Electron Spin Resonance Study of Inversion and Conformations in 1-Hydroxycyclohexyl Radicals

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We have obtained the variable-temperature e.s.r. spectra of the 1-hydroxycyclohexyl, 4-methyl-1-hydroxycyclohexyl, and 4-t-butyl-1-hydroxycyclohexyl radicals by photolysis of the precursor alcohols mixed with di-t-butyl peroxide. From computer analysis of the observed linewidth alternation in the spectra of the first two radicals, we calculate activation energies for chair-to-chair inversion to be 6.6 and 11.4 kcal mol^{-1}, respectively. In order successfully to fit the spectra from the 4-methyl radical it was necessary to include the axial–equatorial energy difference of 1.8 kcal mol^{-1}. The radical sites are probably non-planar and both the radical sites and the rings invert during the hindered motion.

THE conformational equilibria and configurational preferences of cyclohexane and other six-membered rings have long been of interest to chemists. Recently n.m.r. and e.s.r. techniques have been used to study these by investigation of time-dependent processes in molecules such as cyclohexane [1] itself and in related free radicals including the cyclohexyl radical [2] and monosubstituted derivatives.[3] The magnetic resonance methods depend on the fact that any hindered motion which interchanges magnetically distinguishable nuclei in a molecule at rates comparable to the n.m.r. or e.s.r. frequencies will lead to temperature-dependent line broadening in a spectrum. E.s.r. spectra exhibiting selective line broadening (the alternating linewidth effect [4]) have been analysed with the assumption that the cyclic radicals involved were undergoing a chair-to-chair inversion that interchanged axial and equatorial protons on the rings. Barriers for the inversion in the range 4—5 kcal mol^{-1} were obtained for the cyclohexyl,[2] 1-carboxycyclohexyl,[3] and piperidine nitroxyl [5] radicals. The corresponding n.m.r. experiments gave a barrier of 10.8 kcal mol^{-1} for cyclohexane inversion [1] but much lower barriers (5.1—7.7 kcal mol^{-1}) for cyclohexane derivatives containing sp^2-hybridized carbons in the ring.[6]

Temperature-dependent line broadening has previously been observed in e.s.r. spectra of the 1-hydroxycyclohexyl radical formed from cyclohexanol,[7-11] but there has been no quantitative analysis of the results. The popular view is that the inversion is between two equivalent chair forms, although in one study it was suggested that the lowest energy conformation of the radical is the twist-boat rather than the chair.[10] In view of recent theoretical [12] and experimental [13] evidence that α-hydroxy-radicals are non-planar at the radical site, the assumption that the two chair forms are energetically equivalent is not necessarily justified and is obviously not true for disubstituted radicals. Although to our knowledge there have been no studies on disubstituted cyclohexyl radicals, the axial–equatorial energy difference for the methyl group in the 4-methylpiperidine nitroxy radical [5] was measured and found to be similar to the energy difference in methylcyclohexane [14-16] and to the energy difference between *cis*- and *trans*-1,4-dimethylcyclohexane,[17] all in the range 1.5—2.0 kcal mol^{-1}.

The purpose of the present work is to obtain inversion barriers for some 1-hydroxycyclohexyl radicals by means of variable-temperature e.s.r. spectroscopy and with the aid of our recent theoretical calculations [12] to interpret the results in terms of radical structures and mechanisms for the inversion processes.

EXPERIMENTAL

Cyclohexanol, 4-methylcyclohexanol (mixture of isomers), 4-t-butylcyclohexanol, and *cis*- and *trans*-4-methylcyclohexanol (Aldrich), di-t-butyl peroxide (DTBP) (Matheson, Coleman, and Bell), and cyclopropane (Union Carbide) were used as received.

