Supporting Information

Asymmetric Co(II)-Catalyzed Cyclopropanation with Succinimidyl Diazoacetate: General Synthesis of Chiral Cyclopropyl Carboxamides

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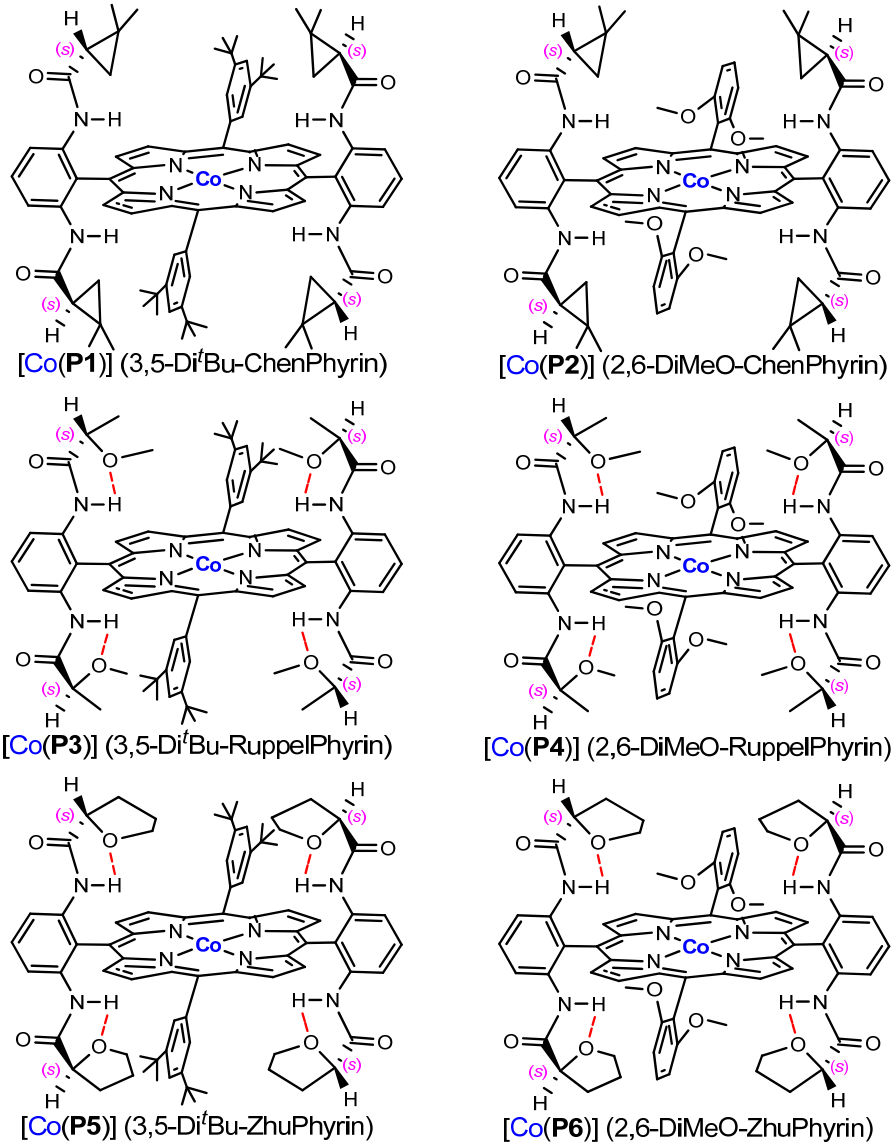
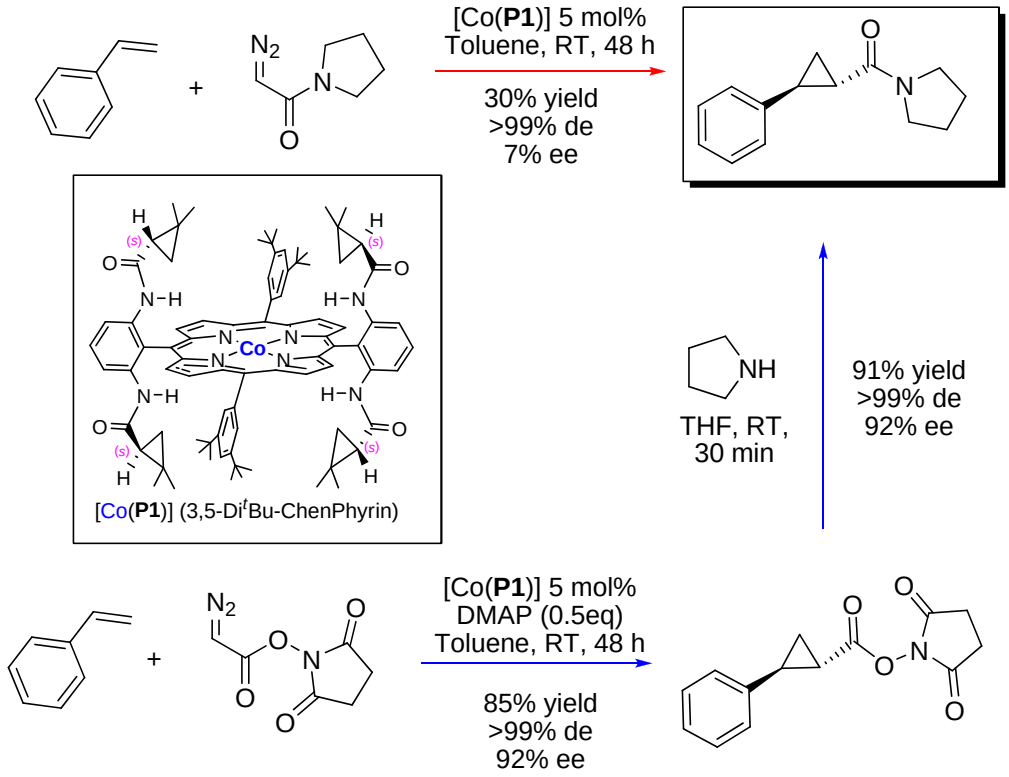


Figure S1. Structures of D_2-Symmetric Chiral Cobalt(II) Porphryins.

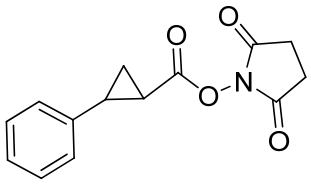
Scheme S1. Comparison of [Co(**P1**)]-Catalyzed Cyclopropanation of Diazoacetamide and Succinimidyl Diazoacetate.



