Hydrogen-Bonded Complex Formation of Oximes with Carboxylic Acids and with Amides. (*E*)-Acetophenone Oxime–Benzoic Acid (1/1) and (*E*)-Benzaldehyde Oxime–Benzamide (1/1)

By Jan K. Maurin

Institute of Atomic Energy, 05-400 Otwock-Świerk, Poland

Małgorzata Winnicka-Maurin

Chemistry Department of Warsaw Agricultural University, Warsaw, Poland

and Iain C. Paul and David Y. Curtin

University of Illinois, Department of Chemistry, Urbana, IL 61801, USA

Abstract

(*E*)-Acetophenone oxime–benzoic acid (1/1), $C_7H_6O_2.C_8H_9NO$, $M_r = 257.29$, monoclinic, $P2_1/c$, $a = 13.666$ (1), $b = 5.413$ (2), $c = 16.298$ (1) Å, $\beta = 108.55$ (1)°, $V = 1282.7$ (2) Å^3, $Z = 4$, $D_x = 1.332$ g cm^{-3}, λ(Mo $K\alpha$) = 0.71073 Å, $\mu = 0.55$ cm^{-1}, $F(000) = 544$, $T = 223$ (2) K, $R = 0.0454$, $wR = 0.0445$ for 1979 reflections [$|F| \geq 3.92\sigma(F)$]. (*E*)-Benzaldehyde oxime–benzamide (1/1), $C_7H_7NO.$-C_7H_7NO, $M_r = 242.28$, monoclinic, $P2_1/n$, $a = 5.283$ (2), $b = 10.478$ (5), $c = 22.893$ (7) Å, $\beta = 99.73$ (6)°, $V = 1249$ (2) Å^3, $Z = 4$, $D_x = 1.288$ g cm^{-3}, λ(Mo $K\alpha$) = 0.71073 Å, $\mu = 0.51$ cm^{-1}, $F(000) = 512$, $T = 223$ (2) K, $R = 0.038$, $wR = 0.036$ for 1266 reflections [$|F| \geq 3.92\sigma(F)$]. Strong hydrogen bonds between the carbonyl or amide and the oxime groups were observed. Fourier-transform infrared (FTIR) spectroscopic studies of complex formation in solution were carried out. A phase diagram for the benzoic acid–acetophenone oxime system was obtained.

Introduction

Previous investigations of compounds containing both carboxyl and oxime groups (Padmanabhan, Paul & Curtin, 1989; Maurin, Paul & Curtin, 1992*a,b*) have suggested a preference for the formation of strong oxime···carboxyl hydrogen bonds rather than centrosymmetrically related ones between like groups. Such studies suggested that if the oxime and acid groups were in different molecules, 1:1 complex formation might be observed. The similarity of the amide group to the carboxyl group has led to the discovery of analogous hydrogen bonding linking molecules containing both the

amide and oxime functions (Maurin, Paul & Curtin, 1992*c,d*).

This paper describes the formation of a crystalline oxime–carboxylic acid complex and an oxime–amide complex and studies of the interaction of oximes and carboxylic acids in solution.

Experimental

Synthesis and infrared spectra of (*E*)-*acetophenone oxime–benzoic acid* (1/1)

Reaction of acetophenone with hydroxylamine hydrochloride in alkaline solution (Fuson, 1962) and purification by recrystallization from ethanol–water solution gave crystals of (*E*)-acetophenone oxime (m.p. 330–331 K). The starting materials were obtained from commercial sources.

Fourier-transform infrared (FTIR) spectra were obtained with an IBM IR-32 spectrometer using 0.1, 0.5, 1.0 and 3.0 mm NaCl cells. The spectra of benzoic acid, acetophenone oxime and 1:1 mixtures of the two components were studied in CCl$_4$ solution at concentrations of 0.2, 0.04, 0.02 and 0.007 *M*. In each case the product of concentration and layer thickness was held approximately constant. The spectra of solid components and 1:1 mixtures ground together in Fluorolube were also obtained. Crystallization of an equimolar mixture of (*E*)-acetophenone oxime and benzoic acid (m.p. 395 K) from ethanol–water (1/1) or ethanol–cyclohexane (1/1) gave crystals of a new solid (m.p. 347–347.5 K) shown by X-ray diffraction to be the 1:1 complex. Infrared spectra indicated that the same complex was obtained by grinding the components together in a ratio of 1:1. Also, X-ray powder diffraction patterns of the grinding product showed lines that are absent

from the powder pattern of either of the base compounds.

Synthesis and infrared spectra of (E)-benzaldehyde oxime–benzamide (1/1)

Attempts at the simultaneous crystallization of the two compounds were carried out with ratios of the two components of 2:1, 1:1 and 1:2 in various organic solvents. Colorless prismatic crystals (m.p. 332 K) of the 1:1 complex were obtained by crystallization from a methylene chloride–methanol (6/1) mixture. Infrared spectra of benzamide and benzaldehyde oxime mixed in a 1:1 ratio (at concentrations of 0.1, 0.02, 0.01 and 0.003 M) were obtained in $CHCl_3$ solution.

