(*d*, 1H, C(21); $J_{20,21} = 5\,\mathrm{Hz}$); 4,67 (*t*, 1H, C(16), $J_{15\alpha,16} = J_{16,17} = 7\,\mathrm{Hz}$); ~4,12 (*m*, 1H, C(3)); 4,1 (*q*, 2H, O—*CH*$_2$—CH$_3$, Ester, $J \approx 7\,\mathrm{Hz}$); ~3,5 (*m*, 2H, O—*CH*$_2$—CH$_3$, Acetal); ~2,9 (*m*, 1H, C(20)); 2,48 (*m*, 2H, C(22)); 1,23 und 1,13 (*t*, je 3H, einander überlagernd, CH$_3$ an —OCH$_2$—, Ester und Acetal); 1,03 und 0,95 (*s*, je 3H, C(18) bzw. C(19)) ppm. Das *Massenspektrum* zeigte die intensivste Spitze bei *m/e* 435, was $M^+ - 29$ (C_2H_5) entspricht.

$C_{27}H_{44}O_6$ (464,6) Ber. C 69,79 H 9,55 C_2H_5O 19,38% Gef. C 70,05 H 9,80 C_2H_5O 19,51%

5.8. *(20S,21R)-3β,14-Dihydroxy-21-methoxy-16β,21-epoxy-24-nor-5β,14β-cholan-23-säure-methylester* (**28**) *aus* **33**. Eine Lösung von 31 mg **33** in 0,5 ml Methanol wurde mit 1,0 ml 10proz. KOH-Lösung in Methanol versetzt und wie bei 5.4 beschrieben behandelt und aufgearbeitet. Das Produkt (28 mg) war nach DC., Smp. und IR.-Spektrum mit authentischem **28** identisch.

5.9. *Hydrolyse von (20S,21R)-3β,14-Dihydroxy-21-methoxy-16β,21-epoxy-24-nor-5β,14β-cholan-23-säure-methylester* (**28**). – 5.9.1. *In Dioxan:* Eine Lösung von 21 mg **28** in 1 ml Dioxan und 2 ml 0,01N H_2SO_4 wurde 14 Std. unter Rückfluss gekocht. Das Hydrolysenprodukt war nach DC., Smp. und IR.-Spektrum mit **33** identisch.

5.9.2. *In Aceton:* Eine Lösung von 571 mg **28** in 50 ml Aceton und 50 ml 0,005N H_2SO_4 wurde 72 Std. bei 20° stehengelassen. Das Rohprodukt (591 mg) wurde an 150 g Kieselgel mit Chloroform/2-Propanol 9:1 chromatographiert. Aus den Frakt. (je 11 ml) Nr. 21–24 resultierten 81 mg Edukt **28**, aus Nr. 27–32 125 mg **33** und aus Nr. 33–39 354 mg **32**, leicht verunreinigt.

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137. The Crystal Structure of Nonactin

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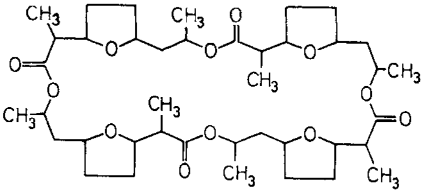
(20. 3. 72)

Summary. An X-ray crystal structure investigation of the macrotetrolide antibiotic nonactin is reported. The shape of the molecule is discussed with special reference to the conformational changes involved in passing from free nonactin to the K$^+$-complex.

Nonactin (1) [1] is a macrotetrolide belonging to a group of antibiotics whose activity depends on the presence or absence of specific alkali cations and is probably associated with transport of cations across biological membranes [2]. The preparation of crystalline complexes of nonactin with alkali cations [3] made it possible to determine the crystal structure of K$^+$NCS$^-$-nonactin [4] [5]. This analysis showed that the

K^+-ion in the complex is not hydrated and that it adopts nearly cubic coordination with four O-atoms of the tetrahydrofurane rings and four carbonyl-O-atoms. The nonactin molecule in the K^+-complex has a crystallographic twofold rotation axis and has approximate S_4 symmetry. The shape of the 32-membered ring can be compared to the seam of a tennis-ball with the K^+-ion in the middle of the ball and hydrophobic groups on the outside. Crystals of nonactin itself give diffraction patterns with unusual symmetry and extinctions [1]; the crystal structure is of the OD (order-disorder) type, which makes a detailed analysis difficult. The structure analysis has now been carried


(1)

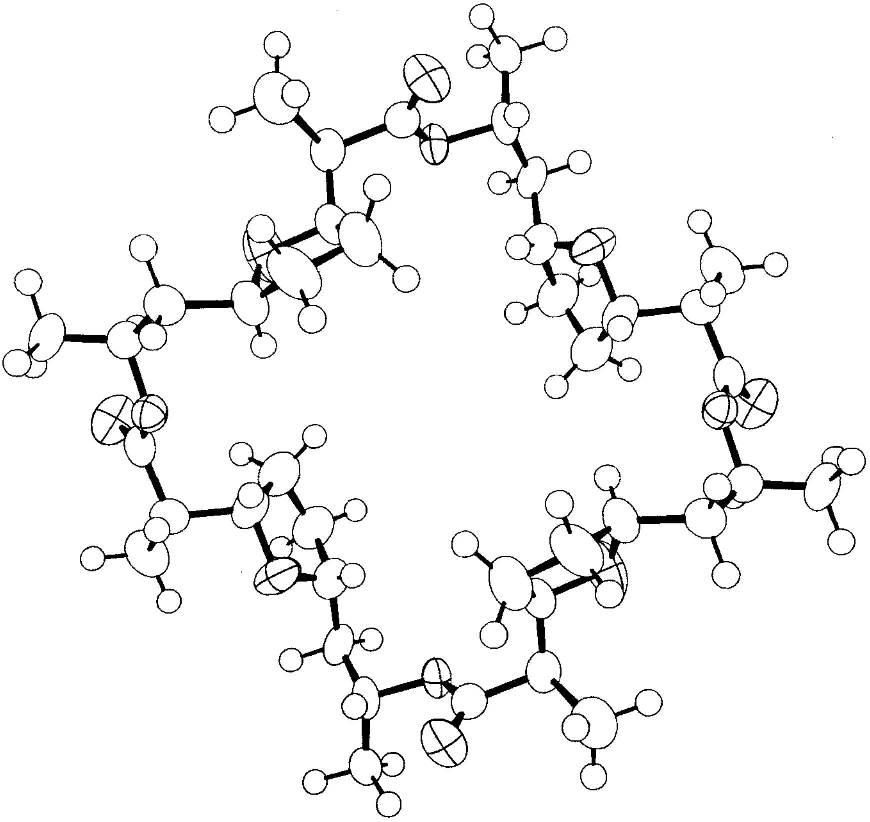


Fig. 1. *The nonactin molecule viewed down the twofold axis showing the thermal motion ellipsoids associated with the atoms. Atoms with principal ellipses are oxygen atoms*

so far as to lead to a reasonably accurate description of the molecular conformation. The most important results can be summarized as follows:

1. The conformation of free nonactin is similar to that of the K^+-complex in that both have approximate S_4 symmetry. The free molecule is, however, much flatter (17 × 17 × 8.5 Å) than the complexed molecule (15 × 15 × 12 Å).

2. The conformational changes involved in passing from free to complexed nonactin affect only eight torsion angles of the 32-membered ring. The other 24 torsion angles remain virtually unchanged.

3. The shape of the uncomplexed nonactin molecule can be described as a torus. The central hole is large enough to allow close approach of a hydrated K^+-ion. Stepwise removal of water molecules may be coupled to the conformational changes involved in complexation.

