MOLLIER, Y. (1985). Private communication.
PAULING, L. (1960). *The Nature of the Chemical Bond*, 3rd ed., p. 260. Ithaca, NY: Cornell Univ. Press.
PEDERSEN, C. TH. (1980). *Sulfur Rep.* 1, 1–96.

ROLLETT, J. S. (1965). *Computing Methods in Crystallography*, p. 114. Oxford: Pergamon Press.
TAYLOR, R. & KENNARD, O. (1982). *J. Am. Chem. Soc.* **104**, 5063–5070.

Structural Characteristics of the Hydroxamic Acid Group. Crystal Structure of Formohydroxamic Acid

BY INGRID KJØLLER LARSEN

Department of Chemistry BC, Royal Danish School of Pharmacy, DK-2100 Copenhagen, Denmark

Abstract

CH_3NO_2, $M_r = 61.04$, monoclinic, Cc, $a = 3.636$ (3), $b = 9.745$ (2), $c = 7.512$ (3) Å, $\beta = 116.56$ (4)°, $V = 238.1$ (2) Å^3, $Z = 4$, D_m (293 K) = 1.64, $D_x = 1.703$ Mg m^{-3}, λ(Mo $K\alpha$) = 0.71073 Å, $\mu = 0.154$ mm^{-1}, $F(000) = 128$, $T = 105$ K, final $R = 0.030$ for 995 unique observed reflections. The conformation of O=CH—NH—OH is synperiplanar (sp) with an O=C—N—O torsion angle of 5.4 (4)°. The crystals are stabilized by a network of intermolecular hydrogen bonds. Data for a series of hydroxamic acids, RCONHOH, and hydroxamate ions and ligands have been retrieved from the Cambridge Structural Database. Bond distances and bond angles as well as conformational parameters of the hydroxamic acid moiety have been analyzed. The antiperiplanar (ap) conformation of the O=C—NH—OH moiety is found to be almost as common in crystals as the sp conformation. Only one case of intramolecular OH$\cdots$O bonding in sp conformers was found. Variations in C=O and C—N bond lengths are correlated. Charge delocalization through the entire hydroxamate moiety is observed in the ligands, but not in the ions. Opening of the O=C—N angle is most pronounced in sp conformers of hydroxamic acids. In hydroxamate ligands this angle is less than 120°.

Introduction

Formohydroxamic acid, HCONHOH, has been reported to show an inhibitory effect on several metal-containing enzymes, *e.g.* the iron-containing enzyme ribonucleotide reductase (Kjøller Larsen, Sjöberg & Thelander, 1982), the nickel-containing enzyme urease (Dixon, Hinds, Fihelly, Gazzola, Winzor, Blakeley & Zerner, 1980), and zinc- or manganese-containing aminopeptidases (Wilkes & Prescott, 1983; Baker, Wilkes, Bayliss & Prescott, 1983). The inhibitory effect

of hydroxamic acids on ribonucleotide reductase has been shown to be due to the ability of the compounds to react with (reduce) the tyrosine free-radical group present in the subunit B2 of this enzyme (Kjøller Larsen *et al.*, 1982). Metal chelation is proposed to be important for the inhibitory effect on the other enzymes mentioned above.

An IR and ^{1}H NMR study of formohydroxamic acid and its sodium salt has been reported (Fritz & von Stetten, 1969), but no detailed experimental structural study has been made so far. On the other hand, several theoretical calculations on the geometry of formohydroxamic acid have been performed in recent years. *Ab initio* SCF MO calculations at the 3-21G level, carried out on formohydroxamic acid (Lipczyńska-Kochany & Iwamura, 1982) indicated an sp (synperiplanar) conformation of O=CH—NH—OH with intramolecular O—H$\cdots$O bonding to be energetically most favourable. This is in agreement with the results of Bock, Trachtman & George (1981, 1982) and George, Bock & Trachtman (1983) in their extensive study of small molecules, forming intramolecular hydrogen-bonded four-, five- or six-membered ring systems, by *ab initio* MO calculations, using the 4-31G set. In addition, semiempirical INDO MO calculations (Hilal & Moustafa, 1984) led to the reverse result, as the ap (antiperiplanar) conformation was found to be more stable than the sp conformation, but the INDO method is hardly as reliable as the *ab initio* methods used by the authors mentioned above. Finally, *ab initio* calculations (STO-3G basis set) have been performed on the tautomer form (see below) of formohydroxamic acid ('hydroxyformaldoxime') by Nguyen, Sana, Leroy, Dignam & Hegarty (1980).

Hydroxamic acids exist in solutions as an equilibrium mixture of the two tautomers: RCONHOH (I) $\rightleftharpoons$ RC(OH)=NOH (II), where (I) is the hydroxyamide (or hydroxamic acid) form, and (II) the hydroxyimine (or

hydroximic acid) form (see *e.g.* Artemenko, Anufriev, Tikunova & Exner, 1980; Kolasa, 1983). The hydroxy-amide form (I) is normally found in the crystalline state of the compounds (Kolasa, 1983) and it has been stated (Smith & Raymond, 1980) that the planar *sp* conformation of (I) is the normal solid-state confor-mation of hydroxamic acids.

