

Aziridination of α,β -Unsaturated Ketones

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Abstract: α,β -Unsaturated ketones are aziridinated by [(arenesulphonyl)oxy]carbamates and CaO (or Cs_2CO_3) or by $\text{N}_3\text{CO}_2\text{Et}$ photolysis. A remote chiral center induced up to 74% d.e. Bis-unsaturated substrates showed scarce regioselectivity under all conditions. © 1998 Elsevier Science Ltd. All rights reserved.

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For a long time we have been interested in amination reactions. More recently we have focused our attention on substituted alkenes like α,β -unsaturated carboxylic esters¹ and nitroalkenes.² The use of ethyl *N*-[(4-nitrobenzenesulphonyl)oxy]carbamate ($\text{NsONHCO}_2\text{Et}$) in the presence of CaO allowed these scarcely nucleophilic olefins to be transformed into the corresponding aziridines in satisfactory yields.

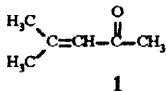
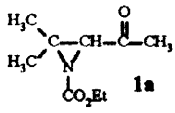
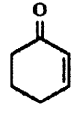
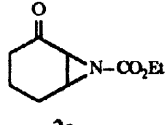
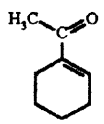
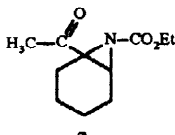
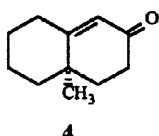
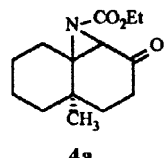
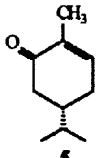
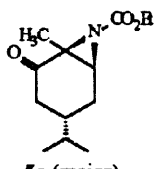
This paper reports results obtained with α,β -unsaturated ketones³ when reacted the above mentioned reagents (route A in Table 1) and in addition with ethyl *N*-[(4-methylbenzenesulphonyl)oxy] carbamate ($\text{TsONHCO}_2\text{Et}$) and Cs_2CO_3 (route B in Table 1).⁴ Under the latter conditions all the substrates tested gave the expected aziridines in yields ranging from 20 to 71%, while $\text{NsONHCO}_2\text{Et}/\text{CaO}$ was not effective with substrates 1 and 4. All the reactions were performed in CH_2Cl_2 and the molar ratios reported in Table 1 were determined on the basis of GC-MS analysis after 24 h.

In order to gain some information about two possible reaction pathways involving either nitrene NCO_2Et addition or the anion $\text{ArSO}_3\text{N}^-\text{CO}_2\text{Et}$ in an initial Michael type addition² we also investigated the photolysis of $\text{N}_3\text{CO}_2\text{Et}$ with the same substrates (route C in Table 1). Only minor differences were observed with respect to the previously described results and the expected aziridines were isolated in the yields reported in Table 1.

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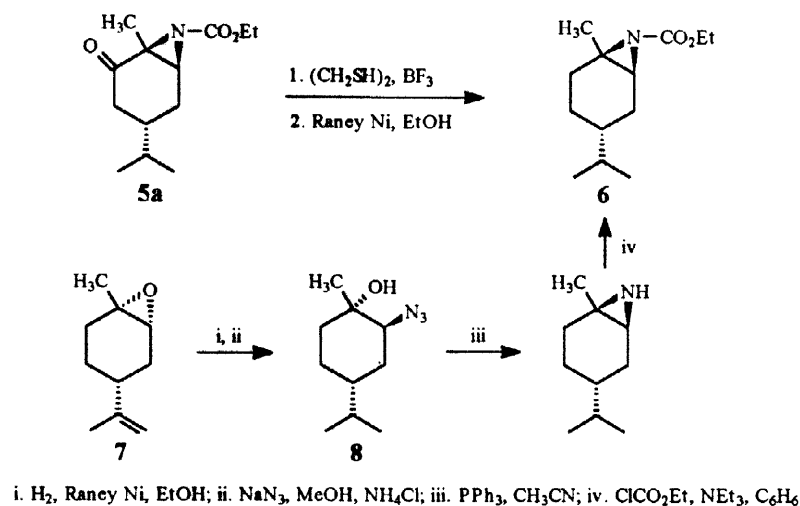
(*R*)-Dihydrocarvone¹ (**5**) gives the expected aziridines with moderate diastereomeric excesses (d.e.) and provides the best result in the photolysis reaction. The aziridines were obtained easily as pure diastereomers after purification by HPLC.

