Carbohydrate Research, 247 (1993) 119–128
Elsevier Science Publishers B.V., Amsterdam

The crystal and molecular structure of threitol

Jürgen Kopf [a,*], Martina Morf [a], Bärbel Zimmer [a], Erhard T.K. Haupt [a], Otto Jarchow [b,*] and Peter Köll [c,*]

[a] *Institute of Inorganic and Applied Chemistry, University of Hamburg, Martin-Luther-King-Pl. 6, D-20146 Hamburg (Germany)*
[b] *Institute of Mineralogy, University of Hamburg, Grindelallee 48, D-20146 Hamburg (Germany)*
[c] *Department of Chemistry, University of Oldenburg, Carl-von-Ossietzky-Str. 9-11, D-26111 Oldenburg (Germany)*

(Received September 18th, 1992; accepted March 26th, 1993)

ABSTRACT

The structure of threitol, $C_4H_{10}O_4$, was determined on a crystal of L-threitol at 293 K. This investigation covers also the racemate, because threitol is one of the rare examples that crystallizes as a conglomerate of the pure enantiomers. In disagreement with a recent publication [Jeffrey and Huang, *Carbohydr. Res.*, 223 (1992) 11–18], the space group of L-threitol is $P3_2$ with nine molecules in a unit cell of $a = 1755.6(1)$, $c = 487.9(1)$ pm. Crystals of threitol are found as twins by merohedry with a twofold twin operation. The asymmetric unit consists of three crystallographically independent, but chemically equivalent molecules. The final conventional R factor is 0.032 for all 3628 symmetry-independent reflections. The molecules have the straight carbon-chain conformation, but do not show C_2 symmetry as was claimed previously. This fact was confirmed by solid state ^{13}C CP/MAS NMR experiments.

INTRODUCTION

Almost all of the structures of the lower alditols were determined many years ago[1], but some still remain. The missing data for D-arabinitol[2], D-altritol[3] ("D-talitol"), and DL-iditol[4] were reported only recently. Another example is threitol, despite the fact that racemic DL-threitol and L-threitol are commercially available, and satisfactory transparent crystals can be grown easily from ethanol or other solvents. Furthermore, from the beginning of the century, it has been known that the racemate (DL-threitol) crystallizes as a conglomerate of the pure enantiomers[5]. Therefore, one structure determination of one of the enantiomers is necessary to describe the complete crystallographic topology of this chiral tetritol diastereomer. The other diastereomer, erythritol, is a *meso* compound.

* Corresponding authors.

Recently, Jeffrey and Huang reported[6] the structure determination of D-threitol (absolute configuration not confirmed) in the trigonal space group $P3_121$ with $a = 1014.05(8)$, $c = 487.67(4)$ pm at 298 K. The conventional R factor was 0.069 for 244 structure factors. With $Z = 3$, single molecules must have twofold axis symmetry and the hydrogens bonded to the secondary oxygen atoms are systematically disordered. A second data set was measured at 119 K and refined within the same model with an R factor of 0.05 for 302 structure factors.

These results do not agree with our investigations and represent only an averaged structure, neglecting an excess in the order of a magnitude of observable reflections and comprising the so-called H cell only. A short account of our work was published[7] in 1990.

TABLE I

Crystallographic data for L-threitol [a]

Formula	$C_4H_{10}O_4$
Mol wt	122.12
Mp (°C)	90–91
Crystal dimensions (mm)	0.6×0.2×0.2
Space group	$P3_2$
Cell parameters (pm)	
a	1755.6(1)
c	487.9(1)
Volume V (pm^3)	$1302.3(3)\times10^6$
Z	9
$F(000)$	594
Calculated density D_x (g×cm^{-3})	1.401
λ (Cu $K\alpha_1$) (pm)	154.051
μ (cm^{-1})	10.9
θ range (deg)	2.5–76.5
Reflections measured	7226
Symmetry independent reflections	3628
Observed reflections with $I > 2\sigma(I)$	3470
Number of refined parameters	233
Final conventional residual factor for all 3628 independent reflections R	0.032
Conventional residual factor for 3470 observed reflections R_{obsd}	0.031
R factor for all intensities $wR_2 = \sqrt{\frac{\Sigma w(F_o^2 - F_c^2)^2}{\Sigma w(F_o^2)^2}}$	0.086
Goodness of fit S for all reflections	1.031
Max electron difference density (e×pm^{-3}) $\Delta\rho_{max}$	0.173×10^6
Min electron difference density (e×pm^{-3}) $\Delta\rho_{min}$	0.159×10^6
Diffractometer	Enraf–Nonius CAD4

[a] Standard deviations in parentheses.

