

The Asymmetric Nature of the Conformation of 4,4,7,7-Tetramethylcyclononane

GERD BORGEN and JOHANNES DALE

Kjemisk Institutt, Universitetet i Oslo, Blindern, Oslo 3, Norway

Dynamic ^{13}C NMR spectroscopy reveals two conformational exchange processes for this nine-membered ring. It must therefore have an asymmetric [234] conformation with the carbonyl group in a non-corner position. This explains earlier difficulties in understanding details of the ^1H spectrum on the basis of a symmetric [333] conformation with the carbonyl group in a corner position.

We have previously reported¹ that a conformational process with very high activation energy ($\Delta G^\ddagger = 65$ kJ/mol) is observed for 4,4,7,7-tetramethylcyclononane by dynamic ^1H NMR spectroscopy, and that the splitting of all chemical shifts into two in the slow-exchange spectrum suggests a triangular [333] conformation * with a two-fold symmetry axis and the carbonyl group in a corner position (A, Fig. 1).

The observation of a different triangular ring skeleton [225] for cyclononane itself in its crystalline HgCl_2 adduct,³ as well as the unsymmetric non-corner position of the carbonyl group both in this adduct and for the free molecule in solution,⁴ would by itself be insufficient as an argument against our assignment. The 1,4-relationship of the gem-dimethyl substituents excludes the [225] skeleton and might be expected to favour the [333] skeleton (A, Fig. 1).

There exists, however, a third type of triangular ring-conformation [234] which is unsymmetric and can also accommodate the methyl groups in corner positions,^{2,5} but will place the carbonyl group next to a corner (B,

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

Figs. 1 and 2). Such a conformation would be in better accord with recently accumulated X-ray, NMR and dipole moment data not only for other medium-ring cycloalkanones, where relief of transannular H–H 1,5-interactions is an energetic advantage, but also for large-ring cycloalkanones and "diametric" cycloalkanediones. In these latter cases only H–H 1,4-interactions (*gauche* interactions) can be invoked to explain that the carbonyl group is never at a corner but usually next to it. Thus, in addition to the data for cyclononane already mentioned, cyclooctanone^{6,7} and cyclooctane-1,5-dione⁷ have both been shown to take the boat-chair or [26] conformation with the carbonyl group(s) next to a corner. Cyclodecanone has the usual [2323] conformation⁴ and 4,4,8,8-tetramethylcyclodecanone the unusual [28] conformation,⁸ both with the carbonyl group next to a corner. Cyclodecane-1,6-dione adopts in the crystal a [2323] conformation with both carbonyl groups next to corners,⁹ and in solution a [1414] conformation with no genuine corners.^{7,10} Cycloundecanone has a crystal conformation of [335] type with the carbonyl group two bonds away from a corner,¹¹ and such a single conformation would be in agreement with data for the solution.⁷ Cyclododecanone,⁴ *cis*-2,12-dibromocyclododecanone,¹² and cyclododecane-1,7-dione¹⁰ all take the familiar [3333] conformation with the carbonyl group(s) next to a corner. Cyclotetradecanone has both in solution⁴ and in the solid¹³ a mixture of conformers, and these are in the solid all of the usual [3434] type with the carbonyl group in any but the corner positions. A similar situation is indicated for

