Supporting Information

Enantioselective Synthesis of Pyrano[2,3-c]pyrrole via Organocatalytic [4+2] Cyclization Reaction of Dioxopyrrolidines and Azlactones

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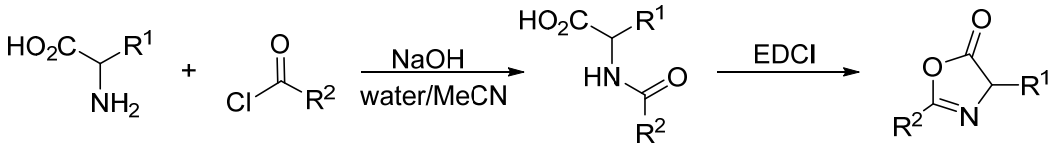
Contents

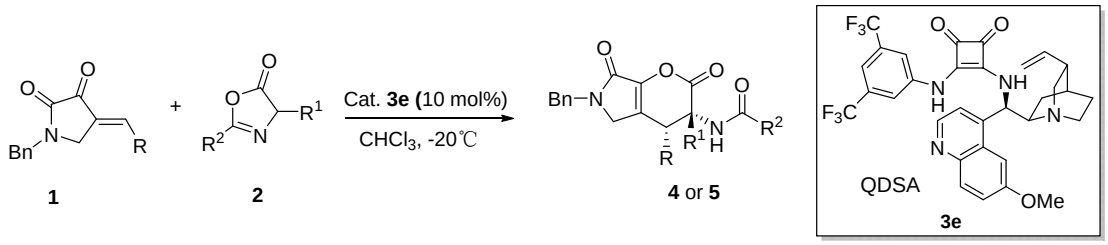
A: General Information and Starting Materials

General Information. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker AV-400 spectrometer (400 MHz and 100 MHz). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CDCl_3$: δ 7.26) Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.16). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz). High resolution mass spectrometry (ESI) were carried out using a TSQ Quantum Access, Thermo Fisher, USA. Optical rotations were measured on an Autopol III automatic polarimeter (Rudolph Research analytical) High performance liquid chromatography (HPLC) was performed on an SHIMADAZU LC-16 series chromatographs using chiral columns (DAICEL CHIRALPAK) as noted.

Starting Materials. All solvents and inorganic reagents were from commercial sources (Adamas-beta®) and used without purification unless otherwise noted. The dioxopyrrolidines **1** were synthesized following the literature procedure.[1] The azlactones **2** were synthesized following the literature procedure.[2]

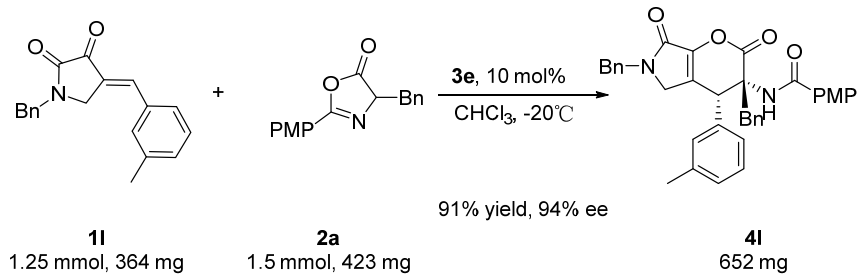


B: General procedure for Asymmetric [4+2] Cyclization of Azlactones



Dioxopyrrolidines **1** (0.1 mmol 1.0 equiv.) and **3e** (0.01 mmol 0.1 equiv.) in $CHCl_3$ (3 mL) were cooled to -20℃, then added azlactones **2** (0.12 mmol 1.2 equiv.) in $CHCl_3$ (1 mL). The reaction stirred at -20℃ for the time indicated at Table 3 and Table 4, and then the solvent was removed under vacuum to give a residue, which was purified by silica gel chromatography to yield the desired product **4** or **5**. The enantiomeric ratio was determined by HPLC analysis on chiral column.

Larger-scale synthesis of 4l



Dioxopyrrolidines **1l** (1.25 mmol, 364 mg, 1.0 equiv.) and **3e** (0.125 mmol 0.1 equiv.) in $CHCl_3$ (40 mL) were cooled to -20℃, then added azlactones **2a** (1.50 mmol, 423 mg 1.2 equiv.) in $CHCl_3$ (10 mL). The reaction stirred at -20℃ for 48h, and then the solvent was removed under vacuum to give a residue, which was purified by silica gel chromatography to yield the desired product **4l** (652 mg, 91% yield). The enantiomeric ratio was determined by HPLC analysis on OD-H chiral column (94% *ee*).

C: Crystallographic Information for Product 4d

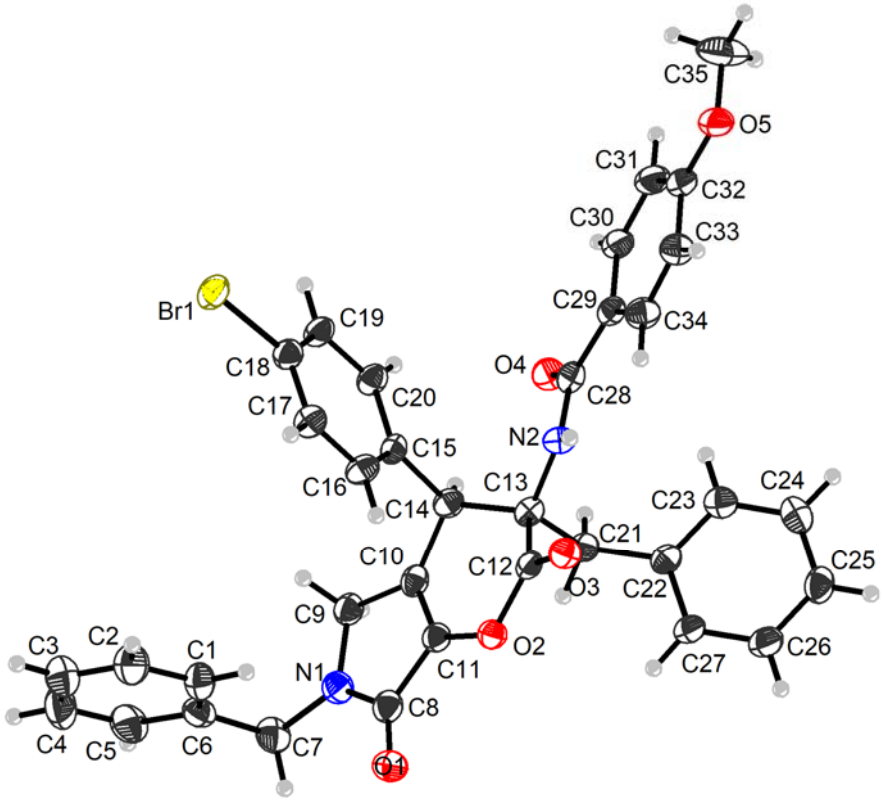
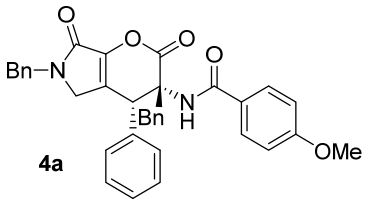


Table 1. Crystal data and structure refinement for 4d

Identification code	**4d**
Empirical formula	$C_{35}H_{29}BrN_2O_5$
Formula weight	637.51
Temperature/K	118.4(8)
Crystal system	orthorhombic
Space group	$P2_12_12$
a/Å	19.3581(2)
b/Å	25.0827(3)
c/Å	6.72000(10)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	3262.92(7)
Z	4
ρ_{calc}g/cm^3	1.298
μ/mm^{-1}	2.063
F(000)	1312.0
Crystal size/mm^3	0.1 × 0.04 × 0.04
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	5.766 to 153.11
Index ranges	$-24 \leq h \leq 21$, $-30 \leq k \leq 30$, $-8 \leq l \leq 6$
Reflections collected	12229
Independent reflections	5985 [R_{int} = 0.0322, R_{sigma} = 0.0388]
Data/restraints/parameters	5985/0/389
Goodness-of-fit on F^2	0.871
Final R indexes [I>=2σ (I)]	R_1 = 0.0304, wR_2 = 0.0692
Final R indexes [all data]	R_1 = 0.0353, wR_2 = 0.0758
Largest diff. peak/hole / e Å^{-3}	0.31/-0.32
Flack parameter	-0.012(9)

D: Characterization Data of Cyclization Products

4a: N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4a

White solid, 50.7 mg, 91% yield, $[\alpha]_D^{20}$ –43.3 (*c* 0.492, CH_2Cl_2), 94% ee.

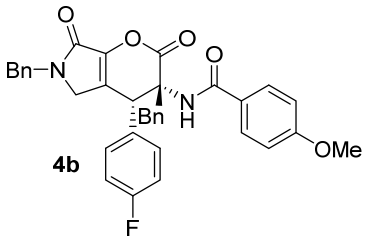
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.28 (m, 6H), 7.21 (d, *J* = 5.9 Hz, 6H), 7.14 (d, 4H), 6.79 (d, *J* = 8.3 Hz, 2H), 6.59 (s, 1H), 5.05 (s, 1H), 4.77 (d, *J* = 14.8 Hz, 1H), 4.61 (d, *J* = 14.8 Hz, 1H), 4.25 (d, *J* = 13.6 Hz, 1H), 3.94 (d, *J* = 18.8 Hz, 1H), 3.78 (s, 3H), 3.70 (d, *J* = 18.8 Hz, 1H), 3.34 (d, *J* = 13.6 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.7, 167.3, 162.3, 162.1, 141.5, 136.2, 135.7, 134.0, 130.1, 129.1, 129.0, 128.5, 128.5, 128.4, 128.3, 128.1, 127.8, 127.7, 126.9, 113.8, 66.2, 55.4, 48.0, 47.7, 46.9, 39.7.

HRMS (ESI) *m/z* calculated for $C_{35}H_{30}N_2O_5$ $[M+H]^+$: 559.2227, found 559.2222.

HPLC analysis: (IB column, Hexane:2-propanol = 80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 15.65 (minor), 20.58 (major).

4b: N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-fluorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4b

White solid, 57.6 mg, 99% yield, $[\alpha]_D^{20}$ –34.4 (*c* 0.487, $CHCl_3$), 91% ee.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.31 (m, 5H), 7.32 – 7.26 (m, 2H), 7.23 (d, *J* = 2.1 Hz, 2H), 7.16 – 7.06 (m, 4H), 6.90 (t, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.61 (s, 1H), 5.05 (s, 1H), 4.77 (d, *J* = 14.9 Hz, 1H), 4.63 (d, *J* = 14.9 Hz, 1H), 4.20 (d, *J* = 13.7 Hz, 1H), 3.93 (d, *J* = 18.9 Hz, 1H), 3.81 (s, 3H), 3.69 (d, *J* = 18.8 Hz, 1H), 3.32 (d, *J* = 13.7 Hz, 1H).

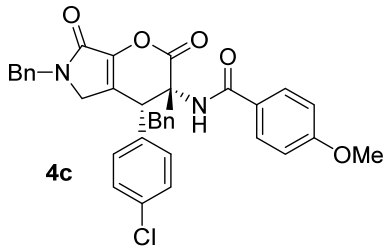
^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.5, 167.2, 162.4, 161.9, 161.2, 141.5, 136.1, 133.8, 131.4, 131.4, 130.0, 129.6, 129.5, 129.0, 128.5, 128.4, 128.3, 128.1, 127.7,

126.61, 116.1, 115.9, 113.8, 66.1, 55.4, 47.5, 47.2, 46.9, 39.6.

HRMS (ESI) *m/z* calculated for $C_{35}H_{29}FN_2O_5$ $[M+H]^+$: 577.2133, found 577.2152.

HPLC analysis: (IB column, Hexane:2-propanol = 80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 24.64 (minor), 27.19 (major).

4c: N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-chlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



White solid, 45.0 mg, 74% yield, $[\alpha]_D^{20}$ –16.5 (*c* 0.285, $CHCl_3$), 95% ee.

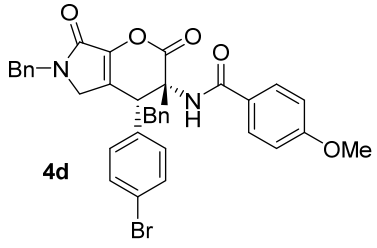
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.32 (m, 5H), 7.30 (d, *J* = 1.5 Hz, 1H), 7.26 – 7.16 (m, 5H), 7.14 – 7.05 (m, 4H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.62 (s, 1H), 5.05 (s, 1H), 4.77 (d, *J* = 14.9 Hz, 1H), 4.63 (d, *J* = 14.9 Hz, 1H), 4.19 (d, *J* = 13.7 Hz, 1H), 3.93 (d, *J* = 18.9 Hz, 1H), 3.81 (s, 3H), 3.66 (s, 1H), 3.32 (d, *J* = 13.7 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.5, 167.2, 162.5, 161.9, 141.7, 136.1, 134.4, 133.8, 130.1, 129.2, 129.2, 129.0, 128.5, 128.4, 128.3, 128.1, 127.8, 127.8, 126.5, 113.9, 66.0, 55.4, 47.5, 47.3, 46.9, 39.7.

HRMS (ESI) *m/z* calculated for $C_{35}H_{29}ClN_2O_5$ $[M+H]^+$:593.1838, found: 593.1843.

HPLC analysis: (IA column, Hexane:2-propanol = 50:50, flow rate = 0.75 mL/min, wavelength = 254 nm): *R*t = 16.98 (minor), 50.91 (major).

4d: N-((3*S*,4*R*)-3,6-dibenzyl-4-(4-bromophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



White solid, 47.2 mg, 74% yield, $[\alpha]_D^{20}$ –13.8 (*c* 0.266, $CHCl_3$), 95% ee.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (td, *J* = 8.9, 2.3 Hz, 6H), 7.29 (d, *J* = 4.4 Hz, 2H), 7.25 – 7.17 (m, 3H), 7.11 (d, *J* = 9.1 Hz, 3H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.62 (s, 1H), 5.04 (s, 1H), 4.77 (d, *J* = 14.9 Hz, 1H), 4.63 (d, *J* = 14.9 Hz, 1H), 4.19 (d, *J* = 13.7 Hz, 1H), 3.93 (d, *J* = 18.9 Hz, 1H), 3.81 (s, 3H), 3.68 (d, *J* =

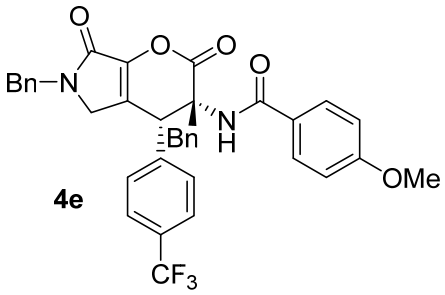
18.8 Hz, 1H), 3.32 (d, *J* = 13.7 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.4, 167.2, 162.5, 161.9, 141.8, 136.1, 134.7, 133.7, 132.2, 130.1, 129.5, 129.0, 128.5, 128.5, 128.3, 128.1, 127.8, 127.7, 126.5, 122.5, 113.9, 65.9, 55.4, 47.5, 47.4, 47.0, 39.7.

HRMS (ESI) *m/z* calculated for $C_{35}H_{29}BrN_2O_5$ $[M+H]^+$:637.1333, found:637.1345.

HPLC analysis: (IA column, Hexane:2-propanol =50:50, flow rate = 0.75 mL/min, wavelength = 254 nm): *R*t = 18.97 (minor), 56.61 (major).

4e: N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(4-(trifluoromethyl)phenyl)-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



White solid, 55.7 mg, 89% yield, $[\alpha]_D^{20}$ –17.8 (*c* 0.298, $CHCl_3$), 95% ee.

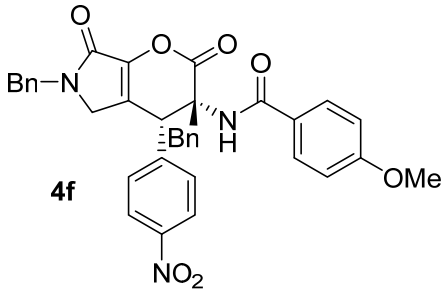
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (d, *J* = 8.1 Hz, 2H), 7.39 – 7.28 (m, 8H), 7.25 – 7.20 (m, 3H), 7.12 (d, *J* = 7.6 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 6.62 (s, 1H), 5.15 (s, 1H), 4.78 (d, *J* = 14.9 Hz, 1H), 4.62 (d, *J* = 14.8 Hz, 1H), 4.21 (d, *J* = 13.7 Hz, 1H), 3.95 (d, *J* = 18.9 Hz, 1H), 3.81 (s, 3H), 3.68 (d, *J* = 18.8 Hz, 1H), 3.34 (d, *J* = 13.7 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.3, 167.3, 162.6, 161.8, 142.0, 139.8, 136.0, 133.6, 131.2, 130.8, 130.5, 130.2, 130.1, 129.0, 128.5, 128.4, 128.3, 128.1, 127.8, 127.7, 127.3, 126.4, 126.1, 126.0, 126.0, 126.0, 125.0, 122.3, 113.9, 65.9, 55.4, 47.7, 47.5, 47.0, 39.7.

HRMS (ESI) *m/z* calculated for $C_{36}H_{29}F_3N_2O_5$ $[M+H]^+$:627.2101, found:627.2115.

HPLC analysis: (IB column, Hexane:2-propanol = 80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 20.37 (major), 27.91 (minor).

4f: N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-nitrophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



Yellow solid, 44.2 mg, 73% yield, $[\alpha]_D^{20}$ –40.5 (*c* 45.8, DCM), 98% ee.

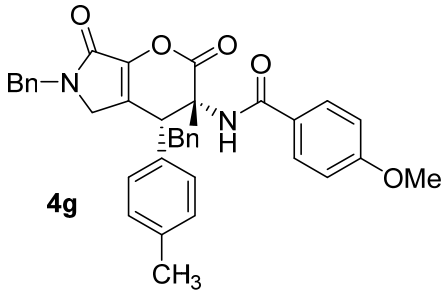
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 8.8 Hz, 2H), 7.39 – 7.31 (m, 6H), 7.30 – 7.27 (m, 2H), 7.24 (t, *J* = 5.5 Hz, 3H), 7.15 – 7.07 (m, 2H), 6.81 (d, *J* = 8.9 Hz, 2H), 6.66 (s, 1H), 5.22 (s, 1H), 4.75 (d, *J* = 14.9 Hz, 1H), 4.64 (d, *J* = 14.9 Hz, 1H), 4.18 (d, *J* = 13.7 Hz, 1H), 3.96 (d, *J* = 19.0 Hz, 1H), 3.80 (s, 3H), 3.66 (d, *J* = 18.9 Hz, 1H), 3.35 (d, *J* = 13.7 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.2, 167.2, 162.7, 161.7, 147.8, 143.1, 142.2, 135.9, 133.4, 130.1, 129.1, 129.0, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 127.9, 126.7, 125.9, 124.2, 114.0, 65.7, 55.4, 47.6, 47.5, 47.0, 39.8.

HRMS (ESI) *m/z* calculated for $C_{35}H_{29}N_3O_7$ $[M+H]^+$:604.2078, found: 604.2101.

HPLC analysis: (IA column, Hexane:2-propanol = 65:35, flow rate = 0.8 mL/min, wavelength = 254 nm): *R*t = 39.43 (minor), 106.27 (major).

4g: N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(*p*-tolyl)-2,3,4,5,6,7-hexahydropyrano-[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



White solid, 49.2 mg, 89% yield, $[\alpha]_D^{20}$ –16.7 (*c* 0.249, $CHCl_3$), 95% ee.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (t, *J* = 7.1 Hz, 4H), 7.31 – 7.27 (m, 2H), 7.22 (d, *J* = 3.7 Hz, 3H), 7.18 – 7.08 (m, 2H), 7.01 (s, 4H), 6.81 (d, *J* = 8.6 Hz, 2H), 6.58 (s, 1H), 5.00 (s, 1H), 4.77 (d, *J* = 14.9 Hz, 1H), 4.62 (d, *J* = 14.9 Hz, 1H), 4.22 (d, *J* = 13.7 Hz, 1H), 3.92 (d, *J* = 18.8 Hz, 1H), 3.81 (s, 3H), 3.70 (d, *J* = 18.8 Hz, 1H), 3.32 (d, *J* = 13.7 Hz, 1H), 2.24 (s, 3H).

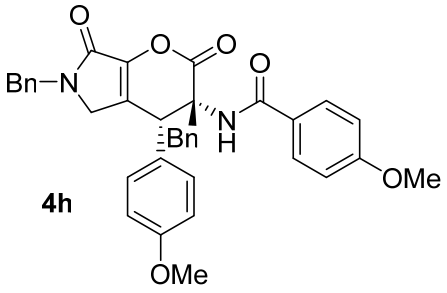
^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.7, 167.2, 162.3, 162.2, 141.4, 138.3, 136.2, 134.1, 132.5, 130.1, 129.7, 129.0, 128.7, 128.5, 128.4, 128.3, 128.0, 127.6, 127.0, 113.7,

66.3, 55.4, 55.4, 47.6, 46.9, 39.6, 21.1.

HRMS (ESI) *m/z* calculated for $C_{36}H_{32}N_2O_5$ $[M+H]^+$: 573.2384, found: 573.2391.

HPLC analysis: (IB column, Hexane:2-propanol = 80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 15.43 (major), 24.03 (minor).

4h: N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-methoxyphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4h

White solid, 43.0 mg, 73% yield, $[\alpha]_D^{20}$ –14.6 (*c* 0.220, $CHCl_3$), 90% ee.

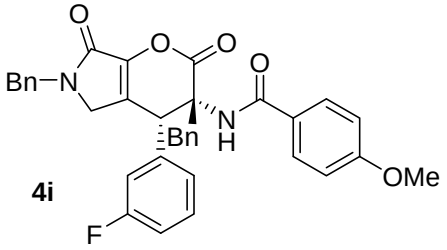
1H NMR (400 MHz, Chloroform-d) δ 7.40 – 7.34 (m, 4H), 7.28 (d, J = 2.3 Hz, 2H), 7.25 – 7.20 (m, 3H), 7.13 (d, J = 9.4 Hz, 2H), 7.04 (d, J = 8.6 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 6.73 (d, J = 8.7 Hz, 2H), 6.59 (s, 1H), 4.99 (s, 1H), 4.77 (d, J = 14.9 Hz, 1H), 4.62 (d, J = 14.9 Hz, 1H), 4.21 (d, J = 13.7 Hz, 1H), 3.92 (d, J = 18.8 Hz, 1H), 3.81 (s, 3H), 3.71 (s, 4H), 3.31 (d, J = 13.7 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.8, 167.2, 162.3, 162.1, 159.5, 141.3, 136.2, 134.1, 130.1, 129.0, 128.9, 128.7, 128.4, 128.3, 128.0, 127.6, 127.4, 127.0, 114.4, 113.8, 66.4, 55.4, 55.2, 47.5, 47.2, 46.9, 39.6.

HRMS (ESI) *m/z* calculated for $C_{36}H_{32}N_2O_6$ $[M+H]^+$:589.2333, found:589.2345.

HPLC analysis: (IA column, Hexane:2-propanol =65:35, flow rate = 0.8 mL/min, wavelength = 254 nm): *R*t = 25.73 (minor), 63.22 (major).

4i: N-((3*R*,4*R*)-3,6-dibenzyl-4-(3-fluorophenyl)-2,7-dioxo-2,3,4,5,6,7 hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4i

White solid, 57.5 mg, 99% yield, $[\alpha]_D^{20}$ -42.6 (*c* 0.495, $CHCl_3$), 94% ee.

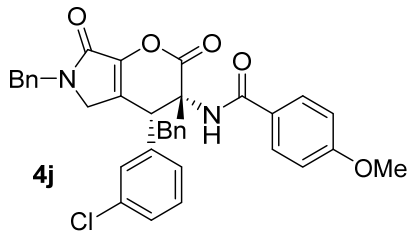
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.32 (m, 4H), 7.29 (d, *J* = 7.7 Hz, 2H), 7.27 – 7.16 (m, 4H), 7.14 – 7.09 (m, 2H), 6.89 (t, *J* = 7.4 Hz, 3H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.62 (s, 1H), 5.06 (s, 1H), 4.79 (d, *J* = 14.8 Hz, 1H), 4.62 (d, *J* = 14.8 Hz, 1H), 4.21 (d, *J* = 13.7 Hz, 1H), 3.93 (d, *J* = 18.9 Hz, 1H), 3.81 (s, 3H), 3.70 (d, *J* = 18.8 Hz, 1H), 3.32 (d, *J* = 13.6 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.4, 167.3, 162.5, 161.9, 141.8, 136.1, 133.7, 130.6, 130.1, 129.0, 128.5, 128.4, 128.3, 128.1, 127.8, 127.6, 126.6, 113.8, 66.0, 55.4, 47.6, 47.5, 47.0, 39.7.

HRMS (ESI) *m/z* calculated for $C_{35}H_{29}FN_2O_5$ $[M+H]^+$:577.2133, found: 577.2152.

HPLC analysis: (OD-H column, Hexane:2-propanol =80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 19.90 (major), 34.12 (minor).

4j: N-((3*R*,4*R*)-3,6-dibenzyl-4-(3-chlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4j

White solid, 59.3 mg, 99% yield, $[\alpha]_D^{20}$-46.4 (c 0.527, CH_2Cl_2), 95% ee.

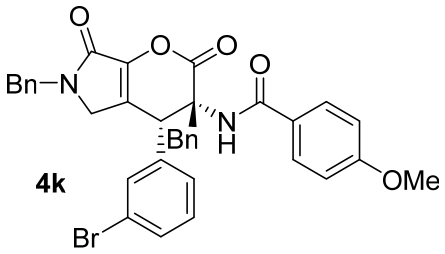
^{1}H NMR (400 MHz, Chloroform-d) δ 7.35 (dd, J = 11.5, 8.1 Hz, 5H), 7.29 (d, J = 7.8 Hz, 2H), 7.24 (d, J = 4.7 Hz, 2H), 7.14 (dd, J = 14.5, 5.3 Hz, 5H), 6.99 (d, J = 6.2 Hz, 1H), 6.83 (d, J = 7.5 Hz, 2H), 6.60 (s, 1H), 5.03 (s, 1H), 4.80 (d, J = 14.8 Hz, 1H), 4.61 (d, J = 14.8 Hz, 1H), 4.20 (d, J = 13.6 Hz, 1H), 3.92 (d, J = 18.8 Hz, 1H), 3.81 (s, 3H), 3.70 (d, J = 18.8 Hz, 1H), 3.31 (d, J = 13.6 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.4, 167.3, 162.5, 161.9, 141.9, 137.6, 136.0, 134.9, 133.7, 130.3, 130.1, 129.0, 128.8, 128.5, 128.4, 128.3, 128.1, 127.8, 127.4, 125.8, 113.9, 66.0, 55.4, 47.6, 47.5, 47.0, 39.7.

HRMS (ESI) m/z calculated for $C_{35}H_{29}ClN_2O_5$ [M+H]+:593.1838, found:593.1843.

HPLC analysis: (IB column, Hexane:2-propanol = 85:15, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 26.82 (major), 33.45 (minor).

4k: N-((3*R*,4*R*)-3,6-dibenzyl-4-(3-bromophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4k

White solid, 52.3mg, 82% yield, $[\alpha]_D^{20}$ -40.8 (*c* 0.497, CH_2Cl_2), 95% ee.

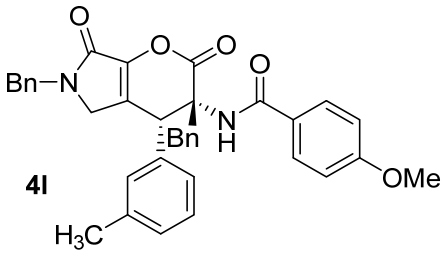
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.29 (m, 8H), 7.24 (d, *J* = 4.7 Hz, 3H), 7.10 (dd, *J* = 13.8, 5.8 Hz, 3H), 7.03 (d, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.60 (s, 1H), 5.02 (s, 1H), 4.80 (d, *J* = 14.8 Hz, 1H), 4.62 (d, *J* = 14.8 Hz, 1H), 4.20 (d, *J* = 13.6 Hz, 1H), 3.92 (d, *J* = 18.8 Hz, 1H), 3.82 (s, 3H), 3.70 (d, *J* = 18.7 Hz, 1H), 3.31 (d, *J* = 13.6 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.4, 167.3, 162.5, 161.9, 141.0, 137.8, 136.0, 133.7, 131.7, 131.1, 130.6, 130.1, 129.0, 128.5, 128.4, 128.3, 128.1, 127.8, 127.4, 126.7, 126.2, 123.0, 113.9, 66.0, 55.4, 55.4, 47.5, 47.0, 39.7.

HRMS (ESI) *m/z* calculated for $C_{35}H_{29}BrN_2O_5$ $[M+H]^+$:637.1332, found:637.1345.

HPLC analysis:(IB column, Hexane:2-propanol = 85:15, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 27.14 (major), 35.37 (minor).

4l: N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(m-tolyl)-2,3,4,5,6,7-hexahydropyrano-[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4l

White solid, 57.2mg, 99% yield, $[\alpha]_D^{20}$ -48.3 (*c* 0.544, $CHCl_3$), 95% ee.

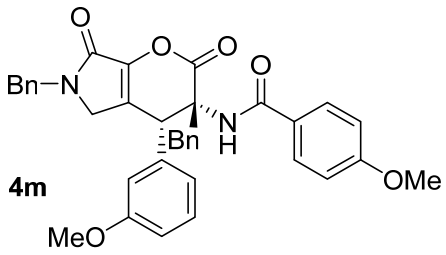
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 6.8 Hz, 1H), 7.25 (d, *J* = 0.8 Hz, 1H), 7.23 (d, *J* = 3.3 Hz, 1H), 7.20 (d, *J* = 2.4 Hz, 2H), 7.18 (s, 1H), 7.12 (d, *J* = 1.7 Hz, 3H), 7.07 – 6.94 (m, 3H), 6.90 (dq, *J* = 7.7, 1.1 Hz, 1H), 6.84 – 6.77 (m, 2H), 6.74 – 6.66 (m, 2H), 6.45 (s, 1H), 4.88 (s, 1H), 4.69 (d, *J* = 14.9 Hz, 1H), 4.51 (d, *J* = 14.9 Hz, 1H), 4.14 (d, *J* = 13.7 Hz, 1H), 3.82 (d, *J* = 18.9 Hz, 1H), 3.71 (s, 3H), 3.61 (d, *J* = 18.8 Hz, 1H), 3.22 (d, *J* = 13.7 Hz, 1H), 2.11 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.6, 167.4, 162.3, 162.1, 141.6, 138.8, 136.2, 135.4, 134.0, 130.1, 129.2, 129.0, 128.9, 128.5, 128.4, 128.4, 128.4, 128.3, 128.1, 127.6, 127.1, 124.8, 113.7, 66.2, 55.4, 47.8, 47.6, 46.9, 39.6, 21.3.

HRMS (ESI) *m/z* calculated for $C_{36}H_{32}N_2O_5$ $[M+H]^+$:573.2384, found:573.2391.

HPLC analysis:(OD-H column, Hexane:2-propanol = 80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 17.17(major), 29.16(minor).

4m: N-((3*R*,4*R*)-3,6-dibenzyl-4-(3-methoxyphenyl)-2,7-dioxo-2,3,4,5,6,7 hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4m

White solid, 46.0 mg, 87% yield, $[\alpha]_D^{20}$-19.2 (*c* 0.289, CH_2Cl_2), 92% ee.

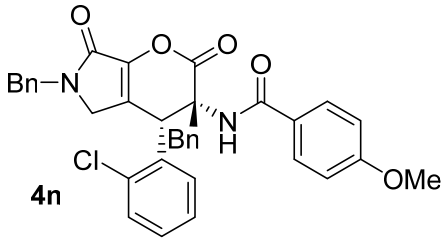
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.30 (m, 6H), 7.25 – 7.19 (m, 3H), 7.19 – 7.08 (m, 3H), 6.81 (d, *J* = 7.0 Hz, 2H), 6.76 – 6.71 (m, 1H), 6.71 – 6.65 (m, 2H), 6.59 (s, 1H), 5.00 (s, 1H), 4.78 (d, *J* = 14.9 Hz, 1H), 4.62 (d, *J* = 14.9 Hz, 1H), 4.24 (d, *J* = 13.7 Hz, 1H), 3.92 (d, *J* = 18.9 Hz, 1H), 3.81 (s, 3H), 3.72 (d, *J* = 18.8 Hz, 1H), 3.65 (s, 3H), 3.32 (d, *J* = 13.7 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.6, 167.3, 162.4, 162.1, 159.9, 141.7, 137.0, 136.2, 134.0, 130.1, 129.0, 128.4, 128.3, 128.2, 128.1, 127.7, 126.9, 119.7, 114.2, 113.8, 113.5, 66.2, 55.4, 55.2, 47.9, 47.6, 46.9, 39.6.

HRMS (ESI) *m/z* calculated for $C_{36}H_{32}N_2O_5$ $[M+H]^+$:589.2333, found:589.2345.

HPLC analysis:(IA column, Hexane:2-propanol = 70:30, flow rate = 0.8 mL/min, wavelength = 254 nm): *R*t = 32.34(minor), 89.85(major).

4n: N-((3*R*,4*S*)-3,6-dibenzyl-4-(2-chlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4n

White solid, 46.2 mg, 78% yield, $[\alpha]_D^{20}$-9.0 (*c* 0.471, CH_2Cl_2), 95% ee.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (dt, *J* = 18.1, 7.0 Hz, 7H), 7.31 – 7.25 (m, 3H), 7.15 (d, *J* = 7.3 Hz, 3H), 7.00 – 6.74 (m, 5H), 5.76 (s, 1H), 4.79 (d, *J* = 14.9 Hz,

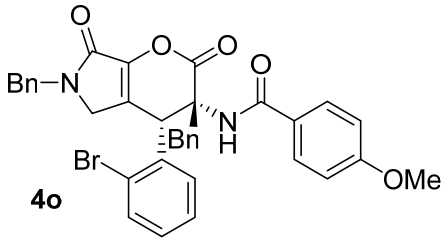
1H), 4.48 (d, *J* = 14.9 Hz, 1H), 4.15 (d, *J* = 13.5 Hz, 1H), 4.03 (d, *J* = 18.9 Hz, 1H), 3.79 (s, 3H), 3.73 (d, *J* = 19.7 Hz, 1H), 3.38 (d, *J* = 13.5 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.4, 166.2, 162.4, 161.9, 136.2, 133.5, 130.2, 129.1, 129.0, 128.5, 128.3, 128.0, 127.8, 127.4, 113.8, 63.7, 55.4, 47.7, 46.9, 44.7, 41.0.

HRMS (ESI) *m/z* calculated for $C_{35}H_{29}ClN_2O_5$ $[M+H]^+$:593.1838, found:593.1843.

HPLC analysis:(IB column, Hexane:2-propanol = 80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 26.49(major), 38.52(minor).

4o: N-((3*R*,4*S*)-3,6-dibenzyl-4-(2-bromophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4o

White solid, 45.5 mg, 71% yield, $[\alpha]_D^{20}$-5.0 (*c* 24.2, CH_2Cl_2), 90% ee.

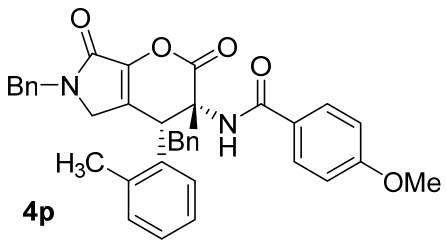
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 (d, *J* = 8.0 Hz, 1H), 7.42 – 7.34 (m, 5H), 7.29 (d, *J* = 4.5 Hz, 2H), 7.26 – 7.18 (m, 3H), 7.12 (d, *J* = 3.9 Hz, 2H), 7.04 (s, 1H), 6.92 (s, 1H), 6.86 – 6.73 (m, 3H), 5.74 (s, 1H), 4.80 (d, *J* = 14.9 Hz, 1H), 4.48 (d, *J* = 15.0 Hz, 1H), 4.14 (d, *J* = 13.6 Hz, 1H), 4.05 (d, *J* = 18.9 Hz, 1H), 3.80 (s, 3H), 3.75 (d, *J* = 18.9 Hz, 1H), 3.37 (d, *J* = 13.5 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.4, 166.1, 162.4, 161.8, 140.0, 136.2, 136.1, 133.6, 133.5, 130.2, 129.3, 129.0, 128.5, 128.5, 128.4, 128.3, 128.0, 127.9, 127.8, 127.6, 126.4, 124.6, 113.7, 63.7, 55.4, 47.7, 47.7, 46.9, 41.1.

HRMS (ESI) *m/z* calculated for $C_{35}H_{29}BrN_2O_5$ $[M+H]^+$:637.1332, found:637.1345.

HPLC analysis:(OD-H column, Hexane:2-propanol = 70:30, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 17.10(major), 28.62(minor).

4p: N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(o-tolyl)-2,3,4,5,6,7-hexahydropyrano-[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4p

White solid, 53.3 mg, 90% yield, $[\alpha]_D^{20}$ -14.8 (*c* 0.450, $CHCl_3$), 99% ee.

