1-Tosyl-1H-pyrrolo[2,3-c]pyridine-5-carboxylic Acid Ethyl Ester

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Abstract

The title compound, $C_{17}H_{16}N_2O_4S$, was synthesized starting from 1H-pyrrole-2-carboxaldehyde under acidic conditions. The X-ray structure determination has proved that the compound was the expected pyrrolo[2,3-c]pyridine derivative and not the pyrrolo[3,2-c]pyridine isomer. The molecules are packed such that the azaindole rings are stacked in one set of parallel planes and the phenyl rings are stacked in another, with interplanar distances of 3.50 (1) and 3.83 (1) Å, respectively, giving the molecule a 'V' shape.

Comment

In connection with studies aimed at the development of new central nervous system agents, we recently prepared the title compound, (1), starting from 1H-pyrrole-2-carboxaldehyde (Dekhane, Potier & Dodd, 1993). As the acidic conditions used to synthesize (1) have been shown to cause substituents at the C2 position of the pyrrole ring to migrate to the C3 position (Carson & Davis, 1981; Desales, Greenhouse & Muchowski, 1982), there was some doubt as to whether the compound isolated was actually an isomer of (1), that is, 1-tosyl-1H-pyrrolo[3,2-c]pyridine-6-carboxylic acid ethyl ester, (2). Such an isomer could not, however, be differentiated from (1) using conventional spectroscopic methods. Therefore, it was necessary to confirm the structure of (1) by an X-ray crystallographic study.
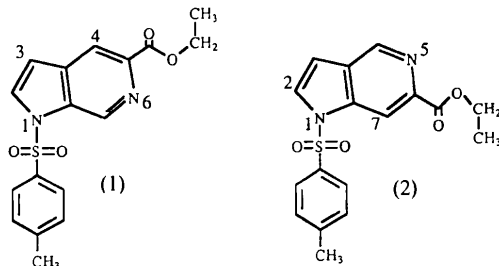
The molecular structure of (1) is shown in Fig. 1. It consists of two planar moieties bridged at the S atom, with a dihedral angle of 95° between the respective

mean planes of the azaindole ring (N1, C2, C3, C3a, C4, C5, N6, C7, C7a) and the phenyl ring. The azaindole ring is perfectly planar [maximum atomic deviation from the mean plane: 0.016 (3) Å] and short distances at C2—C3 [1.335 (5) Å] and N6—C7 [1.325 (4) Å] have been found. Interestingly, the molecules are packed (Fig. 2) such that the azaindole rings on one hand and the phenyl rings on the other are stacked in parallel planes with distances of 3.50 (1) and 3.83 (1) Å, respectively, between the mean planes, giving the molecules a 'V' shape. This specific stacking is also depicted in Fig. 1 where the molecule is shown projected down the crystallographic *a* axis. Consequently, all the molecules obtained by translation along this axis are superimposable.
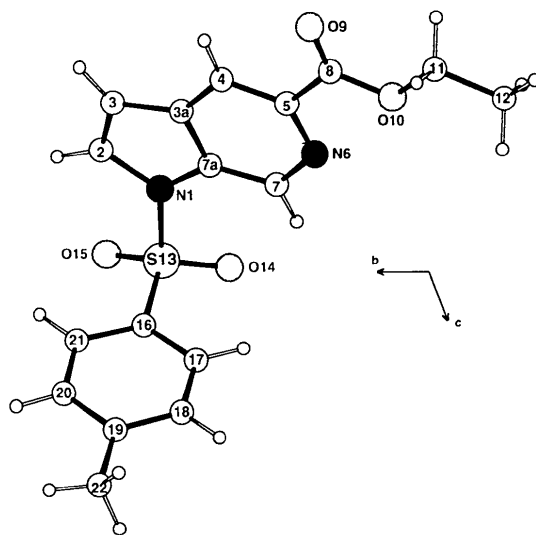

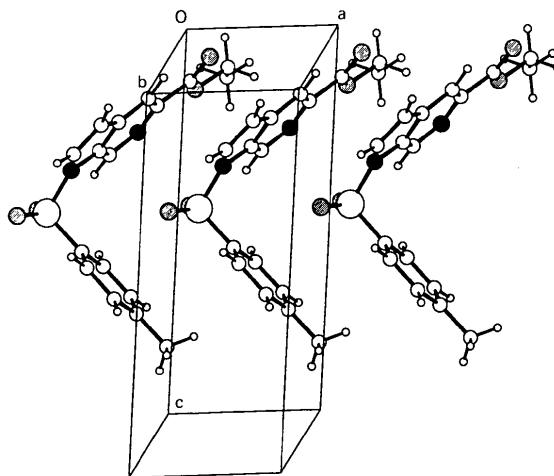Fig. 1. Perspective view of the molecule projected along the *a* axis.

