The failure in this study to find any changes in molecular parameters induced by the introduction of a 4-chloro substituent into PE would therefore indicate that the 4-chloro substituent alone is responsible for the marked difference in the ability of PE and pCPE to interact with the uptake and release of DA and 5HT in the mammalian CNS. X-ray crystallographic studies of a number of phenylethylamines (Carlström, Bergin & Falkenberg, 1973; Paxton & Hamor, 1977) have shown that in all of these in the solid state, the ethylamine side chain adopts an almost identical *trans* conformation. It therefore appears that the side-chain conformation is not an important determinant in the biological activity.

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An X-ray Study of a Very Short, Asymmetric Hydrogen Bond between a Protonated Molecule of 1,5-Dimethyl-1,5-naphthyridine-4(1*H*),8(5*H*)-dione and a CF$_3$COO$^-$ Anion

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Crystals of 1,5-dimethyl-1,5-naphthyridine-4(1*H*),8(5*H*)-dione (DMNDO) obtained from a CF$_3$COOH solution have been studied by X-ray diffraction methods and were found to consist of hydrogen-bonded CF$_3$COOH$\cdots$CF$_3$COO$^-\cdots^+$H(DMNDO)H$^+\cdots$CF$_3$COO$^-\cdots$CF$_3$COOH units situated about crystallographic centers of symmetry. The crystals are monoclinic, space group $P2_1/n$, with $Z = 2$. At $-35\,^{\circ}$C, the unit-cell dimensions are: $a = 16 \cdot 804$ (3), $b = 13 \cdot 959$ (2), $c = 5 \cdot 123$ (1) Å, and $\beta = 90 \cdot 57$ (2)$^{\circ}$. Full-matrix least-squares refinement using 2320 reflections [$I > 2\sigma(I)$] converged at a conventional R of 0·046. All non-hydrogen atoms, including the disordered F atoms of the CF$_3$COOH and CF$_3$COO$^-$ moieties, were refined with anisotropic thermal parameters; the H atoms with isotropic parameters. The protonated keto groups of the DMNDO molecule form very short, asymmetric hydrogen bonds to the O atoms of the CF$_3$COO$^-$ anions. Details of these O–H$\cdots$O bonds are: O$\cdots$O $= 2 \cdot 477$ (2), O–H $= 1 \cdot 09$ (3), H$\cdots$O $= 1 \cdot 39$ (3) Å, O–H$\cdots$O $= 175$ (3)$^{\circ}$. The second O atom of the anion accepts a more normal hydrogen bond from the –OH group of the CF$_3$COOH molecule: O$\cdots$O $= 2 \cdot 594$ (2), O–H $= 0 \cdot 88$ (3), H$\cdots$O $= 1 \cdot 72$ (3) Å, O–H$\cdots$O $= 177$ (3)$^{\circ}$.

Introduction

The structural analysis of 1,5-dimethyl-1,5-naphthyridine-4(1*H*),8(5*H*)-dione (hereinafter referred to as DMNDO) was undertaken as part of a study of the chemistry and spectral properties of substituted naphthyridines (Brown & Dewar, 1976). Recrystallized by slow evaporation from a trifluoroacetic acid

solution, the colorless prisms readily decomposed when the crystals were separated from the mother liquor. It was thus initially assumed that the crystal structure would consist of DMNDO and CF_3COOH molecules. As a result of the structure determination reported herein, however, it was discovered that the basic structural unit is $[(DMNDO)H_2^{2+}][CF_3COO^-]_2$-$[CF_3COOH]_2$ in which the protons of two CF_3COOH molecules have been transferred to the DMNDO molecule, forming a 'very short' hydrogen bond.
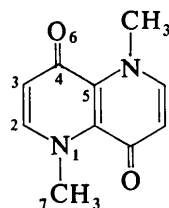
Experimental

Although the crystals decomposed at room temperature, they were found to be quite stable at $-35\,^{\circ}C$, the temperature maintained by the low-temperature apparatus associated with the Syntex $P2_1$ diffractometer (Mo $K\alpha$ radiation, monochromated with a graphite crystal, $\lambda = 0\cdot71069$ Å). The crystal selected for this study was a cleaved fragment which had approximate dimensions $0\cdot41 \times 0\cdot44 \times 0\cdot59$ mm. An initial study showed the crystal to be monoclinic, space group $P2_1/n$; for the structural unit described above, $Z = 2$. The unit-cell parameters at $-35\,^{\circ}C$ were refined by least squares using the Bragg angles ($24^{\circ} < 2\theta < 31^{\circ}$) of 60 reflections: $a = 16\cdot804$ (3), $b = 13\cdot959$ (2), $c = 5\cdot123$ (1), $\beta = 90\cdot57$ (2)$^{\circ}$, $V = 1201\cdot6$ Å³.