In order to get a general picture of the geometry of the hydroxamic acid group, as found in the crystalline state, the data of a series of hydroxamic acids have been retrieved from the Cambridge Structural Data-base (CSD, January 1987 release; Allen *et al.*, 1979), and the structural parameters have been analyzed.

Experimental

Formohydroxamic acid was prepared as previously described (Kjøller Larsen *et al.*, 1982). Crystals suitable for X-ray work were obtained by slow evaporation from a solution in chloroform and ethyl acetate. Hygroscopic, rodlike, colourless crystals with *a* as needle axis, m.p. 351–352 K. D_m measured by flotation. Crystal $0.12 \times 0.20 \times 0.40$ mm chosen for data collection on an Enraf–Nonius CAD-4 dif-fractometer equipped with graphite monochromator and Nonius low-temperature device. The temperature was kept at about 105 K and estimated to be correct within ± 5 K; it was kept constant within 0.5 K. Cell dimensions determined by least-squares fit of angular settings of 18 reflections (θ range 17.05–21.35°). Intensities measured using ω–2θ scan method for θ values up to 45° with $h = \pm 7$, $k = 20$, $l = \pm 16$. Three standard reflections measured every 50 reflections showed no significant variations. Intensities of 2396 reflections measured, 1235 of which are unique (R_{int} = 0.02) and 995 reflections with $I \geq 3.0\sigma(I_o)$ were considered observed. No absorption correction. Struc-ture solved by direct methods using *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980). All H atoms located in a difference Fourier map. Full-matrix least-squares refinement of positional parameters of all atoms, with anisotropic temperature factors for non-H atoms and with fixed, isotropic temperature factors for H atoms. Quantity minimized $w(|F_o| - k|F_c|)^2$, where $w = 1.0/|\sigma^2(F_o) + 0.0005(F_o)^2|$. Average and maximum Δ/σ in final refinement cycle 0.06 and 0.9, respectively. Final $R = 0.030$, $wR = 0.035$, with the $\Delta\rho$ fluctuations ± 0.3 e Å^{-3}. Scattering factors for H those of Stewart, Davidson & Simpson (1965), for O, N and C those of Cromer & Mann (1968). Programs used in refinement from *XRAY*76 (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976).

A search in CSD (version II tailored to VAX systems operating under VMS) of the connectivity file yielded 40 entries on hydroxamic acids. Several of these were discarded for different reasons (*e.g.* low accuracy,

disorder of error flag), resulting in 26 entries on hydroxamic acids determined from X-ray diffractom-eter data and with e.s.d.'s for the C–C bonds less than 0.01 Å. Several structural parameters were calculated for the 26 compounds containing 37 hydroxamic acid moieties.

A search in CSD for the hydroxamate ion yielded 11 entries on alkali-metal salts of hydroxamic acids, one on an amine salt and one on a zwitterion. Five of these entries containing 11 hydroxamate moieties ($R^1COR^2NO^-$, substitution at the N atom in all cases) were included in the sample and structural parameters were calculated as for the free acids. Finally, CSD was searched for transition-metal complexes of hydroxamic acids. Of the 45 entries, 24 were discarded resulting in 21 transition-metal entries (57 hydroxamate moieties), determined from X-ray diffractometer data and with e.s.d.'s less than 0.01 Å or $R \leq 0.076$. Two complexes with N,N' ligands rather than O,O' [bis(glycinhydrox-amato)nickel(II), Brown, Roche, Pakkanen, Pakkanen & Smolander (1982), and sodium bis(aminoaceto-hydroxamato-N,N')nickel(II) trihydrate, Julien-Pouzol, Jaulmes, Laruelle, Carvalho & Paniago (1985)] were not included in the sample.

Discussion

The final atomic parameters of formohydroxamic acid are listed in Table 1.* Bond lengths and angles are given in Table 2. The molecular conformation, atomic numbering scheme and packing arrangement are shown in Fig. 1.

The conformation of the formohydroxamic acid molecule in the crystalline state is *sp*, *i.e.* the con-formation calculated to be the energetically most favourable (Lipczyńska-Kochany & Iwamura, 1982; George *et al.*, 1983), but the intramolecular OH···O bond calculated to stabilize the *sp* conformation (by 29.3 and 38.6 kJ mol^{-1}, respectively) does not exist in the crystal, where strong intermolecular OH···O bonding is preferred (*cf.* Fig. 1). On the other hand, this intermolecular hydrogen bonding has not changed the conformation of the heavy-atom chain of the molecule. Conformational changes in going from the isolated molecule to the intermolecularly hydrogen-bonded molecule in the crystal are often observed, *e.g.* in N,N'-diformylhydrazide (Jeffrey, 1984).