Fig. 2. Packing of the molecules. For clarity the molecules obtained by the centre of symmetry have been omitted.

C20	0.8242 (6)	0.9074 (3)	0.5496 (2)	0.053 (3)
C21	0.6232 (6)	0.8507 (3)	0.4750 (2)	0.051 (3)
C22	1.1853 (7)	0.9051 (4)	0.6782 (2)	0.069 (4)

Experimental

Crystal data

C17H16N2O4S
$M_r = 344.39$
Triclinic
$P\bar{1}$
$a = 5.088$ (3) Å
$b = 11.566$ (8) Å
$c = 14.909$ (12) Å
$\alpha = 110.32$ (3)°
$\beta = 96.62$ (3)°
$\gamma = 91.42$ (3)°
$V = 815.3$ (9) Å^3
$Z = 2$
$D_x = 1.40$ Mg m^{-3}

Cu $K\alpha$ radiation
$\lambda = 1.5418$ Å
Cell parameters from 25
  reflections
$\theta = 9.6–19.4°$
$\mu = 1.93$ mm^{-1}
$T = 293$ K
Prism
$0.40 \times 0.15 \times 0.03$ mm
Colourless

Data collection

Nonius CAD-4 diffractome-
  ter
$\theta/2\theta$ scans
Absorption correction:
  none
2864 measured reflections
2749 independent reflections
1988 observed reflections
  $[I > 3.0\sigma(I)]$

$R_{int} = 0.028$
$\theta_{max} = 64.94°$
$h = -5 \rightarrow 5$
$k = -13 \rightarrow 12$
$l = 0 \rightarrow 17$
3 standard reflections
  frequency: 166 min
  intensity variation: none

Refinement

Refinement on F
$R = 0.043$
$wR = 0.065$
$S = 1.35$
1983 reflections
217 parameters
H-atom parameters not
  refined
Calculated weights
  $w = 1/[\sigma^2(F) + 0.0072F^2]$

$(\Delta/\sigma)_{max} = 0.04$
$\Delta\rho_{max} = 0.22$ e Å^{-3}
$\Delta\rho_{min} = -0.38$ e Å^{-3}
Extinction correction: none
Atomic scattering factors
  from International Tables
  for X-ray Crystallography
  (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij}a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
N1	0.4317 (5)	0.6094 (2)	0.2586 (2)	0.047 (2)
C2	0.4612 (7)	0.6849 (3)	0.2036 (2)	0.060 (4)
C3	0.6202 (8)	0.6347 (3)	0.1371 (2)	0.066 (4)
C3a	0.7071 (6)	0.5232 (2)	0.1492 (2)	0.048 (3)
C4	0.8762 (6)	0.4336 (3)	0.1051 (2)	0.050 (3)
C5	0.9105 (6)	0.3377 (2)	0.1390 (2)	0.041 (3)
N6	0.7893 (5)	0.3230 (2)	0.2104 (2)	0.044 (2)
C7	0.6286 (6)	0.4073 (2)	0.2531 (2)	0.045 (3)
C7a	0.5876 (5)	0.5093 (2)	0.2257 (2)	0.041 (3)
C8	1.0978 (6)	0.2433 (2)	0.0942 (2)	0.045 (3)
O9	1.2249 (5)	0.2499 (2)	0.0325 (2)	0.066 (3)
O10	1.1135 (4)	0.1528 (2)	0.1300 (1)	0.056 (2)
C11	1.3021 (7)	0.0620 (3)	0.0914 (3)	0.060 (3)
C12	1.2735 (7)	-0.0382 (3)	0.1325 (3)	0.068 (4)
S13	0.2934 (1)	0.6534 (1)	0.3608 (1)	0.045 (1)
O14	0.2025 (4)	0.5419 (2)	0.3714 (2)	0.056 (2)
O15	0.1176 (4)	0.7433 (2)	0.3514 (2)	0.060 (2)
C16	0.5541 (5)	0.7261 (2)	0.4535 (2)	0.042 (3)
C17	0.6848 (6)	0.6600 (3)	0.5037 (2)	0.055 (3)
C18	0.8886 (7)	0.7179 (3)	0.5763 (2)	0.061 (4)
C19	0.9616 (6)	0.8424 (3)	0.6004 (2)	0.051 (3)

