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Prenyl carbamates: preparation and deprotection

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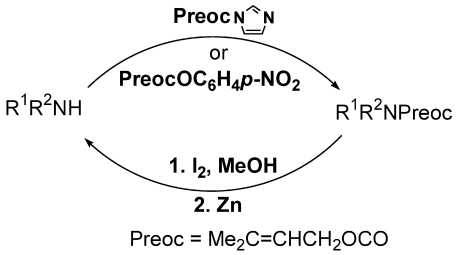
Abstract—Prenyloxycarbonylimidazole (PreocIm) and prenyl *p*-nitrophenyl carbonate (PreocOC_6H_4*p*-NO_2), two substitutes for the unstable prenyl chloroformate, allowed an efficient introduction of the prenyloxycarbonyl group to a variety of primary and secondary amines. Deprotection of prenyl carbamates was readily achieved by, first their conversion to 2-iodo-3-methoxy-3-methylbutyl carbamates with iodine in methanol followed by reductive β-elimination with zinc powder. These reaction conditions are compatible with the presence of a number of functional groups such as Boc and Cbz carbamates, sulfides, double bonds, indoles and aromatic ethers.

1. Introduction

The principle of using carboxyl-protecting groups for the blocking of amines through the conversion of the latter into urethanes (carbamates) was the most successful innovation in peptide synthesis. Since the invention by Bergmann and Zervas in 1932 of the benzyloxycarbonyl group (Cbz group),[1] the first easily and selectively removable carbamate protecting group, an impressive arsenal of amino-protecting groups has been developed.[2] However, because of the increasing complexity of the molecules synthesized, which contain a multiplicity of functional groups, there is a constant need for new protecting groups to overcome the difficulties encountered in the experimental realization of the synthetic plan of these molecules.

In the course of a study devoted to the search of new protecting groups for alcohols and amines,[3] we have recently reported in a preliminary account a mild and chemoselective method for the cleavage of prenyl carbamates.[4]

We now report, in full details, studies of this method of deprotection of prenyl carbamates as well as their efficient preparation using two new and readily available reagents (Scheme 1).



Scheme 1.

2. Results and discussion

2.1. Introduction of the prenyloxycarbonyl amino-protecting group

A survey of the literature revealed that there are only few examples of synthesis of prenyl carbamates.[5] In all cases, prenyl chloroformate was used as a reagent, generated either by reaction of 3-methyl-2-buten-1-ol (prenol) with phosgene[5a] or triphosgene ($Cl_3COCOOCl_3$).[5d]

After several experiments, treatment of 2-phenylethylamine (**3b**), used as a model compound, with 2 equiv. of prenyl chloroformate, made in situ by reaction of commercial phosgene in toluene, in the presence of triethylamine, gave the carbamate **4b** in only 30% yield, after purification on silica gel. An attempt to purify prenyl chloroformate by vacuum distillation (15 mm Hg) in a Kugelrohr apparatus afforded a fraction boiling between 50 and 60 °C containing, except the chloroformate, prenyl chloride and isoprene. Other related substituted allyl chloroformates are known to decompose easily even at room temperature.[6]

Keywords: Amines; Carbamates; Iodine; Prenylation; Protecting groups.
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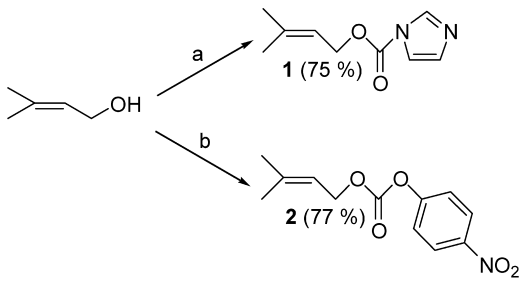
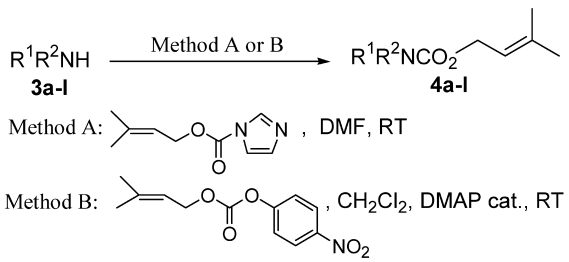
Then, looking for a more efficient and safer method for the synthesis of prenyl carbamates, we turned our attention to an other class of N-alkoxycarbonylation agent: imidazole carboxylic esters.[6b,7] Advantages of imidazolides over chloroformates are their greater stability which allows their purification on silica gel[8] and the use of commercially available *N*,*N*′-carbonyldiimidazole (CDI) for their preparation, a much safer reagent than phosgene. However, imidazolides are less reactive toward amines than chloroformates.

Prenyloxycarbonylimidazole (**1**) was readily prepared in 75% yield by reaction of prenol with CDI in CH_2Cl_2 at room temperature (Scheme 2). Treatment of 2-phenylethylamine (**3b**), a test substrate, with imidazolide **1**, in CH_2Cl_2 at room temperature for 24 h, afforded the corresponding carbamate **4b** in 75% yield. The employment of DMF as solvent instead of CH_2Cl_2 decreased dramatically the reaction time (5 h vs 24 h) and improved the yield (85%).



Scheme 2. Reagents and conditions: (a) CDI, CH_2Cl_2, 4 h, room temperature; (b)*p*-$NO_2C_6H_4OCOCl$, pyridine, 24 h, room temperature.

This mild method for prenyl carbamate formation (Scheme 3) was tested on a number of diversely functionalized amines and the results of this study are shown in Table 1. First, the reaction time of the carbamate formation was very depending on the substrate varying from 4 to 120 h. With most substrates, the *N*-prenyloxycarbonylation proceeded smoothly and in good yields (51–97%). However, with methionine, tryptophan and glucosamine derivatives (entries 15, 17, 21), the reaction was sluggish, providing the corresponding carbamate in low yields (0–33%).[9]



Scheme 3.

Frustrated by the low yielding introduction of the Preoc group to these important natural products, we looked for an other reagent able to form prenyl carbamates under mild conditions and in good yields whatever the amine used. We focused our attention to mixed carbonates activated by a *p*-nitrophenyl moiety, an interesting class of compounds used for the preparation of a large range of carbamates.[10]

Prenyl *p*-nitrophenyl carbonate (**2**), a crystalline solid, was easily made by reaction of prenol, in the presence of pyridine, with commercially available *p*-nitrophenyl chloroformate in CH_2Cl_2 at room temperature for 24 h (Scheme 2).

To evaluate the reactivity of amines toward the mixed carbonate **2**, a 1:1 mixture of L-methionine methyl ester (**3h**) and **2** was dissolved in CH_2Cl_2. Disappointingly, the reaction proceeded quite slowly at room temperature since 48 h were necessary for the reaction to attain completion. Gratifyingly, in the presence of a catalytic amount of DMAP (10 mol%), *N*-prenyloxycarbonyl-L-methionine methyl ester (**4h**) was isolated in 91% yield after stirring for 9 h at room temperature. As seen in Table 1, the mixed carbonate **2**, in the presence of DMAP, is a quite an efficient agent for the introduction of the Preoc group to amines (81–97% yield) except for the glucosamine derivative **3k** (entry 22) which reacted very sluggishly. Furthermore, during workup, *p*-nitrophenol formed during the reaction can be removed from the organic solution by a basic washing (Na_2CO_3) leaving the carbamate pratically pure. As seen in entry 20, the ε-amino group of L-lysine methyl ester derivative **3j** was regioselectively protected by reagent **2** in good yield (81%). Not much reagents are able to accomplish this transformation and anyhow with somewhat inferior yields.[11]

