Supplementary Material (ESI) for Chemical Communications

Electronic Supplementary Information (ESI)

Synthesis of 1,3-dioxo-hexahydro[1,2-c][1,3]diazepine carboxylates, a new bicyclic skeleton formed by ringexpansion-RCM methodology

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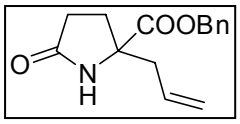
General experimental information:

High resolution ^{1}H-NMR (270 MHz) and ^{13}C-NMR (68 MHz) spectra were run with a Jeol JNM-EX 270 NMR spectrometer or on a Jeol JNM-EX 300 NMR. Peak assignments were obtained with the aid of DEPT, 2D-HETCOR, 2D-COSY spectra. The compounds were diluted in deuterated solvents and the used solvent is indicated for each compound. Mass spectra were recorded on an Agilent 1100 Series VS (ES, 4000V) mass spectrometer. IR-spectra were obtained from a Perkin Elmer Spectrum One infrared spectrometer. For liquid samples the spectra were collected by preparing a thin film of compound between two sodium chloride plates. The crystalline compounds were mixed with potassium bromide and pressed until a transparent potassium bromide plate was obtained. Melting points of crystalline compounds were measured with a Büchi 540 apparatus and are uncorrected. The purification of reaction mixtures was performed by flash chromatography using a glass column with silica gel (Across, particle size 0.035-0.070 mm, Pore diameter ca. 6 nm).

Typical experimental procedure for the alkylation of pyroglutamates at the 2-position:

The pyroglutamate ester (12 mmol) was dissolved in THF (15 mL, freshly distilled from Na metal) and the alkylhalide (48 mmol) was added. The mixture is cooled to -40°C under N_2-atmosphere. Over a period of 30-40 minutes, LiHMDS (25.2 mmol, solution in hexanes) is added at this temperature. The reaction was allowed to stir at room temperature for an additional 2h. The reaction was quenched by addition of saturated aqueous NH_4Cl until the pH was neutral. The mixture was extracted with EtOAc, and the organics were dried ($MgSO_4$) and filtered. The solvent was removed in vacuo.

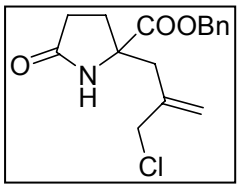
Benzyl 2-allyl-5-oxopyrrolidine-2-carboxylate



^{1}H-NMR (270MHz, $CDCl_3$) δ: 2,09-2,16 (1H, m, $COCH_2C\underline{H}_AH_B$), 2,33-2,47 (4H, m, $COC\underline{H}_2CH_A\underline{H}_B$ + $CC\underline{H}_AH_B$), 2,66 (1H, dd, J = 6,4 Hz, J = 13,7 Hz, $CCH_A\underline{H}_B$), 5,09-5,16 (2H, m, $CH=C\underline{H}_2$), 5,17 (2H, s, $C\underline{H}_2Ph$), 5,61 (1H, dddd, J = 6,6 Hz, J = 8,3 Hz, J = 10,4 Hz, J = 16,7 Hz, $C\underline{H}=CH_2$), 7,33-7,37 (5H, m, Ph). **^{13}C-NMR (68MHz, $CDCl_3$) δ:** 29,72 ($COCH_2\underline{C}H_2$), 30,17

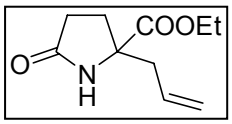
($CO\underline{C}H_2$), 43,45 ($C\underline{C}H_2$), 65,28 (C_q), 67,53 ($\underline{C}H_2Ph$), 120,81 ($CH=\underline{C}H_2$), 128,41 (CH_{ar}), 128,71 (CH_{ar}), 130,78 ($\underline{C}H=CH_2$), 135,09 ($C_{q,ar}$), 172,85 (NHC=O), 176,91 (C=OO). **MS: m/z (%):** 260 ($M+H^+$, 100). **IR (cm^{-1})** ν_{max} : 1703 (C=O), 1736 (C=O). **Chromatography:** Hex/EtOAc (25/75) R_f= 0,31. **Yield:** 83%.

Benzyl 5-oxo-2-(2-chloromethylprop-2-enyl]pyrrolidine-2-carboxylate



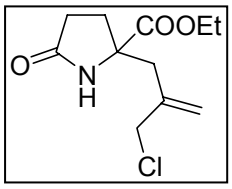
^{1}H-NMR (270MHz, $CDCl_3$) δ: 2,17–2,24 (1H, m, $COCH_2C\underline{H}_AH_B$), 2,37-2,50 (3H, m, $COC\underline{H}_2CH_A\underline{H}_B$), 2,57 (1H, d, *J* =14,5 Hz, $CC\underline{H}_AH_B$), 2,96 (1H, d, *J* =14,5 Hz, $CCH_A\underline{H}_B$), 3,96 (2H, s, CH_2Cl), 5,02 (1H, s, $C=C\underline{H}_AH_B$), 5,20 (1H, d, *J* =12,0 Hz, $C\underline{H}_AH_BPh$), 5,23 (1H, d, *J* =12,0 Hz, $CH_A\underline{H}_BPh$), 5,30 (1H, s, $C=CH_A\underline{H}_B$), 7,40 (5H, s, Ph). **^{13}C-NMR (68MHz, $CDCl_3$) δ:** 29,61 ($COCH_2\underline{C}H_2$), 31,25 ($CO\underline{C}H_2$), 41,71 ($C\underline{C}H_2$), 48,37 ($\underline{C}H_2Cl$), 65,14 (C_q), 67,65 ($\underline{C}H_2Ph$), 120,09 ($C=\underline{C}H_2$), 128,52 (CH_{ar}), 128,68 (CH_{ar}), 134,89 ($C_{q,ar}$), 139,67 ($\underline{C}=CH_2$), 172,97 (NHC=O), 177,18 (C=OO). **MS: m/z (%):** 308 ($M+H^+$,100), 257 (7), 91 (Bn^+,7). **IR (cm^{-1})** ν_{max} : 1701 (C=O), 1735 (C=O). **Chromatography:** Hex/EtOAc (25/75) R_f= 0,45. **Mp** : 47,3-50,3°C. **Yield:** 40%.

Ethyl 2-allyl-5-oxopyrrolidine-2-carboxylate



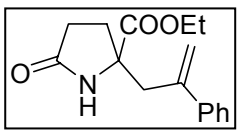
^{1}H-NMR (270MHz, $CDCl_3$) δ: 1,29 (3H, t, *J* = 7,1 Hz, $CH_2C\underline{H}_3$), 2,07-2,17 (1H, m, $COCH_2C\underline{H}_AH_B$), 2,35-2,51 (4H, m, $COC\underline{H}_2CH_A\underline{H}_B$ + $CC\underline{H}_AH_B$), 2,63-2.71 (1H, m, $CCH_A\underline{H}_B$), 4,22 (2H, q, *J* = 7,1 Hz, $C\underline{H}_2CH_3$), 5,14-5,21 (2H, m, $CH=C\underline{H}_2$), 5,69 (1H, dddd, *J* = 6,5 Hz, *J* = 7,9 Hz, *J* = 10,9 Hz, *J* = 16,2 Hz, $C\underline{H}=CH_2$), 6,35 (1H, br. s, NH). **^{13}C-NMR (68MHz, $CDCl_3$) δ:** 14,20 ($CH_2\underline{C}H_3$), 29,88 ($COCH_2\underline{C}H_2$), 30,04 ($CO\underline{C}H_2$), 43,38 ($\underline{C}H_2CH=CH_2$), 61,72 ($\underline{C}H_2CH_3$), 65,35 (C_q), 120,41 ($CH=\underline{C}H_2$), 131,19 ($\underline{C}H=CH_2$), 173,19 (NHC=O), 177,25 (C=OO). **MS: m/z (%):** 198 ($M+H^+$, 100). **IR (cm^{-1})** ν_{max} : 1711 (br. C=O). **Yield:** 72%.

Ethyl 5-oxo-2-(2-chloromethylprop-2-enyl]pyrrolidine-2-carboxylate



^{1}H-NMR (270MHz, $CDCl_3$) δ: 1,31 (3H, t, *J* = 7,1 Hz, $CH_2C\underline{H}_3$), 2,12-2,22 (1H, m, $COCH_2C\underline{H}_AH_B$), 2,37-2,54 (3H, m, $COC\underline{H}_2CH_A\underline{H}_B$), 2,54 (1H, d, *J* =14,5 Hz, $CC\underline{H}_AH_B$), 2,94 (1H, d, *J* =14,5 Hz, $CCH_A\underline{H}_B$), 4,00 (2H, s, $C\underline{H}_2Cl$), 4,22 (2H, q, *J* =7,1 Hz, $C\underline{H}_2CH_3$), 5,06 (1H, s, $C=C\underline{H}_AH_B$), 5,33 (1H, s, $C=CH_A\underline{H}_B$), 6,41 (1H, br. s, NH). **^{13}C-NMR (68MHz, $CDCl_3$) δ:** 14,11 ($CH_2\underline{C}H_3$), 29,69 ($COCH_2\underline{C}H_2$), 31,23 ($CO\underline{C}H_2$), 41,74 ($C\underline{C}H_2$), 48,41 ($\underline{C}H_2Cl$), 61,99 ($\underline{C}H_2CH_3$), 65,07 (C_q), 120,03 ($C=\underline{C}H_2$), 139,91 ($\underline{C}=CH_2$), 173,19 (NHC=O), 177,21 (C=OO). **MS: m/z (%)**: 246 ($M+H^+$, 100). **IR (cm^{-1})** ν_{max}: 1707 (C=O), 1741 (C=O). **Mp**: 55,4-56,6°C. **Yield:** 62%.