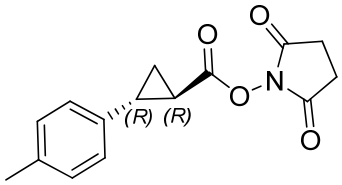
Although the use of diazoacetamides generates the corresponding cyclopropanes in excellent diastereoselectivities in the Co(II)-catalyzed system, the carbene source does not provide for an efficient and highly enantioselective process. On the other hand, the use of succinimidyl diazoacetate can generate the same product in a two step sequence in an overall yield of 77% without loss of the excellent diastereo- and enantioselectivities established during the Co(II)-catalyzed cyclopropanation.

General Considerations. Cyclopropanation reactions were performed under nitrogen in oven-dried glassware following standard Schlenk techniques. Toluene was distilled under nitrogen from sodium benzophenone ketyl prior to use. Succinimidyl diazoacetate was synthesized using reported literature procedure.[1] Olefins were purchased from commercial sources and used without further purification. Thin layer chromatography was performed on Merck TLC plates (silica gel 60 F254). Flash column chromatography was performed with Merck silica gel (60 Å, 230-400 mesh, 32-63 μm). ^{1}H NMR and ^{13}C NMR were recorded on a Varian Inova400 (400 MHz) with chemical shifts reported relative to residual solvent. Infrared spectra were measured with a Nicolet Avatar 320 spectrometer with a Smart Miracle accessory. HRMS data was obtained on an Agilent 1100 LC/MS/TOF mass spectrometer. HPLC measurements were carried out on a Shimadzu Prominence LC-20AT HPLC system with a SPD-N20A diode array detector. Enantiomeric excess was measured using either a Chiralcel OD-H or Chiralcel AD-H chiral HPLC column. Optical rotation was measured on a Rudolf Autopol IV polarimeter.

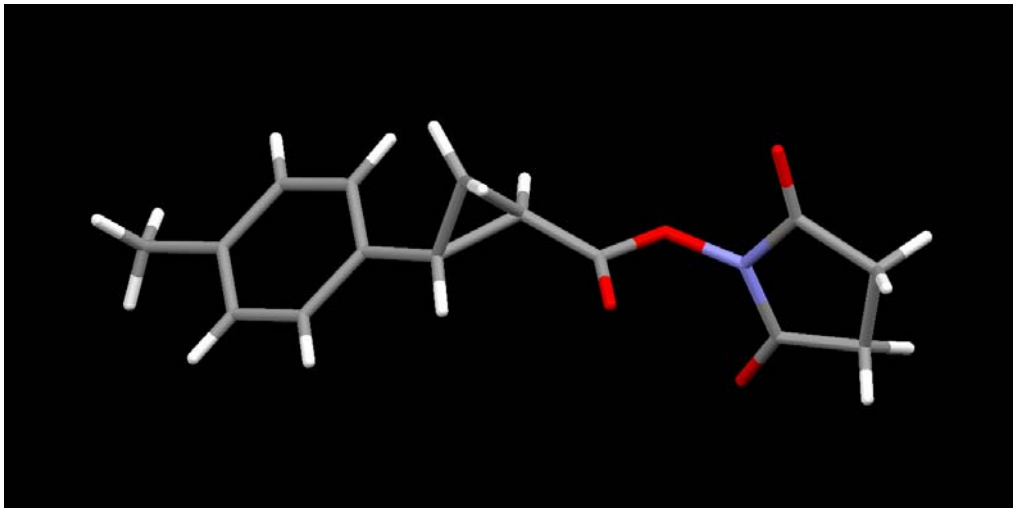
General Procedure for Cyclopropanation. An oven dried Schlenk tube, previously evacuated and backfilled with nitrogen gas, was charged with succinimidyl diazoacetate (0.37 mmol) and catalyst (0.0125 mmol). The Schlenk tube was then evacuated and back filled with nitrogen. The Teflon screw cap was replaced with a rubber septum and a 0.2 ml portion of solvent was added followed by styrene (0.25 mmol), and the remaining solvent (total 1 mL). The Schlenk tube was then purged with nitrogen for one minute and the rubber septum was replaced with a Teflon screw cap. The Schlenk tube was then placed in an oil bath for the desired time and temperature. Following completion of the reaction, the reaction mixture was purified by flash chromatography (hexanes:ethyl acetate = 1:1). The fractions containing product were collected and concentrated by rotary evaporation to afford the compound. In most cases, the product was visualized on TLC using the cerium ammonium molybdate (CAM) stain.



2,5-dioxopyrrolidin-1-yl 2-phenylcyclopropanecarboxylate (**1a**) was obtained as tan oil that solidified upon standing using the general procedure in 86% yield (56.0 mg). R_f=0.47 (hexanes:ethyl acetate = 1:1). $[\alpha]^{20}_D$ = -235 (c = 0.83, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.22 (m, 3H), 7.13-7.11 (m, 2H), 2.82 (bs, 4H), 2.75-2.70 (m, 1H), 2.15-2.11 (m, 1H), 1.80-1.75 (m, 1H), 1.61-1.56 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 168.7, 138.3, 128.6, 127.1, 126.3, 28.23, 25.57, 20.87, 18.37. IR (neat, cm^{-1}): 2980 (C-H), 2890 (C-H), 1800 (C=O), 1773 (C=O), 1732 (C=O). HRMS (ESI): Calcd. for $C_{14}H_{13}NO_4Na$ ($[M+Na]^+$) m/z 282.07368, Found 282.07304. HPLC Chiralcel OD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 92%ee; 25 min (minor) and 29 min (major).



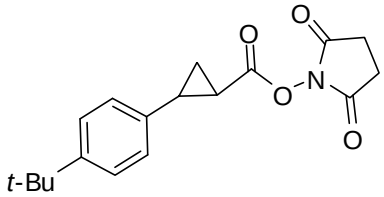
2,5-dioxopyrrolidin-1-yl 2-p-tolylcyclopropanecarboxylate (**1b**) was obtained as tan oil that solidified upon standing using the general procedure in 90% yield (61.7 mg). R_f=0.51 (hexanes:ethyl acetate = 1:1). $[\alpha]^{20}_D$ = -296 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (d, J = 7.8 Hz, 2H), 7.03 (d, J = 7.8 Hz, 2H), 2.82 (bs, 4H), 2.74-2.69 (m, 1H), 2.32 (s, 3H), 2.12-2.08 (m, 1H), 1.78-1.73 (m, 1H), 1.59-1.54 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 168.7, 136.7, 135.2, 129.2, 126.2, 28.03, 25.53, 20.78, 20.77, 18.23. IR (neat, cm^{-1}): 2924 (C-H), 1783 (C=O), 1735 (C=O). HRMS (ESI): Calcd. for $C_{15}H_{19}N_2O_4$ ($[M+NH_4]^+$) m/z 291.13393, Found 291.13339. HPLC Chiralcel OD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 95%ee; 20 min (minor) and 26 min (major).



