

The Conformation of 4,4,8,8-Tetramethylcyclodecanone

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The slow-exchange ^1H NMR spectrum below -100°C shows that 4,4,8,8-tetramethylcyclodecanone has a single unsymmetric conformation. The appearance of one α -proton at very low field and one β -proton at very high field is best explained on the basis of a conformation of boat-chair-chair type. A single exchange process is observed by dynamic NMR spectroscopy ($\Delta G^\ddagger = 9.5-10$ kcal/mol),* although two processes would be expected; both must therefore have the same barrier height.

Dieckmann cyclization of the diethyl ester of 4,4,8,8-tetramethylundecanedioic acid gives, in addition to a good yield of the 20-membered cyclic diketone, a difficultly reproducible and small yield of the 10-membered cyclic monoketone.¹ This compound, 4,4,8,8-tetramethylcyclodecanone, is of particular conformational interest inasmuch as the 1,5-relationship of the two *gem*-dimethyl groups prevents this ring from adopting the generally favoured quadrangular [2323] conformation** of cyclodecane derivatives.³ Fig. 1 demonstrates that one methyl group would then have to point into the ring, which is sterically impossible. Unsubstituted cyclodecanone has been shown⁴ to take this type of conformation with the carbonyl group in the position shown.

Four alternative quadrangular conformations, whose calculated energies⁵ are reasonably low for cyclodecane itself, all have corner atoms in 1,5-relationship and should thus be able to accommodate the two *gem*-dimethyl groups. The resulting possible conformations for 4,4,8,8-tetramethylcyclodecanone are shown in Fig. 2; the ring skeleton [2233] gives conformation A, [1333] gives B, [1324] gives C

* 1 kcal = 4.184 kJ.

** This notation indicates the number of bonds in each "side" separating the "corner" atoms.²

and D, and [1414] gives E.

In the case of a similarly substituted cyclodecane, 4,4,8,8-tetramethylcyclodecanecarboxylic acid, the crystal was found³ to contain a 4:1 mixture of conformations of type A and B. The spectral data for our ketone, however, fit neither of these,* nor a mixture of the two, but are in agreement with a single unsymmetric conformation such as C or D.

PROOF OF CONFORMATIONAL HOMOGENEITY

The infrared spectra of 4,4,8,8-tetramethylcyclodecanone in the crystalline state and in CS_2 -solution show negligible differences. This, together with the relatively high melting point of 105°C , would in itself indicate conformational homogeneity. Since, however, the spectrum in either phase shows broad and numerous absorptions, the possibility that both phases contain the same conformer mixture had to be ruled out. Only an expanded crystal lattice can accept a conformer mixture, and the demonstration by differential scanning calorimetry of a perfectly normal⁶ entropy of melting ($\Delta H_m = 3.9$ kcal/mol; $\Delta S_m = 10.4$ e.u.) and no solid phase transition point down to -80°C ,

* Before having obtained a slow-exchange NMR spectrum, we suggested⁶ conformation A as the most likely candidate.

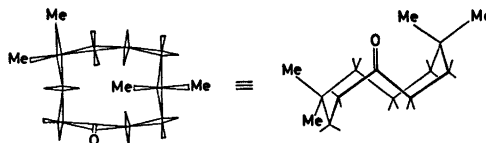


Fig. 1. The sterically impossible [2323] conformation of 4,4,8,8-tetramethylcyclodecanone.

