The Carvoxime System.
V. X-ray Study of a Mixed Crystal of Carvoxime

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A mixed crystal of carvoxime near the ($\pm$) composition is monoclinic, space group $P2_1$, with $Z = 4$, $a = 9.871$ (19), $b = 11.837$ (23), $c = 9.484$ (16) Å, $\beta = 99.13°$. The disordered structure was refined by anisotropic rigid-body least squares, using the molecular geometry previously found in the ($\pm$) crystal. R for reflections with $I \geq 3\sigma(I)$ is 12·6%. The rotational arrangements of the isopropenyl groups are different for the ordered and disordered molecules.

Introduction

The phase and solubility diagrams (Fig. 1) of the carvoxime system suggest a continuous series of mixed crystals. However, it has been reported (Baert & Fouret, 1975; Oonk & Kroon, 1976) that the racemic form does exhibit disorder, and is in fact the most stable structure. Consequently the inactive crystal is a true racemate, and not a pseudoracemate. In the racemate the 1:1 [*i.e.* ($\pm$)] composition is an ordered structure in which (+) molecules are related to (−) molecules through space-group symmetry; they are located on sites which are here referred to as A and B respectively. In the direction of an increasing amount of (−) component, the (+) molecules on the A sites are randomly replaced by (−) molecules. In the opposite direction the B sites are gradually filled by (+) molecules.

In the pseudoracemate the (+) and (−) molecules are randomly distributed over all lattice sites; the 1:1 composition thus has a disordered structure.

To obtain a better understanding of the mechanism of the mutual solubility in the solid state of organic substances, we decided to determine structures of samples with different compositions between (+)- and ($\pm$)-carvoxime. The present communication reports a structural study of a mixed crystal, near the ($\pm$) composition.

Experimental

The crystal, 0·6 × 0·5 × 0·4 mm, had a shape similar to that of ($\pm$)-carvoxime. It was the first crystal
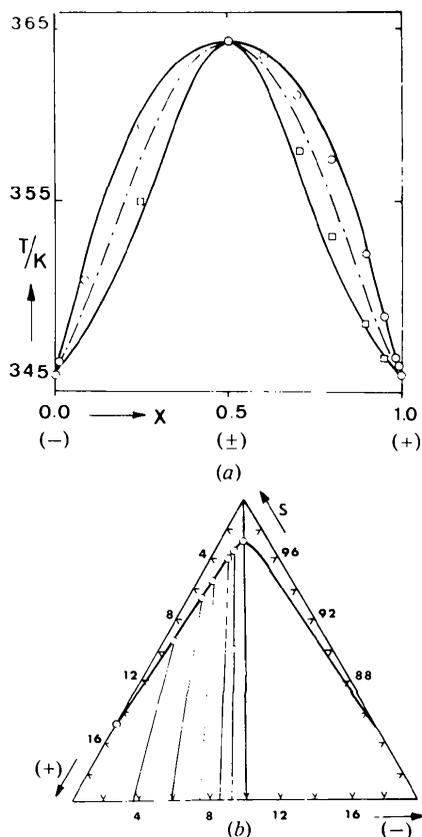
Fig. 1. (*a*) The solid–liquid equilibrium diagram of the system (+)-carvoxime + (−)-carvoxime. O □: liquidus and solidus obtained by Adriani (1900). Solid lines: calculated phase diagram (Oonk, Tjoa, Brants & Kroon, 1977). Dot-dashed line: equal *G* curve. (*b*) The solubility diagram of the system (+)-carvoxime + (−)-carvoxime (Jacques & Gabard, 1972) (*S* = hexane).

Table 1. *Crystal data*

$C_{10}H_{15}NO$, monoclinic, $P2_1$		Z	4
FW	165·23	D_x	$1·12 \text{ g cm}^{-3}$
a	9·871 (19) Å	D_m	1·10
b	11·837 (23)	$\lambda(\text{Cu } K\alpha)$	1·5418 Å
c	9·484 (16)	$\mu(\text{Cu } K\alpha)$	$5·64 \text{ cm}^{-1}$
β	99·13°	$F(000)$	360
V	978·4 Å³	Room temperature	21 (2)°C

obtained by evaporation at 20°C of a solution of equal amounts of (+)- and (±)-carvoxime. The crystallographic data are reported in Table 1. Intensities for 1874 reflections were measured by the ω–2θ scan on a four-circle diffractometer. The width of the scan (°) was 1·6 + 0·16 tg θ. The data were corrected for the Lorentz–polarization factor, but were not corrected for absorption or extinction. 1225 reflections with $I \geq 3\sigma(I)$ were considered in the determination of the structure.

