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STEREOCHEMICAL STUDIES—XXXVI[1]

AN APPROACH TO CONFORMATIONAL ANALYSIS OF MEDIUM RING COMPOUNDS. UNSATURATED TEN-MEMBERED RING DERIVATIVES[2]

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Abstract—It is suggested that bis-*gem*-dimethyl substituted derivatives of medium rings represent useful models for conformational analysis. Relative stabilities and/or enthalpies of hydrogenation of *cis*- and *trans*-monoölefins, diolefins and acetylenes derived from 1,1,4,4-tetramethylcyclodecane have been determined. Large differences were found in the stabilities and enthalpies of hydrogenation between position isomers in each of the three classes of compounds. The results are discussed in conformational terms and it is suggested that, with the possible exception of the monoolefins of *trans* configuration, the most stable unsaturated derivative in each class has the conformation most closely resembling that assumed to exist in the saturated hydrocarbon.

THE great progress achieved in the understanding of the conformation of medium ring compounds is due mainly to the X-ray studies of Dunitz *et al.* on derivatives of the nine-, twelve- and particularly the ten-membered rings.[4] The X-ray method is, however, subject to certain experimental, as well as inherent, limitations, and cannot be expected to clarify all aspects of the problem. Computational approaches to the problem of medium ring conformation recently developed[5] have proved useful although, in the present stage of development they are limited to the simple compounds.

Under these circumstances, and with the essential background information now available from the X-ray work, it seemed timely to investigate systematically the possibility of applying methods of conformational analysis to medium ring systems for the dual purpose of interpreting and predicting reactivity behaviour, and of obtaining information concerning conformational features in these compounds. Such analysis could be applied to the known simple functional derivatives of the cycloalkanes, or, to

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[1] For Paper XXXV see J. Krupička, J. Závada and J. Sicher, *Coll. Czech. Chem. Comm.* in the press.

[2] The results contained in this paper have, in part, been published in preliminary form: P. Goebel, J. Sicher, M. Svoboda and R. B. Turner, *Proc. Chem. Soc.* 237 (1964).

[3] The work at Rice University was supported by a grant from the National Science Foundation.

[4] For a review, see J. D. Dunitz and V. Prelog, *Angew. Chem.* **72**, 896 (1960).

[5] [a] J. B. Hendrickson, *J. Amer. Chem. Soc.* **86**, 4854 (1964); [b] N. L. Allinger, *Ibid.* **81**, 5727 (1959); [c] R. Pauncz and D. Ginsburg, *Tetrahedron* **9**, 40 (1960); [d] K. B. Wiberg, *J. Amer. Chem. Soc.* **87**, 1070 (1965).

the interesting complex naturally occurring medium ring compounds. Such attempts have already been made in a few cases.[5a,6]

The complexity of the conformational situation in the medium rings suggested that more informative data could be obtained if selected model compounds were employed.[7] Our choice, for this purpose, of the bis-*gem*-dialkylcycloalkanes[8] rests on the following considerations, best demonstrated by the ten-membered ring.

From the X-ray data Dunitz *et al.*[4] concluded that there exists one particularly stable conformation of the cyclodecane ring (Fig. 1). The substituent positions on this skeleton fall into two classes: the energetically favourable extra-annular positions (shown by the black dots) and the energetically highly unfavourable intra-annular substituents (shown as circles).[4] A substituted cyclodecane will presumably tend to take up a conformation in which the greatest number of substituents is extra-annular, rather like a polysubstituted cyclohexane derivative will, in general, tend to take up a conformation in which the maximum number of substituents is equatorial. If we now consider a molecule such as 1,1,4,4-tetramethylcyclodecane, and assume that it possesses a conformation of the ring skeleton similar to that of the unsubstituted cyclodecane, then the condition of the maximum number of extra-annular substituents is met only in a single conformer[9] (Fig. 2). If the methyl groups were located in any other (non-equivalent) position then at least one would have to be intra-annular and this would

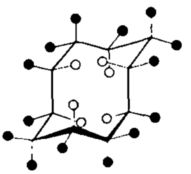

FIG. 1. Schematic representation of conformation of cyclodecane according to Dunitz *et al.*[4] (○ Intra-annular positions; ● extra-annular positions).

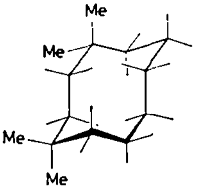

FIG. 2. Schematic representation of postulated conformation of 1,1,4,4-tetramethylcyclodecane.

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[6] V. Prelog, *Pure Appl. Chem.* **6**, 545 (1963); V. Prelog, W. Küng and T. Tomljenović, *Helv. Chim. Acta* **45**, 1352 (1962); J. Dale, *J. Chem. Soc.* 93 (1963).

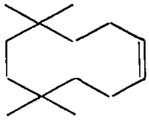
[7] cf. M. Svoboda and J. Sicher, *2nd Internat. Symp. on the Chem. Natural Products (I.U.P.A.C.)*, Prague, August 1962, *Abs. Comm.* p. 39; J. Sicher, *Chimia, Basel* **16**, 300 (1961).

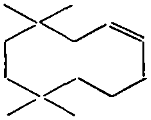
[8] Derivatives of *gem*-dimethylcyclononane and bis-*gem*-dimethylcyclononane have previously been examined by A. T. Blomquist, E. S. Wheeler and Y. Chu, *J. Amer. Chem. Soc.* **77**, 6307 (1955); A. T. Blomquist and G. A. Miller, *Ibid.* **83**, 243 (1961) although in a different context.

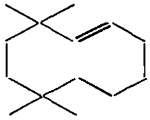
[9] The pair of geminal methyl groups could conceivably enforce a certain (minor) deviation from what otherwise appears to be the most stable arrangement of the carbon skeleton of the ten-membered ring. A decision on this subtle but important point must await the outcome of X-ray studies on derivatives of 1,1,4,4-tetramethylcyclodecane, at present under way in the Laboratory Professor J. D. Dunitz.