RESULTS AND DISCUSSION

Suitable crystals of L-threitol were obtained by crystallization of a commercial sample (Aldrich) from moist ethanol. The structure was solved by direct methods with the program SHELXS-90[8] and refined with SHELXL-92[9]. The refinement was done on F^2 for all reflections. Table I covers some crystallographic properties of L-threitol. The observed threshold $I > 2\sigma(I)$ is used only for calculating R_{obsd} and is given in Table I for comparison with refinements on F.

L-Threitol was found to crystallize in the trigonal space group $P3_2$ with $Z = 9$, and with three independent molecules in the asymmetric unit. All heavy atoms were refined. The hydrogen atoms were positioned theoretically and refined using a riding model with the AFIX options of the program SHELXL-92. This approach is especially useful for hydroxyl groups, where a difference electron density is calculated around the circle which represents the loci of possible hydrogen positions (for a fixed O–H distance and C–O–H angle). The maximum electron density is then taken as the starting position and in subsequent refinement cycles the hydrogens are re-idealized, but the current torsion angle is retained. The final conventional R factor is 0.032 for all 3628 symmetry-independent reflections with the assumption that crystals of L-threitol are twins by merohedry of class II[10]. The twin operation (matrix: $0\bar{1}0\ \bar{1}00\ 00\bar{1}$) is contained in the lattice symmetry, but not in the Laue symmetry of the crystal, with the consequence that twin-related reflections differ in intensity (see Experimental). This kind of calculation can only be done with refinement programs which allow refinement of the structure against intensities (F^2) and which are able to take twinning into consideration.

Table II contains the fractional positional parameters of the C and O atoms and the hydroxyl hydrogens of the three independent molecules. In Table III, bond lengths and bond angles, as well as selected torsion angles, are given. The other data have been deposited* or are described in the Experimental section. The overall geometry of these molecules and the atom numbering scheme can be derived from Fig. 1, which was generated using the program PLATON-92[11]. The three crystallographically independent molecules of the asymmetric unit are chosen in such a way that the molecules are positioned along the direction of the main diagonal of the unit cell. In order to keep the internal geometry correct (best deduced from the selected torsion angles of Table III), molecule II has to be numbered in the reverse direction. Apart from this, the geometries of the three molecules are, obviously, almost identical. The molecules do not have twofold symmetry. No disorder is claimed for any atom.

* Lists of calculated and observed intensities, atomic coordinates of all atoms, including anisotropic thermal displacement factors for C and O, and further information to Table I are deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, Netherlands. Reference should be made to No. BBA/DD/539/*Carbohydr. Res.*, 247 (1993) 119–128.

TABLE II

Fractional positional parameters ($\times 10^4$) and equivalent isotropic thermal parameters U_{eq} [a] ($\times 10^3$) of carbon and oxygen atoms and fractional positional parameters ($\times 10^3$) of hydroxyl hydrogens with isotropic temperature factors U_B [b] ($\times 10^3$) for L-threitol [c]

