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$_4$Cl 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$_2$CH$_2$AHB), 2,33-2,47 (4H, m, COOH$_2$CH$_2$AH + CCH$_3$HB), 2,66 (1H, dd, J = 6,4 Hz, J = 13,7 Hz, CCH$_3$HB), 5,09-5,16 (2H, m, CH=$\equiv$CH$_2$), 5,17 (2H, s, CH$_2$Ph), 5,61 (1H, dddd, J = 6,6 Hz, J = 8,3 Hz, J = 10,4 Hz, J = 16,7 Hz, CH=$\equiv$CH$_2$), 7,33-7,37 (5H, m, Ph). $^{13}$C-NMR (68MHz, CDCl$_3$) δ: 29,72 (COOH$_2$CH$_2$), 30,17
Benzyl 5-oxo-2-(2-chloromethylprop-2-enyl]pyrrolidine-2-carboxylate

\[\text{COC}_2\text{H}, 43,45 (\text{C}_q), 65,28 (\text{C}_q), 67,53 (\text{C}_2\text{H}_3\text{Ph}), 120,81 (\text{CH} = \text{CH}_2), 128,41 (\text{CH}_2\text{ar}), 128,71 (\text{CH}_2\text{ar}), 130,78 (\text{C}_2\text{H} = \text{CH}_2), 135,09 (\text{C}_q,\text{ar}), 172,85 (\text{NHC}=\text{O}), 176,91 (\text{C} = \text{OO}).\]

MS: \(m/z\) (%): 260 (M+H +, 100).

IR (cm\(^{-1}\)) \(\nu_{\text{max}}\): 1703 (C=O), 1736 (C=O).

Chromatography: Hex/EtOAc (25/75) \(R_f = 0.31\).

Yield: 83%.

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

\[\text{COC}_2\text{H}, 29,69 (\text{COCH}_2\text{CH}_3), 31,25 (\text{COCH}_2\text{C}_2\text{H}_5), 41,71 (\text{C}_2\text{H}_3\text{Ph}), 48,37 (\text{C}_2\text{H}_5\text{Cl}), 61,72 (\text{CH}_2\text{C}_2\text{H}_3), 65,35 (\text{C}_q), 120,41 (\text{CH} = \text{CH}_2), 131,19 (\text{CH} = \text{CH}_2), 173,19 (\text{NHC} = \text{O}), 177,25 (\text{C} = \text{OO}).\]

MS: \(m/z\) (%): 198 (M+H+, 100).

IR (cm\(^{-1}\)) \(\nu_{\text{max}}\): 1711 (br. C=O).

Yield: 72%.

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

\[\text{COC}_2\text{H}, 14,11 (\text{CH}_2\text{C}_2\text{H}_3), 29,69 (\text{COCH}_2\text{CH}_3), 31,23 (\text{COCH}_2\text{C}_2\text{H}_5), 41,74 (\text{C}_2\text{H}_3\text{Ph}), 48,41 (\text{C}_2\text{H}_5\text{Cl}), 61,99 (\text{CH}_2\text{C}_2\text{H}_3), 65,07 (\text{C}_q), 120,03 (\text{C} = \text{C}_2\text{H}_3), 139,91 (\text{C} = \text{C}_2\text{H}_5), 173,19 (\text{NHC} = \text{O}), 177,21 (\text{C} = \text{OO}).\]

MS: \(m/z\) (%): 246 (M+H +, 100).

IR (cm\(^{-1}\)) \(\nu_{\text{max}}\): 1707 (C=O), 1741 (C=O).

Yield: 62%.

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

\[\text{COC}_2\text{H}, 1.12 (3H, t, \text{J} = 7.2 \text{ Hz}, \text{CH}_3), 2.05-2.17 (1H, m, \text{COCH}_2\text{H}_3), 2.23-2.36 (2H, m, \text{COCH}_2\text{C}_2\text{H}_5), 2.23-2.49 (1H, m, \text{COCH}_2\text{C}_2\text{H}_3), 2.86 (1H, d, \text{J} = 13.6 \text{ Hz}, \text{C}_2\text{H}_3\text{N}), 3.21 (1H, d, \text{J} = 12.1 \text{ Hz}, \text{C}_2\text{H}_3\text{N}), 3.75 (1H, q, \text{J} = 7.2 \text{ Hz}, \text{CH}_2\text{C}_2\text{H}_3), 3.76 (1H, q, \text{J} = 7.2 \text{ Hz}, \text{CH}_2\text{C}_2\text{H}_3), 5.15 (1H, s; \text{C} = \text{CH}_2\text{N}), 5.33 (1H, d; \text{J} = 1.4 \text{ Hz}, \text{C} = \text{CH}_2\text{N}), 5.98 (1H, br s, \text{NH}), 7.29-7.35 (5H, m, Ph).\]

\[\text{COC}_2\text{H}, 13.97 (\text{CH}_3), 29.60 (\text{CH}_2\text{C}_2\text{H}_3), 30.04 (\text{C}_q), 43.38 (\text{CH}_2\text{C}_2\text{H}_3), 61,72 (\text{CH}_2\text{C}_2\text{H}_3), 65,35 (\text{C}_q), 120,41 (\text{CH} = \text{CH}_2), 131,19 (\text{CH} = \text{CH}_2), 173,19 (\text{NHC} = \text{O}), 177,25 (\text{C} = \text{OO}).\]

MS: \(m/z\) (%): 246 (M+H +, 100).

IR (cm\(^{-1}\)) \(\nu_{\text{max}}\): 1707 (C=O), 1741 (C=O).

