Supporting Information

Efficient Enantioselective Synthesis of Trisubstituted γ-Lactam Via Michael Addition Reaction of 2,3-dioxopyrrolidine with Indole in Aqueous Media.

John Kamanda Mansaray, Yekai Huang, Kuiliang Li, Xiang Sun, Zhenggen Zha, and Zhiyong Wang*

Hefei National Research Center for Physical Sciences at Microscale, CAS Key Laboratory of Soft Matter Chemistry & Center for Excellence in Molecular Synthesis of Chinese Academy of Sciences, Technology & School of Chemistry and Materials Science in University of Science and Technology of China Hefei, Anhui 230026, P. R. China.
*E-mail: zwang3@ustc.edu.cn

Table of contents

Part 1 Experiment Section

1.1 General Information

^{1}H NMR and ^{13}C NMR were recorded on a 400 MHz Nuclear Magnetic Resonance Spectrometer (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz) using TMS as internal reference. The chemical shifts (δ) and coupling constants (J) were expressed in ppm and Hz, respectively. UV-Vis Spectrophotometry was carried out on infrared spectrometer. HPLC analysis was carried out on HPLC with a multiple wavelength detector by commercial chiral columns. Optical rotations were measured on a Polarimeter. HRMS (ESI) were recorded on a Q-TOF Premier. Commercially available compounds were used without further purification. Solvents were purified according to the standard procedures unless otherwise noted. Ligands and various pyrrolidones were prepared according to literature procedures.

1.2 General procedures of Indole-Michael Addition Reaction

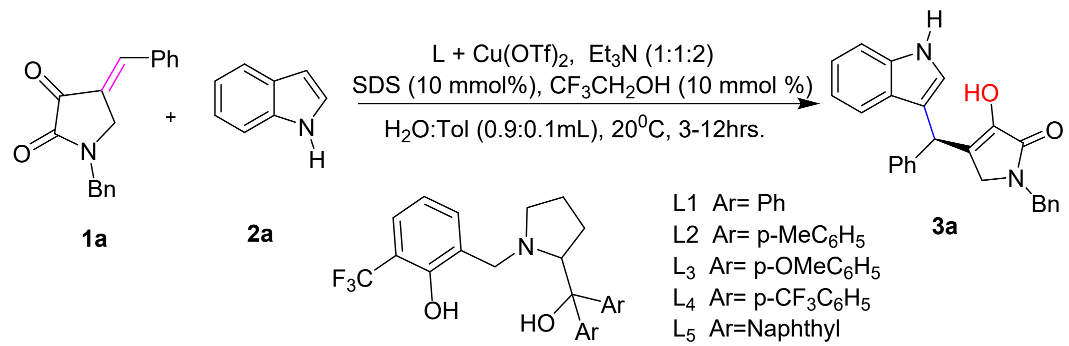
A mixture of Ligand (**L_1**, 10 mol %, 4.3 mg), $Cu(OTf)_2$ (10 mol %, 3.6 mg), Triethylamine (20 mol %, 2.8 μL) and SLS (10 mol %, 2.6 mg) and in corresponding solvent (H_2O/Toluene = 0.9/0.1 mL) was stirred for 2h at 20 °C. Then the corresponding pyrrolidone (0.1 mmol) and Indole (0.15 mmol) was added. After reaction was finished (monitored by TLC), the system was extracted by dichloromethane. The organic phase was dried with anhydrous sodium sulfate, evaporated in vacuo. Purification of the residue by column chromatography (DCM/MeOH = 100/1) afforded the desired Indole-Michael addition adducts. Finally, the product was further recrystallized in ethanol/ water (70/30).

1.3 Procedure for Asymmetric Indole-Michael Addition Reaction on a Gram-scale

A mixture of Ligand (**L_1**, 10 mol %, 215 mg), Cu $(OTf)_2$ (10 mol %, 180 mg), Triethylamine (20 mol %, 140 μL), and SLS (10 mol %, 130 mg) and in corresponding solvent (H_2O/Toluene = 18/2 mL) was stirred for 2h at 20 °C. Then the corresponding pyrrolidone (0.1 mmol) and Indole (0.15 mmol) was added. After reaction was finished (monitored by TLC), the system was extracted by dichloromethane. The organic phase was dried with anhydrous sodium sulfate, evaporated in vacuo. Purification of the residue by column chromatography (DCM/ MeOH = 100/1) afforded the desired Indole-Michael addition adducts.

1.4 Optimization of Reaction Conditions[a-h]

Table S1: Optimization of Reaction Conditions[a-h]



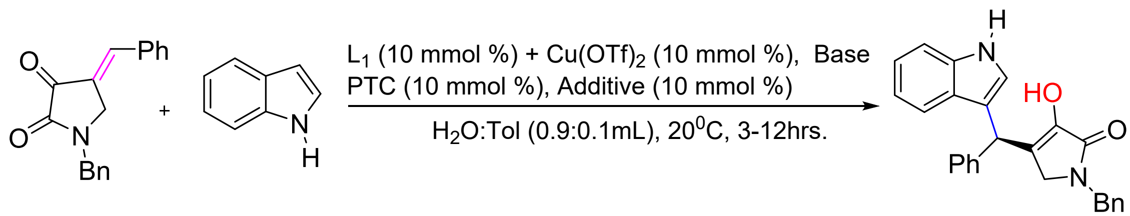
Entry	Ligand	Solvent (1mL)	Yield[b] (%)	ee[c] (%)
1	**L_1**	$CHCl_3$	89	84
2	**L_2**	$CHCl_3$	86	77
3	**L_3**	$CHCl_3$	84	79
4	**L_4**	$CHCl_3$	88	83
5	**L_5**	$CHCl_3$	82	73
6	**L_1**	iPrOH	87	80
7	**L_1**	Toulene	91	85
8	**L_1**	Acetone: MeOH	88	82
9	**L_1**	MTBE	85	83
10	**L_1**	H_20	78	89
11	**L_1**	H_2O/Tol (0.5/05)	83	94
12	**L_1**	H_2O/Tol (0.7/03)	81	93
13	**L_1**	H_2O/Tol (0.9/0.1)	83	94
14[d]	**L_1**	**H_2O/Tol (0.9/0.1)**	**86**	**99**
15[e]	**L_1**	H_2O/Tol (0.9/0.1)	76	41
16[f]	**L_1**	H_2O/Tol (0.9/0.1)	79	77
17[g]	**L_1**	H_2O/Tol (0.9/0.1)	80	96
18[h]	**L_1**	H_2O/Tol (0.9/0.1)	72	74

[a]Unless otherwise noted he reaction was performed with **1a** (0.1 mmol), **2a** (0.15 mmol), **L** (10 mol %), and $Cu(OTf)_2$ (10 mol %), Triethylamine 20 mol %, Sodium dodecyl sulfonate SDS as the surfactant 10 mol % . [b]Isolated yield. [c]Determined by chiral HPLC. [d]CF_3CH_2OH 10 mol% as additive. [e]Triethylamine 10 mol%. [f]Triethylamine 20 mol% [g]Taurdeoxycholate Sodium Salt TSS (10 mol %) as the surfactant and [h]Deoxycholic acid sodium Salt DSS (10 mol %) as the surfactant.

1.5 Optimization of Surfactants, Additives and Bases[a]

In order to study the effect of the surfactant in the reaction, the scope of the surfactant was expanded. Several surfactant (containing lipophilic ions and alkyl chain) were combined with $\mathbf{L_1}$ in an attempt to strengthen the binding ability to form an emulsion to catalyze this asymmetric reaction in water. Various surfacant employed affords a good yield and excellent enantio excess. It was found that SDS was the best in this reaction, which could enhance the reaction yield to 86% and an excellent enantioselectivity 99% ee. Furthermore, the reaction was conducted without a surfactant (Table 2, entry 10) we observed a decrease in the rate of the reaction (24h instead of 3-12h) with similar enantio excess. Hence the addition of the surfacant enhanced the reaction rate however, with no significance influence on the yield and enantiomeric excess.

Table S2: Optimization of Surfactants, Additives and Bases[a]

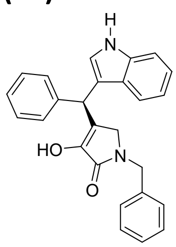


Entry	PTC	Additive	Base	Yield (%)[b]	ee(%)[c]
1	SDS	CF_3CH_2OH	Et_3N	86	99
2	SDS	HFIP	Et_3N	85	92
3	SDS	MeOH	Et_3N	83	98
4	TSS	CF_3CH_2OH	Et_3N	80	96
5	DSS	CF_3CH_2OH	Et_3N	72	74
7	SHS	CF_3CH_2OH	Et_3N	82	96
8	BU_4NI	CF_3CH_2OH	Et_3N	71	99
9	NH_4PF_6	CF_3CH_2OH	Et_3N	63	95
10	-	CF_3CH_2OH	Et_3N	78	96
10	SDS	CF_3CH_2OH	DIPEA	81	98
11	SDS	CF_3CH_2OH	DABCO	79	84
12	SDS	CF_3CH_2OH	N-Morpholine	83	85
13	SDS	CF_3CH_2OH	Piperidine	86	91
14	SDS	CF_3CH_2OH	$CsCO_3$	83	91
15	SDS	CF_3CH_2OH	t-BuOK	82	96

[a]Unless otherwise noted the reaction was performed with **1a** (0.1 mmol), **2a** (0.15 mmol), $\mathbf{L_1}$ (10 mol %), and $Cu(OTf)_2$ (10 mol %). [b]Isolated yield. [c]Determined by chiral HPLC. PTC= Sodium dodecyl sulfonate SDS (10 mol %), Taurdeoxycholate Sodium Salt TSS (10 mol %), Deoxycholic acid sodium Salt DSS (10 mol %), Sodium hexadecane-1-sulfonate SHS (10 mol %), Tetrabutylammonium iodide BU_4NI (10 mol %), Ammonium hexafluorophosphate NH_4PF_6 (10 mol %).

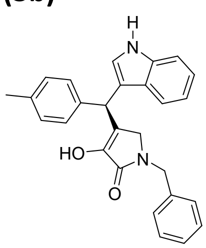
Part 2: The Analytical Data of Products

(S)-4-((1H-indol-3-yl)(phenyl)methyl)-1-benzyl-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3a)



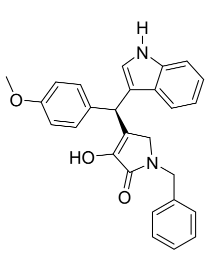
The title compound was prepared according to the general working procedure (6h) and purified by column chromatography (DCM/MeOH = 100/1) to give the product as a white solid 33.9 mg, 86% yield; mp = 193-197 °C; $[\alpha]_D^{20}$ +19.0 (c = 1.0, CH_2Cl_2, 99% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =6.58 min (major), t_R =12.3min (minor); ^{1}H NMR (500 MHz, DMSO) δ 10.92 (s, 1H), 9.53 (s, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.29 – 7.24 (m, 5H), 7.18 – 7.14 (m, 1H), 7.12 (d, *J* = 7.3 Hz, 2H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.96 (s, 1H), 6.87 (t, *J* = 7.4 Hz, 1H), 5.59 (s, 1H), 4.58 – 4.46 (m, 2H), 3.64 (d, *J* = 18.4 Hz, 1H), 3.57 (d, *J* = 18.4 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 166.9, 142.4, 142.1, 137.7, 136.5, 128.7, 128.4, 128.1, 127.3, 127.2, 126.5, 126.4, 123.4, 123.0, 121.18, 118.7, 118.5, 115.2, 111.6, 47.7, 45.5, 38.6. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{26}H_{22}N_2NaO_2$ 417.1573; found 417.1569.

(S)-4-((1H-indol-3-yl)(p-tolyl)methyl)-1-benzyl-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3b)



The title compound was prepared according to the general working procedure (6h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 33.1 mg, 81% yield; mp = 220-225 °C; $[\alpha]_D^{20}$ +5.0 (c = 0.33, CH_2Cl_2, 93% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =27.0 min (major), t_R = 14.6 min (minor); ^{1}H NMR (500 MHz, DMSO) δ 10.97 (s, 1H), 9.53 (s, 1H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.27 (d, *J* = 6.2 Hz, 2H), 7.22 (d, *J* = 6.2 Hz, 1H), 7.19 – 7.10 (m, 5H), 7.09 – 7.02 (m, 3H), 6.96 (s, 1H), 6.88 (d, *J* = 6.3 Hz, 1H), 5.58 (s, 1H), 4.51 (s, 2H), 3.60 (dd, *J* = 44.1, 18.3 Hz, 2H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 167.0, 141.9, 139.3, 137.8, 136.5, 135.3, 129.0, 128.6, 127.9, 127.3, 127.2, 126.5, 123.4, 123.3, 121.1, 118.7, 118.5, 115.3, 111.6, 47.7, 45.5, 38.2, 20.6. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{27}H_{24}N_2NaO_2$ 431.1730 found 431.1730.

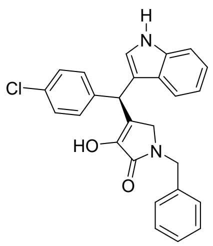
(S)-4-((1H-indol-3-yl)(4-methoxyphenyl)methyl)-1-benzyl-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3c)



The title compound was prepared according to the general working procedure (6h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 35.7 mg, 84% yield; mp =72-76 °C; $[\alpha]_D^{20}$ +22.7 (c = 1.0, CH_2Cl_2, 99% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =7.8 min (major), t_R =4.3 min (minor); ^{1}H NMR (500

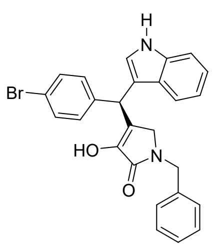
MHz, DMSO) δ 10.90 (s, 1H), 9.49 (s, 1H), 7.27 (ddd, *J* = 33.2, 15.0, 7.7 Hz, 3H), 7.18 – 7.08 (m, 6H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.93 (d, *J* = 1.5 Hz, 1H), 6.90 – 6.77 (m, 3H), 5.52 (s, 1H), 4.50 (s, 2H), 3.70 (s, 3H), 3.58 (dd, *J* = 44.3, 18.4 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 167.0, 157.7, 141.8, 137.8, 136.5, 134.3, 129.0, 128.6, 127.3, 127.2, 126.4, 123.4, 123.3, 121.1, 118.7, 118.4, 115.5, 113.7, 111.6, 47.7, 45.5, 37.8. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{27}H_{24}N_2NaO_3$ 447.1679 found 447.1675.

