O(1)—P(1)—O(2)	103.0 (1)	N(1)—C(2)—C(1)	108.7 (3)
O(1)—P(1)—O(3)	108.6 (2)	N(1)—C(2)—C(3)	108.1 (3)
O(1)—P(1)—O(4)	107.8 (2)	C(1)—C(2)—C(3)	115.0 (3)
O(2)—P(1)—O(3)	113.2 (2)	C(2)—C(3)—C(4)	113.1 (3)
O(2)—P(1)—O(4)	113.5 (2)	N(2)—C(4)—C(3)	120.1 (3)
O(3)—P(1)—O(4)	110.2 (1)	N(2)—C(4)—C(6)	106.7 (3)
P(1)—O(1)—C(1)	117.0 (2)	C(3)—C(4)—C(6)	133.1 (3)
C(4)—N(2)—C(5)	108.2 (3)	N(2)—C(5)—N(3)	109.7 (3)
C(5)—N(3)—C(6)	108.3 (3)	N(3)—C(6)—C(4)	107.5 (3)
O(1)—C(1)—C(2)	108.5 (3)		

Table 3. *Contact distances (Å)*

N(1)···O(2^{i})	2.742 (4)	O(6)···O(2)	3.231 (5)
N(1)···O(4^{ii})	2.768 (4)	O(6)···O(4^{ii})	2.731 (5)
N(1)···O(5^{iii})	2.791 (4)	O(7)···O(6^{vii})	2.727 (5)
N(3)···O(3^{iv})	2.613 (4)	O(7)···O(8^{v})	2.775 (5)
O(2)···N(2^{v})	2.692 (4)	O(8)···O(4)	2.762 (4)
O(5)···O(3)	2.737 (4)	O(8)···O(7^{viii})	2.845 (4)
O(5)···O(7^{vi})	2.879 (4)		

Symmetry codes: (i) $x, y-1, z$; (ii) $1-x, y-\frac{1}{2}, 2-z$; (iii) $1-x, y-\frac{1}{2}, 1-z$; (iv) $-x, y-\frac{1}{2}, 1-z$; (v) $1-x, \frac{1}{2}+y, 1-z$; (vi) $x-1, y, z$; (vii) $x, y, z-1$; (viii) $x-1, y, 1+z$.

H atoms were located in successive difference Fourier syntheses, but those bonded to the O(8) atom could not be found.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1985). Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1985) and *DIRDIF* (Beurskens, 1984). Program(s) used to refine structure: *TEXSAN*. Molecular graphics: *ORTEP*II (Johnson, 1976).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry, together with a packing diagram, have been deposited with the IUCr (Reference: TA1109). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Ames, B. N. & Horecker, B. L. (1956). *J. Biol. Chem.* **220**, 113–128.

Ames, B. N. & Mitchell, H. K. (1955). *J. Biol. Chem.* **212**, 687–697.

Beurskens, P. T. (1984). *DIRDIF. Direct Methods for Difference Structures – an Automatic Procedure for Phase Extension and Refinement of Difference Structure Factors*. Technical Report 1984/1. Crystallography Laboratory, Toernooiveld, 6525 ED Nijmegen, The Netherlands.

Henderson, G. B. & Snell, E. E. (1973). *J. Biol. Chem.* **248**, 1906–1911.

Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

Martin, R. G. & Goldberger, R. F. (1967). *J. Biol. Chem.* **242**, 1168–1174.

Metha, P. K., Hale, T. I. & Christen, P. (1989). *Eur. J. Biochem.* **186**, 249–253.

Metha, P. K., Hale, T. I. & Christen, P. (1993). *Eur. J. Biochem.* **214**, 549–561.

Molecular Structure Corporation (1985). *TEXSAN. TEXRAY Structure Analysis Package*. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.

Molecular Structure Corporation (1988). *MSC/AFC Diffractometer Control Software*. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.

Sheldrick, G. M. (1985). *SHELXS86. Program for the Solution of Crystal Structures*. University of Göttingen, Germany.

