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The Crystal Structure of a 1:1 Nicotine-Salicylic Acid Complex (Nicotinyl Salicylate)

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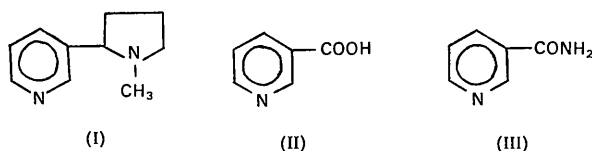
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Crystals of the 1:1 complex of nicotine-salicylic acid, $C_{10}N_2H_{14} \cdot C_7H_6O_3$, are monoclinic, space group $P2_1$, with two formula units in a unit cell, $a = 7.673$ (2), $b = 11.355$ (6), $c = 9.580$ (2) Å, $\beta = 109.34$ (8)°, $D_m = 1.270$ g.cm⁻³ at 20°C. The structure was solved by direct methods using tangent formula phase refinement from 1411 intensities measured with Cu $K\alpha$ radiation on a FACS I automatic diffractometer. The parameters were refined anisotropically to a final R of 0.053. All hydrogen atoms were located on difference synthesis. The quaternary ammonium cation of the nicotine forms a molecular complex with a salicylate anion through a $N^+(H) \cdots O^-$ hydrogen-bond of 2.627 Å. The conformational angle between the best planes of the puckered pyrrolidine and planar pyridine ring of the nicotinyl ion is 77°. In the salicylate anion, the carboxylate group is slightly out of the plane of the ring, by 0.1 Å. As in the free acid, the hydroxyl forms a strong internal hydrogen-bond with a carboxyl oxygen, with a $O(-H) \cdots O$ distance of 2.544 Å.

Introduction

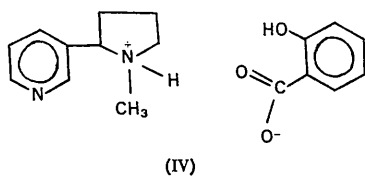
The poisonous alkaloid, nicotine, was first isolated from tobacco by Posselt & Reimann (1828). It is a colorless oily liquid, boiling under atmospheric pressure at 246°C, is levorotatory, soluble in water, and oxidizes in contact with air. The formula (I), α -pyridyl-*N*-methyl-pyrrolidine, was proposed by Pinner (1893), and confirmed by syntheses (Pictet & Crepieux, 1895; Späth & Bretschneider, 1928).

The parent compound has not been studied in the solid state, but crystal structures have been reported for nicotinic acid (II), and nicotinamide (III) (Wright & King, 1953, 1954), familiarly known as the vitamin niacin.



The crystalline complex of nicotine with salicylic acid provides both a means for a structural study of this important molecule and for examining the way in which it can form a hydrogen-bonded complex with an organic acid. As such, this investigation forms part of a general study of hydrogen-bonded complexes, which has included glucose-urea (Snyder & Rosenstein, 1971) and glucitol-pyridine (Kim, Jeffrey & Rosenstein, 1971).

The physiological action of nicotine and chemically related compounds has, not surprisingly, been the subject of research for nearly a century. In 1951, Taylor proposed that the quaternary ammonium cation is the active molecular species at body pH; this is supported by the fact that the monomethiodide has comparable activity (Barlow & Dobson, 1955; Gillis & Lewis, 1956). It also seems likely that it is this cation which occurs naturally in the tobacco plant in combination with maleic and citric acids. This work has confirmed that the salicylic acid complex is, in fact, a molecular crystal of nicotinyl salicylate (IV).



Experimental

Crystals of the 1:1 nicotine-salicylic acid complex were obtained by dissolving salicylic acid in nicotine and cooling slowly the saturated solution. Large transparent crystals were obtained by recrystallization from ethanol. The density was measured at 20°C by flotation in a mixture of n-hexane and tribromomethane. The Picker FACS I diffractometer with Cu K α ($\lambda=1.5418$ Å) was used to measure the cell dimensions and to collect the intensities. The crystal data are as follows;

D- β -Pyridyl- α -N-methylpyrrolidine, *o*-hydroxybenzoic acid complex, C₁₀N₂H₁₄·C₇H₆O₃

F.W. 300.4

m.p. 117.5°C

$a=7.673$ (2), $b=11.355$ (6), $c=9.580$ (2) Å

$\beta=109.34$ (8)°, $Z=2$, $V=787.61$ Å³

$\mu(\text{Cu } K\alpha)=7.2$ cm⁻¹

$D_m=1.270$ g.cm⁻³ at 20°C, $D_x=1.266$ g.cm⁻³

Space group $P2_1$, from systematic absences $0k0$ with k odd.

(The standard deviations given in parentheses refer to the last figure).

