Conversion of carbonimidodithioates to carbamates

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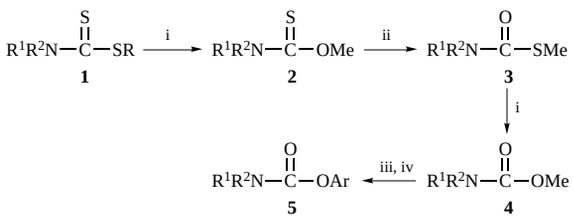
Carbonimidodithioates derived from primary amines or α-amino acid esters have been converted to *N*-benzyloxycarbonyl derivatives under mild conditions by treatment first with sodium benzyl alcoholate and then with water. *N*-Benzyloxycarbonyl α-amino acids have been generated from the methyl esters by alkaline hydrolysis or from the allyl esters by Pd^0-catalysed de-allylation.

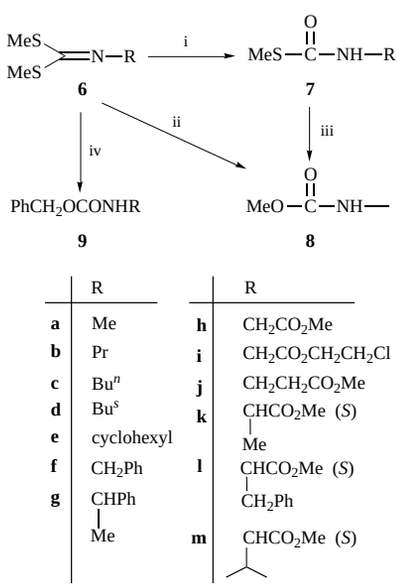
Introduction

Over the past several years, we have been involved in devising synthetic routes for carbamates that do not require the use of phosgene or methyl isocyanate. We had earlier reported the conversion of dithiocarbamates to carbamates in three steps.[1] In that sequence (Scheme 1), a dithiocarbamate **1** was converted first into an *O*-methyl thiocarbamate **2**, which was isomerised in excellent yield to the corresponding *S*-methyl thiocarbamate **3**; the latter could be easily transformed by sodium methoxide in methanol into the methyl carbamate **4**. We had also shown that the *S*-methyl thiocarbamates **7** could be directly prepared from carbonimidodithioates **6** by zeolite-catalysed partial hydrolysis (Scheme 2).[2] This can therefore provide an alternative route to methyl carbamates **4**; $R^2 = H$. The industrial importance of such easy access to alkyl carbamates such as compounds **4** stems from the fact that these can be subjected to transeserification with subsituted phenols, leading to commercially important aryl carbamate pesticides **5**; $R^1 = Me$, $R^2 = H$. This contrathermodynamic transesterification is achieved through a modified Vilsmeier reaction (Scheme 1).[3,4]

We now report, for the first time, the direct conversion of carbonimidodithioates **6** in one step to carbamates **8** (Scheme 2). We further demonstrate the utility of this reaction for the preparation of *N*-benzyloxycarbonyl (Z) α-amino acids.



Scheme 1 *Reagents:* i, NaOMe, MeOH; ii, I_2 or H_2So_4; iii, $POCl_3$; iv, ArOH



Scheme 2 *Reagents and conditions:* i, $ZnCl_2$, MeCN–water (3:1); 60 °C; 6–10 h; (OR) H-Mordenite/toluene, reflux, 24 h; ii, $ZnCl_2$, MeOH–water (3:1), 60–80 °C, 10–12 h; iii, $ZnCl_2$, MeOH, 60 °C, 6 h; iv, $PhCH_2ONa$, THF, 30 °C; 6 h; then water, 30 °C, 15 h

Results and discussion

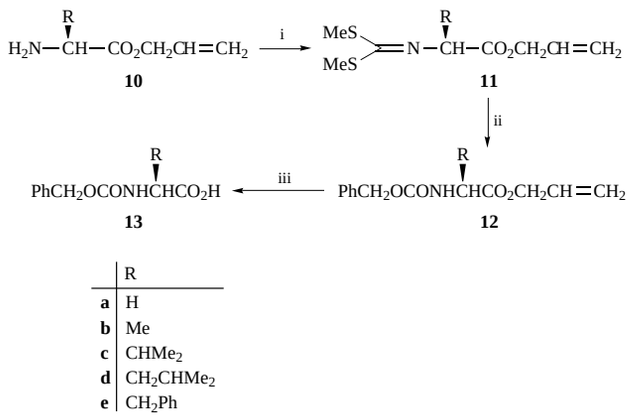
The initial success in this area was based on our discovery that $ZnCl_2$ is an efficient Lewis acid catalyst for the hydrolysis of carbonimidodithioates **6**. The product obtained was dependent on the solvent used for the reaction. In acetonitrile–water (3:1), the $ZnCl_2$-catalysed hydrolysis of the imino sulfide unit in substrates **6** at 60 °C for 6–10 h led to the *N*-alkyl *S*-methyl thiocarbamates **7**. However, if the same reaction was carried out in MeOH–water (3:1) at 60–80 °C for 10–12 h, further methanolysis took place, giving the carbamates **8** in good yields along with small amounts of thiocarbamates **7** in the case of substrates **6a–d**. The intermediate *S*-methyl thiocarbamates **7a–m** were identical with those obtained earlier by zeolite-catalysed hydrolysis.[2,5]

