Application of Electron Spin Resonance Spectroscopy to Problems of Structure and Conformation. XV. Conformational Analysis of Semidiones Derived from Cyclobutane, Cyclopentane, Cyclohexane, and Cycloheptane[1,2]

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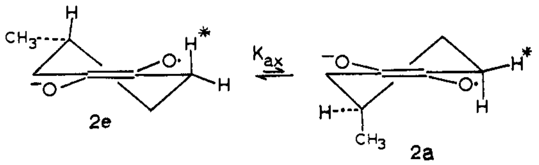
Abstract: The effect of temperature on the esr spectra of a number of medium-sized cycloalkanesemidiones has been investigated. The effect of temperature on the population of the equatorial (more stable) and axial conformations of the methylcyclohexanesemidiones yields enthalpy differences of 0.7 and 1.4 kcal/mole ($\Delta S \cong 0$) for the 3- and 4-methyl substituents. The treatment is extended to di- and trialkylated cyclohexanesemidiones. Cyclohexanesemidione and several symmetrically substituted derivatives yielded coalescence temperatures and demonstrated line-broadening effects above and below the coalescence temperature. Coalescence temperatures occur at conformational lifetimes of $\sim 10^{-7}$ sec. Cyclohexanesemidione undergoes the interconversion of half-chair conformations with an enthalpy of activation of 4.0 kcal/mole, entropy of activation +1 eu. 3,3-Dimethyl- or 4,4-dimethylcyclohexanesemidiones have similar enthalpies of activation (3.9, 3.2 kcal/mole) but less favorable entropies of activation (−6, −8 eu). 3,3,5,5-Tetramethylcyclohexanesemidione has an enthalpy of activation of only 2.6 kcal/mole but the entropy of activation for ring inversion is −8 eu. The treatment has been extended to N-methylpiperidine-3,4-semidione which is much more conformationally stable than cyclohexanesemidione (coalescence temperature ~+60 and −85°, respectively) and to cycloheptanesemidione for which a coalescence temperature could not be observed because of conformational stability.

The oxidation of a variety of ketones in basic solution involves paramagnetic intermediates that have been shown by electron spin resonance spectroscopy to be semidiones (**1**).[3]

$$RCOCH_2R' \xrightarrow{B^-,\ O_2} \underset{\mathbf{1}}{RC(O\cdot){=}C(O^-)R'} \xrightarrow{O_2} RCOCOR'$$

The semidiones can also be conveniently prepared by the reaction of strong bases with many α-diketones and/or α-hydroxy ketones in the absence of oxygen. By analysis of the esr spectra, it has been possible to gain a considerable amount of information regarding the structure and conformation of many acyclic and cyclic semidiones, including those derived from steroidal ketones.[4-6] We have now studied the effect of temperature on the esr spectra of several cyclic semidiones with medium-sized rings in order to obtain thermodynamic data from the rate and equilibrium constants for the ring inversion process. The effect of temperature on the esr spectra of systems capable of undergoing conformational change reveals two distinct behavior patterns depending on whether the possible conformations are equally or unequally populated. For unsymmetrical radicals, *e.g.*, 4-methylcyclohexanesemidione (**2**), wherein two conformations (e and a) of unequal energy exist in rapid equilibrium, the observed hyperfine splitting constant (hfsc) for a particular proton ($a_{\text{obsd}}{}^{\text{H*}}$) is the time average of two limiting values $a_e{}^{\text{H*}}$ and $a_a{}^{\text{H*}}$. The probability (f) of the radical existing in conformation e can be easily calculated provided the limiting values of the hfsc are known (eq 1).

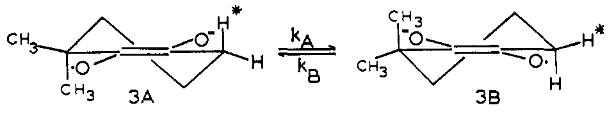


2e 2a

A change in temperature usually results

$$f = (a_{\text{obsd}}{}^{\text{H*}} - a_a{}^{\text{H*}})/(a_e{}^{\text{H*}} - a_a{}^{\text{H*}}) \qquad (1)$$

in a change in the position of the ring inversion equilibrium (K_a) with a resulting change in $a_{\text{obsd}}{}^{\text{H*}}$. If, however, the two conformations are of equal energy and hence equally populated, as in the case of 3,3-dimethylcyclohexanesemidione (**3**), then the mean lifetime of a particular conformation (τ_A or τ_B) is the reciprocal of the rate constant (k_A or k_B).



3A 3B

If rates are sufficiently rapid (*i.e.*, lifetimes sufficiently short) line-width alternation will occur,[7] and under these conditions the increase in full line width at half-height ($\Delta\omega_{1/2}$) of the central absorption peak relative to the wing peaks is related to the mean lifetimes of each conformation by eq 2

$$(\tau_A + \tau_A)/\tau_B T = \pi(\Delta\nu)^2/\Delta\omega_{1/2} \qquad (2)$$

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[1] Aliphatic Semidiones. VII.

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[4] E. R. Talaty and G. A. Russell, *J. Am. Chem. Soc.*, **87**, 4867 (1965).

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where $\Delta\nu$ is the difference (cycles per second) between the limiting values of the axial and equatorial hfsc.[7d] Converting cycles per second to gauss, substituting $k = k_{\mathbf{A}} = k_{\mathbf{B}}$, and rearranging yields eq 3 wherein γ is the gyromagnetic ratio of the electron (17.6×10^6 radians/gauss/sec). When the width is measured in gauss between the maximum and minimum of the first derivative spectrum, k (sec^{-1}) is given by eq 4

$$k = \gamma(a_{\mathbf{A}}^{\mathrm{H}} - a_{\mathbf{B}}^{\mathrm{H}})^2/4\Delta\omega_{1/2} \tag{3}$$

$$k = 2.54 \times 10^6(a_{\mathbf{A}}^{\mathrm{H}} - a_{\mathbf{B}}^{\mathrm{H}})^2/\Delta \text{ width} \tag{4}$$

if the line shape is Lorentzian.

As the exchange rate decreases and the lifetime of a conformational state becomes comparable with the reciprocal of the difference in coupling constants, the expression for the fast exchange line broadening becomes less precise and at the coalescence temperature (the temperature at which the originally degenerate line first separates into a doublet) the rate constant (sec^{-1}) is given by expression 5.[7c] Below the coalescence temperature, separate coupling constants can be observed for hydrogen atoms that spend most of their time in axial ($a_{\mathrm{a}}^{\mathrm{H}}$) or equatorial ($a_{\mathrm{e}}^{\mathrm{H}}$) positions. The rate constant under this condition of slow exchange is given by eq 6.[7c]

$$k = \gamma(a_{\mathbf{A}}^{\mathrm{H}} - a_{\mathbf{B}}^{\mathrm{H}})/2^{3/2} = 6.22 \times 10^6(a_{\mathbf{A}}^{\mathrm{H}} - a_{\mathbf{B}}^{\mathrm{H}}) \tag{5}$$

$$k = 6.22 \times 10^6[(a_{\mathbf{A}}^{\mathrm{H}} - a_{\mathbf{B}}^{\mathrm{H}})^2 - (a_{\mathrm{a}}^{\mathrm{H}} - a_{\mathrm{e}}^{\mathrm{H}})^2]^{1/2} \tag{6}$$

Results

Cyclobutane and Cyclopentanesemidiones. These semidiones are readily prepared by the treatment of the α-hydroxy ketones or β-acetoxy ketones with potassium *t*-butoxide in DMSO or DMF.[6,8] As expected, both spectra consisted of a quintet of sharp lines having intensity ratios of 1:4:6:4:1. This intensity ratio remained unchanged between +70 and −90°. If any conformational changes are involved, they must involve an inversion frequency much greater than the difference between the extreme values of the coupling constants for a given hydrogen atom in the two conformations. For cyclobutanesemidione no significant temperature effect on the value of the hfsc is observed, while for cyclopentanesemidione a gradual increase in the hfsc is noted as the temperature is lowered (Table I).