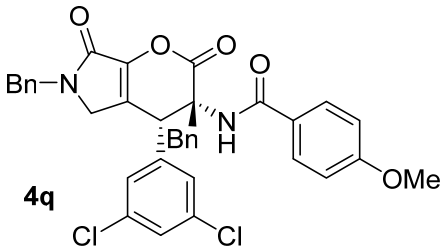
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 (dt, *J* = 12.3, 6.8 Hz, 3H), 7.31 – 7.27 (m, 3H), 7.26 – 7.22 (m, 3H), 7.19 – 7.02 (m, 5H), 6.80 (dd, *J* = 19.3, 8.0 Hz, 3H), 6.70 (s, 1H), 5.28 (s, 1H), 4.83 (d, *J* = 14.9 Hz, 1H), 4.46 (d, *J* = 14.9 Hz, 1H), 4.25 (d, *J* = 13.6 Hz, 1H), 3.93 (d, *J* = 18.5 Hz, 1H), 3.79 (s, 3H), 3.63 (d, *J* = 18.3 Hz, 1H), 3.37 (d, *J* = 13.6 Hz, 1H), 2.47 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.3, 166.8, 162.3, 162.2, 139.9, 136.6, 136.2, 135.2, 133.8, 131.3, 130.2, 130.1, 129.0, 128.9, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 126.8, 126.7, 113.7, 64.8, 55.4, 47.4, 46.8, 44.6, 40.5, 19.7.

HRMS (ESI) *m/z* calculated for $C_{36}H_{32}N_2O_5$ $[M+H]^+$: 573.2384, found: 573.2390.

HPLC analysis:(OD-H column, Hexane:2-propanol = 80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 17.45 (major), 33.15 (minor).

4q: N-((3*R*,4*R*)-3,6-dibenzyl-4-(3,5-dichlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4q

White solid, 42.5 mg, 68% yield, $[\alpha]_D^{20}$ -24.5 (*c* 0.310, $CHCl_3$), 93% ee.

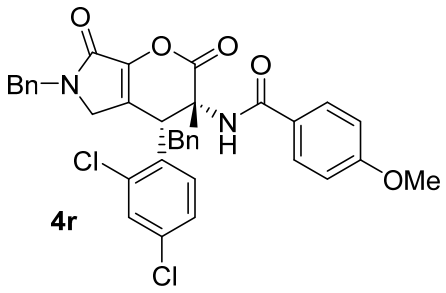
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (d, 2H), 7.22 (dd, *J* = 19.3, 8.2 Hz, 4H), 7.16 – 7.12 (m, 3H), 7.09 (s, 1H), 7.01 (d, *J* = 5.0 Hz, 2H), 6.93 (s, 2H), 6.74 (m, 2H), 6.54 (s, 1H), 4.93 (s, 1H), 4.71 (d, *J* = 14.9 Hz, 1H), 4.52 (d, *J* = 14.9 Hz, 1H), 4.07 (d, *J* = 13.7 Hz, 1H), 3.82 (d, *J* = 18.9 Hz, 1H), 3.72 (s, 3H), 3.60 (d, *J* = 18.9 Hz, 1H), 3.20 (d, *J* = 13.7 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.5, 166.9, 162.6, 161.7, 142.3, 138.9, 135.9, 135.6, 133.5, 130.1, 129.1, 128.9, 128.8, 128.6, 128.5, 128.3, 128.2, 127.9, 126.5, 126.5, 126.3, 113.9, 65.8, 55.4, 47.4, 47.2, 47.0, 39.7.

HRMS (ESI) *m/z* calculated for $C_{35}H_{28}Cl_2N_2O_5$ $[M+H]^+$:627.1448, found:627.1464.

HPLC analysis:(IB column, Hexane:2-propanol = 75:25, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 10.66 (major), 16.31 (minor).

4r: N-((3*R*,4*S*)-3,6-dibenzyl-4-(2,4-dichlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4r

White solid, 49.5 mg, 79% yield, $[\alpha]_D^{20}$-24.5 (*c* 0.310, $CHCl_3$), 99% ee.

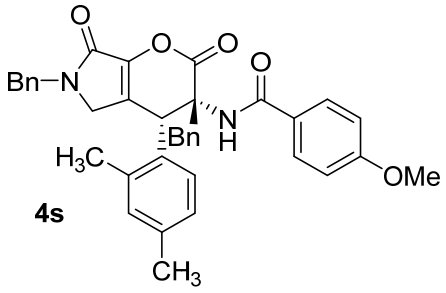
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.28 (m, 2H), 7.25 (d, *J* = 6.1 Hz, 3H), 7.19 – 7.12 (m, 6H), 7.03 (dd, *J* = 9.8, 3.4 Hz, 3H), 6.81 – 6.70 (m, 3H), 5.61 (s, 1H), 4.67 (d, *J* = 14.8 Hz, 1H), 4.41 (d, *J* = 14.9 Hz, 1H), 4.00 (d, *J* = 13.5 Hz, 1H), 3.90 (d, *J* = 18.8 Hz, 1H), 3.71 (s, 3H), 3.60 (d, *J* = 18.7 Hz, 1H), 3.25 (d, *J* = 13.4 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.2, 166.1, 162.5, 161.7, 140.3, 136.1, 134.5, 134.3, 133.3, 133.0, 130.1, 130.0, 129.2, 129.0, 128.5, 128.3, 128.1, 127.9, 127.7, 127.1, 126.0, 113.9, 55.4, 47.6, 46.9, 44.3, 22.7, 14.2.

HRMS (ESI) *m/z* calculated for $C_{35}H_{28}Cl_2N_2O_5$ $[M+H]^+$:627.1448, found:627.1464.

HPLC analysis:(IB column, Hexane:2-propanol = 80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 31.44(major), 53.05 (minor).

4s: N-((3*R*,4*R*)-3,6-dibenzyl-4-(2,4-dimethylphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4s

White solid, 39.9 mg, 68% yield, $[\alpha]_D^{20}$-8.0 (*c* 0.294, CH_2Cl_2), 73% ee.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.35 (m, 2H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.29 (dd, *J* = 7.6, 5.7 Hz, 3H), 7.26 – 7.21 (m, 3H), 7.15 (dd, *J* = 6.5, 2.8 Hz, 2H), 6.89 (d, *J* = 10.2 Hz, 2H), 6.79 (d, *J* = 8.8 Hz, 2H), 6.71 (d, *J* = 7.6 Hz, 2H), 5.23 (s, 1H), 4.83 (d, *J* = 15.0 Hz, 1H), 4.46 (d, *J* = 15.0 Hz, 1H), 4.24 (d, *J* = 13.6 Hz, 1H), 3.92 (d, *J* = 18.5 Hz, 1H), 3.79 (s, 3H), 3.63 (d, *J* = 18.4 Hz, 1H), 3.36 (d, *J* = 13.6 Hz, 1H), 2.42 (s, 3H), 2.19 (s, 3H).

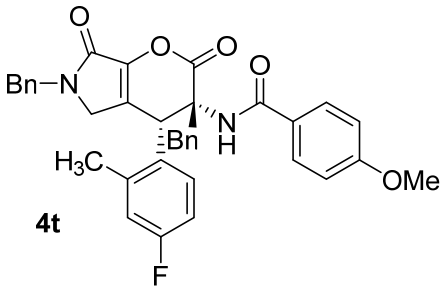
^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.4, 166.7, 162.2, 139.8, 137.5, 136.4, 136.3,

133.9, 132.1, 132.0, 130.2, 129.4, 129.0, 128.4, 128.4, 128.3, 128.0, 127.7, 127.5, 126.9, 126.6, 113.7, 64.9, 55.4, 47.4, 46.8, 44.3, 40.4, 20.9, 19.6.

HRMS (ESI) *m/z* calculated for $C_{37}H_{34}N_2O_5$ $[M+H]^+$:587.2540, found:587.2546.

HPLC analysis:(IB column, Hexane:2-propanol = 80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 17.07(major), 22.88 (minor).

4t: N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-fluoro-2-methylphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4t

White solid, 48.1 mg, 81% yield, $[\alpha]_D^{20}$-4.8 (*c* 0.200, CH_2Cl_2), 98% ee.

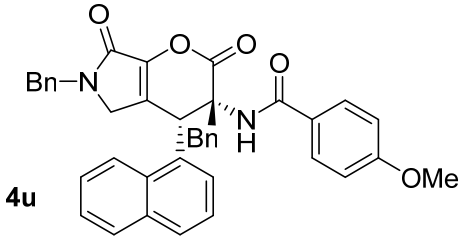
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.31 (m, 5H), 7.28 (d, 1H), 7.26 – 7.21 (m, 3H), 7.13 (d, *J* = 7.6 Hz, 2H), 6.80 (t, *J* = 7.7 Hz, 5H), 6.73 (s, 1H), 5.25 (s, 1H), 4.81 (d, *J* = 15.0 Hz, 1H), 4.50 (d, *J* = 15.0 Hz, 1H), 4.22 (d, *J* = 13.6 Hz, 1H), 3.93 (d, *J* = 18.5 Hz, 1H), 3.80 (s, 3H), 3.61 (d, *J* = 18.4 Hz, 1H), 3.35 (d, *J* = 13.6 Hz, 1H), 2.47 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.3, 166.7, 162.4, 162.1, 160.3, 140.0, 139.3, 136.2, 133.7, 131.1, 130.1, 129.0, 128.8, 128.7, 128.5, 128.4, 128.3, 128.3, 128.1, 127.8, 126.5, 117.9, 117.7, 64.8, 55.4, 47.3, 46.8, 44.0, 40.5, 19.9.

HRMS (ESI) *m/z* calculated for $C_{36}H_{31}FN_2O_5$ $[M+H]^+$:591.2290, found:591.2294.

HPLC analysis: (AD-H column, Hexane:2-propanol = 50:50, flow rate = 0.6 mL/min, wavelength = 254 nm): *R*t = 23.11 (minor), 89.79(major).

4u: N-((3*R*,4*R*)-3,6-dibenzyl-4-(naphthalen-1-yl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4u

White solid, 46.3 mg, 76% yield, $[\alpha]_D^{20}$ 0.65 (*c* 0.249, $CHCl_3$), 85% ee.

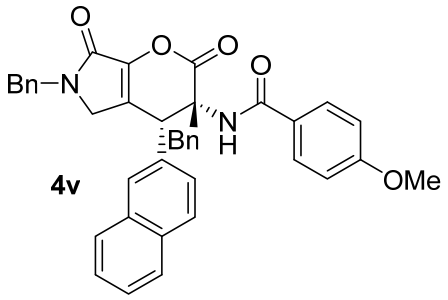
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (d, *J* = 8.6 Hz, 1H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.71 (d, *J* = 8.2 Hz, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.35 (dd, *J* = 14.5, 7.5 Hz, 4H), 7.25 (t, *J* = 5.7 Hz, 4H), 7.19 (d, *J* = 3.4 Hz, 2H), 7.10 (t, *J* = 8.6 Hz, 3H), 6.71 – 6.60 (m, 3H), 5.96 (s, 1H), 4.82 (d, *J* = 15.0 Hz, 1H), 4.42 (dd, *J* = 14.3, 7.5 Hz, 2H), 3.98 (d, *J* = 18.8 Hz, 1H), 3.73 (s, 3H), 3.54 (d, *J* = 4.3 Hz, 1H), 3.49 (s, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.3, 166.9, 162.1, 162.1, 140.6, 136.2, 134.0, 133.8, 132.8, 131.1, 130.2, 129.4, 129.0, 128.9, 128.8, 128.5, 128.2, 128.2, 128.0, 127.8, 126.6, 126.6, 126.0, 125.4, 124.7, 123.4, 113.6, 65.4, 55.3, 47.6, 46.8, 43.2, 40.2.

HRMS (ESI) *m/z* calculated for $C_{39}H_{32}N_2O_5$ $[M+H]^+$:609.2384, found:609.2386.

HPLC analysis: (OD-H column, Hexane:2-propanol = 80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 26.14(major), 54.23 (minor).

4v: N-((3*R*,4*R*)-3,6-dibenzyl-4-(naphthalen-2-yl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4v

White solid, 37.3 mg, 61% yield, $[\alpha]_D^{20}$ -4.2 (*c* 0.249, $CHCl_3$), 99% ee.

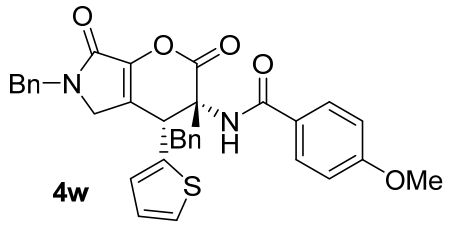
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 – 7.55 (m, 3H), 7.50 (s, 1H), 7.38 – 7.28 (m, 2H), 7.24 – 7.10 (m, 10H), 7.05 (d, *J* = 9.5 Hz, 2H), 6.59 (d, *J* = 8.8 Hz, 2H), 6.50 (s, 1H), 5.12 (s, 1H), 4.68 (d, *J* = 14.9 Hz, 1H), 4.47 (d, *J* = 14.9 Hz, 1H), 4.19 (d, *J* = 13.7 Hz, 1H), 3.84 (d, *J* = 18.9 Hz, 1H), 3.62 (s, 3H), 3.58 (d, *J* = 18.9 Hz, 1H), 3.28 (d, *J* = 13.7 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.7, 167.4, 162.3, 162.2, 141.6, 136.1, 134.0, 133.3, 133.0, 132.9, 130.1, 129.0, 128.9, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.7, 127.6, 127.2, 126.8, 126.6, 126.5, 113.7, 66.3, 55.3, 48.1, 47.6, 47.0, 39.7.

HRMS (ESI) *m/z* calculated for $C_{39}H_{32}N_2O_5$ $[M+H]^+$:609.2384, found:609.2386.

HPLC analysis: (OD-H column, Hexane:2-propanol =80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 24.90(major), 43.28 (minor).

4w: N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(thiophen-2-yl)-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



4w

Yellow solid, 42.4 mg, 79% yield, $[\alpha]_D^{20}$ -17.8 (*c* 0.376, CH_2Cl_2), 71% ee.

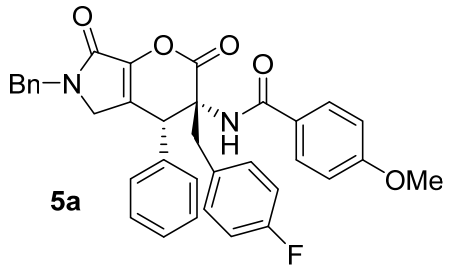
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 4H), 7.15 – 7.11 (m, 3H), 7.07 – 7.00 (m, 3H), 6.75 (d, *J* = 8.3 Hz, 4H), 6.57 (s, 1H), 5.33 (s, 1H), 4.70 – 4.54 (m, 2H), 4.07 (d, *J* = 13.5 Hz, 1H), 3.86 (d, *J* = 18.8 Hz, 1H), 3.77 (d, *J* = 6.5 Hz, 1H), 3.73 (s, 3H). 3.21 (d, *J* = 13.5 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.5, 167.1, 162.5, 162.0, 136.1, 133.9, 130.1, 129.0, 128.6, 128.5, 128.2, 128.1, 128.0, 127.7, 127.3, 127.2, 126.8, 126.0, 113.8, 113.9, 67.0, 55.5, 47.5, 47.0, 42.4, 39.4.

HRMS (ESI) *m/z* calculated for $C_{33}H_{28}N_2O_5S$ $[M+H]^+$:565.1792, found:565.1806.

HPLC analysis: (IB column, Hexane:2-propanol = 80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 18.98 (major), 25.95 (minor).

5a: N-((3*R*,4*R*)-6-benzyl-3-(4-fluorobenzyl)-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



5a

White solid, 43.2 mg, 75% yield, $[\alpha]_D^{20}$ -32.7 (*c* 0.412, CH_2Cl_2), 92% ee.

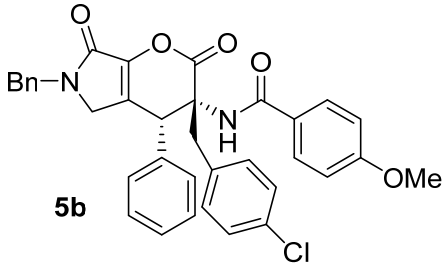
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 – 7.16 (m, 6H), 7.11 (d, *J* = 5.5 Hz, 3H), 7.00 (dt, *J* = 8.4, 4.5 Hz, 4H), 6.80 (t, *J* = 8.5 Hz, 2H), 6.70 (d, *J* = 8.7 Hz, 2H), 6.45 (s, 1H), 4.91 (s, 1H), 4.68 (d, *J* = 14.9 Hz, 1H), 4.50 (d, *J* = 14.9 Hz, 1H), 4.13 (d, *J* = 13.9 Hz, 1H), 3.83 (d, *J* = 18.9 Hz, 1H), 3.69 (s, 3H), 3.60 (d, *J* = 18.8 Hz, 1H), 3.19 (d, *J* = 13.8 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.6, 167.3, 163.5, 162.4, 162.0, 161.1, 141.5, 136.1, 135.5, 131.7, 129.8, 129.7, 129.1, 129.0, 128.5, 128.4, 128.3, 128.3, 128.1, 127.7, 126.7, 115.5, 115.3, 113.8, 66.1, 55.4, 47.9, 47.6, 46.9, 38.8.

HRMS (ESI) *m/z* calculated for $C_{35}H_{29}FN_2O_5$ $[M+H]^+$:577.2133, found:577.2122.

HPLC analysis: (IB column, Hexane:2-propanol = 85:15, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 22.47 (minor), 25.06 (major).

5b: N-((3*R*,4*R*)-6-benzyl-3-(4-chlorobenzyl)-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



5b

White solid, 49.1 mg, 83% yield, $[\alpha]_D^{20}$-9.9 (*c* 0.205, CH_2Cl_2), 77% ee.

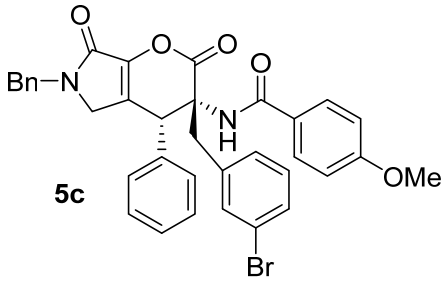
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.26 (m, 6H), 7.20 (t, *J* = 7.3 Hz, 5H), 7.13 – 7.03 (m, 4H), 6.80 (d, *J* = 8.8 Hz, 2H), 6.54 (s, 1H), 5.01 (s, 1H), 4.78 (d, *J* = 14.9 Hz, 1H), 4.61 (d, *J* = 14.9 Hz, 1H), 4.24 (d, *J* = 13.8 Hz, 1H), 3.93 (d, *J* = 18.9 Hz, 1H), 3.81 (s, 3H), 3.71 (d, *J* = 18.9 Hz, 1H), 3.28 (d, *J* = 13.7 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.5, 167.3, 162.4, 162.0, 141.6, 136.1, 135.4, 133.7, 132.4, 131.4, 129.1, 129.0, 128.7, 128.6, 128.4, 128.3, 128.2, 128.1, 127.7, 126.6, 113.8, 66.0, 55.4, 48.0, 47.6, 46.9, 38.9.

HRMS (ESI) *m/z* calculated for $C_{35}H_{29}ClN_2O_5$ $[M+H]^+$:593.1837, found:593.1834.

HPLC analysis: (IB column, Hexane:2-propanol = 80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 16.62 (minor), 19.14 (major).

5c: N-((3*R*,4*R*)-6-benzyl-3-(3-bromobenzyl)-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



5c

White solid, 44.9 mg, 70% yield, $[\alpha]_D^{20}$-28.8 (*c* 0.387, CH_2Cl_2), 79% ee.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.27 (m, 8H), 7.25 – 7.20 (m, 3H), 7.16 – 7.05 (m, 4H), 6.80 (d, *J* = 8.8 Hz, 2H), 6.53 (s, 1H), 5.01 (s, 1H), 4.78 (d, *J* = 14.9

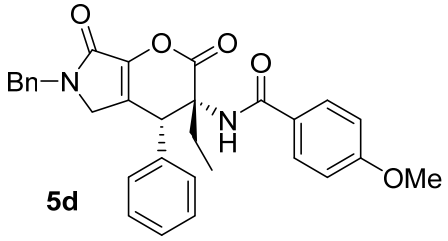
Hz, 1H), 4.60 (d, *J* = 14.9 Hz, 1H), 4.21 (d, *J* = 13.7 Hz, 1H), 3.91 (d, *J* = 14.2 1H), 3.80 (s, 3H), 3.70 (d, *J* = 18.9 Hz, 1H), 3.29 (d, *J* = 13.7 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.6, 167.4, 162.4, 162.0, 141.5, 136.2, 136.1, 135.4, 133.1, 130.9, 130.0, 129.1, 129.0, 128.7, 128.6, 128.4, 128.3, 128.2, 128.0, 127.7, 126.8, 122.5, 113.8, 65.9, 55.4, 47.9, 47.6, 46.9, 39.3.

HRMS (ESI) *m/z* calculated for $C_{35}H_{29}BrN_2O_5$ $[M+H]^+$:637.1332, found:637.1331.

HPLC analysis: (IB column, Hexane:2-propanol = 85:15, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 22.39 (minor), 25.41 (major).

5d: N-((3*R*,4*R*)-6-benzyl-3-ethyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano-[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



5d

White solid, 35.2 mg, 71% yield, $[\alpha]_D^{20}$ -54.1 (*c* 0.330, CH_2Cl_2), 93% ee.

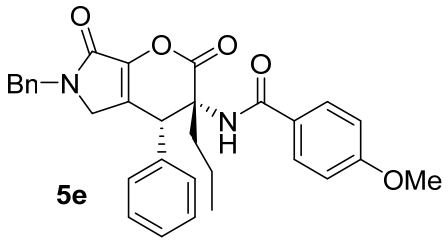
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.28 (m, 5H), 7.25 (d, *J* = 6.5 Hz, 1H), 7.23 – 7.17 (m, 3H), 7.08 (d, *J* = 3.7 Hz, 2H), 6.85 – 6.76 (m, 3H), 4.83 (s, 1H), 4.76 (d, *J* = 14.9 Hz, 1H), 4.56 (d, *J* = 14.9 Hz, 1H), 3.86 (d, *J* = 18.9 Hz, 1H), 3.81 (s, 3H), 3.69 (d, 1H), 3.01 (dd, *J* = 14.3, 7.5 Hz, 1H), 2.07 (dd, *J* = 14.3, 7.2 Hz, 1H). 0.92 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.5, 166.6, 162.3, 162.2, 141.5, 136.2, 135.9, 129.0, 129.0, 128.4, 128.4, 128.3, 128.2, 128.0, 127.6, 126.6, 113.8, 65.5, 55.4, 48.0, 47.6, 46.9, 27.1, 8.6.

HRMS (ESI) *m/z* calculated for $C_{30}H_{28}N_2O_5$ $[M+H]^+$:497.2071, found:497.2071.

HPLC analysis: (IA column, Hexane:2-propanol = 80:20, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 12.88 (minor), 15.48 (major).

5e: N-((3*R*,4*R*)-6-benzyl-2,7-dioxo-4-phenyl-3-propyl-2,3,4,5,6,7-hexahydropy-rano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



5e

White solid, 32.4 mg, 63% yield, $[\alpha]_D^{20}$-60.7 (*c* 0.309, CH_2Cl_2), 90% ee.

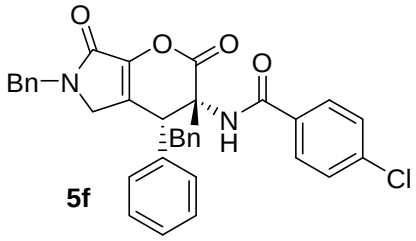
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (d, *J* = 8.8 Hz, 2H), 7.35 (s, 2H), 7.30 (s, 1H), 7.25 (s, 1H), 7.19 (d, *J* = 5.4 Hz, 3H), 7.07 (d, *J* = 3.7 Hz, 2H), 6.92 – 6.86 (m, 3H), 4.83 (s, 1H), 4.73 (d, *J* = 14.9 Hz, 1H), 4.60 (d, *J* = 14.9 Hz, 1H), 3.87 (d, *J* = 18.9 Hz, 1H), 3.81 (s, 3H), 3.66 (d, *J* = 18.8 Hz, 1H), 3.00 – 2.86 (m, 1H), 1.95 (s, 1H), 1.41 (d, *J* = 12.5 Hz, 1H), 1.30 – 1.20 (m, 1H), 0.92 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.7, 166.5, 162.3, 162.2, 141.6, 136.2, 135.8, 129.0, 129.0, 128.4, 128.4, 128.3, 128.2, 128.0, 127.7, 126.6, 113.7, 64.9, 55.4, 48.1, 47.6, 46.9, 36.0, 17.6, 13.6.

HRMS (ESI) *m/z* calculated for $C_{31}H_{30}N_2O_5$ $[M+H]^+$:511.2227, found: 511.2221.

HPLC analysis: (IB column, Hexane:2-propanol = 85:15, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 12.99 (minor), 18.52 (major).

5f: 4-chloro-N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)benzamide



5f

White solid, 56.4 mg, 99% yield, $[\alpha]_D^{20}$-40.7 (*c* 0.543, CH_2Cl_2), 89% ee.

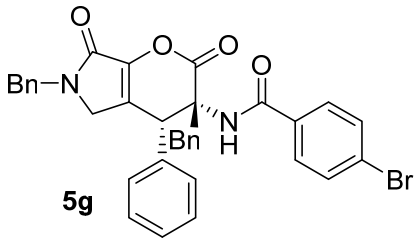
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.33 (m, 3H), 7.31 – 7.19 (m, 12H), 7.12 (dt, *J* = 7.1, 2.7 Hz, 4H), 6.61 (s, 1H), 5.01 (s, 1H), 4.79 (d, *J* = 14.9 Hz, 1H), 4.61 (d, *J* = 14.9 Hz, 1H), 4.20 (d, *J* = 13.8 Hz, 1H), 3.94 (d, *J* = 18.9 Hz, 1H), 3.71 (d, *J* = 18.8 Hz, 1H), 3.36 (d, *J* = 13.7 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 141.5, 138.0, 136.1, 135.5, 133.7, 132.9, 130.0, 129.2, 129.1, 129.0, 128.9, 128.6, 128.5, 128.3, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 66.2, 48.0, 47.6, 46.9, 39.7.

HRMS (ESI) *m/z* calculated for $C_{34}H_{27}ClN_2O_4$ $[M+H]^+$:563.1732, found: 563.1733.

HPLC analysis: (IB column, Hexane:2-propanol = 85:15, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 20.97 (major), 28.41 (minor).

5g: 4-bromo-N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)benzamide



5g

White solid, 22.3 mg, 37% yield, $[\alpha]_D^{20}$ -6.2 (*c* 0.181, CH_2Cl_2), 53% ee.

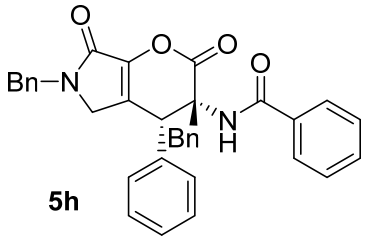
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 (d, *J* = 8.5 Hz, 2H), 7.40 – 7.31 (m, 3H), 7.29 (dd, *J* = 6.1, 2.1 Hz, 2H), 7.26 – 7.20 (m, 6H), 7.17 (d, 1H), 7.16 – 7.07 (m, 5H), 6.61 (s, 1H), 5.01 (s, 1H), 4.79 (d, *J* = 14.9 Hz, 1H), 4.61 (d, *J* = 14.9 Hz, 1H), 4.20 (d, *J* = 13.8 Hz, 1H), 3.94 (d, *J* = 18.9 Hz, 1H), 3.71 (d, *J* = 18.8 Hz, 1H), 3.36 (d, *J* = 13.7 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.5, 166.8, 162.0, 141.5, 136.1, 135.5, 133.7, 133.4, 131.8, 130.0, 129.2, 129.0, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 126.5, 66.2, 48.0, 47.6, 46.9, 39.7.

HRMS (ESI) *m/z* calculated for $C_{34}H_{27}BrN_2O_4$ $[M+H]^+$:607.1227, found: 607.1223.

HPLC analysis: (IB column, Hexane:2-propanol = 75:25, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 13.07 (major), 16.05 (minor).

5h: N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-[1,1'-biphenyl]-4-carboxamid



5h

White solid, 46.8 mg, 84% yield, $[\alpha]_D^{20}$ -40.4 (*c* 0.460, CH_2Cl_2), 83% ee. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 (d, *J* = 3.6 Hz, 1H), 7.36 (q, *J* = 6.7 Hz, 3H), 7.30 (q, *J* = 5.7 Hz, 6H), 7.27 – 7.20 (m, 6H), 7.15 (t, *J* = 6.2 Hz, 4H), 6.65 (s, 1H), 5.05 (s, 1H), 4.79 (d, *J* = 14.4 Hz, 1H), 4.62 (d, *J* = 14.4 Hz, 1H), 4.25 (d, *J* = 13.4 Hz, 1H), 3.94 (d, *J* = 18.6 Hz, 1H), 3.71 (d, *J* = 18.3 Hz, 1H), 3.36 (d, *J* = 13.5 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.9, 167.6, 162.1, 141.6, 136.2, 135.6, 134.7, 133.9, 131.7, 130.1, 129.1, 129.0, 128.6, 128.5, 128.40, 128.3, 128.2, 128.1, 127.8, 127.7, 126.5, 66.2, 48.0, 47.6, 47.0, 39.7.

HRMS (ESI) *m/z* calculated for $C_{34}H_{28}N_2O_4$ $[M+H]^+$:529.2122 found: 529.2129.

HPLC analysis: (IB column, Hexane:2-propanol = 85:15, flow rate = 1.0 mL/min, wavelength = 254 nm): *R*t = 17.43 (major), 25.75 (minor).

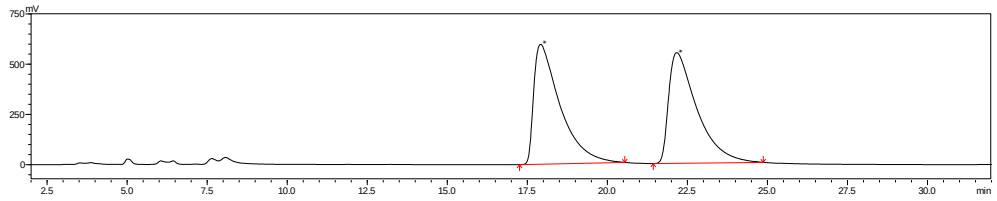
E: References

[1] X. Chen, L. Zhu, L. Fang, S. Yan and J. Lin, *RSC Adv.* **2014**, *4*, 9926.

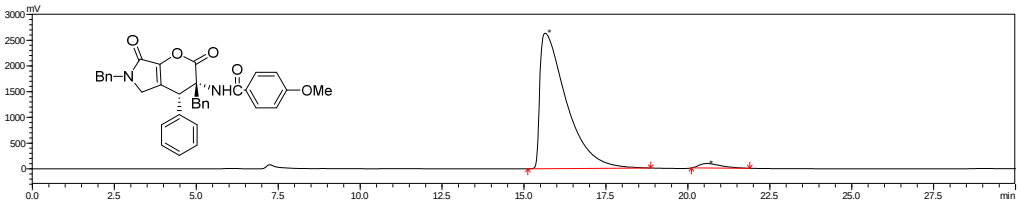
[2] a) A. Karanfil, B. Balta and M. Eskici, *Tetrahedron* **2012**, *68*, 10218; b) D. Beaufils, G. Danger, L. Boiteau, J. C. Rossi and R. Pascal, *Chem. Commun.* **2014**, *50*, 3100.

F: HPLC Charts of Asymmetric Cyclization Products

4a:**N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide**

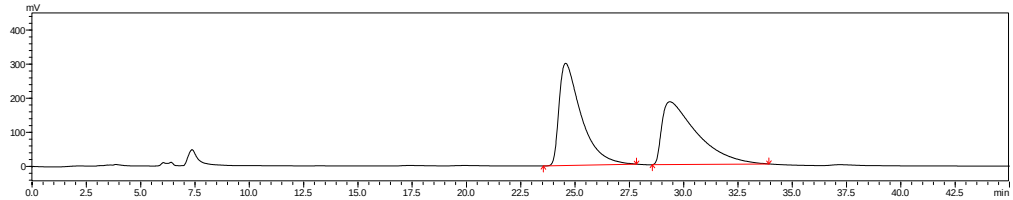


	Retention	Area	High	Area%
1	17.912	34194990	596188	50.200
2	22.165	33922524	551382	49.800

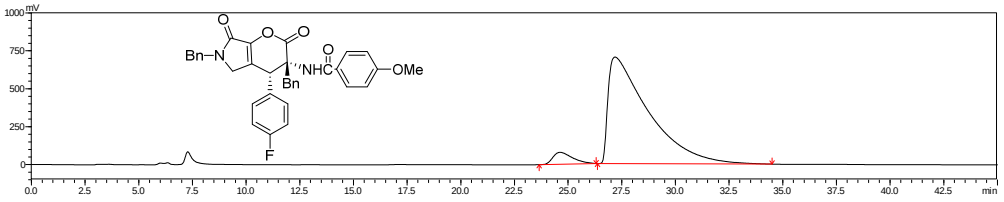


	Retention	Area	High	Area%
1	15.646	148253541	2629870	97.333
2	20.583	4062478	88031	2.667

4b:N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-fluorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

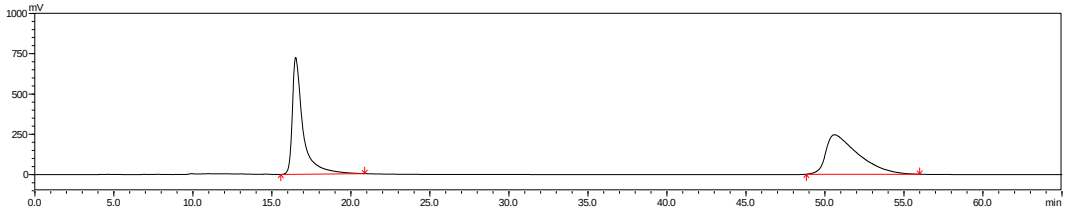


	Retention	Area	High	Area%
1	24.564	21467545	300254	50.422
2	29.362	21108251	184993	49.578

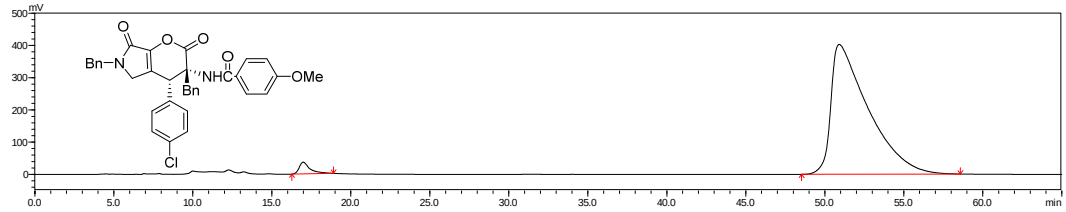


	Retention	Area	High	Area%
1	24.626	4611734	75489	4.776
2	27.187	91956549	702949	95.224

4c:N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-chlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

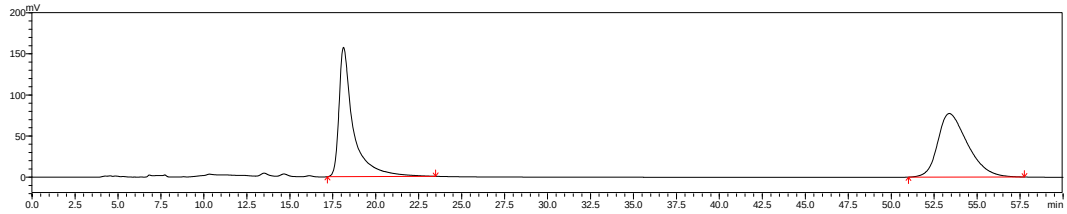


	Retention	Area	High	Area%
1	16.511	34660648	725356	49.839
2	50.605	34884444	244923	50.161

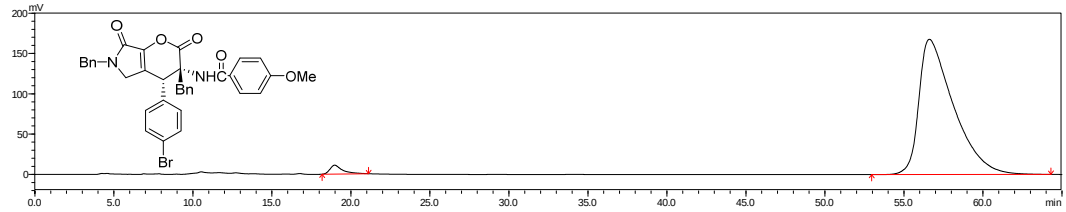


	Retention	Area	High	Area%
1	16.984	1663137	36036	2.425
2	50.913	66360351	402339	97.575

4d:N-((3*S*,4*R*)-3,6-dibenzyl-4-(4-bromophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

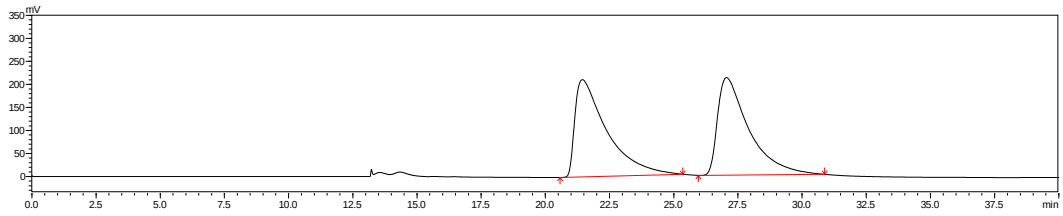


	Retention	Area	High	Area%
1	18.127	9011359	157419	49.479
2	53.381	9201247	76919	50.521

