

# Conformation of 1,3,7,9,13,15,19,21-octaazaquinquecyclo[19.3.1.1<sup>3,7</sup>.1<sup>9,13</sup>.1<sup>15,19</sup>]octacosane

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The tetrameric condensation product of 1,3-propanediamine and formaldehyde has a <sup>1</sup>H NMR spectrum that varies dramatically with temperature over the whole range +100°C to –70°C, whereas the <sup>13</sup>C NMR spectrum is variable only between 0°C and –60°C. It may be concluded that a mixture of the two likely diamond-lattice conformations of *D*<sub>2d</sub> and *S*<sub>4</sub> symmetry is present in toluene solution, whereas the *D*<sub>2d</sub> conformation is almost exclusively present in dichloromethane solution. Crystals from this solvent are shown by X-ray crystallography to contain a 2:1 dichloromethane complex of the *D*<sub>2d</sub> conformer.

When aqueous formaldehyde is mixed with 1,3-propanediamine, a tetrameric condensation product is formed with surprising ease<sup>1</sup> and crystallizes with inclusion of solvents such as benzene, dioxane and dichloromethane (see the preceding paper). Two likely conformations **A** and **B** (Fig. 1) can be envisaged, both of which follow strictly the geometry of the diamond lattice for the central 16-membered ring as well as for the four laterally fused 6-membered rings. Among these conformations, the one of *D*<sub>2d</sub> symmetry (**A**) would be the preferred candidate on the basis of the well-established preference of the –O–CH<sub>2</sub>–O– group to form a *g*<sup>±</sup>*g*<sup>±</sup> ‘corner’ in analogous macrocyclic formals,<sup>2</sup> and because the six-membered rings would thereby become diequatorially *N*-substituted. Nevertheless, the conformation of *S*<sub>4</sub> symmetry (**B**) has been shown by X-ray crystallography to be present in a solid 1:1 clathrate with benzene.<sup>3</sup>

We now report first a dynamic NMR study which shows that a mixture of **A** and **B** is present in toluene solution, and that **A** is practically the sole conformer in dichloromethane

solution. We also report an X-ray structure determination of the dichloromethane 2:1 complex which reveals the same conformation **A** with a well defined interaction between the tertiary amino nitrogens and the hydrogens of dichloromethane.

## NMR studies

We observed (preceding paper) that although the <sup>13</sup>C NMR spectrum of the octaaza compound (crystallized from dioxane) showed, in CDCl<sub>3</sub> at room temperature, the number of sharp lines expected from the constitutional symmetry, the <sup>1</sup>H NMR spectrum had very broad structureless absorptions. This obviously means that geminal exchange within each CH<sub>2</sub> group is moderately slow at room temperature, and a complete dynamic NMR study became necessary.

It should first be noted that the ring fusions in this octaaza compound are all through nitrogen bridgeheads and therefore not configurationally locked but interconvertible through amine inversion, hence to be treated as a

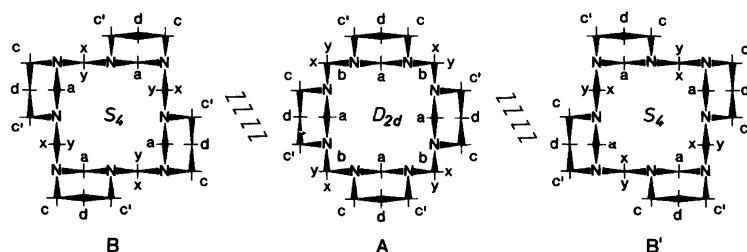


Fig. 1. Interconversion between the possible conformers of octaazaquinquecyclooctacosane. All carbon sites (*a*, *b*, *c*, *d*; *c* = *c'* in **A**), but only the hydrogen sites *x* and *y* on carbon *b* (*x* = *y* in **A**), are exchanged.