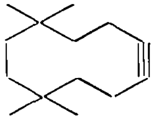
give rise to strain. 1,1,4,4-Tetramethyl substitution should therefore aid in fixing the conformation of the cyclodecane ring.[10]

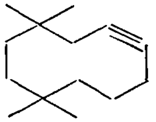
Various derivatives of 1,1,4,4-tetramethylcyclodecane, 1,1,5,5-tetramethylcyclodecane and analogous bis-*gem*-dimethyl derivatives of other medium and large rings have been investigated in the Prague Laboratory; in the present work the relative stabilities of unsaturated derivatives of 1,1,4,4-tetramethylcyclodecane—the mono-olefins *cis*- and *trans*-I, II and III, the acetylenes IV and V and the corresponding dienes have been determined by direct equilibration and/or heats of hydrogenation.


cis-I
trans-I


cis-II
trans-II


cis-III
trans-III


IV


V

If the assumption is made that even in unsaturated derivatives of 1,1,4,4-tetramethylcyclodecane the methyl groups will, if at all possible, occupy extra-annular positions, the C_1–C_4 four-carbon segment will exist in a nearly zig-zag arrangement. This, together with the rather rigid geometry of the C—C═C—C and C—C≡C—C moieties, greatly limits the number of viable conformations for each position isomeric olefin, diene or acetylene. Knowledge of the relative stabilities of the position isomeric olefins, *cis*- and *trans*-I, II and III, the acetylenes IV and V, and of the corresponding dienes should afford information on these conformations and hence on the conformation as well as preferred location of the multiple bond in the unsaturated derivatives of cyclodecane itself. We consider only three alternative positions of the double bond, i.e., 5(6), 6(7) and 7(8); the fourth possible position, 2(3) is not taken into account owing to lack of relevance in the present context.

Data on the relative stabilities of the three olefin pairs I–III could be obtained from equilibration experiments. Four of the olefins (*cis*-I, *trans*-I, *cis*-II and *trans*-II) were available in quantity (see synthesis, below), and all six can be separated and quantitatively estimated by VPC. Acid catalysed equilibration (*p*-toluenesulphonic acid in anhydrous acetic acid) leads, as expected, to a complex mixture, also containing compounds other than the olefins I–III, possibly products of methyl migration and/or bicyclic products, but these were not investigated. Heating with lithium 2-aminoethylamide in ethylenediamine has proved to be an efficient method for bringing about double bond isomerizations,[11] and this method was therefore applied. When any of the four olefins *cis*-I, *trans*-I, *cis*-II or *trans*-II was heated with this reagent to 117° for 3 hr, an olefin mixture of practically identical composition was produced, showing that equilibrium had been attained. The equilibrium composition is shown in Table 1 (column 1).

It is seen at once that very large differences in stability exist among the six olefins concerned, the most striking being that between the three *cis*-olefins. Thus, at equilibrium the *cis*-7(8) isomer (*cis*-I) could not be detected, while the position isomeric

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[10] The application of the t-butyl group as a conformation holding substituent in the eight-membered ring has been examined by N. L. Allinger and S. Greenberg, *J. Amer. Chem. Soc.* **84**, 2394 (1962).

[11] B. S. Tyagi, B. B. Gatge and S. C. Bhattacharyya, *Tetrahedron* **19**, 1189 (1963); L. Reggel, S. Friedman and J. Wender, *J. Org. Chem.* **23**, 1136 (1958); M. D. Carr, J. R. P. Clarke and M. C. Whiting, *Proc. Chem. Soc.* 333 (1963).

cis-6(7) olefin, *cis*-II, is present to the extent of 92·5%; there is also about 1% of the *cis*-5(6) isomer (*cis*-III). In the *trans*-series there is a progressive increase in percentage content on going from the 7(8) to the 5(6) isomer, the last being the most stable of the three *trans*-olefins. The free energy differences between the *cis*-7(8)-olefin and the other olefins of the series cannot be evaluated, since the 7(8) isomer is absent from the chromatographic scans. For this reason, and also in order to obtain data which would make possible an intercomparison with *cis*- and *trans*-cyclodecene, we determined the heats of hydrogenation for the two olefin pairs I and II. The values of the enthalpy of hydrogenation of the olefins are listed in Table 1, column 3.

Table 1. Equilibration of olefins and heats of hydrogenation in acetic acid

Olefin	% of Olefin at equilibrium[a]	ΔG[b] kcal mole^{-1}	ΔH(25°) kcal mole^{-1}	ΔΔH[b] kcal mole^{-1}
cis-7(8) (*cis*-I)	0	v. large	−28·7	−6·7
trans-7(8) (*trans*-I)	0·5	−4·1	−26·0	−4·0
cis-6(7) (*cis*-II)	92·5	0	−22·0	0
trans-6(7) (*trans*-II)	2·0	−3·0	−25·4	−3·4
cis-5(6) (*cis*-III)	1·0	−3·5	—	—
trans-5(6) (*trans*-III)	4·0	−2·5	—	—
cis-Cyclodecene[13]	94·0		−20·7[12]	
trans-Cyclodecene[13]	6·0	−2·1[c]	−24·0[12]	−3·3

[a] With lithium 2-aminoethylamide in ethylene diamine at 117°.
[b] With respect to the most stable olefin, *cis*-6(7) (*cis*-II).
[c] With respect to *cis*-cyclodecene.