---

* Lists of structure factors, anisotropic thermal parameters, CSD reference codes for the hydroxamic acids, hydroxamate ions and ligands, and histograms of C–N–O–H torsion angles, of intra-molecular O···O and O···H distances, of O-to-plane distances, and of O=C–N and C–N–O angles of hydroxamic acids, ions and ligands have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44884 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Fractional atomic coordinates and isotropic thermal parameters

For non-H atoms: $B_{eq} = \frac{1}{3}\sum_i\sum_j B_{ij}a_i^*a_j^*\mathbf{a}_i\cdot\mathbf{a}_j$.

	x	y	z	$B_{eq}/B_{iso}(Å^2)$
O1	0·5000	0·6122 (1)	0·4105	0·93
N2	0·7679 (5)	0·5146 (1)	0·5367 (3)	0·72
C3	0·6613 (5)	0·3850 (1)	0·5044 (3)	0·71
O4	0·3467 (5)	0·3396 (1)	0·3589 (3)	0·77
H1	0·633 (10)	0·677 (3)	0·386 (5)	0·98
H2	0·961 (9)	0·546 (3)	0·656 (4)	0·67
H3	0·853 (9)	0·322 (3)	0·612 (5)	0·62

Table 2. Bond lengths (Å), bond angles (°) and hydrogen-bond geometry (Å, °)

O1–N2	1·388 (2)	O1–H1	0·86 (4)
N2–C3	1·312 (2)	N2–H2	0·91 (3)
C3–O4	1·257 (2)	C3–H3	1·01 (3)

O1–N2–C3	118·3 (1)	H2–N2–C3	123 (2)
N2–C3–O4	125·3 (1)	H3–C3–N2	113 (2)
H1–O1–N2	111 (2)	H3–C3–O4	121 (2)
H2–N2–O1	116 (2)		

X–H$\cdots Y$	$X\cdots Y$	H$\cdots Y$	$\angle X$–H$\cdots Y$	Symmetry code (Y)
O1–H1$\cdots$O4	2·662 (2)	1·82 (3)	166 (4)	$x+\frac{1}{2}, y+\frac{1}{2}, z$
N2–H2$\cdots$O4	2·784 (3)	1·90 (3)	163 (3)	$x+1, -y+1, z+\frac{1}{2}$

Other short distances

N2–H2$\cdots$O1	3·133 (3)	2·55 (3)	122 (2)	$x+1, -y+1, z+\frac{1}{2}$
C3–H3$\cdots$O1	3·207 (3)	2·50 (3)	127 (2)	$x+1, -y+1, z+\frac{1}{2}$
C3–H3$\cdots$O4	3·276 (3)	2·44 (3)	140 (3)	$x+\frac{1}{2}, \frac{1}{2}-y, z+\frac{1}{2}$
C3–H3$\cdots$O1	3·140 (2)	2·73 (3)	104 (2)	$x+\frac{1}{2}, y-\frac{1}{2}, z$

The torsion angle O=C–N–O in the crystal of formohydroxamic acid is 5·4 (4)°, showing that the molecular skeleton is not quite planar, but still planar enough to allow interaction with the free-radical group of the enzyme ribonucleotide reductase (Kjøller Larsen et al., 1982). The average deviation from the least-squares plane through the C, N and O atoms is 0·015 (3) Å (deviations of H atoms not included).
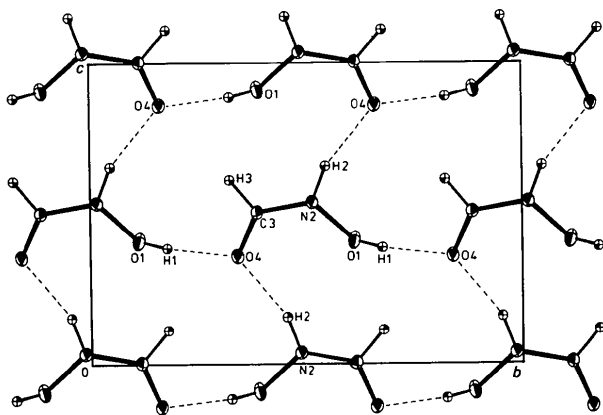

Fig. 1. The structure of formohydroxamic acid viewed along the a^* axis.

Table 3. Comparison of experimental (E) and theoretical (T) bond lengths (Å) and angles (°) of formohydroxamic acid

	Experimental[a]	Theoretical[b]		$\Delta(E-T)^{b,c}$	$\Delta(E-T)^{c,d}$
C=O	1·257	1·220	1·222	+37 +35	+31 (acetamide)
C–N	1·312	1·339	1·334	−27 −22	−23 (acetamide)
N–O	1·388	1·441	1·413	−53 −25	−54 (glyoxime)
∠O=C–N	125·3	—	122·8	— +2·5	Average +1·4
∠C–N–O	118·3	—	119·5	— −1·2	Average ±1·4

Notes: (a) this study; (b) left from Lipczyńska-Kochany & Iwamura (1982), right from C. W. Bock (personal communication); (c) $\Delta(E-T)$ in Å × 10³ or in °; (d) from Jeffrey (1984).

In addition to OH$\cdots$O hydrogen bonds, the molecules of formohydroxamic acid are connected by NH$\cdots$O bonds (cf. Fig. 1 and Table 2). Three short CH$\cdots$O distances were also found, two of which should probably be defined as hydrogen bonds, as the conditions for CH$\cdots$O bonds defined by Taylor & Kennard (1982) are fulfilled.

