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Crystal data of macrotetrolide antibiotics tetranactin and its homologues. By YOSHIHAU NAWATA and KUNIO ANDO, *Research Laboratories, Chugai Pharmaceutical Co. Ltd, Takada, Toshima, Tokyo, Japan* and YOICHI IITAKA, *Faculty of Pharmaceutical Sciences, University of Tokyo, Hongo, Tokyo, Japan*

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Tetranactin crystallizes in the space group $C2/c$ with four molecules in the unit cell having the dimensions $a=25.40$, $b=9.48$, $c=24.49$ Å and $\beta=129^\circ 40'$. Potassium, barium and copper complexes were prepared and their crystal data are given.

Tetranactin, $C_{44}H_{72}O_{12}$, is a new macrotetrolide antibiotic, produced by *Streptomyces aureus*. It is always accompanied by its homologues *A*, $C_{42}H_{68}O_{12}$, and *B*, $C_{43}H_{70}O_{12}$ (Oishi, Sagawa, Okutomi, Suzuki, Hayashi, Sawada & Ando, 1970). The chemical structure of tetranactin was investigated by means of mass spectra, proton magnetic resonance (p.m.r.) and infrared absorption spectra, and was found to be a macrocyclic ester composed of four structural units of homononactinic acid (Ando, Nawata & Murakami, 1971). The homologues *A* and *B* were presumed to be the isomers of dinactin and trinactin, respectively. Table 1 shows the crystal data of the free and complexed molecules of tetranactins (including the homologues *A* and *B*) which were obtained by use of Weissenberg and precession cameras with Cu $K\alpha$ radiation, and also those for nonactin (Dominguez, Dunitz, Gerlach & Prelog, 1962; Dobler, Dunitz & Kilbourn, 1969). The method of preparation and a brief comment on crystal data will be given below.

Tetranactin is rather easily crystallized from common organic solvents (acetone, chloroform, ethyl acetate and so on), forming large prismatic crystals of the monoclinic system (sample No. 1 in Table 1). The space group of tetranactin, $C2/c$, was suggested by the $N(z)$ test on the $hk0$ reflexions (86 planes, excluding $h00$ and $0k0$) which indicated the existence of a centre of symmetry. Accordingly, the tetranactin molecule has either a twofold rotational axis or a centre of symmetry. This is consistent with the data of optical rotation (Ando, Nawata & Murakami, 1971). Crystal structure analysis of tetranactin is now in progress by applying the symbolic addition method. The result will be reported elsewhere.

Homologue A

From homologue *A* it was difficult to grow a suitable crystal for X-ray diffraction, and no detailed crystallographic study has yet been carried out.

Table 1

Sample No.	Sample	Chemical formulae	Mol. wt.	Solvent	Crystal system	a (Å)	b (Å)	c (Å)
1	Tetranactin	$C_{44}H_{72}O_{12}$	792	ea	monoclinic	25.40	9.48	24.49
2	Homologue B	$C_{43}H_{70}O_{12}$	778	ac	triclinic	13.1	28.2	9.5
2'				np		13.2	33.6	9.5
3	Tetranactin	$C_{44}H_{72}O_{12}$	792	ac + me + CaBr ₂	monoclinic	25.36	9.45	24.50
4	Homologue B	$C_{43}H_{70}O_{12}$	778	ac + me + CaBr ₂	monoclinic	25.40	9.45	24.50
5	K ⁺ -tetranactin	$C_{44}H_{72}O_{12} \cdot KSCN$	889.2	ac	monoclinic	30.26	12.43	27.45
5'				ea + ac		15.82	19.98	15.57
6	K ⁺ -homologue B	$C_{43}H_{70}O_{12} \cdot KSCN$	875.2	ac	monoclinic	15.76	20.10	15.76
7	K ⁺ -homologue A	$C_{42}H_{68}O_{12} \cdot KSCN$	861.2	ea + ac	orthorhombic	15.83	19.47	15.33
8	Ba ²⁺ -tetranactin	$C_{44}H_{72}O_{12} \cdot Ba(ClO_4)_2$	1128	ac	monoclinic	26.15	36.59	13.03
9	Ba ²⁺ -homologue B	$C_{43}H_{70}O_{12} \cdot Ba(ClO_4)_2$	1114	ac	monoclinic	26.14	36.83	12.96
10	Ba ²⁺ -homologue A	$C_{42}H_{68}O_{12} \cdot Ba(ClO_4)_2$	1100	ac	orthorhombic	12.55	36.59	10.92
11	Cu ²⁺ -tetranactin	$C_{44}H_{72}O_{12} \cdot CuBr_2$	1015.3	ac	monoclinic	22.33	41.30	15.51
*	Nonactin	$C_{40}H_{64}O_{12}$	736		monoclinic	47.6	31.5	5.70
†	K ⁺ -nonactin	$C_{40}H_{64}O_{12} \cdot KSCN$	833.6		orthorhombic	20.17	15.55	15.53
†	Na ⁺ -nonactin	$C_{40}H_{64}O_{12} \cdot NaSCN$	817.5		monoclinic	15.45	19.52	15.53

