Carbohydrate Research, 229 (1992) 17–32
Elsevier Science Publishers B.V., Amsterdam

The crystal and molecular structures of the hexitol hexa-acetates

Jürgen Kopf [a], Martina Morf [a], Bärbel Zimmer [a], Manfred Bischoff [b], and Peter Köll [b]

[a] *Institute of Inorganic and Applied Chemistry, The University, Martin-Luther-King-Platz 6, D-W2000 Hamburg 13 (Germany)*

[b] *Department of Chemistry, Organic Chemistry, The University, Carl-von-Ossietzky-Str. 9–11, D-W2900 Oldenburg (Germany)*

(Received August 12th, 1991; accepted October 14th, 1991)

ABSTRACT

The structures of the 1,2,3,4,5,6-hexa-acetates derived from allitol, galactitol, D- and DL-mannitol (conglomerate and racemate), D- and DL-iditol, DL-glucitol, and DL-altritol have been determined by X-ray crystallography, using direct methods, and comprise a complete set of solid-state structures. Compared with the parent alditols, the hexa-acetates have much greater freedom to adopt conformations which involve 1,3-parallel interactions of oxygen and carbon atoms. Such interactions of acetoxyl groups do not impose dominating steric constraints. Parallel alignment of the flat acetoxyl groups can result in the thermodynamically most favoured dense packing of molecules in the crystal.

INTRODUCTION

Alditols are model compounds for many stereochemical problems in solution and the solid state related to open-chain compounds which comprise several chiral centres. It is accepted generally that the preferred conformations of alditols are those in which C//C, C//O, and O//O 1,3-parallel interactions are avoided by rotation around C–C bonds, thereby changing the usual planar zigzag conformations into sickle or bent conformations. The avoidance of O//O interactions, which has been observed frequently, has been termed[1] the Hassel–Ottar effect on the basis of a compilation of carbohydrate X-ray structures despite the fact that, in the original paper[2], such an interaction was not claimed to be sterically dominating but the potential effects of intramolecular 1,3 hydrogen bonds were recognised.

Correspondence to: Professor J. Kopf, Institut, für Anorganische und Angewandte Chemie der Universität Hamburg, Martin-Luther-King-Platz 6, D-W2000 Hamburg 13, Germany; or to: Professor P. Köll, Fachbereich Chemie der Universität Oldenburg, Organische Chemie, Carl-von-Ossietzky-Str. 9–11, D-W2900, Oldenburg, Germany.

In connection with the crystal structure of D-*glycero*-L-*allo*-heptitol, Angyal et al.[3] proposed that the influence of C//O interactions may have been overestimated previously[4]. In the crystal state, D-altritol ("D-talitol")[5] and D-*glycero*-D-*manno*-heptitol[6] avoid O//O interactions by adopting sickle conformations, but an easily avoidable C//O interaction was tolerated. Such an interaction involving O-3 and C-6 occurs in the glucitol moiety of cellobiitol[7], and C-3 and O-6 in the same moiety of maltitol[8] and lactitol monohydrate[9], a fact which, regrettably, was not mentioned in previous publications[5,6].

In work on nitroalditols[10–12], it was shown that O//O interactions (violation of the Hassel–Ottar effect[1,2]) are often tolerated in the crystal, with 1-deoxy-1-nitroiditol being the most impressive example. This compound adopts a planar zigzag conformation that involves *two* O//O interactions[11]. Recently, it was reported for the first time that a similar situation occurs in an unsubstituted alditol, namely, L-*galacto*-D-*galacto*-decitol[13]. Other examples, involving *one* such interaction have been reported involving derivatives of D-gluconic acid[14] and

TABLE I

Crystallographic data [a,b] for the hexitol hexa-acetates ($C_{18}H_{26}O_{12}$, mol wt 434.40)

Data	**1** (*allo*)	**2** (*galacto*)	D-**3** (*manno*)	D-**3** (ex conglomerate)
Mp (degrees)	61–62	168–171	124	101(123) [d]
Crystal dimensions (mm)	0.8×0.2×0.1	0.4×0.4×0.2	0.4×0.2×0.2	0.4×0.4×0.1
Space group	$P\bar{1}_1$	$P2_1/n$	$P2_12_12_1$	$P2_12_12_1$
Cell parameters (pm, degrees)				
a	560.3(1)	1067.6(10)	899.1(1)	893.7(1)
b	1020.7(2)	830.9(3)	1201.4(2)	1202.1(1)
c	1050.5(1)	1192.8(11)	1976.0(4)	1977.1(2)
α	62.99(1)	(90)	(90)	(90)
β	84.83(3)	90.44(5)	(90)	(90)
γ	89.26(3)	(90)	(90)	(90)
Volume V (pm×10^6)	532.8(3)	1058(1)	2134.4(6)	2124.0(4)
Z	2/2	4/2	4	4
F(000)	230	460	920	920
Calculated density D_x (g×cm^{-3})	1.354	1.363	1.352	1.358
λ, $K\alpha_1$ (pm)	70.9261(Mo)	70.9261(Mo)	70.9261(Mo)	154.051(Cu)
μ (cm^{-1})	1.1	1.1	1.1	9.5
$2\theta_{max}$ (degrees)	50	48	50	153
Reflections (symmetry independent)	1753	1506	2053	2499
Reflections with $F_o > 3\sigma(F_o)$	1582	983(6σ)	1903	2360
Number of refined parameters	189	189	376	376
Ratio of valued reflections to parameters	8.4	5.2	5.1	6.3
Final residual factors				
R	0.056	0.043	0.049	0.055
R_w	0.051	0.043	0.045	0.051

[a] Enraf–Nonius CAD 4 refractometer except for D-**4** for which a Syntex P21 was used.

D-gluconamides [15] which adopt the planar zigzag conformations and with an O-2//O-4 interaction.

We now report on the conformations of the hexitol hexa-acetates in the solid state as determined by X-ray crystallography, knowing that acetylated oxygens could be less sterically demanding than hydroxyl groups[16]. When this work was started, no crystal structure of an alditol acetate had been reported. Reports on D-glucitol hexa-acetate[17,18] and xylitol penta-acetate[18] have since appeared, and we now give the results of the structure determinations of a further eight hexitol hexa-acetates.

RESULTS AND DISCUSSION

In the hexitol series, six diastereomers are possible, two of which are *meso* compounds, namely, allitol and galactitol. The remaining four can be grouped into two categories: (*a*) mannitol and iditol which have the potential to exhibit C_2 symmetry and (*b*) glucitol and altritol ("talitol") which are asymmetric. Therefore,

DL-**3** (racemate)	D-**4** (*ido*)	DL-**4**	D-**5** (*gluco*) [c]	DL-**5**	DL-**6** (*altro*)
108–109	122	165–166	99	117–118	95–96
0.5×0.3×0.2	0.6×0.6×0.1	0.5×0.4×0.3	0.3×0.3×0.2	0.3×0.3z×0.2	0.5×0.2×0.1
Pbca	$P3_221$	$C2/c$	$P2_1$	$P\bar{1}$	$P\bar{1}$
1839.4(2)	886.7(2)	1560.3(1)	1025.3(1)	883.6(1)	860.1(1)
1012.4(2)	= *a*	884.8(1)	837.0(1)	1074.8(1)	1076.2(1)
2350.7(3)	2401.5(3)	1559.0(1)	1254.8(1)	1184.1(1)	1295.0(1)
(90)	(90)	(90)	(90)	103.08(1)	83.82(1)
(90)	(90)	90.08(1)	95.98(5)	97.57(1)	71.56(1)
(90)	(90)	(90)	(90)	98.73(1)	72.16(1)
4377(1)	1635.2(6)	2152.3(3)	1071.0(2)	1066.4(2)	1082.4(2)
8	3	8/2	2	2	2
1840	690	920	460	460	460
1.318	1.323	1.340	1.347	1.353	1.333
154.051(Cu)	70.9261(Mo)	154.051(Cu)	70.9261(Mo)	154.051(Cu)	154.051(Cu)
9.2	1.1	9.4	1.1	9.5	9.3
153	60	153	50	153	153
3298	1804	2074	1906	4201	4165
2591	1524	1969	1681	3705	3771
375	213	188	375	350	375
6.9	7.2	10.5	4.5	10.6	10.1
0.072	0.082	0.068	0.053	0.069	0.058
0.056	0.061	0.057	0.051	0.059	0.056

[b] Standard deviations in parentheses. [c] Data taken from ref. 17. [d] Individual single crystals.

excluding polymorphs, ten solid-state structures have to be considered for the hexitol hexa-acetates, namely, those of two *meso* compounds, four enantiomers, and four racemates.

In the following discussion, the compounds investigated are treated in a sequence according to the above symmetry properties, namely 1,2,3,4,5,6-hexa-*O*-acetylallitol (**1**), 1,2,3,4,5,6-hexa-*O*-acetylgalactitol (**2**), 1,2,3,4,5,6-hexa-*O*-acetyl-D-mannitol (D-**3**), 1,2,3,4,5,6-hexa-*O*-acetyl-DL-mannitol (DL-**3**), 1,2,3,4,5,6-hexa-*O*-acetyl-D-iditol (D-**4**), 1,2,3,4,5,6-hexa-*O*-acetyl-DL-iditol (DL-**4**), 1,2,3,4,5,6-hexa-*O*-acetyl-D-glucitol (D-**5**)[17,18], and 1,2,3,4,5,6-hexa-*O*-acetyl-DL-glucitol (DL-**5**), 1,2,3,4,5,6-hexa-*O*-acetyl-D-altritol (D-**6**), and 1,2,3,4,5,6-hexa-*O*-acetyl-DL-altritol (DL-**6**).

