Efficient Mitsunobu Reactions with *N*-Phenylfluorenyl or *N*-Trityl Serine Esters

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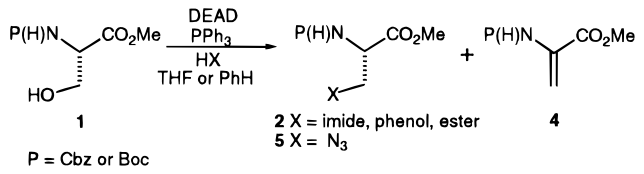
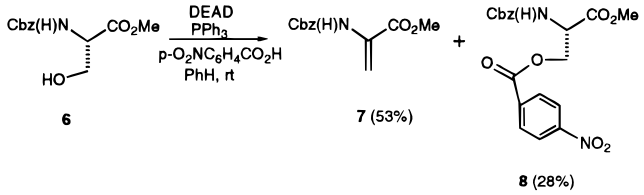
The Mitsunobu reaction[1] is a mild way to convert an alcohol into a wide range of functionality. During the course of a SAR (structure−activity relationship) study, we became interested in the Mitsunobu reaction of serine. It was our intention to use the primary alcohol of L-serine ester **1** as a handle, to which our desired functionality could be attached to give a general derivative **2** (Scheme 1). However, we were concerned that a major problem inherent with this approach would be the well documented[1] β-elimination reaction to yield **4**. In fact, Wjciechowska and co-workers[2] have reported this reaction as an efficient method for producing didehydroalanine derivatives **4** from serine **1** through the action of diethyl azodicarboxylate (DEAD) and PPh_3 (Scheme 1 without an acidic HX present). A literature search on serine-based Mitsunobu reactions yielded mainly references for the intramolecular construction and chemistry of β-lactones,[3] β-lactams,[4] and oxazolines.[5] In fact intermolecular examples, as in Scheme 1, are limited and poor yielding.[6] An exception is the reaction[7] using L-serine with hydrazoic acid under the standard conditions (PPh_3/DEAD/solvent). This reaction converts the alcohol **1** into an azide **5** (∼70% yield) with only a small amount of the elimination product **4** (∼5%) being produced. Our interests were centered on a variety of different nucleophiles (benzoic acids, phenols, and imides) other than hydrazoic acid. We knew, in general, the Mitsunobu reaction with 4-nitrobenzoic acid was a very efficient[8] reaction and thus selected it as a starting point. As we suspected, *N*-Cbz-L-serine **6** with 4-nitrobenzoic acid under standard Mitsunobu conditions (DEAD, PPh_3, and PhH at rt) afforded a large amount (53%) of the didehydroalanine **7** along with a small amount (28%) of the nucleophilic substitution product **8** (Scheme 2).

In order to circumvent this side reaction, we considered the choice of *N*-protecting group. Both *N*-phenylfluorenyl (PhF)[9] and *N*-trityl (Tr)[10] are known to protect the α-center of amino acids from base-promoted racemization. As a result, we postulated these groups might also protect serine from the elimination reaction during a Mitsunobu reaction. When *N*-phenylfluorenyl serine **9** was subjected to the same Mitsunobu reaction with 4-nitrobenzoic acid at room temperature (Scheme 3), *we were pleased to find only the substitution product* ***10*** *in 86% yield*. Hence, by making a simple change in protecting groups, we were able to prevent the elimination reaction completely.

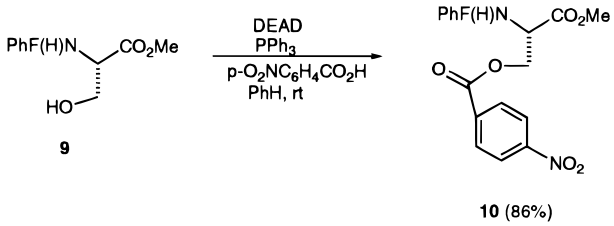
Scheme 1



Scheme 2



Scheme 3



To examine the scope and utility of this reaction, we explored additional examples, the results of which are summarized in Table 1. Entry A indicates that the Mitsunobu reaction with *N*-trityl-L-serine methyl ester and 4-nitrobenzoic acid behaves analogously to give the substitution product **11A** (90% yield) under identical conditions. As mentioned above, we were interested in other acidic moieties like imides and phenols. Phthalimide could also participate in the reaction to give only the addition products **11C** and **11D** for *N*-phenylfluorenyl (entry C) and *N*-trityl (entry D), respectively. One can compare this example to entry B where *N*-Cbz-L-serine methyl ester **6** gave primarily the elimination product **7** (73% yield) and some of the substitution product **11B** (13% yield).