Crystallographic Data. – Crystals of nonactin, $C_{40}O_{12}H_{64}$, molecular weight 737, were grown from methanol. They are small colourless needles with rhombic cross section. Bigger crystals giving identical diffraction patterns and better suited for our purposes can be grown from slightly less purified material (containing about 8% of monactin). The diffraction pattern is unusual. It can be indexed in terms of an orthorhombic unit cell with dimensions $a = 47.57$, $b = 31.40$, $c = 5.69$ Å, V = 8,499 Å^3, $D_m = 1.11-1.15$, $D_x = 1.15$ (assuming Z = 8). The symmetry and the extinctions of the diffraction pattern can be summarized as follows:

Reflection type	Extinction	Symmetry
hkl	$h+k \neq 2n$	$I(hkl) = I(hk\bar{l}) = I(h\bar{k}\bar{l})$ for h, k even $I(hkl) = I(hk\bar{l}) \neq I(h\bar{k}\bar{l})$ for h, k odd
hk0	$h \neq 2n, k \neq 2n$	$I(hk0) = I(h\bar{k}0)$
h0l	$h \neq 4n$	$I(h0l) = I(h0\bar{l})$
0kl	$k \neq 4n$	$I(0kl) = I(0k\bar{l})$
00l	none	

In addition, upper layer photographs with l = 1, 2, 3... show diffuse streaks parallel to a for odd values of k. These findings were first interpreted [6] in terms of a para-orthorhombic arrangement and later [7] [8] in terms of an OD (order-disorder) arrangement.

An OD structure can be thought of being built from equivalent layers, whose internal symmetry is such that pairs of neighbouring layers in different parts of the structure can be equivalent without necessarily producing three-dimensional periodicity.

For an OD structure a superposition structure can be defined [8] as the periodic arrangement consisting of layer L_1, all the n different positions of layer L_2 each with weight $^1/n$, all the n^2 different positions of layer L_3 each with weight $^1/n^2$, etc. It can be shown that in the case of nonactin this superposition structure corresponds to the orthorhombic space group Pbam (D_{2h}^9) with a unit cell of $a/2$, $b/2$, c (Fig. 4). In this superposition structure, the points x, y, z and x, y, $\bar{z}$ are equivalent, but the mirror plane so produced is not present in the real structure. Furthermore, because the asymmetric unit corresponds to only half a molecule, the molecule as a whole must either be centrosymmetric or have a twofold rotation axis. The diffuse reflections with h, k odd do not contribute to the superposition structure; they contain information about the sequence of layer pairs which varies from crystal to crystal. Since there are obvious difficulties in measuring the intensities of these reflections it was decided to attempt

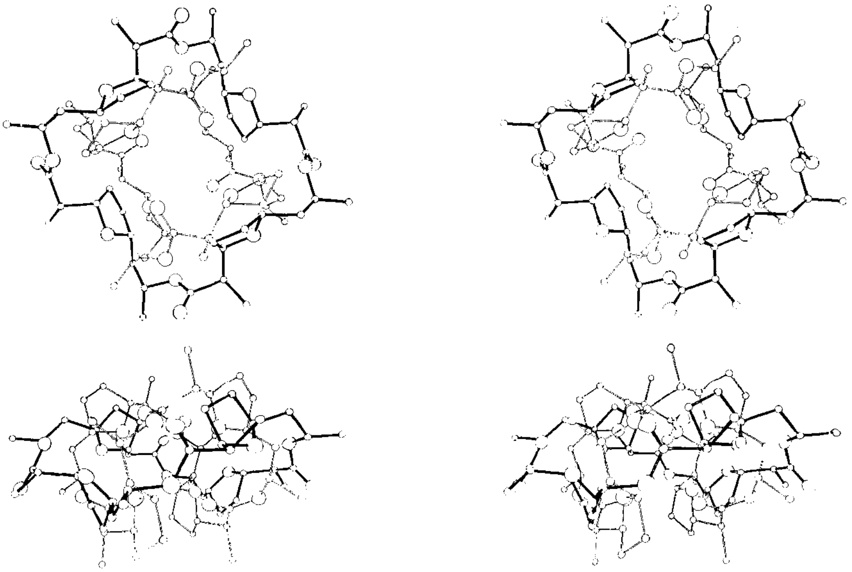


Fig. 2. *Stereographic view of nonactin (solid lines) and its K⁺-complex superimposed. Top view looking down the twofold axis, bottom view with the twofold axis vertical*

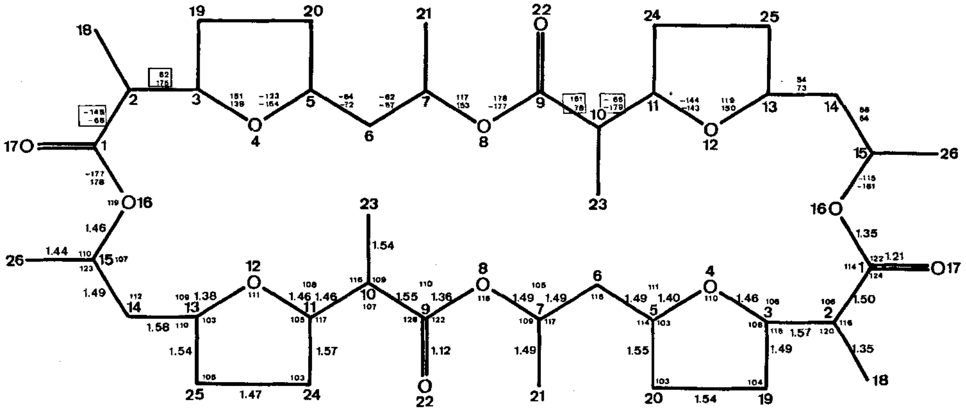


Fig. 3. *Molecular topography*

Top half: torsion angles for the 32-membered ring. First line: K⁺-complex of nonactin; second line: free nonactin

Bottom half: bond lengths and angles

to solve the structure on the basis of the superposition concept, using only the 'sharp' reflections with h, k even.

Intensity measurements. – Intensities of the h, k even reflections were measured out to a limit of $\theta_{\mathrm{Mo}} = 25°$ from a crystal of dimensions $0.2 \times 0.4 \times 0.6$ mm on a computer-controlled four-circle diffractometer (*Hilger & Watts* Y290) with graphite-monochromatized MoK_α radiation. In all, 2,100 reflection intensities were measured, corrected for background and *Lorentz*-polarization effects (but not for absorption) to give relative F_0-values; 1,344 reflections had F_0 values greater than twice their standard deviation.

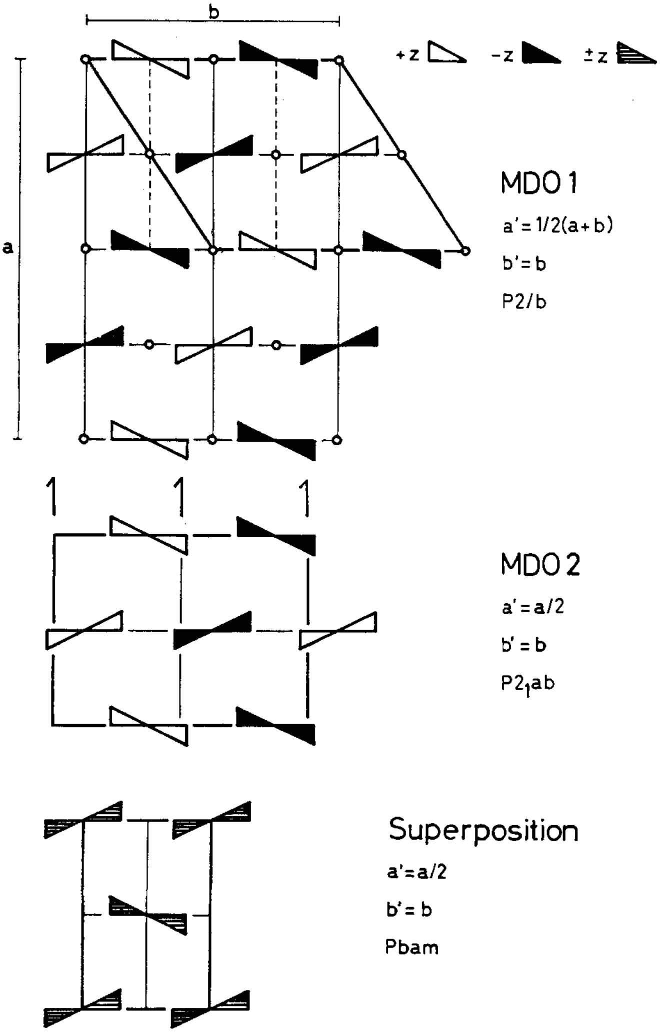


Fig. 4. *Possible arrangements of layer pairs in nonactin crystals. The part indicated by dashed lines in the MDO 1 arrangement is also shown in Fig. 5*