Suitable crystals for X-ray determinations were usually obtained from solutions in ethanol. For **2** and D-**4**, ether was a more appropriate solvent and D-**6** was not obtained crystalline hitherto.

The structures were determined in the usual way by direct methods using the programs SHELXS-90[19] to solve the phase problem and SHELX-76[20] (blocked matrix) for refinement. Table I covers the crystallographic properties of the compounds investigated and Table II contains the fractional positional parameters of the C and O atoms. The other basic data have been deposited*. No unusual bond lengths and angles were observed. The crystal structures are represented as SCHAKAL drawings[21] (Figs. 1–9) which also show the atom numbering.

meso-*Hexitol hexa-acetates*.—1,2,3,4,5,6-Hexa-*O*-acetylallitol (**1**) and 1,2,3,4,5,6-hexa-*O*-acetylgalactitol (**2**) have long been known as crystalline compounds[22,23] and Figs. 1 and 2 show the molecules as found in the crystal. Because of the inherent symmetry, only halves of the molecules are numbered; symmetry-related atoms are enclosed in brackets, e.g., (C-4) is equivalent to C-3 and (C-6) to C-1.

Fig. 1 shows that **1** adopts a bent conformation which results from rotations around the C-2–C-3 and (C-4)–(C-5) bonds in the planar zigzag arrangement and involves two O//O interactions, namely, O-2//(O-4) and O-3//(O-5). These interactions are avoided in allitol by similar rotations, but in opposite directions leading to a conformation which is free of all O//O and C//O interactions[24]. In contrast, the conformation of **1** involves two C//O interactions, namely, between C-1//(O-4) and (C-6)//O-3. The distance between these atoms is 282.0 pm and, as such, is significantly shorter than those in the unsubstituted compounds[3,5,6].

Fig. 2 depicts the shape of the molecules of **2** in the crystal. The carbon chain is planar zigzag as expected because there are no obvious reasons for departing from that conformation, which is also found in galactitol[25]. Nevertheless, the conforma-

* Lists of observed and calculated structure amplitudes, atomic co-ordinates of the atoms, including anisotropic thermal factors for C and O and isotropic factors for H, bond distances and angles, and further information to Table I (173 pages) are deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/495/*Carbohydr. Res.*, 229 (1992) 17–32.

TABLE II

Fractional positional parameters ($\times 10^4$) of carbon and oxygen atoms[a] for the hexitol hexa-acetates

Atom	**1** (*allo*)			**2** (*galacto*)		
	x	*y*	*z*	*x*	*y*	*z*
O-1	−3779(3)	8444(2)	3999(2)	3305(2)	779(3)	−821(2)
O-2	442(3)	7738(2)	2460(2)	1939(2)	−1735(3)	259(2)
O-3	−739(3)	8526(2)	−387(2)	733(2)	436(3)	−1312(2)
O-11	−6601(3)	10121(2)	3578(2)	4749(3)	2621(4)	−485(2)
O-21	−1222(3)	5725(2)	2495(2)	2202(3)	−2290(3)	2091(2)
O-31	4689(3)	7971(2)	−57(2)	1085(3)	3094(3)	−1382(2)
C-1	−2341(4)	9436(2)	2696(2)	2917(3)	897(4)	327(3)
C-2	−1634(3)	8590(2)	1874(2)	1738(3)	−45(4)	516(2)
C-3	−1125(3)	9510(2)	255(2)	577(3)	512(4)	−114(2)
C-11	−5897(3)	8926(3)	4304(2)	4227(4)	1755(5)	−1124(3)
C-12	−7186(3)	7808(3)	5657(3)	4520(3)	1630(5)	−2338(3)
C-21	407(3)	6313(2)	2736(2)	2157(3)	−2734(4)	1139(3)
C-22	2644(3)	5582(3)	3333(3)	2319(4)	−4417(4)	754(3)
C-31	−2682(3)	7788(2)	−450(2)	966(3)	1836(5)	−1851(3)
C-32	−1995(3)	6756(3)	−1037(3)	1066(4)	1564(5)	−3074(3)
	D-**3** (*manno*)			DL-**3**		
O-1	3649(3)	5900(2)	4780(2)	11188(1)	4814(2)	4683(1)
O-2	1203(3)	4456(2)	4427(1)	10360(1)	5482(2)	3766(1)
O-3	4667(3)	4314(2)	3473(2)	9279(1)	2674(2)	4222(1)
O-4	2197(3)	2701(2)	3227(1)	8674(1)	5075(2)	3776(1)
O-5	2840(3)	5084(2)	2159(1)	8951(1)	2156(2)	2907(1)
O-6	551(3)	3448(2)	1790(2)	8348(1)	4450(2)	2351(1)
O-11	6039(4)	6027(3)	5053(2)	12232(2)	3941(3)	4419(2)
O-21	848(4)	2823(3)	4954(2)	10013(2)	7064(3)	4381(1)
O-31	5138(3)	6134(2)	3290(2)	10054(2)	1003(3)	4066(1)
O-41	−309(3)	2709(3)	3343(2)	8884(2)	6697(3)	3144(1)
O-51	5012(4)	4878(3)	1604(2)	8383(2)	571(2)	3414(1)
O-61	28(4)	1652(3)	1685(2)	7321(2)	5490(4)	2155(2)
C-1	3729(5)	4702(4)	4832(2)	10792(2)	3810(4)	4384(2)
C-2	2758(5)	4173(3)	4298(2)	10116(2)	4457(3)	4150(2)
C-3	3074(4)	4519(3)	3576(2)	9649(2)	3486(3)	3810(2)
C-4	2201(4)	3864(3)	3054(2)	9088(2)	4150(3)	3433(2)
C-5	2884(5)	3925(3)	2343(2)	8531(2)	3159(3)	3199(2)
C-6	2139(5)	3204(3)	1817(2)	7978(2)	3740(4)	2799(2)
C-11	4904(5)	6467(4)	4906(2)	11901(3)	4787(4)	4650(2)
C-12	4705(6)	7693(4)	4825(3)	12231(2)	5963(4)	4943(2)
C-21	376(5)	3711(4)	4777(2)	10318(3)	6764(4)	3960(2)
C-22	−1121(5)	4140(4)	4924(3)	10718(3)	7637(4)	3566(2)
C-31	5569(5)	5193(4)	3334(2)	9538(2)	1425(4)	4309(2)
C-32	7137(5)	4820(4)	3247(3)	9079(2)	716(4)	4731(2)
C-41	849(5)	2216(3)	3351(2)	8626(3)	6354(4)	3581(2)
C-42	1021(5)	1015(3)	3501(3)	8227(3)	7175(4)	4002(2)
C-51	4014(5)	5460(4)	1791(2)	8810(2)	862(3)	3057(2)
C-52	3894(5)	6686(4)	1671(3)	9277(3)	−38(4)	2709(2)
C-61	−383(5)	2585(3)	1703(2)	7946(3)	5341(4)	2069(2)
C-62	−1974(5)	2939(4)	1652(3)	8380(3)	6093(5)	1663(2)
	D-**4** (*ido*)			DL-**4**		
O-1	607(5)	8710(5)	2620(2)	638(1)	3862(2)	3765(1)
O-2	2662(3)	7074(3)	2517(1)	1424(1)	976(2)	3823(1)
O-3	4248(3)	8210(2)	1532(1)	874(1)	−79(2)	2321(1)

(continued)

TABLE II (continued)

