Optical Resolution of 1-(3-Methoxyphenyl)ethylamine with Enantiomerically Pure Mandelic Acid, and the Crystal Structure of Less-Soluble Diastereomeric Salt

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Enantiomerically pure 1-(3-methoxyphenyl)ethylamine (**1**), which is a key intermediate of new phenyl carbamate drugs, was obtained by a diastereomeric method with high resolution efficiency (E) by using enantiomerically pure mandelic acid (**2**) as a resolving agent. The first crystallization of the mixture of diastereomeric salts from methanol gave a less-soluble diastereomeric salt in 70% yield with 99% diastereomeric excess. Recrystallization of the salt from 2-propanol gave (R)-**1**·(R)-**2** in 97% yield with 100% diastereomeric excess (total E=68%). The crystal structure of the less-soluble diastereomeric salt, (R)-**1**·(R)-**2**, was determined by X-ray crystallography. The crystal data are: Monoclinic, space group $P2_1$, a=12.642(4), b=5.890(2), c=10.855(4) Å, β=103.68(3)°, V=785.4(5) Å^3, Z=2, R=0.058 for 1450 unique reflections. The X-ray crystallography revealed that the high resolution efficiency was due to a layer-like arrangement of the enantiomerically pure acids, of which two layers sandwiched a layer of the amines by hydrogen bonds, as well as the helical column formed by hydrogen bonds between the acids and the amines, as observed for the less-soluble diastereomeric salt of 1-phenylethylamine with mandelic acid.

Enantiomerically pure 1-(3-methoxyphenyl)ethylamine (**1**) is one of the attractive key intermediates for the synthesis of phenyl carbamate drugs with anti-cholinesterase activity, such as 3-[1-(dimethylamino)ethyl]phenyl ethylmethylcarbamate.[1] Although this drug was initially developed in the (RS)-form, the (S)-enantiomer has been found to show a remarkably stronger activity than the (R)-antipode.[2]

Optically active **1** has been prepared from optically active 1-phenylethanol, obtained by the asymmetric reduction of *m*-methoxyacetophenone with a chiral oxazaborolidine, followed by a S_N2 reaction with hydrogen azide.[3,4] However, this method is not adequate for industrial production, despite the high stereoselectivity of the reactions, because of the required expensive reducing agent and highly toxic and explosive hydrogen azide. On the other hand, it is known that (RS)-**1** can be resolved with (S)- or (R)-malic acid.[5] However, the method requires an equimolar amount of the resolving agent, and recrystallization of the diastereomeric salt must be carried out several times in order to obtain a diastereomerically pure salt. To our knowledge, no resolution of (RS)-**1** with another resolving agent has yet been reported.

We report here on a facile and efficient method for the resolution of (RS)-**1** by using enantiomerically pure mandelic acid (**2**), and the crystal structure of the less-soluble diastereomeric salt.

Results and Discussion

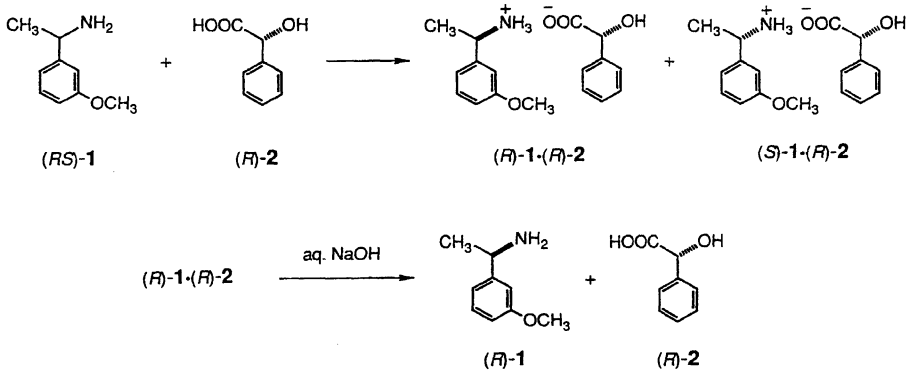
On the basis of the facts that (RS)-1-phenylethylamine can be effectively resolved by enantiomerically pure mandelic acid[6] and that (RS)-**1** has the same fundamental skeleton as (RS)-1-phenylethylamine, the optical resolution of (RS)-**1** was tried by using enantiomerically pure (R)-mandelic acid (**2**) as a resolving agent. In this optical resolution by the diastereomeric method, the less- and more-soluble salts were (R)-**1**·(R)-**2** and (S)-**1**·(R)-**2**, respectively. The diastereomeric excess of the less-soluble salt was determined on the basis of the enantiomeric excess of amine (R)-**1**, obtained upon the decomposition of the less-soluble salt with an aqueous sodium hydroxide solution. The results are given in Table 1 (Scheme 1).

