Acta Cryst. (1984). C**40**, 1441–1443

Structure of 2-[(Methylsulfonyl)acetyl]pyridine,* $C_8H_9NO_3S$: an Immunosuppressive Agent

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(*Received* 10 *January* 1984; *accepted* 11 *April* 1984)

Dedicated to Professor J. D. Dunitz on the occasion of his 60*th birthday*

Abstract. $M_r = 199{\cdot}2$, monoclinic, $P2_1/c$, $a = 11{\cdot}073\ (1)$, $b = 8{\cdot}352\ (1)$, $c = 10{\cdot}489\ (1)$ Å, $\beta = 108{\cdot}85\ (1)°$, $V = 918{\cdot}0\ (3)$ Å^3, $Z = 4$, $D_m = 1{\cdot}45$, $D_x = 1{\cdot}441$ g cm^{-3}, Cu $K\alpha$, $\lambda = 1{\cdot}5418$ Å, $\mu = 28{\cdot}9$ cm^{-1}, $F(000) = 416$, $T = 294$ K, $R = 0{\cdot}031$ for 1282 reflections, $I \geq 3\sigma(I)$. The carbonyl oxygen is directed away from the ring nitrogen and the sulfonyl group is twisted away from the ring. The oxygen atoms of the sulfonyl group take part in a number of C—H···O interactions. There is a partial stacking of the pyridine rings in the crystal structure.

Introduction. Oxisuran, 2-[(methylsulfinyl)acetyl]-pyridine, is a synthetic immunosuppressive drug containing a dimethyl sulfoxide residue. It is used in organ and tissue transplants to suppress cell-mediated immunity as well as to promote graft acceptance without inhibiting humoral antibody formation. It is not cytotoxic and is anti-inflammatory. Oxisuran undergoes three primary attacks in its biotransformation: two are reductive and one is oxidative. Sulfoxide reduction yields oxisuran sulfide, carbonyl reduction forms oxisuran alcohol sulfoxide and sulfoxide oxidation produces oxisuran sulfone (DiCarlo, Crew, Haynes & Gala, 1972). Oxisuran sulfone was observed to have activities significantly different from oxisuran (DiCarlo, 1979). The mechanism of action of these drugs is not well understood, and for this reason it was deemed important to examine the structure of the molecule.

Experimental. Crystals grown by slow evaporation of aqueous solution at room temperature. (Sample kindly supplied by Dr Chheda of our laboratory.) They were very thin needles; D_m by flotation (bromoform/benzene); unit-cell parameters on CAD-4 diffractometer using 25 reflections with $7 \leq \theta \leq 27°$; crystal of dimensions $0{\cdot}55 \times 0{\cdot}2 \times 0{\cdot}1$ mm, three-dimensional data ($2\theta_{\max} = 154°$ for Cu $K\alpha$ radiation), $\omega/2\theta$ scan; ω scan widths $(0{\cdot}65 + 0{\cdot}14\tan\theta)°$, aperture width $(3{\cdot}0 + 1{\cdot}2\tan\theta)$ mm; max. time spent on any reflection measurement 100 s; faster scan used for strong reflections; intensities of three reflections monitored after every hour of exposure; variation in intensity < 2% during complete data collection; orientation matrix checked every 100 reflections; 2083 reflections measured, 1282 significant [$I \geq 3\sigma(I)$]; h 0–13, k 0–10, l 0–±12; Lorentz and polarization corrections; intensities of three reflections at $\chi \sim 90°$ measured for different values of φ from 0 to 360° and resultant curve of transmission as a function of φ used to calculate absorption for all reflections. Max. and min. transmission factors 0·99 and 0·90 with average 0·95. Structure solved using *MULTAN* (Germain, Main & Woolfson, 1971); 160 E values ($|E| \geq 1{\cdot}78$) used as input to *MULTAN* and correct set with highest figure of merit of 1·27 and residual value of 0·148 gave all atoms in the molecule; refinement with anisotropic thermal parameters led to $R = 0{\cdot}054$; difference electron-density maps revealed positions of hydrogen atoms; final cycles of refinement with anisotropic thermal parameters for nonhydrogen atoms, isotropic for hydrogen atoms and extinction parameter refinement ($g = 1{\cdot}3 \times 10^{-5}$) led to R 0·031 for 1282 reflections; $R_w = 0{\cdot}042$, $S = 1{\cdot}33$, $\sum w(|F_o| - 1/k|F_c|)^2$ minimized, $w = 4|F_o|^2/\sigma^2(|F_o|^2)$ and $\sigma^2(|F_o|)^2 = [\sigma^2(I) + p^2I^2]/\mathrm{Lp}$, where $p = 0{\cdot}05$, $\sigma(I)$ is standard deviation of intensity I based on counting statistics; k is scale factor; max. and av. $\Delta/\sigma = 0{\cdot}2$ and 0·01; final $|\Delta\rho| = 0{\cdot}2$ e Å^{-3}. Programs and atomic scattering factors as in Enraf–Nonius (1979) *Structure Determination Package;* Fourier and torsion angle programs by Dr S. T. Rao and *ORTEP* by Johnson (1965).

