

Bridgehead Radicals

John C. Walton

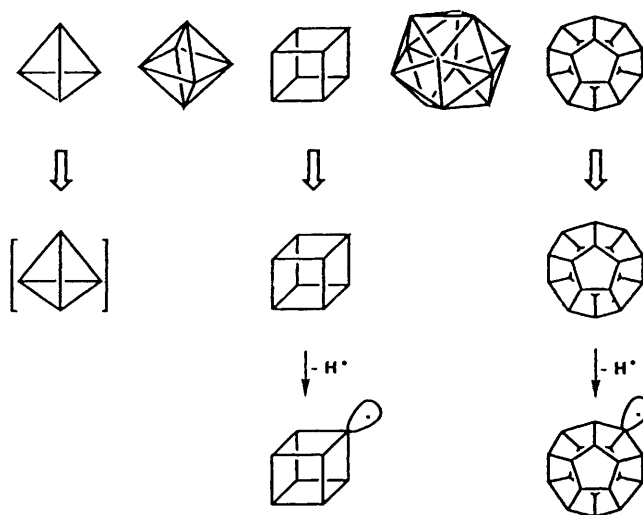
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1 Significance of Bridgehead Radicals

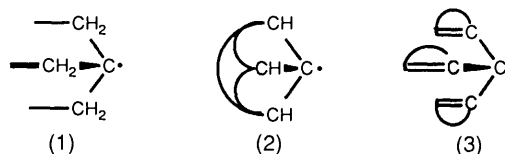
Bridgehead species necessarily have virtually rigid molecular frameworks, with bond angles and dihedral angles which are fixed and known with reasonable certainty. Molecules with such well defined structures are invaluable probes for testing and designing theories about orbital interactions, bond interactions, conformational effects on structure and reactivity, substituent effects, and a host of other geometry-dependent chemical propositions. Many bridgehead species, particularly highly strained ones, have very unusual structures with abnormal bond lengths and angles. They have provided a certain stimulus, notably to those synthetic chemists with well developed pioneering instincts, to invent new and original processes whereby they can be made. Special zest is added to this type of work if it has been predicted by a particular hypothesis that the species in question will be unstable or forbidden. In this way organic structures have been pushed to the limits of stability and reactivity and the amazing flexibility of the carbon atom in adapting itself to virtually any geometry, no matter how distorted, has been highlighted. A remarkable illustration of this type of progress is provided by the chemistry of organic species with structures based on the regular polyhedra. There are only five regular polyhedra, known collectively as the Platonic solids.¹ Three of these, the tetrahedron, the cube and the dodecahedron can serve as models for the structure of hydrocarbons C_nH_n (Scheme 1) in which every methine unit is a bridgehead. Removal of one hydrogen atom from these hydrocarbons yields the corresponding 'Platonic Radicals',² C_nH_{n-1} which are neutral bridgehead species of exceptional symmetry. The Platonic hydrocarbons have stimulated a phenomenal amount of creative research³ and attention has turned recently to the generation and observation of reactive intermediates derived from their basic structures. The parent tetrahedrane is unstable under normal laboratory conditions so it is unlikely that the tetrahedryl radical will be detected, although sterically shielded derivatives are not impossible. The cubyl radical is well characterized (*vide infra*) but rather little work has been done on the dodecahedryl radical and attempts to observe it spectroscopically have not succeeded.⁴

Bridgehead radicals can be distinguished by the number of β -hydrogens they contain. Three limiting types can be specified, firstly, the β -methylene type (1) in which the radical bridgehead is flanked exclusively by methylene groups; examples include the 1-adamantyl and bicyclo[2.2.2]oct-1-yl radicals. Secondly, the β -methine type (2) in which the radical centre is flanked by bridgehead methine groups; examples include the cubyl, dodecahedryl, and prismyl radicals. Thirdly, the β -quaternary type (3) in which the radical centre is flanked by quaternary carbon atoms; the triptycyl radical is an example of this type. Of course, a host of intermediate species exist with mixtures of adjacent methylene, methine, and quaternary groups, and a few bridgehead radicals with β -heteroatoms have also been studied.

Bridgehead radicals differ from other tertiary radicals in a number of important ways. It is known from spectroscopic and

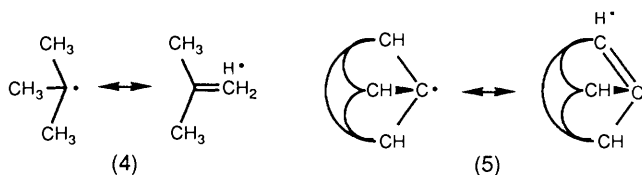


Scheme 1



theoretical work that the *t*-butyl radical is non-planar in its lowest energy configuration. However, the deviation from planarity is small and the barrier to inversion is very low so that for most chemical purposes *t*-butyl radicals behave as if they were planar. Bridgehead radicals are permanently pyramidal and far from planar, inversion is prevented, so their structures are 'unnatural', and they are expected to be destabilized, relative to corresponding acyclic tertiary radicals. The β -carbons of bridgehead radicals are 'tied back' by the cage structure so that the radical centre is sterically uncongested. Obviously, this factor will vary considerably, depending on the details of the structure, but in general bridgehead radicals will be more reactive as a consequence of this. The pyramidal configuration of the bridgehead radical centre ensures that the SOMO will be a σ -orbital with high *s*-character. The orientation of the SOMO with respect to other bonds in the radical differs therefore from that of normal, nearly planar alkyl radicals, and this will particularly influence unimolecular reactions such as decomposition and rearrangement. The marked *s*-character is expected to modify their redox properties relative to acyclic tertiary radicals, making them more nucleophilic in behaviour. The *t*-butyl radical is *ca.* 37 kJ mol⁻¹ more stable than the methyl radical⁵ and this is usually attributed to hyperconjugative and/or inductive effects, (4). In a bridgehead radical the orientation of the SOMO with respect to the orbitals of the β -C-H bonds is usually less favourable for overlap and the rigid structure prevents rotation to improve this. In addition, hyperconjugative structures will contain very strained bridgehead alkene units. For example, in β -methylene bridgehead radicals (1) hyperconjugation leads to an alkene with a single bridgehead. In the β -methine type (2) a double bridgehead structure (5) would be formed; β -quaternary radicals (3) are inherently incapable of

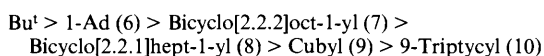
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hyperconjugation. Thus hyperconjugative structures will not make a significantly stabilizing contribution to the ground electronic state of any type of bridgehead radical.

