α -Methylene- β -amino Ketone Derivatives from β -Ketoallylsilanes

M. Antonietta Loreto^{†,‡,*}, *Antonella Migliorini*^{†,‡}, *P. Antonio Tardella*[†]

[†]Dipartimento di Chimica, Università “La Sapienza”, Piazzale Aldo Moro 5, 00185 Rome, Italy;

[‡]Istituto C.N.R. di Chimica Biomolecolare, Sezione Roma, Dipartimento di Chimica, Università “La Sapienza”, Rome, Italy.

mariaantonieta.loreto@uniroma1.it

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General experimental methods

Solvents and common reagents were purchased from commercial sources and used without further purification. All reactions were monitored by GC-MS analysis. Yields are given for isolated products after column chromatography, performed with Merck silica gel 60 (70-230 mesh). ^1H NMR and ^{13}C NMR spectra were recorded on a 200 MHz spectrometer; chemical shifts are expressed in parts per million (δ scale) and are referenced to the carbon and residual protons of the NMR solvent (CHCl_3 : δ 7.26 for ^1H NMR, δ 77.0 for ^{13}C NMR). Infrared (IR) spectra were obtained using a FT-IR; data are presented as the frequency of absorption (cm^{-1}). GC-MS spectrometry analyses were performed on a gas chromatograph with a phenylmethylsilicon capillary column (15m, 0.25 mm i. d.). HRMS spectra were recorded with Micromass Q-TOF *micro* Mass Spectrometer.

Synthesis of silylated ketophosphonates 4a-c.

(2-Oxo-2-phenyl-1-trimethylsilylmethyl-ethyl)-phosphonic acid diethyl ester (4a). To 60% NaH (375 mg, 8.60 mmol; suspension in mineral oil) in anhydrous DME (9 mL), ketophosphonate **5a** (2 g, 7.80 mmol) in anhydrous DME (5 mL) was added dropwise, under argon at 0°C . After 1 h at 0°C and 1 h at room temperature, a solution of iodomethyltrimethylsilane (6.7 g, 31.20 mmol) in anhydrous DME (21 mL) was added and the resulting mixture was heated to 70°C . After being stirred for 7-8 h the mixture was poured into saturated ammonium chloride solution and the aqueous phase was extracted with Et_2O . The combined organic phases were washed with brine and dried over Na_2SO_4 . After solvent evaporation, the crude was purified by chromatography on silica gel (hexane/acetone=7/3) to obtain the product **4a** as a yellow oil (1 g, 3 mmol, 40% yield). IR (CHCl_3): 1681, 1254 cm^{-1} . ^1H NMR (CDCl_3 , 200 MHz) δ -0.07 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 1.12 (t, $J = 7.3$ Hz, 3H, OCH_2CH_3), 1.19-1.30 (m, 4H, OCH_2CH_3 , CHHSi), 1.53-1.71 (m, 1H, CHHSi), 3.90-4.25 (m, 5H, $(\text{OCH}_2\text{CH}_3)_2$, $\text{CHP}=\text{O}$), 7.36-7.61 (m, 3H, $\text{CH}_{\text{arom.}}$), 7.96-8.01 (m, 2H, $\text{CH}_{\text{arom.}}$). ^{13}C NMR

(CDCl₃, 50 MHz) δ -1.3 (Si(CH₃)₃), 13.70 (d, J_{CCP} = 7.6 Hz, CH₂Si), 16.0 (d, J_{CCOP} = 6.1 Hz, OCH₂CH₃), 16.3 (d, J_{CCOP} = 6.1, OCH₂CH₃), 42.7 (d, J_{CP} = 125.1 Hz, CHP=O), 62.5 (d, J_{COP} = 6.1 Hz, OCH₂CH₃), 128.5 (CH_{arom.}), 128.8 (CH_{arom.}), 133.1 (CH_{arom.}), 137.4 (C_{arom.}), 196.4 (C=O). GC-MS m/z 342 [M^+] (1.6%), 105 (100%). HRMS Calculated for C₁₆H₂₇O₄NaPSi: m/z 365.1314. Found: m/z 365.1311.

(2-Oxo-1-trimethylsilanylmethyl-propyl)-phosphonic acid diethyl ester (4b). This compound was prepared from 2 g of ketophosphonate **5b** (10.30 mmol), according to the general procedure described for **4a**. The crude was purified by chromatography on silica gel (hexane/acetone=7/3) to obtain the product as a yellowish oil (1 g, 4 mmol, 40% yield). IR (CHCl₃): 1719, 1252 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ -0.07 (s, 9H, Si(CH₃)₃), 0.83-0.99 (m, 1H, CHHSi), 1.20-1.38 (m, 7H, CHHSi, (OCH₂CH₃)₂), 2.29 (s, 3H, CH₃C=O), 3.14 (ddd, J = 24.9 Hz, J = 11.71 Hz, J = 2.2 Hz, 1H, CHP=O), 3.98-4.15 (m, 4H, (OCH₂CH₃)₂). ¹³C NMR (CDCl₃, 50 MHz) δ -1.6 (Si(CH₃)₃), 12.3 (d, J_{CCP} = 6.1 Hz, CH₂Si), 16.2 (d, J_{CCOP} = 7.6 Hz, OCH₂CH₃), 30.7 (CH₃C=O), 49.0 (d, CHP=O, J_{CP} = 122.1 Hz), 62.5 (d, J_{COP} = 3.0 Hz, OCH₂CH₃), 62.7 (d, J_{COP} = 3.0 Hz, OCH₂CH₃), 203.7 (C=O). GC-MS m/z 280 [M^+] (5.7%), 165 (100%). HRMS Calculated for C₁₁H₂₅NaO₄PSi: m/z 303.1157. Found: m/z 303.1150.