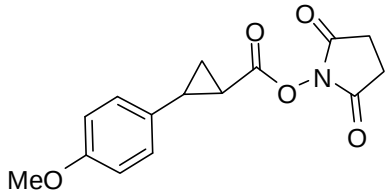
The X-ray intensities were measured using Bruker-APEX2 area-detector CCD diffractometer (CuKa, λ = 1.54178 Å). Indexing was performed using APEX2. Frames were integrated with SAINT V7.51A software package. Absorption correction was performed by multi-scan method implemented in SADABS. The structure was solved using SHELXS-97 and refined using SHELXL-97 contained in SHELXTL v6.10 and WinGX v1.70.01 programs packages.The X-ray Crystal data and refinement conditions are shown in Table S1.

Table S1. Crystal data and structure refinement for **1b.**

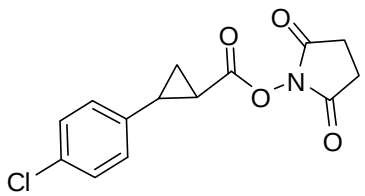
Empirical formula	C15 H15 N O4	
Formula weight	273.28	
Temperature	296(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 5.8676(2) Å	α= 90°.
	b = 8.9556(3) Å	β= 90°.
	c = 27.5262(8) Å	γ = 90°.
Volume	1446.44(8) $Å^3$	
Z	4	
Density (calculated)	1.255 Mg/m^3	
Absorption coefficient	0.760 mm^{-1}	
F(000)	576	
Crystal size	0.35 x 0.20 x 0.08 mm^3	
Theta range for data collection	3.21 to 67.78°.	
Index ranges	-6<=h<=6, -9<=k<=10, -33<=l<=31	
Reflections collected	9269	
Independent reflections	1501 [R(int) = 0.0274]	
Completeness to theta = 67.78°	96.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9417 and 0.7769	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1501 / 0 / 182	
Goodness-of-fit on F^2	1.084	
Final R indices [I>2sigma(I)]	R1 = 0.0392, wR2 = 0.1048	
R indices (all data)	R1 = 0.0520, wR2 = 0.1103	
Absolute structure parameter	10(10)	
Largest diff. peak and hole	0.102 and -0.144 $e.Å^{-3}$	



2,5-dioxopyrrolidin-1-yl 2-(4-tert-butylphenyl)cyclopropanecarboxylate (**1c**) was obtained as tan oil using the general procedure in 80% yield (62.8 mg). R_f=0.52 (hexanes:ethyl acetate = 1:1). $[\alpha]^{20}_D$ = -269 (c = 0.59, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 2.83 (bs, 4H), 2.74-2.70 (m, 1H), 2.15-2.11 (m, 1H), 1.80-1.75 (m, 1H), 1.62-1.57 (m, 1H), 1.31 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 168.7, 150.1, 135.3, 126.0, 125.5, 34.43, 31.26, 27.97, 25.53, 20.84, 18.25. IR (neat, cm^{-1}): 2980 (C-H), 1800 (C=O), 1771 (C=O), 1733 (C=O). HRMS (ESI): Calcd. for $C_{18}H_{21}NO_4$ ($[M+Na]^+$) m/z 338.13628, Found 338.13648. HPLC: Chiralcel OD-H (95 hexanes:5 isopropanol @ 0.8 ml/min): 97%ee; 45 min (minor) and 50 min (major).

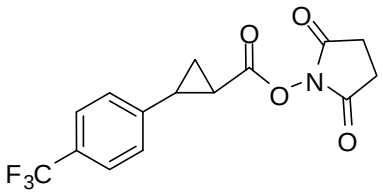


2,5-dioxopyrrolidin-1-yl 2-(4-methoxyphenyl)cyclopropanecarboxylate (**1d**) was obtained as tan oil that solidified upon standing using the general procedure in 71% yield (51.8 mg). R_f=0.39 (hexanes:ethyl acetate = 1:1). $[\alpha]^{20}_D$ = -300 (c = 0.59, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07 (d, J = 8.4 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 3.79 (s, 3H), 2.81 (bs, 4H), 2.73-2.68 (m, 1H), 2.08-2.04 (m, 1H), 1.77-1.72 (m, 1H), 1.57-1.52 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 168.8, 158.7, 130.2, 127.6, 114.0, 55.29, 27.81, 25.54, 20.66, 18.08. IR (neat, cm^{-1}): 1804 (C=O), 1775 (C=O), 1732 (C=O). HRMS (ESI): Calcd. for $C_{15}H_{19}N_2O_5$ ($[M+NH_4]^+$) m/z 307.12885, Found 307.12795. HPLC: Chiralcel OD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 95%ee; 27 min (minor) and 36 min (major).

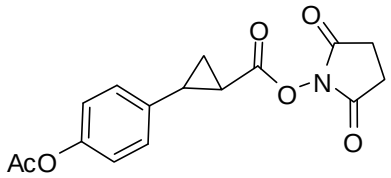


2,5-dioxopyrrolidin-1-yl 2-(4-chlorophenyl)cyclopropanecarboxylate (**1e**) was obtained as tan oil that solidified upon standing using the general procedure in 66% yield (48.9 mg). R_f=0.46 (hexanes:ethyl acetate = 1:1). $[\alpha]^{20}_D$ = -279 (c = 0.40, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, J = 8.4 Hz, 2H), 7.05 (d, J = 8.0 Hz, 2H), 2.81 (bs, 4H), 2.71-2.66 (m, 1H), 2.11-2.07 (m, 1H), 1.79-1.74 (m, 1H), 1.56-1.51 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 169.4, 136.8, 132.8, 128.7, 127.7, 27.47, 25.54, 20.85, 18.22. IR (neat, cm^{-1}): 2980 (C-H), 2890 (C-H), 1802 (C=O), 1773 (C=O), 1730

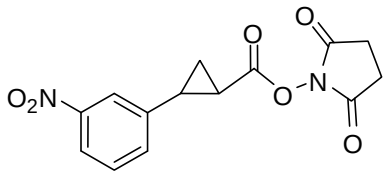
(C=O). HRMS (ESI): Calcd. for $C_{14}H_{12}ClNO_4Na$ ([M+Na]$^+$) m/z 316.03471, Found 316.03380. HPLC: Chiralcel OD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 90%ee; 25 min (minor) and 32 min (major).