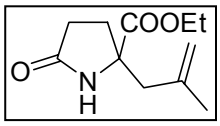
Ethyl 5-oxo-2-(2-phenylprop-2-enyl]pyrrolidine-2-carboxylate



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.12 (3H, t, *J* = 7.2 Hz, CH_3), 2.05-2.17 (1H, m, $COC\underline{H}_AH_B$), 2.23-2.36 (2H, m, $COCH_2C\underline{H}_2$), 2.23-2.49 (1H, m, $COCH_A\underline{H}_B$), 2.86 (1H, d, *J* = 13.6 Hz, $CC\underline{H}_AH_BC$), 3.21 (1H, d, *J* = 12.1 Hz, $CCH_A\underline{H}_BC$), 3.75 (1H, q, *J* = 7.2 Hz, $C\underline{H}_AH_BCH_3$), 3.76 (1H, q, *J* = 7.2 Hz, $CH_A\underline{H}_BCH_3$), 5.15 (1H, s; $C=C\underline{H}_AH_B$), 5.33 (1H, d; *J* = 1.4 Hz, $C=CH_A\underline{H}_B$), 5.98 (1H, br s, NH), 7.29-7.35 (5H, m, Ph). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 13.97 (CH_3), 29.60

($COCH_2\underline{C}H_2$), 31.49 ($CO\underline{C}H_2$), 45.05 ($C\underline{C}H_2C$), 61.69 ($\underline{C}H_2CH_3$), 65.46 (C_q), 118.52 ($C=\underline{C}H_2$), 126.69 (CH_{ar}), 128.15 (CH_{ar}), 128.55 (CH_{ar}), 140.54 ($\underline{C}=CH_2$), 143.68 ($C_{q,ar}$), 172.87 (HNC=O), 176.42 (C=OO). **IR (cm^{-1}) ν_{max}:** 1728 (C=O), 1744 (C=O), 3203 (br NH). **MS: m/z (%):** 274.3 ($M+H^+$, 100). **Mp** : 73,4-74,4°C. **Chromatography:** Hex/EtOAc (4/6) R_f = 0.21. **Yield:** 70%.

Ethyl 2-(2-methylprop-2-enyl)-5-oxopyrrolidine-2-carboxylate

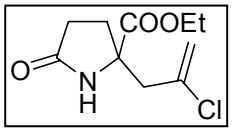


^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.30 (3H, t, *J* = 7.2 Hz, CH_3), 1.72 (3H, s, CH_3), 2.09-2.19 (1H, m, $COCH_A\underline{H_B}$), 2.35-2.52 (3H, m, $COCH\underline{A}H_BC\underline{H_2}$), 2.37 (1H, dd, *J* = 2.6 Hz, *J* = 13.7 Hz, $CC\underline{H_A}H_BC$), 2.69 (1H, d, *J* = 13.7 Hz, $CC\underline{H_A}H_BC$), 4.21 (2H, q, *J* = 7.2 Hz, $C\underline{H_A}H_BCH_3$), 4.76 (1H, s, $C=C\underline{H_A}H_B$), 4.92 (1H, s, $C=CH_A\underline{H_B}$), 6.27 (1H, br s, NH). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.19 ($CH_2\underline{C}H_3$), 23.57 (CH_3), 29.69 ($COCH_2\underline{C}H_2$), 31.66 ($CO\underline{C}H_2$), 47.11 ($C\underline{C}H_2C$), 61.88 ($\underline{C}H_2CH_3$), 65.02 (C_q), 116.11 ($C=\underline{C}H_2$), 139.96 ($CH_3\underline{C}=CH_2$), 173.52 (HNC=O), 176.72 (C=OO). **IR (cm^{-1}) ν_{max}:** 1647 (C=C), 1706 (C=O), 1735 (C=O), 3220 (br NH). **MS: m/z (%):** 212.8 ($M+H^+$, 100). **Yield:** 84%.

Typical experimental procedure for the alkylation of pyroglutamates at the 2-position with base sensitive elektrophiles:

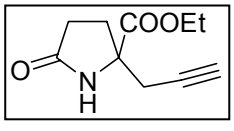
The pyroglutamate ester (12 mmol) was dissolved into THF (15 mL, freshly distilled from Na metal) and the solution is cooled to -40°C under a N_2-atmosphere. LiHMDS (25.2 mmol, solution in hexanes) is added at this temperature and the mixture is stirred for 20 minutes followed by addition of the alkylhalide (48 mmol, dissolved in 5 ml dry THF). The reaction was allowed to stir at room temperature for an additional 2h. The reaction was quenched by addition of saturated aqueous NH_4Cl until the pH was neutral. The mixture was extracted with EtOAc, and the organics were dried ($MgSO_4$) and filtered. The solvent was removed in vacuo, and the residue was purified by flash chromatography (silica gel; hexane/EtOAc).

Ethyl 2-(2-chloroprop-2-enyl)-5-oxopyrrolidine-2-carboxylate



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.30 (3H, t, *J* = 7.2 Hz, CH_3), 2.13-2.23 (1H, m, $COCH_A\underline{H_B}$), 2.36-2.43 (2H, m, $COCH_2C\underline{H_2}$), 2.46-2.56 (1H, m, $COCH_A\underline{H_B}$), 2.71 (1H, d, *J* = 14.3 Hz, $CC\underline{H_A}H_BC$), 3.05 (1H, d, *J* = 14.3 Hz, $CCH_A\underline{H_B}C$), 4.22 (1H, q, *J* = 7.2 Hz, $C\underline{H_A}H_BCH_3$), 4.23 (1H, q, *J* = 7.2 Hz, $CH_A\underline{H_B}CH_3$), 5.25 (1H, t; *J* = 0.7 Hz, $C=C\underline{H_A}H_B$), 5.35 (1H, d; *J* = 1.4 Hz, $C=CH_A\underline{H_B}$), 6.29 (1H, br s, NH). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.18 (CH_3), 29.31 ($COCH_2\underline{C}H_2$), 31.58 ($CO\underline{C}H_2$), 48.13 ($C\underline{C}H_2C$), 62.23 ($\underline{C}H_2CH_3$), 64.72 (C_q), 117.85 ($C=\underline{C}H_2$), 136.20 ($\underline{C}Cl=CH_2$), 172.51 (HNC=O), 176.52 (C=OO). **IR (cm^{-1}) ν_{max}:** 1636 (.C=C), 1715 (C=O), 1741 (C=O), 3195 (br NH). **MS: m/z (%):** 232.7, 234.7 ($M+H^+$, 100). **Mp** : 90,3°C. **Yield:** 46%.

Ethyl 5-oxo-2-prop-2-ynylpyrrolidine-2-carboxylate

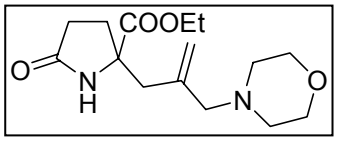


^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.31 (3H, t, *J* = 7.2 Hz, CH_3), 2.08 (1H, t, *J* = 2.2 Hz, CH), 2.12-2.52 (4H, m, $COCH_2\underline{C}H_2$), 2.61 (1H, dd, *J* = 14.3

Hz, *J* = 2.2 Hz, CC$\underline{H}_A H_B$C), 2.82 (1H, dd, *J* = 14.3 Hz, *J* = 2.2 Hz, CC$H_A\underline{H}_B$C), 4.25 (2H, q, *J* = 7.2 Hz, C$\underline{H}_2CH_3$), 5.25 (1H, t; *J* = 0.7 Hz, C=C$\underline{H}_A H_B$), 7.01 (1H, br s, NH). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.13 (CH_3), 29.09 ($COCH_2\underline{C}H_2$), 29.79 ($C\underline{C}H_2C$ + $CO\underline{C}H_2$), 62.15 ($\underline{C}H_2CH_3$), 64.67 (C_q), 72.11 (CH), 78.21 (C), 172.33 (HNC=O), 177.36 (C=OO). **IR (cm^{-1}) ν_{max}:** 1705 (br C=O), 2120 (alkyne), 3283 (br NH). **MS: m/z (%):** 391.7, ($2M+H^+$, 100). **Chromatography:** Hex/EtOAc (2/8) Rf = 0.3. **Yield:** 20%.

Ethyl 2-[2-(morpholin-4-ylmethyl)prop-2-enyl]-5-oxopyrrolidine-2-carboxylate

Ethyl 5-oxo-2-(2-chloromethylprop-2-enyl]pyrrolidine-2-carboxylate (4mmol) was dissolved into THF (20 mL, freshly distilled from Na metal). Morpholine (10 mmol) is added and the mixture is refluxed untill TLC analysis showed that all starting material was consumed. saturated The mixture was cooled and aqueous $NaHCO_3$ (15mL) was added. The mixture was extracted with EtOAc, and the organics were dried ($MgSO_4$) and filtered. The solvent was removed in vacuo, and the residue was purified by flash chromatography.