Yield: 62%. 
(COCH₂CH₂), 31.49 (COCH₂), 45.05 (CCH₂C), 61.69 (CH₂CH₃), 65.46 (C₉), 118.52 (C=CH₂), 126.69 (CH₉), 128.15 (CH₉), 128.55 (CH₉), 140.54 (C=CH₂), 143.68 (C₉), 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) Rf = 0.21. Yield: 70%.

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

**1H-NMR (300 MHz, CDCl₃) δ:** 1.30 (3H, t, J = 7.2 Hz, CH₃), 1.72 (3H, s, CH₃), 2.09-2.19 (1H, m, COCH₂AH₂B), 2.35-2.52 (3H, m, COCH₂AH₂BCH₂), 2.37 (1H, dd, J = 2.6 Hz, J = 13.7 Hz, CCH₂AH₂C), 2.69 (1H, d, J = 13.7 Hz, CCH₂AH₂C), 4.21 (2H, q, J = 7.2 Hz, CH₂AH₂CH₃), 4.76 (1H, s, C=CH₂AH₂), 4.92 (1H, s, C=CH₂AH₂), 5.25 (1H, t; J = 0.7 Hz, C=CH₂AH₂), 5.35 (1H, d, J = 1.4 Hz, C=CH₂AH₂), 6.29 (1H, br s, NH).

**13C-NMR (75 MHz, CDCl₃) δ:** 14.19 (CH₃), 29.31 (COCH₂CH₂), 31.58 (CCH₂C), 48.13 (CCH₂C), 62.23 (CH₂CH₃), 64.72 (C₉), 117.85 (C=CH₂), 136.20 (C=CH₂), 172.51 (HNC=O), 176.52 (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 electrophiles:**

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 N₂-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 NH₄Cl until the pH was neutral. The mixture was extracted with EtOAc, and the organics were dried (MgSO₄) 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**

**1H-NMR (300 MHz, CDCl₃) δ:** 1.30 (3H, t, J = 7.2 Hz, CH₃), 2.13-2.23 (1H, m, COCH₂AH₂B), 2.36-2.43 (2H, m, COCH₂CH₂), 2.46-2.56 (1H, m, COCH₂AH₂B), 2.71 (1H, d, J = 14.3 Hz, CCH₂AH₂B), 3.05 (1H, d, J = 14.3 Hz, CCH₂AH₂B), 4.22 (1H, q, J = 7.2 Hz, CH₂AH₂CH₃), 4.33 (1H, q, J = 7.2 Hz, CH₂AH₂CH₃), 5.25 (1H, t; J = 0.7 Hz, C=CH₂AH₂), 5.35 (1H, d, J = 1.4 Hz, C=CH₂AH₂), 6.29 (1H, br s, NH).

**13C-NMR (75 MHz, CDCl₃) δ:** 14.19 (CH₃), 23.57 (COCH₂CH₂), 31.66 (COC₂H₂), 47.11 (CCH₂C), 61.88 (CH₂CH₃), 65.02 (C₉), 116.11 (C=CH₂), 139.96 (CH₃C=CH₂), 173.52 (HNC=O), 176.72 (C=OO).

IR (cm⁻¹) ν max: 1636 (C=C), 1715 (C=O), 1741 (C=O), 3220 (br NH). MS: m/z (%): 232.7, 234.7 (M+H⁺ , 100).

**Yield:** 46%.

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

**1H-NMR (300 MHz, CDCl₃) δ:** 1.31 (3H, t, J = 7.2 Hz, CH₃), 2.08 (1H, t, J = 2.2 Hz, CH), 2.12-2.52 (4H, m, COCH₂CH₂), 2.61 (1H, dd, J = 14.3 Hz, J = 7.2 Hz, CH₂AH₂B), 2.71 (1H, d, J = 14.3 Hz, C=CH₂AH₂B), 3.05 (1H, d, J = 14.3 Hz, C=CH₂AH₂B), 4.22 (1H, q, J = 7.2 Hz, CH₂AH₂CH₃), 4.33 (1H, q, J = 7.2 Hz, CH₂AH₂CH₃), 5.25 (1H, t; J = 0.7 Hz, C=CH₂AH₂), 5.35 (1H, d, J = 1.4 Hz, C=CH₂AH₂), 6.29 (1H, br s, NH).
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 until TLC analysis showed that all starting material was consumed. The mixture was cooled and aqueous NaHCO₃ (15mL) was added. The mixture was extracted with EtOAc, and the organics were dried (MgSO₄) and filtered. The solvent was removed in vacuo, and the residue was purified by flash chromatography.

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 NH₄Cl until the pH was neutral. The mixture was extracted with EtOAc, and the organics were dried (MgSO₄) 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

**1H-NMR (300 MHz, CDCl3)** δ: 1.25 (3H, t, J = 7.1 Hz, CH3), 2.12-2.30 (2H, m, COCH2CH2), 2.37-2.41 (2H, m, COCH2CH2), 2.51 (1H, dd, J = 13.8 Hz; J = 7.2 Hz, CHA3B3CH), 2.62 (1H, dd, J = 13.8 Hz; J = 7.7 Hz, CHA3B3CH), 4.15 (2H, q, J = 7.1 Hz, CH3CH2), 5.23 (1H, s; HC=CHA3B3), 5.27 (1H, d, J = 1.9 Hz, HC=CH3B3H), 5.70-5.84 (1H, m, HC=CH2), 6.09 (1H, br s, NH), 7.32-7.50 (5H, m, Ph).

