

certed ring contraction. Note that the epoxide oxygen which is involved in this ring contraction reaction is the one on the same side as the methylene of the diazomethane adduct, thus leading to the *cis* ring junction in 4. One would predict on the basis of a concerted ring contraction that rearrangement would be much less favorable, if possible at all, for those epoxy ketones in which the diazomethane attacks from the side opposite the epoxide function. Such systems are currently under investigation and the results along with those obtained concerning the conjugative influences of the epoxide functions on the spectral and chemical properties of compounds such as 1, 2, and 3 will be reported in a subsequent communication.

Experimental Section

Reaction of *trans*-2,3,5,6-diepoxy-2,5-di-*t*-butyl-1,4-benzoquinone (1) with Ethereal Diazomethane.—Excess freshly distilled ethereal diazomethane was added to a solution of 0.318 g (0.00126 mol) of the diepoxide 1 in 50 ml of anhydrous diethyl ether. Nitrogen slowly evolved and the reaction course was followed by glc which showed the progressive appearance of the triepoxide 2 followed by its disappearance and the formation of the tetraepoxide 3 and the ketone 4. After 24 hr the solvent was removed *in vacuo* leaving 0.339 g of a white crystalline product. Glc analysis of this solid showed it to be a mixture of the tetraepoxide 3 and the ketone 4 in a ratio of 98.8:1.2, respectively. Recrystallization of this solid from ethanol gave the pure tetraepoxide 3, mp 114–115°.

Anal. Calcd for C₁₆H₂₄O₄: C, 68.55; H, 8.63. Found: C, 68.52; H, 8.65.

The ring contracted ketone 4 was isolated and purified by preparative glc, mp 105–107°.

Anal. Calcd for C₁₆H₂₄O₄: C, 68.55; H, 8.63. Found: C, 68.43; H, 8.49.

Reaction of the diepoxide 1 with ethereal diazomethane in solvents of varying acidity changed the ratio of the products 3 and 4.

To a solution of 0.278 g (0.0011 mol) of the diepoxide 1 in 100 ml of absolute ethanol was added excess ethereal diazomethane. Concentration of the reaction solution after nitrogen evolution ceased gave 0.292 g (0.0010 mol) of a white crystalline solid. Gas chromatographic analysis of this product showed it to be a mixture of 3 and 4 in a ratio of 79.9 to 20.1, respectively.

Reaction of 0.439 g (0.0017 mol) of 1 in 10 ml of water and 100 ml of absolute methanol with excess ethereal diazomethane gave 0.464 g (0.0017 mol) of a white solid. This solid was shown by gas chromatographic analysis to be a mixture of 3 and 4 in a ratio of 71.7 to 28.3, respectively.

Reaction of 0.387 g (0.0015 mol) of 1 in a solution of 100 ml of absolute methanol and 0.133 g (0.0015 mol) of lithium bromide with excess ethereal diazomethane gave 0.407 g (0.0015 mol) of a white crystalline solid. This solid was isolated by concentration of the reaction mixture followed by repeated washing of the precipitate with water to remove all traces of lithium bromide. Gas chromatographic analysis of this product showed it to be a mixture of 3 and 4 in a relative ratio of 61.8 to 38.2, respectively.

Triepoxide 2.—Reaction of the diepoxide 1 with diazomethane was carried out according to the method described above. The reaction was worked up when the triepoxide 2 was at its maximum concentration (61%) as evidenced by glc (approximately 6 hr). Recrystallization several times from ethanol gave the pure triepoxide 2, mp 111–114°.

Anal. Calcd for C₁₆H₂₂O₄: C, 67.68; H, 8.27. Found: C, 67.65; H, 8.33.

Reaction of the Triepoxide 2 with Deuterated Diazomethane.—Deuterated diazomethane was prepared in a solvent system of tetrahydrofuran, D₂O, and phenol-*O-d*.⁹ One hundred milligrams of the triepoxide 2 was added to this solution and was allowed to react for 12 hr. The solvent was then removed and the product dried *in vacuo*. Gas chromatographic analysis of the product showed only the tetraepoxide 3 and the ketone 4 in approximately a ratio of 98:2, respectively. The products were separated by preparative glc. The nmr spectrum of the tetra-

epoxide showed at least 96% deuterium incorporation at one of exocyclic epoxy methylenes. The mass spectrum of the ketone 4 is described in the text.