Bond lengths and angles of formohydroxamic acid do not deviate much from the mean values obtained for a series of hydroxamic acids from CSD (see below). Direct comparison of the experimental values with those obtained by ab initio MO calculations (Lypczyńska-Kochany & Iwamura, 1982; George et al., 1983; C. W. Bock, personal communication) cannot be made without corrections, e.g. for thermal motion and hydrogen-bonding effects (cf. Jeffrey, 1984, 1985). However, the differences between the experimental and theoretical bond lengths, $\Delta(E-T)$ (Table 3), are comparable with the values found by Jeffrey (1984) for similar small molecules. It appears from Table 3 that the carbonyl bond is found to be longer in the crystal than in the isolated molecule. The C=O bond lengthening in the crystal is probably due to hydrogen bonding (Jeffrey, 1984), the effect being more pronounced the more H bonds the carbonyl O atom accepts. This is also in accordance with the findings of Taylor, Kennard & Versichel (1984), based on an analysis of the data of hydrogen bonds from a large series of compounds in CSD.

The negative values of $\Delta(E-T)$ for the C–N bond indicate bond shortening in the crystal. This is probably due to strong intermolecular NH$\cdots$O bonding (Jeffrey, 1984). The largest discrepancies between experimental and calculated bond lengths are found for the N–O bond as in the studies of Jeffrey. Disagreements between experimental and calculated bond angles are normally found to be small, see Table 3.

Geometry of the hydroxamic acid (HA) group

Analysis of the data retrieved from CSD showed that the assumption of sp conformation as the normal solid-state conformation of hydroxamic acids (Smith & Raymond, 1980) is incorrect. Of the 37 HA moieties in the sample, 20 adopt sp conformation (~54%) and 17

adopt *ap* conformation (~46%), the O=C—N—O torsion angles being $0\pm1\cdot2°$, and $180\pm17°$, respectively (Fig. 2*a*). In 12 of the 20 *sp* conformers, however, the HA moiety is built into a five- or six-membered ring and therefore has to be in the *sp* conformation. Of the 25 HA moieties in which free rotation on the C—N bond is possible, only eight (~32%) have preferred to crystallize in the *sp* conformation. No other conformations (*sc* or *ac*) were found.

As illustrated in Fig. 2(*b*) only two of the 11 hydroxamate moieties in alkali or amine salts of HA's are found to adopt *ap* conformations. The conformation of *O,O'* hydroxamate ligands of the transition-metal complexes (Fig. 2*b*) have to be *sp*. The O=C—N—O torsion angles are distributed in a more narrow range (0 ± 6)° than those of the free HA's.

An analysis of the data of the 15 *sp* HA moieties for which H-atom parameters are available showed that intramolecular OH···O bonding occurs in only one of the compounds [a hydroxypyridinone, Scarrow, Riley, Abu-Dari, White & Raymond (1985)]. In all of the HA moieties the O···O distances are in a range suitable for O—H···O bonding,* but only in the compound mentioned above does the H atom of the OH group have contact with the carbonyl O atom, the H···O distance
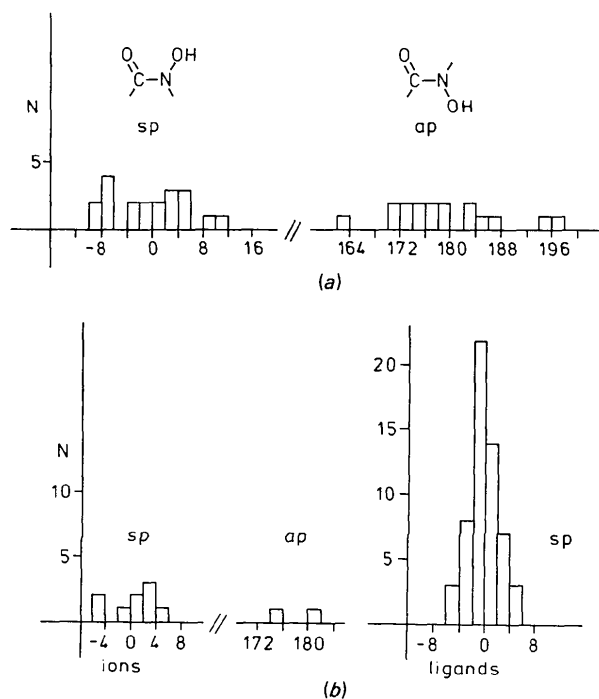
---

* See deposition footnote.

(a)

(b)

Fig. 2. Histograms of O=C—N—O torsion angles (°) of (*a*) *sp* and *ap* conformers of hydroxamic acids and (*b*) hydroxamate ions (alkali salts) and hydroxamate ligands (transition-metal complexes).

being 1·98 Å, and the C—N—O—H torsion angle being 6°. In all other cases the O—H bond is turned out of the plane of the HA group, the C—N—O—H torsion angles being ±(50–140)°, and is probably part of inter- rather than intramolecular hydrogen bonding. This finding was rather surprising, but in accordance with Kroon (1982), who found no evidence suggesting intramolecular hydrogen bonding in α-hydroxycarboxylic acids with *sp* conformation of the O=C—C—OH moiety. The possibility for intermolecular hydrogen bonding is evidently the most important factor determining the conformation in crystals of molecules with strong hydrogen-bonding functional groups (Jeffrey, 1984, 1985).

