Preparation of Enantiomerically Pure Protected 4-Oxo-α-amino Acids and 3-Aryl-α-amino Acids from Serine

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The organozinc reagent **13**, prepared from the protected β-iodo alanine derivative **3c** using ultrasonic activation, is efficiently acylated using acid chlorides in the presence of bis(triphenylphosphine)palladium dichloride to give enantiomerically pure protected 4-oxo-α-amino acids **17** in 39–90% yield (13 examples). Zinc reagent **13** can also be coupled with aryl iodides in the presence of bis(tri-*o*-tolylphosphine)palladium dichloride to give enantiomerically pure protected phenylalanine analogues **26**, **29**, and **30** in 10–67% yield (11 examples). The reaction tolerates the presence of a variety of functional groups in the acid chloride and the aryl iodide and provides derivatives which can be easily deprotected, at either the carboxyl or amino terminus, to give intermediates suitable for peptide synthesis.

New methods for the synthesis of enantiomerically pure α-amino acids have been widely explored.[1] Many of these methods involve formation of one of the four bonds to the α-center.[2] Although this approach is conceptually attractive, primarily due to the flexibility which it offers, the need to induce asymmetry at the α-center necessitates the use of a chiral auxiliary. While many effective auxiliaries have been developed, in almost all cases further synthetic operations are required before the α-amino acid can be isolated in a protected form suitable for incorporation into peptides. These additional steps may place limitations on the functionality which can be incorporated into the target α-amino acid. It is for these two reasons that efforts to develop general approaches to α-amino acid synthesis, principally from α-amino acid precursors,[3] have been investigated more recently.

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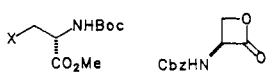
Important goals for such investigations are the development of synthetic equivalents for the alanine β-cation **1** and the alanine β-anion **2**. There are several approaches to the synthon **1**, including 3-iodo- and 3-(tosyloxy)alanine derivatives **3a** and **3b**,[4] the β-lactone **4**,[5] the aziridine **5**,[6] and the sulfamidate **6**,[7] all of which are derived from serine. In addition, an indirect approach using the D-mannitol-derived bis(aziridine) **7** has also been explored.[8] The main limitation of all these approaches is the difficulty in incorporation of functionalized carbon nucleophiles, although carbonyl-stabilized ylides do react with the aziridine **5a** and diethyl malonate reacts with the sulfamidate **6**.



3a, X = I
3b, X = TsO

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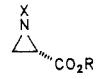
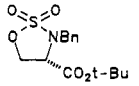


5a, X = pNB, R = Me
5b, X = Ts, R = t-Bu



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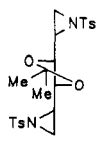

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By contrast, there have been no reports of viable direct approaches to the alanine β-anion **2**, in which the β-anion is not stabilized by an additional functional group.[9] Three indirect approaches, employing the phosphonium salt **8**,[10] the phenyl sulfone **9**,[11] and differentially protected aspartate derivatives **10**[12] have been investigated. Unfortunately, reactions of the phosphorane derived from **8** are low-yielding, and extensively modified reagents are required to allow good yields to be obtained.[13] Similarly, use of the reagents **9** and **10** requires several additional steps to unmask the β-substituted α-amino acid. Very recently, two organometallic derivatives, the chromium carbene complex **11**[14] and the nickellacycle **12**[15] have been reported to react as alanine β-anion equivalents, although their general viability has yet to be established.

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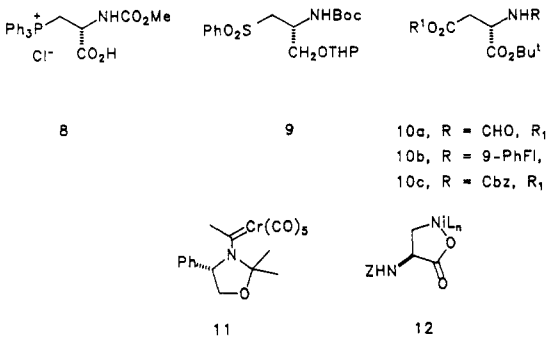


In the context of β-functionalization, β-alanine radicals, prepared from protected 3-iodoalanine, add to acrylic acid and can also react with propargylic and allylic stannanes.[16] Alanine β-radicals can also be derived from aspartic acid derivatives and have been shown to react with halogen transfer reagents and to add to vinylphosphonates and an allylic thioether.[17]

Much recent progress has been made in the use of functionalized zinc reagents in organic synthesis. Functionalized alkylzinc reagents with either ester or ketone functionality may be prepared by treatment of suitably substituted cyclopropanes with zinc chloride[18] or directly from alkyl bromides or iodides using activated zinc.[19] In particular, treatment of ethyl 3-iodopropionate with zinc–copper couple in benzene–dimethylacetamide produces a homoenolate equivalent which couples under palladium catalysis with acid chlorides[19a] and aryl and vinyl iodides (and the corresponding triflates).[19b] A recent advance involves treatment of halozinc reagents, prepared directly from an alkyl halide and activated zinc in THF, with the soluble copper salt CuCN·2LiCl.[20] The mixed zinc/copper reagent thereby formed has been shown to react with a variety of electrophiles.[20] It therefore appeared reasonable to explore the possibility that a more highly functionalized zinc reagent **13**,[21] derived from protected L-iodoalanine, could be prepared and then to explore reactions of this reagent with electrophiles.[22]

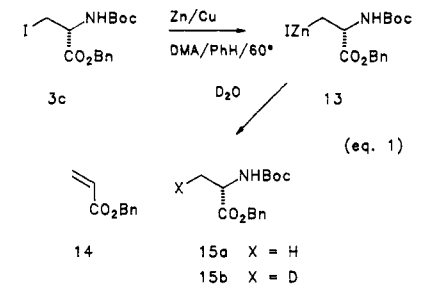
Table I. Preparation of 4-Oxo-α-amino Acid Derivatives 17

substrate	product	R	yield (%)
PhCOCl	**17a**	Ph	70
2-Furoyl chloride	**17b**	2-furyl	90[a]
MeCOCl	**17c**	Me	80[b]
EtCOCl	**17d**	Et	83[c]
Pr^iCH_2COCl	**17e**	Pr^iCH_2	76
Bu^tCH_2COCl	**17f**	Bu^tCH_2	84
$PhCH_2COCl$	**17g**	$PhCH_2$	41
t-PhCH=CHCOCl	**17h**	*t*-PhCH=CH	72
$4\text{-}MeOC_6H_4COCl$	**17i**	$4\text{-}MeOC_6H_4$	43
$4\text{-}AcOC_6H_4COCl$	**17j**	$4\text{-}AcOC_6H_4$	63
$ClCH_2COCl$	**17k**	$ClCH_2$	39[d]
$AcOCH_2COCl$	**17l**	$AcOCH_2$	64
$PhthNCH_2COCl$	**17m**	$PhthNCH_2$	53

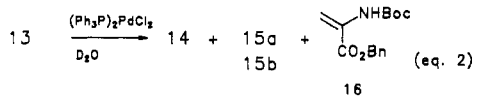
[a] 3-(2-Furoyl)-L-alanine is a naturally occurring compound.[30] [b] 4-Oxonorvaline is an intermediate in the degradation of ornithine by *Clostridium stricklandii*.[31] [c] 4-Oxonorleucine has been isolated from bacteria.[32] For a previous preparation, see ref 24e. [d] The acetyl adduct **17c** was also isolated (8%).

Results and Discussion

Reaction of **3c** with zinc/copper couple in benzene–dimethylacetamide at rt for 1 h, followed by reaction at 60 °C for a further 1 h, gave, after quenching with deuterium oxide, benzyl acrylate **14**, undeuterated protected alanine **15a**, and the corresponding 3-deuterio derivative **15b** (eq 1). Addition of tetrakis(triphenylphosphine)palladium



(6 mol %), prior to quenching with deuterium oxide, resulted additionally in the formation of dehydroalanine **16** (eq 2). These results suggest that zinc reagent formation



was occurring and that although either intra- or intermolecular proton transfer does take place to some extent under the reaction conditions, leading to undeuterated **15a**, the zinc reagent can survive to provide the 3-deuterio derivative **15b**. Formation of dehydroalanine **16** is almost certainly due to elimination of palladium hydride from the palladium intermediate derived from **13** by transmetalation. In order to confirm that the zinc reagent **13** was indeed being formed, the reaction mixture was treated with benzoyl chloride and tetrakis(triphenylphosphine)-palladium (6 mol %), which allowed the isolation of the 4-oxo-α-amino acid derivative **17a** (38%).

