Conformational Studies of Semotiadil (SD-3211), a Novel Ca^{2+} Antagonist

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The stereochemistry of a novel Ca^{2+} antagonist, semotiadil, 1, was investigated using X-ray crystallography and CD. The X-ray structure was analyzed using its diastereomeric salt with (*S*)-(+)-mandelic acid (2); 1 (mandelate). The *R* absolute configuration of 1, which was previously determined by chemical transformation of the optically-active synthetic precursor, was directly confirmed by this analysis. The hydrogen bonding, electrostatic and the hydrophobic interactions, which stabilize the crystal structure, were observed in the crystal. CD spectra of 1 (mandelate) and the hydrogen fumarate of 1 (SD-3211; 1 (fumarate)) in ethanolic solution exhibited similar spectral patterns. The CD bands from each chromophore were unambiguously assigned and the conformation of the benzothiazine ring was determined using the helicity rule. The X-ray and CD data confirmed the *P*-conformation of the benzothiazine ring and the existence of the 2-phenyl ring in an equatorial position in both of the crystal and ethanolic solution states. These findings were in good agreement with our previous results regarding the conformational analysis of 2-arylbenzothiazine derivatives.

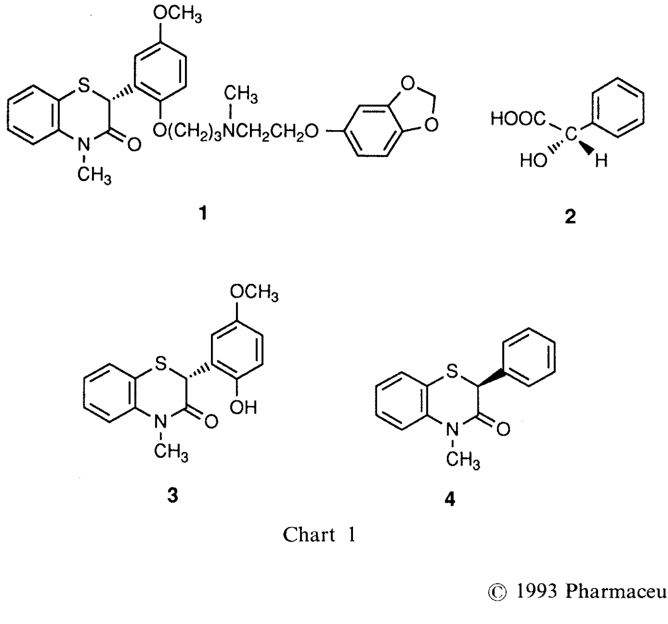
Keywords semotiadil; SD-3211; Ca^{2+} antagonist; molecular conformation; X-ray analysis; CD

Ca^{2+} antagonists have a major advance in the treatment of cardiovascular disorders such as essential hypertension, angina pectoris and certain arrhythmias.[1)] In our recent studies of sulfur-containing heterocycles,[2)] we found a novel Ca^{2+} antagonist, semotiadil[3)] fumarate (SD-3211); **1** (fumarate).[4)]

As part of our stereochemical studies of semotiadil **1**, we previously reported the conformational analysis of 2-arylbenzothiazines, **3** and **4**, compounds related to **1**, using CD spectroscopy.[5)] Here, we report the stereochemistry of **1** using X-ray crystallographic analysis and CD measurements.

Results and Discussion

Crystal Structure of 1 (Mandelate) The X-ray crystal structure of the (*S*)-(+)-mandelate (**1** (mandelate)), recrystallized from benzene, was completely analyzed, although the appropriate crystals of **1** (fumarate) were not obtained. Atomic coordinates of non-H atoms are given in Table I. Tables II and III give the atomic bonds and angles, respectively. The molecular conformation, together with the atomic numbering used, is illustrated in Fig. 1.