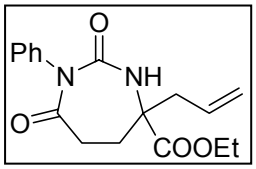


^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.27 (3H, t, *J* = 7.2 Hz, CH_3), 1.98-2.08 (1H, m, COC$\underline{H}_A H_B$), 2.23 (1H, d, *J* = 13.5 Hz, CC$\underline{H}_A H_B$C), 2.31-2.56 (7H, m, COC$H_A\underline{H}_B C\underline{H}_2$ + $C\underline{H}_2NC\underline{H}_2$), 2.75 (1H, d, *J* = 12.1 Hz, NC$\underline{H}_A H_B$C), 2.94 (1H, d, *J* = 12.1 Hz, NC$H_A\underline{H}_B$C), 2.98 (1H, d, *J* = 13.5 Hz, CC$H_A\underline{H}_B$C), 3.68-3.87 (4H, m, $C\underline{H}_2OC\underline{H}_2$), 4.16 (2H, q, *J* = 7.2 Hz, C$\underline{H}_2CH_3$), 5.01 (1H, s; C=C$\underline{H}_A H_B$), 5.07 (1H, s; C=C$H_A\underline{H}_B$), 9.19 (1H, br s, NH). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.35 (CH_3), 30.26 ($COCH_2\underline{C}H_2$), 32.76 ($CO\underline{C}H_2$), 47.54 ($C\underline{C}H_2C$), 53.31 ($\underline{C}H_2N\underline{C}H_2$), 61.49 ($\underline{C}H_2CH_3$), 65.37 ($C\underline{C}H_2N$), 65.94 ($C_q$), 66.73 ($\underline{C}H_2O\underline{C}H_2$), 122.43 (C=$\underline{C}H_2$), 139.22 ($\underline{C}$=$CH_2$), 173.71 (HNC=O), 176.77 (C=OO). **IR (cm^{-1}) ν_{max}:** 1705 (C=O), 1734 (C=O), 3270 (br NH). **MS: m/z (%):** 297.8 ($M+H^+$, 100). **Chromatography:** first 100% EtOAc untill R_f = 0.27 then strip with CH_2Cl_2 + 5% MeOH. **Yield:** 78%.

Typical experimental procedure for the ring-expansion of pyroglutamates functionalized at the 2-position:

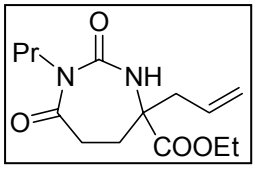
The functionalized pyroglutamate ester (5 mmol) was dissolved into THF (40 mL, freshly distilled from Na metal) and the isocyanate (5.5 mmol) was added followed by NaH (5.5 mmol, washed with hexanes). The reaction was allowed to stir at room temperature for 16h. The reaction was quenched by addition of saturated aqueous NH_4Cl until the pH was neutral. The mixture was extracted with EtOAc, and the organics were dried ($MgSO_4$) and filtered. The solvent was removed in vacuo, and the residue was purified by flash chromatography (silica gel; hexane/EtOAc).

Ethyl 4-allyl-2,7-dioxo-1-phenyl-1,3-diazepane-4-carboxylate



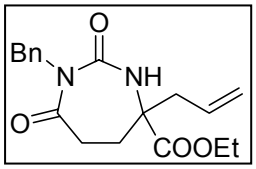
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.25 (3H, t, *J* = 7.1 Hz, CH_3), 2.12-2.30 (2H, m, $COCH_2C\underline{H}_2$), 2.37-2.41 (2H, m, $COC\underline{H}_2CH_2$), 2.51 (1H, dd, *J* = 13.8 Hz; *J* = 7.2 Hz, $C\underline{H}_AH_BCH$), 2.62 (1H, dd, *J* = 13.8 Hz; *J* = 7.7 Hz, $CH_A\underline{H}_BCH$), 4.15 (2H, q, *J* = 7.1 Hz, $C\underline{H}_2CH_3$), 5.23 (1H, s; $HC=C\underline{H}_AH_B$), 5.27 (1H, d, *J* = 1,9 Hz, $HC=CH_AC\underline{H}_B$), 5.70-5.84 (1H, m, $H\underline{C}=CH_2$), 6.09 (1H, br s, NH), 7.32-7.50 (5H, m, Ph). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.24 (CH_3), 28.90 ($CO\underline{C}H_2$), 31.29 ($COCH_2\underline{C}H_2$), 41.75 ($C\underline{C}H_2$), 61.17 ($\underline{C}H_2CH_3$), 64.49 (C_q), 121.73 ($HC=\underline{C}H_2$), 126.32 ($CH_{arom.}$), 128.51 ($CH_{arom.}$), 129.24 ($CH_{arom.}$), 129.86 ($H\underline{C}=CH_2$), 131.44 ($C_{q\ arom.}$). 155.76 (NC=ON), 172.84 (HNC=O), 174.23 (C=OO). **IR (cm^{-1}) ν_{max}:** 1719 (C=O), 1781 (C=O). **MS: m/z (%):** 317.3 ($M+H^+$, 100). **Chromatography:** Hex/EtOAc (1/1) R_f = 0.33. **Yield:** 70%.

Ethyl 4-allyl-2,7-dioxo-1-propyl-1,3-diazepane-4-carboxylate



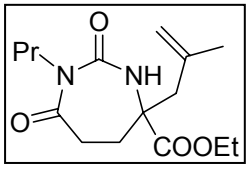
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.92 (3H, t, *J* = 7.4 Hz, $CH_2CH_2C\underline{H}_3$), 1.25 (3H, t, *J* = 7.2 Hz, CH_3), 1.63 (2H, sextet, *J* = 7.4 Hz $CH_2C\underline{H}_2CH_3$), 2.03-2.29 (4H, m, $COC\underline{H}_2C\underline{H}_2$), 2.43 (1H, dd, *J* = 14.0 Hz; *J* = 7.4 Hz, $C\underline{H}_AH_BCH$), 2.50 (1H, dd, *J* = 14.0 Hz; *J* = 7.6 Hz, $CH_A\underline{H}_BCH$), 3.44 (2H, t, *J* = 7.4 Hz, $C\underline{H}_2CH_2CH_3$), 4.13 (2H, q, *J* = 7.2 Hz, $C\underline{H}_2CH_3$), 5.16 (1H, s; $HC=C\underline{H}_AH_B$), 5.20 (1H, d; *J* = 3.3 Hz, $HC=CH_A\underline{H}_B$), 5.59-5.73 (1H, m, $H\underline{C}=CH_2$), 5.88 (1H, br s, NH). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 11.23 ($CH_2CH_2\underline{C}H_3$), 14.21 (CH_3), 21.52 ($CH_2\underline{C}H_2CH_3$), 28.74 ($CO\underline{C}H_2$), 31.05 ($COCH_2\underline{C}H_2$), 40.36 ($\underline{C}H_2CH_2CH_3$), 41.57 (CCH_2), 61.04 ($\underline{C}H_2CH_3$), 64.38 (C_q), 121.34 ($HC=\underline{C}H_2$), 130.02 ($H\underline{C}=CH_2$), 156.97 (NC=ON), 172.86 (HNC=O), 175.29 (C=OO). **IR (cm^{-1}) ν_{max}:** 1642 (C=C), 1713 (br C=O), 1775 (C=O). **MS: m/z (%):** 383.3 ($M+H^+$, 100). **Chromatography:** Hex/EtOAc (1/1) R_f = 0.42. **Yield:** 61%.

Ethyl 4-allyl-2,7-dioxo-1-benzyl-1,3-diazepane-4-carboxylate



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.22 (3H, t, *J* = 7.1 Hz, CH_3), 2.05-2.20 (4H, m, $COC\underline{H}_2C\underline{H}_2$), 2.39 (1H, dd, *J* = 14.0 Hz; *J* = 7.3 Hz, $C\underline{H}_AH_BCH$), 2.47 (1H, dd, *J* = 14.0 Hz; *J* = 7.4 Hz, $CH_A\underline{H}_BCH$), 4.09 (2H, q, *J* = 7.1 Hz, $C\underline{H}_2CH_3$), 4.62 (2H, s, $C\underline{H}_2Ph$), 5.02-5.12 (2H, m; $HC=C\underline{H}_2$), 5.46-5.60 (1H, m, $H\underline{C}=CH_2$), 6.05 (1H, br s, NH), 7.23-7.37 (5H, m, Ph). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.19 (CH_3), 28.67 ($CO\underline{C}H_2$), 31.08 ($COCH_2\underline{C}H_2$), 41.52 (CCH_2), 42.35 ($\underline{C}H_2Ph$), 61.01 ($\underline{C}H_2CH_3$), 64.55 (C_q), 121.36 ($HC=\underline{C}H_2$), 127.97 ($CH_{arom.}$), 128.55 ($CH_{arom.}$), 128.66 ($CH_{arom.}$), 129.83 ($H\underline{C}=CH_2$), 136.03 ($C_{q\ arom.}$). 156.55 (NC=ON), 172.87 (HNC=O), 175.04 (C=OO). **IR (cm^{-1}) ν_{max}:** 1713 (C=O), 1774 (C=O). **MS: m/z (%):** 331.2 ($M+H^+$, 100). **Chromatography:** Hex/EtOAc (55/45) R_f = 0.22. **Yield:** 45%.

