777. *Macrocyclic Compounds. Part V.*[1] *Double-bond Migration in Macrocyclic Alkadienes: Deconjugation of the* 1,3-*Isomers.*

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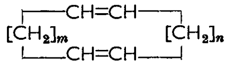
The equilibrium between the different positional isomers of macrocyclic alkadienes at 200° has been established, with triethylborane as a catalyst. The conjugated isomer constitutes only 10% in the case of the 12-membered ring; its proportion increases with ring size to reach a maximum of about 50% for the 15-membered ring, then passes through a minimum (35%) for the 20-membered ring, to increase again for larger rings. The preferences found for certain non-conjugated isomers are explained by conformational considerations.

A STUDY of modified molecular models which allow no Pitzer-strain[2] has shown that ideal strain-free conformations in cyclic alkadienes (I) with a minimum of *gauche*-bonds are only possible when the two double bonds have the *trans*-configuration and are separated by two equal chains each containing an odd number of CH_2 groups. In particular, no conjugated diene (or mono-olefin) below C_{18} can be absolutely strain-free.



$$\begin{array}{ccc} & CH{=}CH & \\ [CH_2]_m & & [CH_2]_n \\ & CH{=}CH & \end{array}$$

(I)

The question arose whether the assumed conformational stability of the symmetrical 14-membered (and possibly the 18- and 22-membered) *trans,trans*-cycloalkadienes might

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[1] Part IV, preceding paper.
[2] Part III, Dale, *J.*, 1963, 93.

compete with the mesomeric stabilization of the corresponding conjugated, but strained, dienes. This has now been found to be so.

Isomerization experiments with cyclic alkadienes having from 12 to 22 ring atoms were carried out at 160—200° with triethylborane[3] as a particularly clean catalyst. It gives no secondary products, and there is no transfer[3] of boron to the ring, as shown by the absence of cyclic alcohols after the oxidation necessary to destroy the catalyst and by the absence of a pressure of ethylene in the reaction tube. This is of course due to the lack of terminal carbon atoms[3] in the ring; in fact, when dodeca-1,11-diene was treated in the same manner, a strong ethylene pressure built up, and the primary alcohol dodec-11-en-1-ol was formed. After destruction of the catalyst, the distribution of positional isomers was determined by the simple semi-quantitative ozonolysis method described in the preceding paper.[1] An illustration of the potentiality of this analytical method is given

TABLE 1.

Incomplete isomerization of symmetrical cyclic dienes ($m = n$) with BEt_3 at 160°.

Ring atoms ($m + n + 4$)	Time (hr.)		Distribution of positional isomers									
12	32	*m*–*n*	4–4	3–5	2–6	1–7	0–8					
		%	7	14	58	8	13					
14	24	*m*–*n*	5–5	4–6	3–7	2–8	1–9	0–10				
		%	49	24	14	10	1·5	1·5				
	(24) *	%	(46)	(21)	(16)	(13)	(2)	(1·5)				
	32	%	49	25	13	11	1·5	1·5				
16	32	*m*–*n*	6–6	5–7	4–8	3–9	2–10	1–11	0–12			
		%	10	27	31	15	8·5	3	5			
18	24	*m*–*n*	7–7	6–8	5–9	4–10	3–11	2–12	1–13	0–14		
		%	17	21	18	19	12	8	1	4·5		
20	24	*m*–*n*	8–8	7–9	6–10	5–11	4–12	3–13	2–14	1–15	0–16	
		%	11	25	23	14	10	4·5	3	1	10	
22	24	*m*–*n*	9–9	8–10	7–11	6–12	5–13	4–14	3–15	2–16	1–17	0–18
		%	14	21	19	18	13	8	5	2	—	1

* With $m = 4$, $n = 6$, as starting material.

TABLE 2.

Isomer equilibrium of cyclic dienes with BEt_3 after 24 hours at 198° ± 2°.