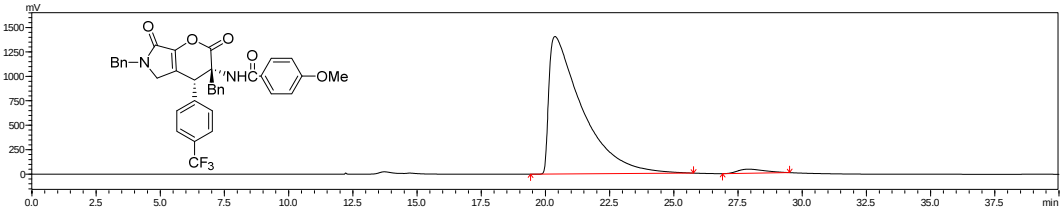


	Retention	Area	High	Area%
1	18.971	592567	10955	2.272
2	56.608	25490651	167517	97.728

4e:N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(4-(trifluoromethyl)phenyl)-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

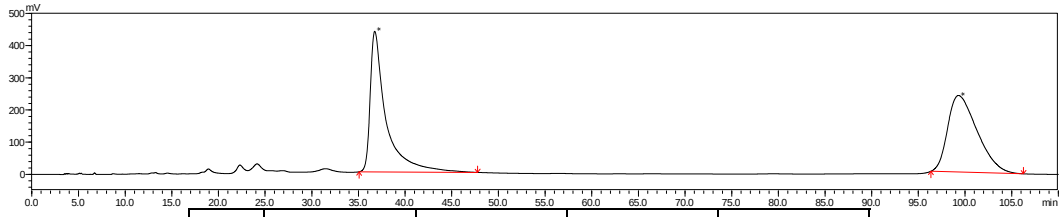


	Retention	Area	High	Area%
1	21.444	18401951	211175	50.398
2	27.055	18111569	212032	49.602

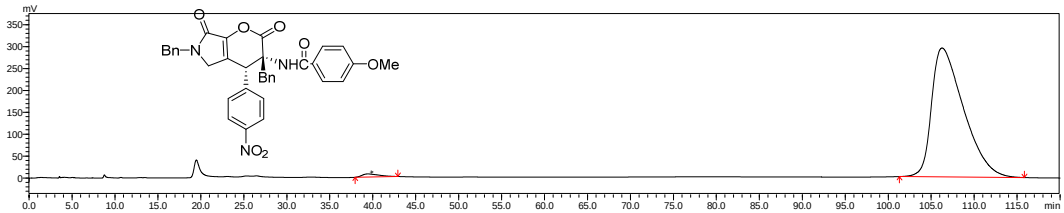


	Retention	Area	High	Area%
1	20.372	125503890	1405912	97.778
2	27.905	2852447	37321	2.222

4f:N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-nitrophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

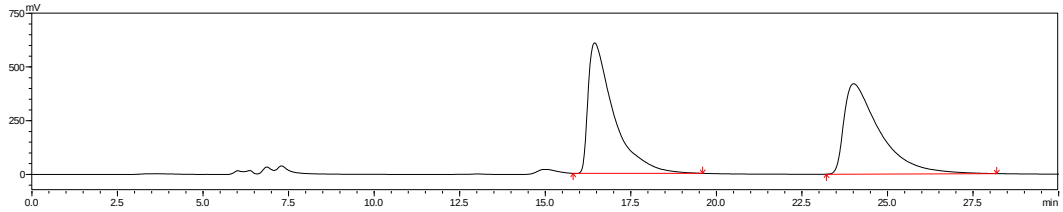


	Retention	Area	High	Area%
1	36.743	51468170	436549	49.594
2	99.303	52310281	237776	50.406

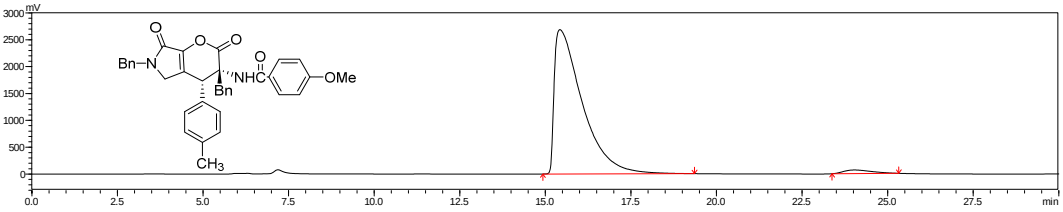


	Retention	Area	High	Area%
1	39.426	945672	6991	1.228
2	106.267	76083383	293980	98.772

4g:N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(*p*-tolyl)-2,3,4,5,6,7-hexahydropy-rano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

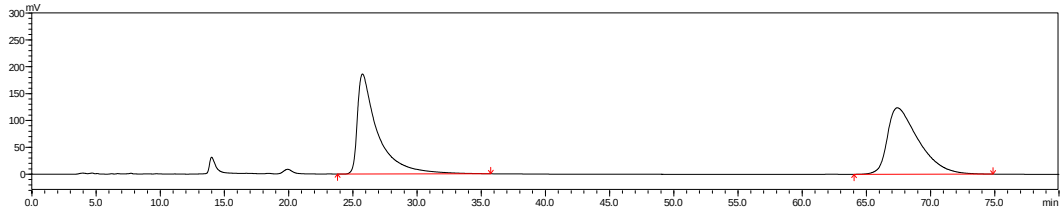


	Retention	Area	High	Area%
1	13.180	30984657	784493	50.684
2	18.845	30147869	545246	49.316

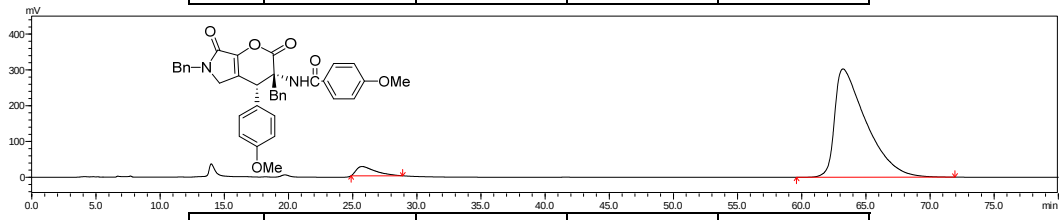


	Retention	Area	High	Area%
1	15.425	151765127	2682916	97.492
2	24.029	3904505	67444	2.508

4h:N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-methoxyphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahy-dropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamid

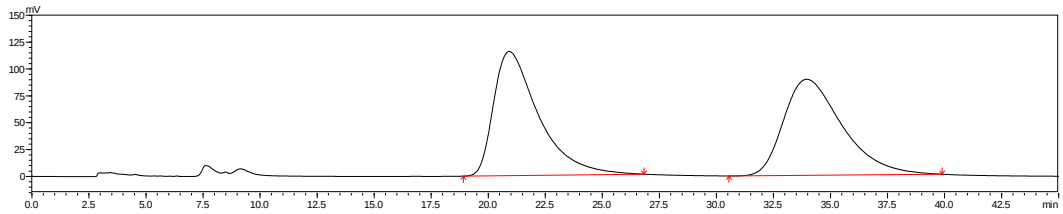


	Retention	Area	High	Area%
1	25.749	20201076	185813	49.548
2	67.413	20569424	123330	50.452

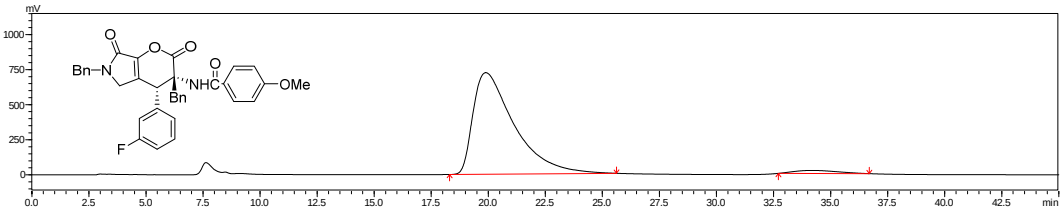


	Retention	Area	High	Area%
1	25.728	2733982	27363	5.034
2	63.217	51577342	302392	94.966

4i:N-((3*R*,4*R*)-3,6-dibenzyl-4-(3-fluorophenyl)-2,7-dioxo-2,3,4,5,6,7 hexahydropy-rano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

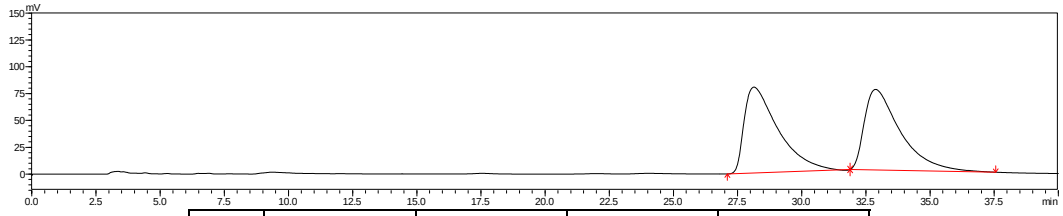


	Retention	Area	High	Area%
1	20.921	15789902	115311	49.715
2	33.962	15970621	89304	50.285

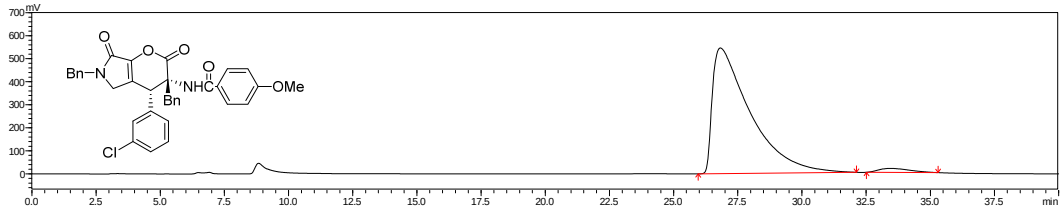


	Retention	Area	High	Area%
1	19.891	92361811	726482	97.068
2	34.188	2789502	21387	2.932

4j:N-((3*R*,4*R*)-3,6-dibenzyl-4-(3-chlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

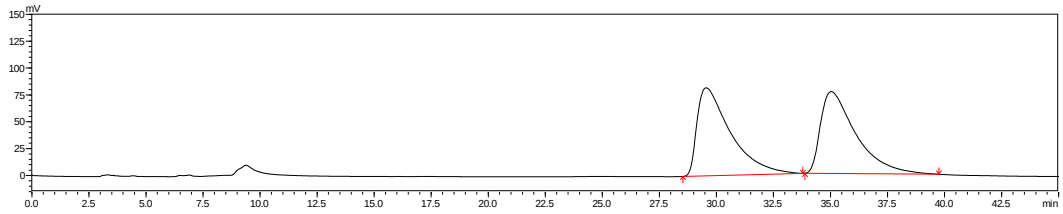


	Retention	Area	High	Area%
1	28.139	7427821	80005	50.674
2	32.879	7230206	75002	49.326

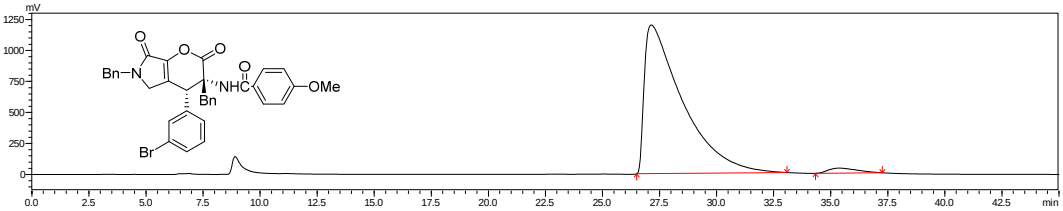


	Retention	Area	High	Area%
1	26.822	55706034	545211	97.402
2	33.450	1485642	17636	2.598

4k:N-((3*R*,4*R*)-3,6-dibenzyl-4-(3-bromophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

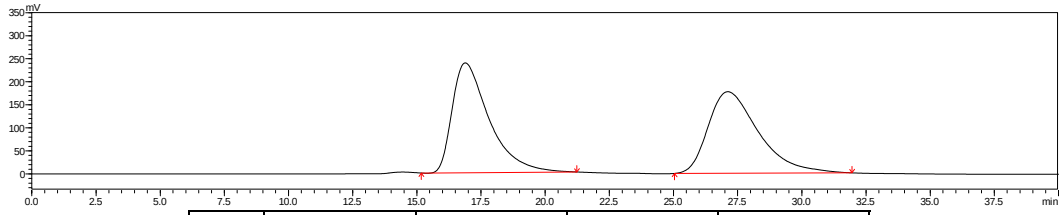


	Retention	Area	High	Area%
1	29.553	8788556	82547	49.435
2	35.035	8989370	78576	50.565

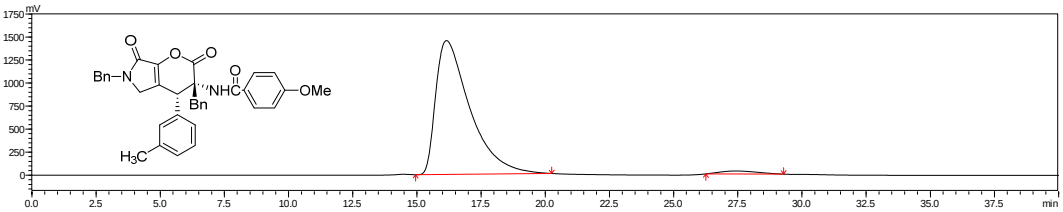


	Retention	Area	High	Area%
1	27.141	140274815	1197533	97.504
2	35.373	3590965	40152	2.496

4l:N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(m-tolyl)-2,3,4,5,6,7-hexahydropy-rano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

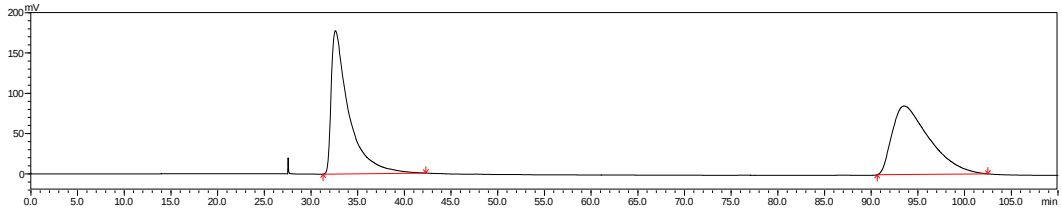


	Retention	Area	High	Area%
1	17.597	34387070	322722	50.077
2	28.197	34281255	228120	49.923

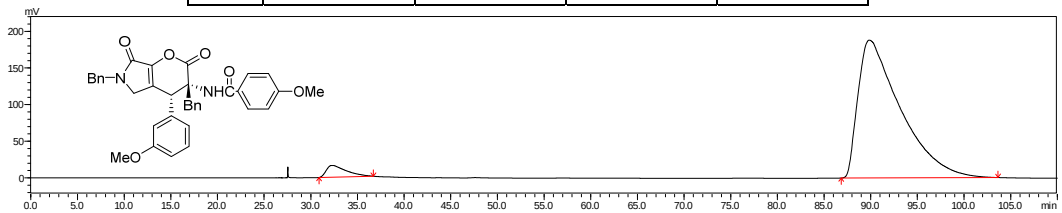


	Retention	Area	High	Area%
1	17.166	137919682	1308615	97.413
2	29.160	3662706	29071	2.587

4m:N-((3*R*,4*R*)-3,6-dibenzyl-4-(3-methoxyphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

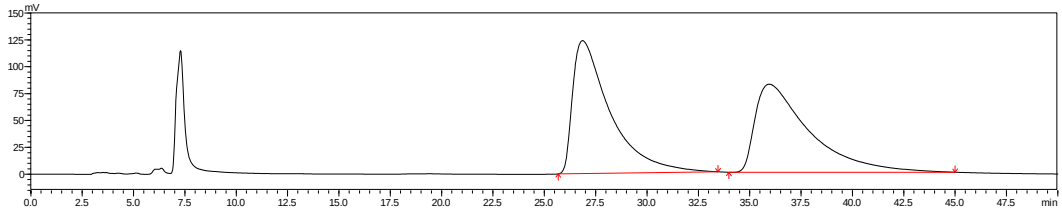


	Retention	Area	High	Area%
1	32.620	22753727	177575	50.837
2	93.510	22004558	81657	49.163

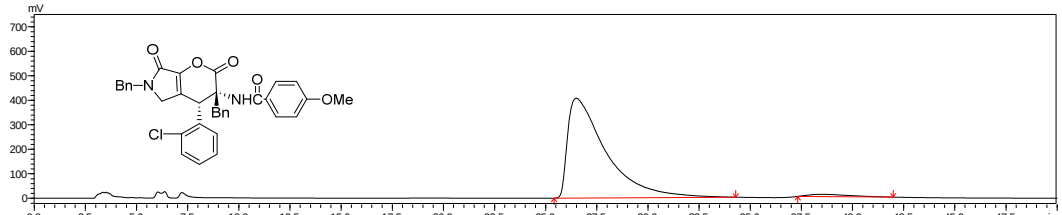


	Retention	Area	High	Area%
1	32.337	2608738	16376	4.203
2	89.851	59466214	188005	95.797

4n:N-((3*R*,4*S*)-3,6-dibenzyl-4-(2-chlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

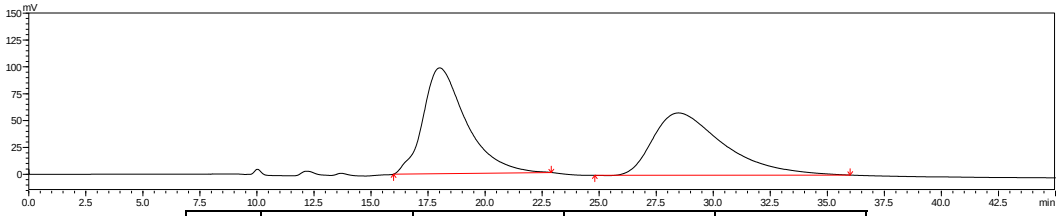


	Retention	Area	High	Area%
1	26.862	15579317	122983	50.520
2	35.950	15258724	82086	49.480

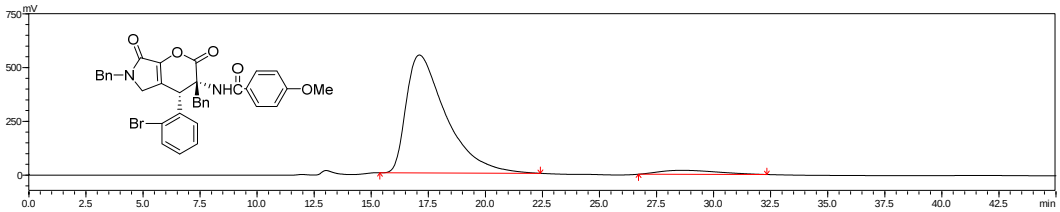


	Retention	Area	High	Area%
1	26.494	53102914	407853	97.638
2	38.517	1284901	8743	2.362

4o:N-((3*R*,4*S*)-3,6-dibenzyl-4-(2-bromophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

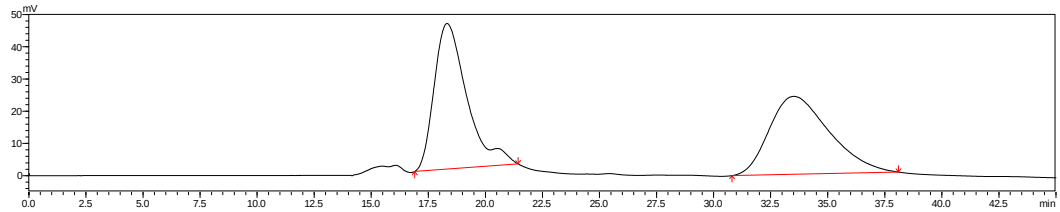


	Retention	Area	High	Area%
1	18.007	12725481	97812	50.975
2	28.475	12238626	57724	49.025

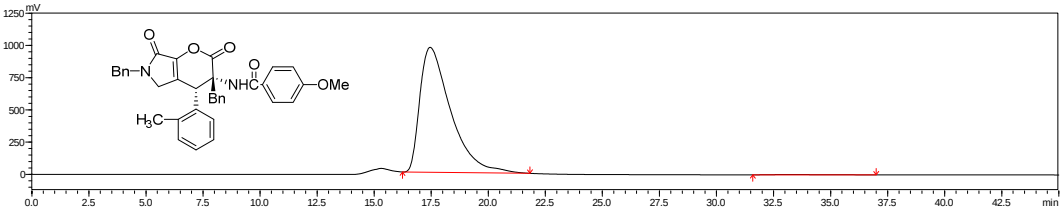


	Retention	Area	High	Area%
1	17.107	65444922	546120	95.334
2	28.622	3203278	18502	4.666

4p:N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(o-tolyl)-2,3,4,5,6,7-hexahydropy-rano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

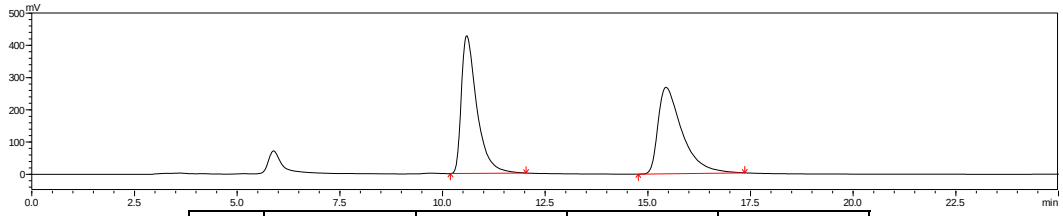


	Retention	Area	High	Area%
1	18.322	4454433	44907	50.597
2	33.516	4349303	23969	49.403

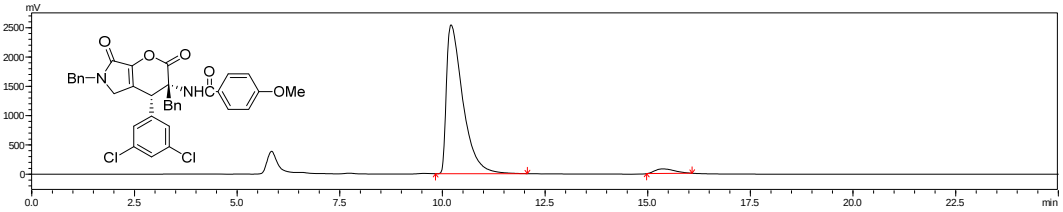


	Retention	Area	High	Area%
1	17.451	88950031	963923	99.822
2	33.149	158964	1449	0.178

4q:N-((3*R*,4*R*)-3,6-dibenzyl-4-(3,5-dichlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

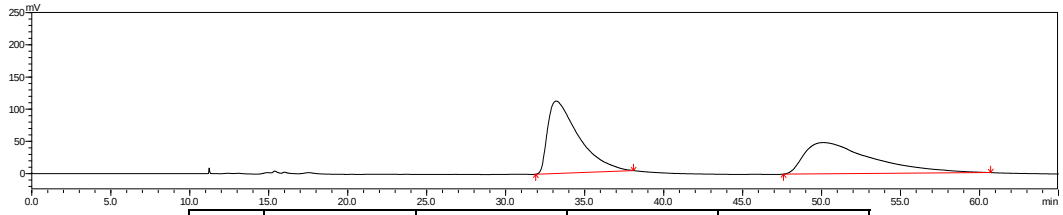


	Retention	Area	High	Area%
1	10.589	11217145	426847	50.520
2	15.443	10986129	268332	49.480

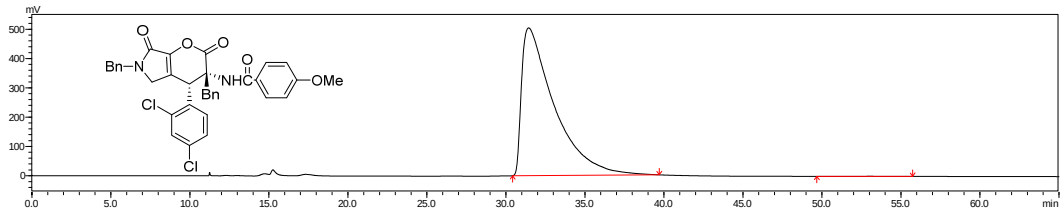


	Retention	Area	High	Area%
1	10.661	71814571	2376201	96.536
2	16.311	2577273	75103	3.464

4r:N-((3*R*,4*S*)-3,6-dibenzyl-4-(2,4-dichlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

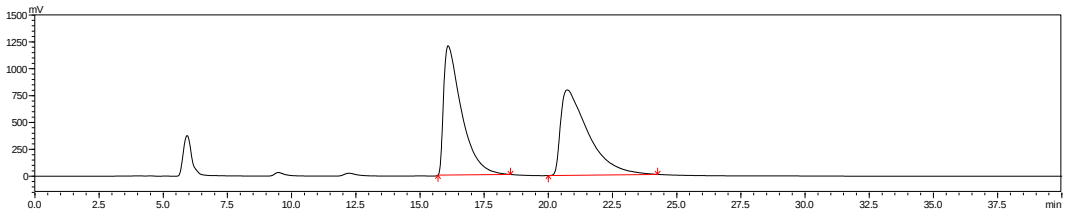


	Retention	Area	High	Area%
1	33.199	15478275	111082	50.738
2	50.093	15027948	48689	49.262

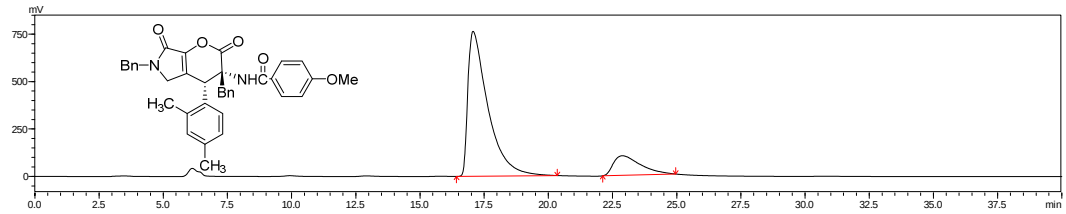


	Retention	Area	High	Area%
1	31.439	74107100	505130	99.892
2	53.053	79818	423	0.108

4s:N-((3*R*,4*R*)-3,6-dibenzyl-4-(2,4-dimethylphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

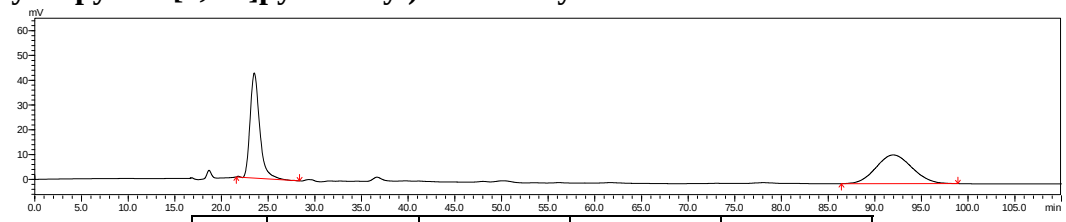


	Retention	Area	High	Area%
1	16.098	59941136	1210600	49.881
2	20.737	60228340	796652	50.119

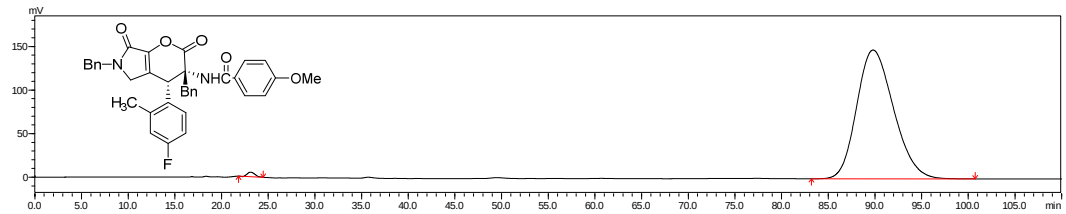


	Retention	Area	High	Area%
1	17.072	41213177	763580	86.571
2	22.884	6392982	95040	13.429

4t:N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-fluoro-2-methylphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

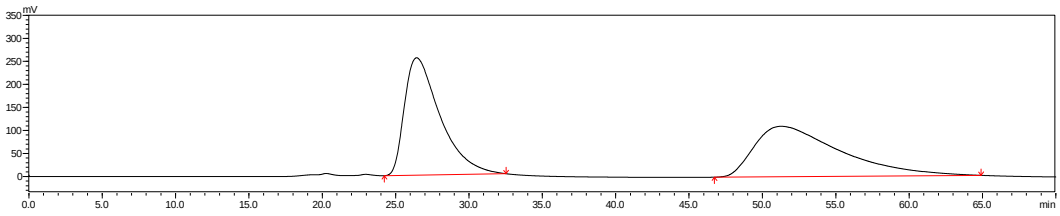


	Retention	Area	High	Area%
1	23.509	2968249	42126	49.237
2	91.960	3060188	11480	50.763

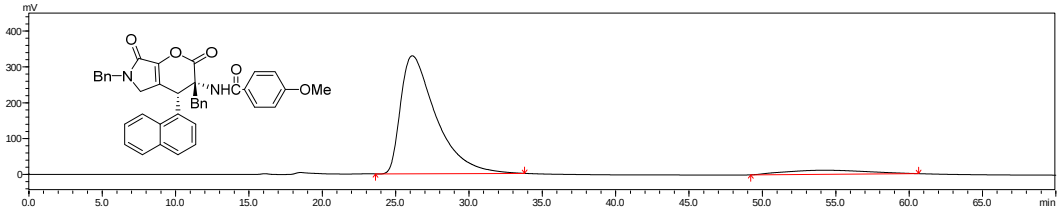


	Retention	Area	High	Area%
1	23.111	281636	5123	0.689
2	89.792	40604129	147738	99.311

4u:N-((3*R*,4*R*)-3,6-dibenzyl-4-(naphthalen-1-yl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

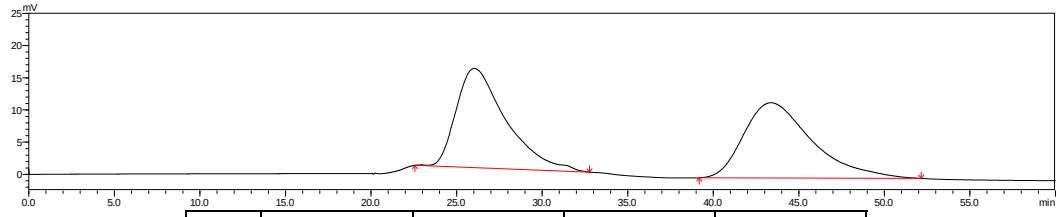


	Retention	Area	High	Area%
1	26.431	44048537	255800	50.523
2	51.279	43136228	108535	49.477

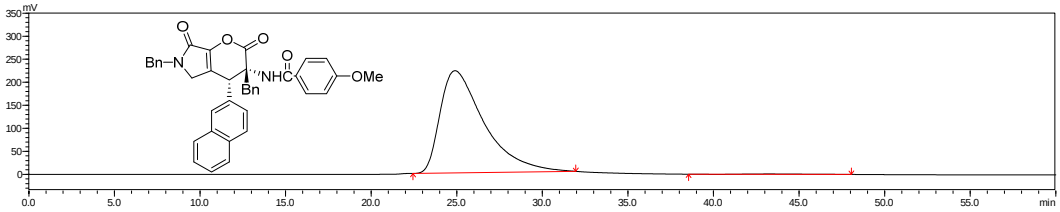


	Retention	Area	High	Area%
1	26.136	55701042	329542	92.477
2	54.234	4531281	11259	7.523

4v:N-((3*R*,4*R*)-3,6-dibenzyl-4-(naphthalen-2-yl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

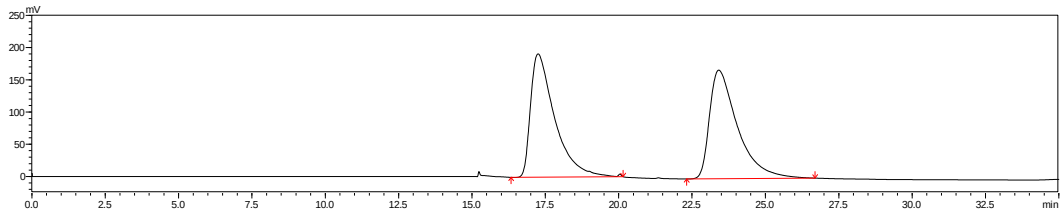


	Retention	Area	High	Area%
1	26.025	3217382	15588	49.448
2	43.362	3289203	11739	50.552

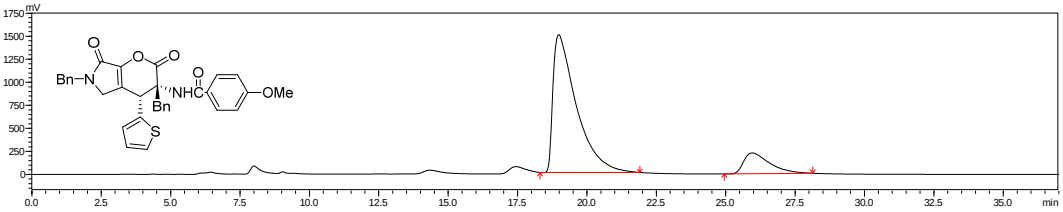


	Retention	Area	High	Area%
1	24.908	38500498	220490	99.669
2	43.277	127715	659	0.331

4w:N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(thiophen-2-yl)-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

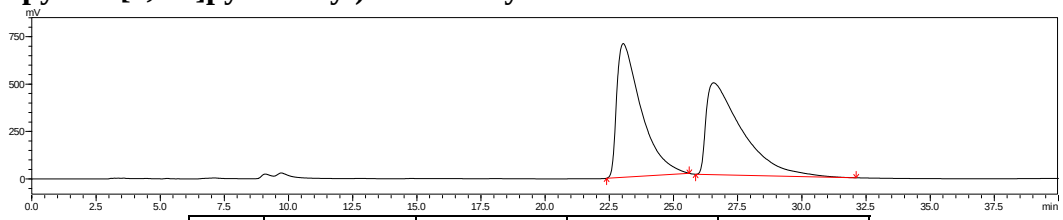


	Retention	Area	High	Area%
1	17.254	10734390	190627	49.930
2	23.412	10764379	167225	50.070

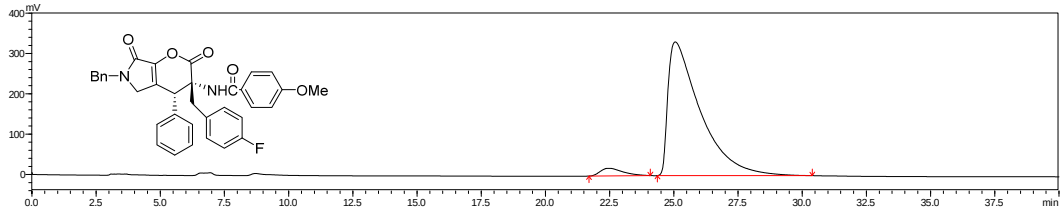


	Retention	Area	High	Area%
1	18.983	88333322	1498922	85.954
2	25.954	14435043	224165	14.046

5a:N-((3*R*,4*R*)-6-benzyl-3-(4-fluorobenzyl)-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

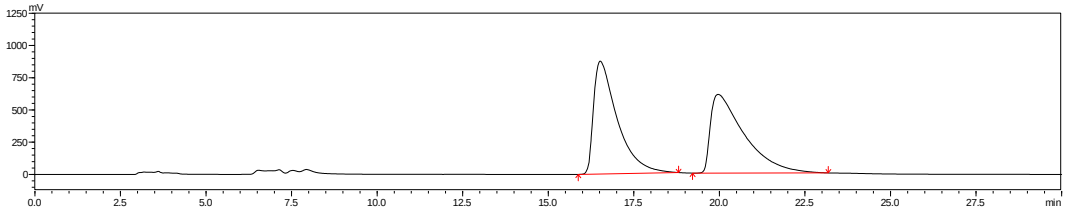


	Retention	Area	High	Area%
1	23.040	47017377	705676	50.600
2	26.564	45903090	482879	49.400

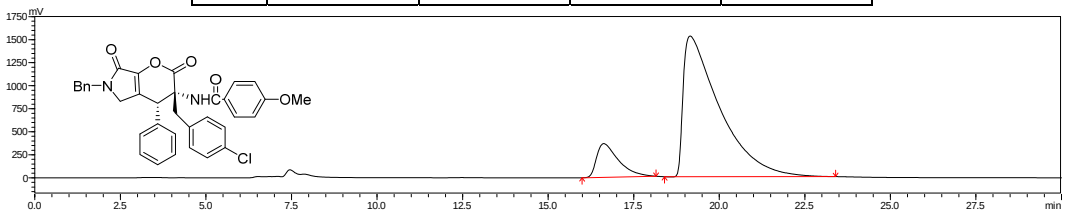


	Retention	Area	High	Area%
1	22.468	1113357	18600	3.756
2	25.058	28525230	330821	96.244

5b:N-((3*R*,4*R*)-6-benzyl-3-(4-chlorobenzyl)-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