This same trend was also noted for phenols. As indicated in entry E, we did not observe any substitution product for the Mitsunobu reaction between *N*-Boc-L-serine methyl ester and methyl 4-hydroxybenzoate. Again, an enhancement was observed with the bulky *N*-protecting groups. When the same Mitsunobu reaction was performed with *N*-trityl serine methyl ester (entry F), the substitution product **11F** was isolated in 63% yield along with the aziridine **14** (Table 1). The aziridine **14** has previously been synthesized (via another route) by Baldwin et al.,[11] and our material compared exactly with their reported characterization. The Mitsunobu reaction with *N*-phenylfluorenyl serine **9** and methyl 4-hydroxybenzoate (entry G) was analogous to this, producing the substitution product **11G** (40% yield) and the corresponding aziridine **15** (24% yield).

(1) (a) Mitsunobu, O. *Synthesis* **1981**, 1. (b) Hughes, D. L. *Org. React.* **1992**, *42*, 335.
(2) Wojciechowska, H.; Pawlowicz, R.; Andruszkiewicz, R.; Grzybowska, J. *Tetrahedron Lett.* **1978**, 4063.
(3) Arnold, L. D.; Kalantar, T. H.; Vederas, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 7105.
(4) Miller, M. J. *Acc. Chem. Res.* **1986**, *19*, 49.
(5) Galeotti, N.; Montagne, C.; Poncet, J.; Jouin, P. *Tetrahedron Lett.* **1992**, 2807. Wipf, P.; Miller, C. P. *Tetrahedron Lett.* **1992**, 6267.
(6) Nagai, U.; Kato, R.; Pavone, V. *Peptide Chem.* **1987**, 187.
(7) (a) Golding, B. T.; Howes, C. *J. Chem. Res. (S)* **1984**, 1. (b) Otsuka, M.; Kittaka, A.; Iimori, T.; Yamashita, H.; Kobayashi, S.; Ohno, M. *Chem. Pharm. Bull.* **1985**, *33*, 509. (c) Fabiano, E.; Golding, B. T.; Sadeghi, M. M. *Synthesis* **1987**, 190.
(8) Martin, S. F.; Dodge, J. A. *Tetrahedron Lett.* **1991**, *32*, 3017.
(9) Christie, B. D.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 1239.
(10) Guthrie, R. D.; Nicolas, E. C *J. Am. Chem. Soc.* **1981**, *103*, 4638.
(11) Baldwin, J. E.; Spivey, A. C.; Schofield, C. J.; Sweeney, J. B. *Tetrahedron* **1993**, *49*, 6309.

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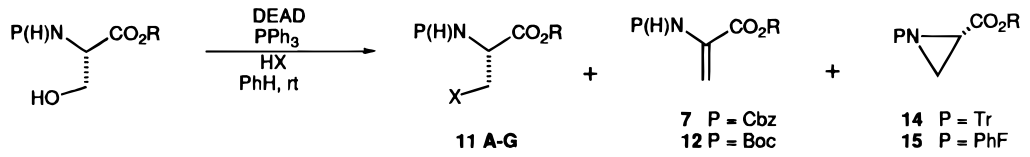
Table 1. Mitsunobu Reactions with *N*-PhF and *N*-Tri-Serine Esters



Entry	P	R	HX	11 (%)[a]	7 or 12 (%)[a]	14 or 15 (%)[a]
A	Tr	Me	p-O_2N-C_6H_4-CO_2H	**11A** (90%)	-	-
B	Cbz	Me	phthalimide	**11B** (13%)	**7** (73%)	-
C	PhF	Me	phthalimide	**11C** (95%)	-	-
D	Tr	Me	phthalimide	**11D** (91%)	-	-
E	Boc	Bn	p-MeO_2C-C_6H_4-OH	**11E** (-)	**12** (91%)	-
F	Tr	Me	p-MeO_2C-C_6H_4-OH	**11F** (63%)	-	**14** (16%)
G	PhF	Me	p-MeO_2C-C_6H_4-OH	**11G** (40%)	-	**15** (24%)

[a] Yields refer to isolated material.