Table I. Variation of Coupling Constant with Temperature[a]

Cyclobutanesemidione		Cyclopentanesemidione	
Temp, °C	a^{H}, gauss	Temp, °C	a^{H}, gauss
+70	13.52 ± 0.04	+85	12.92 ± 0.04
+50	13.57 ± 0.03	+60	12.92 ± 0.04
+30	13.55 ± 0.04	+35	12.95 ± 0.03
+10	13.60 ± 0.04	+10	12.97 ± 0.06
−30	13.60 ± 0.03	−15	13.00 ± 0.03
−50	13.61 ± 0.04	−40	13.08 ± 0.04
−70	13.60 ± 0.03	−65	13.15 ± 0.06
−90	13.67 ± 0.14	−90	13.20 ± 0.07

[a] In dimethylformamide solution in the presence of 0.1 *M* potassium *t*-butoxide.

Cyclohexanesemidiones with Unequally Populated Conformations. The esr spectrum of 4-*t*-butylcyclohexanesemidione at 25° in DMSO solution has been reported previously.[4,9] In DMF solution at 25°, the intensity ratio of the seven lines is 1:2:2.9:4.1:2.9:1.9:0.9, in good agreement with the spectrum expected for two pairs of hydrogen atoms with one pair ($a_{\mathrm{a}}^{\mathrm{H}}$) having twice the hfsc of the other pair ($a_{\mathrm{e}}^{\mathrm{H}}$). A similar spectrum is observed for the $\Delta^{2,3}$-semidione in the decalin system and in the $\Delta^{2,3}$-semidiones in the 19-nor steroids.[4] The fortuitous ratio of $a_{\mathrm{a}}^{\mathrm{H}}/a_{\mathrm{e}}^{\mathrm{H}} = 2.0$ in the half-chair conformation of cyclohexanesemidione reflects the dihedral angles for axial and equatorial hydrogens ($\theta_{\mathrm{a}},\theta_{\mathrm{e}}$) since the hfsc are given by eq 7.[9-11]

$$a^{\mathrm{H}} = \rho_{\mathrm{C}}B\langle\cos^2\theta\rangle \tag{7}$$

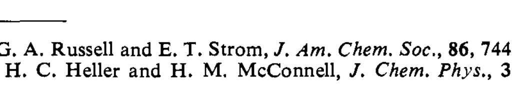
It follows that $a_{\mathrm{a}}^{\mathrm{H}}/a_{\mathrm{e}}^{\mathrm{H}} = \langle\cos^2\theta_{\mathrm{a}}\rangle/\langle\cos^2\theta_{\mathrm{e}}\rangle$. If it is assumed that torsional vibrations within the conformation are small (*i.e.*, $\langle\cos^2\theta\rangle = \cos^2\theta$) then the equilibrium dihedral angle for an axial hydrogen atom is 14°.[9] The intensity ratio observed for 4-*t*-butylcyclohexanesemidione is practically invariant with temperature. However, the total width of the spectrum showed a consistent change with temperature (see Table II). The constancy of the intensity ratio (*i.e.*, the ratio $a_{\mathrm{a}}^{\mathrm{H}}/a_{\mathrm{e}}^{\mathrm{H}}$) is taken as evidence of the population of only one conformation for 4-*t*-butylcyclohexanesemidione over the temperature range studied (with the 4-*t*-butyl group in the equatorial position) and for the absence of significant torsional motion in this conformation.[12] It has been assumed that at all temperatures, *unstrained* cyclohexanesemidiones will possess hfsc for purely axial and equatorial α-hydrogen atoms with a ratio of 2.0.

Table II. Variation of Total Spectrum Width of 4-*t*-Butylcyclohexanesemidione with Temperature[a]

Temp, °C	$2a_{\mathrm{a}}^{\mathrm{H}} + 2a_{\mathrm{e}}^{\mathrm{H}}$, gauss	$a_{\mathrm{a}}^{\mathrm{H}}$ (calcd)[b]
+90	39.4 ± 0.1	13.13 ± 0.03
+70	39.6 ± 0.1	13.20 ± 0.03
+50	39.7 ± 0.1	13.23 ± 0.03
+10	39.7 ± 0.1	13.23 ± 0.03
−30	40.0 ± 0.1	13.33 ± 0.03
−60	40.25 ± 0.1	13.41 ± 0.03

[a] In dimethylformamide solution in the presence of potassium *t*-butoxide. [b] By assuming $a_{\mathrm{a}}^{\mathrm{H}} = 2a_{\mathrm{e}}^{\mathrm{H}}$.

The esr spectra of 3- and 4-methylcyclohexanesemidiones show a significant effect of temperature. This appears reasonable because in both instances an unequally populated mixture of conformations is expected (**2e** ⇄ **2a**, **4e** ⇄ **4a**).[4] Figure 1 gives the esr spectra



4e 4a

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[8] G. A. Russell, R. D. Stephens, and E. R. Talaty, *Tetrahedron Letters*, 1139 (1965).

[9] G. A. Russell and E. T. Strom, *J. Am. Chem. Soc.*, **86**, 744 (1964).

[10] H. C. Heller and H. M. McConnell, *J. Chem. Phys.*, **32**, 1535 (1960).

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[12] If a torsional motion occurs about the dihedral equilibrium angle (θ') the time-average value of $\cos^2\theta$ will be equal to $\cos^2\theta'$ for $\theta' = 45°$ only. Of course no temperature effect will be expected even with significant torsional motion if only a single vibrational energy level is populated at all temperatures studied.

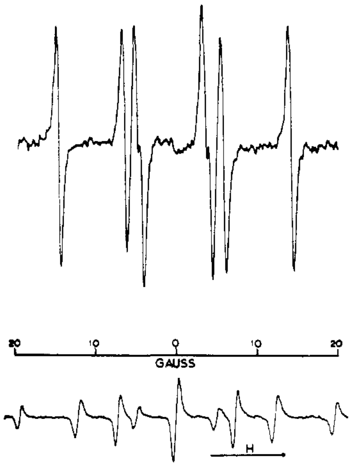


Figure 1. First derivative esr spectra of 3-methylcyclohexanesemidione (top) and 4-methylcyclohexanesemidione (bottom) observed in dimethyl sulfoxide solution at 25° in the presence of 0.1 *M* potassium *t*-butoxide.

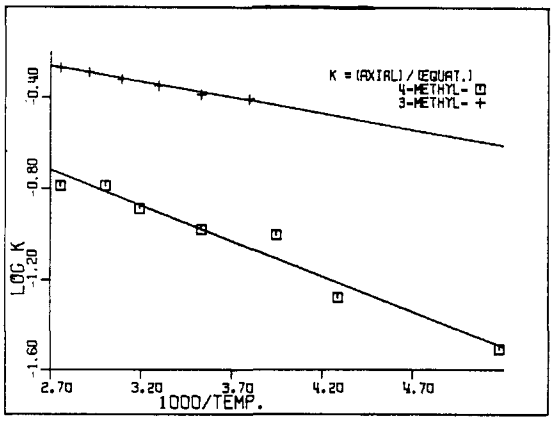


Figure 2. Computer least-squares plot of log K_a (Table III) *vs.* $1/T$ for 3- and 4-methylcyclohexanesemidiones.

