Journal of
Medicinal Chemistry
J. Med. Chem., 1997, 40(4), 559-573, DOI:10.1021/jm960411j

Crystallographic analysis of (*S*)-(+)-2,3-dihydro-2,4,6,7-tetramethyl-2-[(4-phenyl-1-piperidinyl)methyl]-5-benzofuranamine (*S*)-(+)-mandelate

(1)	Unit cell parameters	a= 6.348(2) (Å) b= 17.706(3) (Å) c= 12.356(2) (Å) β= 95.33(2) (degree)
(2)	Formula	$C_{24}H_{32}N_2O \cdot C_8H_8O_3$
	Formula weight	516.68
(3)	Measured density	not detected
	Calculated density	1.241 ($g \cdot cm^{-3}$)
(4)	Space group	$P2_1$
(5)	Wave length	1.5418 (Å)
	Number of total independent reflections	2132
	Number of observed reflections ($\geq 3\sigma$)	1774
	Number of weak reflections ($<3\sigma$)	358

(6) Methods

Intensity data collection

device	RIGAKU AFC5R four circle diffractometer
scan mode	$2\theta-\omega$
scan speed	32 ($degree \cdot min^{-1}$)
range	$3 \leq 2\theta \leq 120$ (degree)

Structure solution

Direct method (MITHRIL in a software package TEXSAN) was used.

MITHRIL: Gilmore, G.J. (1984). *J. Appl. Cryst.* **17**, 42-46.

TEXSAN: Single Crystal Structure Analysis Software, Version 5.0, (1989). Molecular Structure Corporation, The Woodlands, TX. 77381.

Structure refinement

Positions and anisotropic thermal parameters of non-hydrogen atoms were refined by full-matrix least-squares method. We put hydrogen atoms at idealized positions (dC-H = 1.09Å) with isotropic thermal parameters of their parent atoms. Hydrogens were not refined but they were allowed to ride on their parent atoms during refinement.

(7) Final R value

R= 0.049, Rw= 0.045 (unit weight)

(8) Statement on the final difference Fourier map.

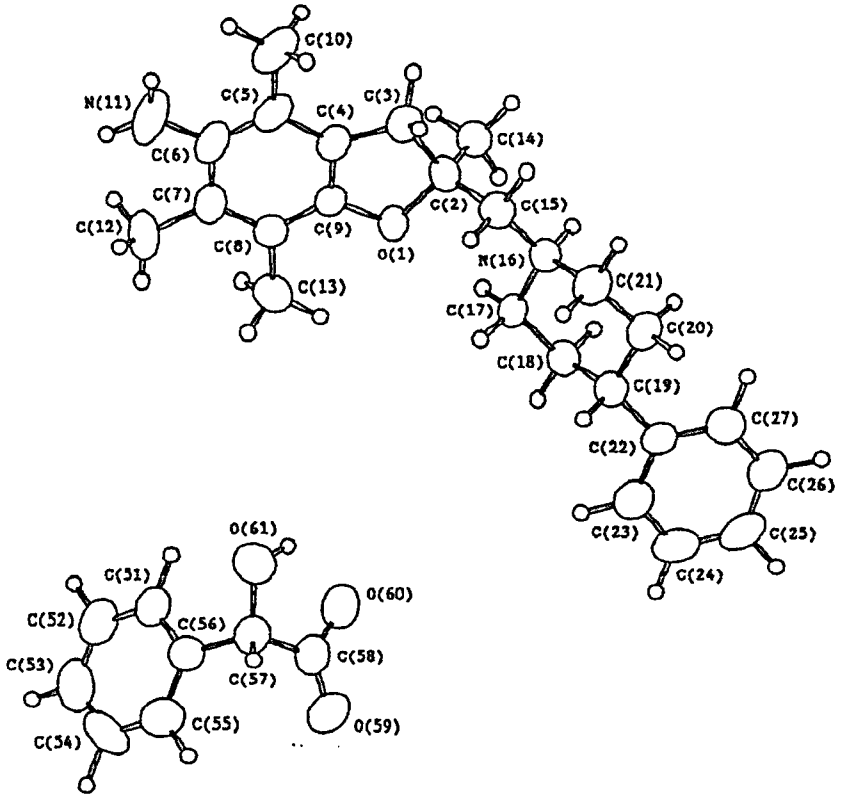
No significant peak is remained in the final difference Fourier map.

The highest remained positive peak is located at near atom H(121) and its height is 0.436 (electron•Å^{-3}). All the other remained peaks are lower than 0.25 (electron•Å^{-3}).

(9) Noteworthy bond length and angles.

None.

(10)



A molecular view and numbering of atoms.