Samples for low temperature runs (< 0 °C) were prepared by mixing approximately equal volumes of the precursor and DTBP in a 4 mm OD Suprasil quartz tube. After thorough degassing of the mixture sufficient cyclopropane was added to make *ca.* 30% of the total and the tube was sealed off under vacuum. For experiments above 0 °C a continuous flow system was used which consisted of a reservoir and heat exchange coil in a constant temperature bath and a peristaltic pump to pump the solution from the reservoir, up through a Suprasil quartz tube in the cavity, and then through the heat exchange coil back to the reservoir. Flow rates were *ca.* 2.5 ml min^{-1}. Nitrogen gas could be continuously bubbled through the sample in the reservoir to remove dissolved oxygen. The samples consisted of equal amounts of precursor and DTBP, with heptane in some cases added as a solvent.

The e.s.r. spectrometer was a Varian E-4 equipped with a variable temperature Dewar for the sealed tube runs. The Dewar had a copper–constantan thermocouple placed just below the cavity, which was calibrated by means of another thermocouple placed in a sample tube at the sample position in the cavity. Temperatures were measured in the flow system by means of a copper–constantan thermocouple permanently mounted in the stream just above the cavity. During either kind of experiment the cavity was continuously irradiated with the light from a 1 kW Hanovia Xe–Hg compact arc lamp in a Schoeffel housing focused onto the cavity through a Suprasil quartz lens. The radicals were formed by hydrogen atom abstraction from the precursor with photolytically produced t-butoxyl radicals.[18]

Computer simulations of the spectra were performed by means of the program ESREXN,[19, 20] which uses the density matrix approach to calculate exchange-broadened e.s.r. spectra. The spectra were analysed on the assumption that observed temperature effects were caused by some process that interchanged the ring β-protons, which were magnetically equivalent in axial and equatorial pairs at low temperatures. The program required a specific exchange mechanism to be chosen, that is, the number of different conformations involved in the exchange process and their relative energies. The required input parameters were then the limiting low temperature hyperfine splittings, the fractional population for each conformer, the rates of exchange between the various conformations, and the width of the non-broadened lines. The lineshapes were assumed to be Lorentzian. Rates were varied until the best visual fits with the experimental spectra were obtained. Error limits were estimated for each case by determination of the range of rates that produced no observable change in the quality of the fit.

RESULTS

Cyclohexanol.—Photolysis of samples of DTBP with cyclohexanol gave e.s.r. spectra that could only be interpreted as arising from the 1-hydroxycyclohexyl radical (1-HCH), formed by abstraction of the tertiary proton by the photolytically generated t-butoxyl radicals. A typical low temperature triplet of triplets spectrum of 1-HCH is shown in Figure 1 and the e.s.r. parameters are listed in Table 1. As can be seen in Figure 2 lines in the spectrum broaden and merge as the temperature is raised and eventually approach the quintet pattern to be expected from four magnetically equivalent protons. Computer simulations obtained from program ESREXN are also shown in Figure 2. The upper temperature limit was imposed by the deteriorating signal to noise ratios of the spectra. The e.s.r. parameters listed in Table 1 and the observed line broadening are both consistent with previous work.[7,10] A g value has not previously been reported for this radical, but our value of 2.0032 is typical of those measured for α-hydroxyalkyl radicals.[21,22]

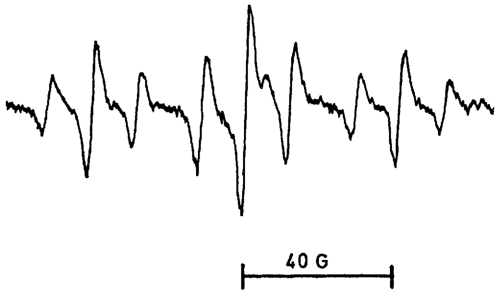


FIGURE 1 The first-derivative e.s.r. spectrum of the 1-HCH radical obtained by photolysis of the alcohol and DTBP in cyclopropane in a sealed tube at 186 K