X-ray structure determinations of complexes

In each case a CAD-4 single-crystal diffractometer was employed using the ω–θ scan mode with graphite-monochromatized Mo $K\alpha$ radiation for data collection. The data were corrected for Lorentz–polarization effects but not for absorption or extinction. The structures were solved by direct methods using the *SHELXS86* program (Sheldrick, 1990) and refined with the *SHELX76* program (Sheldrick, 1976). Scattering factors were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV).

(E)-Acetophenone oxime–benzoic acid (1/1)

Colorless needle-shaped crystals of benzoic acid with (E)-acetophenone oxime suitable for X-ray analysis were obtained from an ethanol–cyclohexane solution. A fragment of dimensions ca $0.30 \times 0.39 \times 0.69$ mm cut from a longer crystal was used for data collection. The unit-cell parameters were obtained by a least-squares refinement of 25 reflections with $18.8 \le 2\theta \le 27.4°$. At 223 (2) K, 3072 independent reflections were collected. Intensities were measured to $2\theta \le 56°$ ($0 \le h \le 18$, $-7 \le k \le 0$, $-24 \le l \le 24$). The systematic absences ($0k0$, k odd; $h0l$, l odd) led to the assignment of space group $P2_1/c$. No significant variations in the intensities of three standard reflections were observed. 1979 reflections were considered observed [$|F| \ge 3.92\sigma(F)$]. All of the non-H atoms were located from an E map. The H atoms attached to C atoms were positioned according to standard geometrical criteria. The two hydroxyl H atoms were located from a $\Delta\rho$ map. Refinement on F of all H-atom positions together with their isotropic displacement parameters and the positional and anisotropic displacement parameters for the other atoms with weights based on $\sigma(F)$ decreased the R factor to 0.045 and wR to 0.044 with $S = 1.445$. The weights used were $1.622/[\sigma(F) + 0.00035F^2]$. The peaks in the final $\Delta\rho$ map were in the range -0.069 to 0.095 e Å^{-3}. The ratios of shifts to e.s.d.'s in the last cycle of refinement were all less than 0.009 with an average of 0.001. The data/parameter ratio was $1979/2321 = 8.53$.*

(E)-Benzaldehyde oxime–benzamide (1/1)

A crystal of dimensions $0.36 \times 0.44 \times 0.55$ mm was used for data collection. The unit-cell parameters were obtained by a least-squares refinement of 24 reflections with $15.9 \le 2\theta \le 23.8°$. 1944 independent reflections were measured at 223 (2) K to $2\theta \le 48°$ ($-6 \le h \le 6$, $0 \le k \le 11$, $0 \le l \le 26$). The non-standard setting $P2_1/n$ for $P2_1/c$ was assigned based on systematic absences ($0k0$, $k = 2n$; $h0l$, $h + l = 2n$). No significant variations in the intensities of three standard reflections were observed. 1266 reflections were considered observed [$|F| \ge 3.92\sigma(F)$]. All of the non-H atoms were located from an E map. All H atoms were located in a $\Delta\rho$ map. Refinement of all H-atom positions together with their isotropic displacement parameters and the positional and anisotropic displacement parameters for the other atoms with weights based on $\sigma(F)$ decreased the R factor to 0.038 and wR to 0.036 with $S = 1.238$. The weights used were $1.675/[\sigma(F) + 0.0004F^2]$. The peaks in the final $\Delta\rho$ map were in the range -0.21 to 0.12 e Å^{-3}. The ratios of shifts to e.s.d.'s in the last cycle of refinement were all less than 0.002 with an average of 0.001. The data/parameter ratio was $1266/219 = 5.78$.*

Phase diagram

The phase diagram of (E)-acetophenone oxime–benzoic acid was obtained by measuring the melting points of ground mixtures with different molar ratios of benzoic acid and acetophenone oxime.

Discussion

(E)-Acetophenone oxime–benzoic acid (1/1)

The formation of a hydrogen-bonded complex by grinding together an equimolar mixture of benzoic acid and (E)-acetophenone oxime is one of an increasing number of examples of 'solid–solid' reactions (Patil, Curtin & Paul, 1984, 1986; Pennington, Patil, Curtin & Paul, 1986; Rastogi, Singh & Singh, 1977; Singh & Singh, 1981). The single crystals needed for X-ray work could, however, only be

---

prepared by crystallization of the 1:1 mixture from ethanol–cyclohexane. The molecular structure of the hydrogen-bonded complex and the numbering of atoms are shown in Fig. 1. The atomic coordinates and the equivalent thermal parameters of the benzoic acid–oxime complex are given in Table 1. The bond lengths and angles involving the non-H atoms are given in Table 2. The structure of the complex consists of a 1:1 arrangement of acetophenone oxime and benzoic acid held together by two hydrogen bonds in a fashion reminiscent of the dimeric structures in crystals of benzoic acid (Feld, Lehmann, Muir & Speakman, 1981) and of acetophenone oxime (Gieren, Hübner & Ruiz-Perez, 1986).*

