Synthesis of Enantiomerically Pure Unsaturated α-Amino Acids Using Serine-Derived Zinc/Copper Reagents

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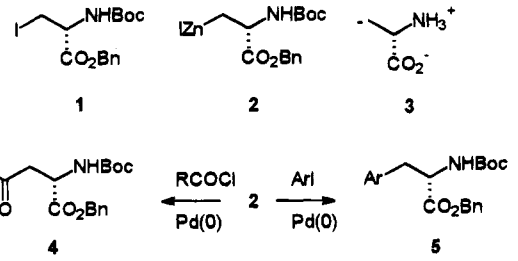
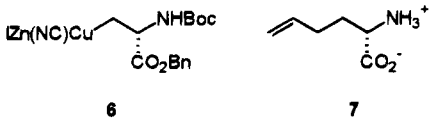
Treatment of the serine-derived organozinc reagent **2**, in benzene/dimethylacetamide, with a THF solution of CuCN·2LiCl gives rise to a zinc/copper reagent **6** which reacts directly with allylic halides and tosylates to give the corresponding enantiomerically pure substitution products **9** in 32–65% yield (11 examples). The reaction proceeds by formal S_N2' displacement of the leaving group. Reaction with propargyl halides gives the corresponding terminal allene **12a**. The zinc reagent **2** may also be prepared directly from protected iodoalanine **1** in THF by the Knochel method. Reaction with propargylic tosylates as electrophiles gives rise to the corresponding protected terminal allenic amino acids in 51–81% yield (four examples); use of enantiomerically enriched propargylic tosylates results in the formation of diastereoisomerically enriched allenic products. Reactions of the zinc/copper reagent **6** with a range of representative electrophiles is explored; use of relatively reactive electrophiles is necessary to obtain satisfactory yields. Finally, the possibility of using the serine-derived iodide **20**, in which the carboxylic acid is protected as a methyl ester, is established. This reagent offers advantages over the corresponding benzyl ester protected reagent **6** for the synthesis of unsaturated amino acids.

There has been continuing interest in the development of new methods for the synthesis of enantiomerically pure α-amino acids.[2] Those approaches which make use of readily available chiral building blocks, for example, by employing derivatives of serine, are especially attractive. Recent work has established that insertion of zinc into the carbon–iodine bond of protected iodoalanine **1**, prepared in four steps from serine, generates a reagent **2** which can function as the synthetic equivalent of the alanine β-anion **3**.[3] Thus, reaction of the zinc reagent **2** with acid chlorides under palladium catalysis gave enantiomerically pure protected 4-oxo amino acids **4**, while reaction with aryl iodides, also under palladium catalysis, gave protected phenylalanine derivatives **5**.[4]



The extensive development by Knochel of functionalized zinc/copper reagents[5] suggested to us that a new alanine β-anion equivalent might be available by treatment of the alanine-derived zinc reagent **2** with CuCN·2LiCl.[6] The enhanced reactivity of zinc/copper reagents, when compared with zinc reagents, implied that such an amino acid derived zinc/copper reagent[7] would be of value in expanding the range of enantiomerically pure amino acids which may be prepared by the alanine β-anion strategy. In this paper we present a full account of our investigations into the synthetic application of the iodoalanine derived zinc/copper reagent **6**.[8] This work has been focussed on the reactions of reagent **6** with allylic and propargylic substrates, as a method for the synthesis of enantiomerically pure unsaturated α-amino acids[9–13] in which the site of unsaturation is remote from the α-center, as for example in butenylglycine **7**.



Results and Discussion

The first investigations into the generation of the amino acid derived zinc/copper reagent **6** were conducted

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(4) Jackson, R. F. W.; Wishart, N.; Wood, A.; James, K.; Wythes, M. J. *J. Org. Chem.* **1992**, *57*, 3397–3404.

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(8) For a preliminary communication, see: Dunn, M. J.; Jackson, R. F. W. *J. Chem. Soc., Chem. Commun.* **1992**, 319–320.

(9) (a) Adlington, R. M.; Baldwin, J. E.; Basak, A.; Kozyrod, R. P. *J. Chem. Soc. Chem. Commun.* **1983**, 944–945. (b) Baldwin, J. E.; Adlington, R. M.; Birch, D. J.; Crawford, J. A.; Sweeney, J. B. *J. Chem. Soc., Chem. Commun.* **1986**, 1339–1340. (c) Baldwin, J. E.; Fieldhouse, R.; Russell, A. T. *Tetrahedron Lett.* **1993**, *34*, 5491–5494.

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(12) Bajgrowicz, J. A.; El Hallaoui, A.; Jacquier, R.; Pigiere, C.; Viallefont, P. *Tetrahedron* **1985**, *41*, 1833–1843.

(13) (a) Chenault, H. K.; Dahmer, J.; Whitesides, G. M. *J. Am. Chem. Soc.* **1989**, *111*, 6354–6364. (b) Baldwin, J. E.; Hulme, C.; Schofield, C. J. *J. Chem. Res. (S)* **1992**, 173; *(M)*, 1517–1526.

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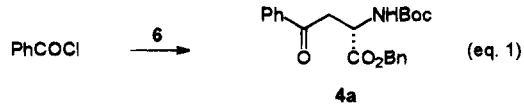
Table 1. Reaction of the Zinc/Copper Reagent 6 with Allylic Substrates

	R^1	R^2	R^3	X	product	yield (%)
8a	H	H	H	Cl	**9a**	65
8b	Ph	H	H	Cl	**9b**	48
8c	H	Me	H	OTs	**9c**	56
8d	CH_2Cl	H	H	Cl	**9d**	44
8e	CH_2Br	H	H	Br	**9e**	48
8f	H	CO_2Me	H	Br	**9f**	51
8g	CO_2Me	H	H	Br	**9g**	49
8h	H	H	CH_2Cl	Cl	**9h**	55
8i	H	Br	H	Br	**9i**	52
8j	H	H	H	Br	**9a**	32
8k	H	H	H	OTs	**9a**	51
8l	Ph	H	H	Br	**9b**	40

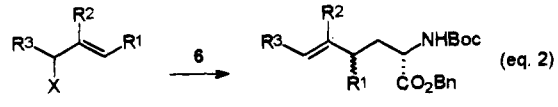
by addition of an equimolar amount of a solution of CuCN·2LiCl in tetrahydrofuran to a solution of the iodoalanine-derived zinc reagent **2** at −10 °C in benzene/dimethylacetamide, followed by brief warming to 0 °C. Recooling of the solution to −25 °C and addition of benzoyl chloride allowed the formation of the 4-oxo α-amino acid **4a** identical to that prepared by the palladium-catalyzed reaction of the zinc reagent **2** with benzoyl chloride, albeit in moderate yield (38%) (eq 1).



