J. CHEM. SOC. FARADAY TRANS., 1990, 86(19), 3237-3241

Cycloalkylmethyl Radicals

Part 7.—Electron Paramagnetic Resonance Characterisation of Axial and Equatorial Centres in Seven-membered Alicyclic Molecules

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The EPR spectra of cycloheptylmethyl, cyclohept-4-enylmethyl and 1,3-dioxacyclohept-5-enylmethyl radicals have been observed. The cycloheptylmethyl radical spectrum shows only a single, average conformation, but for the cycloheptene and dioxacycloheptene rings the $CH_2^{\bullet}$ group proved to be a useful probe of the conformations. The preferred conformation of the 1,3-dioxacycloheptene ring was found to depend on the type of substitution at C(2). For the 2-$CH_2^{\bullet}$ radical, twist-boat and chair conformers were observed with an Arrhenius activation barrier to inversion of 5 kcal mol^{-1}. For the 2-CH_3, 2-$CH_2^{\bullet}$ radical the main conformation was the twist-boat. For the 2-Ph, 2-$CH_2^{\bullet}$ radical the main conformation was the chair; the rotation of the $CH_2^{\bullet}$ group was found to be restricted by a barrier of *ca.* 7.5 kcal mol^{-1}, probably because of steric interaction from two *syn* axial hydrogens on C(4) and C(7).

The methylenyl group, $CH_2^{\bullet}$, when attached to an alicyclic ring, can act as a very useful 'spin probe' for the conformations populated by that molecule. EPR spectra of these transient radicals allow conformational analysis to be carried out, and, in favourable cases, the activation energies of the ring inversion or pseudorotation process can be determined.[1] This method has been successfully applied to six-membered rings.[2,3] and to some larger rings, particularly those with 9–15 C atoms.[4] In this paper we describe our results for seven-membered rings, including cycloheptane, cycloheptene and 1,3-dioxacyclohept-5-ene.

Experimental

EPR spectra were recorded on a Bruker ER 200D spectrometer operating at 9.2 GHz with 100 kHz modulation. Samples were degassed by several freeze–pump–thaw cycles, or by bubbling N_2 for *ca.* 10 min, sealed in Spectrosil tubes and irradiated in the cavity of the spectrometer with light from a 500 W super pressure Hg arc.

Bromomethylcycloheptane

A rapid stream of HBr gas was bubbled through methylenecycloheptane (2.0 g, 18 mmol) in light petroleum (16 cm^3) containing benzoyl peroxide (0.17 g) for 10 min. The solution was swept with nitrogen to remove unreacted HBr, diluted with light petroleum (40 cm^3), washed with 10% $NaHCO_3$ and dried (Na_2SO_4). Distillation gave 2.0 g (57%) of clear liquid b.p. 59 °C at 1.5 Torr.† GLC analysis showed the product to be contaminated with a minor amount of 1-bromo-1-methylcycloheptane and 1-bromo-2-methylcycloheptane. It was purified by preparative GLC on a 10% carbowax 20M column operated at 150 °C. M^+(obs) 190, 192; δ_H(80 MHz), 1.3–1.8(13H, bs), 3.8(2H, d, J = 7 Hz).

Bromomethyl-cyclohept-4-ene[9] and the bromomethyl-1,3-dioxa-cyclohept-5-enes were available from previous work.

Results and Discussion

The cycloalkylmethyl radicals were formed by bromine atom abstraction from the corresponding cycloalkylmethyl bromide with photochemically generated triethylsilyl or trimethyltin radicals in *tert*-butylbenzene at $T > ca.$ 200 K and in cyclopropane or n-propane at lower temperatures.[3]

