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Cocrystalline Salts of Alkynoic Acids. The Crystal and Molecular Structure of 2-Aminopyridinium Butynoate

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COCRYSTALLINE SALTS OF ALKYNOIC ACIDS. THE CRYSTAL AND MOLECULAR STRUCTURE OF 2-AMINOPYRIDINIUM BUTYNOATE.

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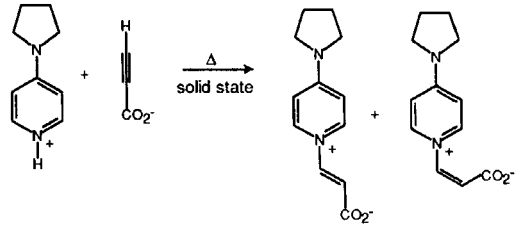
Abstract Mixing 2-butynoic acid and 2-aminopyridine in acetone produces the salt 2-aminopyridinium 2-butynoate (**4**) in high yield. An X-ray structure determination of **4** (Space Group $P2_1/n$, Z = 4) shows it to contain short acetylene-acetylene contacts as well as short contacts between the pyridine N atom and the β-carbon atom of the butynoate moiety. The contacts are between centrosymmetrically-related "dimer pairs" of the cocrystalline salt, and are not part of an infinite array. The material is stable to heating or exposure to ^{60}Co γ-rays.

INTRODUCTION

During a recent investigation[1] of the solid-state properties of cocrystalline salts[2] of substituted pyridines and propynoic acid, we discovered that, although these materials are insensitive to ^{60}Co γ-irradiation, several of the materials are thermally reactive. For example, heating the cocrystalline solid **1** obtained by mixing propynoic acid and 4-(1-pyrrolidino)-pyridine in ethanol converts it, in high yield, to a 19:1 mixture of (*E* and *Z*)-4-(1-pyrrolidino)-pyridinium-1-acrylate (**2,3**). To the best of our knowledge, this is the first example of the addition of a pyridine moiety to an acetylene in the solid state. Michael additions of substituted pyridines to acetylenes



1 **2** **3**

are readily carried out in solution;[3] however, to the best of our knowledge, such additions have not previously been observed in the solid state. In an attempt to understand the thermal and γ-ray induced reactivity of pyridine-containing complexes, we are synthesizing a number of

cocrystals or cocrystalline salts. Here we report the structure and properties of a stable material, the salt 2-aminopyridinium 2-butynoate (**4**).

EXPERIMENTAL SECTION

Instrumentation

Melting points were determined on a Laboratory Devices Mel-Temp apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Varian EM-390 (90 MHz) and XL-300 (300 MHz) spectrometers. Chemical shifts are given in parts per million downfield from 3-(trimethylsilyl)-1-propane sulfonic acid sodium salt. The following abbreviations are used to indicate signal multiplicity (NMR) or spectral characteristics (IR): s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad; sh, shoulder. A Gammacell 220 Irradiator (Atomic Energy of Canada, Ltd.) equipped with a ^{60}Co source was used for all γ-irradiation experiments. The nominal activity of the source as of 1 July 1991 was 0.043 Mrad/h.

2-Aminopyridine 2-Butynoate (4)

To a solution of 2-aminopyridine (0.200 g, 213 mmol) in acetone (10 mL) was added 2-butynoic acid (0.175 g, 208 mmol) in 5 mL of acetone. The solution was stirred for 30 min and concentrated in vacuo (20 torr) to give **4** (0.348 g, 93%) as a colorless solid: Mp 121-123 °C; ^{1}H-NMR (D_2O) δ 7.92 (1 H, ddd, J = 10.0, 7.5, 1.5 Hz), 7.80 (1 H, dd, J = 7.5, 1.5 Hz), 7.01 (1 H, dd, J = 10.0, 1.0), 6.91 (1 H, ddd, J = 7.5, 7.5, 1.0), 1.90 (3 H, s). The thermal reactivity was analyzed by heating samples of the compound for >6 h to temperatures 15 - 30 °C below the melting point; the material was also irradiated with 21.6 Mrad of ^{60}Co γ-rays. The resulting materials were analyzed by ^{1}H NMR. All spectra were identical to those of the starting material.