\*IUPAC recommended name: 1,3,7,9,13,15,19,21-octaazapentacyclo[19.3.1.1<sup>3,7</sup>.1<sup>9,13</sup>.1<sup>15,19</sup>]octacosane.

conformational problem. Geminal site exchange can, in the present molecule, only be studied by  $^1\text{H}$  spectroscopy, and the process involved would consist of a high-barrier multi-step sequence of 6-ring inversions and amine inversions. Whether **A** or **B** are the sole conformers, or whether both are present, is immaterial as long as exchange between them is a much faster process. Interconversion of conformer **A** with conformers **B** and **B'** has the character of a 'pseudorotation' of the 16-membered ring and should involve a sequence of combined bond rotation and amine inversion steps at each of the four 'corners', leaving the 6-membered rings unchanged.<sup>4</sup> This process is most easily studied by  $^{13}\text{C}$  spectroscopy, but is in principle also observable in the  $^1\text{H}$  spectrum, although in practice this is made difficult by the complexity due to the spin-coupling and the multitude of chemical shifts. If only conformer **A** is present, no low-energy process should be observable since **A** already has the constitutional symmetry. If only conformer **B**, which has two different  $\text{CCH}_2\text{N}$  groups, is present, passage over the same barriers via conformer **A** as an intermediate and further to conformer **B'** (which is identi-

cal and *not* enantiomeric) would produce by averaging the same symmetry as **A**.

An unusually wide temperature range ( $+100^\circ\text{C}$  to  $-70^\circ\text{C}$ ) had to be covered, and toluene- $d_8$  was therefore chosen as a solvent.  $^1\text{H}$  NMR spectra at selected temperatures are shown in Fig. 2 with assignments and correlations. The normal fast-exchange spectrum for the four chemically different  $\text{CH}_2$  groups is obtained only above ca.  $100^\circ\text{C}$ . On cooling, only the signals for the three of these that belong to the six-membered ring broaden and split strongly as would be expected because of the very different environments for the axial and equatorial positions. The final slow-exchange spectrum with respect to geminal exchange was obtained at ca.  $0^\circ\text{C}$ . The values for the frequency splittings together with the corresponding coalescence temperatures and calculated  $\Delta G^\ddagger$  values are given in Table 1 and represent three independent estimates of the same barrier, average value ca.  $61\text{ kJ mol}^{-1}$ . That the remaining  $\text{CH}_2$  line, belonging to the 16-membered ring only, did not undergo splitting, is also as expected since in conformer **A** this carbon is situated on a molecular twofold

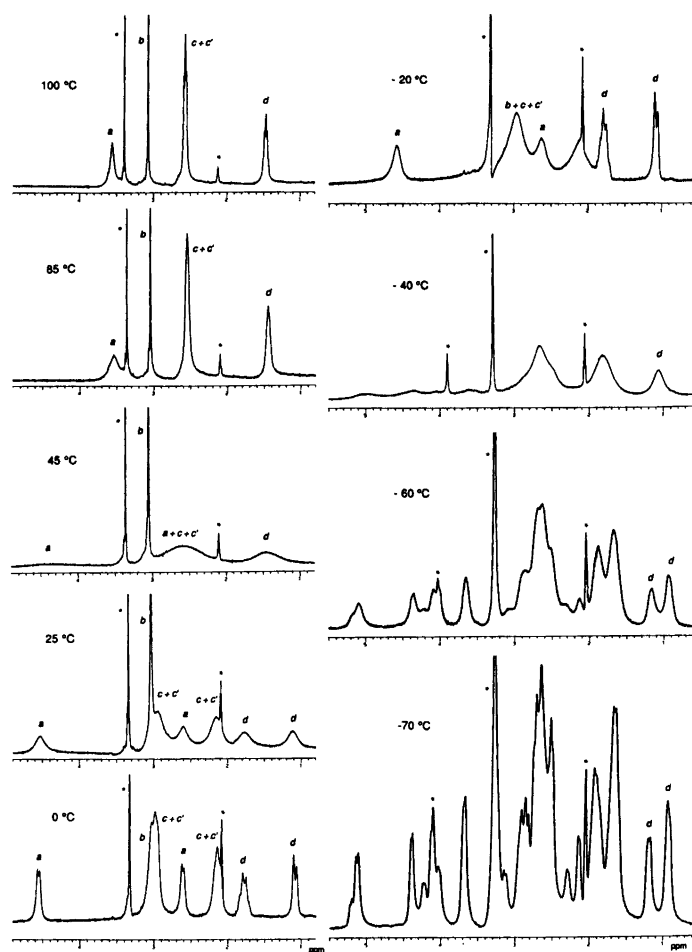


Fig. 2.  $^1\text{H}$  NMR spectra of octaazaquinquecyclooctacosane in toluene- $d_8$  at selected temperatures. The assignments refer to the carbons, as defined in Fig. 1, to which the hydrogens are attached. Peaks marked with an asterisk are due to dioxane (from solvate crystals), toluene- $d_8$ , and condensed water.