The cycloheptylmethyl radical (1) was generated from the corresponding bromide and gave the EPR spectrum shown in fig. 1. This consisted of a double triplet from one β- and two α-hydrogens. The magnitude of $a(H_\beta)$, 3.76 mT at 140 K, and its negative temperature coefficient, indicate that (1) adopts an orientation about the C_β—$C_\alpha^{\bullet}$ bond in which H_β eclipses the p—orbital containing the unpaired electron. Most cycloalkylmethyl radicals show well resolved long-range hyperfine splitting (hfs)[2] but **1** did not; the inset in fig. 1 shows the poorly defined pentet obtained with second-derivative presentation. The spectra showed only a single species throughout the temperature range 110–300 K. The cycloheptane ring

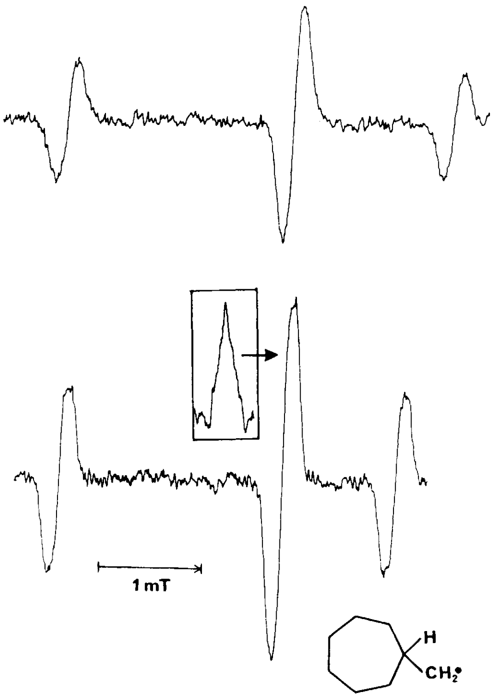

Fig. 1. Low-field half of the 9.2 GHz EPR spectrum of cycloheptylmethyl radicals (**1**): upper trace, 140 K; lower trace, 250 K. The inset shows the $M_\alpha = 0$, $M_\beta = -\frac{1}{2}$ line on the same scale but with second derivative presentation.

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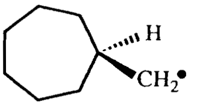
† 1 Torr = 101 325/760 Pa.

Table 1. EPR parameters for seven-membered cycloalkylmethyl radicals[a]

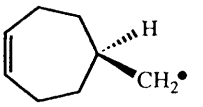
radical	T/K	hfs/mT $a(2H_\alpha)$	$a(H_\beta)$	other	ref.
1	140	2.21	3.76	—	4
2 major	140	2.22	3.67	0.09 (4H)	[b]
2 minor	140	2.22	4.69	—	[b]
3(ce)	140	2.30	2.55	—	[c]
3(tb)	140	2.30	2.30	—	[c]
5	161	2.32	—	0.28 (3H), 0.04 (4H)	[c]
7	239	1.98, 2.03	—	—	[c]
7	295	1.97	—	—	[c]

[a] All g factors 2.003 ± 0.001; [b] this work, see also ref. (9); [c] this work.

conformers are known to interconvert very rapidly by a pseudorotation process with a very low barrier (1.4 kcal mol^{-1},† according to force-field calculations[5]). Thus, dynamic effects in NMR spectra have not been observed[6] except for cycloheptanes with two pairs of geminal substituents.[7,8] It is most probable therefore that the EPR spectrum of (**1**) is the average over all populated ring conformations. In agreement with this, the β-hfs of (**1**) (table 1) is intermediate between that of equatorial radicals (2.8–3.2 mT) and that of axial radicals (3.8–4.1 mT).[4] The fact that the average spectrum is obtained at 110 K shows that the barrier to ring pseudorotation must be $\leqslant 2.7$ kcal mol^{-1}.



