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Lone-Pair Repulsion in Cyclic Hydroxamic Acid *O*-Esters: *N*-Cyclohexyloxy-2(1*H*)-pyridone

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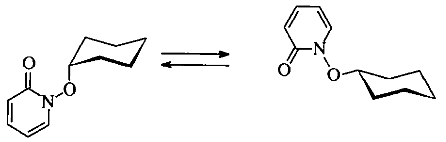
Abstract

The solid-state geometry of the title compound, $C_{11}H_{15}NO_2$, shows a planar pyridone ring. The carbocyclic ring adopts a chair conformation with its substituent located in an axial position. The alkyl substituent of the title compound is twisted by 79.0 (2)° out of the heterocyclic plane. These findings may be interpreted as a consequence of lone-pair repulsion on the adjacent N and O heteroatoms in the hydroxamate moiety. This repulsion will be at its maximum if the C—N—O—C atoms form a plane.

Comment

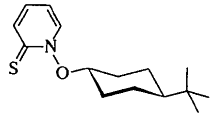
A study of the solution and solid-state geometries of an *N*-alkoxypyridone and its thio analogue, the pyridinethione (2), explains several structural features of both classes of compounds (Hartung, Hiller, Schwarz, Svoboda & Fuess, 1996). Cyclic thiohydroxamic acid esters such as (2) are of current interest in organic chemistry because they are efficient sources of alkoxyl radicals in solution (Hartung & Gallou, 1995; Beckwith & Hay, 1988). The most exciting observation in the previous study on pyridones and on pyridinethiones was that the dihedral angle between the N1—O1—C7 plane and the plane of the heterocyclic rings has always been close to 90° (Hartung *et al.*, 1996). In general, these results indicate that the pyridones, which are by far more stable and convenient to handle than the light-sensitive and thermally-labile pyridinethiones, could be ideally suited for further study of the structural properties of cyclic thiohydroxamates such as (2). Unfortunately, the alkyl residues at the pyridone and at the pyridinethione rings in the previous study were structurally very different. According to a search of the Cambridge Structural Database (Allen, Kennard & Taylor, 1983), no cycloaliphatic ester of the parent acid 1-hydroxy-2(1*H*)-pyridone has been studied previously in the solid state. Thus, we have determined the structure of *N*-cyclohexyloxy-2(1*H*)-pyridone, (1), by X-ray diffraction.

(1)



(1*a*)
axial
Solid state

(1*b*)
equatorial
Solution



(2)

The geometry of the cyclohexyloxypyridone (1) is shown in Fig. 1 and the packing of the ester, (1*a*), as viewed along the crystallographic *z* axis is given in Fig. 2. The N1—O1 axis in *N*-alkoxypyridones is stereogenic unless rotation about this bond occurs, which is unlikely to happen in the solid state. Thus, two enantiomeric esters, (1*a*), exist which differ only in the sign of the torsion angle C2—N1—O1—C7. According to the rules of nomenclature, the enantiomer which is shown in Fig. 1 [C2—N1—O1—C7 79.0 (2)°] has the absolute configuration *M* along the N1—O1 axis (Prelog & Helmchen, 1982). The unit cell, however, shows a 1:1 ratio of the *P* and *M* isomers of (1*a*). The heterocyclic core in (1*a*) is planar [N1—C2—C3—C4 0.7 (3), C2—C3—C4—C5 −1.5 (4) and C3—C4—C5—C6 0.0 (4)°]. As a result of the presence of the hydroxamate group, this ring is slightly distorted from a regular hexagon. The bond angles of the substituents at the carbonyl C atom C2 deviate from 120° [N1—C2—C3 112.4 (2), C2—C3—C4 122.4 (3) and C2—N1—C6 126.4 (2)°]. These findings are also reflected in the coupling constants of vicinal protons in the NMR spectrum of (1) in $CDCl_3$ solution which are larger between H3 and H4 (J = 10 Hz) than between the residual vicinal protons (J = 7 Hz). The bond length of the carbonyl group [C2═O2 1.233 (3) Å] compares well with the corresponding values in previously investigated cyclic hydroxamate esters or with open-chain hydroxamic acids (Hartung *et al.*, 1996; Larsen & Trickey, 1995). The torsion angle C2—N1—O1—C7 [79.0 (2)°] indicates that the cyclohexyl moiety is twisted out of the heterocyclic plane, which is similar to the situation in the thio derivative (2) [C2—N1—O1—C7 84.4 (6)°]. These observations can be rationalized as a consequence of the lone-pair repulsion on the adjacent N and O heteroatoms in the hydroxamate moiety which will be at a maximum if C2—N1—O1—C7 formed a plane.