1 **2** **3** **4**

Chart 1

The *R* absolute configuration of C(2), which was previously determined by chemical transformation from the optically-active synthetic precursor, having the known absolute configuration,[4)] was directly confirmed by measurement of Bijvoet pairs $[|F(hkl)|$ and $|F(\bar{h}\bar{k}\bar{l})|]$ using the abnormal dispersion effect of the sulfur atom. This result was also supported by the analytical data which gave the *S* absolute configuration of the mandelic acid moiety. The 2-phenyl ring exists in an equatorial position. The thiazine ring adopts a twisted boat conformation in which the torsion angles of C(9)–N(4)–C(3)–C(2), S(1)–C(10)–C(9)–N(4) and C(10)–S(1)–C(2)–C(3) are 4.3(5)°, −8.2(4)° and 59.7(3)°, respectively. Thus, the conformation of the thiazine ring was determined as *P*[6)] (discussed later). The aminoalkyl side-chain is folded at the nitrogen and the relative location of the 2-phenyl ring, with regard to the chain, is similar to that of the methylenedioxyphenyl ring; $\mathrm{C(11){-}C(16)\underset{t}{-}O(16)\underset{t}{-}C(18)\underset{-g}{-}C(19)\underset{t}{-}C(20)\underset{+g}{-}N(21)\underset{+g}{-}C(22)\underset{-g}{-}C(23)\underset{t}{-}O(24)\underset{t}{-}C(24){-}C(29)}$.[7)] The distances between (a) the centers of the 2-phenyl and the methylenedioxyphenyl rings, (b) the N(21) atom and the center of the 2-phenyl ring and (c) the N(21) atom and the center of the methylenedioxyphenyl ring are about 7.9, 5.6 and 7.1 Å, respectively.

The crystal packing of **1** (mandelate) is shown in Fig. 2. A hydrogen bond and an electrostatic interaction are found between the semotiadil and (*S*)-(+)-mandelic acid moieties; N(21)···H–O(39) $(x,y,z)=2.67(1)$ Å and N(21)···O(37)–H $(x,y,z)=2.84(1)$ Å, respectively. The O(37)–H is further hydrogen-bonded to the O(38) atom of the neighboring (*S*)-(+)-mandelic acid: O(37)–H···O(38)$(x,y,z-1)=2.67(1)$ Å. The methylenedioxyphenyl ring of the semotiadil moiety is linked with the phenyl ring of the neighboring (*S*)-(+)-mandelic acid moiety by an edge-to-face type hydrophobic interaction. Judging from the fact that **1** (mandelate) was prepared from the free base of the corresponding racemate, by optical resolution with (*S*)-(+)-mandelic acid **2**,[4)] these interactions may play an important role with regard to effective chiral discrimination.

Table I. Atomic Coordinates and Isotropic Thermal Parameters of Non-H Atoms for **1** (Mandelate)