(eq. 1)

4a

Encouraged by this result, which was our first indication that zinc/copper reagents with a β-nitrogen substituent were sufficiently stable to be useful reagents,[14] we set out to explore the reactions of the zinc/copper reagent **6** with allylic halides and tosylates **8**. Moderate to good yields of the expected substitution products **9** were obtained, and in all cases where a distinction was possible, there was only evidence of the formal S_N2' product (eq 2), consistent with the usual behaviour of



(eq. 2)

8 **9**

zinc/copper reagents.[4,5,15] In cases where the formation of two diastereoisomeric products is possible, no significant diastereoselectivity was observed. Our results are summarized in Table 1. In all cases, yields are based on protected iodoalanine and therefore indicate the overall efficiency of the three-step process. Use of limiting amounts of electrophile results in significantly higher yields based on the amount of electrophile used.

Two cases were examined in which the possibility for double substitution existed. Use of 1,3-dichloroprop-1-ene[16] led to the isolation of the 2:1 adduct **10** (eq 3), while use of 3,4-dichlorobut-1-ene gave only the 1:1 adduct **9h**. This is presumably a reflection of the lower reactivity of the internal double bond of the adduct **9h** toward the

(14) For a recent discussion of the preparation of β-amido zinc and zinc/copper reagents, see: Duddu, R.; Eckhardt, M.; Furlong, M.; Knoess, H. P.; Berger, S.; Knochel, P. *Tetrahedron* **1994**, *50*, 2415–2432.

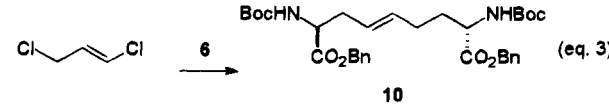
(15) (a) Nakamura, E.; Aoki, S.; Sekiya, K.; Oshino, H.; Kuwajima, I. *J. Am. Chem. Soc.* **1987**, *109*, 8056–8066. (b) Ochiai, H.; Tamaru, Y.; Tsubaki, K.; Yoshida, Z.-i. *J. Org. Chem.* **1987**, *52*, 4418–4420. (c) Sekiya, K.; Nakamura, E. *Tetrahedron Lett.* **1988**, *29*, 5155–5156.

(16) Chen, H. H.; Gage, J. L; Barrett, S. D.; Knochel, P. *Tetrahedron Lett.* **1990**, *31*, 1829–1832.

Table 2. Reaction of the Zinc/Copper Reagent 6 with Propargylic Substrates

	R^1	X	product	yield (%)
11a	H	OTs	**12a**	60
11b	Me	OTs	**12b**	52
11e	H	Cl	**12a**	49
11f	H	Br	**12a**	55

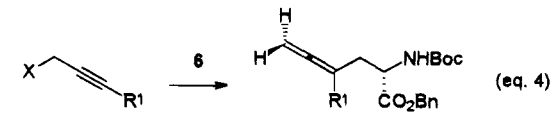
zinc/copper reagent **6**, compared to 3,4-dichlorobutene with a terminal double bond. In cases for which direct comparisons were made, allylic chlorides and allylic tosylates tend to give better yields of product than the corresponding bromides.



(eq. 3)

10

An investigation of the reaction of the zinc/copper reagent **6** with propargylic substrates was carried out as a potential route to allenic amino acids.[17,18] Reaction of reagent **6** with propargylic halides and tosylate **11** gave in each case the expected terminal allenes **12a** and **12b** (eq 4) with no detectable amounts of the corresponding

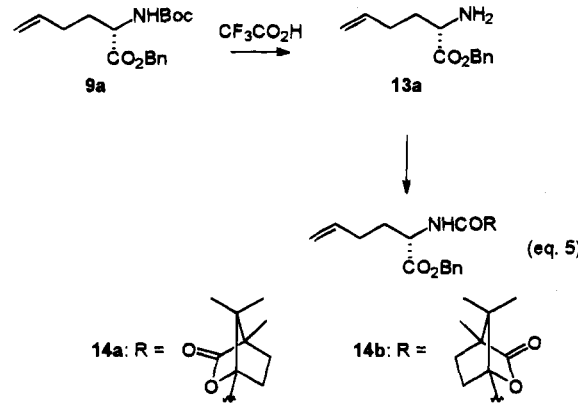


(eq. 4)

11 **12**

acetylenes (Table 2).

Although palladium-catalyzed reactions of the zinc reagent **2** with electrophiles proceed without racemization at the α-center,[3] it was considered essential to establish that this was also the case for reactions of the zinc/copper reagent **6**. The enantiomeric purity of protected butenylglycine **9a** was established by ^1H NMR analysis of the corresponding camphanamides **14a** and **14b**, prepared using standard procedures *via* the free amine **13a** (eq 5).



(eq. 5)

9a **13a**

The enantiomeric purity of protected 2-aminohexa-4,5-dienoic acid **12a** was established directly to a higher level of precision by GLC analysis. Thus, the enantiomeric compound *ent*-**12a** was prepared from (*S*)-iodoalanine

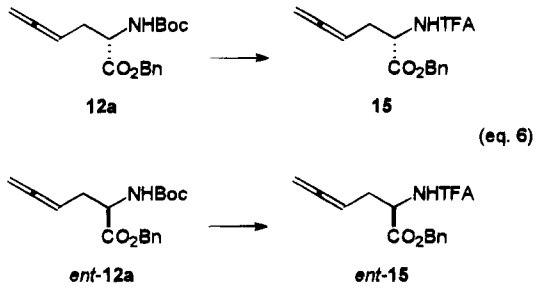
(17) Chilton, W. S.; Tsou, G.; Kirk, L.; Benedict, R. G. *Tetrahedron Lett.* **1968**, 6283–6285.

(18) For approaches to the synthesis of racemic allenic amino acids, see (a) Cazes, B.; Djahanbini, D.; Goré, J.; Genêt, J.-P.; Gaudin, J.-M. *Synthesis* **1988**, 983–985. (b) Black, D. K.; Landor, S. R. *J. Chem. Soc. (C)* **1968**, 281–283. (c) Black, D. K.; Landor, S. R. *J. Chem. Soc. (C)* **1968**, 283–287. For an enantioselective approach, see ref 9.

