Instrumental Achievements

—X-Ray Analysis—

Crystal Structure and Absolute Configuration of
(-)-Amosulalol·L(+)-hemitartrate

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Amosulalol (YM-09538) is a newly developed anti-hypertensive agent with a combined α - and β -adrenoceptor blocking activity.¹ This compound possesses a phenylethanolamine skeleton, which belongs to one of the two typical general structures (arylethanolamine and aryloxypropanolamine) of adrenergic blockers. It has one chiral center.²

The molecular structure and absolute configuration of (-)-amosulalol·L(+)-hemitartrate have been determined by an X-ray diffraction study. Ten Bijvoet pairs which exhibited the greatest effect of anomalous scattering from the S atom were selected. The ratios of $|F_o(hkl)|/|F_o(\bar{h}\bar{k}\bar{l})|$ for an enantiomer were in agreement with the observed values. Consequently, the absolute configuration of this compound was determined to be *R* for benzylic carbinol as well as for two tartrate asymmetric carbons. This result is consistent with the absolute configuration of L(+)-tartaric acid. The atomic coordinates corresponding to this configuration are

Fig. 1 Structure of amosulalol.

Table 1 Crystal and experimental data

Formula:	$C_{18}H_{24}N_2O_5S \cdot 1/2 C_4H_6O_6$
Formula weight:	455.51
Crystal system:	monoclinic
Space group:	$C2$ $Z=4$
a :	28.01(1) Å
b :	7.889(2) Å
c :	9.361(4) Å
V :	2064(1) Å ³
D_x :	1.466 g/cm ³
R :	0.035
No. of reflections used:	1787
Measurement:	Rigaku AFC-5R
Structure determination:	MULTAN 78
Refinement:	block-diagonal least-squares

Fig. 2 Molecular structure and atom numbering of (-)-amosulalol·L(+)-hemitartrate.

Table 2 Fractional coordinates and isotropic temperature factor

Atom	x	y	z	$B_{eq}(Å^2)$
S	0.12968(3)	0.678308	0.55405(9)	2.63<65>
O 1	0.16339(8)	0.7781(3)	0.4810(3)	4.1<14>
O 2	0.13746(8)	0.6568(4)	0.7055(2)	4.3<19>
O 3	0.05138(7)	0.1022(3)	0.1114(2)	2.57<98>
O 4	-0.13656(7)	0.3199(3)	0.0754(2)	3.2<11>
O 5	-0.14250(7)	0.5986(3)	-0.0714(3)	3.9<19>
O 6	0.04825(7)	0.5389(3)	0.9751(2)	2.7<6>
O 7	0.01435(7)	0.5900(3)	0.7073(2)	2.8<8>
O 8	-0.02805(8)	0.8173(3)	0.7604(2)	3.4<21>
N 1	0.07748(9)	0.7617(3)	0.5241(3)	2.7<4>
N 2	-0.04342(8)	0.2277(3)	0.1857(2)	2.2<3>
C 1	0.0875(1)	0.2722(4)	0.3131(3)	2.3<6>
C 2	0.0896(1)	0.4289(4)	0.3813(3)	2.4<6>
C 3	0.1288(1)	0.4718(4)	0.4733(3)	2.4<7>
C 4	0.1670(1)	0.3591(4)	0.5008(3)	2.6<6>
C 5	0.1631(1)	0.2005(5)	0.4354(3)	3.1<8>
C 6	0.1242(1)	0.1582(5)	0.3425(3)	2.8<4>
C 7	0.2114(1)	0.4013(5)	0.5951(4)	3.9<11>
C 8	0.0447(1)	0.2383(4)	0.2076(3)	2.1<6>
C 9	-0.0001(1)	0.2101(4)	0.2879(3)	2.3<4>
C 10	-0.0884(1)	0.1827(5)	0.2563(3)	3.0<8>
C 11	-0.1304(1)	0.1636(5)	0.1493(3)	3.1<6>
C 12	-0.1756(1)	0.3331(5)	-0.0223(3)	2.8<7>
C 13	-0.1786(1)	0.4844(5)	-0.1011(3)	3.0<9>
C 14	-0.2158(1)	0.5090(5)	-0.2028(4)	3.6<6>
C 15	-0.2515(1)	0.3847(5)	-0.2220(4)	3.8<13>
C 16	-0.2491(1)	0.2395(5)	-0.1425(3)	3.7<16>
C 17	-0.2107(1)	0.2119(5)	-0.0428(3)	3.4<8>
C 18	-0.1506(1)	0.7672(5)	-0.1156(4)	4.6<14>
C 19	0.02034(9)	0.6885(4)	0.9491(3)	2.1<5>
C 20	0.0008(1)	0.6971(4)	0.7919(3)	2.3<6>