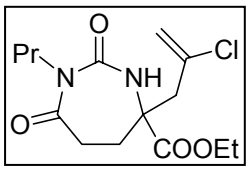
Ethyl 4-(2-methylprop-2-enyl)-2,7-dioxo-1-propyl-1,3-diazepane-4-carboxylate



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.92 (3H, t, *J* = 7.4 Hz, $CH_2CH_2C\underline{H}_3$), 1.25 (1.5H, t, *J* = 7.2 Hz, CH_3), 1.26 (1.5H, t, *J* = 7.2 Hz, CH_3), 1.62 (2H, sextet, *J* = 7.4 Hz $CH_2C\underline{H}_2CH_3$), 1.73 (3H, s, CCH_3), 2.08-2.28 (4H, m, $COC\underline{H}_2C\underline{H}_2$), 2.38 (1H, d, *J* = 13.6 Hz; $CC\underline{H}_AH_BC$), 2.55 (1H, d, *J* = 13.6 Hz; $CCH_A\underline{H}_BCH$), 3.43 (2H, dt, *J* = 2.8 Hz, *J* = 7.4 Hz, $C\underline{H}_2CH_2CH_3$),

4.13 (2H, q, *J* = 7.2 Hz, C$\underline{H}_2$CH$_3$), 4.79 (1H, s, C=C$\underline{H}_A\underline{H}_B$), 4.91 (1H, d, *J* = 1.1 Hz, C=CH$_A\underline{H}_B$), 6.04 (1H, br s, NH). **^{13}C-NMR (75 MHz, CDCl$_3$) δ:** 11.26 (CH$_2$CH$_2\underline{C}$H$_3$), 14.19 (CH$_3$), 21.42 (CH$_2\underline{C}$H$_2$CH$_3$), 24.30 (CH$_3$), 28.76 (CO$\underline{C}$H$_2$), 31.83 (COCH$_2\underline{C}$H$_2$), 40.42 ($\underline{C}$H$_2$CH$_2$CH$_3$), 44.62 (CCH$_2$), 61.07 ($\underline{C}$H$_2$CH$_3$), 64.79 (C$_q$), 116.98 (C=$\underline{C}$H$_2$), 138.75 ($\underline{C}$=CH$_2$), 157.39 (NC=ON), 172.87 (HNC=O), 175.46 (C=OO). **IR (cm^{-1}) ν$_{max}$:** 1646 (C=C), 1713 (br C=O), 1772 (C=O). **MS: m/z (%):** 297.8 (M+H$^+$, 100). **Chromatography:** Hex/EtOAc (4/6) R$_f$ = 0.42. **Yield:** 63%.

Ethyl 4-(2-chloroprop-2-enyl)-2,7-dioxo-1-propyl-1,3-diazepane-4-carboxylate

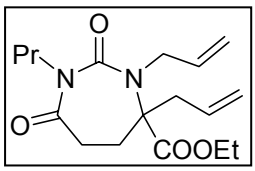


^{1}H-NMR (300 MHz, CDCl$_3$) δ: 0.93 (3H, t, *J* = 7.4 Hz, CH$_2$CH$_2$C$\underline{H}_3$), 1.24 (1.5H, t, *J* = 7.2 Hz, CH$_3$), 1.25 (1.5H, t, *J* = 7.2 Hz, CH$_3$), 1.64 (2H, sextet, *J* = 7.4 Hz CH$_2$C$\underline{H}_2$CH$_3$), 2.11-2.20 (2H, m, COCH$_2$C$\underline{H}_2$), 2.23-2.35 (2H, m, COC$\underline{H}_2$CH$_2$), 2.77 (1H, d, *J* = 14.6 Hz; CC$\underline{H}_A\underline{H}_B$C), 2.87 (1H, d, *J* = 14.6 Hz; CCH$_A\underline{H}_B$CH), 3.45 (2H, t, *J* = 7.4 Hz, C$\underline{H}_2$CH$_2$CH$_3$), 4.12 (1H, q, *J* = 7.2 Hz, C$\underline{H}_A\underline{H}_BCH_3$), 4.13 (2H, q, *J* = 7.2 Hz, CH$_A\underline{H}_B$CH$_3$), 5.28 (1H, s; HC=C$\underline{H}_A\underline{H}_B$), 5.34 (1H, d; *J* = 3.3 Hz, HC=CH$_A\underline{H}_B$), 6.48 (1H, br s, NH). **^{13}C-NMR (75 MHz, CDCl$_3$) δ:** 11.28 (CH$_2$CH$_2\underline{C}$H$_3$), 14.18 (CH$_3$), 21.35 (CH$_2\underline{C}$H$_2$CH$_3$), 28.54 (CO$\underline{C}$H$_2$), 31.34 (COCH$_2\underline{C}$H$_2$), 40.53 ($\underline{C}$H$_2$CH$_2$CH$_3$), 45.97 (CCH$_2$), 61.05 ($\underline{C}$H$_2$CH$_3$), 63.80 (C$_q$), 118.37 (HC=$\underline{C}$H$_2$), 135.25 (H$\underline{C}$=CH$_2$), 156.90 (NC=ON), 172.55 (HNC=O), 174.75 (C=OO). **IR (cm^{-1}) ν$_{max}$:** 1633 (C=C), 1717 (br C=O), 1777 (C=O). **MS: m/z (%):** 317.7, 319.8 (M+H$^+$, 100). **Chromatography:** Hex/EtOAc (6/4) R$_f$ = 0.26. **Yield:** 66%.

Typical experimental procedure for the N-alkylation of alkyl 1,4-dialkyl-2,7-dioxo-1,3-diazepane-4-carboxylates:

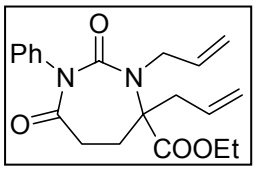
The diazepane (3 mmol) was dissolved into acetone (10 mL) and the alkylhalide (9 mmol) was added followed by K_2CO_3 (15 mmol, finely ground). The reaction was allowed to reflux untill TLC analysis showed that all starting material was consumed. The mixure was filtered and solvent was removed in vacuo. If necessary the residue was purified by flash chromatography (silica gel; hexane/EtOAc).

Ethyl 3,4-diallyl-2,7-dioxo-1-propyl-1,3-diazepane-4-carboxylate



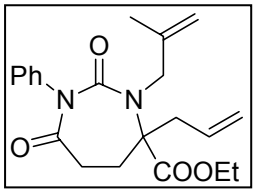
^{1}H-NMR (300 MHz, CDCl$_3$) δ: 0.91 (3H, t, *J* = 7.4 Hz, CH$_2$CH$_2$C$\underline{H}_3$), 1.24 (3H, t, *J* = 7.2 Hz, CH$_3$), 1.61 (2H, sextet, *J* = 7.3 Hz, CH$_2$C$\underline{H}_2$CH$_3$), 2.05-2.20 (4H, m, COC$\underline{H}_2$C$\underline{H}_2$), 2.46-2.60 (2H, m, CC$\underline{H}_2$), 3.44 (2H, dt, *J* = 7.4 Hz, *J* = 1.7 Hz, NC$\underline{H}_2$CH$_2$), 3.82 (1H, dd, *J* = 15.6 Hz, *J* = 6.9 Hz, NC$\underline{H}_A\underline{H}_B$CH), 4.01 (1H, dd, *J* = 15.6 Hz, *J* = 6.5 Hz, NCH$_A\underline{H}_B$CH), 4.11 (2H, q, *J* = 7.2 Hz, C$\underline{H}_2$CH$_3$), 5.10-5.35 (4H, m, 2 x HC=C$\underline{H}_2$), 5.42-5.56 (1H, m, $\underline{H}$C=CH$_2$), 5.85-5.99 (1H, m, $\underline{H}$C=CH$_2$). **^{13}C-NMR (75 MHz, CDCl$_3$) δ:** 11.35 (CH$_2$CH$_2\underline{C}$H$_3$), 14.22 (CH$_3$), 21.57 (CH$_2\underline{C}$H$_2$CH$_3$), 28.33 (CO$\underline{C}$H$_2$), 29.77 (COCH$_2\underline{C}$H$_2$), 39.54 (C$\underline{C}$H$_2$CH), 40.58 ($\underline{C}$H$_2$CH$_2$CH$_3$), 42.87 (NCH$_2$CH), 60.90 ($\underline{C}$H$_2$CH$_3$), 68.09 (C$_q$), 118.93 (HC=$\underline{C}$H$_2$), 121.01 (HC=$\underline{C}$H$_2$), 129.88 (H$\underline{C}$=CH$_2$), 133.32 (H$\underline{C}$=CH$_2$), 156.39 (NC=ON), 172.05 (HNC=O), 174.19 (C=OO). **IR (cm^{-1}) ν$_{max}$:** 1643 (C=C), 1709 (C=O), 1735 (C=O), 1768 (C=O). **MS: m/z (%):** 323.3 (M+H$^+$, 100). **Chromatography:** Hex/EtOAc (6/4) R$_f$ = 0.52. **Yield:** 100%.