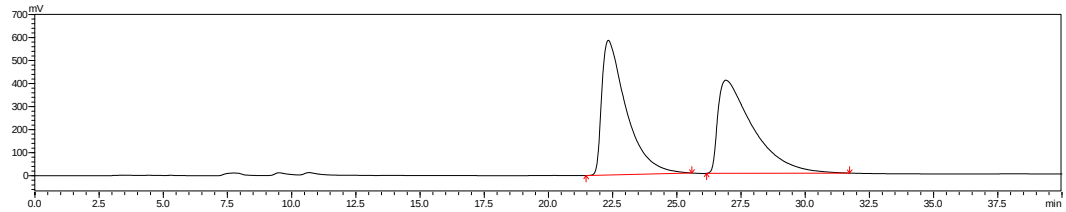


	Retention	Area	High	Area%
1	16.520	41293093	871807	49.526
2	19.964	42082806	610994	50.474

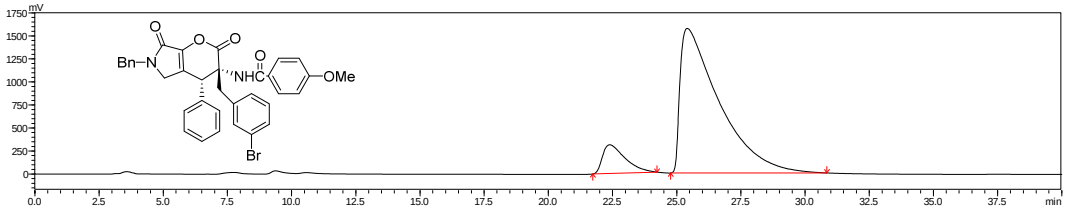


	Retention	Area	High	Area%
1	16.624	14731142	347060	11.564
2	19.149	112660511	1528193	88.436

5c:N-((3*R*,4*R*)-6-benzyl-3-(3-bromobenzyl)-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

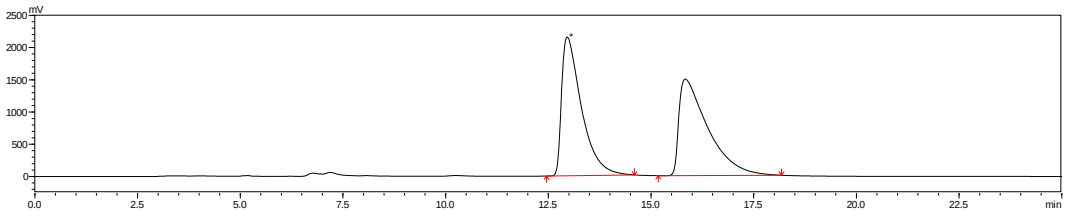


	Retention	Area	High	Area%
1	22.334	38681497	584024	50.319
2	26.914	38191590	404583	49.681

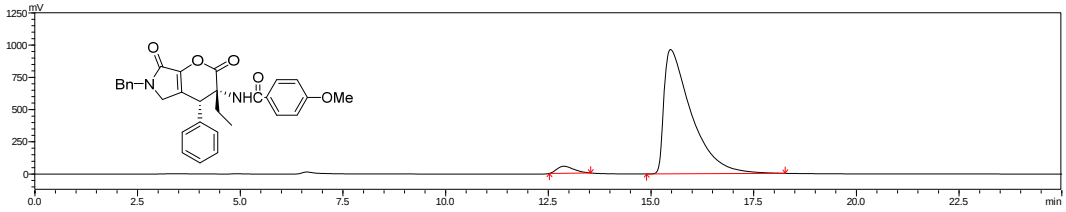


	Retention	Area	High	Area%
1	22.390	19488497	314100	10.448
2	25.411	167046554	1570987	89.552

5d:N-((3*R*,4*R*)-6-benzyl-3-ethyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropy-rano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

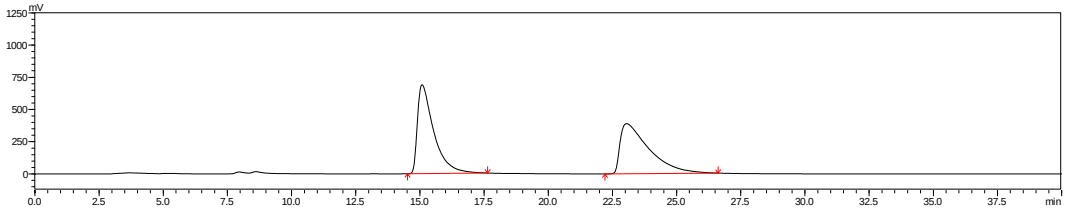


	Retention	Area	High	Area%
1	12.960	72327035	2151567	49.694
2	15.836	73216740	1497262	50.306

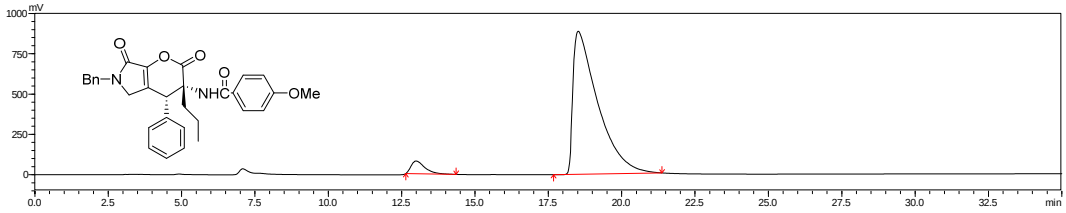


	Retention	Area	High	Area%
1	12.877	1699417	56413	3.675
2	15.476	44540483	964453	96.325

5e:N-((3*R*,4*R*)-6-benzyl-2,7-dioxo-4-phenyl-3-propyl-2,3,4,5,6,7-hexahydropy-rano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

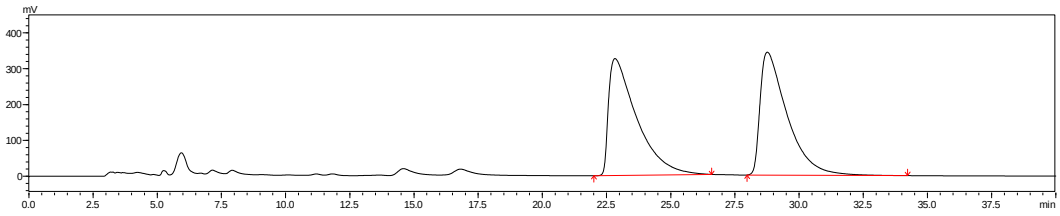


	Retention	Area	High	Area%
1	15.086	30822728	689779	50.069
2	23.053	30737322	389147	49.931

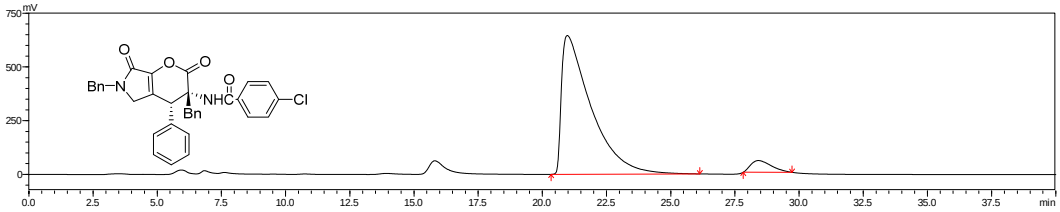


	Retention	Area	High	Area%
1	12.993	2727158	83241	4.900
2	18.518	52933813	888448	95.100

5f:4-chloro-N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)benzamide

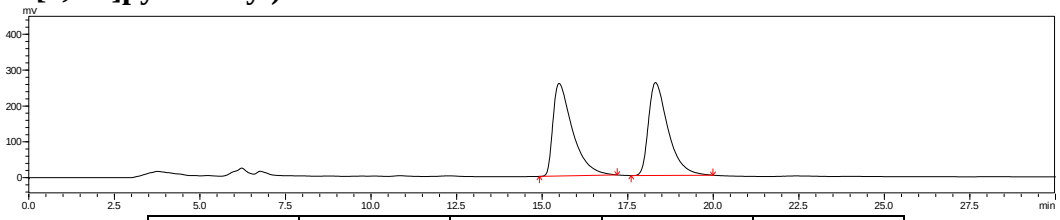


	Retention	Area	High	Area%
1	22.829	24561116	325897	50.238
2	28.763	24328459	339799	49.762

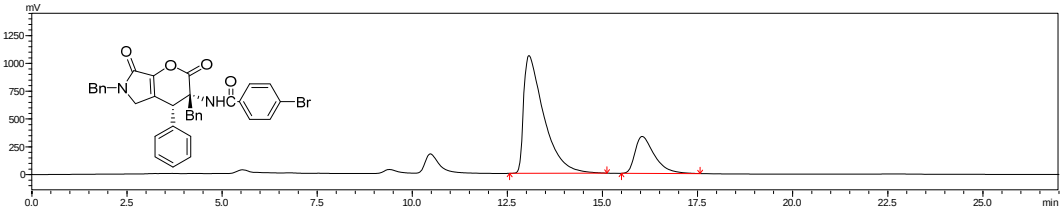


	Retention	Area	High	Area%
1	20.974	51207164	645481	94.047
2	28.415	3241407	56656	5.953

5g:4-bromo-N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)benzamide

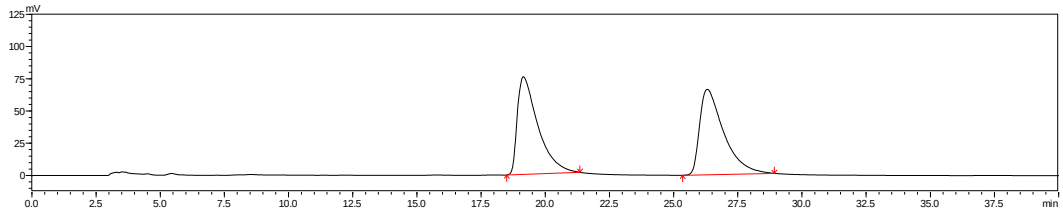


	Retention	Area	High	Area%
1	15.494	10081195	257742	49.840
2	18.312	10145719	258336	50.160

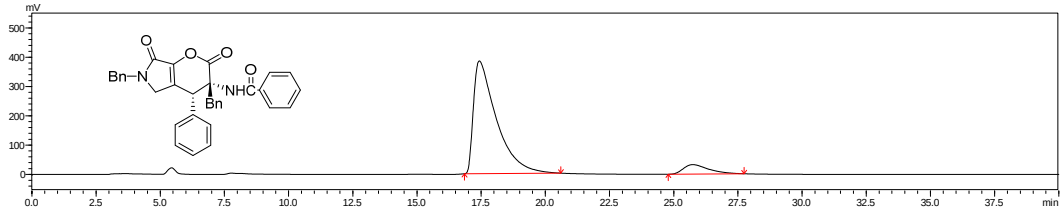


	Retention	Area	High	Area%
1	13.065	38090019	1051826	76.873
2	16.042	11459009	330838	23.127

5h: N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-[1,1'-biphenyl]-4-carboxamid



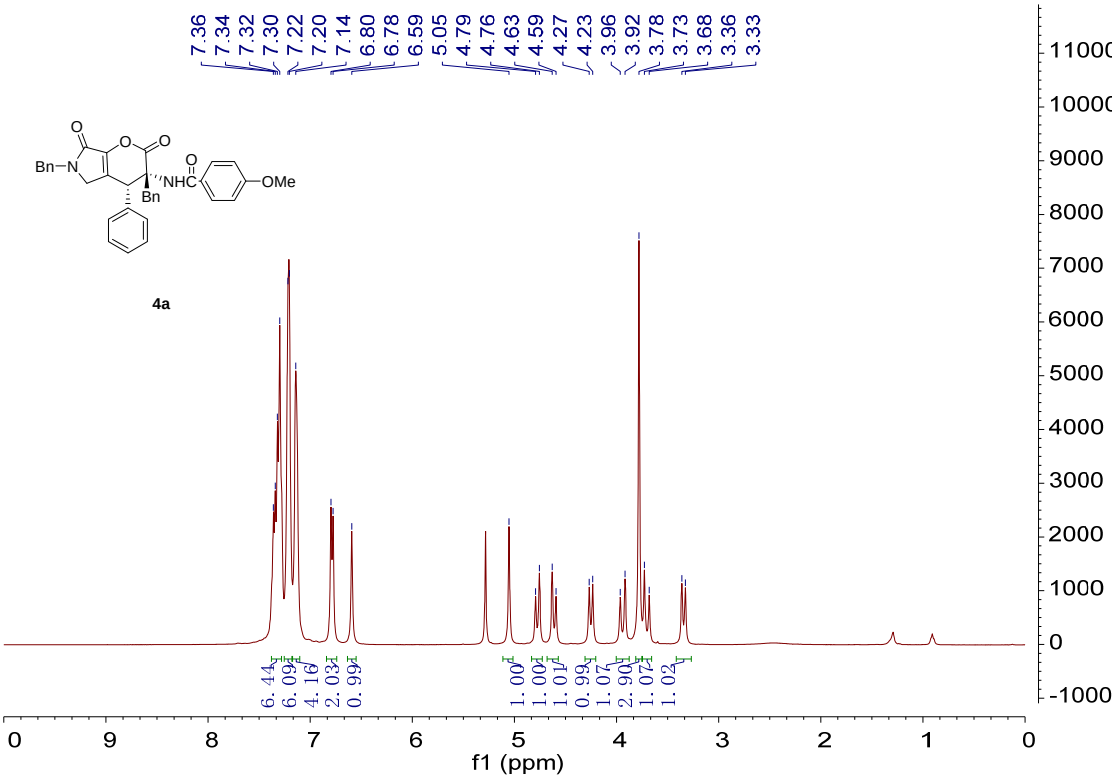
	Retention	Area	High	Area%
1	19.148	4405135	75973	50.223
2	26.311	4366044	66343	49.777

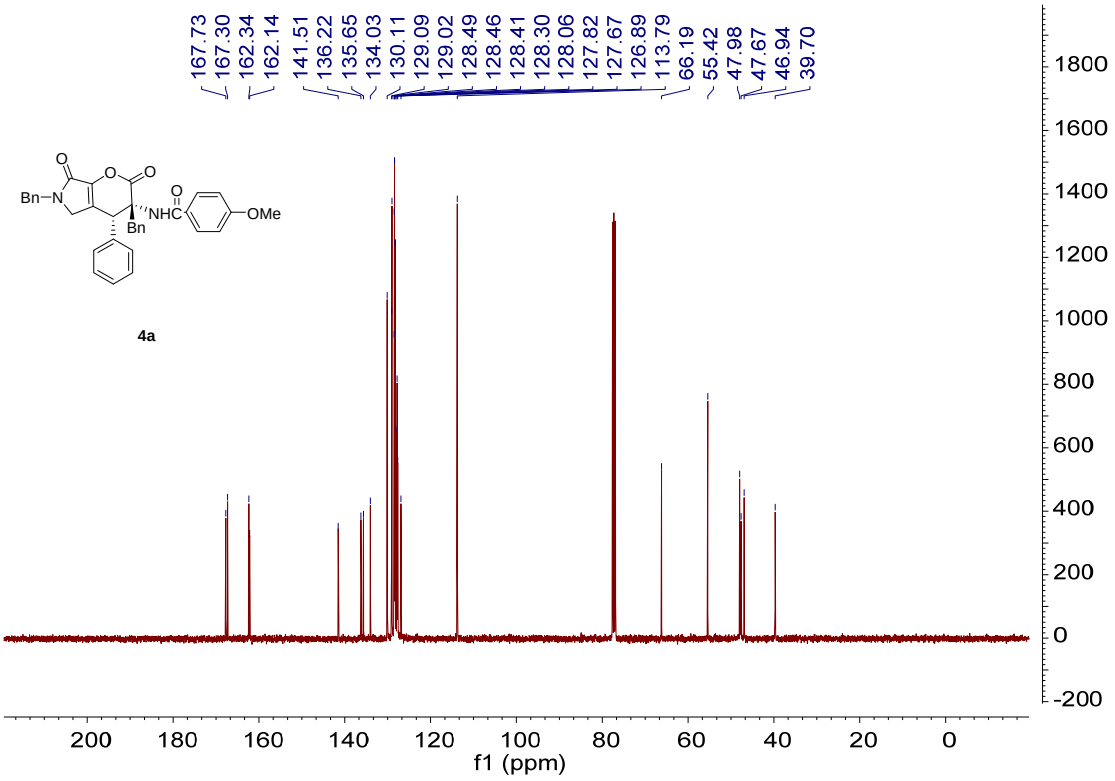


	Retention	Area	High	Area%
1	17.431	24300540	385612	91.759
2	25.745	2182393	32026	8.241

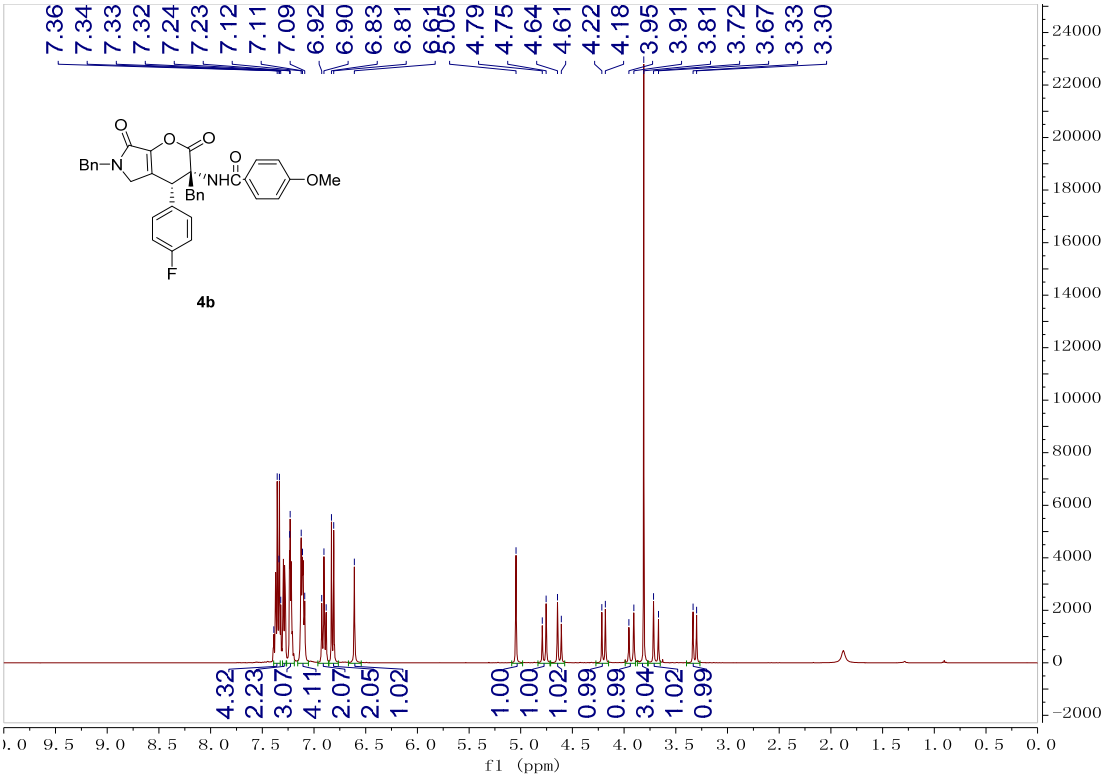
G: NMR Spectra of Asymmetric Cyclization Products

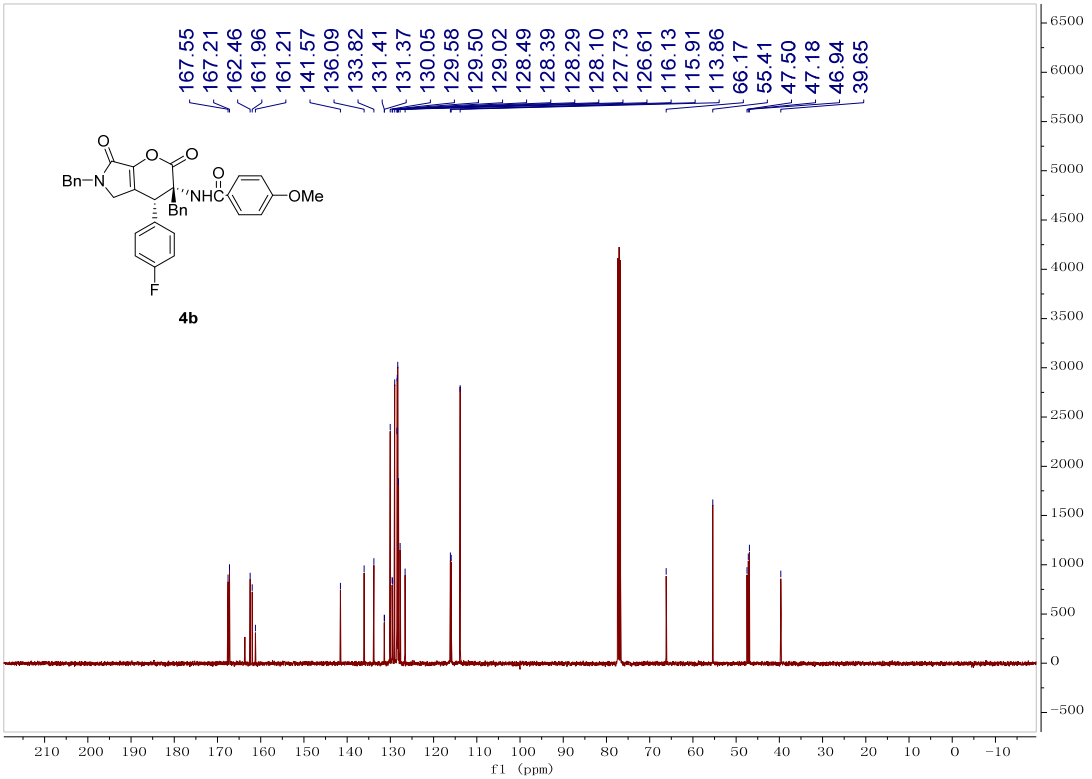
4a:N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

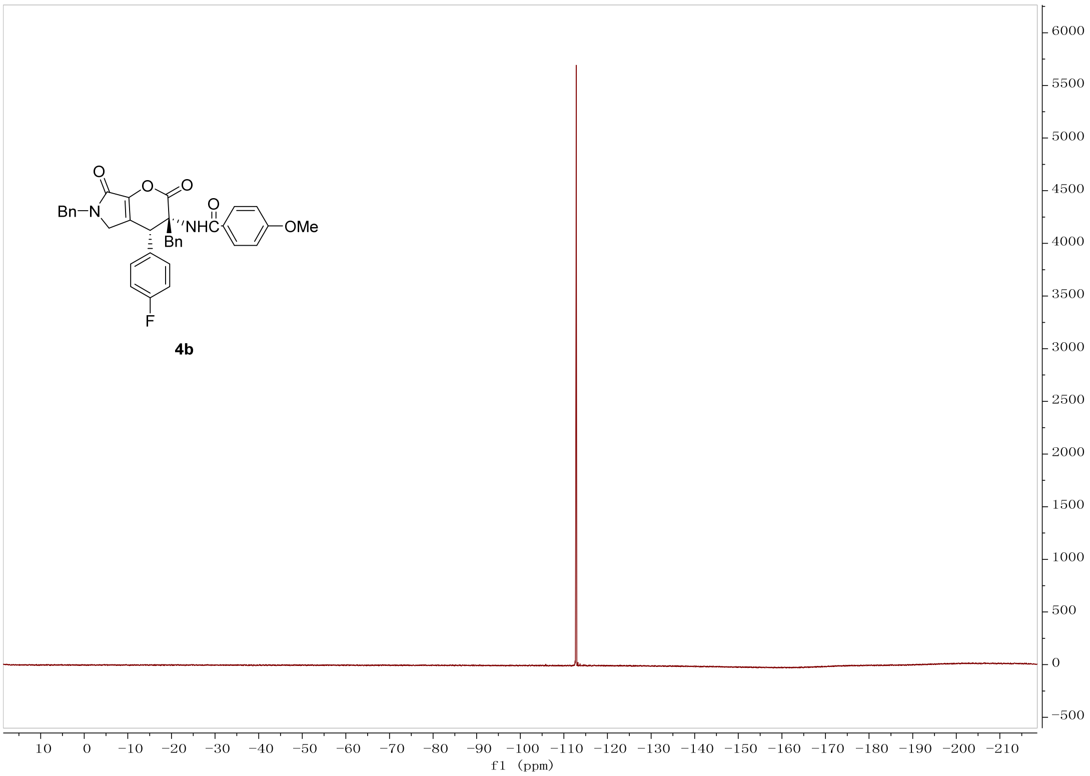




4b:N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-fluorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide






Bn
N
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O
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NHC
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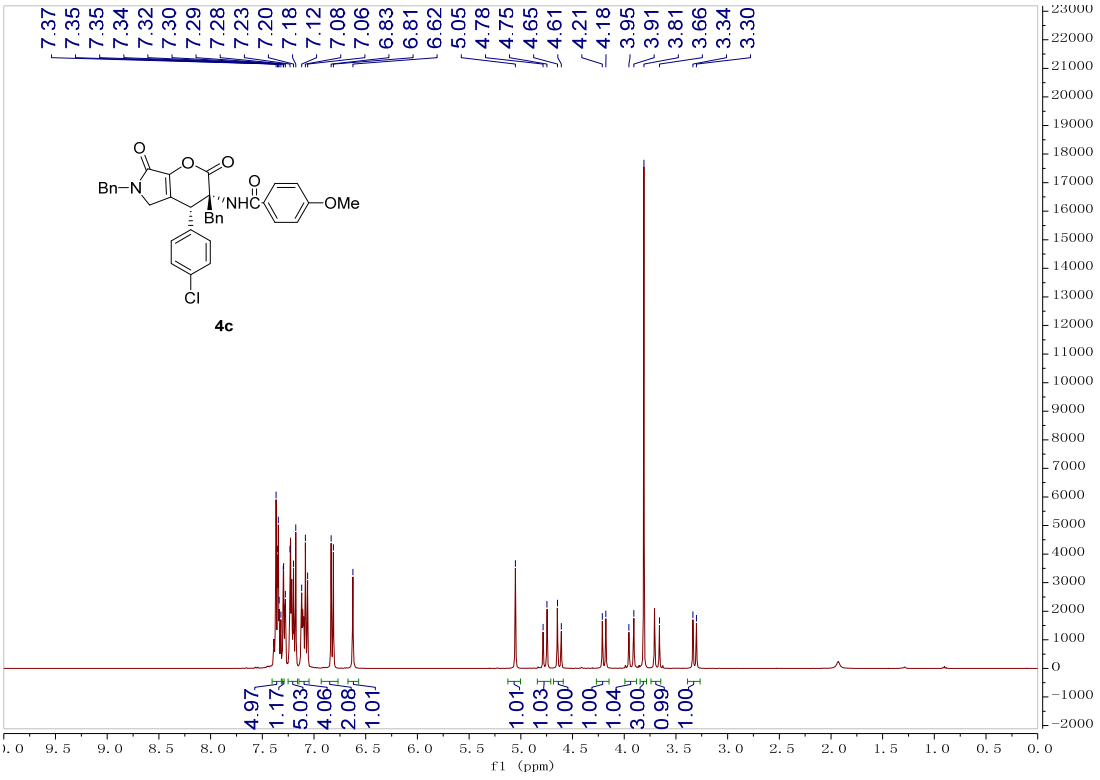
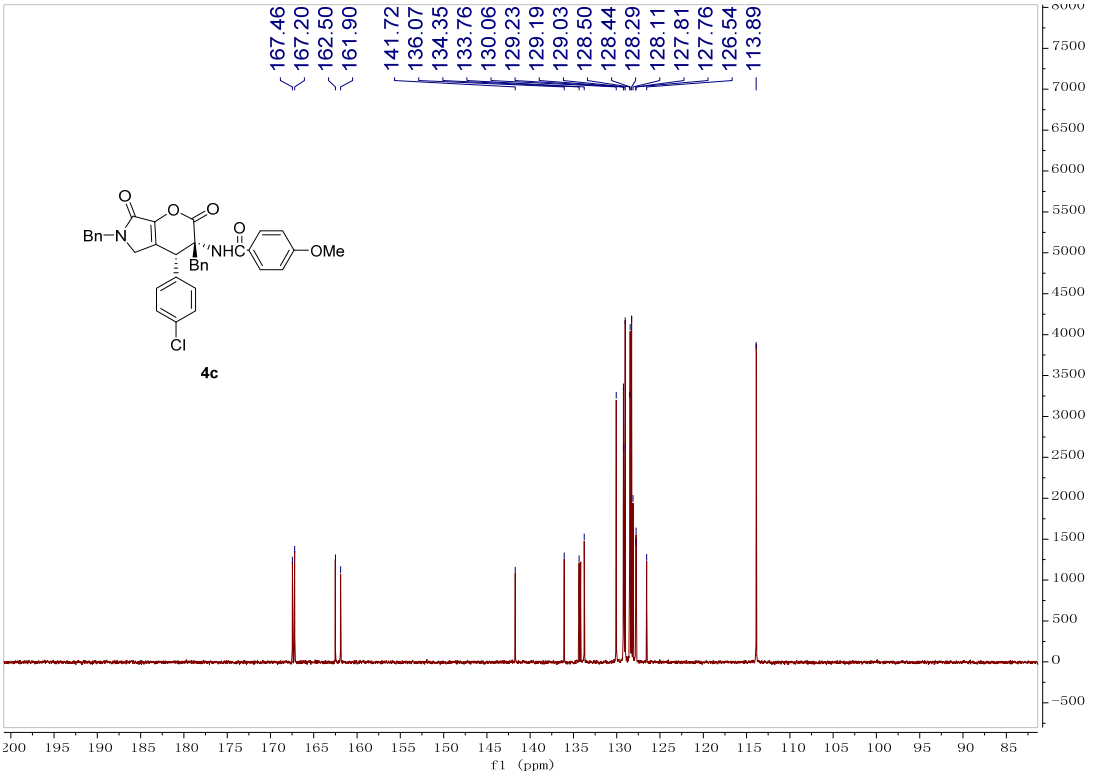
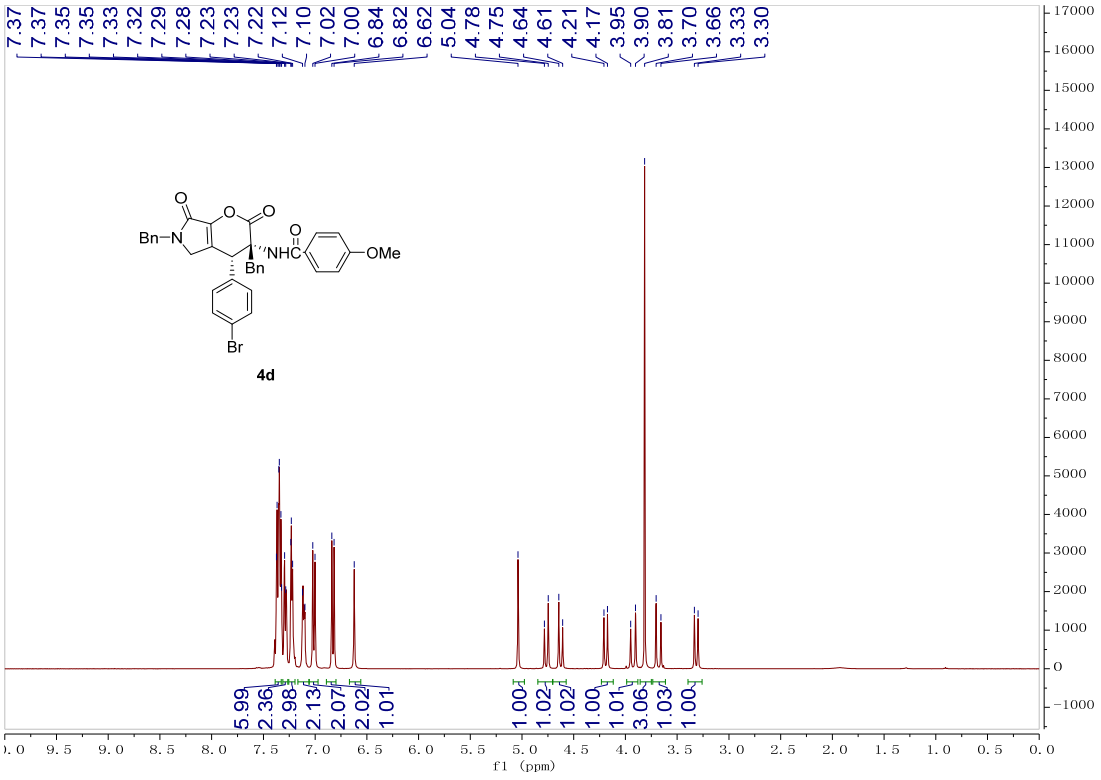
OMe
Bn
F
4b
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
−500
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

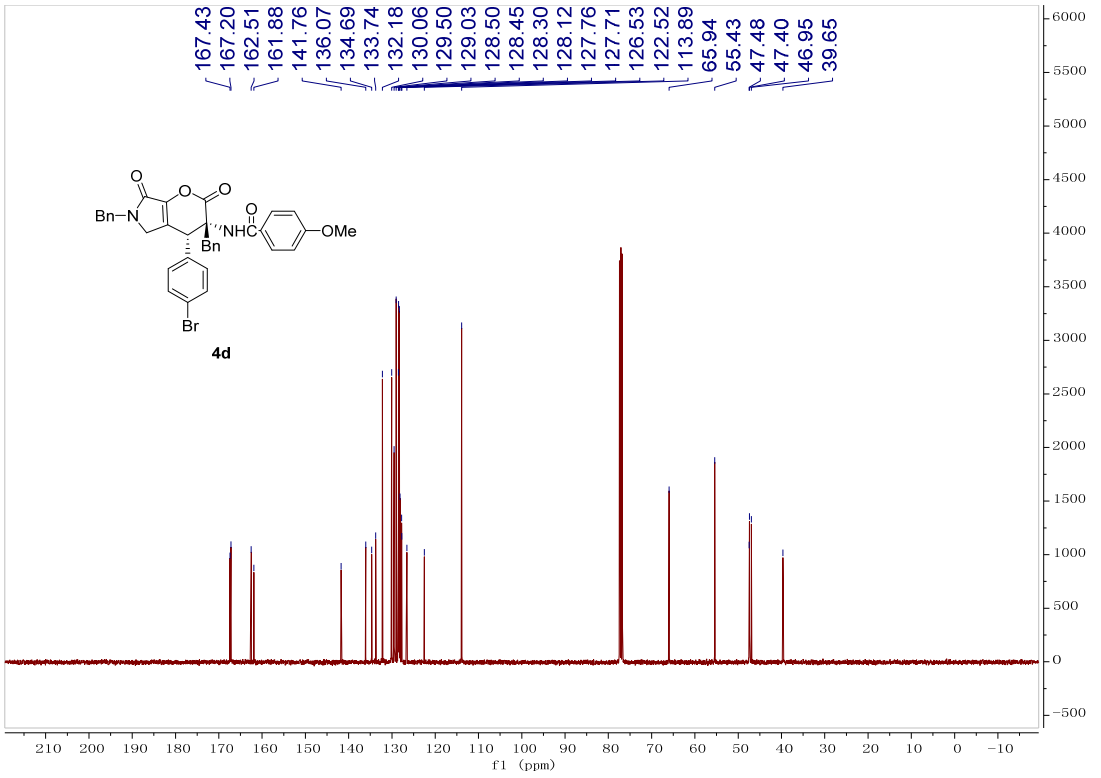
4c:N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-chlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