The enthalpy data show the same trends as the free energy data (ΔG) obtained from the equilibrium runs. The two position isomeric *cis*-isomers, *cis*-7(8) and *cis*-6(7), differ in enthalpy of hydrogenation by 6·7 kcal mole^{-1}. This enormous difference must be conformational in origin, and the following rationalization is put forward. If we assume that 1,1,4,4-tetramethylcyclodecane possesses a conformation such as shown in Fig. 2, with the methyl groups occupying the "corner" positions, the dihedral angle about the 7(8) single bond is approximately 152° and hence may be referred to as "transoid"; the 6(7) single bond has a dihedral angle of about 55° and is thus more nearly "cisoid".[4] A double bond of *cis*-configuration may therefore be incorporated at the 6(7) position of the saturated skeleton (of the type shown in Fig. 2) with relatively little conformational adjustment; on the other hand, introduction of a *cis*-double bond into the 7(8) position necessitates complete departure from a structure of this type.[14]

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[12] R. B. Turner and W. R. Meador, *J. Amer. Chem. Soc.* **79**, 4133 (1957).

[13] Acid catalysed equilibration has afforded very similar results: 96% *cis*-cyclodecene at 100·4° (ΔG −1·9) (A. C. Cope, P. T. Moore and W. R. Moore, *J. Amer. Chem. Soc.* **81**, 3153 (1959).

[14] Construction of specific conformations of "non-rigid" molecules such as the medium and large ring compounds with Dreiding models without the use of some fixing device which prevents "free rotation" about the C—C bonds is very difficult or even impossible. A highly satisfactory way of achieving the required degree of fixation, suggested by Mr. V. Žák of the Prague Institute, consists in converting the sleeve portions of the Dreiding tetrahedra into weak self-locking springs. This is achieved simply by cutting a very thin slot into the tubes, as illustrated in Fig. 3 and slightly compressing them. The model, which by this adjustment loses none of the versatility of the original,

One might, of course, also consider the possibility that the *cis*-7(8) olefin possesses essentially the same conformation of the carbon skeleton as the *cis*-6(7) olefin (with, so to speak, a phase lag of one carbon atom), now necessarily with one of the methyl groups in the energetically unfavourable intra-annular positions. Elsewhere we have put forward evidence that this almost certainly is not so.[15]

Application of an analogous argument to the *trans*-7(8) and *trans*-6(7) olefins is less straightforward. The *trans*-7(8) olefin (*trans*-I) is somewhat less stable than the *trans*-6(7) olefin (*trans*-II), in spite of the fact that the double bond of *trans*-configuration replaces a transoid single bond in the former and a cisoid single bond in the latter. However, we must take into account the fact that replacement of the transoid 7(8) single bond in a structure such as shown in Fig. 2 by a *trans*-double bond moves the two "long" sides of the ring closer towards each other, giving rise to strain. It is also possible that one feature contributing to the higher values of ΔH (and ΔG) of the 7(8) as compared with the 6(7) olefins—*cis* as well as *trans*—is that in the 6(7)-olefins one CH_3—H interaction is relieved relative to the saturated compound. This in itself cannot, of course, account for the very large differences between the *cis*-6(7) and *cis*-7(8) isomers.

The 5(6)-olefins have the additional feature of a quaternary carbon α to the double bond and are hence not strictly comparable with the other olefins. Thus, the relatively strained nature of the *cis*-5(6) olefin finds a ready explanation in the *cis*-relationship of the $C_{(4)}$ quaternary carbon and the $C_{(7)}$ methylene group.

It is instructive also to compare the *cis-trans* stability relationship in the isomer pairs. In cyclodecane itself there is a large difference both in ΔG and ΔH in favour of the *cis*-isomer (Table 1). In the tetramethylcyclodecenes this normal situation holds only in the case of the 6(7) isomer pair. In the 7(8) pair it is reversed, leading to the unexpected situation of a *trans*-cyclodecene being much more stable than a *cis*-cyclodecene.

The conformational situation in cyclodecyne, 1,1,4,4-tetramethylcyclodec-7(8)-yne (IV), 1,1,4,4-tetramethylcyclodec-6(7)-yne (V) and an open-chain model, oct-4-yne have been determined by heats of hydrogenation and the results are listed in Table 2. The fact that the heat of hydrogenation of cyclodecyne is lower than that of oct-4-yne suggests that non-bonded repulsions are more important than strain differences in the corresponding unsaturated derivatives.

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will stay in any rotational conformation into which it is turned while rotation still remains "free". We are greatly indebted to Mr. Žák for this suggestion.

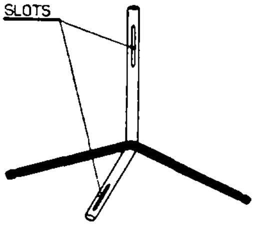

FIG. 3. "Fixation" of Dreiding models.

[15] J. Sicher, M. Svoboda and V. A. Vaver, *Chem. Comm.* 12 (1965).

The heat of hydrogenation of the 7(8)-triple bond isomer IV is less negative than that of the 6(7)-siomer (V) by 2·8 kcal mole^{-1}. Models suggest that incorporation of a 7(8) triple bond requires much less departure from what is believed to be the most stable structure of 1,1,4,4-tetramethylcyclodecane than does the introduction of a 6(7) triple bond. It may also be noted that, as in the case of the corresponding olefins, the heats of hydrogenation of the tetramethylated compounds are higher than those of the corresponding unsubstituted cyclodecane compounds.

TABLE 2. HEATS OF HYDROGENATION OF SOME ACETYLENES IN ACETIC ACID

	ΔH kcal mole^{-1}
Oct-4-yne	−62·8[16]
Cyclodecyne	−56·5[16]
1,1,4,4-Tetramethylcyclodec-7(8)-yne (IV)	−58·9
1,1,4,4-Tetramethylcyclodec-6(7)-yne (V)	−61·7

Further interesting information should be available from base catalysed isomerization of the acetylenes IV and V. As reported previously,[17] the acetylenes IV and V rearrange to the corresponding cyclodeca-1,2-dienes; the allenes, however, are not the most stable species and, heating of either IV or V with a basic catalyst, e.g., potassium t-butoxide in dimethylsulphoxide for 2 hr at 90° in both cases yields a diene, m.p. 29°. Both the double bonds in this compound possess *cis*-configuration (as witnessed by the absence of absorption at ~985 cm^{-1}); their location was established by oxidation with osmium tetroxide (tetrol not identified), followed by potassium periodate and potassium permanganate, which gave 2,2,2′,2′-tetramethylsuberic acid. On this evidence the diene is assigned the structure of 1,1,4,4-tetramethylcyclodeca-*cis*-*cis*-6,8-diene (VI).