Ethyl 3,4-diallyl-2,7-dioxo-1-phenyl-1,3-diazepane-4-carboxylate



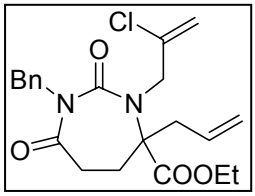
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.24 (3H, t, *J* = 7.1 Hz, CH_3), 2.14-2.38 (4H, m, $COCH_2CH_2$), 2.60 (1H, dd, *J* = 14.2 Hz, *J* = 6.5 Hz, CCH_AH_B), 2.67 (1H, dd, *J* = 14.2 Hz, *J* = 8.0 Hz, CCH_AH_B), 3.91 (1H, dd, *J* = 15.4 Hz, *J* = 6.9 Hz, NCH_AH_BCH), 4.09 (1H, dd, *J* = 15.4 Hz, *J* = 6.6 Hz, NCH_AH_BCH), 4.13 (2H, q, *J* = 7.1 Hz, CH_2CH_3), 5.19-5.40 (4H, m, 2 x $HC=CH_2$), 5.57-5.71 (1H, m, $HC=CH_2$), 5.92-6.06 (1H, m, $HC=CH_2$), 7.32-7.48 (5H, m, Ph). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.24 (CH_3), 28.48 ($COCH_2$), 29.97 ($COCH_2CH_2$), 39.78 (CCH_2CH), 43.16 (NCH_2CH), 61.00 (CH_2CH_3), 68.18 (C_q), 119.28 ($HC=CH_2$), 121.42 ($HC=CH_2$), 126.22 ($CH_{arom.}$), 128.35 ($CH_{arom.}$), 129.13 ($CH_{arom.}$), 129.77 ($HC=CH_2$), 131.52 ($C_{q\ arom.}$). 133.04 ($HC=CH_2$), 155.22 (NC=ON), 171.99 (HNC=O), 173.23 (C=OO). **IR (cm^{-1}) ν_{max}:** 1642 (C=C), 1717 (br C=O), 1772 (C=O). **MS: m/z (%):** 357.2 ($M+H^+$, 100). **Yield:** 100%.

Ethyl 4-allyl-3-(2-methylprop-2-enyl)-1-phenyl-2,7-dioxo-1,3-diazepane-4-carboxylate



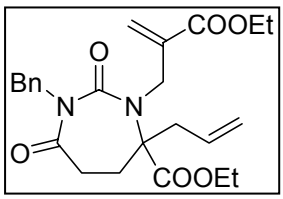
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.24 (3H, t, *J* = 7.2 Hz, CH_3), 1.86 (3H, s, CCH_3), 2.18-2.38 (4H, m, $COCH_2CH_2$), 2.63-2.67 (2H, m, CH_2CH), 3.86 (1H, d, *J* = 15.3 Hz, NCH_AH_BC), 4.03 (1H, d, *J* = 15.3 Hz, NCH_AH_BC), 4.12 (2H, q, *J* = 7.2 Hz, CH_2CH_3), 4.96 (1H, s, $C=CH_AH_B$), 5.02 (1H, s, $C=CH_AH_B$), 5.19 (1H, d, *J* = 3.9 Hz, $HC=CH_AH_B$), 5.24 (1H, d, *J* = 10.7 Hz, $HC=CH_AH_B$), 5.55-5.69 (1H, m, $HC=CH_2$), 7.31-7.48 (5H, m, Ph). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.23 (CH_3), 20.89 (CCH_3), 28.53 ($COCH_2$), 29.95 ($COCH_2CH_2$), 39.72 (CCH_2CH), 46.41 (NCH_2C), 60.97 (CH_2CH_3), 68.44 (C_q), 114.96 ($C=CH_2$), 121.42 ($HC=CH_2$), 126.17 ($CH_{arom.}$), 128.32 ($CH_{arom.}$), 129.12 ($CH_{arom.}$), 129.83 ($HC=CH_2$), 131.65 ($C_{q\ arom.}$). 141.50 ($C=CH_2$), 155.80 (NC=ON), 172.00 (HNC=O), 173.33 (C=OO). **IR (cm^{-1}) ν_{max}:** 1717 (br C=O), 1773 (C=O). **MS: m/z (%):** 371.2 ($M+H^+$, 100). **Yield:** 100%.

Ethyl 4-allyl-1-benzyl-3-(2-chloroprop-2-enyl)-2,7-dioxo-1,3-diazepane-4-carboxylate



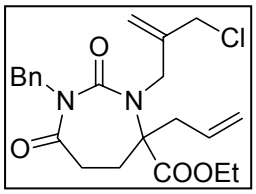
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.22 (3H, t, *J* = 7.0 Hz, CH_3), 2.00-2.28 (4H, m, $COCH_2CH_2$), 2.50 (1H, dd, *J* = 14.5 Hz, *J* = 7.2 Hz, CCH_AH_B), 2.58 (1H, dd, *J* = 14.5 Hz, *J* = 7.3 Hz, CCH_AH_B), 3.90 (1H, d, *J* = 15.8 Hz, NCH_AH_BC), 4.09 (2H, q, *J* = 7.0 Hz, CH_2CH_3), 4.27 (1H, d, *J* = 15.8 Hz, NCH_AH_BC), 4.62 (1H, d, *J* = 14.4 Hz, NCH_AH_BPh), 4.68 (1H, d, *J* = 14.4 Hz, NCH_AH_BPh), 4.93-5.10 (2H, m, $HC=CH_2$), 5.28-5.39 (1H, m, $HC=CH_2$), 5.42 (1H, d, *J* = 1.8 Hz, $C=CH_AH_B$), 5.50 (1H, d, *J* = 1.8 Hz, $C=CH_AH_B$), 7.25-7.39 (5H, m, Ph). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.22 (CH_3), 28.33 ($COCH_2$), 29.95 ($COCH_2CH_2$), 39.54 (CCH_2CH), 42.79 (NCH_2Ph), 46.50 (NCH_2C), 60.84 (CH_2CH_3), 68.38 (C_q), 116.72 ($C=CH_2$), 121.28 ($HC=CH_2$), 128.06 ($CH_{arom.}$), 128.67 ($CH_{arom.}$), 128.75 ($CH_{arom.}$), 129.44 ($HC=CH_2$), 135.88 ($C_{q\ arom.}$). 137.45 (CCl), 156.52 (NC=ON), 172.03 (HNC=O), 173.73 (C=OO). **IR (cm^{-1}) ν_{max}:** 1635 (C=C), 1713 (br C=O), 1772 (C=O). **MS: m/z (%):** 405.2 ($M+H^+$, 100), 407.2 ($M+H^+$, 29). **Chromatography:** Hex/EtOAc (7/3) R_f = 0.35. **Yield:** 70%.

Ethyl 4-allyl-1-benzyl-3-[2-(ethoxycarbonyl)prop-2-enyl]-2,7-dioxo-1,3-diazepane-4-carboxylate



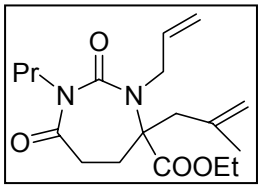
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.16-1.32 (6H, m, 2 x $CH_2C\underline{H}_3$), 1.94-2.15 (4H, m, $COC\underline{H}_2C\underline{H}_2$), 2.60 (1H, dd, *J* = 14.2 Hz, *J* = 6.5 Hz, $CC\underline{H}_AH_B$), 2.52 (2H, d, *J* = 7.2 Hz, $CC\underline{H}_2$), 4.02-4.16 (3H, m, $NC\underline{H}_AH_B$ + $C\underline{H}_2CH_3$), 4.19-4.26 (3H, m, $NCH_A\underline{H}_B$ + $C\underline{H}_2CH_3$), 4.64 (2H, s, $C\underline{H}_2Ph$), 4.91-5.07 (2H, m, $HC=C\underline{H}_2$), 5.22-5.36 (1H, m, $\underline{H}C=CH_2$), 5.99 (1H, d, *J* = 0.8 Hz, $C=C\underline{H}_AH_B$), 6.42 (1H, s, $C=CH_A\underline{H}_B$), 7.24-7.39 (5H, m, Ph). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.21 (2 x CH_3), 28.36 ($CO\underline{C}H_2$), 29.75 ($COCH_2\underline{C}H_2$), 39.40 ($C\underline{C}H_2CH$), 39.75 (NCH_2CH), 42.67 ($\underline{C}H_2Ph$), 60.79 ($\underline{C}H_2CH_3$), 61.36 ($\underline{C}H_2CH_3$), 68.43 (C_q), 121.09 ($HC=\underline{C}H_2$), 128.00 ($CH_{arom.}$), 128.64 ($CH_{arom.}$), 128.73 ($CH_{arom.}$), 129.60 ($\underline{C}=CH_2$), 129.67 ($H\underline{C}=CH_2$), 136.02 ($C_{q\ arom.}$). 156.64 (NC=ON), 165.99 ($C\underline{C}$=O), 171.85 (HNC=O), 174.00 (C=OO). **IR (cm^{-1}) ν_{max}:** 1662 (C=C), 1711 (br C=O), 1770 (C=O). **MS: m/z (%):** 443.2 ($M+H^+$, 100). **Chromatography:** Hex/EtOAc/ether (9/1/2) R_f = 0.07. **Yield:** 45%.