This encouraging result suggested that preparation of the zinc reagent **13** under milder conditions would enable better yields of 4-oxo-α-amino acids[23–25] to be obtained. It

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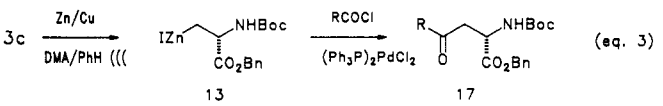
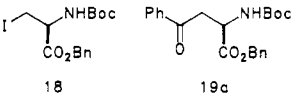
is well established that ultrasonic activation can increase significantly the rate of many reactions,[26] including the insertion of zinc into carbon–halogen bonds.[27] In particular, it has been shown that changes in the morphology of zinc powder, induced by ultrasonic irradiation, lead to a highly reactive metal surface.[28] It is also possible that ultrasonication can increase the rate of zinc insertion into carbon–halogen bonds due to the likely involvement of single-electron transfer in the reaction.[29] It was therefore pleasing to observe that addition of the protected iodoalanine derivative **3c** to a suspension of zinc–copper couple in benzene and dimethylacetamide (DMA), followed by sonication in an ultrasonic cleaning bath for 30 min, during which time the temperature of the bath rose from 22 to 35 °C, resulted in disappearance of **3c**. Addition of catalytic bis(triphenylphosphine)palladium dichloride and then benzoyl chloride and further sonication to 40 °C for 30 min followed by workup and flash chromatography gave the 4-oxo-α-amino acid **17a** in 70% yield. Similar results were obtained using $(Ph_3P)_4Pd$ as catalyst. Due to the greater thermal and air stability of $(Ph_3P)_2PdCl_2$, we have used this catalyst for all our subsequent investigations. Treatment of the β-iodo alanine derivative **18**, derived from D-serine, with benzoyl chloride under the same conditions gave the corresponding protected D-amino acid **19a**, 62%. Application of this procedure to a range of unfunctionalized acid chlorides gave the corresponding 4-oxo-α-amino acids **17a–f** (eq 3) and the results are shown in Table I.



(eq. 3)

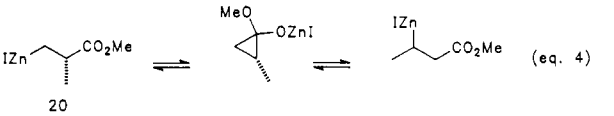
13 17

In all cases the mass balance was accounted for by isolation of protected alanine **15a**, which results from protonation of the zinc reagent **13** either during the reaction or upon quenching.



18 19a

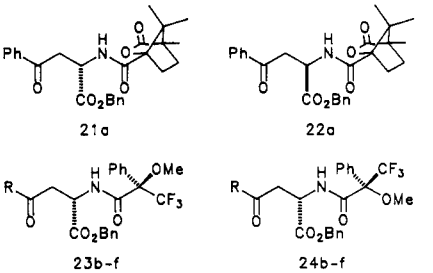
Although the optically active homoenolate **20**, which can in principle racemize via reversible cyclopropanolate formation (eq 4), has been shown to be configurationally



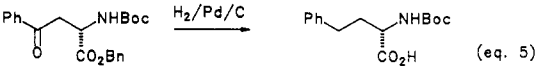
(eq. 4)

20

stable,[33] it was nevertheless considered necessary to establish that no racemization had occurred in the formation of the 4-oxo-α-amino acids **17**. The optical purity of each of the protected α-amino acids **17a–f** was determined by one of two alternative methods. Conversion of compound **17a** to the free amine using trifluoroacetic acid, followed by treatment with (1*S*)-(−)-camphanic chloride gave the camphanamide **21a**. The epimeric camphanamide **22a** was prepared from the protected D-amino acid **19a**.



Examination of the camphanamide derivatives **21a** and **22a** by proton NMR indicated no epimeric contamination. The enantiomeric purities of the remaining protected 4-oxo-α-amino acids **17b–f** were determined by conversion to the (*R*) and (*S*) Mosher amide[34] derivatives **23b–f** and **24b–f**, respectively, in an analogous manner. Here, both ^1H and ^{19}F NMR indicated no detectable epimeric contamination. Further proof of the optical purity of ketone **17a** was provided by catalytic hydrogenation which gave optically pure Boc-homophenylalanine **25** in quantitative yield (eq 5).



(eq. 5)

17a 25

Having established that unfunctionalized acid chlorides could be efficiently coupled to the zinc reagent **13**, the scope of the process was then investigated. Phenylacetyl chloride, with rather acidic α-protons, provided the adduct **17g** in modest yield. Cinnamoyl chloride, 4-methoxybenzoyl chloride, and 4-acetoxybenzoyl chloride gave the adducts **17h**, **17i**, and **17j**, respectively. Compound **17j** is a protected derivative of 4-oxohomotyrosine, which is a degradation product of the cyclic peptide echinocandine B.[35] Chloroacetyl chloride reacted with **13** to give protected 5-chloro-4-oxonorvaline **17k** (39%), provided the solution of zinc reagent **13** and chloroacetyl chloride was stirred rather than sonicated, although even under these conditions protected 4-oxonorvaline **17c** (8%) was also isolated. Compound **17c** presumably arose as a result of reduction of **17k** by highly reactive zinc. Acetoxyacetyl

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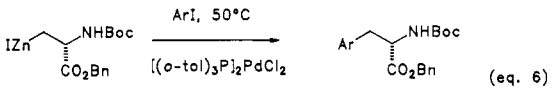
Table II. Preparation of Protected L-β-Aryl Alanines 26

aryl iodide	product	Ar	yield (%)
iodobenzene	**26a**	C_6H_5	55
1-iodonaphthalene	**26b**	1-naphthyl	64
2-acetoxy-1-iodobenzene	**26c**	2-$AcOC_6H_4$	13
2-fluoro-1-iodobenzene	**26d**	2-FC_6H_4	0
1-iodo-2-methoxybenzene	**26e**	2-$MeOC_6H_4$	50
4-acetoxy-1-iodobenzene	**26f**	4-$AcOC_6H_4$	53
4-bromo-1-iodobenzene	**26g**	4-BrC_6H_4	67
4-fluoro-1-iodobenzene	**26h**	4-FC_6H_4	36
1-iodo-4-methylbenzene	**26i**	4-MeC_6H_4	50
1-iodo-4-nitrobenzene	**26j**	4-$NO_2C_6H_4$	61

chloride reacted efficiently with **13** to give protected 5-hydroxy-4-norvaline (HON) **17** (64%).[36,37] Similarly, *N*-phthalimidoglycine acid chloride gave protected 4-oxoornithine **17m** (53%).[38] The results are summarized in Table I.

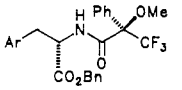
Attention was now directed to the reaction of the organozinc reagent **13** with aryl iodides. This process, if successful, would give access to a variety of enantiomerically pure protected L-β-aryl alanine derivatives **26** from a single precursor. Numerous approaches to the synthesis of enantiomerically pure phenylalanine analogues have been reported, based on either the asymmetric hydrogenation of dehydroarylalanine derivatives[39] or the reaction of chiral nucleophilic glycine equivalents with benzylic halides.[40]

Yoshida's work[19b] suggested that $(Ph_3P)_2PdCl_2$ would not be an efficient catalyst for the coupling of the zinc reagent **13** with aryl iodides. Indeed, treatment of the organozinc reagent **13**, prepared by sonication in the usual way, with $(Ph_3P)_2PdCl_2$ and iodobenzene at 60 °C for 1 h gave a low yield (15%) of protected phenylalanine **26a**. Use of lower reaction temperatures produced no protected phenylalanine **26a**. However, it was pleasing to find that replacement of the catalyst by $[(o\text{-}CH_3C_6H_4)_3P]_2PdCl_2$ (5 mol %), which had previously been shown to be an effective catalyst for coupling of less functionalized zinc reagents with aryl iodides,[19b] allowed reaction to occur at 50 °C within 1 h, yielding the protected phenylalanine derivative **26a**, 55%. An investigation of the scope of the reaction with a variety of functionalized aryl iodides was undertaken, and the results are presented in Table II (eq 6).

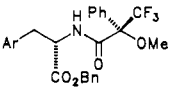


13 26a-j (eq. 6)

Para-substituted aryl iodides react with reasonable efficiency, as does 1-iodonaphthalene. The main problems concern ortho-substituted aryl iodides. This does not appear entirely to be a steric effect, since 1-iodo-2-methoxybenzene does react satisfactorily. In cases where the ortho substituent can act as a leaving group (e.g., AcO **26c** or F **26d**), we have obtained low or negligible yields. An alternative possibility is catalyst inactivation due to coordination of palladium by the ortho substituent.[41] In all cases the mass balance is accounted for by recovery of *N*-Boc-alanine benzyl ester **15a** in an analogous manner to the acid chloride coupling process. Since the temperature used for this coupling reaction was slightly higher than that used for the coupling of acid chlorides (50 versus 40 °C), it was necessary to establish the optical purity of the products. (*R*)-**27** and (*S*)-**28** Mosher amide derivatives of four representative examples (**26a**, **26e**, **26h**, and **26k**) were prepared, and both ^1H and ^{19}F NMR indicated no detectable epimeric contamination. As further confirmation, an authentic sample of **26a** was prepared from commercially available phenylalanine benzyl ester, and the optical rotations of the synthetic and natural material were in good agreement.