In order to find a suitable solvent for the optical resolution, the solubility of a mixture of the diastereomeric salts, prepared from equimolar amounts of (RS)-**1** and (R)-**2**, in several typical solvents such as water, alcohols, benzene, and ethyl acetate were examined at room temperature. As a result, more than 50 parts of water, benzene, or ethyl acetate were required in order to dissolve one part of the mixture, while one part of the mixture dissolved in 6 parts of methanol or 20 parts of ethanol. From the viewpoint of the solvent volume, the alcohols were selected as resolution solvents in this resolution system. The optical resolution of (R)-**2**/(RS)-**1** (1/1) were performed in methanol, ethanol, and 2-propanol, respectively (Table 1, Entries 1, 6, and 8), and the highest resolution efficiency (E) was found to be achieved when methanol was used as a resolution solvent. As can be seen from Table 2, for the solubilities of the less- and more-soluble salts in alcohols the dif-

Table 1. Optical Resolution of (*RS*)-**1** with (*R*)-**2**

Entry	**2**/**1**[a]	Solvent	Solvent/**1**[b]	Yield[c]	De[d]	Resol. efficiency[e]
				%	%	*E*/%
1	1.00	MeOH	3.1	69	89	61
2	0.80	MeOH	2.6	65	96	62
3	0.60	MeOH	3.0	46	100	46
4	0.60	MeOH	2.6	70	99	69
5	0.60	MeOH	1.8	65	82	53
6	1.00	EtOH	5.0	141	14	20
7	0.60	EtOH	5.0	90	57	51
8	1.00	*i*-PrOH	5.6	161	3	5
9	0.60	*i*-PrOH	5.6	106	40	42

a) (*R*)-**2**/(*RS*)-**1** molar ratio. b) Solvent/(*RS*)-**1** ratio in weight. c) Calculated based on a half amount of (*RS*)-**1**. d) Diastereomeric excess. Determined by HPLC (CROWNPAK®) for **1**, which was obtained by decomposition of the salt with a sodium hydroxide solution. e) Resolution efficiency (*E*)(%)=Chemical yield of the crude salt (%)×Diastereomeric excess (%)/100.



Scheme 1.

Table 2. Solubilities of Less- and More-Soluble Diastereomeric Salts in Alcohols[a]

Solvent	Solubilities (g/100 g solvent)	
	Less-soluble salt	More-soluble salt
Methanol	12	32
Ethanol	4	8
2-Propanol	3	4

a) Less-soluble salt: (*R*)-**1**·(*R*)-**2**; More-soluble salt: (*S*)-**1**·(*R*)-**2**.

ference in solubility between the less- and more-soluble salts was extremely larger in methanol than in the other solvents. Therefore, the highest resolution efficiency for the optical resolution in methanol would be explained in terms of a large difference in the solubility between the diastereomeric salts.

The molar ratio of (*R*)-**2** to (*RS*)-**1** also affected the resolution efficiency (*E*) (Table 1, Entries 1, 2, and 4), and the best result was obtained when the molar ratio of (*R*)-**2** to (*RS*)-**1** was 0.6. A similar phenomenon was also observed for the optical resolutions in ethanol or 2-propanol (compare Table 1, Entry 6 with Entry 7, and Entry 8 with Entry 9). This would arise from the solubility of excess free amine **1** in alcohols relatively higher than those of the diastereomeric salts.