(2-Oxo-1-trimethylsilanylmethyl-butyl)-phosphonic acid diethyl ester (4c). This compound was prepared from 2 g of ketophosphonate **5c** (9.60 mmol), according to the general procedure described for **4a**. The crude was purified by chromatography on silica gel (hexane/acetone=7/3) to obtain the product as a yellowish oil (1.3 g, 4.32 mmol, 45% yield). IR (CHCl₃): 1715, 1254 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ -0.03 (s, 9H, Si(CH₃)₃), 0.87-1.04 (m, 1H, CHHSi), 1.06 (t, J = 7.3 Hz, 3H, CH₃CH₂C=O), 1.31 (t, J = 7.3 Hz, 3H, OCH₂CH₃), 1.32 (t, J = 7.3 Hz, 3H, OCH₂CH₃), 1.34-1.46 (m, 1H, CHHSi), 2.48 (dq, J = 18.3 Hz, J = 7.3 Hz, 1H, CH₃CHHC=O), 2.89 (dq, J = 18.3 Hz, J = 7.3 Hz, 1H, CH₃CHHC=O), 3.18 (ddd, J = 24.9 Hz, J = 11.7 Hz, J = 2.2 Hz, 1H, CHP=O), 4.10 (m, 4H, (OCH₂CH₃)₂). ¹³C NMR (CDCl₃, 50 MHz) δ -1.5 ((Si(CH₃)₃), 7.7 (CH₃CH₂C=O),

12.5 (d, $J_{\text{CCP}} = 7.6$ Hz, CH_2Si), 16.3 (d, $J_{\text{CCOP}} = 6.1$ Hz, $(\text{OCH}_2\text{CH}_3)_2$), 37.0 ($\text{CH}_3\text{CH}_2\text{C}=\text{O}$), 48.1 (d, $J_{\text{CP}} = 122.1$ Hz, $\text{CHP}=\text{O}$), 62.6 (d, $J_{\text{COP}} = 6.1$ Hz, $(\text{OCH}_2\text{CH}_3)_2$), 203.5 ($\text{C}=\text{O}$). GC-MS m/z 294 [M^+] (0.8%), 165 (100%). HRMS Calculated for $\text{C}_{12}\text{H}_{27}\text{NaO}_4\text{PSi}$: m/z 317.1314. Found: m/z 317.1310.

By-products **6a**,¹ **6b**,² **6c**,² **7a**,³ **7b**,⁴ **7c** were isolated.

Spectral data of **7c**. IR (CHCl_3): 1710, 1251 cm^{-1} . ^1H NMR (CDCl_3 , 200 MHz) δ 0.89 (t, $J = 7.3$ Hz, 3H, $\text{CH}_3\text{CH}_2\text{CH}$), 1.05 (t, $J = 7.3$ Hz, 3H, $\text{CH}_3\text{CH}_2\text{C}=\text{O}$), 1.30 (t, $J = 7.3$ Hz, 6H, $(\text{OCH}_2\text{CH}_3)_2$), 1.72-2.11 (m, 2H, $\text{CH}_3\text{CH}_2\text{CH}$), 2.45 (dq, $J = 18.3$ Hz, $J = 7.3$ Hz, 1H, $\text{CH}_3\text{CHHC}=\text{O}$), 2.79 (dq, $J = 18.3$ Hz, $J = 7.3$ Hz, 1H, $\text{CH}_3\text{CHHC}=\text{O}$), 3.07 (ddd, $J = 19.8$ Hz, $J = 10.2$ Hz, $J = 3.7$ Hz, 1H, $\text{CHP}=\text{O}$), 4.03-4.18 (m, 4H, $(\text{OCH}_2\text{CH}_3)_2$). GC-MS m/z 236 [M^+] (6.5%), 180 (100%). HRMS Calculated for $\text{C}_{10}\text{H}_{21}\text{NaO}_4\text{P}$: m/z 259.1075. Found: m/z 259.1071.