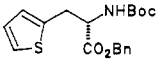


27

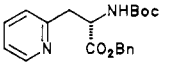


28

A brief investigation of the preparation of β-heteroaryl alanine derivatives was carried out. Reaction of 2-iodothiophene with the organozinc reagent **13** under the usual conditions ($[(o\text{-}CH_3C_6H_4)_3P]_2PdCl_2$, 50 °C, 1 h) gave a poor yield (10%) of the desired protected β-(2-thienyl)alanine **29**.[42] By contrast, 2-bromopyridine reacted satisfactorily with the organozinc reagent **13** under the conditions which had previously been used for coupling with acid chlorides [$(Ph_3P)_2PdCl_2$, 35–40 °C, 30 min] to give protected β-(2-pyridyl)alanine **30**[43] in reasonable yield (59%).[44]



29



30

A final comment about the stability of the zinc reagent **13** is appropriate. There is good evidence that zinc homoenolates derived from simple esters are stabilized by coordination from the ester carbonyl to zinc.[18b] If this coordination also occurs with **13**, then intramolecular NH proton transfer would be expected to be retarded. It is not possible, at present, to rule out an alternative possibility that coordination of the carbamate oxygen to zinc could also be important.

In summary, this work establishes that serine may be easily converted into an organozinc reagent which functions as the synthetic equivalent of the β-alanine anion **2**. This methodology promises to provide a general approach to the synthesis of enantiomerically pure α-amino acids which contain a methylene group adjacent to the α-center.

Experimental Section

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. NMR spectra were recorded for ^1H at 200 or 300 MHz on Bruker instruments. Infrared spectra were obtained on a Nicolet 20SX, and mass spectra were measured on either an AEI MS9 or a Kratos MS80. All solvents were distilled:

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light petroleum refers to that fraction with boiling point between 40 and 60 °C; dry dichloromethane was distilled from phosphorus pentoxide; dry tetrahydrofuran was distilled from potassium benzophenone ketyl; dry diethyl ether was distilled from sodium benzophenone ketyl; dry benzene was obtained from the Aldrich Chemical Co. as an HPLC-grade solvent. Zinc/copper couple was prepared according to the literature procedure.[45] Thin-layer chromatography (TLC) was performed using plates coated with Kieselgel 60 F_{254}, and column chromatography was performed using Kieselgel 60 according to the method of Still et al.[46] Sonication was achieved using a Hillsonic FM 100 cleaning bath. In order to achieve efficient conversion of the iodide **3c** to the zinc reagent **13** it is essential that the flask be correctly positioned in the ultrasonic bath.[47] Using the Hillsonic FM 100 bath, we have found that the best way to achieve this is to place two flasks, one containing the reaction mixture, the other empty, in the bath so that the two flasks are above the two transducers in the base of the bath. The reaction flask should be immersed so that the solution level inside matches the level of the water in the bath. Care should be taken to ensure that the bath is filled with cold (<20 °C) water to the correct level (indicated by an internal lip). The bath is then switched on and "tuned" by altering the positions of both flasks until a standing wave is achieved. This is indicated when the surface of the water in the bath is stationary. At this point degradation of ultrasound to audible frequencies should be minimal. The reaction mixture at this stage should start to foam slightly. The bath was checked at regular intervals throughout the experiment and retuned in a similar fashion whenever necessary. Other ultrasonic baths have also proved satisfactory, although those which incorporate a frequency sweep feature rather than a fixed frequency generator are much less effective.

L-Serine Benzyl Ester Benzenesulfonate (L-Ser-OBn·PhSO$_3$H). A mixture of L-serine (21.02 g, 200.0 mmol), technical-grade benzenesulfonic acid (45.0 g; 90%, 250 mmol), and benzyl alcohol (100 mL) in carbon tetrachloride (250 mL) was distilled gently until no more water formed (6–8 h). Carbon tetrachloride was added periodically to maintain the solvent level. After removal of the remaining solvent by distillation under reduced pressure, diethyl ether (200 mL) was added to the reaction mixture with vigorous shaking. Storage of the resulting oil at 4 °C for 24 h gave a solid product, which was collected, washed with cold ether, and dried. Recrystallization from 2-propanol–anhydrous diethyl ether yielded **L-serine benzyl ester benzenesulfonate** (L-Ser-OBn·PhSO$_3$H) as a white powder (52.29 g, 124.3 mmol, 74%): mp 97–98 °C (lit.[48] 97–98 °C); $[\alpha]^{21}_D$ −2.0° (*c* 1.0 in EtOH); ν_{max} (KBr disk) 3291–2845, 1746.0, and 1608.5 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 3.82 (1 H, dd, $^2J_{AB}$ = 12.5 Hz and $^3J_{AX}$ = 4.5 Hz, C(3)H, 3.92 (1 H, dd, $^2J_{AB}$ 12.5 = Hz and $^3J_{BX}$ = 4.5 Hz, C(3)H), 4.09 (1 H, b, C(2)H), 4.91 (1 H, d, $^2J_{AB}$ = 12.5 Hz, OC*H*$_A$H$_B$Ph), 4.99 (1 H, d, $^2J_{AB}$ = 12.5 Hz, OCH$_A$*H*$_B$Ph), 5.13 (1 H, b, OH), 7.1 (8 H, m, CH_2*Ph* and *m*-, *p*-$PhSO_3^-$), 7.76 (2 H, d, *J* = 7.5 Hz, *o*-$PhSO_3^-$), and 8.04 (3 H, b, NH_3^+). Found: C, 54.3; H, 5.2; N, 3.9. $C_{16}H_{19}NO_6S$ requires C, 54.4; H, 5.4; N, 4.0.

D-Serine benzyl ester benzenesulfonate (D-Ser-OBn·PhSO$_3$H): mp 97–98 °C; $[\alpha]^{21}_D$ +2.1° (*c* 2.2 in EtOH).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-3-hydroxypropionate (Boc-L-Ser-OBn). Di-*tert*-butyl pyrocarbonate (7.20 g, 33.00 mmol) was added to an ice-cooled solution of L-serine benzyl ester benzenesulfonate (10.60 g, 30.00 mmol) in distilled tetrahydrofuran (60 mL) and aqueous sodium hydroxide (30 mL; 1 M). The resulting solution was stirred at room temperature for 1 h, during which time there was significant CO_2 evolution, after which TLC analysis (10% methanol–dichloromethane) showed no remaining benzenesulfonate salt. The solution was concentrated under reduced pressure (ca. 30 mL), cooled in an ice bath, covered with a layer of ethyl acetate (90 mL), and acidified with aqueous potassium hydrogen sulfate (10% w/v) to pH 2–3. The aqueous phase was extracted with ethyl acetate (2 × 30 mL), and the combined organic fractions were washed with distilled water (3 × 30 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure to give a residue which solidified on standing. Recrystallization from ethyl acetate–light petroleum afforded **benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-3-hydroxypropionate (Boc-L-Ser-OBn)** as a white crystalline solid (7.14 g, 24.16 mmol, 81%): mp 70–71 °C; $[\alpha]^{21}_D$ −13.5° (*c* 1.0 in EtOH); ν_{max} (KBr disk) 3420.5, 3365.5, 1760.0, 1670.0, and 1526.5 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.44 (9 H, s, OC(C*H*$_3$)$_3$), 2.1 (1 H, br s, OH), 3.90 (1 H, dd, $^2J_{AB}$ = 11.3 Hz and $^3J_{AX}$ = 3.5 Hz, C(3)H), 3.98 (1 H, dd, $^3J_{AB}$ = 11.2 Hz and $^3J_{BX}$ = 4.0 Hz, C(3)H), 4.42 (1 H, br s, C(2)H), 5.21 (2 H, s, OC*H*$_2$Ph), 5.4 (1 H, br s, NH), and 7.35 (5 H, s, OCH_2Ph); *m*/*z* (FAB) 296 (MH^+, 5), 240 (20, $MH^+ - (CH_3)_2C{=}CH_2$), and 196 (41, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$). Found: C, 61.3; H, 7.1; N, 4.6. $C_{15}H_{21}NO_5$ requires C, 61.0; H, 7.2; N, 4.7.

Benzyl 2(*R*)-[(*tert*-butoxycarbonyl)amino]-3-hydroxypropionate (Boc-D-Ser-OBn): mp 70 °C; $[\alpha]^{21}_D$ +15.8° (*c* 0.9 in EtOH).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-3-*p*-toluenesulfonylpropionate [Boc-L-Ser(Ts)-OBn]. Tosyl chloride (4.911 g, 25.76 mmol) was added to a stirred solution of Boc-L-Ser-OBn (6.915 g, 23.42 mmol) in dry pyridine (40 mL) under nitrogen at −10 °C. The resulting solution was stored under nitrogen at −10 °C for 24 h and then poured into a beaker of ice–water (200 mL). Continued stirring resulted in the production of a white solid, which was filtered, washed with distilled water, and dried in a vacuum desiccator over phosphorus pentoxide. Recrystallization from ethanol yielded **benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-3-*p*-toluenesulfonylpropionate [Boc-L-Ser(Ts)-OBn]** as a white crystalline solid (8.871 g, 19.74 mmol, 84%): mp 95–96 °C; $[\alpha]^{21}_D$ −4.5 ° (*c* 1.0 in EtOH); ν_{max} (Nujol mull) 3374.5, 1753.5, 1694.0, and 1460.5 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.41 (9 H, s, OC(C*H*$_3$)$_3$), 2.43 (3 H, s, O*p*SO$_2$C$_6$H$_4$C*H*$_3$), 4.30 (1 H, dd, $^2J_{AB}$ = 10.0 Hz and $^3J_{AX}$ = 4.0 Hz, C(3)H), 4.42 (1 H, dd, $^2J_{AB}$ = 10.0 Hz and $^3J_{BX}$ = 3.0 Hz, C(3)H), 4.5 (1 H, br s, C(2)H), 5.08 (1 H, d, $^2J_{AB}$ = 11.8 Hz, OC*H*$_A$H$_B$Ph), 5.17 (1 H, d, $^2J_{AB}$ = 11.8 Hz, OCH$_A$*H*$_B$Ph), 5.34 (1 H, bd, *J* = 8 Hz, NH), 7.27 (2 H, d, *J* = 9 Hz, tosyl meta protons), 7.34 (5 H, s, CH_2*Ph*), and 7.71 (2 H, d, *J* = 9 Hz, tosyl ortho protons); *m*/*z* (FAB) 450 (MH^+, 23) and 394 (160, $MH^+ - (CH_3)_2C{=}CH_2$). Found: C, 58.7; H, 5.8; N, 3.0. $C_{22}H_{27}NO_7S$ requires C, 58.8; H, 6.0; N, 3.1.

