Formation of Bicyclo[3.2.1]octane, Bicyclo[4.2.1]nonane, and Bicyclo[3.3.1]nonane by Transannular Radical Cyclisations

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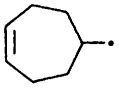
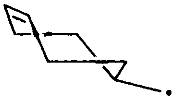
Cyclohept-4-enylmethyl radicals undergo transannular cyclisation to give bicyclo[3.2.1]octane; likewise, bicyclo[4.2.1]nonane and bicyclo[3.3.1]nonane are obtained from cyclo-oct-4-enylmethyl radicals.

The remarkable versatility and utility of the hex-5-enyl radical cyclisation, in various guises, has been demonstrated in many synthetic and mechanistic studies.[1—6] The reaction is very sensitive to stereoelectronic effects, which either impede or facilitate the approach by the radical centre from above one end of the double bond.[2] In a bicyclisation involving intramolecular addition to a ring double bond, as in structure (**1**), the conformations which the hexenyl chain can adopt are severely restricted by the ring geometry. Normally the side chain must be at least two carbon atoms long [(**1**; $n \geqslant 1$)] for significant bicyclisation to occur.

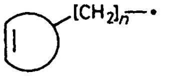
Thus, the cyclohexenylmethyl radical (**2**; R = H) fails to cyclise,[7] although cyclohexenylalkyl and related radicals with longer chains do;[2] as does the cyclopent-3-enylethyl radical (**3**).[8] The ability of cycloalkenylalkyl radicals (**1**) to cyclise depends critically on the preferred conformation(s) of the ring. We have now found two radicals of type (**1**) [cyclohept-4-enylmethyl (**4**) and cyclo-oct-4-enylmethyl (**5**)] with one-carbon-atom side chains [*i.e.* (**1**; $n = 0$)] which readily undergo transannular cyclisation.



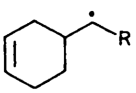
(**4a**)



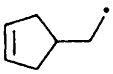
(**4b**)



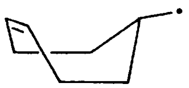
(**1**)



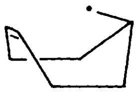
(**2**)



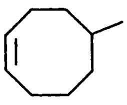
(**3**)



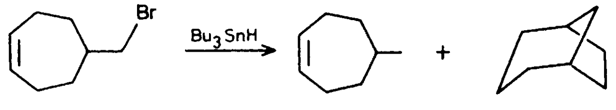
(**4c**)



(**4d**)



(5)



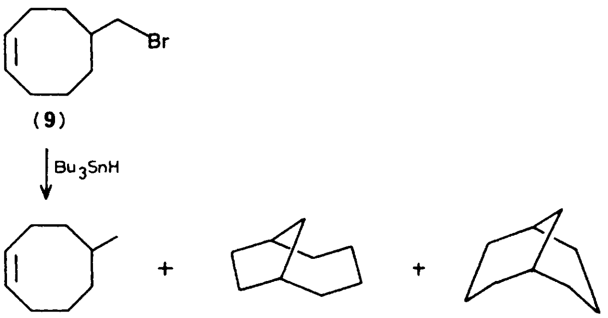
(6) (7) (8)

The radical (4) was generated by bromine abstraction from cyclohept-4-enylmethyl bromide (6) [bromide (6) (30 μl), hexamethylditin (50 μl), and di-t-butyl peroxide (30 μl) in t-butylbenzene (0.5 cm^3), irradiated with a 500 W Hg lamp] and its conformations were examined by e.s.r. spectroscopy. The spectrum showed the presence of a radical with a β-hydrogen hyperfine splitting (h.f.s.) of 3.37 mT at 200 K, which can be attributed[9] to conformer (4b) [or possibly to both (4b) and (4c)] which is expected[10] to be preferred. The spectrum also showed the presence of a second radical (*ca.* 25% of the equatorial species at 200 K) with a β-hydrogen h.f.s. of 4.29 mT at 200 K, which can be attributed to conformer (4d). Models show that there is little steric hindrance between H-4 and -5 and the $CH_2^{\cdot}$ group because both the double bond and the radical centre are planar.

In (4d) the radical centre is very well placed for an intramolecular addition to the double bond. The reduction of the bromide (6) with tri-n-butyltin hydride was therefore examined. The photochemically initiated reaction [bromide (6) (2.0 mM) with Bu_3SnH (4.8 mM) in t-butylbenzene] gave a 70% combined yield of 5-methylcycloheptene (7) and bicyclo[3.2.1]octane (8). The proportion of cyclised product was dependent on temperature and Bu_3SnH concentration, but (8) was the major product for equimolar reactant concentrations at temperatures above 85 °C, and an 80% yield of (8) was obtained at 190 °C in hexadecane as solvent.

Reduction of cyclo-oct-4-enylmethyl bromide (9) under similar conditions gave a mixture of 6-methylcyclo-octene (10) and two transannular cyclisation products, *i.e.* bicyclo-[4.2.1]nonane (11) and bicyclo[3.3.1]-nonane (12). As expected, (11) was the major product and, for example at 150 °C, the proportions were (10) : (11) : (12) 0.2 : 0.7 : 0.1.

The rates of the cyclisations were determined by the usual kinetic treatment for tri-n-butyltin hydride reductions.[11,12] The rate constants ($\times 10^{-5}/\mathrm{s}^{-1}$ at 25 °C) for cyclisation of (4), and cyclisations of (5) to bicyclo[4.2.1]nonyl and bicyclo-[3.3.1]nonyl radicals, were 1.0, 1.5, and 0.3, respectively. Thus (5) cyclises appreciably faster than (4), probably because of the greater ring strain in (8). Both radicals cyclise more slowly than the hex-5-enyl radical ($10^{-5}k/\mathrm{s}^{-1} = 2.5$ at 25 °C).[13] Several factors probably contribute to this, including the fact that for both (4) and (5) ring conformations from which cyclisation cannot occur, *e.g.* (4b), are significantly populated.



(9) (10) (11) (12)

The high rates of cyclisations, and the good yields of (8) and (11) which can be obtained, indicate that these reactions will be synthetically useful.

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