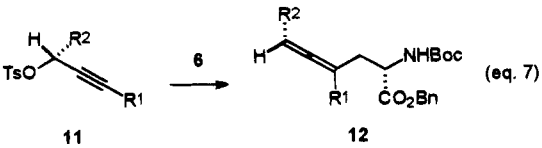
Table 3. Reaction of the Zinc/Copper Reagent 6 with Propargylic Tosylates in THF

	R^1	R^2	product	yield (%)
11a	H	H	**12a**	68
11b	Me	H	**12b**	65
(*R*)-**11c**	H	Me	**12c**	81
(*R*)-**11d**	H	C_5H_{11}	**12d**	51

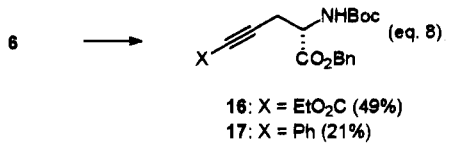
(*ent*-**1**), and both **12a** and *ent*-**12a** were converted to the corresponding *N*-trifluoroacetyl derivatives **15** and *ent*-**15** by sequential treatment with trifluoroacetic acid and then trifluoroacetic anhydride (eq 6). Analysis using a chiral Lipodex E stationary phase indicated that the enantiomeric excess of **15**, and hence of **12a**, was at least 99.5%.



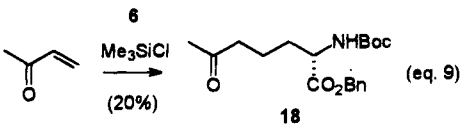
The requirement for benzene, together with the an ultrasonication process which requires close attention to detail,[3] prompted us to investigate alternative methods for zinc and zinc/copper reagent formation. The method of zinc activation and insertion developed by Knochel,[5] using THF as solvent, proved to be the most effective.[19] In order to compare this method with our previous procedure, reaction of zinc/copper reagent **6** with each of the propargylic tosylates previously examined was carried out (Table 3). Reactions with the two secondary tosylates studied were carried out with enantiomerically enriched material prepared from the corresponding acetylenic ketones by reduction with (*R*)-Alpine Borane and subsequent tosylation, so as to examine the stereochemical outcome of the nucleophilic displacement process. In both cases, the enantiomeric purity of the secondary tosylates was reflected in the diastereoisomeric purity of the products formed. Previous observations on the formation of allenes from acyclic propargylic precursors using organocopper reagents, including copper-catalyzed reactions of functionalized zinc reagents,[20] have demonstrated that the reaction proceeds with overall *anti*-stereochemistry and the stereochemistry of the products **12c** and **12d** have therefore been assigned on this assumption (eq 7). In all cases the yields were comparable to those obtained previously.



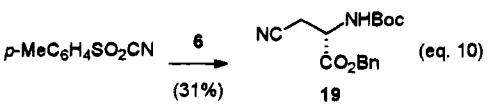
We have carried out a brief survey of the reactions of zinc/copper reagent **6** in THF with some representative electrophiles.[4] While ethyl bromopropiolate reacted reasonably efficiently to give the corresponding adduct **16**,[21] reaction with iodophenylacetylene to give the adduct **17** proceeded in low yield, with significant regeneration of protected iodoalanine **1**, presumably formed by competing nucleophilic attack of the reagent **6** at iodine (eq 8).[22]



Reaction of **6** with methyl vinyl ketone in the presence of chlorotrimethylsilane gave the protected 6-oxo α-amino acid **18**, although in disappointingly low yield (eq 9).



Although it has been reported that functionalized zinc reagents react efficiently with *p*-toluenesulfonyl cyanide to give the corresponding nitriles,[23] the zinc reagent **2** was inert toward this reagent. However, use of the zinc/copper reagent **6** did allow the formation of the corresponding adduct **19** (eq 10). A significantly improved



yield (50%) was obtained when this reaction was carried out using the zinc/copper reagent **6** prepared in the original mixed solvent system of benzene/dimethylacetamide/THF, for which we have no explanation.

The most likely explanation for these poor yields is the relatively low nucleophilicity of the zinc/copper reagent **6** when compared with other zinc/copper reagents which are either less heavily functionalized, or in which the functionality is further removed from the nucleophilic center. Both Yoshida[6] and Knochel[13] have previously commented on the reduced reactivity of zinc/copper reagents in which either electron-withdrawing or potentially coordinating groups are close to the carbon–metal bond.

Finally, the Knochel procedure was also successfully applied to the iodide **20**, the methyl ester analogue of **1**, which allowed the preparation of the three adducts **21a–c** (eq 11). There are some circumstances, especially in the preparation of unsaturated amino acids, when use of benzyl ester protection is not ideal and the compatibility of the methyl ester with this method is a useful extension.[24]

Our overall conclusion is that although the zinc/copper reagent **6** will only give good yields in reactions with relatively reactive electrophiles, use of this reagent does

(19) For a preliminary account of this procedure, see: Dunn, M. J.; Jackson, R. F. W.; Pietruszka, J.; Wishart, N.; Ellis, D.; Wythes, M. J. *Synlett* **1993**, 499–500.

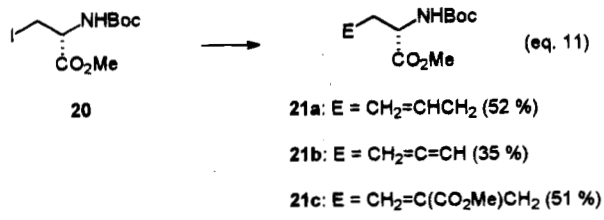
(20) Gooding, O. W.; Beard, C. C.; Jackson, D. Y.; Wren, D. L.; Cooper, G. F. *J. Org. Chem.* **1991**, *56*, 1083–1088.

(21) This compound was incorrectly described as the methyl ester in the preliminary communication.[19]

(22) For a review on acetylenic amino acids, see: Abdulganeeva, S. A.; Erzhanov, K. B. *Russ. Chem. Rev.* **1991**, *60*, 676–688. For an alternative stereoselective synthesis of acetylenic amino acids, see: Hamon, D. P. G.; Massy-Westropp, R. A.; Razzino, P. *J. Chem. Soc., Chem. Commun.* **1991**, 722–724.

(23) Klement, I.; Lennick, K.; Tucker, C. E.; Knochel. P. *Tetrahedron Lett.* **1993**, *34*, 4623–4626.

(24) For the palladium-catalyzed reaction of the zinc reagent derived from **20** with an aryl iodide, see: Smyth, M. S.; Burke, T. R. *Tetrahedron Lett.* **1994**, *35*, 551–554.



significantly enhance the value of the alanine-anion strategy as a method for the preparation of enantiomerically pure amino acids.

