JOC*Note*

1-Benzotriazol-1-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropan-1-ones: Mosher-Bt Reagents

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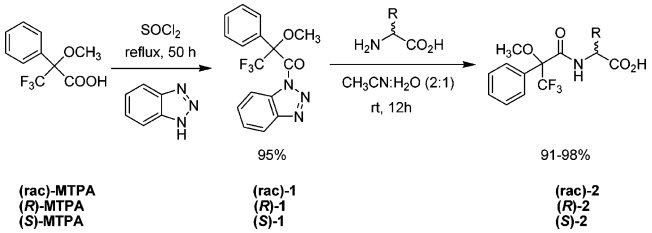
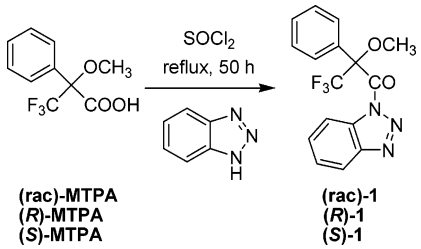


Benzotriazole derivatives of 3,3,3-trifluoro-2-methoxy-2-phenylpropionic acid react with water-soluble amino acids and peptides in an acetonitrile/water (2:1) mixture to give the corresponding amides in quantitative yield.

N-Acylbenzotriazoles, well-established as activated derivatives of carboxylic acids,[1] are easily prepared directly from carboxylic acids by either of two alternative methods: (i) treatment with thionyl chloride and 1*H*-benzotriazole (BtH)[2] or (ii) with $BtSO_2Me$ in the presence of Et_3N. They have been applied for the N-acylation of amines[3] and amides,[3,4] the O-acylation of aldehydes,[5] and the C-acylation of ketones and heteroaromatics,[6] alkyl sulfones,[7] alkyl cyanides,[8] alkylazines,[9] and α-nitroalkanes.[10] Acylations with stable, crystalline *N*-acylbenzotriazoles are of special utility when the corresponding acid chlorides are unstable or difficult to prepare;[11] thus *N*-(α-protected-amino) acylbenzotriazoles provide a simple and efficient method to prepare peptides.[12] They also enable the preparation of esters and amides from unprotected hydroxyaromatic and -aliphatic carboxylic acids,[13] chiral *O*-(α-protected-aminoacyl) steroids,[14] 1,3-benzodioxin-4-one and benzoxazine-2,4-diones,[15] alkyl, unsaturated, (hetero)aryl, and N-protected α-amino ketones, and (α-aminoacyl)oxy-substituted terpenes and alkanes.[16]

SCHEME 1. Synthesis of 1-Benzotriazol-1-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropan-1-one



Mosher's reagent, α-methoxy-α-trifluoromethylphenyl acetic acid (MTPA), reported in 1973 is now the preferred chiral

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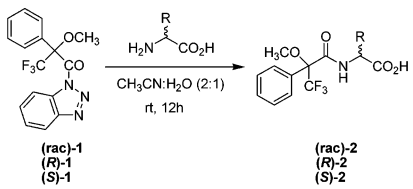
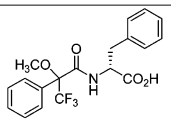
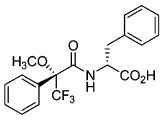
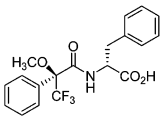
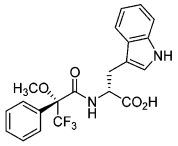
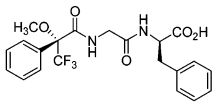
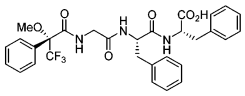
TABLE 1. Reactions of Mosher-Bt Reagent 1 with Chiral Amino Acids and Di- and Tripeptides



(rac)-1
(*R*)-1
(*S*)-1

(rac)-2
(*R*)-2
(*S*)-2

Mosher-Bt **1**	aminoacid and peptide	product structure		yield (%)[a]
(*rac*)-**1**	(*R*)-Phe		(*R*,*R*)- and (*S*,*R*)-**2a**	96
(*R*)-**1**	(*R*)-Phe		(*R*,*R*)-**2a**	96
(*S*)-**1**	(*R*)-Phe		(*S*,*R*)-**2a**	96
(*R*)-**1**	(*R*)-Trp		(*R*,*R*)-**2b**	98
(*R*)-**1**	Gly-(*R*)-Phe		(*R*,*R*)-**2c**	97
(*R*)-**1**	Gly-(*S*)-Phe-(*S*)-Phe		(*R*,*S*,*S*)-**2d**	91