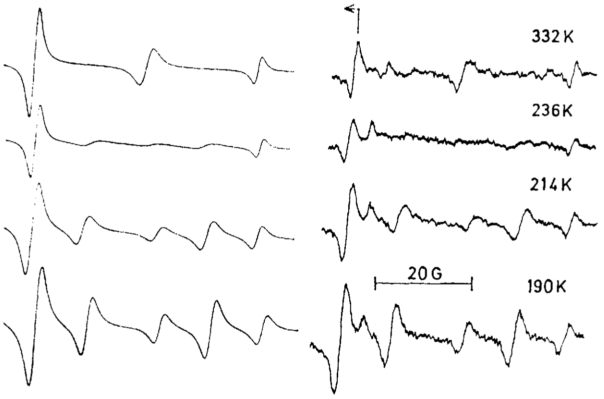


FIGURE 2 Variable-temperature e.s.r. spectra of the 1-HCH radical together with computer simulations calculated by program ESREXN

TABLE 1

E.s.r. parameters for 1-hydroxycyclohexyl radicals

Radical	T/K	$A_{H\beta}$/G[a]	g[b]
1-HCH	190	36.0 ± 0.2 (2) 10.4 (2)	2.0032 ± 0.0002
4-MeHCH	190	34.8 (2), 11.0 (2)	2.0032
4-BuHCH	303	35.5 (2), 11.0 (2)	2.0030

[a] The numbers in parentheses are the number of equivalent protons. [b] Measured relative to DPPH, g 2.0036.

TABLE 2

Kinetic parameters for 1-hydroxycyclohexyl radicals

Radical	T/K	E_a/kcal mol^{-1}	log A
1-HCH	190—330	6.6 ± 0.6	13.7 ± 0.4
4-MeHCH	287—314	8.5 ± 1.0[a]	16.9

[a] This is the barrier for inversion from the less stable to the more stable form.

Figure 3 is an Arrhenius plot of log k *versus* $1/T$, where k is the rate of β-proton exchange at temperature T. The parameters in the Arrhenius equation, $k = Ae^{-E_z/RT}$, were obtained by a linear least-squares fit of the data and are listed in Table 2.

4-Methylcyclohexanol.—In this compound there exists the possibility of the formation of two different tertiary radicals.

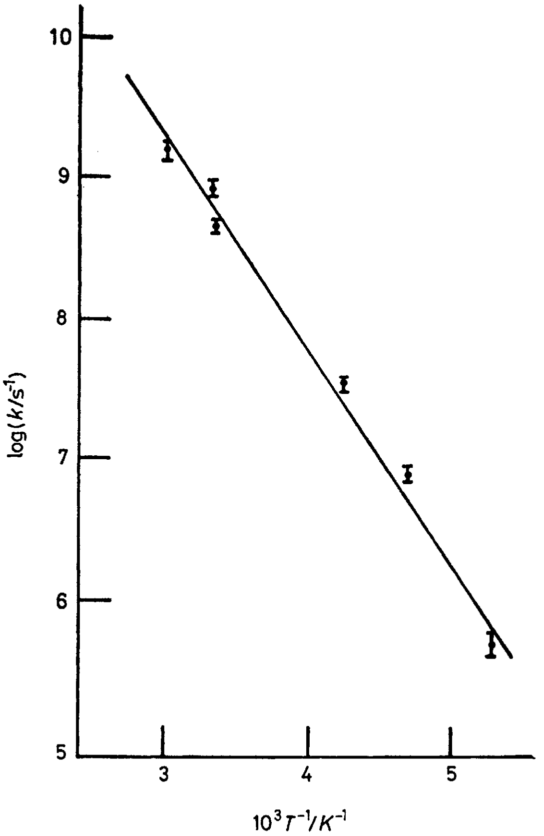


FIGURE 3 Arrhenius plot for the 1-HCH radical of log k *versus* $1/T$, where k is the rate of exchange in program ESREXN that best fits the experimental spectrum

However, the observed spectra were consistent only with the 1-hydroxy-4-methylcyclohexyl radical (4-MeHCH), and the measured e.s.r. parameters (Table 1) are in fact almost identical to those of the unsubstituted 1-HCH radical. There was no indication at any temperature that the 1-methyl radical was formed in detectable amounts. We found it necessary to go to relatively high temperatures (>273 K) before line broadening became noticeable in the spectrum and we were not able to reach the coalescence temperature. Thus the temperature range of our observations was much smaller than for the 1-HCH radical and the error limits on the kinetic parameters are larger.