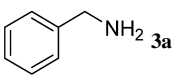
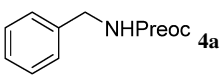
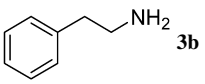
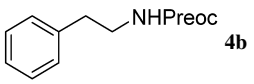
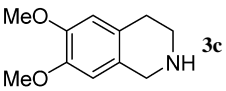
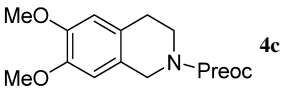
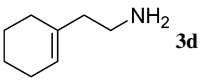
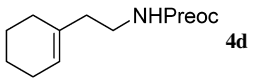
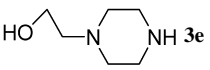
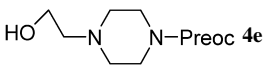
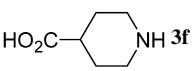
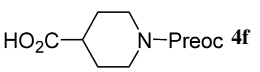
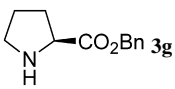
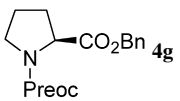
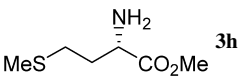
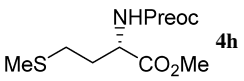
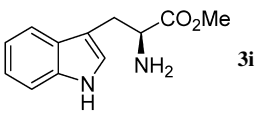
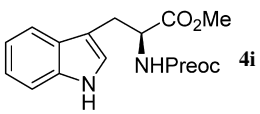
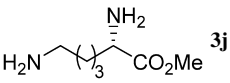
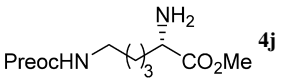
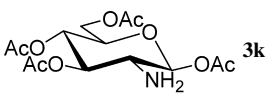
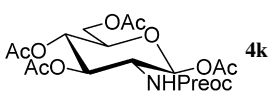
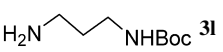
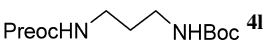
2.2. Cleavage of the *N*-prenyloxycarbonyl protecting group

There is only one method describing in the literature the deprotection of prenyl carbamates, using palladium technology, tested only on two substrates.[5b–c] Convinced that the prenyl moiety should be useful in the protection of functional groups such as acids, alcohols and amines, we first searched for mild method for the deprotection of prenyl ethers. We found that iodine in dichloromethane and dichlorodicyanoquinone in dichloromethane–water could chemoselectively cleave prenyl ethers in good yields.[3a–c] Encouraged by this success in the chemistry of prenyl group, we decided to apply these two techniques of prenyl group removal to amines. In both cases, cleavage of the prenyl carbamate derived from 2-phenylethylamine, compound **4b**, failed, leading to the recovery of the starting material, even after 24 h at room temperature.

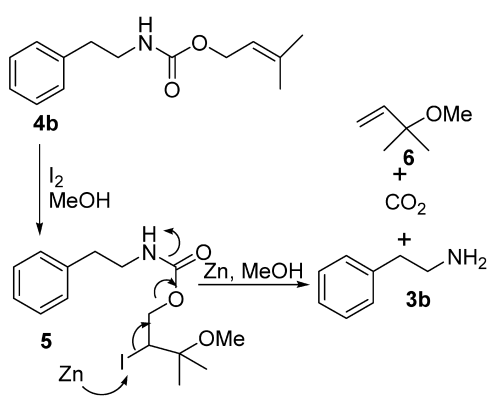
On the other hand, iodine in methanol reacted smoothly with **4b** to afford the 2-iodo-3-methoxy-3-methylbutyl carbamate **5** in 76% yield (Scheme 4). Compounds bearing a 2-haloalkoxycarbonyl system such as **5** are known to fragment in the presence of a metal.[12] Indeed, treatment of **5** with 2 equiv. of zinc in methanol, a good and commonly used electron donor, furnished 2-phenylethylamine (**3b**) in 70% yield (not optimized) (Scheme 4). We did not tried to detect the presence of 3-methoxy-3-methyl-1-butene (**6**), produced during the fragmentation, because of its low boiling point (80 °C).[13]

In order to simplify the process and to improve the overall yield, zinc was directly added to the reaction mixture containing the 2-iodo-3-methoxy-3-methylbutyl carbamate **5** and the excess of iodine. This addition was accompanied

Table 1. Synthesis of Preoc-N-protected amines using *N*-prenyloxycarbonylimidazole or prenyl *p*-nitrophenyl carbonate (**2**) as reagents

Entry	Substrate	Method[a]	Product	Time (h)	Yield (%)
1	 **3a**	A	 **4a**	4	88
2		B		1.5	98
3	 **3b**	A	 **4b**	5	85
4		B		3	97
5	 **3c**	A	 **4c**	48	51
6		B		2	94
7	 **3d**	A	 **4d**	4	97
8		B		3	93
9	 **3e**	A	 **4e**	4	93
10		B		1.5	95
11	 **3f**	A[b]	 **4f**	4	68
12		B[b]		1	91
13	 **3g**	A	 **4g**	120	52
14		B		3	90
15	 **3h**	A	 **4h**	120	33
16		B		9	91
17	 **3i**	A	 **4i**	120	201
18		B		24	85
19	 **3j**	A	 **4j**	24	51
20		B		1.5	81
21	 **3k**	A	 **4k**	48	0
22		B		120	39
23	 **3l**		 **4l**	3	80
24				2	97

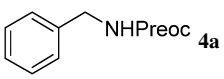
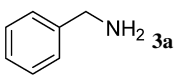
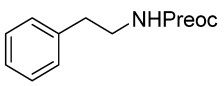
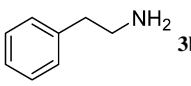
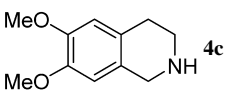
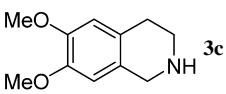
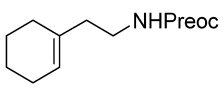
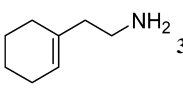
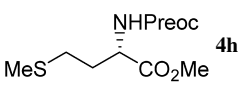
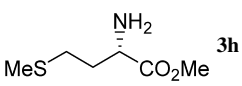
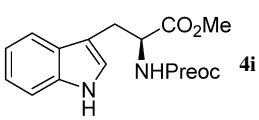
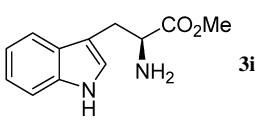
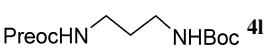
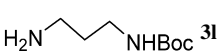
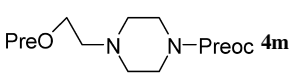
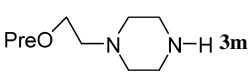
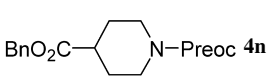
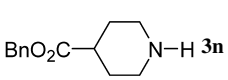
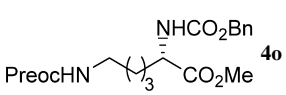
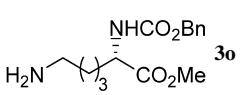
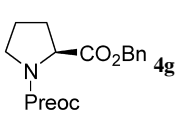
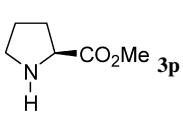
[a] Method A: $(CH_3)_2C{=}CHCH_2OCOlm$, DMF, room temperature. Method B: $(CH_3)_2C{=}CHCH_2OCO_2C_6H_4p\text{-}NO_2$ DMAP cat., CH_2Cl_2, room temperature.
[b] In the case of this amino acid, a 2:1 mixture of dioxane and water was used as solvents.



Scheme 4.