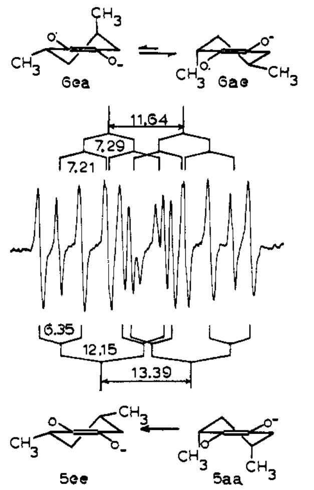


Figure 3. First derivative esr spectrum observed at 25° from oxidation of *cis*- or *trans*-3,5-dimethylcyclohexanone in dimethyl sulfoxide solution containing potassium *t*-butoxide. Hyperfine splitting constants are given in gauss.

observed for these semidiones at 25°. Upon cooling, the spectrum for 4-methylcyclohexanesemidione approaches that of 4-*t*-butylcyclohexanesemidione (*i.e.*, 7 lines, 1:2:3:4:3:2:1). The conformation population fraction (*f*) has been calculated (Table III) by assuming that at all temperatures $a_a^H = 2a_e^H$. For 4-methylcyclohexanesemidione the total spectrum width (Σa^H) is $2(a_a^H + a_e^H)$. It thus follows that $a_a^H = \Sigma a^H/3$. For 3-methylcyclohexanesemidione the sum of the two observed hfsc should be equal to $1.5a_a^H$. Using the values of a_a^H and a_e^H obtained in this manner in eq 1 yielded the values of K_a given in Table III. The values of K_a summarized in Table III have been plotted in Figure 2 and yield enthalpy differences of $H_a - H_e = 1.4$ kcal/mole for **2** and $H_a - H_e = 0.7$ kcal/mole for **4**. In both cases $S_a - S_e = 0.5 \pm 0.5$ eu. The lower conformational stability of the 3-methyl isomer relative to the 4-methyl isomer is presumably due to the methyl–oxygen eclipsing that occurs in **4e** and which destabilizes **4e** relative to **2e** by about 0.7 kcal/mole.[4]

Table III. Effect of Temperature on Hyperfine Splitting Constants of 3- and 4-Methylcyclohexanesemidiones in Dimethylformamide Solution

Substituent	Temp, °C	Obsd hfsc Triplet	Obsd hfsc Doublet	f_e	K_a[a]
4-Methyl	+90	11.69, 7.13	...	0.86	0.163
4-Methyl	+60	11.86, 7.23	...	0.86	0.163
4-Methyl	+40	12.00, 7.10	...	0.885	0.13
4-Methyl	10	12.15, 6.97	...	0.905	0.105
4-Methyl	−20	12.22, 6.96	...	0.91	0.099
4-Methyl	−40	12.47, 6.74	...	0.95	0.0525
4-Methyl	−80	12.96, 6.51	...	0.99 (0.97)[b]	0.01 (0.031)[b]
3-Methyl	+90	10.38	8.52	0.65	0.54
3-Methyl	+70	10.43	8.41	0.66	0.515
3-Methyl	+50	10.55	8.37	0.675	0.48
3-Methyl	+30	10.63	8.29	0.69	0.45
3-Methyl	+10	10.75	8.17	0.71	0.41
3-Methyl	−10	10.85	8.07	0.72	0.39

[a] K_a = [2a]/[2e] or [4a]/[4e]. [b] By use of a_a^H and a_e^H measured for 3,3-dimethylcyclohexanesemidione at −80°.

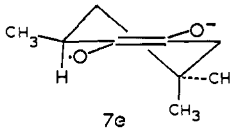
3,5-Dimethylcyclohexanesemidione is a more complicated system since epimerization of the *cis* and *trans* isomers can occur. Treatment of a mixture of isomers of 2-hydroxy-3,5-dimethylcyclohexanone with potassium *t*-butoxide in DMF solution yields the spectrum shown in Figure 3. An elementary consideration of the conformational stabilities of the *cis*- and *trans*-semidiones (**5ee** very much more stable than **5aa**, **6ae** somewhat more stable than **6ea**) leads to the structural assignment of Figure 3. Conformation **5ee** should possess two large (a_a^H) and one small (a_e^H) hfsc while **6ae** should possess two small (a_e^H) and one large (a_a^H) hfsc. As would be expected the spectrum assigned to **5** showed little change of hfsc with temperature indicating that $H_{5aa} - H_{5ee}$ must be >2.5 kcal/mole. However, the spectrum assigned to **6** changed with temperature as expected for an equilibrium between **6ae** and **6ea**. Treatment of the hfsc assigned to **6** in the manner previously employed for the monomethylcyclohexanesemidiones yielded $H_{ea} - H_{ae} = 1.4 \pm 0.2$ kcal/mole and $S_{ae} - S_{ea} = -1.0 \pm 0.5$ eu.

The use of 3- and 4-methylcyclohexanesemidiones as models for the conformational preference of the methyl groups in *trans*-3,5-dimethylcyclohexanesemidione leads to a prediction of $\Delta H° = 0.7 \pm 0.4$ kcal/mole ($1.4 \pm 0.2 - 0.7 \pm 0.2$). In a similar fashion it would be predicted that $H_{5aa} - H_{5ee} = 2.1 \pm 0.4$ kcal/mole (plus whatever destabilization results from the 1,3-diaxial interaction of methyl groups in **5aa**). Temperature has an effect on the ratio of the two semidiones depicted in Figure 3. This is undoubtedly due to the epimerization equilibrium defined as K_{ep} = *cis*-semidione (**5**)/*trans*-semidione (**6**). Figure 4 demonstrates the effect of temperature on this *cis*/*trans* ratio and that $H_6 - H_5 = 0.85 \pm 0.2$ kcal/mole, $S_6 - S_5 = 1 \pm 0.5$ eu. Since **6** exists mainly in the **6ae** conformation, an enthalpy difference of about 0.85 kcal/mole has been assigned to $H_{5ee} - H_{6ae}$. We thus have the approximate experimental enthalpy differences given in kilocalories per mole.

$$\begin{tikzcd}
\mathbf{6ae} \arrow[r, "\Delta H^\circ = +1.4 \pm 0.2"] \arrow[d, leftrightarrow, "\Delta H^\circ = +0.85 \pm 0.2"'] & \mathbf{6ea} \arrow[d, dotted] \\
\mathbf{5ee} \arrow[r, dashed] & \mathbf{5aa}
\end{tikzcd}$$

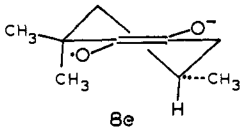
The conversion of **6ea** into **5aa** will involve the conversion of the 3-methyl group from an equatorial to an axial position ($\Delta H^\circ = +0.7$ to $+0.9$ kcal/mole) and the introduction of a 1,3-diaxial interaction of two methyl groups which we will presently show requires at least 1 kcal/mole in the cyclohexene ring. Thus the conversion of **6ea** into **5aa** should be endothermic by at least 1.8 kcal/mole and the conversion of **5ee** into **5aa** endothermic by at least $0.85 + 1.4 + 1.8 \cong 4$ kcal/mole.

