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Crystal and Molecular Structure of Crotonohydroxamic Acid, and a Preliminary Investigation of the Solid-State Reactivity of the Acid and Its Salts

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*The crystal structure of crotonohydroxamic acid, $CH_3CH{=}CHC(O)NHOH$ **5** contains centrosymmetrically-related pairs of acid molecules, with a short contact of 3.36 Å between the α-carbon atoms. The observed arrangement provides excellent alignment for a solid-state ene reaction, but, apparently, the threshold temperature for such a process cannot be realized. The hydrogen bonding patterns observed include C(5) chains and both $R_2^4(10)$ and $R_4^4(18)$ ring systems. Facile preparation of metal salts of the acid is reported, as well as discussion of the effect of heating and ^{60}Co γ-irradiation of the materials.*

Keywords: crystal structure; crotonohydroxamic acid; solid state reaction; hydrogen bonding; γ-irradiation

INTRODUCTION

The *trans*-2-butenoate moiety, typically as a Group Ia or IIa metal salt, is a versatile synthon for solid-state transformations. Thus, heating sodium *trans*-2-butenoate **1** leads to one of two possible diastereomers of disodium 1-hexene-3,4-dicarboxylate **2** [1], while ^{60}Co (γ-irradiation of **1** leads to trimer **3** [2], one of eight possible diastereomeric products. Irradiation of the calcium salt leads to cyclodimer **4**, one of four possible diastereomers [3]. In order to extend the range of possible reactions, and to explore the reactivity of the butenoyl moiety in different chemical and structural environments,

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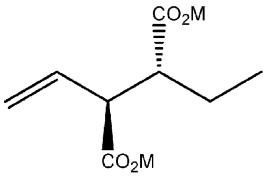
we have synthesized the known crotonohydroxamic acid, CH_3CH=CHC(O)NHOH **5**, determined its crystal structure, and studied its solid-state reactivity. Here we report the structure of the acid, and discuss aspects of hydrogen bonding and contacts between potentially reactive C atoms. We also report the synthesis of the Na, K, Mg, Ca, Ba and Zn salts, and their behavior upon heating and exposure to ionizing radiation.



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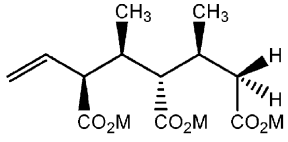

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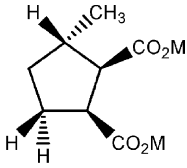

4, M = $Ca_{0.5}$

EXPERIMENTAL SECTION

Instrumentation

NMR spectra were recorded on a Varian XL-400 spectrophotometer. A Gammacell 220 Irradiator (Atomic Energy of Canada Ltd.) equipped with a ^{60}Co source, nominal activity 2.56 kGy d^{-1}, was used for γ-irradiation experiments. A ^{60}Co Gamma reactor at the University of Massachusetts, Lowell, nominal activity 20 kGy h^{-1}, was also used for irradiation experiments.

Synthesis of *trans*-Crotonohydroxamic Acid, CH_3CH=CHCONHOH 5 [4]

To a cooled solution of 50% aqueous hydroxylamine hydrochloride (1.32 mL, 20.0 mmol) in 30 mL of ethanol at 0°C, was added crotonic anhydride (3.08 g, 20.0 mmol). The resulting solution was stirred at 0°C for 2 h and then at room temperature for 18 h. The mixture was concentrated under reduced pressure to give a yellow oil which was dissolved in water and treated with concentrated HCl until the pH reached 4. The aqueous layer was extracted with 3×50 mL portions of methylene chloride. The organic extracts were combined, dried over magnesium sulfate and concentrated in vacuo to give 1.21 g (59.9%) of a light yellow solid, m.p. 111–113°C. Lit. m.p. 109–111°C [4].