The structure of the approximately planar hydrogen-bonded cyclic dimer of benzoic acid has been studied in considerable detail (Feld *et al.*, 1981) because of its remarkable ability to undergo a double proton transfer from the carboxyl O atoms [structure (*A*)] to the pair of O atoms to which they are hydrogen bonded [structure (*B*)]. These proton transfers are rapid in the solid state at room temperature (Agaki, Imashiro, Terao, Hirota & Hayashi, 1987, and work cited therein) so that the structures of benzoic acid and many structurally related acids are disordered, a particular crystal site containing an unequal probability of occupancy by an (*A*) or (*B*) dimer. It has been shown that the unequal occupancy is a consequence of the unsymmetrical crystal environment of the dimer species; the potential molecular plane of symmetry through the two carboxyl C atoms normal to the approximate plane of the dimer unit is broken and the intermolecular forces acting on the two O atoms of the carboxyl group are not equivalent (Leiserowitz, 1976). Were such proton switching to occur in a mixed acid–oxime complex as shown below, it would involve equilibration of an acid–oxime complex (*C*) with a complex (*D*) (an acid molecule hydrogen bonded to a nitrone-like oxime tautomer). Although (*D*) would be expected to be less stable than (*C*), the nitrones

---

* Only the *E* isomer of acetophenone oxime crystallizes in the hydrogen-bonded dimer structure. The *Z* isomer crystallizes as polymeric hydrogen-bonded chains.
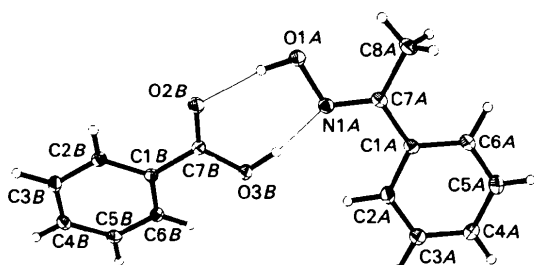
Table 1. *Fractional coordinates and U_{eq} values for (E)-acetophenone oxime–benzoic acid* (1/1)

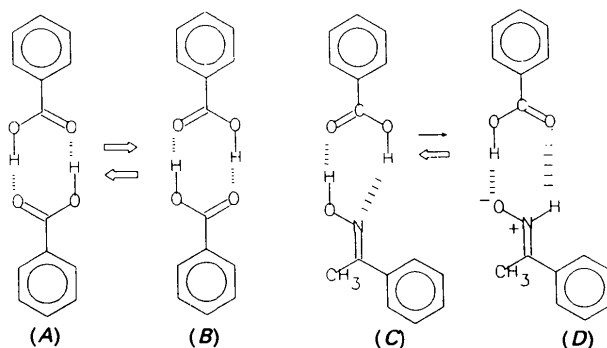$$U_{eq} = (1/3)(U_{11} + U_{22} + U_{33} + U_{13}\cos\beta).$$

	x	y	z	U_{eq} (Å²)
C1*A*	0.4004 (1)	−0.5144 (4)	0.5729 (1)	0.033 (1)
C2*A*	0.4417 (2)	−0.3670 (5)	0.6376 (1)	0.044 (1)
C3*A*	0.5355 (2)	−0.4217 (5)	0.6923 (1)	0.047 (1)
C4*A*	0.5908 (2)	−0.6239 (5)	0.6838 (1)	0.042 (1)
C5*A*	0.5511 (2)	−0.7733 (5)	0.6209 (2)	0.054 (2)
C6*A*	0.4573 (2)	−0.7204 (5)	0.5658 (1)	0.048 (1)
C7*A*	0.2996 (1)	−0.4592 (4)	0.5140 (1)	0.034 (1)
C8*A*	0.2613 (2)	−0.6171 (5)	0.4429 (1)	0.044 (1)
N1*A*	0.2480 (1)	−0.2752 (3)	0.52721 (8)	0.0331 (9)
O1*A*	0.1541 (1)	−0.2363 (3)	0.46805 (8)	0.0389 (8)
C1*B*	0.1371 (1)	0.3894 (4)	0.6558 (1)	0.0281 (9)
C2*B*	0.0629 (1)	0.5681 (4)	0.6231 (1)	0.032 (1)
C3*B*	0.0405 (2)	0.7484 (4)	0.6695 (1)	0.035 (1)
C4*B*	0.0906 (2)	0.7481 (4)	0.7481 (1)	0.036 (1)
C5*B*	0.1639 (2)	0.5698 (4)	0.7811 (1)	0.035 (1)
C6*B*	0.1878 (2)	0.3916 (4)	0.7351 (1)	0.0313 (9)
C7*B*	0.1580 (1)	0.1967 (4)	0.6051 (1)	0.0303 (9)
O2*B*	0.1024 (1)	0.1617 (3)	0.53928 (7)	0.0375 (8)
O3*B*	0.2424 (1)	0.0635 (3)	0.63776 (8)	0.0355 (8)

Table 2. *Bond distances* (Å) *and angles* (°) *involving non-hydrogen atoms for (E)-acetophenone oxime–benzoic acid* (1/1)

C—H and O—H bond lengths are in the range 0.87–1.02 Å.