Structure determination and refinement

The structure was refined from the positions of the atoms of the racemate (Baert & Fouret, 1975). As
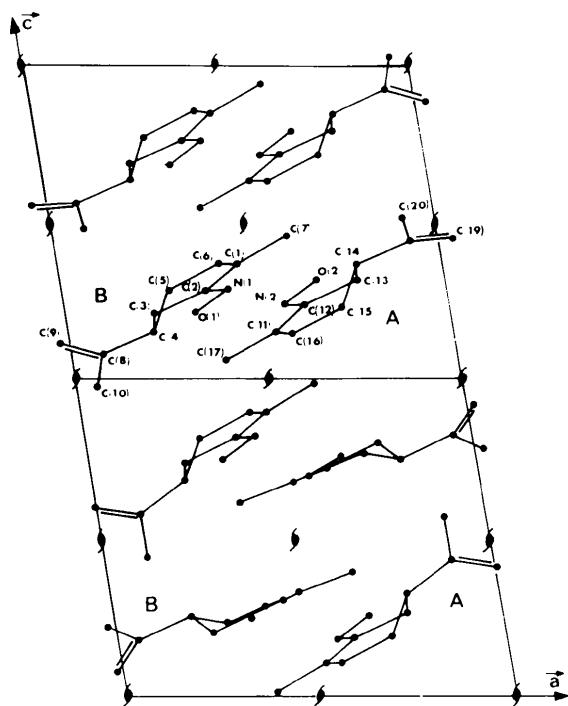
Fig. 2. Projection along **b** of the structure of the mixed crystal: upper part: molecules with an occupancy factor of 0·85; lower part: molecules with an occupancy factor of 0·15.

expected, the full-matrix refinement gave erroneous values for the intramolecular distances, especially near the isopropenyl groups.

R for the 1225 reflections decreased only to 0·21. Moreover, the temperature factors were relatively large. Further refinement by least squares did not prove successful, and conversion to anisotropic temperature factors did not help, as many of the mean-square amplitudes became negative. A difference synthesis revealed only some of the H atoms, and also peaks of $1·5 \text{ e Å}^{-3}$ which could not be interpreted. A disordered structure was postulated to explain all the peaks in the Fourier map. A particular method of refinement was employed to solve our difficulties. At first, the two molecules found were adjusted by least squares on the (+) molecule of the racemic crystal, which was taken as a model. Because of the free rotation around the sp^3–sp^2 [C(4)–C(8)] bond, the adjustment had to be made in two steps: first, we considered the molecule excluding C(9) and C(10) of the isopropenyl group, which could have a different orientation in the mixed crystal (Fig. 2); second, we adjusted the isopropenyl group taking into account the new coordinates obtained for C(4) and C(8) and the approximate positions of C(9) and C(10). In other words, the isopropenyl group is set by geometrical calculations from C(4) and C(8), C(9) and C(10) giving the orientation of the group. In this way the adjusted molecules have coordinates sufficiently near the previous values found from the refinement without constraint and it was expected that convergence would be reached. At this point we used the rigid-body least-squares program *ORION* (André, Fourme & Renaud, 1971) which allows orientational and positional shifts of rigid groups of atoms. Unfortunately a segmented rigid-body refinement around the C(4)–C(8) bonds was not possible.

On a difference synthesis following refinement of this type, it was possible to recognize among the peaks two new molecules occupying the same sites as the previous ones. Evidently these two molecules had to be included in the refinement. The peaks on the difference map had a better resolution than those revealed after a classical least-squares refinement. An estimation of the occupancy factors based on peak heights gave about 0·85 and 0·15 respectively for the two types of molecules (we use unprimed and primed numbering of the atoms to specify these molecules). The same result was found by least squares on the occupancy factors of atoms which were farthest from each other [N–N', O—O', C(4)–C'(4), C(8)–C'(8) (Fig.2)].

After introduction of the two primed molecules, it was possible to distinguish on a difference map some of the H atoms of the unprimed molecules. The remaining H atoms of the latter and those belonging to the cyclohexene ring of the primed molecules were inserted at their expected positions. The final R was 0·105 for the 800 strongest reflections, and 0·126 for the reflections with $I \geq 3\sigma(I)$. Refinement without constraint showed

Table 2. *Positional parameters* ($\times 10^4$, *for* H $\times 10^3$)

The e.s.d.'s are in parentheses. The coordinates of the H atoms belonging to the 'disordered molecules' are not reported.