The PMR spectrum (100 Mc/s in $CDCl_3$ solution using TMS as an internal standard) of the cyclic diene provides further evidence for the proposed structure.[18] The two pairs of methyls appear as two singlets at 0·806 ppm and at 0·925 ppm. The splitting patterns of the allylic protons reflect the symmetry of the molecule. One pair of allylic protons is observed as a doublet of doublets centered at 1·44 ppm, where the larger coupling constant (J = 13·1 c/s) corresponds to geminal coupling between allylic protons and the smaller coupling constants (J = 4·2 c/s) is due to coupling with the vicinal proton of the adjacent double bond. The other pair of allylic protons appears as a triplet centered at 2·39 ppm. For this pair of allylic protons the coupling constant to vicinal proton of the double bond (J = 12·7 c/s) has nearly the same magnitude as the geminal coupling constant (J = 13·1 c/s). The assignment of the allylic protons was confirmed by a spin decoupling experiment. The vinylic protons produce two complicated multiplets located at 5·52 ppm and 5·86 ppm. A more detailed discussion of the spectrum of this compound, as well as of the other olefins here reported, is reserved for a later publication.

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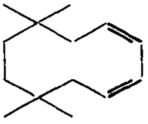
[16] R. B. Turner, P. Goebel, A. D. Jarrett and Barbara Hille, unpublished results.

[17] J. Sicher, M. Svoboda and J. Závada, *Coll. Czech. Chem. Comm.* **30**, 42 (1965).

[18] Our thanks are due to Dr. U. Scheidegger, Varian AG, Zürich, for measuring the spectrum.



VI

The double bonds in the diene, m.p. 29°, thus not only possess the same configuration as the double bond in the most stable mono-olefin, *cis*-II, but also occupy the same position. An examination of models shows that this particular arrangement of the two double bonds is again the only one which, with only relatively little adjustment, can be fitted into a "Dunitz-type" skeleton. Models further indicate that the dihedral angle between the 1,3-double bonds is in the order of 60°, thus accounting for the lack of conjugation as evidenced by the absence of absorption at around 215–230 mμ in the diene.[19]

The isomerization of cyclodecadiene has not been studied. However, in the nine-, fifteen- and twenty-membered rings, the most stable dienes are the *trans,trans* "diametric" olefins (e.g., *trans,trans*-1,5-cyclononadiene).[20] A "diametric" olefin of this type cannot arise in the compounds investigated since double bond migration around the ring is blocked by the *gem* dimethyl groups.

The present results, therefore, indicate that, with the possible exception of the *trans*-monoölefins, the most stable unsaturated isomers in the 1,1,4,4-tetramethylcyclodecane system are those in which the conformation of the carbon skeleton exhibits the minimum necessary deviation from a skeleton of the "Dunitz type". This would suggest that the non-alkylated cyclodecane derivatives, i.e. *cis*-cyclodecene, cyclodecyne as well as cyclodeca-*cis,cis*-1,3-diene probably also preferentially exist in conformations exhibiting the minimum essential deviation from that of cyclodecane. Further work on various aspects of this problem is in progress.

Synthetic studies

Partial reduction on a Lindlar catalyst of 1,1,4,4-tetramethylcyclodec-7(8)-yne (IV) and 1,1,4,4-tetramethylcyclodec-6(7)-yne (V), which were available,[17] were chosen for the synthesis of the *cis*-7(8) and *cis*-6(7) olefins (*cis*-I and *cis*-II), respectively. Reduction of the triple bond in V did, indeed, afford pure *cis*-II in excellent yield. On the other hand, in the case of the hydrogenation of the 7(8)-triple bond, i.e., the acetylene IV, there was an appreciable amount of overreduction and, moreover, the olefin fraction was found to be a mixture consisting of about 68% of the "normal" product, the *cis*-7(8) isomer (*cis*-I), together with about 19% of the corresponding *trans*-olefin (*trans*-I) as well as of the position-isomeric 6(7)-olefins *cis*-II (5%) and *trans*-II (8%). Reduction of V is hence normal, that of IV is accompanied by extensive overreduction and double bond shift.

Although *cis*-I was obtained in pure form by crystallization of the silver nitrate adduct of the olefin mixture prepared by the Lindlar reduction of the acetylene IV, a

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[19] According to Blomquist and Goldstein, *J. Amer. Chem. Soc.* 77, 998 (1955) cyclodeca-*cis,cis*-1,3-diene also shows no absorption in this region.

[20] A. J. Hubert and J. Dale, *J. Chem. Soc.* 4091 (1963); D. Devaprabhakara, C. G. Cardenas and P. D. Gardener, *J. Amer. Chem. Soc.* 85, 1553 (1963).

more advantageous method for its synthesis was found in the diborane reduction[21] of IV, which gave the olefin practically pure and in high yield.

While this work was approaching completion, Corey and Winter[22] published a procedure for the stereospecific conversion of vicinal diols to olefins by reaction of the diol thioncarbonates with trimethyl phosphite. Since 5,5,8,8-tetramethylcyclodecane-*cis*-1,2-diol results from the catalytic reduction of the corresponding acyloin, this procedure was applied to the synthesis of *cis*-I. The olefin thus obtained in good yield was pure by VPC.