(S)-1-benzyl-4-((4-chlorophenyl)(1H-indol-3-yl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3d)



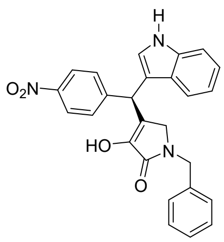
The title compound was prepared according to the general working procedure (6h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 34.7mg, 81% yield; mp =240-245 °C; $[\alpha]_D^{20}$ +63.6 (c = 1.0, CH_2Cl_2, 95% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =31.0min (major), t_R =15.4min (minor); ^{1}H NMR (500 MHz, DMSO) δ 11.03 (s, 1H), 9.60 (s, 1H), 7.28 (ddt, *J* = 20.0, 16.3, 8.6 Hz, 8H), 7.14 (dd, *J* = 11.2, 7.9 Hz, 3H), 7.08 – 7.00 (m, 1H), 6.98 (d, *J* = 1.8 Hz, 1H), 6.88 (t, *J* = 7.4 Hz, 1H), 5.59 (s, 1H), 4.54 (d, *J* = 17.9 Hz, 1H), 4.48 (d, *J* = 15.4 Hz, 1H), 3.60 (q, *J* = 18.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 142.3, 141.4, 137.7, 136.5, 130.8, 129.9, 128.6, 128.3, 127.2, 127.2, 126.2, 123.5, 122.3, 121.2, 118.6, 114.6, 111.6, 47.7, 45.5, 38.0. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{26}H_{21}ClN_2NaO_2$ 451.1184 found 451.1188.

(S)-1-benzyl-4-((4-bromophenyl)(1H-indol-3-yl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3e)



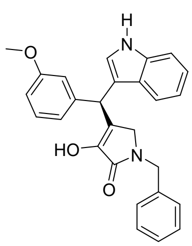
The title compound was prepared according to the general working procedure (6h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 39.6 mg, 84% yield; mp =222-227 °C; $[\alpha]_D^{20}$ +40.3 (c = 1.0, CH_2Cl_2, 96% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =29.7 min (major), t_R =12.4 min (minor); ^{1}H NMR (500 MHz, DMSO) δ 10.97 (s, 1H), 9.58 (s, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.38 – 7.09 (m, 9H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 1.7 Hz, 1H), 6.88 (t, *J* = 7.4 Hz, 1H), 5.55 (s, 1H), 4.51 (dd, *J* = 33.7, 15.5 Hz, 2H), 3.63 (d, *J* = 18.4 Hz, 1H), 3.57 (d, *J* = 18.5 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 167.3, 142.8, 142.3, 138.1, 137.0, 131.7, 131.4, 130.9, 130.7, 129.1, 128.3, 127.7, 127.7, 126.7, 124.0, 122.7, 121.7, 119.8, 119.0, 119.0, 115.0, 112.1, 48.2, 46.0, 38.5. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{26}H_{21}BrN_2NaO_2$ 495.0679 found 495.0683.

(S)-4-((1H-indol-3-yl)(4-nitrophenyl)methyl)-1-benzyl-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3f)



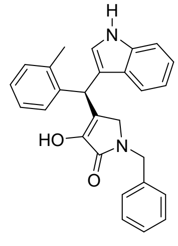
The title compound was prepared according to the general working procedure (8h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a yellow solid 37.8 mg, 86% yield; mp =110-115 °C; $[\alpha]_D^{20}$ +10.9 (c = 0.3, CH_2Cl_2, 99% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R = 26.6 min (major), t_R =13.4 min (minor); ^{1}H NMR (500 MHz, DMSO) δ 11.05 (s, 1H), 9.74 (s, 1H), 8.15 (d, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 8.6 Hz, 2H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.16 (dd, *J* = 19.7, 7.6 Hz, 3H), 7.06 (t, *J* = 7.3 Hz, 2H), 6.90 (t, *J* = 7.4 Hz, 1H), 5.71 (s, 1H), 4.53 (dd, *J* = 40.4, 15.3 Hz, 2H), 3.66 (q, *J* = 18.5 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 167.3, 151.0, 146.5, 143.4, 138.1, 137.0, 129.8, 129.1, 127.8, 127.7, 126.6, 124.3, 124.0, 121.8, 121.5, 119.2, 118.9, 114.4, 112.2, 48.4, 46.0, 39.1. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{26}H_{21}N_3NaO_4$ 462.1424 found 462.1420.

(S)-4-((1H-indol-3-yl)(3-methoxyphenyl)methyl)-1-benzyl-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3g)



The title compound was prepared according to the general working procedure (6h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 36 mg, 86% yield; mp =80-85 °C; $[\alpha]_D^{20}$ +5.4 (c = 1.0, CH_2Cl_2, 99% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R=22.8 min (major), t_R =29.2 min (minor); ^{1}H NMR (500 MHz, DMSO) δ 10.98 (s, 1H), 9.55 (s, 1H), 7.36 – 7.07 (m, 8H), 7.02 (dt, *J* = 7.4, 5.8 Hz, 1H), 6.96 (d, *J* = 1.8 Hz, 1H), 6.88 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 6.76 (dd, *J* = 10.6, 4.2 Hz, 2H), 5.56 (s, 1H), 4.56 – 4.45 (m, 2H), 3.67 (s, 3H), 3.59 (dd, *J* = 27.4, 12.1 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 167.30, 159.7, 144.4, 142.5, 138.2, 136.9, 129.8, 129.1, 127.7, 127.7, 126.9, 123.8, 123.3, 121.6, 120.8, 119.1, 118.9, 115.4, 114.5, 112.0, 111.8, 48.2, 45.9, 39.0. HRMS (ESI TOF) m/z: $[M+H]^+$ calcd for $C_{27}H_{24}N_2NaO_3$ 447.1679 found 447.1669.

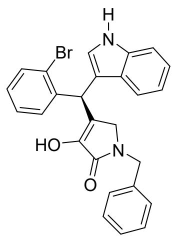
(S)-4-((1H-indol-3-yl)(o-tolyl)methyl)-1-benzyl-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3h)



The title compound was prepared according to the general working procedure (6h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 33.1 mg, 81% yield; mp =77-82°C; $[\alpha]_D^{20}$ +4.3 (c = 1.0, CH_2Cl_2, 90% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =32.2 min (major), t_R =17.4 min (minor); ^{1}H NMR (500 MHz, Acetone) δ 10.20 (s, 1H), 8.26 (s, 1H), 7.49 (d, *J* = 8.1 Hz, 1H), 7.40 (t, *J* = 7.3 Hz, 2H), 7.37 – 7.25 (m, 4H), 7.24 – 7.10 (m, 5H), 7.01 (t, *J* = 7.5 Hz, 2H), 5.94 (s, 1H), 4.69 (q, *J* = 15.2 Hz, 2H), 3.82 (d, *J* = 18.3 Hz, 1H), 3.59 (d, *J* = 18.3 Hz, 1H), 2.16 (dt, *J* =

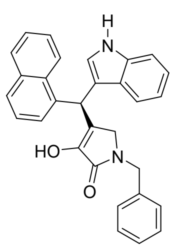
4.3, 2.2 Hz, 4H). ^{13}C NMR (126 MHz, DMSO) δ 167.4, 142.7, 141.0, 138.2, 137.0, 136.1, 130.7, 129.1, 127.9, 127.7, 126.9, 126.7, 126.3, 123.9, 122.6, 121.6, 119.0, 118.9, 115.5, 112.0, 48.3, 45.9, 35.4. HRMS (ESI TOF) m/z: $[M+H]^+$ calcd for $C_{27}H_{25}N_2O_2$ 409.1911 found 409.1906.

(S)-1-benzyl-4-((2-bromophenyl)(1H-indol-3-yl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one
(3i)



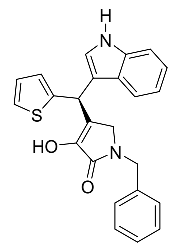
The title compound was prepared according to the general working procedure (6h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 40.0 mg, 85% yield; mp= 101-105°C; $[\alpha]_D^{20}$ +26.2 (c = 0.5, CH_2Cl_2, 99% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2- propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R = 27.4 min (major), t_R =16.2 min (minor); ^{1}H NMR (500 MHz, DMSO) δ 11.01 (s, 1H), 9.49 (s, 1H), 7.61 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.37 – 7.27 (m, 3H), 7.26 – 7.18 (m, 2H), 7.16 – 7.09 (m, 4H), 7.05 (dd, *J* = 15.6, 7.6 Hz, 2H), 6.93 – 6.84 (m, 2H), 5.80 (s, 1H), 4.58 – 4.46 (m, 2H), 3.68 (d, *J* = 18.5 Hz, 1H), 3.42 (s, 1H), 3.41 – 3.41 (m, 1H). ^{13}C NMR (126 MHz, DMSO) δ 167.4, 143.2, 141.7, 138.1, 137.0, 133.1, 130.5, 129.1, 129.0, 128.1, 127.6, 126.6, 124.3, 124.2, 121.7, 121.2, 119.1, 118.8, 114.7, 112.1, 48.6, 46.0, 39.1. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{26}H_{21}BrN_2NaO_2$ 495.0679 found 495.0698.

(S)-4-((1H-indol-3-yl)(naphthalen-1-yl)methyl)-1-benzyl-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3j)



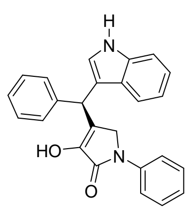
The title compound was prepared according to the general working procedure (6 h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 37.3 mg, 84% yield; mp =232-237 °C; $[\alpha]_D^{20}$ +6.3 (c = 1.0, CH_2Cl_2, 93% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =34.6 min (major), t_R = 8.05 min (minor); ^{1}H NMR (500 MHz, DMSO) δ 10.96 (s, 1H), 9.57 (s, 1H), 7.82 (ddd, *J* = 40.0, 22.9, 18.2 Hz, 4H), 7.44 (ddd, *J* = 9.8, 9.1, 3.7 Hz, 3H), 7.28 (ddd, *J* = 34.4, 22.5, 7.8 Hz, 4H), 7.15 (dd, *J* = 21.4, 7.6 Hz, 3H), 7.09 – 6.98 (m, 2H), 6.86 (t, *J* = 7.5 Hz, 1H), 5.77 (s, 1H), 4.52 (q, *J* = 15.3 Hz, 2H), 3.67 (dd, *J* = 37.7, 18.5 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 167.4, 142.7, 140.5, 138.2, 137.0, 133.5, 132.3, 129.1, 128.3, 128.1, 127.9, 127.7, 127.4, 126.9, 126.5, 126.3, 126.0, 124.0, 123.2, 121.6, 119.1, 119.0, 115.4, 112.1, 48.3, 46.0, 39.2. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{30}H_{24}N_2NaO_2$ 467.1730 found 467.1733.

(S)-4-((1H-indol-3-yl)(thiophen-2-yl)methyl)-1-benzyl-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3k)



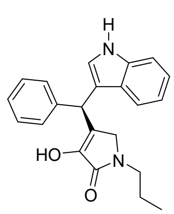
The title compound was prepared according to the general working procedure (6 h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 31.3mg, 81% yield; mp =98-103 °C; $[\alpha]_D^{20}$ +27.0 (c = 1.0, CH_2Cl_2, 69% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2- propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =29.3 min (major), t_R =15.1 min (minor); ^{1}H NMR (500 MHz, DMSO) δ 11.04 (s, 1H), 9.75 (s, 1H), 7.35 (dd, *J* = 10.6, 6.6 Hz, 3H), 7.29 (dd, *J* = 12.5, 7.5 Hz, 3H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.14 – 7.04 (m, 4H), 6.94 (dd, *J* = 11.6, 5.9 Hz, 2H), 6.88 (d, *J* = 2.9 Hz, 1H), 5.92 (s, 1H), 4.55 (d, *J* = 15.3 Hz, 1H), 4.46 (d, *J* = 15.3 Hz, 1H), 3.72 (d, *J* = 18.3 Hz, 1H), 3.53 (d, *J* = 18.3 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 167.1, 146.4, 142.4, 138.1, 136.77, 129.1, 127.7, 127.7, 127.3, 126.6, 125.5, 124.8, 123.7, 123.0, 121.7, 119.1, 118.9, 115.5, 112.1, 47.5, 45.9, 33.99. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{24}H_{20}N_2NaO_2S$ 423.1138 found 423.1143.

(S)-4-((1H-indol-3-yl)(phenyl)methyl)-3-hydroxy-1-propyl-1,5-dihydro-2H-pyrrol-2-one (3l)



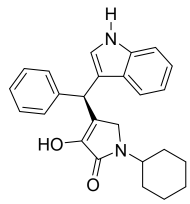
The title compound was prepared according to the general working procedure (6h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 32.7mg, 86% yield; mp =200-205°C; $[\alpha]_D^{20}$ +3.3 (c = 0.5, CH_2Cl_2, 91% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2- propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R = 6.4 min (major), t_R =11.0 min (minor); ^{1}H NMR (500 MHz, DMSO) δ 10.99 (s, 1H), 9.65 (s, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 7.4 Hz, 3H), 7.32 (td, *J* = 7.8, 3.2 Hz, 4H), 7.23 (t, *J* = 7.3 Hz, 2H), 7.17 (d, *J* = 1.8 Hz, 1H), 7.06 (dd, *J* = 11.6, 7.4 Hz, 2H), 6.90 (t, *J* = 7.5 Hz, 1H), 5.66 (s, 1H), 4.27 (d, *J* = 17.8 Hz, 1H), 4.16 (d, *J* = 17.8 Hz, 1H).^{13}C NMR (126 MHz, DMSO) δ 166.3, 142.7, 142.6, 139.8, 136.9, 129.4, 128.9, 128.6, 127.0, 126.9, 124.2, 123.9, 123.7, 121.6, 119.0, 119.0, 118.4, 115.1, 112.0, 48.7, 39.1. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{25}H_{20}N_2NaO_2$ 403.1417 found 403.1415.