Atom	Molecule I				Molecule II				Molecule III			
	x	y	z	U_{eq}/U_B	x	y	z	U_{eq}/U_B	x	y	z	U_{eq}/U_B
O-1	322(2)	7498(2)	3367(5)	38(1)	5916(2)	6395(2)	7987(5)	43(1)	6882(2)	756(2)	3369(5)	37(1)
O-2	264(2)	8976(3)	8504(6)	44(1)	4402(2)	6439(2)	2828(4)	34(1)	6870(2)	2245(2)	8589(5)	36(1)
O-3	922(3)	9785(2)	3353(8)	42(1)	3599(2)	5809(2)	8007(4)	36(1)	7525(2)	3062(2)	3419(5)	37(1)
O-4	2553(2)	9799(2)	8018(5)	41(1)	3593(2)	4188(2)	3334(4)	38(1)	9136(2)	3019(2)	8040(5)	40(1)
C-1	−49(2)	7890(3)	5057(7)	37(1)	5505(2)	6758(2)	6279(7)	33(1)	6529(2)	1160(3)	5042(7)	35(1)
C-2	678(2)	8657(3)	6619(6)	29(1)	4727(2)	6059(2)	4680(6)	28(1)	7267(2)	1922(2)	6685(6)	25(1)
C-3	1334(2)	9395(2)	4796(6)	33(1)	3995(2)	5383(2)	6541(6)	25(1)	7915(2)	2642(2)	4780(6)	27(1)
C-4	2096(3)	10122(2)	6377(7)	35(1)	3266(2)	4636(2)	4964(7)	37(1)	8692(2)	3355(2)	6449(7)	33(1)
H-O1	52(3)	724(3)	437(1)	57(2)	627(3)	631(3)	703(2)	57(2)	708(3)	50(3)	437(1)	57(2)
H-O2	−5(1)	914(1)	761(1)	57(2)	422(1)	673(1)	371(1)	57(2)	656(1)	241(1)	772(1)	57(2)
H-O3	62(1)	945(1)	205(3)	57(2)	368(1)	579(1)	972(1)	57(2)	734(1)	283(1)	186(2)	57(2)
H-O4	289(3)	971(4)	700(2)	57(2)	380(4)	395(3)	437(1)	57(2)	954(3)	301(4)	708(4)	57(2)

[a] $U_{eq} = 1/3\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i \mathbf{a}_j$. [b] One common parameter. [c] Standard deviations in parentheses.

TABLE III

Molecular geometry of L-threitol [a]

	Molecule		
	I	II	III
Bond lengths (pm)			
C-1–O-1	142.3(5)	144.3(5)	141.2(5)
C-4–O-4	143.6(6)	142.6(6)	142.1(5)
C-2–O-2	144.7(6)	140.3(5)	143.7(5)
C-3–O-3	140.8(7)	144.0(5)	139.9(5)
C-1–C-2	151.8(6)	151.8(5)	154.2(5)
C-3–C-4	151.9(5)	150.7(5)	154.4(5)
C-2–C-3	151.8(5)	153.6(5)	152.2(4)
Bond angles (deg)			
O-1–C-1–C-2	109.6(4)	112.7(3)	110.3(3)
O-4–C-4–C-3	112.5(3)	111.3(4)	113.4(3)
O-2–C-2–C-1	107.5(4)	111.2(3)	108.4(3)
O-3–C-3–C-4	107.2(3)	106.6(3)	106.8(3)
O-2–C-2–C-3	110.8(4)	111.5(3)	112.1(3)
O-3–C-3–C-2	110.7(4)	109.1(3)	111.6(3)
C-1–C-2–C-3	113.9(3)	112.8(3)	111.0(3)
C-4–C-3–C-2	113.2(3)	112.9(3)	110.0(2)
Selected torsion angles (deg)			
O-1–C-1–C-2–O-2	−174.3(3)	−173.7(3)	−173.3(3)
O-4–C-4–C-3–O-3	178.0(4)	177.5(2)	177.7(3)
O-1–C-1–C-2–C-3	62.5(5)	60.2(4)	63.3(4)
O-4–C-4–C-3–C-2	55.7(5)	57.8(4)	56.6(4)
O-2–C-2–C-3–O-3	−57.1(4)	−58.2(3)	−54.5(4)
O-2–C-2–C-3–C-4	63.3(5)	60.1(4)	63.9(4)
O-3–C-3–C-2–C-1	64.3(4)	67.8(4)	66.8(4)
C-1–C-2–C-3–C-4	−175.4(4)	−173.9(3)	−174.8(3)

[a] Standard deviations in parentheses.