2 Generation of Bridgehead Radicals

The factors mentioned above seemed to indicate that bridgehead radicals would be a lot more difficult to generate than *t*-butyl radicals. Much of the early work concentrated on comparing the rates of formation of series of bridgehead radicals, derived from various precursors, with the rate of formation of the *t*-butyl radical. Many bridgehead carbo-cations were known to form with extreme difficulty and therefore comparison of their reactivity with that of the corresponding radicals gave additional motivation to this work. There have been three main approaches to the generation of bridgehead radicals. First, particular precursors, designed to yield one specific radical, were carefully synthesized and the rates of radical formation were measured either absolutely, or relative to some standard such as *t*-butyl radicals. Much work was done with bridgehead perester thermolysis, bridgehead azoalkane thermolysis, and tin hydride reduction of bridgehead halides. Appropriate precursors for ketone photolysis, decarbonylation of acyl radicals, and fragmentation of alkoxy radicals were also examined. This work has been reviewed and evaluated by several authors.⁶ Most of these methods indicated that the rates of formation were in the following order:

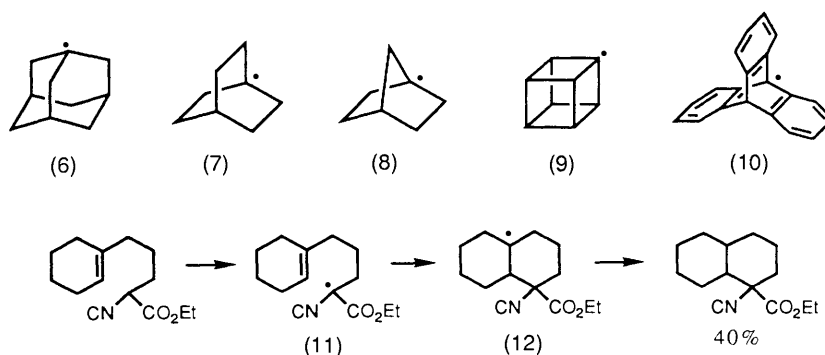


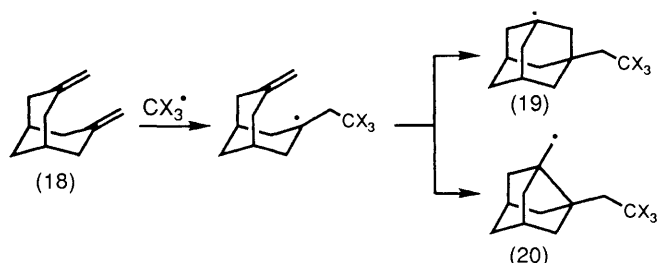
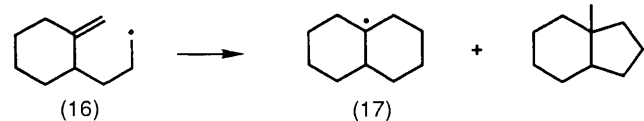
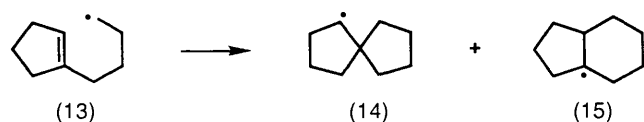
but the relative rates varied greatly depending on the mode of generation, presumably because the extent of development of radical character in the transition state differed from one method to another. Thus, a tendency for more strained radicals to be formed with greater difficulty was perceived, although there were exceptions, such as the cubyl radical. The method which showed the greatest change across the series was usually azoalkane thermolysis, but even this technique showed a range of values far smaller, by many orders of magnitude, than had been observed for the generation of carbo-cations in solvolysis experiments. Thus, although bridgehead radicals are more difficult to generate than *t*-butyl radicals, and are therefore probably thermodynamically less stable, they have a greater toleration for the pyramidal geometry than analogous carbo-cations. This trend is strongly influenced by the amount of strain in the structure.

Secondly, a few bridgehead radicals have been formed in ring closure reactions of alkenylbutyl and alkenylpropyl radicals.

For alkenyl radicals stabilized by electron-withdrawing substituents at the radical centre, *exo*-cyclization is reversible, which leads to thermodynamic control of the process, and consequently the products of *endo*-cyclization are favoured. Julia and Surzur⁷ studied the ring closure of several cyclohexenyl- and cyclopentenyl-alkyl radicals of this type, *e.g.* (11), and showed that the main product was formed *via* the bridgehead radical, (12). Beckwith and co-workers showed that, as expected, cyclization of the 4-cyclopentenylbutyl radical (13) occurred most rapidly in the *exo* mode to give the spiro intermediate (14), but that formation of the bridgehead radical (15) was only about a factor of five slower. In the case of the 3-(2-methylenecyclohexyl)propyl radical (16), where the pattern of substitution disfavors *exo*-cyclization, the bridgehead radical (17) was actually the major cyclized intermediate.⁸ In a particularly interesting study Yurchenko *et al.*⁹ showed that free radical addition of CCl_4 or CBr_4 to diene (18) gave adamantane derivatives, formed *via* bridgehead radical (19), and nor-adamantane derivatives, derived from (20), in the ratio (19):(20) = 1:3. In all these examples the bridgehead species formed quite easily, considering that *endo* cyclizations were involved, and any destabilization of the bridgehead radical seems to have played no part. The reasons for this are that none of the bridgehead radicals studied so far by this method contained much ring strain, but most importantly, that the transition state of intramolecular addition reactions is 'early' and unsymmetrical. That is, the development of bridgehead character in the product radical is not far advanced in the transition state so that its destabilization plays little part in controlling the cyclization.⁸ Obviously, this ring closure method has substantial untapped potential for the production of bridgehead radicals.

