Intermolecular contacts are all of the van der Waals type. Regions of contact which are less than the sum of the van der Waals radii are between N(12) and H(6*b*) ($\frac{1}{2}-x$, $\frac{1}{2}+y$, z) 2·67 (4) Å and O(14) and H(3) ($\frac{1}{2}-x$, $1-y$, $\frac{1}{2}+z$) 2·53 (4) Å.

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Structure of the Hydrate Form of a β-Thiotrifluoromethyl Ketone, a Potent Esterase Inhibitor

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Abstract. 1,1,1-Trifluoro-5-phenyl-4-thiapentane-2,2-diol, $C_{10}H_{11}F_3O_2S$, $M_r = 252{\cdot}25$, $P2_1/c$, $a = 11{\cdot}476$ (4), $b = 10{\cdot}112$ (2), $c = 9{\cdot}794$ (3) Å, $\beta = 104{\cdot}42$ (2)°, $V = 1100{\cdot}7$ (5) Å^3, $Z = 4$, $D_x(130\ K) = 1{\cdot}52$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 3{\cdot}0$ cm^{-1}, $F(000) = 512$, $T = 130$ K, $R = 0{\cdot}039$, 1937 unique reflections. The molecular structure of the hydrated ketone has two equivalent hydroxyl groups bonded to the C atom of the ketone functionality. One of the hydroxyl H atoms is hydrogen bonded across a center of symmetry to another molecule. The other hydroxyl H atom exhibits an intramolecular H bond to the thioether S atom with H···S of 2·37 (5) Å.

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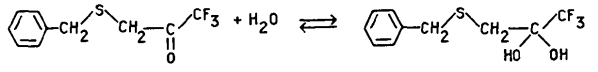
Introduction. Several laboratories have demonstrated that molecules containing the highly polarized trifluoromethylketone functionality can be potent inhibitors of carboxylesterases from a variety of species (Brodbeck, Schweikert, Gentinetta & Rottenberg, 1979; Gelb, Svaren & Abeles, 1985; Abdel-Aal &

Hammock, 1986, and references therein). It was noted that inclusion of a thioether β to the carbonyl group led to a 50- to 100-fold increase in the potency of several series of compounds acting on insect juvenile hormone esterase and several other enzymes (Hammock, Abdel-Aal, Mullin, Hanzlik & Roe, 1984) while also leading to a large decrease in inhibitory potency in other enzymes such as the carboxylesterases found in human liver (Ashour & Hammock, 1987). Since these polarized ketones are putative 'transition state' enzyme inhibitors thought to act by forming a tetrahedral covalent hydrate with a catalytically active serine of carboxylesterases, it became interesting to examine the crystal structure of a thioether-containing member of the series. The structure determination shows that, at least in the solid state, the equilibrium lies to the right.



(1) (2)

Experimental. Colorless plates obtained by recrystallization from hexane, crystal dimensions 0·08 × 0·37 × 0·55 mm; Syntex $P2_1$ diffractometer, locally modified LT-1 apparatus, $T = 130$ K, Mo $K\alpha$ radiation, graphite monochromator; cell dimensions from least-squares fit of 10 reflections with $15 < 2\theta < 22°$; space group $P2_1/c$ (No. 14) based on conditions $0k0$, $k = 2n$, $h0l$, $l = 2n$, no absorption correction (range of absorption correction factors 1·02–1·10); data collected to $2\theta_{max} = 50°$ with hkl ranges 0 to 13, 0 to 12, −11 to 11, respectively; ω scans, 1·2° range, 60° min^{-1} speed (Hope & Nichols, 1981), 1° offset for background; two check reflections monitored every 200 reflections displayed no decay; 2160 reflections measured, 1937 unique data, $R_{int} = 0·020$, 1275 observed $[I > 3\sigma(I)]$ used in the solution and refinement (based on F); structure solved by direct methods; blocked cascade least-squares refinement, 153 parameters; all non-H atoms with anisotropic thermal parameters, isotropic thermal parameters of H atoms set equal to 1·2 times the equivalent U of the bonded C atom. H atoms refined using a riding model with C—H = 0·96 Å except for the two hydroxyl H atoms which refined freely; $R = 0·039$, $wR = 0·039$, $w = 1/[\sigma^2(F_o) + 0·0002F_o^2]$, $S = 1·153$, $(\Delta/\sigma)_{max} = 0·057$ for x of C(7); $(\Delta/\sigma)_{av} = 0·012$; $\Delta\rho$ excursions 0·21 and −0·25 e Å^{-3}; atomic scattering factors and anomalous-dispersion corrections from *International Tables for X-ray Crystallography* (1974); computer programs from the *SHELXTL* (version 3) package (Sheldrick, 1981).