Ethyl 4-allyl-1-benzyl-3-(2-chloroprop-2-enyl)-2,7-dioxo-1,3-diazepane-4-carboxylate



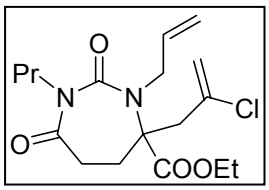
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.22 (3H, t, *J* = 7.1 Hz, CH_3), 2.01-2.20 (4H, m, $COC\underline{H}_2C\underline{H}_2$), 2.48 (1H, dd, *J* = 14.5 Hz; *J* = 7.4 Hz, $C\underline{H}_AH_BCH$), 2.56 (1H, dd, *J* = 14.5 Hz; *J* = 6.9 Hz, $CH_A\underline{H}_BCH$), 3.89-4.12 (4H, m, $NC\underline{H}_2CC\underline{H}_2Cl$), 4.09 (2H, q, *J* = 7.1 Hz, $C\underline{H}_2CH_3$), 4.64 (2H, s, $NC\underline{H}_2Ph$), 4.79-5.08 (2H, m, $HC=C\underline{H}_2$), 5.23 (1H, s, $C=C\underline{H}_AH_B$), 5.23-5.37 (1H, m, $\underline{H}C=CH_2$), 5.37 (1H, s, $C=C\underline{H}_AH_B$), 7.25-7.40 (5H, m, Ph). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.22 (CH_3), 28.32 ($CO\underline{C}H_2$), 29.71 ($COCH_2\underline{C}H_2$), 39.52 ($C\underline{C}H_2CH$), 42.21 (NCH_2CH), 42.73 ($N\underline{C}H_2Ph$), 45.98 ($\underline{C}H_2Cl$), 60.89 ($\underline{C}H_2CH_3$), 68.55 (C_q), 118.50 ($C=\underline{C}H_2$), 121.27 ($HC=\underline{C}H_2$), 128.06 ($CH_{arom.}$), 128.69 ($CH_{arom.}$), 128.78 ($CH_{arom.}$), 129.51 ($H\underline{C}=CH_2$), 135.94 ($C_{q\ arom.}$). 140.87 ($\underline{C}=CH_2$), 156.81 (NC=ON), 171.87 (HNC=O), 173.94 (C=OO). **IR (cm^{-1}) ν_{max}:** 1710 (br C=O), 1769 (C=O). **MS: m/z (%):** 419.2, 421.3 ($M+H^+$, 100). **Chromatography:** Hex/EtOAc (6/4) R_f = 0.63. **Yield:** 72%.

Ethyl 3-allyl-4-(2-methylprop-2-enyl)-1-propyl-2,7-dioxo-1,3-diazepane-4-carboxylate



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.91 (3H, t, *J* = 7.4 Hz, $CH_2CH_2C\underline{H}_3$), 1.24 (3H, t, *J* = 7.2 Hz, CH_3), 1.61 (2H, sextet, *J* = 7.4 Hz, $CH_2C\underline{H}_2CH_3$), 1.63 (3H, s, CCH_3), 1.96-2.22 (4H, m, $COC\underline{H}_2C\underline{H}_2$), 2.49 (1H, d, *J* = 14.4 Hz, $CC\underline{H}_AH_B$), 2.57 (1H, d, *J* = 14.4 Hz, $CCH_A\underline{H}_B$), 3.41 (1H, dt, *J* = 7.4 Hz, *J* = 13.5 Hz, $NC\underline{H}_AH_BCH_2$), 3.45 (1H, dt, *J* = 7.4 Hz, *J* = 13.5 Hz, $NCH_A\underline{H}_BCH_2$), 3.61 (1H, dd, *J* = 15.4 Hz, *J* = 7.7 Hz, $NC\underline{H}_AH_BCH$), 4.11 (2H, q, *J* = 7.2 Hz, $C\underline{H}_2CH_3$), 4.21 (1H, ddt, *J* = 15.4 Hz, *J* = 5.5 Hz, *J* = 1.4 Hz, $NCH_A\underline{H}_BCH$), 4.72 (1H, d, *J* = 0.8 Hz, $C=C\underline{H}_AH_B$), 4.86 1H, t, *J* = 1.5 Hz, $C=CH_A\underline{H}_B$), 5.20 (1H, dd, *J* = 9.9 Hz, *J* = 0.8 Hz, $HC=C\underline{H}_AH_B$), 5.31 (1H, dq, *J* = 17.0 Hz, *J* = 1.4 Hz, $HC=CH_A\underline{H}_B$), 5.87-6.00 (1H, m, $\underline{H}C=CH_2$). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 11.34 ($CH_2CH_2\underline{C}H_3$), 14.24 (CH_3), 21.45 ($CH_2\underline{C}H_2CH_3$), 23.67 ($C\underline{C}H_3$), 28.13 ($CO\underline{C}H_2$), 30.88 ($COCH_2\underline{C}H_2$), 40.58 ($\underline{C}H_2CH_2CH_3$), 42.45 ($C\underline{C}H_2C$), 43.23 ($N\underline{C}H_2CH$), 60.82 ($\underline{C}H_2CH_3$), 67.97 (C_q), 116.58 ($C=\underline{C}H_2$), 118.96 ($HC=\underline{C}H_2$), 133.19 ($H\underline{C}=CH_2$), 138.77 ($\underline{C}=CH_2$), 156.32 (NC=ON), 172.00 (HNC=O), 174.39 (C=OO). **IR (cm^{-1}) ν_{max}:** 1645 (C=C), 1708 (C=O), 1735 (C=O), 1767 (C=O). **MS: m/z (%):** 337.8 ($M+H^+$, 100). **Yield:** 100%.

Ethyl 3-allyl-4-(2-chloroprop-2-enyl)-1-propyl-2,7-dioxo-1,3-diazepane-4-carboxylate

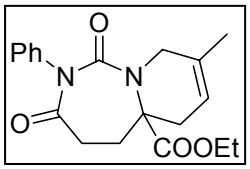


^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.92 (3H, t, *J* = 7.4 Hz, $CH_2CH_2C\underline{H}_3$), 1.24 (1.5H, t, *J* = 7.1 Hz, CH_3), 1.25 (1.5H, t, *J* = 7.1 Hz, CH_3), 1.63 (2H, sextet, *J* = 7.4 Hz, $CH_2C\underline{H}_2CH_3$), 2.01-2.25 (4H, m, $COC\underline{H}_2C\underline{H}_2$), 2.80 (1H, d, *J* = 14.9 Hz, $CC\underline{H}_AH_B$), 2.95 (1H, d, *J* = 14.9 Hz, $CCH_A\underline{H}_B$), 3.42 (1H, dt, *J* = 7.4 Hz, *J* = 11.8 Hz, $NC\underline{H}_AH_BCH_2$), 3.48 (1H, dt, *J* = 7.4 Hz, *J* = 11.8 Hz, $NCH_A\underline{H}_BCH_2$), 3.65 (1H, dd, *J* = 15.6 Hz, *J* = 7.8 Hz, $NC\underline{H}_AH_BCH$), 4.11 (2H, q, *J* = 7.1 Hz, $C\underline{H}_2CH_3$), 4.28 (1H, dd, *J* = 15.6 Hz, *J* = 5.5 Hz, $NCH_A\underline{H}_BCH$), 5.19-5.35 (4H, m, $C=C\underline{H}_2$ + $HC=C\underline{H}_2$), 5.89-6.02 (1H, m, $\underline{H}C=CH_2$). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 11.32 ($CH_2CH_2\underline{C}H_3$), 14.19 (CH_3), 21.32 ($CH_2\underline{C}H_2CH_3$), 27.92 ($CO\underline{C}H_2$), 30.32 ($COCH_2\underline{C}H_2$), 40.70 ($\underline{C}H_2CH_2CH_3$), 43.54 ($C\underline{C}H_2C$ + $N\underline{C}H_2CH$), 60.84 ($\underline{C}H_2CH_3$), 67.49 (C_q), 118.14 ($C=\underline{C}H_2$), 119.02 ($HC=\underline{C}H_2$), 133.13 ($H\underline{C}=CH_2$), 135.09 ($\underline{C}=CH_2$), 156.14 (NC=ON), 171.73 (HNC=O), 173.45 (C=OO). **IR (cm^{-1}) ν_{max}:** 1632 (C=C), 1709 (C=O), 1735 (C=O), 1770 (C=O). **MS: m/z (%):** 357.7, 359.7 ($M+H^+$, 100). **Chromatography:** Hex/EtOAc (2/1) R_f = 0.43. **Yield:** 83%.

Typical experimental procedure for the synthesis of alkyl 2,7-dialkyl-1,3-dioxo-2,3,4,5,6,9-hexahydropyrido[1,2-*c*][1,3]diazepine-5a(1*H*)-carboxylates:

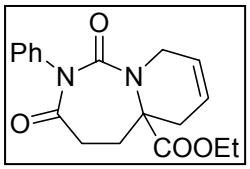
The diazepane (0.6 mmol) was dissolved in CH_2Cl_2 (10 mL, freshly distilled from CaH_2) and the second generation Grubbs' catalyst (0.03 mmol) was added. The reaction was allowed to reflux for 4h under a N_2-atmosphere. The mixure was filtered and solvent was removed in vacuo. The residue was coated on silica gel by removal of the solvent in vacuo and purified by flash chromatography (silica gel; hexane/EtOAc).