Structure Determination of 4

Single crystals were grown by slow evaporation from acetone. Laué photographs and a preliminary X-ray photographic study indicated the crystal to be of excellent quality. The crystal was then transferred to a Supper No. 455 goniometer and optically centered on a Syntex $P2_1$ diffractometer. Operations were performed as described previously.[4] The analytical scattering

factors of Cromer and Waber were used; real and imaginary components of anomalous scattering were included in the calculations.[5] The structure was solved using SHELXS-86;[6] all other computational work was carried out on a VAX 6420 computer using the Enraf-Nonius SDP software package.[7] At the conclusion of least-squares refinement of positional and anisotropic displacement parameters for all nonhydrogen atoms (isotropic displacement parameters for H atoms), R = 0.039 and R_w = 0.048. Complete experimental detail is presented in Table I, atomic coordinates in Table II, and selected bond lengths and angles in Table III. Tables of anisotropic displacement parameters, all bond lengths and angles, and observed and calculated structure amplitudes are available from the authors.

RESULTS AND DISCUSSION

The salt formed from 2-aminopyridine and 2-butynoic acid crystallizes as an eight-membered ring hydrogen-bonded heterodimer (Figure 1; N1-O1, 2.68 Å, N-H···O, 172(1)°; N2-O2, 2.88 Å, N-H···O, 178(2)°). The two moieties are not coplanar, as observed (nearly) for 2-aminopyridinium salicylate (3.9°),[8] but rather are skewed by 15.2(1)°. The sum of the angles (360°) around the amine nitrogen atom (N2) indicates the atom to be mainly sp^2 in character. The amino-nitrogen-to-ring bond length, N2-C4 (1.330(2) Å), is significantly shorter than the N-C distances within the ring (1.345(2) and 1.354(2) Å). The C-C distances within the ring also show a deviation from those found in normal aromatic pyridine structures. The distances C4-C5 (1.406(3) Å) and C6-C7 (1.397(2) Å) are significantly longer than C5-C6 (1.350(3) Å) and C7-C8 (1.345(3) Å). This evidence suggests a considerable degree of double-bond character between N2 and C4 owing to conjugation with the ring (resonance form **5**). These features are in close agreement with those observed for the cation in 2-aminopyridinium salicylate.[8]

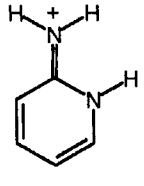


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Table I. Data for the X-ray Diffraction Study of $(C_5H_7N_2)^+(C_4H_3O_2)^-$ (**4**)

(A) Crystal Data at 21(1) °C.

Crystal system : Monoclinic
Space group : $P2_1/n$ [C_{2h}^5; No. 1014]
a = 10.753(3) Å
b = 9.090(3) Å
c = 10.454(3) Å
β = 115.63(2)°
V = 921.3(11) Å^3
Z = 4
Crystal Size : 0.771 x 0.420 x 0.116 mm.
Formula Wt : 178.19
ρ_{obs}[a] = 1.25(2) g·cm^{-3}
ρ_{calc} = 1.285 g·cm^{-3}
μ = 0.868 cm^{-1} (MoKα)

Cell constant determination : 7 pairs of ± (*hkl*) and refined 2θ, ω, χ values in the range 22° ≤ |2θ| ≤ 24° (λ(MoKα) = 0.71073 Å)

(B) Measurement of Intensity Data

Radiation : MoKα, graphite monochromator
Reflections measured : h, k, ±l (3° ≤ 2θ ≤ 50°)
Scan type, speed : θ-2θ, vble, 2.93 - 7.33°·min^{-1}
Scan range : symmetrical, [1.9 + Δ(α_2-α_1)]°
No. of reflections measured : 1718, 1629 in unique set
Standard reflections, period 74 : 105, 051, and 604; variation ≤ ± 3σ(I) for each
Absorption correction : empirical, normalized transmission factors 0.904 - 1.00; 101, 103, 204, 307 reflections
Data reduction : as before[b]
Statistical information : R_{av} = 0.009 (0*kl* reflections)