The next logical step was to extend this sequence to the synthesis of benzyl carbamates derived from α-amino acids. Our first attempt in this direction, by replacing methanol with benzyl alcohol in the $ZnCl_2$-catalysed alcoholysis of the glycine derivative **6h**, proved to be completely futile. Nor could the desired benzyl carbamate be obtained by carrying out the $ZnCl_2$-catalysed alcoholysis under anhydrous conditions, or with other solvents [dimethylformamide, tetrahydrofuran (DMF, THF)]. Replacement of $ZnCl_2$ by $HgCl_2$, lanthanum triflate, RE-Y zeolite or H-Mordenite was equally ineffective. Successful conversion of **6h** to *N*-(benzyloxycarbonyl)glycine methyl ester **9h** was finally achieved by the following protocol. The carbonimidodithioate **6h** was treated with the sodium salt of benzyl alcohol in anhydrous THF at 30 °C for 6 h, after which water was added and the hydrolysis was allowed to proceed overnight at 30 °C. The product **9h** was obtained in 80.8% yield. Similarly, starting materials **6k–m** could be converted to the respective *N*-benzyloxycarbonyl α-amino acid methyl esters **9k–m** in good yields (Scheme 2). Alkaline hydrolysis of these methyl esters at 30 °C led to the required *N*-benzyloxycarbonyl α-amino acids. Although this marked the successful charting out of the synthetic route, we felt it might be desirable to use a protecting group for the carboxy function, one which could be removed under non-racemising conditions. The allyl ester seemed ideal for this purpose, since mild procedures for de-allylation under Pd^0 catalysis have been reported in the literature.[6–10]

Table 1 Yields and physical properties of *N*-benzyloxycarbonyl α-amino acids **13**

Product	R	Yield (%)	Mp (T/°C)[a]	Specific rotation ($[\alpha]_D/10^{-1}$ deg cm^2 g^{-1})
13a	H	83	121 (122–124)	
13b	Me	81	80 (82–84)	−14.1 (−14.20) (*c* 2, HOAc)
13c	$CHMe_2$	79	62 (62–64)	+6.1 (+6.20) (*c* 4, $CHCl_3$)
13d	CH_2CHMe_2	74	50 (52–55)	−16.7 (−16.85) (*c* 2, EtOH)
13e	CH_2Ph	80	86 (87–90)	+4.4 (+4.45) (*c* 5, HOAc)

[a] Values within parentheses are those for authentic samples prepared by standard procedures; the rotations were taken under the same conditions on the same instrument.



Scheme 3 *Reagents and conditions:* i, CS_2, Et_3N; then MeI; ii, $PhCH_2ONa$, THF; then water, 30 °C; iii, MeCN, DBU, morpholine, $Pd(dba)_2$, PPh_3, 30 °C

The carbonimidodithioates **11a–e** derived from the allyl esters of α-amino acids could be transformed into the corresponding benzyl carbamates **12a–e** as before by treatment with sodium benzyl alcoholate in dry THF (30 °C; 6 h) followed by aqueous hydrolysis (30 °C; 15 h). These were then subjected to Pd^0-catalysed de-allylation in the presence of morpholine as the allyl acceptor (Scheme 3).

The *N*-benzyloxycarbonyl α-amino acids **13a–e** were obtained in good to excellent yields (Table 1). The specific rotations of the Z derivatives of the chiral amino acids (compounds **13b–e**) were compared with those of authentic samples prepared by standard procedures (Table 1). As a further check on the enantiomeric purity of the product (*S*)-*N*-benzyloxycarbonylalanine prepared by the de-allylation route was subjected to HPLC analysis using a chiral column (DAICEL CHIRALCEL OD). No trace of the enantiomeric product could be seen under conditions wherein a racemic sample was clearly resolved. Furthermore, the sample of Z-Ala-OH was coupled with (*S*)-proline methyl ester [dicyclohexylcarbodiimide (DCC)] and the ^{1}H NMR spectrum of the product dipeptide was determined. This again showed the presence of only one (*S*,*S*) diastereomer.

Experimental

General

Mps were determined with a microscope hot-stage apparatus, and are uncorrected. IR spectra were determined on a Perkin-Elmer model 599B Infracord spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker-WH-90 (Spectrospin), Bruker-AC-200, Bruker-MSL-300, or Varian-FT-80A instrument for solutions in $CDCl_3$ with tetramethylsilane as internal standard. Coupling constants *J* are given in Hz. Mass spectra were determined on a Finnigan-MAT-1020B spectrometer. Microanalyses were performed at the Organic Chemistry Division, NCL.

General procedure for the conversion of carbonimidodithioates 6 to *N*-alkyl *S*-methyl thiocarbamates 7

A solution of an *N*-alkylcarbonimidodithioate **6a–m** (10 mmol) in MeCN–water (3:1; 10 cm^3) was added dropwise to a stirred solution of $ZnCl_2$ (10 mmol) in the same solvent (10 cm^3). The mixture was further stirred at 60 °C for 6–10 h. A clear solution was obtained at the beginning in which a white precipitate later formed. The reaction mixture was cooled to room temperature and filtered through a sintered funnel. The filtrate was concentrated and the residue was taken up in CH_2Cl_2, washed with brine and dried over anhydrous $MgSO_4$. Evaporation of the mixture gave the product **7a–m**, which was further purified either by column chromatography or by crystallisation.

***S*-Methyl *N*-methyl(thiocarbamate) 7a.** (52%) *Liquid*, bp 70–74 °C/5.0 mmHg; ν_{max}(Nujol)/cm^{-1} 3310, 1670, 1540 and 1230; δ_H($CDCl_3$) 5.50 (1 H, br s, NH), 2.75 (3 H, d, *J* 5.0, NCH_3) and 2.25 (3 H, s, SCH_3); *m*/*z* 105 (M^+, 95%), 75 and 58 (100) (Found: C, 34.28; H, 6.66; N, 13.33. C_3H_7NOS requires C, 34.28; H, 6.67; N, 13.29%).