PhF ≡ 

Each of the *N*-trityl and *N*-phenylfluorenyl substitution products **10**, **11A**, **11C**, **11D**, **11F**, and **11G** were checked by Mosher amide[12] analysis (^{1}H NMR and ^{19}F NMR) for racemization. In each case, the D-serine enantiomer or racemate was carried through the same Mitsunobu reaction and then converted to the Mosher amide for comparison. All the Mosher amides analyzed in this fashion proved to be free of racemization and gave a diastereomeric purity of ≥95%.

In summary, we have shown that with *N*-phenylfluorenyl or *N*-trityl protection, Mitsunobu reactions can be performed quite efficiently with serine. In the cases shown, benzoic acids and imides showed good reactivity, whereas phenols were somewhat less reactive.

Experimental Section

General. All reactions were performed under a nitrogen atmosphere at room temperature unless otherwise noted. The amino acid derivative *N*-phenylfluorenyl-L-serine methyl ester **9** was synthesized according to the procedure of Rapoport.[13] In addition, *N*-Trityl-L-serine methyl ester was synthesized as reported by Baldwin.[11] All other reagents and solvents were purchased from commercial sources and used as received unless otherwise noted. The ^{1}H NMR and ^{13}C NMR were recorded at 300 and 75 MHz, respectively. The chemical shifts are reported in ppm (δ) relative to TMS in the solvent listed. ESMS is the abbreviation for electrospray ionization mass spectroscopy.

General Procedure for *N*-PhF or *N*-Tr-serine Mitsunobu Reactions: *N*-(9-Phenylfluoren-9-yl)-*O*-(4-nitrobenzoyl)-L-serine Methyl Ester (10). The *N*-PhF-L-serine methyl ester **9** (474.4 mg, 1.3 mmol) was dissolved in benzene (15 mL) prior to the addition of PPh_3 (380.8 mg, 1.4 mmol) and 4-nitrobenzoic acid (330.8 mg, 1.9 mmol). After 5 min, DEAD (0.23 mL, 1.4 mmol) was added dropwise. The reaction was stirred for 15 h, after which time the solid urea was removed via filtration. The filtrate was concentrated to an oil, which was purified by flash chromatography (1:5 EtOAc/hexane) to provide the desired product **10** (568.1 mg, 1.1 mmol, 86%) as a white foam: $[\alpha]^{25}_D$ −162.5° (*c* 0.25, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 8.27 (dd, 2H, *J* = 1.8, 8.8 Hz), 8.13 (dd, 2H, *J* = 1.8, 8.8 Hz), 7.7 (t, 2H, *J* = 10.2 Hz), 7.42−7.12 (m, 11H), 4.34 (dd, 1H, *J* = 5.5, 10.6 Hz), 4.25 (dd, 1H, *J* = 5.8, 10.9 Hz), 3.38 (s, 3H), 3.23 (br d, 1H, *J* = 8.4 Hz), 3.04 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 173.62, 164.03, 150.53, 148.60, 148.24, 143.84, 140.98, 139.89, 135.16, 130.69, 128.49, 128.27, 127.95, 127.51, 127.32, 125.97, 125.78, 125.09, 123.44, 120.07, 119.96, 72.71, 67.14, 54.76, 51.97; IR (neat) 3320, 3058, 2952, 1732, 1528, 1272 cm^{-1}; ESMS *m/z* (rel intensity) 509 (M^+ + H, 52), 241 (100). Anal. Calcd for $C_{30}H_{24}N_2O_6$: C, 70.86; H, 4.77; N, 5.52. Found: C, 70.75; H, 4.75; N, 5.37.

The following compounds (see Table 1) were synthesized according to the general procedure:

***N*-(Triphenylmethyl)-*O*-(4-nitrobenzoyl)-L-serine methyl ester (11A):** $[\alpha]^{25}_D$ +58.9° (*c* 0.21, CH_2Cl_2); ^{1}H NMR (DMSO-d_6) δ 8.33 (d, 2H, *J* = 9.2 Hz), 8.11 (d, 2H, *J* = 9.2 Hz), 7.42 (d, 6H, *J* = 7.7 Hz), 7.29−7.15 (m, 9H), 4.51 (dd, 1H, *J* = 5.9, 11.0 Hz), 4.38 (dd, 1H, *J* = 7.5, 11.0 Hz), 3.61 (m, 1H), 3.19 (d, 1H, *J* = 10.2 Hz), 3.12 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 172.69, 164.20, 150.25, 145.34, 135.10, 120.69, 128.57, 127.88, 126.57, 123.50, 70.00, 67.28, 55.36, 51.94; IR (KBr) 3324, 3084, 1734, 1528, 1272 cm^{-1}; CIMS *m/z* (rel intensity) 511 (M^+ + H, 65), 243 (100). Anal. Calcd for $C_{30}H_{26}N_2O_6$: C, 70.58; H, 5.13; N, 5.50. Found: C, 70.50; H, 5.13; N, 5.37.