Benzyl 2(*R*)-[(*tert*-butoxycarbonyl)amino]-3-*p*-toluenesulfonylpropionate [Boc-D-Ser(Ts)-OBn]: mp 95–96 °C; $[\alpha]^{21}_D$ +4.8° (*c* 0.3 in EtOH).

Benzyl 2(*R*)-[(*tert*-Butoxycarbonyl)amino]-3-iodopropionate [Boc-L-Ala(I)-OBn] (3c). A solution of sodium iodide (3.905 g, 26.06 mmol) in dry acetone (20 mL) was added dropwise to a stirred solution of Boc-L-Ser(Ts)-OBn (7.810 g, 17.37 mmol) in dry acetone (20 mL) under nitrogen. The resulting yellow solution was stirred in the dark at ambient temperature for 24 h and then filtered and concentrated under reduced pressure. The residue was dissolved in chloroform (100 mL), washed sequentially with distilled water (2 × 50 mL), sodium thiosulfate (50 mL; 1 M), and distilled water (3 × 50 mL), and then dried over anhydrous sodium sulfate. Concentration under reduced pressure gave a light-sensitive colorless oil which solidified on standing. Recrystallization from a minimum amount of hot ethanol (ca. 5 mL), followed by filtration and trituration with light petroleum, yielded the iodide **3c** as a white crystalline solid (5.665 g, 13.98 mmol, 80%): mp 79–80 °C; [a]$^{21}_D$ −18.6° (*c* 1.0 in EtOH); ν_{max} (KBr disk) 3362.0, 1759.0, 1685.0, and 1515.5 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.45 (9 H, s, OC(C*H*$_3$)$_3$), 3.58 (2 H, m, C(3)H$_2$), 4.55 (1 H, m, C(2)H), 5.18 (1 H, d, $^2J_{AB}$ = 12 Hz, OC*H*$_A$H$_B$Ph), 5.23 (1 H, d, $^2J_{AB}$ = 12 Hz, OCH$_A$*H*$_B$Ph), 5.37 (1 H, bd, *J* = 8 Hz, NH), and 7.38 (5 H, s, CH_2*Ph*); *m*/*z* (FAB) 406 (MH^+, 7), 350 (16, $MH^+ - (CH_3)_2C{=}CH_2$), and 306 (8, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$). Found: C, 44.6; H, 4.8; N, 3.4. $C_{15}H_{20}NO_4I$ requires C, 44.5; H, 5.0; N, 3.4.

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-3-iodopropionate [Boc-D-Ala(I)-OBn] (18): mp 79 °C; $[\alpha]^{21}_D$ +19.4° (*c* 1.0 in EtOH).

The iodides **3c** and **18** were stored in the dark in a vacuum desiccator under nitrogen at ambient temperature. Periodic

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(48) Koehn, P. V.; Kind, C. A. *Arch. Biochem. Biophys.* **1965**, *111*, 614–618.

recrystallization from ethanol (once monthly) removed slight traces of dehydroalanine **16**.

Reactions of Iodide 3c with Zn/Cu Couple under Ultrasonication and General Procedure. A solution of Boc-L-Ala(I)-OBn (**3c**) (0.304 g, 0.75 mmol) in dry benzene (3 mL) and dry DMA (0.20 mL) was added to a dry nitrogen purged flask charged with zinc–copper couple (0.090 g). The resulting mixture was sonicated under nitrogen for 30 min until no starting material remained (as judged by TLC), during which time the bath temperature rose from 22 to 35 °C. Bis(triphenylphosphine)palladium dichloride (0.028 g, 0.04 mmol) was added, followed by the freshly distilled acid chloride (0.75 mmol) and the mixture sonicated under nitrogen for a further 30 min, after which a final bath temperature of 42 °C was recorded. Ethyl acetate (50 mL) was added and the mixture filtered into a separating funnel. Sequential washing with aqueous hydrochloric acid (20 mL; 0.1 M) and distilled water (3 × 20 mL) followed by drying over anhydrous sodium sulfate, filtration, and concentration under reduced pressure gave a crude reaction product. Flash chromatography over silica gel (light petroleum–ethyl acetate gradient) gave the protected 4-oxo-α-amino acid **17**.

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-4-oxo-4-phenylbutanoate (17a): 0.20 g, 0.525 mmol, 70%; mp 82–83 °C (EtOH); $[\alpha]^{23}_D$ +24.7° (*c* 1.0 in CH_2Cl_2); ν_{max} (cap. film) 3463.0, 3373.0, 1743.0, 1713.5 (br), and 1498.5 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.44 (9 H, s, $OC(CH_3)_3$), 3.56 (1 H, dd, $^2J_{AB}$ = 16 Hz and $^3J_{AX}$ = 3 Hz, C(3)H), 3.79 (1 H, dd, $^2J_{AB}$ = 16 Hz and $^3J_{BX}$ = 3 Hz, C(3)H), 4.76 (1 H, m, C(2)H), 5.20 (2 H, s, OCH_2Ph), 5.68 (1 H, d, *J* = 4 Hz, NH), 7.32 (5 H, m, OCH_2Ph), 7.49 (2 H, dd, *J* = 9 and 9 Hz, *m*-PhC=O), 7.60 (1 H, d, *J* = 9 Hz, *p*-PhC=O), and 7.95 (2 H, d, *J* 9 Hz, *o*-PhC=O); δ_H (300 MHz; MeOH-d_4) 1.41 (9 H, s, $OC(CH_3)_3$), 3.56 (2 H, d, *J* = 6 Hz, C(3)H_2), 4.74 (1 H, br t, *J* = 6 Hz, C(2)H), 5.15 (2 H, s, OCH_2Ph), 7.30 (5 H, br s, OCH_2Ph), 7.49 (2 H, dd, *J* = 9 and 9 Hz, *m*-PhC=O), 7.61 (1 H, d, *J* = 9 Hz, *p*-PhC=O), and 7.95 (2 H, d, *J* 9 Hz, *o*-PhC=O); *m*/*z* (FAB) 384 (MH^+, 2), 328 (9, $MH^+ - (CH_3)_2C{=}CH_2$), and 284 (10, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$). Found: C, 68.75; H, 6.6; N, 3.7. $C_{22}H_{25}NO_5$ requires C, 68.9; H, 6.6; N. 3.65.

Benzyl 2(*R*)-[(*tert*-butoxycarbonyl)amino]-4-oxo-4-phenylbutanoate (19a): 0.18 g, 0.48 mmol, 62%; mp 82–83 °C; $[\alpha]^{21}_D$ −23.9° (*c* 1.0 in CH_2Cl_2).

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-4-oxo-4-(2′-furyl)butanoate (17b): 0.252 g, 0.68 mmol, 90%; found M^+ 373.1541, $C_{20}H_{23}NO_6$ requires 373.1525; $[\alpha]^{21}_D$ +27.6° (*c* 1.0 in CH_2Cl_2); ν_{max} (cap. film) 3431.5, 3369.0, 1743.5, 1714.0, 1675.5, and 1499.5 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.41 (9 H, s, $OC(CH_3)_3$), 3.39 (1 H, dd, $^2J_{AB}$ = 17.8 Hz and $^3J_{AX}$ = 4.5 Hz, C(3)H), 3.58 (1 H, dd, $^2J_{AB}$ = 17.8 Hz and $^3J_{BX}$ = 4.5 Hz, C(3)H), 4.71 (1 H, m, C(2)H), 5.15 (1 H, dd, $^2J_{AB}$ = 12.3 Hz, OCH_AH_BPh), 5.20 (1 H, dd, $^2J_{AB}$ = 12.3 Hz, OCH_AH_BPh), 5.6 (1 H, br d, *J* = 8.6 Hz, NH), 6.54 (1 H, dd, *J* = 1.7 and 3.6 Hz, C(4′)H), 7.20 (1 H, dd, *J* = 0.7 and 3.6 Hz, C(3′)H), 7.32 (5 H, m, OCH_2Ph), and 7.59 (1 H, dd, *J* = 0.7 and 1.7 Hz, C(5′)H); *m*/*z* (EI) 373 (MH^+) and 317 ($MH^+ - (CH_3)_2C{=}CH_2$).