Structure Analysis and Refinement. – It was hoped that the use of direct methods, applied to the reflections with h, k even, would yield information about the superposition structure. It was further hoped that with this information, together with the known constitution and configuration of the molecule, the actual structure could be sorted out from its mirror image.

The observed relative F_0-values were put on an absolute scale by *Wilson's* method and converted to E-values. Several tentative sets of signs were derived by the symbolic addition method but they yielded uninterpretable E-maps. Close analysis of the sign-determining process showed that because of the short *c*-axis, relationships connecting reflections with different l index were few in number. The set of relationships thus consisted of several sub-sets with only very weak interconnections, so that the choice of an optimal starting set of reflections was very crucial. The sign-determining process was then carried out with the help of the computer program MULTAN by *Main, Woolfson & Germain* [9], which was mainly intended for non-centrosymmetric space groups. The sign set with the best internal consistency according to the criteria introduced in the program yielded an E-map in which peaks corresponding to 21 of the 26 non-hydrogen atoms in the asymmetric unit could be recognized. These were subsequently used to phase a F_0-*Fourier* which clearly showed the remaining atom positions. Four atoms, C(5), C(18), C(21) and C(23), close to the spurious mirror

Table 1. *Fractional coordinates*
(estimated standard deviations $\times 10^4$ in parentheses)

	x	y	z
C(1)	.2565 (4)	.4701 (7)	.2014 (23)
C(2)	.2776 (4)	.3806 (6)	.1837 (20)
C(3)	.3433 (5)	.3870 (8)	.1576 (23)
O(4)	.3638 (4)	.2995 (5)	.1644 (17)
C(5)	.4057 (4)	.2881 (6)	–.0055 (171)
C(6)	.4084 (4)	.1972 (7)	–.0807 (17)
C(7)	.4320 (4)	.1365 (7)	.0947 (17)
O(8)	.4922 (2)	.1610 (4)	.1168 (11)
C(9)	.5175 (4)	.1424 (6)	.3253 (19)
C(10)	.5787 (4)	.1760 (7)	.3231 (17)
C(11)	.5763 (5)	.2678 (9)	.3654 (27)
O(12)	.6335 (3)	.3012 (7)	.3584 (16)
C(13)	.6403 (4)	.3647 (8)	.5228 (172)
C(14)	.7032 (4)	.3654 (6)	.6107 (19)
C(15)	.7424 (4)	.4007 (6)	.4314 (19)
O(16)	.2734 (3)	.5106 (4)	.3974 (12)
O(17)	.2284 (3)	.5050 (5)	.0528 (19)
C(18)	.2478 (5)	.3287 (7)	.0430 (29)
C(19)	.3630 (6)	.4258 (9)	–.0657 (26)
C(20)	.3877 (6)	.3502 (10)	–.2038 (28)
C(21)	.4286 (3)	.0445 (6)	.0355 (106)
O(22)	.4964 (3)	.1035 (5)	.4639 (59)
C(23)	.6136 (4)	.1239 (6)	.4996 (77)
C(24)	.5520 (6)	.2977 (12)	.6083 (36)
C(25)	.6011 (4)	.3368 (10)	.7239 (24)
C(26)	.8027 (4)	.3937 (6)	.4512 (23)

planes at $z = 0$ and $z = {}^1/_2$ overlapped so strongly with their respective mirror images that their z-coordinate had to be assigned from stereochemical considerations.

The atomic positions were refined by full-matrix least-squares analysis. The z-coordinates of atoms C(5) and C(23) were held constant during the initial refinement cycles; in later cycles the calculated shifts for these atoms were reduced by a factor of 0.25 and finally by a factor of 0.5. In all, two cycles of isotropic and eight cycles of anisotropic refinement were needed to achieve convergence. A difference *Fourier* map, calculated after four cycles of anisotropic refinement, showed maxima for all 32 hydrogen atoms in the asymmetric unit, in good agreement with calculated[1] positions. In the final cycles hydrogen atoms at calculated rather than observed positions were included in the model structure but not refined. Unit weights were used throughout, as seemed justified by the uniform distribution of the quantity $\langle (F_o\text{-}F_c)^2 \rangle$. Final parameters (and estimated standard deviations as calculated by inversion of the least-squares normal-equations matrix) are given in Tables 1, 2 and 3, respectively. The 1,344

Table 2. *Anisotropic vibrational parameters*, expressed in the form $\exp(-2\pi^2(U_{11}a^{*2}h^2 + U_{22}b^{*2}k^2 + U_{33}c^{*2}l^2 + 2U_{12}a^*b^*hk + 2U_{13}a^*c^*hl + 2U_{23}b^*c^*kl))$

	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	.0386	.0698	.0715	−.0024	.0033	.0064
C(2)	.0657	.0563	.0562	−.0029	.0169	−.0015
C(3)	.0615	.0670	.0406	.0197	.0048	.0112
O(4)	.0937	.0572	.0679	.0237	.0148	.0108
C(5)	.0547	.0785	.0559	.0092	.0087	.0235
C(6)	.0431	.0719	.0514	.0150	−.0016	−.0066
C(7)	.0322	.0695	.0469	−.0059	.0033	−.0086
O(8)	.0342	.0723	.0449	−.0019	.0026	.0045
C(9)	.0496	.0528	.0487	.0003	−.0042	.0062
C(10)	.0480	.0693	.0368	.0009	−.0037	.0045
C(11)	.0444	.0657	.0370	−.0104	.0001	.0057
O(12)	.0510	.1195	.0491	−.0308	.0094	−.0107
C(13)	.0534	.0763	.0921	−.0160	−.0204	−.0078
C(14)	.0605	.0566	.0568	−.0063	−.0054	.0108
C(15)	.0478	.0564	.0742	.0029	−.0079	−.0080
O(16)	.0464	.0545	.0555	.0030	−.0041	−.0021
O(17)	.0798	.1066	.0482	.0200	−.0131	−.0137
C(18)	.0760	.0930	.0237	−.0228	.0029	.0052
C(19)	.0787	.0827	.0950	.0165	−.0051	.0078
C(20)	.0805	.0924	.0749	.0215	.0173	.0282
C(21)	.0432	.0720	.0435	−.0089	.0060	−.0071
O(22)	.0773	.0992	.0143	−.0224	−.0046	.0191
C(23)	.0680	.0959	.1042	.0004	.0558	−.0091
C(24)	.0618	.0996	.0909	−.0146	.0319	−.0188
C(25)	.0882	.0972	.0610	−.0338	.0288	−.0078
C(26)	.0488	.0875	.0311	.0186	.0007	.0110

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[1] Positions of hydrogen atoms calculated with the following stereochemical assumptions:
a) methine hydrogen atoms: C—H bond (C—H, 1.09 Å) making equal angles with the three bonds attached to the C-atom;
b) methylene hydrogen atoms: local C_{2v} symmetry, C—H, 1.09 Å; H—C—H, 111°;
c) methyl hydrogen atoms: staggered conformation, C—H, 1.09 Å; H—C—H, 109°.

observable reflections with h, k even form a rather limited set of data for determining 235 independent variables and standard deviations associated with the final parameter values are correspondingly rather large. For most bond lengths they are in the range 0.011–0.025 Å, but they run as high as 0.075 Å when atoms close to the mirror plane are involved. The final R factor was 0.103.