The intensities up to $2\theta=130^\circ$ were measured from an acicular crystal of dimensions 0.30 × 0.38 × 0.26 mm, using the θ - 2θ scanning mode with variable scan width at a 2θ -scan speed of 2° per minute. A 20 second background count was taken at both ends of the scan range for each reflection. Of the 1525 independent reflections in the Cu K α reflection sphere for $2\theta \leq 130^\circ$, 1411 were recorded, of which 212 had intensities less than two standard deviations above background. No absorption corrections were applied in converting the intensities to structure amplitudes.

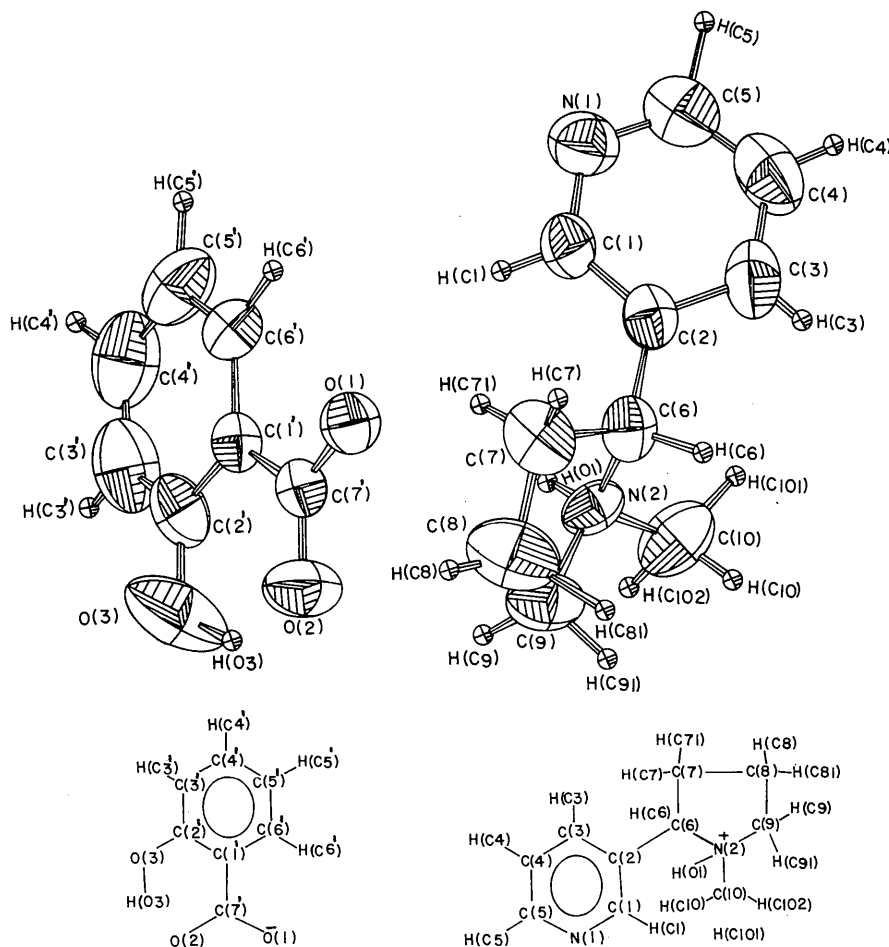


Fig. 1. Molecular conformation observed in the crystal structure of nicotine-salicylic acid complex, with diagrams showing atomic numbering used and the anisotropic thermal ellipsoids.

Table 1. Fractional atomic coordinates and anisotropic thermal parameters in nicotine-salicylic acid complex

Key to atomic numbering is given in Fig. 1. The thermal parameters are given in the form $T = \exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$.