The intramolecular O···O distances of the *sp* hydroxamate ions are in the same range as those of the HA's. The mean value is in both cases 2·68 (2) Å. The O···O distances of the hydroxamate ligands, on the other hand, are considerably shorter, the mean value being 2·533 (5) Å. The O···Tr···O angles are 70·0–81·2°, the NO···Tr distances 1·938–2·121 Å, and the CO···Tr distances 1·971–2·274 Å (where Tr denotes a transition-metal atom: Ti, Cr, Fe, Zn, Mo, Rh or Hf).

The HA moieties are in most cases not quite planar. The deviations of each of the atoms from the least-squares planes defined by *X*—(C=O)—N(*X*)—O are |0–0·240| Å (*X* denotes C, N or H). In order to investigate further this non-planarity, the least-squares planes were calculated with only the four atoms *X*—(C=O)—N defining the planes. These four atoms are in all of the HA's coplanar within |0–0·025| Å, while the O atoms of the hydroxyl groups deviate more or less from these planes. The *sp* conformers are in general slightly more planar than the *ap* conformers, the mean O-to-plane distances being 0·105 (3) and 0·152(5)Å, respectively.* The hydroxamate ions and ligands show a higher tendency to planarity than the HA's, probably because of increased possibilities for π-electron delocalization in the charged groups. The mean O-to-plane distances of ions and ligands are 0·065 (3) and 0·056 (1) Å, respectively.

The non-planarity of the HA moieties can be seen as a consequence of more or less pyramidalization of the N atom, and, much more slightly, of the carbonyl C atom. The distances of the N atoms to the planes formed by the three bonded atoms are |0–0·303| Å [mean 0·11 (2) Å] for the HA's, |0–0·71| Å [mean 0·03 (1) Å] for hydroxamate ions, and |0–0·089| Å [mean 0·037 (6) Å] for hydroxamate ligands. The corresponding distances of the carbonyl C atoms to the planes formed by the three bonded atoms are |0–0·025|Å [mean 0·007 (1) Å] for the HA's, and |0–0·10| Å [mean 0·004 (2) Å] and |0–0·065| Å [mean 0·011 (2) Å] for the hydroxamate ions and ligands, respectively.

---

* See deposition foonote.

Table 4. *Analysis of variations in bond lengths* (Å)

N = number of observations, μ = sample mean, δ = estimated sample standard deviation.

	N	μ	δ
C=O bond			
All HA's	37	1·230 (2)	0·015
sp conformers	20	1·223 (4)	0·016
ap conformers	17	1·238 (2)	0·008
Anions	11	1·232 (5)	0·018
Ligands	57	1·277 (2)	0·016
C—N bond			
All HA's	37	1·355 (5)	0·028
sp conformers	20	1·358 (7)	0·031
ap conformers	17	1·351 (6)	0·023
Anions	11	1·378 (8)	0·027
Ligands	57	1·322 (3)	0·021
N—O bond			
All HA's	34	1·393 (2)	0·011
sp conformers	17	1·389 (2)	0·010
ap conformers	17	1·400 (2)	0·009
Anions	11	1·379 (4)	0·014
Ligands	57	1·376 (1)	0·010

The C=O bond

The variations in the length of this bond are shown in Table 4 and Fig. 3(a). The mean value for the free HA's (1·230 Å) is in agreement with the length of the typical amide C=O bond (~1·23 Å) as found in a CSD search by Schweizer & Dunitz (1982). Table 4 shows that the carbonyl bonds of *ap* conformers are significantly longer than those of *sp* conformers. The reason is probably not increased π-electron delocalization, as the C—N bonds of *ap* conformers are only slightly shorter than those of *sp* conformers.

Investigation of the intermolecular O···X distances (X = O, N), on the other hand, showed that the carbonyl O atoms of *ap* conformers accept more hydrogen bonds than the carbonyl O atoms of *sp* conformers (1·50 per C=O against 1·25), leading to lengthening of the C=O bonds of *ap* conformers (*cf.* discussion of the formohydroxamic acid structure).

The lengths of the carbonyl bonds of the hydroxamate ions (Table 4) are not significantly different from those of the free HA's. The C=O bonds of the HA ligands, on the other hand, are considerably longer because of interactions with the transition-metal atoms and π-electron delocalization.

The C—N bond

Table 4 and Fig. 3(b) show that the lengths of the C—N bonds of HA's are distributed in a broader range than the other bonds of the HA moiety. The mean value for the HA's (1·355 Å) shows that this bond is generally longer than the C—N bonds of amides (1·322–1·346 Å, Schweizer & Dunitz, 1982), but the mean value for the nine HA's with unsubstituted N

atoms [1·332 (6) Å] is close to the values found for secondary amides (1·331–1·332 Å, Schweizer & Dunitz, 1982). Hydrogen bonding is probably the reason for the shortening of this bond compared to the N-substituted HA's. The variations in C—N and C=O bond lengths are correlated (Fig. 4), reflecting π-electron delocalization. No correlations with other parameters, *e.g.* N—O bond lengths, were found.