3,5,5-Trimethylcyclohexanesemidione (**7e**) and 3,3,5-trimethylcyclohexanesemidione (**8e**) appear to have single populated conformations at 25°. Semidione **7** was prepared from the acyloin and examined from 90 to −90°. Over this temperature range the ratios of the three doublet splittings did not change. We conclude that the other possible conformation, **7a**, is at least 2.5 kcal/mole less stable than **7e**. Oxidation of 3,5,5-trimethylcyclohexanone in DMSO solution containing potassium *t*-butoxide yielded a mixture of **7e** and **8e**. Again the ratio of the two hfsc assigned to **8e** did not change with temperature and it is concluded that **8a** is at least 2.5 kcal/mole less stable than **8e**.



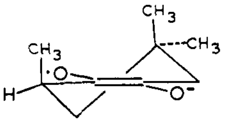
7e

a^H = 13.1, 11.3, 5.6 gauss

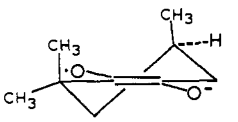


8e

a^H = 12.2, 5.8 gauss



7a



8a

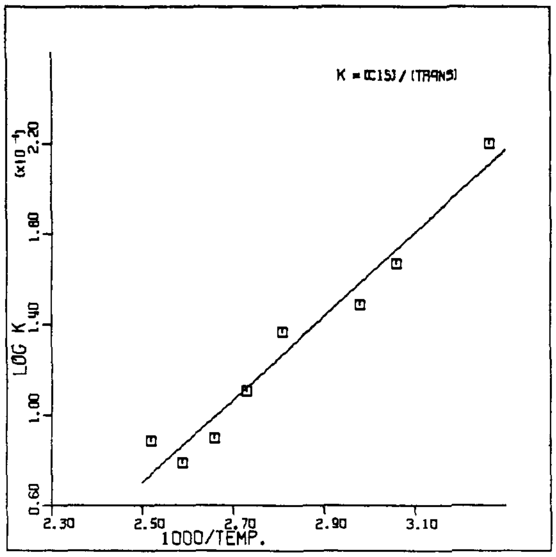
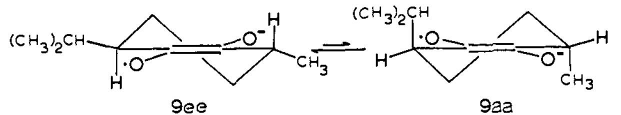


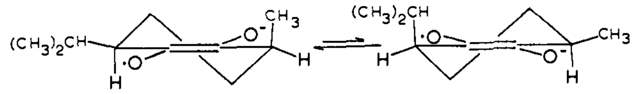
Figure 4. Computer plot of log K_{ep} = log ([**5**]/[**6**]) for *cis*- and *trans*-3,5-dimethylcyclohexanesemidiones.

Oxidation of 2-methyl-5-isopropylcyclohexanone in DMSO solution produces a mixture of two radical anions assigned the *trans* (**9**) and *cis* (**10**) structures. If the hfsc for a pure axial hydrogen is taken as 13.10 gauss at 25° in DMSO,[4] the ratio **9ee**/**9ae** is calculated to be 8.4. The sum of $a_a^H + a_e^H$ for **10** of 17.5 gauss indicates a geometry of **10ae** and/or **10ea** which has deviated considerably from the geometry of the unstrained semidiones ($a_a^H + a_e^H = 19.65$ gauss in DMSO, 25°). However, if it is assumed that $a_a^H = 2a_e^H$ for **10** then a pure axial hydrogen will have a hfsc of 11.6 gauss and the ratio **10ea**/**10ae** is calculated to be 5.8. The free-energy differences at 25° suggest that **9ee** is more stable than **9aa** by 1.3 kcal/mole and that **10ea** is more stable than **10ae** by 1 kcal/mole. Using these data alone leads to the conclusion that an equatorial 3-methyl group is preferred over an axial 3-methyl group by 0.15 kcal/mole and the equatorial 3-isopropyl group preferred over the axial 3-isopropyl group by 1.15 kcal/mole.



9ee 9aa

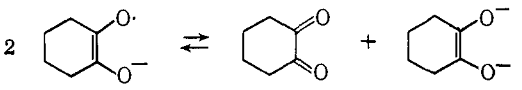
a^H = 12.40, 12.40 gauss



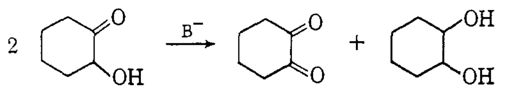
10ea 10ae

a^H = 10.8, 6.7 gauss

Symmetrically Substituted Cyclohexanesemidiones. The esr spectra of cyclohexanesemidione, 3,3-dimethylcyclohexanesemidione, 4,4-dimethylcyclohexanesemidione, and 3,3,5,5-tetramethylcyclohexanesemidione have been investigated at various temperatures. One problem encountered in the low-temperature studies of both symmetrical and unsymmetrical semidiones was the adverse effect of low temperature on the concentration of the semidione. The effect of temperature on the concentration of radical anion was completely reversible below 25° and is apparently connected with the equilibrium



The disproportionation reaction of the radical anion must be strongly exothermic. Measurement of the equilibrium constant for the semidione disproportionation probably is complicated by the occurrence of other oxidation–reduction processes, such as the following.



Reactions of this type are apparently involved in the spontaneous formation of semidiones from α-hydroxy ketones in basic solution.

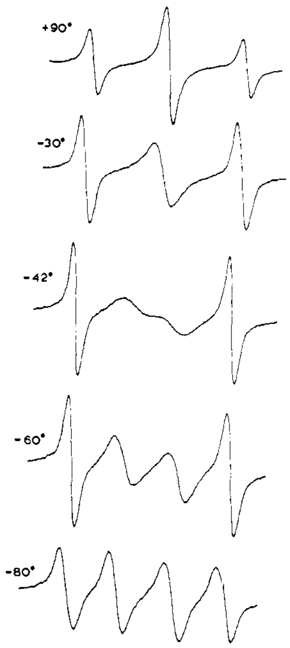


Figure 5. First derivative esr spectrum of 3,3-dimethylcyclohexanesemidione formed by disproportionation of 2-hydroxy-6,6-dimethylcyclohexanone in dimethylformamide solutions of cesium *t*-butoxide.

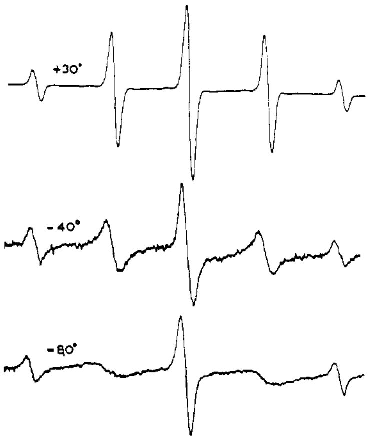


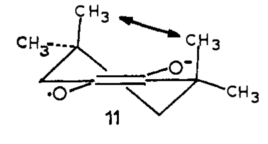
Figure 6. First derivative esr spectra of cyclohexanesemidione prepared by disproportionation of 2-hydroxycyclohexanone in dimethylformamide solutions of cesium *t*-butoxide. Note the decrease in signal intensity as reflected by the signal-to-noise ratio upon cooling.