The packing of the pyridone (1*a*) in the solid state is shown in Fig. 2. The molecules are arranged in layers.

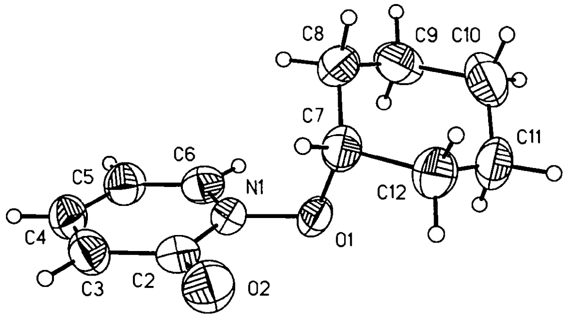


Fig. 1. Molecular structure of *N*-cyclohexyloxy-2(1*H*)-pyridone, (1*a*). Displacement ellipsoids are plotted at the 50% probability level.

The hydrocarbon residues and the pyridone moieties point towards the respective part of the structure in adjacent molecules. Obviously, this arrangement forces the pyridone ring into the axial position of the substituted cyclohexane and imposes conformational strain onto the cycloaliphatic part of the structure. Thus, the cyclohexane ring of (1*a*) is slightly flattened at C7 [C8—C7—C12—C11 49.1 (3) and C12—C7—C8—C9 −50.5 (3)°]. In contrast to the structure of (1*a*) in the condensed phase, the major conformer of (1) in $CDCl_3$ solution at 298 K is the equatorially monosubstituted cyclohexane (1*b*) (^1H NMR analysis).

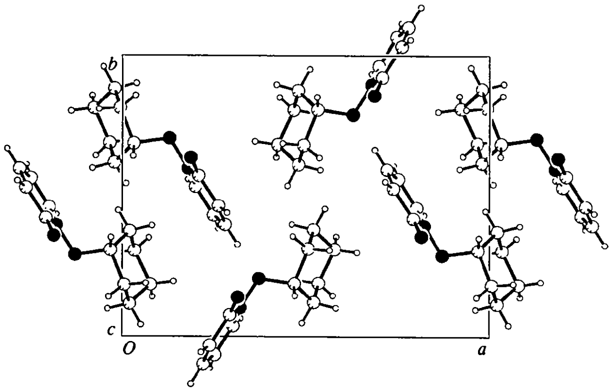
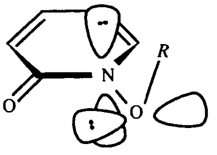


Fig. 2. View of the packing of *N*-cyclohexyloxy-2(1*H*)-pyridone, (1*a*), along the crystallographic *z* axis.



$R = c\text{-}C_6H_{11}$

Fig. 3. Schematic representation of a model of the origin of the alkyl twist out of the heterocyclic plane in cyclic hydroxamic acid derivatives due to a minimization of the lone-pair repulsion on O and one N atom.

In conclusion, the solid-state structure of *N*-cyclohexyloxypyridone (1*a*) shows comparable geometrical parameters in the heterocyclic cores (bond lengths, bond and torsion angles) to the pyridinethione (2). Differences between compounds (1) and (2) originate mainly from the different packing of the more flexible alkyl residue in the monosubstituted cyclohexane derivative (1*a*). Further research will uncover whether pyridones are similar to the thio derivatives as efficient sources of free alkoxyl radicals in solution (Hartung & Gallou, 1995).