Discussion. – In view of the rather large standard deviations associated with some of the atomic parameters a detailed discussion of individual bond lengths, angles, etc. would be unwarranted. Nevertheless, the overall features of the molecular topography are clear.

The nonactin molecule has a crystallographic twofold rotation axis; in addition like the K+-complex [5], it shows approximate S_4 symmetry (Fig. 1). The mean deviation of corresponding atoms of the $C_{10}O_3H_{16}$ units (e.g. C(1) and C(9), C(2) and C(10), etc.) from S_4 symmetry is 0.1 Å in the *a* direction and 0.04 Å in the *b* and *c* directions. Whereas the complexed molecule is roughly spherical in shape with overall dimensions of about 15×15×12 Å along the crystallographic axes, the uncomplexed molecule

Table 3. *Calculated hydrogen atom fractional coordinates*

	x	y	z
H(2)	.271	.355	.359
H(3)	.361	.422	.306
H(5)	.446	.308	.066
H(6)*	.366	.177	–.122
H(6)**	.435	.194	–.237
H(7)	.411	.147	.263
H(10)	.596	.166	.148
H(11)	.552	.297	.225
H(13)	.628	.427	.452
H(14)*	.706	.405	.768
H(14)**	.716	.300	.651
H(15)	.732	.369	.268
H(18)*	.203	.334	.089
H(18)**	.262	.264	.068
H(18)***	.254	.348	–.139
H(19)*	.328	.454	–.161
H(19)**	.395	.474	–.032
H(20)*	.356	.321	–.317
H(20)**	.424	.370	–.308
H(21)*	.384	.026	.019
H(21)**	.448	.008	.175
H(21)***	.450	.034	–.130
H(23)*	.612	.057	.449
H(23)**	.596	.132	.675
H(23)***	.657	.147	.496
H(24)*	.519	.344	.584
H(24)**	.537	.244	.709
H(25)*	.588	.392	.827
H(25)**	.622	.291	.836
H(26)*	.822	.424	.299
H(26)**	.814	.327	.457
H(26)***	.816	.425	.612

is much flatter, 17×17×8.5 Å, as was evident from the short *c* periodicity. Fig. 2 shows the two molecules, uncomplexed and complexed, superimposed. It is noteworthy that the conformational change in the 32-membered ring is achieved mainly by altering only two torsion angles per monomeric unit (see Fig. 3), i.e. around the bond C(2)–C(3) from +175° to +62° (C(10)–C(11) from −179° to −66°) and around the bond C(1)–C(2) from −66° to −146° (C(9)–C(10) from +78° to +151°). The changes in the other 24 torsion angles of the 32-membered ring are all smaller than 37°. In the uncomplexed molecule the planar lactone groups are nearly perpendicular to the mean plane of the ring; in the K^+-complex these groups are tilted so that the carbonyl O-atoms O(17) and O(22) point inwards and the ether O-atoms O(4) and O(16), which do not partake in the complex formation, are on the outside.

Table 4. *Molecular topography. Bond lengths and angles*

C(2)—C(1)—O(16)	1.495	1.347	113.5
C(2)—C(1)—O(17)		1.208	124.3
O(16)—C(1)—O(17)			122.1
C(1)—C(2)—C(3)		1.573	106.3
C(1)—C(2)—C(18)		1.345	115.6
C(3)—C(2)—C(18)			120.4
C(2)—C(3)—O(4)		1.459	105.6
C(2)—C(3)—C(19)		1.485	114.8
O(4)—C(3)—C(19)			107.7
C(3)—O(4)—C(5)		1.401	109.8
O(4)—C(5)—C(6)		1.492	110.5
O(4)—C(5)—C(20)		1.552	103.1
C(6)—C(5)—C(20)			113.8
C(5)—C(6)—C(7)		1.489	115.8
C(6)—C(7)—O(8)		1.489	104.7
C(6)—C(7)—C(21)		1.486	116.7
O(8)—C(7)—C(21)			108.8
C(7)—O(8)—C(9)		1.363	116.3
O(8)—C(9)—C(10)		1.547	109.6
O(8)—C(9)—O(22)		1.118	122.2
C(10)—C(9)—O(22)			128.0
C(9)—C(10)—C(11)		1.462	107.4
C(9)—C(10)—C(23)		1.540	108.7
C(11)—C(10)—C(23)			115.9
C(10)—C(11)—O(12)		1.458	108.3
C(10)—C(11)—C(24)		1.570	117.0
O(12)—C(11)—C(24)			105.0
C(11)—O(12)—C(13)		1.376	110.6
O(12)—C(13)—C(14)		1.578	109.4
O(12)—C(13)—C(25)		1.541	103.2
C(14)—C(13)—C(25)			109.9
C(13)—C(14)—C(15)		1.490	112.3
C(14)—C(15)—O(16)		1.455	106.5
C(14)—C(15)—C(26)		1.443	122.7
O(16)—C(15)—C(26)			109.9
C(1)—O(16)—C(15)			119.0
C(3)—C(19)—C(20)		1.541	104.0
C(5)—C(20)—C(19)			102.6
C(11)—C(24)—C(25)		1.473	103.1
C(13)—C(25)—C(24)			105.4

Prestegard & Chan [10] have used proton magnetic resonance to study the complex formation of nonactin with $KClO_4$. Their results showed that the four sub-units are magnetically equivalent in the free molecule as well as in the complex, in accord with the S_4 symmetry observed in both crystal structures. From changes in coupling constants, using the *Karplus* rule [11], they estimated that the H(2)–C(2)–C(3)–H(3) torsion angle changes from 155° in free nonactin to 180° in the complex. In the crystal structures the corresponding change is from about 55° to 180°. The other important change in torsion angle, around the bond C(1)–C(2), could not, of course, have been predicted from NMR studies.