The longest C—N bonds are found in the 11 hydroxamate ions, indicating that the negative charge is not delocalized to this bond. The shortest C—N bonds are those of the hydroxamate ligands, in which π-electron delocalization seems to be most pronounced, also in accordance with the highest degree of planarity.
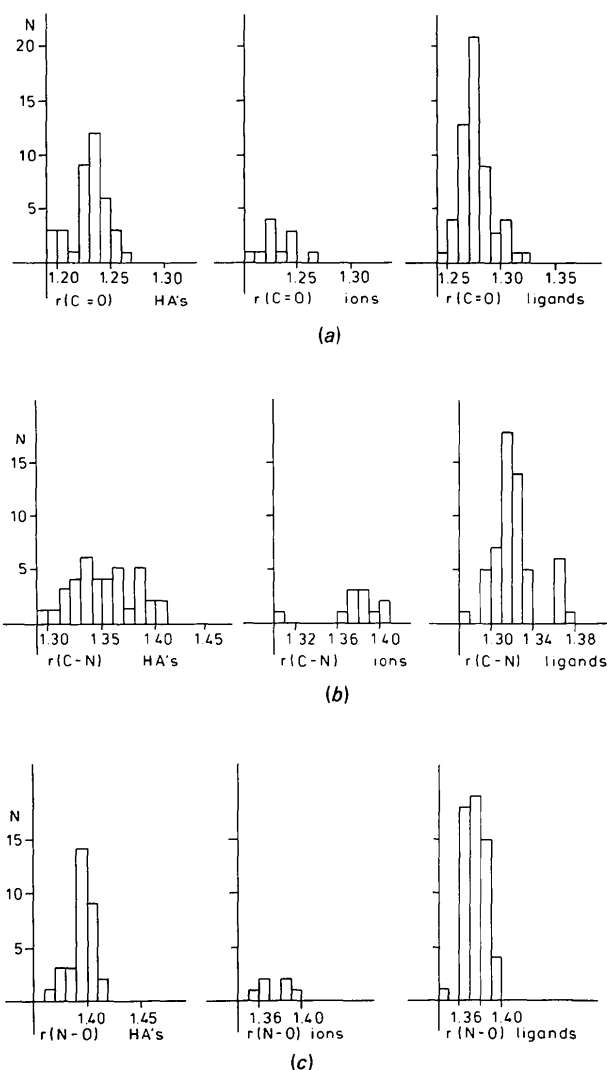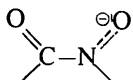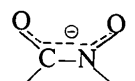

Fig. 3. Histograms of (a) C=O bond lengths, (b) C—N bond lengths, and (c) N—O bond lengths (Å) of HA's, hydroxamate ions and ligands.

The N—O bond

The lengths of the N—O bonds of *ap* and *sp* HA's do not differ significantly, whereas the N—O bonds of hydroxamate ions and ligands are significantly shorter, reflecting more or less delocalization of the negative charge. Thus, the hydroxamate ions and ligands can

probably be represented by the formulas $\overset{O}{\underset{}{C-N}}\overset{\ominus O}{\underset{}{}}$

and $\overset{O \quad \ominus \quad O}{\underset{}{C-N}}$, respectively, *cf*. discussions on C—N and C=O bond lengths.

The bond angles

Variations in the O=C—N and C—N—O bond angles of the HA moiety are shown in Table 5. For nearly all *sp* and *ap* conformers of the HA's and hydroxamate ions the O=C—N angle is found to be larger than the C—N—O angle. The opening of the O=C—N angle is most pronounced in the *sp* conformers, where angles up to 125·9° occur, probably because of repulsion between the two *cis*-situated O atoms. In hydroxamate ligands the difference between the two angles is very small, and both angles are < 120°. Compression of the angles may be due to interactions of the O atoms with the transition-metal atoms and/or steric conditions.

The dimensions of formohydroxamic acid in the present structure agree fairly well with the results of the CSD analysis of the HA's. As can be seen from Table 2

Table 5. *Analysis of variations in bond angles* (°)

N = number of observations, μ = sample mean, δ = estimated sample standard deviation.

	N	μ	δ
∠C—N—O			
All HA's.	37	117·9 (4)	2·3
sp conformers	20	118·5 (6)	2·5
ap conformers	17	117·2 (5)	2·1
Anions	11	118·1 (9)	3·1
Ligands	57	116·5 (2)	1·5
∠O=C—N			
All HA's	37	121·6 (4)	2·2
sp conformers	20	122·6 (5)	2·4
ap conformers	17	120·4 (3)	1·1
Anions	11	121·6 (6)	2·1
Ligands	57	117·8 (2)	1·2

and Fig. 4(*a*) the C=O bond is among the longer ones, and the C—N bond is very short, indicating strong π-electron delocalization in this molecule. The length of the N—O bond is within the accuracy equal to the mean value for *sp* conformers (Table 4). The O=C—N angle in formohydroxamic acid is one of the largest found, see Tables 2 and 5.

