

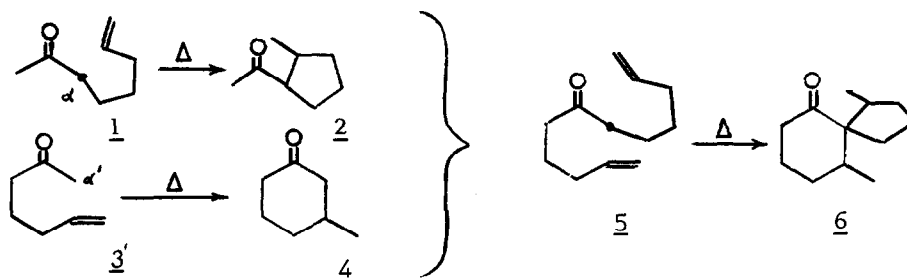
THE DOUBLE THERMAL CYCLISATION OF DIENONES.
A NEW SYNTHETIC ROUTE TO POLYCYCLIC COMPOUNDS.

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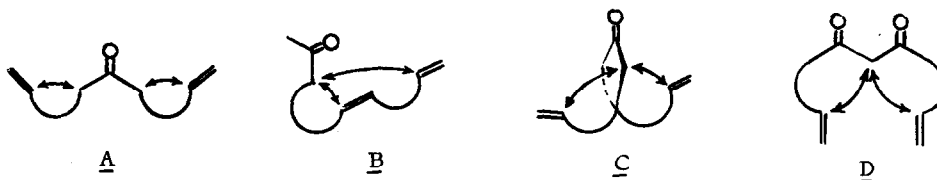
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The thermal cyclisation of ethylenic ketones has found widespread application in the synthesis of organic molecules (for recent reviews, see 1, 2), and involves either α -enolisation (i.e. the formed ring does not contain the carbonyl group, e.g. 1 \rightarrow 2) or α' -enolisation (i.e. the carbonyl group is part of the formed ring, e.g. 3 \rightarrow 4) (3a) or each consecutively as in the sole reported case of a "double cyclisation" reaction (3b) (5 \rightarrow 6).



A challenging task in every organic synthesis being to reduce the number of steps as far as possible, the present communication demonstrates the versatility of "multiple thermal" cyclisation in the rapid construction of polycyclic compounds. Our attention has been focussed in the first instance on the four following types of skeleton :

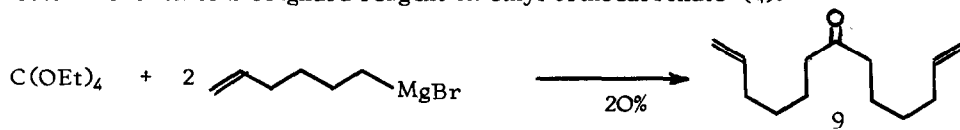


(The double arrows indicate the expected ring closures via the corresponding enol forms)

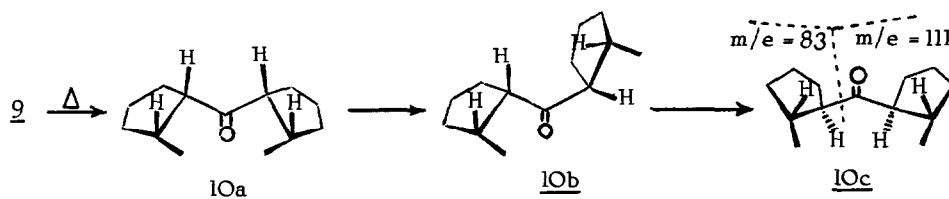
A being a simple example to test the practicability of the method, B a potential precursor of fused bicyclic ketones, C representing an attractive starting point to propellanes and D depicting a case of spiroannellation.

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—The symmetrical trideca-1,12-diene-7-one 9 has been synthesized in one step by the classical reaction of a Grignard reagent on ethyl orthocarbonate (4).