Atom	x	y	z	B_{eq}
Semotiadil part				
S(1)	0.3427 (2)	0.04696 (6)	0.0497 (3)	3.69 (7)
C(2)	0.4483 (4)	0.0350 (1)	−0.1938 (7)	3.1 (2)
C(3)	0.4849 (4)	0.0771 (1)	−0.3137 (7)	3.3 (2)
O(3)	0.6039 (4)	0.0863 (1)	−0.3558 (7)	5.8 (2)
C(4)	0.4042 (5)	0.1426 (1)	−0.5118 (6)	5.4 (2)
N(4)	0.3736 (5)	0.1034 (2)	−0.3795 (8)	3.8 (2)
C(5)	0.1232 (5)	0.1118 (2)	−0.4723 (9)	4.5 (2)
C(6)	−0.0134 (6)	0.1066 (2)	−0.417 (1)	5.0 (2)
C(7)	−0.0439 (5)	0.0853 (2)	−0.2148 (9)	5.5 (2)
C(8)	0.0663 (5)	0.0669 (2)	−0.069 (1)	4.8 (2)
C(9)	0.2362 (6)	0.0952 (2)	−0.330 (1)	3.6 (3)
C(10)	0.2064 (6)	0.0721 (2)	−0.127 (1)	3.4 (3)
C(11)	0.5765 (7)	0.0098 (2)	−0.108 (1)	3.1 (3)
C(12)	0.6634 (6)	0.0223 (2)	0.088 (1)	3.5 (3)
C(13)	0.7803 (6)	−0.0013 (2)	0.160 (1)	3.5 (3)
O(13)	0.8589 (6)	0.0146 (2)	0.355 (1)	5.0 (3)
C(14)	0.8120 (6)	−0.0386 (2)	0.046 (1)	3.3 (3)
C(15)	0.7258 (6)	−0.0518 (2)	−0.150 (1)	3.4 (3)
O(16)	0.5188 (6)	−0.0409 (2)	−0.416 (1)	3.6 (3)
C(16)	0.6090 (6)	−0.0294 (2)	−0.225 (1)	3.2 (3)
C(17)	0.9747 (6)	−0.0110 (2)	0.453 (1)	5.4 (3)
C(18)	0.5613 (7)	−0.0782 (2)	−0.542 (1)	3.7 (3)
C(19)	0.4626 (6)	−0.0837 (2)	−0.765 (1)	4.1 (3)
C(20)	0.3150 (7)	−0.0950 (2)	−0.708 (1)	3.1 (3)
C(21)	0.2019 (6)	−0.0751 (2)	−1.102 (1)	4.2 (3)
N(21)	0.2215 (9)	−0.1099 (3)	−0.920 (1)	3.2 (4)
C(22)	0.2664 (6)	−0.1513 (2)	−1.036 (1)	4.0 (3)
C(23)	0.2662 (6)	−0.1895 (2)	−0.867 (1)	4.5 (3)
C(24)	0.4001 (8)	−0.2199 (3)	−0.536 (1)	4.3 (4)
O(24)	0.3875 (8)	−0.1888 (2)	−0.707 (1)	5.0 (3)
C(25)	0.2995 (7)	−0.2531 (2)	−0.518 (1)	4.4 (3)
C(26)	0.3302 (7)	−0.2819 (2)	−0.336 (1)	4.5 (3)
O(26)	0.2526 (7)	−0.3173 (2)	−0.284 (1)	6.3 (3)
C(27)	0.4465 (7)	−0.2790 (2)	−0.175 (1)	4.7 (3)
O(27)	0.4475 (8)	−0.3129 (2)	−0.020 (1)	6.7 (3)
C(28)	0.5418 (7)	−0.2472 (2)	−0.197 (1)	5.6 (3)
C(29)	0.5195 (8)	−0.2174 (2)	−0.379 (2)	5.5 (4)
C(30)	0.3205 (6)	−0.3343 (2)	−0.072 (1)	7.7 (3)
(*S*)-(+)-Mandelic acid part				
C(31)	−0.1160 (6)	−0.2064 (2)	−0.916 (1)	2.9 (3)
C(32)	−0.0567 (7)	−0.2248 (3)	−1.108 (2)	4.0 (4)
C(33)	−0.0377 (7)	−0.2684 (2)	−1.122 (1)	5.5 (3)
C(34)	−0.0765 (7)	−0.2950 (2)	−0.942 (1)	6.2 (3)
C(35)	−0.1353 (7)	−0.2772 (2)	−0.755 (1)	6.3 (4)
C(36)	−0.1546 (7)	−0.2331 (2)	−0.738 (1)	4.7 (3)
C(37)	−0.1379 (9)	−0.1576 (3)	−0.904 (2)	3.2 (4)
O(37)	−0.0575 (8)	−0.1356 (3)	−1.065 (1)	3.5 (4)
C(38)	−0.094 (1)	−0.1409 (3)	−0.655 (2)	3.1 (4)
O(38)	−0.1816 (7)	−0.1448 (3)	−0.502 (2)	3.4 (4)
O(39)	0.026 (1)	−0.1250 (4)	−0.615 (2)	3.8 (5)

Table II. Bond Length (Å) of **1** (Mandelate)

