Formation of Tetrahydroindanes and Related Systems by Methods Involving Radical Ring Closure

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Treatment with tributylstannane of radical precursors formed by reductive alkylation of benzoic esters with suitable dihalides gives tetrahydroindanes (**2a**—**c**), (**4b**), (**4c**), (**5b**), and (**5c**) and related systems (**9**) and (**10**) in good yields.

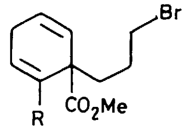
Synthetic applications of radical ring-closure processes, presaged in earlier reviews,[1,2] have recently attracted considerable attention particularly for the construction of fused carbocyclic systems.[3] We now describe intramolecular homolytic additions in some suitably substituted hex-5-enyl, *o*-but-3-enylphenyl, and 2-(but-3-enyl)vinyl radicals which provide an attractive route to tetrahydroindanes and related systems, and which reveal further mechanistic details of the cyclisation process.

Reductive alkylation under Birch conditions of methyl benzoate with the tetrahydropyranyl ether of 3-bromopropanol afforded the expected substitution product† from which the bromide (**1a**) was obtained by standard procedures. In subsequent experiments the bromide (**1a**) was more expeditiously prepared by monosubstitution of 1,3-dibromopropane. Although a small amount of dialkylation product was formed as a mixture of diastereoisomers, it was easily removed by chromatography. Heating of the bromide (**1a**) with a slight molar excess of tributylstannane (0.05 M) and azoisobutyronitrile (AIBN) (0.05 mol. equiv.) as initiator in benzene at 65 °C for 16 h afforded solely the bicyclic compound (**2a**) (88%), the assignment of structure for which rests on its conversion by standard procedures into the saturated acid (**6**), m.p. 39.5—40.5 °C, in good agreement with that (40—42 °C) previously reported for this *cis*-fused compound.[4]

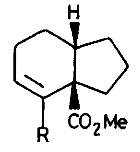
The bromides (**1b**) and (**1c**), prepared by reductive alkylation of *o*-toluic and *o*-anisic esters, when similarly treated with tributylstannane gave solely the cyclised products (**2b**) (79%) and (**2c**) (84%) respectively. Neither the uncyclised reduction product nor compounds arising by ring closure onto the more substituted double bond in the radicals (**11b**) and (**11c**) could be detected by high-field n.m.r. spectroscopy of the mixture or by various chromatographic techniques. Similar treatment of the methoxy bromide (**3c**), however, gave three cyclised products, one of which (**4c**), obtained in 48% relative yield, was formed by ring closure onto the less substituted double bond while the others, obtained in relative yields of 39 and 13%, were tentatively identified as the epimers of the compound (**5c**) arising from the alternative ring closure. Similarly, heating of the bromide (**3b**) with tributylstannane gave the compound (**4b**) (relative yield 32%) and two epimers of the compound (**5b**) in relative yields of 54 and 14%. The aryl iodide (**7**) and the vinyl bromide (**8**) each gave cyclised products (**9**) (85%) and (**10**) (50%) respectively when heated with tributylstannane.

These results conform to previously enunciated guidelines[2,5] for radical ring closures. Thus each of the radicals (**11a**—**c**), (**12b,c**), (**13**), and (**14**) undergoes regiospecific *exo*-cyclisation as expected on stereoelectronic grounds.[2,5] Although accurate rate constants cannot be calculated from the present data, the lower limit ($k \geqslant 5 \times 10^6$ s^{-1} at 65 °C), based on a minimum detection level of 5% for uncyclised reduction products[6] is considerably higher than that ($k = 9 \times 10^5$ s^{-1} at 65 °C)[7] reported for the hex-5-enyl radical presumably because of a favourable *gem*-dialkyl effect.[8] Preliminary experiments indicate that the radical containing a four-carbon alkyl chain, as expected,[1,2] undergoes ring closure much more slowly than its lower homologue (**11a**).

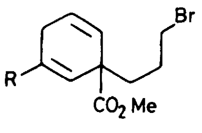
Radicals such as (**11**) and (**12**) are excellent substrates for determining the relative effects of substituents on reaction rates. Although accurate kinetic measurements have not yet been made, the regiospecific ring closure at the less substituted of the two positions available for 1,5-ring closure in each of the radicals (**11b**) and (**11c**) leading eventually to the products



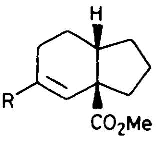
(**1**)



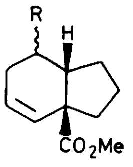
(**2**)



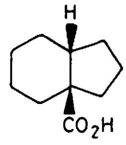
(**3**)



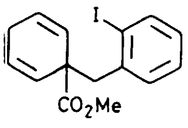
(**4**)



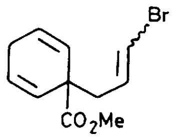
(**5**)



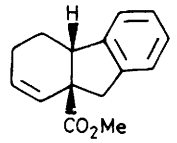
(**6**)



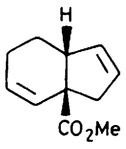
(**7**)



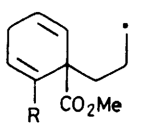
(**8**)



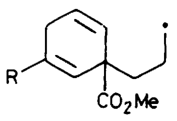
(**9**)



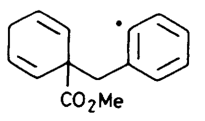
(**10**)



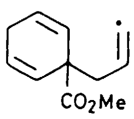
(**11**)



(**12**)



(**13**)



(**14**)

a; R = H
b; R = Me
c; R = OMe

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† New compounds were fully characterised by spectroscopic methods, elemental analysis and/or accurate mass measurement. Yields were not optimised.

(4b) and **(4c)** accords with the view that homolytic addition is retarded by substitution at the seat of attack.[2,5,9] Indeed, our failure to detect products arising from the alternative 1,5-ring closures in the radicals **(11b)** and **(11c)** suggests that the effect of substituents in these systems is more severe than it is for the simple hex-5-enyl system.[2,5,8]

Finally, it is noteworthy that the radicals **(12b)** and **(12c)** each undergo 1,5-ring closure at the two available positions at approximately equal rates. This accords with the view[2] that the transition state energy for intramolecular homolytic addition is only marginally affected by the stability of the product radical.

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