Experimental

N-Cyclohexyloxy-2(1*H*)-pyridone, (1), was prepared by heating 2-ethoxypyridine 1-oxide (Paquette, 1965) (2.00 g, 0.014 mol) and cyclohexyl bromide (20.0 g, 0.120 mol) for 3 h at 423 K. The resulting oil was crystallized from ethyl acetate–petroleum ether to afford the title compound (1) (1.20 g, 0.006 mol). Yield 44% (m.p. 353–355 K). Calculated: C 68.37, H 7.82, N 7.25%; found: C 68.02, H 8.26, N 7.17%. UV/Vis (EtOH): λ_{max} (ε) = 304 nm (5400), 230 (6100). ^1H NMR (250 MHz, $CDCl_3$): δ_H = 1.23–1.49 (*m*, 6H, CH_2), 1.74–1.84 (*m*, 2H, CH_2), 1.96–2.01 (*m*, 2H, CH_2), 4.49 (*tt*, *J* = 4, 10 Hz, 1H, CH), 6.06 (*td*, J_d = 2 Hz, J_t = 7 Hz, 1H, CH), 6.65 (*ddd*, *J* = 1, 2, 10 Hz, 1H, CH), 7.47 (*ddd*, *J* = 2, 6, 10 Hz, 1H, CH), 7.72 (*ddd*, *J* = 1, 2, 7 Hz, 1H, CH). ^{13}C NMR (63 MHz, $CDCl_3$): δ_C = 23.8, 25.4, 30.5, 83.5, 104.3, 122.8, 137.5, 138.3, 150.3.

Crystal data

$C_{11}H_{15}NO_2$
M_r = 193.27
Orthorhombic
$Pna2_1$
a = 14.486 (2) Å
b = 11.1562 (7) Å
c = 6.373 (2) Å
V = 1029.9 (4) Å^3
Z = 4
D_x = 1.246 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.7107 Å
Cell parameters from 25 reflections
θ = 2.80–11.94°
μ = 0.078 mm^{-1}
T = 295 (2) K
Needle
0.88 × 0.10 × 0.10 mm
Colourless

Data collection

Enraf–Nonius Turbo-CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: empirical ψ scans (North, Phillips & Mathews, 1968)
T_{min} = 0.961, T_{max} = 0.990
1552 measured reflections
1290 independent reflections

1173 reflections with $I > 2\sigma(I)$
R_{int} = 0.010
θ_{max} = 23°
$h = -1 \rightarrow 15$
$k = -1 \rightarrow 12$
$l = -7 \rightarrow 4$
3 standard reflections frequency: 90 min intensity decay: 1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.092

$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.196 e Å^{-3}
$\Delta\rho_{min}$ = −0.149 e Å^{-3}

$S = 1.114$
1290 reflections
128 parameters
H atoms refined using a riding model
$w = 1/[\sigma^2(F_o^2) + (0.0624P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
Extinction correction: *SHELXL*93
Extinction coefficient: 0.013 (4)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °)*

C2—O2	1.233 (3)	C7—C8	1.502 (4)
C2—N1	1.373 (3)	C7—C12	1.514 (3)
C2—C3	1.442 (3)	C8—C9	1.505 (4)
C3—C4	1.336 (4)	C9—C10	1.523 (4)
C4—C5	1.387 (4)	C10—C11	1.517 (4)
C5—C6	1.362 (3)	C11—C12	1.501 (4)
C6—N1	1.362 (3)	N1—O1	1.404 (2)
C7—O1	1.479 (3)		
O2—C2—N1	121.8 (2)	N1—C6—C5	118.4 (2)
O2—C2—C3	125.8 (2)	C6—N1—C2	126.4 (2)
N1—C2—C3	112.4 (2)	C6—N1—O1	116.4 (2)
C4—C3—C2	122.4 (3)	C2—N1—O1	117.1 (2)
C3—C4—C5	121.2 (2)	N1—O1—C7	110.15 (14)
C6—C5—C4	119.1 (2)		
O2—C2—C3—C4	−177.3 (3)	C8—C9—C10—C11	−56.3 (3)
N1—C2—C3—C4	0.7 (3)	C9—C10—C11—C12	55.6 (3)
C2—C3—C4—C5	−1.5 (4)	C8—C7—C12—C11	49.1 (3)
C3—C4—C5—C6	0.0 (4)	C5—C6—N1—C2	−3.1 (3)
C4—C5—C6—N1	2.1 (3)	C5—C6—N1—O1	−179.7 (2)
C12—C7—C8—C9	−50.5 (3)	O2—C2—N1—O1	−3.6 (3)
C7—C8—C9—C10	54.5 (3)	C2—N1—O1—C7	79.0 (2)