In the next stage, the effect of the solvent volume was examined (Table 1, Entries 3—5). The highest resolution efficiency was observed when 2.6 parts of methanol were used to one part of (*RS*)-**1**. Upon increasing or decreasing the solvent volume, the resolution efficiency was drastically diminished. These results indicate that the most suitable supersaturation in differentiating the salts in methanol exists around solvent/**1**=2.6.

As shown in Table 3, the recrystallization of the crude salt with low diastereomeric excess (40%de) from methanol or 2-propanol resulted in an improvement in the diastereomeric excess; methanol was better than 2-propanol, although 2-propanol gave a higher total efficiency (Table 3, Entries 1 and 2). In contrast, in the case of crude salt with a higher diastereomeric excess (more than 96%de, Table 3, Entries 3—5), which could be obtained as mentioned above, the highest efficiency was achieved when 2-propanol was used as a recrystallizing solvent. These results would be explained as follows based on the solubility of both diastereomeric salts in the alcohols (Table 2): Since the difference in solubility between the less- and more-soluble diastereomeric salts is extremely larger in methanol than in the other solvents, methanol gave better result than 2-propanol in

Table 3. Recrystallization of Crude (*R*)-**1**·(*R*)-**2** Salt

Entry	De[a] of Salt	Solvent	Solvent/Salt[b]	Yield	De[a]	Total efficiency[c]
	%			%	%	%
1	40	MeOH	3.0	38	97	39
2	40	*i*-PrOH	10.0	60	91	58
3	96	MeOH	2.0	64	100	42
4	96	*i*-PrOH	10.0	85	100	55
5	99	*i*-PrOH	10.0	97	100	68

a) Diastereomeric excess. Determined by HPLC (CROWNPAK®) for **1**, which was obtained by decomposition of the salt with sodium hydroxide solution. b) Solvent/crude salt ratio in weight. c) Total resolution efficiency (%)=Chemical yield of the crude salt (%)×Chemical yield of the recrystallized salt (%)×Final diastereomeric excess (%)/10000.

Table 4. Fractional Atomic Coordinates and Equivalent Isotropic Temperature Factors (B_{eq}) for Non-Hydrogen Atoms with esd's in Parentheses

Atoms	*x*	*y*	*z*	B_{eq}/Å^2
O1	−0.0282(2)	−0.4368(1)	−0.7259(2)	3.98(8)
O2	−0.0321(2)	−0.7226(7)	−0.8603(2)	3.17(7)
O3	−0.0007(2)	−0.7190(7)	−0.5294(2)	3.98(8)
O4	0.3662(2)	−0.3343(9)	−1.3022(3)	5.24(9)
N5	0.0836(3)	−0.6632(8)	−1.0590(3)	3.45(8)
C6	0.3595(3)	−0.498(1)	−1.2160(4)	4.1(1)
C7	−0.0160(3)	−0.6377(9)	−0.7497(3)	2.96(9)
C8	0.2800(3)	−0.680(1)	−1.0609(3)	3.7(1)
C9	0.2780(3)	−0.506(1)	−1.1490(4)	3.8(1)
C10	0.1916(3)	−1.013(1)	−0.6725(4)	4.2(1)
C11	0.3279(4)	−0.668(1)	−0.5575(4)	4.9(1)
C12	0.1481(3)	−0.8282(9)	−0.6248(3)	3.14(9)
C13	0.1972(3)	−0.679(1)	−0.9800(3)	3.7(1)
C14	0.2173(4)	−0.483(1)	−0.8870(4)	5.0(1)
C15	0.2163(3)	−0.656(1)	−0.5658(4)	4.2(1)
C16	0.0257(3)	−0.8053(1)	−0.6401(3)	3.11(9)
C17	0.3026(4)	−1.024(1)	−0.6643(4)	5.2(1)
C18	0.3702(4)	−0.852(1)	−0.6078(4)	5.2(1)
C19	0.4424(4)	−0.829(1)	−1.1065(5)	5.4(1)
C20	0.2800(4)	−0.173(1)	−1.3338(4)	5.0(1)
C21	0.4401(3)	−0.662(1)	−1.1932(4)	5.0(1)
C22	0.3606(3)	−0.838(1)	−1.0390(4)	4.5(1)