Bond	Distance	Bond	Distance
S(1)–C(2)	1.806 (4)	C(21)–N(21)	1.49 (1)
S(1)–C(10)	1.763 (6)	N(21)–C(22)	1.52 (1)
C(2)–C(3)	1.526 (6)	C(22)–C(23)	1.524 (9)
C(2)–C(11)	1.502 (7)	C(23)–O(24)	1.41 (1)
C(3)–O(3)	1.214 (6)	C(24)–O(24)	1.37 (1)
C(3)–N(4)	1.372 (6)	C(24)–C(25)	1.42 (1)
C(4)–N(4)	1.472 (6)	C(24)–C(29)	1.39 (1)
N(4)–C(9)	1.387 (8)	C(25)–C(26)	1.38 (1)
C(5)–C(6)	1.376 (7)	C(26)–O(26)	1.37 (1)
C(5)–C(9)	1.394 (8)	C(26)–C(27)	1.38 (1)
C(6)–C(7)	1.367 (7)	O(26)–C(30)	1.418 (9)
C(7)–C(8)	1.408 (7)	C(27)–O(27)	1.37 (1)
C(8)–C(10)	1.414 (8)	C(27)–C(28)	1.356 (9)
C(9)–C(10)	1.399 (8)	O(27)–C(30)	1.396 (9)
C(11)–C(12)	1.386 (9)	C(28)–C(29)	1.39 (1)
C(11)–C(16)	1.431 (9)	C(31)–C(32)	1.38 (1)
C(12)–C(13)	1.373 (9)	C(31)–C(36)	1.376 (9)
C(13)–O(13)	1.376 (9)	C(31)–C(37)	1.53 (1)
C(13)–C(14)	1.373 (9)	C(32)–C(33)	1.37 (1)
O(13)–C(17)	1.439 (8)	C(33)–C(34)	1.38 (1)
C(14)–C(15)	1.386 (8)	C(34)–C(35)	1.35 (1)
C(15)–C(16)	1.357 (9)	C(35)–C(36)	1.39 (1)
O(16)–C(16)	1.375 (9)	C(37)–O(37)	1.41 (1)
O(16)–C(18)	1.433 (9)	C(37)–C(38)	1.52 (1)
C(18)–C(19)	1.527 (9)	C(38)–O(38)	1.25 (1)
C(19)–C(20)	1.513 (9)	C(38)–O(39)	1.26 (1)
C(20)–N(21)	1.51 (1)		

Table III. Bond Angles (°) of **1** (Mandelate)

Bond	Angle	Bond	Angle
C(2)–S(1)–C(10)	95.3 (2)	C(19)–C(20)–N(21)	114.0 (4)
S(1)–C(2)–C(3)	108.7 (2)	C(20)–N(21)–C(21)	110.9 (4)
S(1)–C(2)–C(11)	110.7 (2)	C(20)–N(21)–C(22)	115.5 (4)
C(3)–C(2)–C(11)	112.2 (3)	C(21)–N(21)–C(22)	110.1 (4)
C(2)–C(3)–O(3)	122.7 (3)	N(21)–C(22)–C(23)	112.2 (4)
C(2)–C(3)–N(4)	115.6 (3)	C(22)–C(23)–O(24)	110.3 (4)
O(3)–C(3)–N(4)	121.7 (3)	O(24)–C(24)–C(25)	122.8 (5)
C(3)–N(4)–C(4)	116.8 (3)	O(24)–C(24)–C(29)	115.8 (5)
C(3)–N(4)–C(9)	124.3 (3)	C(25)–C(24)–C(29)	121.4 (5)
C(4)–N(4)–C(9)	118.9 (3)	C(23)–O(24)–C(24)	117.6 (4)
C(6)–C(5)–C(9)	122.2 (4)	C(24)–C(25)–C(26)	114.9 (5)
C(5)–C(6)–C(7)	120.9 (3)	C(25)–C(26)–O(26)	126.5 (5)
C(6)–C(7)–C(8)	119.0 (3)	C(25)–C(26)–C(27)	124.0 (4)
C(7)–C(8)–C(10)	119.8 (3)	O(26)–C(26)–C(27)	109.5 (4)
N(4)–C(9)–C(5)	121.4 (3)	C(26)–O(26)–C(30)	105.1 (4)
N(4)–C(9)–C(10)	120.9 (3)	C(26)–C(27)–O(27)	109.5 (4)
C(5)–C(9)–C(10)	117.5 (3)	C(26)–C(27)–C(28)	120.0 (4)
S(1)–C(10)–C(8)	119.3 (2)	O(27)–C(27)–C(28)	130.3 (4)
S(1)–C(10)–C(9)	120.2 (2)	C(27)–O(27)–C(30)	105.6 (4)
C(8)–C(10)–C(9)	120.4 (4)	C(27)–C(28)–C(29)	119.2 (5)
C(2)–C(11)–C(12)	122.5 (3)	C(24)–C(29)–C(28)	120.5 (5)
C(2)–C(11)–C(16)	119.7 (3)	O(26)–C(30)–O(27)	109.5 (4)
C(12)–C(11)–C(16)	117.8 (4)	C(32)–C(31)–C(36)	117.9 (5)
C(11)–C(12)–C(13)	120.9 (4)	C(32)–C(31)–C(37)	120.9 (5)
C(12)–C(13)–O(13)	115.4 (4)	C(36)–C(31)–C(37)	121.2 (5)
C(12)–C(13)–C(14)	120.9 (4)	C(31)–C(32)–C(33)	121.4 (4)
O(13)–C(13)–C(14)	123.6 (4)	C(32)–C(33)–C(34)	120.2 (5)
C(13)–O(13)–C(17)	117.8 (4)	C(33)–C(34)–C(35)	118.8 (5)
C(13)–C(14)–C(15)	119.0 (4)	C(34)–C(35)–C(36)	121.4 (4)
C(14)–C(15)–C(16)	121.5 (4)	C(31)–C(36)–C(35)	120.2 (4)
C(16)–O(16)–C(18)	114.4 (4)	C(31)–C(37)–O(37)	111.4 (4)
C(11)–C(16)–C(15)	119.6 (4)	C(31)–C(37)–C(38)	110.5 (5)
C(11)–C(16)–O(16)	116.0 (4)	O(37)–C(37)–C(38)	107.8 (5)
C(15)–C(16)–O(16)	124.3 (4)	C(37)–C(38)–O(38)	117.0 (5)
O(16)–C(18)–C(19)	108.6 (4)	C(37)–C(38)–O(39)	118.6 (6)
C(18)–C(19)–C(20)	112.1 (4)	O(38)–C(38)–O(39)	124.4 (7)