(11) Tables

Table 1. Atomic Positional Parameters of Non-Hydrogen Atoms with Standard Deviations in Parentheses

	x/a	y/b	z/c
O(1)	0.3493(6)	0.2500	0.1804(3)
C(2)	0.2532(9)	0.3262(4)	0.1783(5)
C(3)	0.0353(10)	0.3179(4)	0.1098(5)
C(4)	0.0463(8)	0.2408(4)	0.0648(4)
C(5)	-0.0970(9)	0.2029(4)	-0.0103(5)
C(6)	-0.0463(11)	0.1293(5)	-0.0368(5)
C(7)	0.1370(11)	0.0928(4)	0.0116(5)
C(8)	0.2782(9)	0.1318(4)	0.0847(4)
C(9)	0.2265(9)	0.2055(4)	0.1073(4)
C(10)	-0.2906(10)	0.2412(5)	-0.0602(5)
N(11)	-0.1879(10)	0.0876(4)	-0.1083(5)
C(12)	0.1848(14)	0.0120(5)	-0.0158(6)
C(13)	0.4814(11)	0.0976(4)	0.1377(5)
C(14)	0.4014(10)	0.3800(4)	0.1253(5)
C(15)	0.2143(8)	0.3481(4)	0.2929(5)
N(16)	0.4065(7)	0.3673(3)	0.3705(3)
C(17)	0.5664(8)	0.3049(4)	0.3841(4)
C(18)	0.7469(8)	0.3259(4)	0.4688(5)
C(19)	0.6704(9)	0.3457(4)	0.5780(4)
C(20)	0.5098(10)	0.4101(4)	0.5599(5)
C(21)	0.3279(9)	0.3880(4)	0.4782(5)
C(22)	0.8586(10)	0.3622(4)	0.6620(4)
C(23)	0.9825(11)	0.3015(5)	0.7011(5)
C(24)	1.1607(12)	0.3147(5)	0.7742(6)
C(25)	1.2095(12)	0.3862(6)	0.8101(5)
C(26)	1.0858(13)	0.4446(5)	0.7720(6)
C(27)	0.9109(12)	0.4334(5)	0.6983(6)

Mandelic acid

C(51)	0.2302(10)	0.1401(4)	0.4891(5)
C(52)	0.1382(13)	0.1475(5)	0.3845(6)
C(53)	-0.0696(16)	0.1280(5)	0.3630(7)
C(54)	-0.1849(12)	0.1023(5)	0.4442(9)
C(55)	-0.0906(11)	0.0936(5)	0.5505(7)
C(56)	0.1211(9)	0.1133(4)	0.5724(5)
C(57)	0.2348(10)	0.1011(4)	0.6845(5)
C(58)	0.2998(11)	0.0180(4)	0.6930(5)
O(59)	0.1667(8)	-0.0299(3)	0.7070(4)
O(60)	0.4935(8)	0.0067(3)	0.6835(4)
O(61)	0.4184(8)	0.1491(3)	0.7024(4)

Table 2. Atomic Positional Parameters of Hydrogen Atoms

	x/a	y/b	z/c
H(31)	-0.095	0.323	0.161
H(32)	0.017	0.360	0.045
H(101)	-0.380	0.259	0.007
H(102)	-0.238	0.291	-0.102
H(103)	-0.402	0.212	-0.118
H(111)	-0.146	0.037	-0.136
H(112)	-0.331	0.109	-0.132
H(121)	0.050	-0.022	0.005
H(122)	0.195	0.010	-0.103
H(123)	0.326	-0.016	0.022
H(131)	0.434	0.048	0.181
H(132)	0.572	0.080	0.071
H(133)	0.592	0.128	0.195
H(141)	0.555	0.381	0.172
H(142)	0.420	0.361	0.043
H(143)	0.331	0.436	0.124
H(151)	0.111	0.398	0.288
H(152)	0.133	0.301	0.328
H(161)	0.490	0.414	0.336
H(171)	0.490	0.254	0.410
H(172)	0.630	0.295	0.307
H(181)	0.855	0.278	0.480
H(182)	0.830	0.374	0.439
H(191)	0.589	0.298	0.613
H(201)	0.448	0.424	0.637
H(202)	0.589	0.459	0.530
H(211)	0.246	0.340	0.509
H(212)	0.219	0.435	0.466
H(231)	0.941	0.244	0.675
H(241)	1.261	0.268	0.803
H(251)	1.346	0.396	0.869
H(261)	1.125	0.502	0.800
H(271)	0.814	0.481	0.669

Mandelic acid

H(511)	0.396	0.156	0.507
H(521)	0.229	0.168	0.320
H(531)	-0.145	0.133	0.280
H(541)	-0.352	0.088	0.426
H(551)	-0.181	0.072	0.615
H(571)	0.130	0.116	0.746
H(611)	0.537	0.117	0.700

