Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

3(*S*)-Acetoxymethyl-7-chloro-1,3-dihydro-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one

Aleksandar Višnjevac,[a]* Amir Avdagić[b] and Biserka Kojić-Prodić[a]

[a]Rudjer Bošković Institute, PO Box 180, HR-10002 Zagreb, Croatia, and [b]PLIVA, Pharmaceutical Industry, Inc., Research and Development, Prilaz baruna Filipovića 25, HR-10000 Zagreb, Croatia

Correspondence e-mail: aleksandar.visnjevac@irb.hr

Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.012 Å
R factor = 0.052
wR factor = 0.154
Data-to-parameter ratio = 7.6

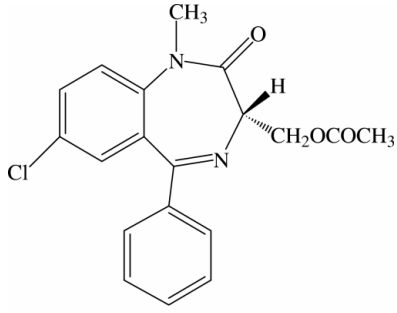
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 6 December 2001
Accepted 7 January 2002
Online 18 January 2002

The enantiomerically pure (*S*) title compound, $C_{19}H_{17}ClN_2O_3$, was crystallized from a 1:1 mixture of ethanol and dichloromethane. The 1,4-diazepine ring has a boat conformation with the C atom in position 3 displaced by 0.729 (4) Å from the plane defined by the atoms in positions 1, 2, 4 and 5. A weak C—H···O interaction, the most prominent feature of the crystal packing, links the molecules into infinite chains stretched along the *c* axis. The title compound, as well as other 1,4-benzodiazepin-2-one derivatives, are suitable precursors for the synthesis of enantiomerically pure α-amino acids and their congeners.

Comment

1,4-Benzodiazepines are of general interest as central nervous system active drugs (Roth *et al.*, 1997). Some derivatives have also been shown to possess substantial antiviral (Hsu & Tam, 1993) and antitumour activity (Kohl *et al.*, 1993). Because of their availability, and specific chemical and conformational features, they are used in the organic synthesis of enantiomerically pure α-amino acids and their congeners. The title compound, (I), as the pure *S* enantiomer, was prepared by a biocatalytic deracemization of its racemic counterpart, en route to the stereocontrolled synthesis of (*S*)-*N*-Cbz-serine (Cbz = benzyloxycarbonyl) and of its (*R*)-enantiomer (Avdagić & Šunjić, 1998).



(I)

As metal complexes of biologically active compounds often show even higher activity than the free ligands themselves, we included compound (I) in a study of metal complexes of chiral 3-substituted 1,4-benzodiazepines. Unsuccessful attempts to prepare complexes of (I) with Cu^{II} and Zn^{II} have, however, emphasised the importance of the substituent at position 5 (Fig. 1) for metal coordination. While its 5-(2-pyridyl) analogue readily reacts with $CuCl_2$ and $ZnCl_2$, giving expected complexes, compound (I) does not show such reactivity (Višnjevac *et al.*, 2001).

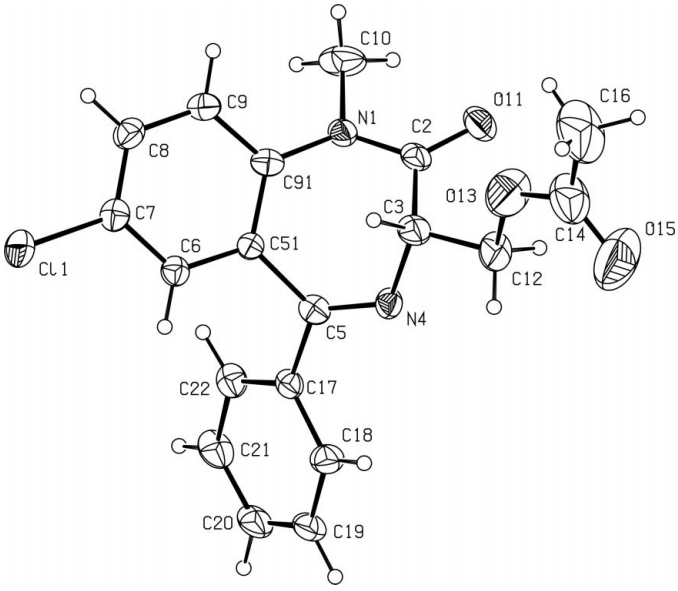


Figure 1
An *ORTEP*II (Johnson, 1976) drawing of (I) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 40% probability level.

The molecular structure of (I) is characterized by a puckered 1,4-diazepine ring in the usual boat conformation where atoms C3, C51, and C91 are displaced by 0.729 (4), 0.794 (7) and 0.765 (5) Å, respectively, from the least-squares plane defined by atoms N1, C2, N4 and C5 [maximum deviation of atom N4 from this plane is equal to 0.026 (4) Å].

A weak C16—H16*B*···O15^{i} [symmetry code: (i) 1+*y*, 1−*x*+*y*, *z*−1/6] interaction [H16*B*···O15^{i} 2.43, C16···O15^{i} 3.39 (2) Å and C16—H16*B*···O15^{i} 173.5°], representing the most prominent feature of the crystal packing, links the molecules into chains along the crystallographic *c* axis.