Reaction of *trans*-2,3,5,6-Diepoxy-2,5-di-*t*-butyl-1,4-benzoquinone (1) with Dimethylsulfonium Methylide.—To a cold, freshly prepared DMSO solution of dimethylsulfonium methylide¹⁰ was added 2.523 g of finely powdered diepoxide 1 as a DMSO slurry. The reaction solution was allowed to warm to room temperature and then poured into 500 ml of water. The white precipitate (1.917 g, 68.5% yield) was collected and shown to be the tetraepoxide 3 by mixture melting point, and comparison of its ir and nmr spectra to those of an authentic sample. Glc analysis of the crude product showed only the tetraepoxide 3.

Reaction of *trans*-2,3,5,6-Diepoxy-2,5-di-*t*-butyl-1,4-benzoquinone with Dimethylsulfonium Methylide.—The reaction of the diepoxide 1 with dimethylsulfonium methylide¹⁰ was carried out in a manner analogous to that described above with dimethylsulfonium methylide. The product was again shown to be only the tetraepoxide 3 by glc, mixture melting point, and its ir and nmr spectra.

Registry No.—1, 10476-78-5; 2, 24903-91-1; 3, 24903-92-2; 4, 24903-93-3; diazomethane, 334-88-3.

Acknowledgment.—The authors are grateful to the National Science Foundation for partial financial support (GP 8706) of this work. We also express appreciation to Dr. Jean-Claude Gramain for helpful discussions.

(10) E. J. Corey and M. Chaykovsky, *ibid.*, **87**, 1357, 1355 (1966).

Applications of Rare Earth Nuclear Magnetic Resonance Shift Reagents.

II.¹ The Assignment of the Methyl Proton Magnetic Resonances of *d*-Camphor

C. C. HINCKLEY

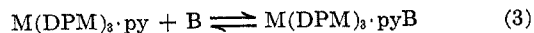
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When the dipyrindine adducts of trisdipivalomethanato rare earth chelates, ²M(DPM)₃·2py, are dissolved in carbon tetrachloride, the molecules dissociate according to equations of the type



If an organic compound, B, having a basic coordinating group is added to the above solution, associations with the metal complexes may occur of the type



Contact shifts in the pmr spectrum of B are a consequence of this association if M is paramagnetic. The phenomenon of contact shifts has been known and studied for many years, as has the requirement for the observation of narrow nmr absorptions in paramagnetic systems, eq 4, where T_e is the electronic relaxation

$$\frac{1}{T_e} > a \quad (4)$$

(1) Part I: C. C. Hinckley, *J. Amer. Chem. Soc.*, **91**, 5160 (1969).

(2) Dipivalomethane, HDPM, is 2,2,6,6-tetramethylheptane-3,5-dione.

time and a is the coupling constant between the electronic and nuclear moments.³ Frequently the condition for narrow nmr absorptions (eq 4) is not met. This is commonly the case for complexes of short transition series metals, many of which have electronic relaxation times long enough for epr spectra to be observed in liquid solutions. In contrast, paramagnetic rare earth complexes (with the exception of gadolinium) are characterized by relatively short electron relaxation times⁴ and solvent nmr resonances of rare earth complex solutions are typically not seriously broadened. Four paramagnetic members (Pr, Nd, Sm, Eu) of the series of rare earth compounds $M(\text{DPM})_3 \cdot 2\text{py}$ exhibit pmr spectra in solution which indicates that the condition of eq 4 is met for those compounds. Additionally, the pmr spectrum of the europium member of the series is silent in the spectral region in which the pmr absorptions of most organic compounds are found. Therefore, $\text{Eu}(\text{DPM})_3 \cdot 2\text{py}$ exhibits a combination of chemical (eq 3) and magnetic properties which make it well suited for use as a probe in the pmr study of a wide variety of organic compounds. Though $\text{Eu}(\text{DPM})_3 \cdot 2\text{py}$ appears to be unique in the above series, this combination of properties should be relatively common for rare earth compounds.