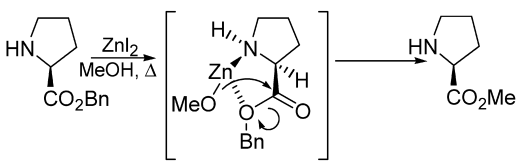
by the discoloration of the solution (ZnI_2 formation), concomitant effervescence as CO_2 liberated and heat formation. 2-Phenylethylamine (**3b**) was obtained in 85% yield which is superior to the 53% yield obtained via the two-step sequence. The reasons for the acceleration of the release of amine **3b** when zinc was added to the reaction mixture are uncertain. Iodine in excess may transform zinc into an active species, as it does with magnesium (Gilman catalyst),[14] achieving its fast oxidative insertion to the C–I bond.[15] An other explanation of the acceleration rate of the deprotection of the carbamate **4b**, under the conditions above, is that zinc iodide, obtained by reaction of zinc with iodine in excess, initiates the formation of the organozinc intermediate as do magnesium halides for Grignard reagents.[16]

Table 2. One-step deprotection of prenyl carbamates with I_2 in MeOH followed by Zn[a]

Entry	Substrate	Product	Yield (%)
1	 **4a**	 **3a**	83
2	 **4b**	 **3b**	85
3	 **4c**	 **3c**	78
4	 **4d**	 **3d**	88
5	 **4h**	 **3h**	83
6	 **4i**	 **3i**	53
7	 **4l**	 **3l**	82
8	 **4m**	 **3m**	63
9	 **4n**	 **3n**	75
10	 **4o**	 **3o**	85
11	 **4g**	 **3p**	70

[a] Reaction conditions: I_2 (2 equiv.), 7 h, room temperature then Zn (4 equiv.), 30 min; entries 4 and 8: I_2 (4 equiv.), Zn (8 equiv.); entry 6: I_2 (2 equiv.), 24 h, room temperature (without Zn).

The applicability of the method for the deprotection of prenyl carbamates was tested on diversely functionalized substrates and the results of this study are presented in Table 2. As depicted in the table, amines **3a**–**p** were obtained in acceptable to excellent yields (53–88%). Commonly used amino protecting groups such as Boc and Cbz groups were found stable under our conditions of Preoc deprotection (entries 7 and 10). In the presence of a double bond, the *N*-Preoc group has been deprotected in an excellent yield (88%) using 4 equiv. of iodine and 8 equiv. of zinc (entry 4). Interestingly, the prenyl carbamate of compound **3m** has been cleaved chemoselectively in the presence of a prenyl ether in an acceptable yield (63%, entry 8). The release of the tetrahydroisoquinoline alkaloid **3c** occurred in good yield (78%) without affecting the two methoxy groups (entry 3). Surprisingly, in the presence of methanol, the liberation of the amine of *N*-Preoc-L-tryptophan methyl ester **4i** happened without the need of adding zinc (entry 6). In the case of this substrate, the 2-iodo-3-methoxy-3-methylbutyl carbamate intermediate was not observed by TLC. We have no rationale to explain this result. Removal of the carbamate of *N*-Preoc proline benzyl ester **4g** occurred with complete transesterification by methanol (entry 11). As no transesterification of the benzyl ester of isonipecotic derivative **3n** was observed, under the same reaction conditions, we assume that the formation of the methyl ester **3p** is very likely the result of an intramolecular delivery of the methoxide anion to the carbonyl site of the ester by zinc, coordinated to the nitrogen of the pyrrolidine ring of the proline derivative (Scheme 5).



Scheme 5.

In order to test this hypothesis, L-proline benzyl ester (**3g**) was treated with 2 equiv. of zinc iodide in refluxing methanol for 30 min (Scheme 5). After a basic workup to extract zinc salts from the organic phase and purification of the residue on silica gel, L-proline methyl ester was obtained in 75% yield, thus confirming our assumption on the mechanism of the transesterification. Unfortunately, *N*-Preoc derivative of 1,3,4,6-tetra-*O*-acetyl-D-glucosamine, compound **4k**, under the conditions of *N*-Preoc deprotection, gave an untractable mixture of compounds.

3. Conclusion

In summary, we have introduced *N*-prenyloxycarbonylimidazole and prenyl *p*-nitrophenyl carbonate as two reagents for a facile installation of the prenyloxycarbonyl group. Both reagents are easily prepared in good yields from commercially available products, much safer and easier to handle than phosgene. If the applicability of the imidazolide is restricted to the protection of reactive primary and secondary amines, that of the mixed carbonate is more general and included amino acids. Another advantage of the carbonate is its high crystallinity which allows its purification by simple crystallization and therefore its preparation on a large scale. Having on hands a variety of prenyl carbamates diversely functionalized, we developed a simple one-pot two-step procedure for the chemoselective unmasking of amino groups. Furthermore, iodine and zinc, involved in this amino deprotection reaction, are cheap and non-toxic reagents. Because of its chemoselectivity and efficiency, this method of cleavage of *N*-prenyloxycarbonyl group should extent the use of prenyl carbamates for the protection of amine compounds.

4. Experimental

4.1. General procedures

^{1}H NMR spectra were recorded in $CDCl_3$ (δ_H=7.25) at ambient probe temperature on a Bruker AC 200 (200 MHz) spectrometer. Data are presented as follows: chemical shift (in ppm on the δ scale relative to δ_{TMS}=0), multiplicity (s=singlet, d=doublet, t=triplet, q=quadruplet, m=multiplet, br=broad), integration, coupling constant and interpretation. ^{13}C NMR spectra were recorded at ambient probe temperature on a Bruker AC 200 (50.3 MHz) in $CDCl_3$ used as reference (δC=77.0). IR spectra were recorded on a Perkin–Elmer 298 spectrophotometer. Optical rotations were measured on a Perkin–Elmer 141 polarimeter at the sodium D line (598 nm). Melting points were determined on a Büchi 530 apparatus and are uncorrected. Combustion analyses were performed by 'Service de Microanalyse', CNRS, Solaize. Reagents and solvents were purified by standard means. Ether and dioxane were distilled from sodium wire/benzophenone and stored under a nitrogen atmosphere. Acetonitrile, dichloromethane, dimethylformamide, pyridine and triethylamine were distilled from calcium hydride. Methanol was distilled from magnesium metal. Zinc dust $<10\mu$m (Aldrich) was used for reductive elimination reactions. All other chemicals were used as received.

4.1.1. (3-Methyl-2-butenyl)oxycarbonylimidazole (1). To a suspension of carbonyldiimidazole (3 g, 18.5 mmol) in CH_2Cl_2 (20 mL), cooled to 0 °C, was added dropwise a solution of 3-methyl-2-buten-1-ol (1.85 mL, 1 equiv.) in CH_2Cl_2 (20 mL). The mixture was allowed to warm up to room temperature and stirred for 4 h. After evaporation of the solution to dryness, the residue was purified by chromatography on silica gel (ether–petroleum ether, 1.5:1) to give the imidazolide **1** as an oil (2.51 g, 75%). IR (film): 1760 cm^{-1}.^{1}H NMR: 1.78 (s, 3H, CH_3), 1.80 (s, 3H, CH_3), 4.88 (d, 2H, J=7.43 Hz, CH_2–CH=CMe_2), 5.44 (brt, 1H, J=7.42 Hz, CH=CMe_2), 7.05 (s, 1H), 7.41 (s, 1H), 8.12 (s, 1H). ^{13}C NMR: 18.0, 25.7, 64.8, 117.0, 117.1, 130.4, 137.0, 141.6, 148.7. Anal. calcd for $C_9H_{12}N_2O_2$: C, 59.99, H, 6.71, N, 15.55, O, 17.76. Found: C, 59.80, H, 6.88, N, 15.37, O, 17.95.