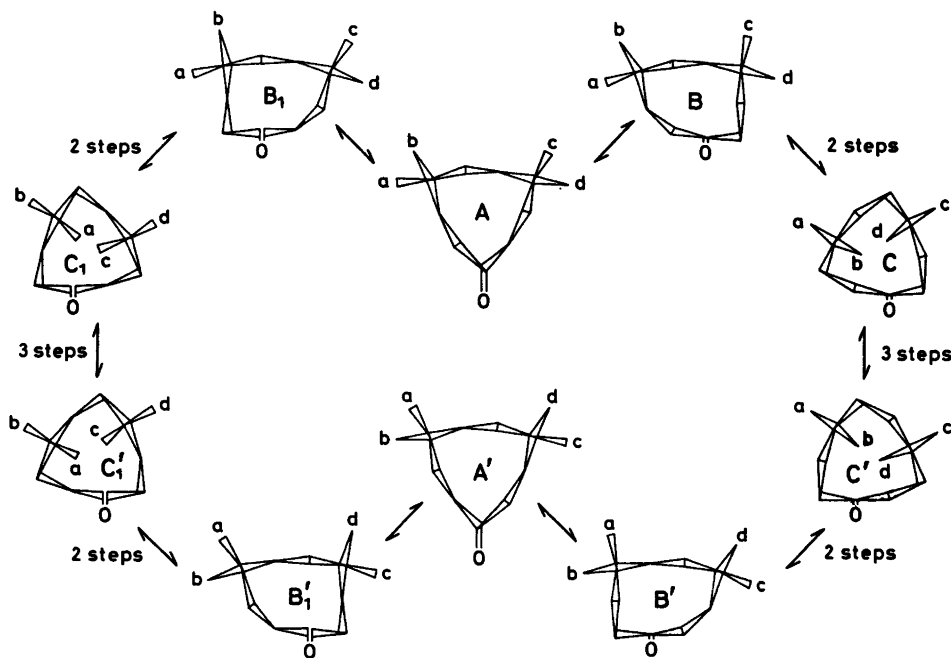


Fig. 1. Conformational interconversion scheme for 4,4,7,7-tetramethylcyclononane.

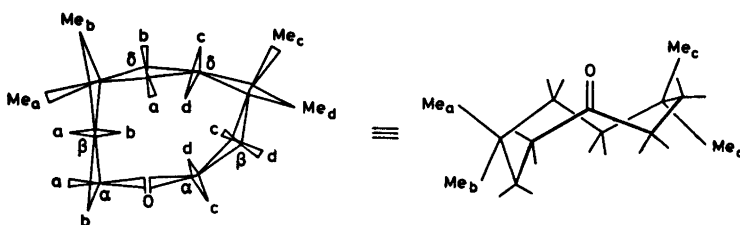


Fig. 2. The [234] conformation of 4,4,7,7-tetramethylcyclononane.

cyclohexadecanone⁴ and cyclohexadecane-1,9-dione.¹⁰

Some anomalies in the ¹H NMR-spectrum of 4,4,7,7-tetramethylcyclononane which we have already noted¹⁴ would become explicable on the basis of the unsymmetric conformation B exchanging rapidly even at low temperature with B₁ via A so as to obtain the apparent symmetry of A. Thus, the observed¹⁴ strong geminal splitting of the chemical shifts of the β- and δ-hydrogens and the methyl groups seems unlikely in conformation A where the anisotropic carbonyl group points outwards from the corner position, but can be readily understood on the basis of an averaging be-

tween B and B₁ where in each (Fig. 2) the carbonyl group comes close to one inner β-hydrogen (c), one inner δ-hydrogen (a), and one methyl group (a). Furthermore, the very small geminal splitting of the α-hydrogens which is observed¹⁴ in the presence of large quantities of europium shift reagent is hardly possible for conformation A, outer and inner hydrogens being very different, but may well result from an averaging between B and B₁. Finally, in view of the very low-field position observed^{4,6,8} for α-hydrogens "eclipsing" the carbonyl group in other medium-ring ketones, the chemical shift is here not at sufficiently low field to correspond to the two carbonyl-

eclipsing α -hydrogens in A, but may well correspond to the averaging of only one low-field and one normal as expected for B and B₁ (a and d in Fig. 2).

NMR-SPECTROSCOPY

Attempts to observe a second process of lower energy in the 100 MHz ¹H NMR-spectrum were inconclusive; signal broadening took place in CHCl₂F from -100 to -130 °C, but no resolved slow-exchange spectrum could be obtained. On the other hand, the 15 MHz ¹³C NMR-spectrum (Fig. 3) has now in fact revealed two processes. In addition to a splitting of the methyl carbon line at 29.2 ppm, identified by its coupling, ($T_c = 37$ °C, $\Delta G^\ddagger = 67$ kJ/mol) corresponding to the process observed earlier in the ¹H spectrum,¹ a further broaden-

