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Short Communications

Contributions intended for publication under this heading should be expressly so marked; they should not exceed about 1000 *words; they should be forwarded in the usual way to the appropriate Co-editor; they will be published as speedily as possible. Publication will be quicker if the contributions are without illustrations.*

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Crystallographic data on the molecular complexes of tetracycline salts.

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Salts of tetracycline (TC) and oxytetracycline (OTC) with inorganic acids form a number of closely related molecular complexes with complexing agents such as aliphatic carboxylic acids or urea derivatives (Ogawa & Inouye, 1960; Inouye, 1961; Inouye & Ogawa, 1961). A general formula of the salt-complexes is 2 TC salt (or 2 OTC salt).complexing agent.xH$_2$O, where x is 10 in the case of sulfate- and fluosilicate-complexes, and 6 in the case of nitrate- and hydrochloride-complexes. The decahydrates are unstable compared with the hexahydrates, and readily lose about 4 molecules of water to convert into hexahydrates when exposed to dry air. Examination of the powder patterns of the salt-complexes revealed the presence of at least four distinct crystal structures, namely, $d\alpha$, $d\beta$, $h\gamma$ and $h\delta$, $d\alpha$ and $d\beta$ being types of decahydrate, and $h\gamma$ and $h\delta$ types of hexahydrate.

Table 1. *Unit cells and crystal densities of salt-complexes*

TC Salt-complex	Type	a (Å)	b (Å)	c (Å)	β	Crystal density: Calculated[1] (g.cm^{-3})	Crystal density: Found (g.cm^{-3})
Sulfate–acetic acid	$d\alpha$	15·87	10·50	17·36	109° 00′	1·49	1·49
Sulfate–aspartic acid	$d\alpha$	15·82	10·50	17·32	109° 12′	1·49[2]	1·49
Sulfate–fumaric acid	$d\alpha$	15·81	10·50	17·34	108° 36′	1·56[3]	1·52
Sulfate–malonic acid	$d\alpha$	15·93	10·50	17·50	109° 12′	—	—
Sulfate–monobromoacetic acid	$d\alpha$	15·79	10·49	17·46	108° 40′	1·58	1·55
Sulfate–monochloroacetic acid	$d\alpha$	15·90	10·50	17·38	108° 48′	1·525	1·52
Sulfate–oxalic acid	$d\alpha$	15·72	10·50	17·44	109° 06′	1·555	1·53
Sulfate–propionic acid	$d\alpha$	15·72	10·49	17·40	108° 24′	1·51	1·49
Sulfate–water[4]	$d\alpha$	15·90	10·50	17·35	109° 12′	1·46	1·47
Sulfate–water[5]	$d\alpha$	15·82	10·49	17·31	109° 00′	1·46	1·47
Fluosilicate–monochloroacetic acid	$d\alpha$	15·91	10·49	17·50	109° 00′	—	—
OTC Sulfate acetic acid	$d\alpha$	15·79	10·50	17·40	108° 12′	1·52	1·515
Sulfate–glutaric acid	$d\beta$	16·05	10·50	32·40	—	—	—
Sulfate–malonic acid	$d\beta$	15·97	10·53	32·13	—	1·55	1·52

(1) Unless otherwise stated, the values were calculated by the formula: 2 TC (or OTC)salt.complexing agent.10 H$_2$O.
(2) Calculated for 2 TC sulfate.2/5 aspartic acid.10 water.
(3) Calculated for 2 TC sulfate.4/5 fumaric acid.10 water.
(4) The dodecahydrate crystallized in the presence of guanidine sulfate.
(5) The dodecahydrate crystallized in the presence of dimethylglyoxime.

In this communication, the lattice parameters and symmetries of the $d\alpha$ and $d\beta$ types are reported and their probable structure principles are proposed.

Table 1 indicates the unit-cell parameters of the $d\alpha$ and $d\beta$ types of the salt-complexes together with the crystal densities. Cell parameters were calculated mainly from the oscillation and $h0l$ Weissenberg photographs about the b axis with Cu $K\alpha$ radiation. Mean errors for the $d\alpha$ cell dimensions were a, $\pm 0{\cdot}04$, b, $\pm 0{\cdot}02$, c, $\pm 0{\cdot}04$ Å; β, $\pm 0{\cdot}2°$. Those for the $d\beta$ cells were a, $\pm 0{\cdot}04$, b, $\pm 0{\cdot}03$, c, $\pm 0{\cdot}05$ Å. The values for densities, which were determined by a flotation method, are not expected to be more accurate than $\pm 0{\cdot}02$ g.cm^{-3}, since the crystals were easily dehydrated. Space groups of the $d\alpha$ and $d\beta$ types were determined as $P2_1$ and $P2_12_12_1$ respectively by considering the optically active character of TC and OTC coupled with the systematic absences, which were $0k0$ when k is odd for the former, $h00$, $0k0$ and $00l$ when h, k and l are odd for the latter.