The experimental spectra (Figure 4) could not be successfully simulated with the two-site model that was used for the 1-HCH radical, and it was necessary to include the effect of conformers with different energies (see Discussion). We assumed that the conformers corresponded to the methyl group being either axial or equatorial with the enthalpy difference between the two forms the same as in methylcyclohexane itself, 1.8 kcal mol^{-1}.[23] The relative populations were then given by the Boltzmann factor. The Arrhenius plot is shown in Figure 5 and the kinetic parameters are listed in Table 2.

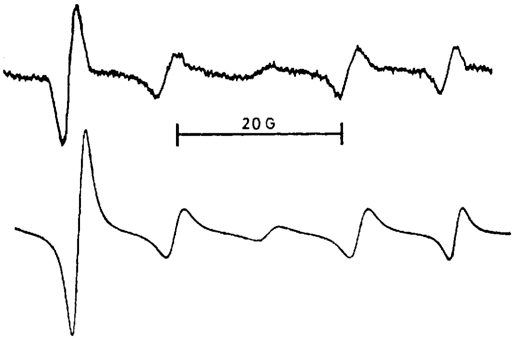


FIGURE 4 A typical first-derivative e.s.r. spectrum for the 4-MeHCH radical, obtained by photolysis of the alcohol and DTBP in the flow system at 301 K, together with a computer simulation calculated by program ESREXN

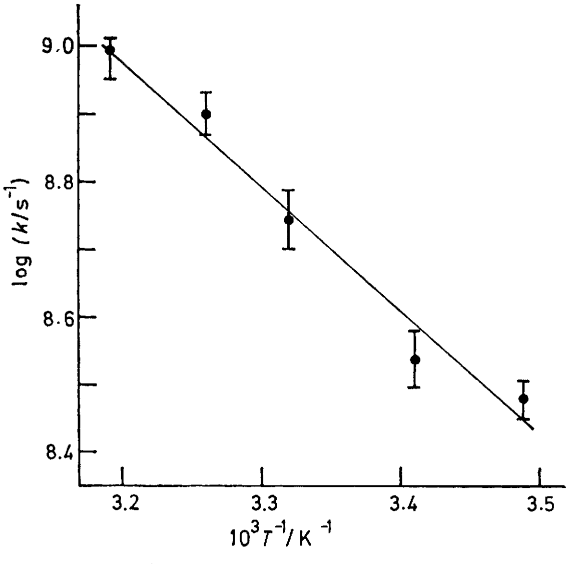


FIGURE 5 Arrhenius plot for the 4-MeHCH radical

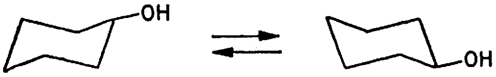
4-t-*Butylcyclohexanol*.—This precursor again gave the possibility of the formation of several different radicals, but the triplet of triplets spectrum was clearly due to the 1-hydroxy-4-t-butylcyclohexyl radical (4-BuHCH) on the basis of its e.s.r. parameters (Table 1), which were similar to those of the other 1-hydroxy-radicals and quite different from the values found for the 1-t-butylcyclohexyl radical (two pairs of protons with hyperfine splittings of 41.5 and 8.0 G, respectively).[24]

DISCUSSION

1-*Hydroxycyclohexyl Radical*.—It is clear from our experimental results that there is hindered motion occurring in this radical, and since the experimental spectra could be successfully simulated with the assumption that there were only two forms with equal populations we can reasonably conclude that this involves interchange of the radical between two energetically equivalent conformers *via* an intermediate that is 6.6 kcal mol^{-1} higher in energy. Further, the motion must be one that interchanges the ring β-protons in pairs.