(C) Refinement

Refinement, with 1254 data for which I > 1.96 σ(I)
Weighting of reflections : as before[c], p = 0.04
Solution : SHELXS-86,[6] difference-Fourier
Refinement[d] : full-matrix least-squares, with:
anisotropic displacement parameters for C, N, and O atoms;
isotropic displacement parameters for H atoms;
secondary extinction parameter, 5.3(2) x 10^{-6};
R = 0.039; R_w = 0.048; *SDU* = 1.627;
R (structure factor calcn with all 1629 reflections) = 0.063
Final difference map : one peak, 0.241 e$^-$/Å^3 near C1, random peaks of -0.145 to +0.139 e$^-$/Å^3.

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[a] Measured by neutral buoyancy in *n*-hexane/1,1-dibromomethane.

[b] Foxman,B.M.;Goldberg,P.L.;Mazurek,H. *Inorg.Chem.* **1981**, *20*, 4381; all computations in the present work were carried out using the ENRAF-NONIUS Structure Determination Package.[7]

[c] Corfield,P.W.R.; Doedens,R.J.; Ibers,J.A. *Inorg.Chem.* **1967**, *6*, 197.

[d] $R_{av} = \Sigma|I-I_{av}|/\Sigma I$; $R = \Sigma||F_o|-|F_c||/\Sigma|F_o|$; $R_w = \{\Sigma w[|F_o|-|F_c|]^2/\Sigma w|F_o|^2\}^{1/2}$
SDU = $\{\Sigma w[|F_o|-|F_c|]^2/(m-n)\}^{1/2}$ where m (=1254) is the number of observations and n (=159) is the number of parameters.

Table II. Atomic Coordinates for $(C_5H_7N_2)^+(C_4H_3O_2)^-$ (4)[a,b]

Atom	x	y	z	B(Å^2)
O1	0.1728(1)	0.3920(2)	0.5314(1)	5.56(3)
O2	0.0611(1)	0.4639(2)	0.3086(1)	5.52(3)
N1	-0.0290(1)	0.2169(1)	0.5289(1)	3.57(3)
N2	-0.1285(2)	0.2307(2)	0.2855(1)	4.48(4)
C1	0.1610(2)	0.4669(2)	0.4260(2)	3.64(4)
C2	0.2753(2)	0.5666(2)	0.4470(2)	3.76(4)
C3	0.3662(2)	0.6502(2)	0.4633(2)	4.09(4)
C4	-0.1259(2)	0.1710(2)	0.4028(2)	3.60(4)
C5	-0.2190(2)	0.0628(2)	0.4037(2)	4.73(4)
C6	-0.2084(2)	0.0099(2)	0.5287(2)	5.48(5)
C7	-0.1069(2)	0.0604(2)	0.6579(2)	5.16(4)
C8	-0.0190(2)	0.1635(2)	0.6540(2)	4.41(4)
C9	0.4772(2)	0.7531(2)	0.4821(2)	5.53(5)
H(N1)	0.038(2)	0.287(2)	0.526(2)	5.4(4)*
HA(N2)	-0.065(2)	0.305(2)	0.292(2)	6.6(5)*
HB(N2)	-0.187(2)	0.189(2)	0.202(2)	6.1(5)*
H5	-0.281(2)	0.031(2)	0.316(2)	5.5(4)*
H6	-0.272(2)	-0.060(2)	0.529(2)	7.0(5)*
H7	-0.097(2)	0.022(2)	0.748(2)	5.8(4)*
H8	0.059(2)	0.209(2)	0.738(2)	6.3(5)*
H9A	0.506(3)	0.802(3)	0.574(2)	10.3(7)*
H9B	0.446(2)	0.816(3)	0.399(2)	9.2(6)*
H9C	0.558(2)	0.701(3)	0.490(2)	9.6(7)*

[a] Atoms refined using anisotropic displacement parameters are given in the form of the isotropic equivalent displacement parameter defined as:

$$1.33\cdot[a^2\cdot B_{11} + b^2\cdot B_{22} + c^2\cdot B_{33} + ab\cdot\cos\gamma\cdot B_{12} + ac\cdot\cos\beta\cdot B_{13} + bc\cdot\cos\alpha\cdot B_{23}]$$

[b] Starred atoms refined using isotropic displacement parameters.