Ethyl 8-methyl-1,3-dioxo-2-phenyl-2,3,4,5,6,9-hexahydropyrido[1,2-*c*][1,3]diazepine-5a(1*H*)-carboxylate



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.23 (3H, t, *J* = 7.2 Hz, $CH_2C\underline{H}_3$), 1.76 (3H, s, $CC\underline{H}_3$), 2.19-2.52 (6H, m, $COC\underline{H}_2C\underline{H}_2$ and $CC\underline{H}_2$), 3.50 (1H, d, *J* = 18.0 Hz, $NC\underline{H}_AH_B$), 4.12 (2H, q, *J* = 7.2 Hz, $C\underline{H}_2CH_3$), 4.34 (1H, d, *J* = 18.0 Hz, $NCH_A\underline{H}_B$), 5.51 (1H, t, *J* = 1.9 Hz, CH), 7.35-7.49 (5H, m, Ph). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.22 ($CH_2\underline{C}H_3$), 20.21 ($C\underline{C}H_3$), 28.79 ($CO\underline{C}H_2$), 29.05 ($COCH_2\underline{C}H_2$), 31.89 ($C\underline{C}H_2CH$), 41.39 (NCH_2), 60.29 (C_q), 61.07 ($\underline{C}H_2CH_3$), 116.05 (CH), 126.26 ($CH_{arom.}$), 128.31 ($CH_{arom.}$), 129.16 ($CH_{arom.}$), 130.57 ($\underline{C}CH_3$), 131.68 ($C_{q\ arom.}$), 153.96 (NC=ON), 172.51 (HNC=O), 174.74 (C=OO). **IR (cm^{-1}) ν_{max}:** 1721 (br C=O), 1775 (C=O). **MS: m/z (%):** 343.2 ($M+H^+$, 100). **Chromatography:** Hex/EtOAc (7/3) R_f = 0.29. **Yield:** 79%.

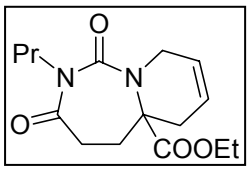
Ethyl 1,3-dioxo-2-phenyl-2,3,4,5,6,9-hexahydropyrido[1,2-*c*][1,3]diazepine-5a(1*H*)-carboxylate



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.23 (3H, t, *J* = 7.2 Hz, $CH_2C\underline{H}_3$), 2.19-2.56 (6H, m, $COC\underline{H}_2C\underline{H}_2$ and $CC\underline{H}_2$), 3.65 (1H, d, *J* = 19.9 Hz + small splitting, $NC\underline{H}_AH_B$), 4.12 (2H, q, *J* = 7.2 Hz, $C\underline{H}_2CH_3$), 4.48 (1H, d, *J* = 19.9 Hz, $NCH_A\underline{H}_B$), 5.78 (1H, m, CH), 7.35-7.50 (5H, m, Ph). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.22 ($CH_2\underline{C}H_3$), 28.94 ($CO\underline{C}H_2$), 28.99 ($COCH_2\underline{C}H_2$), 31.83 ($C\underline{C}H_2CH$), 38.04 (NCH_2), 60.39 (C_q), 61.08 ($\underline{C}H_2CH_3$), 121.71 (CH),

123.25 (CH), 126.25 ($CH_{arom.}$), 128.32 ($CH_{arom.}$), 129.16 ($CH_{arom.}$), 131.65 ($C_{q\ arom.}$), 153.99 (NC=ON), 172.42 (HNC=O), 174.62 (C=OO). **IR (cm^{-1}) ν_{max}:** 1721 (br C=O), 1775 (C=O). **MS: m/z (%):** 329.2 ($M+H^+$, 100). **Mp** : 110-113°C. **Chromatography:** Hex/EtOAc (7/3) R_f = 0.21. **Yield:** 88%.

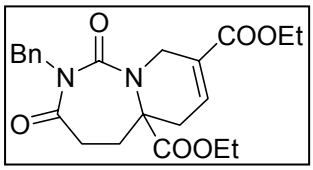
Ethyl 1,3-dioxo-2-propyl-2,3,4,5,6,9-hexahydropyrido[1,2-*c*][1,3]diazepine-5a(1*H*)-carboxylate



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.93 (3H, t, *J* = 7.4 Hz, CH_3 pr), 1.24 (3H, t, *J* = 7.1 Hz, $CH_2C\underline{H}_3$), 1.66 (2H, sextet, *J* = 7.4 Hz, $NCH_2C\underline{H}_2$), 2.05-2.33 (6H, m, $COC\underline{H}_2C\underline{H}_2$ and $CC\underline{H}_2$), 3.49 (2H, dt, *J* = 7.4 Hz, *J* = 1.6 Hz, $NC\underline{H}_2CH_2$), 3.56 (1H, d, *J* = 18.2 Hz + small splitting , $NC\underline{H}_AH_B$), 4.10 (2H, q, *J* = 7.1 Hz, $C\underline{H}_2CH_3$), 4.41 (1H, d, *J* = 18.2 Hz + small splitting, $NCH_A\underline{H}_B$), 5.78 (2H, t, *J* = 1.9 Hz + small splitting, HC=CH). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 11.22 (CH_3 pr), 14.15 ($CH_2\underline{C}H_3$), 21.53 (CH_2 pr), 28.43 ($CO\underline{C}H_2$), 28.80 ($COCH_2\underline{C}H_2$), 31.65 ($C\underline{C}H_2CH$), 37.71 (NCH_2), 40.37 (NCH_2 pr), 60.28 (C_q), 60.87 ($\underline{C}H_2CH_3$), 121.59 (CH), 123.27 (CH), 155.15 (NC=ON), 172.39 (HNC=O), 175.74 (C=OO). **IR (cm^{-1}) ν_{max}:** 1656 (C=C), 1709 (br C=O), 1771 (C=O). **MS: m/z (%):** 295.2 ($M+H^+$, 100). **Chromatography:** Hex/EtOAc (6/4) R_f = 0.25. **Yield:** 93%.

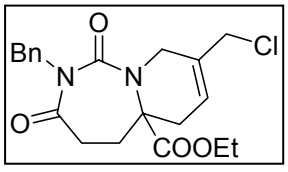
Diethyl 2-benzyl-1,3-dioxo-2,3,4,5,6,9-hexahydropyrido[1,2-*c*][1,3]diazepine-5a,8(1*H*)-dicarboxylate

Instead of the second generation Grubbs' catalyst, the second generation Hoveyda-Grubbs' catalyst was used for this reaction.



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.20 (3H, t, *J* = 7.2 Hz, $CH_2C\underline{H}_3$), 1.30 (3H, t, *J* = 7.0 Hz, $CH_2C\underline{H}_3$), 2.04-2.17 (4H, m, $COC\underline{H}_2C\underline{H}_2$), 2.41 (1H, dq, *J* = 18.4 Hz, *J* = 2.8 Hz, $CC\underline{H}_aH_b$), 2.54 (1H, dd, *J* = 18.4 Hz, *J* = 5.5 Hz, $CCH_a\underline{H}_b$), 3.73 (1H, ddt, *J* = 18.7 Hz, *J* = 3.7 Hz, *J* = 4.1 Hz, $NC\underline{H}_AH_B$), 4.07 (2H, q, *J* = 7.2 Hz, $C\underline{H}_2CH_3$), 4.21 (1H, dq, *J* = 10.6 Hz, *J* = 7.0 Hz, $C\underline{H}_aH_bCH_3$), 4.25 (1H, dq, *J* = 10.6 Hz, *J* = 7.1 Hz, $CH_a\underline{H}_bCH_3$), 4.68 (2H, s, $NC\underline{H}_2Ph$), 4.70 (1H, dt, *J* = 18.7 Hz, *J* = 1.9 Hz, $NCH_A\underline{H}_B$), 6.98 (1H, dd, *J* = 5.8 Hz, *J* = 2.2 Hz, CH), 7.29-7.59 (5H, m, Ph). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.19 ($CH_2\underline{C}H_3$), 14.27 ($CH_2\underline{C}H_3$), 28.61 ($CO\underline{C}H_2$), 28.76 ($COCH_2\underline{C}H_2$), 32.09 ($C\underline{C}H_2CH$), 36.91 (NCH_2), 42.58 (NCH_2Ph), 59.92 (C_q), 60.99 ($\underline{C}H_2CH_3$), 61.16 ($\underline{C}H_2CH_3$), 128.09 (CH), 128.35 (CH), 128.80 (CH), 133.42 ($H\underline{C}$=C), 136.03 (HC=$\underline{C}$), 137.67 ($C_{q,ar}$), 154.61 (NC=ON), 164.28 ($C\underline{C}OOEt$), 172.13 (HNC=O), 174.68 (C=OO). **IR (cm^{-1}) ν_{max}:** 1659 (C=C), 1716 (br C=O), 1774 (C=O). **MS: m/z (%):** 415.3 ($M+H^+$, 100). **Chromatography:** first Hex/EtOAc (3/1) untill R_f = 0.26, then strip with EtOAc + 5% CH_2Cl_2. **Yield:** 55%.