Thirdly, a great variety of bridgehead radicals have been produced by hydrogen abstraction from precursors containing bridgehead hydrogens. Species such as halogen atoms, *t*-butoxy radicals, aminyl radicals, aminium cation radicals, and polyhaloalkyl radicals have been employed. Usually bridgehead hydrogen abstraction takes place in competition with hydrogen abstraction from other sites in the molecule so that an immediate comparison of bridgehead reactivity with bridge reactivity is possible. In molecules like adamantane, bicyclo[2.2.2]octane, or bicyclo[3.2.2]nonane, with little or no ring strain, photochlorination¹⁰ and photobromination take place at about the same rate, on a per hydrogen basis, as in cyclohexane. The selectivity for bridgehead hydrogen, relative to secondary bridge hydrogen, is also similar to that of tertiary hydrogen relative to secondary hydrogen in open chain hydrocarbons. For molecules with more strain, hydrogen abstraction from the bridgehead becomes much more difficult. Bicyclo[2.2.1]heptane (norbornane) is by far the most studied. More than 95% of the reaction with chlorine atoms occurs at the C_2 bridges and only about 0.3% at the bridgehead. Larger radicals show a greater preference for abstraction from the bridgehead,¹¹ *e.g.* the proportion bridgehead products from norbornane increases as shown in Table 1. The factor controlling this selectivity is probably steric. The bridgehead hydrogens are more exposed and therefore larger radicals can approach them more easily than the C_2 -bridge hydrogens. Additional evidence in support of this





conclusion is displayed in Table 2. The extent of steric shielding of the hydrogens in the bridges increases as the size of the bicycloalkane decreases; at the same time, the bridgehead hydrogens become increasingly exposed. In line with this, the proportion of bridgehead hydrogen abstraction increases down the series and increases with the size of the attacking radical. The bridgehead radicals become more destabilized as the ring strain increases and this probably leads to a decrease in the rate of bridgehead H-abstraction, but this factor is evidently not so important as the steric effect. Bicyclo[1.1.1]pentane is a particularly interesting example. The hydrogens from adjacent bridges lie extremely close to one another so that an attacking radical can only approach them with difficulty in 'co-linear' fashion. The majority of abstraction occurs therefore at the exposed bridgehead hydrogens. Competitive experiments showed that the bridgehead hydrogens themselves are deactivated,¹³ as would be expected for such a strained radical.

3 Spectroscopic Studies of Bridgehead Radicals

A few bridgehead radicals have been studied by EPR spectroscopy and the data for most of these are displayed in Table 3. The EPR spectra showed that all these radicals had lifetimes in solution of the same order of magnitude as other transient alkyl radicals. Bicyclo[1.1.1]pent-1-yl (22), cubyl (9), and probably the others, decayed by bimolecular processes – almost certainly

Table 1 Proportion of bridgehead hydrogen abstraction from norbornane by various radicals^{10–12}

Radical	Bridgehead product (%)
Cl [•]	0.3
Bu ^t O [•]	1.3
Et ₂ NH ^{•+}	2.0
Pr ⁱ ₂ NH ^{•+}	4.0
(Me ₃ Si) ₂ N [•]	4.0

Table 2 Proportion of bridgehead hydrogen abstraction (%) from bicyclo[*n.m.1*]alkanes^{10–13}

Bicycloalkane	Cl [•]	Bu ^t O [•]	(Me ₃ Si) ₂ N [•]
	0.3	1.3	4.0
	< 5	~0	29
	62	> 75	—

exclusively combination rather than disproportionation. It is remarkable that radicals with as much strain as (22) and (9) could be directly observed, and this illustrates the difference in reactivity between bridgehead radicals and cations: the bridgehead cubyl and bicyclo[1.1.1]pent-1-yl carbo-cations cannot be observed by low-temperature NMR in super-ionizing media because they react or rearrange too rapidly. The *g*-factors are the same as those of other hydrocarbon radicals, but the hyperfine splittings (hfs) show noteworthy differences. In *t*-butyl radicals the β -hydrogen hfs is 22.9 G and this large value is attributed to hyperconjugation, *i.e.* the SOMO and the C _{β} –H bonds overlap effectively. All the bridgehead radicals have $a(H_{\beta})$ values much