Table 3. Thermal Parameters (U x 10^4, $Å^2$) of Non-Hydrogen Atoms with Standard Deviations in Parentheses

	U11	U22	U33	U12	U13	U23
O(1)	50(2)	43(2)	62(2)	4(2)	-17(2)	-12(2)
C(2)	47(3)	37(3)	61(4)	9(3)	-10(3)	-9(3)
C(3)	52(4)	63(4)	72(4)	12(3)	-19(3)	-12(4)
C(4)	41(3)	57(4)	49(3)	-6(3)	-4(3)	-6(3)
C(5)	48(4)	80(5)	41(3)	-13(3)	-4(3)	-4(3)
C(6)	75(5)	73(5)	43(3)	-27(4)	4(3)	-10(3)
C(7)	90(5)	54(4)	44(4)	-16(4)	13(3)	-9(3)
C(8)	56(3)	49(4)	43(3)	-1(3)	3(3)	0(3)
C(9)	51(4)	44(3)	41(3)	-5(3)	-4(3)	-2(3)
C(10)	47(4)	120(7)	58(4)	-9(4)	-9(3)	-11(4)
N(11)	91(5)	109(6)	90(5)	-32(4)	-16(4)	-42(4)
C(12)	136(7)	58(5)	77(5)	-12(5)	18(5)	-29(4)
C(13)	83(5)	56(4)	66(4)	21(4)	-4(4)	-2(3)
C(14)	65(4)	50(4)	55(3)	1(3)	3(3)	-4(3)
C(15)	34(3)	52(4)	65(4)	2(3)	-2(3)	-1(3)
N(16)	43(3)	43(3)	47(3)	1(2)	9(2)	-4(2)
C(17)	42(3)	44(3)	44(3)	0(3)	2(2)	-9(3)
C(18)	41(3)	47(3)	57(4)	4(3)	1(3)	-7(3)
C(19)	50(3)	45(3)	47(3)	-2(3)	1(3)	0(3)
C(20)	57(4)	64(4)	45(3)	11(3)	6(3)	-10(3)
C(21)	44(3)	71(5)	55(3)	7(3)	8(3)	-9(3)
C(22)	60(4)	59(4)	38(3)	-2(3)	6(3)	3(3)
C(23)	82(5)	74(5)	56(4)	13(4)	-7(4)	-3(4)
C(24)	82(5)	93(6)	71(5)	19(5)	-20(4)	11(4)
C(25)	85(5)	102(6)	46(4)	-6(5)	-10(3)	2(4)
C(26)	88(5)	78(5)	67(5)	-15(4)	-16(4)	-4(4)
C(27)	76(5)	62(5)	71(5)	-3(4)	-9(4)	0(4)

Mandelic acid

C(51)	64(4)	55(4)	66(4)	-6(3)	0(3)	14(3)
C(52)	101(6)	71(5)	69(5)	-10(4)	-2(4)	14(4)
C(53)	121(8)	62(5)	80(6)	15(5)	-29(5)	-2(4)
C(54)	58(5)	77(6)	140(8)	2(4)	-38(5)	-18(6)
C(55)	58(4)	62(5)	108(6)	1(3)	20(4)	5(4)
C(56)	54(4)	37(3)	65(4)	3(3)	3(3)	-3(3)
C(57)	62(4)	47(4)	64(4)	6(3)	6(3)	2(3)
C(58)	73(5)	58(4)	39(3)	2(4)	1(3)	3(3)
O(59)	87(4)	57(3)	91(4)	-16(3)	2(3)	15(3)
O(60)	74(3)	58(3)	78(3)	8(2)	7(2)	13(2)
O(61)	81(3)	53(3)	96(3)	-10(2)	-23(3)	-10(3)

Table 4. Bond Lengths (Å) with Standard Deviations in Parentheses

O(1)	- C(2)	1.480(6)
O(1)	- C(9)	1.383(6)
C(2)	- C(3)	1.561(8)
C(2)	- C(14)	1.529(9)
C(2)	- C(15)	1.510(9)
C(3)	- C(4)	1.478(10)
C(4)	- C(5)	1.407(8)
C(4)	- C(9)	1.365(8)
C(5)	- C(6)	1.390(11)
C(5)	- C(10)	1.486(9)
C(6)	- C(7)	1.414(10)
C(6)	- N(11)	1.409(10)
C(7)	- C(8)	1.395(9)
C(7)	- C(12)	1.507(11)
C(8)	- C(9)	1.381(9)
C(8)	- C(13)	1.518(9)
C(15)	- N(16)	1.518(7)
N(16)	- C(17)	1.499(8)
N(16)	- C(21)	1.509(8)
C(17)	- C(18)	1.524(7)
C(18)	- C(19)	1.516(8)
C(19)	- C(20)	1.532(9)
C(19)	- C(22)	1.536(8)
C(20)	- C(21)	1.513(8)
C(22)	- C(23)	1.392(10)
C(22)	- C(27)	1.368(11)
C(23)	- C(24)	1.401(10)
C(24)	- C(25)	1.367(13)
C(25)	- C(26)	1.356(12)
C(26)	- C(27)	1.384(10)