Single Crystals of *trans*-Crotonohydroxamic Acid 5

100 mg of **5** were placed in a 25 mL beaker and dissolved with 15 mL of acetone. The beaker was covered with parafilm; several small holes were made to allow for slow evaporation of the solvent. After a few hours, plate-like crystals formed and were collected using a Hirsch funnel.

Synthesis of Sodium *trans*-Crotonohydroxamate

To a solution of **5** (100 mg, 0.90 mmol) in 2.5 mL of water, was added NaOH (40 mg, 0.90 mmol) in 2.5 mL of water. The resulting solution was stirred at room temperature for five minutes, concentrated under reduced pressure to give a colorless solid, and washed with acetone several times to remove excess **5**. The final product was a colorless solid, 0.105 g (94%), m.p. $>220^{\circ}$C.

Synthesis of Potassium *trans*-Crotonohydroxamate

To a solution of **5** (100 mg, 0.90 mmol) in 2.5 mL of water, was added KOH (50 mg, 0.90 mmol) in 2.5 mL of water. The resulting solution was stirred at room temperature for five minutes, concentrated under reduced pressure to give a colorless solid, and washed with acetone several times to remove excess **5**. The final product was a colorless solid, 0.123 g (98%), m.p. above $>220^{\circ}$C.

Synthesis of Magnesium *trans*-Crotonohydroxamate

To a solution of **5** (500 mg, 5.00 mmol) in 50 mL of water warmed to 60°C, was added $4\,MgCO_3 \cdot Mg(OH)_2 \cdot 5H_2O$ (2.43 g, 5.00 mmol), in small portions to allow for evolution of CO_2. The saturated solution was stirred at 60°C for 1 h and gravity filtered into a pre-heated flask. The resulting solution was concentrated under reduced pressure to give a colorless solid, 0.278 g (45%) m.p. $>220^{\circ}$C.

Synthesis of Zinc *trans*-Crotonohydroxamate

To a solution of **5** (320 mg, 3 mmol) in 20 mL of water was added zinc oxide (258 mg, 3 mmol). The resulting suspension was stirred at room temperature for 4 h and then filtered to give a colorless solution. The solution was concentrated under reduced pressure to give a colorless solid, 0.312 g (63%) m.p. $>220^{\circ}$C.

Synthesis of Barium *trans*-Crotonohydroxamate

To a solution of **5** (500 mg, 5 mmol) in 15 mL of water was added barium nitrate (653 mg, 25 mmol). The resulting solution was stirred at room temperature for 1 h and concentrated under reduced pressure to give a colorless solid, 0.712 g (60%) m.p. $>220^{\circ}$C.

Synthesis of Calcium *trans*-Crotonohydroxamate

To a solution of **5** (500 mg, 5 mmol) in 50 mL of water was added calcium carbonate (250 mg, 21 mmol). The resulting suspension was stirred at room temperature for 2 h and gravity filtered to give a colorless solution. The solution was concentrated under reduced pressure to give a colorless solid, 0.354 g (51%) m.p. $>220^{\circ}$C.

Solid-State Irradiation of Crotonohydroxamic Acid and its Salts

100 mg of starting material was placed in a 5 mm diameter glass tube sealed at the bottom. A small piece of glass wool was placed on top of the solid and used to pack the sample tightly. A 5 mm septum was used to cover the top of the glass tube and a needle was inserted through the septa to place the sample under vacuum for 2 min. The sample was then sealed under nitrogen using an air/gas flame and exposed to 500 kGy γ-rays.

Thermal Reactions of Crotonohydroxamic Acid and its Salts

100 mg of **5** was placed in a glass vial and heated at various temperatures. The free acid was heated at 50°, 70° and 80°C, while the salts were heated at 125°, 150° and 200°C. The time scale for each sample ranged from 3 to 48 hours.