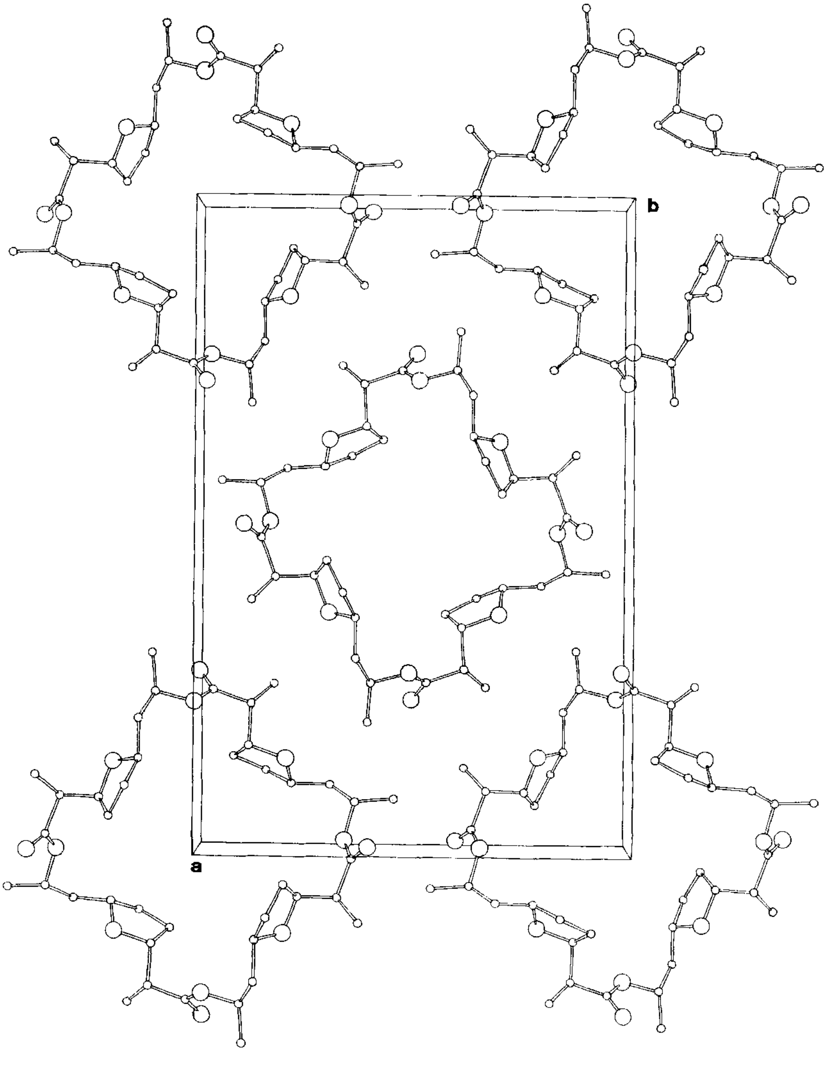

Fig. 5. *Packing of molecules in the unit cell. The arrangement of molecules shown is part of an MDO1 arrangement, shown with dashed lines in the upper part of Fig. 4*

As in the K$^+$-complex the tetrahydrofurane rings are again in the envelope conformation, but it is the methine C-atoms C(5) and C(13), respectively, rather than the methylene C-atoms, C(19) and C(24), that deviate from the plane of the four other atoms. Torsion angles for both rings are given in Table 5. The mean bond angles are 103.8° for methylene C-atoms (102.4° in the K$^+$-complex), 104.8 for methine C-atoms (104.6°) and 110.2° at the O-atom (110.6°). Thus the widening of the C–O–C angle with respect to the others cannot be attributed to any influence of the K$^+$-ion.

The packing of the molecules in the unit cell cannot be described in a straightforward way. The crystal structure is built from perfectly ordered layers in the *b*, *c* directions, but the structure of these layers is such that successive pairs of layers may be stacked in two ways, equivalent with respect to neighbouring layers but distinct with respect to more distant ones. This characterizes the structure as an OD (order-disorder) structure [8]. Two possible arrangements, MDO1 and MDO2, both of 'maximum degree of order' are shown in Fig. 4. A crystal built exclusively from arrangements MDO1 would be monoclinic whereas one built exclusively from MDO2 would be orthorhombic. Occasional substitution of one kind of interlayer relationship for the other leads to a disordered crystal structure. The observed intensities of reflexions with h, k odd vary from crystal to crystal. For some crystals $I(hkl) \neq I(h\bar{k}l)$ for h, k odd, indicating that in these crystals the layers are arranged predominantly as

Table 5. *Molecular topography. Torsion angles for the asymmetric unit of the 32-membered ring and for the two tetrahydrofurane rings*

O(16)—C(1)—C(2)—C(3)	−65.7
C(1)—C(2)—C(3)—O(4)	174.5
C(2)—C(3)—O(4)—C(5)	138.1
C(3)—O(4)—C(5)—C(6)	−153.7
O(4)—C(5)—C(6)—C(7)	−71.6
C(5)—C(6)—C(7)—O(8)	−67.0
C(6)—C(7)—O(8)—C(9)	153.3
C(7)—O(8)—C(9)—C(10)	−177.1
O(8)—C(9)—C(10)—C(11)	78.2
C(9)—C(10)—C(11)—O(12)	−178.7
C(10)—C(11)—O(12)—C(13)	−143.1
C(11)—O(12)—C(13)—C(14)	149.6
O(12)—C(13)—C(14)—C(15)	73.4
C(13)—C(14)—C(15)—O(16)	64.0
C(14)—C(15)—O(16)—C(1)	−161.1
C(15)—O(16)—C(1)—C(2)	177.5
C(19)—C(3)—O(4)—C(5)	14.9
C(3)—O(4)—C(5)—C(20)	−31.7
O(4)—C(5)—C(20)—C(19)	35.8
C(5)—C(20)—C(19)—C(3)	−26.7
C(20)—C(19)—C(3)—O(4)	8.9
C(24)—C(11)—O(12)—C(13)	−17.3
C(11)—O(12)—C(13)—C(25)	32.6
O(12)—C(13)—C(25)—C(24)	−36.0
C(13)—C(25)—C(24)—C(11)	24.7
C(25)—C(24)—C(11)—O(12)	−6.3