	D-**4** (*ido*)			DL-**4**		
	x	*y*	*z*	*x*	*y*	*z*
O-11	797(6)	11096(5)	2236(2)	−485(2)	5313(3)	3975(3)
O-21	4567(3)	7641(3)	3200(1)	1111(1)	−517(3)	4923(2)
O-31	1716(3)	6008(3)	1222(1)	1971(1)	1315(2)	1817(1)
C-1	2419(5)	9552(6)	2755(2)	182(2)	2561(3)	4081(2)
C-2	3427(4)	8930(4)	2399(1)	518(2)	1179(3)	3631(2)
C-3	3389(4)	9081(3)	1769(1)	461(1)	1249(3)	2659(2)
C-11	−42(6)	9653(6)	2385(2)	236(2)	5171(4)	3743(2)
C-12	−1947(6)	8584(9)	2401(3)	790(2)	6432(4)	3459(3)
C-21	3437(4)	6606(4)	2908(1)	1625(2)	21(3)	4457(2)
C-22	2715(5)	4724(5)	2924(2)	2575(2)	−250(5)	4493(2)
C-31	3231(5)	6639(4)	1288(1)	1652(2)	110(3)	1935(2)
C-32	4370(5)	5893(5)	1118(2)	2014(2)	−1398(4)	1711(2)
O-1B	671(5)	8846(5)	2451(2)			
O-11B	66(7)	10640(7)	2869(3)			
C-1B	2426(7)	9730(8)	2662(2)			
C-11B	−425(7)	9429(7)	2568(3)			
C-12B	−2031(7)	8485(7)	2232(3)			
	DL-**5** (*gluco*)			DL-**6** (*altro*)		
O-1	6065(2)	5416(2)	3523(2)	3209(3)	687(2)	2782(2)
O-2	3325(2)	5879(2)	2176(2)	4845(2)	2792(2)	2187(1)
O-3	6985(2)	8042(2)	2563(2)	2880(2)	4140(2)	759(1)
O-4	4348(2)	8541(2)	1198(1)	2173(2)	5453(2)	3361(1)
O-5	6289(2)	10612(2)	3084(1)	68(2)	7028(2)	2242(2)
O-6	3439(2)	10979(2)	1817(2)	1835(2)	8249(2)	225(2)
O-11	8530(3)	5317(4)	3621(3)	789(3)	1491(2)	4098(2)
O-21	2638(3)	4848(3)	271(2)	4792(3)	2382(3)	3933(2)
O-31	7876(2)	8757(3)	4502(2)	542(3)	3648(2)	715(2)
O-41	1738(2)	8037(3)	869(2)	4609(4)	5790(3)	3360(2)
O-51	6637(3)	11718(2)	4983(2)	−110(4)	8960(3)	2829(3)
O-61	1235(3)	11659(4)	2024(3)	4179(3)	8508(2)	460(2)
C-1	5899(3)	5352(3)	2279(3)	2705(4)	1815(3)	2130(2)
C-2	4888(3)	6294(3)	1995(2)	3015(3)	2996(3)	2474(2)
C-3	5419(3)	7677(3)	2763(2)	2243(3)	4255(2)	1925(2)
C-4	4383(3)	8590(3)	2432(2)	2719(3)	5410(2)	2194(2)
C-5	4763(3)	9974(3)	3192(2)	1897(3)	6753(2)	1775(2)
C-6	3568(3)	10808(3)	2999(2)	2331(3)	6894(2)	555(2)
C-11	7414(4)	5341(4)	4084(3)	2100(4)	629(3)	3763(3)
C-12	7430(4)	5407(4)	5340(3)	2652(5)	−589(4)	4369(3)
C-21	2293(3)	5149(3)	1219(3)	5572(4)	2479(3)	3008(2)
C-22	735(3)	4819(3)	1531(3)	7451(4)	2306(3)	2580(3)
C-31	8120(3)	8519(3)	3520(2)	1890(3)	3841(2)	233(2)
C-32	9676(3)	8687(4)	3152(3)	2688(4)	3817(3)	−954(2)
C-41	2927(3)	8230(3)	502(2)	3249(5)	5659(3)	3861(3)
C-42	3055(4)	8153(3)	−747(3)	2499(6)	5666(4)	5053(3)
C-51	7115(3)	11473(3)	4072(2)	−776(4)	8147(3)	2802(3)
C-52	8672(3)	12051(3)	3876(3)	−2619(5)	8241(4)	3329(3)
C-61	2199(3)	11422(3)	1427(3)	2904(3)	8945(3)	183(2)
C-62	2119(4)	11504(4)	191(3)	2366(5)	10273(3)	−274(3)

[a] Standard deviations in parentheses.

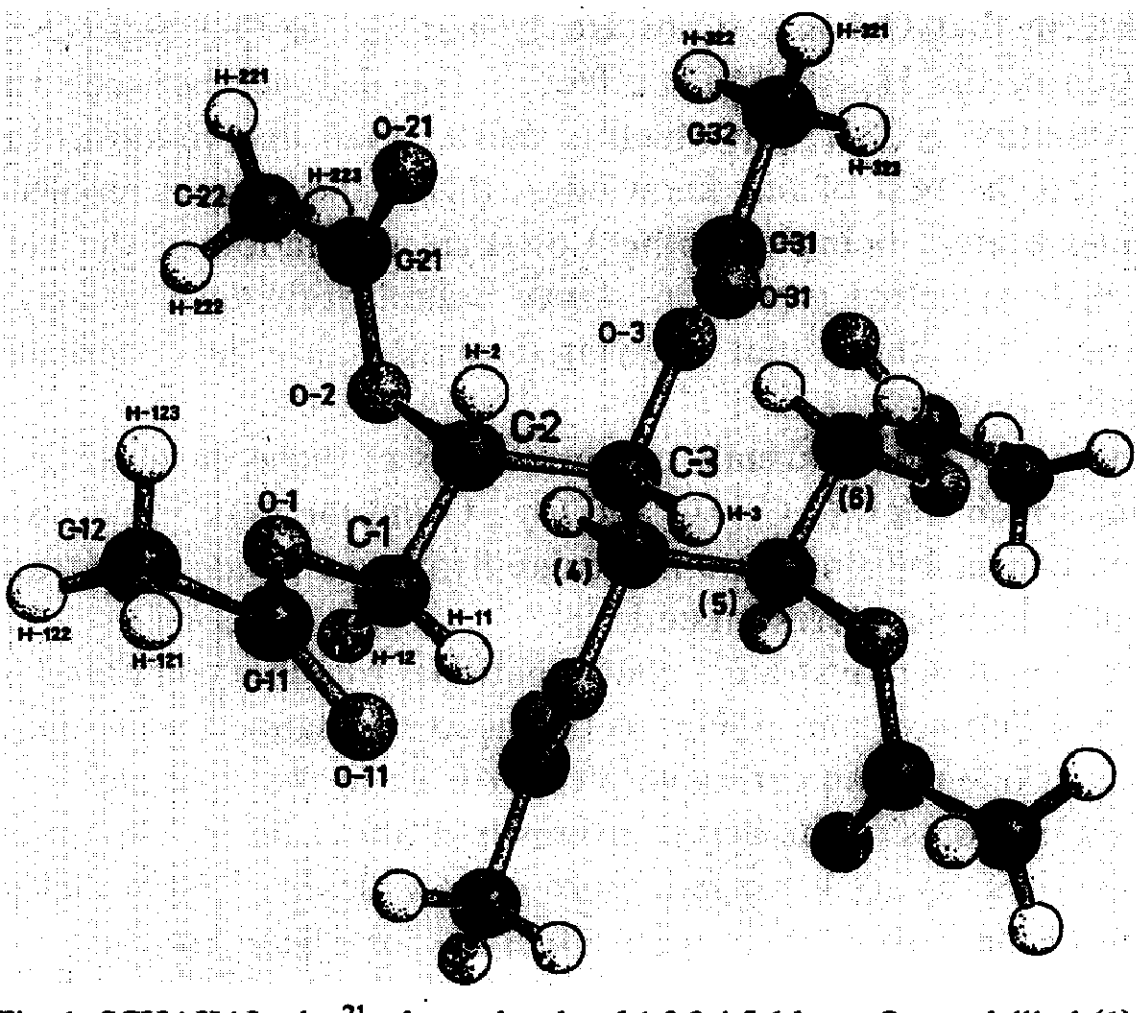

Fig. 1. SCHAKAL plot[21] of a molecule of 1,2,3,4,5,6-hexa-*O*-acetylallitol (**1**).

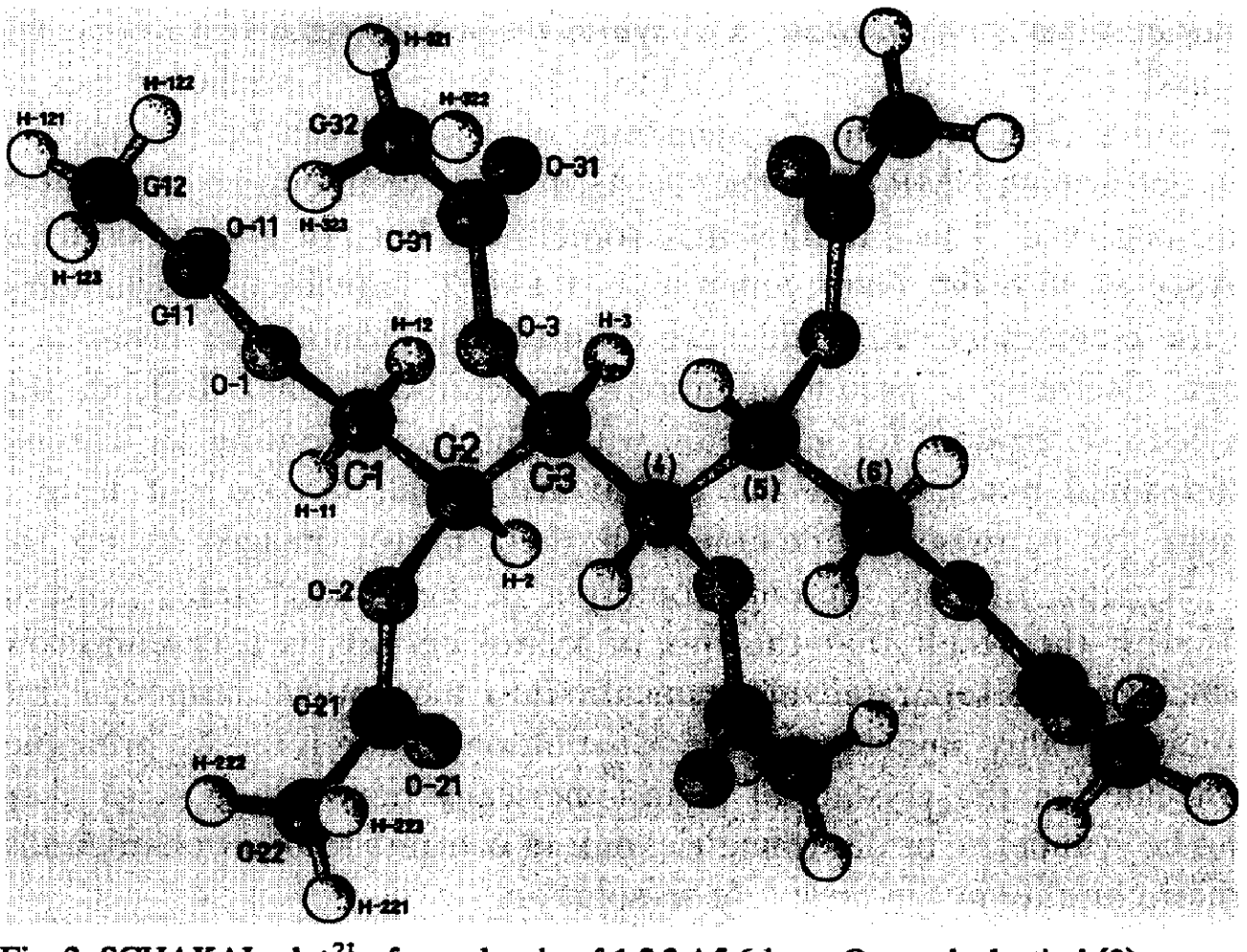

Fig. 2. SCHAKAL plot[21] of a molecule of 1,2,3,4,5,6-hexa-*O*-acetylgalactitol (**2**).

tion of **2** is remarkable in that O-1 and (O-6) are 1,3-parallel to O-3 and (O-4), respectively, in violation of the Hassel–Ottar effect[1,2]. The distance between the oxygen atoms in this situation is 281.7 pm which is shorter than that found in the deoxynitroalditols[11,12]. To the best of our knowledge, this is the second reported example (xylitol penta-acetate[18] being the other) of such a violation of the rule mentioned as far as hydroxymethyl groups in *simple* alditol derivatives are concerned and substantiates the claim that acetylated oxygens are less sterically demanding than hydroxyl groups[16].