[a] Isolated yields of pure products.

derivatizing agent for determining both enantiomeric excess and absolute configurations of synthetic and naturally occurring chiral alcohols and amines by NMR spectroscopy.[17] It is commercially available both as the acid and as the acid chloride.[18] The procedure for determining the absolute configuration starts with the derivatization of a chiral alcohol (or amine) of unknown configuration with (*R*)- and (*S*)-MTPA chloride to yield a pair of diastereoisomeric esters (or amides). The ^{19}F, ^{1}H, or ^{13}C NMR chemical shifts of the diastereomers are then acquired and compared. The absolute configuration of the chiral compound is assigned by interpretation of the signs of $\Delta\delta$ values, using empirical models.[17]

Both enantiomers of commonly used MTPA chloride as chiral derivatizing agents are commercially available; however, they are costly, corrosive, moisture sensitive, and need to be stored tightly closed in a deep freeze. To overcome these problems, we have now prepared the racemic and both enantiomeric versions of 1-benzotriazol-1-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropan-1-one (*rac*)-, (*R*)-, and (*S*)-**1** (Mosher-Bt reagent) from the corresponding MTPA and 1*H*-benzotriazole (BtH) and studied their reactions with representative water-soluble chiral amino acids and di- and tripeptides in acetonitrile/water (2:1) medium in order to find their efficiency as stable chiral derivatizing agents in place of the sensitive MTPA chlorides.

(18) Although derivatization of an alcohol (or amine) with (*R*)-MTPA acid gives the corresponding (*R*)-MTPA ester (or amide), the widely used (*R*)-MTPA acid chloride gives the corresponding (*S*)-MTPA ester (or amide). (a) Joshi, B. S.; Pelletier, S. W. *Heterocycles* **1999**, *51*, 183. (b) Joshi, B. S.; Newton, M. G.; Lee, D. W.; Barber, A. D.; Pelletier, S. W. *Tetrahedron: Asymmetry* **1996**, *7*, 25.

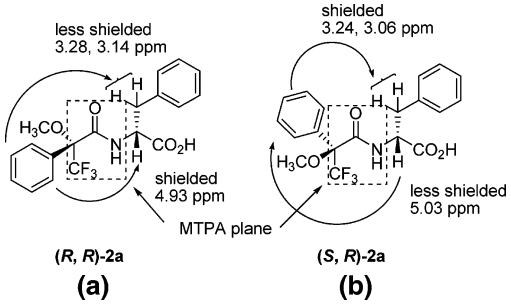


FIGURE 1. MTPA amides of (*R*)-phenylalanine.

The reaction of (*rac*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionic acid (MTPA) with thionyl chloride and 1*H*-benzotriazole (BtH) afforded the benzotriazole derivative, (*rac*)-1-benzotriazol-1-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropan-1-one (*rac*)-**1** as white crystals (mp 99−100 °C), in 95% yield (Scheme 1). The detailed molecular structure of (*rac*)-**1** was established by single-crystal X-ray diffraction analysis (see Supporting Information).

The chiral versions of the Mosher-Bt reagent (*R*)-1-benzotriazol-1-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropan-1-one (*R*)-**1** and (*S*)-1-benzotriazol-1-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropan-1-one (*S*)-**1** were easily prepared from (*R*)-MTPA and (*S*)-MTPA in 95% yield (Scheme 1).