Experimental Section

General experimental procedures have already been described.[3] Specific rotations were measured at 20 °C, unless otherwise stated. NMR spectra were recorded in $CDCl_3$ as solvent, referenced to TMS. Coupling constants are given in Hz. All mass spectral data refer to the isotopes ^{35}Cl and ^{79}Br. Benzyl 2(*R*)-[(*tert*-butoxycarbonyl)amino]-3-iodopropionate [Boc-L-Ala(I)-OBn (**1**)] and its enantiomer *ent*-**1** were prepared by the literature method,[3] and methyl 2(*R*)-[(*tert*-butoxycarbonyl)-amino]-3-iodopropionate [Boc-L-Ala(I)-OMe (**20**)] was likewise prepared by the literature method.[11] Allylic tosylates were synthesized immediately prior to use from the corresponding alcohol (1.0 mmol) *via* deprotonation at −78 °C in dry tetrahydrofuran (2 cm^3) using *n*-butyllithium (1.0 mmol) followed by quenching with solid tosyl chloride (0.1907 g, 1.0 mmol) at 0 °C. Propargylic tosylates were prepared in a similar manner, or using KOH as base in diethyl ether, and purified before use. The optically active tosylates (*R*)-**11c** and (*R*)-**11d** were prepared by tosylation of the corresponding free alcohols, in turn prepared by reduction of the corresponding alkynones using (*R*)-Alpine Borane.[25]

Preparation of 5-Alkenyl and Alken-4,5-dienyl Protected α-Amino Acids. General Procedure. A solution of Boc-L-Ala(I)-OBn (**1**) (0.304 g, 0.75 mmol) in dry benzene (3 cm^3) and dry dimethylacetamide (0.2 cm^3) over zinc/copper couple (0.09 g), under nitrogen, was sonicated for 30 min until no more starting material remained (as judged by TLC 10:1/toluene:ethyl acetate).[3] The stirred flask contents were cooled to −10 °C at which point a solution of copper(I) cyanide−lithium chloride complex (CuCN·2LiCl) (0.75 mmol) in dry tetrahydrofuran [prepared immediately prior to use by stirring copper(I) cyanide (0.067 g, 0.75 mmol) and lithium chloride (0.064 g, 1.5 mmol) in dry tetrahydrofuran (2 cm^3) under nitrogen] was introduced, and then stirring was continued at 0 °C for 10 min. The allylic (or propargylic) halide or tosylate (1 mmol) was added at −25 °C, and the flask contents were stirred at 0 °C for 3 h. The cooling bath was then removed, and once the flask reached room temperature, the mixture was diluted with ethyl acetate (50 cm^3), washed with aqueous sodium hydrogen carbonate (25 cm^3, saturated) and water (3 × 25 cm^3), dried and concentrated under reduced pressure to produce the crude compound. Flash chromatography over silica gel (toluene/ethyl acetate) afforded the pure 5-alkenyl protected amino acid as a colored oil or a white solid.

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]hex-5-enoate (9a). Using allyl bromide as the electrophile gave the product as an oil (0.0768 g, 32%). Use of allyl chloride and allyl tosylate gave the product (0.1579 g, 65%) and (0.1208 g, 51%), respectively. $[\alpha]_D$ + 0.9° (*c* 1.06 in CH_2Cl_2); υ_{max} (cap. film) 3370, 1716, 1500, 1163 cm^{-1}; δ_H (500 MHz) 1.44 (9H, s), 1.76 (1H, m), 1.92 (1H, m), 2.08 (2H, m), 4.37 (1H, d, *J* 7.0), 5.01 (3H, m), 5.14 (1H, d, $^2J_{AB}$ 12.4), 5.20 (1H, d, $^2J_{AB}$ 12.4), 5.75 (1H, m), 7.38 (5H, m); *m*/*z* (EI) 320 (MH^+ 14%), 264 (45, $MH^+ - C_4H_8$), 220 (46, $MH^+ - C_4H_8 - CO_2$). Anal. Found: C 67.64, H 8.15, N 4.67. $C_{18}H_{25}NO_4$ requires C 67.69, H 7.89, N 4.38.

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4(*R*/*S*)-phenylhex-5-enoate (9b). Using cinnamyl bromide as the electrophile yielded the product as an oil (0.1144 g, 0.29 mmol, 40%), as an inseparable mixture of diastereoisomers. Use of cinnamyl chloride gave the product (0.1443 g, 0.36 mmol, 48%) also as a mixture of diastereoisomers in a comparable ratio. Found: $M^+ - C_4H_8$ 339.1508. $C_{20}H_{21}NO_4$ requires 339.1471); υ_{max} (cap. film) 3370, 2978, 1716, 1637, 1167 cm^{-1}; δ_H (200 MHz) 1.43 (9H, s), 1.91−2.33 (2H, m), 3.39 (1H, m), 4.23 (m) and 4.42 (m) together 1H, 4.93−5.20 (5H, m), 5.82−5.99 (1H, m), 7.10−7.41 (10H, m); *m*/*z* (EI) 339 ($M^+ - C_4H_8$, 2%), 295 (30, $M^+ - C_4H_8 - CO_2$).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-5-methylhex-5-enoate (9c). 2-Methyl-2-propenyl tosylate, prepared *in situ*, gave the product as an oil (0.1407 g, 0.42 mmol, 56%). (Found: MH^+ 334.2052. $C_{19}H_{27}NO_4$ requires 334.2018); $[\alpha]_D$ +2.7° (*c* 1.1 in CH_2Cl_2); υ_{max} (cap. film) 3370, 2976, 1716, 1587, 1167 cm^{-1}; δ_H (500 MHz) 1.44 (9H, s), 1.67 (3H, s), 1.77 (1H, m), 2.00 (2H, m), 4.37 (1H, bd), 4.65 (1H, s), 4.72 (1H, s), 5.09 (1H, bd), 5.13 (1H, d, *J* 12.2), 5.21 (1H, d, *J* 12.2), 7.34 (5H, s); *m*/*z* (EI) 334 (MH^+, 8.0%), 278 (57, $MH^+ - C_4H_8$, 234 (68, $MH^+ - C_4H_8 - CO_2$).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4(*R*/*S*)-(chloromethyl)hex-5-enoate (9d). (*E*)-1,4-Dichlorobut-2-ene gave the product as an oil as a mixture of diastereoisomers (0.1215 g, 0.33 mmol, 44%). (Found: $M^+ - C_4H_8 - CO_2$ 267.0972. $C_{14}H_{18}NO_2Cl$ requires 267.1026); υ_{max} (cap. film) 3433, 2980, 1711, 1500, 1165, 758 cm^{-1}; δ_H (200 MHz) 1.43 (9H, s), 1.62−2.2 (2H, m), 2.45 (1H, m), 3.48 (2H, m), 4.41 (1H, m), 4.97 (d, *J* 8.7) and 5.07 (d, *J* 6.6) together 1H, 5.15 (4H, m), 5.65 (1H, m), 7.35 (5H, m); *m*/*z* (EI) 267 ($M^+ - C_4H_8 - CO_2$, 3%), 232 (94, $MH^+ - C_7H_8 - CO_2$).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4(*R*/*S*)-(bromomethyl)hex-5-enoate (9e). (*E*)-1,4-dibromobut-2-ene gave the product as an oil as a separable mixture of diastereoisomers (0.1467 g, 0.36 mmol, 48%); υ_{max} (cap. film) 3370, 2978, 1716, 1653, 1506, 1498, 1165 cm^{-1}; δ_H (300 MHz) (one diastereoisomer) 1.43 (9H, s), 1.89 (2H, m), 2.52 (1H, m), 3.30 (1H, dd, *J* 6.7, 10.0), 3.38 (1H, dd, *J* 5.6, 10.0), 4.36 (1H, m), 4.92 (1H, d, *J* 8.6), 5.19 (4H, m), 5.63 (1H, m), 7.36 (5H, s); $[\alpha]_D$ +6.5° (*c* 1.09 in CH_2Cl_2); δ_H (300 MHz; $CDCl_3$) (one diastereoisomer) 1.43 (9H, s), 1.74 (1H, m), 2.12 (1H, m), 2.52 (1H, m), 3.38 (2H, m), 4.38 (1H, m), 5.06−5.17 (5H, m), 5.62 (1H, m), 7.38 (5H, s); $[\alpha]_D$ + 5.6° (*c* 1.55 in CH_2Cl_2); *m*/*z* (EI) 357 ($M^+ - C_4H_8$, 8.0%), 311 (17, $M^+ - C_4H_8 - CO_2$), 276 (30, $MH^+ - C_7H_8 - CO_2$). Anal. Found: C 55.29, H 6.15, N 3.61. $C_{19}H_{26}NO_4Br$ requires C 55.34, H 6.36, N 3.40.