Synthesis of β -ketoallylsilanes **2a-c** (Method A)

1-Phenyl-2-trimethylsilanylmethyl-propenone (2a).⁵ To a stirred solution of the substrate **4a** (300 mg, 0.88 mmol) in dichloromethane (1 mL) a 50% (w/w) sodium hydroxide aqueous solution (1.05 mL) was added dropwise. After 1 h at room temperature, a 37% (w/w) formaldehyde aqueous solution (73 mg, 0.90 mmol) was added dropwise and the resulting heterogenous mixture was stirred for 6 h. After this period the mixture was extracted with dichloromethane, the organic phase was dried over Na_2SO_4 and evaporated under vacuum. The product **2a** was obtained pure as a yellow oil (163 mg, 0.75 mmol, 85% yield). IR (CHCl_3): 1680 cm^{-1} . ^1H NMR (CDCl_3 , 200 MHz) δ 0.06 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 2.03 (s, 2H, CH_2Si), 5.50 (s, 1H, $\text{C}=\text{CHH}$), 5.72 (s, 1H, $\text{C}=\text{CHH}$), 7.39-7.75 (m, 5H, CH_{arom}). GC-MS m/z 218 [M^+] (14.2%), 73 (100%).

3-Trimethylsilanylmethyl-but-3-en-2-one (2b).⁵ This compound was prepared from 300 mg of **4b** (1.07 mmol), according to the general procedure described for **2a**. The product **2b** was obtained pure as a pale yellow oil (117 mg, 0.75 mmol, 70% yield). IR (CHCl_3): 1680 cm^{-1} . ^1H NMR

(CDCl₃, 200 MHz) δ -0.02 (s, 9H, Si(CH₃)₃), 1.81 (s, 2H, CH₂Si), 2.34 (s, 3H, CH₃C=O), 5.61 (s, 1H, C=CHH), 5.87 (s, 1H, C=CHH). GC-MS m/z 156 [M⁺] (0.7%), 73 (100%).

3-Trimethylsilanylmethyl-pent-3-en-2-one (2c). This compound was prepared from 258 mg of **4c** (0.88 mmol), according to the general procedure described for **2a**. The product **2c** was obtained pure as a pale yellow oil (112 mg, 0.66 mmol, 75% yield). IR (CHCl₃): 1682 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ -0.05 (s, 9H, Si(CH₃)₃), 1.09 (t, J = 7.32 Hz, 3H, CH₃CH₂C=O), 1.79 (s, 2H, CH₂Si), 2.71 (q, J = 7.32 Hz, 2H, CH₃CH₂C=O), 5.54 (s, 1H, C=CHH), 5.84 (s, 1H, C=CHH). GC-MS m/z 170 [M⁺] (0.5%), 73 (100%). HRMS Calculated for C₉H₁₈NaOSi: m/z 193.1025. Found: m/z 193.1018.

Synthesis of β -ketoallylsilanes **2d-i** (Method B)

4-Phenyl-3-trimethylsilanylmethyl-but-3-en-2-one (2d).⁶ To 60% NaH (90 mg, 2.05 mmol; suspension in mineral oil) in anhydrous DME (1.6 mL), the substrate **4b** (411 mg, 1.47 mmol) in anhydrous DME (0.3 mL) was added dropwise, under argon at 0°C. After 1 h at 0°C and 1 h at room temperature, a solution of benzaldehyde (172 mg, 1.62 mmol) in anhydrous DME (0.4 mL) was added at 0°C and the resulting mixture was stirred at room temperature. After being stirred for 10 h the mixture was poured into saturated ammonium chloride solution and the aqueous phase was extracted with Et₂O. The combined organic phases were dried over Na₂SO₄. After solvent evaporation, the crude was purified by chromatography on silica gel (hexane/diethyl ether=98/2) to obtain the pure *Z* isomer (85 mg, 0.37 mmol) as yellowish oil and a mixture of *E/Z* isomers in the ratio of 3/1 (16 mg, 0.07 mmol) (30% total yield). Spectral data of **2d (Z)**: IR (CHCl₃): 1680, 1662 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ -0.04 (s, 9H, Si(CH₃)₃), 2.18 (s, 2H, CH₂Si), 2.48 (s, 3H, CH₃C=O), 7.27-7.43 (m, 6H, CH_{arom.}, C=CHPh). ¹³C NMR (CDCl₃, 50 MHz) δ -0.7 (Si(CH₃)₃), 16.6 (CH₂Si), 25.8 (CH₃C=O), 128.0 (CH_{arom.}), 128.4 (CH_{arom.}), 129.1 (CH_{arom.}), 136.0 (C=CH), 136.6 (C_{arom.}), 141.7 (C=CH), 200.4 (C=O). GC-MS m/z 232 [M⁺] (31.5%), 73 (100%).