It is important to note that the "unusual" conformations of those unsubstituted open-chain compounds which tolerate C//O and O//O interactions[5,6,11–15] cannot always be explained by stabilising intramolecular hydrogen bonds, an effect, which, of course, should not be underestimated[2].

Thus, **1** and **2** in the crystal demonstrate a conformational freedom compared to the "rules"[1,4], which is impressive and points to the need to change the assumptions on conformations of open-chain carbohydrates, at least in the solid state.

The carbon and oxygen atoms in the acetyl groups in **1** and **2** lie in a common plane, and the carbonyl oxygens are arranged, more or less ideally, 1,3-parallel to the adjacent hydrogens of the carbon chain. This effect has long been known[26] and was discussed recently[27]. For the same reasons, one of the hydrogens of the acetoxymethyl groups is in a 1,2-parallel relationship to the carbonyl oxygen which determines the positions of the other two methyl hydrogens.

The primary acetoxyl groups in **1** and **2** are *gauche* to their neighbours. Crystalline allitol[24] and galactitol[25] show the same topology at their termini. These observations can be explained by the general "gauche effect"[28].

Hexitol hexa-acetates with intrinsic C_2 *symmetry*.—1,2,3,4,5,6-Hexa-*O*-acetylmannitol (**3**) and 1,2,3,4,5,6-hexa-*O*-acetyliditol (**4**) are not dissymmetric per se despite being chiral. The inherent C_2 symmetry of **3** and **4** can be observed in solution when performing NMR experiments. As in *meso* compounds, only half of the signals are observed. This situation may sometimes, but not always, occur in the crystal. Also, as with the *meso* compounds **1** and **2**, individual dissymmetric molecules in the elementary cell could have occurred by forming, for instance, a pseudo-racemic assembly of pseudo-enantiomers (enantiomorphs). Indeed, this situation has been observed[25] for galactitol, with xylitol representing an extreme example[29]. Individual molecules in the crystal are chiral, but do not form a pseudo-racemate by pairwise interaction with their mirror images as do the molecules of galactitol. Instead, the enantiomorphs of the same chirality build up single crystals with the result that the mix of xylitol crystals is a (pseudo)conglomerate, which can be separated mechanically into the optical antipodes[1] but which lose their chirality immediately on dissolution. Therefore, in principle, individual molecules in the crystals of enantiomerically pure **3** and **4**, or their racemates, can be symmetric or dissymmetric, but, in contrast to *meso* compounds, do not lose their chirality in the crystal or in solution.

The crystallographic properties (Table I) of D-mannitol hexa-acetate[30] (D-**3**, mp

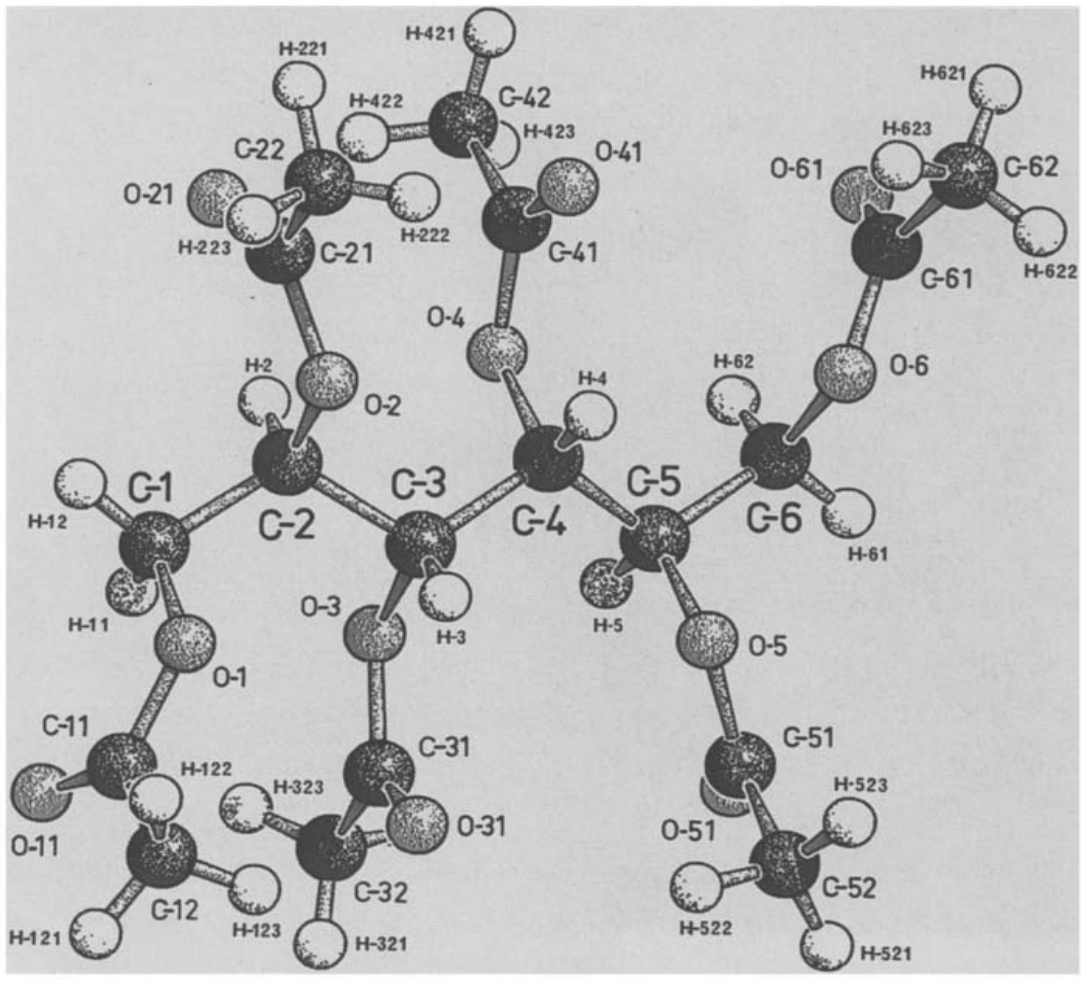

Fig. 3. SCHAKAL plot[21] of a molecule of 1,2,3,4,5,6-hexa-*O*-acetyl-D-mannitol (D-**3**).

124°) are more or less in accord with those in the literature[31]. The space group $P2_12_12_1$ indicates dissymmetric molecules in the elementary cell, one of which is depicted in Fig. 3. As in the polymorphs of D-mannitol[32], molecules of D-**3** are arranged in the planar zigzag conformation which has no 1,3-interactions that involve heavy atoms. The primary acetoxyl groups are *gauche* to their neighbours (see above) as are the primary hydroxyl groups in the parent compound[32] and its racemate[33].

An attempt to prepare crystals of racemic DL-**3** by dissolving equal amounts of D-**3**[30] and L-**3**[34] in hot ethanol or ether and cooling gave crystals which showed crystallographic properties identical to those of the enantiomers as revealed by an independent structure determination (see Table I). The IR spectra were identical, as were the melting points of individual single crystals which had $[\alpha]_D$ values[30,34] around +25° or −25°. Grinding a random sample of the crystals resulted in a dramatic drop of the mp to ~ 101°. Therefore, DL-**3** preferentially crystallises as a conglomerate of pure enantiomers. This is an exceptional situation with few other examples known in carbohydrate chemistry or elsewhere[35]. These example are not only of scientific interest, but also can be exploited for technical purposes, because they allow for simple procedures for the resolution of the racemate[35].