	x	y	z		x	y	z
O(1)	3349 (9)	278 (7)	2096 (10)	O(2)	−3372 (9)	9715 (9)	3136 (10)
N(1)	4281 (7)	1108 (8)	2841 (9)	N(2)	−4294 (7)	8893 (9)	2360 (7)
C(1)	4661 (6)	2978 (10)	3647 (7)	C(11)	−4660 (6)	7034 (10)	1479 (6)
C(2)	3779 (6)	2103 (8)	2826 (7)	C(12)	−3789 (5)	7895 (9)	2346 (6)
C(3)	2309 (5)	2381 (5)	2160 (7)	C(13)	−2352 (5)	7605 (7)	3164 (6)
C(4)	2162 (6)	3565 (4)	1597 (7)	C(14)	−2232 (6)	6394 (7)	3645 (7)
C(5)	2779 (7)	4411 (6)	2854 (5)	C(15)	−2779 (7)	5602 (9)	2238 (8)
C(6)	4205 (7)	4023 (9)	3670 (8)	C(16)	−4205 (7)	5998 (10)	1424 (7)
C(7)	6062 (8)	2658 (12)	4526 (10)	C(17)	−6065 (7)	7361 (11)	603 (8)
C(8)	731 (7)	3866 (2)	778 (9)	C(18)	−785 (7)	6037 (9)	4342 (10)
C(9)	−278 (10)	3241 (2)	1095 (10)	C(19)	372 (9)	6578 (9)	4413 (10)
C(10)	474 (6)	4895 (3)	−272 (12)	C(20)	−855 (6)	4896 (10)	5119 (12)
O'(1)	3496 (52)	155 (28)	2524 (69)	O'(2)	6547 (44)	9719 (27)	2544 (49)
N'(1)	4421 (41)	1036 (30)	3065 (49)	N'(2)	5616 (33)	8899 (29)	1800 (41)
C'(1)	4841 (31)	2962 (32)	3254 (40)	C'(11)	5222 (31)	7033 (31)	1031 (36)
C'(2)	3921 (32)	2023 (29)	2809 (34)	C'(12)	6099 (27)	7900 (27)	1850 (31)
C'(3)	2480 (32)	2239 (29)	2015 (37)	C'(13)	7523 (26)	7609 (27)	2635 (34)
C'(4)	1962 (30)	3329 (31)	2518 (39)	C'(14)	7618 (31)	6428 (28)	3196 (34)
C'(5)	2915 (37)	4316 (28)	2322 (49)	C'(15)	7056 (38)	5584 (27)	1894 (40)
C'(6)	4389 (35)	4002 (30)	3024 (50)	C'(16)	5659 (38)	5985 (30)	1042 (39)
C'(7)	1962 (34)	3329 (42)	2518 (54)	C'(17)	3850 (37)	7364 (40)	118 (52)
C'(8)	496 (32)	3601 (39)	1766 (54)	C'(18)	8891 (39)	6115 (34)	4266 (46)
C'(9)	−92 (36)	2826 (44)	817 (60)	C'(19)	10179 (35)	6660 (42)	4060 (66)
C'(10)	−185 (42)	4701 (45)	2013 (70)	C'(20)	9690 (54)	5140 (41)	5310 (59)
H(O1)	361	−63	167				
H(C3)	197	161	138	H(C13)	−195	832	396
H'(C3)	146	225	257	H'(C13)	−154	771	268
H(C4)	289	377	103	H(C14)	−290	633	430
H(C5)	262	530	253	H(C15)	−262	469	252
H'(C5)	206	438	378	H'(C15)	−205	564	131
H(C6)	471	463	442	H(C16)	−519	544	103
H(C7)*	669	337	463	H(C17)*	−657	784	137
H'(C7)*	594	234	568	H'(C17)*	−594	783	−43
H"(C7)*	647	200	387	H"(C17)*	−663	661	25
H(C9)	−46	242	55	H(C19)	131	612	437
H'(C9)	93	253	189	H'(C19)	40	747	452
H(C10)*	134	505	−81	H(C20)*	−179	481	554
H'(C10)*	−40	475	−115	H'(C20)*	−77	424	426
H"(C10)*	28	559	45	H"(C20)*	−1	481	607
H(O2)	−356	1068	324				

* Expected positions.

that the atoms moved very slightly, R becoming 0·123; the intramolecular distances remained better than those obtained when we ignored the disorder. Unit weights were used throughout. The absolute values of peaks and troughs in the final difference synthesis did not exceed 0·35 e Å^{-3}. The relatively high values of R and the residual density are caused by two main difficulties, *viz* the correlation between the occupancy and the temperature factors, and the fact that we are not sure of the complete homogeneity of the crystal. Scattering factors were those of Hanson, Herman, Lea & Skillman (1964). Final atomic parameters are listed in Table 2.*

Results and discussion

Bond lengths and angles are reported in Table 3; they are mainly those of the molecules of the racemic crystal, owing to the particular mode of refinement.