C1*A*—C2*A*	1.390 (3)	C2*A*—C1*A*—C6*A*	116.9 (2)
C2*A*—C3*A*	1.384 (3)	C2*A*—C1*A*—C7*A*	122.3 (2)
C3*A*—C4*A*	1.366 (3)	C6*A*—C1*A*—C7*A*	120.8 (2)
C4*A*—C5*A*	1.369 (4)	C1*A*—C2*A*—C3*A*	121.6 (2)
C1*A*—C6*A*	1.389 (3)	C2*A*—C3*A*—C4*A*	120.5 (2)
C5*A*—C6*A*	1.385 (4)	C3*A*—C4*A*—C5*A*	118.9 (2)
C1*A*—C7*A*	1.485 (3)	C4*A*—C5*A*—C6*A*	121.1 (2)
C7*A*—C8*A*	1.504 (3)	C1*A*—C6*A*—C5*A*	120.9 (2)
C7*A*—N1*A*	1.287 (3)	C1*A*—C7*A*—C8*A*	120.0 (2)
N1*A*—O1*A*	1.406 (2)	C1*A*—C7*A*—N1*A*	117.1 (2)
C1*B*—C2*B*	1.392 (3)	C8*A*—C7*A*—N1*A*	122.8 (2)
C2*B*—C3*B*	1.390 (3)	C7*A*—N1*A*—O1*A*	113.0 (1)
C3*B*—C4*B*	1.382 (3)	C2*B*—C1*B*—C6*B*	119.6 (2)
C4*B*—C5*B*	1.383 (3)	C2*B*—C1*B*—C7*B*	118.6 (2)
C1*B*—C6*B*	1.394 (2)	C6*B*—C1*B*—C7*B*	121.7 (2)
C5*B*—C6*B*	1.386 (3)	C1*B*—C2*B*—C3*B*	119.8 (2)
C1*B*—C7*B*	1.482 (3)	C2*B*—C3*B*—C4*B*	120.2 (2)
C7*B*—O2*B*	1.217 (2)	C3*B*—C4*B*—C5*B*	120.3 (2)
C7*B*—O3*B*	1.330 (2)	C4*B*—C5*B*—C6*B*	119.9 (2)
		C1*B*—C6*B*—C5*B*	120.2 (2)
		C1*B*—C7*B*—O2*B*	123.1 (2)
		C1*B*—C7*B*—O3*B*	114.4 (1)
		O2*B*—C7*B*—O3*B*	122.6 (2)

and their alkyl and aryl derivatives are a well known family of organic compounds.

Fig. 1. A view of the molecular structure and atomic numbering of the oxime–acid complex.

(*A*)   (*B*)   (*C*)   (*D*)

It has been observed (Dieterich, Paul & Curtin, 1974; Patil, Curtin & Paul, 1985) that a plot of $\Delta\theta$, the difference between the C–C–O angles (corresponding to C1B–C7B–O2B and C1B–C7B–O3B in Fig. 1), versus Δr, the difference in C–O bond lengths (corresponding to C7B–O3B and C7B–O2B in Fig. 1), for a number of crystalline meta- and para-substituted benzoic acids was approximately linear and the position of an acid on the line gave a measure of the extent of imbalance of the proton-switching equilibrium. In the case of the benzoic acid–acetophenone complex discussed here, the value of $\Delta\theta$ (8.7°) and the value of Δr (0.113 Å) fit very well on the line of the plot in the paper cited (Dieterich et al., 1974) at a position indicating a large degree of bias in favour of structure (C) as might be expected from the known stability of oximes relative to their nitrone-like tautomers. However, these results do not rule out the possibility that there is the same kind of dynamic disorder involving (C) and (D) as has been found in the carboxylic acids but with a much more unbalanced ratio of the two tautomers due to the instability of the (D) species relative to the (C) species.

Crystal packing

The crystal is made up of discrete oxime–acid units (Fig. 2). There are no additional strong intermolecular interactions in the crystal. It may be noted that, unlike the cases of the benzoic acid and of the acetophenone oxime cyclic dimers, each hydrogen-bonded complex in the oxime–acid crystal is polar. In other systems, co-crystals made up of chains of polar molecules have been shown to be polar (Etter, Frankenbach & Bernstein, 1989; Etter & Frankenbach, 1989). However, the space group $P2_1/c$ of the present structure dictates that each polar complex must be accompanied by a corresponding complex, related by a centre of symmetry so that the resulting structure is centrosymmetric rather than polar.
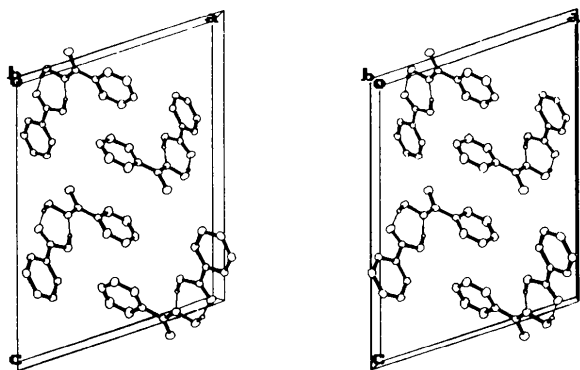
Infrared spectra of the carboxylic acid–oxime complex

Carboxylic acids have been shown to have solid-state infrared spectra which differ according to whether the acid molecules crytallize as hydrogen-bonded eight-membered cyclic dimers [(A) and (B)] or linear catamers (Leiserowitz, 1976; Walborsky, Barsh, Young & Impastato, 1961; Lin, Paul & Curtin, 1974). Since acid–oxime complexes have apparently not previously been prepared, it was of interest to compare the solid-state infrared spectra of the complex with those of its components.