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Complex of a Lisuride Derivative and (*S*)-Naproxen

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Abstract

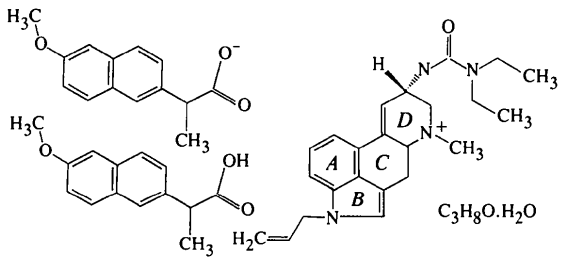
The structure of a complex between (+)-1-allyllisuride and the (+)-(*S*) isomer of 2-(6-methoxy-2-naphthyl)-propionic acid (naproxen), (+)-(5*R*,8*S*)-1-allyl-9,10-didehydro-8-(*N*′,*N*′-diethylureido)-6-methylergolin-6-ium 2-(6-methoxy-2-naphthyl)propionate 2-(6-methoxy-2-naphthyl)propionic acid acetonitrile solvate hydrate, $C_{23}H_{31}N_4O^+.C_{14}H_{13}O_3^-.C_{14}H_{14}O_3.C_3H_8O.H_2O$, has been determined. At the pH of the crystallization conditions, each molecule of allyllisuride is protonated and interacts with two molecules of naproxen in different modes; with one molecule, a π–π interaction seems to occur between aromatic moieties, while with the other, which appears to be deprotonated, hydrogen bonds are present. The electrostatic interactions seem sensitive to the configuration at the asymmetric C atom of naproxen and are likely to be responsible for the enantio-discriminative process. In the asymmetric unit, one molecule of isopropyl alcohol and one molecule of water are present. They are connected through a network of hydrogen bonds to the carbonyl group of allyllisuride and to the carboxyl groups of the two molecules of naproxen.

Comment

The use of liquid chromatography for the resolution of optical isomers requires a chiral selector, usually bonded to an achiral matrix, able to form reversible interactions with the enantiomers and labile diastereoisomeric complexes with different degrees of stability. Since the stability difference between the complexes affects the degree of chiral discrimination and the efficiency of the chiral selector, studies of chiral recognition, which provide the basis for the development of new chiral stationary phases, are particularly relevant.

Recently, new covalently bonded silica-based stationary phases, using ergot alkaloids as chiral selectors, have been developed to resolve optically active isomers (Flieger, Sinibaldi & Castellani, 1994). Lisuride and terguride were considered to have high potential applicability as chiral selectors because of the presence in the molecules of two or three asymmetric C atoms, a π-acceptor represented by the indole ring, basic N atoms as sites of hydrogen bonding and steric hindering groups. They were tested for the enantioselectivities of a series of organic acids, in particular, for a class of non-steroidal anti-inflammatory drugs, the 2-aryl propionic acids, commercialized as racemic mixtures (Castellani, Flieger & Sinibaldi, 1994).

In order to define the mode of interaction and the mechanism of chiral recognition of the ergot alkaloids, an X-ray study of several selector–analyte complexes is being carried out. So far, the crystal structure of the complex between (+)-1-allyl-(5*R*,8*S*)-lisuride and (+)-(*S*)-naproxen, (I), has been determined.



(I)

Bond distances and angles are in the expected ranges. Two independent molecules of naproxen (N*A* and N*B*) are present in the asymmetric unit, together with one molecule each of allyllisuride, isopropyl alcohol and water. The complex formed between one molecule of allyllisuride and two molecules of naproxen is shown in Fig. 1, while allyllisuride and the naproxen N*A* and N*B* molecules are shown with their atom-numbering schemes in Fig. 2.

The ergolene moiety of allyllisuride consists of four fused rings (*A–D*). The indole nucleus (rings *A* and *B*) is planar, while six-membered rings *C* and *D* have twist and envelope conformations, respectively, with atoms C(4) and C(5) of ring *C* and the N(6) atom of ring *D* at the tips. The torsion angles C(2)—C(3)—C(4)—C(5) and C(3)—C(4)—C(5)—N(6), which give the position of N(6) relative to the indole nucleus, have values of $-158.5\,(6)$ and $-165.7\,(4)^\circ$, respectively, thus showing that N(6) lies close to the indole plane. In effect, the ergolene nucleus is approximately planar and a mean

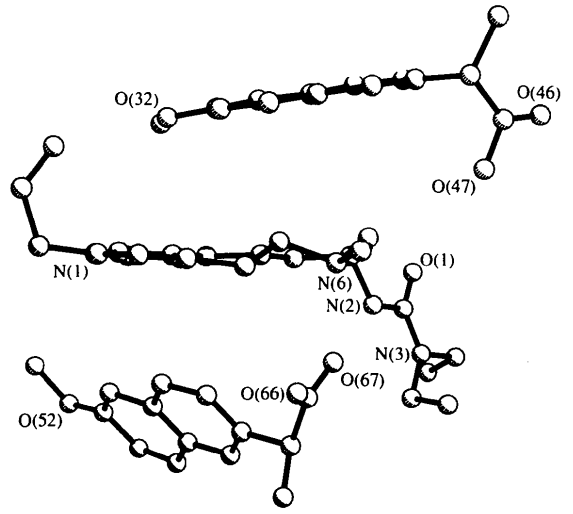


Fig. 1. A perspective view of the 1:2 complex between allyllisuride and naproxen.

