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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 N_3CO_2Et 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 esters[1] and nitroalkenes.[2] The use of ethyl *N*-[(4-nitrobenzenesulphonyl)oxy]carbamate ($NsONHCO_2Et$) 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 ketones[3] when reacted the above mentioned reagents (route A in Table 1) and in addition with ethyl *N*-[(4-methylbenzenesulphonyl)oxy] carbamate ($TsONHCO_2Et$) 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 $NsONHCO_2Et$/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 $ArSO_3N^-CO_2Et$ in an initial Michael type addition[2] we also investigated the photolysis of N_3CO_2Et 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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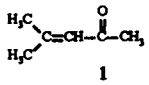
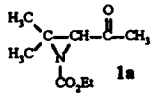
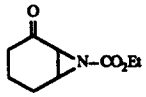
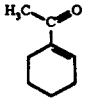
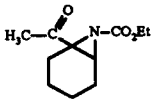
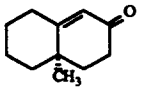
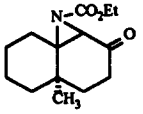
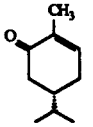
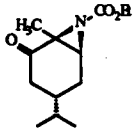
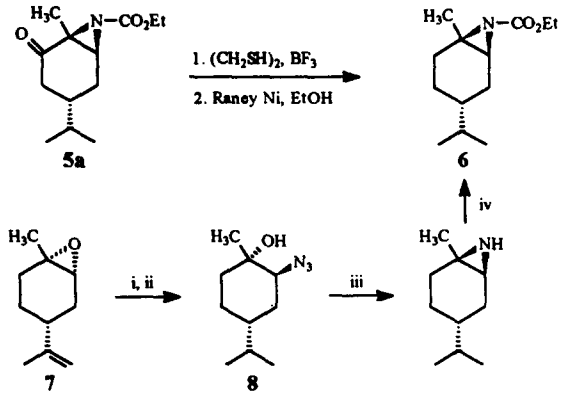
(*R*)-Dihydrocarvone[5] (**5**) gives the expected aziridines with moderate diastereomeric excesses (d.e.) and provides the best result in the photolysis reaction. The aziridines were obtained easily as pure diastereomers after purification by HPLC.

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 ($NsONHCO_2Et/CaO$, route A or $TsONHCO_2Et/Cs_2CO_3$, route B) was used. Route C refers to photolysis reaction of N_3CO_2Et in 1'*M* solutions of ketones in dichloromethane.

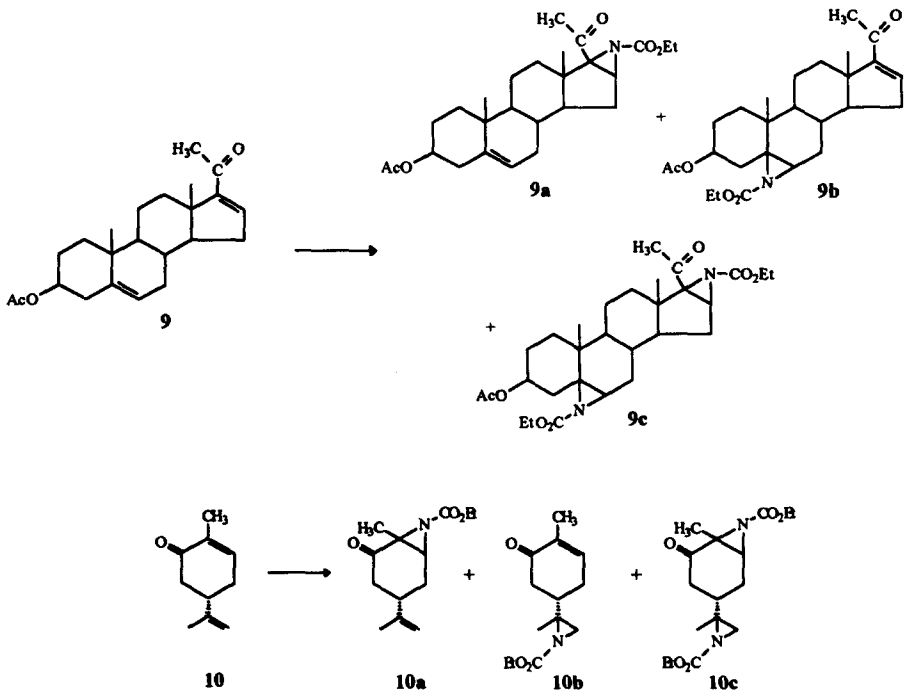
The amination of **5** was attempted with $NsONHCO_2Et$ and CaO by grinding the reactants together with the substrate in a mortar.[2] In this way, **5a** was obtained with a yield comparable to that reported in Table 1, but using a lower molar ratio (**5**:$NsONHCO_2Et$:CaO=1:3:3). In all amination conditions 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.