**13C-NMR (75 MHz, CDCl3)** δ: 14.24 (CH3), 28.90 (COC2H), 31.29 (COCH2C2H2), 41.75 (CCH2), 61.17 (CH2CH3), 64.49 (Cq), 121.73 (HC=C3H2), 126.32 (CH arom.), 128.51 (CH arom.), 129.24 (CH arom.), 129.86 (HC=CH2), 131.44 (Cq arom.), 155.76 (NC=ON), 172.84 (HNC=O), 174.23 (C=OO). **IR (cm⁻¹) νmax:** 1719 (C=O), 1781 (C=O). **MS: m/z (%):** 317.3 (M+H+, 100).

**Chromatography:** Hex/EtOAc (1/1) Rf = 0.33. **Yield:** 70%.

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

**1H-NMR (300 MHz, CDCl3)** δ: 0.92 (3H, t, J = 7.4 Hz, CH2CH2CH3), 1.25 (3H, t, J = 7.2 Hz, CH3), 1.63 (2H, sextet, J = 7.4 Hz CH2CH2CH3), 2.03-2.29 (4H, m, COCH2CH2), 2.35 (1H, dd, J = 14.0 Hz; J = 7.3 Hz, CHA3B3CH), 2.50 (1H, dd, J = 14.0 Hz; J = 7.6 Hz, CH3B3H), 3.44 (2H, t, J = 7.4 Hz, CH2CH2CH3), 4.13 (2H, q, J = 7.2 Hz, CH2CH3), 5.16 (1H, s; HC=CHA3B3), 5.20 (1H, d, J = 3.3 Hz, HC=CH3B3), 5.59-5.73 (1H, m, HC=CH2), 5.88 (1H, br s, NH). **13C-NMR (75 MHz, CDCl3)** δ: 11.23 (CH2CH2CH3), 14.21 (CH3), 21.52 (CH2CH2CH3), 28.74 (COC2H), 31.05 (COCH2CH2), 40.36 (CH2CH2CH3), 41.57 (CCH2), 61.04 (CH2CH3), 64.38 (Cq), 121.34 (HC=CH2), 130.02 (HC=CH2), 156.97 (NC=ON), 172.86 (HNC=O), 175.29 (C=OO). **IR (cm⁻¹) νmax:** 1642 (C=C), 1713 (br C=O), 1775 (C=O). **MS: m/z (%):** 383.3 (M+H+, 100).

**Chromatography:** Hex/EtOAc (1/1) Rf = 0.42. **Yield:** 61%.

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

**1H-NMR (300 MHz, CDCl3)** δ: 1.22 (3H, t, J = 7.1 Hz, CH3), 2.05-2.20 (4H, m, COCH2CH2), 2.39 (1H, dd, J = 14.0 Hz; J = 7.3 Hz, CH3B3H), 2.47 (1H, dd, J = 14.0 Hz; J = 7.6 Hz, CH3B3H), 4.09 (2H, q, J = 7.1 Hz, CH2CH3), 4.62 (2H, s, CH3Ph), 5.02-5.12 (2H, m; HC=CH2), 5.46-5.60 (1H, m, HC=CH2), 6.05 (1H, br s, NH), 7.23-7.37 (5H, m, Ph). **13C-NMR (75 MHz, CDCl3)** δ: 14.19 (CH3), 28.67 (COC2H), 31.08 (COCH2CH2), 41.52 (CCH2), 42.35 (CH3Ph), 61.01 (CH2CH3), 64.55 (Cq), 121.36 (HC=CH2), 127.97 (CH arom.), 128.55 (CH arom.), 128.66 (CH arom.), 129.83 (HC=CH2), 136.03 (Cq arom.), 156.55 (NC=ON), 172.87 (HNC=O), 175.04 (C=OO). **IR (cm⁻¹) νmax:** 1713 (C=O), 1774 (C=O). **MS: m/z (%):** 331.2 (M+H+, 100). **Chromatography:** Hex/EtOAc (55/45) Rf = 0.22. **Yield:** 45%.

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

**1H-NMR (300 MHz, CDCl3)** δ: 0.92 (3H, t, J = 7.4 Hz, CH2CH2CH3), 1.25 (3H, t, J = 7.4 Hz, CH3), 2.05-2.20 (4H, m, COCH2CH2), 2.39 (1H, dd, J = 14.0 Hz; J = 7.3 Hz, CH3B3H), 2.47 (1H, dd, J = 14.0 Hz; J = 7.6 Hz, CH3B3H), 4.09 (2H, q, J = 7.1 Hz, CH2CH3), 4.62 (2H, s, CH3Ph), 5.02-5.12 (2H, m; HC=CH2), 5.46-5.60 (1H, m, HC=CH2), 6.05 (1H, br s, NH), 7.23-7.37 (5H, m, Ph). **13C-NMR (75 MHz, CDCl3)** δ: 14.19 (CH3), 28.67 (COC2H), 31.08 (COCH2CH2), 41.52 (CCH2), 42.35 (CH3Ph), 61.01 (CH2CH3), 64.55 (Cq), 121.36 (HC=CH2), 127.97 (CH arom.), 128.55 (CH arom.), 128.66 (CH arom.), 129.83 (HC=CH2), 136.03 (Cq arom.), 156.55 (NC=ON), 172.87 (HNC=O), 175.04 (C=OO). **IR (cm⁻¹) νmax:** 1713 (C=O), 1774 (C=O). **MS: m/z (%):** 331.2 (M+H+, 100). **Chromatography:** Hex/EtOAc (55/45) Rf = 0.22. **Yield:** 45%.