Ring atoms ($m + n + 4$)		Distribution of positional isomers * (A statistical factor of 2 for the *sym*-isomers is needed in energetic considerations.)									
12	*m*–*n*	4–4	3–5	2–6	1–7	0–8					
	%	11(×2)	16	*57*	6	10					
13	*m*–*n*	4–5	3–6	2–7	1–8	0–9					
	%	16	23	*30*	6	25					
14	*m*–*n*	5–5	4–6	3–7	2–8	1–9	0–10				
	%	*14*(×2)	8	6	*15*	7	*50*				
15	*m*–*n*	5–6	4–7	3–8	2–9	1–10	0–11				
	%	16	9	8	*10*	5	*52*				
16	*m*–*n*	6–6	5–7	4–8	3–9	2–10	1–11	0–12			
	%	5(×2)	*12*	*14*	6	*9*	5	*48*			
18	*m*–*n*	7–7	6–8	5–9	4–10	3–11	2–12	1–13	0–14		
	%	*7*(×2)	9	10	10	8	*9*	4	*45*		
20	*m*–*n*	8–8	7–9	6–10	5–11	4–12	3–13	2–14	1–15	0–16	
	%	5(×2)	*11*	*11*	10	8	7	*9*	4	*35*	
22	*m*–*n*	9–9	8–10	7–11	6–12	5–13	4–14	3–15	2–16	1–17	0–18
	%	3(×2)	6	7	7	6	5	6	*10*	5	*45*

* Main products in italics.

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[3] Brown, *Tetrahedron*, 1961, **12**, 117.

in Fig. 1, which shows the gas-chromatographic separation of diol diacetates obtained at intermediate stages in the isomerization of the 22-membered ring.

The results are shown in Tables 1 and 2 and in Fig. 2. It is clear that the isomerization is too slow at 160° to be of practical interest; even after 32 hours the equilibrium was reached only in the case of the 12-membered ring (Table 1), and the 14-membered ring requires 8 days (Fig. 2). At 200° the equilibrium was reached in less than 2 hours for the 12-membered, and in about 10 hours for the 14-membered ring; for the higher members a time of 24 hours and more was necessary. The advancement of the migration was followed especially carefully in the case of the 14-membered ring, which is the first one that is not necessarily strained,[2] yet is not so large as to resemble open chains. Starting from the symmetrical diene, there were, within the limits of error and reproducibility of the methods, no significant differences either in the manner in which the migration progresses or in the final equilibrium at the temperatures of 160°, 180°, and 200°. Using different time scales, it was therefore possible to fit the three sets of curves to one average diagram (Fig. 2). The curves representing the isomers formed in the first steps pass through maxima, and an induction period is observed before the appearance of the last isomers, *e.g.*, the conjugated diene; both phenomena are to be expected if the migration takes place stepwise [3] along the chain, but not if a transannular mechanism were involved. It was verified that a true equilibrium mixture was obtained by starting, not only from *cis,cis*-cyclotetradeca-1,8-diene (I; $m = n = 5$), but also from the *cis,cis*-1,5-isomer ($m = 2$, $n = 8$), obtained by synthesis, and from the *cis,trans*-1,3-isomer ($m = 0$, $n = 10$), isolated from the equilibrium mixture by chromatography on alumina.

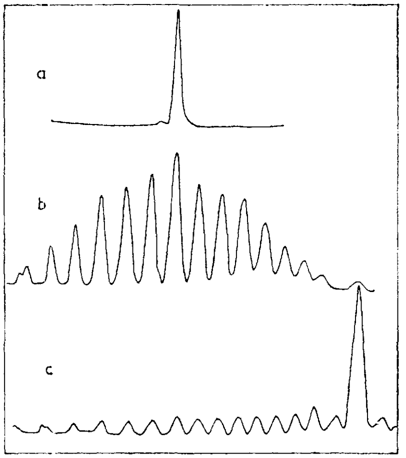

FIG. 1.

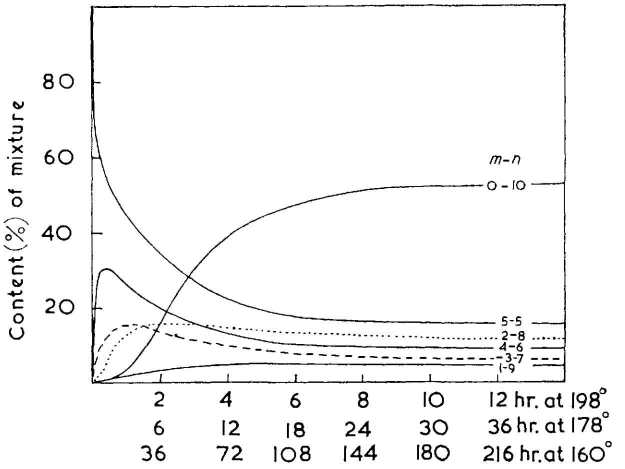

FIG. 2.