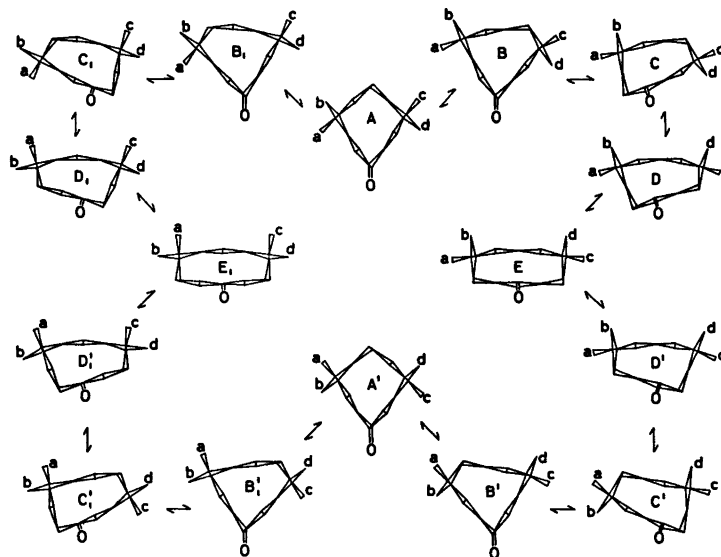


Fig. 2. Conformational interconversion scheme for five possible conformations of 4,4,8,8-tetramethylcyclodecanone.

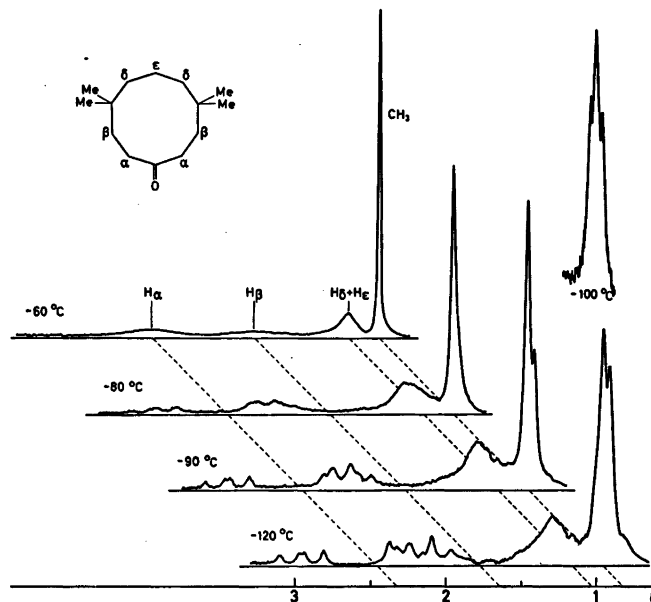


Fig. 3. 100 MHz ^1H NMR-spectra of 4,4,8,8-tetramethylcyclodecanone in CS_2 -solution at -60 , -80 , -90 , and -120 $^\circ\text{C}$. The inset in the upper right-hand corner shows the methyl region in CCl_2F_2 -solution at -100 $^\circ\text{C}$.

excluded a conformer mixture. The numerous and broad IR-absorptions then already suggest that the single conformer might be unsymmetric and perhaps not even very rigid.

THE LOW-TEMPERATURE NMR SPECTRUM

The 100 MHz ^1H NMR-spectrum was of the expected fast-exchange type down to -20 $^\circ\text{C}$.

On further cooling of CS_2 -solutions (Fig. 3) broadening of all methylene signals occurred at about -60°C , the final slow-exchange spectrum being reached at about -100°C (coalescence temp. $\sim -70^\circ\text{C}$). Broadening of the methyl line started at -80°C , the final slow exchange spectrum being reached at about -120°C (coalescence temp. $\sim 85^\circ\text{C}$). One methyl line is at higher field than the remaining mass of presumably three lines, which remain unresolved in this solvent. In CCl_2F_2 -solution at -100°C a methyl line is seen resolved both on the high- and the low-field side of a central mass presumably representing the remaining two methyl groups (Fig. 3). On further cooling this broadens and fuses with the low-field line.

The complexity of this low-temperature spectrum allowed only an indirect interpretation. This was based on integrated intensities of the four main spectral areas and correlation with the chemical shifts of the α, β, δ and ε CH_2 - and the CH_3 -protons in the fast-exchange spectrum. It gave as a result that at all temperatures from -80°C and below the intensities in the four spectral regions $\delta = 3.1 - 2.5$, $2.5 - 1.5$, $1.5 - 0.93$, and $0.93 - 0.5$, represent protons in a ratio close to 1:4.8:13, assuming that a single conformation (26 protons) is present. Thus, the lowest region must represent a single α -proton, the next-lowest region the remaining three α -protons and a single β -proton, the next-highest region the remaining three β -protons and five of the δ - and ε -protons, and the highest region twelve methyl protons and the remaining δ - (or ε -) proton. The latter absorption is actually discernible on the high-field side of the methyl lines.