***N*-(9-Phenylfluoren-9-yl)-β-(phthalimido)-L-alanine methyl ester (11C):** $[\alpha]^{25}_D$ −280.0° (*c* 0.16, CH_2Cl_2); ^{1}H NMR (DMSO-d_6) δ 7.90−7.85 (m, 4H), 7.79 (dd, 2H, *J* = 7.7, 13.9 Hz), 7.36 (t, 1H, *J* = 7.3 Hz), 7.28−7.12 (m, 8H), 6.67 (d, 2H, *J* = 3.4 Hz), 3.64 (dd, 1H, *J* = 9.1, 13.5 Hz), 3.50 (dd, 1H, *J* = 5.5, 13.5 Hz), 3.38 (d, 1H, *J* = 9.89 Hz), 3.34 (s, 3H), 2.74 (ddd, 1H, *J* = 5.48, 9.1, 9.89 Hz); ^{13}C NMR ($CDCl_3$) δ 174.31, 167.84, 133.91, 128.40, 128.31, 127.19, 126.02, 123.29, 120.02, 72.73, 54.42, 52.01, 41.16; IR (KBr) 3472, 3060, 1718, 1394 cm^{-1}; CIMS *m/z* (rel intensity) 489 (M^+ + H, 100). Anal. Calcd for $C_{31}H_{24}N_2O_4$: C, 76.21; H, 4.95; N, 5.73. Found: C, 75.88; H, 4.80; N, 5.59.

***N*-(Triphenylmethyl)-β-(phthalimido)-L-alanine methyl ester (11D):** $[\alpha]^{25}_D$ +16.9° (*c* 0.11, CH_2Cl_2); ^{1}H NMR (DMSO-d_6) δ 7.93−7.85 (m, 4H), 7.38−7.14 (m, 15H), 3.83 (d, 2H, *J* = 7.0 Hz), 3.48 (m, 1H), 3.04−3.01 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 172.89, 167.83, 145.42, 133.93, 128.61, 127.75, 126.36, 123.49, 123.26, 80.90, 55.38, 51.88, 41.62; IR (KBr) 3202, 2950, 1734, 1718, 1394 cm^{-1}; CIMS *m/z* (rel intensity) 491 (M^+ + H, 100). Anal. Calcd for $C_{31}H_{26}N_2O_4$: C, 75.90; H, 5.34; N, 5.71. Found: C, 75.51; H, 5.25; N, 5.59.

***N*-(Triphenylmethyl)-*O*-(4-carbomethoxyphenyl)-L-serine methyl ester (11F):** $[\alpha]^{25}_D$ +96.1° (*c* 0.15, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 7.89 (d, 2H, *J* = 8.9 Hz), 7.43 (d, 6H, *J* = 7.3 Hz), 7.29 (t, 6H, *J* = 7.5 Hz), 7.20 (t, 3H, *J* = 7.1 Hz), 6.97 (d, 2H, *J* = 8.9 Hz), 4.28 (dd, 1H, *J* = 4.9, 9.5 Hz), 4.05 (dd, 1H, *J* = 6.6, 9.5 Hz), 3.81 (s, 3H), 3.56 (ddd, 1H, *J* = 4.9, 6.6, 10.2 Hz),

(12) The substitution product was heated in TFA and CH_2Cl_2 to remove the *N*-phenylfluorenyl or *N*-trityl protecting group. The solution was concentrated and reacted with the (*R*)-Mosher acid chloride (Fluka) to give the corresponding amide: Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(13) Lubell, W.; Rapoport, H. *J. Org. Chem.* **1989**, *54*, 3824.

3.23 (s, 3H), 2.90 (d, 1H, J = 10.2 Hz); ^{13}C NMR ($CDCl_3$) δ 173.24, 162.14, 145.63, 131.55, 128.72, 127.94, 126.58, 123.03, 114.23, 70.99, 70.35, 56.03, 51.96, 51.87; IR (KBr) 3412, 3030, 2950, 1718, 1606 cm^{-1}; CIMS m/z (rel intensity) 496 (M^+ + H, 7), 243 (100). Anal. Calcd for $C_{31}H_{29}NO_5$: C, 75.13; H, 5.91; N, 2.84. Found: C, 75.11; H, 5.73; N, 2.75.