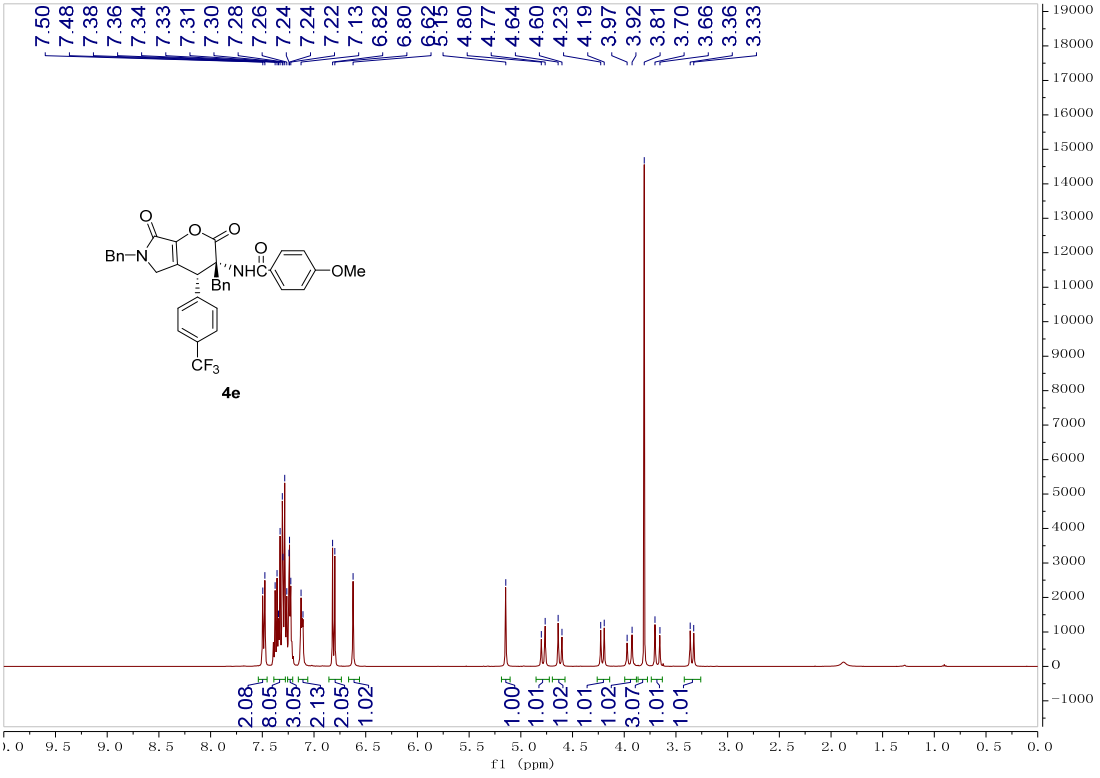


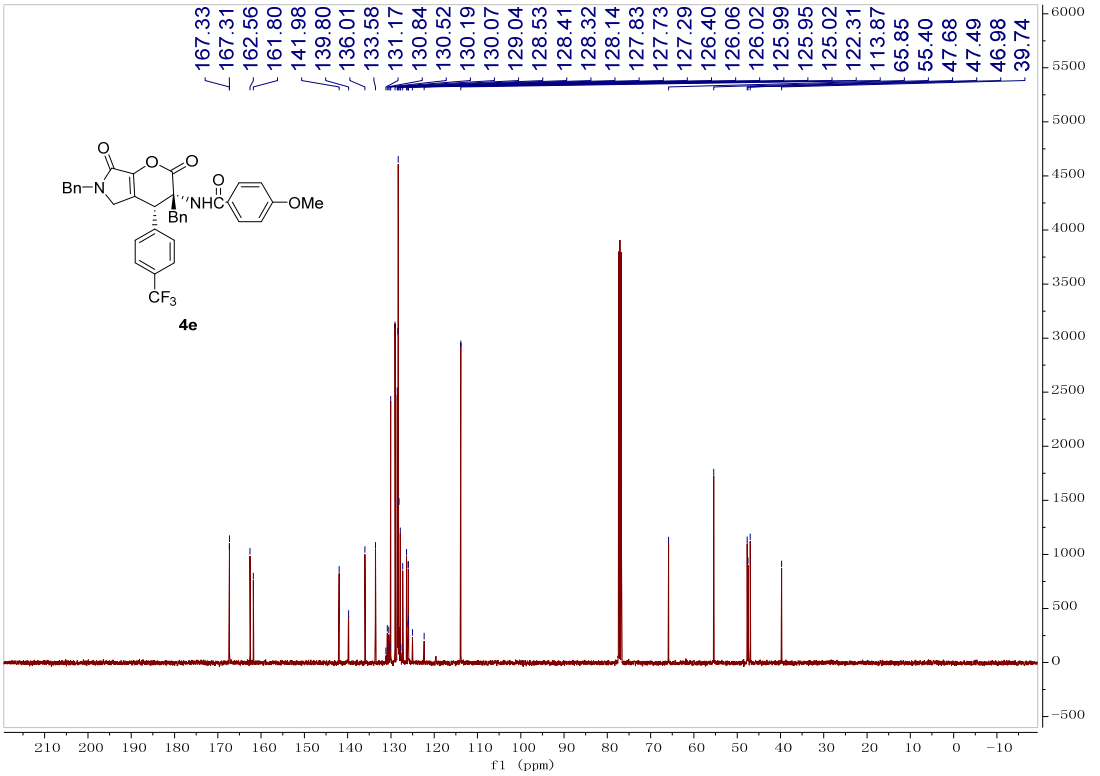
4d:N-((3*S*,4*R*)-3,6-dibenzyl-4-(4-bromophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

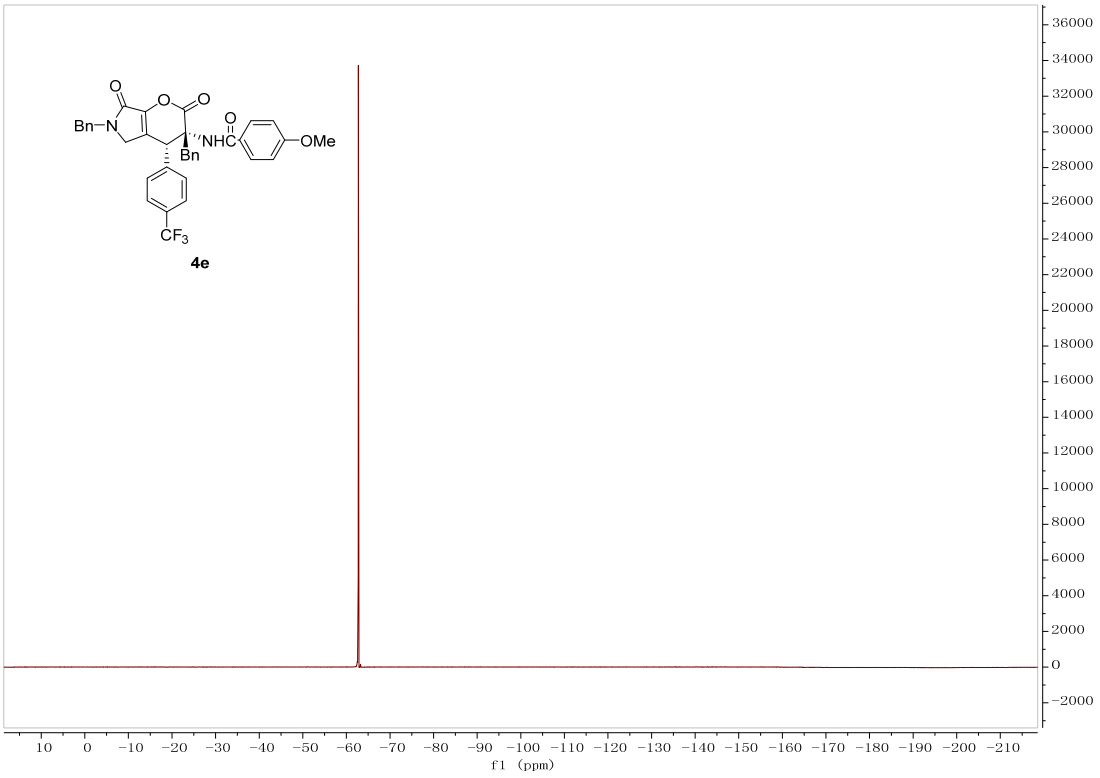




4e:N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(4-(trifluoromethyl)phenyl)-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide






Bn
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NH
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OMe
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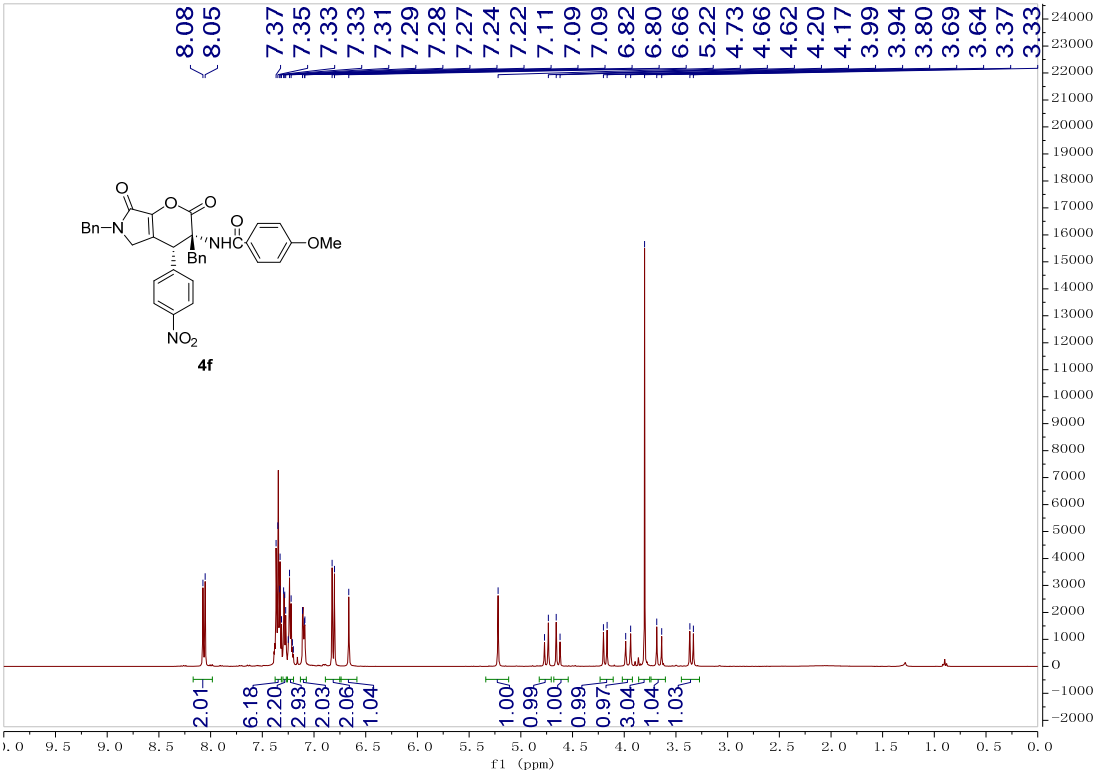
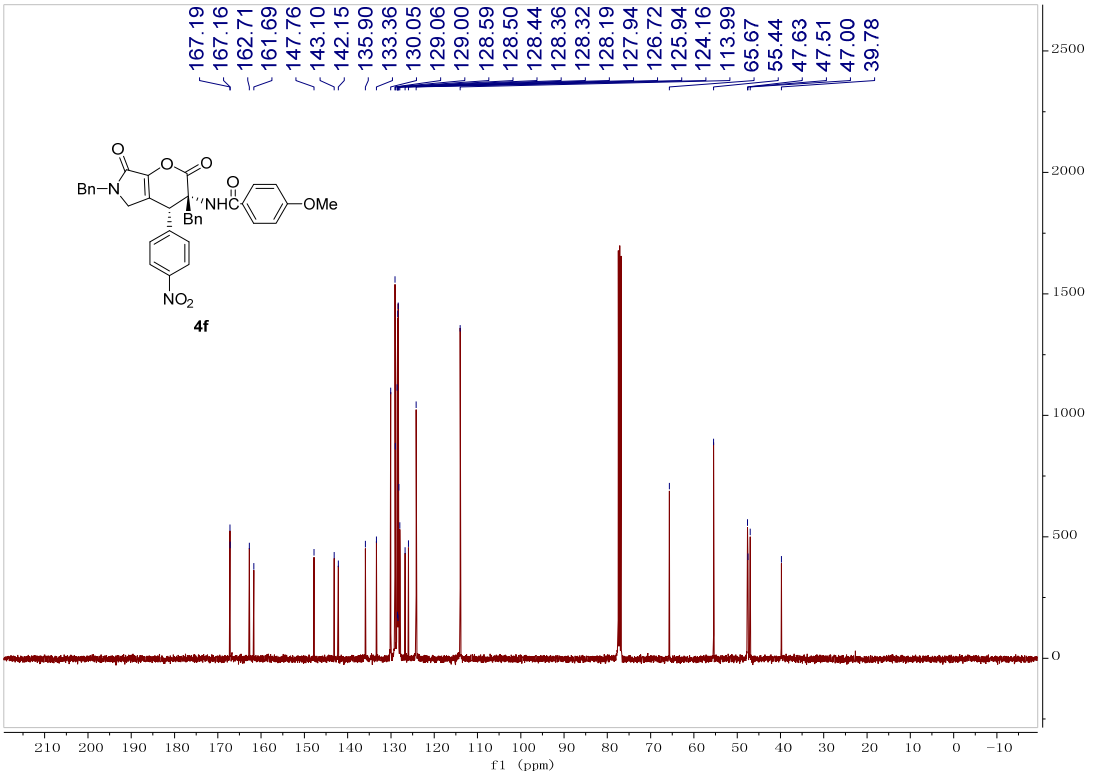
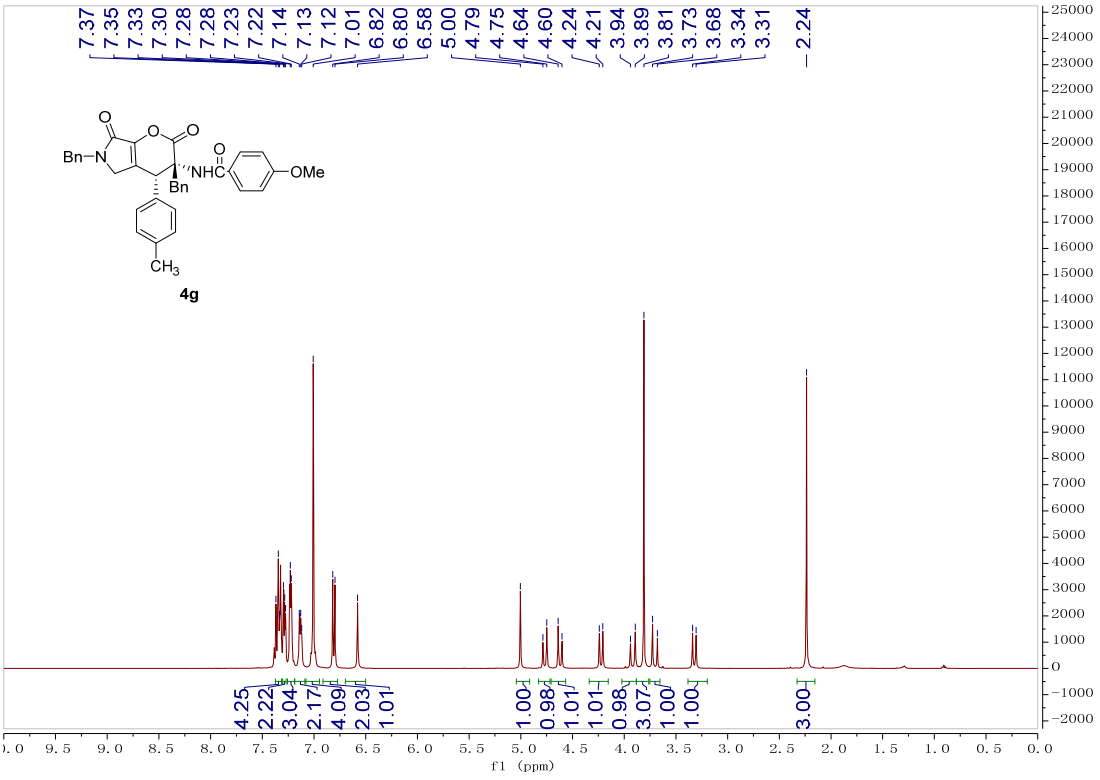
12000
10000
8000
6000
4000
2000
0
−2000
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

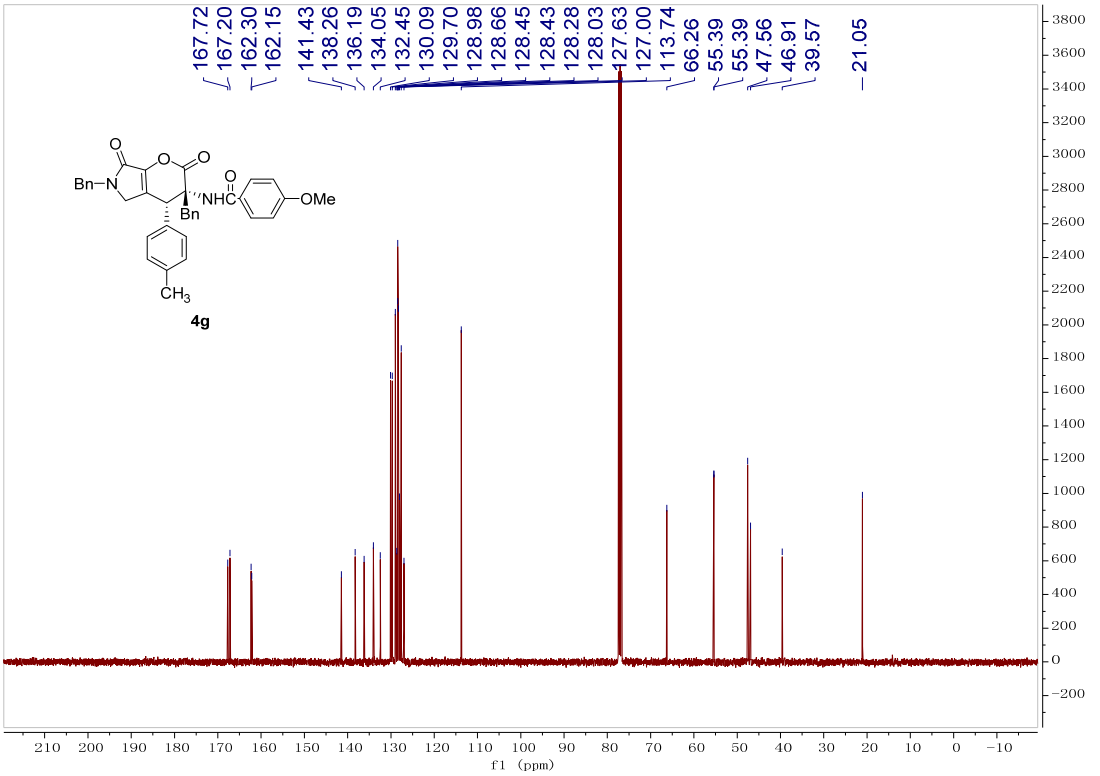
4f:N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-nitrophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



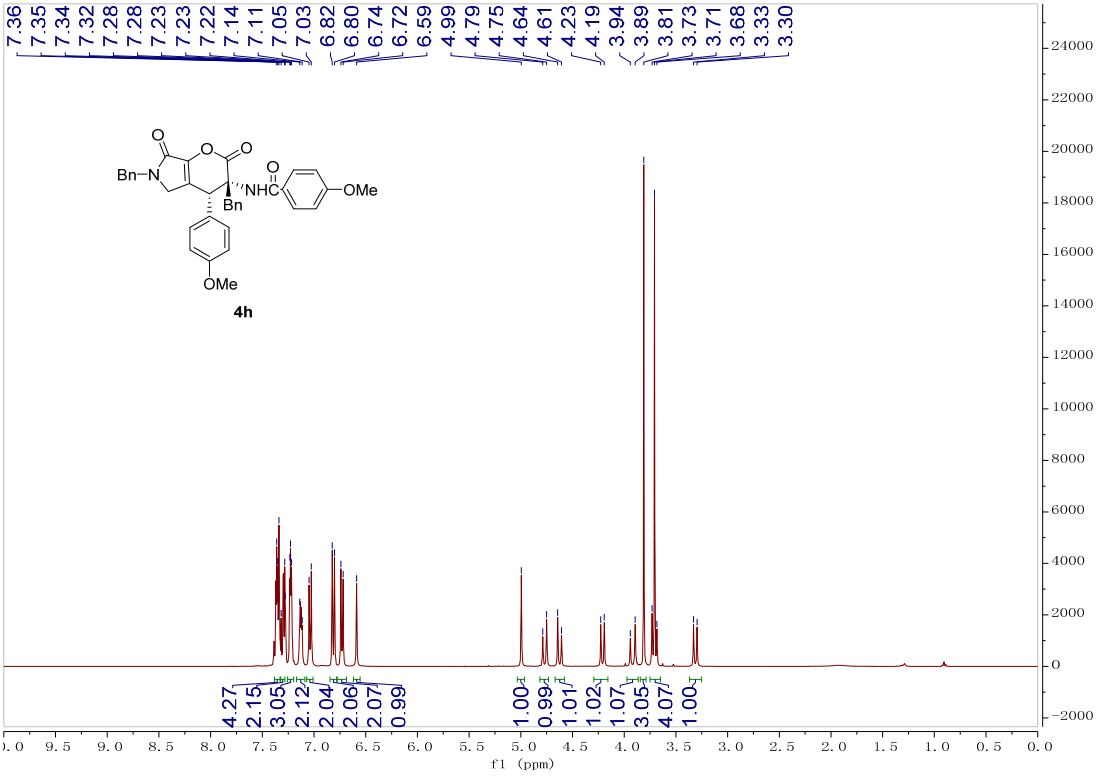


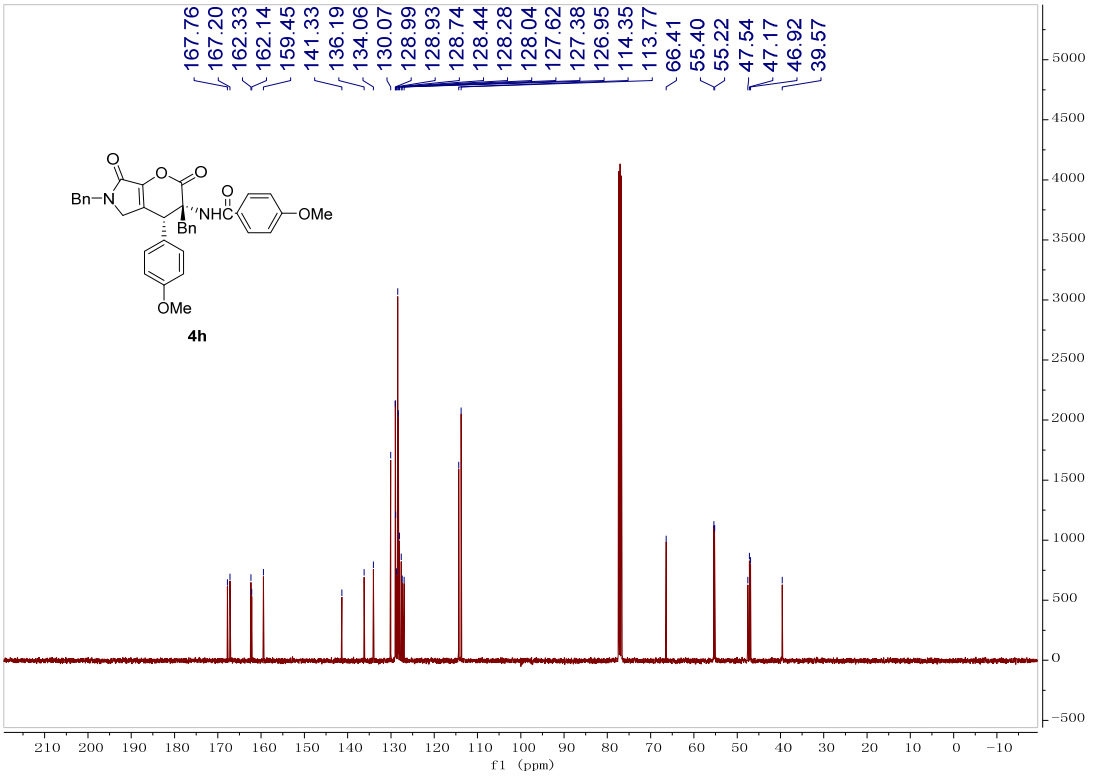
4g:N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(*p*-tolyl)-2,3,4,5,6,7-hexahydropy-rano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



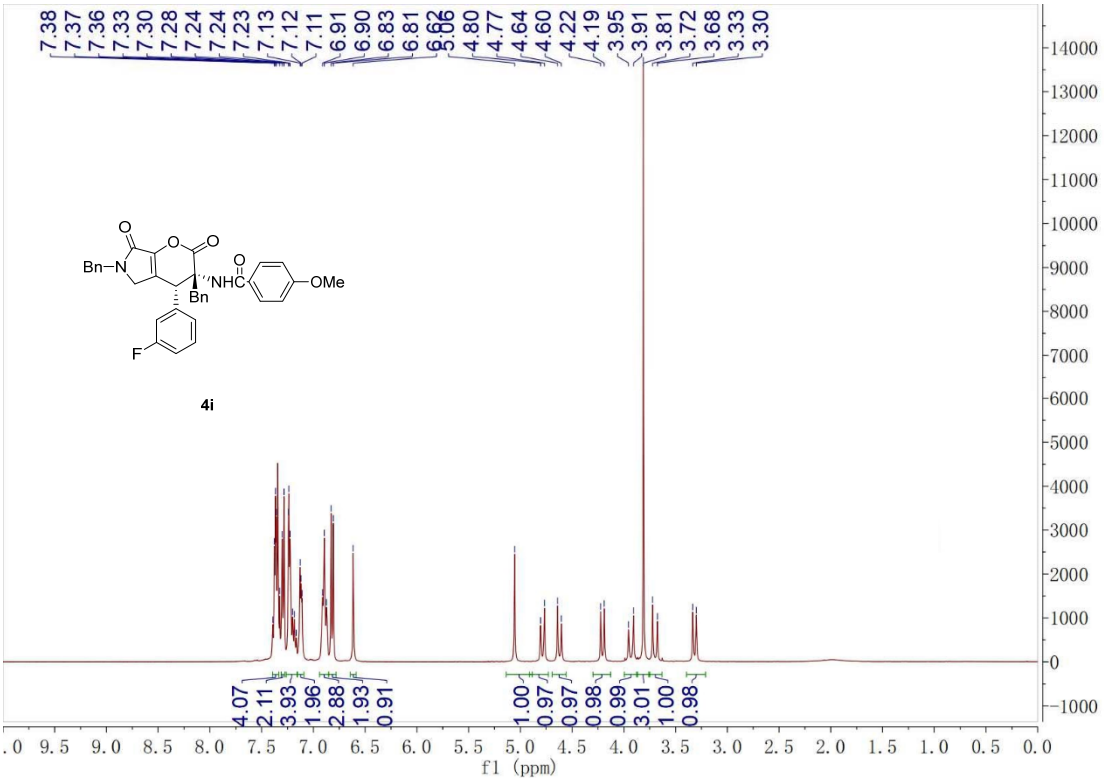


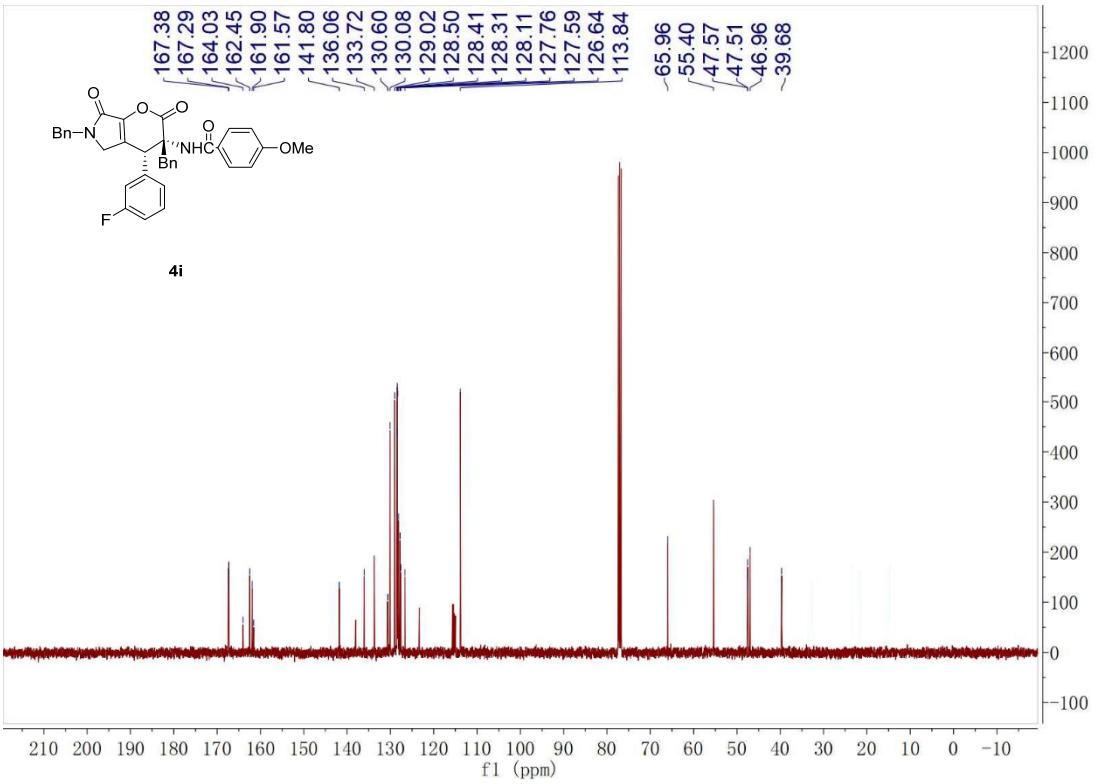
4h:N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-methoxyphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



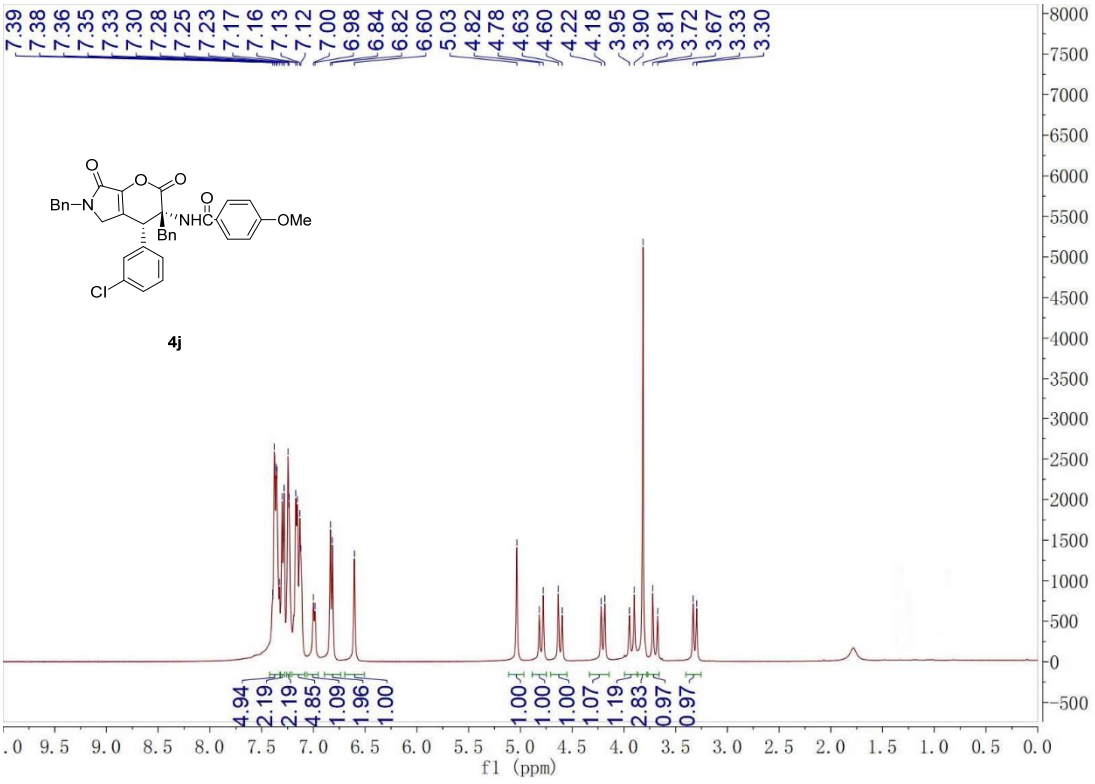


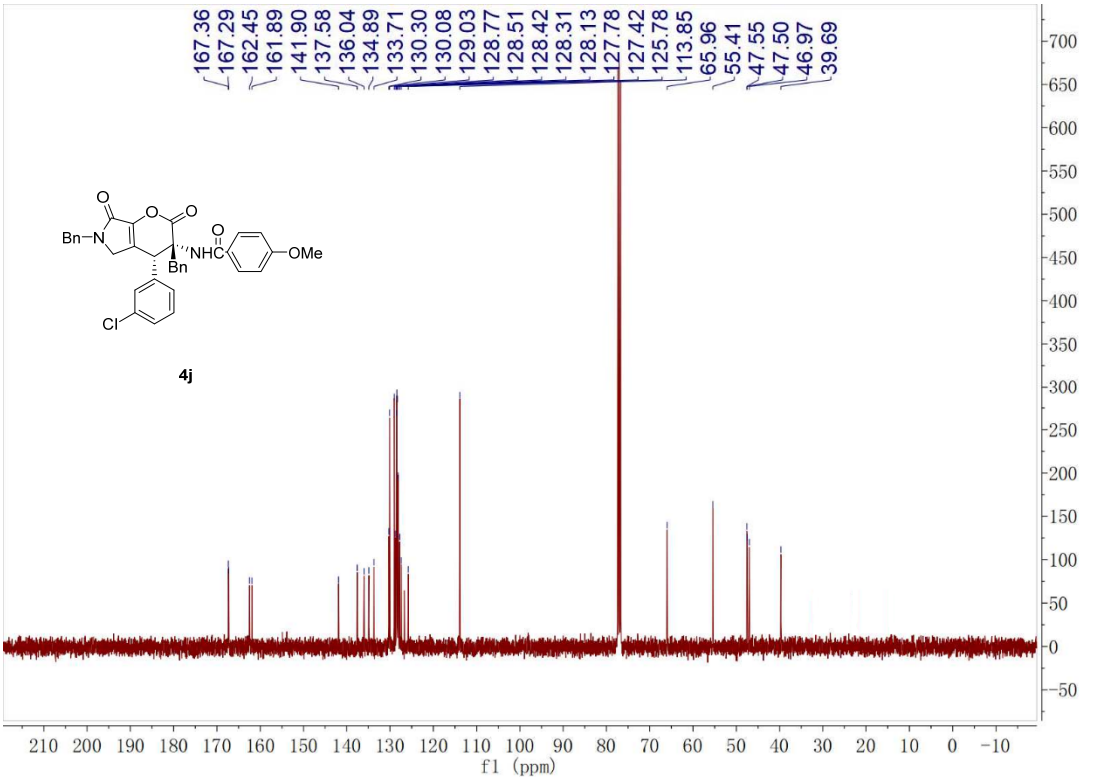
4i:N-((3*R*,4*R*)-3,6-dibenzyl-4-(3-fluorophenyl)-2,7-dioxo-2,3,4,5,6,7 hexahydropy-rano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



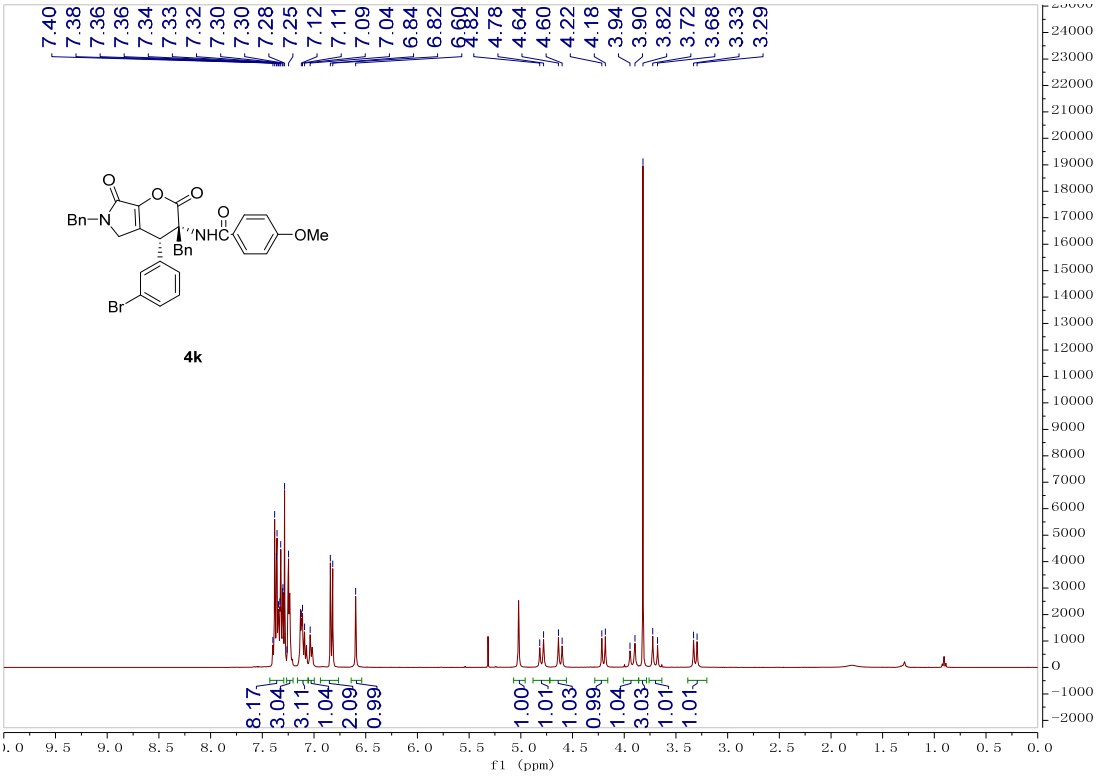


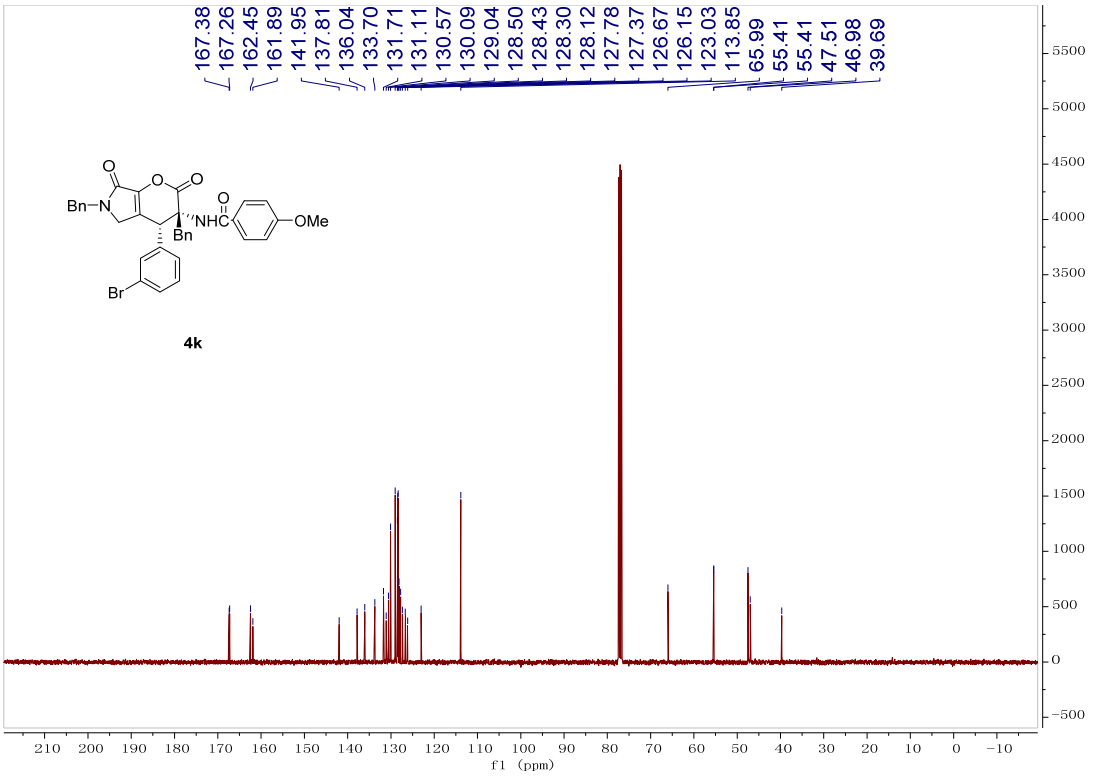
4j:N-((3*R*,4*R*)-3,6-dibenzyl-4-(3-chlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