This unsymmetric intensity distribution, as well as the presence of more than two types of methyl groups, immediately excludes the symmetric conformations A and E. It also excludes conformation B since the local symmetry around the corner position of the carbonyl group would require that not only one, but

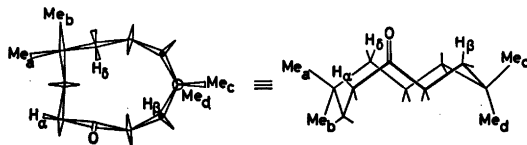


Fig. 4. The [28] conformation of 4,4,8,8-tetramethylcyclodecanone.

two, of the α -protons appear in the lowest region, namely those that are eclipsing the carbonyl group on either side. It is not possible, however, from the NMR-spectra to make a choice between the unsymmetric conformations C and D. These are both based on equivalent mirror image [1324] ring skeletons which are not genuinely quadrangular of type, but also classifiable⁷ as extremes of a biangular family [28] commonly represented (Fig. 4) in the intermediate form, sometimes referred to as boat-chair-chair.* This intermediate [28] conformation is for cyclodecane calculated⁵ to be a low barrier (1 kcal/mol) between two mirror image [1324] minima, but it may instead very well be a shallow energy minimum in our substituted ketone, since the *gem*-dimethyl groups require maximal staggering in the adjoining ring bonds; this can be achieved by moving the inherent partial eclipsing in these bonds of the [1324] forms C and D to the next ring bonds between unsubstituted carbon atoms by passing over to the [28] form (Fig. 4). Also the broad infrared absorptions can be well understood by the existence of a shallow minimum of this type.

All conformations of the [28] family satisfy the symmetry requirements and can explain the unusual chemical shifts observed. The [28] conformation of Fig. 4, chosen for the present discussion but actually representing also the possible conformations C and D, has just one α -proton (marked H_α) eclipsing the carbonyl group and thus expected at unusually low field. In cyclodecanone, where the carbonyl group by symmetry arguments must be similarly situated next to a corner position, one of the four α -protons has been reported⁴ as low as $\delta = 3.41$. Among the β -protons it seems most likely that the one marked H_β is the one at unusually low field, since this is also in the plane of the carbonyl group; this, by the way, might constitute an argument that the [28] form shown in Fig. 4 represents the actual conformation rather than C or D, where this proton gets somewhat out of the carbonyl plane. One of the δ -protons (marked H_δ) sits across the ring just above the carbonyl plane

* The boat-chair of cyclooctane⁸ is closely related and is in our notation given the symbol [26] of a biangular conformation.⁷

and so is expected to come at unusually high field. This is exactly what is observed for the [26] conformation of cyclooctane⁸ where one δ -proton in the same transannular relationship to the carbonyl group comes as high as at $\delta = 0.63$. Similarly, one of the methyl groups of our cyclodecanone (marked Me_a in Fig. 4) is closer to the carbonyl group than the others, and is probably the one which appears at slightly higher field than the other three.

It may be wondered why 4,4,8,8-tetramethylcyclodecanone adopts none of the two conformers A and B, found⁸ for the very closely related 1-carboxylic acid, or the conformer E, largely preferred by cyclodecane-1,6-dione in solution.^{9,10} One reason may be the well-established tendency^{4,9,10} for the carbonyl group of large-ring ketones to avoid corner positions and to prefer to sit next to corners. Another reason may be that the absence of one of the transannular H-H 1,5-interactions, exactly as in the [2323] conformation of cyclodecanone itself and other medium-ring ketones,^{4,9,10} favours the [28] family.