1



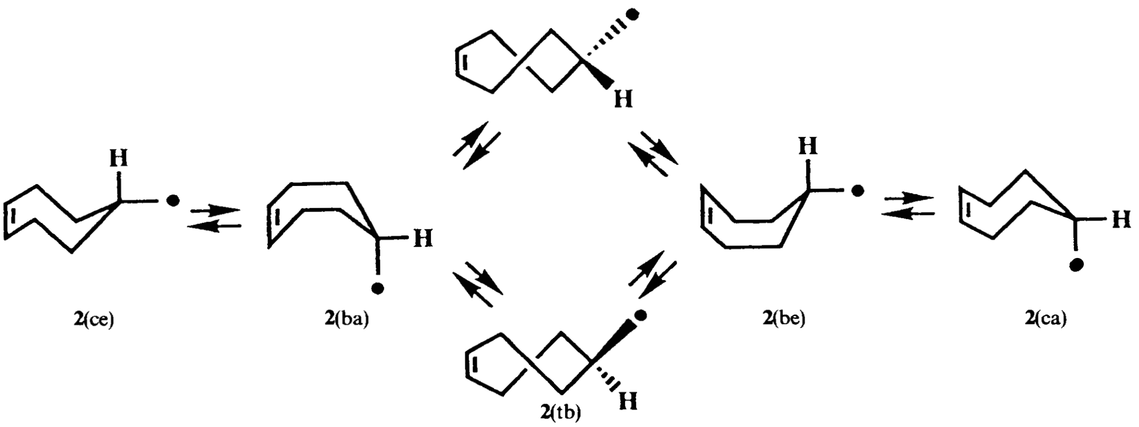
2

The EPR spectrum of cyclohept-4-enylmethyl radicals (**2**) has been reported previously.[9] Two main sets of signals were observed (table 1) but, under high resolution, the major component gave an indication[9] that it could consist of more than one conformation of (**2**). The main conformations of cycloheptene are the chair and twist-boat, but the boat may also be a minimum on the potential-energy surface.[6,10] The five possible conformations of (**2**) and their interconversion are shown in scheme 1. It is probable that the major spectrum with the smaller $a(H_\beta)$ consists of a superposition of the equatorial chair, **2**(ce), and the twist-boat, **2**(tb), conformations. The latter is expected to have a β-H hfs not much different from the equatorial value. The minor spectrum with the larger $a(H_\beta)$ value probably corresponds to the axial form **2**(ca) or **2**(ba) or possibly to a mixture of both.

Above *ca.* 240 K the spectra of **2** weaken and broaden, probably because ring inversion becomes important. The average spectrum could not be observed at higher temperatures, presumably because this radical simultaneously undergoes a transannular cyclisation to give the bicyclo[3.2.1]octan-2-yl radical. A weak spectrum of this latter radical was observed at 340 K.[9] We can estimate, however, that the activation energy for ring inversion in **2** must be $\geqslant 5.0$ kcal mol^{-1}. This compares favourably with the $\Delta G^\ddagger$ value of 5.0 kcal mol^{-1} which was determined by NMR for the inversion of cycloheptene itself.[11]

The EPR spectrum of 1,3-dioxacyclohept-5-enylmethyl radicals (**3**) is shown at three temperatures in fig. 2. In the spectrum at 150 K two different conformations with slightly different H_β hfs were resolved. As T was increased the spectra broadened, coalesced at *ca.* 190 K, and sharpened up to the single average spectrum at 210 K in which $a(H_\beta) = a(2H_\alpha)$ (table 1). For both low-T ring conformations $a(H_\beta)$ is lower than the free rotation average of *ca.* 2.7 mT so that the preferred orientation about the C_α—C_β bond has H_β in the nodal plane of the p orbital containing the unpaired electron (SOMO). The magnitude of $a(H_\beta)$ rules out axial conformations and hence it is probable that the 150 K spectrum shows a *ca.* 50 : 50 mixture of the chair equatorial conformer, **3**(ce), [analogous to **2**(ce), scheme 1] and the twist-boat conformer, **3**(tb), [analogous to **2**(tb), scheme 1]. We tentatively assign the spectrum with the larger H_β hfs to the **3**(ce) conformer (table 1) because models indicate that there is less steric hindrance to rotation about the C_β—$C_\alpha^\bullet$ bond in this conformation and hence the H_β hfs should be closest to the free-rotation limit. From the coalescence temperature and the difference in the $a(H_\beta)$ values the Arrhenius activation energy for interconversion of the conformers was found, by the usual method,[12] to be 5.0 kcal mol^{-1}. (Alternatively, the free energy of activation $\Delta G^\ddagger$ is calculated to be 4.7 kcal mol^{-1} at 190 K.)