1-Benzyl 6-Methyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-5-methylidenehexanedioate (9f). Methyl 2-(bromomethyl)-acrylate gave the product as an oil (0.1439 g, 0.38 mmol, 51%). (Found: MH^+ 378.1878. $C_{20}H_{28}NO_6$ requires 378.1917); $[\alpha]_D$ +1.3° (*c* 0.95 in CH_2Cl_2); υ_{max} (cap. film) 3372, 2978, 1718, 1631, 1167 cm^{-1}; δ_H (200 MHz) 1.44 (9H, s), 1.84 (1H, m), 2.02 (1H, m), 2.34 (2H, t, *J* 7.7), 3.72 (3H, s), 4.36 (1H, m), 5.14 (1H, d, *J* 12.3), 5.15 (1H, m), 5.18 (1H, d, *J* 12.3), 5.53 (1H, d, *J* 1.1), 6.16 (1H, d, *J* 1.1), 7.34 (5H, m); *m*/*z* (EI) 378 (MH^+ 0.1%), 322 (7, $MH^+ - C_4H_8$, 278 (24, $MH^+ - C_4H_8 - CO_2$).

1-Benzyl 5-Methyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4(*R*/*S*)-ethenylpentanedioate (9g). Methyl (*E*)-4-bromocrotonate gave the product as an oil as an inseparable mixture of diastereoisomers (0.1399 g, 0.37 mmol, 49%). υ_{max} (cap. film) 3370, 2978, 1959, 1718, 1500, 1163 cm^{-1}; δ_H (200 MHz) 1.43 (9H, s), 1.81−2.42 (2H, m), 3.16 (1H, dt, *J* 7.2, 7.2), 3.67 (s) and 3.68 (s) together 3H, 4.35 (1H, m), 4.94 (1H, br d, *J* 7.6), 5.01−5.23 (4H, m), 5.68−5.87 (1H, m), 7.36 (5H, m); *m*/*z* (EI) 378 (MH^+ 28%), 322 (87, $MH^+ - C_4H_8$). Found: C 63.67, H 7.24, N 3.73. $C_{20}H_{27}NO_6$ requires C 63.65, H 7.21, N 3.71.

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-7-chlorohept-5-eneoate (9h). 3,4-Dichlorobut-1-ene gave the product as an oil (0.0766 g, 0.21 mmol, 55%). (Found: $M^+ - C_4H_8 - Cl$, 276.1218. $C_{15}H_{18}NO_4$ requires 276.1236); $[\alpha]_D$ +4.3° (*c* 0.97 in CH_2Cl_2); υ_{max} (cap. film) 3433, 2980, 1782, 1732, 1265, 1165, 738 cm^{-1}; δ_H (500 MHz) 1.44 (9H, s), 1.72 (1H, m), 1.92 (1H, m), 2.09 (2H, m), 3.99 (2H, d, *J* 7.0), 4.35 (1H, m), 5.06 (1H, d, *J* 8.1), 5.14 (1H, d, *J* 12.3), 5.20 (1H, d, *J* 12.3), 5.58 (1H, m), 5.70 (1H, m), 7.34 (5H, m); *m*/*z* (EI) 369 (MH_2^+ 44%), 332 (28, $M^+ - Cl$), 276 (10, $M^+ - C_4H_8 - Cl$). Anal. Found: C 62.48, H 7.31, N 4.07. $C_{19}H_{26}NO_4Cl$ requires C 62.03, H 7.12, N 3.80.

(25) Midland, M. M.; Tramontano, A.; Kazubski, A.; Graham, R. S.; Tsai, D. J. S.; Cardin, D. B. *Tetrahedron* **1984**, *40*, 1371−1380.

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-5-bromohex-5-enoate (9i). 2,3-Dibromoprop-1-ene gave the product (0.1552 g, 0.39 mmol, 52%) as a crystalline solid (mp 43–45 °C). $[\alpha]_D$ +7.3° (*c* 1.0 in CH_2Cl_2); ν_{max} (cap. film) 3433, 2982, 2307, 1740, 1714, 1163, 738 cm^{-1}; δ_H (200 MHz) 1.44 (9H, s), 1.87 (1H, m), 2.12 (1H, m), 2.41 (2H, m), 4.37 (1H, m), 5.06 (1H, d, *J* 8.3), 5.16 (1H, d, *J* 12.2), 5.20 (1H, d, *J* 12.2), 5.40 (1H, d, *J* 1.8), 5.55 (1H, d, *J* 1.8), 7.35 (5H, s); *m*/*z* (EI) 398 (MH^+ 0.8%), 342 (7, $MH^+ - C_4H_8$), 298 (6, $MH^+ - C_4H_8 - CO_2$). Anal. Found: C 54.63, H 6.16, N 3.93. $C_{18}H_{24}NO_4Br$ requires C 54.28, H 6.07, N 3.52.