Table 5. Bond Distances (Å) and Angles (°) of (*R*)-**1**·(*R*)-**2** Salt with esd's in Parentheses

Bond distance/Å					
O1–C7	1.229(5)	C7–C16	1.539(6)	C12–C15	1.388(6)
O2–C7	1.272(4)	C8–C22	1.361(7)	C12–C16	1.524(5)
O3–C16	1.415(5)	C8–C9	1.394(7)	C13–C14	1.516(8)
O4–C6	1.361(7)	C8–C13	1.517(6)	C17–C18	1.372(9)
O4–C20	1.425(7)	C10–C12	1.376(7)	C19–C21	1.358(9)
N5–C13	1.491(4)	C10–C17	1.386(6)	C19–C22	1.403(7)
C6–C21	1.381(8)	C11–C18	1.379(9)		
C6–C9	1.396(6)	C11–C15	1.393(6)		
Bond angle/°					
C6–O4–C20		118.0(4)	C10–C12–C16		121.0(4)
O4–C6–C21		117.0(4)	C15–C12–C16		119.3(4)
O4–C6–C9		123.8(5)	N5–C13–C14		108.7(4)
C21–C6–C9		119.1(5)	N5–C13–C8		111.7(3)
O1–C7–O2		125.2(4)	C14–C13–C8		110.9(4)
O1–C7–C16		119.5(3)	C12–C15–C11		120.1(5)
O2–C7–C16		115.3(4)	O3–C16–C12		112.1(3)
C22–C8–C9		120.9(4)	O3–C16–C7		108.6(4)
C22–C8–C13		119.3(4)	C12–C16–C17		107.1(3)
C9–C8–C13		119.5(4)	C18–C17–C10		120.6(6)
C8–C9–C6		119.1(4)	C17–C18–C11		119.9(5)
C12–C10–C17		120.0(5)	C21–C19–C22		119.5(5)
C18–C11–C15		119.8(5)	C19–C21–C6		121.6(5)
C10–C12–C15		119.6(4)	C8–C22–C19		119.7(5)

the case of recrystallization of the diastereomeric salt with low purity. However, when 2-propanol was used as a solvent for the recrystallization of the diastereomeric salt with high purity, its low dissolving ability for both salts resulted in a high recovery of the less-soluble salt, whereas the more-soluble salt, existing in a quite small amount, could dissolve in the solvent during the recrystallization stage.

In order to clarify the recognition mechanism in the salt formation between amine **1** and enantiomerically pure **2** during the optical resolution, the crystal structure of the less-soluble salt, (*R*)-**1**·(*R*)-**2**, was determined by an X-ray crystallographic analysis. The fractional atomic coordinates for non-hydrogen atoms, and the bond distances and angles are listed in Tables 4 and 5, respectively. An ORTEP drawing of (*R*)-**1**·(*R*)-**2** is shown in Fig. 1. The hydrogen-bond network in the crystal viewed along the *a*-axis is shown in Fig. 2.

There is one kind of O–H (hydroxyl)···O (carbonyl) bond between **2** molecules, and one kind of O–H (carboxyl)···N (amine) bond and two kinds of N–H (amine)···O (carbonyl) bonds between **1** molecule and **2** molecule in one crystal lattice to form a hydrogen-bond network. The hydrogen-bond network exists only on the *b*–*c* plane, and there is no hydrogen bond along the *a*-axis. Moreover, a helical column, formed by N–H···O and O–H···N hydrogen bonds between **1** molecule and **2** molecule, is observed along the *b*-axis, the 2_1 screw axis. In addition, neighboring helical columns are connected to each other by O–H···O bonds between the molecules of **2** along the *c*-axis to give a sandwich-like structure of the helical columns. The hydrogen-bond network, helical column, and sandwich-like structure are quite similar to those observed in the less-soluble diastereomeric salt of mandelic acid with 1-phenylethylamine.[7,8] A similar connection of helical columns by O–H···O