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

**1H-NMR (300 MHz, CDCl3)** δ: 1.25 (1.5H, t, J = 7.2 Hz, CH3), 1.26 (1.5H, t, J = 7.2 Hz, CH3), 1.62 (2H, sextet, J = 7.4 Hz CH2CH2CH3), 1.73 (3H, s, CCH3), 2.08-2.28 (4H, m, COCH2CH2), 2.38 (1H, d, J = 13.6 Hz, CH3B3H), 2.55 (1H, d, J = 13.6 Hz, CH3B3H), 3.43 (2H, dt, J = 2.8 Hz, J = 7.4 Hz, CH2CH3).
4.13 (2H, q, J = 7.2 Hz, CH₂CH₃), 4.79 (1H, s, C=CH₂), 4.91 (1H, d, J = 1.1 Hz, C=CH₂), 6.04 (1H, br s, NH).

13C-NMR (75 MHz, CDCl₃) δ: 11.26 (CH₂CH₂C₂H₅), 14.19 (CH₃), 21.42 (CH₂C₂H₃), 24.30 (CH₃), 28.76 (COCH₂), 31.83 (COCH₂), 40.42 (CH₂CH₂CH₃), 44.62 (CCH₂), 61.07 (C=CH₂), 64.79 (C=CH₂), 116.98 (C=CH₂), 138.75 (C=CH₂), 157.39 (NC=ON), 172.87 (HNC=O), 175.46 (C=OO).

IR (cm⁻¹) νmax: 1646 (C=C), 1713 (br C=O), 1772 (C=O).

MS: m/z (%): 297.8 (M+H⁺, 100).

Chromatography: Hex/EtOAc (4/6) Rf = 0.42. Yield: 63%.

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

1H-NMR (300 MHz, CDCl₃) δ: 0.93 (3H, t, J = 7.4 Hz, CH₂CH₂CH₃), 1.24 (1.5H, t, J = 7.2 Hz, CH₃), 1.25 (1.5H, t, J = 7.2 Hz, CH₃), 1.64 (2H, sextet, J = 7.4 Hz CH₂CH₂CH₃), 2.11-2.20 (2H, m, COCH₂CH₂), 2.23-2.35 (2H, m, COCH₂CH₂), 2.77 (1H, d, J = 14.6 Hz; CCH₂AH₂B), 2.87 (1H, t, J = 7.4 Hz, CH₂CH₂CH₃), 4.12 (1H, q, J = 7.2 Hz, CH₂CH₂CH₃), 4.13 (2H, q, J = 7.2 Hz, CH₂CH₂CH₃), 5.28 (1H, s; HC=CH₂), 5.34 (1H, d, J = 3.3 Hz, HC=CH₂), 6.48 (1H, br s, NH). 13C-NMR (75 MHz, CDCl₃) δ: 11.35 (CH₂CH₂CH₃), 14.22 (CH₃), 21.57 (CH₂CH₂CH₃), 28.33 (COCH₂), 29.77 (COCH₂), 39.54 (CH₂CH₂CH₃), 40.58 (CH₂CH₂CH₃), 42.87 (CH₂CH₂CH₃), 60.90 (CH₂CH₂CH₃), 68.09 (C₂), 118.93 (HC=CH₂), 120.01 (HC=CH₂), 129.98 (HC=CH₂), 133.32 (HC=CH₂), 156.39 (NC=ON), 172.05 (HNC=O), 174.19 (C=OO). IR (cm⁻¹) νmax: 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) Rf = 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 K₂CO₃ (15 mmol, finely ground). The reaction was allowed to reflux until TLC analysis showed that all starting material was consumed. The mixture 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

1H-NMR (300 MHz, CDCl₃) δ: 0.91 (3H, t, J = 7.4 Hz, CH₂CH₂CH₃), 1.24 (1.5H, t, J = 7.2 Hz, CH₃), 1.61 (2H, sextet, J = 7.3 Hz, CH₂CH₂CH₃), 2.05-2.20 (4H, m, COCH₂CH₂), 2.46-2.60 (2H, m, CCH₂), 3.44 (2H, dt, J = 7.4 Hz, J = 1.7 Hz, NCH₂CH), 3.82 (1H, dd, J = 15.6 Hz, J = 6.9 Hz, NCH₂CH₂CH₂), 4.01 (1H, dd, J = 15.6 Hz, J = 6.5 Hz, NCH₂CH₂CH₂), 4.11 (2H, q, J = 7.2 Hz, CH₂CH₂CH₃), 5.10-5.35 (4H, m, 2 x HC=CH₂), 5.42-5.56 (1H, m, HC=CH₂), 5.85-5.99 (1H, m, HC=CH₂). 13C-NMR (75 MHz, CDCl₃) δ: 11.35 (CH₂CH₂CH₂C₂H₅), 14.22 (CH₃), 21.57 (CH₂CH₂CH₂C₂H₅), 28.33 (COCH₂), 29.77 (COCH₂), 39.54 (CH₂CH₂CH₂C₂H₅), 40.58 (CH₂CH₂CH₂C₂H₅), 42.87 (NCH₂CH₂), 60.90 (CH₂CH₂CH₂), 68.09 (C₂), 118.93 (HC=CH₂), 120.01 (HC=CH₂), 129.98 (HC=CH₂), 133.32 (HC=CH₂), 156.39 (NC=ON), 172.05 (HNC=O), 174.19 (C=OO). IR (cm⁻¹) νmax: 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) Rf = 0.52. Yield: 100%.
Ethyl 3,4-diallyl-2,7-dioxo-1-phenyl-1,3-diazepane-4-carboxylate

**1H-NMR (300 MHz, CDCl₃)** δ: 1.24 (3H, t, J = 7.1 Hz, CH₃), 2.14-2.38 (4H, m, COCH₂CH₂), 2.60 (1H, dd, J = 14.2 Hz, J = 6.5 Hz, CCH₃H), 2.67 (1H, dd, J = 14.2 Hz, J = 8.0 Hz, CCH₃H), 3.91 (1H, dd, J = 15.4 Hz, J = 6.9 Hz, NCH₂CH₂CH₃), 4.09 (1H, dd, J = 15.4 Hz, J = 6.6 Hz, NCH₂CH₃CH₃), 4.13 (2H, q, J = 7.1 Hz, CH₂CH₃), 5.19-5.40 (4H, m, 2 x HC=CH₂), 5.57-5.71 (1H, m, HC=CH₂), 5.92-6.06 (1H, m, HC=CH₂), 7.32-7.48 (5H, m, Ph).