Acetophenone oxime in carbon tetrachloride solution shows a very sharp O–H stretching absorption at about 3600 cm^{-1}.* In the solid state, however, its structure has been shown (Gieren et al., 1986) to consist of six-membered cyclic dimer units roughly analogous to the eight-membered carboxylic acid dimers characteristic of benzoic acid and its relatives. The solid-state spectrum of acetophenone oxime, like the carboxylic acid dimer spectrum, shows no absorption at 3600 cm^{-1} (free hydroxyl stretching) but only a very broad intense O–H stretching absorption at somewhat lower frequencies (2750–3250 cm^{-1}). The oxime absorption, however, is somewhat more compressed than the corresponding benzoic acid dimer absorption (2150–3150 cm^{-1}). In Fig. 3 the spectrum of the complex in the solid state is compared with the sum of the spectra of the component acid and oxime measured independently. Solution spectra of 1:1 mixtures of oxime and benzoic acid (Fig. 4) show the oxime absorption at 3600 cm^{-1} (free hydroxyl) but its intensity is less than half the intensity of the same band in the absence of benzoic acid. This is consistent with the hypothesis made above that the oxime complexes more strongly with benzoic acid than with itself.

Phase diagram of the acetophenone oxime–benzoic acid mixture

The phase diagram (Fig. 5) is unusual for a system in which complex formation has been demonstrated, in that the sharp melting point for a 1:1 ratio of components does not correspond to a local maximum. The diagram does have some resemblance to those sometimes found for two substances that are miscible (from solid solutions) and form a 1:1 complex (Glasstone, 1940).

Fig. 2. Stereo packing diagram of the oxime–acid complex viewed along b with the intermolecular hydrogen bonds between the oxime and carboxyl groups marked by thin lines.

* A quantitative study of the self-association of acetophenone oxime in carbon tetrachloride solution, taking advantage of the infrared absorption of the unassociated O–H stretching absorption at 3595 cm^{-1} and the associated absorption at 3300 cm^{-1}, has been reported (Ossart, Sauvaitre & Pineau, 1967). The conclusion of these authors was that cyclic dimers were the only associated species present.

(E)-Benzaldehyde oxime–benzamide (1/1)

The oxime–amide complex was much more difficult to obtain than the oxime–acid complex. It
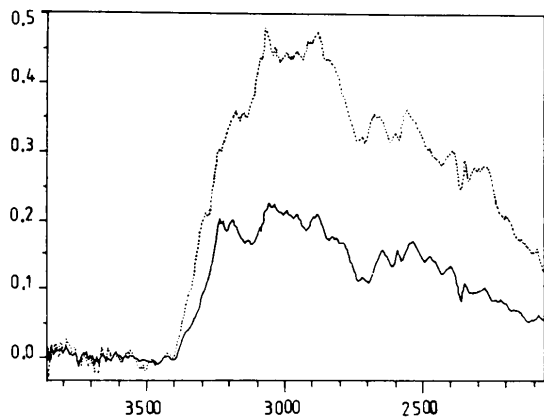

Fig. 3. FTIR spectra of solids in Fluorolube of the acid–oxime complex (solid line) and sum of spectra of the component acid and oxime measured independently (dashed line).
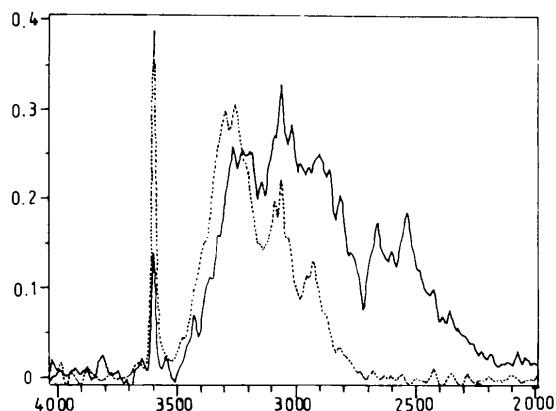

Fig. 4. FTIR spectra of solutions in CCl_4 of 1:1 oxime–acid mixture (solid line) and oxime (dashed line). The oxime concentration was 0.02 *M* in both cases.
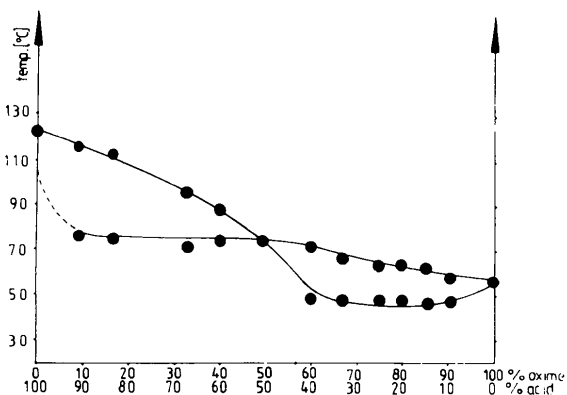

Fig. 5. Liquid–solid phase diagram of the benzoic acid–acetophenone oxime system.

