

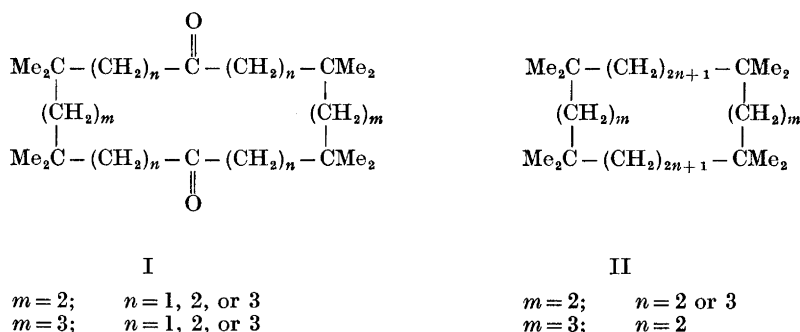
Fourfold *gem*-Dimethyl Substituted Macrocyclic Paraffins

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Of a series of tetrakis(*gem*-dimethyl)cycloalkanediones only those having the carbonyl groups separated from the dimethyl branchings by more than one methylene group can be reduced to the hydrocarbon. Conformational homogeneity is observed for the resulting octamethyl substituted 18- and 20-membered rings.

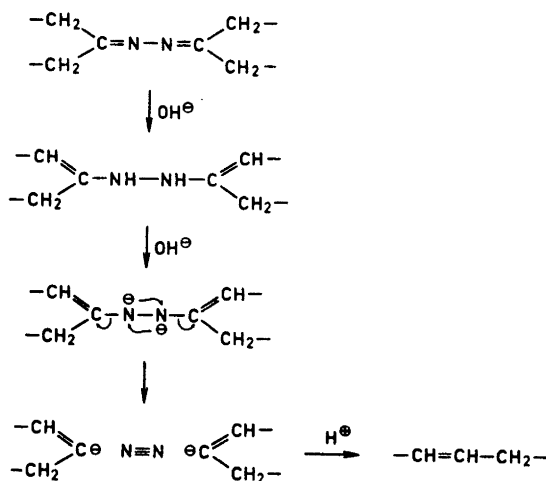
The syntheses of a series of macrocyclic diketones (I) carrying four *gem*-dimethyl substituents were described recently¹ as intermediates for further transformation to the tetrakis(*gem*-dimethyl)cycloalkanes (II), which were of interest as model substances to test earlier conformational predictions.²



Thus, the relative positions of the *gem*-dimethyl groups were designed to fit corner positions on rectangular diamond-lattice conformations,² the only positions that can accommodate two methyl substituents. Such ring conformations should be further favoured over other diamond lattice conformations since no bond in the four polymethylene chains is required to adopt a higher-energy *gauche*-conformation. The perspective drawings in Fig. 1 show that these ring conformations are of two types,² the compact 14-, 18-, and 22-membered rings ($m=2$) and the open 16-, 20-, and 24-membered rings ($m=3$). The former have approximate van der Waals contact between the long sides, the latter an interior hole.

Reduction of the cyclic diketones (I) to saturated hydrocarbons (II) was attempted using the standard Wolff-Kishner method³ (hydrazine and strong alkali in diethyleneglycol). For the 18-membered and higher rings this presented no problem, except that a rather long reaction time was needed. The 14- and 16-membered rings, however, strongly resisted this reduction, presumably because of steric hindrance from the *gem*-dimethyl groups, which are here closer to the carbonyl group ($n=1$) than in the higher homologues. These rings were also difficult to obtain by cyclization.¹

In addition to the normal hydrazone intermediate in the Wolff-Kishner reduction, a yellow polymeric azine was also formed. The tiny amount of hydrocarbon isolated after 20 h at 220° in the case of the 14- and 16-membered diketones showed olefinic infrared absorption bands. Mass spectrometry revealed the presence of both di- and mono-olefin in a ratio of 3:2 and the absence of cycloalkane for the 14-membered ring, while the 16-membered ring gave diolefin, mono-olefin and cycloalkane in the ratio 6:3:1. This may indicate that azines give rise to olefin-formation under these conditions. A possible mechanism, related to the assumed mechanism⁴ for paraffin-formation from hydrazones, can be suggested:



Other methods of reduction were also tried without success, such as the modified Wolff-Kishner reduction claimed to be more effective for hindered carbonyl groups⁵ and the lithium/ethylamine reduction⁶ of the ethylene dithioketal derivatives, which were quite difficult to prepare.

The obtained pure cycloalkanes with 18-, 20-, and 22-membered rings have the properties shown in Table 1. The calorimetric data for the melting process have already been discussed⁷ for the case of the 18-membered ring and shown to be appropriate for a rigid molecule of this symmetry. There is therefore reason to believe that 1,1,4,4,10,10,13,13-octamethylcyclooctadecane is in fact present

Table 1.