X-ray Structure Determination

A single crystal of **5** was selected and mounted on a Pyrex fiber affixed to a brass pin. The crystal was optically centered and placed on an Enraf-Nonius CAD4-Turbo diffractometer. X-ray data were collected using the Enraf-Nonius EXPRESS program [5] (graphite monochromated MoKα radiation, $\lambda = 0.71073$ Å) using the ω-2θ scan technique. The structure was solved by direct methods using SIR-92 [6] and refined using the Oxford CRYSTALS package [7]. Non-hydrogen atoms were refined using anisotropic displacement parameters. The acidic hydrogen atoms were refined using isotropic displacement

TABLE 1 Crystallographic Data for 5

Compound	Crotonohydroxamic acid **5**
Chemical Formula	$C_4H_7NO_2$
a, Å	7.1310(7)
b, Å	8.6195(4)
c, Å	9.2993(7)
α, deg.	90
β, deg.	110.318(6)
γ, deg.	90
V, Å^3	536.02(7)
Z, Z'	4, 1
Formula Wt. g/mol	101.11
Space Group	$P2_1/c$
T,°C	21(1)
λ, Å	0.71073
ρ_{calc}, g cm^{-3}	1.253
ρ_{obs}, g cm^{-3}	1.25(1)
μ, cm^{-1}	1.007
Transmission factors	0.977–1.000
R^a	0.0320
R_w^b	0.0435
S^c	1.048
no. reflections, I > 1.96 σ(I)	799
no. parameters	93
Correction for secondary extinction	53(12)

$^aR = \sum ||F_o| - |F_c|| / \sum |F_o|$
$^bR_w = [\sum w(|F_o| - |F_c|)^2 / \sum w|F_o|^2]^{1/2}$
$S = [\sum w(|F_o| - |F_c|)^2 / (n - m)]^{1/2}$.

parameters. Other H atoms were placed at calculated positions ($d_{C-H} = 0.95$ Å), held fixed during the refinement, and updated after each least-squares cycle. Systematic absences of $h0l$, l odd and $0k0$, k odd indicated that crotonohydroxamic acid, **5** crystallized in the monoclinic space group $P2_1/c$. Final refinement converged at $R = 0.0320$ and $R_w = 0.0435$. Table 1 shows crystallographic data, while Table 2 shows relevant bond lengths.

TABLE 2 Relevant Bond Lengths (Å) and Angles (°) for **5**

O1–C1	1.245(1)	O1–C1–C2	123.1(1)
O2–N1	1.392(1)	O1–C1–N1	122.5(1)
C1–N1	1.321(1)	C2–C1–N1	114.3(1)
C1–C2	1.470(2)	C1–C2–C3	121.8(1)
C2–C3	1.313(2)	C2–C3–C4	125.8(2)
C3–C4	1.489(2)	O2–N1–C1	119.1(1)

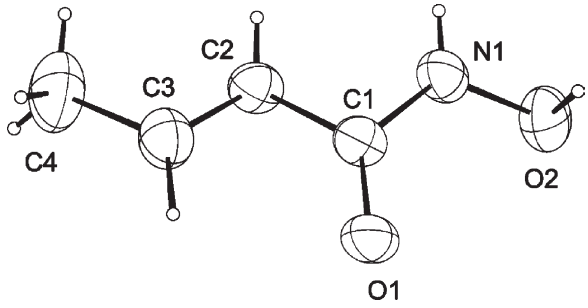

FIGURE 1 Molecular structure of **5**, showing 50% probability ellipsoids.

RESULTS AND DISCUSSION

Molecular Structure of Crotonohydroxamic Acid 5

All bond lengths and angles for **5** lie within normal ranges. The numbering scheme and the molecular structure for **5** are depicted in Figure 1. Crotonohydroxamic acid crystallizes in the monoclinic system, space group $P2_1/c$, and contains two molecules of the acid in the asymmetric unit. The conformation of the O=C–NH–OH moiety is *syn*-periplanar. The *X*–(C=O)–N plane deviates by a range of 0.011–0.025 Å, with the oxygen atom deviating from that plane by 0.011 Å. The O=C–N–O torsion angle is 6.10° and the C–N–O–H torsion angle 121.95°. These values are in agreement with those in the study carried out by Larsen [8].