FIG. 1. Gas-chromatographic separation (temperature programme) of diol diacetates from the ozonolysis of cyclodocosadienes; (a) hendecane-1,11-diol diacetate from the starting material, the 1,12-diene; (b) after isomerization with BEt_3 for 24 hours at 160°; (c) same treatment at 200°.

FIG. 2. Advancement of double-bond migration in cyclotetradecadiene in the presence of BEt_3 starting from the 1,8-isomer (I; $m = n = 5$). Each curve represents at the same time semi-quantitatively the temperatures 160°, 178°, and 198° when referred to the respective time scales given.

With the other ring sizes the equilibrium was established from the symmetrical diene (I; $m = n$) as well as from fractions very rich in the conjugated isomer. Although the distribution pattern was always the same, the actual quantities differed by 10—20 relative percent for the higher members, indicating that the equilibrium had not been completely attained after 24 hours. The equilibrium values in Table 2 represent the mean of the observed values.

Table 2 shows that in all cases the conjugated isomer can be extensively deconjugated, especially in the 12- and 13-membered ring. It is also seen that the symmetrical isomer is, as predicted, the most " stable " of the non-conjugated isomers in the 14- and 18-membered, but not in the 12- and 16-membered rings. It was further expected that in the 16-membered ring the 1,8-isomer ($m = 5, n = 7$) might be favoured, as in the *trans, trans*-configuration it can have a strain-free skeleton if two extra *gauche*-bonds are accepted. However, the 1,7-isomer ($m = 4, n = 8$) was found to be even more preferred, and inspection of the models showed in fact that a slightly strained skeleton was possible by introduction of just one additional *gauche*-bond. An analogous preference for the isomers ($m = 7$, $n = 9$) and ($m = 6, n = 10$) was found in the 20-membered ring. Of particular interest is the surprising predominance of the 1,5-isomer of the 12-membered diene ($m = 2, n = 6$) which persists even in higher-membered isomers having $m = 2$. Probably, the dimethylene group tends to have the two double bonds in *gauche*-position, whereby effectively two of the necessary bends in the ring are taken care of without the expenditure of less favourable di- or mono-alkyl-substituted *gauche*-bonds. It is also noteworthy that the proportion of the conjugated isomer reaches a maximal value at the ring size (C_{14}) which first permits the reasonably strain-free incorporation of a planar *cis,trans*-1,3-diene grouping with our models, then decreases slightly as the number of possible isomers becomes larger, and finally starts to increase again from the ring size (C_{22}) which accommodates a strain-free planar *trans,trans*-1,3-diene grouping. However, a more detailed discussion seems premature, as the information about the *cis,trans*-equilibria is incomplete, and equilibrium measurements over a much larger temperature range are needed to split the free energy into enthalpy and entropy terms. It is encouraging that at least up to the 18-membered ring the expectations are borne out even at a temperature where $\boldsymbol{RT}$ is important compared with the rotational barriers (2—3 kcal. mole^{-1}). Conformational preferences should be more accentuated at low temperatures, and other isomerization catalysts are being investigated.

The isolated cyclotetradeca-1,3-diene shows the two strong infrared bands at 10·17 and 10·53 μ, typical of a conjugated *cis,trans*-diene,[4] sterically the most favourable for this ring size, as well as strong ultraviolet absorption (ε 22,800) at 236 mμ; it melts at 34°. In contrast, a product obtained from a synthesis involving a final dehydration over phosphorus pentoxide has been reported [5] to be liquid and to have $\lambda_{\text{max.}}$ at 232 mμ. We have now found by ozonolysis that the hydrocarbon fraction obtained by dehydration of cyclotetradecane-1,2-diol over alumina contains all possible positional isomers of cyclotetradecadiene, in addition to the mono-olefin and other rearranged products. These observations, together with the knowledge of the composition of the equilibrium mixtures reported in this paper, indicate that all alleged preparations of macrocyclic alka-1,3-dienes which are described in the literature and involve isomerizing conditions should be regarded with scepticism.