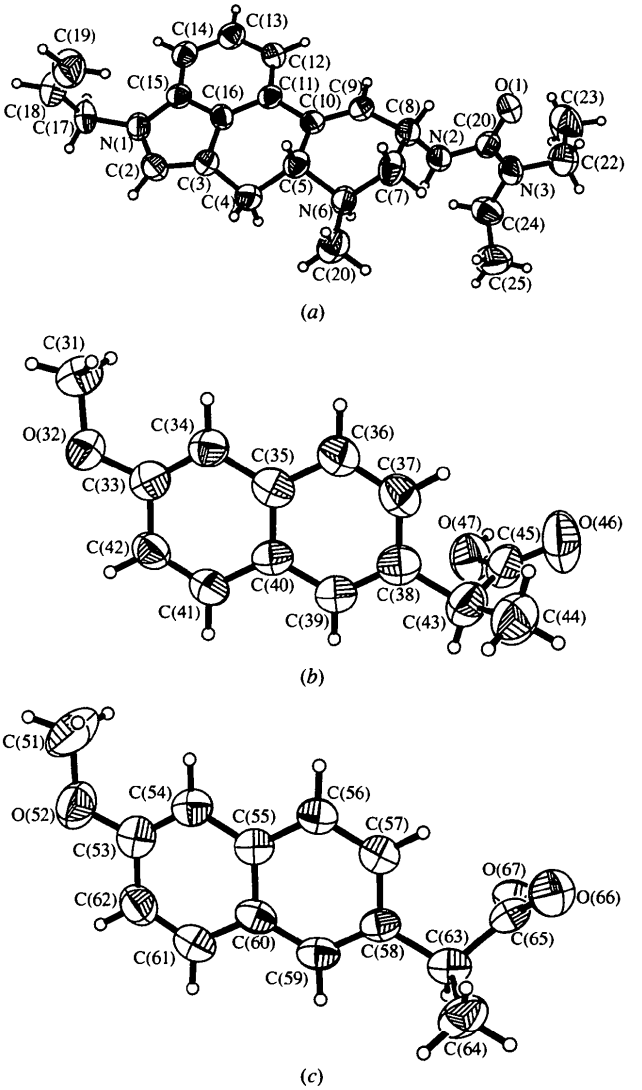


Fig. 2. The independent molecules of (*a*) allyllisuride, (*b*) naproxen N*A* and (*c*) naproxen N*B* in the asymmetric unit, showing the labelling of the non-H atoms. Displacement ellipsoids are shown at 50% probability levels.

plane through it can be defined by excluding atoms C(4), C(5), C(7) and C(8).

The side chains at N(1) and C(8) lie on planes approximately normal to the plane of the ergolene nucleus. On one side of this plane, the diethyl urea chain has an extended conformation and its planar part [C(8), N(2), C(21), O(1), N(3), C(22) and C(24)] forms an angle of 76.2 (1)° with it. Also, the allyl chain has an extended conformation, but on the other side of the plane of the ergolene nucleus, and atoms N(1), C(17), C(18) and C(19) lie on a plane orthogonal to it [91.9 (2)°].

In the two non-equivalent molecules of naproxen (N*A* and N*B*) present in the asymmetric unit, the naphthalene rings are close to planarity since the angles between the planes of the benzene rings in N*A* and N*B* are 1.1 (2) and 2.7 (2)°, respectively, while, in contrast, in the crystal structure of naproxen, the naphthalene system is rather distorted and the benzene rings form an angle of 5.2 (2)° with respect to one another (Ravikumar, Rajan, Pattabhi & Gabe, 1985). The methoxy group tends to be more coplanar with the naphthalene moiety in molecule N*B* [C(54)—C(53)—O(52)—C(51) 4 (1)°] than in molecule N*A* [C(34)—C(33)—O(32)—C(31) 9.8 (8)°], causing a distortion in the geometry [C(34)—C(33)—O(32) 125.9 (6)° in N*A* and C(54)—C(53)—O(52) 126.0 (5)° in N*B*], as already observed and attributed to conjugation between the benzene rings and the O atoms (Domiano, Nardelli, Balsamo, Macchia & Macchia, 1979; Ravikumar *et al.*, 1985). The two molecules differ in terms of the orientation of the carboxyl group with respect to the naphthalene plane. In molecule N*A*, the torsion angles C(37)—C(38)—C(43)—C(45) and C(37)—C(38)—C(43)—C(44) [−59.8 (8) and 64.9 (8)°, respectively] are close to both the theoretical values [60 or 120°] for the configurations of minimum energy of 2-arylpropionic acids (Dupont, Dideberg, Dive, Godfroid & Steiner, 1982) and the experimental values [70.5 (8) and −49.9 (9)°] found in the crystal structure of naproxen (Ravikumar *et al.*, 1985). In contrast, in molecule N*B*, the corresponding torsion angles are not close to the values of the minimum energy configuration [−28.6 (8) and 95.4 (8)°], since the carboxyl group is involved in interactions with allyllisuride.

