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Abstract: The rates and activation parameters describing the interconversion of enantiomers of 15-oxatricyclo[8.2.2.1]pentadeca-4,6,10,12,13-pentaene-11,13-d; (3) \( \Delta E = 11.1 \pm 0.3 \) kcal/mol, \( A = 10^{12.3} \sec^{-1} \), bicyclo[8.2.2]tetradeca-10,12,13-triene-4,7-dione-3,3,5,6,8,11,13-d; (4) \( \Delta E = 9.3 \pm 0.7 \) kcal/mol, \( A = 10^{11.7} \sec^{-1} \), trans-bicyclo[8.2.2]tetradeca-5,10,12,13-tetraene-4,7-dione-3,8,11,13-d; (5) \( \Delta E = 11.2 \pm 0.5 \) kcal/mol, \( A = 10^{12.1} \sec^{-1} \), and trans-bicyclo[8.2.2]tetradeca-5,10,12,13-tetraene-3,8,11,13-d; (7) \( \Delta E = 13.4 \pm 0.7 \) kcal/mol, \( A = 10^{12.7} \sec^{-1} \) have been measured using nmr spectroscopy. These data provide an instructive example of the influence of structural variation on the rates of medium-ring conformational isomerization and a practical check on the precision of kinetic analysis of spin-coupled nmr spectra.

The conformational analysis of medium-ring cycloalkanes has contributed extensive and useful information to the study of the influence of nonbonded interactions and bond-angle deformations on the properties of organic molecules. Of the available spectroscopic techniques, nuclear magnetic resonance has proved to be the best suited for the direct examination of the conformations of this class of compounds in solution. The nmr spectra of these materials are usually very complicated, and in many instances it has been more convenient to investigate the simpler spectra of appropriately substituted medium-ring compounds than the more complex spectra of their unsubstituted parents. In consequence, a number of recent investigations have relied in part on nmr measurements of the rates of interconversion between conformers of substituted cyclic hydrocarbons to provide detailed information concerning not only the structures of these materials themselves, but also by inference information concerning the structures of their unsubstituted analogs. The interpretation of these studies has been complicated by difficulties in isolating the effects of the substituents on the rates, and by uncertainty concerning the extent to which the substituents are capable of influencing the geometry of the con

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(2) (a) National Institutes of Health Predoctoral Fellow, 1963-1966; (b) deceased June 4, 1966.


The observation that the rates obtained from independent line-shape measurements of the aliphatic and aromatic regions of the spectra of compounds 4, 5, and 7 fall on the same straight line (Figure 4) indicates immediately that the rate of rotation of the phenyl group is slow compared to the corresponding rotation for the aliphatic part of these compounds. If the rates of the two processes had been comparable, then the phenyl protons would have appeared to be exchanging more rapidly than their aliphatic counterparts, because both types of conformational interconversion can contribute to the line shapes for the phenyl hydrogens, but only interconversion of enantiomers can contribute to the broadening of the aliphatic resonances.

The conclusion that the phenyl group of compounds 4, 5, and 7 effectively does not rotate can plausibly be extended to the benzene–furan dimer 3, for which no independent measurement of the rate of interchange of the methylene protons was carried out. Thus, the relative rates given in Table II are taken to be the relative rates for the interconversion of enantiomers for each of the compounds examined.

The relative rates reported in Table II are difficult to rationalize in terms of the detailed structures of the compounds involved and suggest that no single structural parameter is of predominant importance in determining the ease with which these interconversions take place. The most obvious structural requirement in the high-energy intermediate conformations involved in the interconversion of enantiomers is that of minimizing the nonbonded repulsions between the aromatic ring and the atoms directly opposed to it. These interactions are sufficiently unfavorable to distort the aromatic moiety from planarity in structurally related compounds, and will undoubtedly be more unfavorable when the bridging group is rotated so that its hydrogen atoms are directed toward the ring. The strain introduced in rotating the alkyl chain could plausibly be partially relieved by spreading the C-C-C bond angles at Cα, Cβ, and Cγ. The tenfold rate increase observed on replacing the allylic methylene groups of 7 with ketone groups (5), with the attendant increase in the Cα and Cβ bond angles, is in qualitative agreement with the idea that angle strain at these atoms may have an important influence on the rates of the interconversions. However, it is clear that other structural features are at least as important in determining the rates as angle strain. For example, saturation of the double bond of 5 increases the rate by a factor of 20. Apparently, the increased bulk of the central methylene groups in 4 is compensated by an increase in the flexibility of the chain. Even shortening the length of the bridging chain (7 → 3) does not permit increase the barrier to rotation. In short, although

it is possible to rationalize the relative rates of Table II
after the fact, it would have been difficult to predict them beforehand. Relatively small changes in structure clearly produce significant changes in the rates of conformational interconversion.

