Electronic Supplementary Information (ESI)

Facile Synthetic Route to Diazepinone Derivatives via Ring Closing Metathesis (RCM) and Its Application for Human Cytidine Deaminase Inhibitors

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1. General Information

Chemical reagents were obtained from Aldrich chemical company. All reaction solvents were dried before use following the literature method. Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 precoated silica gel plate. Subsequent to elution, plates were detection of UV radiation (254 nm). Further visualization was possible by staining with basic solution of phosphomolybdic acid. Column chromatography was performed using E. Merck silica gel 230-400 mesh.

Melting points were determined on a Fisher scientific melting point apparatus. Nuclear magnetic resonance (NMR) spectra were recorded on a VARIAN 500 (500 MHz). Chemical shifts (δ) in CDCl₃ were reported in the scale relative to CDCl₃ (7.26 ppm), CD₃OD (4.87 ppm) for ¹H NMR, and to CDCl₃ (77.0 ppm), CD₃OD (49.1 ppm) for ¹³C NMR. NMR spectra are reported as: s = singlet, d = doublet, dd = doublet of doublets, m = multiplet, brs = broad; coupling constant (s) in Hz; integration. The number of protons (n) for a given resonance is indicated by nH. Coupling constants are reported as a J value in Hz.

LRMS(ESI) spectra were recorded on Shimadzu LCMS 2010 and HRMS(FAB) spectra on JMS-700 Matation.
General procedure for the synthesis of 5 and 44: To a solution of the optically pure amino-1-propanol (3.92 g, 52.2 mmol) in CH₂Cl₂ (100 mL) was added 4Å° molecular sieves (10.0 g) and p-methoxybenzaldehyde (7.11 g, 52.2 mmol). The solution was then stirred at room temperature for 3 h, after the reaction mixture was filtered through the cellite and residue was concentrated under reduced pressure. The solution of residue in EtOH (100 mL) was reacted with NaBH₄ (2.37 g, 62.6 mmol) and the resulting mixture was stirred at room temperature for 2 h. The reaction mixture was addition of a sat. NH₄Cl solution and concentrated under reduced pressure. The solution was neutralized with 1N NaOH, and extracted with CH₂Cl₂ (3 x 75.0 mL). The combined organic extracts were washed with brine and concentrated under vacuum to get as white solid. This compound was used without further purification.

(S)-2-(4-Methoxybenzylamino)propan-1-ol (5): Yield = 9.48 g, 93.0%; mp = 72 °C; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.23 (2H, d, J = 8.3 Hz), 6.85 (2H, d, J = 8.6 Hz), 4.58 (1H, brs), 3.82 (1H, s),

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3.78 (3H, s), 3.67 (1H, d, J = 12.7 Hz), 3.57 (1H, dd, J = 3.9, 10.8 Hz), 3.28 (1H, dd, J = 7.0, 10.6 Hz), 2.82 (1H, m), 2.43 (1H, brs), 1.07 (3H, d, J = 6.6 Hz); 13C NMR (125 MHz; CDCl3; Me4Si) δ 158.7, 129.3, 128.5, 113.9, 65.4, 55.2, 53.9, 50.4, 16.9; LRMS (ESI) m/z 196 [M + H]+.

(R)-2-(4-Methoxybenzylamino)propan-1-ol (44): Yield = 9.44 g, 92.6%; mp = 70 °C; 1H NMR (500 MHz; CDCl3; Me4Si) δ 7.24 (2H, d, J = 8.6 Hz), 6.86 (2H, d, J = 8.6 Hz), 4.59 (1H, brs), 3.83 (1H, s), 3.78 (3H, s), 3.68 (1H, d, J = 13.0 Hz), 3.58 (1H, dd, J = 4.2, 10.8 Hz), 3.30 (1H, dd, J = 6.9, 10.8 Hz), 2.84 (1H, m), 2.70 (1H, brs), 1.09 (3H, d, J = 6.6 Hz); 13C NMR (125 MHz; CDCl3; Me4Si) δ 158.8, 129.3, 128.5, 113.9, 65.3, 55.2, 53.7, 50.2, 16.8; LRMS (ESI) m/z 196 [M + H]+.

General procedure for the synthesis of 6 and 14: A solution of tert-butyldimethylsilyl chloride (5.47 g, 36.3 mmol) in CH2Cl2 (50.0 mL) was added dropwise to a stirred solution of 5 or 44 (6.44 g, 33.0 mmol) and Et3N (9.18 mL, 66.0 mmol) in CH2Cl2 (100 mL). The mixture was stirred at room temperature for 12 h, then sat. NH4Cl solution (50.0 mL) was added, and extracted with CH2Cl2 (3 x 100 mL) and washed with brine. The organic fraction was dried over MgSO4, filtered, and solvent was evaporated under reduced pressure giving relatively pure oil.

(S)-1-(tert-Butyldimethylsilyloxy)-N-(4-methoxybenzyl)propan-2-amine (6): Yield = 10.1 g, 99.0%; 1H NMR (500 MHz; CDCl3; Me4Si) δ 7.26 (2H, d, J = 8.6 Hz), 6.85 (2H, d, J = 8.6 Hz), 3.84 (1H, d, J = 13.0 Hz), 3.78 (3H, s), 3.71 (1H, d, J = 13.2 Hz), 3.57 (1H, dd, J = 4.6 Hz), 3.49 (1H, dd, J = 7.2, 9.9 Hz), 2.79 (1H, m), 1.05 (3H, d, J = 6.6 Hz), 0.89 (9H, s), 0.04 (6H, s); 13C NMR (125 MHz; CDCl3; Me4Si) δ 158.7, 129.4, 127.5, 113.8, 67.1, 55.3, 53.8, 50.3, 25.9, 18.2, 16.4, -5.4; LRMS (ESI) m/z 310 [M + H]+.

(R)-1-(tert-Butyldimethylsilyloxy)-N-(4-methoxybenzyl)propan-2-amine (14): Yield = 10.1 g, 99.4%; 1H NMR (500 MHz; CDCl3; Me4Si) δ 7.24 (2H, d, J = 8.3 Hz), 6.85 (2H, d, J = 8.6 Hz), 3.83 (1H, s), 3.79 (3H, s), 3.68 (1H, d, J = 13.0 Hz), 3.55 (1H, dd, J = 4.7, 9.8 Hz), 3.45 (1H, dd, J = 7.3, 10.0 Hz), 2.80 (1H, m), 1.02 (3H, d, J = 6.4 Hz), 0.89 (9H, s), 0.04 (6H, s); 13C NMR (125 MHz; CDCl3; Me4Si): δ 158.6, 129.2, 127.5, 113.8, 67.1, 55.2, 53.8, 50.5, 25.9, 18.2, 16.7, -5.4; LRMS (ESI) m/z 310 [M + H]+.

General procedure for the synthesis of 9 and 45: To a THF (60.0 mL) solution of crude 6 or 14 (9.48 g, 30.0 mmol) in an ice bath, the allyl isocyanate (3.23 mL, 36.8 mmol) was added dropwise. The reaction temperature was allowed to room temperature over the 18 h. The solvent was removed under vacuum and the residue was purified by column chromatography (8% EtOAc in hexane) to afford compound.

(S)-3-Allyl-1-(1-(tert-butyldimethylsilyloxy)propan-2-yl)-1-(4-methoxybenzyl)urea (9): Yield = 9.15 g, 76.1%; 1H NMR (500 MHz; CDCl3; Me4Si) δ 7.22 (2H, d, J = 8.6 Hz), 6.85 (2H, d, J = 8.6 Hz), 5.76 (1H, m), 4.98 (2H, m), 4.50 (1H, d, J = 17.1 Hz), 4.35 (1H, d, J = 16.9 Hz), 4.26 (1H, m), 3.81 (2H, m), 3.79 (3H, s), 3.56 (2H, m), 1.17 (3H, d, J = 6.9 Hz), 0.87 (9H, s), 0.02 (6H, s); 13C
NMR (125 MHz; CDCl₃; Me₄Si) δ 159.0, 158.7, 135.8, 131.3, 127.9, 115.0, 114.1, 66.5, 55.3, 53.1, 46.7, 43.3, 25.9, 18.2, 15.2, -5.6; LRMS (ESI) m/z 393 [M + H]⁺.

(R)-3-Allyl-1-(1-(tert-butyldimethylsilyloxy)propan-2-yl)-1-(4-methoxybenzyl)urea (45): Yield = 9.38 g, 78.0%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.22 (2H, d, J = 8.3 Hz), 6.85 (2H, d, J = 8.3 Hz), 5.80 (1H, m), 5.00 (2H, m), 4.50 (1H, d, J = 17.1 Hz), 4.35 (1H, d, J = 16.9 Hz), 4.28 (1H, m), 3.81 (2H, m), 3.79 (3H, s), 3.61 (2H, m), 1.17 (3H, d, J = 7.1 Hz), 0.88 (9H, s), 0.02 (6H, s); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 159.0, 158.7, 135.8, 131.3, 127.8, 115.0, 114.1, 66.5, 55.3, 53.1, 46.7, 43.3, 25.8, 18.2, 15.2, -5.6; LRMS (ESI) m/z 393 [M + H]⁺.

**General procedure for the synthesis of 13 and 15:** To a solution of protected urea 9 or 45 (9.38 g, 23.9 mmol), Et₃N (4.32 mL, 31.1 mmol) and DMAP (1.46 g, 11.9 mmol) in 50.0 mL of dry THF at 0 °C was added dropwise di-tert-butyl dicarbonate (6.79 g, 31.1 mmol) in 20.0 mL THF. The reaction mixture was refluxed under N₂ for 24 h. The reaction mixture was quenched with water (20.0 mL) and extracted with EtOAc (3 x 50.0 mL). The combined organic layer was washed with brine, dried over anhydrous MgSO₄, concentrated in vacuo, and purified by column chromatography (6% EtOAc in hexane) to afford an oil.

