**Tetrahedron Letters No.7, pp. 385-389, 1965. Pergamon Press Ltd.
Printed in Great Britain.**

THERMAL VALENCE ISOMERIZATIONS: STEREOCHEMISTRY OF THE 2,4,6-OCTATRIENE TO 5,6-DIMETHYL-1,3-CYCLOHEXADIENE RING CLOSURE

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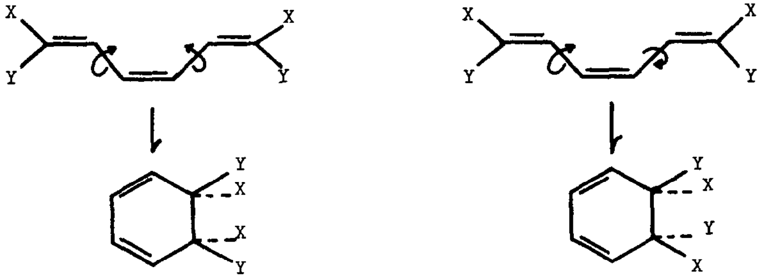
(Received 16 November 1964; in revised form 21 December 1964)

Thermal valence isomerization of conjugated trienes having a central cis double bond to give cyclohexadienes is a well established reaction (1). Most of the known examples involve medium ring trienes, and few provide complete characterization of both valence isomers. Aside from a few tantalizing fragments of information (2), which are more suggestive than definitive, the stereochemistry of this valence isomerization is unknown.

FIG. I. POSSIBLE STEREOPATHS

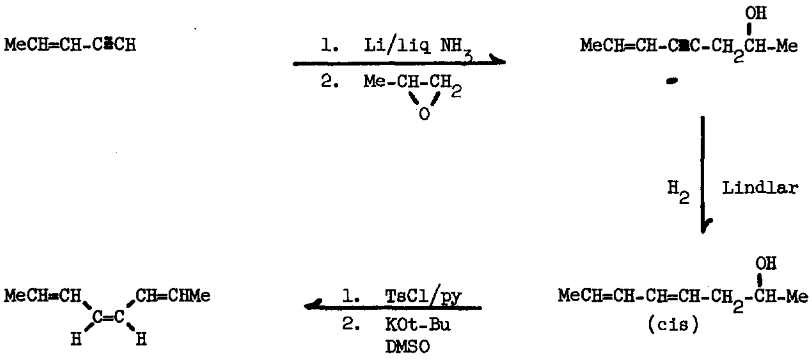


cis trans

Havinga (3) has suggested that stereoelectronic considerations outweigh steric factors and the cis ring closure is preferred. Experimental verification of this suggestion will be presented in this paper (4).

Starting with the known cis- and trans-3-penten-1-ynes (5), we have prepared samples of trans-2,cis-4,trans-6-octatriene (I), cis-2,cis-4, trans-6-octatriene (II) and cis-2,cis-4,cis-6-octatriene (III) via the route of Scheme A. Selectivity in semihydrogenation here is good, about 80% of the product having the desired cis double bond. The elimination reaction gives in each case a mixture of cis and trans isomers for the new double bond. From the tosylate of trans-2,cis-4-octadienol-7 there was obtained approximately 60% I and 40% II, while the cis,cis-dienol gave about 80% II and 20% III. These mixtures were separated by preparative gas chromatography using a Carbowax 20M column.

SCHEME A



The key isomer (I) was obtained in about 95% purity. It was identified by its spectral properties as well as its mode of synthesis (*). It has λ_{max} 255 (33,000), 267 (41,000) and 277 (30,000). The n.m.r. spectrum of the 4,5-dideuterio analog of I showed the AB part of an ABX_3 pattern for the vinyl protons, $\delta_x = 1.76$ ppm., $\delta_B = 5.58$ ppm., $\delta_A = 6.40$ ppm., $J_{BX} = 6.8$ cps. and $J_{AB} = 15$ cps. Both terminal double bonds are thus unequivocally shown to be trans. Both the chemistry (ring closure) and the u.v. spectrum differentiate this from the all trans isomer. II, λ_{max} 257 (32,000), 265 (38,600), 276 (29,200) and III, λ_{max} 258 (32,600),

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(*) Satisfactory analyses for all of the new compounds reported here have been obtained.

268 (35,000), 277 (25,200) were identified by a similar combination of spectral properties and method of synthesis. II is also identified cleanly by its presence as a common constituent in both synthesis products.