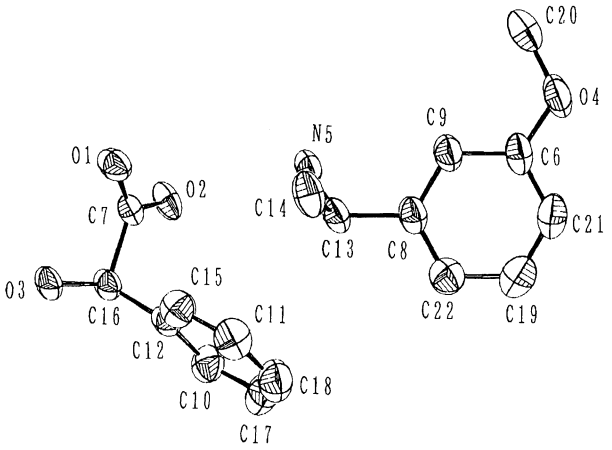


Fig. 1. ORTEP drawing of (*R*)-**1**·(*R*)-**2** salt.

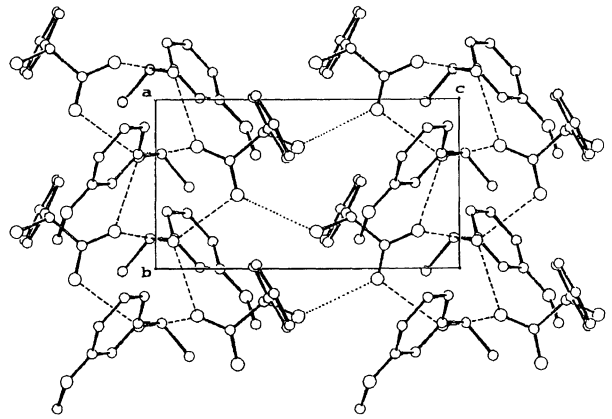


Fig. 2. Crystal structure of (*R*)-**1**·(*R*)-**2** salt and the hydrogen-bond network. The broken lines indicate the N–H···O hydrogen bonds between **1** molecule and **2** molecule. The dotted lines indicate the O–H···O hydrogen bonds between **2** molecules.

bonds was also observed for the less-soluble diastereomeric salt of mandelic acid with ephedrine.[9,10] These results indicate that in the resolution of a racemic amine with enantiomerically pure mandelic acid, the layer-like arrangement of the acid molecules as well as the helical column formation by hydrogen bonds between the acid molecules and the amine molecules would play some role in sufficiently recognizing the racemic amine at the growing site of the crystal, and that the hydrogen bond between the helical columns would make the crystal rigid.

In order to determine the correlation between the crystal growth and the crystal structure, the indices of the planes of a single crystal of (*R*)-**1**·(*R*)-**2** were determined on a goniometer; the longest axis of the single crystal was found to be along the *b*-axis. This fact indicates that the crystal easily grows along the direction where helical columns are developing. On the {010} plane, the most developing surface of the crystal, a molecule of **1** locates between two molecules of (*R*)-**2**, which lay on the both sides of $+c$ and $-c$ to a molecule of **1**, to form a chiral cavity. Racemic **1** would be strictly recognized and discriminated by the cavity, which fits with (*R*)-**1**. After the incorporation of (*R*)-**1** in the cavity, another molecule of (*R*)-**2** is incorporated to form the next layer of the {010} plane.

These observations strongly support the idea that the layer-like arrangement of the enantiomerically pure acids as well as the helical column formation play a very important role in the molecular recognition of the amine in order to achieve highly efficient resolution.

Experimental

General. *m*-Methoxyacetophenone was purchased from Tokyo Kasei Kogyo and used without any purification. The enantiomerically pure mandelic acid (99%ee) used was made by Yamakawa Chemical Industry.

^{1}H NMR spectra were recorded on a JEOL GX-400 or a JEOL JNM-PMX-90 spectrometer. IR spectra were measured on a JASCO IR-700 spectrometer using KBr pellets or films. Mass spectra were obtained with a JEOL JMSDX-303 spectrometer. Optical rotations were measured on a JASCO DIP-370 polarimeter with a circular temperature control unit. High-performance liquid chromatography was performed by a JASCO Intelligent HPLC system equipped with a 875-UV detector. Melting points were determined with a YAMATO MP-21 instrument and are uncorrected.