4-Phenyl-3-trimethylsilanylmethyl-but-3-en-2-one (2e). This compound was prepared from 390 mg of **4c** (1.33 mmol), according to the general procedure described for **2d**, using benzaldehyde. The crude was purified by chromatography on silica gel (hexane/diethyl ether=98/2) to obtain the pure *Z* isomer (98 mg, 0.40 mmol) as a yellow oil, and a mixture of *E/Z* (16 mg, 0.06 mmol) in the ratio of 4/1 (35% total yield). Spectral data of **2e (Z)** IR (CHCl₃): 1672, 1660 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ -0.02 (s, 9H, Si(CH₃)₃), 1.19 (t, *J*= 7.3 Hz, 3H, CH₃CH₂), 2.18 (s, 2H, CH₂Si), 2.86 (q, *J*= 7.3 Hz, 2H, CH₃CH₂), 7.28-7.42 (m, 6H, CH_{arom.}, C=CH). ¹³C NMR (CDCl₃, 50 MHz) δ -1.9 ((Si(CH₃)₃), 8.4 (CH₂Si), 15.7 (CH₃CH₂), 29.3 (CH₃CH₂), 126.6 (CH_{arom.}), 127.3 (CH_{arom.}), 127.9 (CH_{arom.}), 133.4 (C=CH), 135.5 (C_{arom.}), 140.0 (C=CH), 201.9 (C=O). GC-MS *m/z* 246 [M⁺] (18.8%), 73 (100%). HRMS Calculated for C₁₅H₂₂NaOSi: *m/z* 269.1338. Found: *m/z* 269.1333.

3-Trimethylsilanylmethyl-pent-3-en-2-one (2f).⁷ This compound was prepared from 390 mg of **4b** (1.39 mmol), according to the general procedure described for **2d** using acetaldehyde. The crude was purified by chromatography on silica gel (hexane/diethyl ether=98/2) to obtain the pure *Z* isomer (70 mg, 0.41 mmol) as a yellowish oil, and a mixture of *E/Z* isomers in the ratio of 1.2/1 (20 mg, 0.12 mmol). (38% total yield). Spectral data of **2f (Z)** IR (CHCl₃): 1680, 1640 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ -0.03 (s, 9H, Si(CH₃)₃), 1.81-1.84 (m, 5H, C=CH(CH₃), CH₂Si), 2.30 (s, 3H, CH₃C=O), 6.62 (q, *J*= 7.3 Hz, 1H, C=CH). ¹³C NMR (CDCl₃, 50 MHz) δ -0.8 ((Si(CH₃)₃), 15.3 (CH₂Si), 15.6 (C=CH(CH₃)), 25.3 (CH₃C=O), 134.3 (C=CH), 141.8 (C=CH), 202.3 (C=O). GC-MS *m/z* 170 [M⁺] (1.3%), 73 (100%).

4-Trimethylsilanylmethyl-hex-3-en-2-one (2g).⁷ This compound was prepared from 580 mg of **4c** (1.42 mmol), according to the general procedure described for **2d**, using acetaldehyde. The crude was purified by chromatography on silica gel (hexane/diethyl ether=98/2) to obtain the pure *Z* isomer (78 mg, 0.42 mmol) as a yellowish oil, and a mixture of *E/Z* in the ratio of 3/1 (14 mg, 0.08 mmol). (35% total yield). Spectral data of **2g (Z)** IR (CHCl₃): 1680, 1640 cm⁻¹. ¹H NMR (CDCl₃, 200

MHz) δ -0.04 (s, 9H, Si(CH₃)₃), 1.09 (t, J = 7.3 Hz, 3H, CH₃CH₂C=O), 1.78-1.82 (m, 5H, C=CH(CH₃), CH₂Si), 2.67 (q, J = 7.3 Hz, 2H, CH₃CH₂C=O), 6.60 (q, J = 6.6 Hz, 1H, C=CH). ¹³C NMR (CDCl₃, 50 MHz) δ -0.9 (Si(CH₃)₃), 9.2 (CH₃CH₂C=O), 15.2 (CH₂Si), 15.8 (C=CH(CH₃)), 30.1 (CH₃CH₂C=O), 132.7 (C=CH), 141.1 (C=CH), 202.0 (C=O). GC-MS m/z 184 [M⁺] (1.8%), 169 (100%).

(S)-4-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-3-trimethylsilanylmethyl-but-3-en-2-one (2h). This compound was prepared from 282 mg of **4b** (1.01 mmol), according to the general procedure described for **2d** using the (R)-2,2-dimethyl-[1,3]dioxolane-4-carbaldehyde (195 mg, 1.51 mmol). The crude was purified by chromatography on silica gel (hexane/diethyl ether=9/1) to obtain a mixture of *Z/E* (114 mg, 0.44 mmol) in the ratio of 10/1 (44% total yield). Spectral data of **2h (Z)**: IR (CHCl₃): 1672, 1633 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ -0.04 (s, 9H, Si(CH₃)₃), 1.40 (s, 3H, CH₃C-O), 1.46 (s, 3H, CH₃C-O), 1.75 (d, J = 13.2 Hz, 1H, CHHSi), 1.91 (d, J = 13.2 Hz, 1H, CHHSi), 2.33 (s, 3H, CH₃C=O), 3.54-3.64 (m, 1H, CHHO), 4.12-4.19 (m, 1H, CHHO), 4.75-4.86 (m, 1H, C=CH-CHO), 6.33 (d, J = 8.0 Hz, 1H, C=CH). ¹³C NMR (CDCl₃, 50 MHz) δ -1.2 (Si(CH₃)₃), 16.7 (CH₂Si), 25.5 (CH₃C=O), 25.7 (CH₃C-O), 26.7 (CH₃C-O), 68.9 (CH₂O), 73.3 (C=CH(CHO)), 109.7 ((CH₃)₂C), 134.7 (C=CH), 143.1 (C=CH), 199.1 (C=O). GC-MS m/z 256 [M⁺] (<0.1 %), 43 (100%). HRMS Calculated for C₁₃H₂₃NaO₃Si: m/z 279.1392. Found: m/z 279.1387.