The B_{eq} values accompanied by < > are the equivalent isotropic temperature factors calculated from anisotropic thermal parameters using the equation $B_{eq}=8\pi^2(U1+U2+U3)/3$, where $U1$, $U2$ and $U3$ are principal components of the mean square displacement matrix U . Values in < > are anisotropy defined by $(\Sigma(B_{eq}-8\pi^2U_i)^2/3)^{1/2}$ and those in () are e.s.d.'s; they refer to last decimal places.

Table 3 Bond distances (Å) and angles (°)

S -O 1	1.436(2)	S -O 2	1.430(2)	S -N 1	1.611(3)
S -C 3	1.796(3)	O 3-C 8	1.421(4)	O 4-C 11	1.419(4)
O 4-C 12	1.384(4)	O 5-C 13	1.370(4)	O 5-C 18	1.407(5)
O 6-C 19	1.427(4)	O 7-C 20	1.234(4)	O 8-C 20	1.268(4)
N 2-C 9	1.503(4)	N 2-C 10	1.502(4)	C 1-C 2	1.390(4)
C 1-C 6	1.378(4)	C 1-C 8	1.528(4)	C 2-C 3	1.393(4)
C 3-C 4	1.402(4)	C 4-C 5	1.394(5)	C 4-C 7	1.515(5)
C 5-C 6	1.391(5)	C 8-C 9	1.518(4)	C 10-C 11	1.503(5)
C 12-C 13	1.403(5)	C 12-C 17	1.375(5)	C 13-C 14	1.379(5)
C 14-C 15	1.403(5)	C 15-C 16	1.365(5)	C 16-C 17	1.394(5)
C 19-C 20	1.538(4)				

O 1-S	-O 2	118.3(1)	O 1-S	-N 1	108.0(1)
O 1-S	-C 3	106.8(1)	O 2-S	-N 1	107.5(1)
O 2-S	-C 3	107.9(1)	N 1-S	-C 3	108.0(1)
C 11-O	4-C 12	117.0(2)	C 13-O	5-C 18	117.4(3)
C 9-N	2-C 10	111.3(2)	C 2-C	1-C 6	118.7(3)
C 2-C	1-C 8	117.4(3)	C 6-C	1-C 8	124.0(3)
C 1-C	2-C 3	120.5(3)	S	-C 3-C 2	118.0(2)
S	-C 3-C 4	120.5(2)	C 2-C	3-C 4	121.4(3)
C 3-C	4-C 5	116.8(3)	C 3-C	4-C 7	123.8(3)
C 5-C	4-C 7	119.4(3)	C 4-C	5-C 6	121.7(3)
C 1-C	6-C 5	120.8(3)	O 3-C	8-C 1	114.3(2)
O 3-C	8-C 9	110.5(2)	C 1-C	8-C 9	110.2(2)
N 2-C	9-C 8	109.2(2)	N 2-C	10-C 11	111.9(3)
O 4-C	11-C 10	107.6(3)	O 4-C	12-C 13	115.4(3)
O 4-C	12-C 17	124.6(3)	C 13-C	12-C 17	120.0(3)
O 5-C	13-C 12	115.7(3)	O 5-C	13-C 14	124.2(3)
C 12-C	13-C 14	120.0(3)	C 13-C	14-C 15	119.4(3)
C 14-C	15-C 16	120.4(3)	C 15-C	16-C 17	120.4(3)
C 12-C	17-C 16	119.9(3)	O 6-C	19-C 19a	108.3(2)
O 6-C	19-C 20	110.9(2)	C 19a-C	19-C 20	111.3(2)
O 7-C	20-O 8	125.5(3)	O 7-C	20-C 19	118.6(3)
O 8-C	20-C 19	115.9(3)			

given in Table 2. The molecular structure is shown in Fig. 2, together with an atomic numbering scheme. The bond distances and angles are given in Table 3.

References

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