THE CONFORMATIONAL EXCHANGE PROCESS

The multi-step interconversion scheme shown in Fig. 2 has been constructed by employing the type of corner-moving elementary step discussed earlier,^{7,11} which consists in eclipsing the bond between the old and the new corner. The choice of paths becomes restricted by the requirement that *gem*-dimethyl substituted corners cannot be "moved", since this would lead to intermediate conformations with methyl groups pointing into the ring. The only exception is of course the conversion within the [28] family from one extreme C to the other extreme D, whereby the *gem*-dimethyl group moves directly from one non-genuine corner to the next in an outward motion.⁷ It is interesting that no other conformations than the actual low-energy candidates for the stable equilibrium conformation are needed as intermediates. Rapid passage by a certain number of steps along this closed loop will lead to full site exchange for any type of proton on any of the five conformational types, and to a mixing of the NMR-signals from the individual components of any conformer mixture. Whether

one or more processes can be observed by dynamic NMR-spectroscopy will depend⁷ on the symmetry of the conformers and, in the case of a mixture, on the relationship between its constituents.

The situation observed in the present case (Fig. 3) is not a very clear one inasmuch as the spectral changes take place at somewhat different temperatures in the various regions of the spectrum. However, due to the very different magnitudes of the chemical shift splittings, the estimated activation free-energies come out not significantly different in the range 9.5–10 kcal/mol. Also, the clear direct development in the low-temperature NMR spectrum of an α -CH₂ signal corresponding to one proton and a methyl signal corresponding to one methyl group, and not *via* intermediate spectra showing signals corresponding to two of each, is only in accord with a single observed site-exchange process.

Nevertheless, the interconversion scheme in Fig. 2 shows that only if the conformation has a symmetry axis (A) or a symmetry plane (E) will full exchange of all constitutionally equivalent protons be possible in a single process. Thus, A can be converted to its mirror image A' *via* the path $A \rightleftharpoons B \rightleftharpoons C \rightleftharpoons D \rightleftharpoons E \rightleftharpoons D' \rightleftharpoons C' \rightleftharpoons B' \rightleftharpoons A'$ and E can be converted to the identical conformation E₁ *via* the path $E \rightleftharpoons D \rightleftharpoons C \rightleftharpoons B \rightleftharpoons A \rightleftharpoons B_1 \rightleftharpoons C_1 \rightleftharpoons D_1 \rightleftharpoons E_1$, whereby only the critical barrier on each path is observable. In the case of an unsymmetric conformation two processes must in principle be observable.⁷ Thus C may interconvert with its mirror image C' *via* the path $C \rightleftharpoons D \rightleftharpoons E \rightleftharpoons D' \rightleftharpoons C'$ and acquire by averaging an apparent symmetry plane (as in E), whereby *cis*-related methyl groups and methylene hydrogens become equivalent ($a = c, b = d$), or it may interconvert with the identical conformation C₁ *via* the path $C \rightleftharpoons B \rightleftharpoons A \rightleftharpoons B_1 \rightleftharpoons C_1$ and acquire by averaging an apparent twofold symmetry axis (as in A), whereby *trans*-related methyl groups and methylene hydrogens become equivalent ($a = d, b = c$).

The only possible conclusion is that the critical barrier on both interconversion paths have closely similar values. It seems unrealistic to attempt strain energy calculations on these compounds, but for the parent unsubstituted cyclodecane the corresponding barriers have

been reliably calculated.⁵ Fixing the energy of the [1324] conformation (C and D) as zero, the highest barrier on the first path (~ 6 kcal/mol) comes between [1333] and [2233] ($B \rightleftharpoons A$), and the highest barrier on the second path (~ 15 kcal/mol) between [1324] and [1414] ($D \rightleftharpoons E$). It is likely that the former barrier should increase somewhat on *gem*-dimethyl substitution. It is even more likely that the latter barrier should decrease considerably on carbonyl substitution, since the severe transannular H-H 1,5-interaction in the transition state has been relieved by conversion of one CH_2 -group into a carbonyl group, the interaction being now between a δ -hydrogen and the oxygen.

EXPERIMENTAL

Infrared spectra were recorded on a Perkin-Elmer Grating Infrared Spectrophotometer 457.

Calorimetric measurements were performed with a Perkin-Elmer Differential Scanning Calorimeter IB.

¹H NMR spectra were recorded on a Varian HA 100 15D instrument.

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