From what is known about the behaviour of open-chain acetylenes, it might have been assumed that the reduction of IV and V with sodium in liquid ammonia[23] could provide a method for the synthesis of the olefins *trans*-I and *trans*-II, respectively. In the case of the medium ring cycloalkynes,[17] this reaction takes a complicated course and the reduction of the 7(8)acetylene IV with sodium in liquid ammonia gives rise to the pure *cis*-6(7) olefin (*cis*-II), in very high yield, thus providing an advantageous procedure for its synthesis.

The *trans*-olefins thus cannot be obtained by direct reduction from the acetylenes, and elimination procedures were therefore investigated. It was found that pyrolysis of 4,4,7,7-tetramethylcyclodecyltrimethylammonium hydroxide (or methoxide) gives rise, in good yield, to a mixture containing practically equal amounts of the *trans*-7(8) and *trans*-6(7) olefins (*trans*-I and *trans*-II) with only very small amounts of the *cis*-olefins, *cis*-I and *cis*-II. Pyrolysis of 4,4,7,7-tetramethylcyclodecyldimethylamine oxide afforded a mixture containing some two thirds of the *trans*-7(8) isomer (*trans*-I) and one third of the *trans*-6(7) isomer (*trans*-II) and only very small amounts of the corresponding *cis*-olefins, *cis*-I and *cis*-II.[24] The mixture of the two *trans*-olefins, *trans*-I and *trans*-II, can be separated by partition chromatography between aqueous silver nitrate on silica gel and pentane.[25] The 4,4,7,7-tetramethylcyclodecylamine required for these reactions is readily available by reduction of the corresponding acyloin oxime with sodium in butanol, a procedure shown[26] to be very useful for the synthesis of medium and large ring cycloalkylamines.

The only one of the six olefins *cis*- and *trans*-I-III not obtained in a pure state namely *trans*-III was obtained in mixture with *trans*-II by the pyrolysis of 4,4,7,7-tetramethylcyclodecyltrimethylammonium hydroxide. These results will be reported in detail later.

The structure and configuration assigned to the olefins is amply supported by interrelated and mutually consistent evidence. In part, this follows from the methods of synthesis. Thus e.g. the diborane reduction of IV or the Corey–Winter synthesis prove the structure of *cis*-I; the Lindlar reduction of V establishes the structure of

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[21] H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.* **81**, 1512 (1959).

[22] E. J. Corey and R. A. E. Winter, *J. Amer. Chem. Soc.* **85**, 2677 (1963).

[23] [a] K. N. Campell and L. T. Eby, *J. Amer. Chem. Soc.* **63**, 216 (1941); cf. also early reports on steric course of cycloalkyne reductions, [b] A. T. Blomquist, L. -H. Liu and J. C. Bohrer, *Ibid.* **74**, 3643 (1952).

[24] Pyrolysis of cyclodecyltrimethylammonium hydroxide and also of cyclodecyldimethylamine oxide is known to give *trans*-cyclodecene of better than 95% isomeric purity (cf. A. C. Cope, M. Brown and H. H. Lee, *J. Amer. Chem. Soc.* **80**, 2855 (1958); A. T. Blomquist, R. E. Burge and A. C. Sucsy, *Ibid.* **74**, 3636 (1952).

[25] H. L. Goering, W. D. Closson and A. C. Olson, *J. Amer. Chem. Soc.* **83**, 3507 (1961).

[26] J. Sicher and M. Svoboda, *Coll. Czech. Chem. Comm.* **23**, 1252 (1958).

cis-II. The position of the double bonds, particularly for the *trans*-isomers, was confirmed by conversion of the olefins to the corresponding diols by hydroxylation with osmium tetroxide and further oxidation to the known dicarboxylic acids. Such evidence has already been presented in Part XXXI of this series for the olefins *cis*-I and *cis*-III.[17] The configuration assigned on the basis of synthetic evidence are invariably borne out by the IR spectra of the olefins (Fig. 4): the *trans*-isomers exhibit a very strong band in the region of 985 cm^{-1} and this is completely absent in the *cis*-isomers.

EXPERIMENTAL

cis-1,1,4,4-Tetramethycyclodec-7(8)-ene (cis-I)

(a) *By partial catalytic reduction.* A solution of IV[17] (3·84 g) in hexane (10 cc) containing 200 mg Lindlar catalyst was shaken with H_2 at room temp. and press. until the absorption of H_2 slowed down. The crude product was shown by VPC to contain about 8% of the saturated hydrocarbon and a roughly corresponding amount of the starting acetylene; the olefin fraction was found to consist of 68% *cis*-I, 18·5% *trans*-I, 5% *cis*-II and 8·5% *trans*-II.

The olefin was converted to the $AgNO_3$-adduct in the usual manner and the adduct crystallized from MeOH; m.p. with dec. 70–78°. The olefin was liberated from the adduct by shaking with conc. NH_4OH, isolated in the usual manner and distilled, b.p. 111–112°/10 mm. (Found: C, 86·74; H, 13·29. $C_{14}H_{28}$ requires: C, 86·51; H, 13·49%.) The IR spectrum is shown in Fig. 4.

The purified olefin was converted to the vicinal diol m.p. 131–132° by reaction with OsO_4. (Found: C, 73·45; H, 12·19. $C_{14}H_{28}O_2$ requires: C, 73·63; H, 12·36%.)

Oxidation of the diol with periodate, followed by permanganate, afforded 3,3,3′,3′-tetramethylsebacic acid, m.p. 118–121°, undepressed on admixture with an authentic sample.[17]

(b) *By diborane reduction.*[21] A solution of 1,1,4,4-tetramethylcyclodec-7(8)-yne (2·304 g) in dry ether (10 cc) was treated with BF_3-etherate (624 mg, 10% excess), the solution cooled to 0°, flushed with N_2 and an ethereal solution of LAH (containing 131 mg of the hydride) added in the course of 30 min under stirring. Stirring was then continued for 20 min, the mixture treated with glacial acetic acid (4 cc) and allowed to stand overnight. The product, which was isolated in the usual manner, had b.p. 102–104°/8 mm, 2·04 g (87·5%) and was shown by VPC to contain 98% of *cis*-III, the remainder being an impurity which we did not identify.