Table 1. Aziridination of α,β -Unsaturated Ketones.

Substrate	Product	Route	Molar ratio substrate : reagent ^a	% Yield (% d.e.)
 1	 1a	A	1:4	-
		B	1:12	40
		C	1:1	19
 2	 2a	A	1:4	56
		B	1:8	40
		C	1:1	34
 3	 3a	A	1:7	74
		B	1:12	71
		C	1:2	64
 4	 4a	A	1:8	-
		B	1:12	20 (<5)
		C	1:8	29 (18)
 5	 5a (major)	A	1:8	51 (41)
		B	1:12	56 (51)
		C	1:2	60 (74)

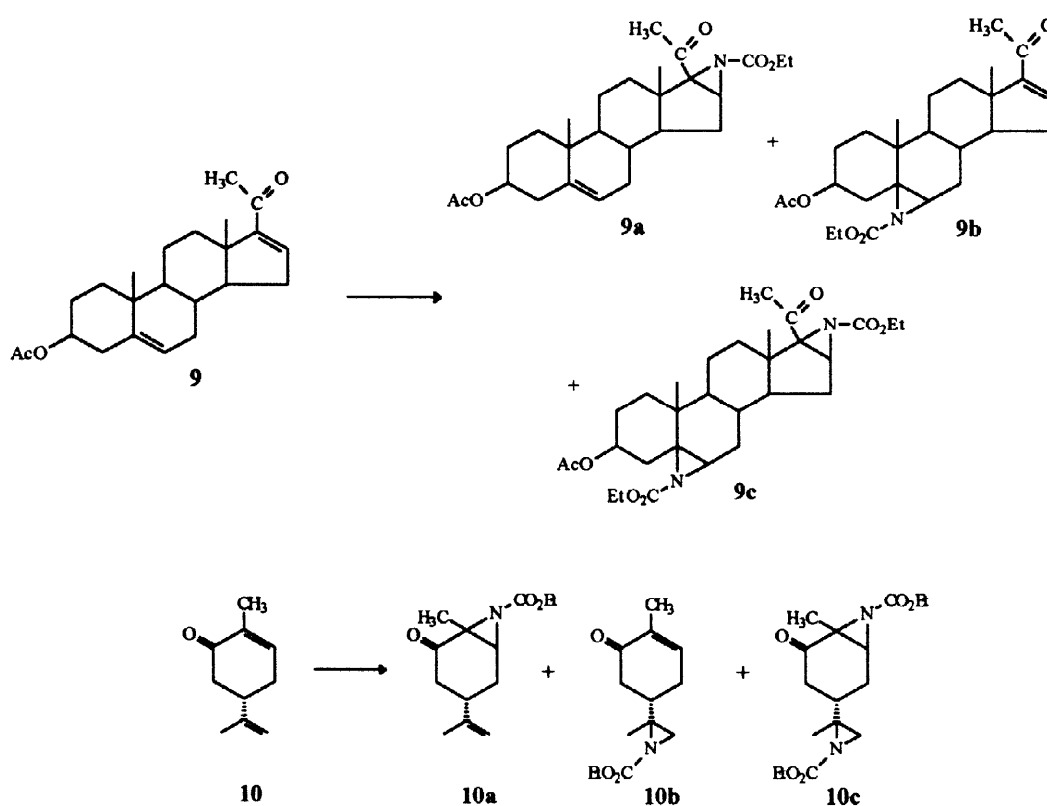
^a An equimolar ratio of the reagents (NsONHCO₂Et/CaO, route A or TsONHCO₂Et/Cs₂CO₃, route B) was used. Route C refers to photolysis reaction of N₃CO₂Et in 1 M solutions of ketones in dichloromethane.