Reaction of (*rac*)-1-benzotriazol-1-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropan-1-one (*rac*)-**1** with water-soluble amino acids such as (*R*)-phenylalanine in an acetonitrile/water (2:1) mixture at rt for 12 h gave the corresponding amide (*R*)-3-phenyl-2-((*R*,*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionylamino)propionic acid (*R*,*R*)- and (*S*,*R*)-**2a** in 96% yield. The ^{1}H NMR spectra of (*R*,*R*)- and (*S*,*R*)-**2a** showed the disappearance of the Bt signals in the aromatic region, indicating the loss of the benzotriazolyl group during the reaction. The ^{13}C NMR spectra of (*R*,*R*)- and (*S*,*R*)-**2a** showed three signals at 175.3, 166.9, and 166.8 ppm corresponding to the carbonyl groups of the product and the disappearance of the signal at 165.7 ppm belonging to the carbonyl group at the α position of the benzotriazolyl group in the starting material (*rac*)-**1**. Similarly, reaction of (*R*)-**1** and (*S*)-**1** with (*R*)-phenylalanine in an acetonitrile/water (2:1) mixture at rt for 12 h gave (*R*)-3-phenyl-2-((*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionylamino)propionic acid (*R*,*R*)-**2a** and (*R*)-3-phenyl-2-((*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionylamino)propionic acid (*S*,*R*)-**2a**, respectively, each in 96% yield. Reaction of (*R*)-**1** with (*R*)-tryptophan, dipeptide Gly-(*R*)-Phe-OH, and tripeptide Gly-(*S*)-Phe-(*S*)-Phe-OH in an acetonitrile/water (2:1) mixture at rt for 12 h gave (*R*)-3-(1*H*-indol-3-yl)-2-((*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionylamino)propionic acid (*R*,*R*)-**2b**, (*R*)-3-phenyl-2-[2-((*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionylamino)acetylamino]propionic acid (*R*,*R*)-**2c**, and (*S*)-3-phenyl-2-{(*R*)-3-phenyl-2-[2-((*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionylamino)acetylamino]propionylamino}-propionic acid (*R*,*S*,*S*)-**2d**, respectively, in 98, 97, and 91% yield (Table 1).

Straightforward assignment of the absolute configuration of (*R*)-phenylalanine using the Mosher-Bt reagent was carried out.

TABLE 2. Chemical Shift (δ) Values in the ^{1}H, ^{13}C, and ^{19}F NMR of MTPA Amides of (*R*)-Phenylalanine

entry	product Mosher amide	abs. config.	δ values (^{1}H NMR) methylene	δ values (^{1}H NMR) methine	δ values (^{13}C NMR) methylene	δ values (^{13}C NMR) methine	δ values (^{19}F NMR) CF_3
1	(*R,R*)-**2a**	(*R,R*)	3.28, 3.14	4.93	37.6	55.4, 55.3	−69.37
2	(*S,R*)-**2a**	(*S.R*)	3.24, 3.06	5.03	37.4	55.0, 55.0	−69.31
		difference	0.04, 0.08	0.1	0.2	0.4, 0.3	0.06

^{1}H NMR analysis of the diastereomers (*R,R*)-**2a** and (*S,R*)-**2a** [MTPA amides of (*R*)-phenylalanine, Figure 1a and b] shows a significant difference in the chemical shift of the methine and methylene signals (Table 2). This difference in chemical shift is because, in one structure, the methine proton and the phenyl ring of the MTPA moiety are on the same side of the MTPA plane shown by dotted lines (Figure 1a), while in the other diastereomer, they are opposite to each other (Figure 1b). The diamagnetic effect of the phenyl ring of the MTPA moiety is more pronounced in the structure where the methine group is on the same side of the phenyl ring (4.93 δ, shielded, Figure 1a) as compared to the structure where the methine group is on the opposite sides of the MTPA plane (5.03 δ, less shielded, Figure 1b). Consequently, the 5.03 δ methine signal should belong to the diastereomer (*S,R*)-**2a** (Figure 1b) and 4.93 δ should belong to the diastereomer (*R,R*)-**2a** (Figure 1a).

To demonstrate that racemization does not occur during the reaction, Mosher amides (*R,R*)- and (*S,R*)-**2a**, and (*R,R*)-**2a** and (*S,R*)-**2a** were subjected to HPLC analysis. As determined by chiral HPLC (using Chirobiotic T column, detection at 254 nm, flow rate 0.1 mL/min, solvent MeOH), (*R,R*)-**2a** and (*S,R*)-**2a** showed single peaks at 6.2 and 6.5 min, respectively, whereas the diastereomeric mixture (*R,R*)- and (*S,R*)-**2a** showed two peaks.

Mosher-Bt reagents can also be used to determine enantiomeric excess of chiral amines. In order to demonstrate this ability, we reacted a mixture of (*R*)- and (*S*)-phenylalanine (3:1 ratio) with the Mosher-Bt reagent (*R*)-**1**. HPLC analysis of the resulting product showed two peaks and their area in the expected 3:1 ratio.

Unfortunately, reaction of (*rac*)-1-benzotriazol-1-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropan-1-one (*rac*)-**1** with alcohols such as α-methylbenzyl alcohol and cholesterol did not give us the desired Mosher ester even under microwave heating conditions. Thus Mosher-Bt reagents are not applicable to determine enantiomeric excess and absolute configuration of chiral alcohols.