Solvent = (ea: ethylacetate, ac: acetone, np: n-pentane, me: methanol).

Density measurements were carried out by the flotation method in the aqueous solutions (NaBr, KI).

* These data are from the papers by Dominguez, Dunitz, Gerlach & Prelog (1962).

† These data are from the papers by Dobler, Dunitz & Kilbourn (1969).

Homologue B

Homologue *B* was crystallized in three forms (Nos. 2, 2' and 4). Two types of triclinic crystals (Nos. 2 and 2') were obtained from acetone and n-pentane solutions respectively, while the monoclinic crystal (No. 4) which was presumed to be isostructural with No. 1 was obtained from an acetone-methanol solution containing an equimolar amount of calcium bromide. In the latter case, chemical analysis, infrared and p.m.r. spectra and crystal density calculation indicated that neither calcium nor bromide ions were included in the crystal and there was no evidence that homologue *B* was complexed with calcium bromide. Furthermore, the characteristic features of X-ray diffraction patterns of No. 1 and No. 4 were very similar to each other except for $h0l$ reflexions which exhibited the absence of reflexions ($l \neq 2n$) in No. 1. In the case of pure tetranactin, the crystal grown from the same solvent (No. 3) showed essentially the same lattice parameters as No. 1. In the methanol solution, there existed almost no interaction between the tetranactins and calcium bromide as evidenced by p.m.r. spectra in CD_3OD solution. While in the acetone solution containing $CaI_2 \cdot 6H_2O$ or $Ca(SCN)_2 \cdot 3H_2O$, ion-dipole interaction between the tetranactins and Ca^{2+} ion was suggested definitely from p.m.r. spectra (Hitachi Perkin-Elmer, R-20A, 60 MHz).

Potassium complexes

Good crystals of complexed compounds of the tetranactins with potassium thiocyanate were prepared from acetone solutions containing an equimolar amount of the salt (Nos.

5, 5', 6 and 7). Tetranactin, and homologue *B* form K^+ complexes which are presumed to be isostructural with each other (Nos. 5' and 6). The space group of No. 7 is $P222$ but $h+l \neq 2n$ in $h0l$, $k+l \neq 2n$ in $0kl$ and $k \neq 2n$ in $hk0$ are very weak, indicating that the space group is approximately $Pnmb$. It should be noted that the lattice parameters of these K^+ complexes closely resemble those found in K^+ complex of nonactin (Dobler, Dunitz & Kilbourn, 1969). Tetranactin forms another type of K^+ complex crystal (No. 5) when crystallized from acetone solution. The infrared spectra (KBr-disc method) of the complexes exhibited remarkable shifts of the absorption bands due to $\nu_{C=O}$ (1730 cm^{-1}) and ν_{C-O-C} (1250 cm^{-1}), which could be explained as a result of the strong interactions between the K^+ ion and the oxygen atoms (both on carbonyl groups and on tetrahydrofuran rings of the tetranactins).