**13C-NMR (75 MHz, CDCl₃)** δ: 14.24 (CH₃), 28.48 (COCH₂), 29.97 (COCH₂CH₂), 39.78 (CCH₂CH₂), 43.16 (NCH₂CH₂), 61.00 (CH₂CH₃), 68.18 (C₂ₐ), 119.28 (HC=CH₂), 121.42 (HC=CH₂), 126.22 (CHₐrοm.), 128.35 (CHₐrοm.), 129.13 (CHₐrοm.), 129.77 (HC=CH₂), 131.52 (C₂ₐrοm.), 133.04 (HC=CH₂), 155.22 (NC=ON), 171.99 (HNC=O), 173.23 (C=OO).

**IR (cm⁻¹)** νmax: 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

**1H-NMR (300 MHz, CDCl₃)** δ: 1.24 (3H, t, J = 7.2 Hz, CH₃), 1.86 (3H, s, CCH₃), 2.18-2.38 (4H, m, COCH₂CH₂), 2.63-2.67 (2H, m, CH₂CH), 3.86 (1H, d, J = 15.3 Hz, NCH₂CH₂C), 4.03 (1H, d, J = 15.3 Hz, NCH₂CH₂C), 4.12 (2H, q, J = 7.2 Hz, CH₂CH₃), 4.96 (1H, s, C=CH₂AH₂), 5.02 (1H, s, C=CH₂AH₂), 5.19 (1H, d, J = 3.9 Hz, HC=CH₂AH₂), 5.24 (1H, d, J = 10.7 Hz, HC=CH₂AH₂), 7.31-7.48 (5H, m, Ph).

**13C-NMR (75 MHz, CDCl₃)** δ: 14.23 (CH₃), 20.89 (CC₂H₃), 28.53 (COCH₂), 29.95 (COCH₂CH₂), 39.72 (CCH₂CH₂), 46.41 (NCH₂C), 60.97 (CH₂CH₃), 68.44 (C₂ₐ), 114.96 (C=CH₂), 121.42 (HC=CH₂), 126.17 (CHₐrοm.), 128.32 (CHₐrοm.), 129.12 (CHₐrοm.), 129.83 (HC=CH₂), 131.65 (C₂ₐrοm.), 141.50 (C=CH₂), 155.80 (NC=ON), 172.00 (HNC=O), 173.33 (C=OO).

**IR (cm⁻¹)** νmax: 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

**1H-NMR (300 MHz, CDCl₃)** δ: 1.22 (3H, t, J = 7.0 Hz, CH₃), 2.00-2.28 (4H, m, COCH₂CH₂), 2.50 (1H, dd, J = 14.5 Hz, J = 7.2 Hz, CCH₃H), 2.58 (1H, dd, J = 14.5 Hz, J = 7.3 Hz, CCH₃H), 3.90 (1H, d, J = 15.8 Hz, NCH₂CH₃C), 4.09 (2H, q, J = 7.0 Hz, CH₂CH₃), 4.27 (1H, d, J = 15.8 Hz, NCH₂CH₃C), 4.62 (1H, d, J = 14.4 Hz, NCH₂CH₃C), 4.68 (1H, d, J = 14.4 Hz, NCH₂CH₃C), 4.93-5.10 (2H, m, HC=CH₂), 5.28-5.39 (1H, m, HC=CH₂), 5.42 (1H, d, J = 1.8 Hz, C=CH₃H), 5.50 (1H, d, J = 1.8 Hz, C=CH₃H), 7.25-7.39 (5H, m, Ph).

**13C-NMR (75 MHz, CDCl₃)** δ: 14.22 (CH₃), 28.33 (COCH₂), 29.95 (COCH₂CH₂), 39.54 (CCH₂CH₂), 42.79 (NCH₂CH₂), 46.50 (NCH₂C), 60.84 (CH₂CH₃), 68.38 (C₂ₐ), 116.72 (C=CH₂), 121.28 (HC=CH₂), 128.06 (CHₐrοm.), 128.67 (CHₐrοm.), 129.85 (CHₐrοm.), 129.94 (HC=CH₂), 135.88 (C₂ₐrοm.), 137.45 (CCL), 156.52 (NC=ON), 172.03 (HNC=O), 173.73 (C=OO).

**MS: m/z (%):** 405.2 (M+H⁺, 100), 407.2 (M+H⁺, 29).

**Chromatography:** Hex/EtOAc (7/3) Rf = 0.35. Yield: 70%.

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

*1H-NMR (300 MHz, CDCl3) δ*: 1.16-1.32 (6H, m, 2 x CH2CH3), 1.94-2.15 (4H, m, COCH2CH2), 2.60 (1H, dd, J = 14.2 Hz, J = 6.5 Hz, C(CH3)H), 2.52 (2H, d, J = 7.2 Hz, CCH2), 4.02-4.16 (3H, m, NCH2AHB + CH2CH3), 4.19-4.26 (3H, m, NCH2AHB + CH2CH3), 4.64 (2H, s, CH2Ph), 4.91-5.07 (2H, m, HC=CH2), 5.22-5.36 (1H, m, HC=CH2), 5.99 (1H, d, J = 0.8 Hz, C=CH2AHB), 6.42 (1H, s, C=CH2AHB), 7.24-7.39 (5H, m, Ph).