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-4-oxopentanoate (17c): 0.192 g, 0.60 mmol, 80%; found M^+ 321.1581, $C_{17}H_{23}NO_5$ requires 321.1576; $[\alpha]^{21}_D$ +14.5° (*c* 1.0 in CH_2Cl_2); ν_{max} (cap. film) 3367.0, 1740–1715, and 1500.0 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 1.42 (9 H, s, $OC(CH_3)_3$), 2.13 (3 H, s, CH_3CO), 2.94 (1 H, dd, $^2J_{AB}$ = 16 Hz and $^3J_{AX}$ = 4 Hz, C(3)H), 3.18 (1 H, dd, $^2J_{AB}$ = 16 Hz and $^3J_{BX}$ = 4 Hz, C(3)H), 4.5 (1 H, m, C(2)H), 5.15 (2 H, s, OCH_2Ph), 5.5 (1 H, br d, NH), and 7.33 (5 H, m, OCH_2Ph); *m*/*z* (EI) 322 (MH^+, 20), 266 (78, $MH^+ - (CH_3)_2C{=}CH_2$), and 222 (56, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$).

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-4-oxohexanoate (17d): 0.210 g, 0.63 mmol, 83%; found MH^+ 336.1834, $C_{18}H_{26}NO_5$ requires 336.1821; $[\alpha]^{21}_D$ +13.4° (*c* 1.0 in CH_2Cl_2); ν_{max} (cap. film) 3371.5, 1740–1715, and 1499.5 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 1.00 (3 H, t, *J* = 7.3 Hz, CH_2CH_3), 1.41 (9 H, s, $OC(CH_3)_3$), 2.39 (2 H, q, *J* = 7.3 Hz, CH_3CH_2CO), 2.90 (1 H, dd, $^2J_{AB}$ = 17 Hz and $^3J_{AX}$ = 4 Hz, C(3)H), 3.16 (1 H, dd, $^2J_{AB}$ = 17 Hz and $^3J_{BX}$ = 4 Hz, C(3)H), 4.55 (1 H, m, C(2)H), 5.11 (1 H, d, $^2J_{AB}$ = 12 Hz, OCH_AH_BPh), 5.19 (1 H, d, $^2J_{AB}$ = 12 Hz, OCH_AH_BPh), 5.55 (1 H, br d, NH), and 7.32 (5 H, m, OCH_2Ph); *m*/*z* (EI) 336 (MH^+, 1), 280 (32, $MH^+ - (CH_3)_2C{=}CH_2$), and 236 (48, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$).

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-4-oxo-6-methylheptanoate (17e): 0.206 g, 0.57 mmol, 76%; found MH^+ 364.2186, $C_{20}H_{30}NO_5$ requires 364.2126; $[\alpha]^{21}_D$ +8.5° (*c* 1.0 in CH_2Cl_2); ν_{max} (cap. film) 3434.0, 3373.0, 1740–1715, and 1449.5 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 0.86 (2 H, d, *J* = 6.5 Hz, $CH(CH_3)_2$), 0.88 (2 H, d, *J* = 6.5 Hz, $CH(CH_3)_2$), 0.98 (2 H, d, *J* = 6.5 Hz, $CH(CH_3)_2$), 1.42 (9 H, s, $OC(CH_3)_3$, 2.06 (1 H, m, $CH_2CH(CH_3)_2$), 2.21 (1.3 H, d, *J* = 2.6 Hz, $CHCH_2CO$), 2.26 (0.7 H, d, *J* = 2.8 Hz, $CHCH_2CO$), 2.9 (1 H, dd, $^2J_{AB}$ = 18 Hz and $^3J_{AX}$ = 4 Hz, C(3)H), 3.2 (1 H, dd, $^2J_{AB}$ = 18 Hz and $^3J_{BX}$ = 4 Hz, C(3)H), 4.5 (1 H, m, C(2)H), 5.15 (2 H, s, OCH_2Ph), 5.58 (1 H, br d, NH), and 7.33 (5 H, m, OCH_2Ph); *m*/*z* (EI) 364 (MH^+, 2), 308 (16, $MH^+ - (CH_3)_2C{=}CH_2$), and 264 (15, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$).

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-4-oxo-6,6-dimethylheptanoate (17f): 0.238 g, 0.63 mmol, 84%, found MH^+ 378.2342, $C_{21}H_{32}NO_5$ requires 378.2280; $[\alpha]^{21}_D$ +11.7° (*c* 1.0 in CH_2Cl_2); ν_{max} (cap. film) 3437.0, 3374.0, 1740–1715, and 1499.5 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 0.96 (9 H, s, $CH_2C(CH_3)_3$), 1.42 (9 H, s, $OC(CH_3)_3$), 2.25 (2 H, s, $COCH_2C(CH_3)_3$), 2.9 (1 H, dd, $^2J_{AB}$ = 18 Hz and $^3J_{AX}$ = 4 Hz, C(3)H), 3.2 (1 H, dd, $^2J_{AB}$ = 18 Hz and $^3J_{BX}$ = 4 Hz, C(3)H), 4.5 (1 H, m, C(2)H), 5.15 (2 H, s, OCH_2Ph), 5.55 (1 H, br d, NH), and 7.33 (5 H, m, OCH_2Ph); *m*/*z* (EI) 378 (MH^+, 12), 322 (57, $MH^+ - (CH_3)_2C{=}CH_2$), and 278 (15, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4-oxo-5-phenylpentanoate (17g). Prepared by the usual method and purified by flash chromatography using 30:1 toluene/ethyl acetate as the eluent: 0.122 g, 0.31 mmol, 41%; found MH^+ 398.1926, $C_{23}H_{28}NO_5$ requires 398.1930; $[\alpha]^{20}_D$ −5.8° (*c* 1.2 in EtOH); ν_{max} (cap. film) 3443, 3379, 1714 (br) and 1496 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 1.40 (9 H, s, $OC(CH_3)_3$), 2.96 (1 H, dd, $^2J_{AB}$ = 18.3 Hz and $^3J_{AX}$ = 4.1 Hz, C(3)H), 3.20 (1 H, dd, $^2J_{AB}$ = 18.3 Hz and $^3J_{BX}$ = 4.1 Hz, C(3)H), 3.65 (2 H, s, $PhCH_2CO$), 4.51 (1 H, m, C(2)H), 5.11 (2 H, s, OCH_2Ph), 5.50 (1 H, br d, NH), and 7.33 (5 H, m, OCH_2Ph); *m*/*z* (EI) 398 (MH^+, 0.4), 342 (7, $MH^+ - (CH_3)_2C{=}CH_2$), 250 (31, $MH^+ - (CH_3)_2C{=}CH_2 - PhCH_3$), and 206 (16, $MH^+ - (CH_3)_2C{=}CH_2 - PhCH_3 - CO_2$).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4-oxo-6-phenyl-(*E*)-hex-5-enoate (17h). Prepared by the usual method and purified by flash chromatography using 30:1 toluene/ethyl acetate as the eluent. Crystallization from EtOH/light petroleum by diffusion gave the product (0.221 g, 0.54 mmol, 72%): mp 92–93 °C; $[\alpha]^{25}_D$ +38.9° (*c* 0.1 in CH_2Cl_2); ν_{max} (cap. film) 3452, 3383, 1745, 1715 (br), 1662, 1610, and 1497 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 1.42 (9 H, s, $OC(CH_3)_3$), 3.23 (1 H, dd, $^2J_{AB}$ = 17.9 Hz and $^3J_{AX}$ = 4.1 Hz, C(3)H), 3.48 (1 H, dd, $^2J_{AB}$ = 17.9 Hz and $^3J_{BX}$ = 4.3 Hz, C(3)H), 4.65 (1 H, m, C(2)H), 5.18 (2 H, s, OCH_2Ph), 5.62 (1 H, br d, NH), 6.69 (1 H, d, *J* = 16.3 Hz, CH=CHCO), and 7.26–7.59 (11 H, m, PhCH=CH, OCH_2Ph, and PhCH=CH); *m*/*z* (EI) 354 ($MH^+ - (CH_3)_2C{=}CH_2$, 2), 310 (5, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$), 262 (11, $MH^+ - (CH_3)_2C{=}CH_2 - PhCH_3$), and 218 (10, $MH^+ - (CH_3)_2C{=}CH_2 - PhCH_3 - CO_2$). Found: C, 70.4; H, 6.65; N, 3.4 $C_{24}H_{27}NO_5$ requires C, 70.2; H, 6.35; N, 3.35.