(S)-4-((1H-indol-3-yl)(phenyl)methyl)-3-hydroxy-1-propyl-1,5-dihydro-2H-pyrrol-2-one (3m)



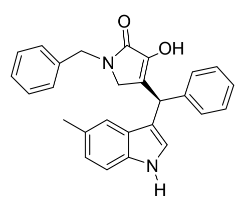
The title compound was prepared according to the general working procedure (6h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 27.0 mg, 78% yield; mp= 92-97°C; $[\alpha]_D^{20}$ +5.3 (c = 1.0, CH_2Cl_2, 99% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =4.85 min (major), t_R = 5.65 min (minor); ^{1}H NMR (500 MHz, DMSO) δ 10.99 (s, 1H), 9.36 (s, 1H), 7.31 (dt, *J* = 14.8, 8.1 Hz, 5H), 7.19 (dd, *J* = 23.9, 7.3 Hz, 2H), 7.07 – 6.98 (m, 2H), 6.87 (t, *J* = 7.4 Hz, 1H), 5.57 (s, 1H), 3.66 (dd, *J* = 40.8, 18.5 Hz, 2H), 3.23 (t, *J* = 7.2 Hz, 2H), 1.43 (dd, *J* = 14.5, 7.3 Hz, 2H), 0.75 (t, *J* = 7.4 Hz, 3H). 13C NMR (126 MHz, DMSO) δ 167.1, 143.0, 142.6, 136.9, 128.8, 128.5, 126.9, 126.7, 123.9, 122.7, 121.6, 119.1, 118.9, 115.7, 112.0, 48.3, 43.9, 39.0, 21.6, 11.6. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{22}H_{22}N_2NaO_2$ 369.1573 found 369.1579.

(S)-4-((1H-indol-3-yl)(phenyl)methyl)-1-cyclohexyl-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3n)



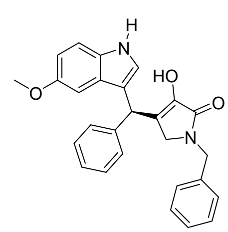
The title compound was prepared according to the general working procedure (6h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 31.3mg, 81% yield; mp =238-243 °C; $[\alpha]_D^{20}$ +4.3 (c = 1.0, CH_2Cl_2, 91% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =6.4 min (major), t_R =11.0 min (minor); ^1H NMR (500 MHz, DMSO) δ 10.98 (s, 1H), 9.34 (s, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.32 – 7.24 (m, 4H), 7.20 (ddd, *J* = 17.5, 10.0, 5.4 Hz, 2H), 7.03 (dd, *J* = 14.9, 4.5 Hz, 2H), 6.88 (t, *J* = 7.4 Hz, 1H), 5.56 (s, 1H), 3.65 (dd, *J* = 43.8, 18.4 Hz, 2H), 1.69 (d, *J* = 11.5 Hz, 2H), 1.57 (t, *J* = 15.7 Hz, 3H), 1.36 – 1.20 (m, 5H). 13C NMR (126 MHz, DMSO) δ 166.5, 143.1, 142.6, 136.9, 128.8, 128.5, 126.9, 126.7, 123.9, 122.8, 121.5, 119.1, 118.9, 115.6, 112.0, 44.7, 39.0, 30.9, 25.6, 25.3. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{25}H_{26}N_2NaO_2$ 409.1886 found 409.1877.

(S)-1-benzyl-3-hydroxy-4-((5-methyl-1H-indol-3-yl)(phenyl)methyl)-1,5-dihydro-2H-pyrrol-2-one (3o).



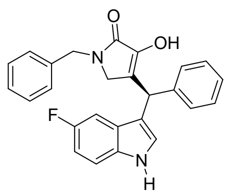
The title compound was prepared according to the general working procedure (12h) and purified by column chromatography (DCM/MeOH=100/1) to give the product as a white solid 33.0 mg, 81% yield; mp=182-187 °C; $[\alpha]_D^{20}$ +27.7 (c = 0.3, CH_2Cl_2, 87% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2- propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =23.6 min (major), t_R =17.0min (minor); ^1H NMR (500 MHz, DMSO) δ 10.74 (s, 1H), 9.50 (s, 1H), 7.31 – 7.17 (m, 10H), 7.14 – 7.09 (m, 3H), 7.00 (d, *J* = 8.1 Hz, 1H), 6.85 (d, *J* = 1.7 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 5.55 (s, 1H), 4.60 – 4.45 (m, 2H), 3.59 (q, *J* = 18.4 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 167.3, 142.9, 142.5, 138.2, 137.4, 130.6, 129.1, 128.8, 128.5, 127.7, 127.7, 126.7, 124.8, 123.5, 123.2, 120.7, 118.8, 115.4, 111.8, 48.1, 45.9, 39.1, 21.8. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{27}H_{25}N_2O_2$ 409.1911 found 409.1911.

(S)-1-benzyl-3-hydroxy-4-((5-methoxy-1H-indol-3-yl)(phenyl)methyl)-1,5-dihydro-2H-pyrrol-2-one (3p).



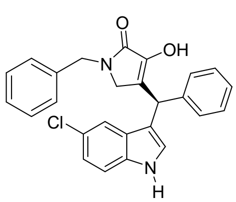
The title compound was prepared according to the general working procedure (6h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 35.6 mg, 84 % yield; mp =93-98°C; $[\alpha]_D^{20}$ +4.5 (c = 1.0, CH_2Cl_2, 99% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =5.0 min (major), t_R =6.3 min (minor). ^{1}H NMR (500 MHz, DMSO) δ 10.76 (d, J = 1.8 Hz, 1H), 9.53 (s, 1H), 7.29 – 7.26 (m, 7H), 7.24 – 7.19 (m, 4H), 7.12 (d, J = 7.1 Hz, 3H), 6.90 (d, J = 2.0 Hz, 1H), 6.70 (dd, J = 8.7, 2.4 Hz, 1H), 6.62 (d, J = 2.3 Hz, 1H), 5.52 (s, 1H), 4.51 (q, J = 15.3 Hz, 2H), 3.61 (d, J = 8.3 Hz, 1H), 3.59 (s, 3H), 3.57 (d, J = 7.0 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 167.3, 161.2, 153.3, 152.6, 142.7, 142.5, 138.2, 132.1, 129.1, 128.8, 128.5, 128.0, 127.7, 127.7, 127.2, 126.8, 124.5, 123.4, 115.3, 112.7, 111.4, 101.0, 55.6, 48.1, 45.9, 39.0. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{27}H_{24}N_2NaO_3$ 447.1679 found 447.1684.

(S)-1-benzyl-4-((5-fluoro-1H-indol-3-yl)(phenyl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3q)



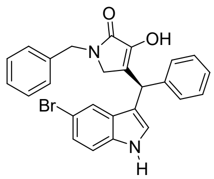
The title compound was prepared according to the general working procedure (10h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 35.4 mg, 86% yield; mp =224-229 °C; $[\alpha]_D^{20}$ +7.7 (c = 1.0, CH_2Cl_2, 81% ee); HPLC: Daicel Chiralpak AD-H, hexane:2- propanol = 60:40, flow rate = 1.0 mL/min, T=23°C, UV = 254 nm, t_R=3.9 min (major), t_R =6.5 min (minor). ^{1}H NMR (500 MHz, DMSO) δ 10.93 (s, 1H), 9.55 (s, 1H), 7.37 – 7.08 (m, 14H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.95 (s, 1H), 6.87 (t, *J* = 7.4 Hz, 1H), 5.58 (s, 1H), 4.50 (s, 2H), 3.60 (dd, *J* = 39.9, 18.4 Hz, 2H).27.69 (d, *J* = 5.8 Hz), 127.04 (d, *J* = 10.0 Hz), 113.04 (d, *J* = 9.8 Hz), 109.72 (d, *J* = 26.0 Hz), 103.62 (d, *J* = 23.2 Hz). ^{13}C NMR (126 MHz, DMSO) δ 167.3, 157.9, 156.1 (s, $^1J_{CF}$ =317 Hz) 142.6, 142.5 (d, $^3J_{CF}$ = 18.3 Hz), 138.2, 133.6, 129.1, 128.9, 128.5, 128.0, 127.7 (d, $^4J_{CF}$ = 5.8 Hz), 127.1, 127.0 (d, $^3J_{CF}$ = 10.0 Hz), 126.9, 126.0, 123.0, 115.8, 115.8, 113.1, 113.0 (d, $^4J_{CF}$ = 9.8 Hz), 109.8 (d, $^2J_{CF}$ = 26.0 Hz), 109.6, 103.7, 103.5, (d, $^2J_{CF}$ = 23.2 Hz). 48.1, 46.0, 39.0. ^{19}F NMR (471 MHz, DMSO) δ-125.1. HRMS (ESI TOF) m/z: $[M+H]^+$ calcd for $C_{26}H_{22}FN_2O_2$ 413.1660 found 413.1666.

(S)-1-benzyl-4-((5-chloro-1H-indol-3-yl)(phenyl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3r)



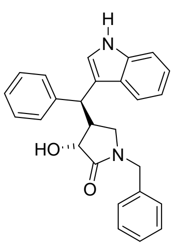
The title compound was prepared according to the general working procedure (10h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 34.2 mg, 80% yield; mp=215-220 °C; $[\alpha]_D^{20}$ +56.6 (c = 0.3, CH_2Cl_2, 87% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R = 17.3 min (major), t_R =14.4 min (minor). ^{1}H NMR (500 MHz, DMSO) δ 11.15 (s, 1H), 9.57 (s, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.34 – 7.18 (m, 10H), 7.18 – 7.09 (m, 2H), 7.05 (d, *J* = 7.1 Hz, 1H), 5.56 (s, 1H), 4.62 – 4.42 (m, 2H), 3.61 (dd, *J* = 41.9, 18.4 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 167.3, 142.7, 142.4, 138.1, 135.4, 129.1, 128.9, 128.7, 128.5, 128.1, 128.0, 127.7, 126.9, 125.7, 124.0, 122.9, 121.6, 118.2, 115.5, 113.6, 48.1, 46.0, 38.9. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{26}H_{21}ClN_2NaO_2$ 451.1184 found 451.1176.

(S)-1-benzyl-4-((5-bromo-1H-indol-3-yl)(phenyl)methyl)-3-hydroxy-1,5-dihydro-2H-pyrrol-2-one (3s)



The title compound was prepared according to the general working procedure (10h) and purified by column chromatography (DCM/MeOH= 100/1) to give the product as a white solid 31.3mg, 81% yield; mp =240-245 °C; $[\alpha]_D^{20}$ +6.7 (c = 0.3, CH_2Cl_2, 92% ee); HPLC: Daicel Chiralpak AD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =17.0 min (major), t_R =15.3 min (minor). ^{1}H NMR (500 MHz, DMSO) δ 11.16 (s, 1H), 9.57 (s, 1H), 7.35 – 7.20 (m, 10H), 7.18 – 7.11 (m, 3H), 7.04 (s, 1H), 5.55 (s, 1H), 4.58 – 4.46 (m, 2H), 3.60 (dd, *J* = 41.8, 18.4 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 167.3, 142.7, 142.4, 138.1, 135.6, 129.1, 128.9, 128.7, 128.5, 127.7, 126.9, 125.6, 124.1, 122.9, 121.2, 115.5, 114.1, 111.6, 48.1, 45.9, 38.9. HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{26}H_{21}BrN_2NaO_2$ 495.0679 found 495.0688.

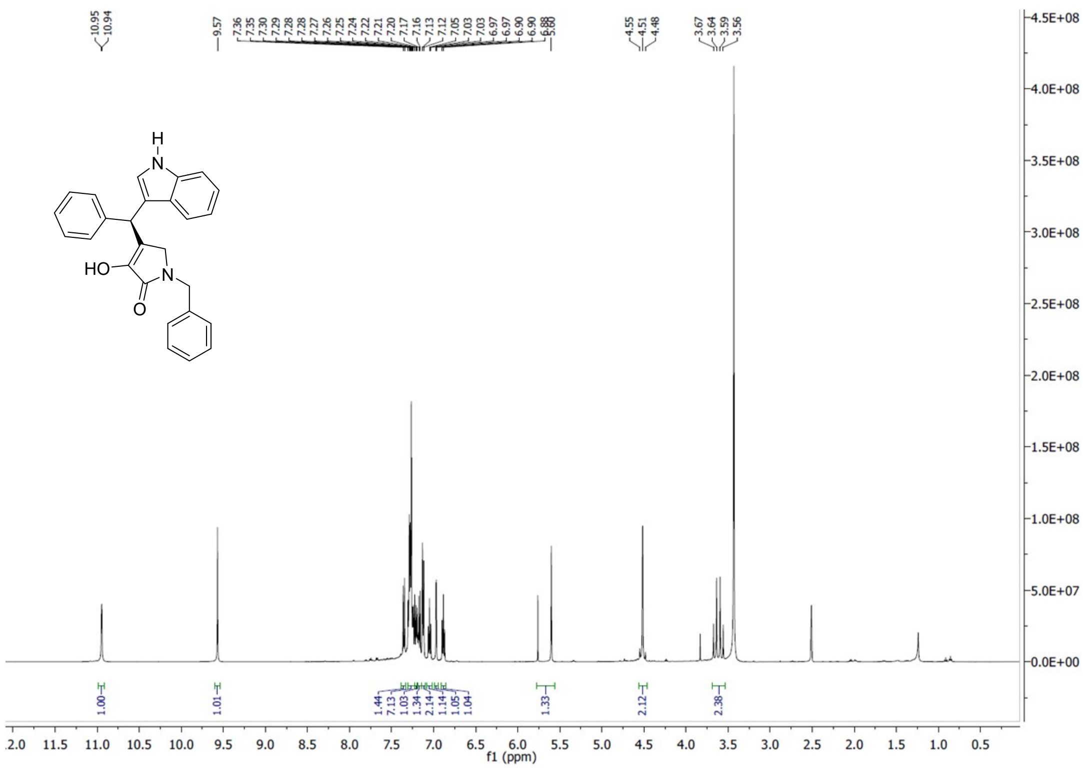
(3R,4R)-4-((S)-(1H-indol-3-yl)(phenyl)methyl)-1-benzyl-3-hydroxypyrrolidin-2-one (4a)