(S)-4-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-3-trimethylsilanylmethyl-pent-3-en-2-one (2i). This compound was prepared from 650 mg of **4c** (2.21 mmol), according to the general procedure described for **2d** using the (R)-2,2-dimethyl-[1,3]dioxolane-4-carbaldehyde (431 mg, 3.31 mmol). The crude was purified by chromatography on silica gel (hexane/diethyl ether=9/1) to obtain a mixture of *Z/E* (239 mg, 0.88 mmol) in the ratio of 10/1 (40% total yield). Spectral data of **2i (Z)**: IR (CHCl₃): 1674, 1634 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ -0.04 (s, 9H, Si(CH₃)₃), 1.07 (t, J = 7.3 Hz, 3H, CH₃CH₂C=O), 1.39 (s, 3H, CH₃C-O), 1.45 (s, 3H, CH₃C-O), 1.76 (d, J = 13.2 Hz, 1H,

CHHSi), 1.91 (d, $J = 13.2$ Hz, 1H, CHHSi), 2.70 (q, 2H, $J = 7.3$ Hz, 3H, CH₃CH₂C=O), 3.55-3.63 (m, 1H, CHHO), 4.11-4.18 (m, 1H, CHHO), 4.74-4.85 (m, 1H, C=CH-CHO), 6.31 (d, $J = 8.8$ Hz, 1H, C=CH). ¹³C NMR (CDCl₃, 50 MHz) δ -1.2 (Si(CH₃)₃), 8.8 (CH₃CH₂C=O), 17.0 (CH₂Si), 25.7 (CH₃C-O), 26.7 (CH₃C-O), 30.5 (CH₃CH₂C=O), 68.9 (CH₂O), 73.2 (C=CH(CHO)), 109.7 ((CH₃)₂C), 133.2 (C=CH), 142.7 (C=CH), 202.0 (C=O). GC-MS m/z 270 [M^+] (<0.1 %), 73 (100%). HRMS Calculated for C₁₄H₂₆NaO₃Si: m/z 293.1549. Found: m/z 293.1542.

General procedure for the synthesis of α -methylene- β -amino ketone derivatives **3a-i**

(2-Benzoyl-allyl)-carbamic acid ethyl ester (3a). To a stirred solution of the substrate **2a** (151 mg, 0.69 mmol) in CH₂Cl₂ (0.2 mL), NsONHCO₂Et (201 mg, 0.69 mmol) and CaO (39 mg, 0.69 mmol) were added every hour, reaching the molar ratio substrate:NsONHCO₂Et:CaO up to 1:3.5:3.5. Because the reaction was exothermic, during the addition the flask was cooled in a water bath to avoid overheating. After 4 h, pentane was added. The organic phase was filtered, concentrated under vacuum and chromatographed on silica gel (hexane: ethyl acetate 7:3) to obtain the product **3a** as a yellow oil (63 mg, 0.27 mmol, 39% yield). IR (CHCl₃): 3500, 1715 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ 1.23 (t, $J = 7.3$ Hz, 3H, OCH₂CH₃), 4.07-4.17 (m, 4H, OCH₂CH₃, CH₂NH), 5.33 (br, 1H, NH), 5.79 (s, 1H, C=CHH), 6.11 (s, 1H, C=CHH), 7.40-7.75 (m, 5H, CH_{arom.}). ¹³C NMR (CDCl₃, 50 MHz) δ 13.4 (OCH₂CH₃), 41.3 (CH₂NH), 59.7 (OCH₂CH₃), 126.4 (C=CH₂), 127.1 (CH_{arom.}), 128.2 (CH_{arom.}), 131.2 (CH_{arom.}), 136.3 (C_{arom.}), 143.1 (C=CH₂), 155.5 (NHC=O), 196.2 (C=O). GC-MS m/z 233 [M^+] (3.7%), 105 (100%). HRMS Calculated for C₁₃H₁₅NNaO₃: m/z 256.0950. Found: m/z 256.0958.