The amination of **5** was attempted with NsONHCO₂Et and CaO by grinding the reactants together with the substrate in a mortar.² In this way, **5a** was obtained with a yield comparable to that reported in Table 1, but using a lower molar ratio (5:NsONHCO₂Et:CaO=1:3:3). In all amination conditions the same major diastereomer was obtained. The relative stereochemistry was determined by conversion of **5a** into **6**, which can be obtained as a pure diastereomer starting from commercial (+)-*trans*-1,2-epoxylimonene (**7**),⁶⁻⁸ as shown in Scheme 1.



Scheme 1

With the aim of distinguishing between the two above mentioned pathways, the regioselective outcome of the reactions run on commercially available bis-unsaturated ketones such as **9** and **10** (Scheme 2) was studied. In both cases aziridines coming from monofunctionalisation of the conjugated double bond and of the unconjugated double bond were obtained and also the products of a double functionalisation were isolated in comparable amounts irrespective of the aminating agent (Table 2).



Scheme 2

In addition, in the photolysis reaction starting from **9**, all the possible aziridines were obtained with yields similar to those reported in the literature,⁹ but using a lower molar ratio between reagents.

Table 2. Aziridination of Polyunsaturated Ketones.

Substrate	Route	Molar ratio ^a substrate:reagent	Product (% Yield)		
			a	b	c
9	A	1:6	traces	7	13
	B	1:12	traces	35	29
	C	1:8	traces	6	19
10	A	1:7	25	33	12
	B	1:12	13	42	18
	C	1:2	traces	27	38

^a See note in Table 1.

The amination reaction on **10** was also performed in a mortar without solvent using a molar ratio 9:NsONHCO₂Et:CaO=1:3:3 and **10a** (47%) was obtained as the major product. In addition, **10b** was formed in 22% yield and **10c** was produced in only trace amounts.

The absence of regioselectivity for bis-unsaturated substrates and the results obtained in the photolysis reactions do not allow a choice between the two possible reaction pathways and both are probably involved.

In conclusion the results reported here show a simple alternative method to other reported ways^{3,9} for the aziridination of α,β -unsaturated ketones. It is known that these aziridines can be easily cleaved to β -amino ketones.^{10,11}

EXPERIMENTAL

GC analyses were performed on a HP 5890 Series II gas chromatograph with a capillary column (methyl silicone, 12.5 m x 0.2 mm). GC-MS were carried out on a HP G1800A GCD System with a capillary column (phenyl methyl silicone, 30 m x 0.25 mm). ¹H NMR and ¹³C NMR spectra were obtained in CDCl₃ on a Varian XL-300 spectrometer, with CHCl₃ as an internal standard. IR spectra in CCl₄ were determined using a Perkin-Elmer 1600 Series FTIR spectrometer. Optical rotations were recorded at the Sodium D line with a Perkin-Elmer 457 polarimeter (1-cm cell). Diastereomeric excesses were determined by both GC and HPLC. The separations by HPLC were performed with a Varian 9001 instrument equipped with a Varian RI-4 differential refractometer. Solvents were HPLC-grade. NsONHCO₂Et,¹² TsONHCO₂Et,⁴ N₃CO₂Et¹³ (CAUTION: explosive and toxic vapours) and (*R*)-dihydrocarvone⁵ **5** were prepared according to literature methods.

(*R*)-**5**: [α]_D +84.3 (*c* = 0.70 in CH₂Cl₂) (lit.¹⁴ [α]_D + 86.0, neat); IR (CCl₄) 1663 cm⁻¹; ¹H NMR (CDCl₃) δ 0.80 [*d*, *J* = 6.8 Hz, 6 H, CH(CH₃)₂], 1.51–1.64 [*m*, 1 H, CH(CH₃)₂], 1.73 (*s*, 3 H, CH₃), 1.92–2.27 [*m*, 5 H, 2 x CH₂, CH], 6.67–6.70 [*m*, 1 H, HC=C]; ¹³C NMR (CDCl₃) δ 15.53, 19.32, 19.38 (CH₃), 20.34, 29.68, 31.86, 42.26 (CH₂, CH), 110.28 (HC=C), 128.16 (HC=C), 200.43 (CO); GC-MS *m/z* 152 (M⁺, 22), 109 (16), 95 (16), 82 (100), 81 (38), 79 (13), 69 (15), 54 (23), 53 (13), 39 (18), 27 (11).