Mandelic acid

C(51)	- C(52)	1.373(9)
C(51)	- C(56)	1.377(9)
C(52)	- C(53)	1.365(13)
C(53)	- C(54)	1.374(14)
C(54)	- C(55)	1.400(13)
C(55)	- C(56)	1.390(9)
C(56)	- C(57)	1.517(9)
C(57)	- C(58)	1.530(10)
C(57)	- O(61)	1.443(8)
C(58)	- O(59)	1.220(9)
C(58)	- O(60)	1.262(9)

Hydrogen Bond

donor	acceptor	symmetry operation	distance between heteroatoms (Å)
N(16)-H(161)...O(60)		(1-x,1/2+y,1-z)	2.650(8)
O(61)-H(611)...O(60)		(x, y, z)	2.581(8)

Table 5. Bond Angles (Degree) with Standard Deviations in Parentheses

C(2)	- O(1)	- C(9)	107.6(4)
O(1)	- C(2)	- C(3)	105.5(5)
O(1)	- C(2)	- C(14)	107.8(5)
O(1)	- C(2)	- C(15)	108.7(5)
C(3)	- C(2)	- C(14)	112.1(5)
C(3)	- C(2)	- C(15)	108.6(5)
C(14)	- C(2)	- C(15)	113.7(5)
C(2)	- C(3)	- C(4)	102.8(5)
C(3)	- C(4)	- C(5)	129.6(6)
C(3)	- C(4)	- C(9)	110.2(5)
C(5)	- C(4)	- C(9)	120.2(6)
C(4)	- C(5)	- C(6)	117.0(6)
C(4)	- C(5)	- C(10)	121.0(7)
C(6)	- C(5)	- C(10)	122.0(6)
C(5)	- C(6)	- C(7)	121.9(6)
C(5)	- C(6)	- N(11)	119.4(6)
C(7)	- C(6)	- N(11)	118.5(7)
C(6)	- C(7)	- C(8)	120.1(7)
C(6)	- C(7)	- C(12)	120.9(6)
C(8)	- C(7)	- C(12)	119.0(6)
C(7)	- C(8)	- C(9)	116.7(5)
C(7)	- C(8)	- C(13)	123.4(6)
C(9)	- C(8)	- C(13)	119.9(5)
O(1)	- C(9)	- C(4)	113.1(5)
O(1)	- C(9)	- C(8)	122.7(5)
C(4)	- C(9)	- C(8)	124.1(6)
C(2)	- C(15)	- N(16)	117.2(4)
C(15)	- N(16)	- C(17)	113.8(5)
C(15)	- N(16)	- C(21)	107.4(4)
C(17)	- N(16)	- C(21)	110.9(4)
N(16)	- C(17)	- C(18)	110.9(5)
C(17)	- C(18)	- C(19)	112.6(4)
C(18)	- C(19)	- C(20)	107.8(5)
C(18)	- C(19)	- C(22)	110.6(5)
C(20)	- C(19)	- C(22)	115.0(5)
C(19)	- C(20)	- C(21)	111.2(5)
N(16)	- C(21)	- C(20)	110.9(5)
C(19)	- C(22)	- C(23)	117.8(6)
C(19)	- C(22)	- C(27)	123.1(6)
C(23)	- C(22)	- C(27)	119.0(6)
C(22)	- C(23)	- C(24)	119.4(7)
C(23)	- C(24)	- C(25)	120.6(8)
C(24)	- C(25)	- C(26)	119.1(7)
C(25)	- C(26)	- C(27)	121.5(8)
C(22)	- C(27)	- C(26)	120.3(7)

Mandelic acid

C(52)	- C(51)	- C(56)	122.4(6)
C(51)	- C(52)	- C(53)	118.6(7)
C(52)	- C(53)	- C(54)	120.8(8)
C(53)	- C(54)	- C(55)	120.8(7)
C(54)	- C(55)	- C(56)	118.4(7)
C(51)	- C(56)	- C(55)	119.1(6)
C(51)	- C(56)	- C(57)	120.1(5)
C(55)	- C(56)	- C(57)	120.7(6)
C(56)	- C(57)	- C(58)	107.6(5)
C(56)	- C(57)	- O(61)	111.4(5)
C(58)	- C(57)	- O(61)	110.3(5)
C(57)	- C(58)	- O(59)	119.5(6)
C(57)	- C(58)	- O(60)	113.8(6)
O(59)	- C(58)	- O(60)	126.7(7)