Stereoselective Substitution in 2-Bromo Amides in the Presence of Ag^+ or Ag_2O

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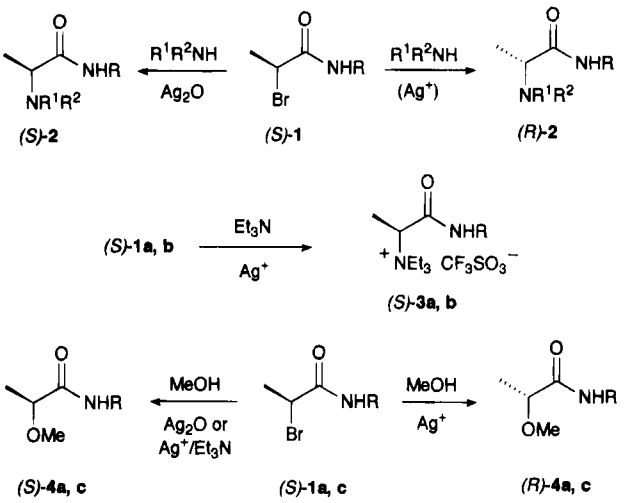
Bromine displacement by a primary, secondary, or tertiary amine, or methanol, in chiral nonracemic (*S*)-2-bromopropanamides **1** occurs with high yields and stereoselectivity. Soluble Ag^+ promotes inversion, and solid Ag_2O promotes retention of configuration. However, in the case of Et_3N, Ag^+ promotes retention. With the hindered 2-bromo-2-methylbutanamide **5**, the displacement by a primary or secondary amine or methanol occurs only in the presence of Ag_2O, possibly with retention of configuration.

In the conversion of *(S)*-2-bromopropanamides **1** into *(S)*- or *(R)*-2-aminopropanamides **2**, whereas soluble Ag^+ favors the *(R)*-products, solid Ag_2O promotes faster formation of the *(S)*-products.[1] We here report new results on the effect of Ag^+ and Ag_2O in the reactions of selected N- or O-nucleophiles with unhindered *(S)*-2-bromopropanamides **1** or hindered (2*S*)- or (2*R*)-2-bromo-2-methylbutanamides **5**.

Whereas **1a** and Et_2NH react with different stereochemical outcomes (Scheme 1 and Table 1, entries 1–3), the reaction of **1a** or **1b** and Et_3N takes place only if promoted by Ag^+, with retention of configuration (entries 4, 9). The absolute configuration of *(S)*-2-triethylammonium *N*-(*m*-bromophenyl)propanamide, trifluoromethanesulfonate (**3b**) has been ascertained by X-ray analysis (Scheme 1 and Figure 1). No reaction between *(S)*-**1a** and methanol occurs in the absence of promoter. However, Ag^+ leads predominantly to the *(R)*-2-methoxy-*N*-phenylpropanamide (**4a**) (Table 1, entry 7), and either Ag_2O or Ag^+/Et_3N give *(S)*-2-methoxy-*N*-phenylpropanamide (entries 5, 6, and 8). Enantiomeric products from *(S)*-**1a** have been differentiated through their optical activities and/or chiral reagent shifts.[1] However, 2-bromo amides **1c** and **5** and their substitution products by amine or methanol carry an additional chiral center in the amide moiety, as well as other features expedient to the formation of resolvable diastereoisomers. HPLC analyses and ^1H NMR spectra of crude reaction products allowed a quantitative determination of diastereomeric distribution. For example, 2-bromo amide **1c** reacts with *tert*-butylamine or methanol, in different conditions, to yield almost pure diastereomeric (2*S*)- or (2*R*)-**2c** or, respectively, (2*S*)- or (2*R*)-**4c** (entries 10–14).

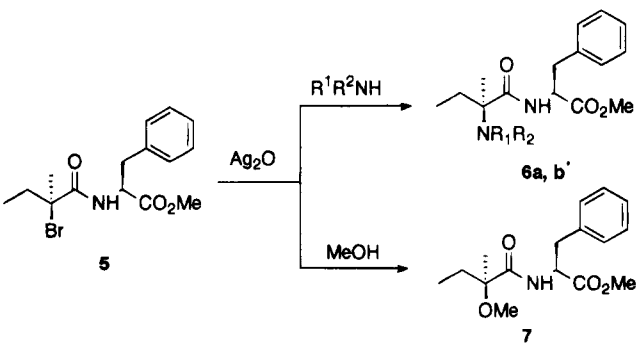
The hindered (2*R*)- or (2*S*)-2-bromo-2-methylbutanamide **5** reacts with *o*-bromobenzylamine or pyrrolidine in the presence of Ag_2O (entries 15 and 16) to yield a single 2-amino amide **6a,b** corresponding to one of the diastereomers **6** obtained from (2*R*,*S*)-**5**. Conversely, neither amine reacts alone or in the presence of Ag^+. It is relevant to mention that pyrrolidine is the fastest amine that we found to react with **1** in the absence of promoters.[1] Compound **5** and methanol again reacted