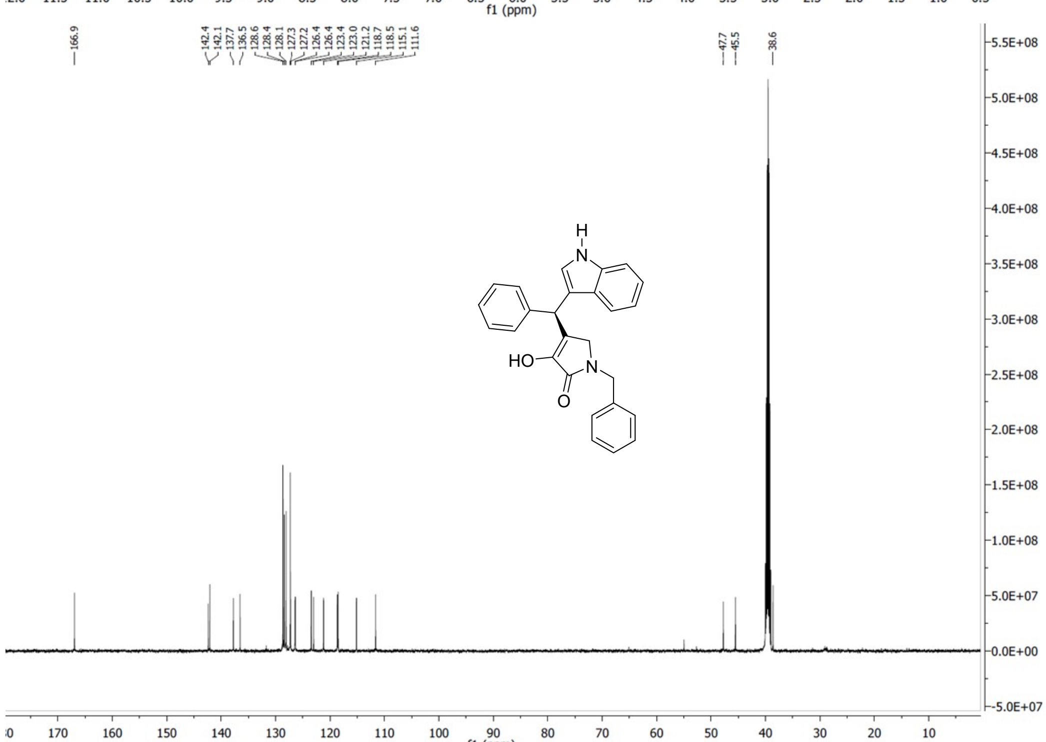


To a solution of pyrrolone **3a** (0.30 mmol) in DCM: CH_3COOH (10:1, v/v, 6 mL), sodium borohydride (0.6 mmol) was added portion wise with stirring at 0°C. After the addition, the reaction mixture was allowed to stir at room temperature for 1 h. Then, a saturated aqueous solution of $NaHCO_3$ (6 mL) was added and extracted with DCM (3x10 mL). The combined organic layer was washed with brine, dried over anhydrous MgSO4 and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate) to get pure pyrrolidinone **4a** as a white solid 79.6 mg, 67% yield; mp = 189-193 °C; $[\alpha]_D^{20}$ +11.7 (c = 1.0, CH_2Cl_2, 88% ee); HPLC: Daicel Chiralpak OD-H, hexane: 2-propanol = 60:40, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R =6.89 min (major), t_R =13.2 min (minor); ^{1}H NMR (500 MHz, DMSO) δ 10.94 (s, 1H), 9.55 (s, 1H), 7.37 – 7.22 (m, 10H), 7.22 – 7.18 (m, 1H), 7.13 (t, *J* = 9.0 Hz, 3H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 1.7 Hz, 1H), 6.87 (t, *J* = 7.4 Hz, 1H), 5.57 (s, 1H), 4.51 (s, 2H), 3.83 (s, 1H), 3.64 (d, *J* = 18.5 Hz, 1H), 3.56 (d, *J* = 18.5 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 167.3, 142.8, 142.5, 138.2, 136.9, 129.1, 128.8, 128.5, 127.7, 127.7, 126.9, 126.8, 123.8, 123.5, 121.6, 119.1, 118.9, 115.5, 112.0, 55.4, 48.1, 45.9, 39.0.HRMS (ESI TOF) m/z: $[M+Na]^+$ calcd for $C_{26}H_{24}N_2NaO_2$ 419.1730; found 417.1726.

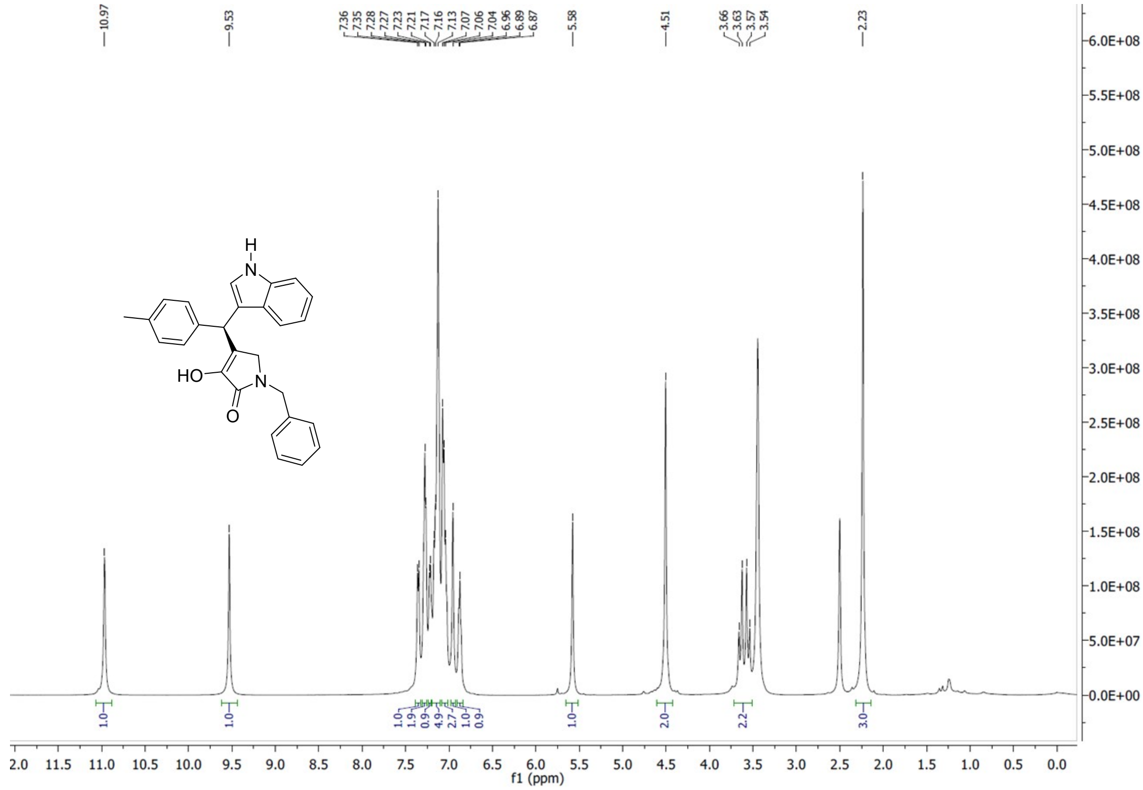
Part 3 : ^{1}H NMR, ^{19}F NMR & ^{13}C NMR