(S)-tert-Butylallyl((1-(tert-butyldimethylsilyloxy)propan-2-yl)(4-methoxybenzyl)carbamoyl)carbamate (13): Yield = 10.3 g, 87.8%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.23 (2H, m), 6.84 (2H, d, J = 8.6 Hz), 5.87(1H, m), 5.22 (1H, m), 5.13 (1H, d, J = 10.3 Hz), 4.40 (1H, d, J = 16.6 Hz), 4.12(1H, d, J = 16.6 Hz), 3.97 (1H, m), 3.80 (3H, s), 3.63 (2H, m), 3.49 (2H, d, J = 5.4 Hz), 1.49 (9H, s), 1.49 (3H, d, J = 6.8 Hz), 0.87 (9H, s), 0.01 (6H, s); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 152.9, 131.2, 128.7, 119.0, 117.7, 113.8, 81.7, 65.3, 55.7, 55.3, 49.4, 45.0, 28.3, 25.9, 18.2, -5.5; LRMS (ESI) m/z 515 [M + Na]⁺.

(R)-tert-Butylallyl((1-(tert-butyldimethylsilyloxy)propan-2-yl)(4-methoxybenzyl)carbamoyl)carbamate (15): Yield = 11.3 g, 96.6%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.23 (2H, m), 6.83 (2H, d, J = 8.3 Hz), 5.87(1H, m), 5.22 (1H, d, J = 17.1 Hz), 5.12 (1H, d, J = 10.0 Hz), 4.44 (2H, m), 4.02 (3H, m), 3.79 (3H, s), 3.61 (2H, m), 1.49 (9H, s), 1.20 (3H, d, J = 6.8 Hz), 0.87 (9H, s), 0.01 (6H, s); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 158.8, 152.9, 133.9, 128.7, 117.6, 113.8, 81.7, 65.2, 55.7, 55.3, 49.4, 28.3, 25.9, 18.2, -5.5; LRMS (ESI) m/z 515 [M + Na]⁺.

**General procedure for the synthesis of 11 and 16:** The compound 13 or 15 (11.3 g, 22.9 mmol) was dissolved in 100 mL of THF and pyridine solution, after added HF-pyridine (70% as hydrogen fluoride). The reaction mixture was stirred at room temperature for 3 h. Then, the reaction mixture was concentrated under reduce pressure. The crude product was purified by column chromatography (30% EtOAc in hexane) to afford alcohol. The free alcohol (6.63 g, 17.5 mmol) was dissolved in a CH₂Cl₂ (100 mL) reacted with Dess-Martin periodiane (65.0 mL, 15% in CH₂Cl₂, 22.8 mmol), initially stirred for 5 min at 0 °C, and then stirred for 1 h at room temperature. The reaction was...
quenched by the addition of sat. NaHCO₃, and the organic material was extracted with CH₂Cl₂ (3 x 50.0 mL). Combined organic extracts were washed with brine, dried over MgSO₄, and concentrated in vacuo. The product was purified by column chromatography (10% EtOAc in hexane) to afford aldehyde as an oil. Finally, the solution of methyltriphenylphosphonium iodide (9.05 g, 22.4 mmol) in anhydrous diethyl ether (200 ml) at 0 °C, NaHMDS (1.0 M in THF, 19.4 mL, 19.4 mmol) was added dropwise and stirred for 30 min under N₂. The aldehyde (5.62 g, 14.9 mmol) in dry ether (100 ml) was added dropwise at 0 °C and stirred for 1 h. The reaction was quenched with sat. NH₄Cl solution and the mixture was extracted with EtOAc (3 x 50.0 mL) and dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography (6% EtOAc in hexane) to afford as an oil. (**S**)-**tert-**Butylallyl(but-3-en-2-yl(4-methoxybenzyl)carbamoyl)carbamate (11): Yield = 4.08 g, 73.0%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.19 (2H, d, J = 7.1 Hz), 6.82 (2H, d, J = 8.8 Hz), 5.89 (1H, m), 5.81 (1H, m), 5.15 (4H, m), 4.67 (1H, m), 4.43 (2H, s), 3.93 (2H, m), 3.78 (3H, s), 1.48 (9H, s), 1.27 (3H, d, J = 6.8 Hz); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 158.7, 156.9, 152.8, 138.2, 133.7, 130.3, 128.6, 118.0, 116.2, 113.7, 81.8, 55.2, 49.3, 28.3, 17.2; LRMS (ESI) m/z 397 [M + Na]⁺.

(**R**)-**tert-**Butylallyl(but-3-en-2-yl(4-methoxybenzyl)carbamoyl)carbamate (16): Yield = 4.16 g, 74.4%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.19 (2H, d, J = 6.6 Hz), 6.82 (2H, d, J = 8.6 Hz), 5.95 (1H, m), 5.81 (1H, m), 5.16 (4H, m), 4.67 (1H, m), 4.24 (2H, s), 3.91 (2H, m), 3.79 (3H, s), 1.47 (9H, s), 1.27 (3H, d, J = 6.8 Hz); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 158.7, 156.9, 152.8, 138.3, 133.7, 130.3, 128.7, 118.0, 116.2, 113.7, 81.8, 55.2, 49.3, 28.3, 17.2; LRMS (ESI) m/z 397 [M + Na]⁺.

**General procedure for the synthesis of 12 and 28:** A round bottomed flask charged with the Grubb’s catalyst 2nd generation (623 mg, 10.0 mol%) was evacuated and filled with argon three times before the addition of the diene 11 or 16 (2.75 g, 7.30 mmol) in CH₂Cl₂ (130 mL). The resulting solution was stirred under argon for 12 h, after 4 h stirred in air. Then, removed the solvent in vacuo gave a black oil residue. The crude product was purified by column chromatography (23% EtOAc in hexane) to afford as light black oil.

(**S**)-**tert-**Butyl-3-(4-methoxybenzyl)-4-methyl-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepine-1-carboxylate (12): Yield = 2.43 g, 95.9%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.25 (2H, d, J = 8.8 Hz), 6.84 (2H, d, J = 8.6 Hz), 5.63 (2H, m), 4.59 (1H, d, J = 14.4 Hz), 4.56 (1H, d, J = 4.8 Hz), 4.47 (1H, d, J = 15.1 Hz), 3.79 (3H, s), 3.75 (1H, d, J = 7.3 Hz), 3.73 (1H, m), 1.50 (9H, s), 1.19 (3H, d, J = 7.1 Hz); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 159.0, 157.3, 152.8, 129.6, 129.2, 125.9, 113.9, 81.4, 55.1, 54.6, 52.2, 42.6, 28.1, 20.5; LRMS (ESI) m/z 369 [M + Na]⁺.

(**R**)-**tert-**Butyl-3-(4-methoxybenzyl)-4-methyl-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepine-1-carboxylate (28): Yield = 2.44 g, 96.0%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.24 (2H, d, J = 8.6 Hz), 6.85 (2H, d, J = 8.6 Hz), 5.64 (2H, m), 4.59 (1H, d, J = 4.8 Hz), 4.47 (2H, d, J = 15.1 Hz), 3.80 (3H, s), 3.75 (1H, d, J = 7.3 Hz), 3.73 (1H, m), 1.59 (3H, d, J = 7.1 Hz), 1.50 (9H, s); ¹³C NMR (125
MHz; CDCl$_3$; Me$_4$Si) $\delta$ 159.1, 157.3, 152.9, 129.7, 129.2, 125.9, 113.9, 81.5, 55.2, 54.6, 52.2, 42.6, 28.2, 20.6; LRMS (ESI) m/z 369 [M + Na]$^+$. 

**General procedure for the synthesis of 33 and 34:** A solution of 12 or 28 (2.12 g, 6.12 mmol) in 40.0 mL of CH$_2$Cl$_2$ was reacted with 10.0 ml of trifluoroacetic acid at room temperature for 3 h. The reaction mixture was concentrated and the residual trifluoroacetic acid was removed by co-evaporation with several portion of CH$_2$Cl$_2$. The residue was neutralized with 1N NaOH, extracted with CH$_2$Cl$_2$ (3 x 75.0 mL) and washed with brine. The organic extracts were dried over MgSO$_4$ and concentrated under vacuum to get crude product as black solid. The residue was purified by column chromatography (3% MeOH in CH$_2$Cl$_2$) to afford as a black oil.

**(S)-4-Methyl-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (33):** Yield = 610 mg, 79.0%; $^1$H NMR (500 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 5.76 (1H, m), 5.65 (1H, m), 5.26 (1H, brs), 4.90 (1H, brs), 4.14 (1H, m), 3.80 (1H, dd, $J$ = 16.6, 3.4 Hz), 3.63 (1H, dd, $J$ = 15.1, 3.5 Hz), 1.30 (3H, d, $J$ = 7.8 Hz); $^{13}$C NMR (125 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 164.1, 133.3, 125.7, 47.1, 40.9, 22.3; LRMS (ESI) m/z 127 [M + H]$^+$; HRMS (FAB) m/z calcd for C$_6$H$_{11}$N$_2$O [M+H]$^+$ 127.0793, found 127.0871.