Scheme 1



Compounds **1-4**: **a**, R = Ph; **b**, R = C_6H_4Br-*m*; **c**, R = *(R)* -CH(Me)Ph;

Scheme 2



a, R^1 = H, R^2 = $CH_2C_6H_4Br$-*o*; **b**, R^1R^2 = $(CH_2)_4$;
C-2 configuration of **5-7** is arbitrary, to show retention.

only in the presence of Ag_2O: the resulting 2-methoxy amide **7** (entry 17) corresponds to one of the two resolvable diastereoisomers resulting from methanol and *(2R,S)*-**5**. Even if none of these products was suitable for X-ray analysis, we consider compounds **6a,b** and **7** as having a retained configuration at the substitution center.

In order to assay if the amide chirality affects the diastereomeric distribution in the displacement, a 1:1 diastereomeric mixture of (2*R*,*S*)-2-bromo-*N*-((1′*R*)-phenylethyl)propanamide (**1c**) was allowed to react with *tert*-

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Table 1. Stereochemistry of Substitution in *(S)*-2-Bromopropanamides 1a–c (Scheme 1) and *(2S)*- or *(2R)*-2-Bromo-2-methylbutanamide 5 (Scheme 2)[a]

						substitution products				
entry	2-bromoamide	nucleophile (equiv)	Ag_2O (equiv)	Ag^+ (equiv)	time (h)	(yield, %)[b]	config[c]	$[\alpha]^{20}_D$	or	de
1	**1a**	Et_2NH (2)			36	**2a** (78)	*R*	−68.0		
2	**1a**	Et_2NH (2)	1		1	**2a** (91)	*S*	+66.0		
3	**1a**	Et_2NH (2)		1	1.5	**2a** (94)	*R*	−67.5		
4	**1a**	Et_3N (2)		1	17	**3a** (75)	*S*	−43.0		
5	**1a**	MeOH (excess)	1		6.5	**4a** (83)	*S*	−57.2		
6	**1a**	MeOH (5)	1		14	**4a** (87)	*S*	−58.9		
7	**1a**	MeOH (5)		1	72	**4a** (66)	*R*	+54.6		
8	**1a**	MeOH (5)		1[d]	2.5	**4a** (93)	*S*	−56.0		
9	**1b**	Et_3N (2)		1	18	**3b** (72)	*S*	−40.0		
10	**1c**	*t*-$BuNH_2$ (2)	1		1	**2c** (95)	*S*			99.5
11	**1c**	MeOH (excess)	1		4	**4c** (97)	*S*			98.5
12	**1c**	MeOH (5)	1		13	**4c** (83)	*S*			99.0
13	**1c**	MeOH (excess)		1	28	**4c** (83)	*R*			99.0
14	**1c**	MeOH (5)		1[d]	23	**4c** (88)	*S*			98.9
15	**5**	*o*-$BrC_6H_4CH_2NH_2$ (2)	1		1.5	**6a** (90)	*S*			99.0
16	**5**	$(CH_2)_4NH$ (2)	1		0.2	**6b** (90)	*S*			99.0
17	**5**	MeOH (excess)	1		0.5	**7** (96)	*S*			99.0

[a] The solvent was toluene, except for entries 5, 11, 13, and 17, which apply to MeOH in methanol. [b] In Tables 1 and 3, the balance was given by unreacted **1**. [c] Configuration at C-2. [d] With 1 equiv of Et_3N.