***S*-Methyl *N*-propyl(thiocarbamate) 7b.** (12%) An *oil*, ν_{max}(neat)/cm^{-1} 3310, 1670, 1540 and 1230; δ_H($CDCl_3$) 5.50 (1 H, br, NH), 3.20 (2 H, q, *J* 3.4, NCH_2), 2.30 (3 H, s, SCH_3) 1.50 (2 H, m, CH_2) and 0.90 (3 H, t, *J* 5.7, CH_3); *m*/*z* 133 (M^+, 95%), 86, 75, 48 and 43 (100) (Found: C, 45.22; H, 8.29; N, 10.53. $C_5H_{11}NOS$ requires C, 45.11; H, 8.27; N, 10.52%).

***S*-Methyl *N*-butyl(thiocarbamate) 7c.** (53%) *Thick liquid*, ν_{max}(neat)/cm^{-1} 3340, 1730, 1520 and 1240; δ_H($CDCl_3$) 4.85 (1 H, br, NH), 3.15 (2 H, q, *J* 5.7, NCH_2), 2.30 (3 H, s, SCH_3), 1.40 (2 H, quintet, CH_2), 1.35 (2 H, m, CH_2) and 0.85 (3 H, t, *J* 5.7, CH_3) (Found: C, 49.09; H, 8.92; N, 9.45. $C_6H_{13}NOS$ requires C, 48.97; H, 8.84; N, 9.52%).

***S*-Methyl *N*-*sec*-butyl(thiocarbamate) 7d.** (40%) *Semisolid*, ν_{max}(neat)/cm^{-1} 3320, 1730, 1670, 1530 and 1220; δ_H($CDCl_3$) 5.30 (1 H, br, NH), 3.55 (1 H, m, CH), 2.35 (3 H, s, SCH_3), 1.45 (2 H, m, CH_2), 1.15 (3 H, d, *J* 7.5, CH_3) and 0.90 (3 H, t, *J* 4.5, CH_3); *m*/*z* 147 (M^+, 75%), 118 (100), 100 and 75 (Found: C, 49.09; H, 8.92; N, 9.45%).

***S*-Methyl *N*-cyclohexyl(thiocarbamate) 7e.** (95%) *Crystalline solid*, mp 103–104 °C (from EtOH); ν_{max}(Nujol)/cm^{-1} 3320, 1660, 1470 and 1220; δ_H($CDCl_3$) 5.30 (1 H, br, NH), 3.65 (1 H, m, CH), 2.35 (3 H, s, SCH_3) and 1.10–2.00 (10 H, m, 5 × CH_2); *m*/*z* 173 (M^+, 75%), 126 and 83 (100) (Found: C, 55.55; H, 8.72; N, 7.89. $C_8H_{15}NOS$ requires C, 55.49; H, 8.67; N, 8.09%).

***S*-Methyl *N*-benzyl(thiocarbamate) 7f.** (97%) *Crystalline solid*, mp 79–80 °C (from EtOH); ν_{max}(Nujol)/cm^{-1} 3320–3420, 1680, 1510 and 1230; δ_H($CDCl_3$) 7.40 (5 H, s, ArH), 5.70 (1 H, br, NH), 4.50 (2 H, d, *J* 6.4, CH_2) and 2.40 (3 H, s, SCH_3); *m*/*z* 181 (M^+, 45%), 133 and 91 (100) (Found: C, 59.77; H, 6.05; N, 7.73. $C_9H_{11}NOS$ requires C, 59.66; H, 6.07; N, 7.73%).

(−)-*S*-Methyl *N*-[(*S*)-1-phenylethyl]thiocarbamate 7g. (98%) Light yellow *crystalline solid*, mp 85 °C (from EtOH); ν_{max}(Nujol)/cm^{-1} 3350, 1640, 1510 and 1230; δ_H($CDCl_3$) 7.35 (5 H, s, ArH), 5.65 (1 H, br, NH), 5.10 (1 H, m, NCH), 2.35 (3 H, s, SCH_3) and 1.55 (3 H, d, *J* 6.5, CH_3); *m*/*z* 195 (M^+, 48%), 147

and 105 (100) (Found: C, 61.75; H, 6.67; N, 7.22. $C_{10}H_{13}NOS$ requires C, 61.53; H, 6.66; N, 7.17%).

Methyl *N*-(methylthiocarbonyl)glycinate 7h. (40%) *Semisolid*, ν_{max}(neat)/cm^{-1} 3350, 1780, 1680, 1530 and 1200; δ_H($CDCl_3$) 6.25 (1 H, br, NH), 4.10 (2 H, d, *J* 5.0, NCH_2), 3.60 (3 H, s, OCH_3) and 2.15 (3 H, s, SCH_3); *m*/*z* 163 (M^+, 20%), 114 (100) 116 and 88 (Found: C, 36.87; H, 5.52; N, 8.56. $C_5H_9NO_3S$ requires C, 36.80; H, 5.52, N, 8.58%).

2-Chloroethyl *N*-(methylthiocarbonyl)glycinate 7i. (43%) *Solid*, mp 73 °C (from EtOH); ν_{max}(Nujol)/cm^{-1} 3410, 1760, 1690, 1500 and 1235; δ_H($CDCl_3$) 5.80 (1 H, br NH), 4.30 (2 H, t, *J* 8.0, CH_2), 4.00 (2 H, d, *J* 6.4, NCH_2), 3.50 (2 H, t, *J* 4.8, CH_2) and 2.20 (3 H, s, SCH_3); *m*/*z* 211 (M^+, 10%), 164 and 136 (100) (Found: C, 34.13; H, 4.82; N, 6.57. $C_6H_{10}ClNO_3S$ requires C, 34.12; H, 4.73; N, 6.63%).