Packing and Hydrogen Bonding Patterns

Examination of the packing diagram for **5** reveals that the crystal structure for crotonohydroxamic acid contains an infinite two-dimensional hydrogen-bonded network, as illustrated in Figures 2–4. The network is made up of two hydrogen bonds, details of which appear in Table 3.

Application of Etter's analysis of hydrogen bond patterns [9] indicates that the crystal structure of **5** is made up of two chains and two rings. Figure 2 illustrates the infinite chain produced from the O(2)–H(2)···O(1) bond, entry 2 in Table 3. The graph set notation for the chain is C(5). Figure 3 illustrates the infinite chain produced from the N(1)–H(2)···O(1), entry **1** in Table 3. The graph set notation for that chain is also C(5). Combining entries 1 and 2 from the table above reveals two rings, graph set notations $R_2^4(10)$ and $R_4^4(18)$, respectively. This pattern is illustrated in Figure 4. The rings which are generated from these hydrogen bonds are both centrosymmetric.

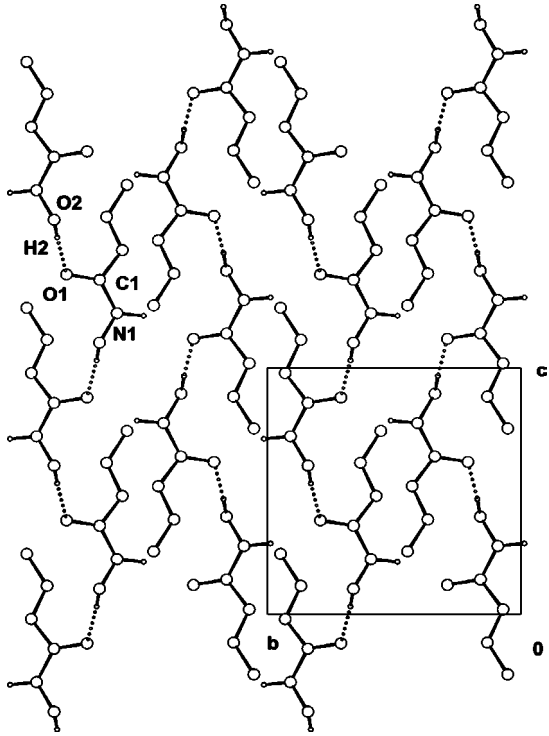

FIGURE 2 C(5) O–H···O hydrogen bonds in **5**. Non-acidic H atoms have been removed for clarity; atoms making up the C(5) chain have been labeled.

Solid-State Reactivity of Crotonohydroxamic Acid, 5 and its Salts

Examination of the intermolecular contacts for **5** indicated the presence of several short carbon-carbon distances. Table 4 lists the observed short contacts (<4.2 Å), including the interlobe distances associated with each contact. Kearsley realized the difficulty of describing the distances and angles, and the parallelism and offset of sets of reactive groups in a crystal, and proposed a simple criterion, which we term the interlobe distance, as a composite parameter for evaluating/rationalizing solid-state reactivity [10]. In short, p_z orbitals are positioned on the atoms in question, the orbitals are assumed to have an extent of 1.8 Å from the atomic centers, and the distances between all potentially reactive orbitals is calculated. The result, that reaction will likely occur for separations $<ca.$ 1.8 Å, is a