Estimated standard deviations from the full matrix calculations are shown in parentheses and refer to the last decimal positions. * fixed y parameter.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C(1)	0.1943 (6)	0.6230 (6)	0.5763 (4)	0.0281 (10)	0.0113 (4)	0.0125 (5)	-0.0018 (6)	0.0066 (5)	-0.0017 (4)
C(2)	0.0606 (6)	0.6172 (5)	0.6440 (4)	0.0267 (9)	0.0073 (3)	0.0112 (4)	-0.0006 (4)	0.0049 (5)	-0.0007 (3)
C(3)	0.1194 (7)	0.5805 (6)	0.7905 (5)	0.0360 (12)	0.0119 (5)	0.0128 (5)	-0.0017 (6)	0.0094 (6)	0.0007 (4)
C(4)	0.3041 (8)	0.5536 (7)	0.8580 (5)	0.0393 (14)	0.0128 (5)	0.0141 (6)	0.0007 (7)	0.0007 (7)	0.0021 (5)
C(5)	0.4234 (7)	0.5621 (7)	0.7807 (6)	0.0301 (11)	0.0127 (5)	0.0197 (7)	-0.0000 (7)	0.0025 (7)	-0.0002 (5)
C(6)	-0.1371 (6)	0.6517 (5)	0.5668 (4)	0.0273 (9)	0.0085 (3)	0.0134 (5)	0.0010 (5)	0.0090 (5)	-0.0020 (3)
C(7)	-0.1713 (8)	0.7623 (6)	0.4716 (6)	0.0333 (12)	0.0078 (4)	0.0197 (7)	0.0022 (6)	0.0058 (7)	-0.0007 (4)
C(8)	-0.3675 (9)	0.7523 (7)	0.3745 (8)	0.0369 (15)	0.0113 (5)	0.0276 (11)	0.0061 (8)	0.0002 (10)	-0.0018 (6)
C(9)	-0.4154 (6)	0.6234 (6)	0.3587 (6)	0.0198 (8)	0.0132 (5)	0.0216 (8)	0.0016 (5)	0.0061 (6)	-0.0035 (5)
C(10)	-0.2789 (8)	0.4503 (6)	0.5215 (7)	0.0357 (13)	0.0095 (4)	0.0296 (10)	-0.0031 (6)	0.0189 (10)	-0.0009 (6)
N(1)	0.3716 (5)	0.5961 (6)	0.6418 (4)	0.0227 (8)	0.0151 (5)	0.0173 (5)	-0.0008 (5)	0.0045 (5)	-0.0025 (4)
N(2)	-0.2440 (4)	0.5608*	0.4548 (4)	0.0199 (6)	0.0078 (3)	0.0169 (5)	0.0004 (3)	0.0090 (4)	-0.0021 (3)
C(1')	-0.1128 (6)	0.3054 (6)	0.0248 (4)	0.0219 (7)	0.0070 (3)	0.0112 (4)	0.0005 (4)	0.0061 (5)	0.0002 (3)
C(2')	-0.0122 (9)	0.2371 (6)	-0.0904 (6)	0.0307 (10)	0.0099 (4)	0.0125 (5)	0.0005 (6)	0.0039 (6)	-0.0011 (4)
C(3')	-0.1756 (9)	0.2385 (6)	-0.0352 (7)	0.0539 (19)	0.0106 (5)	0.0154 (6)	0.0027 (8)	0.0120 (9)	-0.0023 (5)
C(4')	0.2682 (8)	0.3070 (6)	0.0873 (7)	0.0332 (12)	0.0111 (5)	0.0277 (10)	0.0034 (8)	0.0226 (12)	-0.0001 (6)
C(5')	0.1681 (5)	0.3737 (6)	0.1541 (5)	0.0212 (8)	0.0094 (4)	0.0172 (6)	-0.0011 (5)	0.0093 (5)	0.0009 (6)
C(6')	-0.1328 (5)	0.4403 (5)	0.1776 (4)	0.0205 (7)	0.0075 (3)	0.0120 (4)	0.0012 (4)	0.0052 (5)	-0.0001 (3)
C(7')	-0.0449 (4)	0.4980 (4)	0.2907 (3)	0.0238 (5)	0.0097 (2)	0.0132 (3)	-0.0009 (3)	0.0070 (3)	-0.0023 (2)
O(1)	-0.3061 (4)	0.4367 (5)	0.1268 (4)	0.0198 (5)	0.0156 (4)	0.0214 (5)	0.0005 (4)	0.0049 (4)	-0.0047 (4)
O(2)	-0.2945 (6)	0.3013 (6)	-0.0817 (5)	0.0363 (10)	0.0187 (6)	0.0246 (6)	0.0007 (6)	-0.0036 (6)	-0.0077 (3)
O(3)	0.155 (5)	0.649 (4)	0.483 (3)						
H(C1)	0.043 (5)	0.572 (4)	0.829 (4)						
H(C3)	0.348 (6)	0.525 (4)	0.949 (4)						
H(C4)	0.582 (5)	0.553 (4)	0.816 (4)						
H(C5)	-0.191 (5)	0.656 (3)	0.650 (4)						
H(C6)	-0.131 (5)	0.835 (3)	0.530 (4)						
H(C7)	-0.106 (5)	0.768 (4)	0.413 (4)						
H(C71)	-0.394 (5)	0.792 (4)	0.290 (4)						
H(C8)	-0.460 (6)	0.770 (4)	0.450 (5)						
H(C81)	-0.513 (5)	0.591 (4)	0.254 (4)						
H(C9)	-0.360 (6)	0.459 (4)	0.576 (5)						
H(C91)	-0.166 (6)	0.401 (4)	0.618 (5)						
H(C10)	-0.340 (6)	0.406 (4)	0.426 (5)						
H(C101)	0.252 (6)	0.199 (4)	-0.089 (4)						
H(C102)	0.411 (5)	0.313 (4)	0.139 (5)						
H(C3')	0.244 (4)	0.429 (4)	0.249 (4)						
H(C4')	-0.181 (4)	0.536 (3)	0.404 (4)						
H(C5')	-0.360 (6)	0.360 (5)	-0.015 (5)						

Table 3. *Interatomic distances and angles in nicotine-salicylic acid complex*

Estimated standard deviations shown in parentheses refer to the last decimal positions.