Discussion. The final atomic parameters are given in Table 1.† The bond distances and bond angles are given in Fig. 1.

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* 2-(Methylsulfonyl)methyl 2′-pyridyl ketone.

† Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39399 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

0108-2701/84/081441-03$01.50

Table 1. *Final positional parameters, equivalent isotropic thermal parameters for nonhydrogen atoms and isotropic thermal parameters for hydrogen atoms with e.s.d.'s in parentheses*

$$B_{\rm eq} = \tfrac{4}{3}\textstyle\sum_i\sum_j \beta_{ij}\mathbf{a}_i.\mathbf{a}_j$$

	x	y	z	$B_{\rm eq}/B$(Å^2)
S	0·09555 (4)	0·16342 (5)	0·90729 (5)	3·386
N(1)	0·4639 (2)	0·2223 (2)	0·9968 (2)	4·50
C(2)	0·5871 (2)	0·1837 (3)	1·0430 (3)	5·34
C(3)	0·6734 (2)	0·2553 (4)	1·1510 (3)	5·80
C(4)	0·6317 (2)	0·3717 (4)	1·2175 (2)	6·27
C(5)	0·5046 (2)	0·4124 (3)	1·1748 (2)	5·17
C(6)	0·4240 (2)	0·3357 (2)	1·0636 (2)	3·81
C(7)	0·2863 (2)	0·3789 (2)	1·0105 (2)	4·30
O(7)	0·2405 (1)	0·4715 (2)	1·0703 (2)	7·08
C(8)	0·2044 (2)	0·3043 (2)	0·8792 (2)	4·21
C(12)	−0·0154 (2)	0·2761 (3)	0·9550 (2)	4·41
O(10)	0·1659 (1)	0·0633 (2)	1·0174 (2)	5·38
O(11)	0·0307 (1)	0·0883 (2)	0·7802 (2)	5·49
H1(C12)	0·023 (2)	0·322 (3)	1·028 (2)	5·3
H2(C12)	−0·055 (2)	0·352 (3)	0·878 (3)	6·4
H3(C12)	−0·082 (2)	0·199 (3)	0·963 (2)	6·3
H(C4)	0·681 (2)	0·414 (3)	1·278 (3)	7·8
H1(C8)	0·252 (2)	0·240 (3)	0·834 (2)	6·1
H(C3)	0·763 (2)	0·233 (3)	1·178 (2)	6·2
H2(C8)	0·162 (2)	0·373 (3)	0·826 (2)	5·6
H(C5)	0·468 (2)	0·486 (3)	1·204 (2)	5·6
H(C2)	0·614 (2)	0·104 (3)	0·996 (2)	7·3

The bond lengths and angles in the pyridine ring are very similar to the values found in oxisuran (Karle, 1974), picolinamide (Takano, Sasada & Kakudo, 1966) and pyridine.LiCl (Durant, Verkist & Van Meerssche, 1966). The angles alternately have small and large values with extreme values of 116·9 (2)° at N(1) and 124·0 (2)° at C(2), respectively. The carbonyl C(7) is almost in the plane of the pyridine ring [C(2)—N(1)—C(6)—C(7) 179·5 (3)°; N(1)—C(6)—C(7)—O(7) 174·5 (3)°] with the keto oxygen O(7) turned away from the ring nitrogen atom N(1) (Fig. 1). The sulfonyl group is twisted away from the ring [C(6)—C(7)—C(8)—S 109·4 (3)°]. In oxisuran the molecule has a fully extended chain. Other torsional angles in the chain are: C(7)—C(8)—S—O(10) −46·8 (2)°; C(7)—C(8)—S—O(11) −174·7 (2)°; C(7)—C(8)—S—C(12) 69·9 (2)°; C(5)—C(6)—C(7)—C(8) 173·4 (3)°; N(1)—C(6)—C(7)—C(8) −5·5 (3)°. The oxisuran ring is planar to within ±0·008 (3) Å.