In the crystalline state, free carbohydrates are held together by a more or less complex system of hydrogen bonds. For L-threitol, this pattern is given in Table IV. All oxygen atoms are involved as donors and acceptors. Fig. 2 shows this strong cooperative system of hydrogen bonds, which consists of infinite helical chains in the direction of the *c* axis. Three different helices connected with each of the three independent molecules can be discerned. There are two tight helices connecting the hydroxyl groups at the end of each molecule, which have opposite polarities. Along the centres of these helices, pseudo threefold screw-axes can be positioned. The other helical chain is more open and connects the secondary hydroxyl groups to a triad of the same molecule (I, II, and III in Fig. 2). Although these helical chains are positioned along the three crystallographically different 3_2-axes, chain II has the opposite polarity to chains I and III. Nevertheless, all hydrogen bonds are two-centered and intermolecular.

Concerning the lack of C_2 symmetry of individual molecules, a further experimental proof was obtained from a totally different method. In Fig. 3, the ^{13}C

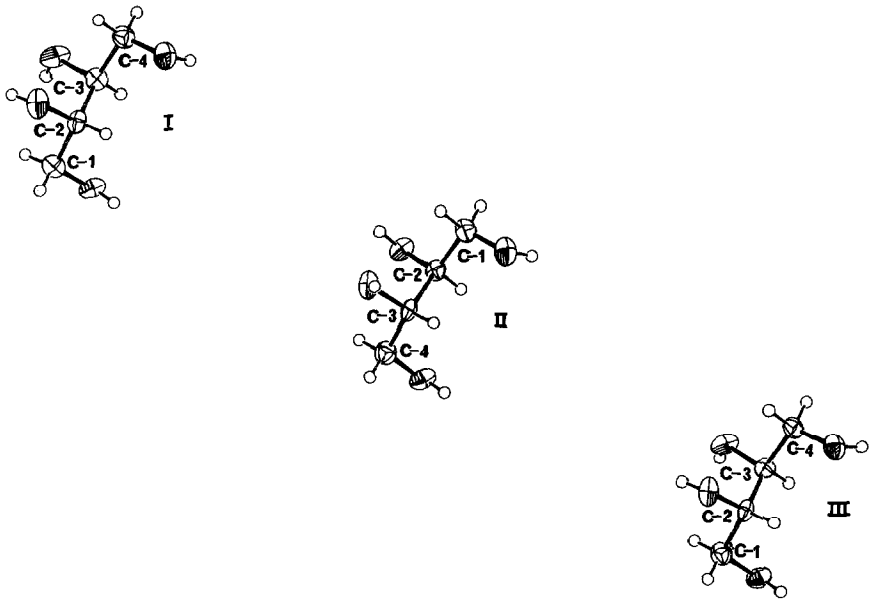

Fig. 1. ORTEP-like plot of the three crystallographically independent, but chemically equivalent, molecules of L-threitol, showing atom numbering and thermal displacement parameters. This drawing was generated using the program PLATON-92[11].

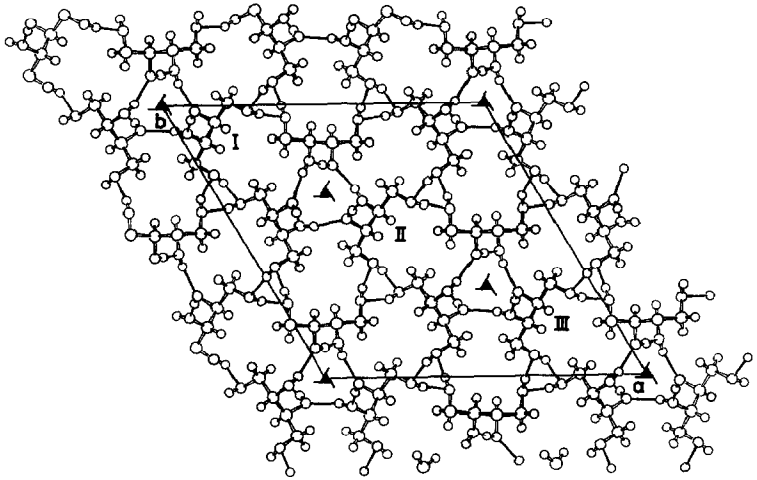

Fig. 2. SCHAKAL-88[14] plot down the *c* axis into the unit cell of L-threitol. Hydrogen bonds are represented as smaller black-bond sticks. Since the molecules are packed directly over each other along the short *c* axis, sometimes individual atoms of a molecule one layer higher or lower are involved in this hydrogen-bonding scheme.