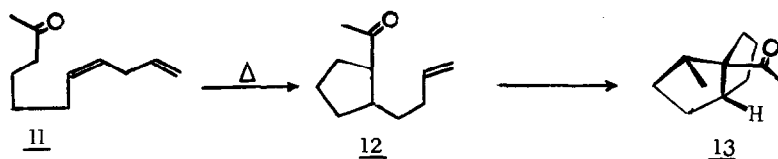


Upon heating in the vapour phase (370° /3 hrs) ketone 9 is converted into three components 10a, 10b and 10c, the two former being completely transformed by further heating into 10c (as shown by g.l.c., Yield : 90%). This latter compound, was indeed assigned the trans-trans structure 10c from the following data : IR 1710 cm^{-1} ; NMR one methyl doublet at 0.98 ppm (J 6 cps, two chemically equivalent methyl groups) (the methyl doublets of cis- and trans-2-acetyl-methylcyclopentane are respectively centered at 0.81 and 1.01 ppm (5)) ; Mass spectrum at 7 ev : only three peaks : $m/e = 194 (M^+)$, 111 and 83.



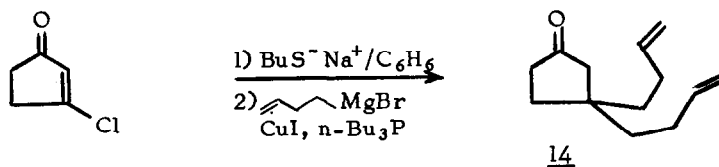
Compound 10c results from the kinetically formed cis-cis product 10a by the double (not unexpected) epimerisation through enolisation on each side of the carbonyl group.

—Undeca-7,10 diene-2-one 11, bearing two unconjugated double bonds on the same side of the carbonyl group, was obtained as a mixture of the cis/trans isomers (in which the cis form predominates) by reaction of the Wittig reagent derived from 4-bromobutene with 6-oxo-heptanal.

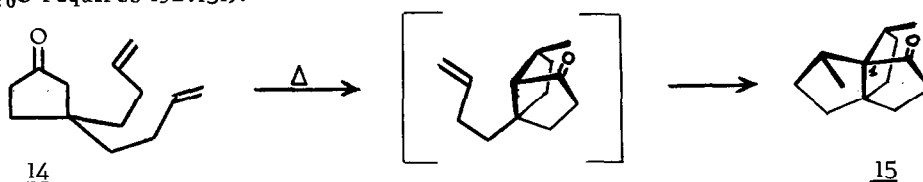


Dienone 11 upon heating in the vapour phase (335° /60hrs) gave a mixture of two components (Yield : 66%). One of them is the monocyclisation product 12 (1/4) : IR $1715, 1650, 990$ and 910 cm^{-1} ; NMR δ ppm 2.05 (s, 3H), 4.80 to 5.50 (m, 3H). The second one [IR 1715 cm^{-1} ; NMR δ ppm : 0.88 (d, J 6.5 cps, 3H), 2.03 (s, 3H), no olefinic protons] is the double cyclisation product : cis-3a-acetyl-3-methyl-cis-perhydropentalene 13 (3/4).

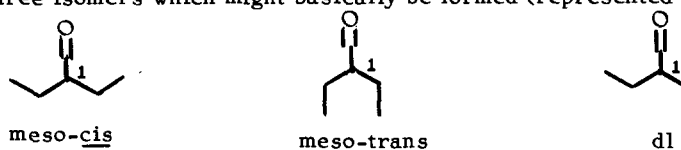
— In order to test the possibility of reaching the propellane system by double thermocyclisation, 3,3-di (but-3'-enyl) cyclopentanone 14 seemed to be a well-suited precursor and has been synthesized in a straightforward manner, the last step involving a modification of Posner's procedure (6) :



On heating ketone 14 as a 10% solution in decalin (sealed tube, 335°/2hrs) one main product has been obtained (50% after isolation by preparative g.l.c.) which showed the following spectroscopic features : IR 1730 cm^{-1} ; NMR δ ppm : 0.95 (d, J 6 cps, 6H, two chemically equivalent methyl groups) ; Mass spectral accurate mass M = 192.150 ($\text{C}_{13}\text{H}_{20}\text{O}$ requires 192.151).