Molecule N*A* lies almost parallel to the mean plane of the ergolene moiety, the two planes making an angle of 12.1 (1)° with one another. A sort of staking takes place between the two molecules with a distance which varies from 3.6 to 4.1 Å for the parts which overlap, *i.e.* the partially aromatic ring *C* and the benzene ring composed of atoms C(33)–C(35) and C(40)–C(42). The methoxy group is also close to the indole ring and is involved in a hydrogen bond with the C(19) atom [C(19)···O(32) 3.36 (1) Å], which seems to anchor the N*A* molecule of naproxen to the allyl chain in a suitable position for a π–π interaction. The formation of the complex between allyllisuride and molecule N*A* thus involves aromatic moieties and the methoxy group of N*A*, but not the carboxyl group, which is free to assume the orientation of minimum energy. The presence of a hydrogen bond with the C(19) atom in the crystal is misleading when evaluating the importance of the π–π interactions, since, for lisuride to be used as a chiral selector, the allyl chain is connected to the silica to form the stationary phase and is thus not available for interactions with the elute.

Molecule N*B* is oriented at an angle of 45.7 (1)° with respect to the mean plane of the ergolene nucleus, with the carboxyl group pointing towards a pocket where asymmetric sites, sites of electrostatic interactions and bulky ethyl groups are close together. Hydrogen bonds connect the O(67) atom of molecule N*B* with the N(6) and N(2) atoms [2.630 (5) and 2.782 (8) Å, respectively], and fix its position. These interactions seem sensitive to the configuration at the asymmetric atom of naproxen and perhaps can account for the process of chiral selection when the ergot alkaloids are used as stationary phase in high-performance liquid chromatography (HPLC).

This hypothesis of a stereoselective 'ion-pairing effect' exerted by the ergot alkaloids towards the arylpropionic acids will be better supported and related with an NMR study of the complexes in solution (Castellani *et al.*, 1994), when the X-ray structures of the complexes with the *R* isomer of naproxen are also available.

A network of hydrogen bonds connects the isopropyl alcohol and water molecules with the O(1) atom and the carboxyl groups of molecules N*A* and N*B* (Fig. 3) [O74···O47^{i} 2.616 (6), O74···O80 2.710 (8), O80···O1^{ii} 2.765 (8) and O80···O66^{iii} 2.733 (8) Å; symmetry codes: (i) $x, y, z-1$; (ii) $1-x, y+\frac{1}{2}, 1-z$; (iii) $1-x, y-\frac{1}{2}, 1-z$].

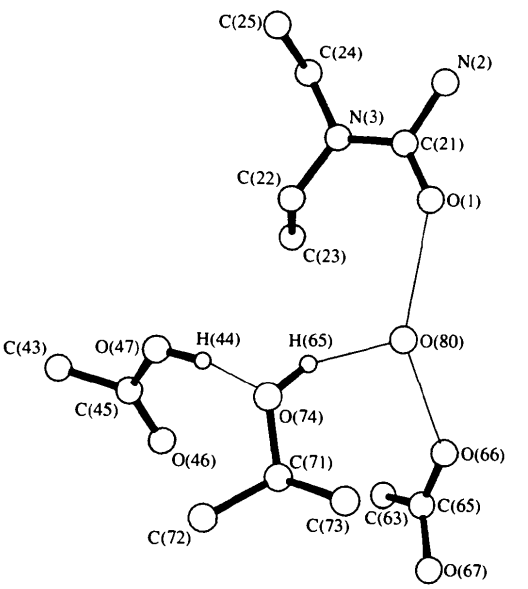


Fig. 3. Hydrogen-bonding scheme around the isopropyl alcohol and water molecules.