ing of most lines, especially the methyl carbon lines, was seen below -100 °C. Since the carbonyl carbon line remains sharp, as does the quaternary γ -carbon line (presumably because both γ -carbons have similar chemical shifts) and of course also signals from the solvent and TMS, the broadening is not ascribed to increased viscosity, but to the freezing of an exchange process. Since this ketone has been shown earlier¹⁵ to be conformationally homogeneous, the only conceivable further spectral change is the splitting of all carbon lines, except that for carbonyl carbon, into just two lines. General viscosity broadening did take place on further cooling in several solvents and prevented the observation of a resolved slow-exchange spectrum. Nevertheless, the free energy barrier for this process can be estimated to be in the range 22–27 kJ/mol, assuming coalescence temperatures from -150 to -160 °C and $\Delta\nu$ from 15 to 60 Hz.*

Thus, the real conformation lacks symmetry, in accord with conformation B, so that also this ketone shows a normal medium-ring behaviour in the sense that the carbonyl group is in a non-corner position.

THE CONFORMATIONAL EXCHANGE MECHANISM

The complete interconversion scheme in Fig. 1 consists of six repetitions of the three-step corner-moving cycle proposed earlier for full site-exchange in the [333] conformation of cyclononane.¹⁶ In each cycle the [234] conformation occurs twice as intermediate; only the low-energy versions B are shown in Fig. 1, the other [234] intermediates with *gem*-dimethyl groups in non-corner positions are of high

* One referee is not convinced that the observed line broadening is due to an exchange process, since quaternary carbons are less influenced by viscosity effects than those carrying hydrogens. We observe, however, identical broadening in vinyl chloride and various mixtures with CHCl₂F, and the ¹³C spectra of similar cyclic ketones^{4,7} in the same solvents show sharp lines for CH₃-carbons down to -175 °C. In the meantime the crystal structure of 4,4,7,7-tetramethylcyclononane has been solved by Per Groth; it reveals the proposed [234] conformation. A low-energy process *must* therefore exist, and it seems unlikely that its activation energy can be lower than the value estimated here.

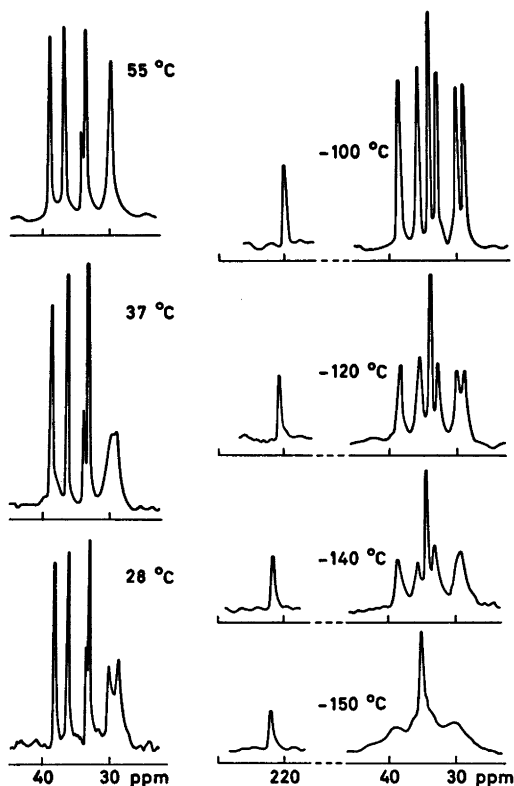


Fig. 3. 15 MHz ¹³C NMR spectra of 4,4,7,7-tetramethylcyclononane in CDCl₃ solution from 28 to 55 °C (left row) and in CHCl₂F/CHCl₃ solution from -100 to -150 °C (right row).

energy and not populated. All [333] intermediates C, on the other hand, are shown, even though these are also of high energy.