4.1.2. (3-Methyl-2-butenyl) 4-nitrophenyl carbonate (2). To a solution of 4-nitrophenyl chloroformate (3.9 g, 19 mmol) in CH_2Cl_2 (28 mL), cooled to 0 °C, was added dropwise a mixture of 3-methyl-2-buten-1-ol (1.93 mL, 1 equiv.) and pyridine (1.63 mL, 1.05 equiv.) in 12 mL of CH_2Cl_2. The reaction mixture was stirred at room temperature for 16 h, diluted with ether, washed once with Na_2CO_3 saturated solution, twice with water. The organic layer was dried (Na_2SO_4) and evaporated to dryness. The residue was crystallized in heptane to afford the carbonate **2** as a crystalline solid (3.75 g, 77%). Mp 72–74 °C. IR (KBr): 1760, 1680 cm^{-1}. ^{1}H NMR: 1.78 (s, 3H, CH_3), 1.81 (s, 3H, CH_3), 4.78 (d, 2H, J=7.42 Hz, CH_2–CH=CMe_2), 5.44 (brt, 1H, J=7.43 Hz, CH=CMe_2), 7.38 (d, 2H, J=9.2 Hz, Ar), 8.27 (d, 2H, J=9.2 Hz, Ar). ^{13}C NMR: 18.2, 25.9, 66.1, 117.1, 121.8 (2C), 125.3 (2C), 141.7, 145.3, 152.6, 155.7. Anal. calcd for $C_{12}H_{13}NO_5$: C, 57.37, H, 5.22, N, 5.58, O, 31.84. Found: C, 57.55, H, 5.29, N, 5.35, O, 31.80.

4.2. General procedures for the preparation of prenyl carbamates

Method A. Using N-prenyloxycarbonylimidazole (**1**) *as reagent*. To 1 mmol of the amine dissolved in DMF (2 mL) was added at room temperature the imidazolide **1** (0.2 g, 1.1 equiv.) in DMF (2 mL). Reaction progress was monitored by TLC (ether–petroleum ether, 2:1). After disappearance of the imidazolide, the mixture was diluted with ether, washed twice with water. The organic phase was dried (Na_2SO_4) and evaporated to dryness. The residue was purified by column chromatography on silica gel. When the hydrochloride salt was used as a starting material, one or two (for the lysine derivative) equivalents of Et_3N were added, prior to the addition of the imidazolide, and the mixture was stirred for 15 min.

Method B. Using prenyl p-nitrophenyl carbonate (**2**) *as a reagent*. To a stirred solution of 1 mmol of the amine dissolved in CH_2Cl_2 (3 mL) were successively added the carbonate **2** (0.276 g, 1.1 equiv.) and DMAP (12 mg, 0.1 equiv.). The solution became quickly yellow due to the formation of *p*-nitrophenol. The reaction mixture was stirred at room temperature until the blue spot of the carbonate observed on TLC (ether–petroleum ether, 1:1, R_f=0.7) became very weak. The reaction mixture was

diluted with ether, washed once with Na_2CO_3 saturated solution, twice with water. The aqueous layer was back extracted once with CH_2Cl_2. The combined organic phases were dried (Na_2SO_4) and evaporated to dryness. The residue was purified by chromatography on silica gel. All compounds prepared by this method have spectroscopic and physical data identical with those a sample synthesized by Method A.

4.2.1. *N*-(3-Methyl-2-butenyl)oxycarbonylbenzylamine (4a). *Method A*. Ether–petroleum ether (1:2), 88% yield, oil. IR (film): 1695, 1530 cm^{-1}. ^1H NMR: 1.72 (s, 3H, Me), 1.77 (s, 3H, Me), 4.36 (d, 2H, J=5.93 Hz, CH_2Ph), 4.60 (d, 2H, J=7.15 Hz, CH_2–CH=CMe$_2$), 5.13 (brs, 2H, NH), 5.36 (brt, 1H, J=7.17 Hz, CH=CMe$_2$), 7.31 (brs, 5H, Ph). ^{13}C NMR: 18.0, 25.8, 45.1, 61.9, 119.2, 127.4, 127.5 (2C), 128.7 (2C), 138.7 (2C), 156.8. Anal. calcd for $C_{13}H_{17}NO_2$: C, 71.21, H, 7.81, N, 6.39, O, 14.49. Found: C, 70.84, H, 7.95, N, 6.41, O, 14.79.

Method B. 98% yield.

4.2.2. *N*-(3-Methyl-2-butenyl)oxycarbonyl-2-phenylethylamine (4b). *Method A*. Ether–petroleum ether (1:1), 85% yield, oil. IR (film): 1690, 1530 cm^{-1}. ^1H NMR: 1.72 (s, 3H, Me), 1.77 (s, 3H, Me), 2.82 (t, 2H, J=7 Hz, CH_2Ph), 3.45 (q, 2H, J=6.8 Hz, CH_2CH$_2$Ph), 4.56 (d, 2H, J=7.17 Hz, CH_2–CH=CMe$_2$), 4.74 (s, 1H, NH), 5.34 (brt, 1H, J=7.16 Hz, CH=CMe$_2$), 7.18–7.36 (m, 5H, Ph). ^{13}C NMR: 18.0, 25.8, 36.2, 42.2, 61.7, 119.3, 126.5, 128.6 (2C), 128.8 (2C), 138.7, 138.8, 156.7. Anal. calcd for $C_{14}H_{19}NO_2$: C, 72.07, H, 8.21, N, 6.0, O, 13.72. Found: C, 72.05, H, 8.37, N, 6.07, O, 13.65.

Method B. 97%.

4.2.3. [*N*-(3-Methyl-2-butenyl)oxycarbonyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (4c). *Method A*. Ether–petroleum ether (3:2), 51% yield, solid, mp 74–75 °C (petroleum ether). IR (KBr): 1700, 1610, 1520 cm^{-1}. ^1H NMR: 1.72 (s, 3H, Me), 1.76 (s, 3H, Me), 2.76 (t, 2H, J=5.71 Hz, ArCH_2CH$_2$), 3.70 (brt, 2H, J=5.5 Hz, ArCH$_2$CH_2), 3.84 (s, 3H, Me), 3.85 (s, 3H, Me), 4.54 (s, 2H, ArCH_2N), 4.62 (d, 2H, J=7.07 Hz, CH_2–CH=CMe$_2$), 5.37 (brt, 1H, J=7.07 Hz, CH=CMe$_2$), 6.59 (s, 1H, Ar), 6.61 (s, 1H, Ar). ^{13}C NMR: 18.1, 25.8, 28.4, 41.5, 45.4, 56.0 (2C), 62.4, 109.2, 111.6, 119.6, 125.1, 126.4, 138.2, 147.7 (2C), 155.9. Anal. calcd for $C_{17}H_{23}NO_4$: C, 66.86, H, 7.59, N, 4.59, O, 20.96. Found: C, 66.68, H, 7.75, N, 4.62, O, 20.93.

Method B. 94% yield.

4.2.4. *N*-(3-Methyl-2-butenyl)oxycarbonyl-2-(1-cyclohexenyl)ethylamine (4d). *Method A*. Ether–petroleum ether (1:2), 97% yield, oil. IR (film): 1705, 1525 cm^{-1}. ^1H NMR: 1.50–1.69 (m, 4H), 1.72 (s, 3H, Me), 1.76 (s, 3H, Me), 1.83–2.07 (m, 4H), 2.12 (t, 2H, J=6.8 Hz, CH_2CH$_2$N), 3.25 (q, 2H, J=6.5 Hz, CH_2N), 4.46 (d, 2H, J=7.2 Hz, CH_2–CH=CMe$_2$), 4.64 (brs, 1H, NH), 5.35 (brt, 1H, J=7.78 Hz, CH=CMe$_2$), 5.46 (brs, 1H, CH=C). ^{13}C NMR: 18.0, 22.4, 22.8, 25.2, 25.8, 27.9, 38.1, 38.7, 61.6, 119.3, 123.6, 134.4, 138.6, 156.6. Anal. calcd for $C_{14}H_{23}NO_2$: C, 70.75, H, 9.77, N, 5.90, O, 13.48. Found: C, 70.45, H, 9.89, N, 5.97, O, 13.76.

Method B. 93% yield.