2,5-dioxopyrrolidin-1-yl 2-(4-(trifluoromethyl)phenyl)cyclopropanecarboxylate (**1f**) was obtained as tan oil that solidified upon standing using the general procedure in 77% yield (63.6 mg). R_f=0.49 (hexanes:ethyl acetate = 1:1). $[\alpha]^{20}_D$ = -226 (c = 0.78, $CHCl_3$). ^{1}H NMR (400 MHz, $CDC1_3$): δ 7.54 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 2.81 (bs, 4H), 2.78-2.73 (m, 1H), 2.19-2.15 (m, 1H), 1.84-1.79 (m, 1H), 1.62-1.57 (m, 1H). ^{13}C NMR (100 MHz, $CDC1_3$): δ 169.0, 168.3, 142.4, 129.5, 126.6, 125.58, 125.54. 27.52, 25.53, 21.07, 18.41. ^{19}F NMR (376 MHz, $CDC1_3$): δ -62.96. IR (neat, cm^{-1}): 2978 (C-H), 2892 (C-H), 1802 (C=O), 1778 (C=O), 1737 (C=O). HRMS (ESI): Calcd. for $C_{15}H_{16}F_3N_2O_4$ ([M+NH$_4$]$^+$) m/z 345.10567, Found 345.10450. HPLC: Chiralcel OD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 90%ee; 22 min (minor) and 26 min (major).

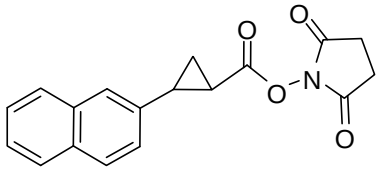


2,5-dioxopyrrolidin-1-yl 2-(4-acetoxyphenyl)cyclopropanecarboxylate (**1g**) was obtained as tan oil using the general procedure in 71% yield (56.8 mg). Isolation was followed by GC and fractions containing product were combined. $[\alpha]^{20}_D$ = -224 (c = 0.45, $CHCl_3$). ^{1}H NMR (400 MHz, $CDC1_3$): δ 7.16 (d, J = 8.8 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H), 2.83 (bs, 4H), 2.76-2.71 (m, 1H), 2.29 (s, 3H), 2.14-2.08 (m, 1H), 1.80-1.76 (m, 1H), 1.59-1.55 (m, 1H). ^{13}C NMR (100 MHz, $CDC1_3$): δ 169.4, 169.0, 168.6, 149.6, 135.8, 127.5, 121.7, 27.67, 25.55, 21.06, 20.81, 18.26. IR (neat, cm^{-1}): 2963 (C-H), 1768 (C=O), 1735 (C=O). HRMS (ESI): Calcd. for $C_{16}H_{16}NO_6$ ([M+H]$^+$) m/z 318.09721, Found 318.09737. HPLC: Chiralcel OD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 91%ee; 45 min (minor) and 57 min (major).

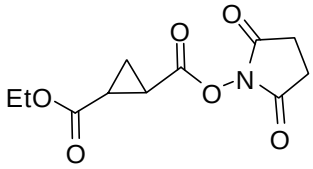


2,5-dioxopyrrolidin-1-yl 2-(3-nitrophenyl)cyclopropanecarboxylate (**1h**) was obtained as tan oil using the general procedure in 50% yield (38.3 mg). Isolation was followed by GC and fractions containing product were combined. $[\alpha]^{20}_D$ = -150 (c = 0.19, $CHCl_3$). ^{1}H NMR (400 MHz, $CDC1_3$): δ 8.11-8.09 (m, 1H), 7.97 (s, 1H), 7.51-7.47 (m, 2H), 2.85-2.80 (m, 5H), 2.26-2.21 (m, 1H), 1.90-1.85 (m, 1H), 1.62-1.63 (m, 1H). ^{13}C

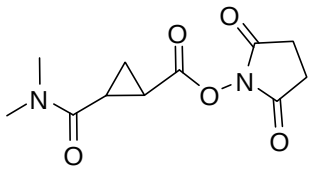
NMR (100 MHz, $CDCl_3$): δ 168.9, 168.1, 148.4, 140.5, 132.9, 129.6, 122.1, 121.0, 27.13, 25.54, 21.11, 18.33. IR (neat, cm^{-1}): 1808 (C=O), 1775 (C=O), 1731 (C=O), 1528 (NO_2), 1350 (NO_2). HRMS (ESI): Calcd. for $C_{14}H_{16}N_3O_6$ ($[M+NH_4]^+$) m/z 322.10336, Found 322.10345. HPLC: Chiralcel AD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 92%ee; 40 min (minor) and 47 min (major).



2,5-dioxopyrrolidin-1-yl 2-(naphthalen-2-yl)cyclopropanecarboxylate (**1i**) was obtained as tan solid using the general procedure in 33% yield (25.6 mg). R_f=0.43 (hexanes:ethyl acetate = 1:1). $[\alpha]^{20}_D$ = -286 (c = 1.06, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81-7.76 (m, 3H), 7.61 (s, 1H), 7.49-7.42 (m, 2H), 7.24-7.22 (m, 1H), 2.94-2.89 (m, 1H), 2.83 (bs, 4H), 2.26-2.22 (m, 1H), 1.88-1.83 (m, 1H), 1.74-1.69 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 168.7, 135.6, 133.2, 132.5, 128.4, 127.6, 127.5, 126.4, 125.8, 125.2, 124.4, 28.48, 25.56, 20.82, 18.27. IR (neat, cm^{-1}): 2980 (C-H), 1802 (C=O), 1774 (C=O), 1739 (C=O). HRMS (ESI): Calcd. for $C_{18}H_{19}N_2O_4$ ($[M+NH_4]^+$) m/z 327.13393, Found 327.13379. HPLC: Chiralcel AD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 91%ee; *trans*: 59 min (minor) and 92 min (major).

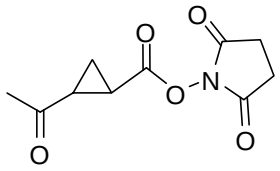


1-(2,5-dioxopyrrolidin-1-yl) 2-ethyl cyclopropane-1,2-dicarboxylate (**1j**) was obtained as tan oil using the general procedure in 57% yield (36.6 mg). Isolation was followed by GC and fractions containing product were combined. $[\alpha]^{20}_D$ = -235 (c = 0.08, $CHCl_3$). $[\alpha]^{20}_D$ = -90 (c = 3.8 mg/mL, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.17 (q, J = 7.2 Hz, 2H), 2.82 (bs, 4H), 2.45-2.41 (m, 1H), 2.37-2.33 (m, 1H), 1.67-1.57 (m, 2H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 168.8, 167.5, 61.53, 25.50, 23.71, 19.05, 16.69, 14.07. IR (neat, cm^{-1}): 2984 (C-H), 1781 (C=O), 1727 (C=O). HRMS (ESI): Calcd. for $C_{11}H_{14}NO_6$ ($[M+H]^+$) m/z 256.08156, Found 256.08129. HPLC: Chiralcel AD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 89%ee; 13 min (minor) and 16 min (major).