**13C-NMR (75 MHz, CDCl3) δ*: 14.21 (2 x CH3), 28.36 (COC2H), 29.75 (COCH2C2H2), 39.40 (CCH2CH), 39.75 (NCH2CH), 42.67 (CH2Ph), 60.79 (CCH2CH3), 61.36 (CCH2CH3), 68.43 (Cq), 121.09 (HC=C2H2), 128.00 (CH arom.), 128.64 (CH arom.), 128.73 (CH arom.), 128.60 (C=CH2), 129.62 (HC=CH2), 136.02 (Cq arom.), 156.64 (NC=ON), 165.99 (C=O), 171.85 (HNC=O), 174.00 (C=O).

**IR (cm^-1)** νmax: 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) Rf = 0.07. **Yield:** 45%.

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

*1H-NMR (300 MHz, CDCl3) δ*: 0.91 (3H, t, J = 7.4 Hz, CH2CH2CH3), 1.24 (3H, t, J = 7.2 Hz, CH3), 1.61 (2H, sextet, J = 7.4 Hz, CH2CH2CH3), 1.63 (3H, s, CCH3), 1.96-2.22 (4H, m, COCH2CH2), 2.49 (1H, d, J = 14.4 Hz, C(CH3)H), 2.57 (1H, d, J = 14.4 Hz, C(CH3)H), 3.41 (1H, dt, J = 7.4 Hz, J = 13.5 Hz, NCH2AHBCH2), 3.45 (1H, dt, J = 7.4 Hz, J = 13.5 Hz, NCH2AHBCH2), 3.61 (1H, dd, J = 15.4 Hz, J = 7.7 Hz, NCH2AHBCH2), 4.11 (2H, q, J = 7.2 Hz, C(CH3)H), 4.21 (1H, ddt, J = 15.4 Hz, J = 5.5 Hz, J = 1.4 Hz, NCH2AHBCH2), 4.72 (1H, d, J = 0.8 Hz, C=CH2AHB), 4.86 (1H, t, J = 1.5 Hz, C=CH2AHB), 5.20 (1H, dd, J = 9.9 Hz, J = 0.8 Hz, H=CH2AHB), 5.31 (1H, dqq, J = 17.0 Hz, J = 1.4 Hz, H=CH2AHB), 5.87-6.00 (1H, m, H=CH2AHB).

**13C-NMR (75 MHz, CDCl3) δ*: 11.34 (CH2CH2CH3), 14.24 (CH3), 21.45 (CH2CH2CH3), 23.67 (CH3), 28.13 (COCH2), 30.88 (COCH2CH2), 40.58 (CH2CH2CH3), 42.45 (CCH2C), 43.23 (NCH2CH), 60.82 (CH2CH3), 67.97 (Cq), 116.58 (C=CH2), 118.96 (HC=CH2), 133.19 (HC=CH2), 138.77 (C=CH2), 156.32 (NC=ON), 172.00 (HNC=O), 174.39 (C=O).

**IR (cm^-1)** νmax: 1710 (br C=O), 1767 (C=O). **MS: m/z (%):** 419.2, 421.3 (M+H+, 100).

**Chromatography:** Hex/EtOAc (6/4) Rf = 0.63. **Yield:** 72%.

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

*1H-NMR (300 MHz, CDCl3) δ*: 1.22 (3H, t, J = 7.1 Hz, CH3), 2.01-2.20 (4H, m, COCH2CH2), 2.49 (1H, d, J = 14.5 Hz, J = 7.4 Hz, CH2AH2CH), 2.56 (1H, dd, J = 14.5 Hz, J = 6.9 Hz, CH2AH2CH), 3.89-4.12 (4H, m, NCH2AH2CH), 4.09 (2H, q, J = 7.1 Hz, CH2AH2CH), 4.64 (2H, s, NCH2Ph), 4.79-5.08 (2H, m, HC=CH2), 5.23 (1H, s, C=CH2AHB), 5.23-5.37 (1H, m, HC=CH2), 5.37 (1H, s, C=CH2AHB), 7.25-7.40 (5H, m, Ph).

**13C-NMR (75 MHz, CDCl3) δ*: 11.34 (CH2CH2C2H3), 14.24 (CH3), 21.45 (CH2CH2CH3), 23.67 (CH3), 28.13 (COCH2), 30.88 (COCH2CH2), 40.58 (CH2CH2CH3), 42.45 (CCH2C), 43.23 (NCH2CH), 60.82 (CH2CH3), 67.97 (Cq), 116.58 (C=CH2), 118.96 (HC=CH2), 133.19 (HC=CH2), 138.77 (C=CH2), 156.32 (NC=ON), 172.00 (HNC=O), 174.39 (C=O).