Table 2. *Selected geometric parameters* (Å, °)

N1—C2	1.406 (4)	C8—O10	1.330 (4)
N1—C7a	1.397 (4)	O10—C11	1.453 (4)
N1—S13	1.674 (2)	C11—C12	1.498 (5)
C2—C3	1.335 (5)	S13—O14	1.424 (2)
C3—C3a	1.436 (5)	S13—O15	1.421 (2)
C3a—C4	1.396 (4)	S13—C16	1.758 (3)
C3a—C7a	1.406 (4)	C16—C17	1.376 (4)
C4—C5	1.376 (4)	C16—C21	1.389 (4)
C5—N6	1.347 (3)	C17—C18	1.378 (5)
C5—C8	1.497 (4)	C18—C19	1.388 (5)
N6—C7	1.325 (4)	C19—C20	1.387 (4)
C7—C7a	1.389 (4)	C19—C22	1.496 (5)
C8—O9	1.206 (4)	C20—C21	1.382 (4)
C2—N1—C7a	107.8 (2)	O9—C8—O10	123.4 (3)
C2—N1—S13	123.8 (2)	C8—O10—C11	115.3 (2)
C7a—N1—S13	126.9 (2)	O10—C11—C12	107.7 (3)
N1—C2—C3	110.0 (3)	N1—S13—O14	105.6 (1)
C2—C3—C3a	107.8 (3)	N1—S13—O15	104.4 (1)
C3—C3a—C4	135.2 (3)	N1—S13—C16	105.6 (1)
C3—C3a—C7a	107.3 (3)	O14—S13—O15	122.1 (1)
C4—C3a—C7a	117.4 (3)	O14—S13—C16	108.8 (1)
C3a—C4—C5	117.5 (3)	O15—S13—C16	109.0 (1)
C4—C5—N6	124.8 (3)	S13—C16—C17	120.0 (2)
C4—C5—C8	117.8 (2)	S13—C16—C21	118.8 (2)
N6—C5—C8	117.3 (2)	C17—C16—C21	121.2 (3)
C5—N6—C7	118.4 (2)	C16—C17—C18	119.6 (3)
N6—C7—C7a	120.9 (3)	C17—C18—C19	120.9 (3)
N1—C7a—C3a	107.1 (2)	C18—C19—C20	118.4 (3)
N1—C7a—C7	132.0 (3)	C18—C19—C22	121.0 (3)
C3a—C7a—C7	120.9 (3)	C20—C19—C22	120.6 (3)
C5—C8—O9	123.1 (3)	C19—C20—C21	121.8 (3)
C5—C8—O10	113.5 (2)	C16—C21—C20	118.2 (3)
C2—N1—S13—C16	-88.3 (2)	N1—S13—C16—C17	-95.0 (2)
C7a—N1—S13—C16	75.8 (2)	N1—S13—C16—C21	85.3 (2)

H atoms of the methyl group of C22 were disordered. Two positions were found with an occupancy factor of 0.50 each. The isotropic displacement parameters of the H atoms were set equal to $1.10U_{eq}$ of the parent atom. Data collection: Enraf–Nonius CAD-4 software. Data reduction: *NONIUS* (Riche, 1989). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1985). Program(s) used to refine structure: *SHELX*76 (Sheldrick, 1976). Molecular graphics: *R3M* (Riche, 1983); *ORTEP* (Johnson, 1965). Software used to prepare material for publication: *ACTACIF* (Riche, 1992).