1,9-Dibenzyl 2(*S*),8(*S*)-Bis[(*tert*-butoxycarbonyl)amino]non-4-enedioate (10). Use of 1,3-dichloropropene (0.375 mmol) gave the product as an oil (0.1029 g, 0.17 mmol, 45%). $[\alpha]_D$ +3.6° (*c* 1.1 in CH_2Cl_2); ν_{max} (cap. film) 3364, 2980, 1741, 1713, 1500, 1163, 738 cm^{-1}; δ_H (500 MHz) 1.43 (9H, s), 1.44 (9H, s), 1.63 (1H, m), 1.89 (1H, m), 2.18 (2H, m), 2.44 (2H, m), 4.34 (1H, m), 4.40 (1H, m), 5.00 (1H, bd), 5.0–5.3 (6H, m), 5.39 (1H, m), 7.33 (5H, s), 7.34 (5H, s); *m*/*z* (EI) 595 ($M^+ - H$, 3%), 529 (16, $M^+ - H - C_4H_8$), 495 (23, $M^+ - H - C_4H_8 - CO_2$), 439 (44, $M^+ - H - 2C_4H_8 - CO_2$).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]hexa-4,5-dienoate (12a). Using purified propargyl tosylate (1 mmol), with reaction at 0 °C for 3 h, the product was obtained as an oil (60%). Propargyl bromide (1 mmol) and propargyl chloride (1 mmol) gave the product in 55 and 49% yields, respectively; $[\alpha]^{22}_D$ −1.1° (*c* 1.02 in $CHCl_3$); ν_{max} (cap. film) 3463, 3373, 2978, 1958, 1748, 1718, 1500, 1456, 1367, 1168 cm^{-1}; δ_H (400 MHz) 1.44 (9H, s), 2.51 (2H, m), 4.38–4.48 (1H, m), 4.63–4.67 (2H, m), 4.97 (1H, tt, *J* 7, 7), 5.13 (1H, d, *J* 12.2), 5.21 (1H, d, *J* 12.2), 5.11–5.15 (1H, br m), 7.35 (5H, s); δ_C (100 MHz) 30.27 (q), 31.69 (t), 53.21 (d), 67.06 (t), 75.29 (t), 79.89 (s), 84.33 (d), 128.27, 123.38, 128.55 (d), 135.34 (s), 155.13 (s), 171.70 (s), 209.63 (s); *m*/*z* (FAB) 318 (MH^+, 23%), 262 (100, $MH^+ - C_4H_8$), 218 (75, $MH^+ - C_4H_8 - CO_2$)]. Anal. Found: C, 68.26; H, 7.3; N, 4.38. $C_{18}H_{23}NO_4$ requires C, 68.12; H, 7.30; N, 4.41.

Benzyl 2(*R*)-[(*tert*-Butoxycarbonyl)amino]hexa-4,5-dienoate (*ent*-12a). This compound was prepared (54%) in an identical fashion to **12a**, but using Boc-D-Ala(I)-OBn *ent*-**1** as starting material. $[\alpha]^{22}_D$ +1.0° (*c* 1.0 in $CHCl_3$).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4-methylhexa-4,5-dienoate (12b). Using purified 1-butyn-3-yl tosylate (1 mmol), with reaction at 0 °C for 3 h, the product was obtained as an oil in 52% yield; $[\alpha]^{22}_D$ +7.0° (*c* 1.1 in $CHCl_3$); ν_{max} (cap. film) 3464, 3374, 2979, 1961, 1746, 1718, 1500, 1456, 1367, 1165 cm^{-1}; δ_H (400 MHz) 1.44 (9H, s), 1.67 (3H, t, *J* 3), 2.36–2.54 (2H, m), 4.47 (1H, m), 4.52–4.64 (2H, m), 5.06 (1H, bd, *J* 6.5), 5.13 (1H, d, *J* 12.2), 5.19 (1H, d, *J* 12.2), 7.35 (5H, s); δ_C (100 MHz) 18.59 (q), 28.30 (q), 36.48 (t), 52.18 (d), 67.03 (t), 74.90 (t), 79.83 (s), 96.11 (s), 2 × 128.32, 128.55 (d), 135.43 (s), 155.20 (s), 172.10 (s), 207.02 (s); *m*/*z* (FAB) 332 (MH^+, 28%), 276 (100, $MH^+ - C_4H_8$), 232 (89, $MH^+ - C_4H_8 - CO_2$). Anal. Found: C, 68.70; H, 7.57. $C_{19}H_{25}NO_4$ requires C, 68.86; H, 7.60.

Preparation of the Zinc/Copper Reagent 6 in THF. A suspension of zinc (0.300 g, 4.5 mmol) in dry THF (0.34 cm^3) and 1,2-dibromoethane (0.0194 cm^3, 0.225 mmol) was heated under nitrogen to 60 °C for 3 min. After cooling the mixture to 35 °C, trimethylsilyl chloride (0.006 cm^3, 0.046 mmol) was added and the mixture was vigorously stirred for 30 min [alternatively, the reaction mixture was placed in an ultrasonic bath (flask positioning appears not to be critical) and the mixture sonicated for 30 min]. At this point the reaction vessel was warmed to 35 °C, Boc-L-Ala-(I)-OBn (**1**) (0.304 g, 0.75 mmol) in dry THF (1.5 cm^3) was slowly added, and the mixture was stirred for 15–40 min until no starting material remained (as judged by TLC). The solution of zinc reagent **2** was then converted to the zinc–copper reagent **6** by the following procedure. The solution of zinc reagent was cooled to −10 °C, and a solution prepared from CuCN (0.067 g, 0.75 mmol) and LiCl (0.064 g, 1.5 mmol) in THF (1.5 cm^3) was added. The mixture was stirred at 0 °C for 10 min and then cooled to the reaction temperature before addition of the electrophile.

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]hexa-4,5-dienoate (12a). Using purified propargyl tosylate (1 mmol), with reaction at 0 °C for 3 h, the product was obtained as an oil in 68% yield; spectroscopic data were identical to those previously described.

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-4-methylhexa-4,5-dienoate (12b). Using purified 1-butyn-3-yl tosylate, with reaction at 0 °C for 3h, the product was obtained as an oil in 65% yield; spectroscopic data were identical to those previously described.