Intensity data for 2762 unique reflections ($4^{\circ} < 2\theta < 55^{\circ}$) were collected using the ω-scan technique. Scans of $1\cdot0^{\circ}$ were employed with scan rates which ranged from $1\cdot0$ to $5\cdot0^{\circ}$ min⁻¹, depending upon the number of counts accumulated in a rapid preliminary scan. Background measurements were taken at both ends of the scan with ω displaced by $\pm1\cdot0^{\circ}$ from the $K\alpha$ peak; the time of each measurement was one-half the scan time. The intensities of four standard reflections were monitored after every 96 reflections; these intensities dropped by an average of 2% over the period of data collection and a correction factor, as a function of exposure time, was applied. The intensities were corrected for Lorentz and polarization effects, but not for absorption ($\mu = 2\cdot17$ cm⁻¹; transmission factors ranged from $0\cdot88$ to $0\cdot92$).

Structure solution and refinement

The structure was solved by direct methods (MULTAN). A difference-density Fourier map was used to locate the H atoms; in addition, it showed that

Table 1. *Final positional and hydrogen isotropic thermal parameters with estimated standard deviations*

	x	y	z	U_{iso} (Å²)
Protonated naphthyridine moiety				
N(1)	0·5999 (1)	0·4493 (1)	0·5517 (3)	
C(2)	0·5849 (1)	0·3855 (1)	0·7379 (3)	
C(3)	0·5116 (1)	0·3740 (1)	0·8457 (3)	
C(4)	0·4483 (1)	0·4300 (1)	0·7645 (3)	
C(5)	0·4615 (1)	0·4956 (1)	0·5519 (3)	
O(6)	0·3791 (1)	0·4272 (1)	0·8771 (3)	
C(7)	0·6848 (1)	0·4601 (2)	0·4761 (5)	
Trifluoroacetic acid molecule				
C(11)	0·0957 (1)	0·4005 (2)	0·5870 (5)	
C(12)	0·1387 (1)	0·3284 (1)	0·7638 (4)	
F(13)*	0·0468 (3)	0·4519 (3)	0·7253 (9)	
F(14)	0·1438 (2)	0·4600 (3)	0·4743 (8)	
F(15)	0·0557 (3)	0·3573 (3)	0·4031 (7)	
F(13)p*	0·136 (2)	0·421 (2)	0·403 (5)	
F(14)p	0·025 (1)	0·365 (2)	0·537 (5)	
F(15)p	0·070 (2)	0·473 (1)	0·707 (5)	
O(16)	0·1961 (1)	0·3696 (1)	0·8919 (4)	
O(17)	0·1180 (1)	0·2467 (1)	0·7741 (3)	
Trifluoroacetate anion				
C(21)	0·3530 (1)	0·1827 (1)	0·5110 (4)	
C(22)	0·3267 (1)	0·2613 (1)	0·3179 (3)	
F(23)†	0·4288 (2)	0·1786 (4)	0·5495 (12)	
F(24)	0·3250 (3)	0·1014 (2)	0·4586 (9)	
F(25)	0·3258 (3)	0·2031 (3)	0·7467 (6)	
F(23)p†	0·300 (1)	0·121 (1)	0·542 (3)	
F(24)p	0·380 (1)	0·212 (1)	0·719 (1)	
F(25)p	0·412 (1)	0·133 (1)	0·403 (2)	
O(26)	0·3799 (1)	0·3188 (1)	0·2598 (3)	
O(27)	0·2567 (1)	0·2585 (1)	0·2475 (3)	
Hydrogen atoms				
H(2)	0·629 (1)	0·350 (1)	0·799 (4)	0·024 (4)
H(3)	0·507 (1)	0·331 (1)	0·970 (4)	0·020 (4)
H(6)	0·380 (2)	0·377 (2)	1·039 (6)	0·082 (9)
H(7A)	0·692 (2)	0·439 (2)	0·292 (6)	0·061 (7)
H(7B)	0·712 (1)	0·420 (2)	0·598 (5)	0·059 (7)
H(7C)	0·702 (1)	0·529 (2)	0·499 (5)	0·052 (7)
H(16)	0·216 (2)	0·333 (2)	1·017 (7)	0·084 (10)

* Occupation factor for F(13–15) is $0\cdot85$: for F(13–15)p, $0\cdot15$.
† Occupation factor for F(23–25) is $0\cdot70$: for F(23–25)p, $0\cdot30$.