(2-Methylene-3-oxo-butyl)-carbamic acid ethyl ester (3b). This compound was prepared from 117 mg of **2b** (0.75 mmol), according to the general procedure described for **3a**. The crude was purified by chromatography on silica gel (hexane/ethyl acetate= 7/3) to obtain the product **3b** as a pale yellow oil (39 mg, 0.23 mmol, 31% yield). IR (CHCl₃): 3455, 1713 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ 1.19 (t, $J = 7.3$ Hz, 3H, OCH₂CH₃), 2.32 (s, 3H, CH₃C=O), 3.91 (d, $J = 6.6$ Hz, 2H,

CH₂NH), 4.07 (q, J = 7.3 Hz, 2H, OCH₃CH₂), 5.18 (br, 1H, NH), 6.01 (s, 1H, C=CHH), 6.09 (s, 1H, C=CHH). ¹³C NMR (CDCl₃, 50 MHz) δ 14.5 (OCH₂CH₃), 25.6 (CH₃C=O), 41.4 (CH₂NH), 60.8 (OCH₂CH₃), 126.8 (C=CH₂), 145.2 (C=CH₂), 156.6 (NHC=O), 199.3 (CH₃C=O). GC-MS m/z 171 [M⁺] (4.2%), 43 (100%). HRMS Calculated for C₈H₁₃NNaO₃: m/z 194.0793. Found: m/z 194.0803.

(2-Methylene-3-oxo-pentyl)-carbamic acid ethyl ester (3c). This compound was prepared from 112 mg of **2c** (0.66 mmol), according to the general procedure described for **3a**. The crude was purified by chromatography on silica gel (hexane/ethyl acetate= 7/3) to obtain the product **3c** as a pale yellow oil (42 mg, 0.22 mmol, 34% yield). IR (CHCl₃): 3437, 1711 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ 1.10 (t, J = 7.3 Hz, 3H, CH₃CH₂C=O), 1.23 (t, J = 7.3 Hz, 3H, OCH₂CH₃), 2.73 (q, J = 7.3 Hz, 2H, CH₃CH₂C=O), 3.96 (d, J = 6.6 Hz, 2H, CH₂NH), 4.10 (q, J = 7.3 Hz, 2H, OCH₂CH₃), 5.11 (br, 1H, NH), 6.00 (s, 1H, C=CHH), 6.11 (s, 1H, C=CHH). ¹³C NMR (CDCl₃, 50 MHz) δ 8.1 (CH₃CH₂C=O), 14.6 (OCH₂CH₃), 30.8 (CH₃CH₂C=O), 41.9 (CHNH), 60.8 (OCH₂CH₃), 125.5 (C=CH₂), 144.6 (C=CH₂), 156.6 (NHC=O), 199.6 (C=O). GC-MS m/z 185 [M⁺] (3.5%), 110 (100%). HRMS Calculated for C₉H₁₅NNaO₃: m/z 208.0950. Found: m/z 208.0959.

(2-Methylene-3-oxo-1-phenyl-butyl)-carbamic acid ethyl ester (3d). This compound was prepared from 90 mg of **2d (Z isomer)** (0.39 mmol), according to the general procedure described for **3a**, reaching the molar ratio substrate: NsONHCO₂Et: CaO up to 1:6:6. The crude was purified by chromatography on silica gel (hexane/ethyl acetate= 7/3) to obtain the product **3d** as a pale yellow oil (40 mg, 0.16 mmol, 41% yield). IR (CHCl₃): 3400, 1714 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ 1.26 (t, J = 7.3 Hz, 3H, OCH₂CH₃), 2.33 (s, 3H, CH₃C=O), 4.14 (q, J = 7.3 Hz, 2H, OCH₂CH₃), 5.71 (br, 2H, NH, CHNH), 6.16 (s, 1H, C=CHH), 6.25 (s, 1H, C=CHH), 7.22-7.38 (m, 5H, CH_{arom.}). ¹³C NMR (CDCl₃, 50 MHz) δ 14.5 (OCH₂CH₃), 26.5 (CH₃C=O), 56.6 (CHNH), 61.0 (OCH₂CH₃), 124.2 (C=CH₂), 126.4 (CH_{arom.}), 127.4 (C_{arom.}), 128.5 (CH_{arom.}), 131.0 (CH_{arom.}), 140.0

(C=CH₂), 155.8 (NHC=O), 201.5 (C=O). GC-MS m/z 247 [M⁺] (2.8%), 174 (100%). HRMS Calculated for C₁₄H₁₇NNaO₃: m/z 270.1106. Found: m/z 270.1101.