Table 6. *Observed structure factors*
Every *hkl$_i$* is followed by values 10 · F$_0$ for l$_i$, l$_{i+1}$, l$_{i+2}$, etc.

```
 0  0  1* 119,1478, 186, 408,  81, 120*  0  2  0*1236, 158, 914, 391, 333, 109,  99*  0  4  0*2343,
 0  4  1*1379,  42,1113, 192, 374,  96*  0  6  0*1802, 774, 358, 397, 190,  13,  20*  0  8  0* 586,
 0  8  1* 780, 262, 384,  58,  76,  25*  0 10  0* 552, 238, 278, 186,  70, 128*  0 12  0* 273,  46,
 0 12  2*  44, 190,  60, 101*  0 14  0* 126,   0,   0, 148, 125*  0 16  0*  72,   0,  24,   0,
 0 18  0*   0,  37*  1  1  0* 726,  74, 947, 121, 146, 295,  55*  1  2  0*  74,2422, 834, 415, 123,
 1  2  5*  23, 180*  1  3  0* 238,   0, 318, 222, 161, 475,  71*  1  4  0* 235, 312, 511,  55, 195,
 1  4  5*  66,  75*  1  5  0* 981,1122, 357, 147, 148,  59,  70*  1  6  0*  62,  58, 222, 180, 154,
 1  6  5*  68,  62*  1  7  0*1048, 231,  70, 188, 270, 108,  80*  1  8  0*  74, 414,  91,   0,  35,
 1  8  5*  58,  40*  1  9  0* 467, 369,  90, 217, 303,  71*  1 10  0* 190, 180, 305, 293,  76,  26,
 1 11  0*  46, 179,  61,  82,  50,  78*  1 12  0*  46, 142, 154, 120,   0,   0*  1 13  0*  64, 100,
 1 13  2* 131, 100, 122*  1 14  0* 117,  32,   0,  97,  23*  1 15  0* 132,  36,  72,  75,   0,
 1 16  0*  80,  54,   0,   0*  1 17  0*   0,  17,  46*  1 18  0*   0,  14*  2  0  0* 550,  94, 224,
 2  0  3*  85,  73, 553,  77*  2  1  0*  56,3654, 225, 836, 118, 116,  91*  2  2  0*2474, 274, 113,
 2  2  3* 177, 292,  67,  55*  2  3  0* 931, 345, 372, 289, 259,  80,  94*  2  4  0* 519, 289, 185,
 2  4  3*   0,  42, 250,   0*  2  5  0* 696, 193, 487, 339, 249,  92,  81*  2  6  0*  68, 114, 547,
 2  6  3* 275, 184, 231,  79*  2  7  0* 112, 354, 374,  56, 122,  77,  57*  2  8  0* 765,  45, 103,
 2  8  3*  20, 144, 191,  31*  2  9  0* 359,  68, 238, 139,  76,   0*  2 10  0* 603, 102,   0,  64,
 2 10  4* 175,   0*  2 11  0* 234, 295,  88, 156,  41,  10*  2 12  0*  77,  31, 300, 208,  89,  53,
 2 13  0*  40, 294,  71,  91,  64*  2 14  0*  78,  61, 104,   0,   0*  2 15  0*   0,  45,  16,  70,
 2 15  4*  53*  2 16  0* 129,  33,  62,  58*  2 17  0*   0,  73,  73*  2 18  0*  67,  34,
 3  1  0*2784, 115, 265, 356, 234,  21, 133*  3  2  0* 134,1620, 104,  63,  35,  63,  68,
 3  3  0*2357, 420, 518, 291, 276, 138, 120*  3  4  0* 788, 497, 491, 207, 213,  86, 179,
 3  5  0* 208, 107, 387, 191, 144,  94,  58*  3  6  0* 712, 671,  70, 134,   0,  48,  71,
 3  7  0* 412, 417, 144,  25, 131,   0,  49*  3  8  0* 343, 549, 286, 197, 248,   0,  46,
 3  9  0* 104, 225,  52, 160, 100,  83*  3 10  0*  80,  83, 286, 109, 125,  67*  3 11  0* 155,  46,
 3 11  2*  56,  60,  61,   0*  3 12  0* 186, 181, 126,  81, 100,  29*  3 13  0*  25,  43,  52,  90,
 3 13  4*   0*  3 14  0* 124,   0,  70,  85,  34*  3 15  0* 125,  48,  36,   0*  3 16  0*  94,  76,
 3 16  2*   0,  10*  3 17  0*  70,   0,  27*  3 18  0*  64,  59*  4  0  0* 217, 454, 701,  32,  40,
 4  0  5*  49,  39*  4  1  0* 651,1394, 872, 137, 111, 116, 134*  4  2  0*2476, 383, 245,   0, 132,
 4  2  5* 203,  63*  4  3  0* 147, 308,  46, 369, 186,  43,  74*  4  4  0*  74,  81, 120,  93, 101,
 4  4  5* 125,  78*  4  5  0*  70, 144, 132, 165, 214,   9, 128*  4  6  0* 512, 871, 400, 279, 278,
 4  6  5*  50,  57*  4  7  0* 533, 329, 291,  87,  48,  53,   0*  4  8  0*1106,  59, 106, 207,  95,
 4  8  5*  85,   0*  4  9  0* 351, 138, 148, 105, 112,  90*  4 10  0*  40, 506, 323,  43, 239,  17,
 4 11  0*  17,  55,  46, 260,  56,   0*  4 12  0* 389, 125, 331,   0, 124,   0*  4 13  0* 187,  31,
 4 13  2*  73,  50,  33*  4 14  0* 140,   0, 143, 160,  76*  4 15  0*  90,  30,   0,  93,
 4 16  0* 108,  68,  32,  83*  4 17  0*  52,  80,  10*  4 18  0*  72,   0*  5  1  0* 474, 127, 275,
 5  1  3* 221, 207, 217,  66*  5  2  0*1001, 491, 249, 535, 238,  21, 122*  5  3  0*1263, 236, 235,
 5  3  3* 122,  61,  99, 113*  5  4  0* 672, 214, 626, 696,  67,   0,   0*  5  5  0* 260, 856, 375,
 5  5  3* 153, 111, 188,  52*  5  5  0* 250,  53,  90,  83,   0,  35,  70*  5  7  0* 328, 524, 192,
 5  7  3* 102,  86, 213,   0*  5  8  0* 527, 174, 147, 126, 101,   0*  5  9  0*  65, 109, 408, 184,
 5  9  4* 165,   0*  5 10  0* 234,  29, 119, 156,  94,   0*  5 11  0* 141,  69, 126, 171,  82,   0,
