Novel Regioselectivity in Radical Addition to a Diene

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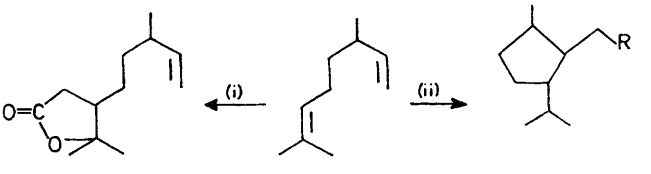
Summary With 3,7-dimethylocta-1,6-diene, carbon radicals $\cdot CH_2CO_2H$, $\cdot CH(COMe)_2$, and $\cdot CH(COMe)CO_2Et$ add at the 6,7-alkene bond, whilst $\cdot CH_2COR$(R = Me, Ph), $\cdot CH(CO_2Me)_2$, oxocyclopentyl, and oxocyclohexyl react at the 1,2-alkene; it is suggested that this behaviour is indicative of reversible addition at the 6,7 positions by the second group of radicals.

WE have found that addition to 3,7-dimethylocta-1,6-diene (**1**) of carbon radicals generated *in situ* by manganese(III) acetate oxidation,[1] shows discrimination between pathways (i) and (ii) depending on the nature of the radical. Radicals $\cdot CH_2CO_2H$, $\cdot CH(COMe)CO_2Et$, and $\cdot CH(COMe)_2$ lead to products of the type exemplified by (**2**). Radicals R = $\cdot CH_2COMe$, $\cdot CH(CO_2Me)_2$, $\cdot CH_2COPh$, oxocyclopentyl, and oxocyclohexyl, on the other hand, yield products of type (**3**). Radicals $\cdot CH_2CO_2H$ and $\cdot CH(COMe)_2$ gave also some product of type (**3**), but $\cdot CH(CO_2Me)_2$ and the ketone radicals gave no evidence of addition at the 6,7-alkene centre.

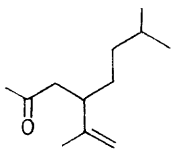
Also, as judged by loss of the brown Mn^{III} colour, reactions following pathway (i) are rapid, whilst reactions *via* (ii) are slower by a factor of *ca.* 100. Conditions have not been optimised, but yields, 25—53% based on diene, varied with the addend.



(2) (1) (3)

In competition for $\cdot CH_2COMe$, generated with $^1/_3$ equiv. of manganese(III) acetate, the diene (**1**), and the isomeric octenes, 2,6-dimethyloct-2-ene and 3,7-dimethyloct-1-ene, gave (**3**; R = CH_2COMe), (**4**), and (**5**) in a ratio 74:21:5

(g.l.c. analysis). Thus the alkene bond located at 6,7 is intrinsically more reactive than the 1,2 alkene.



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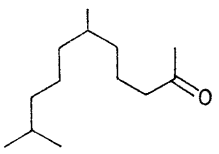

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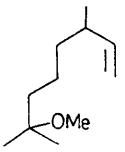

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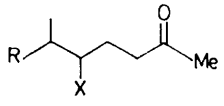

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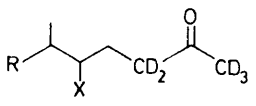


(8)

R = $Me_2C(OMe)[CH_2]_3$-

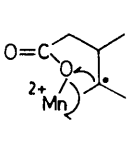
In competition for (**6**), acetone and [$^2H_6$]-acetone with manganese(III) acetate gave (**7**; X = H), (**7**; X = D), (**8**; X = H), and (**8**; X = D) in a ratio 8 : 1·5 : 1·5 : 1 (mass spectral analysis). Hence for acetone addition, radical formation *via* breaking the CH bond is, as expected, rate limiting.

The paradox is that radicals from malonic ester and the ketones apparently fail to show the expected addition at the 6,7-bond. However, in the examples of addition by pathway (i) reaction is completed by irreversible ring closure between the tertiary radical centre and a hydroxy group in the addend unit, *i.e.* leading to (**2**), or, from ethyl acetoacetate or pentane-2,4-dione to a dihydrofuran. Oxidative ring closure should be assisted by the ligand properties of these addends in co-ordinating Mn-ion, *e.g.* as in (**9**).

We infer that $\cdot CH(CO_2Me)_2$ or the ketone radicals do initially react at the 6,7-alkene bond, but, lacking the facility for rapid ring closure to the new radical centre, do so reversibly, *i.e.* with radical transfer to the 1,2-alkene bond followed by ring closure to the cyclopentane (**3**). Precedents[2] do not support reaction *via* a three-centre radical such as (**10**). There is, however, some evidence for reversible addition to an alkene bond,[3] and the present examples appear significantly to extend the phenomenon into the important area of synthesis.

Products both of type (**2**) and of type (**3**) derive ultimately from an intermediate tertiary radical, but reaction pathway (ii) offers the advantage of bonding of the addend to a primary carbon centre with the disadvantage of a larger negative entropy change. Thus the free energy of activation for routes (i) and (ii) may not be very different.

All products were characterised by mass spectral, n.m.r., and correct C and H analyses. Products (**3**) could also be independently synthesised utilising the previously observed[4] reaction of (**1**) with mercury(II) acetate in aqueous tetrahydrofuran. The derived HgOAc adduct (**11**) could be



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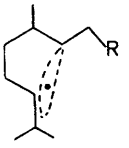

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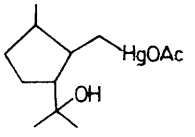

(11)

transformed: $-CH_2HgOAc \rightarrow -CH_2HgBr \rightarrow -CH_2I$, and the propan-2-ol substituent dehydrated: $-C(OH)Me_2 \rightarrow -C(Me)=CH_2$. Condensation with the sodio-derivative of ethyl oxocyclopentanecarboxylate, hydrolysis, and decarboxylation, or with the sodio derivative of dimethyl malonate, gave products which could be hydrogenated to give [**3**; R = $CH(CO_2Me)_2$ or 2-oxocyclopentyl]. The observed identities (mass and n.m.r. spectra and g.l.c.) of these products with those derived by Mn^{III} induced addition to (**1**) also establish the stereochemistry as *r*-1-Pr^i,*t*-2-CH_2R,*c*-3-Me, *cf.* ref. 4.

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