Table III. Bond Lengths (Å) and Angles (°) for $(C_5H_7N_2)^+(C_4H_3O_2)^-$ (**4**)

Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance
O1	C1	1.255(2)	C1	C2	1.464(2)
O2	C1	1.233(2)	C2	C3	1.191(2)
N1	C4	1.345(2)	C3	C9	1.462(3)
N1	C8	1.354(2)	C4	C5	1.406(3)
N1	H(N1)	0.97(2)	C5	C6	1.350(3)
N2	C4	1.330(2)	C6	C7	1.397(2)
N2	HA(N2)	0.94(2)	C7	C8	1.345(3)
N2	HB(N2)	0.91(2)			

Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle
C4	N1	C8	122.6(1)	C1	C2	C3	178.5(2)
C4	N1	H(N1)	116.5(9)	C2	C3	C9	179.5(2)
C8	N1	H(N1)	120.8(9)	N1	C4	N2	118.4(1)
C4	N2	HA(N2)	120.(1)	N1	C4	C5	117.5(2)
C4	N2	HB(N2)	117.(1)	N2	C4	C5	124.1(1)
HA(N2)	N2	HB(N2)	123.(2)	C4	C5	C6	119.5(1)
O1	C1	O2	125.1(2)	C5	C6	C7	121.5(2)
O1	C1	C2	116.4(1)	C6	C7	C8	117.7(2)

The crystal structure is characterized by short N-H···O interactions. The molecules are linked by an infinite chain of HB(N2)···O1 [½ + x, ½ + y, ½ + z] hydrogen bonds (Figure 2). The N-H···O angle is 173(1)° with a N2···O1 distance of 2.82 Å. Figure 3 shows centrosymmetrically related molecules [1 - x, 1 - y, 1 - z] with short C≡C···C≡C contacts. The distance between an α-carbon atom (C2) and the β'-symmetry related atom (C3') is 4.06 Å; the distance between symmetry-related pairs of C3 atoms is 3.80 Å. Note also that the pyridinium cations approach one another (again in centrosymmetric pairs) at an average distance of ≈ 3.5 Å. However, **4** is unreactive towards γ-ray initiation (21.6 Mrad). The solid-state reactivity

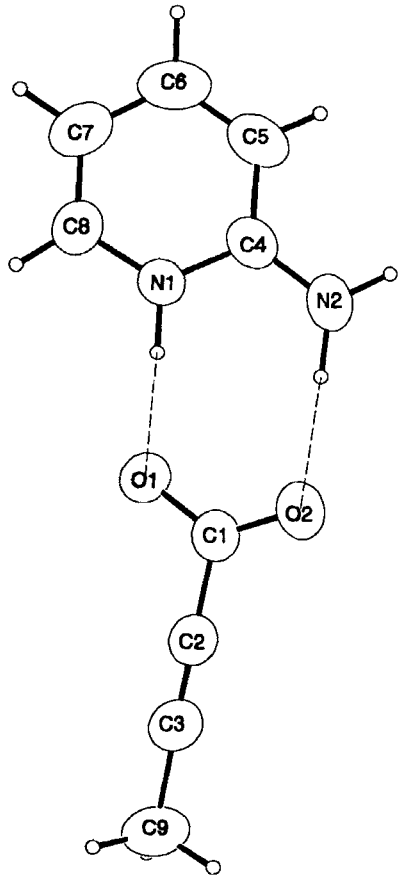

Figure 1. Molecular structure of 1 showing atom labeling scheme.