As was previously demonstrated for the cyclohexyl radical,[13] when hydrogen atoms exchange nonidentical environments at a frequency comparable to the difference in their hfsc, line broadening is observed. Figure 5 illustrates the phenomenon for 3,3-dimethylcyclohexanesemidione wherein the interconversion of **3A** and **3B** causes axial and equatorial hydrogen atoms to exchange places. At 70° the interconversion of **3A** and **3B** is fast and the α hydrogens are magnetically equivalent (a^H = 9.3 gauss) and on a time-average basis spend equal times in axial and equatorial positions. Upon cooling, the central peak broadens until at −42° a coalescence temperature is reached. Below the coalescence temperature the central peak splits into a doublet which becomes sharper as the temperature is decreased until four lines of equal intensity with a_a^H = 13.00 and a_e^H = 6.50 are observed. In a similar manner 4,4-dimethylcyclohexanesemidione yielded a coalescence temperature of −62° and at high temperature a quintet splitting of 9.46 gauss. 3,3,5,5-Tetramethylcyclohexanesemidione gave a triplet splitting of 8.88 gauss at +90° and a coalescence temperature of −85°. Figure 6 illustrates the effect of temperature on cyclohexanesemidione which shows a 1:4:6:4:1 quintet at 25°, a^H = 9.65 gauss in DMF. The second and fourth peaks broaden as the temperature is lowered until at −85° an approximately 1:4:1 triplet is observed for the six magnetic transitions that are unaffected when axial and equatorial hydrogens are interchanged. Below this temperature a seven-line spectrum was observed which approached the 1:2:3:4:3:2:1 multiplicity observed for the frozen conformation of 4-*t*-butylcyclohexanesemidione at 25°.

Table IV. Activation Parameters for Ring Inversion of Symmetrically Substituted Cyclohexanesemidiones

Substituent	$\Delta H^{\ddagger}$, kcal/mole	$\Delta S^{\ddagger}$, eu	Coalescence temp, °C	$\Delta F^{\ddagger}$ at coalescence temp, kcal/mole
None	4.0	+1.0	−85	3.8
3,3-Dimethyl	3.9	−6.0	−62	2.6
4,4-Dimethyl	3.2	−8.0	−42	1.4
3,3,5,5-Tetramethyl	2.6	−8.0	−85	1.2

Treatment of the line-broadening data above the coalescence temperature (eq 4), the coalescence temperature (eq 5), and peak separation below the coalescence temperature (eq 6) yielded rate constants for the ring inversion process plotted in Figure 7. Thermodynamic data obtained from Figure 7 is summarized in Table IV. The significantly lower value of $\Delta H^{\ddagger}$ for the 3,3,5,5-tetramethylcyclohexanesemidione appears to be connected with the diaxial interactions of the methyl groups. It appears this interaction may destabilize **11** by as much as 2.5 kcal/mole (see previous section). This interaction may also change (*i.e.*, flatten) the geometry of the cyclohexene half-chair structure. This is apparent from the fact that a_a^H + a_e^H for **11** was 17.74 gauss at 90°, whereas for the other three cyclohexanesemidiones studied this sum was 19.1 ± 0.2 gauss. Unfortunately the 3,3,5,5-tetra-



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[13] R. W. Fessenden and R. H. Schuler, *J. Chem. Phys.*, **39**, 2147 (1963).

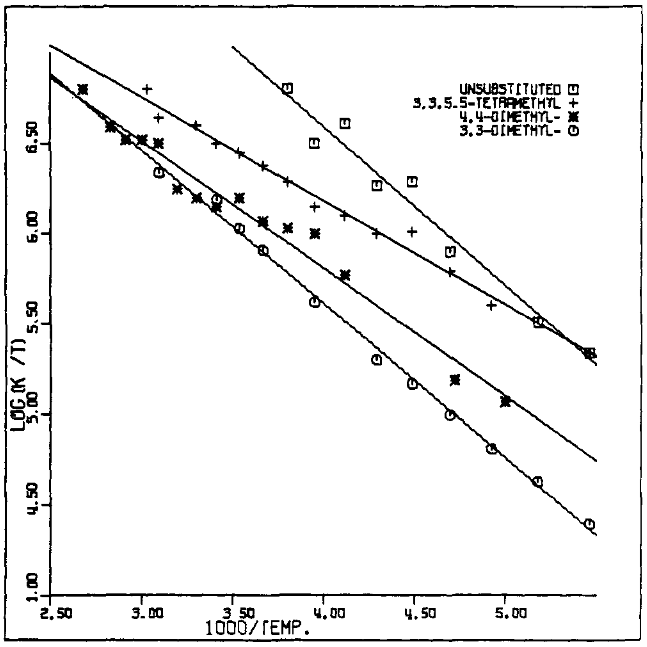


Figure 7. Computer least-squares plot of log k/T *vs.* $1/T$ for the conformational interconversion of symmetrically substituted cyclohexanesemidiones.

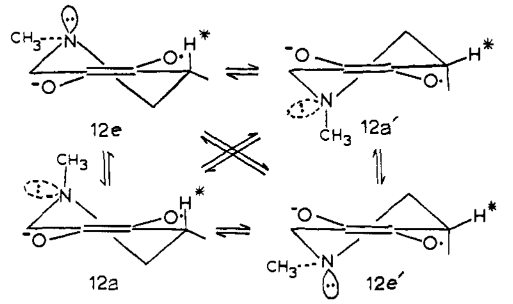


Figure 8. Possible conformational and configurational interconversions for N-methylpiperidine-3,4-semidione.

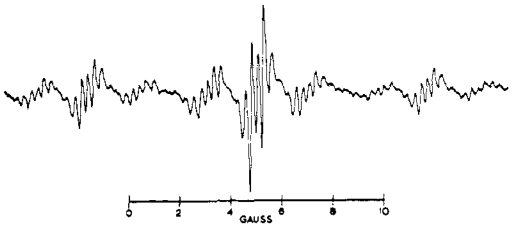


Figure 9. First derivative esr spectrum of cycloheptanesemidione at 25° in dimethyl sulfoxide solution. The semidione was prepared by disproportion of 2-hydroxycycloheptanone in the presence of potassium *t*-butoxide. In addition to the two major triplet splittings additional hyperfine splitting, possibly a 0.52 doublet of 0.26 gauss triplets, is observed.

methylcyclohexanesemidione could not be studied at a low enough temperature to ascertain if the ratio a_a^H/a_e^H deviated substantially from 2.0, as the other data suggest to be the case.

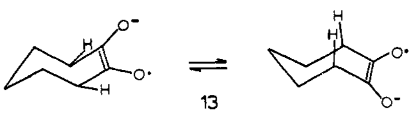
If the 1,3-diaxial interaction of the methyl groups in **11** destabilizes this semidione by 2.5 kcal/mole relative to the cyclohexanesemidione, it follows from the activation parameters of Table IV that such destabilization is reduced in the transition state to 1.1 kcal/mole (2.5 + 2.6 = 4.0 + 1.1). It seems reasonable that the transition state would be more planar than **11** and that 1,3-diaxial interactions as well as alkyl–oxygen eclipsings will be reduced in the transition state.

The rates of ring inversion of 3,3,5,5-tetramethylcyclohexanesemidione were studied in dimethyl sulfoxide, DMF, and 1,2-dimethoxyethane solutions from 0 to 80° with the gegenions cesium, rubidium, and potassium. In this temperature range solvent or gegenions had little if any effect on the rate constant. With lithium or sodium cations hyperfine splitting due to the gegenion was detected at 25°. In DMSO at 80° the splitting by these cations was not observed and rate constants were measured that were within experimental uncertainty equivalent to the rate constants measured with the other cations.

N-Methylpiperidine-3,4-semidione. The effects of inversion of the nitrogen configuration and of the ring conformation are shown in Figure 8. When the semidione is prepared by oxidation of N-methyl-4-piperidone in DMSO in the presence of base at 25° only a single semidione is detected with a^H = 6.4, 6.6, 11.8, 13.2 and $a^N \cong 0.5$ gauss. Upon warming, a coalescence temperature is reached at about +60°. At +110° a 1:4:6:4:1 quintet, a^H = 9.25 gauss, further split by a^N = 0.7 gauss, is observed. It appears certain that above the coalescence temperature the α-hydrogen atoms are spending equal time in axial and equatorial positions, *e.g.*, the conformations involved are equally populated. The simplest explanation to the above facts is that only conformations **12e** and **12e′** are significantly populated.