Determination of Enantiomeric and Diastereomeric Excesses. The enantiomeric excess of **1** was directly determined by HPLC using CROWNPAK CR(+)® (eluent: aqueous perchloric acid solution (pH 1.05), UV: 210 nm, 20 °C). The diastereomeric excess of the salt was based on the enantiomeric excess of the amine, liberated from the salt, without distillation.

Synthesis of (*RS*)-1. To an autoclave (500 ml), containing Raney-nickel catalyst[11] (10 g) and filled with nitrogen were added a methanol solution of ammonia (9.9% (w/v), 115 ml, 0.67 mol) and *m*-methoxyacetophenone **3** (50.0 g, 0.33 mol) at room temperature; the volume of the solution was then adjusted to 300 ml with methanol. The mixture was heated at 110 °C under a hydrogen pressure of about 1 MPa. After the reaction was completed (about 5 h), the mixture was cooled to room temperature and the catalyst was filtered off. The filtrate was dried with anhydrous magnesium sulfate and concentrated under reduced pressure. Distillation of the crude product gave 41.8 g (83%) of (*RS*)-**1** as a colorless oil; bp 81—82 °C (5 mmHg, 1 mmHg=133.322 Pa); 97% chemical purity on the basis of a GLC analysis; IR (neat) 3360, 3300, 2950, 2830, 1595, 1580, 1490, 1455, 1435, 1370, 1315, 1280, 1255, 1150, 1040, 870, 850, 780, and 715 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.30 (d, J=7 Hz, 3H), 2.50 (s, 2H), 3.73 (s, 3H), 4.1 (q, J=7 Hz, 1H), 6.87 (m, 4H); MS (70 eV) m/z (rel intensity) 151 (M^+; 16), 136 (100), 109 (19), 94 (9), and 77 (8).

Optical Resolution of (*RS*)-1. The typical resolution procedure was as follows: To a solution of (*RS*)-**1** (46.1 g, 0.30 mol) in methanol (120 g) was added powdered (*R*)-**2** (27.4 g, 0.18 mol); the mixture was then refluxed with stirring to give a clear solution. Upon cooling to about 50 °C, a few mg of (*R*)-**1**·(*R*)-**2** was seeded to the standing solution. After crystallization started, the solution was allowed to stand at this temperature for 1 h and then cooled to 20

°C over a period of 3 h. Deposited crude salt (*R*)-**1**·(*R*)-**2** was collected by filtration at 20 °C (31.3 g, 0.10 mol, 70% yield, 99%de). The salt (30.0 g) was recrystallized from 2-propanol (300 g) (in order to avoid scaling, the clear solution, obtained upon refluxing, was allowed to stand at 75 °C for 1 h after crystallization started) to give 29.4 g (97%) of diastereomerically pure (*R*)-**1**·(*R*)-**2**.

Enantiomerically pure (*R*)-**1** was obtained from the salt by an ordinary procedure; a suspension of the salt (23.0 g) in water (40 ml) was treated with 0.75 mol dm^{-3} aqueous sodium hydroxide, and the liberated oil was extracted with toluene (200 ml). The organic layer was dried with anhydrous magnesium sulfate and concentrated under reduced pressure. Distillation of the crude product in vacuo gave 10.0 g (87%) of enantiomerically pure (*R*)-**1**, which is highly hygroscopic. Even after repeated drying-distillation for several times, (*R*)-**1** was contaminated with 1/10 equimolar amount of water.

The antipode, (*S*)-**1**, could be obtained in a similar manner. (*S*)-Enriched **1**, recovered from the mother liquor, was treated with (*S*)-**2** to give diastereomerically pure (*S*)-**1**·(*S*)-**2** salt without any recrystallization (62% yield, 100%de). Treatment of the salt with aqueous sodium hydroxide gave enantiomerically pure (*S*)-**1** (87%).