Compared to the corresponding acid chlorides of Mosher-Bt reagents, (*rac*)-, (*R*)-, and (*S*)-**1** have the following advantages: (i) they are noncorrosive, stable to moisture and heat, and can be stored at room temperature indefinitely; thus they are easy to handle as compared to corrosive and moisture-sensitive MTPA chloride; (ii) the carboxyl groups of the amino acids, di- and tripeptides need no protection prior to making their MTPA amides; (iii) high yields of corresponding Mosher's amides are obtained (see Table 1); (iv) their reactions can be carried out in aqueous conditions; (v) unlike MTPA chloride, the absolute configurations of the Mosher-Bt reagent and Mosher's ester or amide are the same simplifying assignment of absolute configuration; and (vi) they are easily prepared in quantitative yield from the corresponding MTPA (250 mg, $36) using 1*H*-benzotriazole (100 g, $25) and are thus more cost-effective as compared to commercially available MTPA chloride (250 mg, $100).

Experimental Section

General Procedure for Synthesis of 1: 3,3,3-Trifluoro-2-methoxy-2-phenylpropionic acid (MTPA) (0.75 g, 3.2 mmol) and thionyl chloride (3 mL) were refluxed together for 50 h. After excess thionyl chloride was removed by vacuum evaporation at rt, the residual oil was dissolved in dry dichloromethane (20 mL) and 3 equiv of 1*H*-benzotriazole (BtH) (1.14 g, 9.6 mmol) was added to it and stirred at rt for 12 h. The volatiles were evaporated. Chloroform (5 mL) was added to the residue and then purified by silica gel column (20 cm × 2 cm) chromatography using chloroform (100 mL) as an eluent to give 1-benzotriazol-1-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropan-1-one.

General Procedure for Synthesis of 2a−d: Benzotriazol-1-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropan-1-one (0.2 g, 0.6 mmol) was added to amino acid, di-, or tripeptide (0.6 mmol) in CH_3CN/water (2:1, 15 mL). Triethyl amine (0.12 mL, 0.9 mmol) was added dropwise to the above reaction mixture and stirred at rt for 12 h. The volatiles were removed, and the residue was added to ethylacetate (50 mL) and washed with 4 N HCl (10 mL); the organic layer was separated and dried over Na_2SO_4, filtered, and evaporated to give the products **2a−d**.

(*rac*)-1-Benzotriazol-1-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropan-1-one ((*rac*)-1): Yield 0.83 g (95%); white crystal; mp 99−100 °C; ^{1}H NMR δ 8.25 (d, J = 8.2 Hz, 1H), 7.93 (d, J = 8.1 Hz, 1H), 7.57 (t, J = 7.7 Hz, 1H), 7.49−7.48 (m, 2H), 7.39 (t, J = 7.7 Hz, 1H), 7.22−7.20 (m, 3H), 3.55 (2s, 3H); ^{13}C NMR δ 165.7, 145.0, 133.1, 131.6, 131.2, 129.7, 128.6, 127.0, 126.4, 123.6 (q, J = 289.1 Hz), 120.6, 114.6, 86.6 (q, J = 26.7 Hz), 56.9, 56.8. Anal. Calcd for $C_{16}H_{12}F_3N_3O_2$: C, 57.32; H, 3.61; N, 12.53. Found: C, 57.43; H, 3.48; N, 12.5.

(*R*)-1-Benzotriazol-1-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropan-1-one ((*R*)-1): Yield 0.83 g (95%); colorless oil; ^{1}H NMR δ 8.38 (d, J = 8.2 Hz, 1H), 8.08 (d, J = 8.1 Hz, 1H), 7.72 (t, J = 7.5 Hz, 1H), 7.66−7.46 (m, 2H), 7.54 (t, J = 7.8 Hz, 1H), 7.42−7.30 (m, 3H), 3.69 (s, 3H); ^{13}C NMR δ 165.6, 144.9, 133.0, 131.5, 131.1, 129.6, 128.5, 126.9, 126.3, 126.3, 123.4 (q, J = 290.7 Hz), 120.6, 114.5, 86.4 (q, J = 26.7 Hz), 56.8, 56.8. Anal. Calcd for $C_{16}H_{12}F_3N_3O_2$: C, 57.32; H, 3.61; N, 12.53. Found: C, 57.24; H, 3.51; N, 12.21.