Amination with *NsONHCO₂Et* and *CaO* or with *TsONHCO₂Et* and *Cs₂CO₃*.

To 3 mmol of substrate in 3 ml of CH₂Cl₂, *NsONHCO₂Et* and *CaO* or *TsONHCO₂Et* and *Cs₂CO₃* were added portionwise in the molar ratio reported in Table 1 and in Table 2. After 24 h of stirring at room temperature, 30 ml of CH₂Cl₂ and 300 ml of petroleum ether were added to precipitate the inorganic salts. After filtration and evaporation of solvents, the products were purified by flash chromatography on silica gel (hexane/ethyl acetate, 8:2). The crude mixture obtained from **5** was separated by HPLC (hexane/ethyl acetate, 8:2). The yields are reported in Table 1 and Table 2.

Photolysis of *N₃CO₂Et*.

The substrate (3 mmol) and the *N₃CO₂Et* in the molar ratio reported in Table 1 and Table 2 in 3 ml of CH₂Cl₂ were photolysed in a quartz vessel under an atmosphere of nitrogen at room temperature, using a medium pressure Hanovia PCR lamp (100 W). When the azide band disappeared in the IR spectrum (*ca* 35 h) the solvent was evaporated *in vacuo*. The products were purified by flash chromatography on silica gel (hexane/ethyl acetate, 8:2). The crude mixture obtained from **5** was separated by HPLC (hexane/ethyl acetate, 8:2). The yields are reported in Table 1 and Table 2.

1a:¹⁵ IR (CCl₄) 1736, 1721 cm⁻¹; ¹H NMR (CDCl₃) δ 1.26 (*t*, *J* = 6.8 Hz, 3 H, CH₂CH₃), 1.27 (*s*, 3 H, CH₃), 1.38 (*s*, 3 H, CH₃), 2.25 (*s*, 3 H, CH₃CO), 3.05 (*s*, 1 H, HC-N), 4.18 (*q*, *J* = 6.8 Hz, 2 H, OCH₂); ¹³C NMR (CDCl₃) δ 14.40 (CH₂CH₃), 19.50, 22.82 (CH₃), 29.12 (CH₃CO), 47.29 (C-N), 52.40 (HC-N), 62.61 (OCH₂), 160.39 (COO), 203.32 (CO); GC-MS *m/z* 185 (M⁺, 6), 143 (16), 142 (100), 70 (66), 43 (77).

2a: IR (CCl₄) 1743, 1728 cm⁻¹; ¹H NMR (CDCl₃) δ 1.25 (*t*, *J* = 6.9 Hz, 3 H, CH₃), 1.51-2.55 (*m*, 6 H, CH₂), 2.95 (*m*, 1 H, CH), 3.11-3.14 (*m*, 1 H, CH), 4.16 (*q*, *J* = 6.9 Hz, 2 H, OCH₂); ¹³C NMR (CDCl₃) δ 14.24 (CH₃), 17.16, 22.58, 36.85 (CH₂), 40.48, 42.94 (CH), 63.16 (OCH₂), 161.61 (COO), 203.80 (CO); GC-MS *m/z* 183 (M⁺, 57), 138 (17), 137 (17), 124 (32), 111 (27), 110 (52), 96 (19), 84 (12), 83 (54), 82 (100), 69 (12), 68 (15), 67 (19), 56 (12), 55 (78), 54 (64), 53 (19), 52 (11), 43 (14), 42 (14), 41 (29); HRMS Calcd for C₉H₁₃NO₃: 183.0895. Found: 183.0887.