<i>i</i>	<i>j</i>	<i>D_{ij}</i>	<i>i</i>	<i>j</i>	<i>k</i>	\angle_{ijk}
C(1)	C(2)	1.384 (7) Å	C(2)	C(1)	N(1)	124.6 (5)°
C(1)	N(1)	1.331 (7)	C(1)	C(2)	C(3)	116.4 (5)
C(2)	C(3)	1.387 (7)	C(1)	C(2)	C(6)	122.7 (4)
C(2)	C(6)	1.502 (7)	C(3)	C(2)	C(6)	120.9 (4)
C(3)	C(4)	1.383 (8)	C(2)	C(3)	C(4)	118.6 (5)
C(4)	C(5)	1.358 (9)	C(3)	C(4)	C(5)	120.0 (6)
C(5)	N(1)	1.314 (8)	C(4)	C(5)	N(1)	122.8 (6)
C(6)	C(7)	1.523 (8)	C(2)	C(6)	C(7)	117.1 (4)
C(6)	N(2)	1.518 (6)	C(2)	C(6)	N(2)	113.0 (4)
C(7)	C(8)	1.489 (9)	C(7)	C(6)	N(2)	101.0 (4)
C(8)	C(9)	1.504 (9)	C(6)	C(7)	C(8)	104.4 (5)
C(9)	N(2)	1.510 (7)	C(7)	C(8)	C(9)	107.5 (6)
C(10)	N(2)	1.472 (7)	C(8)	C(9)	N(2)	105.2 (5)
			C(1)	N(1)	C(5)	117.6 (4)
C(1')	C(2')	1.400 (7)	C(6)	N(2)	C(9)	105.6 (3)
C(1')	C(6')	1.396 (7)	C(6)	N(2)	C(10)	113.9 (4)
C(1')	C(7')	1.486 (6)	C(9)	N(2)	C(10)	114.7 (4)
C(2')	C(3')	1.383 (8)				
C(2')	O(3)	1.318 (7)	C(2')	C(1')	C(6')	117.8 (4)
C(3')	C(4')	1.361 (9)	C(2')	C(1')	C(7')	121.2 (4)
C(4')	C(5')	1.391 (9)	C(6')	C(1')	C(7')	120.9 (4)
C(5')	C(6')	1.377 (8)	C(1')	C(2')	C(3')	121.1 (5)
C(7')	O(1)	1.254 (6)	C(1')	C(2')	O(3)	121.1 (5)
C(7')	O(2)	1.255 (6)	C(3')	C(2')	O(3)	117.7 (5)
			C(2')	C(3')	C(4')	119.7 (6)
C(1)	H(C1)	0.89 (4)	C(3')	C(4')	C(5')	120.9 (6)
C(3)	H(C3)	0.80 (4)	C(4')	C(5')	C(6')	119.5 (6)
C(4)	H(C4)	0.89 (4)	C(1')	C(6')	C(5')	121.0 (5)
C(5)	H(C5)	1.16 (4)	C(1')	C(7')	O(1)	117.8 (4)
C(6)	H(C6)	1.01 (4)	C(1')	C(7')	O(2)	118.9 (4)
C(7)	H(C7)	0.99 (4)	O(1)	C(7')	O(2)	123.3 (4)
C(7)	H(C71)	0.86 (4)				
C(8)	H(C8)	0.89 (5)	C(2)	C(1)	H(C1)	115 (2)
C(8)	H(C81)	1.19 (5)	N(1)	C(1)	H(C1)	120 (2)
C(9)	H(C9)	1.02 (4)	C(2)	C(3)	H(C3)	118 (3)
C(9)	H(C91)	1.04 (4)	C(4)	C(3)	H(C3)	123 (3)
C(10)	H(C10)	0.94 (5)	C(3)	C(4)	H(C4)	122 (3)
C(10)	H(C101)	1.18 (5)	C(5)	C(4)	H(C4)	117 (3)
C(10)	H(C102)	1.02 (5)	C(4)	C(5)	H(C5)	132 (2)
N(2)	H(O1)	0.84 (3)	N(1)	C(5)	H(C5)	105 (2)
			C(2)	C(6)	H(C6)	103 (2)
C(3')	H(C3')	0.95 (4)	C(7)	C(6)	H(C6)	113 (2)
C(4')	H(C4')	1.01 (4)	N(2)	C(6)	H(C6)	109 (2)
C(5')	H(C5')	1.05 (4)	C(6)	C(7)	H(C7)	113 (2)
C(6')	H(C6')	1.10 (4)	C(6)	C(7)	H(C71)	115 (3)
O(3)	H(O3)	1.15 (4)	C(8)	C(7)	H(C7)	118 (2)
			C(8)	C(7)	H(C71)	106 (3)
			H(C7)	C(7)	H(C71)	99 (4)
			C(7)	C(8)	H(C8)	114 (3)
			C(7)	C(8)	H(C81)	107 (2)
			C(9)	C(8)	H(C8)	115 (3)
			C(9)	C(8)	H(C81)	93 (2)
			H(C8)	C(8)	H(C81)	118 (4)
			C(8)	C(9)	H(C9)	116 (2)
			C(8)	C(9)	H(C91)	120 (2)
			N(2)	C(9)	H(C9)	109 (2)
			N(2)	C(9)	H(C91)	101 (2)
			H(C9)	C(9)	H(C91)	105 (3)
			N(2)	C(10)	H(C10)	114 (3)
			N(2)	C(10)	H(C101)	124 (2)
			N(2)	C(10)	H(C102)	98 (3)
			H(C10)	C(10)	H(C101)	94 (4)
			H(C10)	C(10)	H(C102)	111 (4)
			H(C101)	C(10)	H(C102)	118 (4)
			C(9)	N(2)	H(O1)	111 (2)
			C(6)	N(2)	H(O1)	111 (2)
			C(10)	N(2)	H(O1)	101 (2)
			C(2')	C(3')	H(C3')	126 (3)
			C(4')	C(3')	H(C3')	114 (3)