A 0.67 M solution of I in pentane was heated in a sealed tube at 132°. Rearrangement gave a single product, λ_{max} 261 (4100), whose n.m.r. spectrum showed a singlet (olefinic proton, 4H) at 5.88 ppm., the A part of an AXY_3 pattern (allylic proton, 2H, $J_{AX} = 3$ cps., $J_{AY} = 6$ cps.) at 2.42 ppm., and a doublet (methyl, 6H, $J_{AY} = 6$ cps.) at 0.97 ppm. Ozonolysis followed by peroxide oxidation produced meso-2,3-dimethylsuccinic acid, m.p. 205°, liter. 209° (6). The product of the valence isomerization reaction is therefore cis-5,6-dimethyl-1,3-cyclohexadiene (IV). At 132° the rate constant for this valence isomerization, $k = 4.45 \times 10^{-5}$ sec.$^{-1}$ ($E_A = 29.4$ kcal./mole, $\Delta S^{\ddagger} = -7$ e.u. calc'd. at 421.6°). Not more than 0.1% of trans-5,6-dimethyl-1,3-cyclohexadiene (V) could be present in the isomerization product since we found no peak due to this isomer in the gas chromatogram. As far as we are able to ascertain the valence isomerization of I is a stereospecific process.

The thermal behavior of II and III is much more complex. Thermal interconversion of II and III occurs readily at 100°, presumably via consecutive hydrogen shifts. At 109.5° the rate constant for conversion of III to II is about 2×10^{-5} sec.$^{-1}$, while $K = {}^{II}/III \sim 5.5$. The values are only approximate because accurate analysis (gpc) was precluded by overlapping peaks and a small but undetermined amount of rearrangement during passage through the column. Further studies were carried out on a mixture of II and III which contained approximately 80% (II + III).

Rearrangement of the above mixture, 0.66 M in cyclohexane, at 178° gave a mixture containing at least three products. One, which was identified as IV was shown to be derived from an impurity, presumably I, present in the initial mixture. A second, λ_{max} 263 (4000), having an n.m.r. spectrum containing a doublet (methyl, 6H, J = 6 cps.) at 1.01 ppm., a multiplet (allylic protons, 2H) centered at 122 cps. and a broad singlet peak (olefinic protons, 4H) at 5.68 ppm., was identified as V. This product gave on ozonolysis followed by peroxide oxidation dl-2,3-dimethylsuccinic acid, m.p. 123-125°, liter. 125-127° (6). The third product, λ_{max} 263 (6500), exhibited four peaks in the n.m.r., a doublet (methyl, 3H, J = 6.5 cps.) at 0.97 ppm., a singlet (allylic methyl, 3H) at 1.80 ppm., a multiplet (allylic protons, 3H) centered at 131 cps., and a broad singlet (olefinic protons, 3H) at 5.61 ppm. On the basis of this spectral evidence and an analysis we assign the third product the structure of 1,6-dimethyl-1,3-cyclohexadiene (VI).

Rate studies show that the disappearance of the mixture of (II + III) at 178° is first order (with respect to the sum of II + III) with $k = 1.5 \times 10^{-5}$ sec.$^{-1}$. A sample of V rearranges to VI via a first order process at 178° with $k = 0.60 \times 10^{-5}$ sec.$^{-1}$. Assuming the mechanism, $\text{III} \rightleftarrows \text{II} \rightarrow \text{V} \rightarrow \text{VI}$, calculation of the concentration of V at various times during a kinetic run can be made using the measured rate constants determined separately (7). Although this concentration term is not particularly sensitive to the ratio of the rate constants for the last two steps, a reasonable fit to the experimental points is obtained. Our data are in good accord with the assumption that V is the primary product of the rearrangement of II. Once again then the preferred stereopath is cis. Because of uncertainties introduced by working with a mixture we have been unable to show whether the reaction is stereospecific, but it is certainly greater than 90% stereoselective.

The rate constant for the valence isomerization of II corrected for the equilibrium between II and III is 2.2×10^{-5} sec.$^{-1}$ at 178°. This is slower than the reaction of I by a factor of at least 100. We attribute this to a steric effect due to the cis methyl group on one of the terminal double bonds. It is quite reasonable that III with two cis methyl groups should undergo valence isomerization to a cyclohexadiene so much more slowly than II, that III is converted to V via the path $\text{III} \rightarrow \text{II} \rightarrow \text{V}$ rather than undergoing a direct ring closure.

If, as seems likely, pyro- and isopyrocalciferols are formed from precalciferol (2) that reaction provides a further example of this valence isomerization with the same stereochemistry. These results point to a general cis ring closure for thermal triene to cyclodiene valence isomerizations.

Very recently Lewis and Steiner (8) have reported a study of the kinetics of.ring closure of cis-hexatriene. No stereochemical conclusions can be drawn from their work, but it seems appropriate to note here that those authors have unfortunately chosen the activated complex leading to a trans stereochemistry as the basis for their theoretical calculations.

Acknowledgement. We are pleased to note the generous financial support of this work by the National Science Foundation under grant G-23072.

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