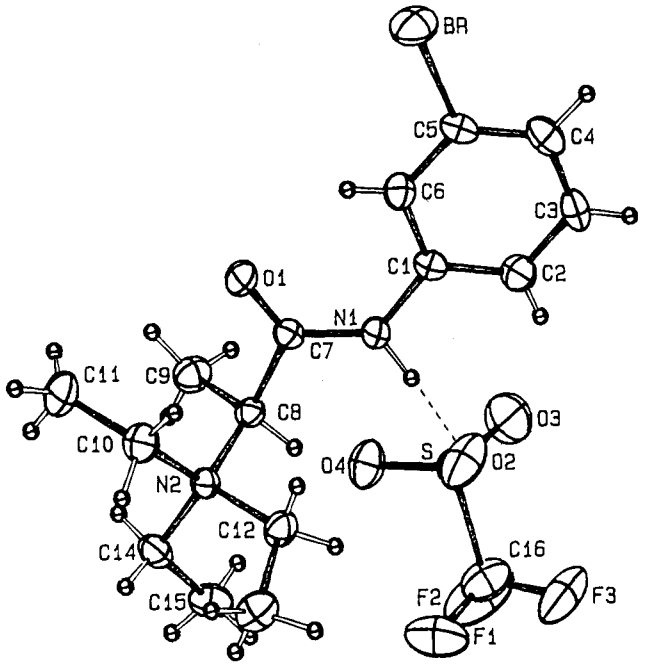

Figure 1. ORTEP (C. K. Johnson, ORTEP II, Report ORNL-5138, Oak National Laboratory, Oak Ridge, TN, 1976) drawing of *(S)*-**3b** (30% probability thermal ellipsoids). The two ions are linked by means of the N1–H···O2 hydrogen bond (N1···O2 = 2.900(6) Å).

$BuNH_2$ in the presence or absence of Ag_2O. No influence by the chiral amide center was observed.[2]

The use of a more polar solvent (Table 2) or less than 1 equiv of Ag_2O (Table 3) showed an adverse effect on the chemical and/or sterical yields, respectively, of **2c** and **2a**, the trend varying somehow according to the nucleophile.

Whereas in DMF the pK_a of conjugated acids of amines are typically within the range 9–10.5,[3] the pK_a of, *e.g.*, **1a** is much higher, being ca. 19.[4] Taking into account

Table 2. Effect of the Solvent in the Reaction of (2S,1′R)-1c[a] with *t*-*Bu*NH_2 and Ag_2O, yielding (2S,1′R)-2c vs (2R,1′R)-2c[b]

entry	solvent	time (h)	de
1	toluene	1	99.5[c]
2	THF	6	98.7[c]
3	CH_3CN	7	84.8[c]
4	DMF	9	75.5[c]
5	DMSO	18	27.4[d]

[a] See ref 10. [b] In entries 1–5 the molar ratio was 1:2:1; time as needed to obtain about 80% conversion. [c] (2S,1′R)-**2c** > (2R,1′R)-**2c**. [d] (2S,1′R)-**2c** < (2R,1′R)-**2c**.

Table 3. Effect of Different Amounts of Ag_2O on the Conversion of (S)-1a into 2a

			2a		
entry	nucleophile (equiv)	Ag_2O (equiv)	yield (%)	$[\alpha]^{20}_D$	main outcome
1	Et_2NH (2)	1	95	+63.4	retention
2	Et_2NH (2)	0.5	91	+63.9	retention
3	Et_2NH (2)	0.25	49	+61.1	retention
4	Et_2NH (2)	0.1	24	+31.1	
5	$PhCH_2NH_2$ (2)	1	91	−11.9	retention
6	$PhCH_2NH_2$ (2)	0.5	92	−4.2	

such data and the short lifetime of the conjugated 2-bromoamide anion,[5] we assume that inversion of configuration is due to S_N2 reaction of the amine with the neutral molecule of **1**. The fact that Ag^+ does not change the stereochemical outcome may be due to electrophilic assistance by the soft Lewis acid.[6] In the faster reactions proceeding with retention of configuration,[7] solid Ag_2O would behave as both a Lewis acid and Brønsted base,

(2) The diastereoselective formation of *(S)*-2-amino- or *(S)*-2-aryloxy esters from *(R)*-pantonolactone esters of racemic 2-bromo acids has been explained, in turn, *via* epimerization at the C–Br bond by Br^- and different S_N2 rates due to the ester auxiliary center. Koh, K.; Ben, R. N.; Durst, T. *Tetrahedron Lett.* **1993**, *34*, 4473. Durst, T.; Koh, K. *J. Org. Chem.* **1994**, *59*, 4683.