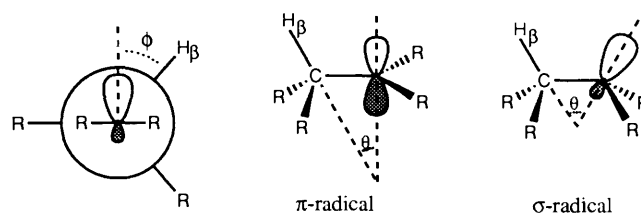


Table 3 EPR Parameters of bridgehead radicals

Radical	<i>g</i> -Factor	Hfs/G*	
		$a(H_{\beta})$	$a(\text{other})$
1-Adamantyl (6) ¹⁶	—	6.6(6H)	4.7(3H _{γ}), 3.1(3H _{δ}), 0.8(3H _{ϵ})
Bicyclo[2.2.2]oct-1-yl (7) ¹⁶	—	6.6(6H)	0.9(6H _{γ}), 2.7(1H _{br})
Quinuclidine ^{•+} (51) ²⁹	—	9.4(6H)	2.4(6H _{γ}), 14.3(H _{br}), 25.1(N)
Quinuclidin-4-yl (52) ²⁹	2.0029	7.0(6H)	1.8(N)
Bicyclo[2.2.1]hept-1-yl (8)	2.0026	9.8(H _{2,6^{exo}}) 2.4(2H ₇) 0.5(H _{2,6^{endo}}) 5.0(H _{5,6^{exo}}) 2.0(H _{5,6^{endo}})	1.23(H _{3,5^{exo}}), 2.5(H _{br}) 0.36(H _{3,5^{endo}})
Bicyclo[2.1.1]hex-1-yl (21)	2.0026	1.2(6H)	22.5(H _{br}), 0.84(H _{other})
Bicyclo[1.1.1]pent-1-yl (22) ¹³	2.0028	12.4(3H)	69.6(H _{br}) 8.2(3H), 6.3(H _{br})
Cubyl (9) ³³	2.0028		

* 1G = 0.1mT

lower in magnitude. Two factors contribute to this. First, for the bridgehead radicals of Table 3, the dihedral angle ϕ is non-zero (except for cubyl) and is fixed by the cage structure. In addition, the SOMO points away from the orbitals of the C_β -H bond, *i.e.* the angle θ between the axis of the SOMO and the orbitals of the C_β -H bond, is greater than in planar π -radicals. Thus orbital overlap is diminished in comparison with *t*-butyl radicals. Secondly, hyperconjugative structures are of high energy, and will not contribute to the ground state, because they contain bridgehead alkene units. Hence, even in the cubyl radical (9), where the dihedral angle ϕ is zero, and thus optimum for overlap, $a(H_\beta)$ is still small.

Most of the bridgehead radicals show large long-range hfs. Of particular interest are the splittings from bridgehead hydrogens elsewhere in the structures. In bicyclo[2.2.2]oct-1-yl (7), bicyclo[1.1.1]pent-1-yl (22), and cubyl (9) radicals the SOMO and the orbitals of the C-H_{br} bond are exactly in line and at an angle of 180°. In bicyclo[2.1.1]hex-1-yl (21) and bicyclo[2.2.1]hept-1-yl radicals (8) deviations from this ideal co-linearity are fairly small. Figure 1 shows a plot of the hfs from the bridgehead

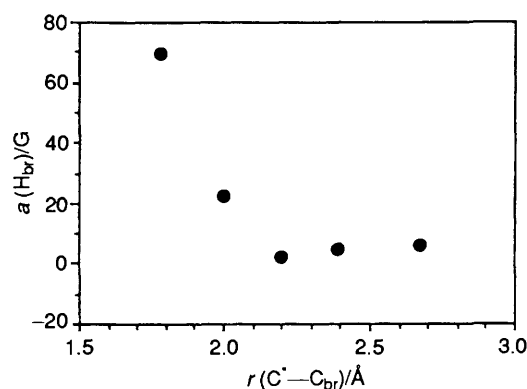


Figure 1

hydrogens, $a(H_{br})$, against the distance in space between the radical centre and the carbon atom to which the bridgehead hydrogen is bonded, $r[C^*-C_{br}]$, as calculated by the semi-empirical AM1 method. Radical (22) shows an enormous hfs from the γ -bridgehead hydrogen which is probably the result of reinforcement between through space (TS) and through bond (TB) effects. There is a steep decrease in $a(H_\beta)$ as $r[C^*-C_{br}]$ increases up to *ca.* 2.1 Å, followed by a gentle increase. It seems probable that the sharp decrease results from a rapid fall off in the TS effect with increasing distance; this effect being negligible much above 2.1 Å. Other evidence^{14,15} shows that TS effects are not important beyond this distance in radicals. It is known, however, that TS effects between pairs of double bonds, and in cations, are transmitted much further than this. The reason for the difference observed for radicals remains puzzling. The TB effect should also die away as the number of intervening bonds increases, but this will be strongly modified by the dihedral angles between the bonds. It appears that for the cubyl radical (9) the orbital arrangement permits significant spin density to reach the bridgehead δ -hydrogen so that the graph shows an apparent increase; more data are needed to disclose the true trends. The hfs from bridgehead hydrogens which are not co-linear with the SOMO, *e.g.* the γ -hydrogens in the adamantyl radical, are not aligned with those in Figure 1.

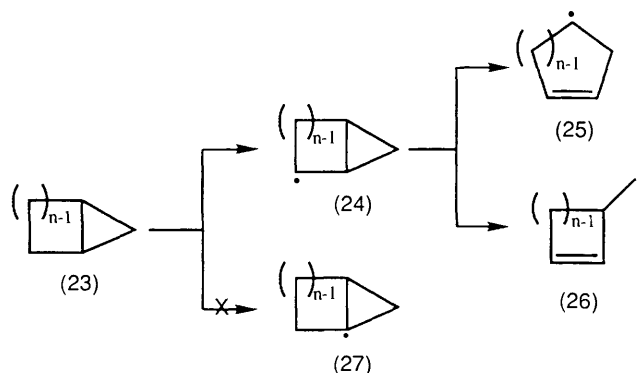
Comparison of the experimental H_β hfs with values calculated by the INDO method suggested that the radical centres in adamantyl (6) and bicyclo[2.2.2]oct-1-yl radicals (7) were pyramidal but slightly flattened out of the true tetrahedral geometry.¹⁶ The best experimental evidence about the geometry at bridgehead radical centres would come from the EPR ¹³C hfs. However, to date, $a(^{13}C_{br})$ has only been obtained for the adamantyl radical.¹⁷ The observed value, of $a(^{13}C_{br}) = 136.7$

G, showed that only slight relaxation towards planarity had occurred.