(c) *From 5,5,8,8-tetramethylcyclodecane-*cis-1,2*-diol.*[22] A solution of 5,5,8,8-tetramethylcyclodecan-2-olone (22·8 g) in MeOH (100 cc) was shaken with H_2 at room temp. and press. in the presence of Adams' catalyst (1·0 g). The catalyst was removed and the solvent distilled off; the residual crystals, m.p. 125°, and after one crystallization from benzene, m.p. 131–132°, yield 16·3 g (73%). The diol was identical with a sample prepared from *cis*-I and OsO_4.

A solution of the diol (8·2 g), N,N′-thiocarbonyldiimidazole[27] (7·1 g, 10% excess) in toluene (50 cc) was refluxed for 30 min, cooled, diluted with ether and water, the organic layer washed with water to remove the imidazole, dried over $MgSO_4$, evaporated and the residue crystallized 3 times from benzene, m.p. 139–140°, yield 7·2 g (74%). (Found: C, 66·73; H, 9·67. $C_{15}H_{26}O_2S$ requires: C, 66·63; H, 9·69%.)

A solution of the above thiocarbonyl derivative (7·2 g) in trimethylphosphite (20 cc) was heated for 74 hr to 110–115° in a sealed tube under N_2, the cooled colourless solution was shaken with a solution of NaOH (32 g) in water (100 cc) for 30 min and extracted with pentane. The pentane extracts afforded 4·95 g (96%) of the required olefin, containing, according to VPC, less than 2% of *trans*-I.

cis-1,1,4,4-*Tetramethylcyclodec-6(7)-ene* (cis-II)

A solution of V (200 mg) was reduced on a Lindlar catalyst, as described for the reduction of the position isomer IV. The product was shown by VPC to be identical with the product obtained by reduction of IV with Na in liquid ammonia; the identity of this product as *cis*-II has been established previously.[17]

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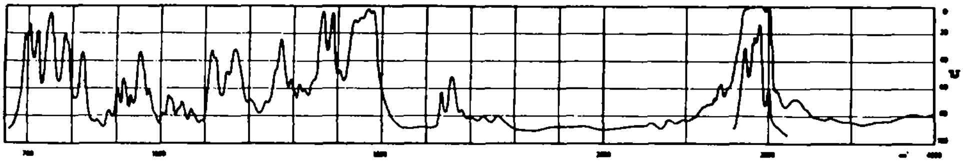
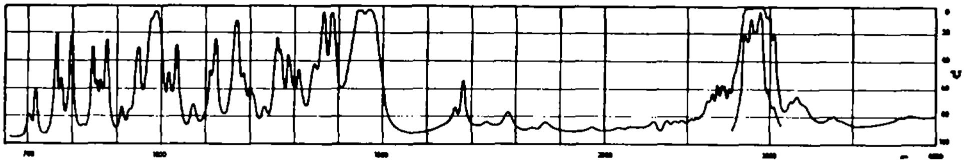
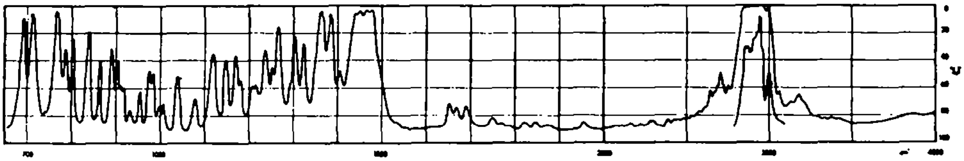
[27] H. A. Staab and G. Walther, *Liebigs Ann.* **657**, 98 (1962).



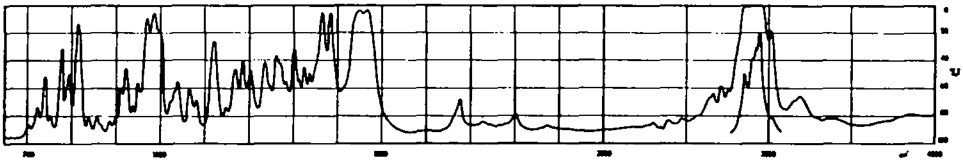
1,1,4,4-Tetramethyl-*cis*-cyclodec-7(8)-ene (*cis*-I)



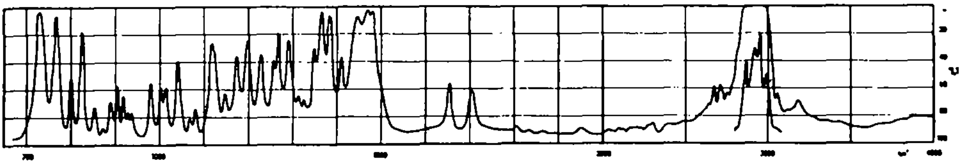
1,1,4,4-Tetramethyl-*trans*-cyclodec-7(8)-ene (*trans*-I)



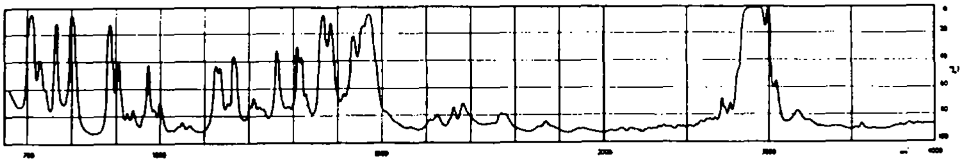
1,1,4,4-Tetramethyl-*cis*-cyclodec-6(7)-ene (*cis*-II)



1,1,4,4-Tetramethyl-*trans*-cyclodec-6(7)-ene (*trans*-II)



1,1,4,4 Tetramethyl-*cis*-cyclodec-5(6)-ene (*cis*-III)



1,1,4,4-Tetramethylcyclodeca-*cis*,*cis*-6,8-diene (VI)

FIG. 4. IR spectra (Recorded on a Zeiss-Jena UR-10 Infrared spectrometer. I–V: neat, cell-thickness 0·072 mm and for the 2850–3050 cm^{-1} region in CS_2 solution, cell thickness 0·12 mm. VI: neat, cell thickness 0·039 mm.)