The linearity of the rate plots from the analysis of the aromatic and aliphatic regions serves another useful purpose. It permits an empirical comparison of the accuracy of kinetic analysis of a spin-coupled

\[ l(\omega) = Re((p-r)^2, (p+r)^2, (p+r)^2, (p+r)^2) \times \]

\[ \begin{pmatrix} -\alpha_1 - (p+r)^2/\tau & (p^2 - r^2)/\tau & 0 & 0 \\ (p^2 - r^2)/\tau & -\alpha_2 - (p+r)^2/\tau & 0 & 0 \\ 0 & 0 & -\alpha_3 - (p+r)^2/\tau & 0 \\ 0 & 0 & 0 & -\alpha_4 - (p+r)^2/\tau \end{pmatrix} \]

The line-shape function \( l(\omega) \) can be shown as in eq 1 where as usual

\[ \alpha = \frac{\omega_k - \omega_k}{1/T_k} \] and the subscript \( k \) refers to the observed lines in the AB spectrum. Here, \( \tau \) is the preexclusion lifetime in sec, \( \omega_k \) is the frequency of the \( k \)th observed line in radians/sec, and \( T_k \) is the relaxation time characterizing that line. The lines are numbered consecutively in order of increasing frequency.

Calculation of the aromatic region of carbon gas using a flow rate and 7 as carried out by superimposing an AB spectrum with \( J = 0 \) and relative area 2.8 on an AB spectrum with the same chemical shifts, having \( J = 0 \) and relative area 1.0. This ratio of areas, derived from the mass spectral analysis of \( p \)-xylene-2,5-dt, satisfactorily accounts for the mixture of isotopic species present. No corrections were made for isotopic impurities in the aromatic region.

Calculation of the aromatic region of 5 in Table II was carried out by 4.94, with an empirical comparison of the results of independent kinetic analysis of the two types of spectra. This comparison is unfortunately less clear-cut than it might ideally be, because the isotopic impurities in the aromatic regions of these compounds complicate their line shapes appreciably. Nonetheless, the two types of analyses do lead to very similar results as evidenced by the agreement obtained from the two spectral regions at the common temperatures examined (Figure 4). Moreover, the close similarity between the values of \( A \) obtained for these compounds and the high correlation coefficients for the corresponding Arrhenius plots indicate that these data are at least internally consistent and suggest that kinetic analyses of line shapes in coupled spectra are of comparable accuracy to those of uncoupled spectra. Experimental Section

Nmr spectra were taken of approximately 10% solutions in carbon disulfide. Theoretical spectra were calculated using a

(15) In a, the oxygen atom rather than the CH=CH group is almost certainly the part of the furan moiety which actually passes through the loop of the ring. Hence, elimination of the nonbonded repulsions between the hydrogen atoms of the alkyl chain and the benzene ring is probably important in explaining the lower relaxation rate. Note also that in this compound, the two conformations involved in the equilibration are enantiomeric only by virtue of the deuteration substitution on the aromatic ring.


(17) Independent least-squares analysis of the data from the aliphatic and aromatic regions of 5 and 7 gave values for \( \epsilon \), differing by approximately 0.5 kcal/mol from those given in Table II. The correlation coefficients for the Arrhenius plots were approximately the same as those in the table.

(18) Melting points were taken on a Kofler hot stage; boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 217B grating spectrophotometer. Mass spectra were measured on a Hitachi Perkin-Elmer Model RMU-60 mass spectrometer. Vapor phase chromatographic analyses were performed on an F & M Model 720 gas chromatograph with helium as carrier gas at a flow rate of 1 see.

Nmr spectra were taken at 60 MHz on a Varian A-60 spectrometer, equipped with a V-6040 variable-temperature probe and controller. Sweep widths were calibrated using a Krohn-Hite Model 450 pushbutton oscillator. Deuterium-decoupling experiments were carried out using an Nmr Specialties Model HD-60A decoupler. Calibration of the temperature controller was accomplished by measuring peak separations in a methanol or ethylene glycol sample.

(19) This method is not the most efficient in terms of total computer time for calculating AB special line shapes; however, in this instance it fits conveniently into the format of a program normally used for a somewhat different type of calculation.