Table 3 (cont.)

<i>i</i>	<i>j</i>	<i>k</i>	\angle_{ijk}
C(3')	C(4')	H(C4')	121 (3)
C(5')	C(4')	H(C4')	118 (3)
C(4')	C(5')	H(C5')	127 (2)
C(6')	C(5')	H(C5')	114 (2)
C(5')	C(6')	H(C6')	118 (2)
C(1')	C(6')	H(C6')	121 (2)
C(2')	O(3)	H(O3)	110.4(2)

were consistent with a chemically reasonable model. The remaining three heavy atoms were located from the subsequent Fourier syntheses. The initial structure factor calculation for the 19 atoms gave a discrepancy index of $R=0.38$, with a uniform isotropic temperature factor. The structure was refined isotropically and anisotropically to $R=0.07$ using an IBM 1130 block-diagonal least-squares program by Shiono (1968). All hydrogen atoms were located on the difference syntheses. A final refinement with full-matrix least-squares (Shiono, 1966) included all parameters except the thermal parameters of hydrogen atoms. The temperature factors for the hydrogen atoms were the same as those for the atom to which they are bonded. The quantity minimized was $\sum_i w_i (K|F_o| - |F_c|)^2$ where $w_i = (a + b|F_o| + c|F_o|^2)^{-1}$, $a = 2|F_{\min}| = 16.24$, $b = 1.0$ and $c = 2/|F_{\max}| = 0.0043$. The last cycle of refinement gave $R=0.053$ for all reflections and 0.045 for observed only, with insignificant parameter shifts. The value of $\sum w \Delta^2 / (m-n) = 0.1513$; the average value of shift/ σ was 0.18 and the maximum 1.45 for the x coordinate of O(3). The final parameters are given in Table 1 and the corresponding structure factors in Table 2. The atomic scattering factors used were those of Cromer & Waber (1965) for carbon, nitrogen and oxygen, and by Stewart, Davidson & Simpson (1965) for hydrogen. The conformation and thermal parameters of the molecule are illustrated by an ORTEP plot in Fig. 1, with a diagram of the atomic notation. The bond lengths and angles are listed, with their standard deviations, in Table 3.

Description of the crystal structure

The structure is illustrated in Figs. 2 and 3, as viewed down the a and b axes respectively. There is no continuous hydrogen bonding framework as observed in structures with more functional groups, such as glucose-urea. The complex consists of well-defined salt molecules consisting of a nicotinyl cation and a salicylate anion, *i.e.* the crystal is nicotinyl salicylate. These molecules stack in a characteristic herring-bone 'van der Waals' manner to form sheets parallel to (100).

The molecular ions are linked into a salt-like pair by a strong hydrogen-bond type interaction $+N(2)-H \cdots -O(1)-C$ between the quaternary nitrogen and the carboxylate group. This is indicated by the dotted line with an arrow in Figs. 2 and 3. The $+N(H) \cdots O^-$ separation of 2.627 Å is significantly shorter than that commonly found in the zwitterion association of amino acids

which range from 2.80 to 2.85 Å (Marsh & Donohue, 1967). The hydrogen atom H(O1) lies on the line of centers, about 0.8 Å from the nitrogen, within the experimental uncertainty. The coordination about the quaternary nitrogen is approximately tetrahedral.