***N*-(Triphenylmethyl)aziridine-(2*S*)-carboxylic acid methyl ester (14):** $[\alpha]^{25}_D$ −85.9° (c 0.09, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 7.51−7.19 (m, 15H), 3.76 (s, 3H), 2.26 (dd, 1H, J = 1.4, 2.6 Hz), 1.89 (dd, 1H, J = 2.6, 6.2 Hz), 1.41 (dd, 1H, J = 1.4, 6.2 Hz); ^{13}C NMR ($CDCl_3$) δ 172.20, 143.53, 129.24, 128.98, 128.55, 128.36, 127.90, 127.83, 127.75, 127.56, 126.84, 126.55, 74.30, 51.98, 31.61, 28.57; IR (KBr) 3434, 3060, 1744, 1490, 1448, 1284, 1242 cm^{-1}; CIMS m/z (rel intensity) 344 (M^+ + H, 21), 243 (100); HRMS calcd for $C_{23}H_{22}NO_2$ (M^+ + H), 344.1650; found 344.1664.

***N*-(9-Phenylfluoren-9-yl)-*O*-(4-carbomethoxyphenyl)-L-serine methyl ester (11G):** $[\alpha]^{25}_D$ −62.5° (c 0.11, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 7.90 (dd, 2H, J = 1.8, 8.8 Hz), 7.69 (t, 2H, J = 6.6 Hz), 7.44−7.16 (m, 11H), 6.71 (dd, 2H, J = 2.2, 9.1 Hz), 4.00 (dd, 1H, J = 5.1, 9.5 Hz), 3.92 (dd, 1H, J = 2.9, 6.6 Hz), 3.87 (s, 3H), 3.36 (s, 3H), 3.20 (br d, 1H, J = 8.8 Hz), 3.05 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 174.06, 166.66, 161.97, 148.90, 148.46, 143.99, 140.88, 140.07, 131.39, 128.46, 128.24, 127.94, 127.54, 127.29, 126.00, 125.71, 125.05, 122.78, 120.07, 119.96, 114.06, 72.74, 70.00, 54.94, 51.83, 51.72; IR (film) 3320, 2950, 1716 cm^{-1}; ESMS m/z (rel intensity) 494 (M^+ + H, 41), 241 (100). Anal. Calcd for $C_{31}H_{27}NO_5$: C, 75.44; H, 5.51; N, 2.85. Found: C, 75.57; H, 5.41; N, 2.80.

***N*-9-Phenylfluoren-9-ylaziridine-(2*S*)-carboxylic acid methyl ester (15):** $[\alpha]^{25}_D$ −124.1° (c 0.94, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 7.69 (td, 2H, J = 2.5, 4.8 Hz), 7.41−7.33 (m, 4H), 7.28−7.18 (m, 7H), 3.69 (s, 3H), 2.19 (dd, 1H, J = 2.9, 6.2 Hz), 2.09 (dd, 1H, J = 1.1, 2.9 Hz), 1.55 (dd, 1H, J = 1.1, 6.2 Hz); ^{13}C NMR ($CDCl_3$) δ 171.40, 147.24, 146.05, 142.95, 141.20, 140.29, 128.90, 128.71, 128.25, 127.77, 127.64, 127.14, 126.90, 126.21, 126.23, 119.95, 119.90, 75.72, 52.11, 33.18, 29.76; IR (KBr) 3058, 1748, 1448 cm^{-1}; HRMS calcd for $C_{23}H_{20}NO_2$ (M^+ + H), 342.149404; found 342.147554.

Mitsunobu Reaction between *N*-Cbz-L-Serine Methyl Ester (6) and 4-Nitrobenzoic Acid. The reaction was performed as described in the general procedure. Starting with *N*-Cbz-L-serine methyl ester (**6**) (283.0 mg, 1.1 mmol), 4-nitrobenzoic acid (280.2 mg, 1.7 mmol), PPh_3 (322.5 mg, 1.2 mmol), and DEAD (0.19 mL, 1.2 mmol) gave the β-elimination product **7** (141 mg, 0.6 mmol, 53%) and the substitution product **8** (126 mg, 0.3 mmol, 28%).