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4-oxo-4-(4′-methoxyphenyl)butanoate (17i). Prepared by the usual method and purified by flash chromatography using 30:1 toluene/ethyl acetate as the eluent. Crystallization from EtOH/light petroleum by diffusion gave the product (0.133 g, 0.32 mmol, 43%): mp 92–93 °C; $[\alpha]^{16}_D$ +10.5° (*c* 0.21 in EtOH); ν_{max} (cap. film) 3442, 3392, 1713 (br), 1504, and 1259 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 1.42 (9 H, s, $OC(CH_3)_3$), 3.46 (1 H, dd, $^2J_{AB}$ = 18.0 Hz and $^3J_{AX}$ = 4.1 Hz, C(3)H), 3.72 (1 H, dd, $^2J_{AB}$ = 18.0 Hz and $^3J_{BX}$ = 4.2 Hz, C(3)H), 3.86 (3 H, s, *Me*O), 4.72 (1 H, m, C(2)H), 5.17 (2 H, s, OCH_2Ph), 5.70 (1 H, br d, NH), 6.92 (2 H, m), 7.29 (5 H, m, OCH_2Ph), and 7.90 (2 H, m); *m*/*z* (EI) 414 (MH^+, 3), 358 (15, $MH^+ - (CH_3)_2C{=}CH_2$), 314 (21, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$), 266 (8, $MH^+ - (CH_3)_2C{=}CH_2 - PhCH_3$) and 222 (20, $MH^+ - (CH_3)_2C{=}CH_2 - PhCH_3 - CO_2$). Found: C, 66.8; H, 6.6; N, 3.4. $C_{23}H_{27}NO_6$ requires C, 66.4; H, 6.45; N, 3.4.

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4-oxo-4-(4′-acetoxyphenyl)butanoate (17j). Prepared by the usual method and purified by flash chromatography using 30:1 toluene/ethyl acetate as the eluent to give the product as an oil (0.212 g, 0.48 mmol, 63%); found $MH^+ - (CH_3)_2C{=}CH_2$ 386.1286, $C_{20}H_{20}NO_7$ requires 386.1281; $[\alpha]^{17}_D$ +23.7° (*c* 1.0 in CH_2Cl_2); ν_{max} (cap. film.) 3441, 3387, 1755, 1714, and 1500 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 1.42

(9 H, s, $OC(CH_3)_3$), 2.32 (3 H, s, $MeCO_2$), 3.50 (1 H, dd, $^2J_{AB}$ = 18.1 Hz and $^3J_{AX}$ = 4.1 Hz, C(3)H), 3.73 (1 H, dd, $^2J_{AB}$ = 18.1 Hz and $^3J_{BX}$ = 4.3 Hz, C(3)H), 4.72 (1 H, m, C(2)H), 5.17 (2 H, s, OCH_2Ph), 5.66 (1 H, br d, NH), 7.19 (2 H, m), 7.29 (5 H, m, OCH_2Ph) and 7.94 (2 H, m); *m/z* (EI) 386 ($MH^+ - (CH_3)_2C{=}CH_2$, 40), 294 (15, $MH^+ - (CH_3)_2C{=}CH_2 - PhCH_3$), and 250 (51, $MH^+ - (CH_3)_2C{=}CH_2 - PhCH_3 - CO_2$).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4-oxo-5-chloropentanoate (17k). The zinc reagent **13** (0.75 mmol) was prepared using the general procedure. Bis(triphenylphosphine)palladium dichloride (0.028 g, 0.04 mmol) was then added followed by freshly distilled chloroacetyl chloride (0.060 mL, 0.085 g, 0.75 mmol) and the mixture stirred at room temperature for 30 min. Usual workup and flash chromatography over silica gel gave the following: a high-running component, the chloro ketone **17k** as a colored oil, which solidified on standing (0.103 g, 0.29 mmol, 39%) [mp 71–73 °C; found MH^+ 356.1359, $C_{19}H_{23}NO_5Cl$ requires 356.1254; $[\alpha]^{21}_D$ +32.0° (*c* 0.8 in EtOH); ν_{max} (KBr disk) 3329.5, 1740–1717, 1695.0, and 1531.5 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 1.42 (9 H, s, $OC(CH_3)_3$), 3.14 (1 H, dd, $^2J_{AB}$ = 18.1 Hz and $^3J_{AX}$ = 4.7 Hz, C(3)H), 3.29 (1 H, dd, $^2J_{AB}$ = 18.1 Hz and $^3J_{BX}$ = 4.5 Hz, C(3)H), 4.04 (2 H, s, $ClCH_2CO$), 4.62 (1 H, m, C(2)*H*), 5.16 (2 H, s, OCH_2Ph), 5.47 (1 H, br d, *J* = 8 Hz, NH), and 7.33 (5 H, m, OCH_2Ph); *m/z* (EI) 356 (MH^+, 4), 300 (28, $MH^+ - (CH_3)_2C{=}CH_2$), and 256 (22, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$)], and a low-running component, identified as benzyl 2-(*S*)-[(*tert*-butoxycarbonyl)amino]-4-oxopentanoate (**17c**) (0.020 g, 0.06 mmol, 8%).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4-oxo-5-acetoxypentanoate (17l). A solution of Boc-L-Ala(I)-OBn (**3c**) (1.216 g, 3.00 mmol) in dry benzene (5 mL) and dry DMA (0.80 mL) was added to a dry nitrogen-purged flask charged with zinc–copper couple (0.40 g). The resulting mixture was sonicated under nitrogen for 1 h until no starting material remained (as judged by TLC). Bis(triphenylphosphine)palladium dichloride (0.112 g, 0.16 mmol) was added followed by freshly distilled acetoxyacetyl chloride (0.323 mL, 0.410 g, 3.00 mmol) and the mixture sonicated under nitrogen for a further 1 h. Ethyl acetate (50 mL) was added, and the flask contents were filtered into a separating funnel. Sequential washing with aqueous hydrochloric acid (20 mL; 0.1 M) and distilled water (3 × 20 mL) followed by drying over anhydrous sodium sulfate, filtration, and concentration under reduced pressure gave a crude reaction product. Flash chromatography over silica gel (light petroleum–ethyl acetate gradient) gave the acetoxy ketone **17l** as a colored oil, which solidified on standing (0.726 g, 1.91 mmol, 64%): mp 74–75 °C (EtOH); $[\alpha]^{21}_D$ −17.1° (*c* 1.0 in EtOH); ν_{max} (KBr disk) 3357.5, 1757.0, 1733.0, 1675.5, and 1519.8 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.42 (9 H, s, $OC(CH_3)_3$), 2.16 (3 H, s, CH_3CO), 2.99 (1 H, dd, $^2J_{AB}$ = 18.0 Hz and $^3J_{AX}$ = 4.4 Hz, C(3)H), 3.11 (1 H, dd, $^2J_{AB}$ = 18.0 Hz and $^3J_{BX}$ = 4.5 Hz, C(3)H), 4.58 (1 H, m, C(2)H), 4.59 (2 H, s, $AcOCH_2CO$), 5.16 (2 H, s, OCH_2Ph), 5.49 (1 H, br d, *J* = 8 Hz, NH), and 7.33 (5 H, m, CH_2Ph); *m/z* (EI) 380 (MH^+, 2), 324 (8, $MH^+ - (CH_3)_2C{=}CH_2$), and 280 (5, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$). Found: C, 60.3; H, 6.7; N, 3.45. $C_{19}H_{25}NO_7$ requires C, 60.2; H, 6.6; N, 3.7.

***N*-Phthaloylglycine Acid Chloride (PhthGlyCl).** Oxalyl chloride (0.270 mL, 0.393 g, 3.10 mmol) was added to a stirred suspension of *N*-phthaloylglycine (0.616 g, 3.00 mmol) in dry benzene (2 mL). Dry *N*,*N*-dimethylformamide (DMF) (ca. 0.010 mL) was then added cautiously. The resulting mixture was stirred under nitrogen at room temperature until it became homogeneous (ca. 30 min) and then used directly in the following reaction.

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4-oxo-5-[(phthaloyl)amino]pentanoate (17m). The zinc reagent was prepared on a 3 mmol scale as described above. Bis(triphenylphosphine)palladium dichloride (0.112 g, 0.16 mmol) was added followed by a freshly prepared solution of *N*-phthaloylglycine acid chloride (3.00 mmol) in dry benzene (2 mL) and the mixture sonicated under nitrogen for a further 1 h. Ethyl acetate (50 mL) was added and the mixture filtered into a separating funnel. Sequential washing with aqueous hydrochloric acid (20 mL; 0.1 M) and distilled water (3 × 20 mL) followed by drying over anhydrous sodium sulfate, filtration, and concentration under reduced pressure gave a crude reaction product. Flash chromatography over silica gel (light petroleum–ethyl acetate gradient) gave the amino ketone **17i** as a colored oil, which solidified on standing (0.736 g, 1.58 mmol, 53%): mp 80–81 °C (EtOH); $[\alpha]^{21}_D$ −9.0° (*c* 1.0 in EtOH); ν_{max} (KBr disk) 3356.0, 1776.0, 1750–1700, 1680.5, and 1519.8 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.43 (9 H, s, $OC(CH_3)_3$), 3.10 (1 H, dd, $^2J_{AB}$ = 18.0 Hz and $^3J_{AX}$ = 4.3 Hz, C(3)H), 3.27 (1 H, dd, $^2J_{AB}$ = 18.0 Hz and $^3J_{BX}$ = 4.4 Hz, C(3)H), 4.45 (1 H, d, $^2J_{AB}$ = 17 Hz, NCH_AH_BCO), 4.55 (1 H, d, $^2J_{AB}$ = 17 Hz, NCH_AH_BCO), 4.60 (1 H, m, *J* = 4.2 Hz, C(2)H), 5.12 (1 H, d, $^2J_{AB}$ = 12 Hz, OCH_AH_BPh), 5.17 (1 H, d, $^2J_{AB}$ = 12 Hz, OCH_AH_BPh), 5.47 (1 H, br d, *J* = 5 Hz, NH), 7.33 (5 H, m, CH_2Ph), 7.75 (2 H, dd, *J* = 3.1 and 5.5 Hz, C(2′)H and C(3′)H phthaloyl), and 7.88 (2 H, dd, *J* = 3.0 and 5.3 Hz, C(1′)H and C(4′)H phthaloyl); *m/z* (EI) 467 (MH^+, 0.1), 410 (22, $MH^+ - (CH_3)_2C{=}CH_2$), and 367 (81, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$). Found: C, 64.6; H, 5.6; N, 5.9. $C_{25}H_{26}N_2O_7$ requires C, 64.4; H, 5.6; N, 6.0.