The first band in the photoelectron spectrum of the adamantyl radical (6) was observed on flash vacuum photolysis of 1-adamantyl nitrite.¹⁸ The adiabatic ionization energy, IE_a , of 6.21 eV was about as expected for a large tertiary radical. The sizeable difference between this and the vertical ionization energy, 6.36 eV, together with the band shape, indicated that a substantial geometrical reorganization took place upon ionization, *i.e.* that the 1-adamantyl carbo-cation is much more flattened than the radical.

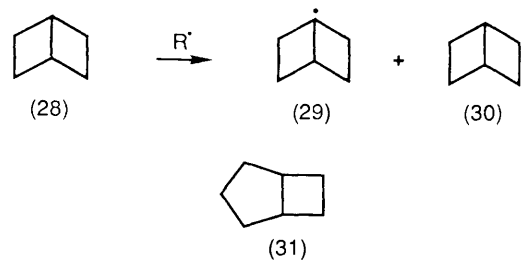
4 Homolytic Reactions at Bridgeheads

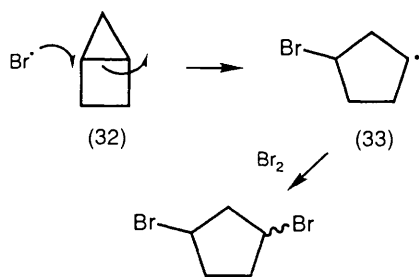
Hydrogen and halogen abstraction from bridgehead sites have been referred to above. For highly strained bicycloalkanes containing small rings, radicals such as $CCl_3\cdot$, $(Me_3Si)_2N\cdot$, and $ButO\cdot$, do not transfer hydrogen from the bridgehead, but attack at the bridge(s) of the larger ring.¹⁹ In the bicyclo[*n*.1.0]alkanes (23) attack normally occurs in the larger ring, adjacent to the bridgehead, to give a bicyclo[*n*.1.0]alk-2-yl radical (24) which rearranges rapidly by β -scission to either the cycloalk-3-enyl radical (25) or, for $n > 3$, to the cycloalkenylmethyl radical (26).



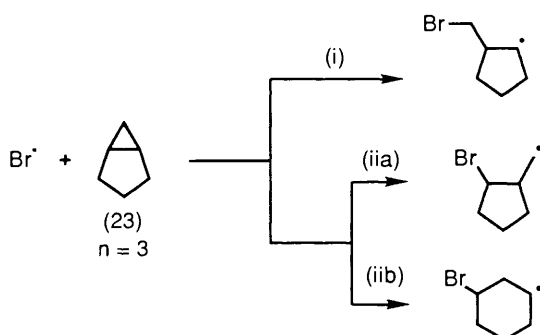
One consequence of this is that the smallest possible bridgehead radicals, (27) $n = 1, 2$ etc., in which the bridgehead forms part of a 3-membered ring, have never been generated, or studied experimentally. Interestingly, with bicyclo[2.2.0]hexane (28), hydrogen abstraction *does* take place at the bridgehead as well as at the methylene adjacent to the bridgehead,²⁰ and the bicyclo[2.2.0]hex-1-yl radical (29) was observed by EPR spectroscopy. This surprising selectivity does not denote any increased reactivity of the bridgehead hydrogens, but is probably a consequence of steric shielding of the bridge hydrogens. For the larger members of the bicyclo[*n*.2.0]alkane series, *e.g.* (31), abstraction did not take place at the bridgehead.

For bicycloalkanes where the bridgehead forms part of a 3-membered ring, a second reaction can occur. This is homolytic substitution (S_H2) (also known as displacement). Strangely, with only a few exceptions, the attacking radical must be a halogen atom for this reaction to supplant hydrogen abstraction. Bromine atoms attack both bicyclo[1.1.0]butane and bicyclo[2.1.0]pentane (32) exclusively at the bridgehead position, with cleavage of the inter-ring bond to give a 3-substituted cycloalkyl





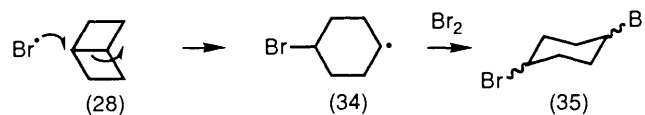
radical such as (33). For the higher homologues, attack occurred at the bridgehead and at the C_1 bridge, e.g. for (23, $n = 3$) reactions (i) and (ii) were in competition. The ratio of outer- to inter-ring bond scission *i.e.* [(i) + (iia)]/(iib) rose from zero for (23) $n = 1$ and $n = 2$ to 0.6 and 6 for $n = 3$ and $n = 4$, respectively. The ring strain released by inter-ring bond cleavage decreases sharply with increase in ring size and this accounts for the changeover. Chlorine atoms, and sometimes iodine atoms, behave similarly.



Recently, the scope of this type of process has increased substantially with the discovery that halogen atoms also take part in S_H2 reactions at bridgeheads in polycycloalkanes containing condensed cyclobutane rings. Photobromination of bicyclo[2.2.0]hexane (28) leads to the formation of *trans*- and *cis*-dibromocyclohexane (35) *via* the S_H2 process. The homolytic substitution reactions which [1.1.1]propellane (36) takes part in²¹ are even more remarkable. A variety of radicals such as MeCO^\cdot , CCl_3^\cdot , PhS^\cdot , PhSe^\cdot , ButO^\cdot , and halogen atoms cleave the unique inter-ring bond to give substituted bicyclo[1.1.1]hexanes (38). This is, of course, a new way of generating bridgehead radicals (37). It is evident that the bridgehead bicyclo[1.1.1]hexyl radical (37) also substitutes at the quaternary carbon atom of (36) because dimers (39) and even oligomers (40) have been isolated in some instances. Bicyclo[1.1.0]butane reacts in a similar way with several free radicals, but only halogen atoms cleave the inter-ring bond of bicyclo[2.1.0]pentane.