2-Hydroxy-5,5,8,8-tetramethylcyclodecanone oxime

A solution of 5,5,8,8-tetramethylcyclodecan-2-olone (45·2 g, 0·2 mole) in EtOH (300 cc) was treated with a solution of hydroxylamine hydrochloride (27·8 g) in water (150 cc) and sodium acetate trihydrate (55 g) in water (150 cc). Crystals of the oxime began to separate almost at once, the mixture was diluted with water and the product filtered off and washed with light petroleum m.p. 179–183°, 43·1 g (89%). Crystallization from ethyl acetate, benzene and EtOH raised the m.p. (to 181–185°) but did not narrow the rather large range; moreover the m.p. was found to depend somewhat on the rate of heating. (Found: C, 69·66; H, 11·28; N, 5·80. $C_{14}H_{27}NO_2$ requires: C, 69·71; H, 11·33; N, 5·82%.) The crude oxime was used for further work.

4,4,7,7-Tetramethylcyclodecylamine. To a solution of the above oxime (31·4 g, 0·13 mole) in dry n-butanol (1·1) was added in the course of about 15 min 50 g of Na, the rate of addition being such as to keep the solution vigorously refluxing, and heating was continued till all the Na had passed into solution (about 30 min). The resulting light yellow solution was acidified with HCl and the butanol removed by steam distillation. The aqueous residue was made strongly alkaline with KOH and the organic base taken up in ether. The ethereal extracts were dried over KOH, the ether distilled off and the residue separated into two fractions by distillation. The lower boiling fraction, b.p. 146–155°/12 mm, consisted of the crude amine (19·3 g, 70%); and a higher boiling fraction (3·66g), b.p. 125–135°/0·05 mm, consisting of a mixture of the two possible 2-aminocyclodecanol derivatives was discarded. The crude amine fraction was taken up in a small volume of EtOH, treated with ethereal HCl and the precipitated hydrochloride crystallized once from water, m.p. 251–253° (dec). (Found: C, 68·22; H, 12·23; N, 5·48. $C_{14}H_{30}ClN$ requires: C, 67·84; H, 12·20; N, 5·68%.)

The amine was liberated from the hydrochloride in the usual manner and distilled, b.p. 139–140°/12 mm, 14·46 g (51·5%).

4,4,7,7-Tetramethylcyclodecyldimethylamine. The above amine (3·17 g) was refluxed with formic acid and 25% aqueous formaldehyde for 18 hr, acidified with HClaq and evaporated and after adding another 40 cc 1:1 HCl was again evaporated to dryness. The residue was dissolved in 40 cc 1:1 HCl and treated with a solution of 3 g $NaNO_2$ in 10 cc water, allowed to stand at room temp (or 30 min, shaken with ether, the aqueous layer made alkaline and the base taken up in ether. The ethereal extracts were dried over NaOH and the base distilled, b.p. 99–101°/0·5 mm, yield 3·13 g (88%). (Found: C, 80·27; H, 13·84; H, 5·80. $C_{16}H_{33}N$ requires: C, 80·26; H, 13·89; N, 5·85%.)

4,4,7,7-Tetramethylcyclodecyltrimethylammonium iodide

(a) A solution of 4,4,7,7-tetramethylcyclodecyldimethylamine (1·2 g, 0·005 mole) and MeI (1·45 g) in MeOH (5 cc) was refluxed for 1 hr. The solution was evaporated and the residue recrystallized from MeOH, yield 1·45 g (61%), m.p. 244–245° (dec). (Found: C, 53·65; H, 9·63; N, 3·67. $C_{17}H_{36}IN$ requires: C, 53·54; H, 9·51; N, 3·67%.)

(b) A solution of 4,4,7,7-tetramethylcyclodecylamine (8·46 g, 0·04 mole) and MeI (11·36 g) in MeOH (20 cc) was refluxed for 1 hr, treated with MeONa (prepared from 0·92 g Na) in MeOH, the solution briefly heated, a second lot of MeI (11·36 g) added and refluxed for 1 hr. Finally, methanolic MeONa (from 0·92 g Na) was added, the solution partially evaporated and the crystalls filtered off. Crystallization from water afforded 11·38 g (75%) of the quaternary salt, m.p. 244–245°.

1,1,4,4-*Tetramethyl*-trans-*cyclodec*-7(8)-*ene* (trans-I) and
1,1,4,4-*Tetramethyl*-trans-*cyclodec*-6(7)-ene (trans-II)

(a) *Pyrolysis of* 4,4,7,7-*tetramethylcyclodecyltrimethylammonium methoxide.* The quaternary base was liberated from the above salt (26 g) using Ag_2O in MeOH. The methanolic solution was taken to dryness under red. press., the residue heated to 200° and the distillate collected in a flask cooled with EtOH–dry ice. The distillate was taken up in pentane, the extracts washed with very dil H_2SO_4aq, water, $NaHCO_3$aq and again with water and finally dried over $MgSO_4$. The residue was distilled, b.p. 108–110°/13 mm, 11·6 g (87%), and the product found to consist of a mixture of four olefins: 3% *cis*-II, 1% *cis*-I, 46% *trans*-II and 50% *trans*-I, listed in the order of emergence in VPC. The mixture was subjected to partition chromatography between pentane and $AgNO_3$aq on silica gel[26] (1 part $AgNO_3$, 4 parts water, 10 parts silica gel). The order of emergence of the olefins in this system is the same as in VPC. The composition of the individual fractions was controlled by VPC.