i. H_2, Raney Ni, EtOH; ii. NaN_3, MeOH, NH_4Cl; iii. PPh_3, CH_3CN; iv. $ClCO_2Et$, NEt_3, C_6H_6

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**:$NsONHCO_2Et$: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). ^{1}H NMR and ^{13}C NMR spectra were obtained in $CDCl_3$ on a Varian XL-300 spectrometer, with $CHCl_3$ as an internal standard. IR spectra in CCl_4 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. $NsONHCO_2Et$,[12] $TsONHCO_2Et$,[4] N_3CO_2Et[13] (*CAUTION: explosive and toxic vapours*) and (*R*)-dihydrocarvone[5] **5** were prepared according to literature methods.

(*R*)-5: $[\alpha]_D$ +84.3 (*c* = 0.70 in CH_2Cl_2) (lit.[14] $[\alpha]_D$ + 86.0, neat); IR (CCl_4) 1663 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80 [*d*, *J* = 6.8 Hz, 6 H, $CH(CH_3)_2$], 1.51-1.64 [*m*, 1 H, $CH(CH_3)_2$], 1.73 (*s*, 3 H, CH_3), 1.92-2.27 (*m*, 5 H, 2 × CH_2, CH), 6.67-6.70 (*m*, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) δ 15.53, 19.32, 19.38 (CH_3), 20.34, 29.68, 31.86, 42.26 (CH_2, 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 $NsONHCO_2Et$ and CaO or with $TsONHCO_2Et$ and Cs_2CO_3.

To 3 mmol of substrate in 3 ml of CH_2Cl_2, $NsONHCO_2Et$ and CaO or $TsONHCO_2Et$ and Cs_2CO_3 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 CH_2Cl_2 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 N_3CO_2Et.

The substrate (3 mmol) and the N_3CO_2Et in the molar ratio reported in Table 1 and Table 2 in 3 ml of CH_2Cl_2 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 disapparead 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 (CCl_4) 1736, 1721 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (*t*, *J* = 6.8 Hz, 3 H, CH_2CH_3), 1.27 (*s*, 3 H, CH_3), 1.38 (*s*, 3 H, CH_3), 2.25 (*s*, 3 H, CH_3CO), 3.05 (*s*, 1 H, HC-N), 4.18 (*q*, *J* = 6.8 Hz, 2 H, OCH_2); ^{13}C NMR ($CDCl_3$) δ 14.40 (CH_2CH_3), 19.50, 22.82 (CH_3), 29.12 (CH_3CO), 47.29 (C-N), 52.40 (HC-N), 62.61 (OCH_2), 160.39 (COO), 203.32 (CO); GC-MS *m/z* 185 (M^+, 6), 143 (16), 142 (100), 70 (66), 43 (77).

2a: IR (CCl_4) 1743, 1728 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (*t*, *J* = 6.9 Hz, 3 H, CH_3), 1.51-2.55 (*m*, 6 H, CH_2), 2.95 (*m*, 1 H, CH), 3.11-3.14 (*m*, 1 H, CH), 4.16 (*q*, *J* = 6.9 Hz, 2 H, OCH_2); ^{13}C NMR ($CDCl_3$) δ 14.24 (CH_3), 17.16, 22.58, 36.85 (CH_2), 40.48, 42.94 (CH), 63.16 (OCH_2), 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 $C_9H_{13}NO_3$: 183.0895. Found: 183.0887.

3a: IR (CCl_4) 1775, 1732 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14 (*t*, *J* = 6.8 Hz, 3 H, CH_2CH_3), 1.7-2.3 (*m*, 8 H, CH_2), 2.14 (*s*, 3 H, CH_3), 2.81 (*m*, 1 H, CH), 4.03 (*q*, *J* = 6.8 Hz, 2 H, OCH_2); ^{13}C NMR ($CDCl_3$) δ 14.27 (CH_2CH_3), 19.46, 19.56, 22.94, 23.87 (CH_2), 27.12 (CH_3), 42.53 (CH), 49.47 (C-N), 62.04 (OCH_2), 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 $C_{11}H_{17}NO_3$: 211.1208. Found: 211.1216.