Discussion. The final atomic coordinates and isotropic thermal parameters for the compound are given in Table 1.* The structure (Fig. 1) consists of hydrogen-bonded pairs of $C_6H_5CH_2SCH_2C(OH)_2CF_3$ molecules. In addition, there is an intramolecular H bond between H(1) and the thioether sulfur. The relevant distances and angles are included in Table 2. Fig. 2 depicts the molecular packing and the intermolecular hydrogen bonding across a center of symmetry. There are no unusual features of the molecular geometry.

The existence of the hydrated structure even after two recrystallizations from hexane provides further indirect support for a similar structure mimicking a transient intermediate or transition state of the interaction of a carboxylesterase with its substrate. The relatively short intramolecular hydrogen bond with the thioether could help to stabilize the tetrahedral structure of the hydrate in some enzyme catalytic sites and thus increase potency. It also raises the possibility that the

* Lists of structure factors, anisotropic thermal parameters and calculated H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43960 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Atomic coordinates* (× 10^4) *and isotropic thermal parameters* (Å^2 × 10^3) *for* $C_{10}H_{11}F_3O_2S$

	x	y	z	U_{eq}/U_{iso}
S	2059 (1)	740 (1)	6723 (1)	30 (1)*
F(1)	5769 (2)	2336 (2)	10447 (2)	39 (1)*
F(2)	4262 (2)	3681 (2)	10012 (2)	41 (1)*
F(3)	5215 (2)	3283 (2)	8415 (2)	37 (1)*
O(1)	4624 (2)	664 (2)	8357 (2)	25 (1)*
O(2)	3572 (2)	1064 (2)	10069 (2)	24 (1)*
C(1)	4805 (3)	2723 (3)	9450 (3)	28 (1)*
C(2)	3949 (3)	1577 (3)	8920 (3)	21 (1)*
C(3)	2835 (3)	2064 (3)	7816 (3)	23 (1)*
C(4)	1293 (3)	−116 (3)	7901 (3)	29 (1)*
C(5)	208 (3)	569 (3)	8113 (3)	23 (1)*
C(6)	−920 (3)	324 (4)	7226 (4)	35 (1)*
C(7)	−1930 (3)	907 (4)	7462 (5)	54 (2)*
C(8)	−1836 (4)	1750 (4)	8590 (5)	60 (2)*
C(9)	−723 (4)	2027 (4)	9471 (4)	48 (2)*
C(10)	292 (3)	1432 (3)	9247 (3)	29 (1)*
H(1)	4085 (25)	343 (39)	7744 (37)	50 (13)
H(2)	4085 (25)	668 (27)	10477 (28)	25 (8)

* Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.

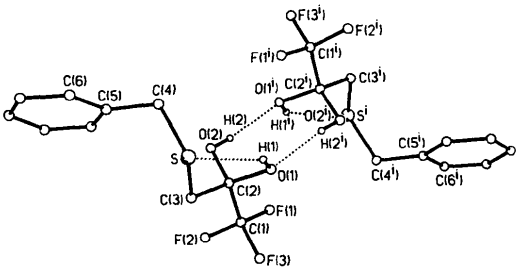


Fig. 1. A view of the hydrogen-bonded pairs of $C_6H_5CH_2SCH_2C(OH)_2CF_3$. The dotted lines indicate hydrogen-bonding interactions.