Experimental

Crystals of the title complex were obtained by co-crystallization from isopropyl alcohol in the presence of acetate buffer at pH $\simeq$ 4. The chiral recognition operates in a pH interval between 2.5 and 5.0, with the carboxylic acids being dissociated.

Crystal data

$C_{23}H_{31}N_4O^+.C_{14}H_{13}O_3^-.C_{14}H_{14}O_3.C_3H_8O.H_2O$
M_r = 917.16
Monoclinic
$P2_1$
a = 12.688 (2) Å
b = 11.894 (4) Å
c = 16.876 (2) Å
β = 101.78 (1)°
V = 2493 (1) Å^3
Z = 2
D_x = 1.222 Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
λ = 1.54178 Å
Cell parameters from 15 reflections
θ = 30–40°
μ = 0.668 mm^{-1}
T = 295 K
Prism
0.8 × 0.2 × 0.1 mm
Colourless

Data collection

Rigaku AFC-5*R* diffractometer
Profile data from ω–2θ scans
Absorption correction: none
4295 measured reflections
3930 independent reflections
3350 observed reflections [$I > 3\sigma(I)$]

R_{int} = 0.0254
θ_{max} = 60°
$h = 0 \rightarrow 14$
$k = 0 \rightarrow 13$
$l = -18 \rightarrow 18$
3 standard reflections monitored every 97 reflections
intensity decay: none

Refinement

Refinement on F
R = 0.0490
wR = 0.0566
S = 2.030
3350 reflections
603 parameters
H atoms riding
$w = 1/[\sigma^2(F_o)]$
$(\Delta/\sigma)_{max}$ = 0.05

$\Delta\rho_{max}$ = 1.4 e Å^{-3}
$\Delta\rho_{min}$ = −1.65 e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Tables 2.2A, 2.2C and 2.3.1)