Data collection: *CAD*-4 *Express* (Enraf–Nonius, 1994). Cell refinement: *CAD*-4 *Express*. Data reduction: *CAD*-4*red* (Geselle, 1994). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1985). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *Xtal*3.2 (Hall, Flack & Stewart, 1992).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: KA1240). Services for accessing these data are described at the back of the journal.

References

Allen, F. H., Kennard, O. & Taylor, R. (1983). *Acc. Chem. Res.* **16**, 146–153.
Beckwith, A. L. J. & Hay, B. P. (1988). *J. Org. Chem.* **54**, 4330–4334.
Enraf–Nonius (1994). *CAD*-4 *Express*. Version 5.1/1.2. Enraf–Nonius, Delft, The Netherlands.
Geselle, M. (1994). *CAD-4red. Data Reduction Program for Enraf–Nonius CAD-4*. PhD thesis, Technische Hochschule Darmstadt, Germany.
Hall, S. R., Flack, H. D. & Stewart, J. M. (1992). Editors. *Xtal*3.2 *Reference Manual*. Universities of Western Australia, Australia, Geneva, Switzerland, and Maryland, USA.
Hartung, J. & Gallou, F. (1995). *J. Org. Chem.* **60**, 6710–6716.
Hartung, J., Hiller, M., Schwarz, M., Svoboda, I. & Fuess, H. (1996). *Liebigs Ann.* pp. 2091–2097.
Larsen, I. K. & Trickey, P. (1995). *Acta Cryst.* **C51**, 125–127.
North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* **A24**, 351–359.
Paquette, L. A. (1965). *J. Am. Chem. Soc.* **87**, 5186–5190.
Prelog, V. & Helmchen, G. (1982). *Angew. Chem.* **94**, 614–631; *Angew. Chem. Int. Ed. Engl.* **21**, 567–620.
Sheldrick, G. M. (1985). *SHELXS86. Program for the Solution of Crystal Structures*. University of Göttingen, Germany.
Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.

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Hydrogen Bonding in 1-Hydroxy-4(1*H*)-pyridinethione

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Abstract

The crystal lattice of the title compound, C_5H_5NOS, a vinylogous cyclic thiohydroxamic acid, comprises a network of hydrogen bonds [O—H 1.16 (3), O···S 2.971 (2), H···S 1.82 (3) Å and O—H···S 171 (1)°], with the hydroxyl moiety as hydrogen-bond donor and the S atom as acceptor. According to the observed C—S distance of 1.718 (2) Å, the sulfur–carbon bond in the title compound is closer to a single than a double bond. The sum of bond angles at N1 is 360.8° which suggests a planar arrangement of the N—O group with respect to the carbon framework of the heterocycle.

Comment

The interest in thiohydroxamic acids and their derived *O*-esters has been renewed as a result of their fascinating properties as precursors of free alkoxyl radicals in synthetic organic chemistry and medicine (Hartung & Gallou, 1995; Adam, Ballmeier, Epe, Grimm & Saha-Möller, 1995). These transformations generally involve the 2-isomer, (2), of the title compound 1-hydroxy-4(1*H*)-pyridinethione, (1). The pyridinethiones (1) and (2) have been known for almost 40 years and have been studied extensively in solution with respect to their tautomeric equilibria between the thiol [*e.g.* (1*c*)] and