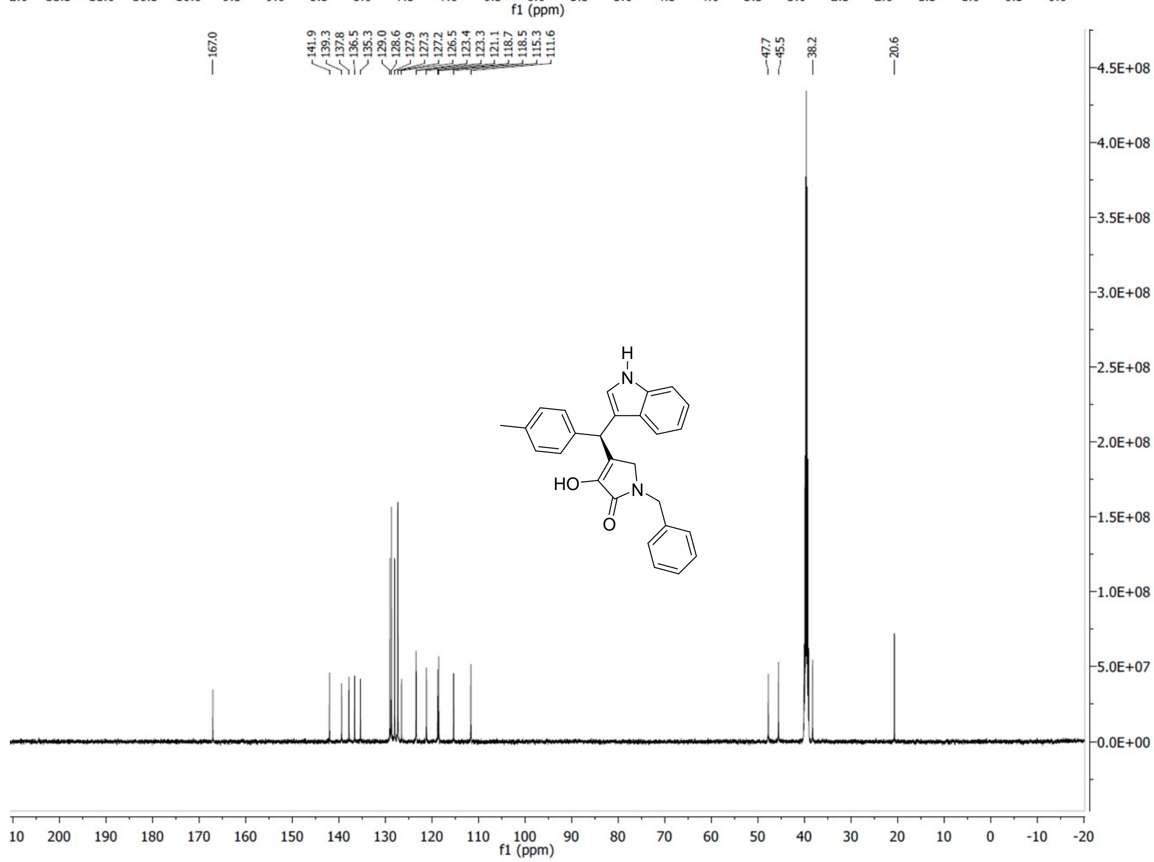
^{1}H NMR and ^{13}C NMR of **3a**



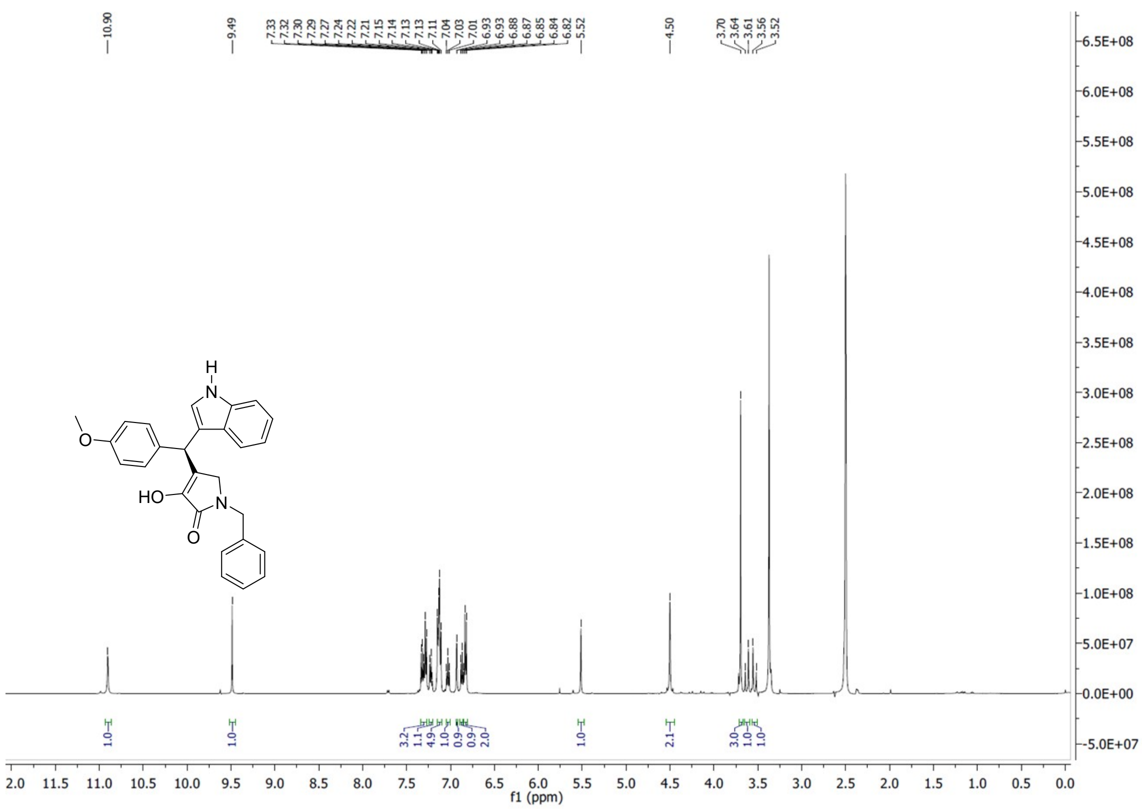


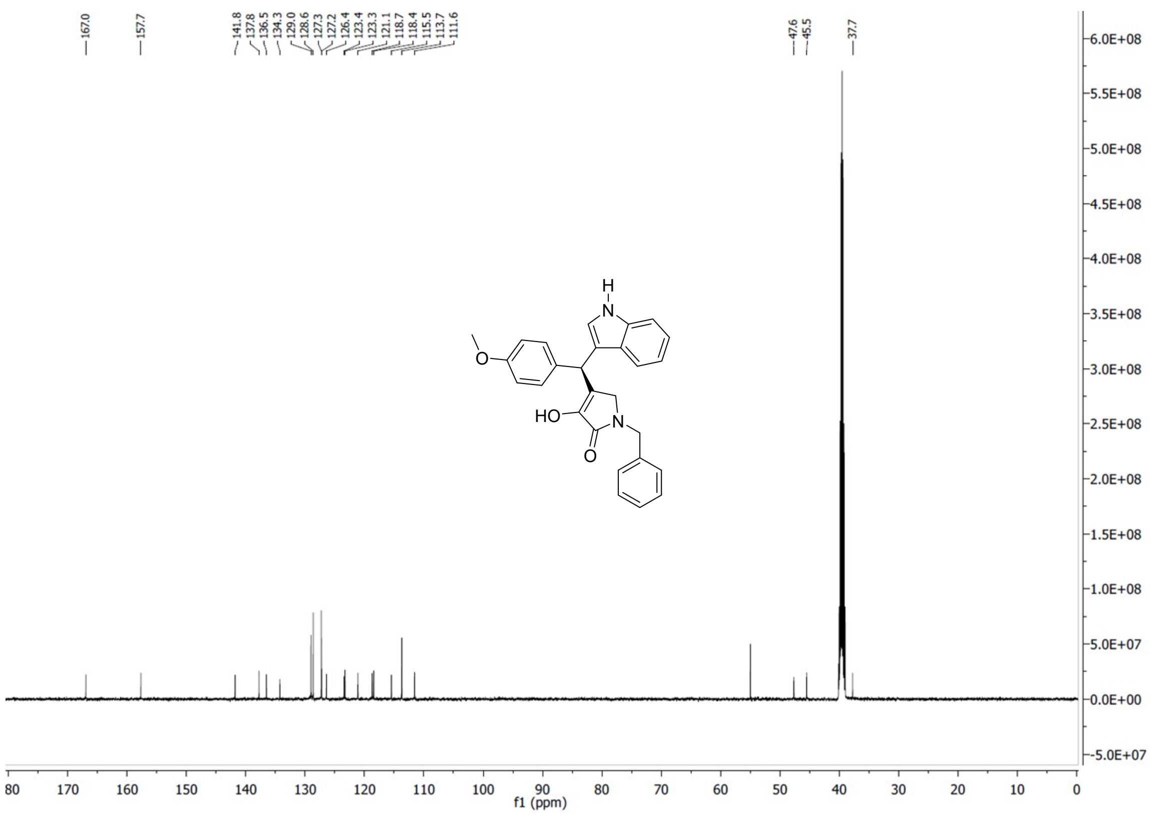
[1]H NMR and [13]C NMR of **3b**



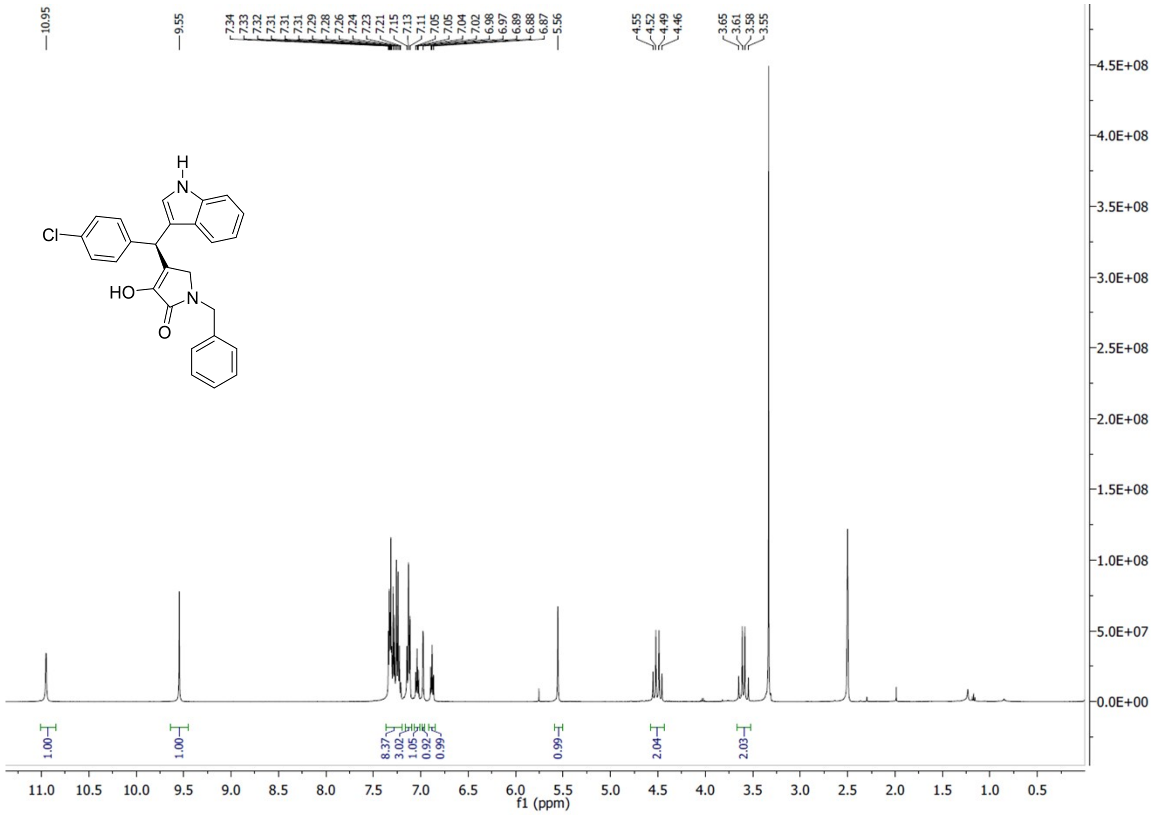


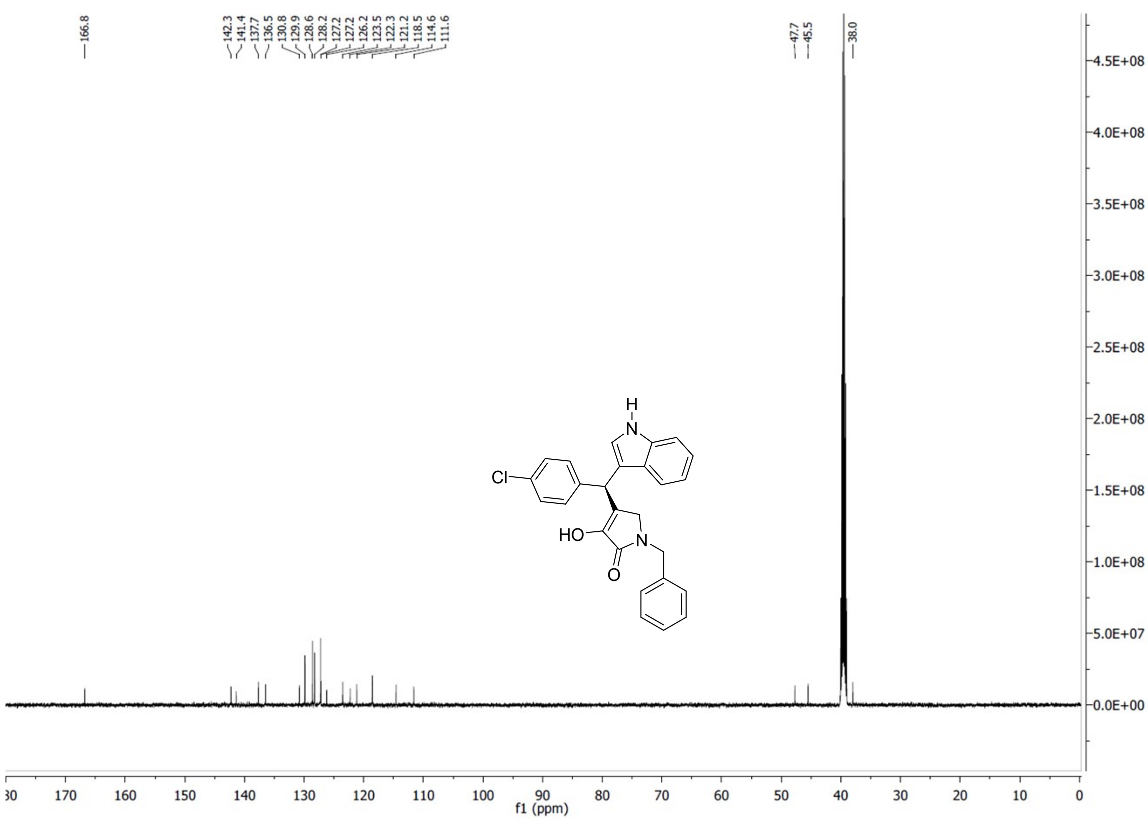
[1]H NMR and [13]C NMR of **3c**