CD Spectra of 1 (Fumarate) and 1 (Mandelate) Figure 3 shows the CD spectra of **1** (fumarate) and **1** (mandelate) in ethanolic solution. These compounds exhibit a similar spectral pattern, where the positive bands are observed in the 340—285 nm, 285—265 nm (shoulder), 265—250 nm and 230—215 nm regions, while the regions 250—230 nm and <215 nm are negative. Furthermore, the CD spectrum of **1** (fumarate) was almost the same as that of the corresponding free base (data is not shown). The CD spectrum of (*S*)-(+)-mandelic acid (**2**) is also shown in Fig. 3. Since **2** shows only a positive maximum at approximately 225 nm, the CD spectrum of **1** (mandelate) seems to correspond to the summation of the spectra of **1** (fumarate) (or its free

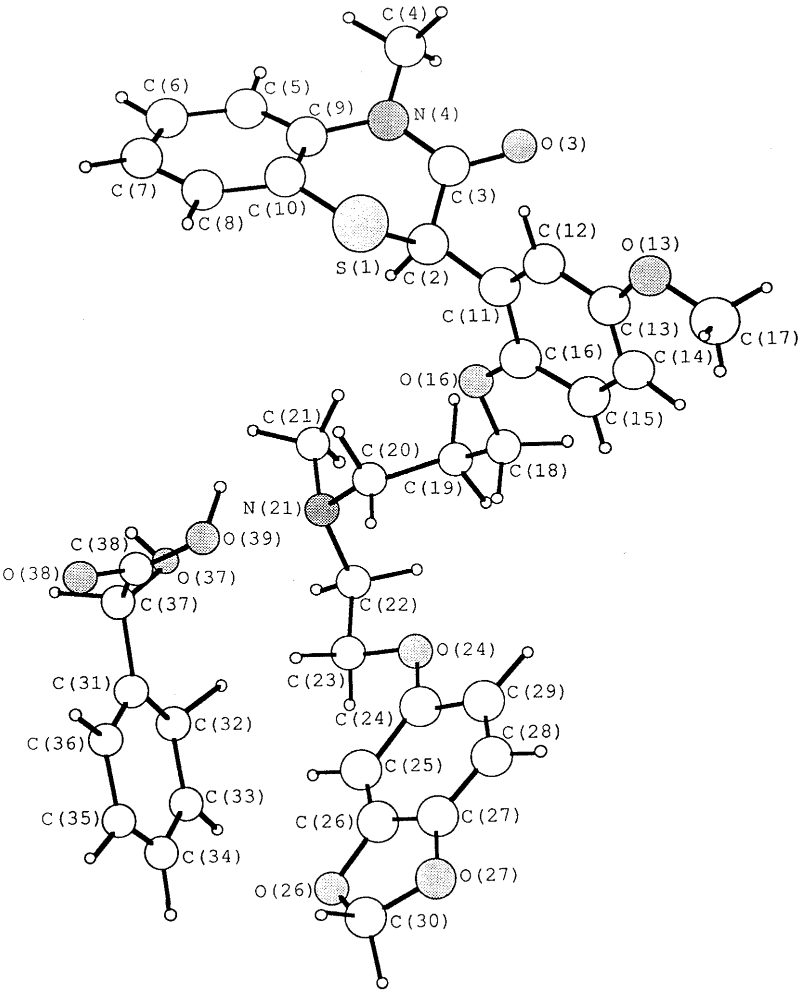


Fig. 1. Perspective View of the Molecular Conformation of **1** (Mandelate), together with the Atomic Numberings

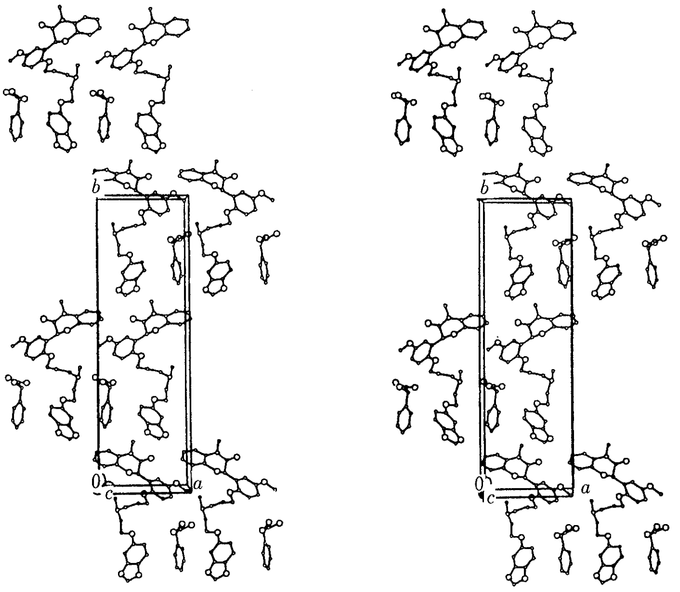