 5 12  0* 117, 202,  93,  67,   0,   0*  5 13  0* 274, 220,   0,  33,   0*  5 14  0*  49, 156,  39,
 5 14  3* 105,   0*  5 15  0* 156,  96,  78,  91*  5 16  0*   0,  97,  61,  40*  5 17  0* 100,  42,
 5 17  2*  48*  5 18  0*   0,  65*  6  0  0*2607,1421,  78,1073, 189, 320,  95*  6  1  0* 237, 657,
 6  1  2* 407, 257, 147, 141,  86*  6  2  0*  62, 155,  25, 322, 132, 114,  64*  6  3  0* 837, 304,
 6  3  2* 365, 483, 171,  49,  67*  6  4  0*1521, 156, 709,  43,  45,  36,  79*  6  5  0* 385, 111,
 6  5  2* 321, 225,  18, 126,  83*  6  6  0* 911, 224, 115, 140, 248,  28,  10*  6  7  0* 330, 248,
 6  7  2* 197, 303,  81,  13,  49*  6  8  0*   0,  18, 129,  80, 179,  90*  6  9  0* 290, 383, 185,
 6  9  3* 345,  96,  85*  6 10  0*  94,  58, 138, 138, 129,  81*  6 11  0*  71,  53,  60,  51, 111,
 6 11  5*   0*  6 12  0*  29, 256,  89, 105,  27*  6 13  0*   0,  70,  44,   0,   0*  6 14  0*  53,
 6 14  1*  63,  90,  62,   0*  6 15  0* 172,   0,  74,   0*  6 16  0*  44,   0,  59,  63,
 6 17  0*  82,  72,   0*  6 18  0*  44, 102*  7  1  0* 421,1550, 351, 193, 106, 111,   0,
 7  2  0*1034,  84, 480, 354, 138, 113,  57*  7  3  0*  71, 655, 436, 121, 146,  37,   0,
 7  4  0* 350, 202, 400,   0,   0, 158,  57*  7  5  0* 560,  95, 193, 106,  86, 110,  89,
 7  6  0*  48, 275, 250, 107,  74,  87,  46*  7  7  0* 583,  84, 283,   0, 244,  36,   0,
 7  8  0* 181, 136,  99, 223, 133,  36*  7  9  0* 312, 441, 101, 254, 148, 117*  7 10  0*  72,  79,
 7 10  2*  59,  94,  42,  64*  7 11  0* 158,   0, 240, 191,  89,   0*  7 12  0*  95,  64,  98,  44,
 7 12  4*  48*  7 13  0* 205,   0,  81,  51, 161*  7 14  0*  68, 157,   0,  53,   0*  7 15  0* 129,
 7 15  1*  83,  17, 110*  7 16  0*   0,   0,   0,  42*  7 17  0*  68,   0,  10*  7 18  0*  43,
 8  0  0*2391,  55, 281, 636, 176,   9,  57*  8  1  0*  59, 278, 416, 191, 197,  77,   0,
 8  2  0* 217, 593, 143, 142,  29,  37,  30*  8  3  0* 403,  78, 381,  85,  80,  79,  59,
 8  4  0* 628, 512, 293, 222, 142, 135, 110*  8  5  0*  60, 381,  94,  92,  50,  71,  59,
 8  6  0* 720, 406, 206,   0,  85,  60,  56*  8  7  0* 100, 101, 274,   0,   0,  43*  8  8  0*  10,
 8  8  1* 355, 256,  87, 212,   0*  8  9  0*  59, 139, 194, 149, 111,  56*  8 10  0* 284,  77, 157,
 8 10  3*   0,  60,  36*  8 11  0* 136, 195,  61, 124,  67,   0*  8 12  0* 232, 228, 155,  77,  59,
 8 13  0* 306,  38,   0, 106,  10*  8 14  0*  35,   9,  59,  84,   0*  8 15  0*   0,   0,  37,  38,
 8 16  0*  64,   0,   0*  8 17  0*   0,   0,  64*  9  1  0* 190, 153, 602, 209,  97, 252,   0,
 9  2  0* 936, 793, 169,  25, 121,  61,   0*  9  3  0* 393, 547, 473, 209, 206,  75,  38,
 9  4  0* 336,  75,  99, 167,  88,  53,   0*  9  5  0* 298, 748,  42,  91, 177,   0,  83,
 9  6  0*  69, 323,  81, 374, 102,  89,  52*  9  7  0* 148, 430, 288,  25, 164, 111*  9  8  0*  73,
 9  8  1*  39,  54, 253, 181, 120*  9  9  0* 195, 120,  62,   0, 185,   0*  9 10  0* 178, 174, 257,
 9 10  3*  42, 198,  34*  9 11  0*  44, 363, 151,  41,  52,  52*  9 12  0*  92, 150,   0, 271,  83,
 9 13  0*  48, 181,  24,  32,  90*  9 14  0*  18, 103,  67,  46*  9 15  0*  72,  40,  59,   0,
 9 16  0*  81,  31,  87*  9 17  0*   0,  38* 10  0  0* 195, 439, 182,  64, 204, 228,   0,
10  1  0* 260, 292, 534, 216, 120,  34,  73* 10  2  0* 461, 672,  74,  37,  74,  48,  66,
10  3  0* 576, 440, 184,  57,  69,  56,  48* 10  4  0* 962, 558, 134, 195,  57,   0,  53,
10  5  0* 147, 211, 105,  90,  52,  74,   0* 10  6  0* 206, 270, 386,   0, 208,  84* 10  7  0*  12,
10  7  1*  36, 101, 212,  32,  97* 10  8  0* 207, 331,  74,  84,   0,  30* 10  9  0* 226,   0,  58,
10  9  3*  36,  76,  28* 10 10  0* 265,  64, 280,   0, 239,  36* 10 11  0* 220,  78, 107, 111,  78,
10 12  0* 111,   0, 210, 135,  76* 10 13  0* 165,  72,   0,  43,   0* 10 14  0*   0, 128,  64,  86,
10 15  0*  49,  91,  58,  56* 10 15  0*   0,  67,  59* 10 17  0*  34,  95* 11  1  0*1638, 834, 159,
11  1  3* 309, 128,  84,  42* 11  2  0* 162,   0, 125,  53, 126,   0,   0* 11  3  0*1377, 209, 116,
11  3  3* 263, 155, 207,  46* 11  4  0* 265, 239, 278, 234,  57,  52,   0* 11  5  0* 104, 156, 512,
11  5  3* 127, 433,  82* 11  6  0*   0,  56, 252, 110,  89, 102* 11  7  0* 207, 300,   0,  50,  44.
11  7  5*  20* 11  8  0* 136, 154,  68, 100, 119,  72* 11  9  0*  87, 505,  59, 221,   0,   0,
```