**(R)-4-Methyl-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (34):** Yield = 610 mg, 79.0%; $^1$H NMR (500 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 5.79 (1H, m), 5.68 (1H, m), 5.44(1H, brs), 5.06 (1H, brs), 4.18 (1H, m), 3.82 (1H, dd, $J$ = 16.6, 4.9 Hz), 3.65 (1H, dd, $J$ = 16.5, 4.8 Hz), 1.31 (3H, d, $J$ = 7.1 Hz); $^{13}$C NMR (125 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 163.8, 133.4, 125.8, 47.0, 40.7, 22.2; LRMS (ESI) m/z 127 [M + H]$^+$; HRMS (FAB) m/z calcd for C$_6$H$_{11}$N$_2$O [M+H]$^+$ 127.0793, found 127.0871.

**(R)-2-((tert-Butyldimethylsilyloxy)methyl)pyrrolidine (17):** A solution of tert-butyldimethylsilane chloride (3.27 g, 21.8 mmol) in CH$_2$Cl$_2$ (50.0 mL) was added dropwise to a stirred solution of (R)-pyrrolidin-2-ylmethanol (2.00 g, 19.8 mmol) and Et$_3$N (3.58 mL, 25.7 mmol) in CH$_2$Cl$_2$ (100 mL). The mixture was stirred at room temperature for 12 h, then washed with brine and extracted with
CH₂Cl₂ (3 x 100 mL). The organic fraction was dried over MgSO₄, filtered, and solvent was evaporated under reduced pressure to afford a crude oil (4.54 g, 99.9%). ^1^H NMR (500 MHz; CDCl₃; Me₄Si) δ 3.59 (1H, m), 3.52 (1H, m), 3.17 (1H, m), 2.98 (1H, m), 2.84 (1H, m), 2.36 (1H, brs), 1.75 (3H, m), 1.44 (1H, m), 0.89 (9H, m); ^13^C NMR (125 MHz; CDCl₃; Me₄Si) δ 65.6, 60.0, 46.4, 28.6, 27.4, 25.9, 25.3, 23.2, 18.3, -5.4; LRMS (ESI) m/z 216 [M + H]^+. (R)-tert-Butylallyl(2-((tert-butyldimethylsilyloxy)methyl)pyrrolidine-1-carbonyl)carbamate (18): The TBS protected product 17 (4.50 g, 20.9 mmol) was dissolved in 60.0 mL of dried THF and the solution was cooled in an ice bath. After the allyl isocyanate (2.04 mL, 23.2 mmol) was added quickly dropwise. The solution was then stirred at room temperature for 18 h. The solvent was removed in vacuo and the residue was purified by column chromatography (10% EtOAc in hexane) to afford a white solid. To the solution of the protected urea (3.40 g, 11.5 mmol) and DMAP (700 mg, 5.75 mmol) in 30.0 mL of dry THF was added Et₃N (42.40 mL, 17.3 mmol) at 0 °C. The reaction mixture was stirred at the same temperature for 0.5 h and was then added dropwise a solution of di-tert-butyl dicarbonate (5.01 g, 23.0 mmol) in THF (20.0 ml). The reaction mixture was then refluxed under N₂ for 24 h. The reaction mixture was quenched with water (10.0 mL) and extracted with EtOAc (3 x 30.0 mL). The combined extracts were washed with brine, dried over anhydrous MgSO₄, concentrated in vacuo, and purified by column chromatography (10% EtOAc in hexane) to afford 18 (3.99 g, 87.0%) as a yellowish oil. ^1^H NMR (500 MHz; CDCl₃; Me₄Si) δ 5.86 (1H, m), 5.19 (1H, d, J=17.12, 0.98 Hz), 5.11 (1H, d, J=9.54 Hz), 4.03 (3H, m), 3.86 (1H, brs), 3.42 (4H, m), 1.95 (4H, m), 1.77 (1H, brs), 1.46 (9H, s), 0.87 (9H, s), 0.03 (6H, s); ^13^C NMR (125 MHz; CDCl₃; Me₄Si) δ 154.9, 133.8, 117.5, 81.3, 62.7, 59.4, 48.6, 28.2, 25.8, 23.9, 18.2, 5.5; LRMS (ESI) m/z 421 [M + Na]^+. (R)-tert-Butylallyl(2-vinylpyrrolidine-1-carbonyl)carbamate (19): Compound 18 (982 mg, 3.50 mmol) was dissolved in 10.0 mL of MeOH and to the solution was added catalytic amount of p-toluenesulfonic acid. The reaction mixture was stirred at room temperature for 6 h. The reaction mixture was then concentrated in vacuo. The residue was extracted with EtOAc (3 x 20.0 ml) and the extracts were washed with brine, dried over MgSO₄, and concentrated in vacuo. The crude product was purified by column chromatography (50% EtOAc in hexane) to afford an alcohol. The free alcohol (343 mg, 1.20 mmol) was dissolved in CH₂Cl₂ (10 mL) and to this was added Dess-Martin periodiand (7.4 mL 15.0% in CH₂Cl₂, 2.60 mmol) under N₂. The reaction mixture was stirred for 5 min at 0 °C and then stirred for 1 h at room temperature. The reaction was quenched by addition of sat. NaHCO₃ and extracted with CH₂Cl₂ (3 x 15.0 mL). The combined organic extracts were washed with brine, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography (10% EtOAc in hexane) to afford aldehyde as an oil. Finally, To the solution of methyltriphenylphosphonium iodide (199 mg, 0.49 mmol) in anhydrous diethyl ether (10.0 ml) at 0 °C was added dropwise NaHMDS (1.0 M solution in THF, 0.43 mL, 0.43 mmol) and the mixture was stirred for 30 min under N₂. Then the aldehyde (92.7 mg, 0.33 mmol) in dry ether (5.00 ml) was
added dropwise to the above solution at 0 °C and stirred for 1 h. The reaction was quenched with a sat. NH₄Cl solution, and extracted with EtOAc (3 × 15 mL), dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography (33% EtOAc in hexane) to afford 19 (65.8 mg, 71.2%) as an oil.; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 5.86 (1H, m), 5.69 (1H, brs), 5.13 (4H, m), 4.46 (1H, brs), 4.02 (2H, brs), 3.46 (2H, brs), 2.07 (1H, m), 1.78 (3H, m), 1.43 (9H, s); ¹³C NMR (125 MHz; CDCl₃; Me₄Si): δ 154.8, 152.3, 140.0, 134.0, 117.5, 115.0, 81.5, 60.2, 48.8, 47.7, 31.1, 28.2, 23.8; LRMS (ESI) m/z 303 [M + Na]+.

(R)-tert-Butyl 1-oxo-5,6,7,8-tetrahydro-1H-pyrrolo[1,2-c][1,3]diazepine-2(3H)-carboxylate (29): A round bottomed flask charged with the Grubb’s catalyst 2nd generation (44.0 mg, 10.0 mol%) was evacuated and filled with argon three times before the addition of the diene (19) (72.7 mg, 0.26 mmol) in CH₂Cl₂ (5 mL). The resulting solution was stirred under argon for 12 h and then stirred for 4 h exposed to the air, removed the solvent to get black oil residue. The crude product was purified by column chromatography (25% EtOAc in hexane) to afford 29 (71.4 mg, 98.0%) as colorless oil. ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 5.59 (1H, m), 5.52 (1H, m), 4.48 (2H, m), 3.68 (1H, d, J=18.10 Hz), 3.62 (1H, m), 3.40 (1H, m), 2.22 (1H, m), 1.80 (4H, m), 1.43 (9H, s); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 155.0, 152.8, 129.2, 127.5, 81.3, 55.5, 47.2, 43.2, 33.8, 28.2, 23.5; LRMS (ESI) m/z 275 [M + Na]+.

(R)-2,3,5,6,7,8-Hexahydro-1H-pyrrolo[1,2-c][1,3]diazepin-1-one (35): To the solution of (R)-tert-butyl-1-oxo-5,6,7,8-tetrahydro-1H-pyrrolo[1,2-c][1,3]diazepine-2(3H)-carboxylate (29) (71.4 mg, 0.28 mmol) in 5.00 mL of CH₂Cl₂ was added 3.50 ml of trifluoroacetic acid and stirred at room temperature for 3 h. The reaction mixture was concentrated and the residual trifluoroacetic acid was removed by co-evaporation with several portion of CH₂Cl₂. The residue was neutralized with 1N NaOH, and extracted with CH₂Cl₂ (3 × 20 mL), washed with brine and concentrated under vacuum to get crude product. The residue was purified by column chromatography (5% MeOH in CH₂Cl₂) to afford 35 (29.8 mg, 70.0%) as a black oil.; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 5.64 (2H, m), 4.96 (1H, brs), 4.26 (1H, s), 3.60 (3H, m), 3.26 (1H, m), 2.11 (1H, s), 1.66 (3H, m); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 162.7, 131.0, 126.7, 55.8, 47.6, 42.2, 34.2, 22.6; LRMS (ESI) m/z 153 [M + H]+; HRMS (FAB) m/z calcd for C₇H₁₃N₂O [M+H]+ 153.0950, found 153.1028.
(R)-Methyl-3-(tert-butyldimethylsilyloxy)-2-(4-methoxybenzylamino)propanoate (20): To a solution of the D-serine methyl ester hydrochloride (3.50 g, 22.9 mmol) in CH2Cl2 (100 mL) was added 4 Å molecular sieves (10.0 g), Et3N (3.83 mL, 27.5 mmol) and p-methoxybenzaldehyde (3.11 g, 22.9 mmol). After 3 h at room temperature without stirring, then suspension was filtered through the cellite and filtrate was concentrated under reduced pressure. Further, the residue was dissolved in EtOH (50 mL) and reacted with NaBH4 (1.02 g, 27.0 mmol) at room temperature for 2 h. The reaction mixture was addition of a sat. NH4Cl solution and concentrated under reduced pressure to remove the EtOH. The aqueous solution was neutralized with 1N NaOH, and extracted with CH2Cl2 (3 x 75.0 mL), washed with brine and concentrated under vacuum to get crude product as a white solid (5.55 g, 90.2%). This compound was used further without purification. Next, a solution of tert-butylidimethylsilane chloride (4.20 g, 27.8 mmol) in CH2Cl2 (40 mL) was added dropwise to a stirred solution of (R)-methyl-3-hydroxy-2-(4-methoxybenzylamino)propanoate (5.50 g, 23.2 mmol) and Et3N (3.87 mL, 27.83 mmol) in CH2Cl2 (70.0 mL). The mixture was stirred at room temperature for 12 h, then sat. NH4Cl solution (50.0 mL) was added, and extracted with CH2Cl2 (3 x 100 mL) and combined extracts were washed with brine. The organic fraction was dried over MgSO4, filtered, and solvent was evaporated under reduced pressure to obtain oil (7.47 g, 92.7%). This product was used for next reaction without further purification.; 1H NMR (500 MHz; CDCl3; Me4Si) δ 7.24 (2H, d, J = 8.31 Hz), 6.86 (2H, d, J = 6.35 Hz), 3.83 (5H, m), 3.72 (3H, s), 3.66 (1H, dd, J = 14.67 Hz), 3.61 (1H, m), 3.55(1H, m, J = 4.89 Hz), 0.87 (9H, s), 0.03 (6H, s); 13C NMR (125 MHz; CDCl3; Me4Si) δ
173.8, 158.7, 132.0, 129.4, 113.8, 64.6, 62.1, 55.3, 51.6, 51.3, 25.7, 18.2, -5.6; LRMS (ESI) m/z 376 [M + Na]+.