Fig. 2 shows the disordered structure. For clarity, the unprimed molecules are separated from the primed. Sites A and B of the upper part of the drawing are occupied by a right and a left molecule with an occupancy factor of 0·85. In the lower part, the two molecules are both right, the weight being 0·15. If now we look at site B we observe that the left molecule of the (±) crystal has been substituted by a right one, whereas at site A the two molecules are both right. The mixed crystal can be described as being built up mainly of unit cells with (±) molecules. How the molecules are distributed on sites A and B in the solid state is still to

Table 3. *Bond lengths* (Å) *and bond angles* (°) *with e.s.d.'s in parentheses for the heavy atoms*

N(1)–O(1)	1·423 (12)	O(1)–N(1)–C(2)	114·1 (7)	N(2)–O(2)	1·421 (12)	O(2)–N(2)– C(12)	114·5 (7)
C(2)–N(1)	1·277 (13)	N(1)–C(2)–C(1)	116·7 (7)	C(12)–N(2)	1·282 (14)	N(2)–C(12)–C(11)	116·8 (7)
C(1)–C(2)	1·458 (12)	N(1)–C(2)–C(3)	123·6 (7)	C(11)–C(12)	1·455 (12)	N(2)–C(12)–C(13)	122·7 (7)
C(2)–C(3)	1·508 (8)	C(1)–C(2)–C(3)	119·3 (6)	C(12)–C(13)	1·517 (7)	C(11)–C(12)·C(13)	120·4 (6)
C(3)–C(4)	1·481 (8)	C(2)–C(3)–C(4)	111·5 (5)	C(13)–C(14)	1·490 (14)	C(12)–C(13)–C(14)	111·7 (6)
C(4)–C(5)	1·518 (9)	C(3)–C(4)–C(5)	113·0 (5)	C(14)–C(15)	1·546 (11)	C(13)–C(14)–C(15)	111·7 (6)
C(5)–C(6)	1·537 (10)	C(4)–C(5)–C(6)	110·8 (6)	C(15)–C(16)	1·539 (10)	C(14)–C(15)–C(16)	110·1 (6)
C(1)–C(6)	1·317 (15)	C(5)–C(6)–C(1)	124·3 (7)	C(11)–C(16)	1·310 (15)	C(15)–C(16)· C(11)	124·2 (8)
C(1)–C(7)	1·511 (10)	C(6)–C(1)–C(2)	119·7 (8)	C(11)–C(17)	1·516 (9)	C(16)–C(11)–C(12)	119·7 (7)
C(4)–C(8)	1·514 (9)	C(6)–C(1)–C(7)	121·0 (8)	C(14)–C(18)	1·516 (9)	C(16)–C(11)–C(17)	120·8 (8)
C(8)–C(9)	1·303 (8)	C(2)–C(1)–C(7)	119·1 (7)	C(18)–C(19)	1·303 (11)	C(12)–C(11)· C(17)	119·3 (7)
C(8)–C(10)	1·507 (7)	C(3)–C(4)–C(8)	114·0 (5)	C(18)–C(20)	1·509 (14)	C(13)–C(14)–C(18)	113·8 (6)
		C(5)–C(4)–C(8)	114·0 (5)			C(15)–C(14)–C(18)	108·7 (6)
		C(4)–C(8)–C(9)	121·2 (5)			C(14)–C(18)–C(19)	121·3 (7)
		C(4)–C(8)–C(10)	117·3 (6)			C(14)–C(18)–C(20)	130·2 (8)
		C(9)–C(8)–C(10)	121·2 (6)			C(19)–C(18)–C(20)	108·3 (7)

O(1)–H	1·17	C(9)–H'(C9)	1·08	O(2)–H	1·16	C(16)· H(C16)	1·17
C(3)–H(C3)	1·13	C(7)–H'(C7)	1·07	C(13)–H(C13)	1·12	C(14)–H(C14)	0·93
C(3)–H'(C3)	0·97	C(10)–H(C10)	1·06	C(13)–H'(C13)	0·96	C(19)–C(C19)	1·08
C(5)–H(C5)	1·09	C(10)–H'(C10)	1·07	C(15)–H(C15)	1·10	C(19)–H'(C19)	1·07
C(5)–H'(C5)	1·14	C(10)–H''(C10)	1·07	C(15)–H'(C15)	1·14	C(20)–H(C20)	1·07
C(6)–H(C6)	1·04	C(7)–H(C7)	1·06	C(17)–H(C17)	1·07	C(20)–H'(C20)	1·07
C(4)–H(C4)	0·96	C(7)–H''(C7)	1·05	C(17)–H'(C17)	1·06	C(20)–H''(C20)	1·06
C(9)–H(C9)	1·07			C(17)–H''(C17)	1·07		