Cycloalkane (II)	Number of ring atoms	Melting point	ΔH_m (kcal/mol)	ΔS_m (e.u.)	Beginning broadening in NMR
$m=2, n=2$	18	165° ^a	6.1 ^a	13.8 ^a	-30°
$m=3, n=2$	20	166°	11.4	26.4	-50°
$m=2, n=3$	22	138°	14.0	34.1	-60°

^a Total melting. Part of the melting process takes place at a transition point at 155° ($\Delta H_{tr}=1.4$ kcal/mol, $\Delta S_{tr}=3.2$ e.u.; $\Delta H_m=4.7$ kcal/mol, $\Delta S_m=10.6$ e.u.).

exclusively in the rectangular conformation shown in Fig. 1, while 1,1,10,10-tetramethylcyclooctadecane^{7,8} and cyclooctadecane itself⁷ have melting entropies higher by factors of 1.9 and 2.2 and therefore must consist in the melt of conformer mixtures. For the octamethyl substituted 20- and 22-membered rings the calorimetric data (see Table 1) are more difficult to interpret. The much higher observed melting entropies would have indicated conformer mixtures in the melt only if the melting enthalpies had remained relatively constant.² As these increase by roughly the same factor, the crystal forces must be quite different, and no clear conclusion can be drawn.

From the infrared spectra in Figs. 2, 3, and 4 the situation seems more clear. Thus, octamethylcyclooctadecane (Fig. 2) shows no bands in solution in addition to those present in the crystal spectrum, in contrast to the situation

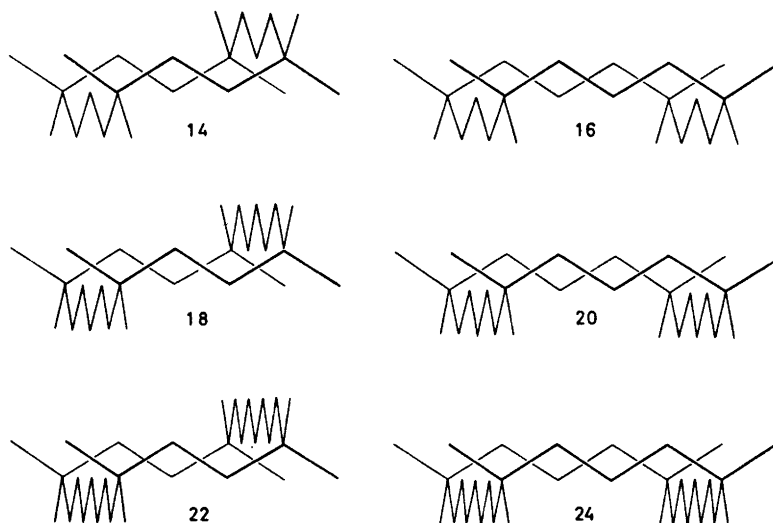


Fig. 1. Proposed conformations for tetrakis(*gem*-dimethyl)cycloalkanes (II). The number of ring atoms ($2m + 4n + 6$) is marked.

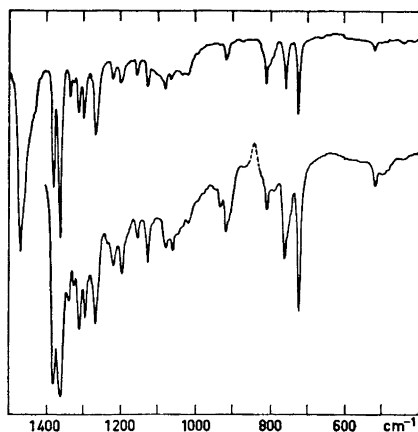


Fig. 2. Infrared spectra of 1,1,4,4,10,10,13,13-octamethylcyclooctadecane as KBr-disc (upper curve) and in CS_2 -solution (lower curve).

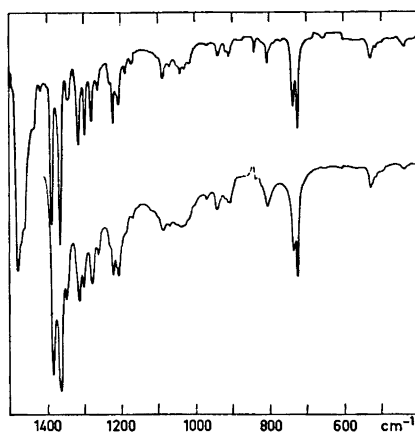


Fig. 3. Infrared spectra of 1,1,5,5,11,11,15,15-octamethylcycloeicosane as KBr-disc (upper curve) and in CS_2 -solution (lower curve).

for 1,1,10,10-tetramethylcyclooctadecane⁸ and particularly cyclooctadecane itself⁹ where broad new absorption regions in solution and melt betray conformer mixtures.