From the comparison of the powder patterns, it was further indicated that the decahydrates of the following salt-complexes also have the same monoclinic cell dimensions as those of the $d\alpha$ crystals given in Table 1: TC sulfate–acrylic acid, –cyanamide, –dicyanodiamide, –formic acid, –glycolic acid, –hydantoin, –methyl hydrogen oxalate, –pyrazine, –succinimide, and –thioacetic acid complexes; TC fluosilicate–acetic acid, –dicyanodiamide, –formamide, –formic acid, –hydantoin, and –succinimide complexes; OTC sulfate–monochloroacetic acid and –propionic acid complexes. On the other hand, two members of the decahydrates of TC sulfate-complexes (–ascorbic acid and –parabanic acid complexes) were found to belong to the orthorhombic $d\beta$ type.

Although the crystals of these salt-complexes contain a variety of complexing agents of varied types and sizes, the unit-cell dimensions are nearly constant. Furthermore, the reflection intensities of the different kinds of $d\alpha$ crystals, which were examined mainly on the $h0l$ and hll Weissenberg photographs of the sulfate-complexes listed in Table 1, showed a striking similarity to one another. This fact suggests that the crystal structure of the $d\alpha$ crystals consists of an almost identical framework which encloses spaces capable of containing a complexing agent isomorphously. It also suggests that the location or orientation of the complexing agent in the cavity may be statistically random. These results, however, seem to be not in accordance with those which may be obtained in the case of a coordination compound such as tetraethylammonium bromide succinimide complex, because the formation of a coordination compound is restricted not only by charge distribution of a complexing agent but also by dimensional factors (Powell, 1958). Therefore, the most probable structure of the $d\alpha$ type is that of a clathrate (Palin & Powell, 1948).

The orthorhombic $d\beta$ structure is a polymorphic modification of the monoclinic $d\alpha$, since TC sulfate–malonic acid complex crystallizes in both of them. Comparison of the cell parameters between the two structures shows that a and b are almost identical, while $c_{d\beta}$ corresponds to $2\,c_{d\alpha}\sin\beta$. Hence, if two monoclinic cells of the $d\alpha$ are twinned as shown in Fig. 1, where the twinning axis is the twofold screw axis lying at $y=\frac{1}{4}$ or $\frac{3}{4}$ in [001], the newly formed orthorhombic cell

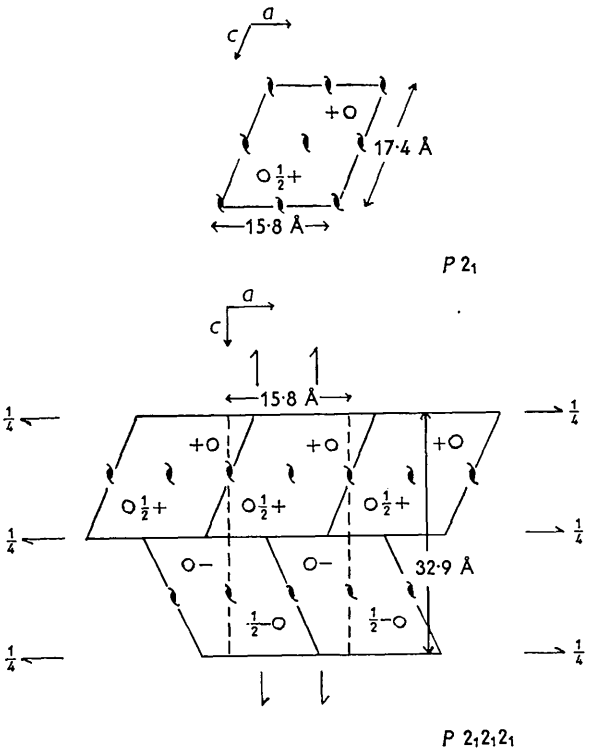

Fig. 1. Relationship between the $d\alpha$ type monoclinic cell ($P2_1$) and the $d\beta$ type orthorhombic cell ($P2_12_12_1$). Projections along [010].

has nearly the same cell dimensions, and the same space group, as the $d\beta$ cell. It is, therefore, possible that the $d\beta$ structure is really a monoclinic one submicroscopically twinned, having essentially the same molecular packing as in the $d\alpha$ type.* In this connection, it is interesting to note that the $d\alpha$ crystals are often twinned macroscopically on {001}.

Full details of this paper will be published elsewhere.

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* Such microscopic twinning is widely recognized (Ito, 1950).