4a: major diastereomer: IR (CCl_4) 1738, 1708 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 (*s*, 3 H, CH_3), 1.25 (*t*, *J* = 7.1 Hz, 3 H, CH_2CH_3), 1.3-2.4 (*m*, 12 H, CH_2), 2.83 (*s*, 1 H, CH), 4.12 (*q*, *J* = 7.1 Hz, 2 H, OCH_2); ^{13}C NMR ($CDCl_3$) δ 14.11 (CH_2CH_3), 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 (OCH_2), 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 $C_{14}H_{21}NO_3$: 251.1521. Found: 251.1523; minor diastereomer: ^{13}C NMR ($CDCl_3$) δ 14.40 (CH_2CH_3), 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 (OCH_2), 160.13 (COO), 206.40 (CO).

5a: major diastereomer: $[\alpha]_D$ -84.1 (*c* = 0.73 in CH_2Cl_2); IR (CCl_4) 1730, 1707 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.81 [*d*, *J* = 6.8 Hz, 3 H, $CH(CH_3)$], 0.83 [*d*, *J* = 6.8 Hz, 3 H, $CH(CH_3)$], 1.22 (*t*, *J* = 7.1 Hz, 3 H, CH_2CH_3), 1.27 (*s*, 3 H, CH_3), 1.45-2.52 (*m*, 6 H, CH_2, CH), 2.90 (*m*, 1 H, HC-N), 4.10 (*q*, *J* = 7.1 Hz, 2 H, OCH_2); ^{13}C NMR ($CDCl_3$) δ 13.84, 14.09, 18.95, 19.37 (CH_3), 26.37 (CH_2), 31.69, 34.36 (CH), 40.73 (CH_2CO), 44.68 (HC-N), 46.29 (C-N), 62.57 (OCH_2), 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 $C_{13}H_{21}NO_3$: 239.1521. Found: 239.1515; minor diastereomer:[16] $[\alpha]_D$ +7.3 (*c* = 0.12 in CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 0.83 [*d*, *J* = 7.0 Hz, 6 H, $CH(CH_3)_2$], 1.31 (*s*, 3 H, CH_3), 1.40 (*t*, *J* = 7.1 Hz, 3 H, CH_2CH_3), 1.41-2.63 (*m*, 6 H, CH_2, CH), 2.91 (*d*, *J* = 7.0 Hz, 1 H, HC-N), 4.18 (*q*, *J* = 7.1 Hz, 2 H, OCH_2); ^{13}C NMR ($CDCl_3$) δ 13.47, 14.12, 18.75, 18.97 (CH_3), 26.12 (CH_2), 32.10, 38.88 (CH), 44.77 (CH_2CO), 47.83 (HC-N), 53.29 (C-N), 62.63 (OCH_2), 160.49 (COO), 207.78 (CO).

9a: IR (CCl_4) 1747, 1738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (*s*, 3 H, CH_3), 1.04 (*s*, 3 H, CH_3), 1.36 (*t*, *J* = 7.0 Hz, 3 H, CH_2CH_3), 1.03-2.58 (*m*, 17 H, CH_2, CH), 2.04 (*s*, 3 H, CH_3CO), 2.18 (*s*, 3 H, CH_3CO), 3.41 (*m*, 1 H, HC-N), 4.36 (*q*, *J* = 7.0 Hz, 2 H, OCH_2), 4.51-4.62 (*m*, 1 H, HC-O), 5.35-5.42 (*m*, 1 H, HC=C).

9b: IR (CCl_4) 1737, 1669 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (*s*, 3 H, CH_3), 1.06 (*s*, 3 H, CH_3), 1.22 (*t*, *J* = 7.0 Hz, 3 H, CH_2CH_3), 1.01-2.38 (*m*, 17 H, CH_2, CH), 2.01 (*s*, 3 H, CH_3CO), 2.23 (*s*, 3 H, CH_3CO), 2.62 (*m*, 1 H, HC-N), 4.15 (*q*, *J* = 7.0 Hz, 2 H, OCH_2), 4.81-4.93 (*m*, 1 H, HC-O), 6.67-6.72 (m, 1 H, HC=C); ^{13}C NMR ($CDCl_3$) 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 (CCl_4) 1736, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84 (*s*, 3 H, CH_3), 1.04 (*s*, 3 H, CH_3), 1.25 (*t*, *J* = 7.0 Hz, 6 H, 2 × CH_2CH_3), 1.09-2.48 (*m*, 17 H, CH_2, CH), 2.01 (*s*, 3 H, CH_3CO), 2.13 (*s*, 3 H, CH_3CO), 2.60 (*m*, 1 H, HC-N), 3.36 (*m*, 1 H, HC-N), 4.11 (*q*, *J* = 7.0 Hz, 4 H, 2 × OCH_2), 4.78-4.92 (*m*, 1 H, HC-O); ^{13}C NMR ($CDCl_3$) 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 (CCl_4) 1733, 1709 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (*t*, *J* = 7.1 Hz, 3 H, CH_2CH_3), 1.36 (*s*, 3 H, CH_3), 1.70 (*s*, 3 H, CH_3), 1.75-2.80 (*m*, 5 H, 2 × CH_2, CH), 2.98-3.01 (*m*, 1 H, HC-N), 4.10 (*q*, *J* =