References

ALLEN, F. H., BELLARD, S., BRICE, M. D., CARTWRIGHT, B. A., DOUBLEDAY, A., HIGGS, H., HUMMELINK, T., HUMMELINK-PETERS, B. G., KENNARD, O., MOTHERWELL, W. D. S., RODGERS, J. R. & WATSON, D. G. (1979). *Acta Cryst.* B35, 2331–2339.

ARTEMENKO, A. I., ANUFRIEV, E. K., TIKUNOVA, I. V. & EXNER, O. (1980). *Zh. Prikl. Spektrosk.* 33, 131–135; *Chem. Abstr.* 94, 46316b.

BAKER, J. O., WILKES, S. H., BAYLISS, M. E. & PRESCOTT, J. M. (1983). *Biochemistry*, 22, 2098–2103.

BOCK, C. W., TRACHTMAN, M. & GEORGE, P. (1981). *Chem. Phys.* 62, 303–318.

BOCK, C. W., TRACHTMAN, M. & GEORGE, P. (1982). *J. Comput. Chem.* 3, 512–524.

BROWN, D. A., ROCHE, A. L., PAKKANEN, T. A., PAKKANEN, T. T. & SMOLANDER, K. (1982). *J. Chem. Soc. Chem. Commun.* pp. 676–677.

CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A24, 321–324.

DIXON, N. E., HINDS, J. A., FIHELLY, A. K., GAZZOLA, C., WINZOR, D. J., BLAKELEY, R. L. & ZERNER, B. (1980). *Can. J. Biochem.* 58, 1323–1334.

FRITZ, H. P. & VON STETTEN, O. E. (1969). *Z. Naturforsch. Teil B*, 24, 947–949.

GEORGE, P., BOCK, C. W. & TRACHTMAN, M. (1983). *J. Mol. Struct. Theor. Chem.* 92, 109–139.

HILAL, R. & MOUSTAFA, H. (1984). *Int. J. Quantum Chem.* 26, 183–196.

JEFFREY, G. A. (1984). *J. Mol. Struct. Theor. Chem.* 108, 1–15.

JEFFREY, G. A. (1985). *J. Mol. Struct. Theor. Chem.* 130, 43–53.

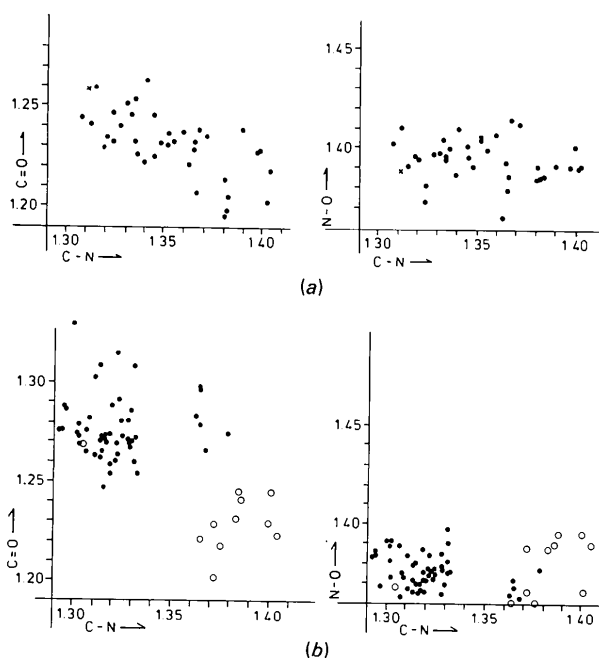JULIEN-POUZOL, M., JAULMES, S., LARUELLE, P., CARVALHO, S. & PANIAGO, E. D. (1985). *Acta Cryst.* C41, 712–715.

Fig. 4. Scatterplots of C—N bond lengths *versus* C=O and N—O bond lengths (Å) of (*a*) the HA's (× present study), and (*b*) the hydroxamate ions (○) and ligands (●).

KjØller Larsen, I., Sjöberg, B.-M. & Thelander, L. (1982). *Eur. J. Biochem.* **125**, 75–81.

Kolasa, T. (1983). *Tetrahedron*, **39**, 1753–1759.

Kroon, J. (1982). *Molecular Structure and Biological Activity*, edited by J. F. Griffin & W. L. Duax. Amsterdam: Elsevier.

Lipczyńska-Kochany, E. & Iwamura, H. (1982). *J. Org. Chem.* **47**, 5277–5282.

Main, P., Fiske, S. J., Hull, S. E., Lessinger, L., Germain, G., Declercq, J.-P. & Woolfson, M. M. (1980). *MULTAN80. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

Nguyen, M.-T., Sana, M., Leroy, G., Dignam, K. J. & Hegarty, A. F. (1980). *J. Am. Chem. Soc.* **102**, 573–580.

