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Convenient Preparation of *tert*-Butyl *β*-(Protected amino)esters

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Abstract: Refluxing an aldehyde **1** with benzotriazole and benzylcarbamate in the presence of a catalytic amount of *p*-TsOH gave the corresponding benzyloxycarbonylamino-1-(1-benzotriazolyl)alkane **2** in good yields. Compounds **2** treated with substituted *tert*-butyl acetates **3** using LDA as a base afford smoothly and under mild conditions the *N*-2-protected 3-aminoalkanoic esters **4**.

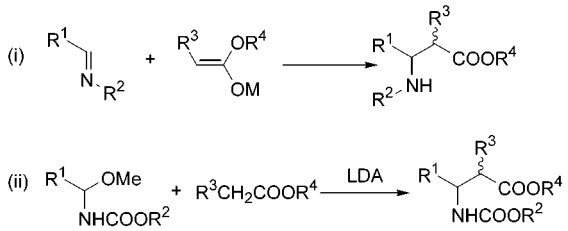
Two popular methods for the synthesis of *β*-amino acids utilize formation of the Cα-C*β* bond[1a,b] (Scheme 1): (i) the treatment of imines with ester enolates or ketene acetals,[2a−e] which is particularly convenient for making *N*-substituted *β*-amino acids, and (ii) the treatment of *N*-alkoxycarbonyl-1-methoxyamines with esters,[3a,b] which can be applied to prepare *N*-unsubstituted *β*-amino acids.

In an extension of our previous work on the synthesis of *β*- amino acids,[4a,b] we have now shown that reactions of benzyloxycarbonylamino-1-(1-benzotriazolyl)alkanes **2a**−**e** with substituted *tert*-butyl acetates **3x**−**z** using LDA as a base afford smoothly and under mild conditions the *N*-protected 3-aminoalkanoic esters **4ax**−**cz**, **4dx**−**dy**, and **4ey** (Scheme 2, Table 1).

The starting benzotriazole derivatives **2a**−**e** were easily prepared according to our previously published method.[4a] The reactions of intermediates **2a**−**e** with *tert*-butyl acetates **3x**−**z** are discussed in two subsections according to the reaction results.

(i) Reactions of Intermediates 2a−e with *tert*-Butyl Acetates 3x,y. Treatment of a mixture of a benzyl *N*-[1-(1-benzotriazol-1-yl)arylalkyl]carbamate **2a**−**d** and *tert*-butyl acetate **3x** in THF with 2.5 equiv of LDA ranging from −78 to 0 °C gave *β*-amino acid derivatives **4ax**, **4bx**, **4cx**, and **4dx**. Analogously, treatment of carbamate **2a**−**e** and *tert*-butyl acetate **3y** gave **4ay**, **4by**, **4cy**, **4dy,** and **4ey**. For each of these nine products, the ^{1}H and ^{13}C NMR spectra showed only a single set of signals for the appropriate protons and carbons because there is only one chiral center in each of these compounds.

SCHEME 1



SCHEME 2

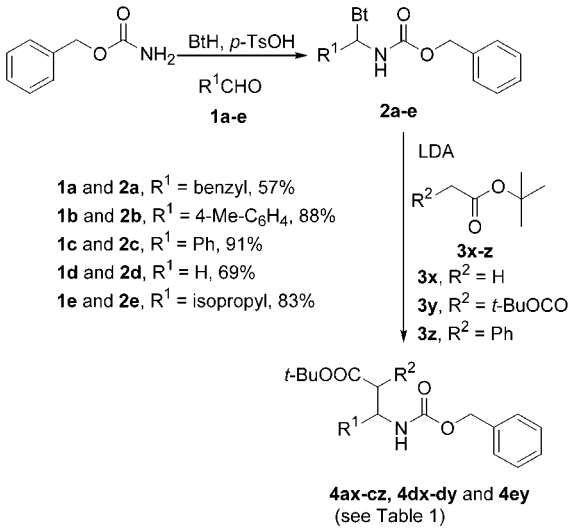


TABLE 1. Preparation of *β*-Amino Acid Derivatives 4

4	R^1	R^2	yield (%)
ax	benzyl	H	63
ay	benzyl	*t*-BuOCO	53
az	benzyl	Ph	45 (72:28)[a]
bx	4-MeC_6H_4	H	43
by	4-MeC_6H_4	*t*-BuOCO	53
bz	4-MeC_6H_4	Ph	67 (71:29)[a]
cx	Ph	H	53
cy	Ph	*t*-BuOCO	65
cz	Ph	Ph	73 (82:18)[a]
dx	H	H	35
dy	H	*t*-BuOCO	59
ey	isopropyl	*t*-BuOCO	70