Nevertheless, in some preparations, which could not be reproduced deliberately, the bulk of rhombohedric, enantiomerically pure crystals was accompanied by a small proportion of needle-shaped crystals with mp 108–109° and different crystallographic properties (see Table I). The space group *Pbca* indicates an

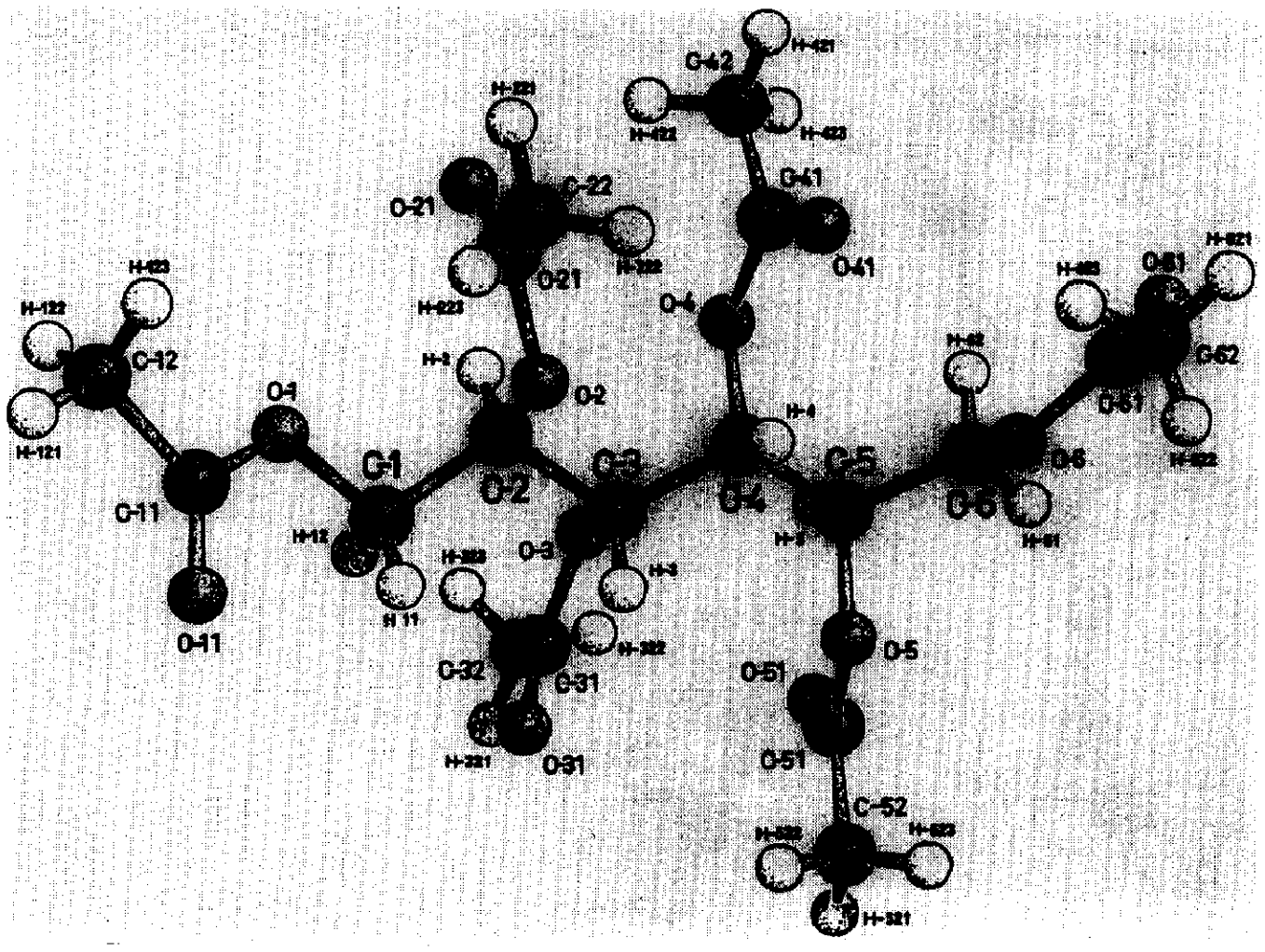

Fig. 4. SCHAKAL plot[21] of a molecule of the D enantiomer in the metastable morph of 1,2,3,4,5,6-hexa-*O*-acetyl-DL-mannitol (DL-**3**).

enantiomeric pair (a racemate) of dissymmetric molecules in the elementary cell, one of which (D) is shown in Fig. 4. O-1 (D) extends the planar zigzag carbon chain, but a *gauche* arrangement to its neighbour is still favoured (see above). As can be seen by comparing Figs. 3 and 4, the molecules in these racemic crystals of DL-**3** are less compact, which results in a lower density than that of the pure enantiomers (see Table I). Thus, it is concluded that the crystals of racemic DL-**3** are thermodynamically unstable at room temperature, an assumption which is substantiated by the lower melting point (108°) as compared to that (124°) of the enantiomers.

Although crystals of 1,2,3,4,5,6-hexa-*O*-acetyl-D-iditol[36] (D-**4**) were obtained easily from ether, the elucidation of the solid state structure was not simple. The best solution was achieved only by assuming a symmetric molecule in which the primary acetoxyl groups can adopt two equally populated positions with respect to the α-hydrogens. Fig. 5 shows one of these situations with the carbonyl oxygens at the termini orientated 1,3-parallel to H-11 and (H-61), respectively. Due to the assumed disorder, the carbonyl oxygens mentioned arrange equally often 1,3-syn-periplanar to H-12 and (H-62). The carbon chain is doubly bent by rotations around the C-2–C-3 and (C-4)–(C-5) bonds in the planar zigzag arrangement. Therefore, the overall geometry is different from those for D-iditol[24] and DL-iditol[37]. In these compounds, a single twist around the central C-3–C-4 bond in the planar zigzag conformation leads to a bent conformation in which all O//O and C//O

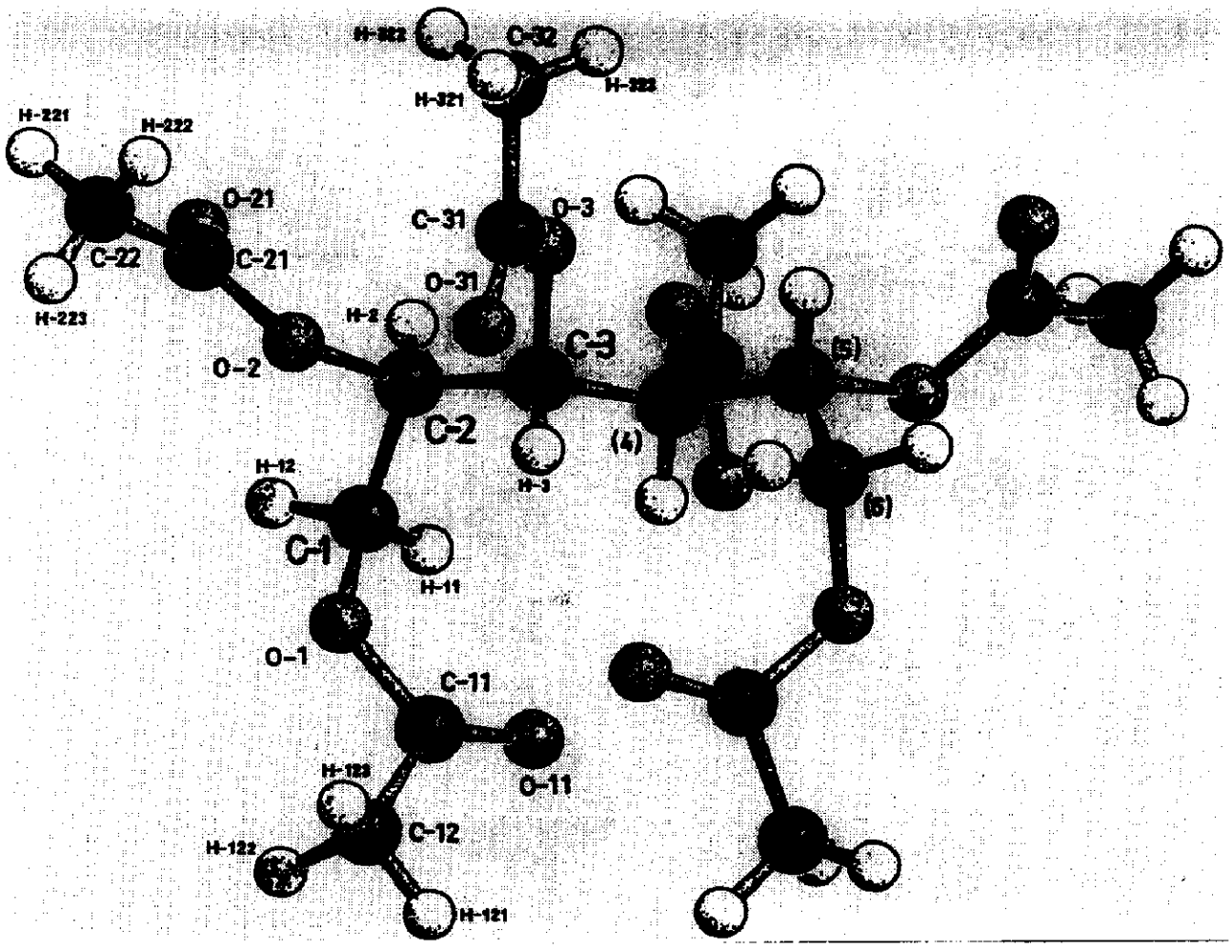

Fig. 5. SCHAKAL plot[21] of a molecule of 1,2,3,4,5,6-hexa-*O*-acetyl-D-iditol (D-**4**); disordered structure: only one of the two rotamers involving the C-1(6), O-1(6) bonds are given.

interactions are avoided. The general orientation of each primary acetoxyl group in D-**4** is *gauche* to its neighbour as is each primary hydroxyl group in D-iditol[24].

DL-**4**[36] Crystallises as a racemate (mp 165°, cf. mp 122° for D-**4**). The molecules of DL-**4** (Fig. 6) are symmetric and adopt the same overall conformation as observed for D-**4** but without exhibiting disorder at the acetoxyl termini. In accordance with the Wallach rule[35], the calculated density D_x is higher for the racemate than for the enantiomers, as expected from considerations of entropy. The conformation of individual molecules in DL-iditol[37] is different, not only from that observed in D-iditol[24] but also from that found in DL-**4** insofar as only one primary hydroxyl group is *gauche* to its neighbour and the other is *trans*.