If the stable conformation had been the symmetric one A as concluded earlier, the only possible interconversion would have been with the mirror image A' to exchange geminal methyls and hydrogens *via* a nine-step path $A \rightleftharpoons C \rightleftharpoons C' \rightleftharpoons A'$ (or $A \rightleftharpoons C_1 \rightleftharpoons C_1' \rightleftharpoons A'$). The critical barrier should occur in one of the steps between C and C' when the 5-6 bond passes *syn*-eclipsing, since then the inner methyl groups b and d interact strongly. This interaction between two methyl groups in 1,4-relationship can never be bypassed in any scheme for geminal exchange in such ring systems, and explains why the observed barrier (67 kJ/mol) is so much higher than for 4,4,8,8-tetramethylcyclodecanone (~42 kJ/mol) where the methyl groups are in 1,5-relationship and the most severe 1,4-interaction occurs between one methyl group and one hydrogen.⁸ The possible importance of an additional strain due to ring size cannot be excluded, however, although nine- and ten-membered rings are not very different with respect to ring strain. The observed barrier for geminal exchange in cyclodecanone (30.6 kJ/mol) is in fact even higher than in cyclononane (27.2 kJ/mol).⁴

If B is taken as the stable conformation, as now shown, a partial exchange with the identical conformation B₁ over two identical barriers *via* the already mentioned two-step path $B \rightleftharpoons A \rightleftharpoons B_1$ becomes possible; all *trans*-related substituents (Fig. 2) thereby become pairwise identical (a=d; b=c). One would expect these barriers to be less strongly increased by the presence of the *gem*-dimethyl groups as compared to the barrier observed⁴ by ¹³C spectroscopy in cyclononane (21 kJ/mol) for the same type of partial exchange, as indeed now found to be the case (22-27 kJ/mol). Exchange of B with its mirror image B' *via* the seven-step path $B \rightleftharpoons C \rightleftharpoons C' \rightleftharpoons B'$ over the very high critical barrier already discussed makes all *cis*-related substituents pairwise identical (a=c; b=d). Full exchange requires that both processes occur.

EXPERIMENTAL

The ¹³C NMR spectra were recorded in a Jeol Fourier transform instrument (JNM-FX 60) operating at 15 MHz using external deuterium lock. For the higher temperatures the solvent was CDCl₃, for the lower temperatures a mixture of CHCl₃ and CHCl₂F. The number of pulses varied from 400 to 900, pulse intervals were 4 s. The lines were identified by their coupling pattern in the off-resonance decoupled spectrum. Ppm is given relative to tetramethylsilane.

REFERENCES

1. Borgen, G., Dale, J. and Schaug, J. *Acta Chem. Scand.* 26 (1972) 1073.
2. Dale, J. *Acta Chem. Scand.* 27 (1973) 1115.
3. Dahl, S. and Groth, P. *Acta Chem. Scand.* 25 (1971) 1114.
4. Anet, F. A. L., Cheng, A. K. and Krane, J. *J. Am. Chem. Soc.* 95 (1973) 7877.
5. Dale, J. *Acta Chem. Scand.* 27 (1973) 1149.
6. Anet, F. A. L. In Chiurdoglu, G., Ed., *Conformational Analysis*, Academic, New York 1971, p. 15.
7. Anet, F. A. L., St. Jacques, M., Henrichs, P. M., Cheng, A. K., Krane, J. and Wong, L. *Tetrahedron* 30 (1974) 1629.
8. Borgen, G. and Dale, J. *Acta Chem. Scand. B* 30 (1976) 711.
9. Germain, G. Cited by Dunitz, J. D. *Perspectives in Structural Chemistry* 2 (1968) 1.
10. Alvik, T., Borgen, G. and Dale, J. *Acta Chem. Scand.* 26 (1972) 1805.
11. Groth, P. *Acta Chem. Scand. A* 28 (1974) 294.
12. Dehli, J. and Groth, P. *Acta Chem. Scand.* 23 (1969) 587.
13. Groth, P. *Acta Chem. Scand. A* 29 (1975) 374.
14. Borgen, G. *Acta Chem. Scand.* 26 (1972) 1740.
15. Borgen, G. and Dale, J. *Chem. Commun.* (1970) 1105.
16. Dale, J. *Acta Chem. Scand.* 27 (1973) 1130.

Received March 19, 1976.