**IR (cm^-1)** νmax: 1645 (C=C), 1708 (C=O), 1735 (C=O), 1767 (C=O). **MS: m/z (%):** 419.2, 421.3 (M+H+, 100). **Yield:** 100%.
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(1H)-carboxylates:

The diazepane (0.6 mmol) was dissolved in CH2Cl2 (10 mL, freshly distilled from CaH2) and the second generation Grubbs’ catalyst (0.03 mmol) was added. The reaction was allowed to reflux for 4h under a N2-atmosphere. The mixture 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(1H)-carboxylate

1H-NMR (300 MHz, CDCl3) δ: 1.23 (3H, t, J = 7.2 Hz, CH2CH3), 1.76 (3H, s, CCH3), 2.19-2.52 (6H, m, COCH2CH2 and CCH3), 3.50 (1H, d, J = 18.0 Hz, NCH2CH3), 4.12 (2H, q, J = 7.2 Hz, CH2CH3), 4.34 (1H, d, J = 18.0 Hz, NCH2CH3), 5.51 (1H, t, J = 1.9 Hz, CH), 7.35-7.49 (5H, m, Ph).

13C-NMR (75 MHz, CDCl3) δ: 14.22 (CH2CH3), 20.21 (CCH3), 28.79 (COCH2), 29.05 (COCH2CH2), 31.89 (CCH2CH3), 41.39 (NCH2), 60.29 (Cq), 61.07 (CH2CH2), 116.05 (CH), 121.71 (CH), 126.26 (CH), 128.31 (CH), 129.16 (CH), 130.57 (CCH3), 131.68 (Cq), 153.96 (NC=ON), 172.58 (HNC=O), 174.74 (C=CO). MS: m/z (%): 343.2 (M+H+, 100). IR (cm⁻¹) νmax: 1721 (br C=O), 1775 (C=O).

Chromatography: Hex/EtOAc (7/3) Rf = 0.29. Yield: 79%.
1H-NMR (300 MHz, CDCl3) δ: 0.93 (3H, t, J = 7.4 Hz, CH3 pr), 1.24 (3H, t, J = 7.1 Hz, CH2CH3), 1.66 (2H, sextet, J = 7.4 Hz, NCH2CH2), 2.05-2.33 (6H, m, COCH2CH2 and CCH2), 3.49 (2H, dt, J = 7.4 Hz, J = 1.6 Hz, NCH2CH2), 3.56 (1H, d, J = 18.2 Hz + small splitting, NCHAHB), 4.10 (2H, q, J = 7.1 Hz, CH2CH3), 4.41 (1H, d, J = 18.2 Hz + small splitting, NCHAHB), 5.78 (2H, t, J = 1.9 Hz + small splitting, HC=CH).

13C-NMR (75 MHz, CDCl3) δ:
- 11.22 (CH3 pr), 14.15 (CH2CH3), 21.53 (CH2 pr), 28.43 (COCH2), 28.80 (COCH2CH2), 31.65 (CH2CH2), 37.71 (NCH2), 40.37 (NCH2 pr), 60.28 (Cq), 60.87 (CH2CH3), 121.59 (CH), 123.27 (CH), 155.15 (NC=ON), 172.39 (HNC=O), 175.74 (C=OO).

IR (cm⁻¹) νmax: 1656 (C=C), 1709 (br C=O), 1771 (C=O).

MS: m/z (%): 295.2 (M+H+, 100).

Chromatography: first Hex/EtOAc (3/1) untill Rf = 0.26, then strip with EtOAc + 5% CH2Cl2. Yield: 55%.

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

1H-NMR (300 MHz, CDCl3) δ:
- 1.20 (3H, t, J = 7.2 Hz, CH2CH3), 1.30 (3H, t, J = 7.0 Hz, CH2CH3), 2.04-2.17 (4H, m, COCH2CH2), 2.41 (1H, dq, J = 18.4 Hz, J = 2.8 Hz, CCH2H6), 2.54 (1H, dd, J = 18.4 Hz, J = 5.5 Hz, CCH2H6), 3.73 (1H, ddt, J = 18.7 Hz, J = 1.9 Hz, NCHAHB), 4.07 (2H, q, J = 7.2 Hz, CH2CH3), 4.21 (1H, dq, J = 10.6 Hz, J = 7.0 Hz, CH2H2CH3), 4.25 (1H, dq, J = 10.6 Hz, J = 7.1 Hz, CH2H2CH3), 4.68 (2H, s, NCH2Ph), 4.70 (1H, dt, J = 18.7 Hz, J = 1.9 Hz, NCH2H6), 6.98 (1H, dd, J = 5.8 Hz, J = 2.2 Hz, CH), 7.29-7.59 (5H, m, Ph).

13C-NMR (75 MHz, CDCl3) δ:
- 14.19 (CH2CH3), 14.27 (CH2CH3), 28.61 (COCH2), 28.76 (COCH2CH2), 32.09 (COCH2CH2), 36.91 (NCH2), 42.58 (NCH2Ph), 59.92 (Cq), 60.99 (CH2CH3), 61.16 (CH2CH3), 128.09 (CH), 128.35 (CH), 133.42 (HC=C), 136.03 (HC=C), 137.67 (Cq), 154.61 (NC=ON), 164.28 (CCOOEt), 172.13 (HNC=O), 174.68 (C=OO).

IR (cm⁻¹) νmax: 1659 (C=C), 1716 (br C=O), 1774 (C=O).

MS: m/z (%): 415.3 (M+H+, 100).

Chromatography: first Hex/EtOAc (6/4) Rf = 0.25. Yield: 93%.

Instead of the second generation Grubbs’ catalyst, the second generation Hoveyda-Grubbs’ catalyst was used for this reaction.
NCHaH, bPh), 5.88 (1H, q-like, J = 2.4 Hz, CH), 7.28-7.41 (5H, m, Ph).