Fig. 2. Stereoscopic Drawing of the Molecular Packing of **1** (Mandelate) Viewed along the *c*-Axis

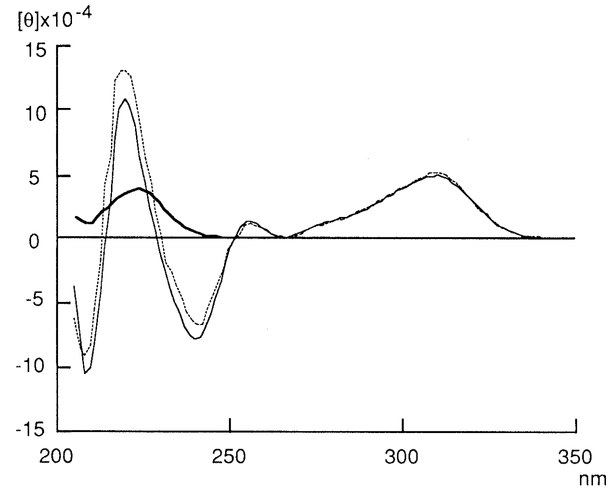


Fig. 3. CD Spectra of **1** (Fumarate) (——), **1** (Mandelate) (------), and **2** (——) in Ethanol at 25 °C

base) and **2**. Since the spectral patterns of **1** (fumarate) and **1** (mandelate) are similar to that of **3**, reported in our previous paper,[5] this suggests that the flexible aminoalkyl-side chain moves freely in solution and the methylenedioxyphenyl chromophore has almost no effect on the CD spectra. Furthermore, the conformation of the 2-phenylbenzothiazine nucleus of **3** might be similar to that of **1** (fumarate), **1** (mandelate) and also their corresponding free base. Based on the CD data of **3**, each chromophore, except that of the methylenedioxyphenyl ring, is assigned for **1** (fumarate) and **1** (mandelate) as given in Table IV.