4.2.5. 4-(3-Methyl-2-butenyl)oxycarbonyl-1-(2-hydroxyethyl)piperazine (4e). *Method A*. Ether–MeOH (9:1), 93% yield, oil. IR (film): 3440, 1700 cm^{-1}. ^1H NMR: 1.72 (s, 3H, Me), 1.77 (s, 3H, Me), 2.49 (t, 4H, J=4.9 Hz, 2CH_2N), 2.57 (t, 2H, J=5.34 Hz, CH_2CH$_2$OH), 3.51 (t, 4H, J=4.94 Hz, CH_2N), 3.67 (t, 2H, J=5.44 Hz, CH_2OH), 4.50 (d, 2H, J=7.07 Hz, CH_2CH=CMe$_2$), 5.36 (brt, 1H, J=7.1 Hz, CH=CMe$_2$),. ^{13}C NMR: 18.0, 25.7, 43.7, 52.7 (3C), 58.0, 59.7, 62.3, 119.3, 138.1, 155.5. Its spectroscopic data were in perfect agreement with those described in the literature.[5c]

Method B. 95% yield.

4.2.6. *N*-(3-Methyl-2-butenyl)oxycarbonyl isonipecotic acid (4f). *Method A*. In the case of this substrate, the reaction was effected in a mixture dioxane–water (2:1) in the presence of 1 equiv. of triethylamine. After stirring for 4 h at room temperature, the reaction mixture was acidified with 1N HCl solution, extracted twice with CH_2Cl_2. The residue was purified by flash chromatography on silica gel, eluent: ether–petroleum ether (2:1) then CH_2Cl_2–MeOH (9:1) to give **4f** (68% yield) as a crystalline solid, mp 80 °C (isopropyl ether). IR (KBr): 3180, 1730, 1670 cm^{-1}. ^1H NMR: 1.61 (qd, 2H, J=2.5, 13 Hz, H-3a and H-5a), 1 67 (s, 3H, Me), 1.72 (s, 3H, Me), 1.90 (brd, 2H, J=13.3 Hz, H-3e and H-5e), 2.47 (m, 1H, CHCO$_2$H), 2.89 (td, 2H, J=2.7, 12.5 Hz, H-2a and H-6a), 4.03 (brd, 2H, J=13.2 Hz, H-2e and H-6e), 4.55 (d, 2H, J=7.07 Hz, CH_2-CH=CMe$_2$), 5.31 (brt, 1H, J=7.1 Hz, CH=CMe$_2$), 11.0 (brs, CO$_2$$H$). ^{13}C NMR: 18.0, 25.8, 27.7, 30.3, 40.7, 43.1 (2C), 62.5, 119.3, 138.3, 155.7, 179.7. Anal. calcd for $C_{12}H_{19}NO_4$: C, 59.73, H, 7.94, N, 5.81, O, 26.52. Found: C, 59.72, H, 8.10, N, 5.76, O, 26.41.

Method B. 91% yield.

4.2.7. *N*-(3-Methyl-2-butenyl)oxycarbonyl-L-proline benzyl ester (4g). *Method A*. AcOEt–petroleum ether (1:3), 52% yield, oil, $[\alpha]_D^{20}=-53.3$ (c 0.5, CHCl$_3$). IR (film): 1475, 1705 cm^{-1}. ^1H NMR (2 rotamers): 1.66 (s, 3H, Me), 1.70 (s, 6H, 2Me), 1.75 (s, 3H, Me), 1.91 (m, 6H), 2.22 (m, 2H), 3.58 (m, 4H, 2CH_2N), 4.34 (dd, 1H, J=3.8, 8.5 Hz, CHCO$_2$Bn), 4.42 (dd, 1H, J=3.7, 8.4 Hz, CHCO$_2$Bn), 4.6 (m, 4H, 2 CH_2-CH=CMe$_2$), 5.16 (m, 5H, 2CH_2Ph, CH=CMe$_2$), 5.36 (brt, 1H, J=7 Hz, CH=CMe$_2$), 7.34 (brs, 10H, Ph). ^{13}C NMR (2 rotamers): 18.1 (2C), 23.6, 24.4, 25.75, 26.0, 29.9, 30.9, 46.4, 46.8, 59.0, 59.3, 62.2, 62.3, 66.6, 66.7, 119.4, 119.5, 128.0 (4C), 128.2, 128.3, 128.6 (4C), 135.8 (2C), 137.97, 138.07, 154.7, 155.3, 172.6, 172.8. Anal. calcd for $C_{18}H_{23}NO_4$: C, 68.12, H, 7.30, N, 4.41, O, 20.16. Found: C, 67.91, H, 7.44, N, 4.48, O, 20.15.

Method B. 90% yield.

4.2.8. *N*-(3-Methyl-2-butenyl)oxycarbonyl-L-methionine methyl ester (4h). *Method A*. Ether–petroleum ether (1:1), 33% yield, crystalline solid, mp 34–35 °C, $[\alpha]_D^{20}=+23.15$ (c 1.7, CHCl$_3$). IR (film): 3340, 1740, 1700, 1530 cm^{-1}. ^1H

NMR: 1.68 (s, 3H, Me), 1.73 (s, 3H, Me), 1.95 (m, 1H, C*H*CH_2S), 2.06 (s, 3H, Me), 2.11 (m, 1H, C*H*CH_2S), 2.51(t, 2H, *J*=7.5 Hz, CH_2S), 3.73 (s, 3H, Me), 4.45 (q, 1H, *J*=7.6, 13 Hz, C*H*CO_2Me), 4.55 (d, 2H, *J*=7.18 Hz, CH_2-CH=CMe_2), 5.31 (brt, 1H, *J*=7.15 Hz, C*H*=CMe_2), 5.40 (brs, 1H, NH). ^{13}C NMR: 15.4, 18.0, 25.7, 29.9, 32.1, 52.5, 53.1, 62.1, 118.9, 138.9, 156.1, 172.6. Anal. calcd for $C_{12}H_{21}NO_4S$: C, 52.34, H, 7.69, N, 5.09, O, 23.24, S, 11.64. Found: C, 52.28, H, 7.80, N, 5.09, O, 23.16, S, 11.67.

Method B. 91% yield.

4.2.9. *N*-(3-Methyl-2-butenyl)oxycarbonyl-L-tryptophan methyl ester (4i). *Method A*. Ether–petroleum ether (2:1), 20% yield, crystalline solid, mp 102–104 °C, $[\alpha]_D^{20}$=+51.2 (*c* 0.5, $CHCl_3$). IR (KBr) 3370, 3340, 1735, 1700, 1620, 1540 cm^{-1}. ^{1}H NMR: 1.71 (s, 3H, Me), 1.76 (s, 3H, Me), 3.31 (d, 2H, *J*=5.2 Hz, CH_2-CHCO_2Me), 3.68 (s, 3H, Me), 4.57 (d, 2H, *J*=7.04 Hz, CH_2–CH=CMe_2), 4.72 (q, 1H, *J*=5.5, 13.4 Hz, C*H*CO_2Me), 5.3 (m, 2H, NH and C*H*=CMe_2), 7.0 (d, 1H, *J*=2 Hz, NC*H*=), 7.12 (t, 1H, *J*=6.9 Hz, Ar), 7.21(t, 1H, *J*=6.7 Hz, Ar), 7.34 (d, 1H, *J*=7.5 Hz, Ar), (7.56 (d, 1H, *J*=7.4 Hz, Ar), 8.4 (brs, 1H, NH). ^{13}C NMR: 18.1, 25.8, 28.0, 52.4, 54.6, 62.2, 109.8, 111.4, 118.6, 118.9, 119.6, 122.2, 123.0, 127.6, 136.3, 138.9, 156.2, 172.7. Anal. calcd for $C_{18}H_{22}N_2O_4$: C, 65.44, H, 6.71, N, 8.48, O, 19.37. Found: C, 65.23, H, 6.92, N, 8.44, O, 19.47.

Method B. 85% yield.