It has been shown by nmr spectroscopy that N-methylpiperidine exists mainly or completely with the N-methyl group in an equatorial position.[14] Whether the interconversion of **12e** to **12e′** involves **12a** or **12a′** as an intermediate cannot be answered. However, the greater conformational stability of the N-methylpiperidinesemidione relative to cyclohexanesemidione (coalescence temperature −85°) is apparently due to the requirement of both a ring and a nitrogen atom inversion to convert **12e** into **12e′**. Whether the nitrogen inversion can occur simultaneously with ring inversion (**12e** ⇄ **12e′**) or must be a slow step following or preceding the ring inversion (**12e** → **12a′** → **12e′** or **12e** → **12a** → **12e′**) cannot be specified. It is our feeling that the observed coalescence temperature of +60° is connected with the direct process (**12e** ⇄ **12e′**) since the conformational lifetimes of ~10^{-7} sec appear too short for a nitrogen inversion process, even the exothermic conversion of **12a** into **12e′**.

Cycloheptanesemidione gave a spectrum (Figure 9) that was a triplet of triplets between +30 and −80°. As shown in Table V little change in hfsc was observed over the temperature range studied. Cycloheptanesemidione is conformationally more stable than cyclohexanesemidione. This is apparently due to the fact that cycloheptanesemidione can assume a chairlike structure (**13**) that would be expected to have an energy



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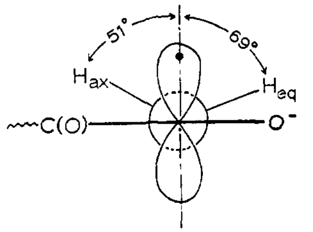
[14] J. B. Lambert and R. G. Keske, *J. Am. Chem. Soc.*, **88**, 620 (1966).

Table V. Hyperfine Splitting Constants for Cycloheptanesemidiones[a]

	Hyperfine splitting constants,[b] gauss	
Temp, °C	Unsubstituted[c]	3,3-Dimethyl[d]
+60		10.00
+30	6.63, 2.00	10.00
+10	6.61, 2.02	10.00
−20	6.62, 2.05	10.02
−40	6.62, 2.05	10.05
−60	6.64, 2.07	10.05
−80	6.61, 2.11	10.05

[a] Prepared by oxidation of the acyloin in DMF in the presence of potassium *t*-butoxide. [b] +0.05 gauss. [c] Triplet splittings. [d] Doublet splitting.

of activation for ring inversion comparable to that of cyclohexane (10–12 kcal/mole). The dihedral angles for the α-hydrogen atoms calculated from the observed hfsc are −51 and +69° for the quasi-axial and quasi-equatorial carbon–hydrogen bonds (**14**).[15] Nmr spectroscopy has provided a measurement of $\theta_a = -19°$ and $\theta_e = 79°$ for cycloheptene.[16] For cyclohexene the nmr method yields $\theta_a = -13°$, $\theta_e = 47°$,[16] in excellent agreement with the estimates made by esr examination of the semidiones. Since the quasi-axial hydrogen atoms actually point into the center of the cycloheptene ring, it follows that serious diaxial interactions between the 3,7 positions of the cycloheptene ring may occur. To test this postulate 3,3-dimethylcycloheptanesemidione was prepared. The spectrum was a doublet of 10.0 gauss between −60 and +60°. The lines were somewhat broad (~2 gauss) but no further hfs could be detected. We conclude that in 3,3-dimethylcycloheptanesemidione $a_e^H = 10.0$, $a_e^H \ll 1$ gauss. Apparently the methyl at the axial position at C-3 has repelled the axial hydrogen at C-7 until the equatorial hydrogen at C-7 resides close to the nodal plane ($\theta_e = 90°$). Taking $\theta_a = -30°$ for the hydrogen at the 7 position leads to $B\rho_C = 12.5$ gauss for 3,3-dimethylcycloheptanesemidione. The lack of a significant temperature effect on the hfsc as well as a value of a_e^H close to zero rule out significant torsional motion of the α-methylene group in cycloheptanesemidione and justify the calculation of dihedral angles *via* the Heller–McConnell equation.



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Discussion

Cycloheptene apparently has much greater conformational stability than cyclohexene. The results observed with cycloalkanesemidiones suggest the possibility of observing 3 or 4 position symmetrically substituted cycloheptenes as optically active disymmetric chromophores.

The temperature effect observed for the hfsc of cyclopentane- and cyclohexanesemidiones appears to be connected with some sort of molecular motion since the more rigid cyclobutane- and cycloheptanesemidiones do not show a significant variation in hfsc. However, the interpretation of this effect is by no means obvious. We have argued that it is not the result of torsional or rocking motion of the α-methylene group. *trans*-Biacetyl radical anion shows a similar temperature effect ($a_{CH_3}^H$ increases as the temperature is decreased). This excludes a torsional explanation because $a_{CH_3}^H = (B\rho_C/3)[\cos^2\theta + \cos^2(\theta + 120°) + \cos^2(\theta + 240°)]$ is independent of the value of θ. Ion pairing between the semidione and the cation is apparently excluded since *trans*- and *cis*-semidiones show similar effects. Population of a transition state conformation (*e.g.*, half-boat conformation for cyclohexane would appear capable of explaining the observed temperature effect for cyclohexanesemidiones but seems incapable of explaining the effect observed for the biacetyl radical anion or cyclopentanesemidione. If the effect of temperature on hfsc is connected with some vibrational motion of the α-methylene group, a deviation in a^H/a^D from the value of 6.514 (*i.e.*, the ratio of nuclear magnetic moments) would be expected since the vibrational amplitudes of carbon–hydrogen and carbon–deuterium bonds are different. This should be true whether the vibration is torsional or a breathing vibration involving changes in the C_π–C_α–H angle. Actually, the observed isotope effects are very close to the theoretical value. Preparation of cyclohexanesemidione in DMSO-d_6 yielded a nonet with intensities 1:4:10:16:19:16:10:4:1 and $a^D = 1.465 \pm 0.005$ gauss at 25°. The value of a^H in DMSO is 9.68 ± 0.03 gauss and $a^H/a^D = 6.60$.

In a similar fashion cyclopentanesemidione yielded $a^H = 13.12 \pm 0.05$, $a^D = 1.00 \pm 0.01$, $a^H/a^D = 6.60$ in DMSO at 25°. We conclude that the value of a^H is not particularly influenced by any vibrational motion of the α-carbon–hydrogen bond. Incidentally, the observed hfsc can be interpreted as showing that in situations wherein an unpaired spin is delocalized by hyperconjugation ($\cdot$C–C–H(D) $\leftrightarrow$ C=C H$\cdot$(D$\cdot$)) that $\rho_H = \rho_D$, *i.e.*, deuterium and hydrogen undergo hyperconjugation to the same degree.

Perhaps the increase in hfsc with a decrease in temperature is connected with the spin density of the carbonyl carbon atoms. This in turn could be controlled by the planarity of the dicarbonyl system. Both cyclobutane- and cycloheptanesemidiones have values of $B\rho_C$ greater than cyclohexanesemidione and show little effect of temperature on hfsc. Perhaps these are highly planar structures as far as the four atoms in the π system are concerned and ρ_C is a maximum. For cyclohexane, cyclopentane-, and biacetylsemidiones the degree of planarity may increase as the temperature is lowered with a resulting increase in ρ_C. If this is the case, it is surprising that the natures of the cation and solvent do not have a larger effect on the value of the hfsc since chelation of a *cis*-semidione would be expected to increase the planarity of the system.