Table 1. Barrier to geminal site exchange of CH<sub>2</sub> groups, average for conformers **A** and **B**, detected by <sup>1</sup>H NMR spectroscopy.

Signal used	T <sub>c</sub> /°C	Δν/Hz	k/s <sup>-1</sup>	ΔG <sup>‡</sup> /kJ mol <sup>-1</sup>
CH <sub>2</sub> -a	~60	582	1293	~62
CH <sub>2</sub> -c	~40	254	564	~60
CH <sub>2</sub> -d	~35	201	447	~60

Table 2. Barrier to site exchange between conformers **A** and **B**, or **B** and **B'**, determined by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy.

Signal used	T <sub>c</sub> /°C	Δν/Hz	k/s <sup>-1</sup>	ΔG <sup>‡</sup> /kJ mol <sup>-1</sup>
CH <sub>2</sub> -d	-50	76	168	~45
C-a	-40	232	515	~44
C-b	-40	420	933	~43
C-d	-45	172	382	~44
C-c + C-c'	-55	94	209	~43

symmetry axis, and in conformer **B** the inner and outer hydrogen atoms exchange their sites rapidly at these temperatures when conformer **B** is converted via **A** into **B'** (Fig. 1).

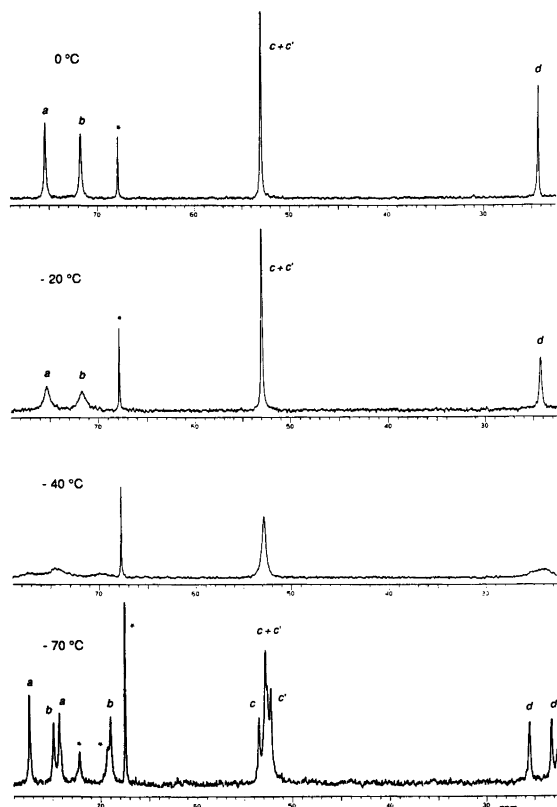


Fig. 3. <sup>13</sup>C NMR spectra of octaazaquinquecyclooctacosane in toluene-*d*<sub>6</sub> at selected temperatures. For the assignments refer to Fig. 1. Peaks labelled with an asterisk are due to dioxane and (at -70 °C) accumulated impurities when the product crystallizes.

On further cooling, a new broadening sets in, followed by further splitting and finally a sharpening of the new lines to give the final slow-exchange spectrum now also with respect to the interconversion between comparable quantities of **A** and **B** at ca. -70 °C (Fig. 2). The 17 chemical shifts expected (10 for **B**, 7 for **A**) can be recognized only with difficulty, and the spectra are too complex to be analysed for estimation of the barrier heights except for one of the *d* protons (Table 2).

Fortunately, this process could be more clearly observed in the <sup>13</sup>C spectrum which has only four sharp lines down to about 0 °C (Fig. 3). On further cooling, these broaden and split into two sets of lines of roughly equal intensity. One set consists of four lines corresponding to conformer **A** (CCH<sub>2</sub>N has double weight), the other set has five lines of equal intensity corresponding to conformer **B**. The slow-exchange spectrum is obtained at ca. -70 °C, and the values for the frequency splitting of each signal and the corresponding coalescence temperatures and calculated ΔG<sup>‡</sup> values are given in Table 2. Three of these values represent independent observations of the same barrier separating conformers **A** and **B**, average value ca. 44 kJ mol<sup>-1</sup>. The fourth value was obtained from the splitting of the frequency of the CCH<sub>2</sub>N line of conformer **B** into two due to its lower symmetry and therefore represents strictly the