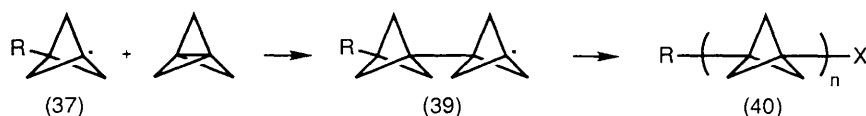
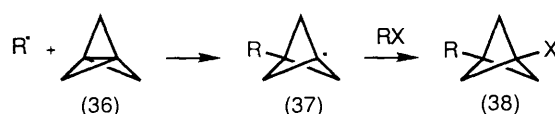
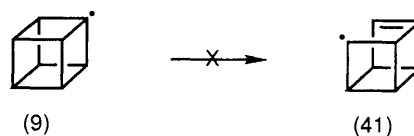
5 Reactions of Bridgehead Radicals

Bridgehead radicals will add to unsaturated molecules, abstract hydrogen or halogen, and take part in combination reactions in solution in the normal way *via* chain processes. In one of the most studied systems, bridgehead radicals were generated from



the corresponding perester, and allowed to abstract halogen from a mixture of CCl_4 and CCl_3Br . From the ratio of the bridgehead bromide to chloride produced in this way the relative rate constants for bromine and chlorine abstraction were determined for a series of bridgehead radicals.²² The difference in activation enthalpies $\Delta H_{\text{Cl}}^\ddagger - \Delta H_{\text{Br}}^\ddagger$ was found to increase from homocubyl (and cubyl) to norborn-1-yl to bicyclo[2.2.2]oct-1-yl to 1-adamantyl. This order agrees with expectation because the radical centres become progressively less exposed (*i.e.* front strain increases) along this series and ring strain decreases. The relative rates were also influenced by entropic factors but, in the appropriate temperature range, homocubyl (and cubyl) radicals were the *least* selective, and adamantyl radicals were the most selective of this series.

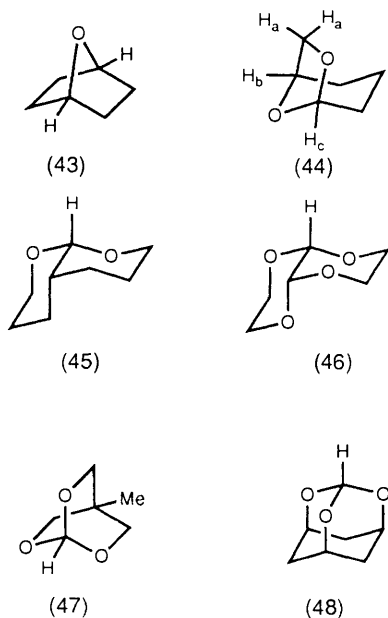
The main type of rearrangement open to bridgehead radicals is β -scission. For free radicals in general only species containing 3- or 4-membered rings readily undergo β -scission under normal solution phase conditions. Thus, facile rearrangements are not expected for adamantyl, bicyclo[2.2.2]oct-1-yl, norborn-1-yl *etc.* radicals, except in high temperature or high energy situations.¹⁸ It seems to be characteristic of bridgehead radicals that even highly strained ones rearrange with great reluctance. The cubyl radical, which contains *ca.* 14 kcal mol⁻¹ of strain per C—C bond (*cf.* cyclobutyl which contains *ca.* 6 kcal mol⁻¹ of strain per C—C bond) takes part in reactions at 100°C and above without rearrangement. This is easily explained because β -scission of (9) would produce the high energy bridgehead alkene (41). However, even bridgehead radicals with potentially strongly exothermic ring opening processes, such as bicyclo[1.1.1]pent-1-yl (22), bicyclo[2.1.1]hex-1-yl, or bicyclo[2.2.0]hex-1-yl (28), require forcing conditions for β -scission to occur. This is exemplified by (22), for which β -scission is of the well known cyclobutylmethyl to pent-1-enyl type, and should give the 3-methylene cyclobutyl radical (42). In fact rearranged products were not observed even at 150°C; the activation energy for β -scission being > 26 kcal mol⁻¹.^{13,23} This can be accounted for in stereoelectronic terms. The SOMO and the orbitals of the bond due to break, $C_\beta-C_\gamma$, are very poorly aligned for overlap; in addition a great deal of structural reorganization must take place during rearrangement. Kinetically, therefore, rearrangement is disfavoured.



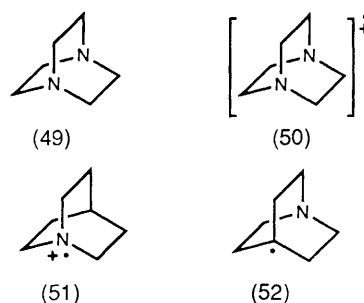
Because bridgehead radicals maintain their structural integrity so tenaciously, homolytic methods have frequently been employed for manipulation of functional groups at bridgeheads, and for other synthetic purposes. Several syntheses of the cubane skeleton, including the original method of Eaton and Cole,²⁴ produce cubane-1,4-dicarboxylic acids which may be converted into the hydrocarbon *via* thermal decomposition of the perester. In recent years the Barton decarboxylation *via* the *N*-hydroxypyridine-2-thione esters has replaced perester thermolysis as the method of choice. This procedure was used to make a variety of highly strained bridgehead derivatives,^{23,25} including bromo- and iodo-cubanes, -bicyclo[1.1.1]pentanes, and -bicyclo-[2.1.1]hexanes. Cubane was directly converted into mono- and poly-iodides by photochemical reaction with *t*-butyl hypiodite.²⁶ The photochemical reaction of bicyclo[1.1.1]pentane with oxalyl chloride gave the corresponding bridgehead acyl chloride.²⁷