Fractions enriched in the olefin *trans*-I and *trans*-II in the first run were re-chromatographed, and some 2·5–3·0 g of pure samples of *trans*-I (Found: C, 86·49; H, 13·28. $C_{14}H_{26}$ requires: C, 86·51; H, 13·49%) and *trans*-II (Found: C, 86·45; H, 13·53. $C_{14}H_{26}$ requires: C, 86·51; H, 13·49%) were obtained.

(b) *Pyrolysis of* 4,4,7,7-*tetramethylcyclodecyldimethylamine oxide.* A solution of 4,4,7,7-tetramethylcyclodecyldimethylamine (1·4 g) in MeOH (5 cc) was treated at 0° with 5 cc of 30% H_2O_2 and the solution shaken for 6 hr at room temp. Pt black (0·15 g) was carefully added to the reaction mixture under N_2, the mixture filtered and the filtrate evaporated under red. press. The viscous residue was heated to 110–160° at 14 mm, the distillate taken up in ether, washed with dil HCl, water, dried over $MgSO_4$ and distilled. The product (0·65 g) gave a satisfactory analysis for the olefin $C_{14}H_{26}$ and was shown by VPC to consist of 66% *trans*-I, 31% *trans*-II, and a trace of *cis*-I and 3% *cis*-II.

Equilibration of the 1,1,4,4-*tetramethylcyclodecenes*

Li (300 mg) was added to carefully dried ethylene diamine (15 cc) in a flask fitted with a reflux condenser under dry purified N_2[11]. A 100 mg sample of the olefin (*cis*-I, *cis*-II, *trans*-I or *trans*-II) was added to the discoloured solution of lithium 2-aminoethylamide and the solution heated for 3 hr to 117°. (In the case of *trans*-II, the equilibration proceeded more slowly, and heating was therefore continued for 7 hr.) The cooled reaction mixture was diluted with water, shaken with pentane, the pentane extracts repeatedly washed with dil HCl and water, the extracts dried over $MgSO_4$ and the pentane removed by distillation through a column. The crude residue was directly analysed by VPC.

The analyses are listed in Table 3.

TABLE 3

Starting olefin	Product composition *cis*-I	*trans*-I	*cis*-II	*trans*-II	*cis*-III	*trans*-III
cis-I	0	0·5	92·8	2·3	0·8	3·6
trans-I	0	0·5	92·8	2·1	0·8	3·8
cis-II	0	0·5	92·8	2·1	0·8	3·8
trans-II	0	0·5	92·5	2·0	1·0	4·0

Base-catalysed isomerization of the acetylenes IV *and* V

A solution of freshly sublimed potassium t-butoxide (200 mg) and IV or V (100 mg) in dry dimethylsulphoxide[18] (2·5 cc) was heated in a sealed tube for 6 hr to 90°. All manipulations previous to the sealing were carried out in a "dry-box" under N_2. The reaction mixture was taken up in pentane, the pentane solution extracted with water, dried over $MgSO_4$ and the solvent carefully distilled off. The crude residue was shown by VPC ot contain 97% of 1,1,4,4-tetramethylcyclodeca-*cis*,*cis*-6,8-diene, irrespective whether IV or V was used; the remaining 3% were products not identical with either the starting IV or V or the allenes, described in our previous paper.[17]

An experiment carried out on a preparative scale (from 1 g IV) afforded a residue which by distillation gave 0·9 g (90%) crystals which, after crystallization from MeOH had m.p. 29°. Purification may advantageously be effected by way of the $AgNO_3$-adduct. (Found: C, 87·54; H, 12·41. $C_{14}H_{24}$ requires: C, 87·42; H, 12·58%.) The IR spectrum (Fig. 4) shows no absorption at ~985 cm^{-1}.

The same results were obtained when the isomerization was carried out using lithium 2-aminoethylamide in ethylene diamine (under the same conditions as in the case of the olefins, cf. above).

In hydrogenation of this compound 2 equivs H_2 were taken up and the resulting saturated hydrocarbon was identical by VPC with 1,1,4,4-tetramethylcyclodecane.

Oxidation of 1,1,4,4-*tetramethylcyclodeca*-6,8-*diene*

The diene (80 mg) was oxidized, under standard conditions, successively with OsO_4, sodium periodate and $KMnO_4$, without purification of intermediates. The crude acid obtained was esterified

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[18] A. Schriesheim, R. J. Muller, C. A. Rowe, *J. Amer. Chem. Soc.* **84**, 3164 (1962).

with diazomethane; the practically uniform product was identical, according to VPC on 2% poly(1,4-butylene)glycoladipate–tetracyanoethoxyerythritol (1:1), with authentic dimethyl 2,2,2′,2′-tetramethylsuberate.[29]

Heats of hydrogenation

Heats of hydrogenation of the various compounds reported in this paper were obtained in acetic acid solution at 25° according to the previously described method.[30] The results were: *cis*-I, −28·71 ± 0·14 kcal/mole; *trans*-I, −26·05 ± 0·11 kcal/mole; *cis*-II, −22·03 ± 0·17 kcal/mole; *trans*-II, −25·45 ± 0·05 kcal/mole; IV (7,8) −58·93 ± 0·20 kcal/mole; V (6,7), −61·68 ± 0·07 kcal/mole. The data represent averages of two determinations, except in the case of *cis*-I where 3 runs were carried out. As noted earlier[30] the deviations reported here are experimental, and the overall accuracy of the method is probably of the order of ±1%.

Acknowledgement—We wish to express our gratitude to Professors V. Prelog and J. D. Dunitz (Eidgenössische Technische Hochsule, Zürich) for most valuable discussions.

[29] S. F. Birch, V. E. Gripp, D. T. McAllen and W. S. Nathan, *J. Chem. Soc.* 1363 (1952).

[30] R. B. Turner, W. R. Meador and R. E. Winkler, *J. Amer. Chem. Soc.* **79**, 4116 (1957).