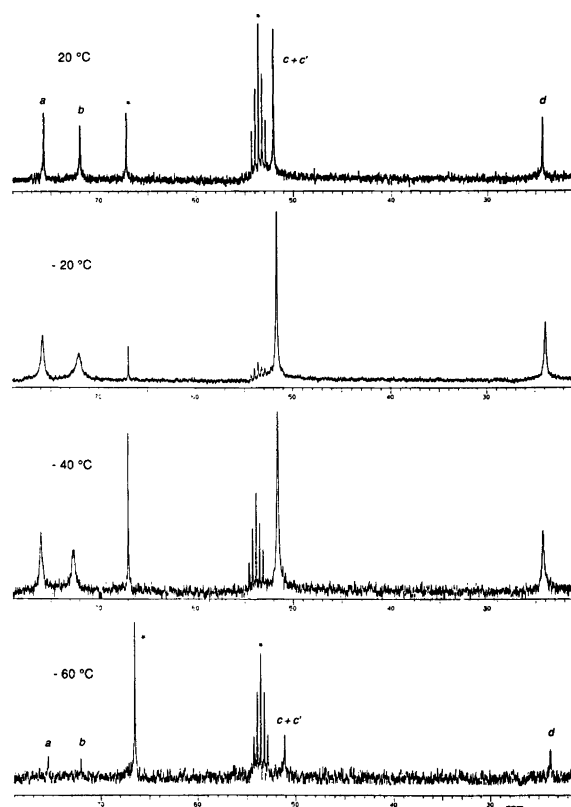


Fig. 4. <sup>13</sup>C NMR spectra of octaazaquinquecyclooctacosane in CD<sub>2</sub>Cl<sub>2</sub> at selected temperatures. Peaks that remain sharp at -20 and -40 °C are due to dioxane and CD<sub>2</sub>Cl<sub>2</sub>.

barrier between **B** and **B'**. That this barrier height is so close (ca. 43 kJ mol<sup>-1</sup>) confirms our assumption implied in Fig. 1 that **B** passes through **A** as an intermediate in order to exchange sites with **B'**.

When CD<sub>2</sub>Cl<sub>2</sub> was tried to obtain better solubility at these low temperatures, no line splitting was observed in the <sup>13</sup>C NMR spectrum even down to -60°C (Fig. 4). Clearly, this solvent favours the *D*<sub>2d</sub> conformer **A** so completely that specific complexation requiring the *D*<sub>2d</sub> symmetry must be postulated. It is easy to see on space-filling molecular models that the *D*<sub>2d</sub> conformer has a cleft on either side that can be filled with a dichloromethane molecule in contact with four nitrogen lone pairs each, whereby not a loose clathrate but a well-defined 2:1 complex can be formed. This complex was easily crystallized, enabling our conclusion to be verified by crystal structure analysis (below).

A closer inspection of the <sup>13</sup>C spectra in Fig. 4 reveals that conformer **B** cannot be completely absent in CD<sub>2</sub>Cl<sub>2</sub> solution. At intermediate temperatures (-20 to -40°C), where the coalescence might have been expected, all four lines undergo pronounced broadening before they sharpen again, suggesting exchange with a 'hidden partner'.<sup>5</sup> The partner in this case can only be conformer **B** in a concentration too low to rise above the noise level at slow exchange, at which temperature decreased solubility becomes a problem. A similar temporary broadening on cooling is also observed in the <sup>1</sup>H spectrum: The sharply structured bands at -20°C are broad and diffuse at -40°C and reappear with unchanged structure at -60°C.

### Crystal structure of the dichloromethane complex

The complex crystallizes in the orthorhombic space group *Fddd* with eight formula units in the unit cell. It thus possesses 222 symmetry (*D*<sub>2</sub>) in the crystal. The situation is illustrated in Fig. 5 where ORTEP plots of the complex are shown as seen along two of the twofold axes. Both dichloromethane molecules are situated on the same twofold axis and are disordered.

The ring conformation is shown to be that of **A** (Fig. 1) in contrast with that of the 1:1 clathrate with benzene (**B**, Fig. 1).<sup>3</sup> Conformation **A** has been assumed<sup>3</sup> to be less favourable because of dipole-dipole repulsion between the axial lone pairs on the nitrogen atoms. However, in the present structure the axial lone pairs are engaged in intermolecular interactions with the hydrogen atoms of the dichloromethane molecules.