(*R*)-1·(*R*)-2 Salt: White needles; mp 149.0—149.5 °C; 100%de; $[\alpha]_D^{20}$ −46.3° (*c* 2, MeOH); IR (KBr) 3400, 3030, 2920, 2850, 2640, 2520, 2200, 1600, 1560, 1465, 1400, 1340, 1260, 1220, 1160, 1090, 1060, 1020, 855, 780, 730, 695, 625, and 490 cm^{-1}; ^{1}H NMR (DMSO) δ=1.42 (d, J=7 Hz, 3H), 3.73 (s, 3H), 4.26 (q, J=7 Hz, 1H), 4.55 (s, 1H), 6.9—7.4 (m, 9H), 1.5—7.5 (ultra broad, 4H); MS (70 eV) *m/z* (rel intensity) 152 (M^+; 9), 151 (M'^+; 12), 136 (88), 109 (13), 108 (12), 107 (100), 105 (7), 94 (7), 79 (52), 77 (39), 51 (13), 44 (11). Found: C, 67.40; H, 7.12; N, 4.71%. Calcd for $C_{17}H_{21}NO_4$: C, 67.30; H, 6.98; N, 4.62%.

(*S*)-1·(*S*)-2 Salt: White needles; mp 149.0—150.0 °C; 100%de; $[\alpha]_D^{20}$ +47.0° (*c* 2, MeOH); The IR, ^{1}H NMR and MS spectra were identical with those of (*R*)-**1**·(*R*)-**2** salt. Found: C, 67.18; H, 6.94; N, 4.67%. Calcd for $C_{17}H_{21}NO_4$: C, 67.30; H, 6.98; N, 4.62%.

(*R*)-1 (contained 1/10 equimolar amount of water since (*R*)-**1** was highly hygroscopic): Colorless oil; 100%ee; $[\alpha]_D^{20}$ +17.6° (*c* 2, MeOH); IR (neat) 3350, 3295, 2950, 2830, 1590, 1580, 1480, 1450, 1430, 1360, 1315, 1280, 1250, 1150, 1035, 865, 840, 780, and 695 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.33 (d, J=7 Hz, 3H), 1.66 (s, 2H), 3.8 (s, 3H), 4.1 (q, J=7 Hz, 1H), and 6.7—7.3 (m, 4H); MS (70 eV) *m/z* (rel intensity) 151 (M^+; 14), 136 (100), 109 (20), 94 (11), 77 (10), and 44 (23). Found: C, 70.86; H, 8.76; N, 9.04%. Calcd for $C_9H_{13}NO{\cdot}1/10H_2O$: C, 70.64; H, 8.70; N, 9.16%.

(*S*)-1 (contained 1/10 equimolar amount of water since (*S*)-**1** is highly hygroscopic): Colorless oil; 100%ee; $[\alpha]_D^{20}$ −17.8° (*c* 2, MeOH); The IR, ^{1}H NMR and MS spectra were identical with those of (*R*)-**1**. Found: C, 70.65; H, 8.74; N, 9.21%. Calcd for $C_9H_{13}NO{\cdot}1/10H_2O$: C, 70.64; H, 8.70; N, 9.16%.

X-Ray Crystal Structure Analysis. A colorless long needle-like single crystal of (*R*)-**1**·(*R*)-**2** salt (0.80×0.10×0.05 mm) was grown from a saturated 2-propanol solution of the recrystallized salt. The X-ray intensities were measured up to 2θ=130° with graphite monochromated Cu $K\alpha$ radiation (λ=1.54178 Å) on a MAC Science MXC18 four-circle diffractometer by the ω–2θ scan. Standard reflections showed no significant intensity change. The structure was solved and refined by CRYSTAN. The scattering factors were taken from "International Table for X-Ray Crystallography."[12] The function minimized was sum $[\omega(|F_o|^2-|F_c|^2)^2]$, where $\omega=1.0/[(\sigma|F_o|)^2+0.0007|F_o|^2]$.

Crystallographic details: $C_{17}H_{21}NO_4$, FW=303.4, monoclinic, space group $P2_1$, a=12.642(4), b=5.890(2), c=10.855(4) Å, V=785.4(5) Å^3, β=103.68 (3)°, Z=2, D_c=1.28 g cm^{-3}, μ=6.61 cm^{-1}, R=0.058, Rw=0.066 with GOF=1.91 for 1450 unique reflections. Maximum shift in final step=0.09, residual density=0.22 to −0.33 e Å^{-3}.

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