6 Bridgehead Radicals Containing Heteroatoms

According to an interesting stereoelectronic hypothesis, the SOMO on C_a of a radical should interact (by conjugative electron delocalization) with the *p*-type lone pair of an adjacent oxygen.²⁸ Consequently, any weakening of the C–H bond adjacent to oxygen in the parent ether, and concomitant acceleration of hydrogen abstraction, would be at a maximum when the dihedral angle ϕ between the C–H bond and the *p*-type orbital on the oxygen(s) is 0° , and would be at a minimum when this angle is 90° . Hydrogen abstraction from a number of cyclic and bicyclic ethers was investigated in order to test this hypothesis.²⁸ The hydrogens adjacent to oxygen in tetrahydrofuran, for which $\phi = 30^\circ$, were found to be about 2900 times as reactive as those of cyclopentane, whereas hydrogen abstraction from (43), where $\phi = 90^\circ$ for the two bridgehead hydrogens adjacent to the oxygen, was undetectably slow. For (44) only the radical formed by abstraction of H_a ($\phi = 30^\circ$) was detected, with no trace of the radical which would be formed by loss of H_b ($\phi = 70^\circ$), nor even that which would be formed by loss of H_c though this has *two* neighbouring oxygens ($\phi = 50^\circ$ and 70°). The bridgehead hydrogens in (45) and (46) ($\phi = 30^\circ$ and 70°) were abstracted in preference to other hydrogens in these molecules. In (47) and (48) the bridgehead hydrogens adjacent to three oxygens ($\phi = 90^\circ, 90^\circ, 90^\circ$) were not abstracted. This, together with other evidence, showed that a pronounced stereoelectronic effect of the type outlined above is of crucial importance in hydrogen abstraction from ethers.



A series of aza- and di-azabicyclo[2.2.2]octyl species has been investigated. For diazabicyclo[2.2.2]octane itself (49), and its radical cation (50), experimental and theoretical evidence showed that there is a very strong stabilizing interaction between the nitrogen orbitals.^{15,29} The magnitudes of the EPR $a(H_{br})$ values for the mono-aza quinuclidine cation radical (51) and the quinuclidin-4-yl radical (52) (see Table 3) indicate however that while there is some TB coupling to the 4-position it is not particularly strong. Chemical studies revealed that (52) is formed only three times faster than the hydrocarbon radical (7), free-radical chlorination of (52–H) showed normal bridgehead reactivity, and electrochemical reduction of the bromide precursors of (52) and (7) showed that they have similar reduction potentials. It can be concluded that radicals (7), (51), and (52) are not stabilized by long-range electron delocalization. It is likely that (49) and (50) represent special cases in which electron delocalization, and hence stabilization, result from symmetry-induced degeneracy of the interacting orbitals.²⁹



7 Thermochemistry of Bridgehead Radicals

Thermochemical and kinetic data provide the best means of quantifying the stability and reactivity of free radicals and are extremely useful aids to mechanistic analysis and in the design of syntheses. The enthalpies of formation of bridgehead radicals, $\Delta H_f^\circ(R_{br}^\cdot)$, and the C–H_{br} bond dissociation energies of the corresponding hydrocarbons, $DH^\circ(R-H_{br})$, summarize and organize key facts. Leading information is thereby made available in a readily usable form which enables one radical to be meaningfully compared with another, and with other reactive intermediates. A start has been made in the collection of this type of data for bridgehead radicals, but so far theoretical predictions outnumber reliable experimental facts.

The heat of formation of the norbornyl radical (8) was derived from a study of the reaction of norbornyl iodide with hydrogen iodide.³⁰ Recent work on this type of iodination system has indicated that radical heats of formation and the corresponding C–H bond dissociation energies can only be obtained accurately if the individual rates of the reactions of each radical with HI are determined.⁵ For secondary and tertiary alkyl radicals this leads to an increase of *ca.* 3 kcal mol⁻¹ over previous $\Delta H_f^\circ(R^\cdot)$ and $DH^\circ(R-H)$ values. If we arbitrarily assume that a similar correction of the original results is needed for the norbornyl radical then the estimated ΔH_f° (norbornyl) and DH° (norbornyl–H) values become 35.6 and 99.7 kcal mol⁻¹ respectively.

In a different approach, the rates of abstraction of iodine by phenyl radicals from a series of alkyl iodides, including 1-iodoadamantane, 1-iodobicyclo[2.2.2]octane, and 1-iodobicyclo[2.2.1]heptane, were measured relative to the rate of bromine abstraction from bromotrichloromethane.³¹ The relative rates were corrected for polar effects by use of the Taft σ^* parameters. A linear correlation of these modified rate constants $[k_1/k_{Br}]_{cor}$ with the $DH^\circ(R-H)$ values of the corresponding hydrocarbons was obtained. The bond dissociation energies of the bridgehead compounds were derived by comparing their corrected relative rates with this correlation. If the most recent values⁵ of $DH^\circ(R-H)$ are used for this correlation it becomes:

Table 4 Thermochemical data for bridgehead and related radicals^a

Radical	$DH^0(\text{R-H})$ Exptl.	$DH^0(\text{R-H})$ AM1	$\Delta H_f(\text{R}^\cdot)$ Exptl.	$\Delta H_f(\text{R}^\cdot)$ AM1
Bu ^t	95.9 ^b	78.8	11.6 ^b	-2.7
Methyl	104.8 ^b		34.9 ^b	
Cyclopropyl	106.3	93.5		59.2
1-Adamantyl (6)	99.6 ^c	88.0	15.7 ^c	-7.3
1-Adamantyl (6)	97.0 ^d		13.3 ^d	
Bicyclooct-1-yl (7)	97.7 ^d	89.4	22.0 ^d	1.3
Bicyclohept-1-yl (8)	97.7 ^d	99.7	35.6 ^d	33.1
Bicyclohept-1-yl (8)	101.8 ^e		36.7 ^e	
Cubyl (9)	106.8 ^f	110.7	205.9 ^f	209.8
Bicyclo[1.1.0]but-1-yl (23, $n = 1$)		116.7		142.7
Bicyclo[2.1.0]pent-1-yl (23, $n = 2$)		109.7		103.4
Bicyclo[3.1.0]hex-1-yl (23, $n = 3$)		102.2		58.7
Bicyclo[2.2.0]hex-1-yl (28)		100.9		70.0
Bicyclo[3.2.0]hept-1-yl (31 ^g)		92.1		29.5
Bicyclo[1.1.1]hex-1-yl (22)		108.7		136.6
Bicyclo[2.1.1]hept-1-yl (21)		105.9		82.9

^a Data in kcal mol⁻¹. ^b From ref. 5. ^c From PES data, see ref. 18 and text. ^d From correlation of relative rates of iodine abstraction by Ph[·] radicals with DH^0 data, see ref. 31 and text. ^e From reaction of 1-iodonorbornane with HI, see ref. 30 and text. ^f From *ab initio* computed energy relative to t-butyl, see ref. 32 and text.

$$DH^0(\text{R-H})/\text{kcal mol}^{-1} = 96.0 - 8.021 \log[k_1/k_{\text{Br}}]_{\text{cor}}$$

with $r^2 = 0.975$; the thermochemical data estimated from this equation are given in Table 4.

From the difference in ionization energies of the t-butyl and 1-adamantyl radicals, and the known difference in hydride affinities of the corresponding cations, the bridgehead bond dissociation energy of adamantane was found to be 3.7 kcal mol⁻¹ greater than the tertiary C-H bond dissociation energy of isobutane.¹⁸ Using the most recent value for this latter quantity (95.9 kcal mol⁻¹)⁵ we find $DH^0(\text{Ad-H}) = 99.6$ kcal mol⁻¹.

Experimental data are not available for any highly strained bridgehead radicals. The closest approach we can make to this comes from *ab initio* calculations comparing the computed energy of cubyl with that of t-butyl radicals.³² Incorporation of the experimental enthalpies of formation of cubane, t-butyl, *etc.* gives: $DH^0(\text{cubyl-H}) = 106.8$ kcal mol⁻¹. Thermochemical parameters for a series of strained bridgehead and related radicals, computed using the semi-empirical AM1 approach, are also displayed in Table 4.

The two experimental $DH^0(\text{R-H})$ values for the norbornyl radical (8) are nearly in agreement; there is a greater discrepancy in the adamantyl data, but it is probably not beyond the combined experimental error. The $DH^0(\text{R-H})$ values increase through the series from radical (6) to radical (9) (ignoring the higher experimental value for adamantyl); this is in line with the increase in internal strain through this series, the increasing s -character of the orbitals, and the decrease in front strain. For radicals (6)–(8) the $DH^0(\text{R-H})$ values are all greater than that of isobutane, and less than that of methane, as would be expected. The 'experimental' C-H bond dissociation energy for cubane looks reasonable for such a strained molecule in that it is slightly greater than that of methane and comparable to that of cyclopropane. When Bu^tO[·] radicals abstracted hydrogen from a mixture of cubane and cyclopropane, both cyclopropyl and cubyl radicals were detected,³³ which indicates that their bond dissociation energies are not very different. Unfortunately, the AM1 calculated $DH^0(\text{R-H})$ values show large differences from the experimental values (including the well established experimental values for methane, isobutane, *etc.*). The computed results are probably least reliable for radicals containing 3- and 4-membered rings; the limitations of the semi-empirical methods for these species are well known. However, the trend of increasing $DH^0(\text{R-H})$ from radical (6) to (9) is reproduced by the calculations. The computed value for bicyclo[1.1.1]pent-1-yl (22) is greater than that of cyclopropyl; this agrees with experiment in that only cyclopropyl radicals were detected on hydro-

gen abstraction from a mixture of cyclopropane and bicyclo[1.1.1]pentane.¹³ The computations also predict very high bridgehead C-H bond dissociation energies in bicyclo[1.1.0]butane and bicyclo[2.1.0]pentane which is in line with expectation and suggests that these particular bridgehead radicals will be very difficult to generate and detect.

8 Conclusions

Bridgehead radicals are strongly pyramidal, much more so than acyclic tertiary radicals, yet they can be generated and observed with ease by the usual methods employed for free radicals. They do not disproportionate because this would produce highly strained bridgehead alkenes. Bridgehead radicals, even those with extremely high internal strain, either fail to rearrange, or do so reluctantly. Sometimes this is because β -scission would produce an anti-Bredt alkene, in other cases unfavourable stereoelectronic effects inhibit rearrangement. In general, bridgehead radicals take part in conventional abstraction and addition reactions, but are more reactive and less selective than t-butyl radicals. Internal strain and the degree of steric 'exposure' of the radical centre play important parts in governing the reactivity. The well defined geometries possessed by bridgehead radicals have made them ideal tools for testing theories about hyperconjugation, through-space and through-bond effects, stereoelectronic effects, *etc.* Although a great variety of bridgehead radical reactions have been examined, and some of these are synthetically useful, quantitative studies of their thermochemistry and stability are in their infancy. The same is true of spectroscopic studies leading to structural information such as the extent of pyramidality at the radical centre. These are conspicuous areas for profitable future research.

9 References and Notes

- None of the Kepler-Poinsot polyhedra such as the *stella octangula*, or other combinations of the basic Platonic structures, are applicable as models of organic structures.
- The name implies a self-contradictory character for these species!
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