Apart from this strong association, all other interion-pair distances are greater than 3.09 Å. They are given

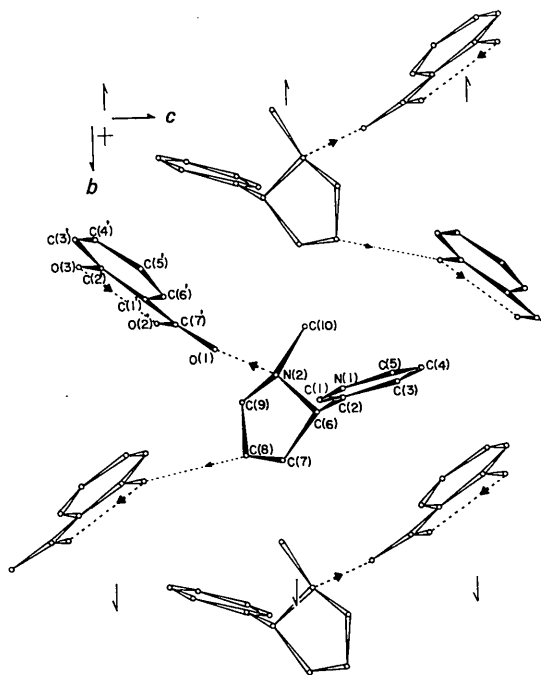


Fig. 2. The crystal structure of nicotine-salicylic acid viewed down the a axis. Solid lines indicate C-C, C-N, and C-O bonds. Dotted lines indicate hydrogen bonds with arrows pointing in the donor direction.

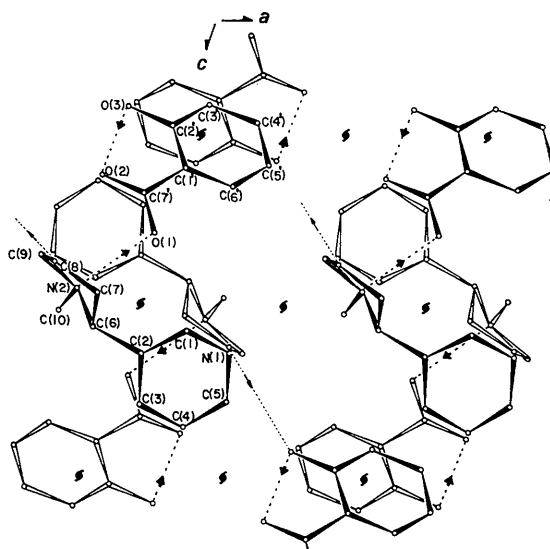


Fig. 3. The crystal structure of nicotine-salicylic acid viewed down the b axis. Solid and dotted lines are as in Fig. 2.

Table 4. *Interionic and intermolecular distances shorter than 3.6 Å in nicotine-salicylic acid complex*

Interionic distances			Intermolecular distances		
N(2)	O(1)	2.627* Å	C(3)	C(2'a)	3.411 Å
	C(7')	3.339	C(4)	O(2b)	3.497
	O(2)	3.331		O(3a)	3.551
O(1)	C(1)	3.089	C(5)	C(5'c)	3.598
	C(2)	3.482		O(2b)	3.573
	C(6)	3.432	C(7)	O(1a)	3.549
	C(9)	3.429	C(8)	O(3d)	3.175†
	C(10)	3.321	C(9)	O(3d)	3.488
			C(3')	O(1e)	3.435
			C(4')	O(1e)	3.580

Symmetry code:

<i>a</i>	- <i>x</i>	$\frac{1}{2} + y$	1 - <i>z</i>
<i>b</i>	1 + <i>x</i>	<i>y</i>	1 + <i>z</i>
<i>c</i>	1 - <i>x</i>	$\frac{1}{2} + y$	1 - <i>z</i>
<i>d</i>	-1 - <i>x</i>	$\frac{1}{2} + y$	- <i>z</i>
<i>e</i>	- <i>x</i>	$-\frac{1}{2} + y$	- <i>z</i>

* Strong hydrogen bond

† Weak hydrogen bond

in Table 4 together with the intermolecular distances which are less than 3.6 Å. The shortest of these is the separation of C(8)---O(3) of 3.175 Å. This corresponds to a distance of 2.56 Å from the methylene H(C8) to the hydroxyl oxygen O(3) in the direction of the lone pairs of the oxygen. This is just about the sum of the van der Waals radii, but might also be regarded as a very weak C-H...O hydrogen bond interaction. It is the only interaction less than 3.4 Å across the layers parallel to (100); indicated as the dotted line with a thin arrow in Figs. 2 and 3. The absence of (100) cleavage suggests that, in fact, this interaction gives cohesion between the sheets of stacked ion pairs.