TABLE IV

Hydrogen-bond pattern [a] in L-threitol (bond lengths in pm, angles in degrees) [b]

Pattern $D^{\overset{185(5)}{\cdots}}H\cdots A$	Symmetry operation on A	Distance D···A	Angle D–H···A
Molecule I			
O-1–H-O1$^{\overset{190(4)}{\cdots}}$O-4(II)	$-x+y, -x+1, z+1/3$	272.2(5)	163(5)
O-2–H-O2$^{\overset{192(2)}{\cdots}}$O-3(I)	$-x+y-1, -x+1, z+1/3$	270.3(8)	153(2)
O-3–H-O3$^{\overset{188(1)}{\cdots}}$O-2(I)	$x, y, z-1$	270.3(5)	161(2)
O-4–H-O4$^{\overset{185(5)}{\cdots}}$O-1(II)	$-y+1, x-y+1, z-1/3$	269.2(5)	178(4)
Molecule II			
O-1–H-O1$^{\overset{184(5)}{\cdots}}$O-4(III)	$-y+1, x-y, z-1/3$	268.5(5)	175(4)
O-2–H-O2$^{\overset{194(2)}{\cdots}}$O-3(II)	$-y+1, x-y+1, z-1/3$	273.0(5)	155(2)
O-3–H-O3$^{\overset{194(1)}{\cdots}}$O-2(II)	$x, y, z+1$	268.0(3)	145(1)
O-4–H-O4$^{\overset{191(5)}{\cdots}}$O-1(III)	$-x+y+1, -x+1, z+1/3$	272.0(5)	161(6)
Molecule III			
O-1–H-O1$^{\overset{191(4)}{\cdots}}$O-1(I)	$-x+y, -x, z+1/3$	273.3(5)	164(5)
O-2–H-O2$^{\overset{191(2)}{\cdots}}$O-3(III)	$-x+y+1, -x+1, z+1/3$	271.8(6)	158(2)
O-3–H-O3$^{\overset{185(1)}{\cdots}}$O-2(III)	$x, y, z-1$	269.9(4)	176(2)
O-4–H-O4$^{\overset{185(5)}{\cdots}}$O-4(I)	$-y+2, x-y+1, z-1/3$	269.5(5)	167(6)

[a] A, Acceptor oxygen; D, Donor oxygen. [b] Standard deviations in parentheses.

CP/MAS NMR spectrum of L-threitol is presented. It shows two separated signals for the secondary carbons and a broad, but nevertheless split signal for the primary carbons (DL-threitol gives the same spectrum). Therefore, the C_2 symmetry of individual molecules can definitely be excluded. Furthermore, the different chemical shifts of the secondary carbon atoms can be interpreted with respect to the arrangement of the secondary hydroxyl hydrogens to the neighbouring primary ones[12]. For C-2, this arrangement is *trans*, while for C-3 it is *cis* for all molecules I to III in Fig. 1. The result is a considerable difference in the distances C-2–O-2 compared to C-3–O-3 and in the torsion angles O-1–C-1–C-2–O-2 compared to O-4–C-4–C-3–O-3 (see Table III).

The observed twinning (compare Experimental) can now be explained. The unit cell contains nine molecules of which three molecules in the direction of the main diagonal are connected via a pseudotranslation $\pm(-1/3, 1/3, 0)$ (see Fig. 2). The reason for the observed twinning is that the CH_2OH groups at the termini of individual molecules fulfil the pseudosymmetry $H3_212$ of the cell, while the central part of the molecule, composed of two stereogenic secondary carbons, has only the