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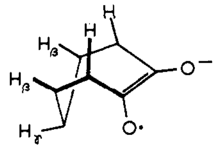
(15) By simultaneous solution of the Heller–McConnell equations, $a^H = \rho_C B \cos^2\theta$. For cycloheptane there are two possible solutions, $\theta_a = +3°$, $B\rho_C = 6.8$ gauss, or $\theta_a = 51°$, $B\rho_C = 16.4$ gauss. For 4-*t*-butylcyclohexanesemidione only a single solution is realistic; $\theta_a = 14°$, $B\rho_C = 14$ gauss. For cyclopentanesemidione with $\theta_a = 30°$, $B\rho_C$ must be 17.6. It seems most reasonable for cycloheptanesemidione that $B\rho_C$ will be 16.4 gauss and that $\theta_a = -51°$. We had indicated previously that $\theta_a = +3°$ might be the preferred geometry.

(16) G. V. Smith and H. Kriloff, *J. Am. Chem. Soc.*, **85**, 2016 (1963).

We have assumed from elementary considerations of nonbonding interactions that the preferred conformation of cycloheptanesemidione is that resembling a chair structure.[17] However, our results do not exclude the conformation **15**.[18] Boat conformations of cycloheptene derivatives are required to explain certain solvolytic results, for example, the conversion of 4-cycloheptenylmethyl derivatives to *endo*-2-bicyclo[3.2.1]octane derivatives.[19] However, there is no evidence of participation by the double bond in the products observed from 4-cycloheptenyl brosylate.[20]



15

Extensive long-range hfs has been noted in bicyclic and tricyclic semidiones that could be taken as models for **13** and **15**.[21,22] Bicyclo[3.2.1]octane-6,7-semidione. prepared by oxidation of the monoketone, appears to be a model for **15**. In this semidione hfsc of 5.51, 4.03 (two), and 0.53 (three or five) gauss are observed.[22] The β- and γ-methylene groups are extensively involved.

Tricyclo[3.2.1^{3,8}]nonane-6,7-semidione, prepared by oxidation of the monoketone,[23] gives rise to a complicated spectrum, apparently showing hfs by all ten hydrogen atoms. A possible assignment of hfsc for this model of **13** is a^{H} = 6.15 (two), 2.60, 2.34 (two), 0.40 (two), 0.25 (two), and 0.20 gauss.[24] It thus appears that the observed long-range hfs by β- and γ-hydrogen atoms in cycloheptanesemidione could be consistent with either structure **13** or **15**.

It is pertinent that a cycloheptene derivative, 1,1,4,4-tetramethyl-6,7-benzocycloheptene, has been extensively studied by pmr and an enthalpy difference between the chair and boat conformations of only 317 cal/mole found.[25] Enthalpies of activation for the interconversion of these conformations (boat $\rightleftarrows$ boat, boat $\rightleftarrows$ chair, chair $\rightleftarrows$ chair) were in the range of 10 kcal/mole,[25] consistent with our observation of a frozen conformation for cycloheptanesemidione in the time scan of $\sim 10^{-7}$ sec.

A comparison of the enthalpy of activation for ring inversion of cyclohexanesemidione with estimates for cyclohexene[26] and 4-bromocyclohexene[27] is of interest. From pmr spectroscopy a coalescence temperature of −164° has been observed for *cis*-3,3,4,5,6,6-d_6-cyclohexane in bromotrifluoromethane solution.[26] This corresponds to a $\Delta H^{\ddagger}$ of 5.3 kcal/mole if $\Delta S^{\ddagger}$ is zero. For 4-bromocyclohexene a coalescence temperature is observed at −145° and a value of $\Delta H^{\ddagger}$ = 6.1 kcal/mole estimated.[27] Experimental values of $\Delta H^{\ddagger}$ are 2–3 kcal/mole lower for the cyclohexanesemidiones. Apparently the lowered double bond character in the semidione (standard HMO calculations indicate a bond order, $1 + \Sigma N c_i c_j$, of 1.6 between the carbonyl carbon atoms) facilitates the ring inversion process. The repulsion of the negatively charged oxygen atoms may also contribute to the lowered energy barrier although this effect may be offset by chelation between the semidione and alkali metal cation.

It is difficult to assess the reliability of the values of $\Delta S^{\ddagger}$ reported in Table IV. The values of $\Delta H^{\ddagger}$ appear reliable to ±0.5 kcal/mole and the values of $\Delta F^{\ddagger}{}_{\text{coales}}$ should be accurate to ±0.3 kcal/mole, provided that our approach to the measurement of rate constants from line broadening is valid. It is apparent for cyclohexanesemidione and its 3,3,5,5-tetramethyl derivative that a considerable difference in $\Delta S^{\ddagger}$ exists (in the range of 9 eu). In addition to the usual symmetry considerations, variations in the absolute value of $\Delta S^{\ddagger}$ may reflect ionic association and solvation, as well as restricted motion due to steric considerations in the ground and transition states.

Experimental Section

Preparation and Detection of Semidiones. Radical anions were prepared by the disproportionation of the appropriate α-hydroxy ketones in DMSO containing excess potassium *t*-butoxide or in DMF containing excess cesium *t*-butoxide.[4,28] In a typical experiment equal volumes of deoxygenated solutions of the hydroxy ketone (0.05 *M*) and base (0.1 *M*) were mixed in the inverted U-cell described previously.[29] The esr spectra were measured using a Varian Associates V-4500 epr spectrometer with 100-kcps field modulation and with a 9-in. magnet, regulated by a Fieldial control. Variable-temperature experiments were performed using a Varian Associates V-4540 variable-temperature controller which was found to reproducibly yield temperatures within ±1°. The temperature of the sample was calibrated by a copper–constantan thermocouple which was immersed into the sample in the cavity. All spectra were recorded in flat, fused silica cells. At ambient temperatures the Varian Associates V-4548 aqueous sample cell was used. For thermostated experiments a special cell (V-4548-1) to fit within the dewar insert was obtained from Varian Associates.

Field scans were calibrated by *p*-benzosemiquinone in 85% ethanol (a^{H} = 2.368 gauss).[30] Line widths were measured as the difference between maxima and minima of the first derivative spectra. The wing peaks of the spectrum were used as internal standards for line width. Other peaks were compared with the standard line widths by alternately scanning the standard and broadened peaks. A large number of scans (10–30) were recorded at each temperature. For cyclohexane- and 4,4-dimethylcyclohexanesemidiones the broadened peaks examined were the $M_I = \pm 1$ lines and the standards were the $M_I = \pm 2$ lines. Calculations were based on the average values for the two sets of data. For 3,3-dimethyl- and 3,3,5,5-tetramethylcyclohexanesemidione the $M_1 = +1$ and -1 lines were scanned and averaged to yield the standard line width at each temperature. There was a tendency for the standard line width to change with time, perhaps because of exchange broadening. However, $\Delta\omega_{1/2}$ showed no change with time. We did not find the precision improved by the use of second derivative spectra.