Asymmetric hexitol hexa-acetates.—The structure of 1,2,3,4,5,6-hexa-*O*-acetyl-D-glucitol (D-**5**) has been published recently[17,18] and the conformation of the individual molecules is shown in Fig. 7. In contrast to the molecules of D-glucitol, which adopt[38] a sickle conformation*, the molecules of D-**5** adopt the planar zigzag conformation which involves an O-2//O-4 interaction (cf. ref. 14). Furthermore, O-1 and O-3 are found in the same steric relationship and O-1 is *gauche* to O-2 as is O-6 to O-5. Another *gauche* position free of O//O interactions is viable

* The structure of only one of the polymorphs of D-glucitol has been reported hitherto, which, because of its low melting point[38], should not be the one usually encountered.

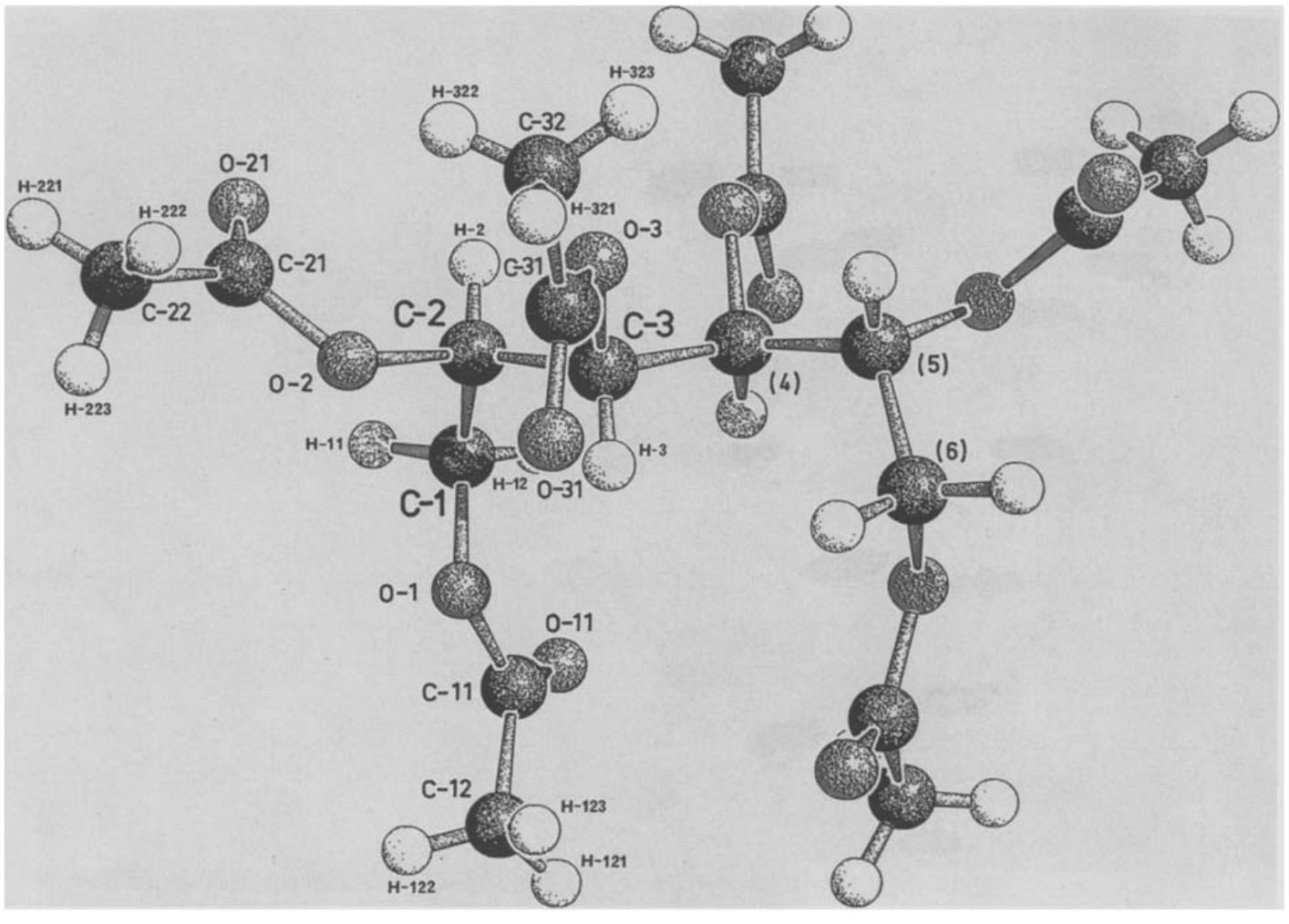

Fig. 6. SCHAKAL plot[21] of a molecule of the D enantiomer in 1,2,3,4,5,6-hexa-*O*-acetyl-DL-iditol (DL-4).

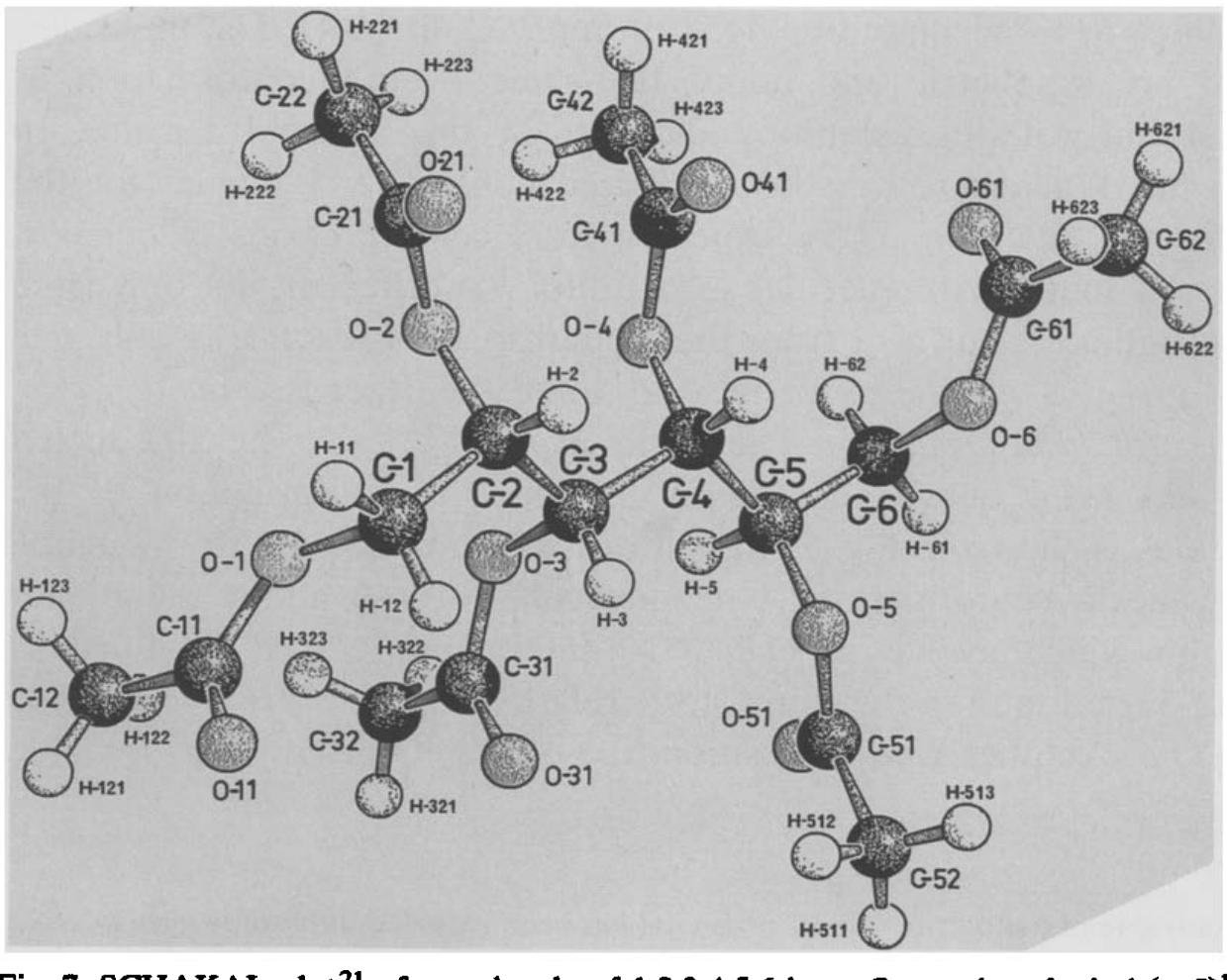

Fig. 7. SCHAKAL plot[21] of a molecule of 1,2,3,4,5,6-hexa-*O*-acetyl-D-glucitol (D-5)[17,18].