4.2.10. N^{ε}-(3-Methyl-2-butenyl)oxycarbonyl-L-lysine methyl ester (4j). *Method A*. In the case of this substrate, 1 mmol of lysine methyl ester·2HCl was dissolved in dioxane–H_2O (1:1). The reaction mixture was diluted with water and extracted three times with CH_2Cl_2. Chromatography on silica gel of the residue (CH_2Cl_2–MeOH, 92:8) gave the N-monoprotected lysine derivative **4j**, obtained as an oil (51% yield). ^{1}H NMR: 1.40 (m, 6H, 3CH_2), 1.51 (brs, 2H, NH_2), 3.1 (dd, 2H, *J*=6.3, 12.6 Hz, CH_2N), 3.36 (t, 1H, *J*=7.1 Hz, C*H*CO_2Me), 3.64 (s, 3H, Me), 4.46 (d, 2H, *J*=7.12 Hz, CH_2-CH=CMe_2), 4.96 (brs, 1H, NH), 5.24 (brs, 1H, *J*=7.1 Hz, C*H*=CMe_2). Compound **4j** was characterized as its hydrochloride salt. To 1 mmol of **4j** dissolved in 5 mL of dry ether, cooled to 0 °C, was added 4 N HCl in dioxane (0.35 mL, 1.5 equiv.). After stirring the reaction mixture for 30 min, the precipitate was filtered and washed with dry ether to give the hydrochloride salt (0.363 g, 90% yield). Mp 98–99 °C, $[\alpha]_D^{20}$=+14.6 (*c* 1.2, H_2O). IR (KBr): 3360, 1745, 1690, 1600, 1525 cm^{-1}. ^{1}H NMR (D_2O):1.53 (m, 4H), 1.74 (s, 3H, Me), 1.79 (s, 3H, Me), 2.0 (m, 2H), 3.15 (t, 2H, *J*=6.3 Hz, CH_2N), 3.88 (s, 3H, Me), 4.19 (t, 1H, *J*=7.1 Hz, C*H*–CO_2Me), 4.57 (d, 2H, *J*=7.02 Hz, CH_2–CH=CMe_2), 5.38 (brt, 1H, *J*=7.05 Hz, C*H*=CMe_2). ^{13}C NMR: 19.9, 24.0, 27.6, 31.0, 32.0, 42.5, 55.4, 56.1, 64.8, 120.7, 143.5, 151.2, 173.3. Anal. calcd for $C_{13}H_{25}ClN_2O_4$: C, 50.56, H, 8.16, Cl, 11.48, N, 9.07. Found: C, 50.87, H, 8.38, Cl, 11.50, N, 9.02.

Method B. 81% yield.

4.2.11. 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(3-methyl-2-butenyl)oxycarbonylamino-β-D-glucopyranose (4k). *Method A*. 0% yield; several products were observed by TLC (ether).

Method B. The reaction was effected in DMF. After a usual workup, the solid residue was purified by flash chromatography on silica gel (ether–petroleum ether, 4:1) to give the N-protected sugar **4k** in 39% yield obtained as a white crystalline solid, mp 121–124 °C, $[\alpha]_D^{20}$=+17.7 (*c* 1.2, $CHCl_3$). IR (KBr): 3350, 1745, 1705, 1530 cm^{-1}. ^{1}H NMR: 1.66 (s, 3H, Me), 1.70 (s, 3H, Me), 2.0 (s, 6H, 2OAc), 2.04 (s, 3H, OAc), 2.07 (s, 3H, OAc), 3.80 (m, 1H, H-5), 3.93 (m, 1H, H-2), 4.08 (brd, 1H, *J*=12.4 Hz, H-6), 4.27 (dd, 1H, *J*=4.3, 12.4 Hz, H-6), 4.51 (d, 1H, *J*=6.7 Hz, C*H*–CH=CMe_2), 5.05 (t, 1H, *J*=9.5 Hz, H-3 or H-4), 5.12–5.4 (m, 3H, H-3 or H-4, N*H*, C*H*=CMe_2), 5.65 (d, 1H, *J*=8.5 Hz, H-1). ^{13}C NMR: 18.0, 20.6 (2C), 20.7, 20.8, 25.7, 54.8, 61.8, 62.2, 68.2, 72.5, 72.7, 92.6, 118.9, 138.8, 156.2, 169.5(2C), 170.7, 170.8. Anal. calcd for $C_{20}H_{29}NO_{11}$: C, 52.28, H, 6.36, N, 3.05, O, 38.31. Found: C, 52.54, H, 6.60, N, 3.01, O, 37.84.

4.2.12. 1-*N*-tert-Butoxycarbonyl-3-*N*-(methyl-2-butenyl)oxycarbonyl-1,3-diaminopropane (4l). *Method A*. Ether–petroleum ether (1.5:1), 80% yield, crystalline solid, mp 47–48 °C. ^{1}H NMR: 1.42 (s, 9H, C$(CH_3)_3$), 1.61 (q, 2H, *J*=6.3 Hz, CH_2), 1.70 (s, 3H, Me), 1.74 (s, 3H, Me), 3.18 (m, 4H, 2 CH_2N), 4.54 (d, 2H, *J*=7.12 Hz, CH_2–CH=CMe_2), 4.90 (brs, 1H, NH), 5.18 (brs, 1H, NH), 5.32 (brt, 1H, *J*=7.11 Hz, C*H*=CMe_2). ^{13}C NMR: 18.0, 25.8, 28.4 (3C), 30.6, 37.2, 37.7, 61.7, 79.3, 119.3, 138.5, 156.4, 157.1. Anal. calcd for $C_{14}H_{26}N_2O_4$: C, 58.72, H, 9.15, N, 9.78, O, 22.35. Found: C, 58.50, H, 9.38, N, 9.67, O, 22.37.

Method B. 97% yield.

4.2.13. 1-[2-(3-Methyl-2-butenyl)oxyethyl]-4-(3-methyl-2-butenyl)oxycarbonylpiperazine (4m). To a solution of the alcohol **4e** (0.52 g, 2.1 mmol) in DMF (5 mL), cooled to −50 °C, were successively added NaH (60% dispersion in mineral oil, 0.104 g, 1.2 equiv) and prenyl bromide (0.29 mL, 1.5 equiv.). The reaction mixture was allowed to warm up to 0 °C (90 min), diluted with ether, washed with water. The aqueous phase was extracted once with ether. The combined organic phases were dried (Na_2SO_4) and concentrated. The residue was purified by chromatography on silica gel (ether) to give **4m** (0.492 g, 74% yield) obtained as a yellow oil. IR (film): 1700 cm^{-1}.^{1}H NMR: 1.67 (s, 3H, Me), 1.71 (s, 3H, Me), 1.75 (s, 6H, 2Me), 2.45 (t, 4H, *J*=5.1 Hz, 2 CH_2N), 2.59 (t, 2H, *J*=5.8 Hz, CH_2–CH_2OPre), 3.49 (t, 4H, *J*=5.2 Hz, 2CH_2N), 3.54 (t, 2H, *J*=5.8 Hz, CH_2OPre), 3.97 (d, 2H, *J*=6.91 Hz, OCH_2–CH=CMe_2), 4.57 (d, 2H, *J*=7.05 Hz, NCO_2CH_2-CH=CMe_2), 5.34 (m, 2H, 2C*H*=CMe_2). ^{13}C NMR: 18.0 (2C), 25.7, 25.8, 43.6, 53.3 (3C), 58.0, 62.3, 67.3, 67.5, 119.5, 121.1, 136.9, 138.0, 155.6. Anal. calcd for $C_{17}H_{30}N_2O_3$: C, 65.77, H, 9.74, N, 9.02, O, 15.46. Found: C, 65.77, H, 9.90, N, 8.76, O, 15.50.