was highly sensitive to the conditions employed. Amides are poorer hydrogen donors than carboxylic acids but stronger hydrogen-bond acceptors and it has been found that carboxylic acids undergo self-association in nonpolar solvents to a substantially greater extent than amides (Joeston & Shaad, 1974). It is perhaps not unexpected, then, that the formation of an oxime–amide complex might be less favoured than the acid–oxime complex discussed above.
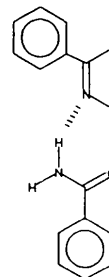
The molecules of benzaldehyde oxime and benzamide that are complexed by hydrogen bonding, together with the numbering of their atoms, are shown in Fig. 6. The atomic coordinates and the equivalent thermal parameters are given in Table 3. The bond lengths and angles involving the non-H atoms are given in Table 4. Fig. 7 shows a stereo packing diagram of a view along the *c* axis with the intermolecular hydrogen bonds between the oxime and the amide groups marked as dashed lines.
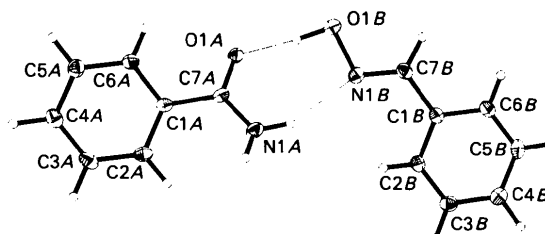

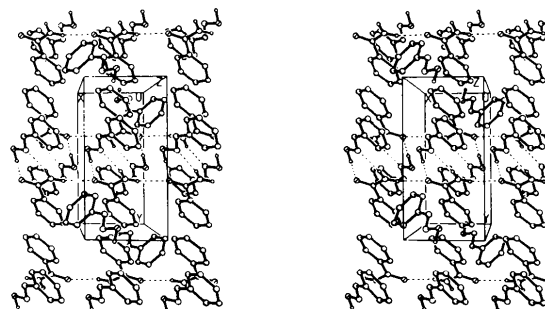Fig. 6. Benzaldoxime–benzamide complex and numbering of atoms.

Fig. 7. Stereo packing diagram of the oxime–amide complex.

Table 3. *Fractional coordinates and U_{eq} values for (E)-benzaldehyde oxime-benzamide* (1/1)

$$U_{eq} = (1/3)(U_{11} + U_{22} + U_{33} + U_{13}\cos\beta).$$

	x	y	z	U_{eq} (Å^2)
C1A	0.4915 (4)	0.2127 (2)	0.52361 (9)	0.034 (1)
C2A	0.7020 (4)	0.1329 (3)	0.5243 (1)	0.045 (2)
C3A	0.7600 (5)	0.0420 (3)	0.5680 (1)	0.050 (2)
C4A	0.6135 (5)	0.0305 (3)	0.6119 (1)	0.048 (2)
C5A	0.4053 (5)	0.1097 (3)	0.6115 (1)	0.047 (2)
C6A	0.3440 (4)	0.1995 (3)	0.5677 (1)	0.040 (1)
C7A	0.4134 (4)	0.3105 (2)	0.47720 (9)	0.038 (1)
N1A	0.5922 (4)	0.3580 (2)	0.4487 (1)	0.049 (1)
O1A	0.1864 (3)	0.3461 (2)	0.46541 (7)	0.047 (1)
C1B	0.3846 (4)	0.6551 (2)	0.28320 (9)	0.036 (1)
C2B	0.5787 (4)	0.5687 (3)	0.2780 (1)	0.041 (1)
C3B	0.7165 (5)	0.5785 (3)	0.2325 (1)	0.046 (2)
C4B	0.6637 (5)	0.6747 (3)	0.1908 (1)	0.050 (2)
C5B	0.4730 (5)	0.7608 (3)	0.1956 (1)	0.051 (2)
C6B	0.3346 (5)	0.7517 (3)	0.2415 (1)	0.046 (2)
C7B	0.2297 (4)	0.6462 (3)	0.3302 (1)	0.041 (1)
N1B	0.2560 (3)	0.5544 (2)	0.36667 (8)	0.040 (1)
O1B	0.0838 (3)	0.5640 (2)	0.40694 (7)	0.052 (1)

Table 4. *Bond distances (Å) and angles (°) involving non-hydrogen atoms for (E)-benzaldehyde oxime-benzamide* (1/1)

C—H, N—H and O—H bond lengths are in the range 0.89–1.03 Å.