The nicotinyl cation

The nicotinyl cation consists of a puckered pyrrolidine ring linked to a planar pyridine ring by a normal C-C bond of length 1.502 Å. The dihedral angle between the best planes of these two rings (see Table 5),

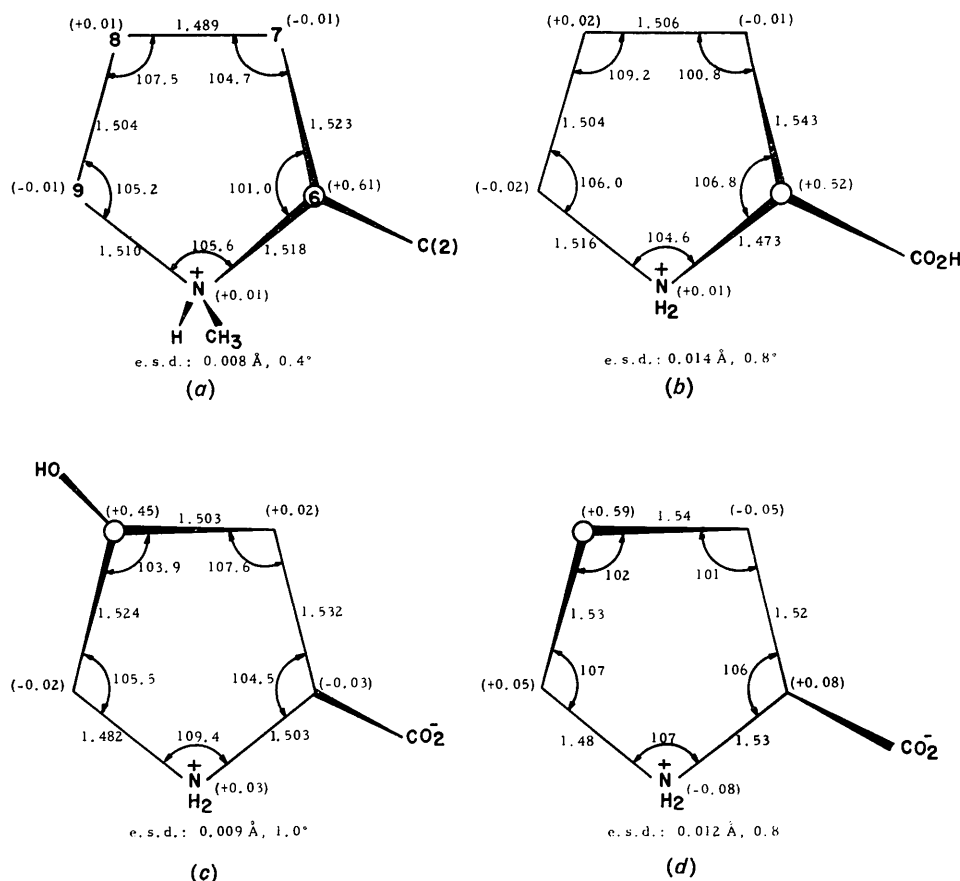


Fig. 4. Comparison of the geometry of the pyrrolidine ring with that observed in proline and its derivatives. Encircled atoms lie out of the plane formed by the other four atoms in the ring and decimal values in parentheses denote the deviations of atoms; bond lengths are in (Å) and bond angles in (°). (a) Pyrrolidine ring (present study), (b) DL-proline-HCl (Mitsui, Tsuboi & Iitaka, 1969), (c) hydroxy-L-proline (Donohue & Trueblood, 1952), (d) L-proline (Kayushina & Vainshtein, 1965).

with respect to the connecting bond, is 77° . The pyrrolidine ring has four atoms in a plane, C(7), C(8), C(9) and N(2) with the fifth, C(6), displaced by 0.605 \AA . The geometry of the ring is compared with that observed in proline and its derivatives in Fig 4. It is clear that any systematic variations in bond lengths or bond angles which may occur between these molecules are small and are obscured by the experimental errors. As with the tetrahydrofuran ring in ribofuranyl and fructofuranyl residues (*e.g.* Sundaralingam, 1965), there are two distinct conformations involving different out-of-plane atoms, one adjacent to the heteroatom and one across the ring.

The C-N⁺ distances around the quaternary nitrogen are unusual in that the N⁺-CH₃ bond length of 1.472 \AA is shorter than the two ring bonds, 1.510 and 1.518 \AA . The shorter distance agrees well with the mean value of 1.487 \AA in the amino acid zwitterion structures (Marsh & Donohue, 1967). A similar variation in lengths for single C_{sp³}-N_{sp³}⁺ bonds has been observed recently in the crystal structure of 1,5-endomethylenequinolizidinium *p*-toluenesulphonate (Huber, 1969), where the shorter bonds (1.487 , 1.516 \AA) are in six-membered rings and the longer bonds (1.527 , 1.533 \AA) are in a four-membered ring. These observations have in common that the longer C-N⁺ bonds subtend the smallest valence angle, which is 88° for the four-membered ring and 105° for the five-membered ring.

