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 H₂O from the molecular ion.

The nmr spectrum of **2** (0.31 mmol) in 0.5 ml of CDCl₃ 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

(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]
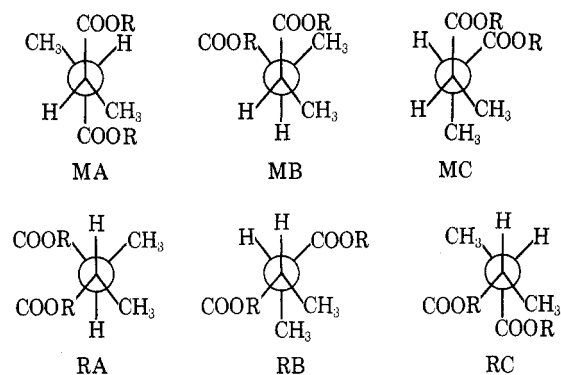
It has been reported[4] that the meso isomer, as predicted, was experimentally determined to be more stable than the racemate and this result has been generally cited[2,5] as an example of diastereoisomer equilibrium. However, Eberson[1] more recently found that the racemate was somewhat more stable 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 find-

TABLE I

RESULTS OF THE EQUILIBRIUM EXPERIMENTS

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

ing 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.

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-

(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).

soned that the "steric interaction" argument might hold true for the diesters in producing a more stable meso form. The results of the equilibrium experiments with methyl and isopropyl esters of 2,3-dimethylsuccinic acid are given in Table I. The methyl esters of the meso and racemic diastereoisomers are present in almost equal amounts at equilibrium, whereas in the case of the isopropyl esters, the meso is definitely the more stable form. Presumably the steric interaction of the more bulky isopropyl groups outweighs any interaction of the polar portions of the molecule.

In the glc analysis of the diastereoisomer esters, the racemic methyl and isopropyl esters were found to have greater retention times than those of the corresponding meso ones (Table II). This was expected[8] as was the

TABLE II

RELATIVE RETENTION TIMES OF THE DIASTEREOISOMERS
OF 2,3-DIMETHYLSUCCINIC ACID AND ITS ESTERS[a]

Diastereoisomers	Relative retention time, racemate/meso
Acids	0.76
Methyl esters	1.18
Isopropyl esters	1.05
Trimethylsilyl esters	1.00

[a] All esters were chromatographed under the same conditions.

observation that the presumably hydrogen-bonded racemic acid had a retention time less than that of the meso form. The direction of the change in the relative retention time of the methyl (1.18), isopropyl (1.05), and trimethylsilyl (1.00) esters can be explained by the increased shielding of the polar groups in going to the more bulky ester groups.

The ratios of the two diastereoisomeric dimethyl esters present in partly esterified mixtures, shown in Table III, indicate that the racemic acid esterifies

TABLE III

RESULTS OF THE ESTERIFICATION EXPERIMENTS

% acid groups reacted (a)	% of the methyl ester diastereoisomers		$k_{racemate}/k_{meso}$
	Meso (m)	Racemate (r)	
32	30.2	69.8	1.30
74	30.9	69.1	1.33
90	34.7	65.3	1.23
(100)	37.2	62.8	

faster than the meso. Unimolecular rate constants for the two acid forms were compared as if the two acid groups esterify independently. From these calculations, discussed in the Experimental Section, a rate constant 30% greater for the racemic acid is indicated. An actual determination of the esterification rates k_1 and k_2 for each acid form would be necessary in order to interpret the esterification rate differences.

Experimental Section

Materials.—By means of melting point and gas–liquid chromatography, 2,3-dimethylsuccinic acid (K and K Laboratories, Plainview, N. Y.) was found to consist of 99.8% of the meso form. Mixtures of the meso and racemic acid forms from which esters were prepared were obtained by heating the meso form with 5 N hydrochloric acid. The trimethylsilyl esters were pre-

(8) D. Nurok, G. L. Taylor, and A. M. Stephen, *J. Chem. Soc. B*, 291 (1968).

pared with the silylation reagent Tri-Sil (Pierce Chemical Co., Rockford, Ill.).

Gas–Liquid Chromatography.—For chromatography of the esters, a 20 ft × $^1/_8$ in. column packed with 3% XE-60 on 80–100 mesh Chromosorb W was used. The column temperature was 200° and the helium flow was 30 ml/min. Even when chromatographed separately (a sample of the racemic acid was obtained from the equilibrium mixture of the acids by means of crystallization from concentrated hydrochloric acid), the retention times of the two trimethylsilyl esters showed no difference. The acid diastereoisomers were chromatographed on a column 6 ft × $^1/_8$ in. packed with 20% diethylene glycol adipate and 3% phosphoric acid on 60–80 mesh Gas-Chrom P. Peak shapes for the acids were distorted so that this method would not be suitable for analytical purposes.

Equilibrium Experiments.—Samples of the meso acid, approximately 0.2 g in 10 ml of 5 N hydrochloric acid, were sealed in glass tubes and kept at 125°. Analysis of the samples by glc of the methyl esters showed that equilibrium had been reached within 100 hr. Methyl and isopropyl esters prepared from the meso acid, approximately 0.2-g samples in 10 ml of the corresponding alcohol containing 0.1 N sodium alcoholate, reached equilibrium within 50 hr. Analyses of the diastereoisomers are based on peak–area measurements. Results are given in Table II.

Relative Esterification Rates.—A sample of the meso acid heated to 125° in 5 N hydrochloric acid for 80 hr provided a mixture of 37.2% meso and 62.8% racemic acids. Samples of this acid mixture (0.2 g) were partly esterified by refluxing in 25 ml of methanol containing 0.1 g of concentrated sulfuric acid for approximately 12, 30, and 60 min. The per cent of carboxylic acid groups reacted was determined by titration and the ratio of the two diesters formed was analyzed by glc. Relative esterification rates of the two acids were calculated on the assumption that the acid groups react independently, by use of the equation

$$\frac{k_{racemate}}{k_{meso}} = \frac{\log\,[1\,-\,(\text{fraction of racemate diester formed})^{1/2}]}{\log\,[1\,-\,(\text{fraction of meso diester formed})^{1/2}]}$$

$$= \frac{\log\,[1\,-\,(a/100)(r/62.8)^{1/2}]}{\log[\,1\,-\,(a/100)(m/37.2)^{1/2}]}$$

where a is the per cent of the acid groups reacted, and m and r are the per cent areas of the chromatogram for the meso and racemate diesters. The results are shown in Table III.

Registry No.—*meso*-2,3-Dimethylsuccinic acid, 608-40-2; *rac*-2,3-dimethylsuccinic acid, 608-39-9; meso methyl ester, 29800-12-2; racemic methyl ester, 29913-52-8; meso isopropyl ester, 29800-13-3; racemic isopropyl ester, 29800-14-4; meso trimethylsilyl ester, 29800-15-5; racemic trimethylsilyl ester, 29800-16-6.

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¹³C–H Coupling Constants as a Probe of Ortho-Substituent Effects

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Although attempts at semiquantitative correlations of structure with reactivity in substituted aromatics have been made, ortho substituents are usually not included in linear free energy relationships. It has generally been assumed that steric factors as well as electronic ones would be an important consideration in