(2-Methylene-3-oxo-1-phenyl-butyl)-carbamic acid ethyl ester (3e). This compound was prepared from 95 mg of **2e (Z isomer)** (0.39 mmol), according to the general procedure described for **3a**, reaching the molar ratio substrate: NsONHCO₂Et: CaO up to 1:6:6. The crude was purified by chromatography on silica gel (hexane/ethyl acetate= 7/3) to obtain the product **3e** as a pale yellow oil (31 mg, 0.12 mmol, 30% yield). IR (CHCl₃): 3439, 1713 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ 1.03 (t, J = 7.3 Hz, 3H, CH₃CH₂C=O), 1.26 (t, J = 7.3 Hz, 3H, OCH₂CH₃), 2.70 (q, J = 7.3 Hz, 2H, CH₃CH₂C=O), 4.14 (q, J = 7.3 Hz, 2H, OCH₂CH₃), 5.72 (m, 2H, NH, CHNH), 6.10 (s, 1H, C=CHH), 6.23 (s, 1H, C=CHH), 7.19-7.34 (m, 5H, CH_{arom.}). ¹³C NMR (CDCl₃, 50 MHz) δ 7.9 (CH₃CH₂C=O), 14.5 (OCH₂CH₃), 31.6 (CH₃CH₂C=O), 56.9 (CHNH), 61.0 (OCH₂CH₃), 124.0 (C=CH₂), 126.3 (CH_{arom.}), 127.3 (C_{arom.}), 128.5 (CH_{arom.}), 130.9 (CH_{arom.}), 140.1 (C=CH₂), 155.8 (NHC=O), 201.6 (C=O). GC-MS m/z 261 [M⁺] (2.9%), 188 (100%). HRMS Calculated for C₁₅H₁₉NNaO₃: m/z 284.1263. Found: m/z 284.1270.

(1-Methyl-2-methylene-3-oxo-butyl)-carbamic acid ethyl ester (3f). This compound was prepared from 60 mg of **2f (Z isomer)** (0.35 mmol), according to the general procedure described for **3a**, reaching the molar ratio substrate: NsONHCO₂Et: CaO up to 1:4:4. The crude was purified by chromatography on silica gel (hexane/ethyl acetate= 7/3) to obtain the product **3f** as a pale yellow oil (22 mg, 0.12 mmol, 34% yield). IR (CHCl₃): 3436, 1707 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ 1.22 (t, J = 7.3 Hz, 3H, OCH₂CH₃), 1.30 (d, J = 6.6 Hz, 3H, CHCH₃), 2.34 (s, 3H, CH₃C=O), 4.08 (q, J = 7.3 Hz, 2H, OCH₂CH₃), 4.49-4.64 (m, 1H, NHCH), 5.32 (br, 1H, NH), 5.95 (s, 1H, C=CHH), 6.03 (s, 1H, C=CHH). ¹³C NMR (CDCl₃, 50 MHz) δ 14.6 (OCH₂CH₃), 21.2 (CHCH₃), 26.5 (CH₃C=O), 49.2 (CHNH), 60.8 (OCH₂CH₃), 124.3 (C=CH₂), 144.7 (C=CH₂), 155.8 (NHC=O), 202.0 (C=O). GC-MS m/z 185 [M⁺] (2.2%), 112 (100%). HRMS Calculated for C₉H₁₅NNaO₃: m/z 208.0950. Found: m/z 208.0959.

(1-Methyl-2-methylene-3-oxo-pentyl)-carbamic acid ethyl ester (3g). This compound was prepared from 60 mg of **2g (Z isomer)** (0.33 mmol), according to the general procedure described for **3a**, reaching the molar ratio substrate: $\text{NsONHCO}_2\text{Et}$: CaO up to 1:4:4. The crude was purified by chromatography on silica gel (hexane/ethyl acetate= 7/3) to obtain the product **3g** as a pale yellow oil (30 mg, 0.15 mmol, 44% yield). IR (CHCl_3): 3436, 1705 cm^{-1} . ^1H NMR (CDCl_3 , 200 MHz) δ 1.08 (t, $J = 7.3$ Hz, 3H, $\text{CH}_3\text{CH}_2\text{C}=\text{O}$), 1.21 (t, $J = 7.3$ Hz, 3H, OCH_2CH_3), 1.30 (d, $J = 7.3$ Hz, 3H, CHCH_3), 2.70 (q, $J = 7.3$ Hz, 2H, $\text{CH}_3\text{CH}_2\text{C}=\text{O}$), 4.08 (q, $J = 7.3$ Hz, 2H, OCH_2CH_3), 4.49-4.64 (m, 1H, NHCH), 5.35 (br, 1H, NH), 5.90 (s, 1H, $\text{C}=\text{CHH}$), 6.01 (s, 1H, $\text{C}=\text{CHH}$). ^{13}C NMR (CDCl_3 , 50 MHz) δ 8.1 ($\text{CH}_3\text{CH}_2\text{C}=\text{O}$), 14.6 (OCH_2CH_3), 21.2 (CHCH_3), 31.6 ($\text{CH}_3\text{CH}_2\text{C}=\text{O}$), 49.5 (CHNH), 60.7 (OCH_2CH_3), 124.2 ($\text{C}=\text{CH}_2$), 144.3 ($\text{C}=\text{CH}_2$), 155.7 ($\text{NHC}=\text{O}$), 202.1 ($\text{C}=\text{O}$). GC-MS m/z 199 [M^+] (2.3%), 126 (100%). HRMS Calculated for $\text{C}_{10}\text{H}_{17}\text{NNaO}_3$: m/z 222.1106. Found: m/z 222.1101.