2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4-phenylbutanoic Acid 25. Palladium on charcoal (5%) (0.10 g; 50% wet) was added to a solution of benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-4-oxo-4-phenylpropionate (**17a**) (0.170 g, 0.44 mmol) in ethanol (5 mL) and water (1 mL). The resulting mixture was agitated under a hydrogen atmosphere at 40 psi for 24 h, after which TLC analysis (20% ethyl acetate–light petroleum) showed no starting material remained. The reaction mixture was then filtered through a Celite pad and concentrated under reduced pressure to give Boc-homophenylalanine **25** as a foam (0.120 g, 0.43 mmol, 98%): $[\alpha]^{25}_D$ +5.9° (*c* 1.4 in EtOH) (lit.[49] +6.0° (*c* 1.0 in EtOH)); ν_{max} (cap. film) 3335, 2978, and 1720 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.48 (9 H, s, $OC(CH_3)_3$), 2.05 (1 H, m,C(3)H), 2.22 (1 H, m, C(3)H), 2.75 (2 H, m, $C(4)H_2$), 4.40 (1 H, m, C(2)H), 5.16 (1 H, br d, *J* = 6 Hz, NH), 7.23 (3 H, m, *o*-, *p*-Ph), and 7.32 (2 H, m, *m*-Ph); *m/z* (FAB) 624 [$(2MNa + Na)^+$ 17], and 324 [7, $(MNa + Na)^+$].

Preparation of Protected 3-Aryl Alanines. General Procedure. A solution of Boc-L-Ala(I)-OBn (**3c**) (0.304 g, 0.75 mmol) in dry benzene (3 mL) and dry DMA (0.20 mL) was added to a dry nitrogen-purged flask charged with zinc–copper couple (0.090 g). The resulting mixture was sonicated under nitrogen for 30 min until no starting material remained (as judged by TLC). Bis(tri-*o*-tolylphosphine)palladium dichloride (0.035 g, 0.04 mmol) was added followed by the aromatic iodide (0.75 mmol). The resulting mixture was stirred under nitrogen at 50 °C for 1 h and then allowed to cool. Ethyl acetate (50 mL) was added and the mixture filtered into a separating funnel. Sequential washing with aqueous hydrochloric acid (20 mL; 0.1 M) and distilled water (3 × 20 mL) followed by drying over anhydrous sodium sulfate, filtration, and concentration under reduced pressure gave a crude reaction product. Flash chromatography over silica gel (light petroleum–ethyl acetate gradient) then afforded the protected 3-aryl alanine.

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-3-phenylpropionate (Boc-L-Phe-OBn) (26a): 0.146 g, 0.42 mmol, 55%; mp 62–63 °C; found MH^+ 356.1864, $C_{21}H_{26}NO_4$ requires 356.1862; $[\alpha]^{21}_D$ −10.0° (*c* 1.0 in EtOH); ν_{max} (KBr disk) 3365.5, 1732.0, 1684.0, and 1524.0 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.41 (9 H, s, $OC(CH_3)_3$), 3.08 (2 H, m, *J* = 5 Hz, $C(3)H_2$), 4.63 (1 H, m, *J* = 6 Hz, C(2)H), 4.97 (1 H, br d, *J* = 8 Hz, NH), 5.10 (1 H, d, $^2J_{AB}$ = 12.2 Hz, OCH_AH_BPh), 5.17 (1 H, d, $^2J_{AB}$ = 12.2 Hz, OCH_AH_BPh), 7.05 (2 H, m, *o*-$PhCH_2C$), and 7.35 (8 H, m, OCH_2Ph and *m*-, *p*-$PhCH_2C$); *m/z* (FAB) 356 (MH^+, 52), 300 (85, $MH^+ - (CH_3)_2C{=}CH_2$), and 256 (88, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$).

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-3-(1′-naphthyl)propionate (26b): 0.192 g, 0.48 mmol, 64%; mp 95–96 °C; found MH^+ 406.2017, $C_{25}H_{28}NO_4$ requires 406.2017; $[\alpha]^{21}_D$ −16.6° (*c* 1.0 in EtOH); ν_{max} (cap. film) 3370.0, 1750–1698, and 1499.0 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.38 (9 H, s, $OC(CH_3)_3$), 3.49 (1 H, dd, $^2J_{AB}$ = 14.1 Hz and $^3J_{AX}$ = 6.6 Hz, C(3)H), 3.60 (1 H, dd, $^2J_{AB}$ = 14.2 Hz and $^3J_{BX}$ = 6.7 Hz, C(3)H), 4.78 (1 H, m, C(2)H), 5.08 (3 H, m, OCH_2Ph and NH), 7.18 (2 H, m, C(2′)H and C(3′)H), 7.35 (5 H, m, OCH_2Ph), 7.50 (2 H, m, C(6′)H and C(7′)H), 7.74 (1 H, d, *J* = 8 Hz, C(4′)H), 7.85 (1 H, d, *J* = 7 Hz, C(5′)H), and 8.07 (1 H, d, *J* = 8 Hz, C(8′)H); *m/z* (FAB) 406 (MH^+, 4), 350 (20, $MH^+ - (CH_3)_2C{=}CH_2$), and 306 (32, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$).

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-3-(2′-acet-

(49) Weller, H. N.; Gordon, E. M. *J. Org. Chem.* **1982**, *47*, 4160–4161.

oxyphenyl)propionate (26c): 0.040 g, 0.097 mmol, 13%; found MH^+ 414.1903, $C_{23}H_{28}NO_6$ requires 414.1917; $[\alpha]^{21}_D$ −11.0° (*c* 0.2 in EtOH); ν_{max} (cap. film) 3377.5, 1748.0, 1717.0, and 1499.0 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.39 (9 H, s, $OC(CH_3)_3$), 2.27 (3 H, s, CH_3CO), 2.90 (1 H, dd, $^2J_{AB}$ = 14.1 Hz and $^3J_{AX}$ = 7.2 Hz, C(3)H), 3.03 (1 H, dd, $^2J_{AB}$ = 14.0 Hz and $^3J_{BX}$ = 6.0 Hz, C(3)H), 4.62 (1 H, m, *J* = 7 Hz, C(2)H), 5.08 (1 H, br, NH), 5.12 (2 H, s, OCH_2Ph), 7.04 (1 H, d *J* = 8 Hz, C(6′)H), 7.10 (2 H, m, C(4′)H and C(5′)H), and 7.25–7.35 (6 H, m, OCH_2Ph and C(3′)H); *m/z* (FAB) 414 (MH^+, 1), 358 (6, $MH^+ - (CH_3)_2C{=}CH_2$), and 314 (22, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$).

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-3-(2′-methoxyphenyl)propionate (26e): 0.139 g, 0.38 mmol, 50%; mp 71–72 °C; found MH^+ 386.1970, $C_{22}H_{28}NO_5$ requires 386.1967; $[\alpha]^{21}_D$ −10.9° (*c* 1.0 in EtOH); ν_{max} (cap. film) 3418.5, 1760–1701, and 1496.0 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.41 (9 H, s, $OC(CH_3)_3$), 3.12 (2 H, d, *J* = 6 Hz, C(3)H_2), 3.82 (3 H, s, $ArOCH_3$), 4.61 (1 H, m, *J* = 7 Hz, C(2)H), 5.12 (1 H, d, $^2J_{AB}$ = 12.4 Hz, OCH_AH_BPh), 5.17 (1 H, d, $^2J_{AB}$ = 12.4 Hz, OCH_AH_BPh), 5.27 (1 H, br d, *J* = 8 Hz, NH), 6.90 (2 H, d, C(3′)H and C(5′)H), 7.07 (1 H, d *J* = 6 Hz, C(6′)H), and 7.35 (6 H, m, OCH_2Ph and C(4′)H); *m/z* (FAB) 386 (MH^+, 2), 330 (8, $MH^+ - (CH_3)_2C{=}CH_2$), and 286 (39, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$).