4.2.14. 1-(3-Methyl-2-butenyl)-4-(benzyloxycarbonyl)-piperidine (4n). To a solution of the acid **4f** (0.3 g, 1.2 mmol) in acetonitrile (3 mL), cooled to 0 °C, was added DBU (0.21 mL, 1.16 equiv.). After stirring for 15 min at

0 °C, benzyl bromide (0.18 mL, 1.25 equiv.) was added. The reaction mixture was stirred for 2 h at room temperature, diluted with ether, washed once with water. The organic layer was dried (Na_2SO_4), evaporated and the residue was purified by chromatography on silica gel (ether–petroleum ether, 1:2) to afford the benzyl ester **4n** as an oil (0.367 g, 89% yield). IR (film): 1730, 1695 cm^{-1}.^{1}H NMR: 1.64 (m, 2H, H-3a and H-5a), 1.71 (s, 3H, Me), 1.76 (s, 3H, Me), 1.93 (brd, 2H, J=13.1 Hz, H-3e and H-5e), 2.52 (m, 1H, C*H*–CO_2H), 2.89 (td, 2H, J=2.3, 12.3 Hz, H-2a and H-6a), 4.07 (brd, 2H, J=12.4 Hz, H-2e and H-6e), 4.58 (d, 2H, J=6.8 Hz, CH_2-CH=CMe_2), 5.13 (s, 2H, CH_2Ph), 5.35 (brt, 1H, J=7.20 Hz, C*H*=CMe_2), 7.35 (s, 5H, Ar). ^{13}C NMR: 18.1, 25.8, 27.9 (2C), 41.1, 43.2 (2C), 62.3; 66.3, 119.5, 128.1 (2C), 128.3, 128.6 (2C), 136.0, 138.1, 155.5, 174.2. Anal. calcd for $C_{19}H_{25}NO_4$: C, 68.86, H, 7.60, N, 4.23, O, 19.31. Found: C, 68.81, H, 7.88, N, 4.21, O, 19.57.

4.2.15. N^{α}-Benzyloxycarbonyl-N^{ε}-(3-methyl-2-butenyl)oxycarbonyl-L- lysine methyl ester (4o). To a solution of the N^{ε}-protected lysine derivative **4j** (0.5 g, 1.8 mmol) in CH_2Cl_2 (10 mL), cooled to 0 °C, were successively added triethylamine (0.4 mL, 1.5 equiv.) and benzyl chloroformate (0.38 mL, 1.5 equiv.). The reaction mixture was stirred for 2 h at room temperature, diluted with ether, washed twice with water, dried (Na_2SO_4) and evaporated. The residue was chromatographed on silica gel (ether–petroleum ether, 2:1) to furnish the di-N protected lysine **4o** (0.51 g, 69% yield) as a colorless oil. IR (film): 3330, 1740, 1700, 1530 cm^{-1}.^{1}H NMR: 1.38 (m, 4H), 1.64 (s, 3H, Me), 1.69 (s, 3H, Me), 3.09 (dd, 2H, J=6.5, 12 Hz, CH_2N), 3.67 (s, 3H, OMe), 4.3 (dd, 1H, J=5.7, 12 Hz, C*H*CO_2Me), 4.49 (d, 2H, J=6.92 Hz, CH_2–CH=CMe_2), 5.01 (brs, 1H, N*H*), 5.05 (s, 2H, CH_2Ph), 5.27 (brt, 1H, J=7.20 Hz, C*H*=CMe_2), 5.68 (d, 1H, J=7.9 Hz, N*H*), 7.28 (brs, 5H, Ph). ^{13}C NMR: 18.0, 22.4, 25.7, 29.4, 32.0, 40.4, 52.3, 53.8, 61.6, 66.9, 119.3, 128.0 (2C), 128.1, 128.5 (2C), 136.3, 138.3, 156.1, 156.9, 173.0. Anal. calcd for $C_{21}H_{30}N_2O_6$: C, 62.05, H, 7.44, N, 6.89, O, 23.62. Found: C, 61.87, H, 7.57, N, 6.98, O, 24.07.

4.3. General procedure for the deprotection of prenyl carbamates

To a well-stirred solution of 1 mmol of the prenyl carbamate in methanol (6 mL) was added, at room temperature, iodine (0.508 g, 2 equiv.). The reaction progress was monitored by TLC. In most cases, the spot of the 2-iodo-3-methoxy-3-methylbutyl carbamate was slightly more polar than that of the starting material and was well UV-absorbing (254 nm). After disappearance of the starting material, zinc (0.26 g, 4 equiv.) was added and the stirring was continued for 30 min. After concentration, CH_2Cl_2 and saturated Na_2CO_3 solution were added and the formed precipitate and zinc in excess were filtered on a funnel. The aqueous layer was extracted once with CH_2Cl_2. The combined organic phases were washed once with brine, dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography on silica gel. Most amines were characterized as their hydrochloride salts, prepared by dissolving 0.5 mmol of the amine in dry ether (4 mL), cooling the solution to 0 °C, and adding 4 N HCl solution in dioxane (0.25 mL, 2 equiv.). The precipitate was filtered and washed with dry ether, dried.

4.3.1. Benzylamine (3a). Reaction time: 5 h; CH_2Cl_2–MeOH–Et_3N (85:10:5), 83% yield, liquid. ^{1}H NMR: 1.82 (brs, 2H, NH_2), 3.83 (s, 2H, PhCH_2), 7.30 (m, 5H, Ar). ^{13}C NMR: 46.4, 126.9, 127.2 (2C), 128.6 (2C), 143.1. Its spectroscopic data are in agreement with those of an authentic sample.

4.3.2. 2-Phenylethylamine (3b). Reaction time: 5 h; CH_2Cl_2–MeOH–Et_3N (85:10:5), 85% yield, liquid. ^{1}H NMR: 1.27 (s, 2H, NH_2), 2.75 (t, 2H, J=6.6 Hz, PhCH_2), 2.97 (t, 2H, J=6.7 Hz, C$H_2$$NH_2$), 7.18–7.34 (m, 5H, Ph). ^{13}C NMR: 40.2, 43.6, 126.2, 128.5 (2C), 128.9 (2C), 139.9. Its spectroscopic data were in accordance with those of an authentic sample.

4.3.3. 6,7-Dimethoxy-1,2,3,4-tetrahydroisoquinoline (3c). Reaction time: 6 h, CH_2Cl_2–MeOH–Et_3N (86:10:4), 78% yield. It was characterized as its hydrochloride salt: mp 258–260 °C. ^{1}H NMR (D_2O): 3.04 (t, 2H, J=6.2 Hz, ArC$H_2$$CH_2$$NH_2^+$), 3.49 (t, 2H, J=6.3 Hz, ArCH_2C$H_2$$NH_2^+$), 3.81 (s, 3H, OMe), 3.82 (s, 3H, OMe), 4.28 (s, 2H, ArC$H_2$$NH_2^+$), 6.81 (s, 1H, Ar), 6.87 (s, 1H, Ar).^{13}C NMR (D_2O): 24.5, 42.1, 44.5, 55.9, 56.0, 109.7, 111.9, 120.0, 124.2, 147.4, 148.1. Its spectroscopic data were agreement with those of a commercial sample.

4.3.4. 2-(1-Cyclohexenyl)ethylamine (3d). Reaction time: 7 h, CH_2Cl_2–MeOH–Et_3N (85:10:5), 88% yield, liquid. ^{1}H NMR: 1.49–1.66 (m, 4H, 2CH_2), 1.85–2.0 (m, 4H, 2CH_2), 2.06 (t, 2H, J=6.8 Hz, C$H_2$$CH_2$N), 2.09 (s, 2H, N$H_2$), 2.74 (t, 2H, J=6.7 Hz, C$H_2$$NH_2$), 5.43 (brs, 1H, C*H*=C). ^{13}C NMR: 22.5, 22.9, 25.3, 28.1, 39.7, 41.7, 123.2, 134.9. Its spectroscopic data were in accordance with those of an authentic sample.

4.3.5. L-Methionine methyl ester (3h). Reaction time: 7 h, CH_2Cl_2–MeOH (95:5), oil, 83% yield. It was characterized as its hydrochloride salt: mp 145–149 °C, $[\alpha]_D^{20}$=+23.4 (*c* 1.2, H_2O) [Lit.[17] $[\alpha]_D^{20}$=+25.2 (*c* 5.1, H_2O), mp 147–150 °C]. ^{1}H NMR: 2.14 (s, 3H, Me), 2.29 (sextuplet, 2H, J=6.3, 7.2 Hz, SCH_2CH_2), 2.72 (t, 2H, J=7.2 Hz, SCH_2), 3.88 (s, 3H, OMe), 4.34 (t, 1H, J=6.3 Hz, C*H*CO_2Me). ^{13}C NMR: 14.4, 28.9, 29.2, 52.2, 54.1, 171.0. These NMR data were in agreement with those of a commercial sample.