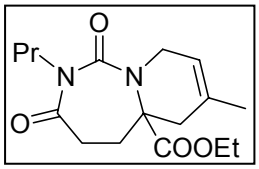
Ethyl 2-benzyl-8-(chloromethyl)-1,3-dioxo-2,3,4,5,6,9-hexahydropyrido[1,2-*c*][1,3]diazepine-5a(1*H*)-carboxylate



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.20 (3H, t, *J* = 7.1 Hz, $CH_2C\underline{H}_3$), 2.05-2.21 (4H, m, $COC\underline{H}_2C\underline{H}_2$), 2.23-2.43 (2H, m, CCH_2), 3.59 (1H, dq, *J* = 18.0 Hz, *J* = 2.4 Hz, $NC\underline{H}_AH_B$), 4.05 (2H, s, CH_2Cl), 4.07 (2H, q, *J* = 7.1 Hz, $C\underline{H}_2CH_3$), 4.54 (1H, d, *J* = 18.0 Hz, $NCH_A\underline{H}_B$), 4.67 (1H, d, *J* = 15.0 Hz, $NC\underline{H}_aH_bPh$), 4.68 (1H, d, *J* = 15.0 Hz,

NCH_aH_bPh), 5.88 (1H, q-like, J = 2.4 Hz, CH), 7.28-7.41 (5H, m, Ph). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.21 (CH_2CH_3), 28.62 ($COCH_2$), 28.73 ($COCH_2CH_2$), 31.58 (CCH_2CH), 38.38 (NCH_2), 42.56 (NCH_2Ph), 45.83 (CH_2Cl), 60.30 (C_q), 60.97 (CH_2CH_3), 121.85 (CH), 128.06 ($CH_{arom.}$), 128.55 ($CH_{arom.}$), 128.80 ($CH_{arom.}$), 131.45 (CCH_2Cl), 136.08 ($C_{q\ arom.}$), 154.77 (NC=ON), 172.33 (HNC=O), 175.00 (C=OO). **IR (cm^{-1}) ν_{max}:** 1713 (br C=O), 1771 (C=O). **MS: m/z (%):** 391.2/393.2 ($M+H^+$, 100). **Chromatography:** Hex/EtOAc (7/3) R_f = 0.18. **Yield:** 85%.

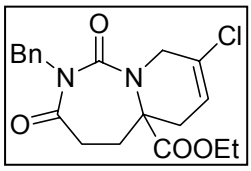
Ethyl 7-methyl-1,3-dioxo-2-propyl-2,3,4,5,6,9-hexahydropyrido[1,2-*c*][1,3]diazepine-5a(1*H*)-carboxylate



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.93 (3H, t, J = 7.4 Hz, $CH_2CH_2CH_3$), 1.24 (3H, t, J = 7.2 Hz, CH_2CH_3), 1.66 (2H, sextet, J = 7.4 Hz, NCH_2CH_2), 1.74 (3H, s, CCH_3), 2.05-2.24 (6H, m, $COCH_2CH_2$ and CCH_2), 3.49 (2H, dt, J = 7.4 Hz, J = 1.7 Hz, NCH_2CH_2), 3.51 (1H, dddd, J = 17.9 Hz, J = 12.5 Hz, J = 4.6 Hz, J = 2.2 Hz, NCH_AH_B), 4.10 (2H, q, J = 7.2 Hz, CH_2CH_3), 4.36 (1H, d, J = 17.9 Hz, NCH_AH_B), 5.44 (1H, s, CH). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 11.29 (CH_3 pr), 14.22 (CH_2CH_3), 21.60 (CH_2 pr), 23.51 (CCH_3), 28.55 ($COCH_2$), 28.85 ($COCH_2CH_2$), 36.38 (CCH_2C), 37.72 (NCH_2), 40.42 (NCH_2 pr), 60.93 (C_q + CH_2CH_3), 116.78 (CH), 129.42 (C), 155.24 (NC=ON), 172.48 (HNC=O), 175.81 (C=OO). **^{13}C-NMR (75 MHz, C_6D_6) δ:** 11.05 (CH_3 pr), 13.92 (CH_2CH_3), 21.60 (CH_2 pr), 22.93 (CCH_3), 28.73 ($COCH_2$), 28.85 ($COCH_2CH_2$), 35.95 (CCH_2C), 37.43 (NCH_2), 40.12 (NCH_2 pr), 60.41 (CH_2CH_3), 60.64 (C_q), 116.83 (CH), 128.83 (C), 154.98 (NC=ON), 171.90 (HNC=O), 175.26 (C=OO). **IR (cm^{-1}) ν_{max}:** 1712 (br C=O), 1770 (C=O). **MS: m/z (%):** 309.8 ($M+H^+$, 100). **Chromatography:** Hex/EtOAc (7/3) R_f = 0.27. **Yield:** 86%.

Ethyl 2-benzyl-8-chloro-1,3-dioxo-2,3,4,5,6,9-hexahydropyrido[1,2-*c*][1,3]diazepine-5a(1*H*)-carboxylate

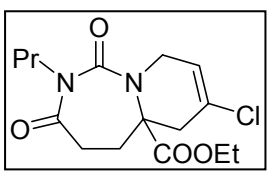
Instead of refluxing in CH_2Cl_2, the reaction was refluxed in dry benzene for 16 hours.



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.20 (3H, t, J = 7.1 Hz, CH_3), 2.00-2.33 (4H, m, $COCH_2CH_2$), 2.39-2.41 (2H, m, CH_2CH), 3.63 (1H, dq, J = 17.9 Hz, J = 2.6 Hz, NCH_AH_BCCl), 4.07 (2H, q, J = 7.1 Hz, CH_2CH_3), 4.49 (1H, dq, J = 17.9 Hz, J = 2.2 Hz, NCH_AH_BCCl), 4.67 (2H, s, NCH_2Ph), 5.86 (1H, dq, J = 1.6 Hz, J = 3.5Hz, CH), 7.27-7.39 (5H, m, Ph). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 14.19 (CH_3), 28.48 ($COCH_2$), 28.71 ($COCH_2CH_2$), 32.61 (CCH_2CH), 41.87 (NCH_2C), 42.64 (NCH_2Ph), 60.07 (C_q), 61.02 (CH_2CH_3), 119.28 (CH), 127.31 (CCl), 128.14 ($CH_{arom.}$), 128.52 ($CH_{arom.}$), 128.83 ($CH_{arom.}$), 135.91 ($C_{q\ arom.}$), 154.51 (NC=ON), 172.20 (HNC=O), 174.49 (C=OO). **IR (cm^{-1}) ν_{max}:** 1660 (C=C), 1714 (br C=O), 1775 (C=O). **MS: m/z (%):** 377.2/379.2 ($M+H^+$, 100). **Chromatography:** Hex/EtOAc (7/3) R_f = 0.29. **Yield:** 75%.

Ethyl 7-chloro-1,3-dioxo-2-propyl-2,3,4,5,6,9-hexahydropyrido[1,2-*c*][1,3]diazepine-5a(1*H*)-carboxylate

Instead of refluxing in CH_2Cl_2, the reaction was refluxed in dry benzene for 16 hours.



^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.93 (3H, t, J = 7.4 Hz, $CH_2CH_2CH_3$), 1.24 (3H, t, J = 7.2 Hz, CH_2CH_3), 1.66 (2H, sextet, J = 7.4 Hz,

$NCH_2C\underline{H_2}$), 2.07-2.36 (4H, m, $CO\underline{CH_2}\underline{CH_2}$), 2.51 (1H, d, J = 17.4 Hz, $CC\underline{H_A}H_BC$), 2.64 (1H, dq, J = 17.4 Hz, J = 3.1 Hz, $CCH_A\underline{H_B}C$), 3.49 (2H, dt, J = 7.4 Hz, J = 2.2 Hz, $NC\underline{H_2}CH_2$), 3.61 (1H, dq, J = 18.4 Hz, J = 3.2 Hz, $NC\underline{H_A}H_B$), 4.11 (2H, q, J = 7.2 Hz, $C\underline{H_2}CH_3$), 4.49 (1H, dt, J = 18.4 Hz, J = 3.2 Hz, $NCH_A\underline{H_B}$), 5.90 (1H, q, J = 3.2 Hz, CH). **^{13}C-NMR (75 MHz, $CDCl_3$) δ:** 11.26 (CH_3 pr), 14.21 ($CH_2\underline{C}H_3$), 21.52 (CH_2 pr), 28.70 ($CO\underline{C}H_2\underline{C}H_2$), 38.16 ($NCH_2$), 38.77 ($C\underline{C}H_2C$), 40.64 ($NCH_2$ pr), 61.08 ($\underline{C}H_2CH_3$), 61.55 (C_q), 120.17 (CH), 126.86 (CCl), 154.97 (NC=ON), 172.20 (HNC=O), 174.29 (C=OO). **IR (cm^{-1}) ν_{max}:** 1663 (C=C), 1713 (br C=O), 1774 (C=O). **MS: m/z (%):** 329.8, 331.7 ($M+H^+$, 100). **Chromatography:** Hex/EtOAc (2/1) R_f = 0.43. **Yield:** 77%.