Benzyl 2(*S*),4a(*S*)-[(*tert*-Butoxycarbonyl)amino]hepta-4,5-dienoate (12c). Starting from optically active 3-butyn-2-yl tosylate (ee = 88%), we obtained product in 81% yield. The reaction time was 1 h at 0 °C to prevent racemization of the allenic moiety.[26] The (2*S*,4a*S*)-diastereoisomer was formed in 89% de (as judged by GLC, 25 m fused silica capillary column, coated with a 1:1 mixture of heptakis(6-*O*-methyl-2,3-di-*O*-n-pentyl)-β-cyclodextrin - OV1701: 135 °C; carrier gas, hydrogen, 55 kPa). The (2*S*,4a*R*)-diastereoisomer has identical spectroscopic properties, but the two doublets of the benzyl group have slightly different chemical shifts (5.14 and 5.19, J_{AB} = 12 Hz) in the proton NMR; $[\alpha]_D$ +19.6° (*c* 0.7 in $CHCl_3$); ν_{max} (cap. film) 3464, 3373, 2978, 1967, 1744, 1718, 1500, 1456, 1367, 1250, 1170 cm^{-1}; δ_H (400 MHz) 1.43 (9H, s), 1.62 (3H, dd, *J* 7, 3.5), 2.40–2.53 (2H, m), 4.45 (1H, m), 4.90 (1H, m), 5.06 (1H, m), 5.13 (1H, b), 5.13 (1H, d, *J* 12.5), 5.21 (1H, d, *J* 12.5), 7.35 (5H, s); δ_C (100 MHz) 14.28 (q), 28.33 (q), 32.08 (t), 53.14 (d), 67.03 (t), 79.85 (s), 83.82 (d), 86.46 (s), 128.23, 128.39, 128.60 (d), 135.46 (s), 155.18 (s), 171.84 (s), 206.24 (s); *m*/*z* (FAB) 332 (MH^+, 31%), 276 (100, $MH^+ - C_4H_8$), 232 (61, $MH^+ - C_4H_8 - CO_2$). Anal. Found: C, 68.86; H, 7.61; N, 4.13. $C_{19}H_{25}NO_4$ requires C, 68.86; H, 7.60; N, 4.23.

Benzyl 2(*S*),4a(*S*)-[(*tert*-Butoxycarbonyl)amino]undeca-4,5-dienoate (12d). Starting from optically active 1-octyn-3-yl tosylate (ee 85%), we obtained the product (51%) with a de = 88% (as judged by ^1H NMR analysis) after 1 h reaction time at 0 °C. $[\alpha]_D$ +23.8° (*c* 1.15 in $CHCl_3$); ν_{max} (cap. film) 3449, 3374, 2930, 2858, 1964, 1745, 1718, 1499, 1456, 1367, 1170 cm^{-1}; δ_H (400 MHz) 0.88 (3H, t, *J* 7), 1.27–1.44 (6H, m), 1.44 (9H, s), 1.95 (2H, ddt, *J* 3, 7, 7), 2.42–2.56 (2H, m), 4.35–4.48 (1H, m), 4.92 (1H, m), 5.06–5.11 (2H, m), 5.13 (1H, d, *J* 12.5), 5.20 (1H, d, $^2J_{AB}$ 12.5), 7.35 (5H, s); δ_C (100 MHz) 13.98 (q), 22.38 (t), 28.59 (t), 31.23 (t), 28.25 (q), 28.67 (t), 32.22 (t), 53.14 (d), 66.92 (t), 79.72 (s), 84.86 (d), 91.76 (d), 128.13 (d), 128.28 (d), 128.49 (d), 135.39 (s), 155.13 (s), 171.77 (s), 205.41 (s); *m*/*z* (FAB) 388 (MH^+, 29) 332 (100, $MH^+ - C_4H_8$), 288 (98, $MH^+ - C_4H_8 - CO_2$). Anal. Found: C, 71.34; H, 8.57; N, 3.50. $C_{23}H_{33}NO_4$ requires C, 71.28; H, 8.58; N, 3.61.

NMR Data for the (2*S*,4a*R*)-diastereoisomer: δ_H (400 MHz) 0.88 (3H, t, *J* 7), 1.27–1.44 (6H, m), 1.44 (9H, s), 1.95 (2H, ddt, *J* 3, 7, 7), 2.38–2.52 (2H, m), 4.35–4.48 (1H, m), 4.92 (1H, m), 5.06–5.11 (2H, m), 5.14 (1H, d, $^2J_{AB}$ 12.5), 5.19 (1H, d, $^2J_{AB}$ 12.5), 7.35 (5H, s); δ_C (100 MHz) 13.98 (q), 22.38 (t), 28.59 (t), 31.23 (t), 28.25 (q), 28.67 (t), 32.22 (t), 53.14 (d), 66.92 (t), 79.72 (s), 85.00 (d), 91.87 (d), 128.13 (d), 128.28 (d), 128.49 (d), 135.39 (s), 155.13 (s), 171.77 (s), 205.37 (s).

1-Benzyl 6-Ethyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-hex-4-ynedioate (16). Cuprate formation was as described above. At −55 °C, with stirring, a solution of ethyl 3-bromoprop-2-ynoate (0.177 g, 1.0 mmol) in dry tetrahydrofuran (2 cm^3) was introduced followed by stirring at this temperature for 20 h. Quenching with aqueous ammonium chloride (5 cm^3, saturated) and standard workup gave the product **16** as a colored oil (0.138 g, 0.37 mmol, 49%). (Found: MH^+ 376.1825. $C_{20}H_{26}NO_6$ requires 376.1760); $[\alpha]_D$+ 11.1° (*c* 1.06 in CH_2Cl_2); ν_{max} (cap. film) 3379, 2980, 2241, 1713, 1255, 1165 cm^{-1}; δ_H (200 MHz) 1.30 (3H, t, *J* 7.1), 1.44 (9H, s), 2.90 (2H, d, *J* 5.0), 4.20 (2H, q, *J* 7.1), 4.56 (1H, m), 5.21 (1H, d, *J* 12.1), 5.23 (1H, d, *J* 12.1), 5.39 (1H, br d, *J* 8), 7.35 (5H, s); *m*/*z* (EI) 376 (MH^+, 1.0%), 320 (17, $MH^+ - C_4H_8$), 276 (33, $MH^+ - C_4H_8 - CO_2$).

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-5-phenylpent-4-yneoate (17). A solution of 1-iodo-2-phenylethyne (0.228 g, 1.0 mmol) in dry tetrahydrofuran (2 cm^3) was syringed into a stirred solution of the cuprate at −78 °C. After 6 h the flask was permitted to warm up overnight, worked up, and purified as above to afford benzyl 2(*S*)-[(*tert*-butoxy-

(26) Claesson, A.; Olsson, L-I.; *J. Chem. Soc., Chem. Commun.* **1979**, 524–525.

carbonyl)amino]-5-phenylpent-4-ynoate as a white solid (0.06 g, 0.16 mmol, 21%) (mp 65–66 °C). (Found: M^+ 379.1752. $C_{23}H_{25}NO_4$ requires 379.1783); $[\alpha]_D$ −0.1° (*c* 1.15 in CH_2Cl_2); ν_{max} (cap. film) 3429, 2932, 1745, 1716, 1491, 1367, 1165 cm^{-1}; δ_H (200 MHz) 1.45 (9H, s), 2.90 (1H, dd, *J* 17.0, 5.0), 3.01 (1H, dd, *J* 17.0, 4.8), 4.60 (1H, bd), 5.21 (1H, d, *J* 12.3), 5.25 (1H, d, *J* 12.3), 5.41 (1H, bd), 7.32 (10H, s); *m/z* (EI) 379 (M^+, 0.1%), 144 (18, $MH^+ - C_7H_8 - C_4H_8 - 2CO_2$).