Recently,¹ a study was reported of contact shifts produced in the pmr spectrum of cholesterol through association with $\text{Eu}(\text{DPM})_3 \cdot 2\text{py}$ in carbon tetrachloride solution. Among other things it was found that substantial paramagnetic shifts could be induced in the pmr spectrum of cholesterol without serious broadening effects and that the shifts produced were predominantly the result of pseudocontact interactions⁵ (equation 5).

$$\frac{\Delta H_j}{H_j} = -\epsilon \frac{(g_1 + g_2 + g_3)}{R_j^3} \left[\left(g_1 - \frac{1}{2}g_2 - \frac{1}{2}g_3 \right) (\cos^3 X_j - 1) - \frac{1}{2}(g_2 - g_3) \sin^2 X_j \cos 2\Omega_j \right] \quad (5)$$

The study of cholesterol and studies of other compounds⁶ using $\text{Eu}(\text{DPM})_3 \cdot 2\text{py}$ further indicate that the pseudocontact shifts induced are dominated by the distance parameter, R (eq 4). Magnitudes of the observed contact shifts depend upon the relative concentration of the metal complex, which indicates a rapid chemical exchange between associated and unassociated B, and the equilibrium constant for the association (eq 3) as well as the distance, R , from the metal ion to the proton in the metal chelate-organic substrate complex. Association constants, as reflected in observed contact shift magnitudes, correlate well with the basicity of the coordinating groups. Shifts of several hundred cycles, without appreciable broadening, have been obtained in

the pmr spectra of organic molecules with amine and hydroxyl functional groups through association with $\text{Eu}(\text{DPM})_3 \cdot 2\text{py}$. Compounds having a functional groupings less basic than amines and alcohols, such as esters, carbonyls, ether linkages, sulfides, sulfoxides, and others, generally associate with the metal complex to a lesser degree. These findings suggest that the compound, $\text{Eu}(\text{DPM})_3 \cdot 2\text{py}$, and others with similar magnetic and chemical properties would be useful in pmr spectral analysis. Specifically, the sensitive distance dependence of the pseudocontact shift should indicate relative distances of protons from coordinating groups and allow assignment of resonance lines on this basis. A typical application would include the following steps. (1) Pmr spectra of the organic compound B dissolved in carbon tetrachloride are recorded after successive dropwise additions of $\text{Eu}(\text{DPM})_3 \cdot 2\text{py}$ solution and the field position of the nmr lines are plotted as a function of metal concentrations. A concentration study is not necessary in principle as the paramagnetic shifts measured for a single metal concentration are sufficient, but since the shifts produced may be substantial, this procedure may help keep track of the resonances and allows finer control over the shifts induced. (2) A molecular model of the compound is constructed and distances, R , from the center of the metal ion (ionic radius of $\text{Eu}^{3+} = 0.950 \text{ \AA}$) at the point of coordination to the various protons are measured. Resonances of protons closest to the coordinated metal ion will be shifted the most and assignments are made accordingly. Since the pseudocontact interaction dominates the observed shifts in aliphatic systems, many ambiguities may be resolved by plotting the measured shifts for the particular metal concentration chosen *vs.* $1/R^3$.

d-Camphor was chosen to demonstrate the above technique with the aim of confirming the methyl resonance assignments. Kumler, Shoolery, and Brucher⁷ reported initial assignments in 1958 and Tori, Hamashima, and Takamizawa⁸ proposed assignments in 1964 of τ 9.02 for the C(10) methyl and 9.08 and 9.15 for the C(9) and C(8) methyls respectively in chloroform. Connolly and McCrindle⁹ found apparently anomalous solvent shifts for *d*-camphor and in 1965 reassigned the resonances by deuterium substitution experiments. These corrected assignments are τ 9.02 for the C(9) methyl, 9.08 for C(10), and 9.15 for C(8) and relieve the solvent shifts of anomaly.

Pmr spectra of *d*-camphor (Figure 1) were taken with a Varian HA100 pmr spectrometer and the field positions of the methyl resonances were plotted as a function of $\text{Eu}(\text{DPM})_3 \cdot 2\text{py}$ concentration (Figure 2). A molecular model (scale: 1 inch/ \AA) of *d*-camphor was constructed and approximate metal ion-methyl group distances were measured (Table I).