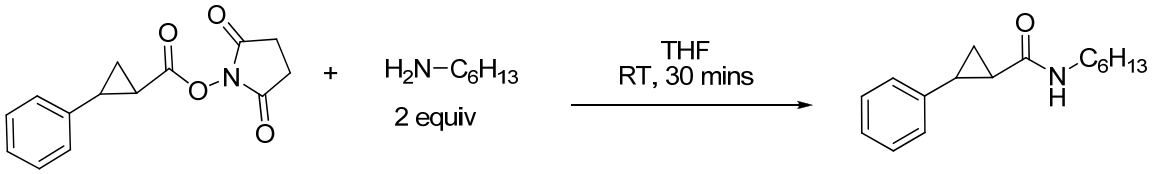


2,5-dioxopyrrolidin-1-yl 2-(dimethylcarbamoyl)cyclopropanecarboxylate (**1k**) was obtained as tan oil using the general procedure in 52% yield (33.4 mg). Isolation was followed by GC and fractions containing product were combined. $[\alpha]^{20}_D$ = -101 (c = 0.16, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.17 (s, 3H), 2.97 (s, 3H), 2.82 (bs, 4H), 2.51-2.47 (m, 1H), 2.45-2.40 (m, 1H), 1.70-1.65 (m, 1H), 1.56-1.51 9m, 1H). ^{13}C NMR (100

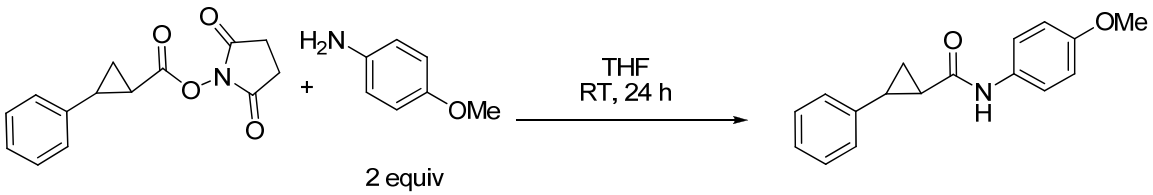
MHz, $CDC1_3$): δ 168.9, 168.6, 168.4, 37.27, 35.96, 25.52, 22.66, 18.77, 16.31. IR (neat, cm^{-1}): 2924 (C-H), 2854 (C-H), 1782 (C=O), 1740 (C=O), 1637 (C=O). HRMS (ESI): Calcd. for $C_{11}H_{18}N_3O_5$ ($[M+NH_4]^+$) m/z 272.12410, Found 272.12386. HPLC: Chiralcel AD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 96%ee; 19 min (minor) and 36 min (major).



2,5-dioxopyrrolidin-1-yl 2-acetylcyclopropanecarboxylate (**1l**) was obtained as tan oil using the general procedure in 55% yield (31.1 mg). Isolation was followed by GC and fractions containing product were combined. $[\alpha]^{20}_D$ = -231 (c = 0.25, $CHCl_3$). ^{1}H NMR (400 MHz, $CDC1_3$): δ 2.81 (bs, 4H), 2.65-2.60 (m, 1H), 2.45-2.41 (m, 1H), 2.35 (s, 3H), 1.60-1.56 (m, 2H). ^{13}C NMR (100 MHz, $CDC1_3$): δ 203.9, 168.8, 167.6, 30.99, 30.37, 25.51, 20.63, 18.30. IR (neat, cm^{-1}): 2924 (C-H), 1780 (C=O), 1735 (C=O), 1704 (C=O). HRMS (ESI): Calcd. for $C_{10}H_{11}NO_5Na$ ($[M+Na]^+$) m/z 248.05294, Found 248.05239. HPLC: Chiralcel AD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 91%ee; 22 min (minor) and 39 min (major).

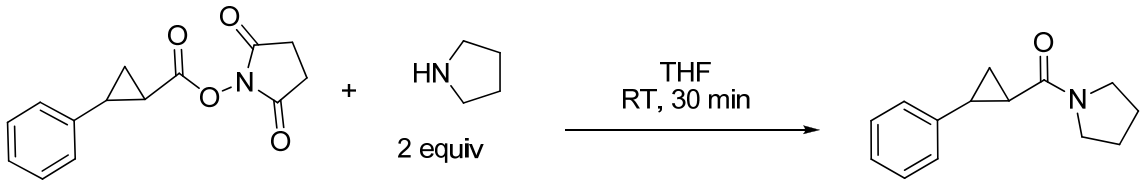


N-hexyl-2-phenylcyclopropanecarboxamide (**2aa**) was obtained as oil in 92% yield (29.1 mg). R_f=0.80 (hexanes:ethyl acetate = 1:1). $[\alpha]^{20}_D$ = -242 (c = 0.49, $CHCl_3$). ^{1}H NMR (400 MHz, $CDC1_3$): δ 7.25-7.22 (m, 2H), 7.17-7.15 (m, 1H), 7.06-7.04 (m, 2H), 5.65 (bs, 1H), 3.26-3.22 (m, 2H), 2.45-2.43 (m, 1H), 1.58-1.51 (m, 2H), 1.47-1.45 (m, 2H), 1.26 (bs, 6H), 1.21-1.18 (m, 1H), 0.85 (m, 3H). ^{13}C NMR (100 MHz, $CDC1_3$): δ 171.6, 140.9, 128.4, 126.1, 125.9, 39.86, 31.44, 29.64, 26.81, 26.57, 24.85, 22.51, 15.80, 13.97. IR (neat, cm^{-1}): 3295 (N-H), 2956 (C-H), 2925 (C-H), 2857 (C-H), 1634 (C=O). HRMS (ESI): Calcd. for $C_{16}H_{24}NO$ ($[M+H]^+$) m/z 246.1858, Found 246.1861. HPLC Chiralcel AD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 90%ee; 6 min (minor) and 8 min (major).