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

$B_{eq} = (4/3)\sum_i\sum_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}
O(1)	0.4536 (3)	−0.0847 (5)	0.7982 (2)	4.7 (1)
N(1)	0.6873 (3)	0.5140	0.4827 (2)	4.1 (1)
N(2)	0.4519 (3)	0.1023 (5)	0.7736 (2)	4.1 (1)
N(3)	0.3074 (3)	0.0172 (5)	0.8131 (3)	4.8 (1)
N(6)	0.6308 (3)	0.2919 (5)	0.7909 (2)	3.7 (1)
C(2)	0.7078 (4)	0.5401 (6)	0.5643 (3)	4.1 (1)
C(3)	0.6763 (4)	0.4535 (6)	0.6070 (3)	3.6 (1)
C(4)	0.6671 (4)	0.4356 (5)	0.6933 (3)	4.0 (1)
C(5)	0.6679 (3)	0.3096 (6)	0.7123 (3)	3.7 (1)
C(7)	0.6392 (4)	0.1705 (6)	0.8132 (3)	4.4 (2)
C(8)	0.5601 (4)	0.1016 (6)	0.7546 (3)	4.0 (1)
C(9)	0.5546 (4)	0.1395 (6)	0.6696 (3)	3.8 (1)
C(10)	0.5993 (3)	0.2333 (5)	0.6484 (3)	3.3 (1)
C(11)	0.5949 (3)	0.2653 (5)	0.5628 (3)	3.3 (1)
C(12)	0.5545 (4)	0.2010 (6)	0.4941 (3)	4.1 (1)
C(13)	0.5603 (4)	0.2400 (6)	0.4165 (3)	4.5 (2)
C(14)	0.6059 (4)	0.3419 (6)	0.4043 (3)	4.1 (1)
C(15)	0.6444 (4)	0.4083 (5)	0.4724 (3)	3.6 (1)
C(16)	0.6369 (4)	0.3687 (5)	0.5492 (3)	3.4 (1)
C(17)	0.7213 (4)	0.5839 (6)	0.4211 (3)	4.6 (2)
C(18)	0.8339 (5)	0.5666 (7)	0.4129 (4)	5.5 (2)
C(19)	0.8976 (5)	0.4926 (7)	0.4487 (5)	7.1 (2)
C(20)	0.6960 (4)	0.3612 (6)	0.8584 (3)	5.4 (2)
C(21)	0.4068 (4)	0.0065 (6)	0.7959 (3)	3.9 (1)
C(22)	0.2574 (5)	−0.0818 (7)	0.8424 (4)	6.4 (2)
C(23)	0.1840 (7)	−0.1422 (8)	0.7753 (5)	9.1 (3)
C(24)	0.2514 (5)	0.1248 (6)	0.8113 (4)	5.6 (2)
C(25)	0.2834 (6)	0.1886 (7)	0.8891 (4)	7.7 (3)
C(31)	0.8426 (5)	0.1681 (7)	0.5076 (4)	5.7 (2)
O(32)	0.8958 (3)	0.2554 (5)	0.5563 (2)	5.5 (1)
C(33)	0.9191 (4)	0.2414 (6)	0.6381 (3)	4.5 (2)
C(34)	0.9095 (4)	0.1449 (6)	0.6779 (3)	4.3 (2)
C(35)	0.9365 (4)	0.1433 (6)	0.7643 (3)	4.4 (2)
C(36)	0.9274 (4)	0.0451 (6)	0.8085 (3)	5.1 (2)
C(37)	0.9516 (5)	0.0481 (6)	0.8915 (4)	5.3 (2)
C(38)	0.9870 (4)	0.1437 (6)	0.9346 (3)	5.0 (2)
C(39)	0.9976 (4)	0.2396 (6)	0.8927 (3)	4.7 (2)
C(40)	0.9730 (4)	0.2424 (6)	0.8069 (3)	4.1 (1)
C(41)	0.9837 (4)	0.3407 (6)	0.7624 (3)	4.6 (2)
C(42)	0.9566 (4)	0.3412 (6)	0.6813 (3)	4.7 (2)
C(43)	1.0083 (5)	0.1440 (7)	1.0272 (3)	5.8 (2)
C(44)	1.1004 (5)	0.0669 (7)	1.0644 (4)	7.3 (2)
C(45)	0.9054 (5)	0.1144 (7)	1.0543 (4)	5.6 (2)
O(46)	0.8957 (4)	0.0310 (6)	1.0941 (3)	9.1 (2)
O(47)	0.8259 (3)	0.1802 (5)	1.0268 (3)	6.6 (1)
C(51)	0.2718 (7)	0.2712 (9)	0.1984 (4)	9.3 (3)
O(52)	0.1782 (3)	0.2542 (5)	0.2317 (2)	6.7 (1)
C(53)	0.1856 (5)	0.2858 (6)	0.3102 (3)	4.9 (2)
C(54)	0.2707 (4)	0.3370 (6)	0.3575 (3)	4.4 (1)
C(55)	0.2694 (4)	0.3647 (6)	0.4388 (3)	3.9 (1)
C(56)	0.3583 (4)	0.4151 (6)	0.4898 (3)	4.5 (2)
C(57)	0.3580 (4)	0.4365 (6)	0.5694 (3)	4.3 (2)
C(58)	0.2691 (4)	0.4105 (5)	0.6036 (3)	3.7 (1)
C(59)	0.1811 (4)	0.3624 (6)	0.5543 (3)	4.4 (2)
C(60)	0.1784 (4)	0.3386 (6)	0.4721 (3)	4.3 (1)
C(61)	0.0904 (4)	0.2866 (6)	0.4194 (4)	5.1 (2)
C(62)	0.0944 (5)	0.2588 (7)	0.3420 (4)	5.4 (2)
C(63)	0.2714 (4)	0.4356 (6)	0.6926 (3)	4.3 (1)
C(64)	0.2181 (5)	0.5491 (6)	0.7019 (3)	6.0 (2)
C(65)	0.3867 (4)	0.4310 (6)	0.7402 (3)	4.0 (1)
O(66)	0.4416 (3)	0.5175 (5)	0.7555 (2)	5.6 (1)
O(67)	0.4229 (3)	0.3340 (5)	0.7611 (2)	4.5 (1)
C(71)	0.6182 (6)	−0.0081 (7)	0.0341 (4)	6.3 (2)
C(72)	0.6671 (6)	−0.0638 (7)	−0.0311 (4)	7.1 (2)
C(73)	0.5025 (6)	−0.0386 (8)	0.0271 (4)	8.3 (3)
O(74)	0.6311 (3)	0.1114 (5)	0.0304 (3)	6.2 (1)
O(80)	0.5280 (4)	0.1981 (5)	0.1422 (3)	7.2 (2)