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Product of a Paterno–Büchi Reaction of Pentafluorobenzaldehyde and 4-*tert*-Butyl-1-acetoxycyclohexene

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Abstract

The stereochemistry of the product of the photoaddition of pentafluorobenzaldehyde to 4-*tert*-butyl-1-acetoxycyclohexene, 4-*tert*-butyl-8-pentafluorophenyl-7-oxabicyclo[4.2.0]oct-1-yl acetate, $C_{19}H_{21}F_5O_3$, has been established. The ring fusion is *cis*, and the aryl and acetoxy substitutents are *trans* to the tertiary butyl group.

Comment

In the course of developing a synthesis for the 3-acetoxyoxetane subunit in the antineoplastic agent taxol (Wani, Taylor, Wall, Coggan & McPhail, 1971), we examined the prospects for using a Paterno–Büchi reaction (Paterno & Chietti, 1909; Büchi, Imman & Lipinsky, 1954) of enol acetates and benzaldehydes to introduce this particular moiety. The success of the methodology would depend upon the yields of the photoaddition reaction as well as of the subsequent oxidative degradation of the aromatic ring and a decarboxylation. Prior reports of the photoaddition reactions of enol ethers and trimethylsilyl enol ethers with aromatic aldehydes suggested that the regiochemistry desired in the taxol situation was favored (Jones, 1981). The photolysis of

variously substituted benzaldehydes with enol acetates had not, however, been investigated (Vasudevan, Brock, Watt & Morita, 1994). The photolysis of 4-*tert*-butyl-1-acetoxycyclohexene (1) and pentafluorobenzaldehyde (2) gave preferentially a 2-aryl-3-acetoxyoxetane with the expected *cis* relationship between the pentafluorophenyl and acetoxy groups. It was difficult, however, to resolve the remaining stereochemical issue regarding the selectivity of the facial attack by (2): attack on the diastereotopic faces of (1) would lead either to the oxetane (3) or the oxetane (4). The structure determination confirmed that the product was, in fact, the oxetane (3).
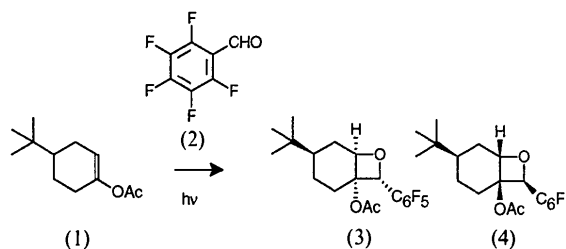
In forming the oxetane (3) rather than (4), the pentafluorobenzaldehyde (2) underwent a preferential *syn* addition with respect to the *tert*-butyl group in the enol acetate (1). The factors which guide this unexpected diastereospecificity in this situation are unclear, but the steric influence of the *tert*-butyl group on attack by the triplet state of (2) would appear to be minimal. A kinetic preference for addition to the *re* face of the enol acetate (1) may reflect a transition state in which the acetyl group preferentially shields the *si* face. Molecular-mechanics calculations for 4-*tert*-butyl-1-acetoxycyclohexene (1) suggested that a conformation with the acetyl group twisted toward the *si* face (*i.e.* *syn* to the *tert*-butyl group) was more stable than other conformations with the acetyl in a quadrant above the *re* face. This same preference, if present in the transition state, would favor the formation of (3).
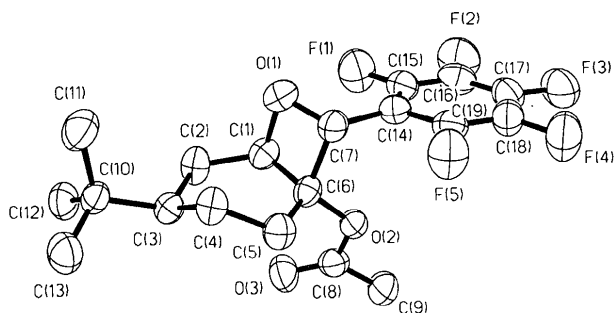

Fig. 1. Perspective drawing showing the molecular structure and the atom-numbering scheme. The shapes of the ellipsoids correspond to 50% probability contours of atomic displacement. The H atoms have been omitted for the sake of clarity.