2-Substituted derivatives of 1,3-dioxacyclohept-5-ene[13] and 1,3-dioxa-5,6-benzocycloheptene[14] have been studied by St.-Jacques and co-workers using ^1H and ^{13}C NMR spectroscopy. They found that the twist-boat and the chair equatorial were the most stable conformations, the balance being easily



Scheme 1.

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† 1 cal = 4.18 J.

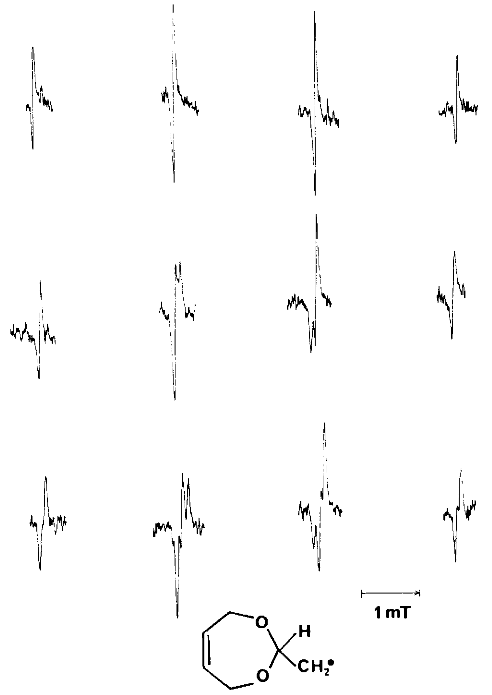
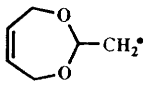


Fig. 2. 9.2 GHz EPR spectrum of 1,3-dioxacyclohept-5-enylmethyl radicals (**3**) in cyclopropane solution: top, 210 K; centre, 170 K; bottom 150 K.



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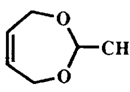

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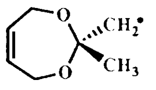

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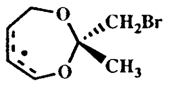

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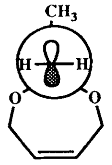
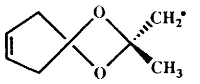
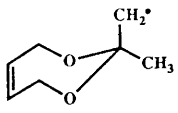


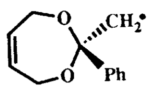
5(a)



5(tb)



5(ca)



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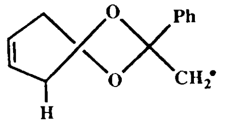


7(tb)

tipped in favour of one or the other by small changes in the substitution at C(2). For the 2-methyl derivative (**4**), which is structurally very similar to **3**, they found the most stable conformation to be the chair equatorial with a possible minor contribution from the twist-boat. The free energies of activation ($\Delta G^{\ddagger}$) for pseudorotation of the twist-boat conformers were <5, 6.8 and 5.2 kcal mol^{-1} for the parent (unsubstituted), 2,2-dimethyl- and 2-methoxy-derivatives, respectively. These activation parameters correspond to the pseudorotation that interconverts the twist-boat conformers. In the radical **3** the measured free-energy barrier corresponds to the ring-inversion process that interconverts the chair and twist-boat conformers *via* the boat (see scheme 1). Intuitively, we would have expected the ring-inversion process to have a higher energy barrier than the ring pseudorotation. The above comparison indicates, however, that, to within the combined experimental error, the two processes have roughly equal barriers for the 1,3-dioxacyclohept-5-ene ring.