Data for **7**: ^{1}H NMR ($CDCl_3$) δ 7.37 (m, 5H), 7.24 (br s, 1H), 6.25 (br s, 1H), 5.79 (d, 1H, J = 1.5 Hz), 5.16 (s, 2H), 3.83 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 164.07, 153.02, 135.76, 130.91, 128.51, 128.27, 128.13, 105.98, 66.95, 52.79; IR (KBr) 3412, 1742, 1500 cm^{-1}; CIMS (NH_3) m/z (rel intensity) 253 (M^+ + NH_4, 100), 236 (M^+ + H, 19); HRMS calcd for $C_{12}H_{14}NO_4$ (M^+ + H), 236.092283; found 236.091810.

Data for **8**: $[\alpha]^{25}_D$ +38.0° (c 0.67, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 8.27 (dd, 2H, J = 1.8, 7.0 Hz), 8.13 (dd, 2H, J = 2.2, 7.0 Hz), 7.35 (s, 5H), 5.64 (br d, 1H, J = 7.7 Hz), 5.13 (s, 2H), 4.81 (m, 1H), 4.69 (m, 2H), 3.81 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 169.66, 164.11, 155.64, 150.77, 135.88, 134.64, 130.81, 128.57, 128.35, 128.16, 123.66, 67.37, 65.37, 53.34, 53.05; IR (KBr) 3424, 1754, 1730, 1718, 1536 cm^{-1}; ESMS m/z (rel intensity) 403 (M^+ + H, 100). Anal. Calcd for $C_{19}H_{18}N_2O_8$: C, 56.72; H, 4.52; N, 6.96. Found: C, 56.53; H, 4.58; N, 6.83.

Mitsunobu Reaction between *N*-Cbz-L-Serine Methyl Ester (6) and Phthalimide. The reaction was performed as described in the general procedure. Starting with *N*-Cbz-L-Serine methyl ester (**6**) (443.2 mg, 1.7 mmol), phthalimide (382.5 mg, 2.6 mmol), PPh_3 (505.8 mg, 1.9 mmol), and DEAD (0.31 mL, 1.9 mmol) gave the β-elimination product **7** (301.6 mg, 1.3 mmol, 73%) and the substitution product **11B** (87 mg, 0.22 mmol, 13%).

Data for **7**: See above.

Data for **11B**: $[\alpha]^{25}_D$ +12.0° (c 0.22, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 7.84 (m, 2H), 7.73 (m, 2H), 7.31 (s, 5H), 5.69 (br d, 1H, J = 7.3 Hz), 5.07 (s, 2H), 4.68 (br q, 1H, J = 5.5 Hz), 4.22−4.04 (m, 2H), 3.79 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.13, 168.02, 155.70, 136.06, 134.11, 131.65, 128.34, 127.98, 127.91, 123.46, 66.95, 53.27, 52.80, 39.03; IR (KBr) 3312, 1772, 1752, 1726, 1684 cm^{-1}; CIMS (NH_3) m/z (rel intensity) 400 (M^+ + NH_4, 100), 383 (M^+ + H, 27); HRMS calcd for $C_{20}H_{19}N_2O_6$ (M^+ + H), 383.124312; found 383.125009.

Mitsunobu Reaction between *N*-Boc-L-Serine Benzyl Ester (entry E) and Methyl 4-Hydroxybenzoate. The reaction was performed as described in the general procedure. Starting with *N*-Boc-L-serine benzyl ester (517.7 mg, 1.7 mmol), methyl 4-hydroxybenzoate (399.4 mg, 2.6 mmol), PPh_3 (505.8 mg, 1.9 mmol), and DEAD (0.31 mL, 1.9 mmol) gave the β-elimination product **12** (442.5 mg, 1.6 mmol, 91%): ^{1}H NMR ($CDCl_3$) δ 7.37 (m, 5H), 7.03 (br s, 1H), 6.17 (br s, 1H), 5.79 (d, 1H, J = 1.5 Hz), 5.26 (s, 2H), 1.48 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 163.86, 152.53, 135.21, 131.38, 128.63, 128.50, 128.18, 105.43, 80.67, 67.60, 28.23; IR (KBr) 3456, 3420, 2978, 1718 cm^{-1}; HRMS calcd for $C_{15}H_{20}NO_4$ (M^+ + H), 278.139233; found 278.138973.

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