[a] These yields are the total yield of anti and syn adducts; the ratios are anti/syn.

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(ii) Reactions of Intermediates 2a−c with *tert*-Butyl Acetate 3z. The intermediates **2a−c** reacted with *tert*-butyl acetate **3z** under the same conditions as used above to give **4az**, **4bz,** and **4cz**, each as a mixture of two diastereoisomers. According to the integrated intensities of the two singlets near 1.10−1.40 ppm (assigned to the *tert*-butyl group) and the two doublets near 3.60−4.00 ppm (assigned to the proton α to the carbonyl group), the ratios are approximately 72:28, 71:29, and 82:18, respectively. Two sets of signals were also found in the ^{13}C NMR spectra. According to Kise's mechanistic study,[3b] the anti adducts were expected to be obtained preferentially. We successfully separated mixtures of diastereoisomers to obtain these six pure compounds, including good crystals of one of the **4cz** isomers, whose ^{1}H NMR spectrum shows the *J* value assigned to the proton α to the carbonyl group to be 5.4 Hz. X-ray analysis of this isomer confirmed that it is the anti stereoisomer, ***4cz-anti***. We can deduce that the other isomer of **4cz** (the *J* value is 10.3 Hz) is the syn adduct, ***4cz-syn***.

Furthermore, from comparisons of the ^{1}H NMR spectra of the three pairs of diastereoisomers, we can deduce the structure of **4az** and **4bz**. Compound ***4az-anti*** clearly has a *J* value 6.2 Hz and ***4bz-anti*** of 5.9 Hz. These anti adducts are the major products. The syn adducts are the minor products: the *J* value of ***4az-syn*** is 8.7 Hz, and the *J* value of ***4bz-syn*** is 10.4 Hz. Using similar reaction conditions, but in the presence of Ti(OPr-*i*)$_4$, for the preparation of **4cz**, the yield is 73%, and the ratio of anti:syn decreased to 66:34 from 82:18 without Ti(OPr-*i*)$_4$. Our ratios of anti:syn are a little higher than Kise's;[3b] the higher stereoselectivity may be due to the greater bulk of *tert*-butyl acetates **3z**.

The present work is conceptually similar to the innovative and successful method of Kise[3a,b] but avoids the anodic oxidation. Our starting materials are stable, cheap, and easy to prepare, and the yields are useful. Moreover, we prepare *β*-amino acids with differential protection at the amine and carboxyl group. The reactions give anti adducts preferentially.

Experimental Section

General Methods. Melting points were determined on a hot-stage apparatus and are uncorrected. NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 with TMS as the internal standard for ^{1}H (300 MHz) or a solvent as the internal standard for ^{13}C (75 MHz). Microanalyses were performed on a Carlo Erba-1106 elemental analyzer. Benzene and toluene were dried over molecular sieves. Column chromatography was conducted with silica gel 200−425 mesh.

General Procedure for the Preparation of Benzyloxycarbonylamino-1-(1-benzotriazolyl)alkanes 2. A mixture of benzotriazole (5.95 g, 50 mmol), benzyl carbamate (7.55 g, 50 mmol), a catalytic amount of *p*-TsOH (0.95 g, 5 mmol), and the corresponding aldehyde **1** (50 mmol) in toluene (70 mL) was refluxed for 6−10 h. Water formed during the reaction was removed azeotropically with a Dean−Stark apparatus. Toluene was then removed in vacuo. The residue was poured into diethyl ether/hexanes (1:2, v/v) and filtered to get the precipitate, which was collected and recrystallized from the appropriate solvent.