The EPR spectrum of the 2-methyl substituted radical (**5**) is shown in fig. 3. This spectrum was essentially unchanged in the range 150–190 K, but quickly weakened in intensity at higher temperatures. The only radical that could be detected above this range was the allyl type **6**, formed by hydrogen abstraction from C(4) or C(7). The comparatively clear resolution in fig. 3 suggests that only one conformation makes a significant contribution. The large quartet hfs from the γ-Hs of the methyl group indicates[15] that the CH_3 group eclipses the SOMO, **5**(a), and that rotation about the $C_{\beta}-C_{\alpha}^{\bullet}$ bond must be slow. Further long-range splittings are resolved, in contrast to the spectra from **3**. The data are not sufficient to establish definitely the ring conformation, but the twist-boat, **5**(tb), or the chair axial, **5**(ca), are the main possibilities. In view of the contrast between the spectrum of **5** and that of the 2-phenyl radical (**7**) (see below) the twist-boat **5**(tb) seems most likely. For the structurally similar 2,2-dimethyl-1,3-dioxacycloheptene, NMR data suggested that the twist-boat was the preferred conformation.[13]

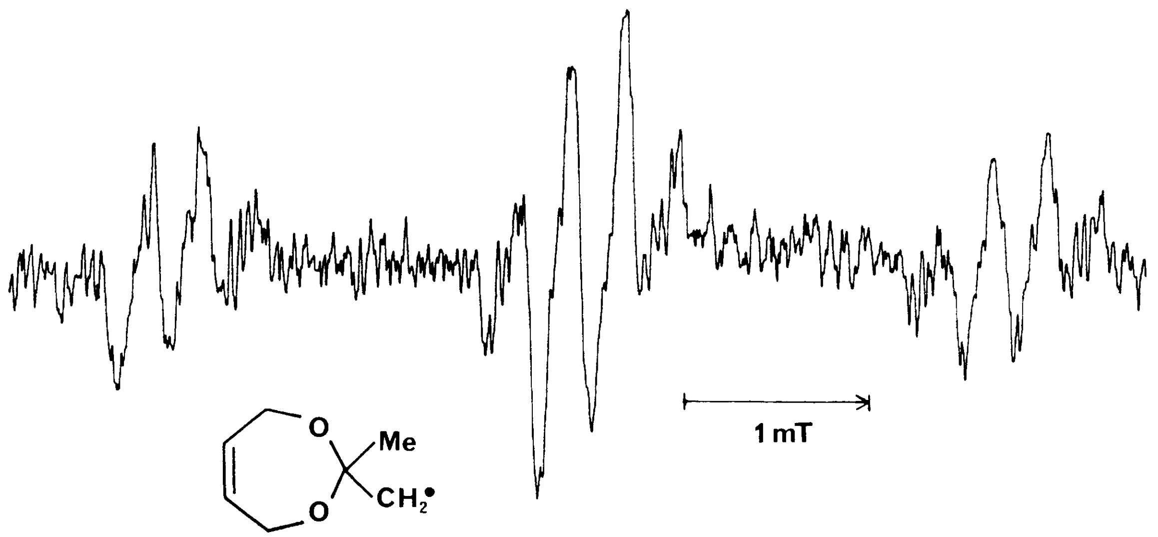


Fig. 3. 9.2 GHz EPR spectrum of 2-methyl-1,3-dioxacyclohept-5-enylmethyl radicals (**5**) in cyclopropane at 161 K.