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acting synergically on the substrate. The fact that with the system **1a**/Ag^+/Et_3N triethylamine undergoes alkylation, whereas with the system **1a**/Ag^+/Et_3N/MeOH it is methanol that undergoes the alkylation, indicates that relative concentration, as well as nucleophilicity and basicity,[8] play a composite role. No Favorskij-like rearranged products were observed either in the presence or absence of Ag_2O, contrary to related base-promoted reactions of *N*-(mesyloxy)-*N*-alkylamides with amines.[9]

To conclude, chiral 2-bromo amides do show high stereoselectivity in reactions with nucleophiles and can lead one to expect either substitution product starting from a single enantiomeric center.

Experimental Section[1]

HPLC analysis was performed on a Bruker LC 313 UV variable-wavelength detector. Recording and quantification were accomplished with a chromatographic data processor Epson computer system (QX-10). Vydac C_{18} columns (analytical HPLC: 150 × 4.5 mm i.d., 5 μm particle size, flow rate 1.0 mL/min; preparative HPLC: 150 × 32 mm i.d., 10 μm particle size, flow rate 30 mL/min) were used for **2c** and **6b**. Analytical and preparative processes were carried out by a gradient made up of A = 10% acetonitrile in water and B = 60% acetonitrile in water, both containing 0.1% TFA. A 25 min linear gradient was run from 0% to 50% of B; λ = 220 nm. Säulentechnik silica columns, packed with Eurosphere 100 (analytical HPLC: 250 × 4.6 mm i.d., 5 μm particle size, flow rate 1.0 mL/min; preparative HPLC: 25 × 16 mm i.d., 7 μm particle size, flow rate 15 mL/min) were used for **1c**, **4c**, **5**, **6a**, and **7** with isocratic systems (see below); λ = 254 nm. Retention times (t_R) are reported. Elemental analyses are reported for compounds **3b** and **4c**; other products gave C, H, N with errors of ±0.5%. A sonicator Microson XL 2005 with standard microprobe was used for the reactions promoted by Ag_2O. Cu_2O or CaO proved far less active than Ag_2O as promoters. We checked that sonication did not affect the outcome of magnetically stirred reactions. Reagents, promoters, and 2-bromopropanamides **1a**,**c** were described.[1,10] *(R)*- and *(S)*-2-bromopropanoic acid are from Fluka and *(R,S)*-**1a** is from Aldrich.

***(S)*-2-Triethylammonium *N*-(*m*-Bromophenyl)propanamide, trifluoromethanesulfonate [*(S)*-3b].** *(S)*-2-Bromo-N-(*m*-bromophenyl)propanamide (**1b**) (307 mg, 1 mmol) and $Ag^+CF_3SO_3^-$ (257 mg, 1 mmol) were dissolved in toluene (5 mL). Triethylamine (0.7 mL, 5 mmol) was added, and the mixture was magnetically stirred for 18 h. The AgBr formed was removed by filtration, and the solution was concentrated to an oil that was purified through column chromatography on SiO_2. A first elution (hexane/EtOAc 1:1) gave few byproducts. Then, methanol eluted an oil (518 mg) that was dissolved in EtOAc (10 mL) and extracted with water (3 × 3 mL). The water extract was again concentrated to an oil. Trituration with Et_2O (3 × 3 mL) gave a solid (343 mg, 72%): mp 97–8 °C; $[\alpha]^{20}_D$ −40.0; ^{1}H NMR δ 1.47 (t, 9H, *J* = 7.3 Hz), 1.74 (d, 3H, *J* = 7 Hz), 3.56–3.80 (m, 6H), 4.68 (q, 1H, *J* = 7 Hz), 7.15–8.07 (m, 4H), 10.15 (s, 1H). Anal. Calcd for $C_{16}H_{24}BrF_3N_2O_4S$: C, 40.26; H, 5.07; Br, 16.74; N, 5.87. Found: C, 39.15; H, 5.20; Br, 16.68; N, 5.80. Single prisms were obtained upon recrystallization from water as well as from dioxane. X-ray analysis was run on a crystal obtained from dioxane.