There is one dichloromethane molecule situated on each side of the general plane of the 16-membered ring. One half of a dichloromethane molecule has its hydrogen atoms pointing in the general direction of the N(1) atoms situated diametrically across the ring, the other half points its hydrogen atoms towards N(2) atoms. The two halves of the other dichloromethane molecule are situated on the other side of the ring plane and engage the remaining nitrogen atoms in a corresponding manner.

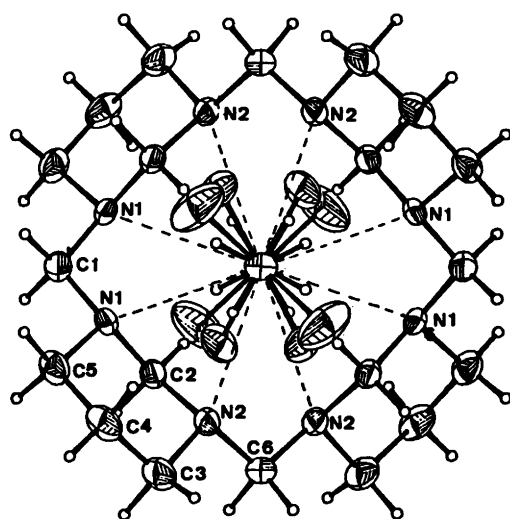
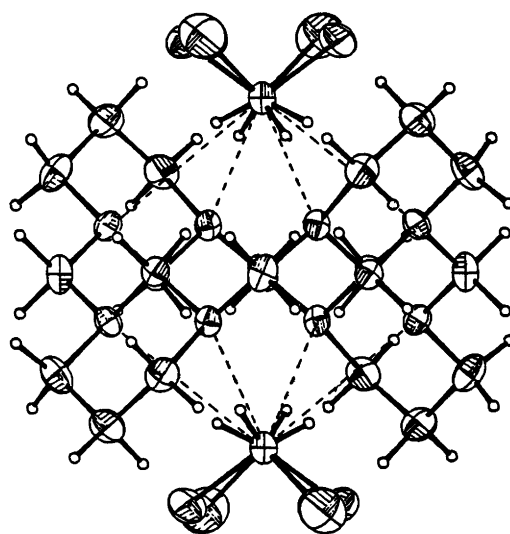


Fig. 5. ORTEP plot of the 2:1 complex as seen along two of the twofold axes. Hydrogen bonds are depicted by broken lines.

The distance between the dichloromethane carbon and the nitrogen atoms is 3.6 Å. Allowing 1.0 Å for the C-H bond, this corresponds to a 2.46 Å separation between the hydrogen and nitrogen atoms as compared with the sum of van der Waals' radii of 2.7 Å. We conclude that the interaction must be characterized as a weak hydrogen bond.

### Experimental

**NMR spectroscopy.** The NMR spectra were recorded on a Varian XL-300 instrument operating at 300 MHz for <sup>1</sup>H and 75.4 MHz for <sup>13</sup>C.

**X-Ray diffraction.** Crystals of the complex were formed by recrystallization of the parent compound from dichloromethane. Crystal data and conditions for the data collec-

Table 3. Crystal and experimental data for the 2:1 dichloromethane complex.

Compound	C <sub>20</sub> H <sub>40</sub> N <sub>8</sub> · 2CH <sub>2</sub> Cl <sub>2</sub>
Recrystallization	from dichloromethane
Diffractometer	NICOLET P3/F
Radiation	Mo K <sub>α</sub> (λ = 0.71069 Å)
Crystal system	Orthorhombic
a/Å	10.577(2)
b/Å	17.419(4)
c/Å	31.889(9)
V/Å <sup>3</sup>	5875.4(1.9)
T/K	138
Space group	Fddd (No. 70, origin at $\bar{1}$ )
M	562.46
F(000)	2400
Z	8
D <sub>c</sub> /g cm <sup>-3</sup>	1.272
Crystal size/mm	0.3 × 0.3 × 0.3
μ(Mo K <sub>α</sub> )/cm <sup>-1</sup>	1.06
Scan mode	ω
Scan speed (ω)/deg min <sup>-1</sup>	2.0
Scan range (ω)/deg	1.4
Maximum (sin θ/λ)/Å <sup>-1</sup>	0.70
Stability monitoring	3 Test refl./100 observ.
No. of indep. meas.	1191
No. with I > 2.5σ(I)	766
Weighting scheme	w = [σ <sup>2</sup> (F)] <sup>-1</sup>
No. of parameters refined	125
R = Σ  F <sub>o</sub> - F <sub>c</sub>   /Σ F <sub>o</sub>	0.049
R <sub>w</sub> = [Σw(F <sub>o</sub> - F <sub>c</sub> ) <sup>2</sup> /ΣwF <sub>o</sub> <sup>2</sup> ] <sup>1/2</sup>	0.040
S = [Σw(F <sub>o</sub> - F <sub>c</sub> ) <sup>2</sup> /(n - m)] <sup>1/2</sup>	1.60