Scarrow, R. C., Riley, P. E., Abu-Dari, K., White, D. L. & Raymond, K. N. (1985) *Inorg. Chem.* **24**, 954–967.

Schweizer, W. B. & Dunitz, J. D. (1982). *Helv. Chim. Acta.* **65**, 1547–1562.

Smith, W. L. & Raymond, K. N. (1980). *J. Am. Chem. Soc.* **102**, 1252–1255.

Stewart, J. M., Machin, P. A., Dickinson, C. W., Ammon, H. L., Heck, H. & Flack, H. (1976). *The XRAY76 system.* Tech. Rep. TR-446. Computer Science Center, Univ. of Maryland, College Park, Maryland, USA.

Stewart, R. F., Davidson, E. R. & Simpson, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

Taylor, R. & Kennard, O. (1982). *J. Am. Chem. Soc.* **104**, 5063–5070.

Taylor, R., Kennard, O. & Versichel, W. (1984). *Acta Cryst.* **B40**, 280–288.

Wilkes, S. H. & Prescott, J. M. (1983). *J. Biol. Chem.* **258**, 13517–13521.

Crystal Structures and Photochemistry of α-Cyclopentyl-4-carboxypropiophenone* and α-Cyclooctyl-4-carboxypropiophenone†–Acetic Acid (1:1 Mixed Carboxylic Acid Dimer)

By Stephen V. Evans and James Trotter

Department of Chemistry, University of British Columbia, Vancouver, BC, Canada V6T 1Y6

Abstract

The structures and photochemistry of two α-cycloalkylpropiophenones have been studied for comparison with related acetophenones. Crystal data: Cu $K\alpha_1$, $\lambda = 1\cdot54056$ Å, $T = 295$ K; cyclopentyl derivative, $C_{15}H_{18}O_3$, $M_r = 246\cdot31$, triclinic, $P\bar{1}$, $a = 5\cdot867$ (1), $b = 10\cdot291$ (1), $c = 11\cdot583$ (2) Å, $\alpha = 87\cdot43$ (1), $\beta = 80\cdot11$ (1), $\gamma = 78\cdot25$ (1)°, $V = 674\cdot5$ (5) Å³, $Z = 2$, $D_x = 1\cdot212$ g cm⁻³, $\mu = 6\cdot4$ cm⁻¹, $F(000) = 264$, $R = 0\cdot076$ for 1328 reflections; cyclooctyl derivative, $C_{18}H_{24}O_3.C_2H_4O_2$, $M_r = 348\cdot44$, triclinic, $P\bar{1}$, $a = 7\cdot1567$ (5), $b = 7\cdot7031$ (5), $c = 18\cdot1728$ (2) Å, $\alpha = 97\cdot162$ (5), $\beta = 94\cdot670$ (6), $\gamma = 104\cdot331$ (6)°, $V = 956\cdot5$ (1) Å³, $Z = 2$, $D_x = 1\cdot209$ g cm⁻³, $\mu = 6\cdot6$ cm⁻¹, $F(000) = 376$, $R = 0\cdot044$ for 1586 reflections. The α-methyl substituents have resulted in large changes in molecular conformation relative to the acetophenone analogues, with rotations of about 100° about the C(carbonyl)—C(α) bonds, and rotations of the carbonyl groups out of the aromatic planes by 27°. The cyclopentyl ring is disordered over two envelope conformations and the cyclooctyl ring has a boat–chair

---

* α-Cyclopentyl-α-methyl-4-carboxyacetophenone; 1-(4-carboxyphenyl)-2-cyclopentylpropan-1-one; 4-(2-cyclopentylpropionyl)-benzoic acid.

† α-Cyclooctyl-α-methyl-4-carboxyacetophenone; 1-(4-carboxyphenyl)-2-cyclooctylpropan-1-one; 4-(2-cyclooctylpropionyl)-benzoic acid.

conformation; the propiophenone moieties occupy equatorial sites on the cycloalkyl rings, with molecular parameters being favourable for photochemical reaction *via* hydrogen abstraction. The photoproduct ratios are relatively insensitive to reaction medium, with a trend to increased amounts of cyclization products with increasing cycloalkyl ring size. The cyclopentyl crystal structure contains the usual hydrogen-bonded carboxylic acid dimers, but the cyclooctyl compound exhibits an unusual arrangement, each α-cyclooctyl-4-carboxypropiophenone molecule forming a pair of hydrogen bonds with an acetic acid molecule, *i.e.* the structure contains a mixed acid dimer.

Introduction

Previous crystal structure studies of α-cycloalkylacetophenones (Fig. 1, Z = H) have given detailed information on the structural aspects of the photochemical fragmentation or cyclization reactions (Norrish type II reaction) in the solid state and in solution (Evans & Trotter, 1988a,b). These reactions are believed to proceed *via* γ-H abstraction to give a 1,4-biradical, which either undergoes cleavage of the α–β bond to yield cycloalkene and acetophenone, or cyclizes to cyclobutanols (Fig. 2). Correlation of the structural and photochemical data leads to several important conclusions. (1) The acetophenone grouping occupies an equatorial site on the non-planar cycloalkyl ring in all