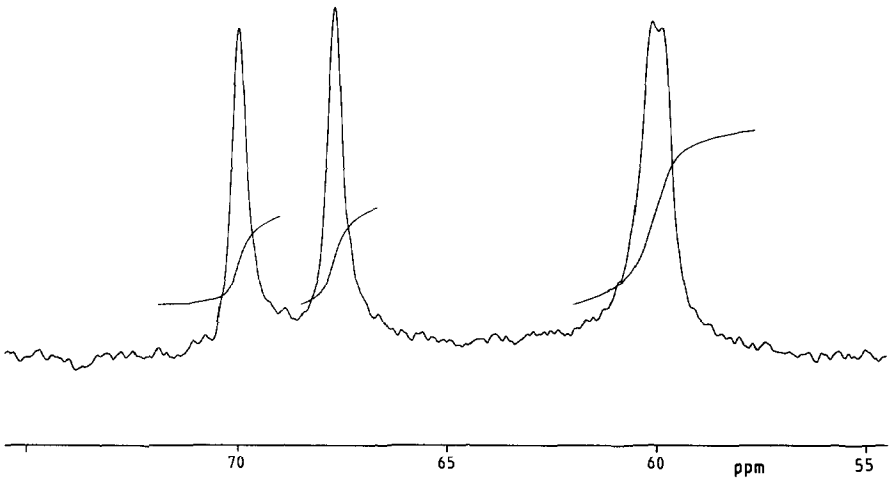

Fig. 3. ^{13}C CP/MAS NMR spectrum of L-threitol. Chemical shifts are 70.0, 67.7, 60.1, and 59.8 ppm, respectively. The spectrum of DL-threitol is identical.

lower symmetry $P3_211$. There are two options for twinning. If the z coordinate of the central CHOH part is designated with (+), it should be possible to translate two neighbouring molecules along the main diagonal $[\bar{1}10]$ via $-1/3$, $1/3$, 0 into each other and the third molecule via a translation plus a rotation around the twofold pseudoaxis $[\bar{x}xz]$. In a symbolic representation, the sequence of molecules along the main diagonal is (+ − +) in one individual and (− + −) in its twin or *vice versa*.

Therefore, our measured data set of L-threitol contains many superstructure reflections of minor mean intensity. Only the central CHOH groups support these reflections, whereas the CH_2OH groups at the termini are located in positions of the sublattice described by the H cell and thus only supporting reflections with $-h + k = 3n$, but this together with all other atoms. The observed differences in the intensities between the main and the superstructure reflections are thus explained as well as the observed pseudo extinction rule $(hh0)h = 3n$ (see Experimental).

The geometrical information, as given in Table III, as well as the solid state NMR spectrum (Fig. 3) are in accordance with this interpretation. The end groups are not absolutely in general positions, due to the specific effects of the differing geometries of the neighbouring secondary partners. Therefore, a small splitting for these carbon atoms is observed in the NMR spectrum, and bond lengths and angles vary slightly. The (+ − +) pattern of the central part of the three individual molecules in the asymmetric unit is best observed by comparing the bond lengths C-2–O-2 and C-3–O-3. The different polarities of the three more open helices of hydrogen bonds also follow this pattern.

Recently, we reported the structure determination of D-iditol hexaacetate in the trigonal space group $P3_221$ with disorder at C-1 and C-6[13]. The similarities to the

situation in L-threitol are obvious. We intend to reinvestigate this compound with the help of the program SHELXL-92[9].

EXPERIMENTAL

Crystallography.—From rotation- and Weissenberg-photographs of different crystals of L-threitol and several other crystals randomly chosen from the DL conglomerate, the Laue class $\bar{3}12/m$ was determined in all cases. The intensity measurement was done on an Enraf–Nonius CAD4 diffractometer; 7226 intensities (ca. 70% of the Cu-limiting sphere with a theta-range of $\theta = 2.25 \rightarrow 76.5°$) were measured. From these measurements, it is found that the intensities of the reflections with $-h + k = 3n$ are significantly higher. With the same setting to this selection of intensities belongs an averaged structure with the so-called H cell, while the remaining reflections with $-h + k \neq 3n$ are superstructure reflections, which are supported, obviously, only by a fraction of the atoms.

In connection with the known chirality of the molecules (the measured crystal was dissolved after the data collection on the CAD4 and the sign of the rotatory power was determined with a Perkin–Elmer 2043 polarimeter) and the observed extinction conditions $l = 3n$ for $00l$ reflections [a pseudo extinction rule $(hh0)$ $h = 3n$ is observed as well], the only space group is $P3_212$. All attempts to refine direct methods solutions consistently ended in conventional R values of ca. 20%. Split positions gave evidence that the data set obtained is not of a single crystal but of a twin, thus calling for a decrease in symmetry.

