Radical and Electrophile Induced Cyclisations of Germacrene

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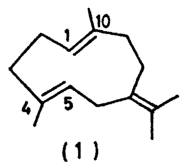
Summary Phenylthio- and trichloromethyl radicals cyclise the cyclodeca-1,5-diene system of germacrene to selinane derivatives; evidence is presented that cyclisations of germacrene are concerted reactions.

CATION-INDUCED cyclisations of cyclodeca-1,5-dienes and their derived oxides are now established as processes exhibiting high stereoselectivity.[1] We now show that radical induced cyclisations show similar stereoselectivity. Irradiation of germacrene (**1**) and benzenethiol in cyclohexane yields (**2**) (34%) [λ_{max} (EtOH) 216 (ϵ 10,900) and 257 nm (ϵ 8700); τ ($CDCl_3$) 9·08 (3H, d, *J* 7 Hz), 8·97 (3H, s), 8·40 (6H, s), 7·34 (1H, dd, $w_{\frac{1}{2}}$ 15 Hz)]. Successive reduction (Li–EtNH$_2$), and ozonolysis of (**2**) gave (**6**) identical with the major isomer formed on catalytic reduction of (**7**).[2] Germacrene (**1**) on being irradiated in the presence of diphenyl disulphide gave an adduct (**3**) (51%) λ_{max} (EtOH) 219 (ϵ 19,700) and 259 nm (ϵ 9500); τ ($CDCl_3$) 8·87 (3H, s), 8·78 (3H, s), 8·34 (3H, s), 8·20 (3H, s) 6·68 (1H, dt, $w_{\frac{1}{2}}$ 14 Hz)]. Hydrogenolysis of (**3**) (Li–EtNH$_2$) gave a mixture of hydrocarbons which, after ozonolysis, gave (**6**) and (**8**) in a 1:9 ratio. The above evidence establishes the structures proposed except for the stereochemistry of (**3**) at C-4 which is assigned by analogy to (**2**); the $w_{\frac{1}{2}}$ (0·8 Hz relative Me_4Si) value is consistent with the methyl being axial.[3]

Irradiation of (**1**) in carbon tetrachloride yielded (**4**) (32%) [τ($CDCl_3$) 8·74 (3H, s), 8·48 (3H, s), 8·38 (3H, s), 8·32 (3H, s), 6·94 (1H, dd, $w_{\frac{1}{2}}$ 14 Hz)]. Structure (**4**) is assigned on the basis of analogy and spectroscopic data and is supported by reduction (Li–NH$_3$) to a hydrocarbon mixture, the major components of which are (**9**) (in accord with the C-4 stereochemistry depicted) and (**10**), which can be ozonized to (**11**) [ν_{max} 1710 cm^{-1}, τ (Me_2CO) 9·22 (3H, d, *J* 6 Hz), 9·15 (3H, d, *J* 6 Hz), 9·05 (3H, s)].

Previously we[4] and others[5] have shown that reductive cyclisation of a carbonyl group on to an olefinic double bond is possible; replacement of carbonyl by oxiran also leads to cyclisation under reductive conditions since the oxide (**12**) on reaction with lithium in ethylamine generates a product (10%) the spectral properties of which are consistent with (**13**) [ν_{max} 3460 cm^{-1}, τ ($CDCl_3$) 9·13 (3H, d, *J* 6·5 Hz), 8·77 (3H, s), 8·35 (6H, s); *M* (mass spec.) 222].



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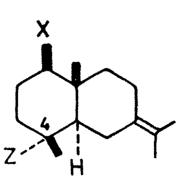
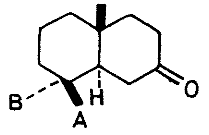
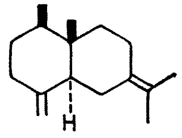


(2) X=SPh, Z=H
(3) X=Z=SPh
(4) X=CCl$_3$, Z=Cl
(5) X=H, Z=OH



(6) A=Me, B=H
(7) A, B= =CH$_2$
(8) A=H, B=Me



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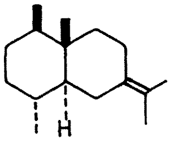

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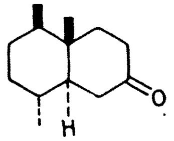

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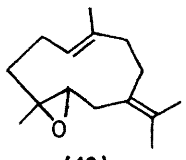

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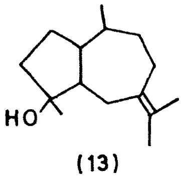

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In none of the cyclisations described were we able to obtain evidence for formation of stereoisomers other than those indicated.‡ The direction and stereoselectivity of the radical cyclisations are similar to those effected by electrophiles and we postulate that in both types of cyclisation

† Part of this work was carried out at the Chemistry Department, Imperial College, London S.W.7.
‡ The by-products were ill defined and most probably polymeric.

C–X and C–C bonding are synchronous. The most clearcut case is the acid-catalysed cyclisation of (**1**) to (**5**) (98%) which, when effected in D_2O, leads to incorporation of only one D atom.§ This selective attack of an electrophile at the 1,10-bond is to be contrasted with that of electrophilic peroxyacetic acid where the relative reactivity of the 4,5 and 1,10 bonds is 7 : 3; this ratio has been explained on the basis of relief of sp^2–sp^2 torsional strain.[6] Formation of a carbonium ion (or radical) at C-4 should be competitive with formation of such a centre at C-10 (indeed the former would be favoured if there is relief of strain relative to protonation of an unstrained bond). Our results then require that there is no other reaction pathway open to the C-4 carbonium ion other than stereospecific elimination of a proton to regenerate (**1**). This appears unlikely so we postulate that C–X and C-5–C-10 bonding are synchronous, generating a transition state which is geometrically like a *trans*-decalin; the alternative cyclisation (C-1 to C-4), which also leads to a tertiary cation, would have the geometrically less favoured bicyclo-[6,2,0]decane-like transition state, so accounting for the observed formation of decalin derivatives.

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