Methyl *N*-(methylthiocarbonyl)-β-alaninate 7j. (47%) *Semisolid*, ν_{max}(Nujol)/cm^{-1} 3320, 1760, 1670, 1510 and 1450; δ_H($CDCl_3$) 5.90 (1 H, br, NH), 3.55 (3 H, s, OCH_3), 3.40 (2 H, q, *J* 8.0, NCH_2), 2.45 (2 H, t, *J* 6.4, CH_2) and 2.10 (3 H, s, SCH_3); δ_C($CDCl_3$) 172.52, 167.86, 51.65, 36.52, 33.78 and 12.08; *m*/*z* 177 (M^+, 7%), 130, 98 (100), 75, 70 and 59 (Found: C, 40.52; H, 6.25; N, 7.98. $C_6H_{11}NO_3S$ requires C, 40.67; H, 6.21; N, 7.90%).

Methyl (*S*)-*N*-(methylthiocarbonyl)alaninate 7k. (50%) An oil, ν_{max}(neat)/cm^{-1} 3320, 1770, 1680, 1520 and 1200; δ_H($CDCl_3$) 5.90 (1 H, br, NH), 4.50 (1 H, m, NH), 3.85 (3 H, s, OCH_3), 2.55 (3 H, s, SCH_3) and 1.55 (3 H, d, *J* 7.8, CH_3); *m*/*z* 177 (M^+, 5%) and 130 (100%) (Found: C, 40.75; H, 6.24; N, 7.82%).

Methyl (*S*)-*N*-(methylthiocarbonyl)phenylalaninate 71. (48%) Light yellow *solid*, mp 85–87 °C (from EtOH); ν_{max}(Nujol)/cm^{-1} 3400, 1740, 1670, 1500 and 1220; δ_H($CDCl_3$) 7.10–7.45 (5 H, m, ArH), 5.95 (1 H, br, NH), 4.90 (1 H, q, *J* 5.4, NCH), 3.70 (3 H, s, OCH_3), 3.10 (2 H, d, *J* 6.4, CH_2) and 2.35 (3 H, s, SCH_3); *m*/*z* 253 (M^+, 2%), 206, 194, 162 (100), 146, 134 and 91 (Found: C, 57.22; H, 5.98; N, 5.42. $C_{12}H_{15}NO_3S$ requires C, 56.91; H, 5.92; N, 5.53%).

Methyl (*S*)-*N*-(methylthiocarbonyl)valinate 7m. (45%) Thick *liquid*, ν_{max}(neat)/cm^{-1} 3360, 1750, 1680 and 1540; δ_H($CDCl_3$) 5.80 (1 H, br s, NH), 4.40 (1 H, d, *J* 5.7, NCH), 3.55 (3 H, s, OCH_3), 2.05 (1 H, m, CH) and 0.89 (6 H, m, 2 × CH_3); *m*/*z* 205 (M^+), 158, 146 and 130 (100%) (Found: C, 46.79; H, 7.37; N, 6.71. $C_8H_{15}NO_3S$ requires C, 46.82; H, 7.31; N, 6.82%).

General procedure for the conversion of carbonimidodithioates 6 to *N*-alkylcarbamates 8

A solution of an *N*-alkylcarbonimidodithioate **6a–g** and **6k–m** (10 mmol) in MeOH–water (3:1; 10 cm^3) was added dropwise at room temperature to a stirred solution of $ZnCl_2$ (10 mmol) in the same mixture of solvents (10 cm^3). The reaction mixture was further stirred at 60–80 °C. TLC after 5 h showed the formation of both the thiocarbamate and the corresponding carbamate. The reaction was complete after 10–12 h; the mixture was then cooled to room temperature and filtered through a sintered funnel. The filtrate was concentrated and the residue was taken up in CH_2Cl_2, washed with brine and dried over anhydrous $MgSO_4$. Evaporation of the mixture gave the products **8a–g** and **8k–m**.

Methyl *N*-methylcarbamate 8a. (52%) An *oil*, bp 52–54 °C/4.4 mmHg; ν_{max}(neat)/cm^{-1} 3350–3460, 1720, 1520 and 1230; δ_H($CDCl_3$) 75 (1 H, br, NH), 3.65 (3 H, s, OCH_3) and 2.75 (3 H, d, *J* 4.0, NCH_3) (Found: C, 40.57; H, 7.97; N, 15.69. $C_3H_7NO_2$ requires C, 40.44; H, 7.86; N, 15.73%).

Methyl *N*-propylcarbamate 8b. (84%) An *oil*, ν_{max}(neat)/cm^{-1} 3320–3450, 1700, 1520 and 1220; δ_H($CDCl_3$) 4.95 (1 H, br, NH), 3.55 (3 H, s, OCH_3), 3.15 (2 H, q, NCH_2), 1.45 (2 H, m, CH_2) and 0.95 (3 H, t, *J* 6.7, CH_3) (Found: C, 51.41; H, 9.80; N, 11.82. $C_5H_{11}NO_2$ requires C, 51.28; H, 9.40; N, 11.96%).

Methyl *N*-butylcarbamate 8c. (87%) *Thick liquid*, ν_{max}(neat)/cm^{-1} 3340, 1700, 1520 and 1240; δ_H($CDCl_3$) 4.85 (1 H, br, NH), 3.50 (3 H, s, OCH_3), 3.15 (2 H, m, NCH_2), 1.40 (2 H, quintet, CH_2), 1.35 (2 H, m, CH_2) and 0.85 (3 H, t, *J* 6.7, CH_3) (Found: C, 54.64; H, 10.10; N, 10.62. $C_6H_{13}NO_2$ requires C, 54.96; H, 9.92; N, 10.68%).