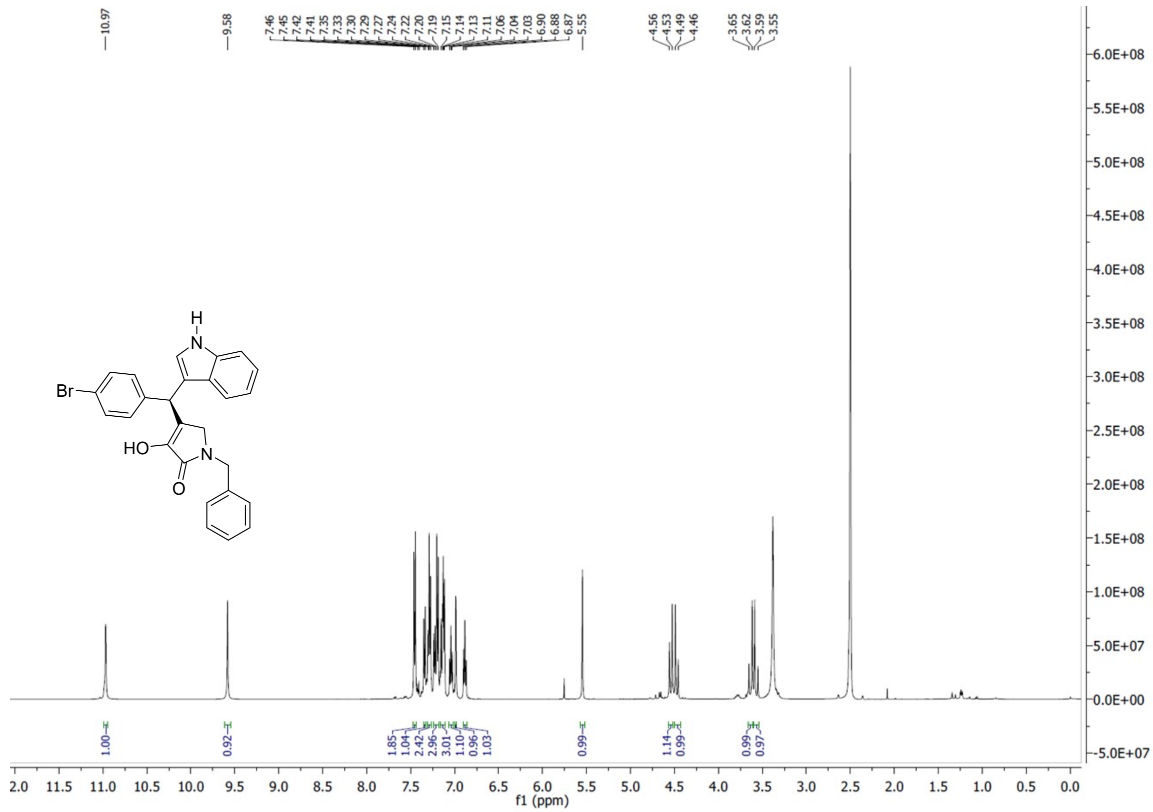


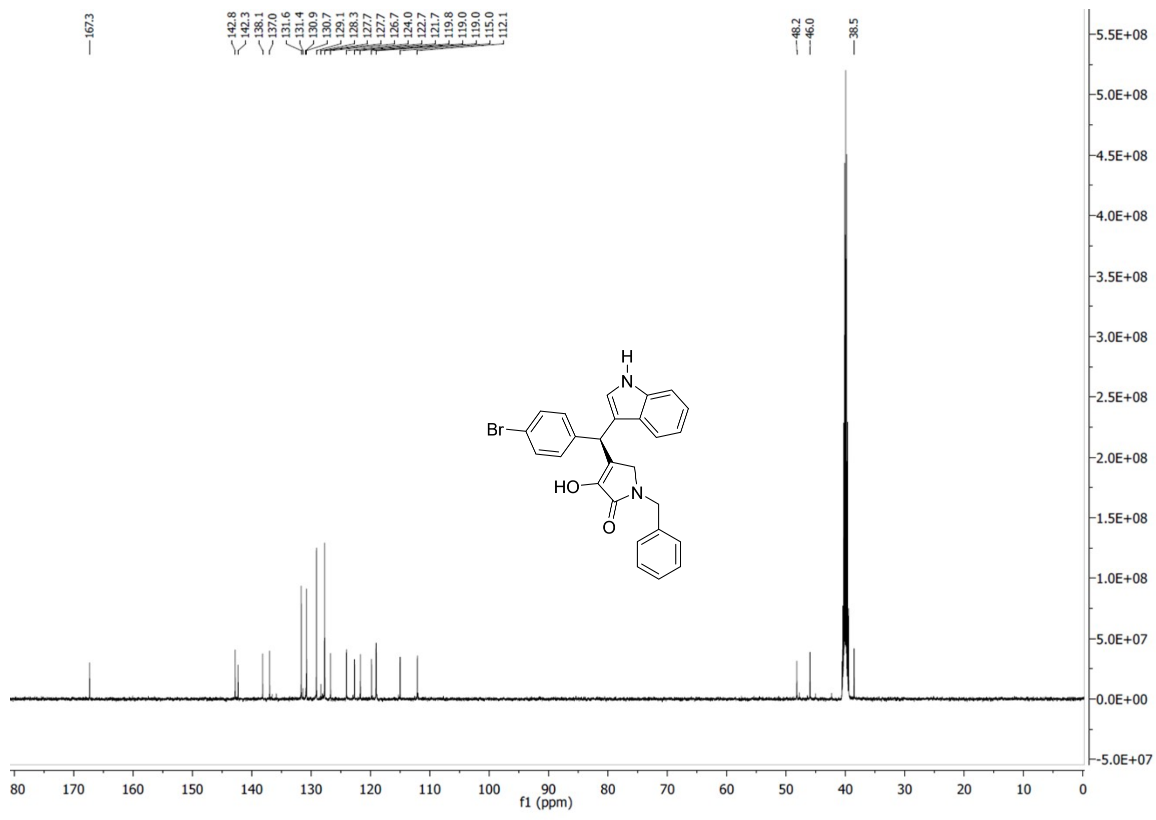
^1H NMR and ^{13}C NMR of **3d**



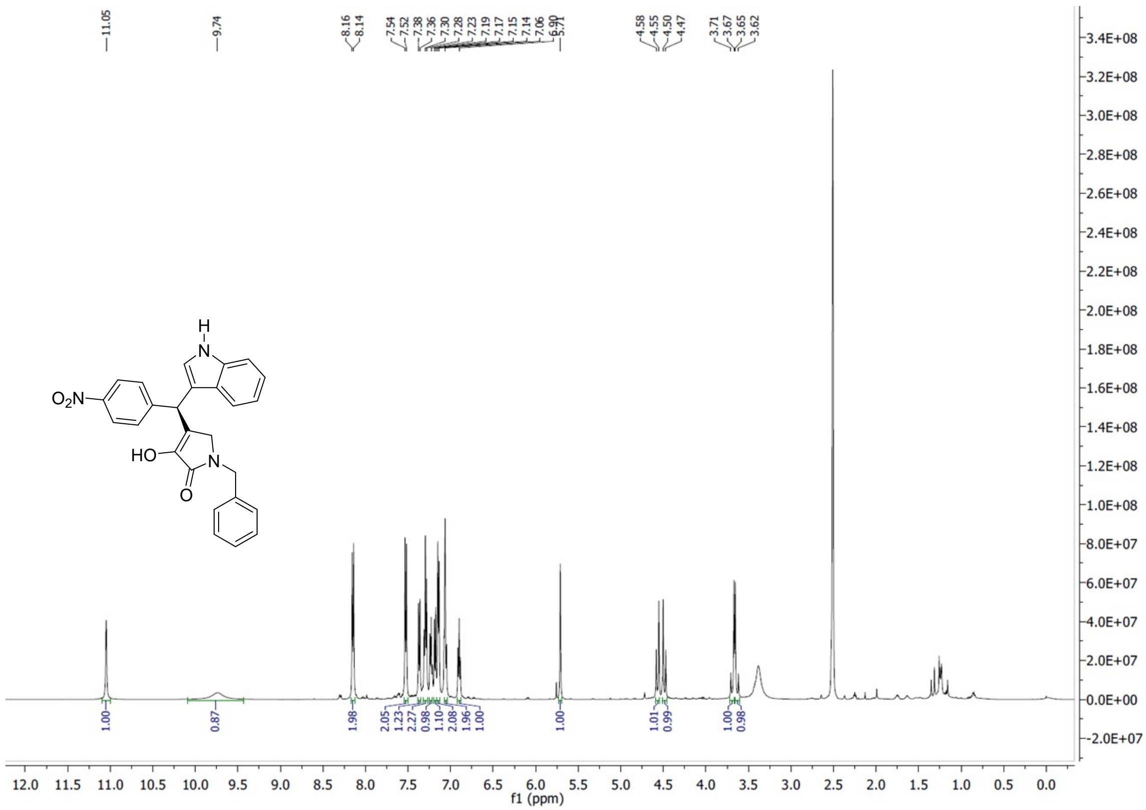


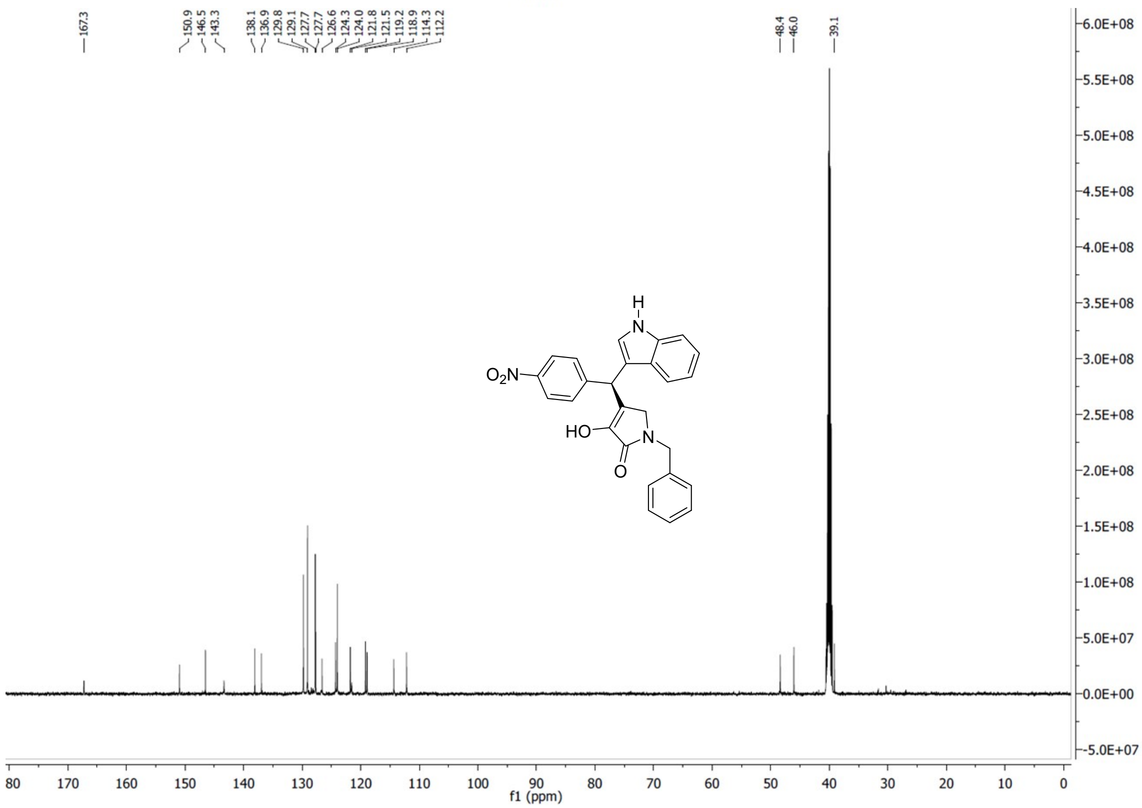
^{1}H NMR and ^{13}C NMR of **3e**



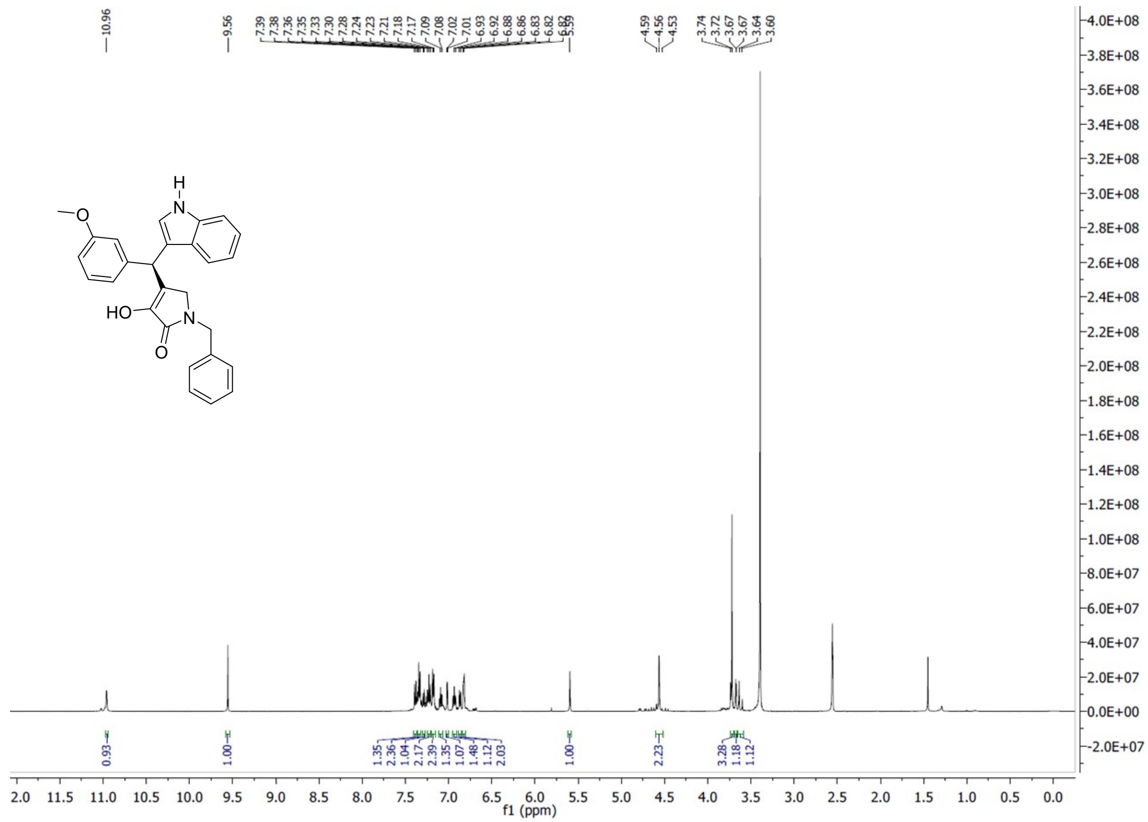


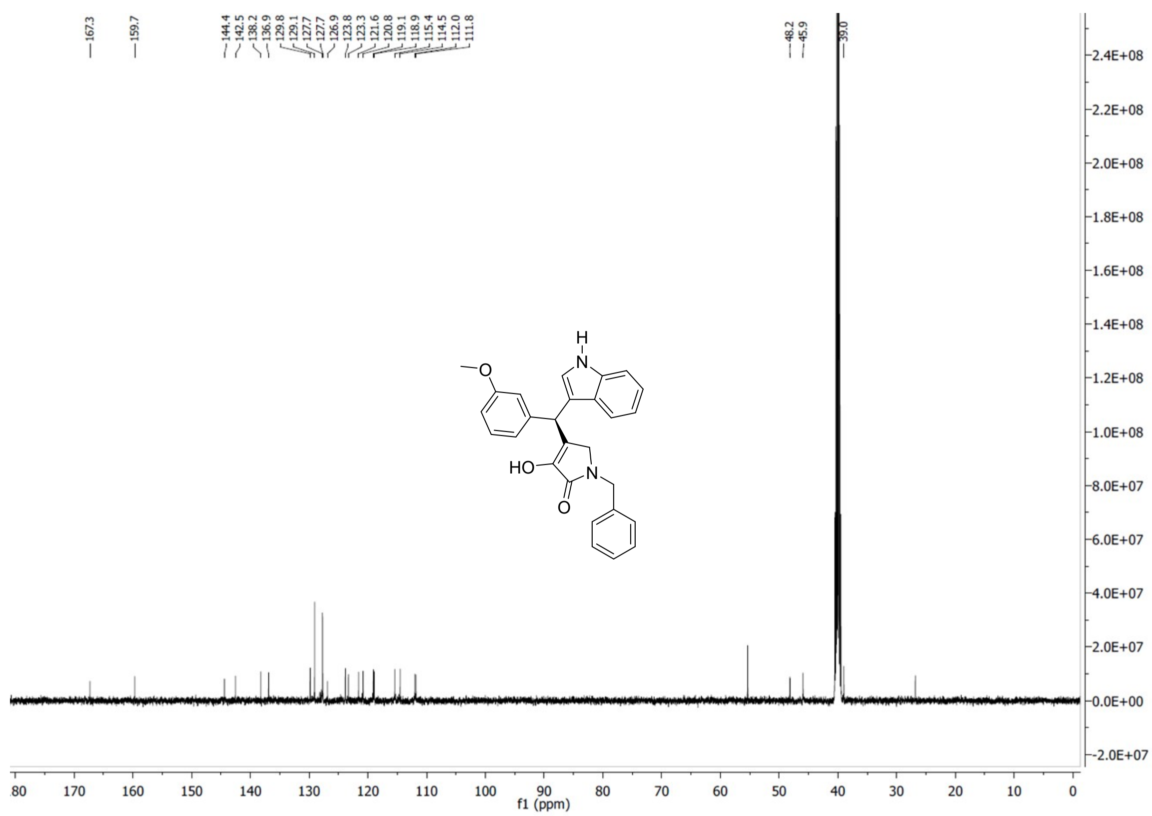
[1]H NMR and [13]C NMR of **3f**