Benzyl *N*-[1-(1-benzotriazol-1-yl)-2-phenylethyl]carbamate (2a): white needles (hexanes); mp 118−120 °C (57%) (mp 117−120 °C[4a]); ^{1}H NMR *δ* 3.60−3.77 (m, 2H), 4.91, 5.07 (AB, *J* = 12.3 Hz, 2H), 6.64−6.72 (m, 1H), 6.86 (d, *J* = 9.6 Hz, 1H), 7.06−7.28 (m, 11H), 7.35 (t, *J* = 8.1 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR *δ* 40.6, 66.0, 67.2, 109.8, 118.3, 119.4, 124.0, 127.1, 127.5, 127.8, 128.1, 128.3, 128.5, 129.0, 132.9, 134.8, 135.5, 145.3, 155.5.

Benzyl *N*-[1-benzotriazol-1-yl(4-methylphenyl)methyl]-carbamate (2b): white plates (diethyl ether); mp 129−131 °C (57%); ^{1}H NMR *δ* 2.29 (s, 3H), 5.02, 5.14 (AB, *J* = 12.0 Hz, 2H), 6.69 (d, *J* = 12.0 Hz, 1H), 7.08−7.18 (m, 4H), 7.25−7.42 (m, *J* = 7H), 7.55 (d, *J* = 7.7 Hz, 1H); 7.64 (d, *J* = 9.4 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR *δ* 21.0, 67.3, 67.6, 109.8, 119.9, 124.1, 126.1, 126.6, 127.7, 128.1, 128.3, 128.5, 129.6, 132.4, 135.4, 139.2, 145.9, 155.3. Anal. Calcd for $C_{22}H_{20}N_4O_2$: C, 70.95; H, 5.41; N, 15.04. Found: C, 70.03; H, 4.99; N, 14.99.

Benzyl *N*-[1-benzotriazol-1-yl-benzyl]carbamate (2c): white needles (hexanes); mp 136−137 °C (91%) (mp 115−117 °C[4a]); ^{1}H NMR *δ* 5.04, 5.13 (AB, *J* = 12.0 Hz, 2H), 7.18−7.45 (m, 12H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.86 (d, *J* = 9.0 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 9.30 (d, *J* = 9.3 Hz, 1H); ^{13}C NMR *δ* 65.7, 67.3, 109.9, 118.3, 122.9, 125.4, 126.2, 126.9, 127.2, 127.5, 127.7, 130.7, 134.7, 134.8, 144.7, 154.9. Anal. Calcd for $C_{21}H_{18}N_4O_2$: C, 70.38; H, 5.06; N, 15.63. Found: C, 70.44; H, 5.30; N, 15.71.

Benzyl *N*-(1-benzotriazol-1-ylmethyl)carbamate (2d): white crystals (toluene); mp 122−123 °C (69%) (mp 124 °C[5]); ^{1}H NMR *δ* 5.12 (s, 2H), 6.02 (d, *J* = 7.0 Hz, 2H), 6.43 (t, *J* = 6.8 Hz, 1H), 7.26−7.40 (m, 6H), 7.42−7.53 (t, *J* = 7.5 Hz, 1H), 7.89 (d, *J* = 8.3 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR *δ* 53.3, 67.5, 110.7, 119.6, 124.2, 127.9, 128.1, 128.3, 128.5, 132.3, 135.5, 146.0, 156.1.

Benzyl *N*-[1-(1-benzotriazol-1-yl)-2-methylpropyl]carbamate (2e): white crystals (benzene); mp 171−172 °C (83%) (mp 170−172 °C[5]); ^{1}H NMR *δ* 0.75, (d, *J* = 6.4 Hz, 3H), 1.19 (d, *J* = 6.6 Hz, 3H), 2.65−2.90 (m, 1H), 4.96 (d, *J* = 12.2 Hz, 1H), 5.10 (d, *J* = 12.2 Hz, 1H), 6.13 (t, *J* = 9.6 Hz, 1H), 6.49 (d, *J* = 9.7 Hz, NH), 7.20−7.43 (m, 6H), 7.43−7.55 (m, 1H), 7.77 (d, *J* = 8.2 Hz, 1H), 8.05 (d, *J* = 9.5 Hz, 1H); ^{13}C NMR *δ* 18.6, 19.0, 33.0, 67.2, 70.4, 109.8, 119.7, 124.1, 127.7, 127.9, 128.2, 128.4, 133.2, 135.6, 145.3, 155.8.