***(S)*-2-Methoxy-*N*-phenylpropanamide [*(S)*-4a].** *(S)*-2-Bromo-*N*-phenylpropanamide (**1a**) (228 mg, 1 mmol) was dissolved in toluene (5 mL), and Ag_2O (232 mg, 1 mmol) and MeOH (0.2 mL, 5 mmol) were added. The mixture was sonicated for 14 h at 20 °C and then centrifuged. On concentration, the solution gave an oil that was purified by chromatography (SiO_2, hexane/EtOAc 4:1) to give *(S)*-**4a**: oil (156 mg, 87%); $[\alpha]^{20}_D$ −58.9° (lit.[11] mp 46 °C; $[\alpha]^{20}_D$ −89° ($CHCl_3$); −125° (EtOH)]; ^{1}H NMR δ 1.46 (d, 3 H, *J* = 6.8 Hz), 3.48 (s, 3 H), 3.87 (q, 1 H, *J* = 6.8 Hz), 7.11–7.61 (m, 5 H), 8.34 (br s, 1H).

***(2S)*-2-(*tert*-Butylamino)-*N*-((1′*R*)-phenylethyl)propanamide [(2*S*),(1′*R*)-2c].** To a solution of (2*S*)-2-bromo-*N*-((1′*R*)-phenylethyl)propanamide (**1c**)[10] [256 mg, 1 mmol, t_R = 10.55 (cyclohexane/EtOAc 83:17)] [t_R of (2*R*,1′*R*)-**1c** = 7.42] in toluene (5 mL), *tert*-butylamine (114 mg, 2 mmol), and Ag_2O (232 mg, 1 mmol) were added. The suspension was sonicated (1 h) and then centrifuged. The supernatant was concentrated and the crude mixture was separated on a SiO_2 column to give (2*S*,1′*R*)-**2c**: oil (236 mg, 95%); de 99.5% (HPLC, reversed phase, see introduction to Experimental Section); t_R = 16.20; ^{1}H NMR δ 1.11 (s, 9 H), 1.29 (d, 3 H), 1.49 (d, 3 H), 3.32 (q, 1 H), 5.07–5.20 (m, 1 H), 7.15–7.42 (m, 5 H), 8.10 (br d, 1 H).

The diastereomeric (2*R*,1′*R*)-**2c** was identified in an identical reaction starting from (2*R*,*S*,1′*R*)-**2c**: t_R = 14.94; ^{1}H NMR δ 0.97 (s, 9 H), 1.33 (d, 3 H), 1.47 (d, 3 H), 3.25 (q, 1 H), 5.04–5.13 (m, 1 H), 7.21–7.38 (m, 5 H), 8.03 (br d, 1 H).

(2*S*)-2-Methoxy-*N*-((1′*R*)-phenylethyl)propanamide [(2*S*,1′*R*)-4c]. (2*S*)-2-Bromo-*N*-((1′*R*)-phenylethyl)propanamide (**1c**) (256 mg, 1 mmol) was dissolved in methanol (5 mL), Ag_2O (232 mg, 1 mmol) was added, and the suspension was sonicated for 14 h. Workup as for *(S)*-**4a** gave (2*S*,1′*R*)-**4c**: oil [201 mg, 97%, t_R = 15.0 (cyclohexane/EtOAc 70:30)]; de 98.5%; ^{1}H NMR δ 1.35 (d, 3 H, *J* = 7 Hz), 1.52 (d, 3 H, *J* = 7 Hz), 3.40 (s, 3 H), 3.77 (q, 1 H), 5.13 (m, 1 H), 6.78 (br s, 1 H), 7.25–7.35 (m, 5 H). Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 68.32; H, 8.31; N, 6.69.

(2*R*)-2-Methoxy-*N*-((1′*R*)-phenylethyl)propanamide [(2*R*,1′*R*)-4c]. From **1c** and MeOH in the presence of Ag^+: t_R = 12.9; ^{1}H NMR δ 1.40 (d, 3 H), 1.50 (d, 3 H), 3.35 (s, 3 H), 3.73 (q, 1 H), 5.13 (m, 1 H), 6.8 (br s, 1 H), 7.26–7.35 (m, 5 H).