4.3.6. L-Tryptophan methyl ester (3i). For this substrate, after stirring for 24 h, at room temperature, the prenyl carbamate of tryptophan methyl ester **4i** in methanol (6 mL), in the presence of two equivalents of iodine (0.508 g), the mixture was concentrated. The residue was diluted with CH_2Cl_2, washed with saturated sodium thiosulfate solution. The aqueous phase was extracted twice with CH_2Cl_2 and the combined organic phases were washed once with brine, dried (Na_2SO_4), evaporated to dryness. The residue was purified by flash chromatography on silica gel (CH_2Cl_2–MeOH, 95:5) to give compound **3i** as a yellow oil (0.115 g, 53% yield). It was characterized as its hydrochloride salt: mp 215–216 °C, $[\alpha]_D^{20}$=+17.1 (*c* 0.5, MeOH) [Lit.[18] mp 213–214 °C, $[\alpha]_D$=+17 (*c* 2, MeOH)]. ^{1}H NMR: 3.36 (d, 2H, J=5.65 Hz, CH_2CHCO_2Me), 3.77 (s,

3H, OMe), 4.35 (t, 2H, J=6.1 Hz, C*H*CO_2Me), 7.21 (t, 1H, J=6.8 Hz, Ar), 7.24 (t, 1H, J=7 Hz, Ar), 7.25 (brs, 1H, NCH=), 7.50 (d, 1H, J=7.1 Hz, Ar), 7.55 (d, 1H, J=6.9 Hz, Ar). ^{13}C NMR: 26.1, 53.8, 54.1, 106.4, 112.6, 118.5, 120.1, 122.7, 125.9, 126.9, 136.8, 170.9. These spectroscopic data were in accordance with those of a commercial sample.

4.3.7. 1-*tert*-Butoxycarbonyl-1,3-diaminopropane (3l). Reaction time: 4 h, CH_2Cl_2–MeOH–Et_3N (85:10:5), oil, 82% yield.^{1}H NMR: 1.39 (s, 9H, C(CH_3)$_3$), 1.57 (quintuplet, 2H, J=6.7 Hz, $CH_2CH_2CH_2$), 2.74 (t, 2H, J=6.7 Hz, CH_2NH_2), 2.87 (s, 2H, NH_2), 3.16 (q, 2H, J=6.4 Hz, CH_2NHBoc), 5.1 (brs, 1H, NH). ^{13}C NMR: 28.4 (3C), 33.5, 38.4, 39.7, 79.0, 156.2. Spectroscopic data were in accordance with those of an authentic sample.

4.3.8. 1-[2-(3-Methyl-2-butenyl)oxyethyl]piperazine (3m). In the case of this substrate, 4 equiv. of iodine and 8 equiv. of zinc were added. Reaction time: 7 h, CH_2Cl_2–MeOH–Et_3N (85:10:5), 63% yield, oil. It was characterized as its dihydrochloride salt: mp 160–162 °C (dec.). ^{1}H NMR (D_2O): 1.72 (s, 3H, Me), 1.78 (s, 3H, Me), 3.55 (t, 2H, J=6 Hz, NCH_2CH_2O), 3.7 (m, 8H, 4 CH_2), 3.87 (t, 2H, J=6 Hz, NCH_2CH_2O), 4.11 (d, 2H, J=7.2 Hz, CH_2-CH=CMe_2), 5.40 (t, 1H, J=7.1 Hz, C*H*=CMe_2). ^{13}C NMR (D_2O): 17.8, 25.4, 41.0 (2C), 49.1 (2C), 56.9, 62.6, 67.6, 119.2, 141.4. Anal. calcd for $C_{11}H_{22}N_2O$·2HCl: C, 48.71, H, 8.92, Cl, 26.14, N, 10.33, O, 5.90. Found: C, 48.84; H, 9.02, Cl, 25.84, N, 10.10, O, 6.2.

4.3.9. 4-(Benzyloxycarbonyl)piperidine (3n). Reaction time: 5 h, CH_2Cl_2–MeOH–Et_3N (86:10:4), 77% yield, oil. Characterized as its hydrochloride salt. Mp 145–147 °C (dec.). ^{1}H NMR (D_2O): 1.86 (m, 2H, H-3a and H-5a), 2.16 (dd, 2H, J=3.3, 13.5 Hz, H-3e and H-5e), 2.76 (m, 1H, C*H*CO_2Bn), 3.06 (td, 2H, J=2.7, 12.5 Hz, H-2a and H-6a), 3.43 (dt, 2H, J=3.5, 12 Hz, H-2e and H-6e), 5.16 (s, 2H, CH_2Ph), 7.43 (s, 5H, Ph). ^{13}C NMR (D_2O): 24.8 (2C), 38.6, 43.4 (2C), 67.7, 128.7 (2C), 129.2, 129.4 (2C), 136.0, 175.7. Anal. calcd for $C_{13}H_{18}ClNO_2$: C, 61.05, H, 7.09, Cl, 13.86, N, 5.48, O, 12.51. Found: C, 61.24, H, 7.45, Cl, 14.1, N, 5.35, O, 12.24.

4.3.10. N^{α}-Benzyloxycarbonyl-L-lysine methyl ester (3o). Reaction time: 5 h, CH_2Cl_2–MeOH–Et_3N (85:10:5), oil, 85% yield. This compound was characterized as its N^{ε}-Boc derivative (Boc_2O, Et_3N, CH_2Cl_2, 2 h, room temperature), 74% yield, oil, $[\alpha]_D^{20}$=+4.2 (*c* 0.15, $CHCl_3$), $[\alpha]_D^{20}$=−9.2 (*c* 0.34, acetone). [Lit.[19,20] $[\alpha]_D^{20}$=+3.8 (*c* 2, $CHCl_3$), $[\alpha]_D^{28}$=−10 (*c* 1, acetone)]. ^{1}H NMR: 1.3–1.55 (m, 13H, $2CH_2$ and C(CH_3)$_3$), 1.6–1.85 (m, 2H, CH_2), 3.08 (m, 2H, CH_2NBoc), 3.73 (s, 3H, OMe), 4.35 (q, 1H, J=6.8, 12.8 Hz, C*H*CO_2Me), 4.61 (brs, 1H, N*H*Boc), 5.1 (s, 2H, CH_2Ph), 5.46 (d, 1H, J=7.5 Hz, N*H*Z), 7.34 (s, 5H, Ph). ^{13}C NMR: 24.4, 28.4 (3C), 29.6, 32.2, 40.1, 52.4, 53.8, 79.2, 128.2, 128.5 (4C), 136.3, 156.1, 172.9. ^{13}C NMR data were identical with those described in the literature.[20]

4.3.11. L-Proline methyl ester (3p). Reaction time: 5 h, CH_2Cl_2–MeOH–Et_3N (85:15), oil, 70% yield. Characterized as its hydrochloride salt. Mp 67–69 °C (ether), $[\alpha]_D^{20}$=−31.6 (*c* 1.6, H_2O) [lit.[21] mp 71 °C, $[\alpha]_D^{20}$=−32.6 (*c* 2.1, MeOH). ^{1}H NMR (D_2O): 2.03–2.3 (m, 3H), 2.51 (m, 1H), 3.46 (m, 2H, CH_2N), 3.88 (s, 3H, OMe), 4.54 (dd, 1H, J=7, 8.5 Hz, C*H*CO_2Me). ^{13}C NMR (D_2O): 23.8, 28.6, 46.8, 54.3, 60.0, 170.9. Its spectroscopic data were consistent with those of a commercial sample.

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