Methyl *N*-*sec*-butylcarbamate 8d. (82%) An *oil*, ν_{max}(neat)/cm^{-1} 3320–3430, 1710, 1510 and 1220; δ_H($CDCl_3$) 4.40 (1 H, br, NH), 3.55 (1 H, m, CH), 3.60 (3 H, s, OCH_3), 1.40 (2 H, m, CH_2), 1.15 (3 H, s, CH_3) and 0.95 (3 H, t, *J* 5.6, CH_3) (Found: C, 54.62; H, 10.14; N, 10.58%).

Methyl *N*-cyclohexylcarbamate 8e. (97%) *Solid*, mp 57 °C (from EtOH); ν_{max}(Nujol)/cm^{-1} 3320, 1720, 1510 and 1230; δ_H($CDCl_3$) 4.55 (1 H, br, NH), 3.70 (3 H, s, OCH_3), 3.55 (1 H, br, CH) and 1.10–2.00 (10 H, m, CH_2) (Found: C, 61.16; H, 9.64; N, 8.82. $C_8H_{15}NO_2$ requires C, 61.14; H, 9.55; N, 8.91%).

Methyl *N*-benzylcarbamate 8f. (98%) *Solid*, mp 49.8 °C (from EtOH); ν_{max}(Nujol)/cm^{-1} 3440–3460, 1730, 1520 and 1230; δ_H($CDCl_3$) 7.35 (5 H, s, ArH), 5.00 (1 H, br, NH), 4.40 (2 H, s, CH_2Ph) and 3.70 (3 H, s, OCH_3) (Found: C, 65.47; H, 6.68; N, 8.47. $C_9H_{11}NO_2$ requires C, 65.45; H, 6.66; N, 8.48%).

(−)-Methyl *N*-[(*S*)-1-phenylethyl]carbamate 8g. (98%) *Solid*, mp 50–51 °C (from EtOH); ν_{max}(Nujol)/cm^{-1} 3440, 1720, 1520 and 1230; δ_H($CDCl_3$) 7.35 (5 H, m, ArH), 5.00 (1 H, br, NH), 4.90 (1 H, m, CH), 3.70 (3 H, s, OCH_3) and 1.50 (3 H, d, *J* 7.1, CH_3); *m*/*z* 179 (M^+, 25%), 164 (100), 125, 105, 77 and 42 (Found: C, 66.59; H, 7.66; N, 7.92. $C_{10}H_{13}NO_2$ requires C, 67.03; H, 7.26; N, 7.82%).

Methyl (*S*)-*N*-(methoxycarbonyl)alaninate 8k. (88%) *Thick liquid*, ν_{max}(neat)/cm^{-1} 3440, 1720, 1520, 1460 and 1220; δ_H($CDCl_3$) 5.40 (1 H, br, 1 H), 4.40 (1 H, br m, CH), 3.80 (3 H, s, OCH_3), 3.70 (3 H, s, OCH_3) and 1.45 (3 H, d, *J* 8.0, CH_3) (Found: C, 44.84; H, 6.89; N, 8.58. $C_6H_{11}NO_4$ requires C, 44.72; H, 6.83; N, 8.69%).

Methyl (*S*)-*N*-(methoxycarbonyl)phenylalaninate 81. (89%) *Thick liquid*, ν_{max}(neat)/cm^{-1} 3430, 1740, 1520 and 1230; δ_H($CDCl_3$) 7.20 (5 H, m, ArH), 5.20 (1 H, br, NH), 4.55 (1 H, br, CH), 3.65 (3 H, s, OCH_3), 3.55 (3 H, s, OCH_3) and 3.05 (2 H, d, *J* 6.7, CH_2) (Found: C, 60.50; H, 6.81; N, 5.82. $C_{12}H_{15}NO_4$ requires C, 60.75; H, 6.32; N, 5.90%).

Methyl (*S*)-*N*-(methoxycarbonyl)valinate 8m. (84%) *Thick liquid*, ν_{max}(neat)/cm^{-1} 3430, 1720, 1510 and 1220; δ_H($CDCl_3$) 5.15 (1 H, br, NH), 4.30 (1 H, br s, NCH), 3.55 (3 H, s, OCH_3), 3.50 (3 H, s, OCH_3), 1.95 (1 H, m, CH) and 0.75 (6 H, m, 2 × CH_3) (Found: C, 50.49; H, 8.09; N, 7.26. $C_8H_{15}NO_4$ requires C, 50.79; H, 7.93; N, 7.40%).

Preparation of carbonimidodithioates 11a–e from α-amino acid allyl esters 10

α-Amino acid allyl esters **10a–e** were prepared by the published procedure.[11] These were converted to the corresponding dimethyl carbonimidodithioates **11a–e** by the usual procedure[12,13] involving condensation with CS_2, followed by methylation.

***N*-[Bis(methylthio)methylene]glycine allyl ester 11a.** (69%) *Pale yellow oil*, ν_{max}(neat)/cm^{-1} 2900, 2100, 1740, 1580, 1410 and 1170; δ_H($CDCl_3$) 2.40 (3 H, s, SCH_3), 2.60 (3 H, s, SCH_3), 4.25 (2 H, s, NCH_2), 4.75 (2 H, m, OCH_2) and 5.30 (2 H, m, $=CH_2$); δ_C($CDCl_3$) 14.46, 14.75, 54.04, 65.16, 117.98, 132,02, 162.86 and 169.43; *m*/*z* 219 (M^+), 172 (100%), 157, 144, 127, 116, 101 and 87 (Found: C, 43.54; H, 5.92; N, 5.94. $C_8H_{13}NO_2S_2$ requires C, 43.83; H, 5.93; N, 6.39%).