EXPERIMENTAL

Isomerization Method.—A reservoir of triethylborane (~0·5 g.) and several weighed tubes, each fitted with a breakable glass point and containing a weighed quantity (~0·1 g.) of the olefin

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[4] Jackson, Paschke, Tolberg, Boyd, and Wheeler, *J. Amer. Oil Chemists' Soc.*, 1952, **29**, 229.
[5] Ingraham, MacDonald, and Wiesner, *Canad. J. Res.*, 1950, **28***B*. 453.

to be isomerized, were connected by ground-glass joints to a high-vacuum line. The triethylborane was distilled directly into the tubes by cooling them one by one with liquid nitrogen, then sealing them off; the tubes were then weighed again with their respective glass joints.

When several samples with exactly the same concentration were required for kinetic measurements, a four-times larger sample was prepared by the same procedure, but in a larger tube having four smaller side tubes (not cooled) each fitted with a breakable glass point (Fig. 3). After sealing off at constriction *a* the mixture was distributed into the side-tubes by pouring. The side-tubes were then cooled simultaneously in a larger Dewar flask and sealed off at points *b*.

The sealed tubes were heated in an oil-bath for the required time and at the desired temperature. After cooling, the open part (*c*, Fig. 3) of each tube was filled with hexane and the glass point broken with a glass rod, so that the hexane was sucked into the tube. The dilution thus obtained was necessary to enable the sample to be poured, without flaming, into the mixture of 30% hydrogen peroxide and 3N-aqueous sodium hydroxide used to destroy the catalyst. The isomerized olefin was extracted with hexane and evaporated, then ozonolysed in propanol solution, reduced, acetylated, and analysed by gas chromatography,[1] It was verified that the peak areas of the diol diacetates were proportional to weight percentages; an additional check was obtained by calculating each isomer independently from each of the two fragments to which in general it gives rise.

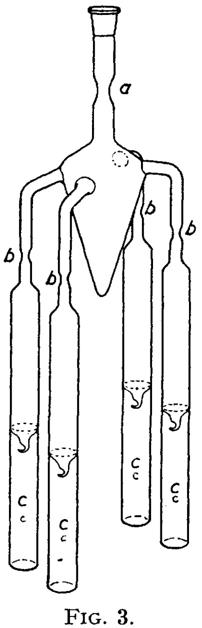

FIG. 3.

Preparation of Cycloalkadienes.—Most of the *cis,cis*-cycloalkadienes used for isomerization have already been described.[6] A new 14-membered diene (I; $n = 2$, $m = 8$) was prepared in a similar manner: Disodiohexa-1,5-diyne and 1,8-dibromo-octane in liquid ammonia gave the *cyclotetradeca-*1,5-*diyne* (7% yield), m. p. 10—12° (Found: C, 88·3; H, 10·4. $C_{14}H_{20}$ requires C, 89·3; H, 10·7%). Reduction on a Lindlar catalyst gave the cis,cis-*cyclotetradeca-*1,5-*diene* (70%) as a liquid (Found: C, 86·0; H, 12·3. $C_{14}H_{24}$ requires C, 87·4; H, 12·6%). Ozonolysis [1] showed only the two expected fragments C_4 and C_{10}.

Isolation of cis,trans-*Cyclotetradeca-*1,3-*diene.*—*cis,cis*-Cyclotetradeca-1,8-diene (5 g.) was heated with triethylborane (10 g.) at 200° for 24 hr. After destruction of the catalyst the mixture of isomers was chromatographed on highly activated alumina. The fractions eluted with hexane were examined in the ultraviolet spectrometer at 235 mμ; the extinction at this wavelength increased from zero for the first fractions to about 23,000 for the last ones. Those fractions having $\varepsilon \geqslant 20{,}000$ were combined and recrystallized from ethanol, to give the pure cis,trans-1,3-*isomer*, m. p. 32—34·5° (Found: C, 87·3; H, 12·4. $C_{14}H_{24}$ requires C, 87·4; H, 12·6%). The yield of isolated pure product was only 10% although the mixture contained about 50%. The ultraviolet spectrum (in hexane) showed maxima at 229, 236, and 242 mμ (sh) (ε 21,400, 22,800, and 14,600). The infrared spectrum showed the two strong bands typical of conjugated *cis,trans*-dienes,[4] at 10·17 and 10·53 μ; additional olefinic bands were at 3·33, 5·96w, 6·06w, 6·21w, and 14·2 μ. Ozonolysis [1] gave exclusively the two expected fragments C_2 and C_{12}.