Table 2. *Bond lengths* (Å) *and bond angles* (°) *for* $C_{10}H_{11}F_3O_2S$

S–C(3)	1·804 (3)	S–C(4)	1·832 (4)
F(1)–C(1)	1·339 (3)	F(2)–C(1)	1·342 (4)
F(3)–C(1)	1·344 (4)	O(1)–C(2)	1·404 (4)
O(1)–H(1)	0·789 (34)	O(2)–C(2)	1·402 (4)
O(2)–H(2)	0·741 (26)	C(1)–C(2)	1·524 (4)
C(2)–C(3)	1·535 (4)	C(4)–C(5)	1·484 (5)
C(5)–C(6)	1·391 (4)	C(5)–C(10)	1·397 (4)
C(6)–C(7)	1·370 (6)	C(7)–C(8)	1·378 (7)
C(8)–C(9)	1·381 (5)	C(9)–C(10)	1·376 (6)

C(3)–S–C(4)	102·7 (2)	C(2)–O(1)–H(1)	101·6 (29)
C(2)–O(2)–H(2)	105·6 (24)	F(1)–C(1)–F(2)	107·2 (2)
F(1)–C(1)–F(3)	107·0 (3)	F(2)–C(1)–F(3)	106·9 (3)
F(1)–C(1)–C(2)	111·8 (3)	F(2)–C(1)–C(2)	111·2 (3)
F(3)–C(1)–C(2)	112·3 (2)	O(1)–C(2)–O(2)	112·5 (2)
O(1)–C(2)–C(1)	105·2 (3)	O(2)–C(2)–C(1)	108·1 (2)
O(1)–C(2)–C(3)	112·2 (2)	O(2)–C(2)–C(3)	108·3 (3)
C(1)–C(2)–C(3)	110·5 (2)	S–C(3)–C(2)	112·4 (2)
S–C(4)–C(5)	114·7 (2)	C(4)–C(5)–C(6)	120·8 (3)
C(4)–C(5)–C(10)	120·6 (3)	C(6)–C(5)–C(10)	118·5 (3)
C(5)–C(6)–C(7)	120·9 (3)	C(6)–C(7)–C(8)	120·1 (3)
C(7)–C(8)–C(9)	120·1 (4)	C(8)–C(9)–C(10)	120·0 (4)
C(5)–C(10)–C(9)	120·4 (3)		

Hydrogen-bonding dimensions

O(1)···O(2^{i})	2·851 (4)	O(1)···S	2·981 (3)
O(2^{i})–H(2^{i})···O(1)	172 (3)	O(1)–H(1)···S	135 (2)
H(2^{i})···O(1)	2·11 (3)	H(1)···S	2·37 (2)

Symmetry code: (i) $1-x, -y, 2-z$.

thioether hydrogen bonds with an amino acid in juvenile hormone esterase.

The inability to isolate a ketone structure provides further evidence that these compounds exist predominantly in the hydrated state. Although the X-ray structure presented here is likely to approximate the ultimate structure of the inhibitor in the catalytic site, it is not known if the inhibitor approaches the enzyme as the abundant hydrated form or the more substrate-like but rare carbonyl compound.

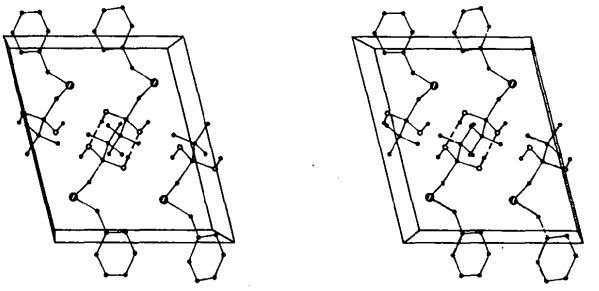


Fig. 2. Stereoview of the molecular packing as viewed down **b**. S atoms are shown as shaded circles, O atoms as open circles, and the remaining atoms as solid circles.

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Heterocyclic Tautomerism. III.* The Structure of the Product of Dimerization of 2-Pyridylacetonitrile

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Abstract. (*E*)-3-Amino-2,4-di(2-pyridyl)-2-butenenitrile, $C_{14}H_{12}N_4$, $M_r = 236·3$, orthorhombic, *F*2*dd*, $a = 4·693$ (1), $b = 20·023$ (5), $c = 49·636$ (21) Å, $V = 4664$ Å^3, $Z = 16$, $D_m = 1·33$, $D_x = 1·34$ Mg m^{-3}, Mo $K\alpha$, $\lambda = 0·71069$ Å, $\mu = 0·079$ mm^{-1}, $F(000) = 1984$, $T = 140$ K, $R = 0·037$ for 1195

* Part II. O'Connell, Ramsay & Steel (1985).

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