The derivation of eq 4 follows directly from eq 8,[7d] where $\tau = \tau_A\tau_B/(\tau_A+\tau_B)$,[7c] P_A and P_B are the fractional populations of the two conformations **A** and **B**, $\delta\nu$ is the difference in hfsc for a given hydrogen atom in conformations **A** and **B**, and $\Delta\omega_{1/2}$ is the total line width at half-height for a Lorentzian absorption curve. When

$$^1/_2\tau = 2\pi P_A P_B(\delta\nu)^2(\Delta\omega_{1/2})^{-1} \qquad (8)$$

$P_A = P_B$ $(\tau_A = \tau_B)$ it follows that $\tau_A = {}^1/_2\tau = k_A$. Substituting $\nu = \gamma H/2\pi$ and $\Delta\omega_{1/2} = \sqrt{3}(\Delta \text{ width})(\gamma/2\pi)$ to convert to cycles

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(17) N. L. Allinger and W. Szkrybalo, *J. Org. Chem.*, **27**, 722 (1962).

(18) R. Pauncz and D. Ginsberg, *Tetrahedron*, **9**, 40 (1960).

(19) G. Le Ny, *Compt. Rend.*, **251**, 1526 (1960).

(20) A. C. Cope, C. H. Park, and P. Scheiner, *J. Am. Chem. Soc.*, **84**, 4862 (1962).

(21) G. A. Russell, K.-Y. Chang, and C. W. Jefford, *ibid.*, **87**, 4383 (1965).

(22) G. A. Russell, G. Holland, K.-Y. Chang, and L. H. Zalkow, *Tetrahedron Letters*, 1955 (1967).

(23) A. Nickon, H. Kwasnik, T. Swartz, R. O. Williams, and J. B. DiGiorgio, *J. Am. Chem. Soc.*, **87**, 1615 (1965).

(24) K.-Y. Chang, unpublished results.

(25) E. Grunwald and E. Price, *J. Am. Chem. Soc.*, **87**, 3139 (1965).

(26) F. A. L. Anet and M. Z. Haq, *ibid.*, **87**, 3147 (1965).

(27) F. R. Jensen and C. H. Bushweller, *ibid.*, **87**, 3285 (1965).

(28) G. A. Russell and E. T. Strom, *ibid.*, **86**, 744 (1964).

(29) G. A. Russell, E. G. Janzen, and E. T. Strom, *ibid.*, **86**, 1807 (1964).

(30) B. Venkataraman, B. G. Segal, and G. K. Fraenkel, *J. Chem. Phys.*, **30**, 1006 (1959).

per second and to correct for the difference in full line widths between the absorption curve at half-height and the first derivative curve between maximum and minimum leads to eq 9 which is equivalent to eq 4.

$$k = (17.6 \times 10^6)(a_{\mathbf{A}}{}^{\mathrm{H}} - a_{\mathbf{B}}{}^{\mathrm{H}})/4\sqrt{3}(\Delta \text{ width}) \quad (9)$$

Materials. 2-Acetoxycyclobutanone,[31] 2-hydroxycyclopentanone,[32] 2-hydroxy-6-methylcyclohexanone,[33] 2-acetoxy-4-methylcyclohexanone,[34] 2-bromo-6,6-dimethylcyclohexanone,[35] 2-acetoxy-4,4-dimethylcyclohexanone,[36] 2-acetoxy-3,5-dimethylcyclohexanone,[37] 2-hydroxy-3,5,5-trimethylcyclohexanone,[38] 2-acetoxy-3,3,5,5-tetramethylcyclohexanone,[39] 2-hydroxycycloheptanone,[40] 2,2-dimethylcycloheptanone,[41] and 2-hydroxymenthone[42] were prepared according to the literature.

2-Hydroxy-6,6-dimethylcyclohexanone was prepared from the bromo ketone. The bromo ketone (100 mg) was dissolved in ethanol (2 ml) and a solution of potassium carbonate (50 mg) in water (1 ml) was added. The solution was heated to reflux for 0.5 hr at which time the reaction (monitored by tlc) appeared complete. The solution was cooled and extracted with five 2-ml portions of methylene chloride. The combined extracts were washed once with water, evaporated free of solvent, and dried by azeotropic distillation with benzene. The crude material was purified by glpc on a 5-ft column of 20% SF-96 on firebrick at 180°. The retention time of the product was 11.5 min while under identical conditions the starting material had a retention time of 6.5 min. The product was a colorless liquid: $n^{25}\mathrm{D}$ 1.4305; mass spectrum, parent peak at *m/e* 140. *Anal.* Calcd for $C_8H_{12}O_2$: C, 68.6; H, 8.57. Found: C, 68.5; H, 8.56. The ketone gave a phenylhydrazone (methanol–water) of mp 137–139° dec whose mass spectrum gave a parent peak at *m/e* 208. *Anal.* Calcd for $C_{14}H_{20}N_2O$: N, 13.45. Found: N, 13.5.

2-Acetoxy-7,7-dimethylcycloheptanone was prepared. 2,2-Dimethylcycloheptanone (1 g) was dissolved in glacial acetic acid (300 ml) and to the mixture was added boron trifluoride diethyl etherate (6 ml) and lead tetraacetate (1.90 g). The mixture was stirred at room temperature for 4 hr, at 50° for 4 hr, and at 80° for 4 hr. The mixture was cooled and the excess of acetic acid was removed at an aspirator. When the volume was reduced to 10 ml, the distillation was stopped, the solution was diluted with water (200 ml) and extracted with four 100-ml portions of benzene. The combined extracts were washed once with saturated sodium bicarbonate solution (20 ml) and once with water (10 ml) and the benzene was removed by distillation. The light brown oil (1 g) was distilled, bp 100° (2 mm). Final purification was effected by glpc on a 5-ft column of 20% SF 96 on firebrick. The retention time of the product was 11.0 min, while that of the starting material under identical conditions was 5.5 min. *Anal.* Calcd for $C_{11}H_{18}O_3$: C, 70.2; H, 9.6. Found: C, 70.2; H, 9.5. The ketone yielded a phenylhydrazone, mp 144–145°. *Anal.* Calcd for $C_{17}H_{24}N_2O_2$: C, 70.9; H, 8.33. Found, C, 71.2; H, 8.2.

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Secondary Deuterium Isotope Effects. β-Kinetic Effects in SN2 Reactions of N,N-Dimethylaniline and Dimethylphenylphosphine with Methyl *p*-Toluenesulfonate and Comparison with Observed and Calculated Vibrational Frequencies of Deuterated and Undeuterated Dimethylaniline and Trimethylanilinium Ion[1]

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Abstract: The rates of reaction, in nitrobenzene at 51.29°, of methyl *p*-toluenesulfonate with N,N-dimethylaniline and N,N-dimethyl-d_6-aniline to form trimethylphenylammonium and methyldimethyl-d_6-phenylammonium *p*-toluenesulfonates, respectively, and with dimethylphenylphosphine and dimethyl-d_6-phenylphosphine to form the corresponding phosphonium salts, were determined conductiometrically. The secondary isotope effects observed are small and inverse: 1.133 ± 0.008 for the amines, and 1.050 ± 0.002 for the phosphines. The result for the amines is discussed in relation to the equilibrium isotope effect calculated using information obtained from the observed infrared spectra of the reactants and products. Though uncertainties in the assignment of spectral bands exist, it appears that there is very little shift in CH(CD) stretching force constants. The inverse effect is, therefore, very probably due to increased force constants for lower frequency vibrations, such as for bending. This interpretation is consistent with a steric explanation for the isotope effects. Inductive effects are expected to produce changes in the stretching force constants.

The origin of secondary deuterium isotope effects[3] is understood, in terms of the general theory of isotope effects,[4] to be changes in vibrational force constants[5] (along with possible changes in mass and mo-

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(1) For further details, *cf.* E. D. Kaplan, Ph.D. Dissertation in Chemistry, University of Pennsylvania, 1966; submitted to University Microfilms.

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