13C-NMR (75 MHz, CDCl3) δ: 14.21 (CH2C6H3), 28.62 (COC6H2), 28.73 (COCH2C6H2), 31.58 (CC6H2CH), 38.38 (NCH2), 42.56 (NC6H2Ph), 45.83 (CH2Cl), 60.30 (Cq), 60.97 (CH3C6H2), 121.85 (CH), 128.06 (CH arom.), 128.50 (CH arom.), 128.80 (CH arom.), 131.45 (CCH2Cl), 136.08 (Cq arom.), 154.77 (NC=ON), 172.33 (HNC=O), 175.00 (C=OO).

IR (cm−1) νmax: 1713 (br C=O), 1771 (C=O).

MS: m/z (%): 391.2/393.2 (M+H+, 100).

Chromatography: Hex/EtOAc (7/3) Rf = 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(1H)-carboxylate

Instead of refluxing in CH2Cl2, the reaction was refluxed in dry benzene for 16 hours.

1H-NMR (300 MHz, CDCl3) δ: 0.93 (3H, t, J = 7.4 Hz, CH2CH2CH3), 1.24 (3H, t, J = 7.2 Hz, CH2CH3), 1.66 (2H, sextet, J = 7.4 Hz, NCH2CH2), 1.74 (3H, s, CCH3), 2.05-2.24 (6H, m, COCH2CH2 and CCH2), 3.49 (2H, dt, J = 7.4 Hz, J = 1.7 Hz, NCH2CH2), 3.51 (1H, dddd, J = 17.9 Hz, J = 12.5 Hz, J = 4.6 Hz, J = 2.2 Hz, NCH2AHB), 4.10 (2H, q, J = 7.2 Hz, CH2CH3), 4.36 (1H, d, J = 17.9 Hz, NCH2H2B), 5.44 (1H, s, CH).

13C-NMR (75 MHz, CDCl3) δ: 11.29 (CH3 pr), 14.22 (CH2C6H3), 21.60 (CH2 pr), 22.93 (CC6H3), 28.48 (COC6H2), 28.71 (COCH2C6H2), 35.95 (CC6H2C), 37.43 (NCH2), 40.12 (NCH2 pr), 60.41 (CH2CH3), 60.64 (Cq), 116.83 (CH), 128.83 (C), 154.98 (NC=ON), 171.90 (HNC=O), 175.26 (C=OO).

IR (cm−1) νmax: 1712 (br C=O), 1770 (C=O).

MS: m/z (%): 309.8 (M+H+, 100).

Chromatography: Hex/EtOAc (7/3) Rf = 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(1H)-carboxylate

Instead of refluxing in CH2Cl2, the reaction was refluxed in dry benzene for 16 hours.

1H-NMR (300 MHz, CDCl3) δ: 1.20 (3H, t, J = 7.1 Hz, CH3), 2.00-2.33 (4H, m, COCH2CH2), 2.39-2.41 (2H, m, CH2CH), 3.63 (1H, dq, J = 17.9 Hz, J = 2.6 Hz, NCH4H2CCL), 4.07 (2H, q, J = 7.1 Hz, CH2CH3), 4.49 (1H, dq, J = 17.9 Hz, J = 2.2 Hz, NCH4H2CCL), 4.67 (2H, s, NCH2Ph), 5.86 (1H, dq, J = 1.6 Hz, J = 3.5 Hz, CH), 7.27-7.39 (5H, m, Ph).

13C-NMR (75 MHz, CDCl3) δ: 14.19 (CH3), 28.48 (COC6H2), 28.71 (COCH2C6H2), 32.61 (CC6H2CH), 41.87 (NCH2C), 42.64 (NCH2Ph), 60.07 (Cq), 61.02 (CH2CH3), 119.28 (CH), 127.31 (CCI), 128.14 (CH arom.), 128.52 (CH arom.), 128.83 (CH arom.), 135.91 (Cq arom.), 154.51 (NC=ON), 172.20 (HNC=O), 174.49 (C=OO).

IR (cm−1) νmax: 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) Rf = 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(1H)-carboxylate

Instead of refluxing in CH2Cl2, the reaction was refluxed in dry benzene for 16 hours.

1H-NMR (300 MHz, CDCl3) δ: 0.93 (3H, t, J = 7.4 Hz, CH2CH2CH3), 1.24 (3H, t, J = 7.2 Hz, CH2CH3), 1.66 (2H, sextet, J = 7.4 Hz,
NCH₂CH₂), 2.07-2.36 (4H, m, COCH₂CH₂), 2.51 (1H, d, J = 17.4 Hz, CCH₃H₆C), 2.64 (1H, dq, J = 17.4 Hz, J = 3.1 Hz, CCH₃H₆C), 3.49 (2H, dt, J = 7.4 Hz, J = 2.2 Hz, NCH₂CH₂), 3.61 (1H, dq, J = 18.4 Hz, J = 3.2 Hz, NCH₃H₆b), 4.11 (2H, q, J = 7.2 Hz, CH₂CH₃), 4.49 (1H, dt, J = 18.4 Hz, J = 3.2 Hz, NCH₃H₆b), 5.90 (1H, q, J = 3.2 Hz, CH). **¹³C-NMR (75 MHz, CDCl₃) δ:** 11.26 (CH₃ pr), 14.21 (CH₂CH₃), 21.52 (CH₂ pr), 28.70 (COCH₂CH₂), 38.16 (NCH₂), 38.77 (CCH₂C), 40.64 (NCH₂ pr), 61.08 (CH₂CH₃), 61.55 (Cₙ), 120.17 (CH), 126.86 (CCI), 154.97 (NC=ON), 172.20 (HNC=O), 174.29 (C=OO). **IR (cm⁻¹) νmax:** 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) Rₕ = 0.43. **Yield:** 77%. 