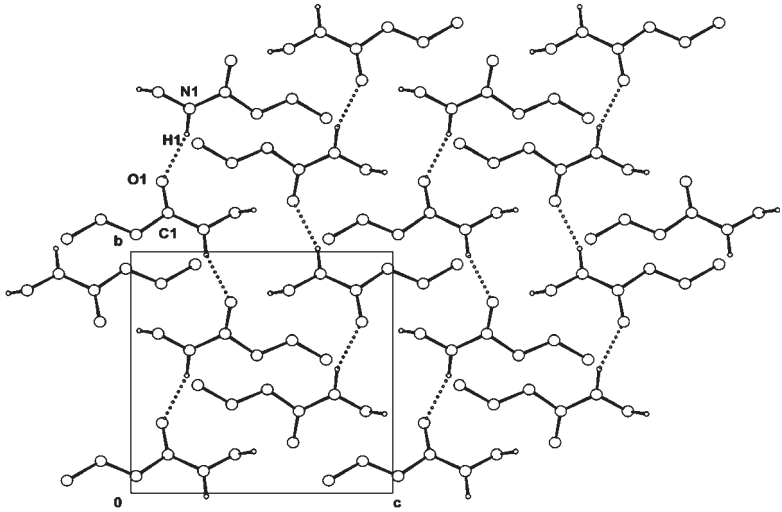

FIGURE 3 C(5) N–H···O hydrogen bonds in **5**. Non-acidic H atoms have been removed for clarity; atoms making up the C(5) chain have been labeled.

rather good predictor of photochemical reactivity, and has been used by us in a number of cases to rationalize radiation-induced reactions.

The shortest distance, 3.362 Å, illustrated in Figure 5, suggests the possibility of an ene reaction, analogous to the production of **2** upon heating **1** [1]. Crotonohydroxamic acid **5**, was placed in a glass vial and heated at 50, 70, and 80°C. In all three cases, the acid appeared to decompose as the colorless solid became brown after prolonged heating. Small aliquots were removed for ^{1}H NMR analysis at 3, 6, 18, 24 and 48 hour intervals. Heating for 24 hours at 70°C caused no change in **5**. After 48 hours, the solid began to turn yellow. The NMR spectrum from a small sample taken at 48 hours revealed that the major component (∼95%) was the starting material. After eight days, a sample was removed once again and NMR analysis indicated that the major component was still the starting material (∼90%). The minor products (∼10%) showed the most distinctive peaks in the region at δ 1.21–1.43 and δ 2.40–2.68, with smaller peaks at δ 2.81–2.96 and δ 3.56–3.68. The identity of the minor products could not be determined from NMR as they appeared to be mixtures. No significant difference was observed after heating at higher temperatures. Thus, although molecules appear to be well-oriented to undergo an ene reaction, the low melting point and decomposition behavior of **5** intervene against a thermally-accessible, chemospecific ene reaction. On the other hand, heating solid sodium *trans*-2-butenoate at the

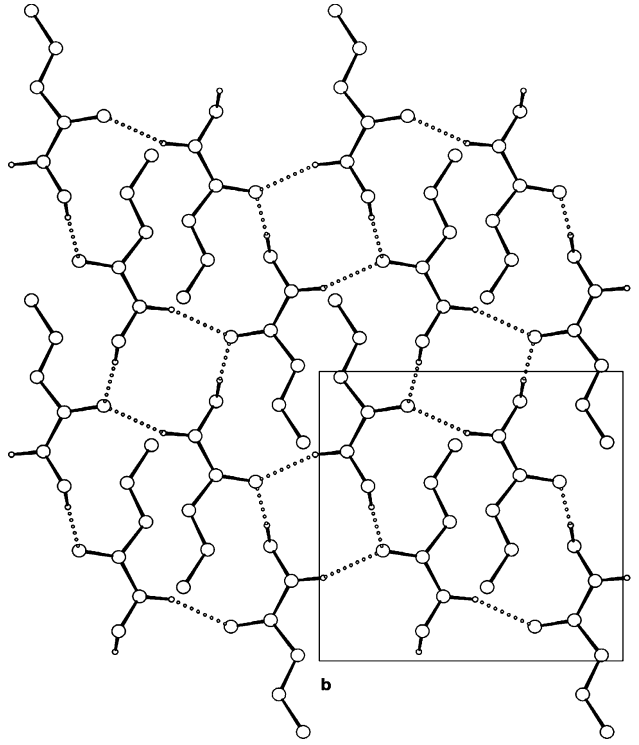

FIGURE 4 Ring motifs R_2^4 (10) and R_4^4 (18), generated by combining the two C(5) chains in. Figures 2 and 3; Non-acidic H atoms have been removed for clarity.

relatively high temperature of 320°C for 4 h produces, chemospecifically, a single diastereomer of the disodium salt of 1-hexene-3,4-dicarboxylic acid in 84% yield [1].