the F atoms of the CF_3COOH molecule and CF_3COO^- anion were slightly disordered. The occupation factors for the disordered atoms were initially included in the refinement in order to determine their approximate values; they were later fixed (see Table 1). The refinement of the structure by the full-matrix least-squares method was carried out using only those 2320 reflections for which $I > 2\sigma(I)$. Included in the refinement were anisotropic thermal parameters for the non-hydrogen atoms and isotropic thermal parameters for the H atoms. The refinement of 272 variables converged at a conventional R of $0\cdot046$ and a weighted R
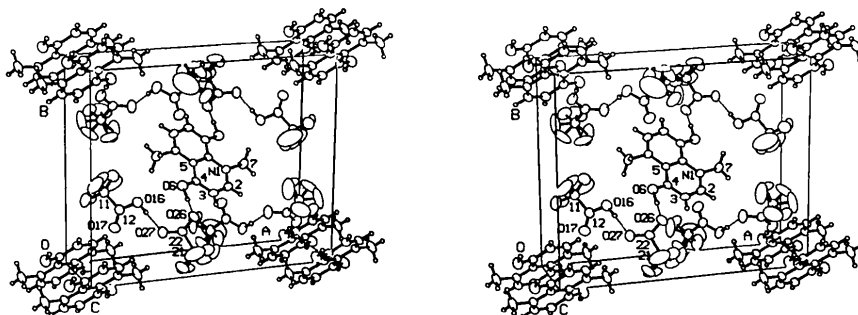
Fig. 1. Packing diagram and atom-numbering scheme. Each H atom is numbered in accordance with the C or O atom to which it is bonded. The thin lines represent hydrogen bonds.

of 0·058, although convergence was hindered by large correlations between the variables associated with the disordered F atoms. (All data, $R = 0·056$, $R_w = 0·059$.) The H atoms refined normally, and there is no reason to believe that the disorder of the F atoms had any effect on the H positions. The refinement was stopped when the largest shift in any parameter among the non-fluorine atoms was $0·04\sigma$; the largest shift for the F atoms was $0·75\sigma$. The final positional (and, for H, thermal) parameters are listed in Table 1.* The largest peak in the final difference map had a magnitude of $0·23$ e Å^{-3} and was located in the neighborhood of F(24) and F(25)p. The mathematical and computational details are noted elsewhere (Harlow & Simonsen, 1976).

Discussion

Hydrogen-bonding scheme

The crystal structure consists of hydrogen-bonded $CF_3COOH \cdots CF_3COO^- \cdots ^+H(DMNDO)H^+ \cdots CF_3COO^- \cdots CF_3COOH$ units which are located about crystallographic centers of symmetry. Fig. 1 shows the spatial arrangement of one such unit situated about the inversion center at $\frac{1}{2},\frac{1}{2},\frac{1}{2}$. The two O atoms, O(26) and O(27), of each trifluoroacetate anion serve as hydrogen-bond acceptors. The hydrogen bond formed between O(27) and the −OH function of the CF_3COOH molecule is a typical 'short' bond with an O···O distance of $2·594$ (2) Å and a nearly linear O−H···O angle of 177 (3)°. The hydrogen bond between the protonated DMNDO molecule and O(26) must, however, be classed as a 'very short' bond (Speakman, 1972) with its O···O distance of $2·477$ (2) Å. Furthermore, with the location and refinement of the H atom, it is obvious that the hydrogen bond is asym-
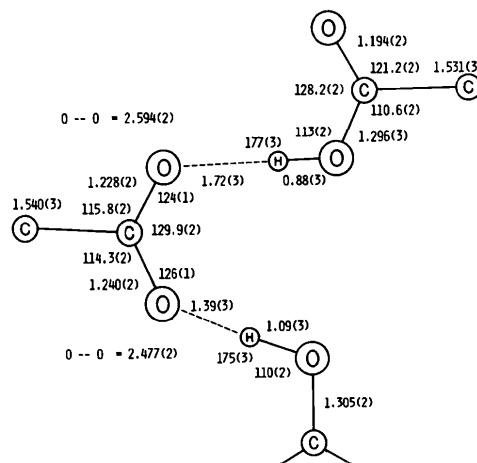
* Lists of structure amplitudes and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33432 (16 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Fig. 2. Bond distances (Å) and angles (°) for the CF_3COOH and CF_3COO^- moieties and their relation within the hydrogen-bonding scheme. The disordered F atoms of the acid and the anion have been omitted. The molecular fragment at the bottom is the DMNDO cation.

metric in nature with the H atom being much closer to the O atom of the DMNDO molecule, $1·09$ (3) Å, than to the O atom of the anion, $1·39$ (3) Å. The positioning of the H atom does appear to be quite reasonable when the O−H and O···O distances here are compared with those graphed by Speakman. Details of the hydrogen-bonding scheme are given in Fig. 2.