3a: IR (CCl₄) 1775, 1732 cm⁻¹; ¹H NMR (CDCl₃) δ 1.14 (*t*, *J* = 6.8 Hz, 3 H, CH₂CH₃), 1.7-2.3 (*m*, 8 H, CH₂), 2.14 (*s*, 3 H, CH₃), 2.81 (*m*, 1 H, CH), 4.03 (*q*, *J* = 6.8 Hz, 2 H, OCH₂); ¹³C NMR (CDCl₃) δ 14.27 (CH₂CH₃), 19.46, 19.56, 22.94, 23.87 (CH₂), 27.12 (CH₃), 42.53 (CH), 49.47 (C-N), 62.04 (OCH₂), 160.14 (COO), 204.52 (CO); GC-MS *m/z* 211 (M⁺, 3), 139 (31), 138 (38), 124 (33), 110 (12), 96 (100), 95 (11), 94 (13), 79 (10), 69 (17), 68 (18), 67 (16), 43 (68), 42 (13), 41 (21), 29 (25), 27 (12); HRMS Calcd for C₁₁H₁₇NO₃: 211.1208. Found: 211.1216.

4a: major diastereomer: IR (CCl₄) 1738, 1708 cm⁻¹; ¹H NMR (CDCl₃) δ 1.02 (*s*, 3 H, CH₃), 1.25 (*t*, *J* = 7.1 Hz, 3 H, CH₂CH₃), 1.3-2.4 (*m*, 12 H, CH₂), 2.83 (*s*, 1 H, CH), 4.12 (*q*, *J* = 7.1 Hz, 2 H, OCH₂); ¹³C NMR (CDCl₃) δ 14.11 (CH₂CH₃), 19.41, 20.76, 22.65, 27.97, 32.39, 33.61, 34.56, 36.63, 49.68 (HC-N), 57.61 (C-

N), 62.72 (OCH₂), 160.57 (COO), 207.15 (CO); GC-MS *m/z* 251 (M⁺, 30), 205 (13), 190 (11), 177 (21), 178 (100), 165 (17), 162 (13), 150 (10), 133 (12), 134 (16), 91 (10), 67 (12), 41 (10); HRMS Calcd for C₁₄H₂₁NO₃: 251.1521. Found: 251.1523; minor diastereomer: ¹³C NMR (CDCl₃) δ 14.40 (CH₂CH₃), 19.59, 21.12, 22.48, 28.83, 33.23, 33.49, 34.55, 36.76, 50.21 (HC-N), 57.46 (C-N), 62.71 (OCH₂), 160.13 (COO), 206.40 (CO).

5a: major diastereomer: [α]_D -84.1 (*c* = 0.73 in CH₂Cl₂); IR (CCl₄) 1730, 1707 cm⁻¹; ¹H NMR (CDCl₃) δ 0.81 [*d*, *J* = 6.8 Hz, 3 H, CH(CH₃)], 0.83 [*d*, *J* = 6.8 Hz, 3 H, CH(CH₃)], 1.22 (*t*, *J* = 7.1 Hz, 3 H, CH₂CH₃), 1.27 (*s*, 3 H, CH₃), 1.45-2.52 (*m*, 6 H, CH₂, CH), 2.90 (*m*, 1 H, HC-N), 4.10 (*q*, *J* = 7.1 Hz, 2 H, OCH₂); ¹³C NMR (CDCl₃) δ 13.84, 14.09, 18.95, 19.37 (CH₃), 26.37 (CH₂), 31.69, 34.36 (CH), 40.73 (CH₂CO), 44.68 (HC-N), 46.29 (C-N), 62.57 (OCH₂), 160.70 (COO), 205.42 (CO); GC-MS *m/z* 239 (M⁺, <1), 196 (17), 170 (10), 168 (26), 142 (87), 138 (11), 130 (13), 124 (16), 11 (21), 110 (13), 97 (35), 96 (27), 83 (11), 82 (13), 81 (11), 70 (27), 69 (100), 68 (34), 67 (11), 56 (12), 55 (79), 54 (27), 53 (16), 43 (25), 42 (50), 41 (44), 39 (17), 29 (74), 27 (29); HRMS Calcd for C₁₃H₂₁NO₃: 239.1521. Found: 239.1515; minor diastereomer: ¹⁶ [α]_D +7.3 (*c* = 0.12 in CH₂Cl₂); ¹H NMR (CDCl₃) δ 0.83 [*d*, *J* = 7.0 Hz, 6 H, CH(CH₃)₂], 1.31 (*s*, 3 H, CH₃), 1.40 (*t*, *J* = 7.1 Hz, 3 H, CH₂CH₃), 1.41-2.63 (*m*, 6 H, CH₂, CH), 2.91 (*d*, *J* = 7.0 Hz, 1 H, HC-N), 4.18 (*q*, *J* = 7.1 Hz, 2 H, OCH₂); ¹³C NMR (CDCl₃) δ 13.47, 14.12, 18.75, 18.97 (CH₃), 26.12 (CH₂), 32.10, 38.88 (CH), 44.77 (CH₂CO), 47.83 (HC-N), 53.29 (C-N), 62.63 (OCH₂), 160.49 (COO), 207.78 (CO).