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11 10  0* 310,  72,  67, 192,  43, 112* 11 11  0* 289, 146,   0,  34,  73* 11 12  0* 327,  31, 108,
11 12  3*  62,  23* 11 13  0* 200,  37,  26,  32,  23* 11 14  0*  68,  87,   0,  55* 11 15  0*  36,
11 15  1*  55,  68,  40* 11 16  0* 119,   0,  62* 11 17  0*  50* 12  0  0* 760, 782, 245,  91,  60,
12  0  5* 147,  49* 12  1  0* 202, 498, 433, 167,  86,  81,  39* 12  2  0* 101, 323, 240, 226,  91,
12  2  5* 138,  61* 12  3  0* 664, 469,  87, 278, 113,  77,   0* 12  4  0* 159, 122,  60,  81, 113,
12  4  5* 160* 12  5  0* 103, 261, 244, 236, 117,   0* 12  6  0*  43, 516,  66,  30,   0, 120,
12  7  0*  97,  99,  55,   0, 199,  41* 12  8  0*  45, 102, 166,  86, 111,   0* 12  9  0* 244,  64,
12  9  2*   0, 201,  31,  79* 12 10  0* 157, 107, 153,  78, 112* 12 11  0*  61, 240, 155, 216,  76,
12 12  0* 124, 183,   0,  60,  34* 12 13  0* 164,  24,  54,  26* 12 14  0* 177,   0,  38,   0,
12 15  0* 100,  46,  14* 12 16  0* 195,  57* 13  1  0* 140, 653, 159, 233, 116, 107* 13  2  0* 393,
13  2  1* 324, 138, 302,  75,  95* 13  3  0* 561, 196, 371,  77, 189,   0* 13  4  0* 254, 329, 271,
13  4  3* 416,   0,  82* 13  5  0* 416, 306,  59, 100,  83,  58* 13  6  0*  56,  95,   0, 185,  81,
13  6  5* 150* 13  7  0* 231, 348,  80,  93, 133,  52* 13  8  0* 282,   8,   0, 137,  49,  73,
13  9  0* 684,  89, 108,  59,  96,  31* 13 10  0* 431,  29,  42,   0,  84* 13 11  0*  72,  69,  74,
13 11  3*   0,   0* 13 12  0* 144,  34,  59,  42,   0* 13 13  0*  60, 156,   0, 118* 13 14  0*  82,
13 14  1*  67, 104,  64* 13 15  0*   0,  33,   0* 13 16  0*  88, 132* 14  0  0*1260,  53, 183,  64,
14  0  4* 380, 147* 14  1  0* 415, 266, 260,  65,  92,   0* 14  2  0* 202, 295, 345,  79, 204,   0,
14  3  0* 213,  84, 237, 271,  52,   0* 14  4  0* 146, 169,  69, 282,   0, 118* 14  5  0*  61, 181,
14  5  2* 177, 158, 157,  22* 14  5  0*  52, 121,  72,   0, 175,  72* 14  7  0*  83,   0, 178,  73,
14  7  4*  43,   0* 14  8  0* 166,  89,  96, 101,  19,   0* 14  9  0* 104,   0,  35, 243,  82,
14 10  0*  39,  34, 192,  94,  53* 14 11  0* 272,  99,  77,  96,  59* 14 12  0* 123,  24,  55,  36,
14 13  0* 148, 144, 129,  55* 14 14  0* 148,  34,   0* 14 15  0* 113,   0,  53* 14 16  0*  86,
15  1  0* 585, 136,   0, 249,  51,   0* 15  2  0*  28, 132, 342, 176, 133,  39* 15  3  0*  14, 490,
15  3  2*  90, 142, 143, 167* 15  4  0*  81, 187, 182, 151,  43,  42* 15  5  0* 446,  82,   0, 172,
15  5  4* 103,   0* 15  6  0* 100, 156, 197,  61, 138,  68* 15  7  0* 435,  69, 257, 113, 257,  25,
15  8  0* 421, 142, 113, 176,  26* 15  9  0*  42, 173, 145, 126,  76* 15 10  0* 116, 287,   0,   0,
15 10  4*  48* 15 11  0*  13, 456,  40,  47,  39* 15 12  0* 145, 102,   0,  53* 15 13  0*  19,  39,
15 13  2*  82,  31* 15 14  0*  95,  51,  84* 15 15  0* 218,  73* 16  0  0* 474, 236, 166, 153,  71,
16  0  5*  28* 16  1  0*   0, 359, 252, 360,  59,   0* 16  2  0*  65, 177, 143,  56, 189,  28,
16  3  0* 289, 160, 286, 122,  39,  78* 16  4  0* 362,  99, 485,   0,  35, 101* 16  5  0*  93, 128,
16  5  2*  42, 146,   9,   0* 16  6  0*  63, 366, 180,  91,  73,  57* 16  7  0*  46, 189,  62,  75,
16  7  4* 102* 16  8  0* 251,  17, 147,   0,  45* 16  9  0* 315,  61,  62,  85,   0* 16 10  0*  95,
16 10  1* 407,  99,   0,  48* 16 11  0*  73, 222,  65,  33* 16 12  0*  81, 139,  22,  73,
16 13  0* 113, 179,  49* 16 14  0* 104,  73, 110* 16 15  0*   0,   0* 17  1  0* 181, 203, 289,  80,
17  1  4*  28,  81* 17  2  0* 517,  76, 266, 290, 132,   0* 17  3  0* 254, 149, 156, 185,  13,  10,
17  4  0*  24,   0,  65,  12, 147,  52* 17  5  0* 260, 213,   0, 107,  47,  57* 17  6  0* 397,  65,
17  6  2*  19, 434,   0* 17  7  0* 118,  62, 159,  77,  20* 17  8  0* 274, 267,  82, 124,   0,
17  9  0*  70,   0,  54,   0,  14* 17 10  0* 312,  50,  94,   0,   0* 17 11  0* 225, 119,  36,   0,
17 12  0* 103,  62,   0,  47* 17 13  0*  99,  60,   0* 17 14  0*  98,  60* 18  0  0* 214,  82,  43,
18  0  3* 307,  34,  50* 18  1  0* 121, 114,   0, 258,  58,  31* 18  2  0* 389,  94, 123, 182, 120,
18  2  5*   0* 18  3  0* 255, 222, 119, 148,   0,   0* 18  4  0*  52, 199, 199, 254,   0,   0,
18  5  0* 109,   0,  69, 113, 100* 18  6  0* 202,  78,  28,  61,  76* 18  7  0* 262, 129,  33, 125,
18  7  4*   0* 18  8  0* 306, 196,  24,   0,  72* 18  9  0* 230, 139, 104,  46,   0* 18 10  0*   0,
18 10  1*  89,  32,  36* 18 11  0* 144,  54,  71,  86* 18 12  0*  67,  70,   0* 18 13  0*  52,  66,
18 13  2*  86* 18 14  0*   0,  40* 19  1  0* 121, 237,  94, 171,   0* 19  2  0* 100, 527,  77,  87,
19  2  4*  44* 19  3  0*  35,   0, 203,  65,   0* 19  4  0*  68,  90,   0,  49,  73* 19  5  0*  17,
19  5  1* 114, 218,  43, 150* 19  6  0* 431, 144,  83,   0, 138* 19  7  0* 165,  51, 107,  78,  70,
19  8  0* 128,  30, 121,  77,  61* 19  9  0* 123, 232,   0,   0* 19 10  0*  58,  63,   8,   0,
19 11  0*  91,   0,  61,   0* 19 12  0*  22,  89,  72* 19 13  0*   0,  14* 20  0  0*  60,  14, 186,
20  0  3* 288,  91* 20  1  0* 150,  71,   0,  67,  65* 20  2  0* 176, 218, 256,  70,  44,
20  3  0* 135, 133,  79, 113,   0* 20  4  0* 323, 220, 208,  13,  71* 20  5  0* 280, 183,  82, 146,
20  5  4*  53* 20  6  0* 128, 173,  84,  53,  69* 20  7  0*  98,  54,  76,  83,  48* 20  8  0*  68,
20  8  1* 100,   0,  47* 20  9  0* 175, 207, 110, 103* 20 10  0*  93,   0, 129,   0* 20 11  0* 103,
20 11  1* 131,  77* 20 12  0*  52,  96* 20 13  0*  75* 21  1  0* 211,   0,  88,  58,   0,
21  2  0* 150,   0,  82,  72,  91* 21  3  0*  39, 175,   0,  85,  35* 21  4  0*  33,   0, 101,  68,
21  4  4*  25* 21  5  0*  61,  57,  68,  67,  37* 21  6  0* 195,  57,  81,   0* 21  7  0*  30, 178,
21  7  2*  13,  30* 21  8  0*  32,  52,  50,  58* 21  9  0*  60,  37,   0,  61* 21 10  0* 138,  42,
21 10  2*  74* 21 11  0* 149,  43,  96* 21 12  0*   0,  81* 22  0  0* 102,  42, 133,   0,   0,
22  1  0* 172,  65,   0,  35,  75* 22  2  0*  69, 106,   0,   0,  46* 22  3  0*  85,   0,  43, 132,
22  3  4*  54* 22  4  0* 297,  68,  67,  62* 22  5  0*   0,  77,  56,  61* 22  6  0*  51,  94,  49,
22  6  3*   0* 22  7  0*  94,  70,  14,  14* 22  8  0* 143,  43,  76,  57* 22  9  0*  65,  30,  30,
22 10  0* 303,  59,  74* 22 11  0*   0,   0* 23  1  0*   9,  42,  94,  56* 23  2  0* 147,   0,   0,
23  2  3*  59* 23  3  0*   0,  73,   0,  65* 23  4  0* 190,  13,  27,  80* 23  5  0*   0, 110,   0,
23  5  3*  68* 23  6  0*  31,   0,  96,  56* 23  7  0*   0,   0,   0* 23  8  0* 235,  77,   0,
23  9  0*  89,   0,  60* 23 10  0*  56,  80* 24  0  0*   0,  25,   8,   0* 24  1  0*  96, 102,  82,
24  1  3*  40* 24  2  0* 145,   0,  94, 106* 24  3  0* 122, 138,   0,   0* 24  4  0*  16,   8,  92,
24  4  3*  68* 24  5  0*  70,   0,  64,   0* 24  6  0*  52, 102,  70* 24  7  0*  34,  99,   0,
24  8  0* 154,  64,   0* 24  9  0* 150, 145* 25  1  0*  57,  58, 108,   0* 25  2  0*  74, 112,  28,
25  2  3*  23* 25  3  0* 140,  42,  51* 25  4  0* 168,   0,  36* 25  5  0*  67,   0,  50,
25  6  0* 110,  53,   0* 25  7  0*  67, 104* 25  8  0*  73,   0* 26  0  0*  54,  82,   0,
26  1  0*  37,   0,  58* 26  2  0* 132,  77, 113* 26  3  0*  86,  62,  34* 26  4  0*  28,   0,  50,
26  5  0*  76,  54* 26  6  0*   0,  63* 26  7  0*  80* 27  1  0* 118,   0* 27  2  0*  34,  51,
27  3  0*   0,  96* 27  4  0*  61, 109* 27  5  0*   0* 28  0  0*   0* 28  1  0*  41* 28  2  0*   0,
```

in the MDO1 arrangement (Fig. 5). Contact distances between molecules in adjacent layers are the same for both types of arrangements. There are 8 H–H contacts shorter than 2.50 Å between molecules in different layers (none between molecules of a layer along *b*); the shortest is 2.15 Å, between a methyl hydrogen of C(26) and a methylene hydrogen of C(6). Careful examination of the difference *Fourier* map failed, not surprisingly perhaps, to show any sign of the additional methyl group at C(21) or C(26) of the monactin impurity (8%) in the crystals used for this analysis. It should also be mentioned again that crystals of very pure nonactin show the same disorder effects.

Upon complexation, the alkali cation must be stripped of its hydration shell as it enters the nonactin molecule. The loss of hydration energy, about 80 kcal/mole, must be compensated by interactions between the cation and its eight coordinated oxygen atoms in the complex. It has been shown that complex formation is very fast and it has been postulated [12] that fast conformational changes to form an optimal cavity, with stepwise substitution of solvent molecules, are essential for this process. Inspection of space-filling models shows that a hydrated K^+-cation can be inserted into the central cavity of a nonactin molecule with formation of hydrogen bonds between its water molecules and the various oxygen atoms of the prospective ligand. The actual complexation can be imagined to take place by a stepwise process in which removal of successive water molecules is coupled to conformational changes of the ligand, leading to gradual envelopment of the cation in the central cavity. It may be important in this connection that as the four ester groups tilt in the course of complexation, the four uncoordinated O-atoms move to the outside of the molecule. Their role could be to assist complex formation by removing hydrogen-bonded water molecules from the cavity.

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