**(S)-tert-Butyl-1-(tert-butyldimethylsilyloxy)but-3-en-2-yl(4-methoxybenzyl)carbamate (21):** To the solution of protected urea 20 (4.26 g, 12.0 mmol) in 25.0 mL of dry THF at 0 °C was added Et$_3$N (2.52 mL, 18.1 mmol) and stirred at same temperature for 0.5 h, then added dropwise 20.0 mL solution of di-tert-butyl dicarbonate (3.94 g, 18.1 mmol) in THF. After addition the reaction mixture was refluxed under N$_2$ for 24 h. The reaction mixture was quenched with water (10.0 mL) and extracted with EtOAc (3 x 30.0 mL). The combined extracts were washed with brine, the organic layer was dried over anhydrous MgSO$_4$ concentrated in vacuo and purified by column chromatography (10% EtOAc in hexane) to afford an oil. Then, diisobutyl aluminum hydride, 1.0 M in toluene (4.40 mL, 4.40 mmol,) was added to slurry of crude compound (1.00 g, 2.20 mmol) in water (15.0 mL) at -78 °C under vigorous stirring. After addition the reaction mixture was stirred at -78°C for 15 min. The reaction mixture was quenched with water (10.0 mL) and extracted with EtOAc (3 x 20.0 mL). The combined extracts were washed with brine, the organic layer was dried over anhydrous MgSO$_4$, concentrated in vacuo and purified by column chromatography (12% EtOAc in hexane) to afford a colorless oil. Finally, the aldehyde compound (53.0 mg, 0.12 mmol) was dissolved in 3.00 mL of THF, and added Tabbe’s reagent (0.5 M in toluene in Toluene, 0.30 ml, 0.15 mmol). The reaction mixture was stirred at room temperature for 2 h. The reaction mixture was quenched with 1N NaOH aqueous solution and extracted with ether (3 x 20 mL). The combined extracts were washed with brine, the organic layer was dried over anhydrous MgSO$_4$, concentrated in vacuo and purified by column chromatography (13% ethyl acetate in hexane) to afford a colorless oil 21 (38.0 mg, 72.1%).

$^1$H NMR (500 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 7.24 (2H, m), 6.86 (2H, m), 5.94 (1H, m), 5.11 (2H, brs), 4.31 (3H, m), 4.12 (1H, m), 3.80 (3H, s), 3.73 (1H, brs), 1.48 (9H, m), 0.88 (9H, s), 0.02 (6H, s); $^{13}$C NMR (125 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 158.5, 135.3, 128.6, 113.6, 79.1, 60.3, 55.2, 49.5, 28.4, 25.8, 21.0, 18.2, 14.2, -5.4; LRMS (ESI) m/z 444 [M + Na]$^+$.  

**(S)-1-(tert-Butyldimethylsilyloxy)-N-(4-methoxybenzyl)but-3-en-2-amine (22):** To a solution of 21 (30.0 mg, 0.07 mmol) in CH$_2$Cl$_2$ (3.00 mL) was added TMEDA (9.92 mg, 0.08 mmol) and TMSOTf (0.01 mL, 0.08 mmol). The mixture was stirred at room temperature for 24 h, then water (10.0 mL) was added, and mixture was extracted with CH$_2$Cl$_2$ (3 x 10.0 mL) and washed with brine. The organic fraction was dried over MgSO$_4$, filtered, and solvent was evaporated under reduced pressure and purified by column chromatography (5% EtOAc in hexane) to afford an oil 22 (20.0 mg, 87.7%).

$^1$H NMR (500 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 7.24 (2H, d, $J$ = 8.3 Hz), 6.86 (2H, d, $J$ = 8.3 Hz), 5.65 (1H, m), 5.22 (2H, m), 3.80 (3H, s), 3.72 (1H, m), 3.60 (2H, m), 3.53 (2H, m), 3.21 (1H, m), 0.89 (9H, s), 0.04 (6H, s); $^{13}$C NMR (125 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 158.5, 132.8, 129.2, 117.6, 113.8, 66.2, 62.4, 55.3, 50.5, 25.9, 18.2, -5.4; LRMS (ESI) m/z 322 [M + H]$^+$.  

S11
(S)-tert-Butylallyl[(1-(tert-butyldimethylsilyloxy)but-3-en-2-yl)(4-methoxybenzyl)carbamoyl]carbamate (23): The TBS product 22 (20.0 mg, 30.0 mmol) was dissolved in of dried THF and the solution was cooled in an ice bath. After the allyl isocyanate (6.00 ml, 0.06 mmol) was added quickly dropwise. The solution was then stirred at room temperature for 18 h. The solvent was removed in vacuum and the residue is was purified by column chromatography (5% EtOAc in hexane) to afford urea compound. To the solution of protected urea (20.0 mg, 0.04 mmol) and DMAP (3.00 mg, 0.02 mmol) in 3.00 mL of dry THF was added Et₃N (10.4 ml, 0.07 mmol) at 0 °C. The reaction mixture was stirred at the same temperature for 0.5 h and was added dropwise solution of di-tert-butyl dicarbonate (16.2 mg, 0.07 mmol) in THF. The reaction mixture was then refluxed under N₂ for 24 h. The reaction mixture was quenched with water (5.00 mL) and extracted with EtOAc (3 x 10.0 mL). The combined organic extracts were washed with brine, dried over anhydrous MgSO₄, concentrated in vacuo and purified by column chromatography (10% EtOAc in hexane) to afford an oil 23 (10.3 mg, 51.5%).; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.23 (2H, d, J = 8.3 Hz), 6.83 (2H, d, J = 8.6 Hz), 5.91 (2H, brs), 5.17 (4H, m), 4.47 (3H, brs), 3.78 (7H, m), 1.48 (9H, s), 0.86 (9H, s), 0.02 (6H, s); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 158.8, 152.8, 134.2, 133.9, 128.9, 118.2, 117.5, 113.7, 81.8, 64.3, 62.3, 55.3, 49.4, 28.3, 25.8, 18.2, -5.5; LRMS (ESI) m/z 527 [M + Na]⁺.

(S)-tert-Butyl-4-((tert-butyldimethylsilyloxy)methyl)-3-(4-methoxybenzyl)-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepine-1-carboxylate (30): A round bottomed flask charged with the Grubb’s catalyst 2nd generation (373 mg, 10 mol%) was evacuated and filled with argon three times before the addition of the diene (23) (1.10 g, 2.20 mmol) in degassed CH₂Cl₂ (55.0 mL). The resulting solution was stirred under argon for 12 h and then stirred for 4 h exposed to the air, removed the solvent in vacuo to obtain a black oil residue. The crude product was purified by column chromatography (15% EtOAc in hexane) to afford 30 (988 mg, 95.1%) as colorless oil.; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.18 (2H, d, J = 8.6 Hz), 6.83 (2H, d, J = 8.6 Hz), 5.74 (1H, m), 5.62 (1H, m), 4.93 (2H, d, J = 14.9 Hz), 4.61 (1H, m), 4.33 (1H, d, J = 14.9 Hz), 4.11 (1H, d, J = 7.3 Hz), 3.78 (3H, s), 3.68(2H, m), 1.51 (9H, s), 0.87 (9H, s), 0.00 (6H, s); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 159.1, 157.2, 153.2, 129.1, 127.8, 128.0, 114.0, 81.6, 66.1, 61.0, 55.2, 53.4, 42.7, 28.2, 25.8, 18.1, -5.3; LRMS (ESI) m/z 499 [M + Na]⁺.