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

O(1)—C(21)	1.234 (9)	C(11)—C(16)	1.378 (8)
N(1)—C(2)	1.383 (7)	C(12)—C(13)	1.404 (7)
N(1)—C(15)	1.367 (6)	C(13)—C(14)	1.376 (9)
N(1)—C(17)	1.465 (7)	C(14)—C(15)	1.397 (8)
N(2)—C(8)	1.472 (6)	C(15)—C(16)	1.400 (7)
N(2)—C(21)	1.363 (8)	C(17)—C(18)	1.477 (8)
N(3)—C(21)	1.356 (6)	C(18)—C(19)	1.26 (1)
N(3)—C(22)	1.470 (9)	C(22)—C(23)	1.49 (1)
N(3)—C(24)	1.461 (9)	C(24)—C(25)	1.50 (1)
N(6)—C(5)	1.510 (6)	C(31)—O(32)	1.408 (9)
N(6)—C(7)	1.490 (9)	O(32)—C(33)	1.363 (7)
N(6)—C(20)	1.509 (8)	C(43)—C(44)	1.52 (1)
C(2)—C(3)	1.362 (8)	C(43)—C(45)	1.510 (8)
C(3)—C(4)	1.501 (7)	C(45)—O(46)	1.22 (1)
C(3)—C(16)	1.422 (8)	C(45)—O(47)	1.287 (9)
C(4)—C(5)	1.532 (9)	C(51)—O(52)	1.429 (9)
C(5)—C(10)	1.537 (8)	O(52)—C(53)	1.362 (7)
C(7)—C(8)	1.501 (9)	C(63)—C(64)	1.53 (1)
C(8)—C(9)	1.491 (7)	C(63)—C(65)	1.519 (8)
C(9)—C(10)	1.333 (8)	C(65)—O(66)	1.240 (8)
C(10)—C(11)	1.484 (7)	C(65)—O(67)	1.265 (9)
C(11)—C(12)	1.397 (8)		

C(15)—N(1)—C(2)	108.9 (4)	C(14)—C(15)—N(1)	133.5 (5)
C(17)—N(1)—C(2)	123.8 (4)	C(16)—C(15)—N(1)	106.9 (5)
C(17)—N(1)—C(15)	126.8 (4)	C(16)—C(15)—C(14)	119.5 (5)
C(21)—N(2)—C(8)	121.3 (5)	C(11)—C(16)—C(3)	127.8 (5)
C(22)—N(3)—C(21)	118.7 (6)	C(15)—C(16)—C(3)	108.4 (5)
C(24)—N(3)—C(21)	123.1 (6)	C(15)—C(16)—C(11)	123.8 (5)
C(24)—N(3)—C(22)	117.9 (4)	C(18)—C(17)—N(1)	114.7 (5)
C(7)—N(6)—C(5)	109.8 (4)	C(19)—C(18)—C(17)	126.2 (6)
C(20)—N(6)—C(5)	111.4 (4)	N(2)—C(21)—O(1)	121.1 (5)
C(20)—N(6)—C(7)	109.7 (4)	N(3)—C(21)—O(1)	122.6 (6)
C(3)—C(2)—N(1)	109.9 (5)	N(3)—C(21)—N(2)	116.3 (6)
C(4)—C(3)—C(2)	135.2 (6)	C(23)—C(22)—N(3)	112.0 (6)
C(16)—C(3)—C(2)	105.9 (4)	C(25)—C(24)—N(3)	112.4 (6)
C(16)—C(3)—C(4)	118.6 (5)	C(33)—O(32)—C(31)	118.7 (6)
C(5)—C(4)—C(3)	110.1 (5)	C(34)—C(33)—O(32)	125.9 (6)
C(4)—C(5)—N(6)	109.3 (4)	C(42)—C(33)—O(32)	113.4 (6)
C(10)—C(5)—N(6)	107.4 (4)	C(44)—C(43)—C(38)	112.4 (5)
C(10)—C(5)—C(4)	116.9 (4)	C(45)—C(43)—C(38)	109.0 (5)
C(8)—C(7)—N(6)	111.0 (5)	C(45)—C(43)—C(44)	112.0 (6)
C(7)—C(8)—N(2)	112.4 (4)	O(46)—C(45)—C(43)	123.2 (7)
C(9)—C(8)—N(2)	110.2 (4)	O(47)—C(45)—C(43)	114.3 (6)
C(9)—C(8)—C(7)	111.3 (5)	O(47)—C(45)—O(46)	122.3 (6)
C(10)—C(9)—C(8)	125.0 (5)	C(53)—O(52)—C(51)	116.5 (6)
C(9)—C(10)—C(5)	121.1 (5)	C(54)—C(53)—O(52)	126.0 (5)
C(11)—C(10)—C(5)	115.7 (5)	C(62)—C(53)—O(52)	114.1 (6)
C(11)—C(10)—C(9)	122.9 (5)	C(64)—C(63)—C(58)	110.6 (5)
C(12)—C(11)—C(10)	127.0 (5)	C(65)—C(63)—C(58)	109.6 (4)
C(16)—C(11)—C(10)	117.0 (5)	C(65)—C(63)—C(64)	112.0 (5)
C(16)—C(11)—C(12)	116.0 (5)	O(66)—C(65)—C(63)	121.3 (6)
C(13)—C(12)—C(11)	120.9 (6)	O(67)—C(65)—C(63)	115.8 (5)
C(14)—C(13)—C(12)	122.3 (6)	O(67)—C(65)—O(66)	122.9 (5)
C(15)—C(14)—C(13)	117.5 (5)		