It has been tacitly assumed [2] that the motion in cyclohexyl radicals involves chair-to-chair inversion, but the experimental evidence by itself does not explicitly require this. Our *ab inito* theoretical study of the 1-HCH radical [12] shows that the chair does have the lowest energy (by 5—7 kcal mol^{-1}) of those forms considered, chair, boat, and twist-boat, contrary to the suggestion of Corvaja *et al.* that the twist-boat is lowest. The latter suggestion was based on comparison of the observed β-proton hyperfine splittings with values calculated from the well known relationship of the β-proton hyperfine splittings to the dihedral angle between the β-C–H bond and the unpaired electron orbital. However, the calculations were based on geometries that included planar radical sites, which is not in accord with recent evidence.[12,13]

The barrier for inversion of the hydroxy-group at the radical site without ring inversion was calculated [12] to be *ca.* 3.5 kcal mol^{-1}, much lower than the experimental value, and also this motion alone would not properly interchange the β-protons. The mechanism which best accounts for the above observations is in fact chair-to-chair inversion of the ring with concerted inversion of the hydroxy-group on the non-planar radical carbon, in order to maintain the equivalence of the two chair conformers (Scheme 1). We suggest that the likeliest intermediate is the twist-boat and that the classical boat is a high energy form not involved in the inversion process.

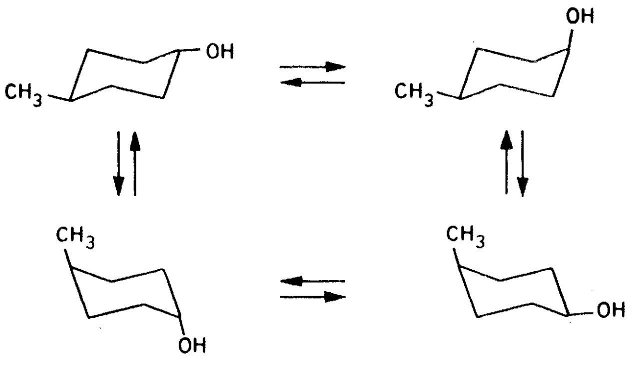


SCHEME 1

The somewhat higher activation energy that we observed for this radical compared to the unsubstituted cyclohexyl radical (6.6 *versus* 4.9 kcal mol^{-1}) is probably related to the non-planarity of the radical site. It has been suggested that substituted cyclopentyl radicals which are non-planar at the radical site have higher barriers to inversion than planar radicals.[25] In the 1-carboxycyclohexyl[3] radical the β-proton hyperfine splitting and the lower inversion barrier (4.0 kcal mol^{-1}) are similar to the values for the unsubstituted cyclohexyl radical,[2] indicating that these two radicals have a similar planar radical site hybridization. There is evidence that substitution of a carboxy-group for an α-proton leads to stabilization of a π structure and sp^2 hybridization at the radical site.[26]

1-*Hydroxy*-4-*methylcyclohexyl Radical*.—As mentioned above it was necessary to consider the axial–equatorial energy difference of the methyl group in the simulations. With this difference taken to be the same as in methylcyclohexane (1.8 kcal mol^{-1}, corresponding to *ca*. 95% equatorial methyl and 5% axial methyl at room temperature), we were able to obtain satisfactory simulations with the four site mechanism shown in Scheme 2.