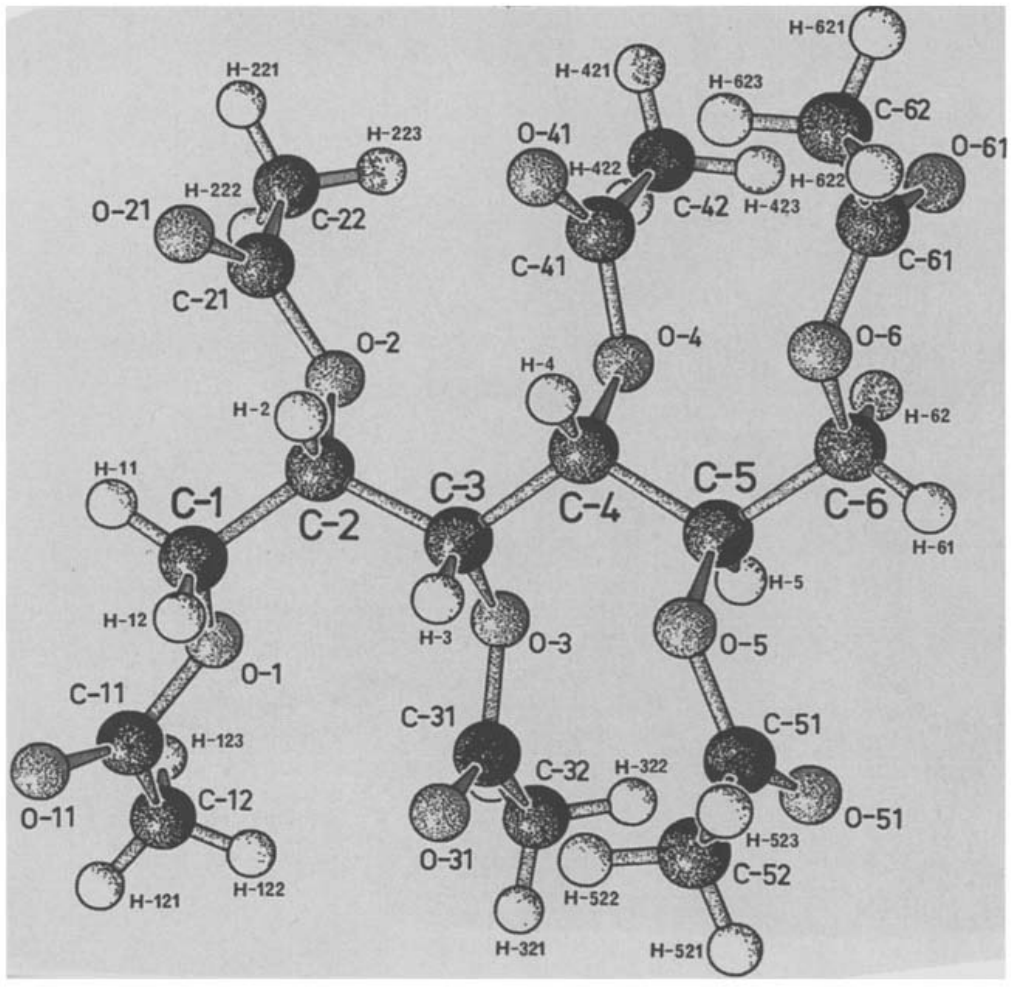

Fig. 8. SCHAKAL plot[21] of a molecule of the D enantiomer in 1,2,3,4,5,6-hexa-*O*-acetyl-DL-glucitol (DL-**5**).

for O-1 as in galactitol hexa-acetate (**2**), which exhibits similar remarkable conformational features.

Crystallisation of a mixture of equal amounts of D- and L-**5** (mp 99°) gave DL-**5** (mp 117°)[39]. The X-ray structure determination revealed a slightly higher density D_x for DL-**5** than for D-**5** (Table I) in support of the Wallach rule[35]. Nevertheless, the geometries of individual molecules in D-**5** and DL-**5** are the same as seen by comparision of Figs. 7 and 8. The crystal structure of DL-glucitol is not known.

To the best of our knowledge, the hexa-acetate of enantiomerically pure altritol ("talitol") never has been crystallised[40], but acetylation of DL-altritol[41] gave 1,2,3,4,5,6-hexa-*O*-acetyl-DL-altritol[42] (DL-**6**), mp 95–96°. Fig. 9 shows a D molecule which is in a sickle conformation but, as with D-altritol[5], not the alternative one in which the O-3//C-6 interaction would have been avoided. The distance between these atoms is 285.1 pm (cf. 297.6 pm in D-altritol[5]). The orientation of the acetoxyl groups at both termini again is *gauche* to its neighbours.

In each of the compounds investigated, the acetoxyl groups show normal geometry and arrange more or less synperiplanar[43] to the adjacent hydrogens of the carbon chain as usual[26,27]. The primary acetoxyl groups are always *gauche* (synclinal[43]) to the neighbouring oxygen substituent.

The avoidance of 1,3-parallel O//O interactions (Hassel–Ottar effect[1,2]) is of minor importance in determining the conformation of the hexa-acetates compared to the situation in the parent compounds. Due to this effect, **1**, **4** (D and DL), and

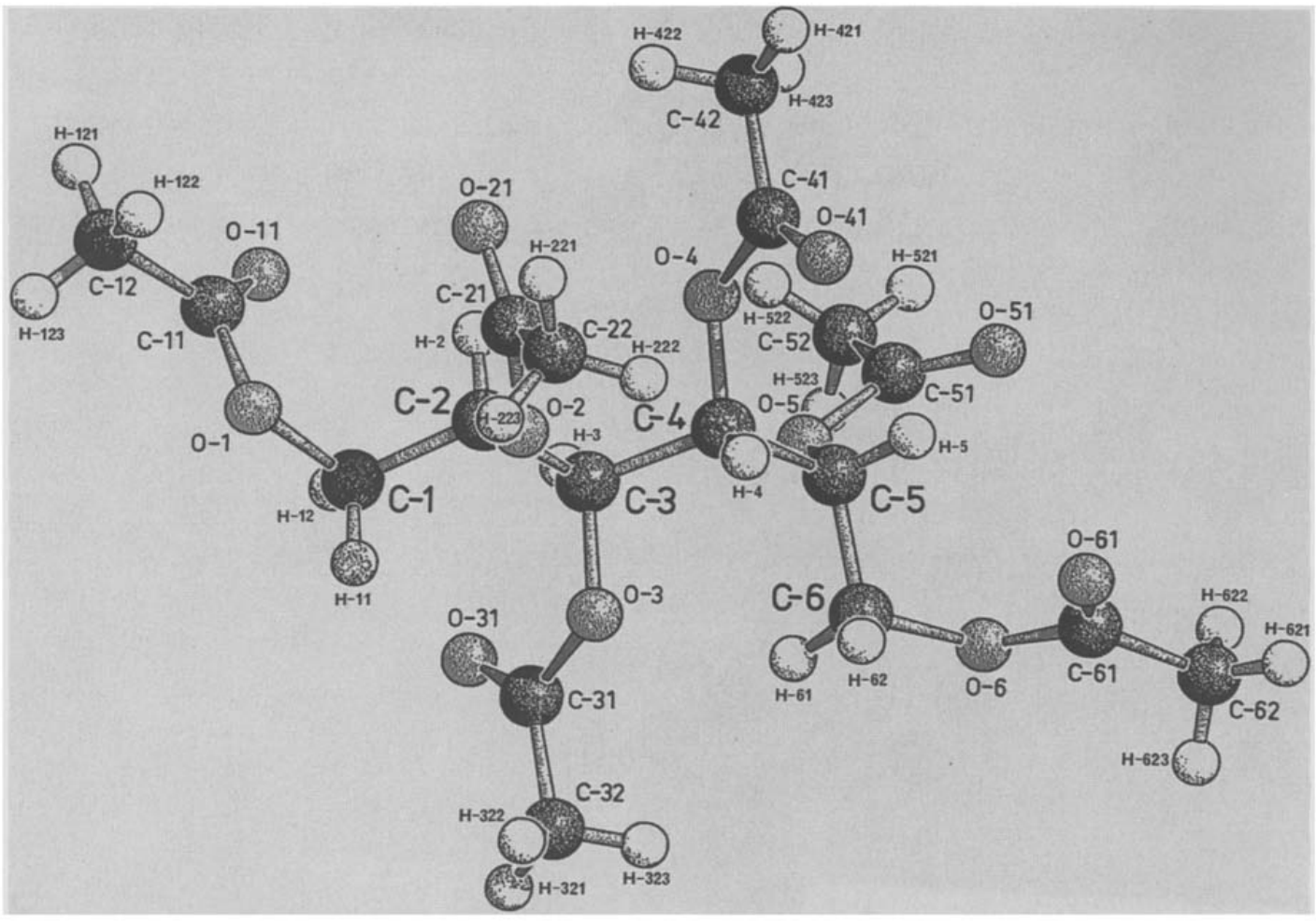

Fig. 9. SCHAKAL plot[21] of a molecule of the D enantiomer in 1,2,3,4,5,6-hexa-*O*-acetyl-DL-altritol (DL-**6**).

DL-**6** adopt bent conformations, but not **5** (D and DL) and xylitol penta-acetate[18]. Furthermore, such interactions are tolerated between primary substituents and acetoxyl groups in the γ-positions in **2**, **4** (D and DL), and xylitol penta-acetate[18], despite the fact that they could be avoided easily by a simple rotation, which would not change the overall geometry of the carbon chain. Two other structures have been reported where, at one terminus of a *manno* compound with a planar zigzag chain, a 1,3-parallel interaction between acetoxyl groups is observed[44]. The steric requirements of acetoxyl groups are lower than those of hydroxyl groups[16], which allow more dense packings in the crystal.