General Procedure for the Preparation of *β*-Amino Acid Derivatives 4. A mixture of benzyloxycarbonylamino-1-(1-benzotriazolyl)alkanes **2** (1 mmol) and *tert*-butyl esters **3** (1.1 mmol) in THF (5 mL) was added to a solution of LDA (2.5 mmol) in THF (10 mL) at −78 °C and the mixture was stirred for 12 h. The reaction temperature was raised to 0 °C and kept at this temperature for several hours until compound **2** was consumed. The mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with brine and dried over Na_2SO_4. The solvent was removed in vacuo, and the residue was purified by column chromatography to afford the pure samples of **4**.

***tert*-Butyl 3-[(benzyloxy)carbonyl]amino-4-phenylbutanoate (4ax):** white needles (hexanes/ethyl acetate); mp 78−79 °C (oil, no mp[6]) (63%); ^{1}H NMR *δ* 1.44 (s, 9H), 2.29−2.46 (m, 2H), 2.77−2.96 (m, 2H), 4.15−4.24 (m, 1H), 5.06 (s, 2H), 5.39 (d, *J* = 8.5 Hz, 1H), 7.16−7.36 (m, 10H); ^{13}C NMR *δ* 28.0, 38.6, 40.2, 49.5, 66.4, 81.1, 126.5, 128.0, 128.4, 128.5, 129.3, 136.5, 137.6, 155.5, 170.8. Anal. Calcd for $C_{22}H_{27}NO_4$: C, 71.52; H, 7.37; N, 3.79. Found: C, 71.54; H, 7.69; N, 3.75.

Di-*tert*-butyl 2-(1-[(benzyloxy)carbonyl]amino-2-phenylethyl)malonate (4ay): white needles (hexanes/ethyl acetate); mp 64−66 °C (53%); ^{1}H NMR *δ* 1.46 (s, 9H), 1.58(s, 9H), 2.81−2.89 (m, 1H), 3.06−3.14 (m, 1H), 3.37 (d, *J* = 4.2 Hz, 1H), 4.50−4.60 (m, 1H), 5.13 (s, 2H), 6.09 (d, *J* = 9.6 Hz, 1H), 7.20−7.40 (m, 10H); ^{13}C NMR *δ* 27.7, 27.9, 39.9, 52.4, 54.7, 66.4, 82.2, 82.3, 126.6, 127.8, 127.9, 128.3, 128.5, 129.2, 136.5, 137.3, 155.2, 167.0, 167.9. Anal. Calcd for $C_{27}H_{35}NO_6$: C, 69.06; H, 7.51; N, 2.98. Found: C, 69.11; H, 7.56; N, 2.98.

tert*-Butyl 3-[(benzyloxy)carbonyl]amino-2,4-diphenylbutanoate (4az):** two stereoisomers, **4az-*anti*/4az-*syn = 72:28.

***tert*-Butyl (2*R**,3*R**)-3-[(benzyloxy)carbonyl]amino-2,4-diphenylbutanoate (4az-*anti*):** white powder (methylene

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chloride); mp 102−103 °C (32%); ^{1}H NMR δ 1.41 (s, 9H), 2.70−2.90 (m, 2H), 3.65 (d, J = 6.2 Hz, 1H), 4.20−4.40 (m, 1H), 4.98 (s, 2H), 5.67 (d, J = 9.5 Hz, 1H), 7.05−7.50 (m, 15H); ^{13}C NMR δ 27.9, 39.4, 54.2, 55.6, 66.3, 81.6, 126.5, 127.4, 127.9, 128.3, 128.4, 128.5, 128.6, 129.3, 136.4, 136.7, 137.7, 155.6, 171.8. Anal. Calcd for $C_{28}H_{31}NO_4$: C, 75.48; H, 7.01; N, 3.14. Found: C, 75.39; H, 7.08; N, 3.22.

