chem. Soc.*, 3722 (1954).

[5] E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 139.

[6] J. Cason and F. J. Schmitz, *J. Org. Chem.*, **28**, 555 (1963).

[7] L. Paolillo and P. A. Temussi, *Ric. Sci.*, **37**, 687 (1967).