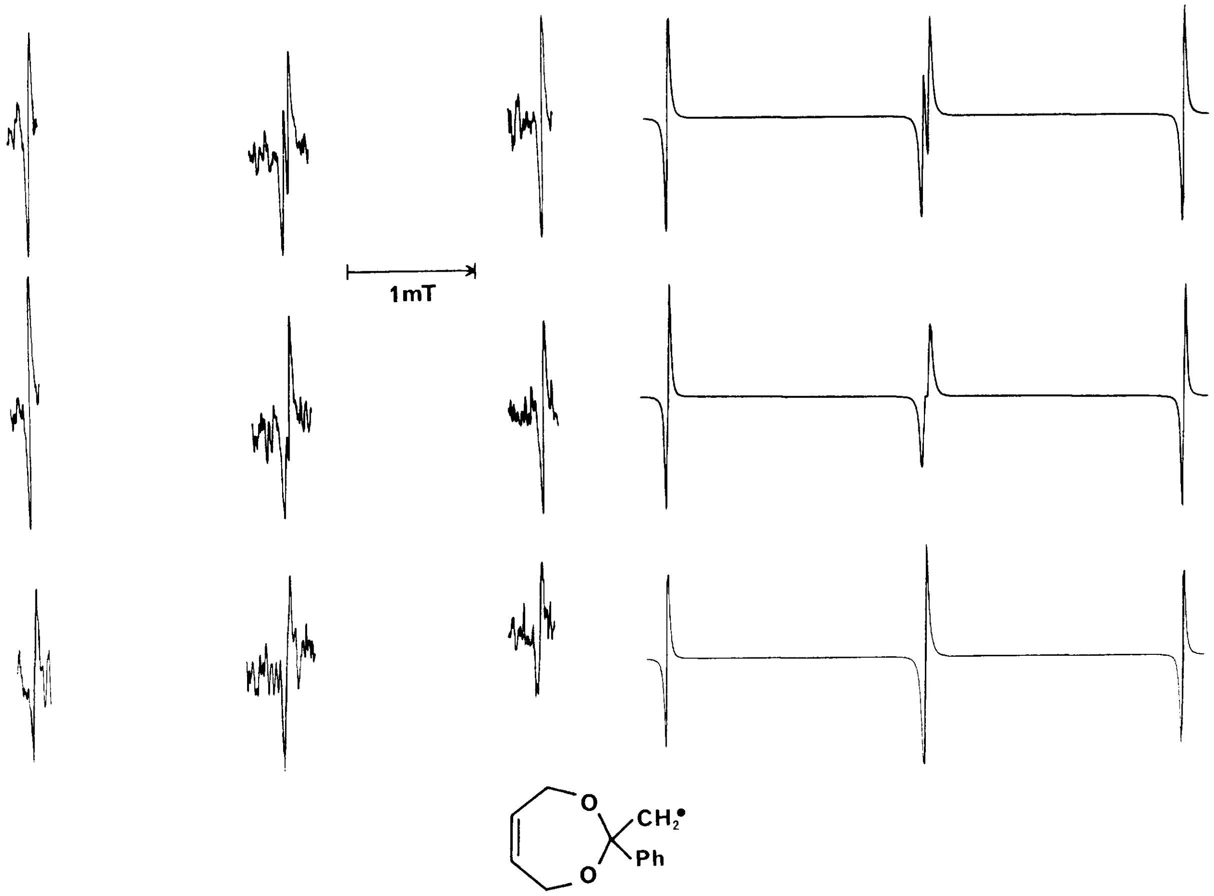
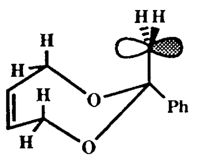


Fig. 4. 9.2 GHz EPR spectra of 2-phenyl-1,3-dioxacyclohept-5-enylmethyl radicals 7 in t-butylbenzene: left-hand side, experimental spectra at, from the top, 239, 262 and 295 K; right-hand side, simulations with, from the top, ($/10^6$ k s^{-1}), 0.6, 1.7 and 10.0.