7.1 Hz, 2 H, OCH_2), 4.80 (*d*, *J* = 3 Hz, 2 H, C=CH_2); ^{13}C NMR ($CDCl_3$) δ 14.16, 15.64, 20.40 (CH_3), 28.19, 35.75, 40.72 (CH_2, CH), 42.12 (C-N), 44.21 (HC-N), 62.33 (OCH_2), 110.40 (*C*=CH_2), 146.63 (C=*C*H_2), 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 $C_{13}H_{19}NO_3$: 237.1365. Found: 237.1357.

10b (d.e. 10%): IR (CCl_4) 1710, 1677 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (*s*, 3 H, CH_3), 1.23 (*t*, *J* = 7.1 Hz, 3 H, CH_2CH_3), 1.73 (*s*, 3 H, CH_3), 2.10-2.50 (*m*, 5 H, 2 × CH_2, CH), 2.51-2.62 (*m*, 2 H, N-CH_2), 4.10 (*q*, *J* = 7.1 Hz, 2 H, OCH_2), 6.68-6.79 (*m*, 1 H, C=CH); ^{13}C NMR ($CDCl_3$) δ 14.47, 15.66, 16.90, 17.33 (CH_3), 27.79, 28.36, 35.90, 36.41 (CH_2), 39.96, 40.57 (N-CH_2), 41.06, 41.55 (CH), 44.71, 44.74 (N-C), 62.32 (OCH_2), 135.44, 135.58 (*C*=CH), 143.88, 144.26 (C=*C*H), 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 $C_{13}H_{19}NO_3$: 237.1365. Found: 237.1354.

10c (d.e. <5): IR (CCl_4) 1742, 1709 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (*s*, 3 H, CH_3), 1.26 (*t*, *J* = 7.1 Hz, 6 H, 2 × CH_2CH_3), 1.31 (*s*, 3 H, CH_3), 2.10-2.50 (m, 5 H, CH_2, CH), 2.51-2.62 (*m*, 2 H, N-CH_2), 2.92-2.99 (*m*, 1 H, N-CH), 4.16 (*q*, *J* = 7.1 Hz, 4 H, 2 × OCH_2); ^{13}C NMR ($CDCl_3$) δ 13.60, 13.96, 14.02, 14.23, 14.37, 14.47, 17.35, 17.44 (CH_3), 24.90, 25.61, 34.31, 34.42, 35.73, 36.24, 38.71, 39.59, 44.62, 44.65 (CH_2, CH), 62.36, 62.86 (OCH_2), 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 $C_{16}H_{24}N_2O_5$: 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/H_2O (8:1) was treated with NaN_3 (50 mmol) and NH_4Cl (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 H_2O and then with a saturated solution of NaCl. The solvent was evaporated and **8** was obtained with 95% of yield: $[\alpha]_D$ +58.2 (*c* = 0.42 in CH_2Cl_2); IR (CCl_4) 3469, 2094 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86-0.89 (2 *d*, *J* = 7.0 Hz, 6 H, 2 × CH_3), 1.22 (*s*, 3 H, CH_3), 1.13-1.78 (*m*, 9 H, CH_2, CH, OH), 3.46 (*m*, 1 H, HC-N); ^{13}C NMR ($CDCl_3$) δ 19.65, 27.28, 31.52, 32.45, 36.90 (CH, CH_3), 23.90, 24.85, 28.94 (CH_2), 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 PPh_3 (10 mmol) in CH_3CN (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**: $[\alpha]_D$ +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 × 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 $C_{13}H_{23}NO_2$: 225.1729. Found: 225.1731.

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