The packing of the molecules is illustrated in Fig. 2. The oxygen atoms of the sulfonyl group take part in a number of C—H···O interactions, the strongest of which are: C(4)···O(10) 3·357 (3) Å, H(C4)···O(10) 2·58 (3) Å, C(4)—H(C4)···O(10) 175 (1)°; and C(12)···O(10) 3·349 (3) Å, H3(C12)···O(10) 2·41 (3) Å, C(12)—H3(C12)···O(10) 157 (1)°. There is a partial stacking of the pyridine rings, so that molecules related by the center of inversion are on top of each other at a distance of 3·45 Å.

This structure determination formed the summer project of Mr Vladimir Vitkin, a summer student in our department in 1982. My thanks are due to him for his participation in this project. My thanks are also due to Dr R. Parthasarathy for use of the crystallographic facilities and helpful discussions, to Dr G. B. Chheda for crystals of oxisuran sulfone and to Ms J. Mann for technical help. This work was supported by Institutional Research Grant IN-54W8 from the American Cancer Society.

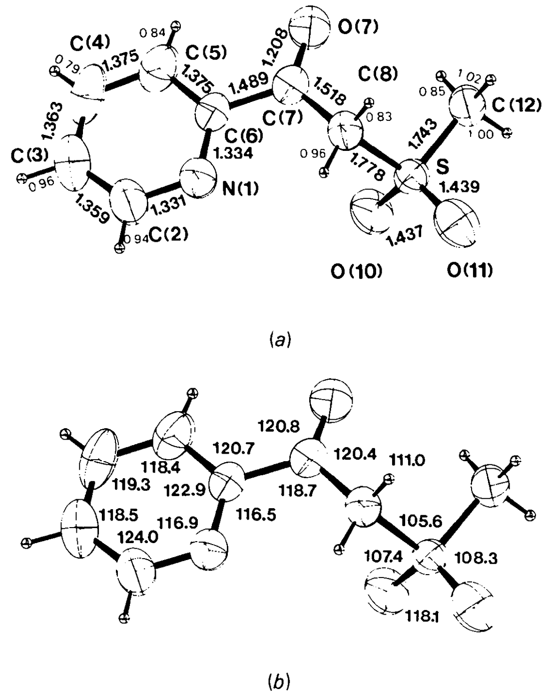

Fig. 1. (*a*) Bond lengths (Å) and (*b*) bond angles (°). The e.s.d.'s are 0·002–004 Å (0·2 Å for C—H) and 0·1–0·3°. Angles C(8)—S—O(11) = 107·4 (1) and O(10)—S—C(12) = 109·5 (1)°. The thermal ellipsoids are drawn at 50% probability.

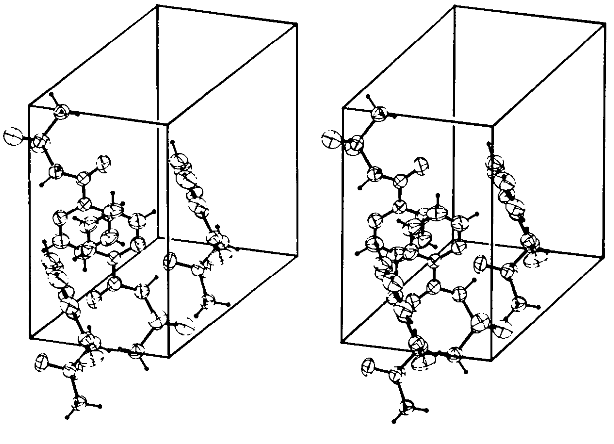

Fig. 2. Stereoview of the packing of the molecules in the unit cell. The oxygen atoms of the sulfone group take part in a number of C—H···O interactions (see text for details). The axial directions are **a** vertically upwards, **b** horizontally to the right, **c** out of the page.

References

DiCarlo, F. J. (1979). *Drug Metab. Rev.* **10**, 225–237.

DiCarlo, F. J., Crew, M. C., Haynes, L. J. & Gala, R. L. (1972). *Xenobiotica*, **2**, 159–168.

Durant, F., Verkist, J. & Van Meerssche, M. (1966). *Bull. Soc. Chim. Belg.* **75**, 806.