*Preparation of Cyclotetradecane-*1,2-*diol.*—Ethyl hydrogen suberate [7] was electrolysed [8] at 50° in methanol containing 0·02 equivalents of sodium methoxide, at a current density of 0·15—0·2 amp./cm.^{2}, to give diethyl dodecane-1,12-dicarboxylate (53%). An acyloin condensation [9] gave 2-hydroxycyclotetradecanone (57%), which was reduced by lithium aluminium hydride in ether to the diol (85%), m. p. 126°.

*Dehydration of Cyclotetradecane-*1,2-*diol.*—When the diol was passed over alumina at 320—330°, dehydration was incomplete, and the liquid part consisted mainly of the ketone with very little olefin. Chromatography on alumina gave a hydrocarbon fraction, n_D^{24} 1·4815, eluted with pentane, which showed infrared bands at 10·18 and 10·55 μ (conjugated *cis,trans*-diene [4]) and considerably stronger bands at 10·34 (isolated *trans*-) and 14·1 μ (isolated *cis*-olefin). The

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[6] Part I, Dale, Hubert, and King, *J.*, 1963, 73.

[7] *Org. Synth.*, Coll. Vol. II, p. 276 (1943).

[8] Weedon, *Quart. Rev.*, 1952, **6**, 380.

[9] Prelog, Frenkiel, Kobelt, and Barman, *Helv. Chim. Acta*, 1947, **30**, 1741.

ultraviolet band at 235 mμ had an extinction of only 4500 (corresponding to 20% of conjugated diene).

When the diol was passed over alumina at 375°, more hydrocarbon, n_D^{25} 1·4833, was formed, but the infrared bands at 10·18 and 10·55 μ were very weak compared with those at 10·34 and 14·1 μ, and the intensity at 235 mμ was only 2800 (~12% of conjugated diene). Gas chromatography showed one main broad peak (~80%) followed by a second major peak (~15%, conjugated diene); but after ozonolysis, reduction, and acetylation, all the possible diol acetates from C_2 to C_{12} were shown to be present; the C_{14}-fragment (from the mono-olefin) was, surprisingly, observed as the main product. The nuclear magnetic resonance spectrum was very complex and indicated even the presence of methyl-substituted double bonds. Apparently, both transfer of hydrogen (carbon is formed on the catalyst) and ring opening had occurred.

Preparation and Isomerization of Dodeca-1,11-*diene*.—Dodeca-1,11-diyne[6] absorbed 2 mol. of hydrogen on a Lindlar catalyst, to give the liquid diene whose infrared spectrum shows the bands typical of terminal double bonds and the absence of internal double bonds, ethynyl, or methyl groups.

This diene (0·9 g.) was isomerized with triethylborane (0·4 g.) at 160° for 24 hr. When the tube was opened an ethylene pressure was observed. Ozonolysis gave the following distribution of diol diacetates ($\mathrm{AcO{\cdot}[CH_2]_{\mathit{r}}{\cdot}OAc}$):

r	6	7	8	9	10	11
%	2·5	12	14	11	45	17

The fragment with $r = 11$ can only have arisen from $\mathrm{CH_2{=}CH{-}[CH_2]_{10}{\cdot}B}<$ formed by permanent transfer of boron.

Preparation and Isomerization of cis,cis-*Trideca*-3,10-*diene*.—The disodium salt of nona-1,8-diyne and ethyl bromide in liquid ammonia gave trideca-3,10-diyne, which absorbed 2 mol. of hydrogen on a Lindlar catalyst, to give the liquid *cis,cis*-trideca-3,10-diene; its infrared spectrum had the expected bands for *cis*-double bonds.

Isomerization of this diene (0·8 g.) with triethylborane (0·6 g.) at 157° for 24 hr. and subsequent ozonolysis gave the following diol diacetate distribution:

r	4	5	6	7	8	9
%	4·5	14	23	29	20	9

It is evident that no equilibrium was reached under these conditions, as no conjugated diene ($r = 2$) or transfer of boron ($r \geqslant 10$; pressure of ethylene) was observed.

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