(*S*)-*N*-[Bis(methylthio)methylene]alanine allyl ester 11b. (73%) *Pale yellow oil*, ν_{max}(neat/cm^{-1} 2990, 2910, 2020, 1740, 1570, 1420 and 1370; δ_H($CDCl_3$) 1.45 (3 H, d, *J* 6.2, CH_3), 2.40 (3 H, s, SCH_3), 2.55 (3 H, s, SCH_3), 4.55 (1 H, q, *J* 7.5, NCH), 4.65 (2 H, m, OCH_2), 5.25 (2 H, m, $=CH_2$) and 5.95 (1 H, m, =CH); δ_C($CDCl_3$) 14.32, 14.53, 18.18, 19.13, 59.70, 64.77, 117.35, 118.80, 131.88, 160.77 and 171.50; *m*/*z* 233 (M^+), 186 (100%),158, 148, 130, 114, 89, 75 and 60 (Found: C, 46.73; H, 6.62; N, 5.94. $C_9H_{15}NO_2S_2$ requires C, 46.35; H, 6.43; N, 6.00%)

(*S*)-*N*-[Bis(methylthio)methylene]valine allyl ester 11c. (71%) *Pale yellow oil*, ν_{max}(neat)/cm^{-1} 2960, 2920, 2080, 1730, 1580 and 1430; δ_H($CDCl_3$) 1.00 (6 H, m, 2 × CH_3), 2.35 (1 H, m,

CH), 2.45 (3 H, s, SCH_3), 2.60 (3 H, s, SCH_3), 4.20 (1 H, d, *J* 6.7, NCH), 4.65 (2 H, m, OCH_2), 5.35 (2 H, m, $=CH_2$) and 5.95 (1 H, m, CH); $\delta_C(CDCl_3)$ 14.38, 14.62, 17.82, 19.12, 32.17, 64.60, 65.11, 117.49, 131.86, 161.19 and 170.31; *m*/*z* 261 (M^+), 214, 199, 186, 171, 128, 114 (100%), 103 and 91 (Found: C, 50.91; H, 7.22; N, 5.79. $C_{11}H_{19}NO_2S_2$ requires C, 50.57; H, 7.27; N, 5.36%).

(*S*)-*N*-[Bis(methylthio)methylene]leucine allyl ester 11d. (65%) *Pale yellow oil*, ν_{max}(neat)/cm^{-1} 2920, 2060, 1740, 1570, 1430, 1560 and 1220; $\delta_H(CDCl_3)$ 0.90 (3 H, d, *J* 7.8, CH_3), 0.95 (3 H, d, *J* 7.3, CH_3), 1.55 (1 H, m, CH), 2.60 (2 H, dd, CH_2), 2.40 (3 H, s, SCH_3), 2.80 (3 H, s, SCH_3), 4.50 (1 H, t, *J* 7.4, NCH), 4.65 (2 H, m, OCH_2), 5.30 (2 H, m, $=CH_2$) and 5.95 (1 H, m, =CH); $\delta_C(CDCl_3)$ 14.34, 14.60, 21.80, 22.70, 24.68, 42.21, 63.01, 64.70, 117.30, 131.92, 16.96 and 170.99; *m*/*z* (275 (M^+), 260, 228, 200, 172, 142, 95 and 69 (100%) (Found: C, 52.59; H, 7.70; N, 5.20. $C_{12}H_{21}NO_2S_2$ requires C, 52.36; H, 7.63; N, 5.09%).

(*S*)-*N*-[Bis(methylthio)methylene]phenylalanine allyl ester 11e. (77%) *Pale yellow oil*, ν_{max}(neat)/cm^{-1} 3000, 2905, 2020, 2010, 1725, 1560, 1490 and 1410; $\delta_H(CDCl_3)$ 2.40 (3 H, s, SCH_3), 2.50 (3 H, s, SCH_3), 3.20 (2 H, m, CH_2), 4.60 (1 H, t, *J* 5.7, NCH), 4.65 (2 H, m, OCH_2), 5.25 (2 H, m, $=CH_2$), 5.90 (1 H, m, =CH) and 7.25 (5 H, m, ArH); $\delta_C(CDCl_3)$ 14.65, 14.94, 39.59, 65.05, 66.38, 117.70, 126.30, 127.99, 131.89, 137.56, 162.35 and 170.52; *m*/*z* 309 (M^+), 262, 218, 188, 162, 143, 128, 103 and 91 (100%) (Found: C, 58.59; H, 6.09; N, 4.85. $C_{15}H_{19}NO_2S_2$ requires C, 58.25; H, 6.14; N, 4.53%).

General procedure for the conversion of carbonimidodithioates 6 or 11 to benzyl carbamates 9 or 12

Sodium benzyl alcoholate (2 mmol) was taken up in dry THF (10 cm^3). To this was added the appropriate carbonimidodithioate (2 mmol) and the mixture was stirred at 30 °C for 6 h. The sodium salt slowly went into solution as the reaction progressed. The reaction was monitored by TLC. After complete disappearance of the starting material, water (0.1 cm^3) was added to the mixture, which was then stirred overnight at 30 °C. The THF was removed by distillation *in vacuo*, and the aqueous residue was extracted with EtOAc (25 cm^3). The organic layer was washed successively with water (2 × 20 cm^3), 1% HCl (2 × 20 cm^3) and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the product was purified by chromatography on a silica column [1:9 acetone–light petroleum (60–80 °C)].