(*S*)-1-Benzotriazol-1-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropan-1-one ((*S*)-1): Yield 0.83 g (95%); colorless oil; ^{1}H NMR δ 8.38 (d, J = 8.2 Hz, 1H), 8.08 (d, J = 8.2 Hz, 1H), 7.72 (t, J = 8.2 Hz, 1H), 7.66−7.58 (m, 2H), 7.54 (t, J = 8.1 Hz, 1H), 7.40−7.30 (m, 3H), 3.69 (s, 3H); ^{13}C NMR δ 165.7, 145.0, 133.1, 131.6, 131.3, 130.7, 129.8, 129.1, 128.6, 127.0, 126.5, 123.4 (q, J = 290.7 Hz), 120.7, 114.7, 86.4 (q, J = 26.7 Hz), 57.0, 56.9. Anal. Calcd for $C_{16}H_{12}F_3N_3O_2$: C, 57.32; H, 3.61; N, 12.53. Found: C, 57.08; H, 3.54; N, 12.37.

(*R*)-3-Phenyl-2-((*rac*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionylamino)propionic Acid ((*R,R*)- and (*S,R*)-2a): Yield 0.22 g (96%); colorless oil; ^{1}H NMR δ (1:1 mixture of diastereomers) 7.54−7.46 (m, 1H), 7.44−7.28 (m, 5H), 7.24−7.14 (m, 3H), 7.05 (d, J = 8.5 Hz, 1H), 6.96 (2d, J = 7.4 Hz, 1H), 5.01 (ddd, J = 8.2, 7.4, 5.2 Hz, 1H), 4.94 (ddd, J = 8.2, 7.4, 5.2 Hz, 1H), 3.39 (2s, 1.5H), 3.28 (2dd, J = 14.3, 5.5 Hz, 1H), 3.19 (s, 1.5H), 3.08 (2dd, J = 14.1, 7.4 Hz, 1H); ^{13}C NMR δ 175.8, 166.7, 166.6, 135.4, 135.4, 132.5, 132.0, 129.8, 129.7, 129.5, 129.4, 129.0, 128.9, 128.8, 128.8, 128.1, 127.6, 127.6, 127.5, 55.4, 55.0, 53.1, 52.8, 37.6, 37.4.

Anal. Calcd for $C_{19}H_{18}F_3NO_4$: C, 59.84; H, 4.76; N, 3.67. Found: C, 59.72; H, 4.85; N, 3.73.

(*R*)-3-Phenyl-2-((*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionylamino)propionic Acid ((*R*,*R*)-2a): Yield 0.22 g (96%); white crystal; mp 110−112 °C; ^{1}H NMR δ 8.79 (s, 1H), 7.54−7.44 (m, 2H), 7.44−7.23 (m, 7H), 7.22−7.12 (m, 2H), 4.93 (ddd, J = 7.8, 7.7, 5.2 Hz, 1H), 3.28 (dd, J = 14.1, 5.3 Hz, 1H), 3.18 (s, 3H), 3.14 (dd, J = 14.1, 7.4 Hz, 1H); ^{13}C NMR δ 175.9, 166.7, 135.4, 131.9, 129.8, 129.4, 129.0, 128.8, 128.6, 128.1, 127.9, 127.6, 123.8 (q, J = 290.3 Hz), 84.2 (q, J = 26.3 Hz), 55.0, 55.0, 53.1, 37.4; ^{19}F NMR δ −69.37 (s, 3F). Anal. Calcd for $C_{19}H_{18}F_3NO_4$: C, 59.84; H, 4.76; N, 3.67. Found: C, 59.46; H, 5.19; N, 3.54.

(*R*)-3-Phenyl-2-((*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionylamino)propionic Acid ((*S*,*R*)-2a): Yield 0.22 g (96%); white crystal; mp 107−108 °C; ^{1}H NMR δ 10.14 (s, 1H), 7.46−7.28 (m, 6H), 7.24−7.10 (m, 3H), 6.97 (2d, J = 7.7 Hz, 1H), 5.03 (ddd, J = 7.8, 7.7, 5.2 Hz, 1H), 3.38 (2s, 3H), 3.24 (dd, J = 14.1, 5.2 Hz, 1H), 3.06 (dd, J = 14.1, 7.4 Hz, 1H); ^{13}C NMR δ 175.6, 166.7, 135.4, 132.4, 129.7, 129.4, 128.8, 128.7, 127.6, 127.4, 126.4, 123.7 (q, J = 290.3 Hz), 115.1, 84.0 (q, J = 26.3 Hz), 55.3, 52.9, 37.6; ^{19}F NMR δ −69.31 (s, 3F). Anal. Calcd for $C_{19}H_{18}F_3NO_4$: C, 59.84; H, 4.76; N, 3.67. Found: C, 59.57; H, 4.89; N, 3.59.