TABLE I

APPROXIMATE METAL-METHYL DISTANCES	
Methyl group	R
C(8)	5.25
C(9)	7.0
C(10)	4.5

(7) W. D. Kumler, J. N. Schoolery, and F. V. Brucher, Jr., *J. Amer. Chem. Soc.*, **80**, 2533 (1958).

(8) K. Tori, Y. Hamashima, and A. Takamizawa, *Chem. Pharm. Bull.*, **12**, 924 (1964).

(9) J. D. Connolly and R. McCrindle, *Chem. Ind. (London)*, 379 (1969).

(3) Recent reviews include (a) M. Base, *Progr. Nucl. Magn. Resonance Spectrosc.*, **4**, 335 (1969); (b) D. R. Eaton, "Physical Methods in Advanced Inorganic Chemistry," H. A. D. Hill and P. Day, Ed., Interscience, New York, N. Y., 1968, p 462.

(4) A. Carrington and A. D. McLachlan, "Introduction to Magnetic Resonance," Harper and Row, New York, N. Y., 1967, p 173.

(5) This equation is an example taken from G. N. La Mar, W. DeW. Horrocks, and L. C. Allen, *J. Chem. Phys.*, **41**, 2126 (1964), for shifts, ΔH , produced in the resonance of the j th proton in a metal complex having a totally anisotropic g -factor. R_j is the distance from the metal to the j th proton and X_j and Ω_j are angles taken from the symmetry axes of the complex. The derivation of this equation includes assumptions appropriate to short transition series metals and is not directly applicable to rare earth complexes. However, the R parameterization is appropriate and equations for rare earth complexes are under study.

(6) C. C. Hinckley, unpublished research.

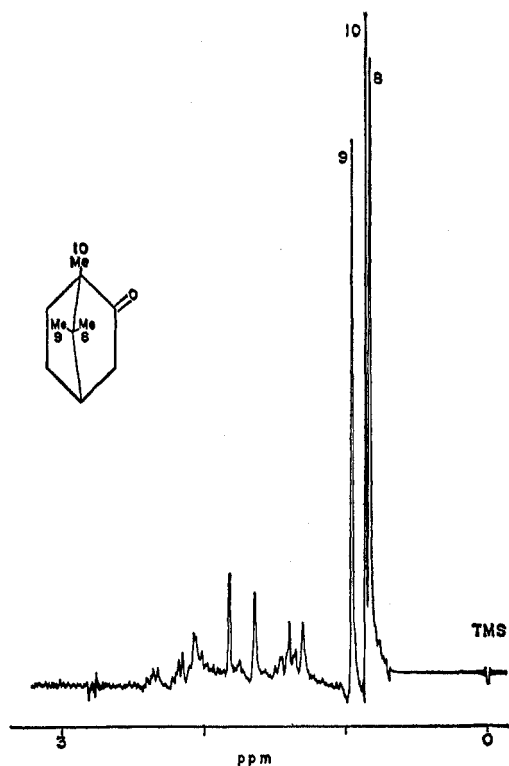


Figure 1.—Pmr spectrum of *d*-camphor. Methyl resonance assignments are indicated by number according to the accompanying diagram.

Bonding between the metal ion and the carbonyl group of *d*-camphor is expected to involve the non-bonding electron pairs of the oxygen which places the metal ion in the plane defined by the carbonyl group and the two adjacent ring carbons. Consideration of steric interference suggests that the C–O–Eu bond is bent away from the 10 methyl group. The C–O–Eu bond angle is unknown but should be between 120 and 180°. Metal ion–methyl distances to the 8 and 9 methyl groups are insensitive to the C–O–Eu angle in that portion of the plane.