Barium complexes

Complex compounds of tetranactin or the homologue *B* with a Ba^{2+} ion were precipitated from acetone solution [containing equal mole of tetranactins and $Ba(ClO_4)_2 \cdot 2H_2O$] as monoclinic crystals (Nos. 8 and 9), while an unstable orthorhombic crystal of the Ba^{2+} complex was obtained for the homologue *A* (No. 10). Distinct differences were observed in the infrared spectra (KBr-disc method) among the Ba^{2+} complexes of the different crystal systems.

Copper complex

A complex compound of tetranactin with a Cu^{2+} ion was precipitated from acetone solution (containing an equi-

Crystal data

α	β	γ	Cell volume (\AA^3)	Z	$\rho(\text{cal})$ (g.cm^{-3})	$\rho(\text{obs})$ (g.cm^{-3})	Systematic absences	Space group
$90^\circ 0'$	$129^\circ 40'$	$90^\circ 0'$	4540	4	1.158	1.18	$\left\{ \begin{array}{l} hkl \\ h0l \end{array} \right. \begin{array}{l} h+k \neq 2n \\ l \neq 2n \end{array}$	$C2/c$
$99^\circ 11'$	$111^\circ 57'$	$141^\circ 49'$	2130	2	1.21		none	$P1$
$96^\circ 24'$	$112^\circ 20'$	$134^\circ 50'$	2170	2	1.19	1.19		
$90^\circ 0'$	$129^\circ 40'$	$90^\circ 0'$	4532	4	1.16	1.15	$\left\{ \begin{array}{l} hkl \\ h0l \end{array} \right. \begin{array}{l} h+k \neq 2n \\ l \neq 2n \end{array}$	$C2/c$
$90^\circ 0'$	$130^\circ 0'$	$90^\circ 0'$	4502	4	1.15	1.14	$hkl \quad h+k \neq 2n$	$C2$
$90^\circ 0'$	$97^\circ 54'$	$90^\circ 0'$	10228	8	1.15		$\left\{ \begin{array}{l} hkl \\ h0l \end{array} \right. \begin{array}{l} k+l \neq 2n \\ h \neq 2n \end{array}$	$A2/a$ or Aa
$90^\circ 0'$	$90^\circ 0'$	$90^\circ 0'$	4921	4	1.20	1.19	$\left\{ \begin{array}{l} h0l \\ 0k0 \end{array} \right. \begin{array}{l} h+l \neq 2n \\ k \neq 2n \end{array}$	$P2_1/n$
$90^\circ 0'$	$90^\circ 0'$	$90^\circ 0'$	4995	4	1.16	1.18	$0k0 \quad k \neq 2n$	$P2_1$
$90^\circ 0'$	$90^\circ 0'$	$90^\circ 0'$	4725	4	1.21	1.18	$0k0 \quad k \neq 2n$	$P222$
$90^\circ 0'$	$124^\circ 30'$	$90^\circ 0'$	10276	8	1.46	1.44	$\left\{ \begin{array}{l} h0l \\ 0k0 \end{array} \right. \begin{array}{l} h \neq 2n \\ k \neq 2n \end{array}$	$P2_1/a$
$90^\circ 0'$	$124^\circ 30'$	$90^\circ 0'$	10280	8	1.44		$\left\{ \begin{array}{l} 0k0 \\ h00 \end{array} \right. \begin{array}{l} k \neq 2n \\ h \neq 2n \end{array}$	$P2_1$
$90^\circ 0'$	$90^\circ 0'$	$90^\circ 0'$	5014	4	1.46		$\left\{ \begin{array}{l} 0k0 \\ 00l \end{array} \right. \begin{array}{l} k \neq 2n \\ l \neq 2n \end{array}$	$P2_12_12_1$
$90^\circ 0'$	$132^\circ 30'$	$90^\circ 0'$	10543	8	1.28	1.25	$\left\{ \begin{array}{l} h0l \\ 0k0 \end{array} \right. \begin{array}{l} h \neq 2n \\ k \neq 2n \end{array}$	$P2_1/a$
$90^\circ 0'$	$90^\circ 0'$	$90^\circ 0'$	8546	8	1.15		$\left\{ \begin{array}{l} hkl \\ hk0 \\ h0l \end{array} \right. \begin{array}{l} h+k \neq 2n \\ h \neq 2n, k \neq 2n \\ h \neq 4n \end{array}$	$C2/b$
$90^\circ 0'$	$90^\circ 0'$	$90^\circ 0'$	4808	4	1.15		$0kl \quad k \neq 4n$	$Pnna$
$90^\circ 0'$	$90^\circ 0'$	$90^\circ 0'$	4620	4	1.17			$C2/c$