Assuming the lower symmetric space group $P3_2$ for the single individuals, the Laue class is $\bar{3}$ and $\bar{3}12'/m'$ for the twin (primed symmetry elements correspond to twin operations). This includes $\bar{3}11$ as a white subclass of the Laue class for the individual. Such twins, where the Laue class of the individual is lower than that of the twinned crystal but both Laue classes belong to the same crystal system, are called twins by merohedry of class II[10]. All individuals have a common lattice; therefore, superposition of all reflections occurs and, with the contribution of equal volumes of the individuals in the twinned crystal, the Laue class is lowered.

In point group 311 for the individual, the hexagonal crystal system allows 321, 312, and 6 as twin classes for an enantiomorphic structure; 312 agrees with the experiments. The successful refinement of the structure in $P3_2$ with the twin-LSQ part of SHELXL-92[9] confirmed the above assumed twinning by merohedry. The final $wR2$ factor for all 3628 intensities is 0.0861. The corresponding conventional R factor for all structure factors is 0.032. In all LSQ-calculations, it is assumed that the volumes of the twins are equal. This can be justified by the fact that the observed Laue class for all twins is $\bar{3}12'/m'$.

Solid state NMR spectroscopy.—^{13}C CP/MAS NMR spectra were recorded at 75.47 MHz with a Bruker MSL-300 spectrometer under conditions of the Hartmann–Hahn match, using 90° pulses of 4.5 μs, contact times of ca. 1 ms, and a 4-s recycle delay. Samples ($\sim$ 400 mg each) were examined in powder form in rotors

(i.d. 7 mm) constructed of Al_2O_3, and a spinning rate of ca. 4 kHz was applied at the magic angle in a double bearing spinner assembly, using air as the driving gas. Chemical shifts are referenced against the CO signal of solid glycine assumed to resonate at 176.09 ppm (δ with respect to Me_4Si).

ACKNOWLEDGMENTS

The authors thank Professor G.M. Sheldrick (University of Göttingen) for giving access to the new program SHELXL-92, Dipl. Chem. M. Bischoff (Oldenburg) for preparing drawings, and Cornelia Topf (Hamburg) for technical assistance. The Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie gave financial support.

REFERENCES

1 G.A. Jeffrey, *Acta Crystallogr., Sect. B*, 46 (1990) 89–103.
2 J. Kopf, M. Morf, B. Zimmer, and P. Köll, *Carbohydr. Res.*, 218 (1991) 9–13.
3 J. Kopf, M. Bischoff, and P. Köll, *Carbohydr. Res.*, 217 (1991) 1–6.
4 J. Kopf, M. Morf, B. Zimmer, M. Bischoff, and P. Köll, *Acta Crystallogr., Sect. C*, 48 (1992) 339–342.
5 L. Maquenne and G. Bertrand, *C.R. Acad. Sci.*, 132 (1901) 1565–1567.
6 G.A. Jeffrey and D. Huang, *Carbohydr. Res.*, 223 (1992) 11–18.
7 J. Kopf, P. Köll, M. Morf, B. Zimmer, and O. Jarchow, *Abstracts of Papers*, 15th Congress of the International Union of Crystallography, Bordeaux, France, 1990, C-194.
8 G.M. Sheldrick, *Acta Crystallogr., Sect. A*, 46 (1990) 467–473.
9 G.M. Sheldrick, SHELXL-92, Crystal structure refinement, University of Göttingen, Germany, 1992 (Beta-Test Version).
10 M. Catti and G. Ferraris, *Acta Crystallogr., Sect. A*, 32 (1976) 163–165.
11 A.L. Spek, PLATON-92, *Acta Crystallogr., Sect. A*, 46 (1990) C31.
12 T.B. Grindley, M.S. McKinnon, and R.E. Wasylishen, *Carbohydr. Res.*, 197 (1990) 41–52.
13 J. Kopf, M. Morf, B. Zimmer, M. Bischoff, and P. Köll, *Carbohydr. Res.*, 229 (1992) 17–32.
14 E. Keller, SCHAKAL-88, *Chem. Unserer Zeit*, 20 (1986) 178–181.