be investigated. To have a pseudoracemate the substitution should be at both sites *A* and *B*, and the symmetry centre would become a statistical one. Our study shows that the laws of Kitaigorodsky (1973) about general mixed crystals work well when the crystal consists of enantiomorphs. The substitution is possible because the (+) and (−) molecules are very similar: $\varepsilon = 1 - (\Delta/\Gamma)$ (where Δ and Γ are the non-overlapping and overlapping volumes respectively) is 0·78 which means that there are no appreciable changes in the number of contacts and no drastic modifications in

Fig. 4. Hydrogen-bond geometry in the mixed crystal for the unprimed molecules. The values for (±)-carvoxime are given in square brackets. Distances are in Å, angles in degrees.

intermolecular distances. An energy calculation between (+)–(+) and (+)–(−) molecules gave −21·9 and −23·0 kcal mol⁻¹.

The different conformations of the carvoxime molecule are illustrated in Newman projections along C(4)–C(8) (Fig. 3).

The hydrogen bond O–H···N is part of a six-membered ring as in the (±) and (−) compounds (Kroon, van Gurp, Oonk, Baert & Fouret, 1976)); the parameters of the ring are altered, but this may be owing to difficulties in locating the H atoms (Fig. 4).

Fig. 3. Newman projections along the C(4)–C(8) bonds of the carvoxime molecules: (*a*) molecules at site *B* are enantiomorphs, (*b*) at site *A* only (+) molecules occur.

the solubility diagram, and Dr Riche for measuring the intensities.

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Strukturaufklärung von 5-Azido-5-desoxy-1,2-O-isopropyliden-3-O-mesyl-β-L-iduronsäurediethylamid

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5-Azido-5-desoxy-1,2-O-isopropylidene-3-O-mesyl-β-L-iduronic acid diethylamide (ADIMID) crystallizes in space group $P2_1$ with four molecules per unit cell. Lattice constants are $a = 12.650$ (4), $b = 10.753$ (2), $c = 15.208$ (4) Å, $\beta = 106.94$ (2)°. The structure was solved by direct methods and refined to a final R value of 0.05. The R configuration exists at C(5) of the compound. The two symmetrically independent molecules in the crystal have a different arrangement of the azido groups and different conformations of the furanose rings. The furanose ring has E_4 conformation (phase angle $P = 55°51'$) in one molecule and $^3T_4$ conformation (phase angle $P = 35°59'$) in the other molecule.

Einleitung

5-Amino-hexuronsäuren sind Hauptbausteine der bakteriell und fungizid wirksamen Antibiotika des Polyoxin-Komplexes, die zur Bekämpfung von Pilzkrankheiten der Reispflanzen eingesetzt werden (Isono, Asahi & Suzuki, 1969). Freie 5-Amino-Zucker zeigen ferner ein Gleichgewicht zwischen stickstoff- und sauerstoffhaltigen Halbacetalformen (Paulsen & Todt, 1968; Paulsen & Mäckel, 1973). Synthetische Untersuchungen in dieser Substanzklasse sind somit von erheblichem Interesse. Um zu einer 5-Amino-hexuronsäure zu gelangen, haben wir nach Fig. 1 1,2-O-Isopro-

pyliden-3,5-di-O-mesyl-α-D-glucuronsäurediethylamid (I) mit Natriumazid zu einem 5-Azido-Zucker (II) umgesetzt (Paulsen & Günther, 1977). Azido-Zucker
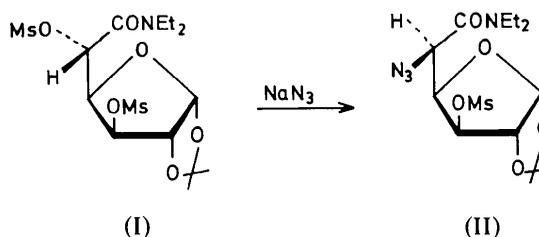
Fig. 1. Reaktion von 1,2-O-Isopropyliden-3,5-di-O-mesyl-α-D-glucuronsäurediethylamid (I) zu 5-Azido-5-desoxy-1,2-O-isopropyliden-3-O-mesyl-β-L-iduronsäurediethylamid (II) (abgekürzt ADIMID).

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