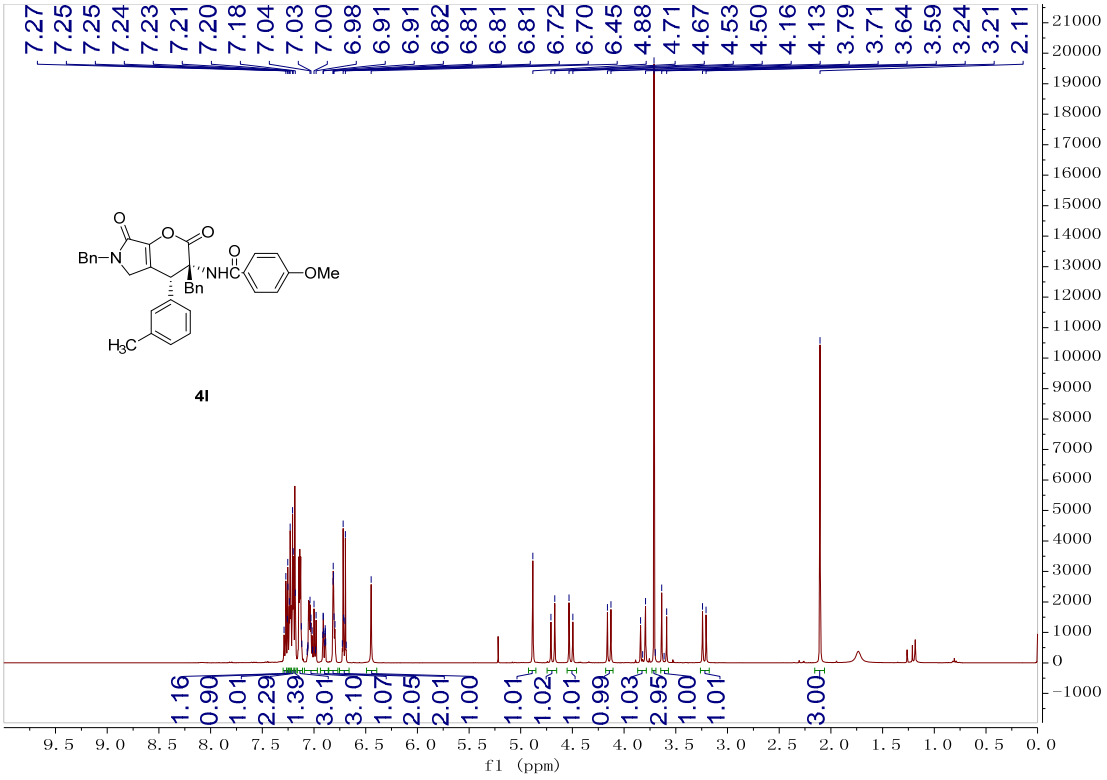


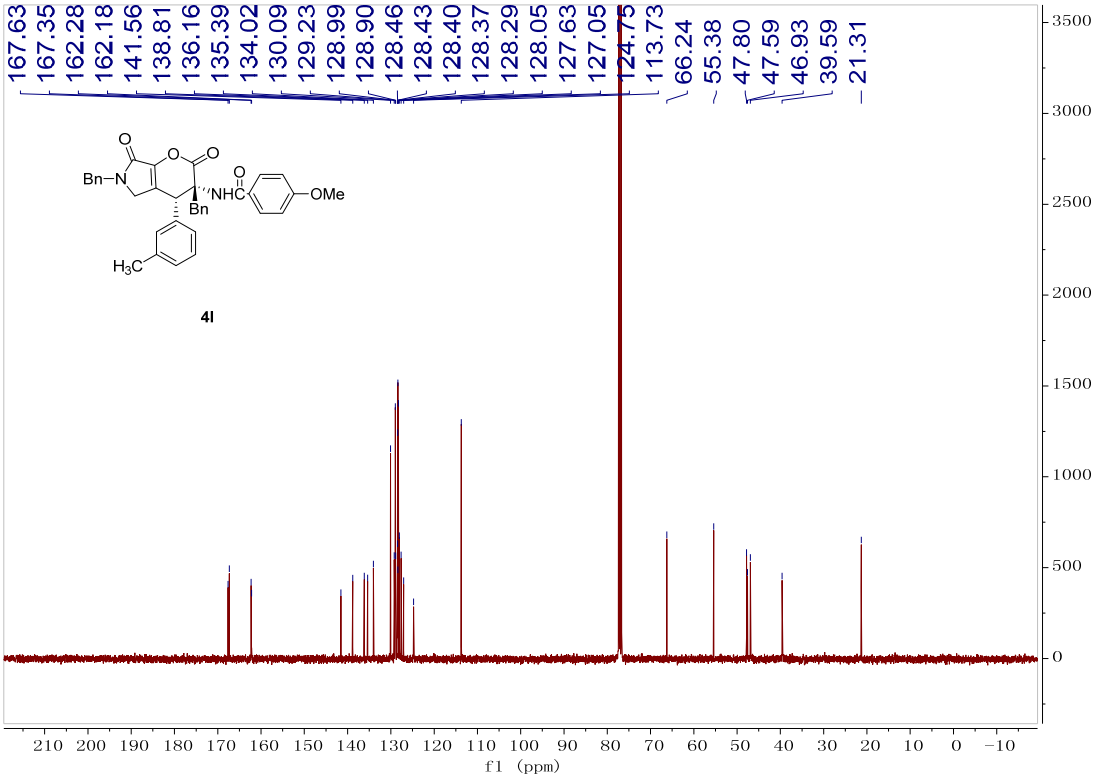
4k:N-((3*R*,4*R*)-3,6-dibenzyl-4-(3-bromophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



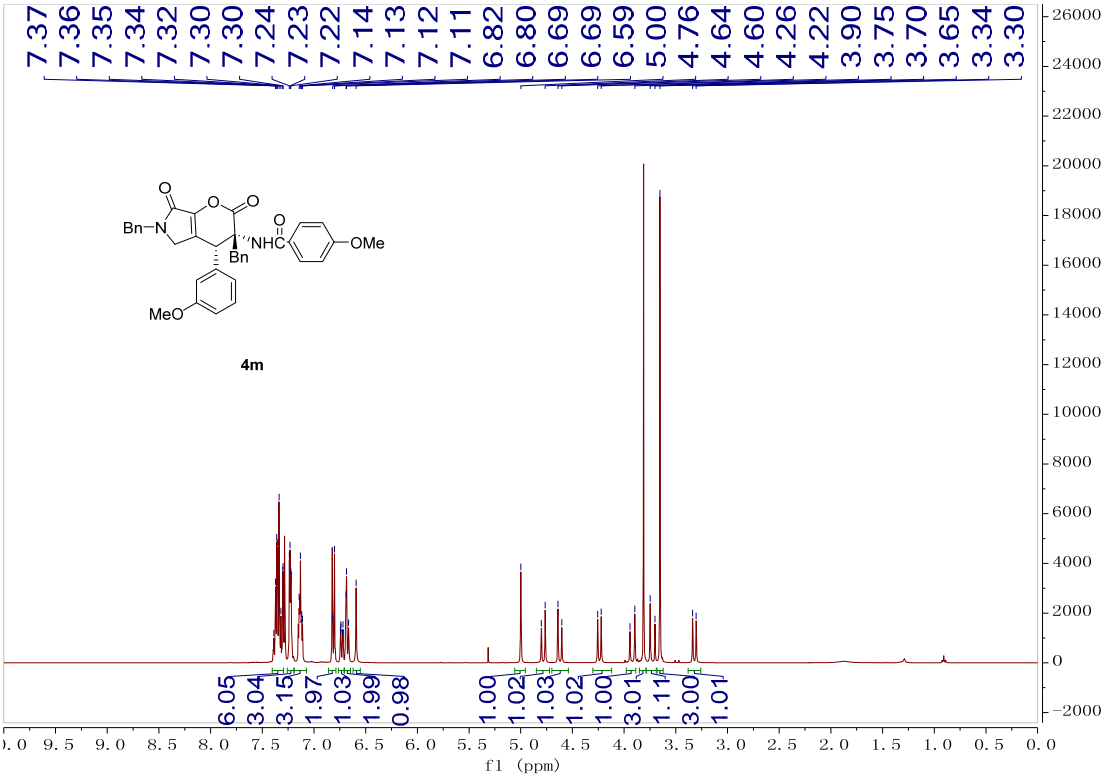


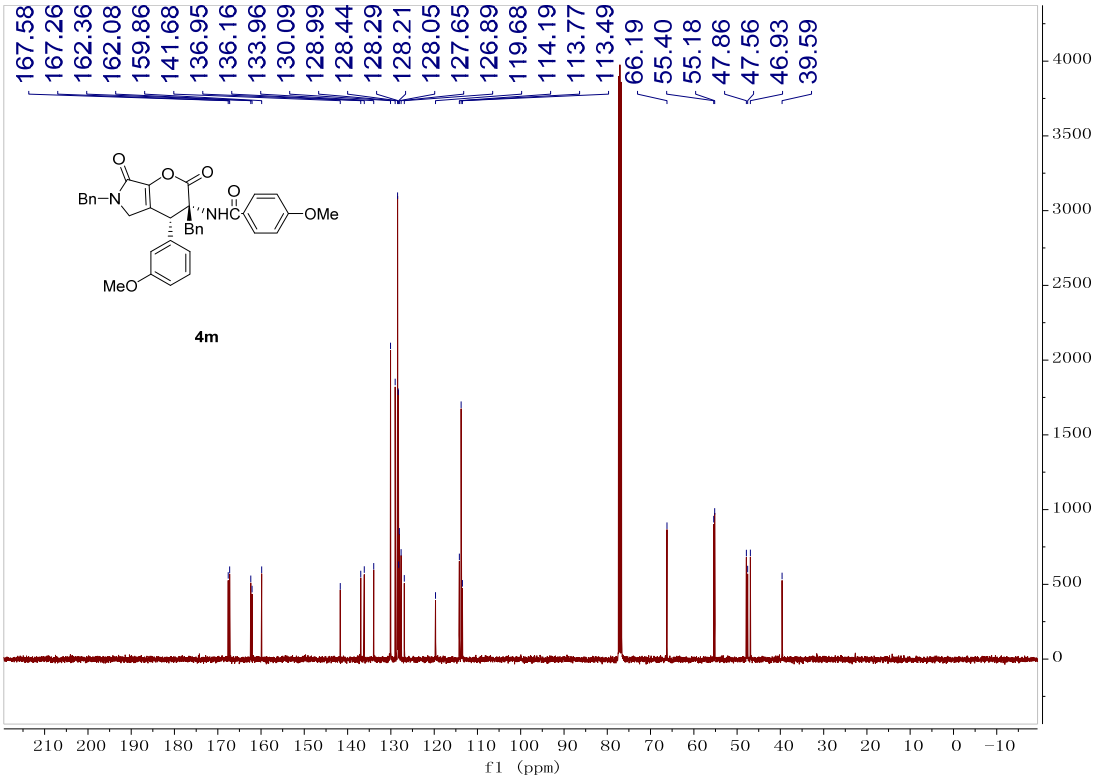
4l:N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(m-tolyl)-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



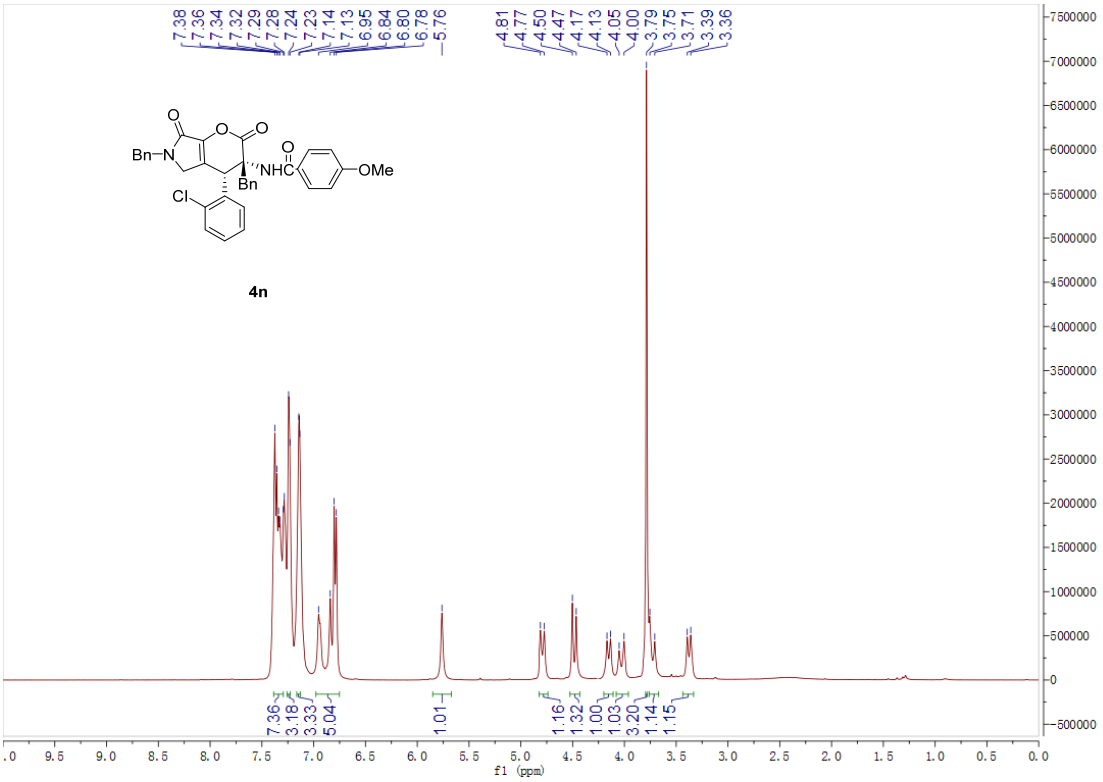


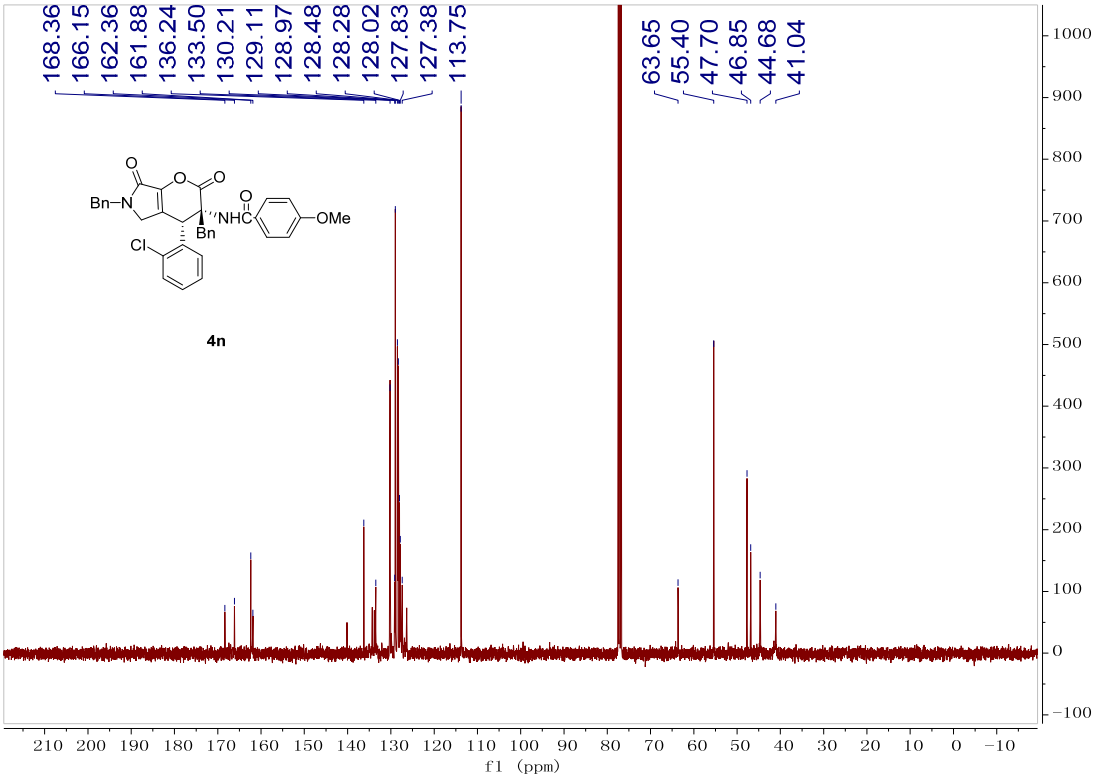
4m:N-((3*R*,4*R*)-3,6-dibenzyl-4-(3-methoxyphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



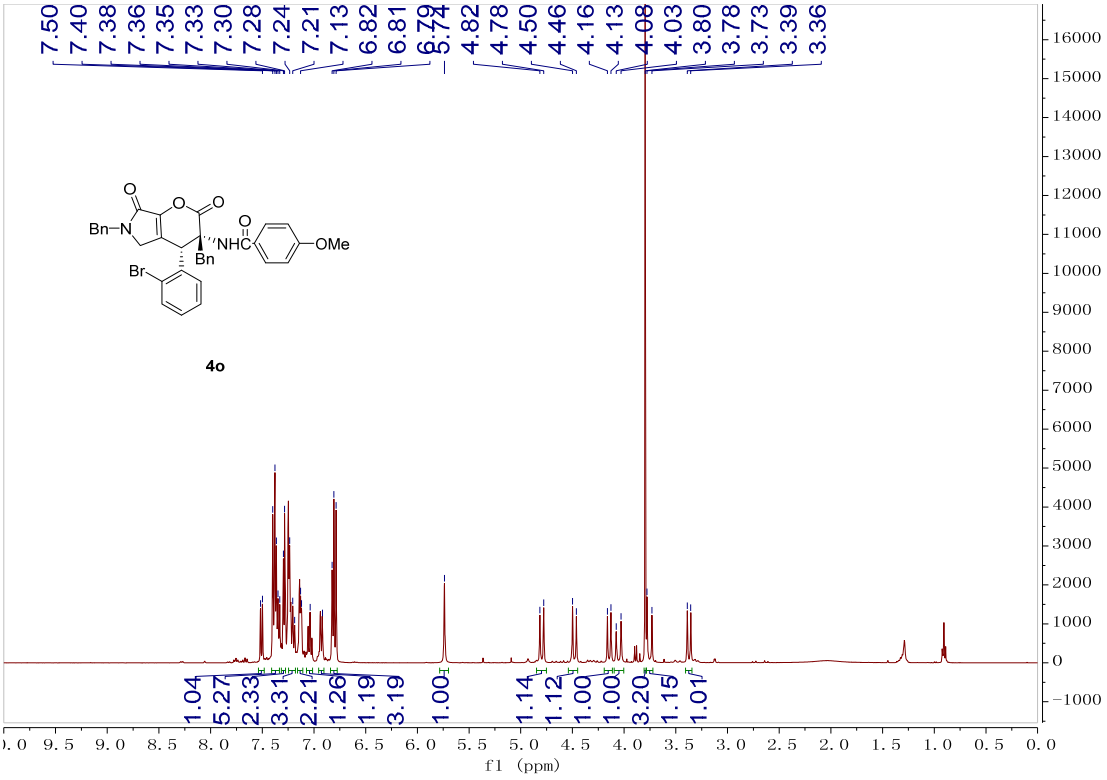


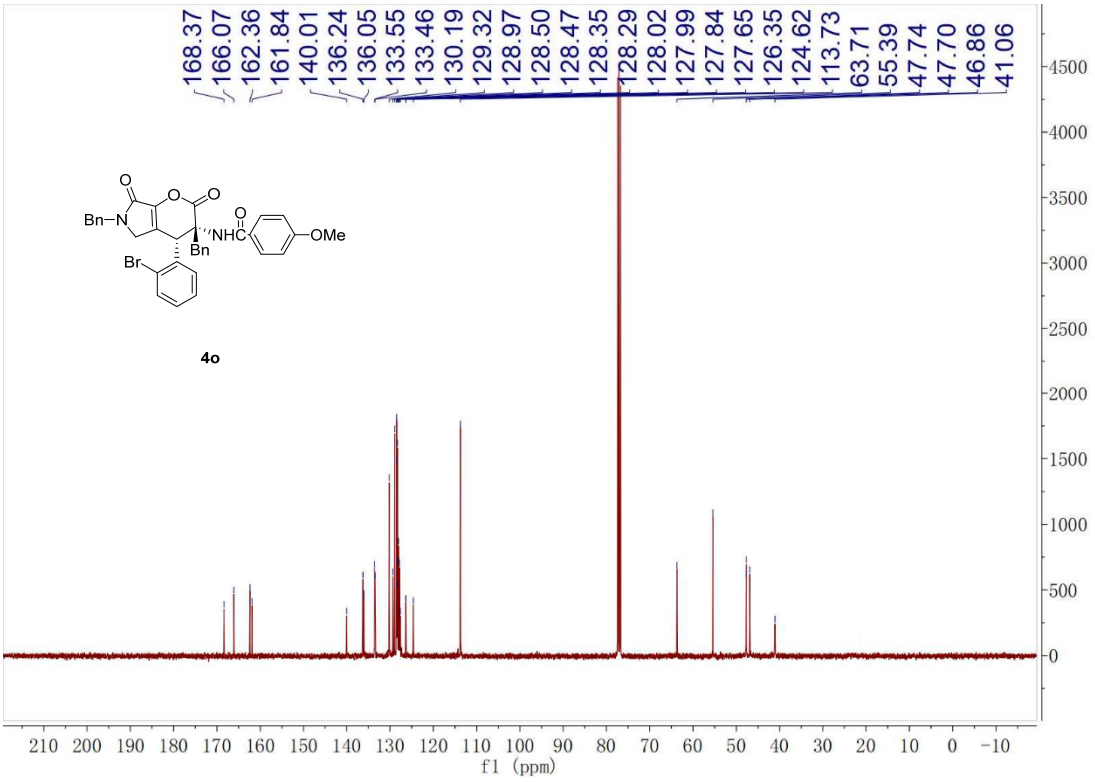
4n:N-((3*R*,4*S*)-3,6-dibenzyl-4-(2-chlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



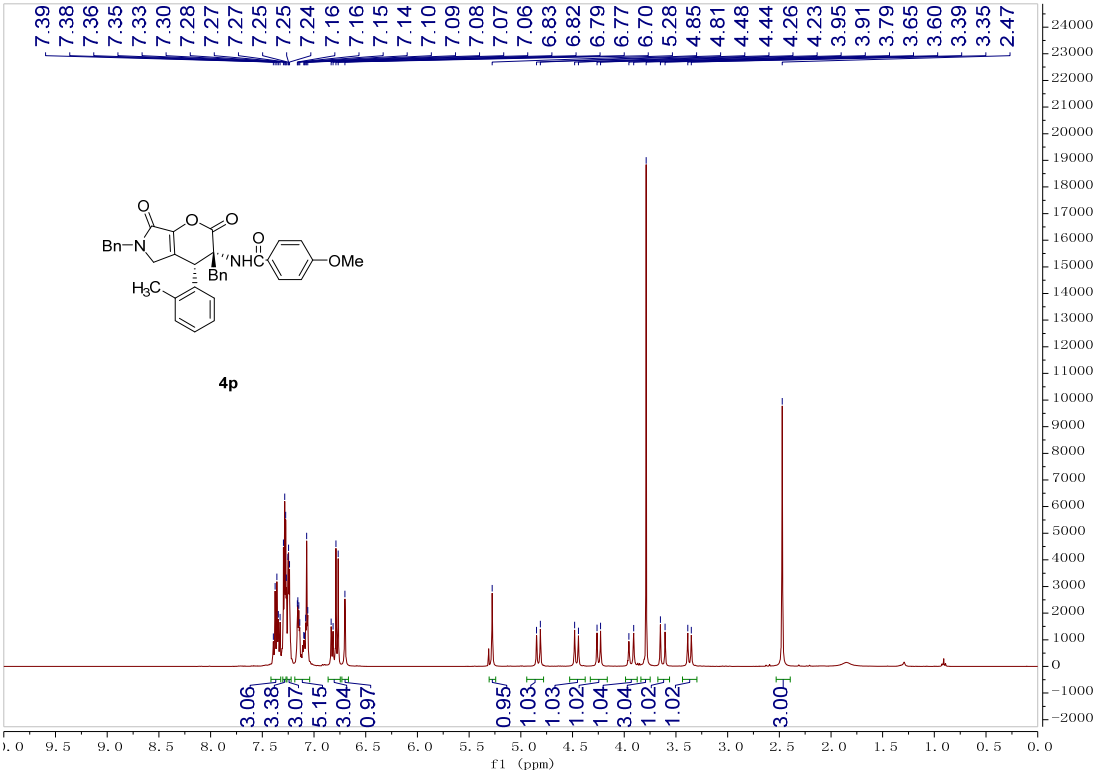


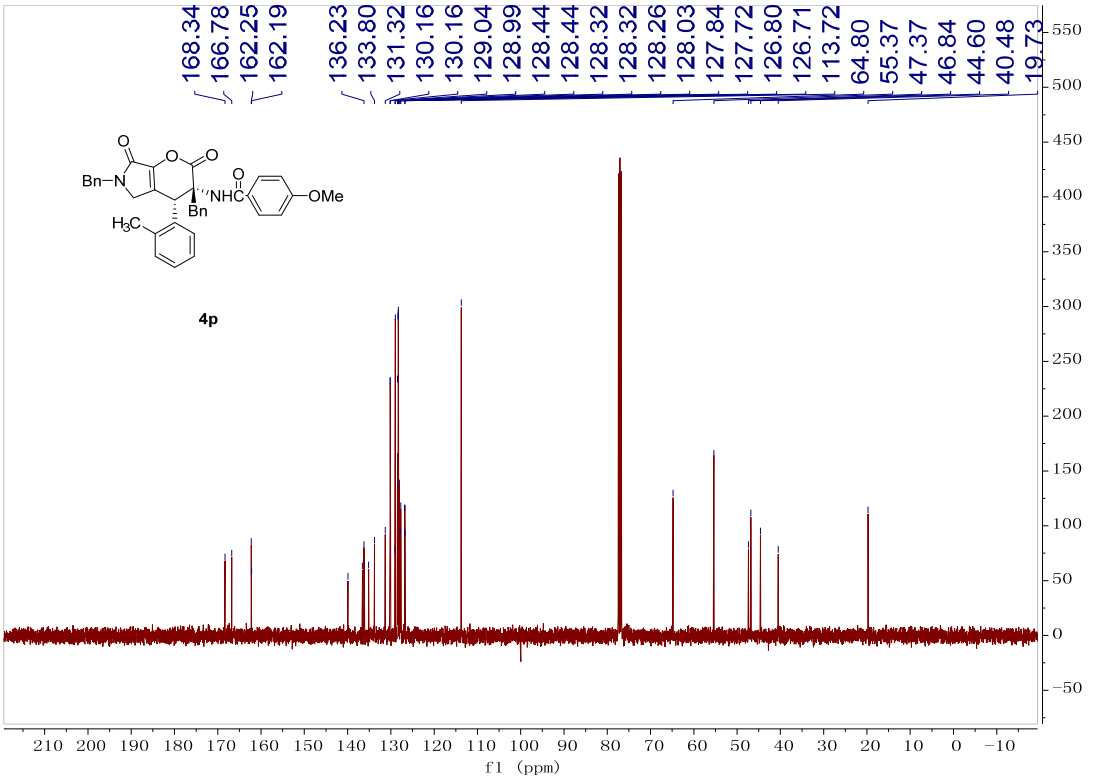
4o:N-((3*R*,4*S*)-3,6-dibenzyl-4-(2-bromophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



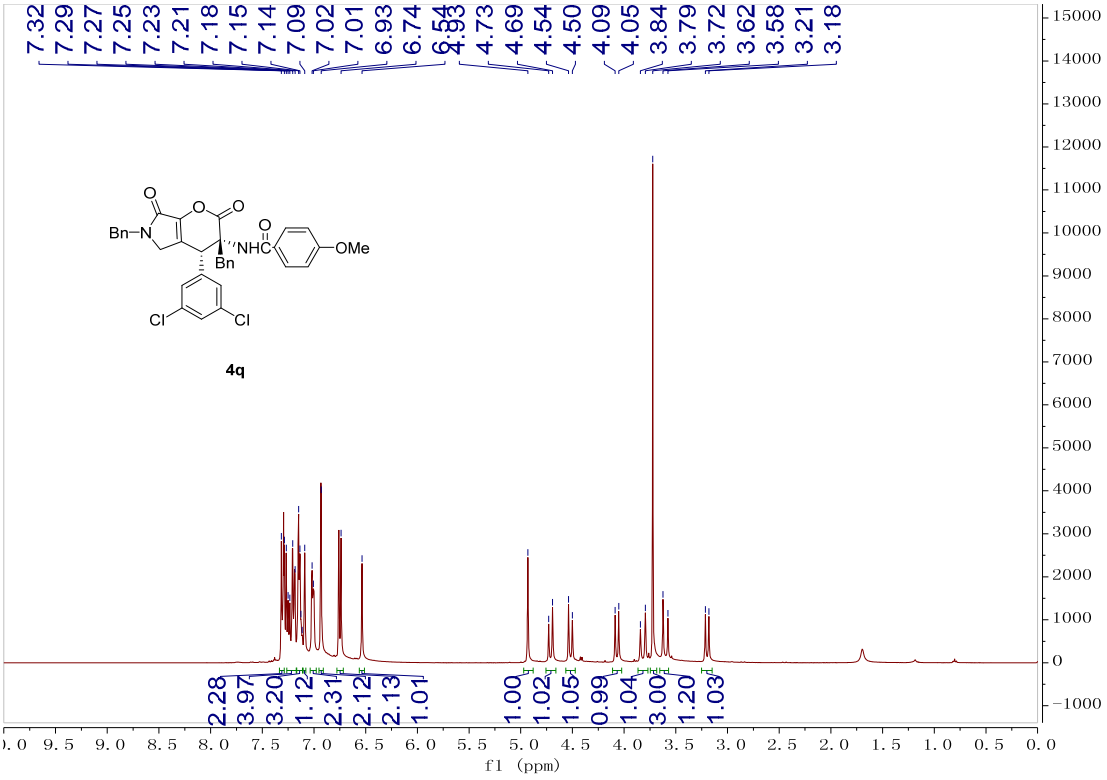


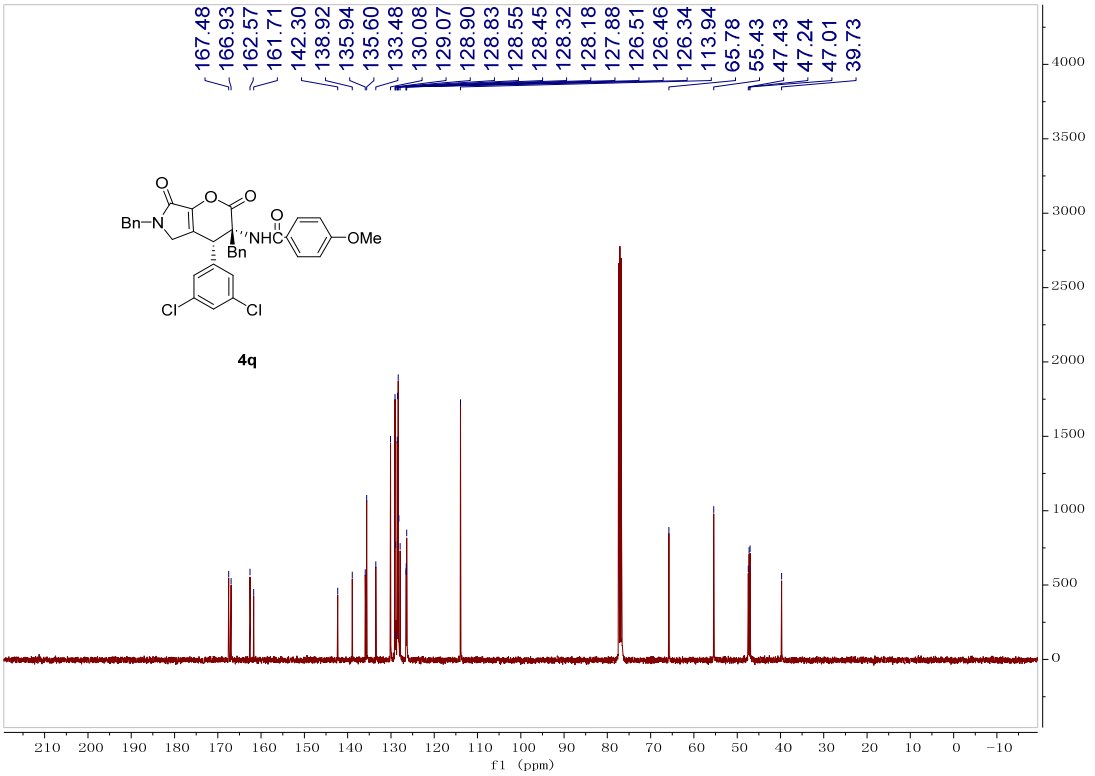
4p:N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(o-tolyl)-2,3,4,5,6,7-hexahydropy-rano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