9a: IR (CCl₄) 1747, 1738 cm⁻¹; ¹H NMR (CDCl₃) δ 0.91 (*s*, 3 H, CH₃), 1.04 (*s*, 3 H, CH₃), 1.36 (*t*, *J* = 7.0 Hz, 3 H, CH₂CH₃), 1.03-2.58 (*m*, 17 H, CH₂, CH), 2.04 (*s*, 3 H, CH₃CO), 2.18 (*s*, 3 H, CH₃CO), 3.41 (*m*, 1 H, HC-N), 4.36 (*q*, *J* = 7.0 Hz, 2 H, OCH₂), 4.51-4.62 (*m*, 1 H, HC-O), 5.35-5.42 (*m*, 1 H, HC=C).

9b: IR (CCl₄) 1737, 1669 cm⁻¹; ¹H NMR (CDCl₃) δ 0.85 (*s*, 3 H, CH₃), 1.06 (*s*, 3 H, CH₃), 1.22 (*t*, *J* = 7.0 Hz, 3 H, CH₂CH₃), 1.01-2.38 (*m*, 17 H, CH₂, CH), 2.01 (*s*, 3 H, CH₃CO), 2.23 (*s*, 3 H, CH₃CO), 2.62 (*m*, 1 H, HC-N), 4.15 (*q*, *J* = 7.0 Hz, 2 H, OCH₂), 4.81-4.93 (*m*, 1 H, HC-O), 6.67-6.72 (*m*, 1 H, HC=C); ¹³C NMR (CDCl₃) δ 13.86, 14.47, 15.78, 19.81, 21.31, 21.64, 21.78, 26.88, 27.09, 28.39, 31.21, 34.66, 34.72, 35.19, 35.43, 45.34, 45.93, 49.10, 49.63, 56.17, 61.99, 64.66, 61.99, 70.86, 144.23 (HC=C), 155.24 (HC=C), 161.61, 170.52 (COO), 196.60 (CO).

9c: IR (CCl₄) 1736, 1720 cm⁻¹; ¹H NMR (CDCl₃) δ 0.84 (*s*, 3 H, CH₃), 1.04 (*s*, 3 H, CH₃), 1.25 (*t*, *J* = 7.0 Hz, 6 H, 2 × CH₂CH₃), 1.09-2.48 (*m*, 17 H, CH₂, CH), 2.01 (*s*, 3 H, CH₃CO), 2.13 (*s*, 3 H, CH₃CO), 2.60 (*m*, 1 H, HC-N), 3.36 (*m*, 1 H, HC-N), 4.11 (*q*, *J* = 7.0 Hz, 4 H, 2 × OCH₂), 4.78-4.92 (*m*, 1 H, HC-O); ¹³C NMR (CDCl₃) δ 13.96, 14.14, 14.23, 15.13, 19.56, 21.10, 21.39, 25.62, 26.61, 28.03, 28.79, 29.51, 30.94, 32.26, 34.66, 34.95, 35.16, 40.71, 45.06, 45.20, 46.86, 48.75, 49.34, 53.33, 60.31, 62.01, 62.41, 70.74, 160.18, 161.74, 171.81 (COO), 202.31 (CO).