molar amount of tetranactin and CuBr_2) as dark green needles with monoclinic symmetry (No. 11). The complex formation was proved by the infrared spectra which indicated complicated shifts in $\nu_{\text{C}-\text{O}-\text{C}}$ bands, while $\Delta\nu_{\text{C}-\text{O}}$ (ca. 4 cm^{-1}) was rather small compared with those found in K^+ (15 cm^{-1}) and Ba^{2+} (45 cm^{-1}) complexes.

The spectral data (infrared and p.m.r.) on the free and the complexed molecules of the tetranactins will be published elsewhere.

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The crystal structures of racemic 3-benzylamino-4-hydroxypent-2-enoic acid lactone hydrochloride and of spontaneously resolved 3-benzylamino-4-hydroxypent-2-enoic acid lactone hydrobromide. By PEI-TAK CHENG, CHUNG HOE KOO, IAN P. MELLOR, S. C. NYBURG AND JOHN M. YOUNG, *Lash Miller Chemical Laboratories, University of Toronto, Toronto 181, Ontario, Canada*

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In *Acta Cryst.* (1970) B26, 1139 the compounds are erroneously named and pent-2-enoic should read pentanoic.

In a paper of the above title (Cheng, Koo, Mellor, Nyburg & Young, 1970), the compounds are erroneously named. 3-Benzylamino-4-hydroxypent-2-enoic acid should read 3-benzylamino-4-hydroxypentanoic acid throughout.

Reference

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Refinement of the crystal structure of lithium hydroxide monohydrate. By N.W. ALCOCK, *School of Molecular Sciences, University of Warwick, Coventry CV4 7AL, England*

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The crystal structure of lithium hydroxide monohydrate, $\text{LiOH}\cdot\text{H}_2\text{O}$, has been refined from the data of Rabaud & Gay to locate the hydrogen atoms. The R value was reduced from 0.085 to 0.065 and the hydrogen atoms were shown to be ordered.

Rabaud & Gay (1957) determined the crystal structure of $\text{LiOH}\cdot\text{H}_2\text{O}$ from three-dimensional data, using for refinement difference syntheses in two-dimensional projections. They located the hydroxyl hydrogen atom (in a special position) but could not find that of the water molecule (in a general position) and they suggested that it was disordered. However, the deuteron magnetic resonance (d.m.r.) spectrum of the compound, which has been studied in this laboratory (Clifford, Dixon & Smith, 1967; Smith & Clifford, 1971), indicates strongly that the water molecule is not disordered. The X-ray data has therefore been re-examined to resolve this discrepancy.

Experimental

Crystal data

Monoclinic, $a=7.37$, $b=8.26$, $c=3.19\text{ \AA}$;
 $\beta=110^\circ 18'$; $Z=4$;
 Space group $C2/m$ (from Rabaud & Gay, 1957).

Form factors for Li^+ and O were from *International Tables for X-ray Crystallography*, (1962), for H from McWeeny (1951). Two cycles of full-matrix least-square refinement on the lithium and oxygen atoms with anisotropic temperature factors for each reduced the R value to 0.073 (Rabaud & Gay (1957) quote 0.085 as their final figure). A difference Fourier synthesis showed the largest peak in special position $i(x,0,z)$ with $x=0.26$, $z=0.64$, equivalent to the hydroxyl hydrogen found by Rabaud & Gay. There were two peaks of nearly equal height in general positions, but after one cycle of refinement including the first hydrogen atom, H(1), only one of these two peaks remained strong. The second hydrogen atom, H(2), was therefore added at this position and the data finally refined to $R=0.065$. It was found necessary to damp the hydrogen atom shifts by 0.5 to avoid oscillations; of the 167 reflexions, three (400, 021, 002) showing extinction effects were given zero weight, with the rest having unit weights. The final parameters are shown in Table 1. Following the original nomenclature,

References

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