Enraf–Nonius (1979). *Structure Determination Package.* Enraf–Nonius, Delft.

Germain, G., Main, P. & Woolfson, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

Johnson, C. K. (1965). *ORTEP.* Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.

Karle, I. (1974). *Acta Cryst.* B**30**, 527–528.

Takano, T., Sasada, Y. & Kakudo, M. (1966). *Acta Cryst.* **21**, 514–522.

Acta Cryst. (1984). C**40**, 1443–1445

cis-1,5-Diphenyl-3-(diphenylmethylene)-4-morpholinocarbonyl-2-pyrrolidinone, $C_{34}H_{30}N_2O_3$

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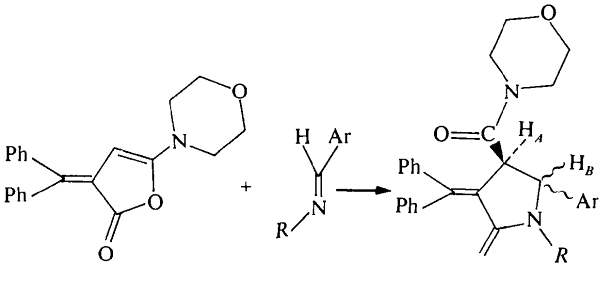
(*Received* 29 *February* 1984; *accepted* 18 *April* 1984)

Abstract. $M_r = 514{\cdot}6$, orthorhombic, $Pbca$, $a = 18{\cdot}262\,(5)$, $b = 23{\cdot}285\,(7)$, $c = 12{\cdot}798\,(3)$ Å, $V = 5442\,(2)$ Å^3, $Z = 8$, $D_x = 1{\cdot}256$ Mg m^{-3}, Cu $K\alpha$ radiation, $\lambda = 1{\cdot}54184$ Å, $\mu = 0{\cdot}648$ mm^{-1}, $F(000) = 2176$, $T = 293$ K, final $R = 0{\cdot}056$ for 2527 significant reflections. The morpholinocarbonyl and phenyl substituents at the 4 and 5 positions in the γ-lactam ring are *cis*-orientated with respect to the ring plane. All four aromatic rings are planar. The pyrrolidine ring has a C(4) envelope conformation and the morpholine ring a chair conformation. There are no intermolecular separations significantly less than the sum of the van der Waals radii.

Introduction. We recently reported a general synthesis of γ- and δ-lactones by the 'acyl-ene' reaction (Boyd, Monteil, Lindley & Mahmoud, 1978) and its extension to the preparation of α-(diphenylmethylene)-γ-lactones from the morpholinobutenolide (I) and aromatic aldehydes (Baydar & Boyd, 1978). We have found that imines, ArCH=N*R*, react with the butenolide in an analogous fashion, yielding α-(diphenylmethylene)-γ-lactams (II). The ^{1}H NMR spectra of the crude products showed the presence of two geometrical isomers with J_{AB} 8·6–9·5 and 4·0–6·0 Hz, the former predominating. We tentatively assigned the larger coupling constants to the *cis* isomers on the basis of the Karplus equation (Sternhell, 1969), but it was desirable to obtain independent confirmation since the equation does not strictly apply to strained systems, as in the present case. We therefore determined the X-ray structure of the major product (II; Ar = *R* = Ph) of the reaction of the butenolide (I) with *N*-benzylideneaniline and found that it has, indeed, the *cis* geometry.



(I) (II)

Experimental. Material prepared by heating under reflux morpholinobutenolide (I) (1·00 g) and *N*-benzylideneaniline (0·54 g, 1 mol) in acetonitrile for 10 min. ^{1}H NMR spectrum of the reaction mixture showed presence of *cis*- and *trans*-lactams ($J_{AB} = 8{\cdot}6$ and 6·0 Hz respectively) in the ratio 6:1. *cis*-1,5-Diphenyl-3-(diphenylmethylene)-4-morpholinocarbonyl-2-pyrrolidinone (II, Ar = *R* = Ph) (1·14 g; 74% yield) crystallized from ethanol. Spectral parameters: $\nu_{\max}$ (Nujol) 1698 (cyclic CO), 1630 (acyclic CO), 1600 and 1120 (morpholino) cm^{-1}; $\delta(CF_3CO_2D)$ 2·7–3·8 (*m*,8H, morpholino), 4·74 (*d*, H_B), 5·87 (*d*, H_A)

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