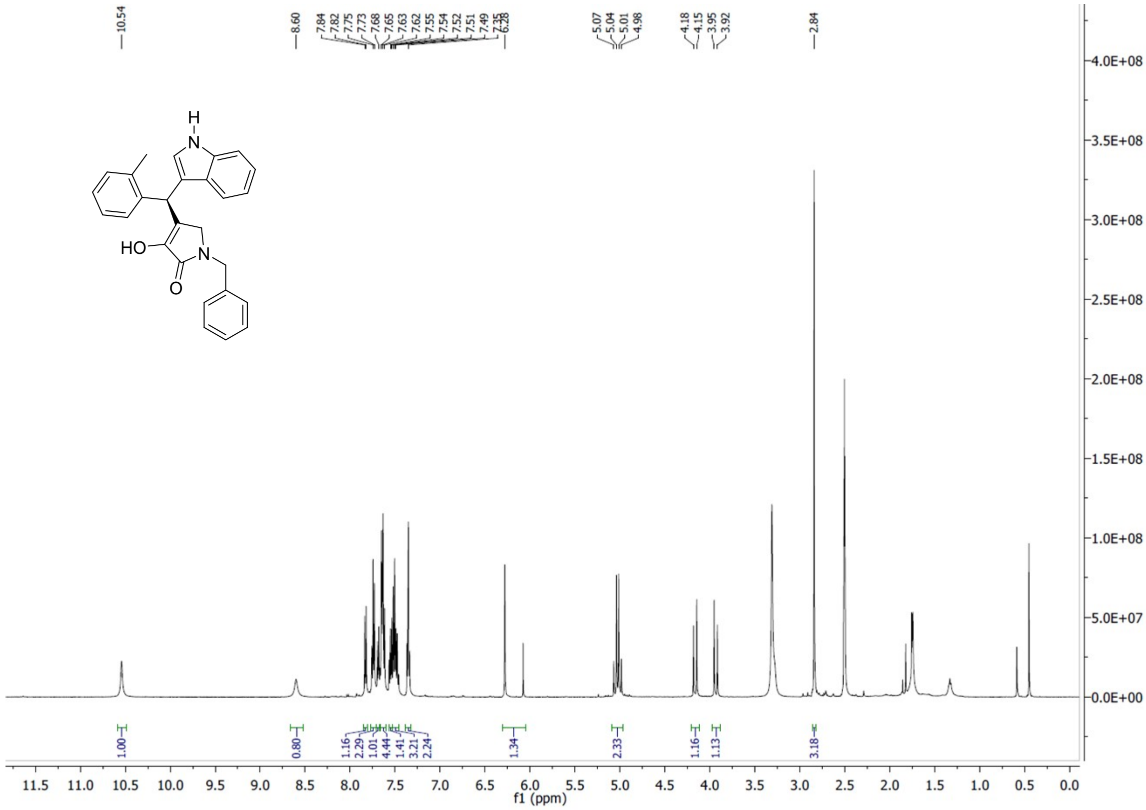


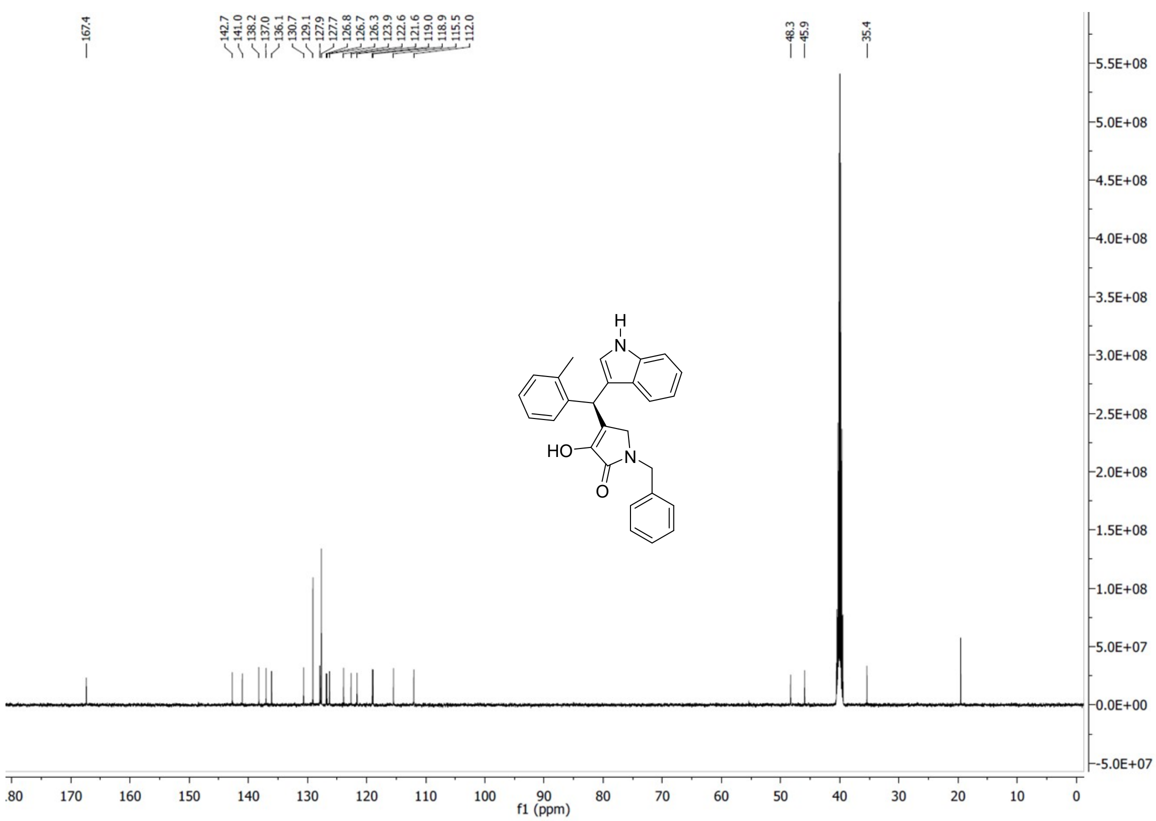
^{1}H NMR and ^{13}C NMR of **3g**



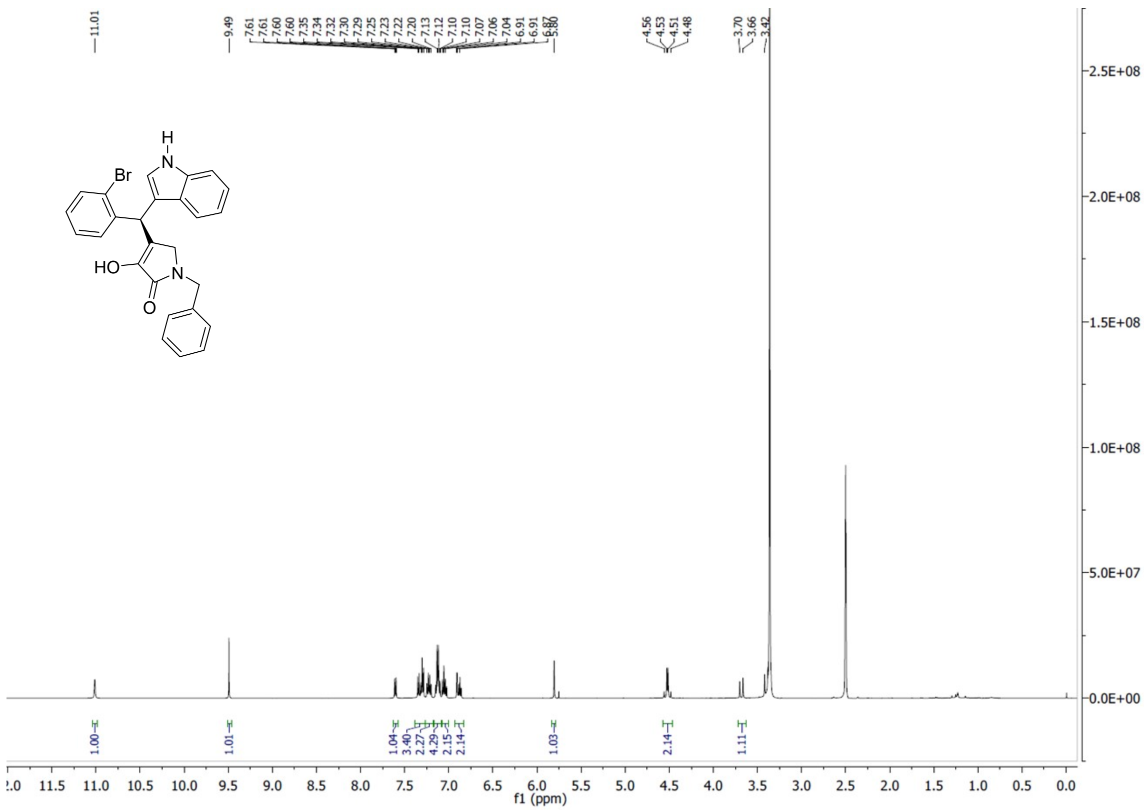


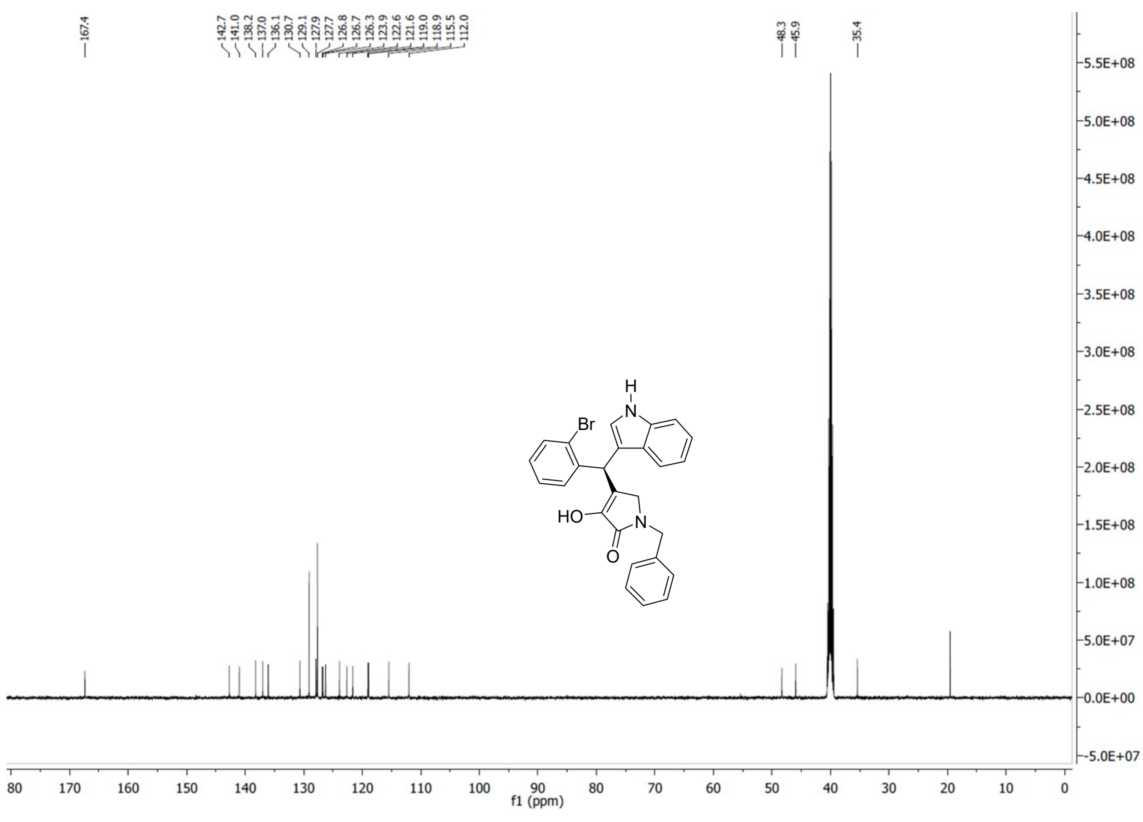
^{1}H NMR and ^{13}C NMR of **3h**



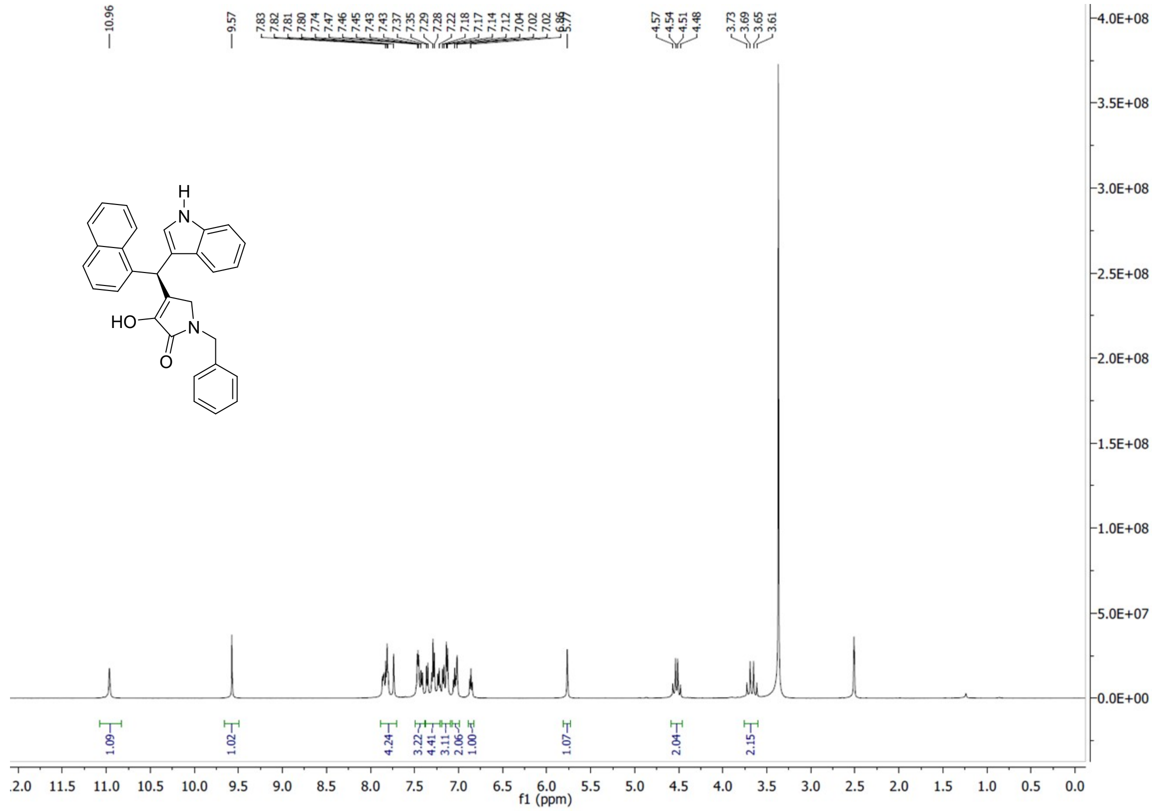


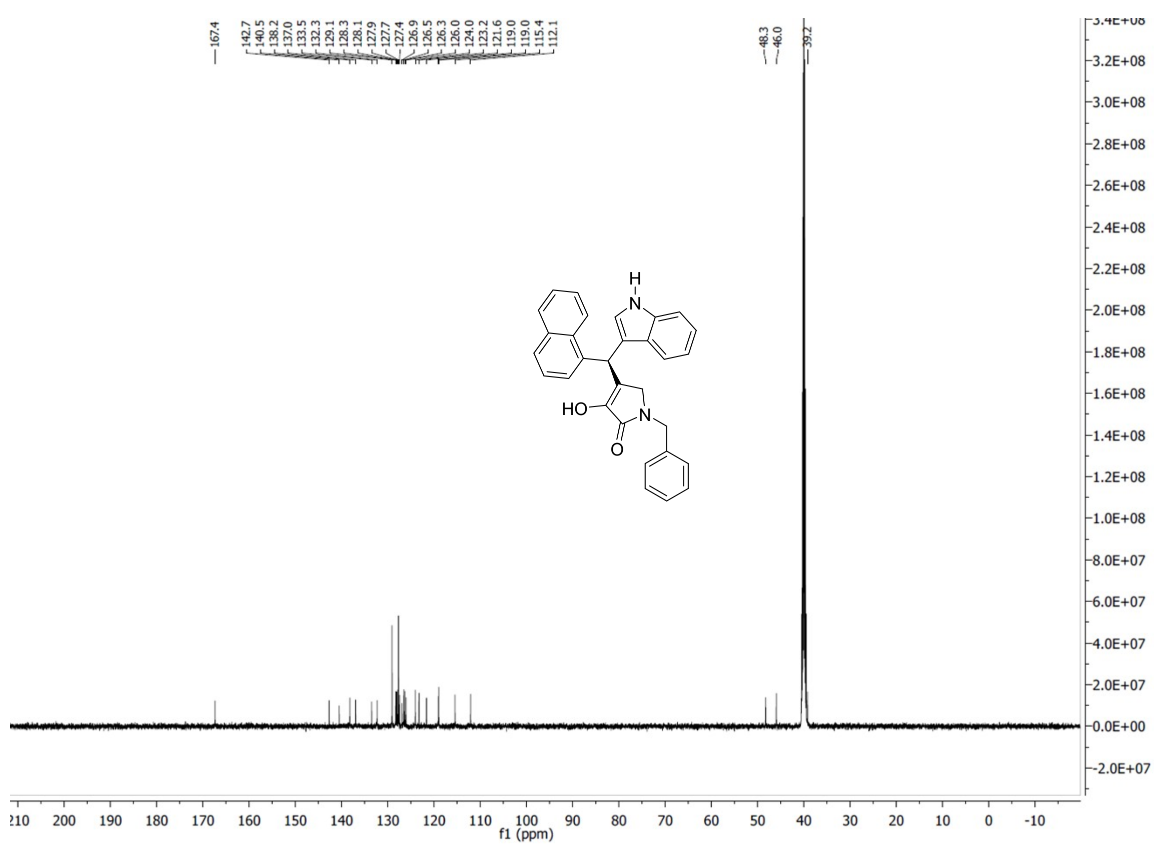