(S)-4-(Hydroxymethyl)-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (36): To the solution of (S)-tert-butyl-4-((tert-butyldimethylsilyloxy)methyl)-3-(4-methoxybenzyl)-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepine-1-carboxylate (30) (930 mg, 1.95 mmol) in 40.0 mL of CH₂Cl₂ was added 10.0 ml of trifluoroacetic acid and stirred at room temperature for 3 h. The reaction mixture was concentrated and the residual trifluoroacetic acid was removed by co-evaporation with several portion of CH₂Cl₂. The residue was neutralized with 1N NaOH, and extracted with CH₂Cl₂ (3 x 30.0 mL), washed with brine, dried over MgSO₄ and concentrated under vacuum to get crude product. The residue was purified by
column chromatography (3% MeOH in CH₂Cl₂) to afford 36 (106 mg, 38.2%) as a colored solid. mp 120 °C; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 6.04 (1H, brs), 5.87 (1H, m), 5.63 (1H, m), 4.59 (1H, brs), 4.00 (1H, s), 4.82 (1H, d, J = 18.6 Hz), 3.68 (1H, m), 3.59 (1H, m), 3.46 (1H, s); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 164.5, 127.6, 64.9, 54.1, 40.7; LRMS (ESI) m/z 143 [M + H]+; HRMS (FAB) m/z calcd for C₆H₁₁N₂O₂ [M+H]⁺ 143.0742, found 143.0821.

H₂N

CHO

MeO

N

PMB

N

N

PMB

Boc

N

N

O

Boc

HN

N

H

O

R = H

R = CH₃

R = H, CH₃

R = H,

R = CH₃

Grubb’s catalyst 2nd generation (10 mol%) excess TFA

CH₂Cl₂, RT

3 hrs, 79%

1. Et₃N, THF, 0 °C-RT, 12 hrs

2. (Boc)₂O, Et₃N, DMAP, Reflux, THF, 97%

General procedure for the synthesis of 24 and 26: To a solution of amine Hydrochloride (5.00 g, 53.4 mmol) in CH₂Cl₂ (100 mL) was added 4 Å molecular sieves (10.0 g) and p-methoxybenzaldehyde (7.27 g, 53.4 mmol). The solution was then stirred at room temperature for 3 h, after the reaction mixture was filtered through the cellite and residue was concentrated under reduced pressure. The solution of residue in EtOH (100 mL) and reacted with NaBH₄ (1.68 g, 64.1 mmol) at room temperature for 2 h. The reaction mixture was addition of a sat. NH₄Cl solution and concentrated under reduced pressure to remove EtOH. Further, the solution was neutralized with 1N NaOH, and extracted with CH₂Cl₂ (3 x 75.0 mL), washed with brine and concentrated under vacuum to get product as an oil.

N-(4-Methoxybenzyl)prop-2-en-1-amine (24): Yield = 8.60 g, 90.7%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.23 (2H, d, J = 8.3 Hz), 6.87 (2H, m), 5.59 (1H, m), 5.18 (1H, dd, J = 17.1, 1.2 Hz), 5.10 (1H, dd, J = 10.3, 1.1 Hz), 4.59 (1H, brs), 3.79 (3H, s), 3.71 (2H, s), 3.25 (2H, d, J = 5.9 Hz); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 158.8, 136.7, 129.3, 128.5, 115.9, 113.8, 55.2, 52.6, 51.6; LRMS (ESI) m/z 178 [M + H]+.

N-(4-Methoxybenzyl)-2-methylprop-2-en-1-amine (26): Yield = 9.47 g, 99.9%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.24 (2H, d, J = 8.8 Hz), 6.86 (2H, d, J = 8.6 Hz), 4.48 (2H, d, J = 20.5 Hz), 3.77 (3H, s), 3.68 (2H, s), 3.16 (2H, s), 2.31 (1H, brs), 1.77 (3H, s); ¹³C NMR (125 MHz; CDCl₃;
General procedure for the synthesis of 25 and 27: The amine product 24 or 26 (8.60 g, 48.0 mmol) was added 60.0 mL of dried THF and the solution was cooled in an ice bath. After the allyl isocyanate (5.11 mL, 58.0 mmol) was added quickly dropwise. The solution was allowed to stir and gradually equilibrate to room temperature over the course of 18 h. The solvent was removed under vacuum and the residue was purified by column chromatography (20 % ethyl acetate in hexane) to afford urea compound. Next, To the solution of protected urea (6.32 g, 24.0 mmol) and DMAP (1.48 g, 12.0 mmol) in 50.0 mL of dry THF at 0 °C was added Et₃N (7.00 mL, 48.0 mmol) and stirred at same temperature for 0.5 h. Then add dropwise di-tert-butyldicarbonate (20.9 g, 96.0 mmol) in 20.0 mL of THF. After addition, the reaction mixture was refluxed under N₂ for 24 h. After the reaction mixture was quenched with water (20.0 mL) and extracted with EtOAc (3 x 50.0 mL). The combined extracts were washed with brine, the organic layer was dried over anhydrous MgSO₄, concentrated in vacuo and purified by column chromatography (8% EtOAc in hexane) to afford an oil 25 or 27.

**tert-Butylallyl(allyl(4-methoxybenzyl)carbamoyl) (25):** Yield = 8.22 g, 93.9%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.17 (2H, m), 6.84 (2H, d, J = 8.6 Hz), 5.87 (1H, m), 5.74 (1H, m), 5.25 (2H, d, J = 5.1 Hz), 5.18 (2H, m), 5.14 (2H, d, J = 5.1 Hz), 4.45 (2H, m), 4.06 (2H, d, J = 6.4 Hz), 3.78 (3H, s), 1.44 (9H, s); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 159.1, 156.6, 152.7, 133.6, 129.5, 128.4, 118.1, 113.9, 81.8, 55.2, 49.1, 28.2; LRMS (ESI) m/z 383 [M + Na]⁺.

**tert-Butylallyl((4-methoxybenzyl)(2-methylallyl)carbamoyl)carbamate) (27):** Yield = 8.32 g, 95.0%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.19 (2H, m), 6.84 (2H, d, J = 8.3 Hz), 5.90 (1H, m), 5.24 (2H, dd, J = 17.1, 1.5 Hz), 5.15 (2H, dd, J = 10.3, 1.2 Hz), 4.94 (2H, s), 4.85 (2H, s), 4.05 (2H, d, J = 6.4 Hz), 3.78 (3H, s), 1.69 (3H, s), 1.47 (9H, s); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 159.1, 157.1, 152.7, 140.1, 133.8, 129.7, 128.5, 117.9, 113.9, 105.0, 81.9, 55.2, 49.5, 28.2, 20.2; LRMS (ESI) m/z 397 [M + Na]⁺.

General procedure for the synthesis of 31 and 32: A round bottomed flask charged with the Grubb’s catalyst 2nd generation (470 mg, 10 mol%) was evacuated and filled with argon three times before the addition of the diene 25 or 27 (2.00 g, 5.50 mmol) in CH₂Cl₂ (130 mL). The resulting solution was stirred under argon for 12 h and then stirred for 4 h exposed to the air, removed the solvent in vacuo to get a black oil. The crude product was purified by column chromatography (15% EtOAc in hexane) to afford a colorless oil.

**tert-Butyl-3-(4-methoxybenzyl)-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepine-1-carboxylate (31):** Yield = 1.86g, 99.9%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 7.23 (2H, d, J = 8.3 Hz), 6.85 (2H, d, J = 8.6 Hz), 5.70 (2H, d, J = 1.7 Hz), 4.55(2H, s), 4.20 (1H, s), 3.80 (3H, s), 3.79 (2H, m), 3.68 (1H, s), 3.62 (1H, s), 3.24 (1H, s), 2.76 (1H, s), 2.45 (1H, m), 2.10 (1H, s), 1.83 (1H, s), 1.67 (1H, m), 1.56 (1H, m), 1.43 (9H, s); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 167.6, 133.1, 129.3, 125.0, 123.4, 121.4, 113.8, 55.1, 49.5, 28.2, 20.2; LRMS (ESI) m/z 397 [M + Na]⁺.
1.50 (9H, s); $^{13}$C NMR (125 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 159.2, 157.6, 152.7, 129.1, 128.5, 123.6, 114.0, 81.6, 55.2, 51.8, 45.0, 43.3, 28.3; LRMS (ESI) m/z 355 [M + Na]$^+$. 

tert-Butyl-3-(4-methoxybenzyl)-5-methyl-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepine-1-carboxylate (32): Yield = 1.77 g, 95.0%; $^1$H NMR (500 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 7.15 (2H, m), 6.77 (2H, m), 5.25 (1H, m), 4.46 (2H, d, $J$ = 3.7 Hz), 4.06 (2H, m), 3.71 (3H, s), 3.51 (2H, m), 1.94 (3H, s), 1.46 (9H, s); $^{13}$C NMR (125 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 159.0, 157.4, 152.5, 131.7, 128.9, 128.4, 121.4, 113.7, 81.1, 54.9, 51.6, 49.4, 42.9, 28.0, 23.2; LRMS (ESI) m/z 369 [M + Na]$^+$. 

**General procedure for the synthesis of 37 and 38:** A solution of 31 or 32 (685 mg, 2.10 mmol) in 20.0 mL of CH$_2$Cl$_2$ was taken and then added 15.0 mL of trifluoroacetic acid followed by stirring at room temperature for 3 h. The reaction mixture was concentrated and the residual trifluoroacetic acid was removed by co-evaporation with several portion of CH$_2$Cl$_2$. The residue was neutralized with 1N NaOH, and extracted with CH$_2$Cl$_2$ (3 x 30.0 mL), washed with brine and concentrated under vacuum to get crude product as a black solid. The residue was purified by column chromatography (3% MeOH in CH$_2$Cl$_2$) to afford 37 or 38.

3,4-Dihydro-1H-1,3-diazepin-2(7H)-one (37): Yield = 222 mg, 96.0%; mp 72 $^\circ$C; $^1$H NMR (500 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 5.88 (2H, m), 5.44 (1H, brs), 3.74 (4H, m); $^{13}$C NMR (125 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 165.2, 128.9, 41.3; LRMS (ESI) m/z 113 [M + H]$^+$; HRMS (FAB) m/z calcd for C$_5$H$_9$N$_2$O [M+H]$^+$ 113.0637, found 113.0715.