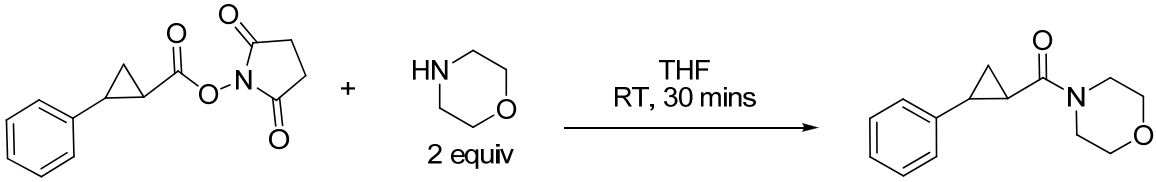


N-(4-methoxyphenyl)-2-phenylcyclopropanecarboxamide (**2ab**) was obtained as tan oil that solidified in 62% yield (27.4 mg). R_f=0.79 (hexanes:ethyl acetate = 1:1). $[\alpha]^{20}_D$ = -252 (c = 0.54, $CHCl_3$). ^{1}H NMR (400 MHz, $CDC1_3$): δ 7.39 (d, J = 8.0 Hz, 2H), 7.34

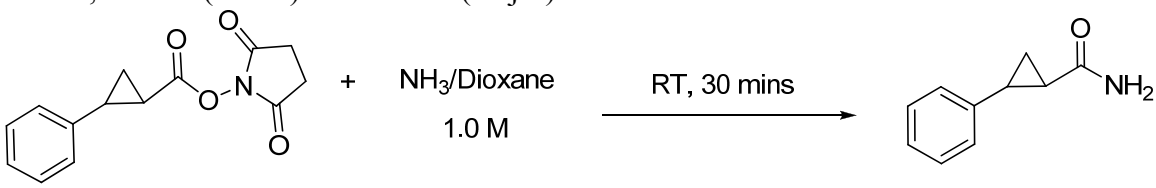
(bs, 1H), 7.29-7.24 (m, 2H), 7.20-7.19 (m, 1H), 7.09 (d, *J* = 7.6 Hz, 2H), 6.82 (d, *J* = 7.6 Hz, 2H), 3.76 (s, 3H), 2.55-2.54 (m, 1H), 1.70-1.68 (m, 2H), 1.32-1.30 (m, 1H). ^{13}C NMR (100 MHz, $CDC1_3$): δ 170.2, 156.5, 140.8, 131.3, 128.7, 126.5, 126.2, 121.8, 114.3, 55.69, 27.74, 25.90, 16.46. IR (neat, cm^{-1}): 3274 (N-H), 2980 (C-H), 1643 (C=O). HRMS (ESI): Calcd. for $C_{17}H_{18}NO_2$ ($[M+H]^+$) m/z 268.1337, Found 268.1337. HPLC Chiralcel AD-H (90 hexanes:10 isopropanol @ 1.0 ml/min): 89%ee; 16 min (major) and 28 min (minor).



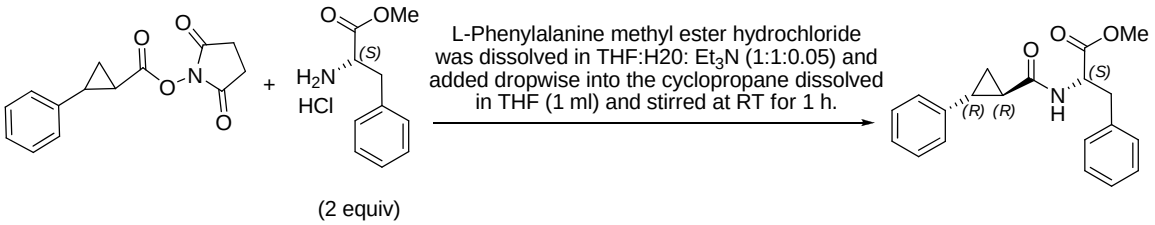
(2-phenylcyclopropyl)(pyrrolidin-1-yl)methanone (**2ac**) was obtained as tan oil that solidified upon standing in 91% yield (32.4 mg). R_f=0.28 (hexanes:ethyl acetate = 1:1). $[\alpha]^{20}_D$ = -376 (c = 0.30, $CHCl_3$). ^{1}H NMR (400 MHz, $CDC1_3$): δ 7.27-7.23 (m, 2H), 7.18-7.14 (m, 1H), 7.11-7.09 (m, 2H), 3.61-3.53 (m, 2H), 3.48 (t, *J* = 6.8 Hz, 2H), 2.52-2.47 (m, 1H), 1.97 -1.81 (m, 5H), 1.65-1.61 (m, 1H), 1.25-1.21 (m, 1H). ^{13}C NMR (100 MHz, $CDC1_3$): δ 170.4, 141.2, 128.3, 126.1 (2 Ar), 46.58, 46.01, 25.99, 25.39, 24.58, 24.40, 16.26. IR (neat, cm^{-1}): 2979 (C-H), 2873 (C-H), 1607 (C=O). HRMS (ESI): Calcd. for $C_{14}H_{18}NO$ ($[M+H]^+$) m/z 216.13829, Found 216.13775. HPLC Chiralcel OD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 92%ee; 7 min (minor) and 8 min (major).



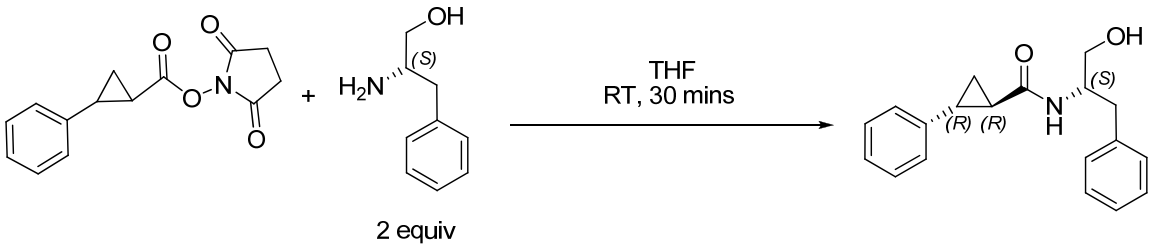
morpholino(2-phenylcyclopropyl)methanone (**2ad**) was obtained as oil that solidified upon standing in 95% yield (40.9 mg). R_f=0.37 (hexanes:ethyl acetate = 1:1). $[\alpha]^{20}_D$ = -178 (c = 0.48, $CHCl_3$). ^{1}H NMR (400 MHz, $CDC1_3$): δ7.28-7.25 (m, 2H), 7.20-7.16 (m, 1H), 7.10-7.08 (m, 2H), 3.66-3.61 (m, 8H), 2.50-2.45 (m, 1H), 1.93-1.89 (m, 1H), 1.69-1.63 (m, 1H), 1.30-1.24 (m, 1H). ^{13}C NMR (100 MHz, $CDC1_3$): δ 170.6, 140.7, 128.4, 126.3, 125.9, 66.78 (2 C), 45.95, 42.53, 25.52, 22.91, 16.15. IR (neat, cm^{-1}): 2980 (C-H), 2890 (C-H), 1632 (C=O). HRMS (ESI): Calcd. for $C_{14}H_{18}NO_2$ ($[M+H]^+$) m/z 232.13321, Found 232.13339. HPLC Chiralcel OD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 92%ee; 11 min (minor) and 17 min (major).