Irradiation of crotonohydroxamic acid with 500 kGy γ-rays also produced no detectable product (NMR analysis of dissolved material).

TABLE 3 Hydrogen Bond Parameters in **5**

No.	Bond Type	X···H (Å)	X···Y (Å)	Angle (°) −X−H···Y	Symmetry Operation
1	N(1)−H(1)···O(1)	0.88(2)	2.780(1)	162.6(15)	*1-x*, $1/2-y$, $-z-1/2$
2	O(2)−H(2)···O(1)	0.89(2)	2.680(1)	178.4(18)	x, $1/2-y$, $1/2+z$

TABLE 4 Short Contacts and Interlobe Distances in **5**

Carbon Atoms	Distances (Å)	Symmetry Operation	Interlobe Distances
C2···C2	3.362	*1 − x, 1 − y, 1 − z*	0.88
C2···C3	3.889	*1 − x, 1 − y, 1 − z*	2.14
C3···C4	4.007	*−x, y − 1/2, −z + 1/2*	—

As noted in Table 4, there is a short contact between a methyl C atom and the β-carbon atom of a symmetry-related molecule of 4.007 Å; potentially, upon γ-irradiation, this could lead to a radical addition process, such as that observed for the formation of **3** [3]. Nonetheless, the lack of sensitivity to γ-rays is consistent with our observations that (to date), we have only been able to effect radical addition reactions in metal salts or complexes of the *trans*-2-butenoate (crotonate) moiety.

The solid-state reactivity of the synthesized metal salts of crotonohydroxamic acid was also investigated. Sodium, potassium, magnesium, zinc, barium, and calcium crotonohydroxamate were prepared and irradiated with ^{60}Co γ-rays (500 kGy dose). No detectable product was observed after these irradiation experiments. Attempts to grow single crystals of the salts from various solvents were unsuccessful, therefore structure/reactivity correlations cannot be made at this time. Additionally, the metal salts of crotonohydroxamic acid were heated at 100, 150, 175 and 200°C for 3, 6, 12, 18 and 48 hour time intervals. No change was observed in any of the salts when heated at 100, 150 and 175°C for 48 hours. Heating at 200°C for 3 h resulted

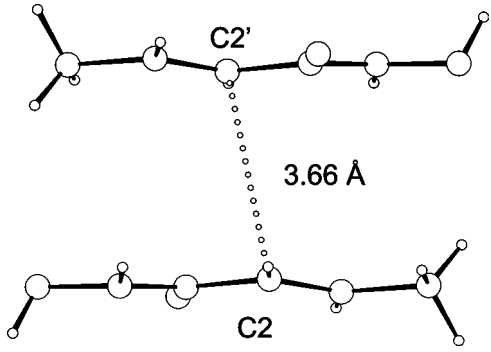

FIGURE 5 Paired molecules of **5**, related by (*1 − x, 1 − y, 1 − z*).

in the appearance of a light yellow color in the salts. A small sample of each salt was removed for NMR analysis, which revealed that no reaction had occurred. Heating the salts for 6 hours at 200°C resulted in a dark brown pasty material that covered the glass vial. It thus appears that the metal salts decompose and are not thermally stable at higher temperatures.

In conclusion, the structure of **5** shows excellent alignment for a solid-state ene reaction, but, apparently, the threshold temperature for such a process cannot be realized. Facile preparation of the salts of this acid provide a possible entry into the study of reactivity for other, yet-to-be synthesized salts. When single crystals of the salts become available, it will be possible to explore the structure-reactivity relationships implied by this work.

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