10a (d.e. <5%): IR (CCl₄) 1733, 1709 cm⁻¹; ¹H NMR (CDCl₃) δ 1.29 (*t*, *J* = 7.1 Hz, 3 H, CH₂CH₃), 1.36 (*s*, 3 H, CH₃), 1.70 (*s*, 3 H, CH₃), 1.75-2.80 (*m*, 5 H, 2 × CH₂, CH), 2.98-3.01 (*m*, 1 H, HC-N), 4.10 (*q*, *J* =

7.1 Hz, 2 H, OCH₂), 4.80 (*d*, *J* = 3 Hz, 2 H, C=CH₂); ¹³C NMR (CDCl₃) δ 14.16, 15.64, 20.40 (CH₃), 28.19, 35.75, 40.72 (CH₂, CH), 42.12 (C-N), 44.21 (HC-N), 62.33 (OCH₂), 110.40 (C=CH₂), 146.63 (C=CH₂), 161.94 (COO), 199.62 (CO); GC-MS *m/z* 237 (*M*⁺, <1), 168 (51), 166 (44), 148 (11), 140 (12), 129 (25), 122 (16), 109 (18), 96 (56), 95 (25), 94 (27), 81 (18), 79 (16), 68 (100), 67 (32), 56 (14), 57 (18), 53 (21), 42 (53), 29 (60). HRMS Calcd for C₁₃H₁₉NO₃: 237.1365. Found: 237.1357.

10b (d.e. 10%): IR (CCl₄) 1710, 1677 cm⁻¹; ¹H NMR (CDCl₃) δ 1.22 (*s*, 3 H, CH₃), 1.23 (*t*, *J* = 7.1 Hz, 3 H, CH₂CH₃), 1.73 (*s*, 3 H, CH₃), 2.10–2.50 (*m*, 5 H, 2 × CH₂, CH), 2.51–2.62 (*m*, 2 H, N-CH₂), 4.10 (*q*, *J* = 7.1 Hz, 2 H, OCH₂), 6.68–6.79 (*m*, 1 H, C=CH); ¹³C NMR (CDCl₃) δ 14.47, 15.66, 16.90, 17.33 (CH₃), 27.79, 28.36, 35.90, 36.41 (CH₂), 39.96, 40.57 (N-CH₂), 41.06, 41.55 (CH), 44.71, 44.74 (N-C), 62.32 (OCH₂), 135.44, 135.58 (C=CH), 143.88, 144.26 (C=CH), 161.94 (COO), 201.02 (CO); GC-MS *m/z* 237 (*M*⁺, <1), 148 (100), 135 (14), 133 (16), 108 (16), 105 (14), 91 (14), 82 (23), 54 (18), 39 (18), 29 (20); HRMS Calcd for C₁₃H₁₉NO₃: 237.1365. Found: 237.1354.

10c (d.e. <5): IR (CCl₄) 1742, 1709 cm⁻¹; ¹H NMR (CDCl₃) δ 1.21 (*s*, 3 H, CH₃), 1.26 (*t*, *J* = 7.1 Hz, 6 H, 2 × CH₂CH₃), 1.31 (*s*, 3 H, CH₃), 2.10–2.50 (*m*, 5 H, CH₂, CH), 2.51–2.62 (*m*, 2 H, N-CH₂), 2.92–2.99 (*m*, 1 H, N-CH), 4.16 (*q*, *J* = 7.1 Hz, 4 H, 2 × OCH₂); ¹³C NMR (CDCl₃) δ 13.60, 13.96, 14.02, 14.23, 14.37, 14.47, 17.35, 17.44 (CH₃), 24.90, 25.61, 34.31, 34.42, 35.73, 36.24, 38.71, 39.59, 44.62, 44.65 (CH₂, CH), 62.36, 62.86 (OCH₂), 161.05, 161.92 (COO), 201.03, 204.00 (CO); GC-MS *m/z* 324 (*M*⁺, <1), 223 (15), 222 (100), 150 (35), 135 (11), 107 (10), 79 (11), 30 (12), 29 (29); HRMS Calcd for C₁₆H₂₄N₂O₅: 324.1685. Found: 324.1672.