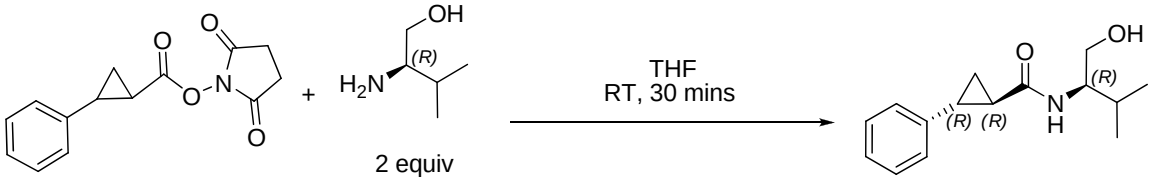
2-phenylcyclopropanecarboxamide (**2ae**) was obtained as white solid in 93% yield (29.6 mg). Isolation was performed by simple filtration. $[\alpha]^{20}_D$ = -290 (c = 0.14, $CHCl_3$). ^{1}H NMR (400 MHz, $CDC1_3$): δ 7.25-7.22 (m, 2H), 7.19-7.16 (m, 1H), 7.08-7.05 (m, 2H), 5.82-5.71 (bd, 2H), 2.49-2.45 (m, 1H), 1.68-1.61 (m, 1H), 1.60-1.56 (m, 1H), 1.27-1.23 (m, 1H). ^{13}C NMR (100 MHz, $CDC1_3$): δ 174.1, 140.5, 128.4, 126.3, 126.0, 25.83, 25.66, 16.29. IR (neat, cm^{-1}): 3382 (N-H), 3201 (N-H), 2922 (C-H), 1647 (C=O). HRMS (ESI): Calcd. for $C_{10}H_{12}NO$ ($[M+H]^+$) m/z 162.09134, Found 162.09066. HPLC Chiralcel OD-H (80 hexanes:20 isopropanol @ 0.8 ml/min): 94%ee; 8 min (major) and 10 min (minor).



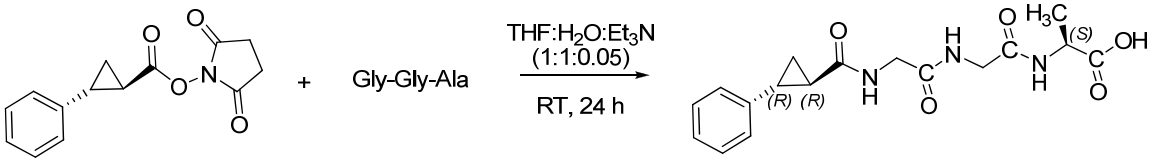
(2S)-methyl 3-phenyl-2-(2-phenylcyclopropanecarboxamido)propanoate (**2af**) was obtained as oil that solidified upon standing in 66% yield (17.3 mg). $[\alpha]^{20}_D$ = -46 (c = 0.34, $CHCl_3$). ^{1}H NMR (400 MHz, $CDC1_3$): δ 7.29-7.17 (m, 6H), 7.08-7.06 (m, 4H), 6.10 (d, J = 7.6 Hz, 1H), 4.94-4.89 (m, 1H), 3.71 (s, 3H), 3.18-3.06 (m, 2H), 2.48-2.43 (m, 1H), 1.60-1.57 (m, 2H), 1.26-1.22 (m, 1H). ^{13}C NMR (100 MHz, $CDC1_3$): δ 172.1, 171.4, 140.5, 135.7, 129.2, 128.5, 128.4, 127.1, 126.3, 126.1, 53.28, 52.30, 37.99, 26.38, 25.41, 15.82. IR (neat, cm^{-1}): 3312 (N-H), 3033 (C-H), 2950 (C-H), 1741 (C=O), 1639 (C=O). HRMS (ESI): Calcd. for $C_{20}H_{22}NO_3$ ({$M+H]^+$) m/z 324.1599, Found 324.1597.



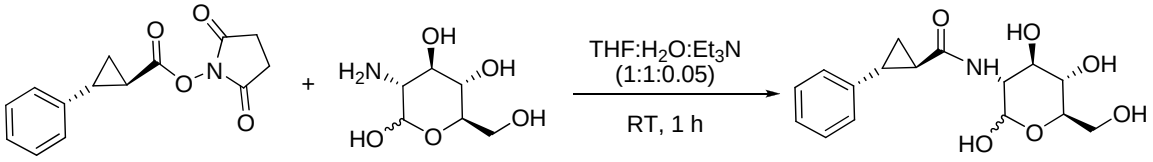
N-((S)-1-hydroxy-3-phenylpropan-2-yl)-2-phenylcyclopropanecarboxamide (**2ag**) was obtained as oil that solidified upon standing in 93% yield (20.8 mg). R_f=0.36 (hexanes:ethyl acetate = 1:1). $[\alpha]^{20}_D$ = -161 (c = 0.40, $CHCl_3$). ^{1}H NMR (400 MHz, $CDC1_3$): δ 7.29-7.16 (m, 8H), 7.05-7.03 (m, 2H), 6.00 (d, J = 28.8 Hz, 1H), 4.19-4.17 (m, 1H), 3.68-3.66 (m, 1H), 3.59-3.55 (m, 1H), 2.91 (bs, 1H), 2.86 (d, J = 7.2 Hz, 2H), 2.45-2.40 (m, 1H), 1.60-1.53 (m, 2H), 1.24-1.18 (m, 1H). ^{13}C NMR (100 MHz, $CDC1_3$): δ 172.5, 140.5, 137.5, 129.2, 128.6, 128.4, 126.6, 126.2, 126.0, 64.01, 53.14, 37.07, 26.63, 25.16, 15.94. IR (neat, cm^{-1}): 3284 (O-H, N-H), 2954 (C-H), 1633 (C=O). HRMS (ESI): Calcd. for $C_{19}H_{22}NO_2$ ($[M+H]^+$) m/z 296.1650, Found 296.1650.



N-((R)-1-hydroxy-3-methylbutan-2-yl)-2-phenylcyclopropanecarboxamide (**2ah**) was obtained as oil that solidified upon standing in 54% yield (11.2 mg). R_f=0.28 (hexanes:ethyl acetate = 1:1). $[\alpha]^{20}_D$ = -156 (c = 0.22, $CHCl_3$). ^{1}H NMR (400 MHz, $CDC1_3$): δ 7.27-7.23 (m, 2H), 7.19-7.17 (m, 1H), 7.07-7.05 (m, 2H), 5.87 (d, *J* = 7.2 Hz, 1H), 3.74-3.72 (m, 1H), 3.65-3.64 (m, 2H), 2.78 (bs, 1H), 2.47-2.44 (m ,1H), 1.63-1.60 (m, 2H), 1.24-1.21 (m, 1H), 0.945 (m, 6H). ^{13}C NMR (100 MHz, $CDC1_3$): δ 172.9, 140.7, 128.4, 126.2, 125.9, 64.21, 57.56, 29.13, 26.78, 25.21, 19.43, 18.75, 16.17. IR (neat, cm^{-1}): 3287 (O-H, N-H), 2924 (C-H), 1637 (C=O). HRMS (ESI): Calcd. for $C_{15}H_{22}NO_2$ ({M+H]$^+$) m/z 248.1650, Found 248.1655.