tert*-Butyl (2*R**,3*S**)-3-[(benzyloxy)carbonyl]amino-2,4-diphenylbutanoate (4az-*syn*):** contains about 50% **4az-*anti; white powder (methylene chloride) (13%); ^{1}H NMR δ 1.44 (s, 9H), 2.90−3.00 (m, 2H), 3.76 (d, J = 8.7 Hz, 1H), 4.40−4.53 (m, 1H), 4.90 (s, 2H), 5.67 (d, J = 9.5 Hz, 1H), 7.04−7.30 (m, 15H); ^{13}C NMR δ 27.9, 39.3, 54.5, 56.1, 66.2, 81.4, 126.5, 127.4, 127.7, 127.9, 128.4, 128.5, 128.7, 129.6, 136.1, 136.7, 137.6, 155.4, 171.3. Anal. Calcd for $C_{28}H_{31}NO_4$: C, 75.48; H, 7.01; N, 3.14. Found: C, 75.39; H, 7.08; N, 3.22.

***tert*-Butyl 3-[(benzyloxy)carbonyl]amino-3-(4-methylphenyl)propanoate (4bx):** white needles (hexanes/ethyl acetate); mp 79−81 °C (43%); ^{1}H NMR δ 1.33 (s, 9H), 2.32(s, 3H), 2.69−2.78 (m, 1H), 5.05, 5.12 (AB, J = 12.3 Hz, 2H), 5.68−5.76 (brs, 1H), 7.15 (dd, J = 18.6, 7.8 Hz, 4H), 7.25−7.37 (m, 5H); ^{13}C NMR δ 21.0, 27.9, 41.9, 51.6, 66.7, 81.2, 117.8, 126.1, 128.0, 128.4, 129.2, 136.5, 137.1, 137.9, 155.5, 170.1. Anal. Calcd for $C_{22}H_{27}NO_4$: C, 71.52; H, 7.37; N, 3.79. Found: C, 71.49; H, 7.60; N, 3.81.

Di-*tert*-butyl 2-[[(benzyloxy)carbonyl]amino(4-methylphenyl)methyl]malonate (4by): white needles (hexanes/ethyl acetate); mp 74−76 °C (78%); ^{1}H NMR δ 1.32 (s, 9H), 1.40 (s, 9H), 2.30 (s, 3H), 3.70 (s, 1H), 5.04, 5.12 (AB, J = 12.3 Hz, 2H), 5.43 (brs, 1H), 6.54 (d, J = 8.4 Hz, 1H), 7.10 (d, J = 7.5 Hz, 4H), 7.19 (d, J = 7.2 Hz, 2H), 7.24−7.36 (m, 5H); ^{13}C NMR δ 21.0, 27.7, 53.8, 58.3, 66.6, 82.3, 82.6, 126.2, 127.9, 128.0, 128.3, 129.0, 136.4, 137.0, 155.6, 166.3, 167.5. Anal. Calcd for $C_{27}H_{35}NO_6$: C, 69.06; H, 7.51; N, 2.98. Found: C, 69.41; H, 7.82; N, 3.00.

tert*-Butyl3-[(benzyloxy)carbonyl]amino-3-(4-methylphenyl)-2-phenylpropanoate (4bz):** two stereoisomers, **4bz-*anti*/4bz-*syn = 71:29.

***tert*-Butyl (2*R**,3*S**)-3-[(benzyloxy)carbonyl]amino-3-(4-methylphenyl)-2 phenylpropanoate (4bz-*anti*):** white needles (chloroform); mp 60−61 °C (48%); ^{1}H NMR δ 1.31 (s, 9H), 2.29 (s, 3H), 3.96 (d, J = 5.9 Hz, 1H), 4.94, 5.04 (AB, J = 12.2 Hz, 2H), 5.16−5.22 (m, 1H), 6.33 (d, J = 8.7 Hz, 1H), 7.07 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 7.20−7.38 (m, 10H); ^{13}C NMR δ 21.0, 27.7, 57.4, 57.7, 66.5, 81.8, 126.4, 127.4, 127.9, 127.9, 128.3, 128.4, 128.5, 129.0, 135.9, 136.6, 136.9, 137.4, 155.7, 171.5. Anal. Calcd for $C_{28}H_{31}NO_4$: C, 75.48; H, 7.01; N, 3.14. Found: C, 75.20; H, 6.58; N, 3.22.