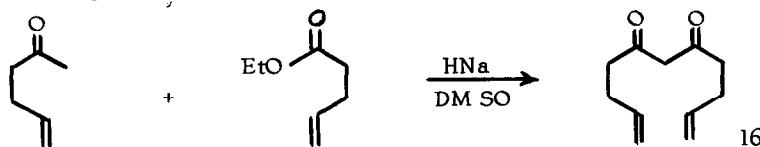


Among the three isomers which might basically be formed (represented in Newman projection) :

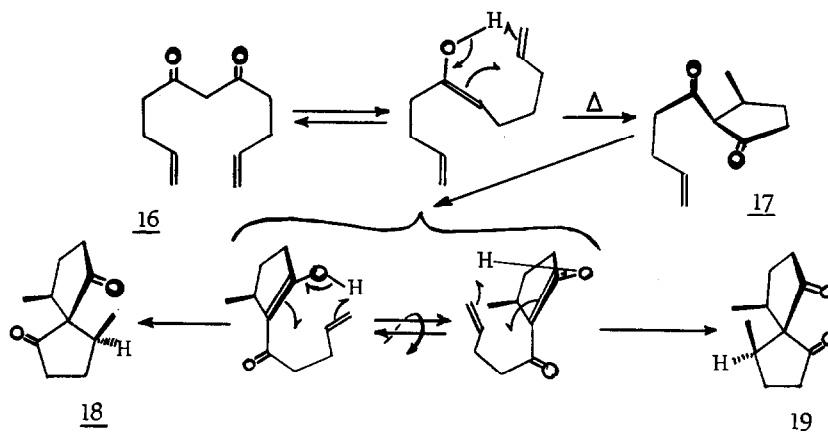


the dl form can be ruled out on the basis of NMR evidence : no splitting of the methyl doublet occurs with any change of solvent or by LIS experiments. The meso-trans structure is very unlikely owing to the cis stereospecificity always observed in five-membered ring formation by thermal cyclisation of ϵ -ethylenic ketones (5,7). It follows that the double cyclisation product can be reasonably assigned the meso-cis structure : 8R,9S-dimethyl [3,3,3]propellan-2-one 15.

— Methods leading to spiro- β -diones are sparse (8,9,10). The "double cyclisation" reaction was felt to be a good way to such structures. Undeca-1,10-diene-5,7-dione 16 has therefore been synthesized and Bloomfield's procedure (11) has been used :



After purification via its cuprous chelate, dienedione 16 was thermolysed (330°/48 hrs, vapour phase) to give a mixture of three main products (Yield : 40%) 1:1:2 respectively . To the first one has been ascribed structure 17 : IR 3080, 1730, 1710, 1670, 1645, 990 and 910 cm^{-1} ; NMR δ ppm : 1.45 (d, J 6 cps, 3H), 4.90 to 6.10 (m, 3H) ; Mass spectral accurate mass : 180.115 ($\text{C}_{11}\text{H}_{16}\text{O}_2$ requires 180.115). To the two others have



been ascribed the double cyclisation structures **18** and **19**. Effectively, the cyclisation of **17** can proceed from the two conformations of the ethylenic side-chain in the transition state (12). One of them leads to the symmetrical 4S,9S-dimethyl-spiro [4,4]nonane-1,6-dione **18** [δ ppm (CDCl₃) 1.05 (d, J 6 cps, 6H); (C₆H₆) 0.88 (d, J 6 cps, 6H), no olefinic protons] which exhibits two chemically equivalent methyl groups. The other conformation leads to the unsymmetrical 4R,9S-dimethyl-spiro [4,4]nonane-1,6-dione **19** which shows in NMR two methyl doublets: δ ppm (CDCl₃): 1.05 (d, J 6 cps, 3H) and 1.14 (d, J 6 cps, 3H); (C₆H₆): 0.74 (d, J 6 cps, 3H) and 0.83 (d, J 6 cps, 3H); no olefinic protons.

These examples and especially the two last ones show clearly how "double thermal cyclisation" reactions can provide a new approach to the problem of building up various polycyclic compounds.

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* NMR spectra were run in CCl₄ unless otherwise stated; d, doublet; m, multiplet.