For octamethylcycloeicosane (Fig. 3) the situation is essentially the same; no new bands appear in solution, although some bands become broader. An additional argument that the single conformation common for the crystal and the solution is the open one shown in Fig. 1 is the marked tendency for the crystals to retain solvent molecules¹⁰ (methanol, CCl_4 , water). No such tendency is shown by cycloeicosane itself, and in this case the IR-spectrum of the solution is clearly different from that of the solid.

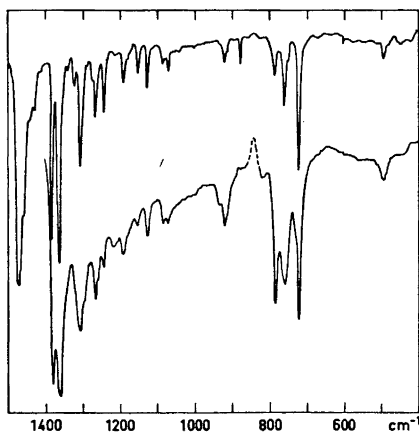


Fig. 4. Infrared spectra of 1,1,4,4,12,12,15,15-octamethylcyclodocosane as KBr-disc (upper curve) and in CS_2 -solution (lower curve).

Finally, octamethylcyclodocosane show marked differences between solid and solution spectra (Fig. 4). Nevertheless, all main peaks of the solid remain the main peaks in solution, and no really new absorption peaks appear. It therefore seems as if the changes are chiefly due to band broadening so as to suggest that the solution consists essentially of the same conformation, but with larger deformation amplitudes and hence a less perfect symmetry than when held rigidly in the crystal lattice (*cf.* the large melting enthalpy).

Evidence has been given earlier¹¹ that unsubstituted cyclotetradecane has a single diamond lattice conformation under all circumstances, while unsubstituted cyclohexadecane is a conformer mixture in solution, in the melt and in a high-temperature solid phase, but selects the open square diamond-lattice conformation (Fig. 1) below the solid-solid transition point. Higher unsubstituted cycloalkanes are, as already mentioned, conformationally inhomogeneous in solution. Since proper fourfold *gem*-dimethyl substitution has now been shown to bias a single conformation of not only the "compact", but also of the "open" type (Fig. 1), and of rings as large as 18, 20, and possibly 22 members, it seems quite certain that also 1,1,4,4,8,8,11,11-octamethylcyclotetradecane and 1,1,5,5,9,9,13,13-octamethylcyclohexadecane, if they could be prepared, would prove to be conformationally homogeneous under all circumstances. The corresponding diketones were in fact the only members of the series II ($m = 2$ and 3 , $n = 1$) which proved to be conformationally homogeneous.¹²

EXPERIMENTAL

1,1,4,4,10,10,13,13-Octamethylcyclooctadecane. Potassium hydroxide tablets (0.35 g) were dissolved by heating in diethyleneglycol (8 ml). To the cooled solution were added 4,4,7,7,13,13,16,16-octamethylcyclooctadecane-1,10-dione (0.53 g) and 99 % hydrazine hydrate (3 ml). After refluxing overnight, hydrazine and water was distilled off until the temperature reached 190°, and the residue refluxed at that temperature for 20 h. Water (20 ml) was added, the solution was extracted with pentane, the pentane solution washed with water and dried over magnesium sulphate. Evaporation of the pentane left the 1,1,4,4,10,10,13,13-octamethylcyclooctadecane (0.25 g = 51 %), m.p. 165° after crystallization from methanol. Mol. wt. 364 (mass spectrometry). (Found: C 85.40; H 14.30. Calc. for C₂₆H₅₂: C 85.63; H 14.37.)

1,1,5,5,11,11,15,15-Octamethylcycloeicosane. In the same way as described above, 4,4,8,8,14,14,18,18-octamethylcycloeicosane-1,11-dione (0.8 g) was reduced with hydrazine hydrate and gave the 1,1,5,5,11,11,15,15-octamethylcycloeicosane (0.5 g = 66 %), m.p. 166°. Mol.wt. 392 (mass spectrometry). The elemental analysis failed because the substance absorbed solvents and moisture.

1,1,4,4,12,12,15,15-Octamethylcyclodocosane. By reduction of 5,5,8,8,16,16,19,19-octamethylcyclodocosane-1,12-dione (1.0 g) with hydrazine hydrate and recrystallization from CCl₄ the 1,1,4,4,12,12,15,15-octamethylcyclodocosane was obtained (0.7 g = 74 %), m.p. 139°. Mol. wt. 420 (mass spectrometry). (Found: C 84.88; H 14.73. Calc. for C₃₀H₆₀: C 85.63; H 14.73.)

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