Benzyl 2(*S*)-[(tert-Butoxycarbonyl)amino]-6-oxoheptanoate (18). Trimethylsilyl chloride (0.543 g, 83 μL, 5 mmol) and methyl vinyl ketone (0.070 g, 1.0 mmol) in dry tetrahydrofuran (2 cm^3) were added dropwise to a solution of the cuprate **6** at −78 °C and stirred at this temperature for 3 h, followed by warming to room temperature overnight. The usual workup gave benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-6-oxoheptanoate as a colored oil (0.051 g, 0.15 mmol, 20%). $[\alpha]_D$ −4.5° (*c* 0.95 in CH_2Cl_2); ν_{max} (cap. film) 3366, 2976, 1714, 1500, 1165 cm^{-1}; δ_H (200 MHz) 1.43 (9H, s), 1.45–2.08 (4H, m), 2.10 (3H, s), 2.43 (2H, m), 4.31 (1H, m), 5.10 (1H, br m), 5.16 (1H, d, *J* 12.3), 5.18 (1H, d, *J* 12.3), 7.35 (5H, s); *m/z* (EI) 350 (MH^+, 8.0%), 294 (44, $MH^+ - C_4H_8$), 250 (29, $MH^+ - C_4H_8 - CO_2$). Anal. Found: C 65.46, H, 7.77, N, 3.99. $C_{19}H_{27}NO_5$ requires C 65.31, H, 7.79, N, 4.01.

Benzyl 2(*S*)-[(*tert*-Butoxycarbonyl)amino]-3-cyanopropionate (19). *p*-Toluenesulfonyl cyanide (0.181 g, 1.0 mmol) in dry THF (2 cm^3) was added to a solution of the cuprate at −25 °C and then stirred at 0 °C for 3 h. Workup and purification gave benzyl 2(*S*)-[(*tert*-butoxycarbonyl)amino]-3-cyanopropionate as a white, crystalline solid (0.1138 g, 0.37 mmol, 31%) (mp 99–100 °C). $[\alpha]_D$ +17.4° (*c* 1.04 in CH_2Cl_2); ν_{max} (cap. film) 3360, 2974, 2253, 1730, 1680, 1645, 1298, 1196 cm^{-1}; δ_H (200 MHz) 1.45 (9H, s), 2.97 (2H, m), 4.53 (1H, m), 5.25 (2H, s), 5.48 (1H, br d, *J* 7.0), 7.38 (5H, s); *m/z* (EI) 305 (MH^+, 6.0%), 249 (59, $MH^+ - C_4H_8$), 205 (5, $MH^+ - C_4H_8 - CO_2$). Anal. Found: C 63.50, H 6.70, N 8.79. $C_{16}H_{20}N_2O_4$ requires C 63.15, H 6.62, N 9.20.

Reactions of the Zinc/Copper Reagent Derived from Boc-L-Ala(I)-OMe 20. The same procedure as described above for conversion of the the benzyl ester **1** into the corresponding zinc and zinc/copper reagents in THF was employed for the conversion of the methyl ester **20** into the corresponding zinc and zinc/copper reagents. Reactions of the zinc/copper reagent derived from **20** with allylic halides was also carried out according to the same procedure.

Methyl 2(*S*)-[N-(*tert*-Butoxycarbonyl)amino]hex-5-enoate (21a). Reaction with allyl chloride (1 mmol) gave the product as an oil (52%). $[\alpha]_D$ −18.7° (*c* 0.97 in MeOH); lit. −17.0° (*c* 1.2 in MeOH); (Found: MH^+ 244.1539. $C_{12}H_{22}O_4N$ requires 244.1549); ν_{max} (cap. film) 3368, 2980, 2955, 2932, 1746, 1715, 1509 cm^{-1}. δ_H (200 MHz) 1.43 (9H, s). 1.74 (1H, m), 1.91 (1H, m), 2.1 (2H, m), 3.72 (3H, s), 4.30 (1H, m), 4.98–5.10 (3H, m), 5.8 (1H, m). *m/z* (EI) 244 (MH^+, 4%), 188 (61, $MH^+ - C_4H_8$), 144 (73, $MH^+ - C_4H_8 - CO_2$).

Methyl 2(*S*)-[N-(*tert*-Butoxycarbonyl)amino]hexa-4,5-dienoate (21b). Reaction with propargyl chloride (1 mmol) gave the product as an oil (35%). $[\alpha]_D$ +26.5° (*c* 0.77 in CH_2Cl_2); (Found: MH^+ 242.1405. $C_{12}H_{20}O_4N$ requires 242.1392); ν_{max} 3368, 2980, 2934, 1958, 1717, 1509 cm^{-1}. δ_H (200 MHz) 1.45, (9H, s), 2.47 (2H, m), 3.7 (3H, s), 4.43 (1H, m), 4.73 (2H, m), 4.97 (1H, tt, *J* 7, 7), 5.06 (1H, m). *m/z* (EI) 242 (MH^+, 24%), 186 (76, $MH^+ - C_4H_8$), 142 (80, $MH^+ - C_4H_8 - CO_2$).

1,6-Dimethyl 2(*S*)-[*N*-(*tert*-Butoxycarbonyl)amino]-5-methylidenehexane (21c). Reaction with methyl 2-(bromomethyl)acrylate (1 mmol) gave the product as an oil (51%). $[\alpha]_D$ +17.3° (*c* 1.76 in CH_2Cl_2); (Found: MH^+ 302.1607. $C_{14}H_{24}O_6N$ requires 302.1604); ν_{max} 3372, 2978, 2955, 1719, 1631, 1518 cm^{-1}. δ_H (200 MHz) 1.42 (9H, s), 1.90 (2H, m), 2.35 (2H, t, *J* 7), 3.72 (3H, s), 3.73 (3H, s), 4.29 (1H, m), 5.05 (1H, d, *J* 8.1), 5.58 (1H, d, *J* 1.1), 6.17 (1H, d, *J* 1.1). *m/z* (EI) 302 (MH^+, 33%), 246 (72, $M^+ - C_4H_8$), 202 (86, $MH^+ - C_4H_8 - CO_2$).

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Supplementary Material Available: Experimental procedures for the preparation of the camphanamides **14a** and **14b**. ^1H NMR spectra for the amino acid derivatives **9b–f**, **10**, **16**, **17**, and **21a–c** (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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