(2*S*)-L- and (2*R*)-L-2-Bromo-2-(methylbutanoyl)phenylalanine, Methyl Ester [(2*S*)-L-5 and (2*R*)-L-5]. A solution of (2*R*,*S*)-2-bromo-2-methylbutanoyl bromide (2.04 g, 8.3 mmol) in chloroform (8 mL) was dropped onto a suspension of L-phenylalanine methyl ester hydrochloride (1.8 g, 8.3 mmol) and triethylamine (1.69 g, 16.7 mmol) in chloroform (8 mL) under magnetic stirring in an ice–water bath. The mixture was stirred for 14 h at rt. The resulting solution was washed with 2 N HCl (2 × 7 mL), brine (7 mL), and saturated $NaHCO_3$ (2 × 7 mL) and dried (Na_2SO_4). Evaporation gave an oil consisting only of the two diastereoisomers (2.63 g, 92%, ^{1}H NMR, see below). HPLC resolution (cyclohexane/EtOAc 95:5) gave the following: oil; t_{R1} = 23.5; ^{1}H NMR δ 0.67 (t, 3 H), 1.65 (t, 3 H), 2.16 (m, 2 H), 3.19 (m, 2 H), 3.83 (s, 3 H), 4.80 (m, 1 H), 7.10–7.30 (m, 6 H); oil; t_{R2} = 25.9; ^{1}H NMR δ 0.88 (t, 3 H), 1.69 (t, 3 H), 2.10 (m, 2 H), 3.13 (m, 2 H), 3.74 (s, 3 H), 4.81 (m, 1 H), 7.12–7.30 (m, 6 H).

(2*R*,*S*)-2-[(*o*-bromobenzyl)amino]-2-(methylbutanoyl)-L-phenylalanine, Methyl Ester [(2*R*,*S*)-L-6a]. A sample of *o*-bromobenzylamine hydrochloride (258 mg, 1.16 mmol) was stirred for 1.5 h with Amberlyst A-21 (Fluka) (1.16 g) in toluene (5 mL). The resin was filtered off, (2*R*,*S*)-L-**5** (0.2 g, 0.58 mmol) and Ag_2O (0.135 g, 0.58 mmol) were added to the solution, and the suspension was sonicated for 1.5 h at about 20 °C. Centrifugation of the mixture gave an oil that was purified by column chromatography (silica gel; hexane/EtOAc 4:1). A pure diastereomeric mixture *(2R,S)*-L-**6a** (0.23 g, 90%) was obtained: oil; analytical HPLC (cyclohexane/EtOAc 90:10) showed two identical peaks, t_{R1} = 35.5 and t_{R2} = 36.6; ^{1}H NMR δ 0.76 and 0.91 (2t, 3 H), 1.26 and 1.35 (2s, 3 H), 1.62 and 1.76 (2q, 2 H), 2.98 and 3.21 (m, 2 H), 3.42–3.78 (m, 2 H), 3.70 and 3.71 (2s, 3 H), 4.80–4.94 (m, 1 H), 7.04–7.55 (m, 9 H), 7.81 (br d, 1 H).

(2*R*)-L-6a or (2*S*)-L-6a. A sample of (2*R*)-L-**5** or (2*S*)-L-**5** (t_R = 23.5, de 99%) was treated with *o*-bromobenzylamine and Ag_2O as described above for (2*R*,*S*)-L-**5**: oil (90%); HPLC *single* peak, t_R = 33.5; ^{1}H NMR δ 0.91 (t, 3 H), 1.26 (s, 3 H), 1.76 (q,

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2 H), 2.98–3.25 (2 AB, 2 H), 3.41–3.91 (2 AB, 2 H), 3.71 (s, 3 H), 4.80–4.90 (m, 1 H), 7.04–7.55 (m, 9 H), 7.80 (br d, 1 H).

(2*R*,*S*)-2-Pyrrolidino-2-(methylbutanoyl)-L-phenylalanine, Methyl Ester [(2*R*,*S*)-L-6b]. To the solution of (2*R*,*S*)-L-**5** (0.21 g, 0.6 mmol) in toluene (3 mL) were added Ag_2O (0.14 g, 0.6 mmol) and pyrrolidine (0.086 g, 1.2 mmol), and the suspension was sonicated for 15 min at 20 °C. The mixture was centrifuged, the solid was washed (EtOAc) and the solution and washing were concentrated. The residue was chromatographed (SiO_2, hexane/EtOAc 1:8) to give an oil (0.18 g, 92%): analytical HPLC (reversed phase, see introduction to Experimental Section) showed two identical peaks: t_{R1} = 9.60, t_{R2} = 10.3; ^{1}H NMR δ 0.60 and 0.86 (2t, 3H), 1.03 and 1.05 (2s, 3H), 1.49–1.69 (m, 8H), 2.45–2.52 (m, 2H), 3.01–3.20 (m, 2H), 3.71 and 3.73 (2s, 3H), 3.77–3.90 (m, 1H), 7.14–7.34 (m, 5H), 7.56 and 7.70 (2d, 1H).