C(2)—C(3)—C(4)—C(5)	−158.5 (6)
C(3)—C(4)—C(5)—N(6)	−165.7 (4)
C(34)—C(33)—O(32)—C(31)	9.8 (8)
C(37)—C(38)—C(43)—C(44)	64.9 (8)
C(37)—C(38)—C(43)—C(45)	−59.8 (8)
C(54)—C(53)—O(52)—C(51)	4 (1)
C(57)—C(58)—C(63)—C(65)	−28.6 (8)
C(57)—C(58)—C(63)—C(64)	95.4 (8)

An ω-scan width of $(1.21 + 0.30\tan\theta)°$, an ω-scan rate of 4° min^{-1} and background counts at the beginning and end of each scan, each for 50% of the total scan time, were used. The weak reflections, $I < 6\sigma(I)$, were rescanned (maximum of three rescans) and the counts accumulated to insure good counting statistics. Azimuthal scans of several reflections indicated no need for an absorption correction. The structure was solved by direct methods and refined by full-matrix least-squares methods. All the non-H atoms were refined anisotropically. The H atoms were introduced at calculated positions and refined as riding on the corresponding C atoms. Some H atoms were introduced only before the last cycles of refinement and after an accurate inspection of the structure. On the basis of C—O bond distances and consideration of intramolecular distances, which showed a network of hydrogen bonds, the following choices could be made: (*a*) the carboxyl group in molecule N*A* was considered undissociated and the H(44) atom was generated bound to O(47) and *trans* to C(43); (*b*) the carboxyl group in molecule N*B* was considered dissociated; (*c*) atom N(6) was considered protonated and H(66) was generated bound to N(6); (*d*) in the isopropyl alcohol, H(65) was generated bound to O(74) and *trans* to C(72); (*e*) the H atoms of the water molecule were neglected.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1985). Program(s) used to solve structure: *TEXSAN*. Program(s) used to refine structure: *CAOS* (Cerrini & Spagna, 1977). Molecular graphics: *TEXSAN*.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: NA1243). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Castellani, L., Flieger, M., Mannina, L., Sedmera, P., Segre, A. L. & Sinibaldi, M. (1994). *Chirality*, **6**, 543–548.

Castellani, L., Flieger, M. & Sinibaldi, M. (1994). *J. Liq. Chromatogr.* **17**, 3695–3703.

Cerrini, S. & Spagna, R. (1977). 4th European Crystallographic Meeting, Oxford. Abstracts, p. 7.

Domiano, P., Nardelli, M., Balsamo, A., Macchia, B. & Macchia, F. (1979). *Acta Cryst.* B**35**, 1363–1372.

Dupont, L., Dideberg, O., Dive, G., Godfroid, J. J. & Steiner, E. (1982). *Acta Cryst.* B**38**, 2409–2411.

Flieger, M., Sinibaldi, M. & Castellani, L. (1994). *Chirality*, **6**, 549–554.

Molecular Structure Corporation (1985). *TEXSAN. TEXRAY Structure Analysis Package*. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.

Molecular Structure Corporation (1988). *MSC/AFC Diffractometer Control Software*. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.

Ravikumar, K., Rajan, S. S., Pattabhi, V. & Gabe, E. J. (1985). *Acta Cryst.* C**41**, 280–282.

Acta Cryst. (1997). C**53**, 140–143

1,5-Bis[4,4-dimethyl-1-(4-methylphenyl)-5-(1-piperidinio)-1-penten-3-ylidene]-carbonohydrazide Dichloride Methanol Solvate

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Abstract

The title compound, $C_{39}H_{58}N_6O^{2+}.2Cl^-.CH_3OH$, was synthesized as the lead molecule of a novel group of anticancer agents. The biscarbonohydrazide group in the molecule forms a complex conjugated resonance system involving the two 4-methylstyryl groups. Although the chemical bonding implies that the bonds of the molecule should have a mirror plane of symmetry, the molecule adopts an asymmetric bonding conformation.