(3R,4S)-[1-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-2-methylene-3-oxo-butyl]-carbamic acid ethyl ester (3h). This compound was prepared from 104 mg of **2h (mixture Z/E= 10/1)** (0.41 mmol), according to the general procedure described for **3a**, reaching the molar ratio substrate: $\text{NsONHCO}_2\text{Et}$: CaO up to 1:5.5:5.5. The crude was purified by chromatography on silica gel (hexane/ethyl acetate= 7/3) to obtain the product **3h** as a pale yellow oil (68 mg, 0.25 mmol, 60% yield). Spectral data of the main diastereomer: IR (CHCl_3): 3433, 1715 cm^{-1} . ^1H NMR (CDCl_3 , 200 MHz) δ 1.19 (t, $J = 7.3$ Hz, 3H, OCH_2CH_3), 1.27 (s, 3H, $\text{CH}_3\text{-C}$), 1.38 (s, 3H, $\text{CH}_3\text{-C}$), 2.34 (s, 3H, $\text{CH}_3\text{C}=\text{O}$), 3.79 (dd, $J = 5.1$ Hz, $J = 8.8$ Hz, 1H, CHHO) 3.95-4.13 (m, 3H, OCH_2CH_3 , CHHO), 4.17-4.45 (m, 2H, CHCHO , NHCH), 5.61 (br, 1H, NH), 6.03 (s, 1H, $\text{C}=\text{CHH}$), 6.18 (s, 1H, $\text{C}=\text{CHH}$). ^{13}C NMR (CDCl_3 , 50 MHz) δ 14.4 (OCH_2CH_3), 25.1 ($\text{CH}_3\text{-C}$), 26.3 ($\text{CH}_3\text{C}=\text{O}$), 26.7 ($\text{CH}_3\text{-C}$), 56.8 (NHCH), 61.0 (OCH_2CH_3), 67.1 (CH_2O), 75.9 (CHO), 109.8 ($\text{C}(\text{CH}_3)_2$), 129.8 ($\text{C}=\text{CH}_2$), 144.9 ($\text{C}=\text{CH}_2$), 156.0 ($\text{NHC}=\text{O}$), 200.1 ($\text{C}=\text{O}$). $[\alpha]_D^{20} = +10.7$ (c 3, CHCl_3). GC-MS m/z

271 [M^+] (< 0.01%), 101 (100%). HRMS Calculated for $C_{13}H_{21}NNaO_5$: m/z 294.1317. Found: m/z 294.1310.

(3R,4S)-[1-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-2-methylene-3-oxo-pentyl]-carbamic acid ethyl ester (3i). This compound was prepared from 130 mg of **2i** (mixture *Z/E*= 10/1) (0.48 mmol), according to the general procedure described for **3a**, reaching the molar ratio substrate: $NaONHCO_2Et$: CaO up to 1:5.5:5.5. The crude was purified by chromatography on silica gel (hexane/ethyl acetate= 7/3) to obtain the product **3i** as a pale yellow oil (63 mg, 0.22 mmol, 44% yield). Spectral data of the main diastereomer: IR ($CHCl_3$): 3431, 1714 cm^{-1} . 1H NMR ($CDCl_3$, 200 MHz) δ 1.08 (t, J = 7.3 Hz, 3H, $CH_3CH_2C=O$), 1.21 (t, J = 7.3 Hz, 3H, OCH_2CH_3), 1.28 (s, 3H, CH_3-C), 1.39 (s, 3H, CH_3-C), 2.74 (q, J = 7.3 Hz, 2H, $CH_3CH_2C=O$), 3.81 (dd, J = 5.1 Hz, J = 8.8 Hz, 1H, $CHHO$) 3.96-4.15 (m, 3H, OCH_2CH_3 , $CHHO$), 4.21-4.46 (m, 2H, $CHCHO$, $NHCH$), 5.64 (br, 1H, NH), 5.99 (s, 1H, $C=CHH$), 6.18 (s, 1H, $C=CHH$). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 7.9 ($CH_3CH_2C=O$), 14.5 (OCH_2CH_3), 25.2 (CH_3-C), 26.7 (CH_3-C), 31.3 ($CH_3CH_2C=O$), 57.1 ($NHCH$), 61.0 (OCH_2CH_3), 67.2 (CH_2O), 76.0 (CHO), 109.8 ($C(CH_3)_2$), 128.3 ($C=CH_2$), 144.4 ($C=CH_2$), 156.0 ($NHC=O$), 202.8 ($C=O$). $[\alpha]_D^{20}$ = +7.1 (c 3.6, $CHCl_3$). GC-MS m/z 285 [M^+] (< 0.01%), 101 (100%). HRMS Calculated for $C_{14}H_{23}NNaO_5$: m/z 308.1474. Found: m/z 308.1471.

4a

4b

4c

2b

2c

2d

2e

2f

2g

2h (Z/E= 10/1)

2i (Z/E= 10/1)

3a

S25

3b

3c

3d

3e

3f

3g

3h

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