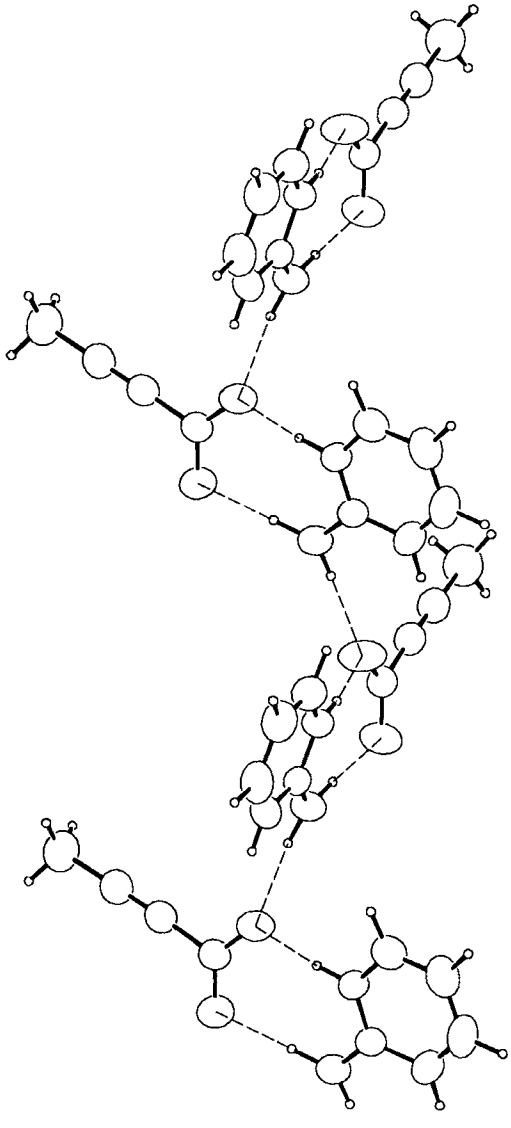

Figure 2. View of 1 showing the N-H···O hydrogen bond patterns.

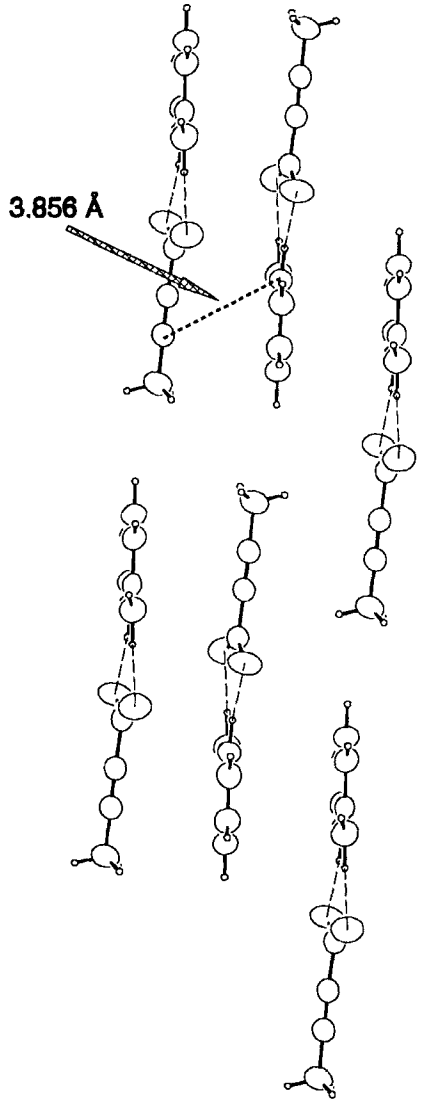

Figure 3. View of 1 showing the short N1···C3, C≡C···C≡C, and pyridine-pyridine contacts.

(thermal or γ-ray) of isolated pairs of monoacetylenes has not yet been observed. If we consider the possible addition of the pyridine moiety to β-carbon atom of the propynoate, there is a short intermolecular distance (N1···C3, 3.86 Å), and a C2-C3···N1 angle of 59°. This angle is near the value (60°) proposed by Baldwin for ring closures of alkynes;[9] however, this value was revised (120°) by Eisenstein, Procter and Dunitz for nucleophilic addition to a triple bond.[10] The lack of reactivity in the present case could well be due to other factors; for similar solution reactions the reactivity of the butynoate moiety is drastically reduced in contrast to the analogous propynoate.[11] Answers to such questions must await a full study of the solid-state reactivity of cocrystals and/or cocrystalline salts of alkynoic acids.

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