CF_3COO^- anion and CF_3COOH molecule

In addition to the location of the H atoms, the C−O and C−C−O bond parameters serve to differentiate these two species (Fig. 2). The geometry of the acid molecule is similar to that expected for a dimeric, hydrogen-bonded organic acid; the C−O distances of $1·194$ (2) and $1·296$ (3) Å clearly distinguish between the C=O and C−OH bonds. In the anion, these two distances are nearly equivalent, $1·228$ (2) and

Table 2. *Comparison of the trifluoroacetate geometry with the* O—H *distance*

The O—H distances include the normal O—H distance found in the molecular acid and those O···H distances associated with very short hydrogen bonds (O···O distance less than 2·5 Å).

Species	O—H/O···H	C=O	C—O	C—C=O	C—C—O	O=C—O
^{a} CF$_3$COOH	0·88 (3) Å	1·194 (2) Å	1·296 (3) Å	121·2 (2)°	110·6 (2)°	128·2 (2)°
^{b} (CF$_3$COO···H···OCOCF$_3$)$^-$	1·22	1·214 (2)	1·266 (3)	119·5 (1)	111·2 (1)	129·3 (2)
^{a} CF$_3$COO$^-$···H$^+$	1·39 (3)	1·228 (2)	1·240 (2)	115·8 (2)	114·3 (2)	129·9 (2)
^{c} CF$_3$COO$^-$		1·252 (8)	1·263 (8)	116·5 (6)	115·4 (6)	128·0 (6)

(a) Present work. (b) Macdonald, Speakman & Hadzi (1972). The O···H distance assumes a symmetric hydrogen bond. (c) Cruickshank, Jones & Walker (1964). The shortest C—O distance is listed under the C=O column only for consistency. Within the experimental error, the two C—O distances are equivalent.
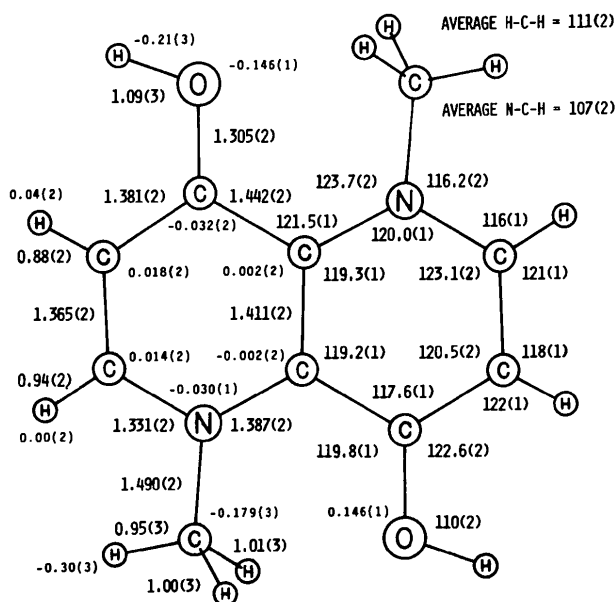

Fig. 3. Molecular geometry of the (DMNDO)H$_2^{2+}$ cation. The bond distances (Å) and angles (°) are given in large type: the small numbers are deviations (Å) from the least-squares mean plane of the 10 ring atoms.

(DMNDO)H$_2^{2+}$ cation

Of the bond distances and angles for the (DMNDO)-H$_2^{2+}$ cation (Fig. 3), only the C—O and O—H distances are fairly interesting. The C—O bond length of 1·305 (2) Å falls between the values reported for the two tautomeric forms of 4-hydroxypyridine in which the C=O distance is 1·253 (7) Å while the C—OH distance is 1·321 (6) Å (Boer, Turley & van Remoortere, 1972). This intermediate C—O distance appears to be consistent, however, with the exceptionally long O—H bond of 1·09 (3) Å.

The non-planarity of the fused-ring system gives the naphthyridine ring a slight 'chair' conformation when viewed parallel to the central C(5)—C(5)' bond. This distortion from planarity is induced by the repulsive interactions between the exocyclic —OH$^+$ and —CH$_3$ substituents; the naphthyridine ring of a similar compound, 4,8-dimethoxy-1,5-naphthyridine, where such an interaction is not possible, was found to be quite planar (Harlow & Simonsen, 1977).

1·240 (2) Å, with the longer C—O distance being linked with the shorter O···H hydrogen bond. The C—C—O angles are also indicative of an acid on one hand, where the angle opposite the C=O bond is much smaller than the angle opposite the C—OH bond, and of an anion on the other, where the angles are nearly equal. As the H ion of the acid molecule is drawn away from the O atom, one would expect the conformation of the trifluoroacetate residue to approach that of the CF$_3$COO$^-$ anion. The results of several trifluoroacetate structures (Table 2) clearly indicate that such is the case. The O—C—O angle appears to be quite independent of the O—H distance.

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