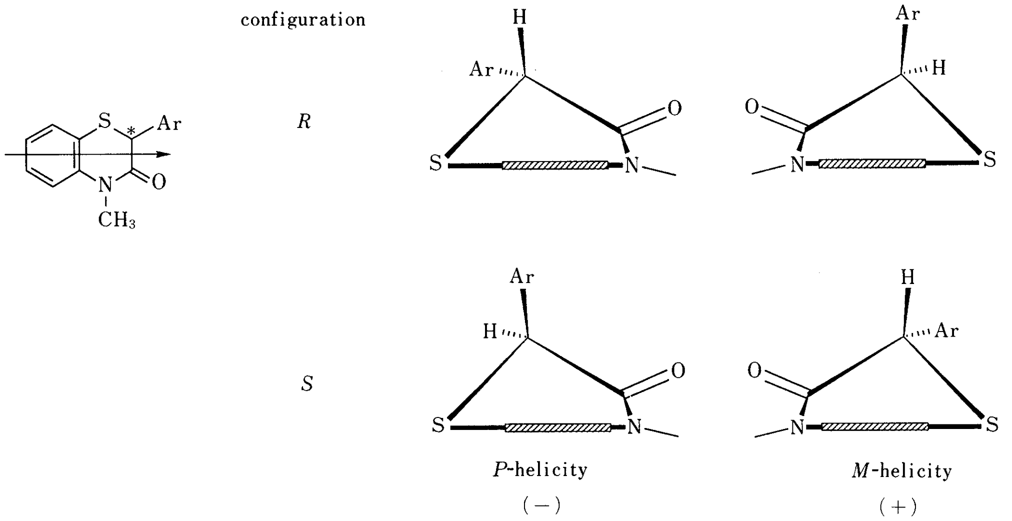


Fig. 4. Schematic Projection for the Structure of 2-Aryl-2*H*-1,4-benzothiazin-3(4*H*)-one Derivatives

The arrow indicates the direction of projection. The signs given are those for contributions to the ^1L_a band CD of the benzene chromophore of the benzothiazine ring, according to the helicity rule.

TABLE IV. CD Data of **1** (Fumarate) and **1** (Mandelate) in Ethanol at 25 °C

Chromophore	**1** (Fumarate)		**1** (Mandelate)	
	Wavelength	Sign	Wavelength	Sign
^1L_b of benzene (2-phenyl ring)	340—285 nm	+	340—285 nm	+
^1L_b of benzene (benzothiazine ring)	285—265 nm[a)]	+	285—267 nm[a)]	+
Not assigned	265—252 nm	+	267—252 nm	+
^1L_a of benzene (benzothiazine ring)	252—229 nm	−	252—231 nm	−
n-π* of amide (benzothiazine ring)	229—214 nm	+	231—213 nm	+
^1L_a of benzene (2-phenyl ring)	214— nm	−	213— nm	−

a) Shoulder.

In our previous study of the relationship between the stereochemistry and the CD spectral patterns of 2-aryl-2*H*-1,4-benzothiazin-3(4*H*)-one derivatives using the helicity rule,[8] it was shown that the sign of the ^1L_a CD band for the benzene chromophore of the benzothiazine ring correlates with the conformation of that thiazine ring; positive and negative signs correspond to *M*-[6] and *P*-conformers, respectively (see Fig. 4).[5]

Since the sign of the ^1L_a band is negative and the absolute configuration for **1** is *R*, the conformation of the thiazine ring in solution could be predicted to be the *P*-conformer and the 2-phenyl ring would exist in an equatorial position as it does in the crystalline state.

The X-ray[4,9] and the CD[5] investigations previously reported show that the 2-phenyl ring orientation for 2-hydroxyphenylbenzothiazine **3** is axial in its crystalline state and equatorial in ethanolic solution, while the orientation for 2-unsubstituted-phenylbenzothiazine **4** is equatorial in both the crystalline and solution states. We assume that the axial orientation of the 2-phenyl ring in the crystal of **3** is caused by the intermolecular hydrogen bond between the amido carbonyl and phenolic hydroxyl groups of neighboring molecules. This is supported by the fact that the 2-phenyl ring exists in an equatorial position in the crystalline form of **1** (mandelate), where no such intermolecular hydrogen bonding is present.