We cannot distinguish between this mechanism, consisting of ring inversion followed by rapid radical site inversion, and a mechanism in which the two inversions are simultaneous, but in either case the barrier for passage from the axial methyl conformer to the equatorial methyl conformer is found to be 8.5 kcal mol^{-1}. According to this mechanism it would not matter which isomer of the starting material (*cis*- or *trans*-4-methylcyclohexanol) was used as the radical precursor, and we did not in fact observe any differences between experiments in which the two different pure isomers were used as starting materials.



SCHEME 2

The value of E_a is higher than that reported for the parent cyclohexyl radical or for cyclohexyl derivatives, including the 6.9 kcal mol^{-1} found for 4-methylpiperidine nitroxyl.[5] However, the nitroxyl group again is thought to be planar[27] in contrast to the non-planar radical site in 4-MeHCH. This increase in the barrier upon disubstitution is in contrast to the results found for substituted cyclohexanes, which have barriers nearly the same as for cyclohexane itself.[28] For example, the value of $\Delta H^{\ddagger}$ for *cis*-1,4-dimethylcyclohexane was found to be 11.0 kcal mol^{-1} compared to 10.8 for cyclohexane. These results may mean that because of the disubstitution the geometry of the 4-MeHCH radical is constrained to be closer to cyclohexane than to cyclohexyl radical.

Finally, we were able to resolve further hyperfine splittings in the spectrum by observation of the centre line of the spectrum with low modulation amplitude, as shown in Figure 6. The computer simulation (Figure 6, bottom) required hyperfine splitting of 0.78 (2 H) and 0.39 G (3 H) plus the expected second-order splitting for two protons of 34.8 G,[29] with a first derivative peak-to-peak linewidth of 0.40 G. A sample of 4-methylcyclohexanol with the hydroxy-group deuteriated by refluxing with acidified D_2O (>90% deuteriation by ^1H n.m.r.) gave the same spectrum, showing that the hydroxy-proton was not involved Under the same experimental conditions we were not able to resolve any further splittings in the spectrum of the 1-HCH radical, in agreement with the observations of Corvaja *et al.*,[10] who stated that 1-HCH had broader lines in its spectrum than other 1-hydroxycycloalkyl radicals.

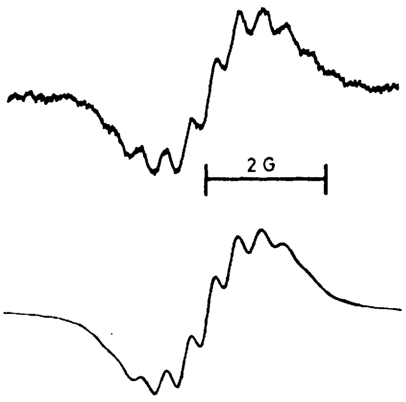


FIGURE 6 The centre line of the 4-MeHCH radical spectrum, run with expanded scale

Fessenden and his co-workers[2,30] observed a splitting of 0.71 G from two protons in the spectrum of the cyclohexyl radical which they assigned to the δ-protons on the basis that inversion of the radical at rates sufficiently fast to average the β-protons should also average the four γ-protons. However, we were not able to achieve a satisfactory fit of the spectrum with any hyperfine splitting from a set of four equivalent protons and this radical does not have two δ-protons. Therefore, we tentatively assign the splittings to two of the γ-protons and to a long-range interaction with the methyl protons.

1-*Hydroxy*-4-*t-butylcyclohexyl Radical*.—The spectrum of this radical was qualitatively different from the others in that no temperature-dependent conformational changes were observed. Because of this well known preference of the t-butyl group for the equatorial position we believe that the e.s.r. parameters reported for the 4-Bu^{t}HCH radical represent true limiting values for a ' frozen ' 1-hydroxycyclohexyl radical and it is gratifying to note that they are essentially the same as the ' low temperature ' values used in the kinetic analyses of the other radicals.

We conclude that the 1-hydroxycyclohexyl and 1-

hydroxy-4-methylcyclohexyl radicals have non-planar radical sites and that they invert between chair conformers through a higher energy intermediate that is most likely a twist-boat form.

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