5-Methyl-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (38): Colored Oil; Yield = 208 mg, 90.0%; $^1$H NMR (500 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 10.71 (1H, brs), 6.94 (1H, brs), 5.87 (1H, m), 3.79 (4H, m), 1.97 (3H, s); $^{13}$C NMR (125 MHz; CDCl$_3$; Me$_4$Si) $\delta$ 163.9, 137.1, 122.1, 44.8, 40.0, 22.5; LRMS (ESI) m/z 127 [M + H]$^+$; HRMS (FAB) m/z calcd for C$_6$H$_{11}$N$_2$O [M+H]$^+$ 127.0793, found 127.0874.
Ribofuranosyl bromide (39): Hydrogen bromide gas (KBr+H₂SO₄) was bubbled in to an ice cold solution of 1-O-acetyl-2,3,5-tribenzoyl-β-D-ribofuranose (252 mg, 5.00 mmol) in CH₂Cl₂ (15.0 mL) for 15 min. After the reaction mixture had been stirred at 0 °C for 2 h and at room temperature for 30 min, it was concentrated under vacuum to thin syrup. Then 3 times with 3.00 mL of CH₂Cl₂ and 3.00 mL of toluene were successively distilled in vacuum from the syrup which was then used immediately for the condensation reaction.

General procedure e for the synthesis of 40, 41 and 42: 37 or 33 or 34 (90.0 mg, 0.70 mmol) was dissolved in 5.00 mL of CH₃CN and treated with an excess of BSTFA (2.50 mL) at room temperature for 1 h. After the completion of reaction the solvent and excess reagent were removed under vacuum. The residue was dissolved in anhydrous benzene (5.00 mL). The solution was slowly added to a mixture of HgO (263 mg, 1.20 mmol) and HgBr₂ (265 mg, 0.73 mmol) in refluxing benzene 5.00 mL. Immediately a benzene solution containing ribofuranosyl bromide (39) was added dropwise to the refluxing mixture and heating and stirring were continued for 12 h. After cooling the reaction mixture was filtered through cellite, the organic filtrate was washed twice with sat. NaHCO₃ solution and H₂O. The organic layer was dried over MgSO₄, concentrated under vacuum and the residue was purified by column chromatography (50% EtOAc in hexane) to afford 40 or 41 or 42.

(2R,3R,4R,5R)-2-(Benzoyloxymethyl)-5-(2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepin-1-yl)tetrahydrofuran-3,4-diyl dibenzoate (40): Colored Oil; Yield = 204 mg, 50.0%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 8.14 (2H, dd, J=8.2, 0.9 Hz), 7.94 (4H, m), 7.59 (1H, m), 7.51 (4H, m), 7.35 (4H, m), 6.13 (1H, d, J=7.1 Hz), 5.79 (1H, dd, J=6.0, 3.3 Hz), 5.65 (1H, m), 5.58 (2H, m), 4.93 (1H, brs), 4.80 (1H, m), 4.57 (2H, m), 3.86 (1H, d, J=15.9 Hz), 3.74 (2H, m), 3.57 (1H, d, J=18.8 Hz); ¹³C NMR (125 MHz ; CDCl₃; Me₄Si) δ 166.0, 165.4, 165.3, 165.2, 133.4, 133.3, 133.2, 133.0, 129.7, 129.6, 129.5, 128.9, 128.8, 128.6, 128.3, 128.2, 126.9, 125.5, 83.3, 78.7, 71.5, 70.8, 64.3, 60.3, 43.0, 41.2, 20.9, 14.1

(2R,3R,4R,5R)-2-(Benzoyloxymethyl)-5-((S)-4-methyl-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepin-1-yl)tetrahydrofuran-3,4-diyl dibenzoate (41): Colored Oil; Yield = 163 mg, 40.0%; mp: 88 °C; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 8.15 (2H, m), 7.96 (4H, m), 7.61 (2H, m), 7.53 (3H, m), 7.36 (4H, m), 6.16 (1H, d, J=7.3 Hz), 5.78 (1H, dd, J=6.1, 3.4 Hz), 5.64 (1H, dd, J=7.1, 6.4 Hz), 5.48 (2H, m), 4.81 (1H, d, J=3.9 Hz), 4.57 (2H, m), 4.28 (1H, s), 3.86 (1H, m), 3.69 (1H, m), 1.22 (3H, d, J=6.8 Hz); ¹³C NMR (125 MHz; CDCl₃; Me₄Si) δ 166.1, 165.5, 165.3, 164.4, 133.5, 133.4, 133.3, 132.8, 129.8, 129.9, 129.7, 129.6, 129.0, 128.9, 128.6, 128.4, 128.3, 124.7, 88.2, 78.9, 71.5, 70.9, 64.3, 48.9, 41.0, 22.5; LRMS (ESI) m/z 571 [M + H]+.

(2R,3R,4R,5R)-2-(Benzoyloxymethyl)-5-((R)-4-methyl-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepin-1-yl)tetrahydrofuran-3,4-diyl dibenzoate (42): Colored Oil; Yield = 175 mg, 43.0%; ¹H NMR (500 MHz; CDCl₃; Me₄Si) δ 8.16 (2H, m), 7.94 (4H, m), 7.61 (2H, m), 7.53 (3H, m), 7.36 (4H, m), 6.19
(1H, d, J=8.1 Hz), 6.05 (1H, d, J=7.3 Hz), 5.79 (1H, m), 5.63 (1H, m), 5.52 (2H, s), 4.80 (1H, dd, J=4.6 Hz), 4.57 (3H, m), 3.86 (1H, m), 3.67 (1H, m), 3.67 (1H, dd, J=16.4, 4.2 Hz), 1.14 (3H, m), 1.14 (3H, d, J=6.8 Hz); 13C NMR (125 MHz; CDCl3; Me4Si) δ 166.0, 165.4, 165.2, 164.1, 133.4, 133.3, 132.6, 129.8, 129.7, 129.6, 129.5, 128.9, 128.8, 128.6, 128.4, 128.3, 124.2, 87.6, 79.0, 71.6, 70.7, 64.4, 49.9, 40.5, 22.7, 14.1; LRMS (FAB) m/z 571 [M + H]+.

General procedure for the synthesis of 1, 2 and 3: The compound 40 or 41 or 42 (95.0 mg, 0.16 mmol) was dissolved in 20.0 mL of sat. methanolic ammonia and stirred at room temperature for 30 h, then remove of the solvent under vaccum gave a white foam. The residue was purified by column chromatography (12% MeOH in CH2Cl2) to afford 1 or 2 or 3.

1-((2R,3R,4S,5R)-3,4-Dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (1): Colored Oil; Yield = 41.7 mg, 97.0%; 1H NMR (500 MHz, CD3OD) δ 5.89 (2H, m), 5.53 (1H, m), 4.04 (2H, m), 3.88 (4H, m), 3.77 (1H, m), 3.72 (1H, m), 3.68 (2H, m); 13C NMR (125 MHz, CD3OD) δ 167.6, 128.9, 127.9, 92.7, 95.0, 73.1, 71.8, 63.5, 43.4, 42.8

(S)-1-((2R,3R,4S,5R)-3,4-Dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-4-methyl-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (2): Colored Oil; Yield = 40.9 mg, 95.0%; 1H NMR (500 MHz, CD3OD) δ 5.83 (1H, m), 5.66 (1H, m), 5.52 (1H, d, J=5.6 Hz), 4.13 (1H, m), 4.02 (3H, m), 3.83 (2H, m), 3.74 (2H, dd, J=4.6, 3.2 Hz), 3.66 (1H, dd, J=5.4 Hz), 1.30 (3H, m); 13C NMR (125 MHz, CD3OD) δ 166.7, 134.6, 126.5, 92.7, 85.0, 73.1, 71.9, 63.4, 50.3, 42.6, 22.8; LRMS (FAB) m/z 259 [M + H]+; HRMS (FAB) m/z calcd for C11H19N2O5 [M+H]+ 259.1216, found 259.1294.

(R)-1-((2R,3R,4S,5R)-3,4-Dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-4-methyl-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (3): Colored Oil; Yield = 43.0 mg, 99.9%; 1H NMR (500 MHz, CD3OD) δ 5.86 (1H, m), 5.73 (1H, m), 5.55 (1H, d, J=5.6 Hz), 4.01 (3H, m), 3.87 (2H, m), 3.77 (2H, m), 3.68 (1H, dd, J=12.0, 4.2 Hz), 1.35 (3H, m); 13C NMR (125 MHz, CD3OD) δ 167.1, 134.2, 128.1, 92.2, 85.0, 73.3, 71.8, 63.5, 51.2, 42.3, 23.1; LRMS (FAB) m/z 259 [M + H]+; HRMS (FAB) m/z calcd for C11H19N2O5 [M+H]+ 259.1216, found 259.1294.
III. Enzyme assay

Cloning and purification of human CDA: Human CDA gene (IMAGE consortium) was amplified by PCR with synthetic primer set (5’ primer: gga att cca tat gaa gec tga tgt tgt cca gca gct (NdeI site marked in bold type letter), 3’ primer: tgg tgc tcg agt tat ttt tgt aaa tct ata ata tgc (XhoI site marked in bold type letter)). Human CDA gene encoding amino acid sequence 11-146 was cloned into pET28a vector (Novagen) with NdeI/XhoI cleavage site. The resulting N-terminal His-tagged hCDA construct was transformed into E. coli Rosetta (DE3) (Novagen). Cells were grown at 37 °C in LB medium until the optical density at $A_{600}$ reached to 0.6-0.8 and hCDA protein was expressed by adding 1 mM IPTG at 18 °C for 18 h. Cells were harvested, washed with buffer A (50 mM Tris pH 7.5, 250 mM NaCl, 5% glycerol, 1 mM β-mercaptoethanol) and lysed using ultrasonication. After centrifugation (29,820 g for 30 min), the supernatant was incubated with a cobalt affinity resin (TALON®, Clontech) on a rocker for 1 h at 4 °C and washed with buffer A containing 10 mM imidazole. The proteins were eluted from the metal affinity resin by buffer A supplemented with 100 mM imidazole, concentrated to 2 mg/ml, and stored -80 °C.