Experimental

The title compound was prepared according to a previously described procedure (Avdagić & Šunjić, 1998). Single crystals were obtained by evaporation of a 1:1 mixture of ethanol and dichloromethane at room temperature.

Crystal data

$C_{19}H_{17}ClN_2O_3$
M_r = 356.80
Hexagonal, $P6_1$
a = 11.075 (5) Å
c = 24.40 (4) Å
V = 2592 (5) Å^3
Z = 6
D_x = 1.371 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 20 reflections
θ = 4.9–20.3°
μ = 0.24 mm^{-1}
T = 293 (2) K
Prismatic, colourless
0.20 × 0.20 × 0.18 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\theta/2\theta$ scans
2904 measured reflections
1796 independent reflections
798 reflections with $I > 2\sigma(I)$
R_{int} = 0.113
θ_{max} = 26.3°
$h = -13 \rightarrow 0$
$k = 0 \rightarrow 13$
$l = -30 \rightarrow 0$
3 standard reflections
frequency: 120 min
intensity decay: none

Refinement

Refinement on F^2
$R\{F^2 > 2\sigma(F^2)\}$ = 0.052
$wR(F^2)$ = 0.154
S = 0.97
1796 reflections
236 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0712P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.29 e Å^{-3}
$\Delta\rho_{min}$ = −0.27 e Å^{-3}
Absolute structure: Flack,1983; no Friedel pairs
Flack parameter = 0.1 (2)

Table 1
Selected geometric parameters (Å, °).

Cl1—C7	1.736 (9)	N1—C91	1.406 (11)
O11—C2	1.221 (12)	N4—C3	1.476 (9)
O13—C12	1.443 (11)	N4—C5	1.262 (10)
O13—C14	1.261 (17)	C2—C3	1.506 (15)
O15—C14	1.260 (17)	C5—C51	1.502 (11)
N1—C2	1.357 (11)	C51—C91	1.395 (12)
N1—C10	1.462 (14)		
C12—O13—C14	120.7 (9)	N4—C3—C12	106.0 (6)
C2—N1—C10	117.4 (8)	C2—C3—C12	115.0 (9)
C2—N1—C91	122.2 (8)	N4—C5—C51	123.4 (7)
C10—N1—C91	119.2 (7)	O13—C12—C3	106.5 (7)
C3—N4—C5	118.3 (6)	O13—C14—O15	119.2 (11)
O11—C2—N1	121.1 (9)	O13—C14—C16	115.9 (12)
O11—C2—C3	122.4 (8)	O15—C14—C16	124.9 (13)
N1—C2—C3	116.3 (8)	C5—C51—C91	120.9 (7)
N4—C3—C2	109.1 (7)	N1—C91—C51	122.9 (7)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C16—H16*B*···O15^{i}	0.96	2.43	3.39 (2)	174

Symmetry code: (i) $1 + y, 1 - x + y, z - \frac{1}{6}$.

H atoms were placed in positions calculated on stereochemical grounds and included in the refinement in the riding-motion approximation. Their U_{iso} values were constrained to be $1.2U_{eq}$ of the carrier atom ($1.5U_{eq}$ in the case of the methyl H atoms). Even though the high s.u. value for the Flack (1983) parameter does not make determination of the absolute configuration on the basis of anomalous scattering very convincing, it in fact points to the correct configuration, *i.e.* the one which should have been expected on the basis of the synthetic route.

Data collection: *CAD*-4 Software (Enraf–Nonius, 1989); cell refinement: *SET*4 and *CELDIM* in *CAD*-4 *Software*; data reduction: *HELENA* (Spek, 1997); program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *PLATON* (Spek, 1990).

References

Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Moliterni, A. G. G., Burla, M. C., Polidori, G., Camalli, M. & Spagna, R. (1997). *SIR*97. Universities of Bari, Perugia, and Rome, Italy.
Avdagić, A. & Šunjić, V. (1998). *Helv. Chim. Acta*, **81**, 85–92.
Enraf–Nonius (1989). *CAD*-4 *Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.

Hsu, M.-C. & Tam, S. (1993). *The Search for Antiviral Drugs*, edited by L. Adams and V. J. Merluzzi, p. 15. Boston: Birkhauser.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Kohl, N. E., Mosser, S. C., de Solms, S. J., Giuliani, E. A., Pompliano, D. L., Graham, S. L., Smith, R. L., Scolnick, E. M., Oliff, A. & Gibbs, J. B. (1993). *Science*, **260**, 1934–1937.
Roth, K. J., Kleemann, A. & Besswenger, T. (1997). *Pharmaceutical Chemistry*, Vol. 1. New York: J. Wiley.
Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.
Spek, A. L. (1990). *Acta Cryst.* A**46**, C-34.
Spek, A. L. (1997). *HELENA*. University of Utrecht, The Netherlands.
Višnjevac, A., Tušek-Božić, Lj., Majerić-Elenkov, M., Šunjić, V. & Kojić-Prodić, B. (2001). *Eur. J. Inorg. Chem.* pp. 2647–2654.