***tert*-Butyl (2*R**,3*R**)-3-[(benzyloxy)carbonyl]amino-3-(4-methylphenyl)-2 phenylpropanoate (4bz-*syn*):** white needles (chloroform); mp 172−173 °C (19%); ^{1}H NMR δ 1.18 (s, 9H), 2.33 (s, 3H), 3.84 (d, J = 10.4 Hz, 1H), 4.80−5.00 (m, 3H), 5.22−5.37 (m, 1H), 7.05−7.20 (m, 4H), 7.20−7.45 (m, 10H); ^{13}C NMR δ 21.1, 27.6, 57.0, 58.9, 66.5, 77.2, 81.3, 127.3, 127.8, 127.9, 128.3, 128.6, 128.7, 129.1, 135.6, 136.3, 137.4, 155.3, 170.0. Anal. Calcd for $C_{28}H_{31}NO_4$: C, 75.48; H, 7.01; N, 3.14. Found: C, 75.29; H, 7.11; N, 3.08.

***tert*-Butyl 3-[(benzyloxy)carbonyl]amino-3-phenylpropanoate (4cx):** white needles (hexanes/ethyl acetate); mp 89−91 °C (53%); ^{1}H NMR δ 1.31 (s, 9H), 2.69−2.78 (m, 2H), 5.04−5.14 (m, 2H), 5.80 (brs, 1H), 7.23−7.40 (m, 10H); ^{13}C NMR δ 27.8, 41.8, 51.8, 66.8, 81.3, 126.2, 127.5, 128.1, 128.4, 128.5, 136.3, 140.8, 155.5, 170.0. Anal. Calcd for $C_{22}H_{27}NO_4$: C, 71.52; H, 7.37; N, 3.79. Found: C, 70.97; H 7.10; N 3.94.

Di-*tert*-butyl 2-[[(benzyloxy)carbonylamino)benzyl]malonate (4cy): white needles (hexanes/ethyl acetate); mp 167−169 °C (87%); ^{1}H NMR δ 1.30 (s, 9H), 1.40 (s, 9H), 3.75 (d, J = 4.2 Hz, 1H), 5.04, 5.13 (AB, J = 12.3 Hz, 2H), 5.51 (brs, 1H), 6.61 (d, J = 9.3 Hz, 1H), 7.22−7.36 (m, 10H); ^{13}C NMR δ 27.5, 27.6, 53.8, 58.1, 66.6, 82.2, 82.5, 126.2, 127.3, 127.8, 128.0, 128.2, 136.3, 139.3, 155.5, 166.1, 167.3. Anal. Calcd for $C_{27}H_{35}NO_6$: C, 69.06; H, 7.51; N, 2.98. Found: C, 68.54; H, 7.32; N, 3.08.

tert*-Butyl 3-[(benzyloxy)carbonyl]amino-2,3-diphenylpropanoate (4cz):** two stereoisomers, **4cz-*anti*/4cz-*syn = 82:18.

***tert*-Butyl (2*R**,3*S**)-3-[(benzyloxy)carbonyl]amino-2,3-diphenylpropanoate (4cz-*anti*):** white needles (ethanol); mp 129−130 °C (60%); ^{1}H NMR δ 1.30 (s, 9H), 3.98 (d, J = 5.4 Hz, 1H), 4.86, 4.95 (AB, J = 12.3 Hz, 2H), 5.18−5.24 (m, 1H), 6.40 (d, J = 8.7 Hz, 1H), 7.20−7.35 (m, 15H); ^{13}C NMR δ 27.7, 57.4, 57.9, 66.6, 81.9, 126.5, 127.3, 127.5, 127.9, 127.9, 128.2, 128.3, 128.4, 128.5,135.8, 136.5, 140.4, 155.7, 171.4.