C1A—C2A	1.389 (3)	C2A—C1A—C6A	118.8 (2)
C2A—C3A	1.378 (4)	C2A—C1A—C7A	123.3 (2)
C3A—C4A	1.373 (4)	C6A—C1A—C7A	117.9 (2)
C4A—C5A	1.377 (4)	C1A—C2A—C3A	120.2 (2)
C1A—C6A	1.382 (3)	C2A—C3A—C4A	120.6 (2)
C5A—C6A	1.374 (4)	C3A—C4A—C5A	119.4 (2)
C1A—C7A	1.484 (3)	C4A—C5A—C6A	120.5 (2)
C7A—N1A	1.332 (3)	C1A—C6A—C5A	120.6 (2)
C7A—O1A	1.241 (3)	C1A—C7A—N1A	118.3 (2)
C1B—C2B	1.388 (3)	C1A—C7A—O1A	120.3 (2)
C2B—C3B	1.371 (3)	N1A—C7A—O1A	121.3 (2)
C3B—C4B	1.384 (4)	C2B—C1B—C6B	118.4 (2)
C4B—C5B	1.371 (4)	C2B—C1B—C7B	122.4 (2)
C1B—C6B	1.385 (3)	C6B—C1B—C7B	119.2 (2)
C5B—C6B	1.381 (4)	C1B—C2B—C3B	120.7 (2)
C1B—C7B	1.460 (3)	C2B—C3B—C4B	120.5 (2)
C7B—N1B	1.266 (3)	C3B—C4B—C5B	119.3 (2)
N1B—O1B	1.404 (2)	C4B—C5B—C6B	120.4 (3)
		C1B—C6B—C5B	120.7 (2)
		C1B—C7B—N1B	121.4 (2)
		C7B—N1B—O1B	111.6 (2)

Benzaldehyde oxime in $CHCl_3$ solution has an absorption in the infrared at 3580 cm^{-1} which is due to a free O–H stretching mode. A comparison of the $CHCl_3$ solution spectra of the 1:1 mixtures (various concentrations) of benzaldehyde oxime and benzamide with those of the individual compounds (same concentrations) shows that the intensity of the absorption at 3580 cm^{-1} is reduced by about one-half when benzamide is present, indicating that complex formation takes place in solution as well as in the solid state.

Hydrogen-bonding dimensions in the two complexes

In the acetophenone oxime–benzoic acid complex the O–H$\cdots$O distance is 2.725 (2) Å with an O–H$\cdots$O

angle of 168 (3)° and the O–H$\cdots$N distance is 2.749 (2) Å with an O–H$\cdots$N angle of 170 (3)°. The hydrogen-bonding dimensions in the benzaldehyde oxime–benzamide complex are O–H$\cdots$O 2.656 (3) Å with an angle of 176 (3)° and N–H$\cdots$N 3.129 (3) Å with an angle of 156 (2)°, while the amide–amide N–H$\cdots$O hydrogen bond has a length of 3.150 (3) Å and the N–H$\cdots$O angle is 162 (2)°.

The distances in the oxime–acid complex, albeit involving either different donors or acceptors, are intermediate between the lengths typically found in acid–acid dimers, for example 2.627 (1) Å in benzoic acid (Feld *et al.*, 1981), and those found in oxime–oxime dimers, for example 2.81 (2) Å in the α form of (E)-acetophenone oxime (Gieren *et al.*, 1986). By contrast, the O–H$\cdots$O distance in the oxime–amide complex is quite short, indeed comparable to those generally found in acid–acid dimers, whereas the N–H$\cdots$N distance is quite long. Although benzoic acid dimers show dynamic disorder of the hydroxylic protons whereas the oxime–acid complexes are essentially ordered, it has been pointed out by Leiserowitz (1976) that there seems to be no correlation between the O–H$\cdots$O distance and the degree of disorder in dimers of crystalline carboxylic acids. The N–H$\cdots$O hydrogen-bond length linking benzamide–oxime complexes together is also longer than those normally found cross-linking amide dimers, but this finding is not without precedent.

The two molecules of the benzoic acid–oxime complex are not coplanar; the dihedral angle between the planes of the two benzene rings is 22.76°. The oxime group is almost coplanar with the ring to which it is bonded (dihedral angle of 4.85°) whereas the dihedral angle between the carboxyl group and the attached ring is 13.44°. The two functional groups are rotated with respect to one another by an angle of 8.1°

References

AGAKI, T., IMASHIRO, F., TERAO, T., HIROTA, N. & HAYASHI, S. (1987). *Chem. Phys. Lett.* **139**, 331–335.

DIETERICH, D. A., PAUL, I. C. & CURTIN, D. Y. (1974). *J. Am. Chem. Soc.* **96**, 6372–6380.

ETTER, M. C. & FRANKENBACH, G. M. (1989). *Chem. Mater.* **1**, 10–12.

ETTER, M. C., FRANKENBACH, G. M. & BERNSTEIN, J. (1989). *Tetrahedron Lett.* **30**, 3617–3620.

FELD, R., LEHMANN, M. S., MUIR, K. W. & SPEAKMAN, J. C. (1981). *Z. Kristallogr.* **157**, 215–231.

FUSON, R. C. (1962). *Reactions of Organic Compounds*, pp. 406 ff. New York: John Wiley.

GIEREN, A., HÜBNER, T. & RUIZ-PEREZ, C. (1986). *Chem. Z.* **110**, 73–78.

GLASSTONE, S. (1940). *Text Book of Physical Chemistry*, pp. 732 ff. New York: Van Nostrand.