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-3-(4′-acetoxyphenyl)propionate (26f): 0.165 g, 0.39 mmol, 53%; mp 88–89 °C (EtOH); $[\alpha]^{21}_D$ −17.7° (*c* 0.8 in EtOH); ν_{max} (cap. film) 3374.0, 1745.0, 1717.0, and 1508.5 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.41 (9 H, s, $OC(CH_3)_3$), 2.29 (3 H, s, CH_3CO), 3.07 (2 H, m, C(3)H_2), 4.62 (1 H, m, *J* = 6 Hz, C(2)H), 5.00 (1 H, br d, *J* = 8 Hz, NH), 5.09 (1 H, d, $^2J_{AB}$ = 12.2 Hz, OCH_AH_BPh), 5.18 (1 H, d, $^2J_{AB}$ = 12.2 Hz, OCH_AH_BPh), 6.94 (2 H, d, *J* = 8 Hz, C(2′)H and C(6′)H), 7.02 (2 H, d *J* = 8 Hz, C(3′)H and C(5′)H), and 7.35 (5 H, m, OCH_2Ph); *m/z* (FAB) 414 (MH^+, 0.5), 358 (3, $MH^+ - (CH_3)_2C{=}CH_2$), and 314 (20, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$). Found: C, 66.4; H, 6.6; N, 3.4. $C_{23}H_{27}NO_6$ requires C, 66.8; H, 6.6; N, 3.4.

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-3-(4′-bromophenyl)propionate (26g): 0.217 g, 0.50 mmol, 67%; mp 88–89 °C (EtOH); $[\alpha]^{21}_D$ −11.3° (*c* 1.0 in EtOH); ν_{max} (cap. film) 3366.0, 1750–1699, and 1489.0 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.41 (9 H, s, $OC(CH_3)_3$), 3.03 (2 H, m, C(3)H_2), 4.63 (1 H, m, *J* = 6 Hz, C(2)H), 4.98 (1 H, br, d, *J* = 9 Hz, NH), 5.08 (1 H, d, $^2J_{AB}$ = 12.1 Hz, OCH_AH_BPh), 5.17 (1 H, d, $^2J_{AB}$ = 12.1 Hz, OCH_AH_BPh), 6.87 (2 H, d, C(2′)H and C(6′)H), and 7.36 (7 H, m, OCH_2Ph, C(3′)H and C(5′)H); *m/z* (FAB) 434 (MH^+, 1), 378 (6, $MH^+ - (CH_3)_2C{=}CH_2$), and 334 (5, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$). Found: C, 58.5; H, 5.4; N, 3.1. $C_{21}H_{24}NO_4Br$ requires C, 58.1; H, 5.6; N, 3.2.

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-3-(4′-fluorophenyl)propionate (26h): 0.100 g, 0.27 mmol, 36%; mp 73–74 °C; found MH^+ 374.1774, $C_{21}H_{25}NO_4F$ requires 374.1768; $[\alpha]^{21}_D$ −22.0° (*c* 0.8 in EtOH); ν_{max} (cap. film) 3366.0, 1750–1697, and 1510.5 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.41 (9 H, s, $OC(CH_3)_3$), 3.05 (2 H, m, C(3)H_2), 4.58 (1 H, m, *J* = 8 Hz, C(2)H), 4.98 (1 H, br d, *J* = 8 Hz, NH), 5.09 (1 H, d, $^2J_{AB}$ = 12.1 Hz, OCH_AH_BPh), 5.18 (1 H, d, $^2J_{AB}$ = 12.1 Hz, OCH_AH_BPh), 6.91 (4 H, m, 4-FC_6H_4), and 7.36 (5 H, m, OCH_2Ph); *m/z* (FAB) 374 (MH^+, 3), 318 (36, $MH^+ - (CH_3)_2C{=}CH_2$), and 274 (19, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$).

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-3-(4′-methylphenyl)propionate (26i): 0.139 g, 0.38 mmol, 50%; mp 71–72 °C; found MH^+ 370.2019, $C_{21}H_{26}NO_4$ requires 370.2018; $[\alpha]^{21}_D$ −15.1° (*c* 1.0 in EtOH); ν_{max} (cap. film) 3370.0, 1750–1713, and 1499.0 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.41 (9 H, s, $OC(CH_3)_3$), 2.30 (3 H, s, $ArCH_3$), 3.04 (2 H, br d, *J* = 6 Hz, C(3)H_2), 4.59 (1 H, m, C(2)H), 4.95 (1 H, br d, *J* = 8 Hz, NH), 5.09 (1 H, d, $^2J_{AB}$ = 12.3 Hz, OCH_AH_BPh), 5.17 (1 H, d, $^2J_{AB}$ = 12.2 Hz, OCH_AH_BPh), 6.91 (2 H, d, C(2′)H and C(6′)H), 7.03 (2 H, d, *J* = 8 Hz, C(3′)H and C(5′)H), and 7.34 (5 H, m, OCH_2Ph); *m/z* (FAB) 370 (MH^+, 4), 314 (20, $MH^+ - (CH_3)_2C{=}CH_2$), and 270 (35, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$).

Benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-3-(4′-nitrophenyl)propionate (26j): 0.186 g, 0.46 mmol, 61%; mp 82–83 °C; found MH^+ 401.1714, $C_{21}H_{25}NO_6$ requires 401.1726; $[\alpha]^{21}_D$ −19.2° (*c* 1.0 in EtOH); ν_{max} (cap. film) 3426.0, 1742.0, 1713.0, and 1522.0 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.42 (9 H, s, $OC(CH_3)_3$), 3.12 (1 H, dd, $^2J_{AB}$ = 13.6 Hz and $^3J_{AX}$ = 5.9 Hz, C(3)H), 3.22 (1 H, dd, $^2J_{AB}$ = 13.6 Hz and $^3J_{BX}$ = 6.1 Hz, C(3)H), 4.65 (1 H, m, *J* = 7 Hz, C(2)H), 5.08 (1 H, br, NH), 5.09 (1 H, d, $^2J_{AB}$ = 12.0 Hz, OCH_AH_BPh), 5.22 (1 H, d, $^2J_{AB}$ = 12.0 Hz, OCH_AH_BPh), 7.14 (2 H, d, *J* = 8 Hz, C(2′)H and C(6′)H), 7.35 (5 H, m, OCH_2Ph), and 8.02 (2 H, d, *J* = 8 Hz, C(3′)H and C(5′)H); *m/z* (FAB) 401 (MH^+, 0.1) and 345 (3, $MH^+ - (CH_3)_2C{=}CH_2$).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-3-(2′-thienyl)propionate (29). This compound was prepared from 2-iodothiophene (0.75 mmol) according to the general procedure for aryl iodide coupling: 0.025 g, 0.075 mol, 10%; mp 62–63 °C; found MH^+ 362.1408, $C_{19}H_{24}NO_4S$ requires 362.1426; $[\alpha]^{21}_D$ −8.9° (*c* 1.2 in EtOH); ν_{max} (cap. film) 3372.0, 1748.0, 1717.0, and 1499.0 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.44 (9 H, s, $OC(CH_3)_3$), 3.35 (2 H, d, *J* = 5 Hz, C(3)H_2), 4.62 (1 H, m, *J* = 8 Hz, C(2)H), 5.14 (1 H, br, NH), 5.15 (2 H, s, OCH_2Ph), 6.70 (1 H, m, C(3′)H), 6.89 (1 H, dd, *J* = 3.4 and 5.1 Hz, C(4′)H), 7.15 (1 H, dd, *J* = 5.1 and 1.1 Hz, C(5′)H), and 7.35 (5 H, m, OCH_2Ph); *m/z* (FAB) 723 (M_2H^+, 4), 362 (22, MH^+), 306 (90, $MH^+ - (CH_3)_2C{=}CH_2$), and 262 (100, $MH^+ - (CH_3)_2C{=}CH_2 - CO_2$).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-3-(2′-pyridyl)propionate (30). This compound was prepared from 2-bromopyridine (0.75 mmol) according to the general procedure for acid chloride coupling: 0.157 g, 0.44 mol, 59%; mp 38–40 °C; found M^+ 356.1778, $C_{20}H_{24}N_2O_4$ requires 356.1736; $[\alpha]_D^{21}$ −19.9° (*c* 1.2 in EtOH); ν_{max} (cap. film) 3371.0, 1745.0, 1713.0, and 1499.0 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 1.42 (9 H, s, $OC(CH_3)_3$), 3.25 (1 H, dd, $^2J_{AB}$ = 14.8 Hz and $^3J_{AX}$ = 4.8 Hz, C(3)H), 3.35 (1 H, dd, $^2J_{AB}$ = 14.7 Hz and $^3J_{BX}$ = 4.7 Hz, C(3)H), 4.74 (1 H, m, C(2)H), 5.06 (1 H, d, $^2J_{AB}$ = 12.4 Hz, OCH_AH_BPh), 5.16 (1 H, d, $^2J_{AB}$ = 12.4 Hz, OCH_AH_BPh), 5.98 (1 H, br d, *J* = 8 Hz, NH), 7.01 (1 H, d, *J* = 8 Hz, C(3′)H), 7.11 (1 H, m, C(5′)H), 7.42 (6 H, m, OCH_2Ph and C(4′)H), and 8.44 (1 H, br d, *J* = 4 Hz, C(6′)H); *m/z* (EI) 356 (MH^+) and 300 ($MH^+ - (CH_3)_2C{=}CH_2$).

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Supplementary Material Available: Experimental details for the reactions of the iodide **3c** with Zn/Cu couple under thermal conditions and for the establishment of optical purity for 4-oxo-α-amino acid derivatives **17a–f** and the protected phenylalanine analogues **26a**, **26e**, **26g**, and **26j**, and ^1H NMR spectra of **17a–17m**, **26b**, **26c**, **26e–26j**, **29**, and **30** (35 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.