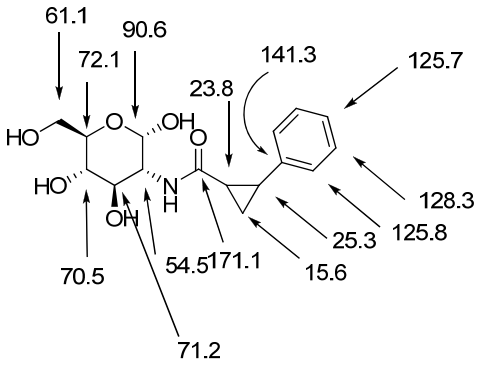
2-(2-(2-(2-phenylcyclopropanecarboxamido)acetamido)acetamido)propanoic acid[2] (**2ai**) was obtained as white solid in 60% yield (30.8 mg). The cyclopropyl peptide was purified by preparatory HPLC using a Dionex Summit HPLC equipped with the Waters Radial Compression column (300 mm x 25 mm, 15 micron particle size, 300 Angstrom pore size, C4) utilizing a gradient solvent system of acetonitrile and water (5% MeCN/H_20 – 50%MeCN/H_20) with a flow rate of 20 ml/min. $[\alpha]^{20}_D$ = -185 (c = 0.19, IPA). ^{1}H NMR (400 MHz, D_2O): δ 7.24-7.20 (m, 2H), 7.15- 7.12 (m, 1H), 7.09-7.08 (m, 2H), 4.24 (t, *J* = 7.6 Hz, 1H), 3.84-3.82 (m, 4H), 2.36-2.31 (m, 1H), 1.88-1.83 (m, 1H), 1.42-1.37 (m, 1H), 1.32-1.25 (m, 4 H). ^{13}C NMR (100 MHz, D_2O): δ 179.4, 178.9, 175.1, 173.7, 143.1, 131.4, 129.3, 128.8, 51.55, 45.67, 44.86, 28.26, 27.69, 18.95, 18.32. IR (neat, cm^{-1}): 3303 (O-H, N-H), 2979 (C-H), 1651 (C=O), 1635 (C=O). HRMS (ESI): Calcd. for $C_{17}H_{22}N_3O_5$ ([M+H]$^+$) m/z 348.1559, Found 348.1550.



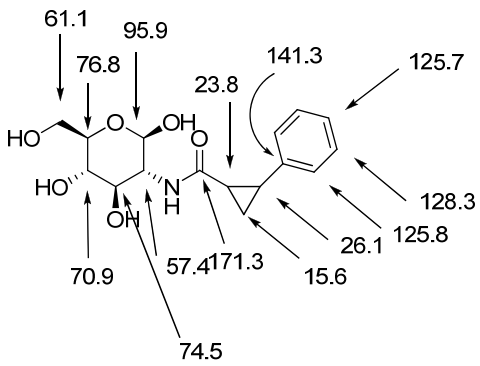
N-(2-phenylcyclopropanecarboxamido)-D-glucosamine (**2aj**) was obtained as white solid in 47 % yield (20.4 mg) as a mixture of anomers (α:β = 1.6:1) as determined by HPLC. The product was purified by preparatory HPLC using a Dionex Summit HPLC equipped with the Supelcosil PLC-8 column (250 mm x 21.2 mm, 12 micron particle size, C8) utilizing a gradient solvent system of acetonitrile in water (5% MeCN:H_2O – 30% MeCN:H_2O) with a flow rate of 20 ml/min. $[\alpha]^{20}_D$ = -51 (c = 0.78, DMSO). ^{1}H

NMR (400 MHz, DMSO) (anomeric mixture α:β = 2:1): δ 8.02 (d, J = 8.4 Hz, 1H, β anomer), 7.95 (d, J = 8.0 Hz, 1H, α anomer), 7.29-7.25 (m, 2H, anomeric mixture), 7.18-7.14 (m, 1H, anomeric mixture), 7.10-7.09 (m, 2H, anomeric mixture), 6.52 (d, J = 6.4 Hz, 1H, β anomer), 6.41 (d, J = 4.4 Hz, 1H, α anomer), 4.94-4.92 (m, 1H, mixture of anomers), 4.88 (d, J = 5.6 Hz, 1H, α anomer), 4.85 (d, J = 5.6 Hz, 1H, β anomer), 4.65 (d, J = 5.6 Hz, 1H, α anomer), 4.50 (t, J = 5.6 Hz, 1H, β anomer), 4.45-4.40 (m, 1H), 3.69-3.56 (m, 2H, anomeric mixture), 3.53-3.30 (m, 3H, anomeric mixture), 3.27 (m, 1H, β anomer), 3.11 (m, 1H, α anomer), 3.05 (m, 1H, anomeric mixture), 2.26-2.18 (m, 1H, anomeric mixture), 2.13-2.09 (m, 1H, α anomer), 1.89-1.85 (m, 1H, β anomer), 1.36-1.30 (m, 1H, anomeric mixture), 1.20-1.10 (m, 1H, anomeric mixture). ^{13}C NMR (100 MHz, DMSO) (α anomer): δ 171.1, 141.3, 128.3 (2), 125.8, 125.7 (2), 90.58, 72.05, 71.22, 70.50, 61.14, 54.47, 25.32, 23.83, 15.59. ^{13}C NMR (100 MHz, DMSO) (β anomer): δ 171.13, 141.3, 128.3 (2), 125.8, 125.7 (2), 95.49, 76.77, 74.45, 70.88, 61.14, 57.39, 26.11, 23.83, 15.59. IR (neat, cm^{-1}): 3285 (O-H, N-H), 1637 (C=O), 1613 (C=O), 1563 (C=C). HRMS (ESI): Calcd. for $C_{16}H_{22}NO_6$ ([M+H]$^+$) m/z 324.1447, Found 324.1469.

Carbon Assignments:



alpha-anomer



beta-anomer

[1] (a) Blankley, C. J.; Sauter, F. J.; House, O. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. V, p 258. (b) Doyle, M. P.; Kalinin, A. V. *J. Org. Chem*. **1996**, *61*, 2179. (c) Ouihia, A.; Rene, L.; Guilhem, J.; Pascard, C.; Badet, B. *J. Org. Chem*. **1993**, *58*, 1641.

[2] Triethylamine remains as an impurity as seen by residual solvent peaks in the ^{1}H NMR and ^{13}C NMR. The amine and carboxylic acid protons were not observed in D_2O.