Compounds **1** and DL-**6** adopt bent conformations, but not those expected[4], by tolerating C//O interactions which could have been avoided by a simple rotation without disturbing the conformation of the carbon chain. Considering those examples where such interactions have been observed in alditols[3,5–8], it is clear that such a situation is not very unfavourable[3] and always occurs in compounds with a sequence of three centres of same chirality with one separated from the other two by a centre of the opposite configuration. The higher conformational freedom, which should make the topology of alditol acetates even less predictable in the crystal than that of parent compounds[5,6,13], is also observed in solution and has been discussed in detail[3]. This general situation is more complex[45] for a penta-*O*-acetyl derivative of 7-deoxy-7-nitro-D-*glycero*-L-*gulo*-heptitol[45] [the configurational assignments do not agree with the results reported and the name of the

compound investigated should be (*Z*)-1,2,3,4,5-penta-*O*-acetyl-8-amino-7-*C*-carboxyethyl-6,7,8,9-tetradeoxy-6-*C*-nitromethyl-D-*glycero*-L-*gulo*-non-7-enitol; furthermore, the first digit of the *x* co-ordinate reported for "O-61" should read 4 instead of 7]. In this compound, an O//O interaction is avoided by a twist of the central chain which leads to an almost parallel orientation (synperiplanar[43]) of two vicinal acetoxyl groups (dihedral angle between the oxygens of 6°).

EXPERIMENTAL

The compounds investigated were prepared by the procedures cited. The X-ray structure determinations were performed at ~20° and the results are given in Table I or are deposited. Calculations of geometries were executed by using the PLATON program[46].

ACKNOWLEDGMENTS

We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support, and Mrs. C. Topf (Hamburg) and Mr. H. Komander (Oldenburg) for technical assistance.

REFERENCES

1 G.A. Jeffrey, *Acta Crystallogr., Sect. B*, 46 (1990) 89–103.
2 O. Hassel and B. Ottar, *Acta Chem. Scand.*, 1 (1947) 929–942.
3 S.J. Angyal, J.K. Saunders, C.T. Grainger, R. LeFur, and P.G. Williams, *Carbohydr. Res.*, 150 (1986) 7–21.
4 G.A. Jeffrey and H.S. Kim, *Carbohydr. Res.*, 14 (1970) 207–216.
5 J. Kopf, M. Bischoff, and P. Köll, *Carbohydr. Res.*, 217 (1991) 1–6.
6 P. Köll, H. Komander, S.J. Angyal, M. Morf, B. Zimmer, and J. Kopf, *Carbohydr. Res.*, 218 (1991) 55–62.
7 W.P.J. Gaykema and J.A. Kanters, *Acta Crystallogr., Sect. B*, 35 (1979) 1156–1162.
8 S. Ohno, M. Hirao, and M. Kido, *Carbohydr. Res.*, 108 (1982) 163–171.
9 J.A. Kanters, A. Schouten, and M. van Bommel, *Acta Crystallogr., Sect. C*, 46 (1990) 2408–2411.
10 P. Köll, C. Stenns, W. Seelhorst, and H. Brandenburg, *Liebigs Ann. Chem.*, (1991) 201–206; P. Köll, H. Brandenburg, W. Seelhorst, C. Stenns, and H. Kogelberg, *ibid.*, (1991) 207–211.
11 J. Kopf, H. Brandenburg, W. Seelhorst, and P. Köll, *Carbohydr. Res.*, 200 (1990) 339–354.
12 P. Köll, B. Malzahn, and J. Kopf, *Carbohydr. Res.*, 205 (1990) 1–17.
13 P. Köll, J. Kopf, M. Morf, B. Zimmer, and J.S. Brimacombe, *Carbohydr. Res.*, (1992) in press.
14 C.D. Littleton, *Acta Crystallogr.*, 6 (1953) 775–781; N.C. Panagiotopoulos, G.A. Jeffrey, S.J. LaPlaca, and W.C. Hamilton, *ibid., Sect. B*, 30 (1974) 1421–1430; T. Lis, *ibid., Sect. C*, 40 (1984) 374–376, 376–378; S. Bhattachargee, G.A. Jeffrey, and J.W. Goodby, *Mol. Cryst. Liq. Cryst.*, 131 (1985) 245–255.
15 L.O.G. Satzke and M.F. Mackey, *Acta Crystallogr., Sect. B*, 31 (1975) 2722–2724; A.C. Smidt and M.F. Mackey, *ibid., Sect. B*, 33 (1977) 2659–2662; N. Darbon, Y. Oddon, J.M. Lacombe, E. Decoster, A.A. Pavia, and J.P. Reboul, *ibid., Sect. C*, 40 (1984) 1105–1107; N. Darbon-Meyssonnier, Y. Oddon, E. Decoster, A.A. Pavia, G. Pèpe, and J.P. Reboul, *ibid., Sect. C*, 41 (1985) 1324–1327; A. Müller-Fahrnow, V. Zabel, M. Steifa, and R. Hilgenfeld, *J. Chem. Soc., Chem. Commun.*, (1986) 1573–1574; V. Zabel, A. Müller-Fahrnow, R. Hilgenfeld, W. Saenger, B. Pfannemüller, V. Enkelmann, and W. Welte, *Chem. Phys. Lipids*, 39 (1986) 313–327; A. Müller-Fahrnow, R. Hilgenfeld, H. Hesse, W. Saenger, and B. Pfannemüller, *Carbohydr. Res.*, 176 (1988) 165–174.

16 R.U. Lemieux and A.A. Pavia, *Can. J. Chem.*, 47 (1969) 4441–4446; H. Paulsen and M. Friedmann, *Chem., Ber.*, 105 (1972) 705–717.
17 J. Kopf, C. Topf, M. Morf, B. Zimmer, and P. Köll, *Acta Crystallogr., Sect. C*, 47 (1991) 2186–2188.
18 Y.J. Park, M.H. Park, and J.M. Shin, *Daehan Hwahak Hwoejee*, 34 (1990) 517–526; *Chem. Abstr.*, 114 (1991) 82345a.
19 G.M. Sheldrick, *Acta Crystallogr., Sect. A*, 46 (1990) 467–473.
20 G.M. Sheldrick, SHELX-76. Programs for Crystal Structure Determination, University of Cambridge, 1976.
21 E. Keller, *Chem. Unserer Zeit*, 14 (1980) 56–60.
22 J. Wiemann, *Ann. Chim. (Paris)*, 5 (1936) 267–336; M.L. Wolfrom, B.W. Lew, and R.M. Goepp, *J. Am. Chem. Soc.*, 68 (1946) 1443–1448.
23 H. Rogerson, *J. Chem. Soc.*, 101 (1912) 1040–1052.
24 N. Azarnia, G.A. Jeffrey, and M.S. Shen, *Acta Crystallogr., Sect. B*, 28 (1972) 1007–1013.
25 H.M. Berman and R.D. Rosenstein, *Acta Crystallogr., Sect. B*, 24 (1968) 435–441.
26 H.M. Mathieson, *Tetrahedron Lett.*, 1965, 4137–4143.
27 J. Kopf and P. Köll, *Carbohydr. Res.*, 164 (1987) 161–176, and references therein.
28 S. Wolfe, *Acc. Chem. Res.*, 5 (1972) 102–111; A.J. Kirby, *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*, Springer Verlag, Berlin, 1983.
29 H.S. Kim and G.A. Jeffrey, *Acta Crystallogr., Sect. B*, 25 (1969) 2607–2613.
30 A.P.N. Franchimont, *Ber.*, 12 (1879) 2059; T.S. Patterson and A.R. Todd, *J. Chem. Soc.*, (1929) 2876–2889; W.M. Higgins and M.F.W. Dunker, *J. Am. Chem. Soc.*, 67 (1945) 153–154.
31 D. French, *Acta Crystallogr.*, 7 (1954) 136–137.
32 H.M. Berman, G.A. Jeffrey, and R.D. Rosenstein, *Acta Crystallogr., Sect. B*, 24 (1968) 442–449; H.S. Kim, G.A. Jeffrey, and R.D. Rosenstein, *ibid*, 24 (1968) 1449–1455.
33 J.A. Kanters, G. Roelofsen, and D. Smits, *Acta Crystallogr., Sect. B*, 33 (1977) 3635–3640.
34 E. Baer and H.O.L. Fischer, *J. Am. Chem. Soc.*, 61 (1939) 761–765.
35 J. Jacques, A. Collet, and S.H. Wilen, *Enantiomers, Racemates and Resolution*, Wiley, New York, 1981.
36 R.M. Hann and C.S. Hudson, *J. Am. Chem. Soc.*, 64 (1942) 925–928.
37 J. Kopf, M. Morf, B. Zimmer, M. Bischoff, and P. Köll, *Acta Crystallogr., Sect. C*, in press.
38 Y.J. Park, G.A. Jeffrey, and W.C. Hamilton, *Acta Crystallogr., Sect. B*, 27 (1971) 2393–2401.
39 M.L. Wolfrom, B.W. Lew, R.A. Hales, and R.M. Goepp, *J. Am. Chem. Soc.*, 68 (1946) 2342–2343; R.K. Ness, H.G. Fletcher and C.S. Hudson, *J. Am. Chem. Soc.*, 73 (1951) 4759–4761.
40 J.M. Sugihara and G.U. Yuen, *J. Am. Chem. Soc.*, 79 (1957) 5780–5782.
41 F.L. Humoller, M.L. Wolfrom, B.W. Lew, and R.M. Goepp, *J. Am. Chem. Soc.*, 67 (1945) 1226–1227.
42 L. Wright and L. Hartmann, *J. Org. Chem.*, 26 (1961) 1588–1956.
43 W. Klyne and V. Prelog, *Experientia*, 16 (1960) 521–523.
44 E.R. Galan, D.J. Hodgson, Y. Yokomori, E.L. Eliel, M.B. Martinez, and J.A.S. Blazquez, *Carbohydr. Res.*, 180 (1988) 263–276.
45 R. Vega, M.J. Diánez, A. López-Castro, and R. Márquez, *Acta Crystallogr., Sect. C*, 40 (1984) 1941–1944.
46 A.L. Spek, PLATON, in D. Sayre (Ed.), *Computational Crystallography*, Clarendon Press, Oxford, 1982, p. 528.