Inhibitory assay of compounds 1, 2 and 3 against cytidine deamination by human CDA: Cytidine deaminase activity was monitored by the loss of absorbance of cytidine at 282 nm ($\Delta\varepsilon = -3600$) during the deamination reaction. hCDA (12.5 nM of final concentrations) was added to cytidine (0, 12.5, 25, 50, 100 and 200 µM of the final concentration) in pH 7.4 PBS buffer and the absorbance change was monitored at 282 nm on a DU 800 UV-VIS Spectrophotometer (Beckman Coulter). $K_m$ value was calculated to be 26 µM using Hyper32 (version 1.0.0 http://homepage.ntlworld.com/john.easterby/hyper32.html). The synthetic inhibitors (1 and 3: 31.25, 62.5, 125, 250 nM of the final concentrations; 2: 1.25, 2.5, 5, 10 µM of the final concentrations) were added to hCDA (12.5 nM of final concentration) in pH 7.4 PBS buffer. The enzyme reaction was started by addition of substrate solution (cytidine: 2.5, 25, 50, 100 µM of final concentrations). Each initial velocity was measured by monitoring disappearance of cytidine and analyzed by Lineweaver-Burk plot and secondary plot to determine inhibition constant ($K_i$) (Figure S1).
**Figure S1.** The initial velocities were analyzed by Lineweaver-Burk plot, and the resulting slopes of the grapes were plotted against the corresponding inhibitor concentrations (secondary plots), where x-intercept corresponds to $-K_i$. (a) Compound 1; (b) Compound 2; (c) Compound 3

<table>
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<th>Compound</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<tbody>
<tr>
<td>$K_i$</td>
<td>35.33 ± 0.49 nM</td>
<td>2.56 ± 0.18 µM</td>
<td>145.97 ± 4.87 nM</td>
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IV NMR spectra

1H-NMR (CDCl₃, 500 MHz):
(S)-2-(4-methoxybenzylamino)propan-1-ol (5)

13C-NMR (CDCl₃, 125 MHz):
(S)-2-(4-methoxybenzylamino)propan-1-ol (5)
\( ^1 \text{H-NMR (CDCl}_3, 500 \text{ MHz):} \)

\((S)-1\text{-}(\text{tert-butylimethylsilyloxy})\text{-N-}(4\text{-methoxybenzyl})\text{propan-2-amine (6)}\)

\( ^{13} \text{C-NMR (CDCl}_3, 125 \text{ MHz):} \)

\((S)-1\text{-}(\text{tert-butylimethylsilyloxy})\text{-N-}(4\text{-methoxybenzyl})\text{propan-2-amine (6)}\)
$^1$H-NMR (CDCl$_3$, 500 MHz):
(S)-3-allyl-1-(1-((tert-butyldimethylsilyloxy)propan-2-yl)-1-(4-methoxybenzyl)urea (9)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(S)-3-allyl-1-(1-((tert-butyldimethylsilyloxy)propan-2-yl)-1-(4-methoxybenzyl)urea (9)
$^1$H-NMR (CDCl$_3$, 500 MHz):
(S)-tert-butyl allyl[(1-(tert-butyldimethylsilyloxy)propan-2-yl)(4-methoxybenzyl)carbamoyl]carbamate (13)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(S)-tert-butyl allyl[(1-(tert-butyldimethylsilyloxy)propan-2-yl)(4-methoxybenzyl)carbamoyl]carbamate (13)
$^1$H-NMR (CDCl$_3$, 500 MHz):

(S)-tert-butyl allyl(but-3-en-2-yl(4-methoxybenzyl)carbamoyl)carbamate (11)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):

(S)-tert-butyl allyl(but-3-en-2-yl(4-methoxybenzyl)carbamoyl)carbamate (11)
$^1$H-NMR (CDCl$_3$, 500 MHz):
(S)-tert-butyl 3-(4-methoxybenzyl)-4-methyl-2-oxo-2,3,4,7-tetrahydro-1$H$-1,3-diazepine-1-carboxylate (12)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(S)-tert-butyl 3-(4-methoxybenzyl)-4-methyl-2-oxo-2,3,4,7-tetrahydro-1$H$-1,3-diazepine-1-carboxylate (12)
$^1$H-NMR (CDCl$_3$, 500 MHz):
(S)-4-methyl-3,4-dihydro-$1^H$-1,3-diazepin-2($7^H$)-one (33)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(S)-4-methyl-3,4-dihydro-$1^H$-1,3-diazepin-2($7^H$)-one (33)
COSY-Spectrum (CDCl₃, 500 MHz):
(S)-4-methyl-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (33)
$\text{H-NMR (CDCl}_3, 500 \text{ MHz):}$

(R)-2-(4-methoxybenzylamino)propan-1-ol (44)

$\text{C-NMR (CDCl}_3, 125 \text{ MHz):}$

(R)-2-(4-methoxybenzylamino)propan-1-ol (44)
$^1$H-NMR (CDCl$_3$, 500 MHz):
(R)-1-(tert-butyldimethylsilyloxy)-N-(4-methoxybenzyl)propan-2-amine (14)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(R)-1-(tert-butyldimethylsilyloxy)-N-(4-methoxybenzyl)propan-2-amine (14)
$^1$H-NMR (CDCl$_3$, 500 MHz):
(R)-3-allyl-1-(1-(tert-butyldimethylsilyloxy)propan-2-yl)-1-(4-methoxybenzyl)urea (45)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(R)-3-allyl-1-(1-(tert-butyldimethylsilyloxy)propan-2-yl)-1-(4-methoxybenzyl)urea (45)
$^{1}$H-NMR (CDCl$_3$, 500 MHz):
(R)-tert-butyl allyl\(((1-(\text{tert-}	ext{butyldimethylsilyloxy})\text{propan-2-yl})(4\text{-} \text{methoxybenzyl})\text{carbamoyl})\text{carbamate (15)}$

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(R)-tert-butyl allyl\(((1-(\text{tert-}	ext{butyldimethylsilyloxy})\text{propan-2-yl})(4\text{-} \text{methoxybenzyl})\text{carbamoyl})\text{carbamate (15)}$
$^1$H-NMR (CDCl$_3$, 500 MHz):
(R)-tert-butyl allyl(but-3-en-2-yl(4-methoxybenzyl)carbamoyl)carbamate (16)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(R)-tert-butyl allyl(but-3-en-2-yl(4-methoxybenzyl)carbamoyl)carbamate (16)
$^1$H-NMR (CDCl$_3$, 500 MHz):
(R)-tert-butyl 3-(4-methoxybenzyl)-4-methyl-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepine-1-carboxylate (28)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(R)-tert-butyl 3-(4-methoxybenzyl)-4-methyl-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepine-1-carboxylate (28)
$^1$H-NMR (CDCl$_3$, 500 MHz):
(R)-4-methyl-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (34)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(R)-4-methyl-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (34)
COSY- Spectrum (CDCl₃, 500 MHz):
(R)-4-methyl-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (34)
$^1$H-NMR (CDCl$_3$, 500 MHz):

(R)-2-(((tert-butyldimethylsilyloxy)methyl)pyrrolidine (17)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):

(R)-2-(((tert-butyldimethylsilyloxy)methyl)pyrrolidine (17)
\( ^1\text{H-NMR (CDCl}_3, 500 \text{ MHz):} \)

(R)-\text{tert-buty}l 2-(\text{[(tert-butyldimethylsilyloxy)methyl]}\text{pyrrolidine-1-carbonyl(ethyl)carbamate (18)}

\( ^1\text{C-NMR (CDCl}_3, 125 \text{ MHz):} \)

(R)-\text{tert-buty}l 2-(\text{[(tert-butyldimethylsilyloxy)methyl]}\text{pyrrolidine-1-carbonyl(ethyl)carbamate (18)}
$^1$H-NMR (CDCl$_3$, 500 MHz):
(R)-tert-butyl allyl(2-vinylpyrrolidine-1-carbonyl)carbamate (19)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(R)-tert-butyl allyl(2-vinylpyrrolidine-1-carbonyl)carbamate (19)
1H-NMR (CDCl3, 500 MHz):
(R)-tert-butyl 1-oxo-5,6,7,8-tetrahydro-1H-pyrrolo[1,2-c][1,3]diazepine-2(3H)-carboxylate (29)

13C-NMR (CDCl3, 125 MHz):
(R)-tert-butyl 1-oxo-5,6,7,8-tetrahydro-1H-pyrrolo[1,2-c][1,3]diazepine-2(3H)-carboxylate (29)
$^{1}H$-NMR (CDCl$_3$, 500 MHz):

(R)-2,3,5,6,7,8-hexahydro-1$H$-pyrrolo[1,2-c][1,3]diazepin-1-one (35)

$^{13}C$-NMR (CDCl$_3$, 125 MHz):