(2*R*)-L-6b or (2*S*)-L-6b. A sample of (2*R*)-L-**5** or (2*S*)-L-**5** (t_R = 25.95, de 99%) was treated with pyrrolidine and Ag_2O as described above for (2*R*,*S*)-L-**5**: oil (90%); HPLC (reversed phase, see introduction to Experimental Section) *single* peak, t_R = 10.3; ^{1}H NMR δ 0.61 (t, 3 H), 1.05 (s, 3 H), 1.47–1.68 (m, 8 H), 2.45–2.52 (m, 2 H), 3.01–3.15 (m, 2 H), 3.71 (s, 3 H), 3.70–3.90 (m, 1 H), 7.14–7.29 (m, 5 H), 7.68 (d, 1 H).

(2*R*,*S*)-2-Methoxy-2-(methylbutanoyl)-L-phenylalanine, Methyl Ester [(2*R*,*S*)-L-7]. To the solution of (2*R*,*S*)-L-**5** (0.14 g, 0.42 mmol) in MeOH (3 mL) was added Ag_2O (0.1 g, 0.42 mmol), and the suspension was sonicated for 0.5 h and centrifuged. Concentration gave an oil (115 mg, 93%): R_f (hexane/EtOAc 1:1) 0.5 and 0.6; analytical HPLC (cyclohexane/EtOAc 85:15) showed two identical peaks t_{R1} = 18.3, t_{R2} = 23.1; ^{1}H NMR δ 0.65 and 0.79 (2 t, 3 H), 1.25 and 1.30 (2 s, 3 H), 1.50–1.83 (m, 2 H), 3.02–3.20 (m, 2 H), 3.12 and 3.19 (2s, 3 H), 3.72 (s, 3 H), 4.78–5.02 (m, 1H), 7.10–7.30 (m, 6 H).

(2*R*)-L-7 or (2*S*)-L-7. A sample of (2*R*)-L-**5** or (2*S*)-L-**5** (t_R = 25.95, de 99%) was treated with MeOH and Ag_2O as described above for (2*R*,*S*)-L-**5**: oil (96%); R_f = 0.45 (hexane/EtOAc 1:1); HPLC (cyclohexane/EtOAc 85:15) *single* peak, t_R = 18.27; ^{1}H NMR δ 0.64 (t, 3 H), 1.30 (s, 3 H), 1.50–1.75 (m, 2 H), 3.02–3.20 (m, 2 H), 3.19 (s, 3 H), 3.71 (s, 3 H), 4.84–5.02 (m, 1 H), 7.12–7.29 (m, 6 H).

Crystal Data. (*S*)-**3b**: $C_{15}H_{24}N_2OBr^+SO_3CF_3^-$, orthorombic $P2_12_12_1$ (No. 19) a = 7.302(1) Å, b = 10.270(2) Å, c = 27.713(6) Å, V = 2078.0(6) Å^3, Z = 4, D_{calcd} = 1.53 g cm^{-3}, μ = 21.01 cm^{-1}. Of the 2892 unique measured reflections 1774 with $I \geq 2\sigma(I)$ were used in the refinement. Full-matrix least-squares refinement with all non-hydrogen atoms anisotropic and hydrogen atoms isotropic. R(on F) = 0.046, R_w = 0.041. The data were collected on an Enraf-Nonius CAD-4 diffractometer with graphite monochromated Mo Kα radiation, $\omega/2\theta$ scan technique ($2 \leq \theta \leq 28°$). Cell parameters were determined and refined from 25 reflections in the range $10 < \theta < 15°$; three standard reflections monitored every 2 h showed no significant variation during data collection. All data were collected for Lorentz, polarization, and absorption (ψ scan method, minimum transmission factor 69.9%). The structure was solved by direct methods with the SIR88 system of programs (Burla, M. C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Polidori, G.; Spagna, R.; Viterbo, D. SIR88, A Direct Methods Program for the Authomatic Solution of Crystal Structures. *J. Appl. Crystallogr.* **1989**, *22*, 389). All other calculations were accomplished by the MolEN system of programs (MolEN, An Interactive Structure Solution Procedure, Enraf-Nonius, Delft, The Netherlands, 1990). Both enantiomorphous structures were refined with final disagreement factors R_1 = 0.046, R_{1w} = 0.041 and R_2 = 0.071, R_{2w} = 0.070 for the two enantiomers, respectively. The correct absolute configuration was assigned to the enantiomer displaying the lower values of the disagreement factors.[12]

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(12) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.