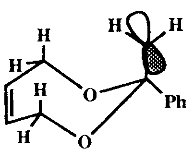
The EPR spectra from the 2-phenyl radical (7) at three temperatures are shown in fig. 4. Solubility problems prevented us from obtaining satisfactory spectra below *ca.* 200 K in cyclopropane. The spectra show only one conformation; the absence of long-range splittings suggests that in 7 the orientation about the C_β—$C_\alpha^•$ bond is different from that in 5, or the ring conformation is different, or both. The remarkable feature of these spectra is that at $T < ca.$ 250 K the two H_α show non-equivalent hfs. The exchange broadening was simulated using Heinzer's program,[16] assuming a two-jump model. The best-fit rate constants, *k*, are given in table 2. Linear regression gave the following Arrhenius parameters: $\log(A/\text{s}^{-1}) = 12.5 \pm 0.3$, $E_a = 7.4 \pm 0.3$ kcal mol^{-1} ($r^2 = 99.1\%$), [alternatively $\Delta G^‡$ (260 K) = 7.7 kcal mol^{-1}]. Obviously this is an exceptionally high barrier for a $CH_2^•$ rotor. In the twist-boat conformation 7(tb) the two H_α are non-equivalent irrespective of the preferred conformation about the C_β—C_α bond. Thus, the EPR spectra could correspond to 7(tb). However, in this conformation the large phenyl substituent experiences greater steric constraint from the hydrogens on C(7) than it would in the alternative chair conformation 7(ac). The $CH_2^•$ rotor experiences very little steric constraint in 7(tb) because it is impeded by only one *syn* axial hydrogen on C(4). There is therefore no reason to expect a large barrier to $CH_2^•$ rotation in 7(tb). By analogy with radical 5, which probably does prefer the twist-boat conformer, resolved long-range hfs would be expected from 7 if it too adopted the twist-boat conformation, whereas none were observed. It is most likely, therefore, that the 2-phenyl radical adopts the chair conformation with the $CH_2^•$ group axial, 7(ca), and the phenyl group equatorial. The large phenyl group experiences least steric strain in this conformation, which is consequently 'locked' on the EPR timescale. NMR studies indicated that both 1,3-dioxacycloheptenes[13] and 1,3-dioxa-5,6-benzocycloheptenes[14] with bulky 2-substituents such as t-butyl prefer the chair conformation. For radical 7 in the chair conformation there are two possible minimum energy orientations of the $CH_2^•$ group about the C_β—C_α bond. In the first of these, 7′(ac), the two α-H are always equivalent and therefore this is not consistent with the observed EPR spectrum. In 7(ac), however, where the phenyl substituent lies in the nodal plane of the SOMO, the two α-H can jump between two different sites so that this structure fits the observations. In 7(ac) the $CH_2^•$ rotor experiences steric interaction from two *syn* axial hydrogens on C(4) and C(7); a higher than normal barrier to rotation would therefore be expected.

Table 2. Best-fit rate constants for spectra in fig. 4.

T/K	228	239	250	262	273	284	295
$10^6k/\text{s}^{-1}$	0.2	0.6	1.0	1.7	3.0	6.0	10.0

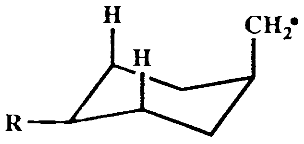


7′(ac)



7(ac)

The barriers to rotation of several radicals of the type $R_2CHCH_2^•$, including cycloalkylmethyls, have been determined from the variation in $a(H_\beta)$ with temperature[17,18] and



8(ca)

these are all <1 kcal mol^{-1}. However, a high barrier of *ca.* 6 kcal mol^{-1} was previously observed for $CH_2^{\bullet}$ rotation in chair axial cyclohexylmethyl radicals, **8**(ca), in which again steric hindrance from two *syn* axial hydrogens occurs.[19] In the case of **8**(ca) the barrier height was deduced from changes in long-range hfs with temperature, so that we now have two different approaches, both of which show that axial radicals with the $CH_2^{\bullet}$ group sterically hindered by two *syn* axial hydrogens have exceptionally high rotation barriers.

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Paper 0/01421D; *Received* 30*th March*, 1990