Experimental

X-Ray crystallographic data were obtained on **1** (mandelate), $C_{29}H_{32}N_2O_6S \cdot C_8H_8O_3$, F.W. = 688.80, monoclinic, space group $P2_1$, $a = 9.564(3)$ Å, $b = 31.077(9)$ Å, $c = 5.643(1)$ Å, $\beta = 94.40(2)°$, $V = 1672.3(8)$ Å^3, $Z = 2$ and $D_{calcd} = 1.368$ gm cm^{-3}. Crystals were grown in benzene by allowing the solvent to evaporate slowly at 25 °C. A clear, colorless crystal, 0.5 × 0.5 × 0.2 mm, was used for the structural determination. Cell constants were obtained by a least-squares refinement, using centered reflections within $30° \leq 2\theta \leq 60°$. A computer-controlled diffractometer (Rigaku AFC, with graphite-monochromated Cu K_α radiation, wavelength = 1.5418 Å) was used for data collection. A total of 1773 reflections were measured in the $\omega - 2\theta$ mode to $2\theta_{max} = 130°$. Corrections were applied for Lorentz and polarization effects. The structure was solved by direct methods with the aid of the program SAYTAN,[10] and non-H atoms were refined by using the full-matrix least-squares method with anisotropic temperature factors.[11] Hydrogen atoms were refined by difference Fourier syntheses. The final *R* factor for 1745 reflections ($I > 2\sigma(I)$) was $R = 0.0433$ and $R_w = 0.0578$.[12] CD spectra were measured at 25°C using a 10 mm cell and a JASCO J-500 spectropolarimeter. All samples were 0.03 mM ethanolic solutions. (*R*)-(+)-2-[5-Methoxy-2-[3-[methyl-[2-[3,4-(methylenedioxy)phenoxy]ethyl]amino]propoxy]phenyl]-4-methyl-2*H*-1,4-benzothiazin-3(4*H*)-one **1** (hydrogen fumarate **1** (fumarate), (*S*)-(+)-mandelate **1** (mandelate)) were synthesized as previously described.[4] (*S*)-(+)-Mandelic acid **2** was purchased from Yamakawa Chemical Industry Co., Ltd.

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References and Notes

1) A. Fleckenstein, *Circ. Res.*, **52** (Suppl. I), 3 (1983); G. Das, *Int. J. Clin. Pharmacol. Ther. Toxicol.*, **26**, 575 (1988).
2) K. Yamamoto, M. Fujita, K. Tabashi, Y. Kawashima, E. Kato, M. Oya, T. Iso, J. Iwao, *J. Med. Chem.*, **31**, 919 (1988); M. Fujita, A. Ota, S. Ito, K. Yamamoto, Y. Kawashima, *Synthesis*, **1988**, 599; M. Fujita, A. Ota, S. Ito, K. Yamamoto, Y. Kawashima, T. Iso, J. Iwao, *Chem. Pharm. Bull.*, **38**, 936 (1990).
3) This generic name is a Proposed International Nonproprietary Name (Prop. INN).
4) M. Fujita, S. Ito, A. Ota, N. Kato, K. Yamamoto, Y. Kawashima, H. Yamauchi, J. Iwao, *J. Med. Chem.*, **33**, 1898 (1990).
5) A. Ota, H. Suhara, Y. Kawashima, *Chem. Pharm. Bull.*, **40**, 833 (1992).
6) Concerning the definition of *P*- and *M*-conformers, see R. S. Cahn, Ch. Ingold, V. Prelog, *Angew. Chem.*, **78**, 413 (1966).
7) The subscripts, *t*, −*g* and +*g*, are *trans*, −*gauche* and +*gauche*, respectively.

8) M. Kajtár, J. Kajtár, J. Röhricht, J. G. Ángyán, *Croat. Chem. Acta*, **62**, 245 (1989).
9) K. Yamamoto, M. Fujita, K. Fujimura, Y. Kawashima, "in preparation".
10) T. Debaerdemaeker, G. Germain, P. Main, C. Tate, M. M. Woolfson, A System of Computer Programs for the Automatic Solution of Crystal Structure from X-Ray Diffraction Data, Univs. of York, England, Louvain, Belgium, 1987.
11) The Universal Crystallographic Computing System-Osaka, The Computation Center, Osaka University, Japan, 1979.
12) Tables of anisotropic temperature factors of non-H atoms, and fractional coordinates and isotropic temperature factors of H atoms are available from one of authors (A. O.) on request.