Synthesis of 8.

Following the procedures reported in literature,^{6,7} (+)-*trans*-1,2-epoxylimonene (*Fluka*, 13 mmol) was hydrogenated at atmospheric pressure and at room temperature in the presence of Raney Ni (6 g) in 80 ml of MeOH for 1 h. The obtained (+)-carvomenthene epoxide (10 mmol) in 24 ml of MeOH/H₂O (8:1) was treated with NaN₃ (50 mmol) and NH₄Cl (22 mmol) and the mixture was stirred at 80 °C for 18 h. After evaporation of the solvents, the residue was diluted with ethyl acetate and the salts were filtered. The residue was washed first with H₂O and then with a saturated solution of NaCl. The solvent was evaporated and **8** was obtained with 95% of yield: [α]_D +58.2 (*c* = 0.42 in CH₂Cl₂); IR (CCl₄) 3469, 2094 cm⁻¹; ¹H NMR (CDCl₃) δ 0.86–0.89 (2 *d*, *J* = 7.0 Hz, 6 H, 2 × CH₃), 1.22 (*s*, 3 H, CH₃), 1.13–1.78 (*m*, 9 H, CH₂, CH, OH), 3.46 (*m*, 1 H, HC-N); ¹³C NMR (CDCl₃) δ 19.65, 27.28, 31.52, 32.45, 36.90 (CH, CH₃), 23.90, 24.85, 28.94 (CH₂), 43.26 (HC-N), 71.08 (C); GC-MS *m/z* 169 (*M*⁺-28, <1), 126 (11), 98 (21), 71 (22), 58 (11), 56 (14), 43 (100), 41 (18).

Synthesis of 6.

According to typical procedures,⁸ a mixture of **8** (10 mmol) and PPh₃ (10 mmol) in CH₃CN (10 ml) was stirred at room temperature for 2 h and then at reflux overnight. After cooling and evaporation of the solvent,

10 mmol of anhydrous Et_3N and 13 mmol of ethyl chloroformate were added at 0 °C dropwise to the crude mixture in 20 ml of anhydrous Et_2O . The reaction mixture was stirred for 2 h at room temperature. The solvents were removed under reduced pressure and the product was purified by flash chromatography on silica gel (hexane/ethyl acetate, 9:1). **6** was obtained in 52% of yield. According to a standard method,^{17,18} **6** was also obtained by treating **5a** (2 mmol) with 1,2-ethanedithiol (10 mmol) and 0.83 ml of BF_3 . After work-up, 9.3 g of Raney Ni in 30 ml of EtOH was added to the crude mixture under a hydrogen atmosphere. After 4 h of stirring, **6** was purified by HPLC (hexane/ethyl acetate, 95:5) with 30% of yield. **6**: $[\alpha]_{\text{D}} +11.8$ ($c = 0.90$ in CH_2Cl_2); IR (CCl_4) 1724 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.85–0.90 (2 d, $J = 6.8$ Hz, 6 H, $2 \times \text{CH}_3$), 1.19 (t, $J = 7.1$ Hz, 3 H, CH_3), 1.21 (s, 3 H, CH_3), 1.29–2.05 (m, 8 H, CH_2 , CH), 2.46 (m, 1 H, HC-N), 4.08 (q, $J = 7.1$ Hz, 2 H, OCH_2); ^{13}C NMR (CDCl_3) δ 14.44, 15.47, 19.56, 22.80 (CH_3), 24.99, 27.96, 29.58 (CH_2), 31.62, 35.39 (CH), 42.97 (C), 44.41 (HC-N), 61.74 (OCH_2), 162.25 (CO); GC-MS m/z 225 (M^+ , 2), 196 (29), 182 (17), 155 (11), 137 (11), 136 (49), 135 (10), 96 (10), 94 (16), 93 (100), 92 (45), 91 (20), 90 (43), 82 (22), 81 (19), 79 (17), 77 (16), 67 (10), 43 (23), 41 (25); HRMS Calcd for $\text{C}_{13}\text{H}_{23}\text{NO}_2$: 225.1729. Found: 225.1731.

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