Methyl *N*-(benzyloxycarbonyl)glycinate 9h. (81%) *Oil*, ν_{max}(neat)/cm^{-1} 3360, 3040, 2960, 1740, 1710, 1520, 1510 and 1440; $\delta_H(CDCl_3)$ 3.75 (3 H, s, OCH_3), 4.00 (2 H, d, *J* 5.0, NCH_2), 5.15 (2 H, s, OCH_2), 5.35 (1 H, br, NH) and 7.35 (5 H, m, ArH); $\delta_C(CDCl_3)$ 42.40, 51.94, 66.75, 127.85, 128.29, 136.25, 156.48 and 170.55; *m*/*z* 223 (M^+), 189, 164, 120, 108 and 91 (100%) (Found: C, 59.15; H, 5.96; N, 6.12. $C_{11}H_{13}NO_4$ requires C, 59.19; H, 5.82; N, 6.27%).

Methyl (*S*)-*N*-(benzyloxycarbonyl)alaninate 9k. *Oil*, (86%) ν_{max}(neat)/cm^{-1} 3320, 2930, 1720, 1540, 1460 and 1220; δ_H 1.40 (3 H, d, *J* 8.7, CH_3), 3.75 (3 H, s, OCH_3), 4.40 (1 H, m, NCH), 5.10 (2 H, s, CH_2Ph), 5.55 (1 H, br, NH) and 7.35 (5 H, m, Ph); $\delta_C(CDCl_3)$ 18.19, 49.55, 52.19, 66.71, 127.96, 128.36, 136.35, 155.69 and 173.43; *m*/*z* 237 (M^+), 218, 178, 156, 141, 115 and 91 (100%) (Found: C, 60.64; H, 6.02; N, 5.69. $C_{12}H_{15}NO_4$ requires C, 60.75; H, 6.32; N, 5.90%).

Methyl (*S*)-*N*-(benzyloxycarbonyl)phenylalaninate 9l. *Oil*, (80%) ν_{max}(neat)/cm^{-1} 3460, 3020, 1720, 1540, 1510, 1460 and 1220; $\delta_H(CDCl_3)$ 3.15 (2 H, t, *J* 5.5, CH_2), 3.75 (3 H, s, OCH_3), 4.70 (1 H, q, *J* 7.8, NCH), 5.15 (2 H, s, CH_2Ph), 5.30 (1 H, br, NH) and 7.10–7.45 (10 H, m, 2 × Ph); $\delta_C(CDCl_3)$ 38.00, 52.12, 66.77, 127.00, 127.99, 128.46, 128.53, 129.30, 136.33, 136.58, 155.98 and 172.23; *m*/*z* 313 (M^+), 270, 252, 228, 210, 192, 178, 162 and 91 (100%) (Found: C, 68.87; H, 6.01; N, 4.32. $C_{18}H_{19}NO_4$ requires C, 69.00; H, 6.07; N, 4.47%).

Methyl (*S*)-*N*-(benzyloxycarbonyl)valinate 9m. *Oil*, (85%) ν_{max}(neat)/cm^{-1} 3360, 2990, 1730, 1540, 1510, 1450 and 1220; $\delta_H(CDCl_3)$ 0.95 (6 H, q, *J* 8.5, 2 × CH_3), 2.25 (1 H, m, CH), 3.75 (3 H, s, OCH_3), 4.30 (1 H, q, *J* 4.7, NCH), 5.15 (2 H, s, CH_2Ph), 5.20 (1 H, br, *J* 7.4, NH) and 7.40 (5 H, m, Ph); $\delta_C(CDCl_3)$ 17.50, 18.79, 31.09, 51.86, 59.08, 66.78, 127.94, 128.35, 128.76, 136.35, 156.21 and 172.41; *m*/*z* 265 (M^+), 218, 206, 162, 108 and 91 (100%) (Found: C, 63.51; H, 7.30; N, 5.37. $C_{14}H_{19}NO_4$ requires C, 63.39; H, 7.16; N, 5.28%).

Allyl *N*-(benzyloxycarbonyl)glycinate 12a. (79%) *Oil*, ν_{max}(neat)/cm^{-1} 3350, 3020, 2940, 1740, 1720, 1520, 1480 and 1230; $\delta_H(CDCl_3)$ 4.00 (2 H, d, *J* 6.7, NCH_2), 4.65 (2 H, d, *J* 5.5, OCH_2), 5.15 (2 H, s, OCH_2Ph), 5.15 (2 H, m, $=CH_2$), 5.40 (1 H, br, NH), 5.90 (1 H, m, =CH) and 7.35 (5 H, m, ArH); $\delta_C(CDCl_3)$ 42.39, 65.40, 66.57, 118.21, 127.71, 128.15, 131.45, 136.19, 156.41 and 169.68; *m*/*z* 249 (M^+), 206, 192, 170, 158, 107 and 91 (100%) (Found: C, 62.47; H, 6.28; N, 5.35. $C_{13}H_{15}NO_4$ requires C, 62.65; H, 6.02; N, 5.62%).

Allyl (*S*)-*N*-(benzyloxycarbonyl)alaninate 12b. (80%) *Oil*, ν_{max}(neat)/cm^{-1} 3360, 3080, 2980, 1740, 1750, 1510, 1460 and 1260; $\delta_H(CDCl_3)$ 1.45 (3 H, d, *J* 8.7, CH_3), 4.45 (1 H, t, *J* 8.5, NCH), 4.65 (2 H, d, *J* 5.6, OCH_2), 5.10 (2 H, s, OCH_2Ph), 5.30 (2 H, m, $=CH_2$), 5.45 (1 H, br, NH), 5.90 (1 H, m, $=CH_2$) and 7.35 (5 H, m, ArH); $\delta_C(CDCl_3)$ 18.36, 49.69, 65.76, 66.80, 118.51, 128.04, 128.44, 131.64, 136.37, 155.72 and 172.69; *m*/*z* 263 (M^+), 172, 134, 108, 91 (100%), 79 and 65 (Found: C, 64.18; H, 6.44; N, 5.06. $C_{14}H_{17}NO_4$ requires C, 63.87; H, 6.46; N, 5.32%).