Crystal data for 4cz-*anti*: $C_{27}H_{29}NO_4$, MW 431.51, orthorhombic, $Pca2_1$, a = 10.238(6) Å, b = 12.267(7) Å, c = 38.013(22) Å, V = 4774(5) Å^3, Z = 8, T = −105 °C, F(000) = 1840, μ(Mo Kα) = 0.080 mm^{-1}, D_{calcd} = 1.201 g·cm^{-3}, $2\theta_{max}$ 45° (CCD area detector, 99.9% completeness), wR(F^2) = 0.1178 (all 6224 data), R = 0.0505 (2867 data with $I > 2\sigma I$).

***tert*-Butyl (2*R**,3*R**)-3-[(benzyloxy)carbonyl]amino-2,3-diphenylpropanoate (4cz-*syn*):** white needles (ethanol); mp 180−181 °C (13%); ^{1}H NMR δ 1.16 (s, 9H), 3.86 (d, J = 10.3 Hz, 1H), 4.82−5.00 (m, 3H), 5.26−5.40 (m, 1H), 7.07−7.16 (m, 2H), 7.23−7.44 (m,13H); ^{13}C NMR δ 27.6, 57.3, 58.9, 66.6, 81.4, 127.4, 127.8, 127.9, 127.9, 128.4, 128.4, 128.7, 128.7,135.5, 136.3, 140.5, 155.3, 170.0. Anal. Calcd for $C_{27}H_{29}NO_4$: C, 75.15; H, 6.77; N, 3.25. Found: C, 75.47; H, 6.69; N 3.25.

***tert*-Butyl 3-[[(benzyloxy)carbonyl]amino]propanoate (4dx):** colorless oil[7] (35%); ^{1}H NMR δ 1.43 (s, 9H), 2.43 (t, J = 6.1 Hz, 2H), 3.35−3.48 (m, 2H), 5.08 (s, 2H), 5.42 (bs, 1H), 7.25−7.40 (m, 5H); ^{13}C NMR δ 27.9, 35.4, 36.6, 66.4, 80.8, 127.9, 128.3, 136.4, 156.2, 171.5.

Di-*tert*-butyl 2-([[(benzyloxy)carbonyl]amino]methyl)-malonate (4dy): colorless oil (59%); ^{1}H NMR δ 1.44 (s, 18H), 3.44 (t, J = 6.2 Hz, 1H), 3.62 (t, J = 6.2 Hz, 2H), 5.08 (s, 2H), 5.46 (bs, 1H), 7.25−7.40 (m, 5H); ^{13}C NMR δ 27.7, 39.5, 53.4, 66.5, 81.9, 127.9, 128.3, 136.3, 156.0, 167.3. Anal. Calcd for $C_{20}H_{29}NO_6$: C, 63.31; H, 7.70; N, 3.69. Found: C, 63.68; H, 8.08; N, 4.28.

Di-*tert*-butyl 2-(1-[[(benzyloxy)carbonyl]amino]-2-methylpropyl)malonate (4ey): colorless oil (70%); ^{1}H NMR δ 0.92−1.00 (m, 6H), 1.39 (s, 9H), 1.47 (s, 9H), 1.67−1.82 (m, 1H), 3.52 (d, J = 4.4 Hz, 1H), 3.94−4.05 (m, 1H), 5.07 (s, 2H), 5.96 (d, J = 10.3 Hz, 1H), 7.24−7.40 (m, 5H); ^{13}C NMR δ 19.2, 19.7, 27.6, 27.8, 32.2, 54.7, 56.6, 66.3, 82.1, 82.3, 127.8, 128.0, 128.3, 136.6, 156.1, 167.2, 168.2. Anal. Calcd for $C_{23}H_{35}NO_6$: C, 65.53; H, 8.37; N, 3.32. Found: C, 65.31; H, 8.70; N, 3.93.

Supporting Information Available: X-ray crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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