(*R*)-3-(1*H*-Indol-3-yl)-2-((*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionylamino)propionic Acid ((*R*,*R*)-2b): Yield 0.25 g (98%); white crystal; mp 78−80 °C; ^{1}H NMR δ 8.30 (s, 1H), 7.80−7.52 (m, 1H), 7.52−7.27 (m, 8H), 7.23 (t, J = 7.6 Hz, 1H), 7.07 (t, J = 7.7 Hz, 1H), 6.80 (d, J = 2.2 Hz, 1H), 5.09 (ddd, J = 8.2, 6.2, 3.4 Hz, 1H), 3.37 (t, J = 5.8 Hz, 2H), 3.32 (s, 3H); ^{13}C NMR δ 176.2, 167.1, 136.3, 132.5, 129.7, 128.7, 127.6, 127.5, 123.5, 122.4, 120.0, 118.4, 11.6, 109.1, 84.0 (q, J = 26.3 Hz), 55.2, 53.0, 27.5. Anal. Calcd for $C_{21}H_{19}F_3N_2O_4$: C, 60.00; H, 4.56; N, 6.66. Found: C, 59.65; H, 4.48; N, 6.77.

(*R*)-3-Phenyl-2-[2-((*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionylamino)acetylamino]propionic Acid ((*R*,*R*)-2c): Yield 0.13 g (97%); white crystal; mp 84−86 °C; ^{1}H NMR δ 7.78 (br s, 1H), 7.54−7.42 (m, 2H), 7.40−7.30 (m, 3H), 7.30−7.16 (m, 3H), 7.16−7.06 (m, 2H), 6.87 (br s, 2H), 4.75 (dd, J = 12.6, 6.9 Hz, 1H), 4.09 (dd, J = 16.8, 6.0 Hz, 1H), 3.84 (dd, J = 16.6, 4.9 Hz, 1H), 3.31 (s, 3H), 3.08 (dd, J = 13.9, 4.9 Hz, 1H), 2.82 (dd, J = 13.9, 7.0 Hz, 1H); ^{13}C NMR δ 174.2, 168.6, 167.8, 136.0, 132.0, 129.9, 129.5, 128.9, 128.8, 128.0, 127.4, 123.9 (q, J = 290.9 Hz), 84.3 (q, J = 26.9 Hz), 55.2, 53.7, 42.8, 37.5. Anal. Calcd for $C_{21}H_{21}F_3N_2O_5$: C, 57.53; H, 4.83; N, 6.39. Found: C, 57.21; H, 4.92; N, 6.21.

(*S*)-3-Phenyl-2-{(*S*)-3-phenyl-2-[2-((*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionylamino)acetylamino]propionylamino}-propionic Acid ((*R*,*S*,*S*)-2d): Yield 0.16 g (91%); white crystal; mp 169−170 °C; ^{1}H NMR (DMSO-d_6) δ 8.45 (d, J = 7.8 Hz, 1H), 8.40 (t, J = 5.9 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 7.56−7.36 (m, 6H), 7.32−7.12 (m, 9H), 4.58 (ddd, J = 8.5, 8.9, 4.4 Hz, 1H), 4.44 (ddd, J = 8.2, 8.2, 5.4 Hz, 1H), 3.82 (dd, J = 16.5, 6.2 Hz, 1H), 3.61 (dd, J = 16.5, 5.8 Hz, 1H), 3.49 (s, 1H), 3.42 (s, 3H), 3.12−2.88 (m, 4H), 2.71 (dd, J = 13.9, 9.3 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 172.8, 171.1, 167.8, 165.7, 137.6, 137.4, 133.1, 129.4, 129.3, 129.2, 128.3, 128.2, 128.0, 127.5, 126.5, 126.3, 125.8, 121.9, 83.5 (q, J = 24.6 Hz), 55.0, 53.5. Anal. Calcd for $C_{30}H_{30}F_3N_3O_6$: C, 61.53; H, 5.16; N, 7.18. Found: C, 61.14; H, 5.55; N, 6.87.

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Supporting Information Available: Spectral data for new compounds and details for the crystal structure of (*rac*)-**1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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