The pyridine ring is planar, but (C6) lies out of the

plane by 0.044 \AA . The C-C bond lengths range from 1.358 to 1.387 \AA with a mean of 1.378 \AA , the C-N bond lengths are 1.314 and 1.331 \AA . The ring angles vary from 116 to 125° . The greatest differences which are between C(2)-C(3) and C(4)-C(5), and angles C(1)-C(2)-C(3) and C(3)-C(4)-C(5), correspond to 2.5σ and 5.6σ respectively. Similar variations have been reported in some of the more recent studies of *m*-substituted pyridine derivatives, such as β -pyridyl carbinol hydrochloride (Kupfer-Tsoucaris, 1964), β -picolylamine hydrochloride (Genet, 1965), and in more complex molecules, such as pyridoxal phosphate oxide (Barrett & Palmer, 1969) and 2-amino-3-hydroxy-4-hydroxymethyl-7-methyl- Δ^2 -furo[2,3-*c*]pyridine phosphate hydrobromide (Yoshino, Iitaka, Takanashi & Tamura, 1970). More precise measurements on simpler compounds are necessary to establish the reality and rationale of these variations in bond lengths and valence angles.

The salicylate anion

As in the crystal structures of the acid (Cochran, 1953; Sundaralingam & Jensen, 1965), there is a strong internal hydrogen bond between the hydroxyl and a carboxylate oxygen. The O-(H)···O separation is 2.544 \AA and the hydrogen atom is 0.44 \AA off the line of centers, thereby making an O-H···O angle of 140.8° . This compares with 2.620 \AA and 145.8° in the acid.

The C-C bond lengths do not differ significantly from

Table 5. Least-squares planes in nicotine-salicylic acid complex

Equation for plane: $Ax + By + Cz = D$, where x, y, z are in \AA .

Atoms in plane	Atoms out of plane	Distance from best plane	Given constant
A. Pyridine ring			
C(1)		0.001 \AA	$A = 0.0963$
C(2)		0.001	$B = 0.9502$
C(3)		-0.003	$C = 0.2479$
C(4)		0.003	$D = 8.2319$
C(5)		-0.000	
N(1)		-0.002	
	C(6)	0.044	
B. Pyrrolidine ring			
C(7)		-0.009	$A = -0.6063$
C(8)		0.014	$B = 0.0735$
C(9)		-0.014	$C = 0.9479$
N(2)		0.009	$D = 5.7244$
	C(2)	0.357	
	C(6)	0.605	
	C(10)	0.684	
C. Salicylate anion			
C(1')		-0.006	$A = 0.2295$
C(2')		0.009	$B = 0.7669$
C(3')		-0.005	$C = -0.6415$
C(4')		-0.002	$D = 2.6042$
C(5')		0.005	
C(6')		-0.001	
	C(7)	-0.095	
	O(1)	-0.132	
	O(2)	-0.119	
	O(3)	0.003	
	H(O3)	-0.012	

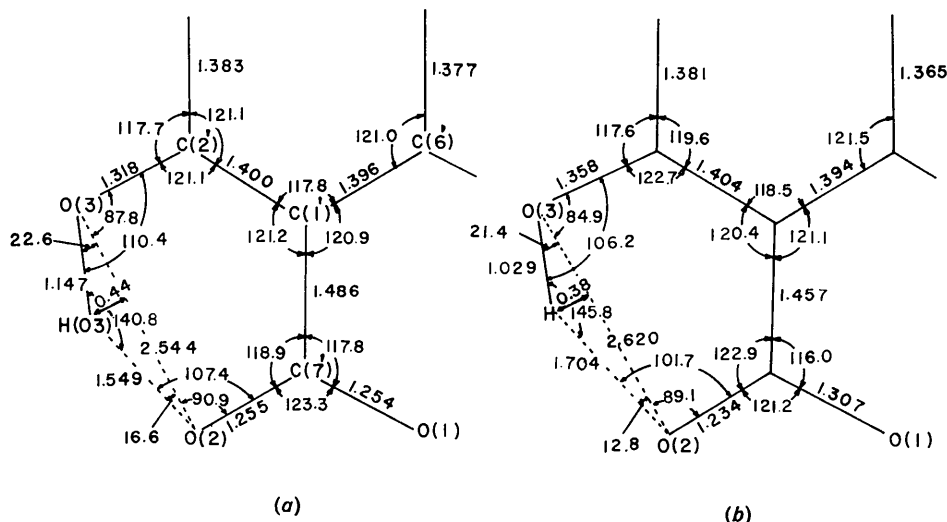


Fig. 5. Bond lengths (Å) and bond angles (°) around the intramolecular hydrogen bond (a) for salicylate anion in nicotine-salicylic acid complex, (b) for salicylic acid.

those observed in the acid, with mean and maximum differences of 0.010, 0.029 Å between the two structures. The C-O bonds of 1.254 and 1.255 Å are normal values for the carboxylate group. The C-OH of 1.318 Å is 0.04 Å shorter than observed in the acid and this difference is associated with the stronger hydrogen bond (*i.e.* 0.08 Å shorter). The carboxylate group is slightly out of the plane of the benzene ring, by 3.1° as compared with 1.1° in the acid. The small differences in the geometry of the internal hydrogen bond between the ion in this complex and the free acid presumably arises from the ionic charge; they are compared in Fig. 5. It will be noted that the geometry of the ion is slightly more favorable for internal hydrogen bonding.

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