Figure 2 shows that each methyl resonance is effected by the contact shift to a different degree and assignments are made accordingly (Figure 1). The 10 methyl group will be closest to the metal ion in the complex and is therefore assigned the resonance at 0.86 ppm which undergoes the greatest shift. The resonance at 0.83 ppm is shifted by an intermediate amount and is assigned to the 8 methyl. The remaining, least affected resonance, at 0.95 ppm is assigned to the 9 methyl which is furthest removed from the metal ion on coordination. These assignments are the same as those reported by Connolly and McCrindle when the solvent change from chloroform to carbon tetrachloride is taken into account.¹⁰

d-Camphor is a rigid structure of relatively low base strength. Comparable studies with alcohols and amines yield shifts of a greater order of magnitude. When the subject molecule, B, is flexible so that there is substantial internal rotation in the metal chelate–organic substrate complex, resonances are shifted by increments appropriate to the average distance from the

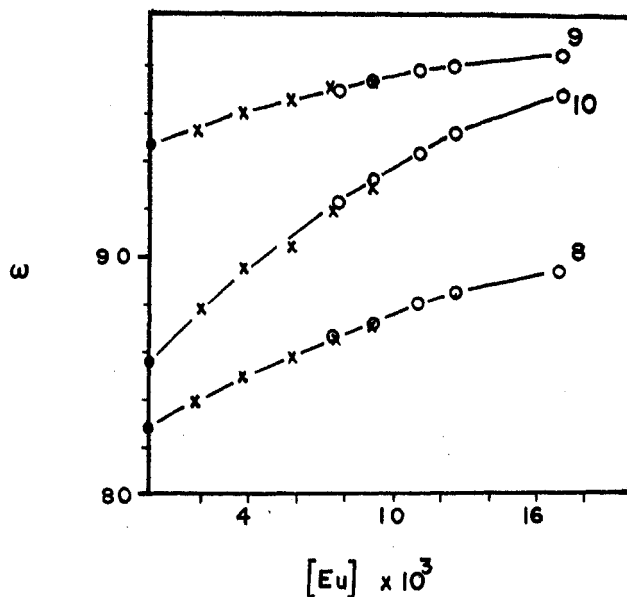


Figure 2.—Field position of the *d*-camphor methyl resonances plotted as a function of $\text{Eu}(\text{DPM})_3 \cdot 2\text{py}$ concentration in cps downfield from the tetramethylsilane resonance.

metal in the complex. In such cases all ambiguities may not be removed. However, the use of rare earth induced contact shifts in pmr spectral analysis¹¹ should be applicable to studies of a wide variety of compounds and is simple enough to be routinely applied.¹²

Experimental Section

Preparation of $\text{Eu}(\text{DPM})_3 \cdot 2\text{py}$.—The europium chelate $\text{Eu}(\text{DPM})_3$ was prepared by the method of Eisentrant and Sievers¹⁴ and the dipyrindine adduct obtained by recrystallization from pyridine.

Pmr Spectra.—Pmr spectra were obtained using a Varian HA100 nmr spectrometer. To 50 drops of a 0.2 *M* *d*-camphor solution in carbon tetrachloride in an nmr sample tube, 5 drops of TMS internal standard was added. Spectra were recorded and line positions measured after successive dropwise additions of 0.1 *M* $\text{Eu}(\text{DPM})_3 \cdot 2\text{py}$ in carbon tetrachloride.

Registry No.— $\text{Eu}(\text{DPM})_3 \cdot 2\text{py}$, 24189-43-3; *d*-camphor, 464-49-3.

Acknowledgment.—Conversations with Dr. C. Y. Meyers of Southern Illinois University and his research group were extremely helpful. Dr. A. M. Malte graciously provided important literature references unknown to the author. The Varian HA100 nmr spectrometer was purchased with the aid of a grant from the National Science Foundation.

(11) Recent studies using Co^{2+} complexes in a similar context are: (a) C. C. McDonald and W. D. Phillips, *Biochem. Biophys. Res. Commun.*, **35**, 43 (1969); (b) W. A. Szarek, E. Dent, T. B. Grindley, and M. C. Baird, *Chem. Commun.*, **D17**, 953 (1969).

(12) Sanders and Williams¹³ have shown that the chelate $\text{Eu}(\text{DPM})_3$ produces shifts approximately four times larger than the dipyrindine adduct, and have suggested additional applications. Their studies show that pyridine is not an essential component.

(13) J. K. M. Sanders and D. H. Williams, *Chem. Commun.*, **D7**, 422 (1970).

(14) K. J. Eisentrant and R. E. Sievers, *J. Amer. Chem. Soc.*, **87**, 5254 (1965).

(10) J. D. Connolly and R. McCrindle, *J. Chem. Soc. C*, 1613 (1966).