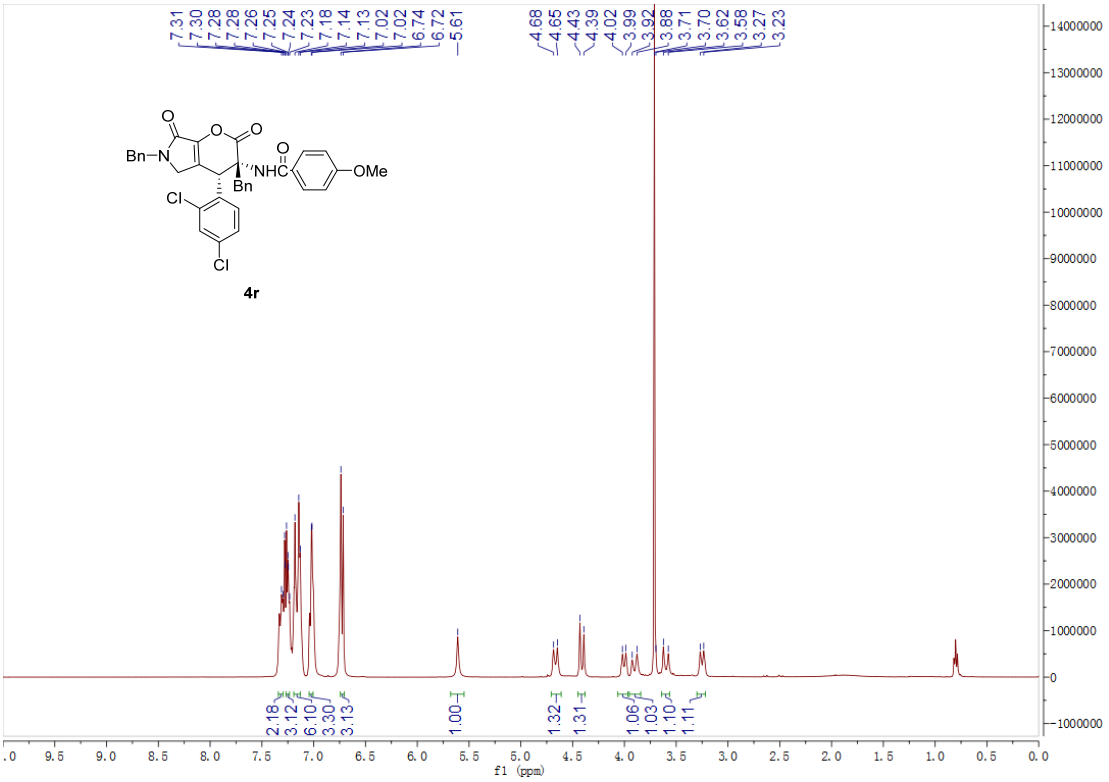


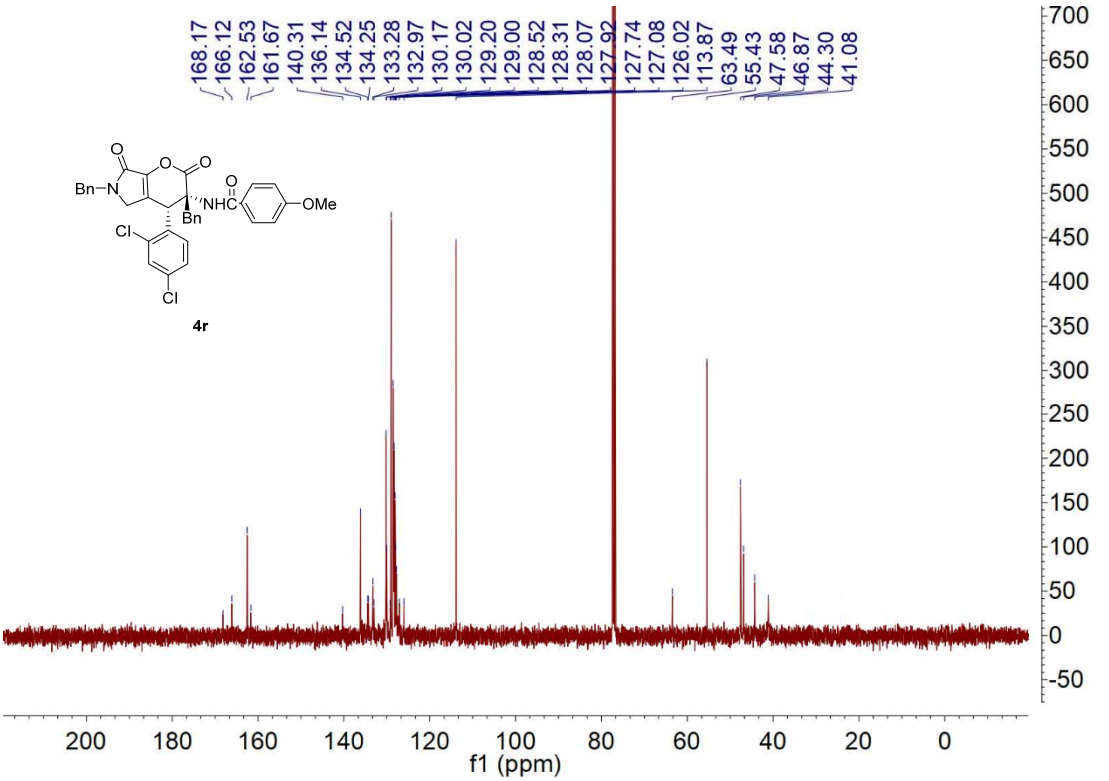
4q:N-((3*R*,4*R*)-3,6-dibenzyl-4-(3,5-dichlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



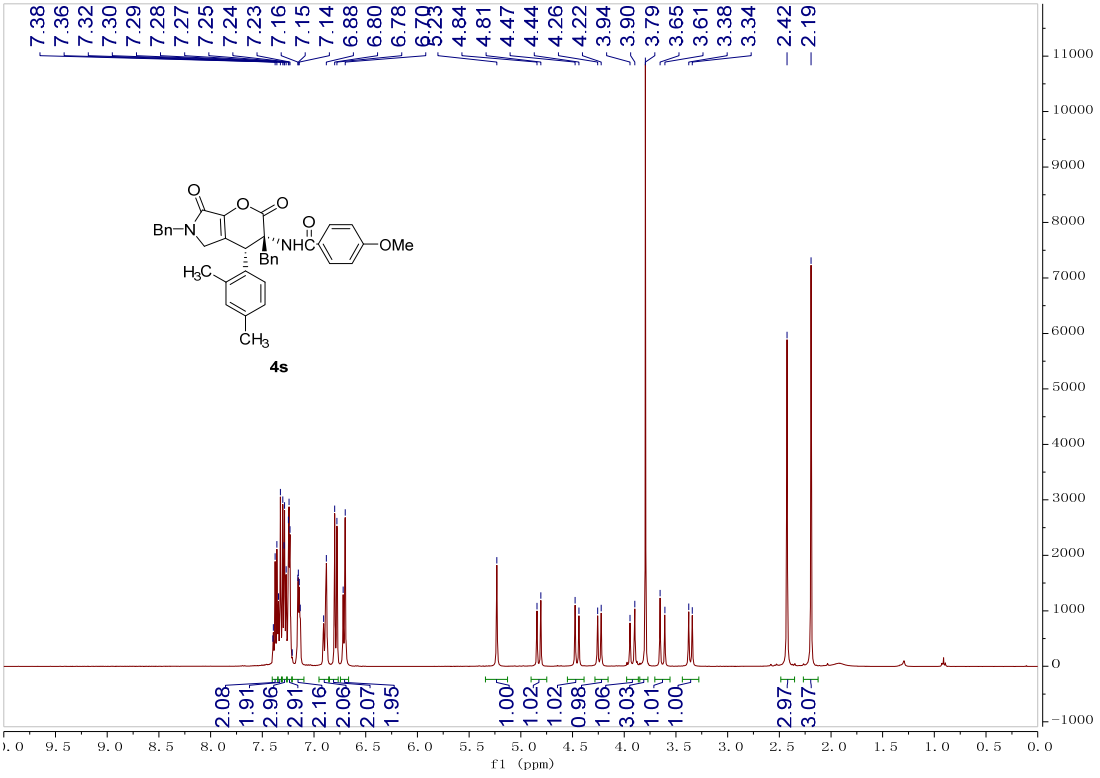


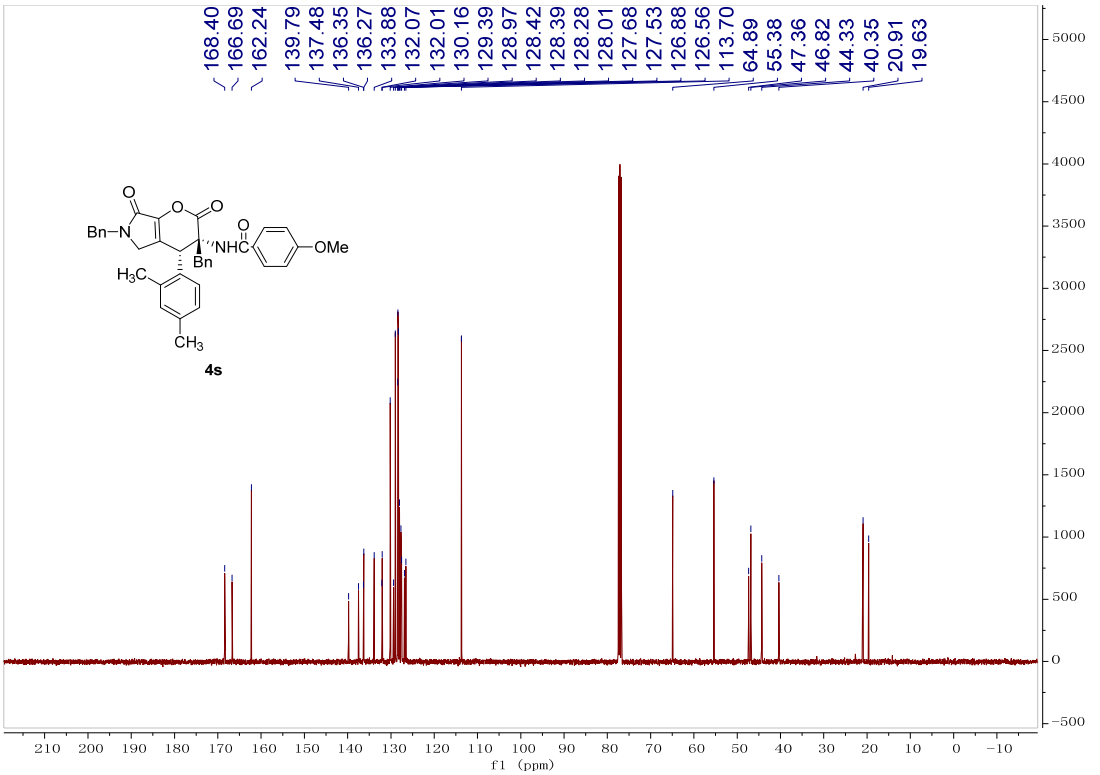
4r:N-((3*R*,4*S*)-3,6-dibenzyl-4-(2,4-dichlorophenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



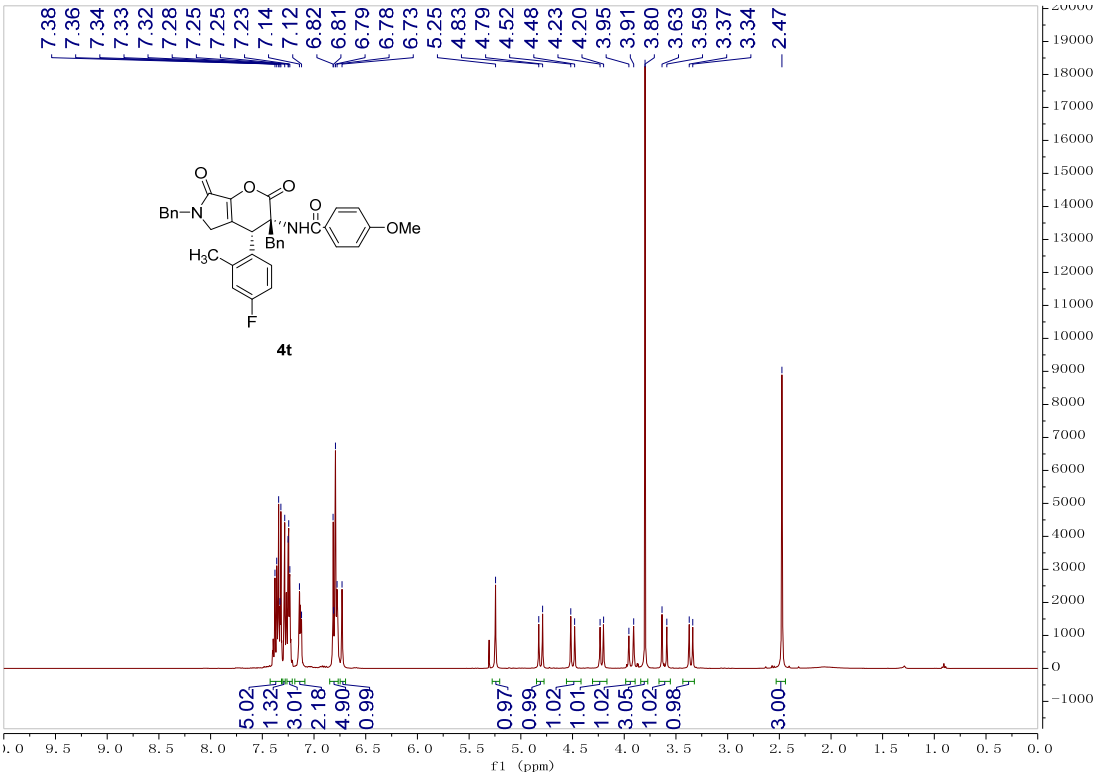


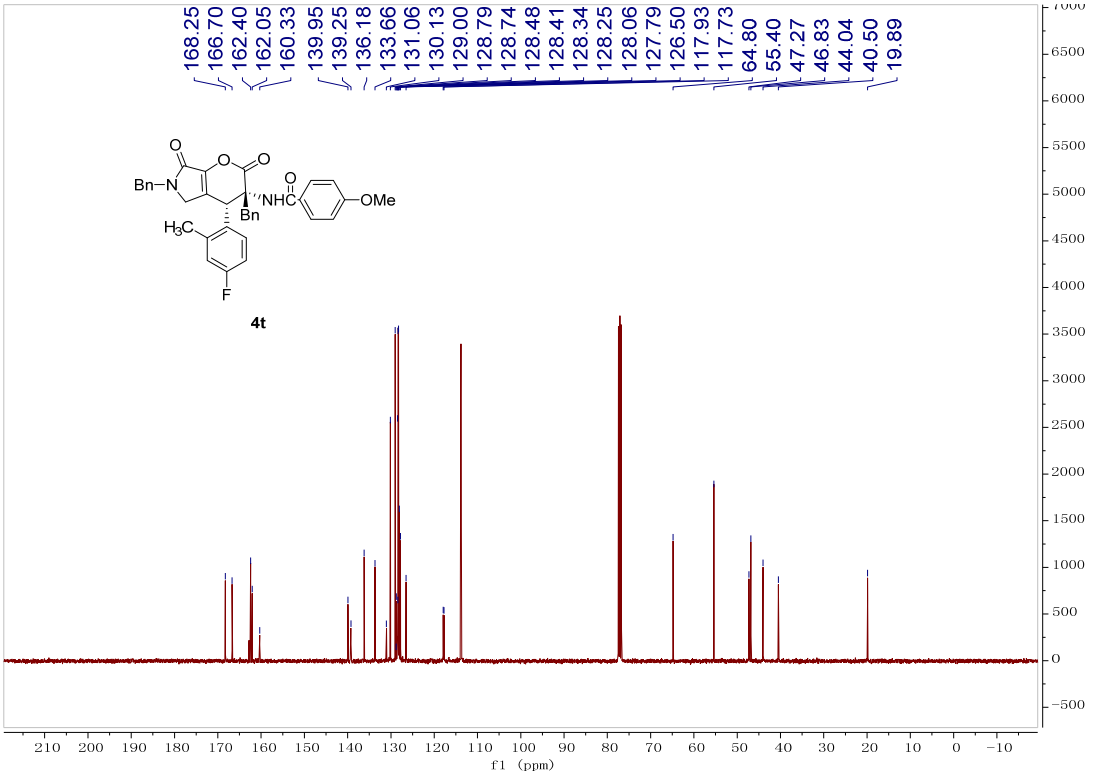
4s:N-((3*R*,4*R*)-3,6-dibenzyl-4-(2,4-dimethylphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

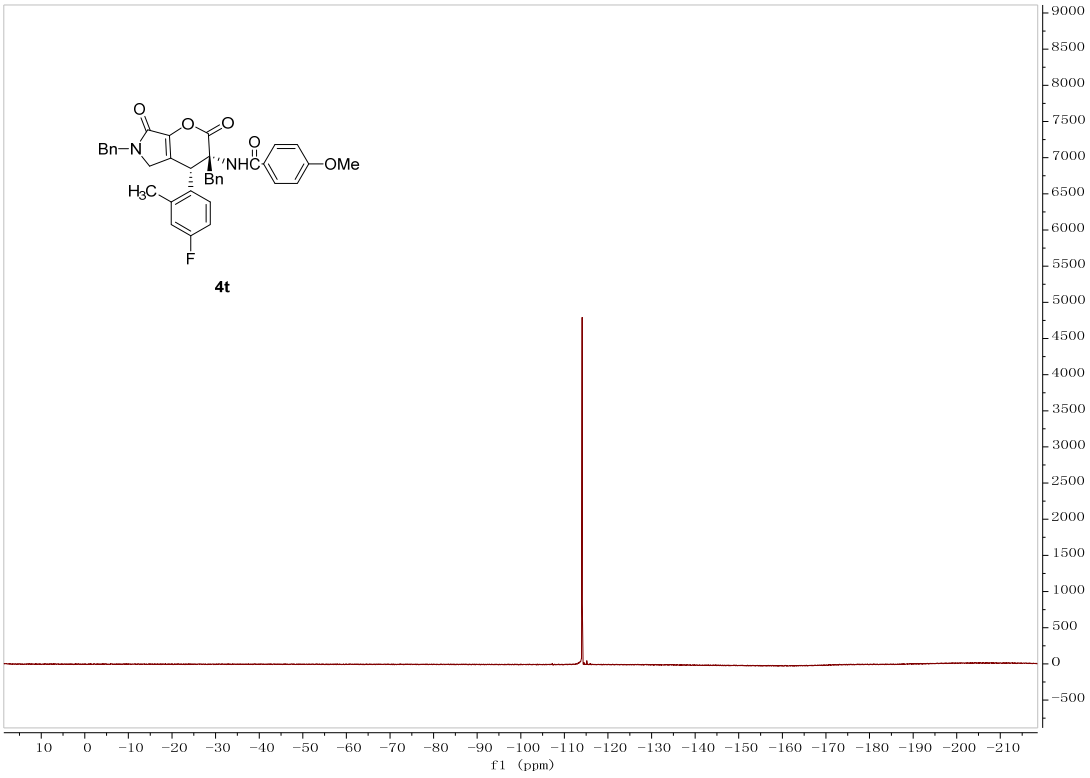




4t:N-((3*R*,4*R*)-3,6-dibenzyl-4-(4-fluoro-2-methylphenyl)-2,7-dioxo-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide






Bn
N
NH
OMe
Bn
H3C
F
4t
9000
8500
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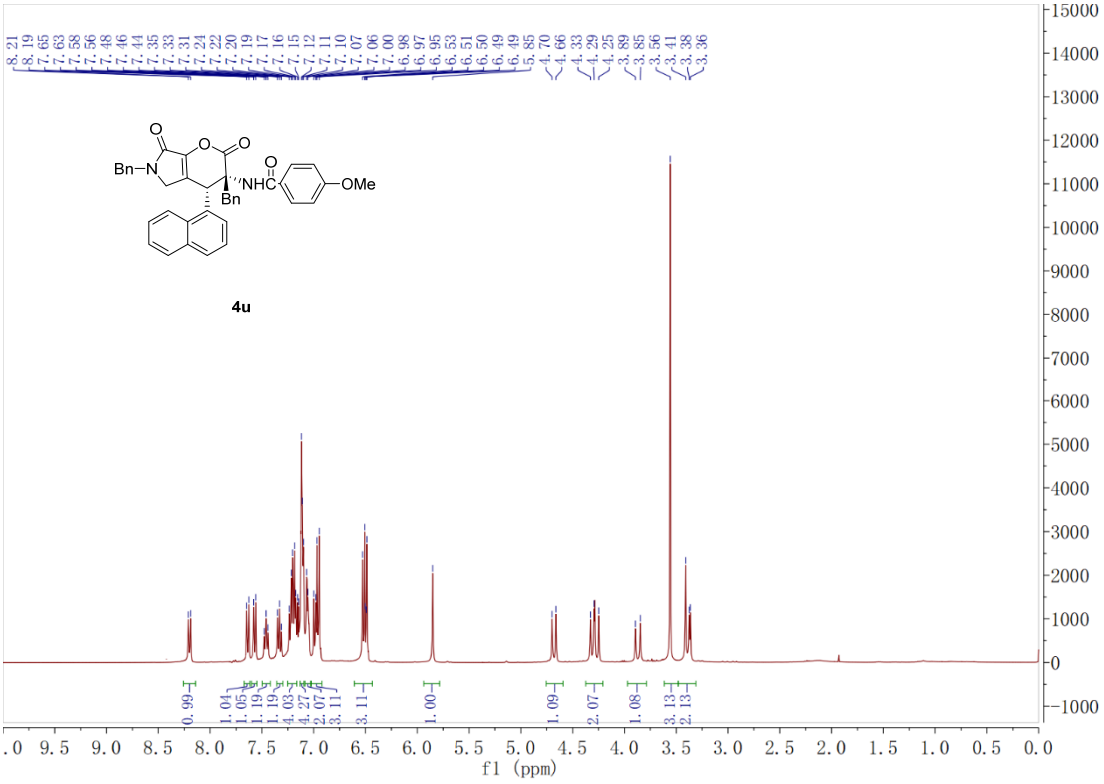
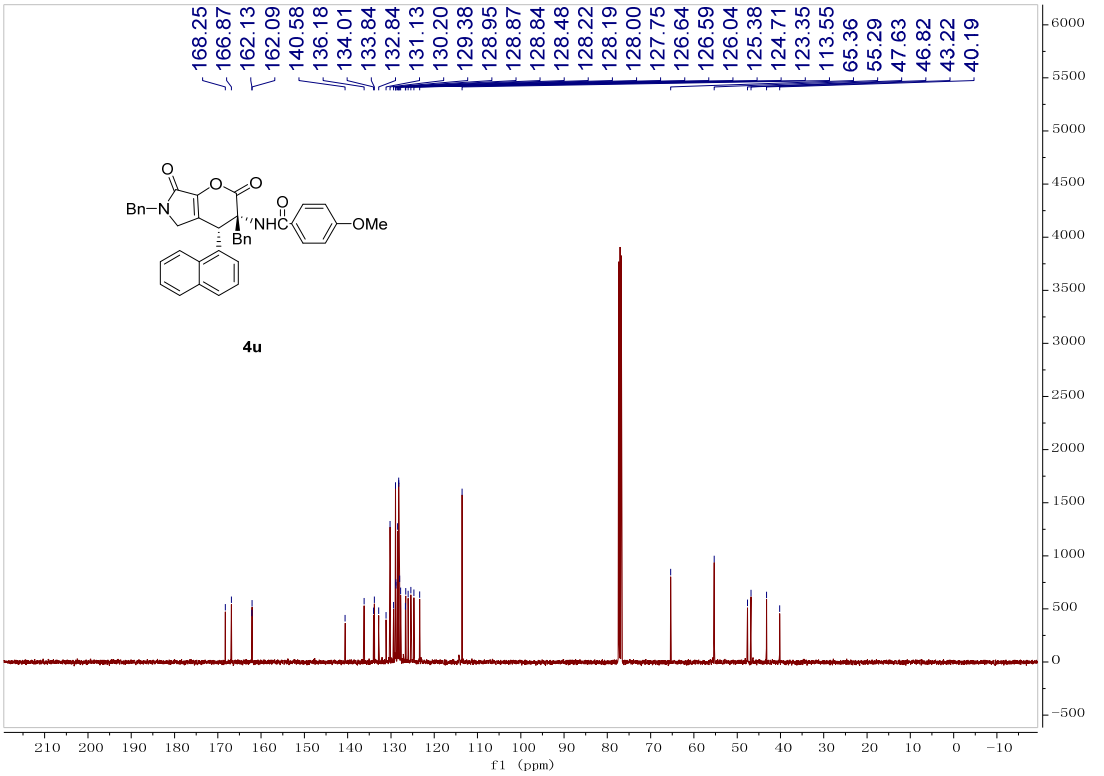
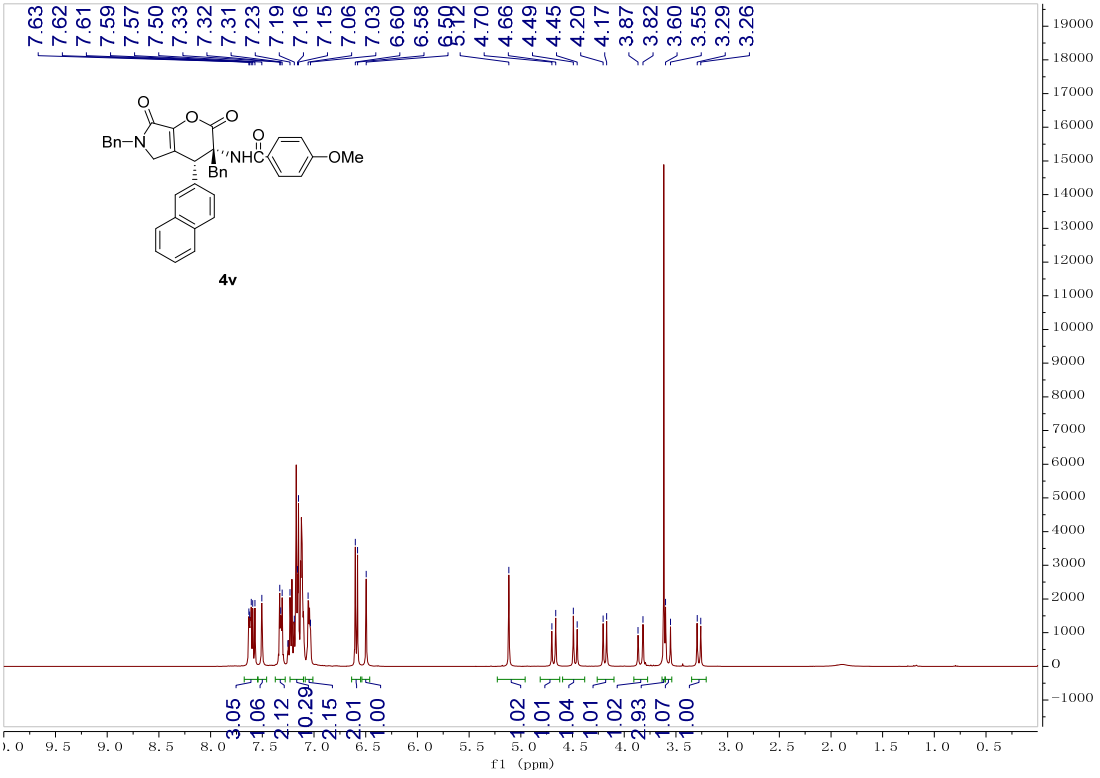
−500
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

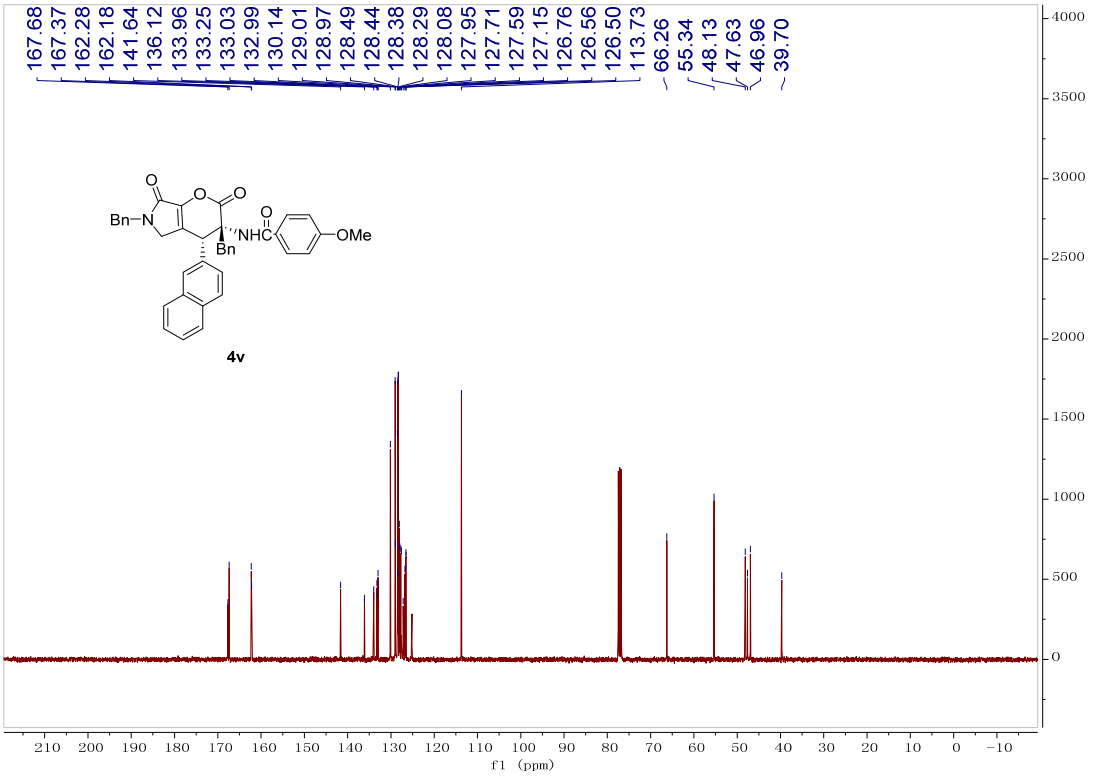
4u:N-((3*R*,4*R*)-3,6-dibenzyl-4-(naphthalen-1-yl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



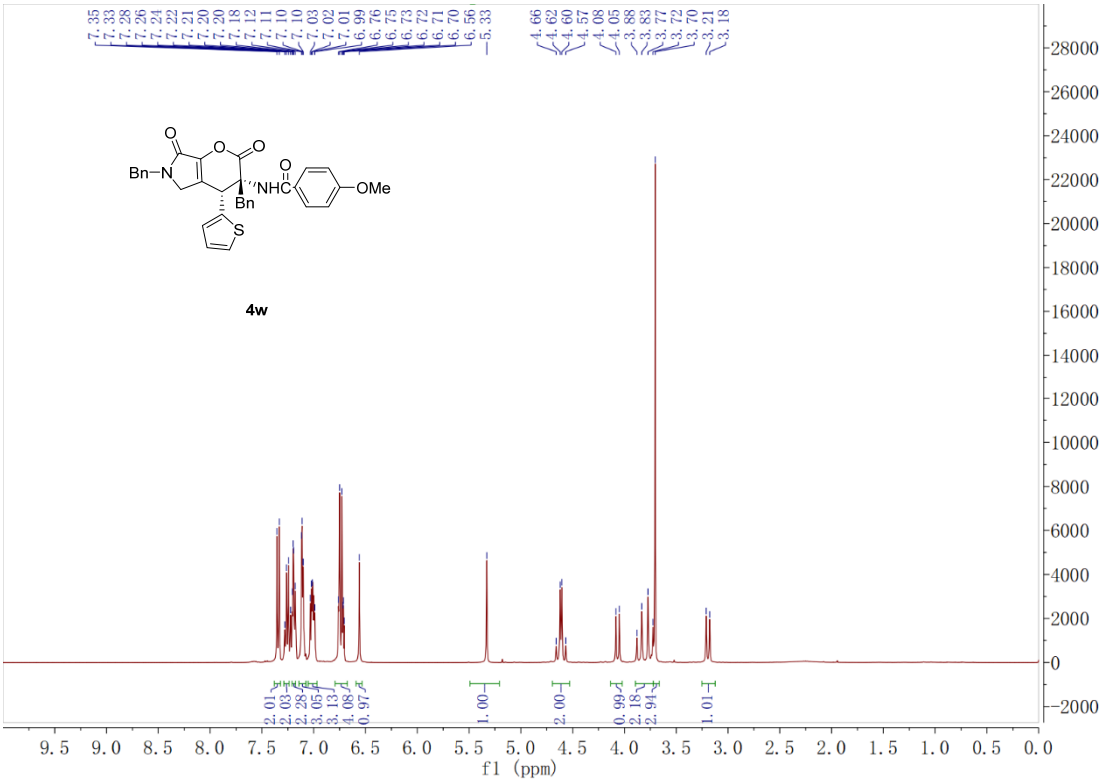


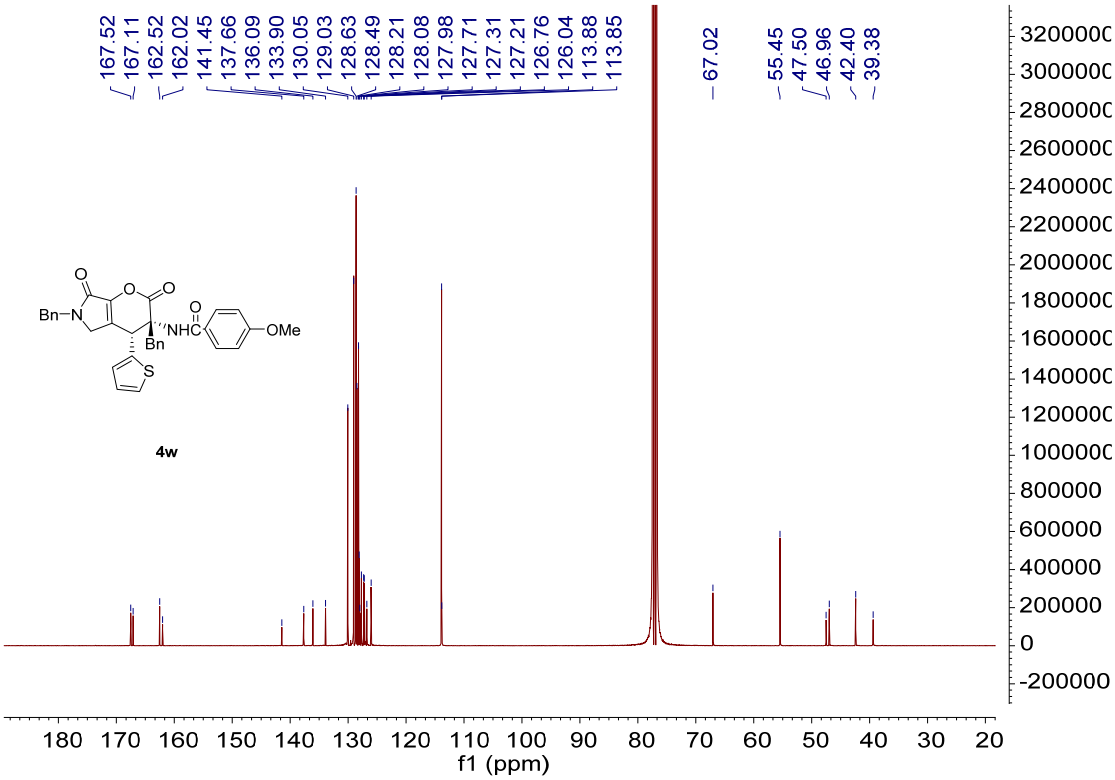
4v:N-((3*R*,4*R*)-3,6-dibenzyl-4-(naphthalen-2-yl)-2,7-dioxo-2,3,4,5,6,7-hexahydro-pyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



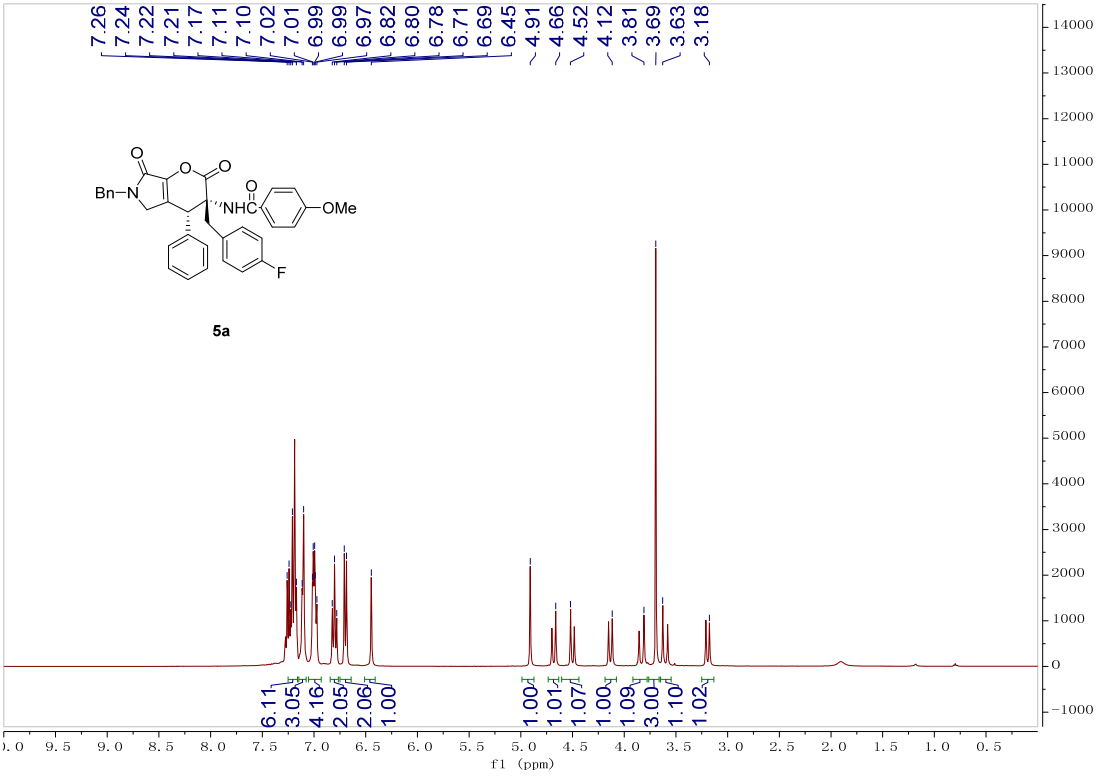


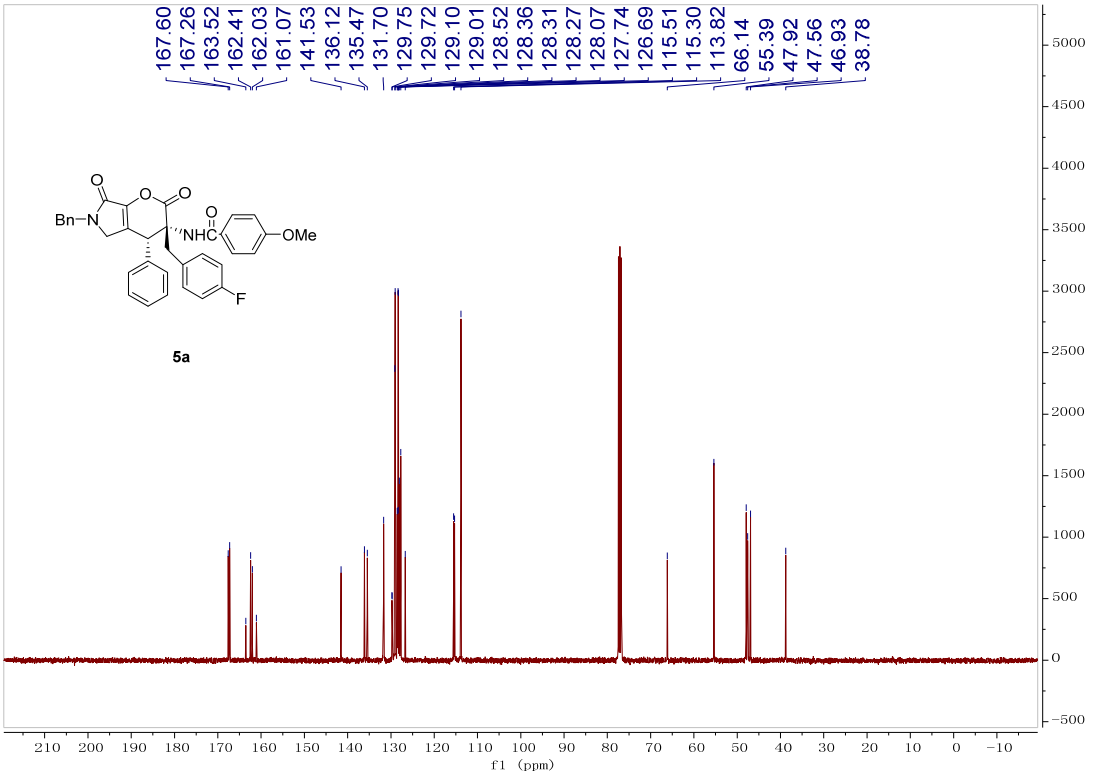
4w:N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-(thiophen-2-yl)-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide

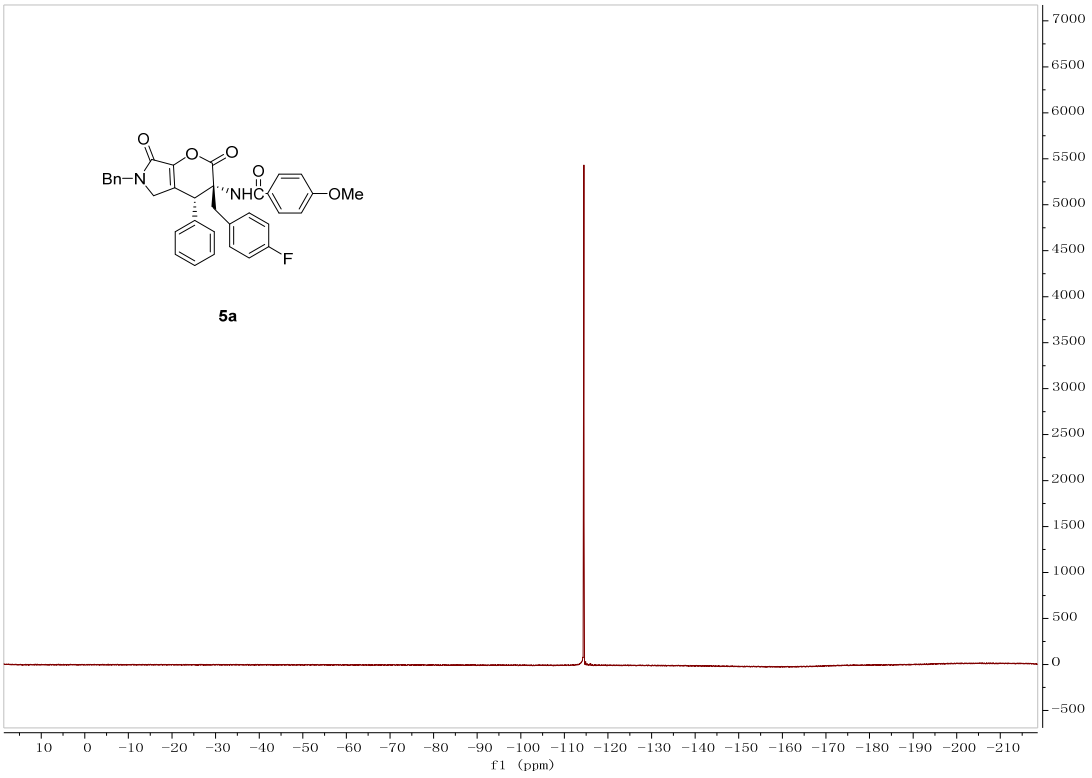




5a:N-((3*R*,4*R*)-6-benzyl-3-(4-fluorobenzyl)-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide






Bn–N
O
O
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NHC
O
OMe
F
5a
7000
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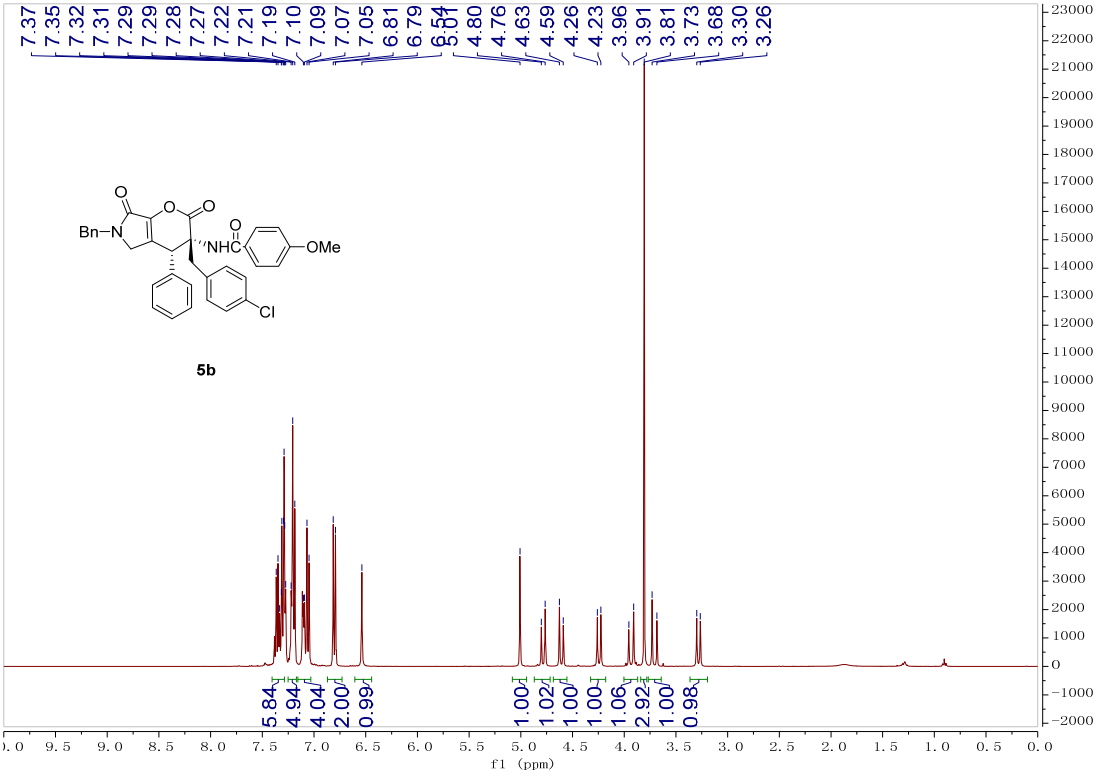
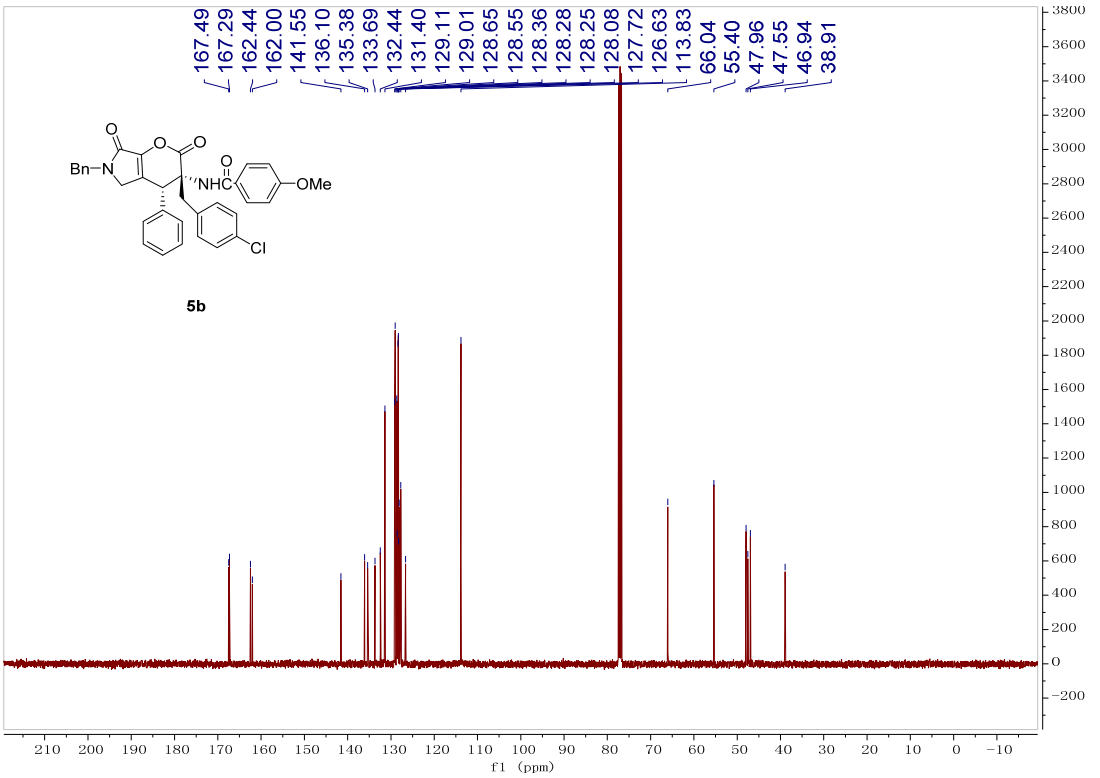
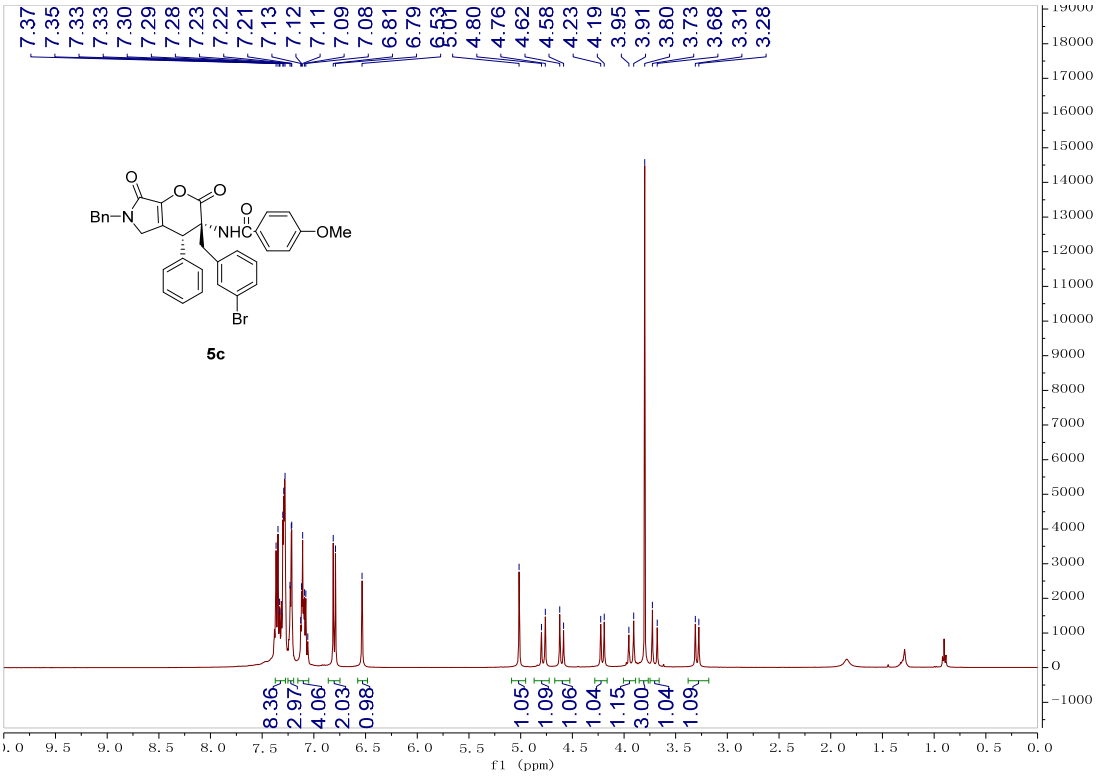
−500
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

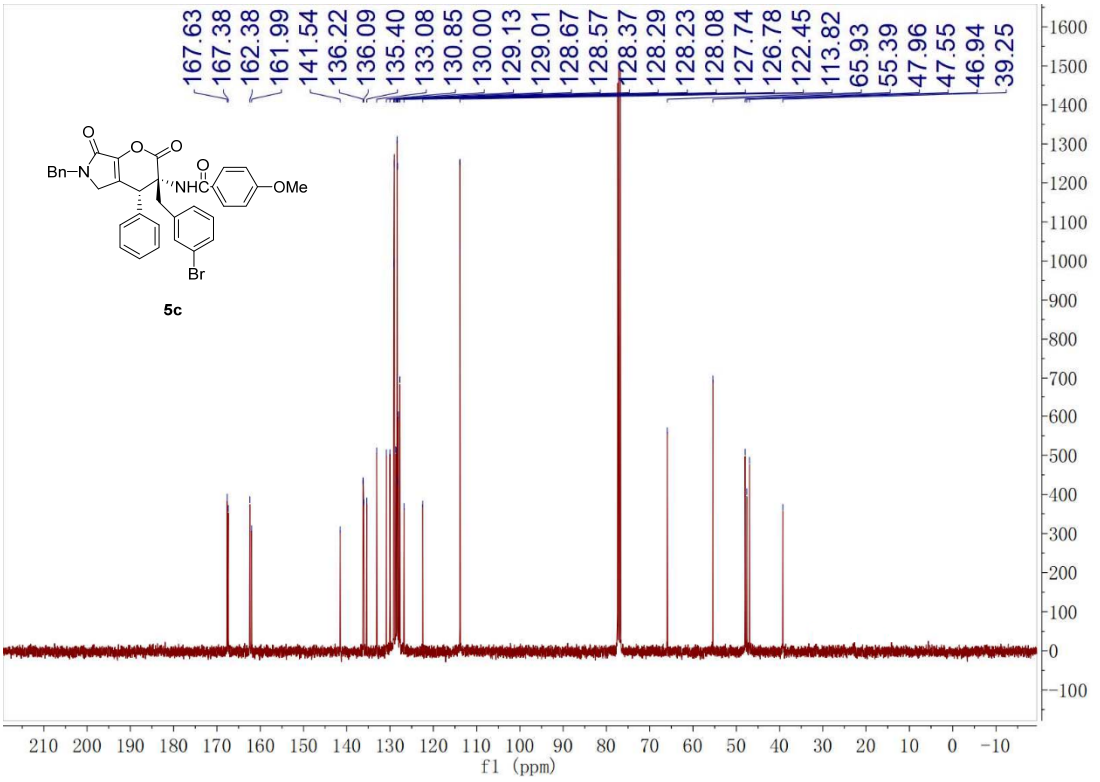
5b:N-((3*R*,4*R*)-6-benzyl-3-(4-chlorobenzyl)-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexa-hydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



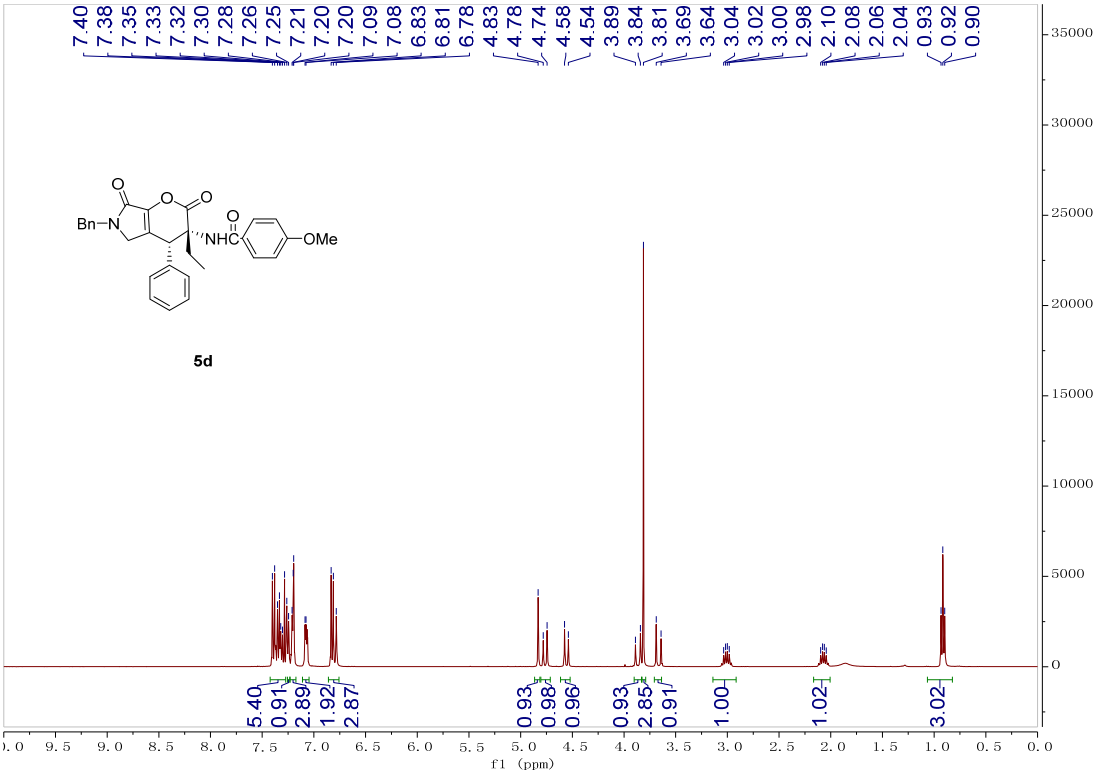


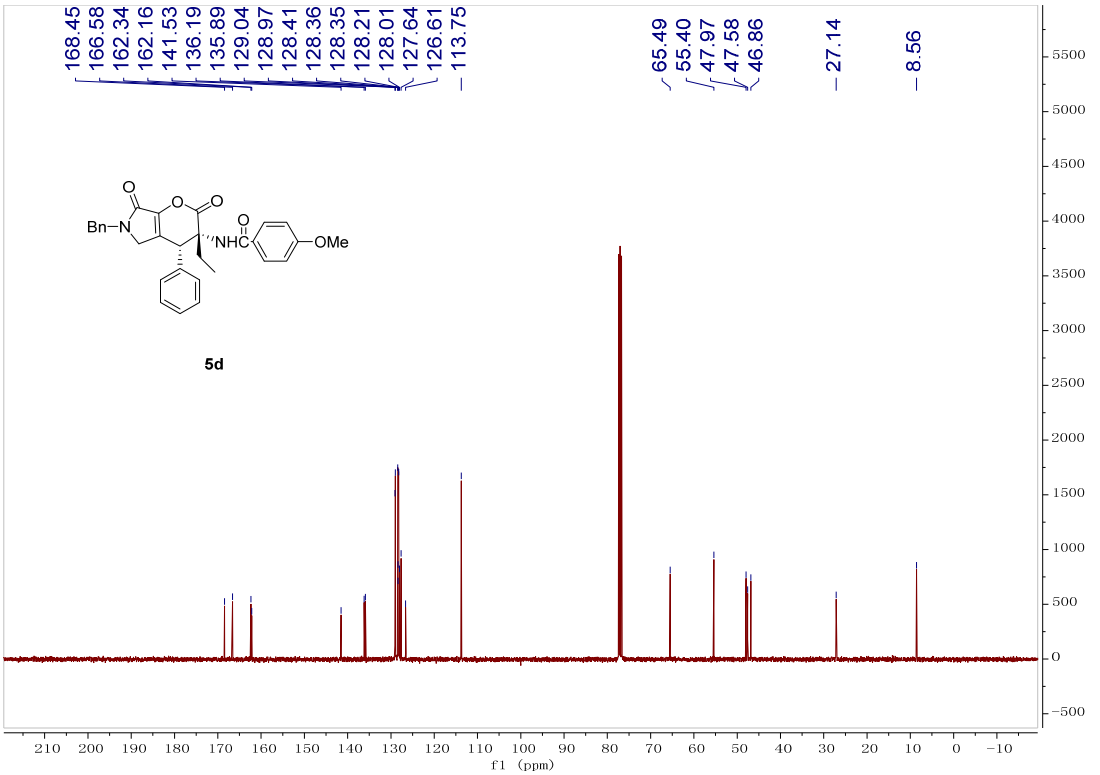
5c:N-((3*R*,4*R*)-6-benzyl-3-(3-bromobenzyl)-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexa-hydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



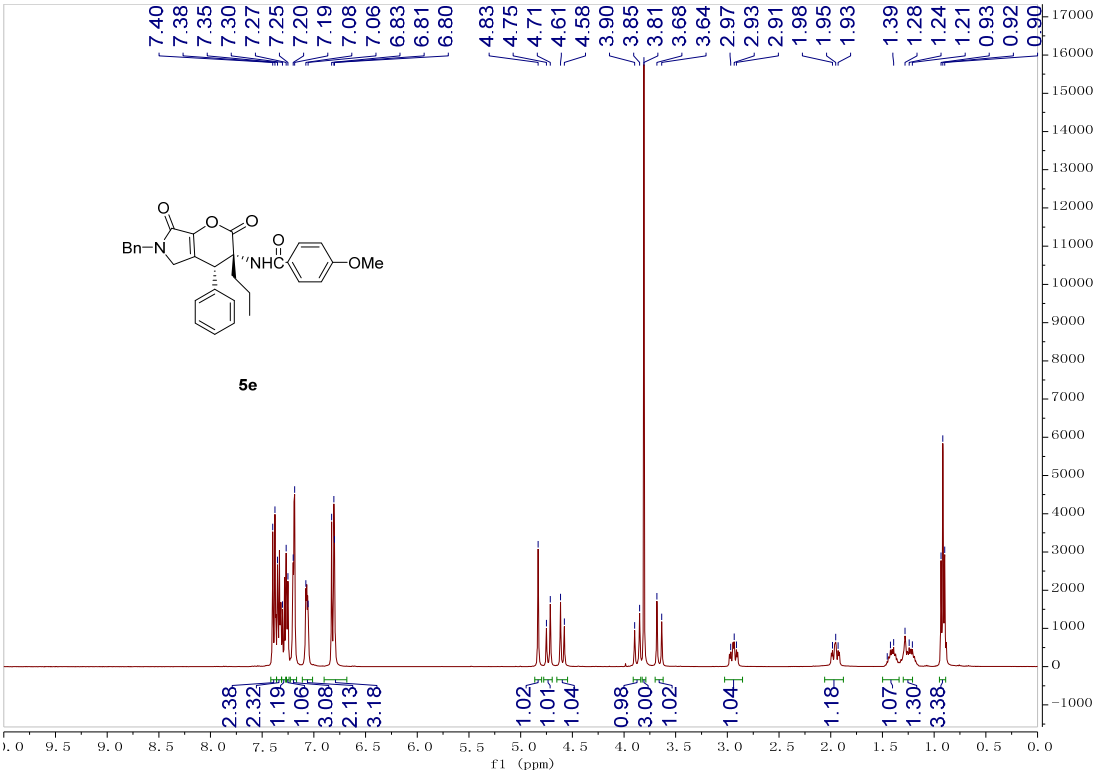


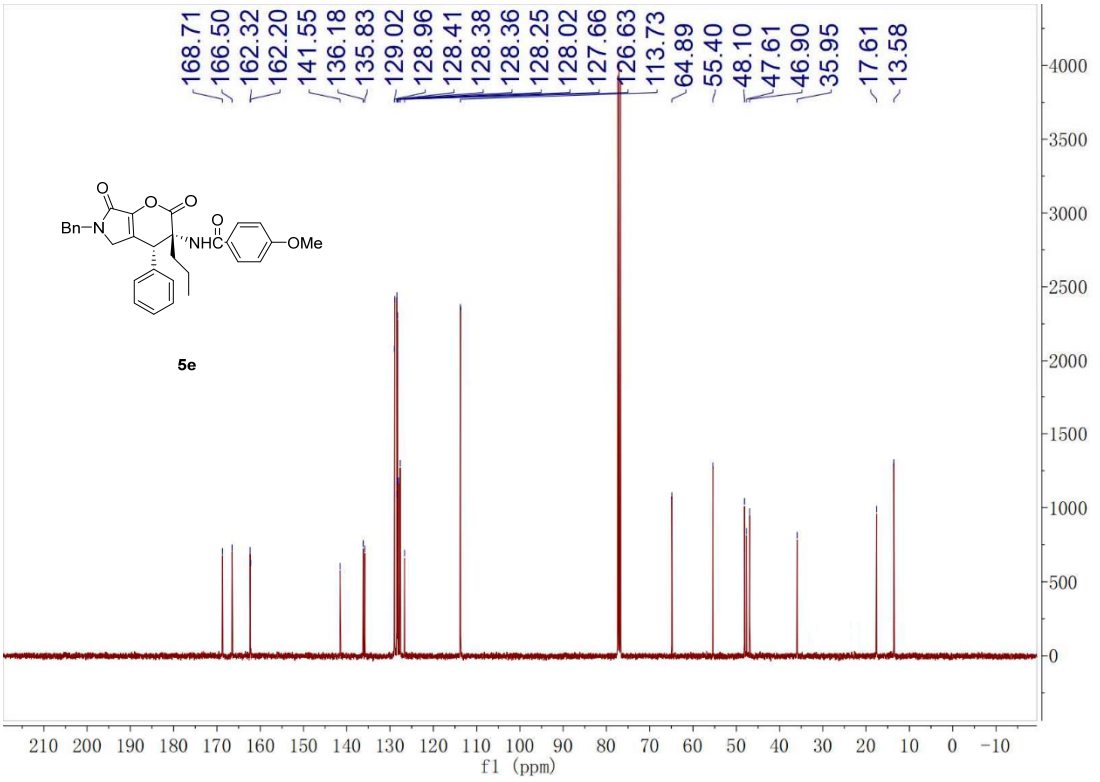
5d:N-((3*R*,4*R*)-6-benzyl-3-ethyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropy-rano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



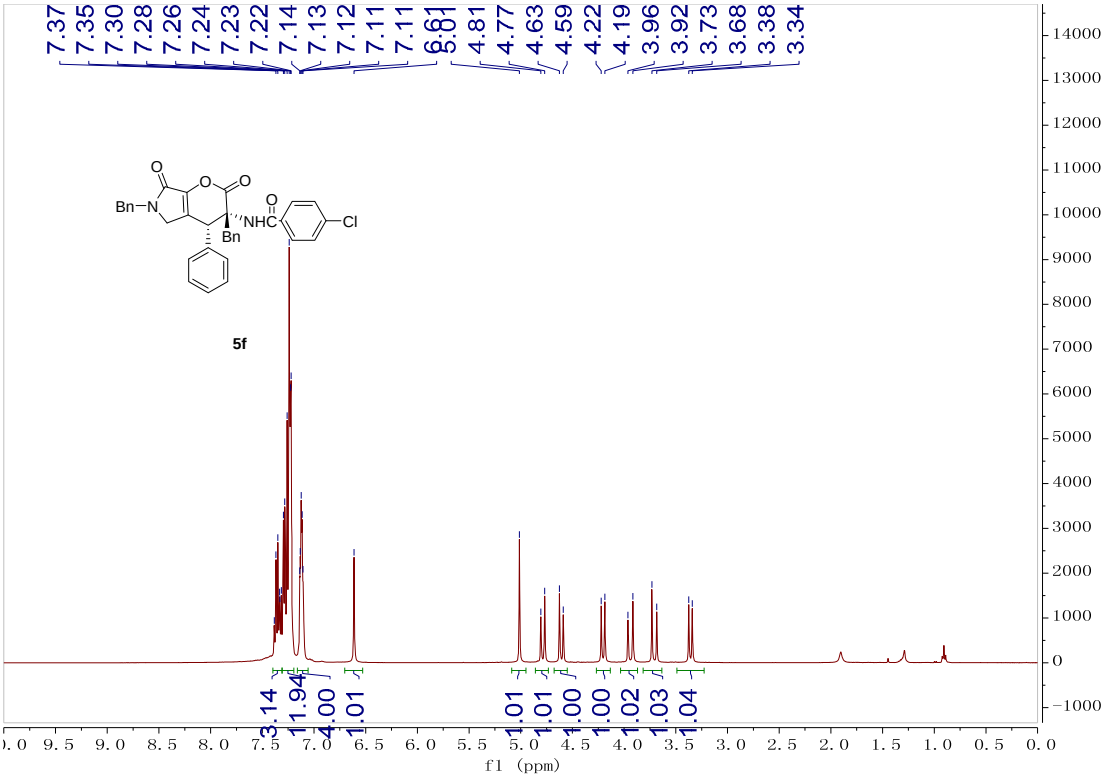


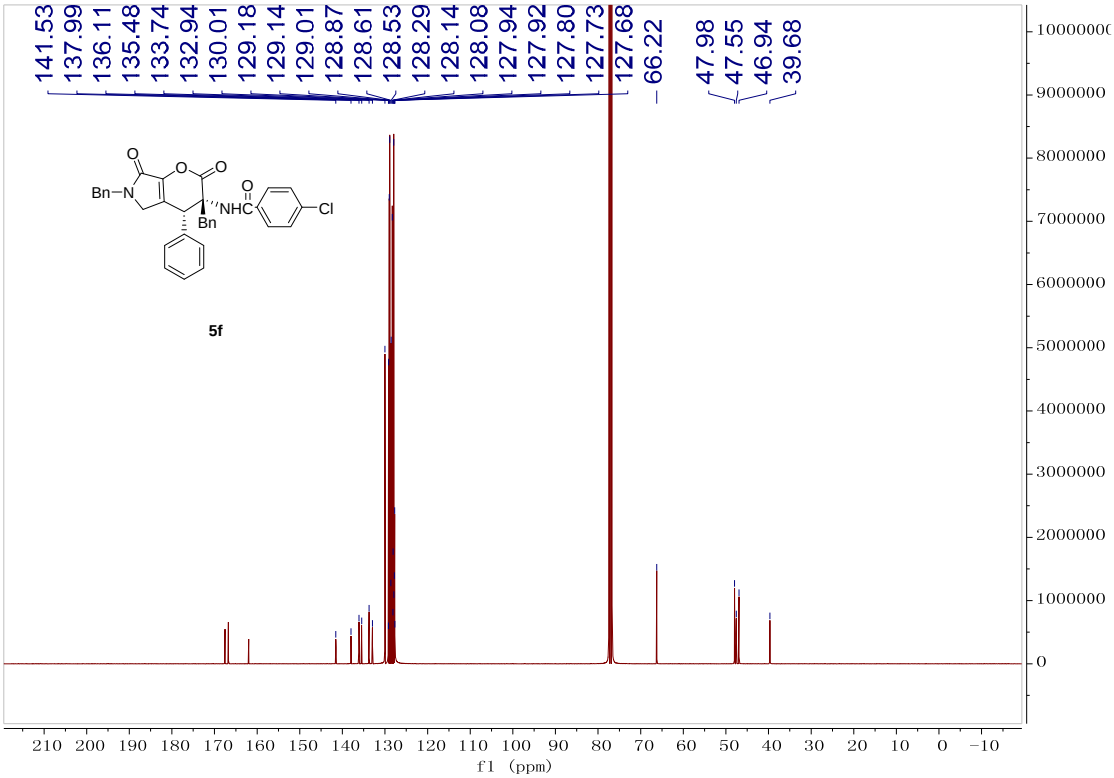
5e:N-((3*R*,4*R*)-6-benzyl-2,7-dioxo-4-phenyl-3-propyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-4-methoxybenzamide



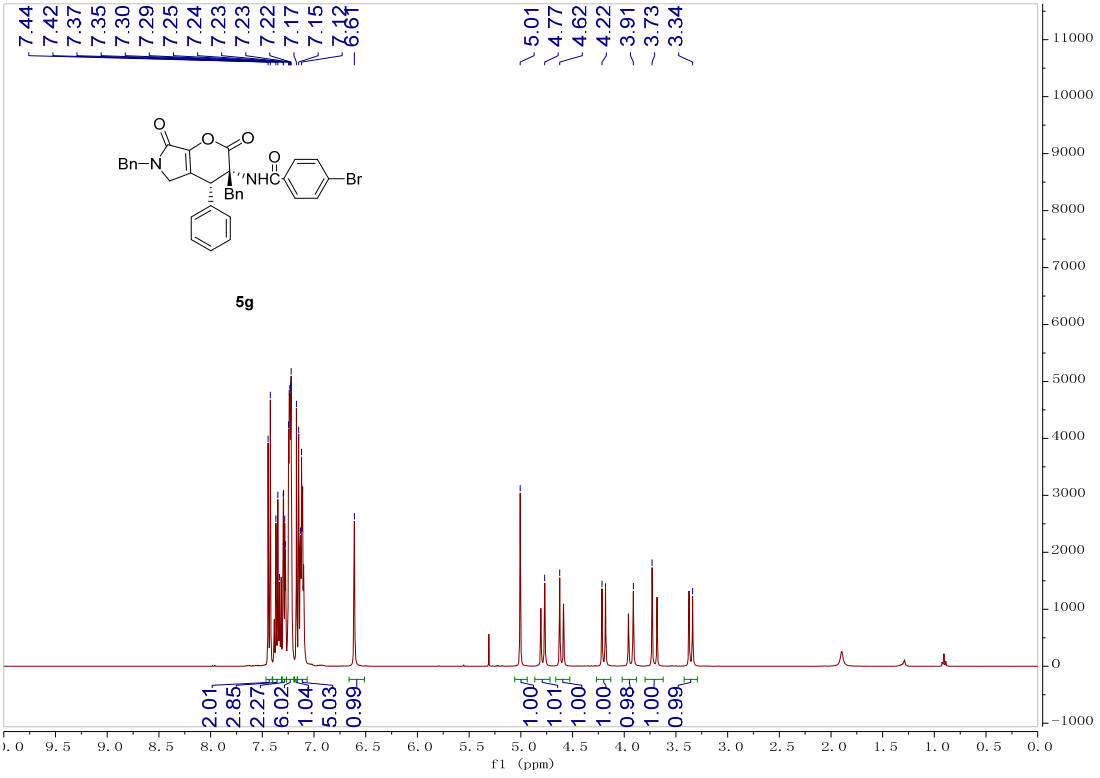


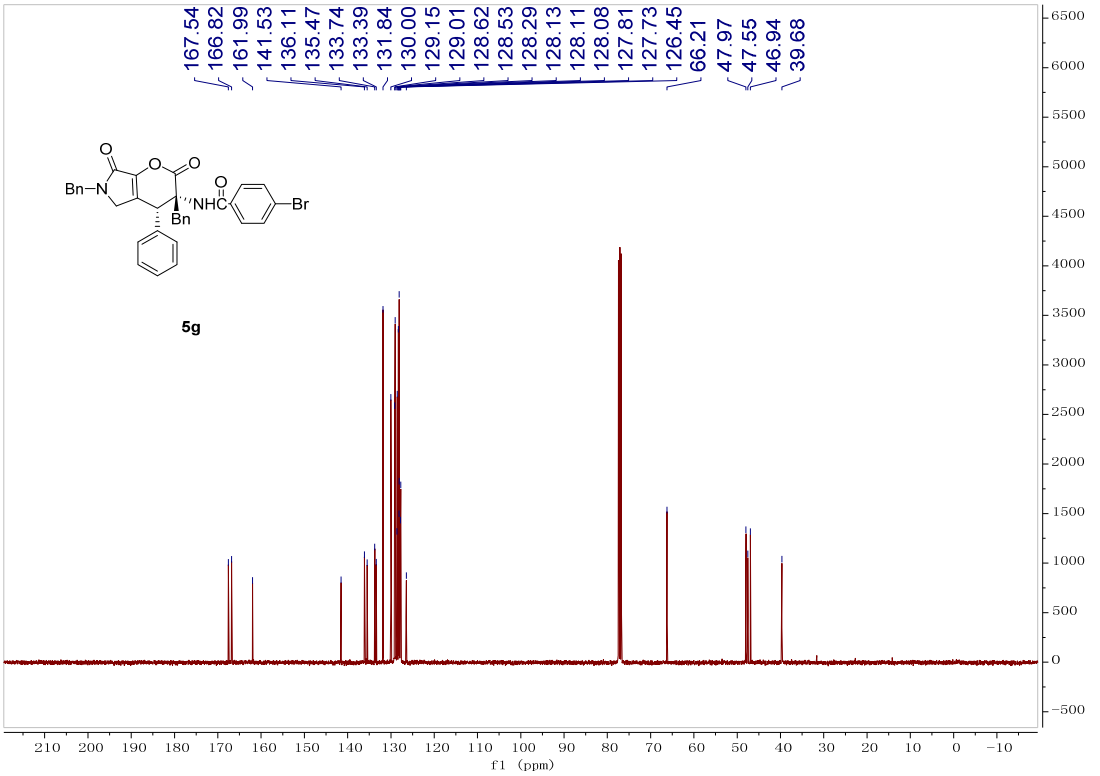
5f:4-chloro-N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropy-rano[2,3-c]pyrrol-3-yl)benzamide





5g:4-bromo-N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)benzamide





5h: N-((3*R*,4*R*)-3,6-dibenzyl-2,7-dioxo-4-phenyl-2,3,4,5,6,7-hexahydropyrano[2,3-c]pyrrol-3-yl)-[1,1'-biphenyl]-4-carboxamide