Allyl (*S*)-*N*-(benzyloxycarbonyl)valinate 12c. (72%) *Oil*, ν_{max}(neat)/cm^{-1} 3320, 3060, 3020, 2940, 1725, 1710, 1510, 1450 and 1290; $\delta_H(CDCl_3)$ 0.90 (3 H, d, *J* 6.7, CH_3), 1.00 (3 H, d, *J* 6.5, CH_3), 2.20 (1 H, m, CH), 4.35 (1 H, br, NH), 4.15 (2 H, d, *J* 5.8, $=CH_2$), 5.15 (2 H, s, OCH_2Ph), 5.35 (2 H, m, OCH_2), 5.40 (1 H, br, NH), 5.95 (1 H, m, =CH) and 7.40 (5 H, m, ArH); $\delta_C(CDCl_3)$ 17.40, 18.78, 31.00, 59.08, 65.44, 66.66, 118.51, 127.84, 128.25, 131.59, 134.64, 136.33, 156.19, 166.19 and 171.58; *m*/*z* 295 (M^+), 206, 162, 127, 107 and 91 (100%) (Found: C, 65.59; H, 7.54; N, 5.23. $C_{16}H_{21}NO_4$ requires C, 65.97; H, 7.21; N, 4.81%).

Allyl (*S*)-*N*-(benzyloxycarbonyl)leucinate 12d. (74%) Oil, ν_{max}(neat)/cm^{-1} 3350, 3070, 3015, 2945, 1730, 1510 and 1450; $\delta_H(CDCl_3)$ 1.00 (6 H, 2 d, *J* 7.6, 2 × CH_3), 1.65 (3 H, m, CH and CH_2), 4.45 (1 H, m, CH), 4.75 (2 H, d, *J* 7.7, OCH_2), 5.15 (2 H, s, OCH_2Ph), 5.30 (2 H, m, $=CH_2$), 5.40 (1 H, br, NH), 5.95 (1 H, m, =CH) and 7.35 (5 H, m, ArH); $\delta_C(CDCl_3)$ 21.85, 22.90, 24.79, 41.68, 52.68, 65.81, 66.96, 118.65, 128.12, 128.54, 131.77, 136.45, 156.11 and 172.91; *m*/*z* 305 (M^+), 220, 186, 171, 155, 141, 127, 107, 91 (100%) and 81 (Found: C, 66.85; H, 7.54; N, 4.54. $C_{17}H_{23}NO_4$ requires C, 66.88; H, 7.54; N, 4.59%).

Allyl (*S*)-*N*-(benzyloxycarbonyl)phenylalaninate 12e. (73%) *Oil*, ν_{max}(neat)/cm^{-1} 3340, 3060, 3020, 2940, 1730, 1710, 1520, 1450 and 1295; $\delta_H(CDCl_3)$ 3.35 (2 H, d, *J* 4.2, CH_2), 4.65 (2 H, d, *J* 6.5, OCH_2), 4.75 (1 H, m, NCH), 5.15 (2 H, s, OCH_2Ph), 5.30 (2 H, m, $=CH_2$), 5.40 (1 H, br, NH), 5.90 (1 H, m, =CH) and 7.25 (10 H, m, ArH); $\delta_C(CDCl_3)$ 38.17, 55.00, 65.95, 66.88, 118.87, 127.07, 128.04, 128.51, 129.35, 131.52, 135.89, 136.38, 155.74 and 171.31; *m*/*z* 339 (M^+), 296, 278, 254, 210, 188 and 91 (100%) (Found: C, 70.70; H, 5.90; N, 4.06. $C_{20}H_{21}NO_4$ requires C, 70.79; H, 6.19; N, 4.12%).

Hydrolysis of *N*-(benzyloxycarbonyl)glycine methyl ester 9h

A solution of compound **9h** (1 mmol) in MeOH (5 cm^3) was stirred with aq. NaOH (1.1 mmol in 5 cm^3) at 30 °C for 6 h. The MeOH was removd *in vacuo*, the residue was diluted with water and acidified to pH 2 by addition of conc. HCl. The product was extracted with EtOAc (3 × 15 cm^3), the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The solvent was then removed to give the TLC-pure *N*-(benzyloxycarbonyl)glycine **13a**, mp 120 °C, in 84% yield.

The hydrolysis could similarly be carried out with substrates **9k**, **9l** and **9m** to give the corresponding *N*-benzyloxycarbonyl-α-amino acids.

General procedure for de-allylation of allyl esters

To a solution of an allyl ester **12** (1 mmol) in dry MeCN (5 cm^3) were added 1,8-diazabicyclo [5.4.0]undec-7-ene (DBU) (1 mmol), and morpholine (3 mmol) and the mixture was stirred under argon at 30 °C. To this was added $Pd(dba)_2$† (5 mol%), followed by PPh_3 (10 mol%). The reaction mixture became clear in about 15–20 min. The mixture was stirred at 30 °C for 12 h. The progress of the reaction was monitored by TLC. After completion of the reaction, it was quenched by the addition of aq. HCl (5%; 5–6 cm^3). The aqueus solution was extracted with EtOAc (5 × 15 cm^3), and the organic layers were combined, washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the product **13** was purified by recrystallisation. The yields and physical data are presented in Table 1.

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† dba = dibenzylideneacetone.

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