tion are given in Table 3. Lattice parameters were determined from the accurate setting angles for 25 reflections.

The intensity data were corrected for Lorentz and polarization effects but not for absorption and extinction. The standard deviation for the intensities were taken as given in eqn. (1), where C<sub>T</sub> is the total number of counts and C<sub>N</sub> is the net count.

$$\sigma(I) = [C_T + (0.01 C_N)^2]^{1/2} \quad (1)$$

The atomic coordinates of all non-hydrogen atoms were determined by direct methods (MITHRIL).<sup>6</sup> Refinements were performed by least-squares calculations; hydrogen positions were calculated and included in the refinements. The non-hydrogen atoms were refined with anisotropic thermal parameters, the hydrogen atoms were assumed to behave isotropically with a common thermal parameter.

The computer programs employed have been described.<sup>7</sup> Final figures of merit based on the refinement of 125 parameters are included in Table 3. Positional parameters are

Table 4. Fractional coordinates and equivalent isotropic thermal parameters<sup>a</sup> for the dichloromethane complex.

Atom	x	y	z	U <sub>eq</sub> /Å <sup>2</sup>
Cl(11)	0.9750(9)	0.1468(6)	0.3441(3)	0.070
Cl(12)	0.9415(8)	0.1513(5)	0.3348(3)	0.039
N(1)	0.6303(3)	0.3290(2)	0.3463(1)	0.021
N(2)	0.7892(3)	0.3290(2)	0.2938(1)	0.023
C(1)	0.5540(6)	0.375	0.375	0.030
C(2)	0.7045(4)	0.3770(2)	0.3187(1)	0.023
C(3)	0.7143(5)	0.2781(3)	0.2668(1)	0.035
C(4)	0.6274(5)	0.2286(3)	0.2932(2)	0.036
C(5)	0.9478(5)	0.2776(3)	0.3221(1)	0.032
C(6)	0.875	0.375	0.2685(2)	0.031
C(7)	0.875	0.2069(4)	0.375	0.028
H(11)	0.501(3)	0.340(2)	0.392(1)	0.028(3)
H(21)	0.753(3)	0.413(2)	0.335(1)	
H(22)	0.647(3)	0.410(2)	0.299(1)	
H(31)	0.769(4)	0.246(2)	0.254(1)	
H(32)	0.659(3)	0.309(2)	0.246(1)	
H(41)	0.673(3)	0.192(2)	0.312(1)	
H(42)	0.572(4)	0.198(2)	0.276(1)	
H(51)	0.488(3)	0.310(2)	0.306(1)	
H(52)	0.500(3)	0.246(2)	0.341(1)	
H(61)	0.824(3)	0.413(2)	0.248(1)	
H(71)	0.946(8)	0.243(5)	0.387(3)	
H(72)	0.830(9)	0.231(6)	0.351(3)	

$$^a U_{eq} = 1/3 \sum U_{ij}$$

given in Table 4. Anisotropic thermal parameters and the structure factor listings may be obtained from C.R. upon request.

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## References

1. Krässig, H. *Makromol. Chem.* 17 (1955) 77.
2. Dale, J. *Tetrahedron* 30 (1974) 1683.
3. Murray-Rust, P. *Acta Crystallogr. Sect. B* 31 (1975) 583.
4. Dale, J. *Top. Stereochem.* 9 (1976) 199.
5. Anet, F. A. L. and Basus, V. J. *J. Magn. Reson.* 32 (1978) 339.
6. Gilmore, C. J. *Appl. Crystallogr.* 17 (1984) 42.
7. Mallinson, P. R. and Muir, K. W. *J. Appl. Crystallogr.* 18 (1985) 51.

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