Joeston, M. D. & Shaad, L. J. (1974). *Hydrogen Bonding*, pp. 287–290. New York: Marcel Dekker.
Leiserowitz, L. (1976). *Acta Cryst.* **B32**, 775–802.
Lin, C. T., Paul, I. C. & Curtin, D. Y. (1974). *J. Am. Chem. Soc.* **96**, 3699–3701.
Maurin, J. K., Paul, I. C. & Curtin, D. Y. (1992a). *Acta Cryst.* C48. In the press.
Maurin, J. K., Paul, I. C. & Curtin, D. Y. (1992b). *Acta Cryst.* C48. In the press.
Maurin, J. K., Paul, I. C. & Curtin, D. Y. (1992c). *Acta Cryst.* C48, 1819–1821.
Maurin, J. K., Paul, I. C. & Curtin, D. Y. (1992d). *Acta Cryst.* C48, 1821–1823.
Ossart, A., Sauvaitre, H. & Pineau, P. (1967). *J. Chim. Phys. Phys. Chim. Biol.* **64**, 953–956.
Padmanabhan, K., Paul, I. C. & Curtin, D. Y. (1989). *Acta Cryst.* B45, 411–416.

Patil, A. O., Curtin, D. Y. & Paul, I. C. (1984). *J. Am. Chem. Soc.* **106**, 348–353.
Patil, A. O., Curtin, D. Y. & Paul, I. C. (1985). *Isr. J. Chem.* **25**, 320–326.
Patil, A. O., Curtin, D. Y. & Paul, I. C. (1986). *J. Chem. Soc. Perkin Trans.* 2, pp. 1687–1692.
Pennington, W. T., Patil, A. O., Curtin, D. Y. & Paul, I. C. (1986). *J. Chem. Soc. Perkin Trans.* 2, pp. 1693–1700.
Rastogi, R. P., Singh, N. B. & Singh, R. P. (1977). *J. Solid State Chem.* **20**, 191–200.
Singh, N. B. & Singh, R. P. (1981). *J. Solid State Chem.* **38**, 211–218.
Sheldrick, G. M. (1976). *SHELX76.* Program for crystal structure determination. Univ. of Cambridge, England.
Sheldrick, G. M. (1990). *Acta Cryst.* A46, 467–473.
Walborsky, H. M., Barsh, L., Young, A. E. & Impastato, F. J. (1961). *J. Am. Chem. Soc.* **83**, 2517–2525.

Structural Studies on DNA-Binding Drugs: Crystal Structure and Molecular Dynamics Studies of Triazoloacridinones

By P. Arjunan and S. K. Arora*

Department of Crystallography, University of Pittsburgh, Pittsburgh, PA 15260, USA

and W. Chalody

Department of Pharmaceutical Technology, Technical University of Gdansk, 80952 Gdansk, Poland

(*Received* 16 *January* 1992; *accepted* 18 *June* 1992)

Abstract

Structural and conformational studies on two 8-substituted triazoloacridinone antitumor agents, C1295 and C1303, have been carried out to compare the conformation of the (aminoalkyl)amino side chain and the effect of C-8 substitution. Crystal data for 5-[2-(diethylamino)ethylamino]-8-methyl-6H-[1,2,3]-triazolo[4,5,1-de]acridin-6-one (C1295), $C_{20}H_{23}N_5O$, $M_r = 349.4$, triclinic, $P\bar{1}$, $a = 12.200$ (1), $b = 14.890$ (1), $c = 5.185$ (1) Å, $\alpha = 93.54$ (1), $\beta = 102.21$ (1), $\gamma = 80.61$ (1)°, $V = 907.9$ (1) Å³, $Z = 2$, $D_x = 1.278$ g cm⁻³, λ(Cu $K\alpha$) = 1.54178 Å, $\mu = 6.2$ cm⁻¹, $F(000) = 372$, $T = 293$ K, $R = 0.061$ for 1631 observed reflections; for 5-[2-(diethylamino)-ethylamino]-8-hydroxy-6H-[1,2,3]triazolo[4,5,1-de]-acridin-6-one (C1303), $C_{17}H_{17}N_5O_2$, $M_r = 323.4$, monoclinic, $P2_1/n$, $a = 15.823$ (2), $b = 5.790$ (1), $c = 16.856$ (2) Å, $\beta = 98.59$ (1)°, $V = 1526.9$ (2) Å³, $Z = 4$, $D_x = 1.404$ g cm⁻³, λ(Cu $K\alpha$) = 1.54178 Å, $\mu = 7.5$ cm⁻¹, $F(000) = 680$, $T = 293$ K, $R = 0.054$ for 1303 observed reflections. There is a difference in the orientation of the (aminoalkyl)amino side chain in the two compounds in the solid state, but molecular dynamics simulations indicate that in the gas phase the orientation is very similar. This difference could result from the different crystal packing in the case of C1303, due to the presence of an intermolecular hydrogen bond. Preliminary drug–DNA modeling studies indicate that the higher biological activity of C1303 may be attributed to the availability of the OH group which could form an extra hydrogen bond with DNA.

Introduction

There has been great interest recently in the development of synthetic antineoplastic agents that complex with DNA (Zee-Cheng & Cheng, 1978; Zee-Cheng, Podrebarac, Mennon & Cheng, 1979; Showalter, Johnson, Werbel, Leopold, Jackson & Elslager, 1984). The availability of a large number of synthetic intercalating antitumor drugs has led to renewed interest in the mode of action of intercalators. Structural studies show that the DNA-intercalating agents currently under development as antitumor drugs share the common structural feature of an aromatic