(R)-2,3,5,6,7,8-hexahydro-1$H$-pyrrolo[1,2-c][1,3]diazepin-1-one (35)
$^1$H-NMR (CDCl$_3$, 500 MHz):
(R)-methyl 3-(tert-butyldimethylsilyloxy)-2-(4-methoxybenzylamino)propanoate (20)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(R)-methyl 3-(tert-butyldimethylsilyloxy)-2-(4-methoxybenzylamino)propanoate (20)
$^1$H-NMR (CDCl$_3$, 500 MHz):
(S)-tert-butyl 1-(tert-butyldimethylsilyloxy)but-3-en-2-yl(4-methoxybenzyl)carbamate (21)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(S)-tert-butyl 1-(tert-butyldimethylsilyloxy)but-3-en-2-yl(4-methoxybenzyl)carbamate (21)
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$^{1}H$-NMR (CDCl$_3$, 500 MHz):  
(S)-1-(tert-butyldimethylsilyloxy)-N-(4-methoxybenzyl)but-3-en-2-amine (22)

$^{13}C$-NMR (CDCl$_3$, 125 MHz):  
(S)-1-(tert-butyldimethylsilyloxy)-N-(4-methoxybenzyl)but-3-en-2-amine (22)
$^1$H-NMR (CDCl$_3$, 500 MHz):
(S)-tert-butyl allyl(1-(tert-butyldimethylsilyloxy)but-3-en-2-yl)(4-methoxybenzyl)carbamoyl)carbamate (23)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(S)-tert-butyl allyl(1-(tert-butyldimethylsilyloxy)but-3-en-2-yl)(4-methoxybenzyl)carbamoyl)carbamate (23)
**1H-NMR (CDCl₃, 500 MHz):**

(S)-tert-butyl 4-((tert-butyldimethylsilyloxy)methyl)-3-(4-methoxybenzyl)-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepine-1-carboxylate (30)

**13C-NMR (CDCl₃, 125 MHz):**

(S)-tert-butyl 4-((tert-butyldimethylsilyloxy)methyl)-3-(4-methoxybenzyl)-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepine-1-carboxylate (30)
$^1$H-NMR (CDCl$_3$, 500 MHz):
(S)-4-(hydroxymethyl)-3,4-dihydro-1$H$-1,3-diazepin-2(7$H$)-one (36)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
(S)-4-(hydroxymethyl)-3,4-dihydro-1$H$-1,3-diazepin-2(7$H$)-one (36)
$^1$H-NMR (CDCl$_3$, 500 MHz):
$N$-(4-methoxybenzyl)prop-2-en-1-amine (24)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
$N$-(4-methoxybenzyl)prop-2-en-1-amine (24)
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**1H-NMR (CDCl₃, 500 MHz):**

*tert*-butyl allyl(allyl(4-methoxybenzyl)carbamoyl)carbamate (25)

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**13C-NMR (CDCl₃, 125 MHz):**

*tert*-butyl allyl(allyl(4-methoxybenzyl)carbamoyl)carbamate (25)
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**1H-NMR (CDCl₃, 500 MHz):**

*tert*-butyl 3-(4-methoxybenzyl)-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepine-1-carboxylate (31)

**13C-NMR (CDCl₃, 125 MHz):**

*tert*-butyl 3-(4-methoxybenzyl)-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepine-1-carboxylate (31)
$^1$H-NMR (CDCl$_3$, 500 MHz):
3,4-dihydro-$1H$-$1,3$-diazepin-$2(7H)$-one (37)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
3,4-dihydro-$1H$-$1,3$-diazepin-$2(7H)$-one (37)
$^{1}H$-NMR (CDCl$_3$, 500 MHz): N-(4-methoxybenzyl)-2-methylprop-2-en-1-amine (26)

$^{13}C$-NMR (CDCl$_3$, 125 MHz): N-(4-methoxybenzyl)-2-methylprop-2-en-1-amine (26)
\[ ^1H\text{-NMR (CDCl}_3, 500 MHz): \]
\[ \text{tert-butyl allyl(4-methoxybenzyl)(2-} \text{methylallyl)carbamoyl)carbamate (27)} \]

\[ ^13C\text{-NMR (CDCl}_3, 125 MHz): \]
\[ \text{tert-butyl allyl(4-methoxybenzyl)(2-} \text{methylallyl)carbamoyl)carbamate (27)} \]
$^1$H-NMR (CDCl$_3$, 500 MHz):

$\text{tert-}-\text{butyl 3-}(\text{4-methoxybenzyl})\text{-5-methyl-2-oxo-2,3,4,7-tetrahydro-1}^H\text{-1,3-diazepine-1-carboxylate (32)}$

$^1$C-NMR (CDCl$_3$, 125 MHz):

$\text{tert-}-\text{butyl 3-}(\text{4-methoxybenzyl})\text{-5-methyl-2-oxo-2,3,4,7-tetrahydro-1}^H\text{-1,3-diazepine-1-carboxylate (32)}$
$^1$H-NMR (CDCl$_3$, 500 MHz):
5-methyl-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (38)

$^{13}$C-NMR (CDCl$_3$, 125 MHz):
5-methyl-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (38)
1H-NMR (CDCl₃, 500 MHz):

(2R,3R,4R,5R)-2-(benzoyloxymethyl)-5-(2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepin-1-yl)tetrahydrofuran-3,4-diyl dibenzoate (40)

13C-NMR (CDCl₃, 125 MHz):

(2R,3R,4R,5R)-2-(benzoyloxymethyl)-5-(2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepin-1-yl)tetrahydrofuran-3,4-diyl dibenzoate (40)
COSY-Spectra (CDCl₃, 500 MHz):
(2R,3R,4R,5R)-2-(benzoyloxymethyl)-5-(2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepin-1-yl)tetrahydrofuran-3,4-diyl dibenzoate (40)
$^{1}$H-NMR (CDCl$_3$, 500 MHz):

\[
(2R,3R,4R,5R)-2-(\text{benzoyloxymethyl})-5-((S)-4\text{-methyl-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepin-1-yl})\text{tetrahydrofuran-3,4-diyl dibenzoate (41)}
\]

$^{13}$C-NMR (CDCl$_3$, 125 MHz):

\[
(2R,3R,4R,5R)-2-(\text{benzoyloxymethyl})-5-((S)-4\text{-methyl-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepin-1-yl})\text{tetrahydrofuran-3,4-diyl dibenzoate (41)}
\]
COSY-Spectra (CDCl₃, 500 MHz):

\[ (2R,3R,4R,5R)-2-(benzoyloxymethyl)-5-((S)-4-methyl-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepin-1-yl)tetrahydrofuran-3,4-diyl dibenzoate \] (41)

correlation between signals of \( 1'H \) (6.16 ppm) and \( 2'H \) (5.64 ppm).

NOESY- Spectra (CDCl₃, 500 MHz):

\[ (2R,3R,4R,5R)-2-(benzoyloxymethyl)-5-((S)-4-methyl-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepin-1-yl)tetrahydrofuran-3,4-diyl dibenzoate \] (41)

correlation between signals of \( 1'H \) (6.16 ppm), \( 2'H \) (5.64 ppm), \( 7H \) (3.69 ppm) and \( 6H \) (5.48 ppm).

Electronic Supplementary Material (ESI) for Chemical Communications
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$^{1}H$-NMR (CDCl$_3$, 500 MHz):

(2$R$,3$R$,4$R$,5$R$)-2-(benzoyloxymethyl)-5-((($R$)-4-methyl-2-oxo-2,3,4,7-tetrahydro-1$H$-1,3-diazepin-1-yl)tetrahydrofuran-3,4-diyl dibenzoate (42)

$^{13}C$-NMR (CDCl$_3$, 125 MHz):

(2$R$,3$R$,4$R$,5$R$)-2-(benzoyloxymethyl)-5-((($R$)-4-methyl-2-oxo-2,3,4,7-tetrahydro-1$H$-1,3-diazepin-1-yl)tetrahydrofuran-3,4-diyl dibenzoate (42)

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COSY- Spectra (CDCl₃, 500 MHz):
(2R,3R,4R,5R)-2-(benzoyloxyethyl)-5-((R)-4-methyl-2-oxo-2,3,4,7-tetrahydro-1H-1,3-diazepin-1-yl)tetrahydrofuran-3,4-diyl dibenzoate (42)
\[ 1\text{-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (1)} \]

\[ ^{13}\text{C-NMR (CD}_3\text{OD, 125 MHz):} \]

\[ 1\text{-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (1)} \]
COSY- Spectra (CD$_3$OD, 500 MHz):
1-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (1)
$^1$H-NMR (CD$_3$OD, 500 MHz):
(S)-1-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-4-methyl-3,4-dihydro-1$H$-1,3-diazepin-2(7$H$)-one (2)

$^{13}$C-NMR (CD$_3$OD, 125 MHz):
(S)-1-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-4-methyl-3,4-dihydro-1$H$-1,3-diazepin-2(7$H$)-one (2)
COSY- Spectra (CD$_3$OD, 500 MHz):
(S)-1-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-4-methyl-3,4-dihydro-1H-1,3-diazepin-2(7H)-one (2)
\[ ^{1}H\text{-NMR (CD}_{3}\text{OD, 500 MHz):} \]
(R)-1-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-4-methyl-3,4-dihydro-1\text{-}H\text{-}1,3-diazepin-2(7\text{H})\text{-}one (3)

\[ ^{13}C\text{-NMR (CD}_{3}\text{OD, 125 MHz):} \]
(R)-1-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-4-methyl-3,4-dihydro-1\text{-}H\text{-}1,3-diazepin-2(7\text{H})\text{-}one (3)
COSY- Spectra (CD$_3$OD, 500 MHz):

(R)-1-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-4-methyl-3,4-dihydro-1H-1,3-
diazepin-2(7H)-one (3)