^{1}H NMR and ^{13}C NMR of **3i**



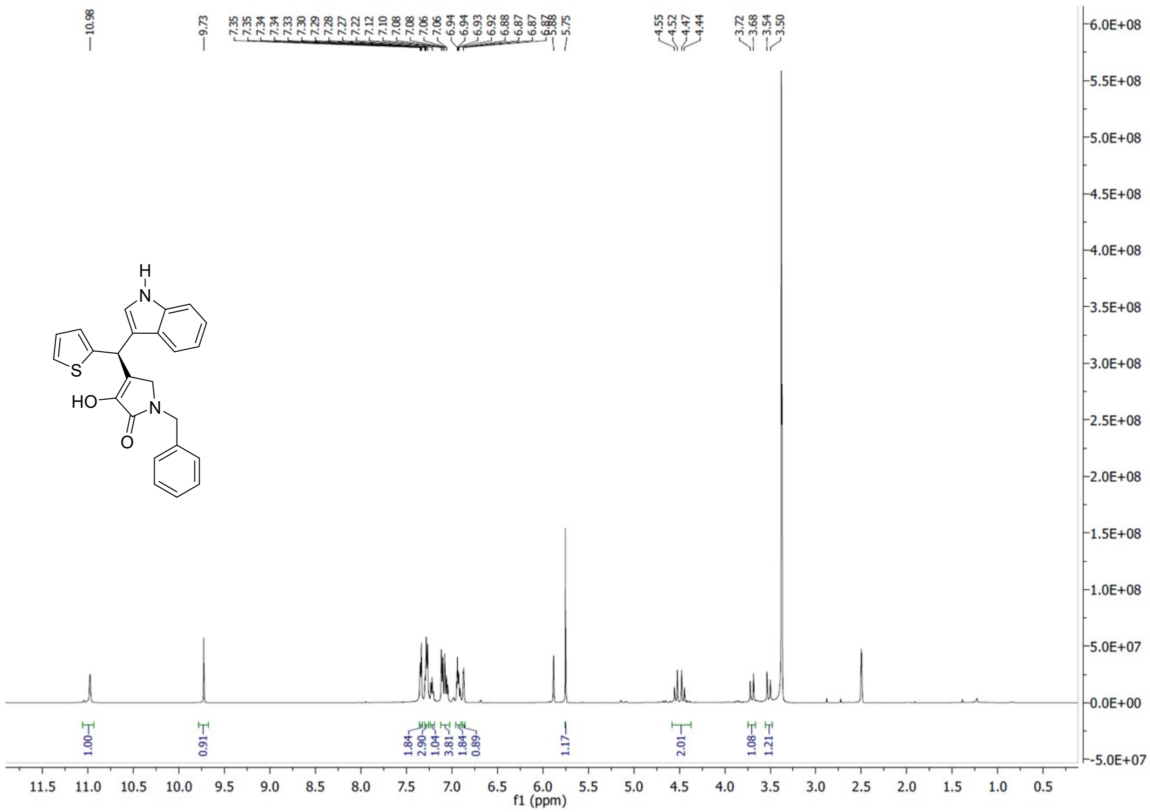


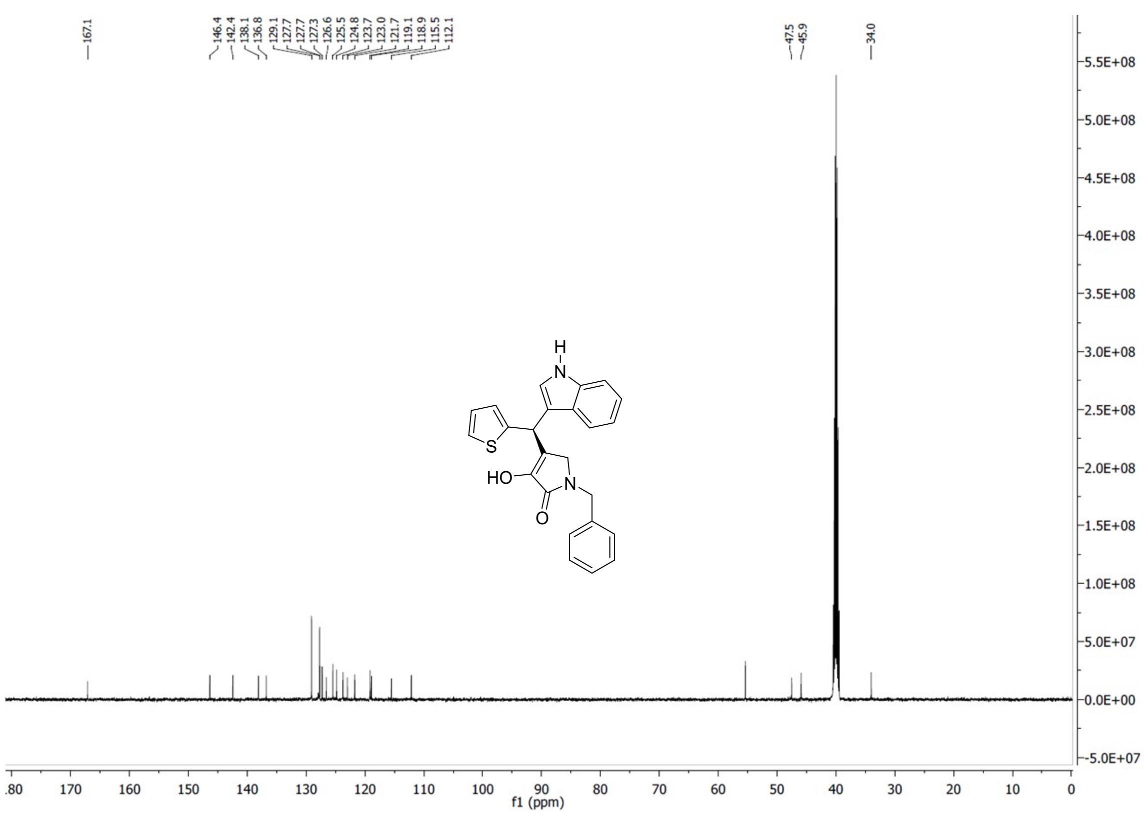
^{1}H NMR and ^{13}C NMR of **3j**



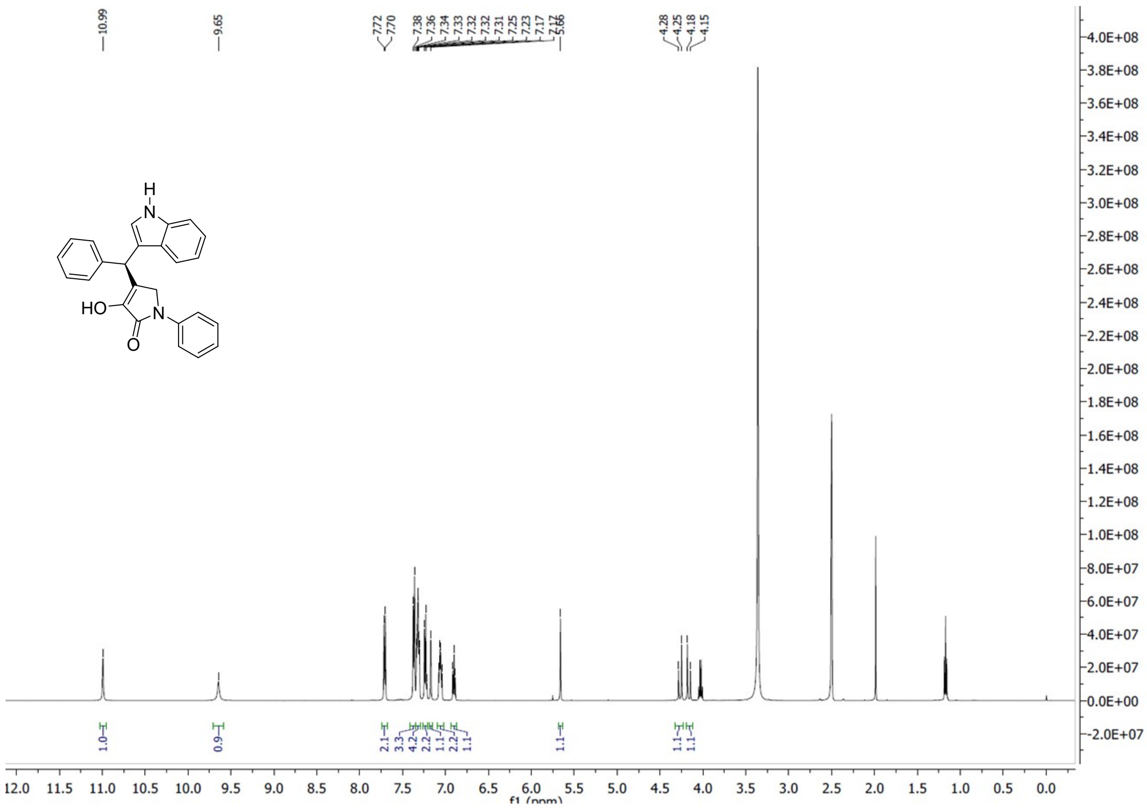


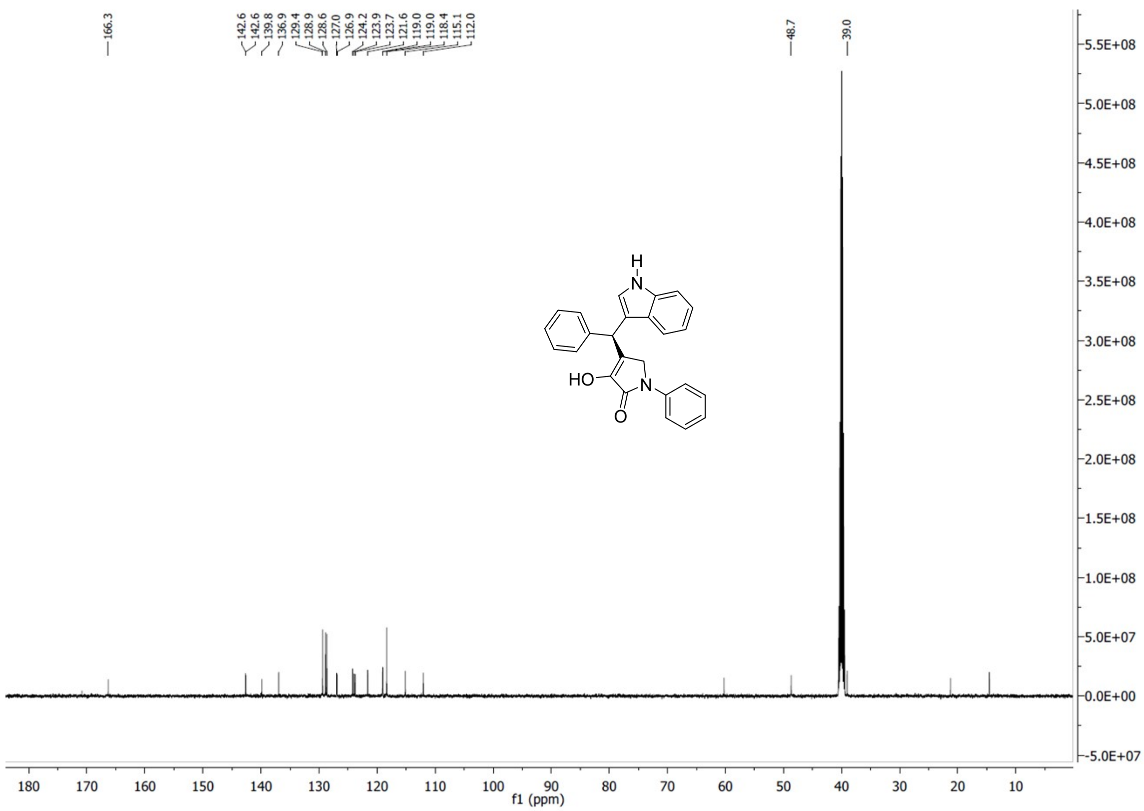
^{1}H NMR and ^{13}C NMR of **3k**



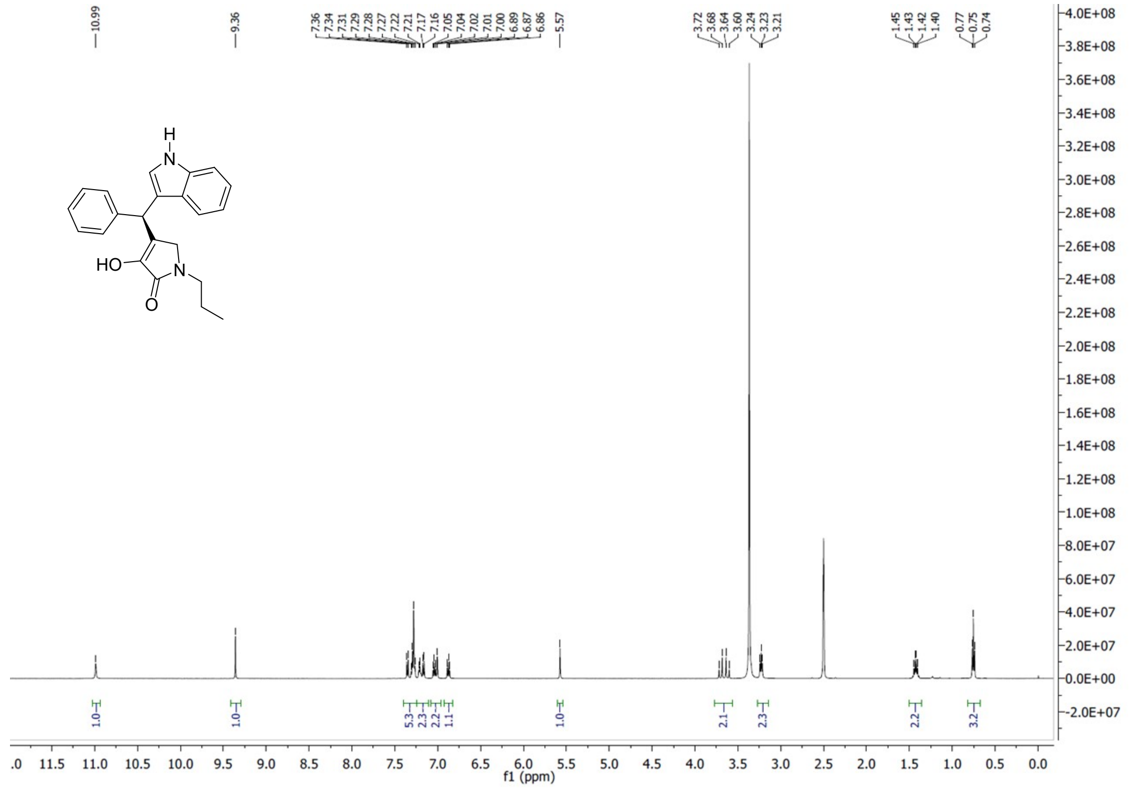


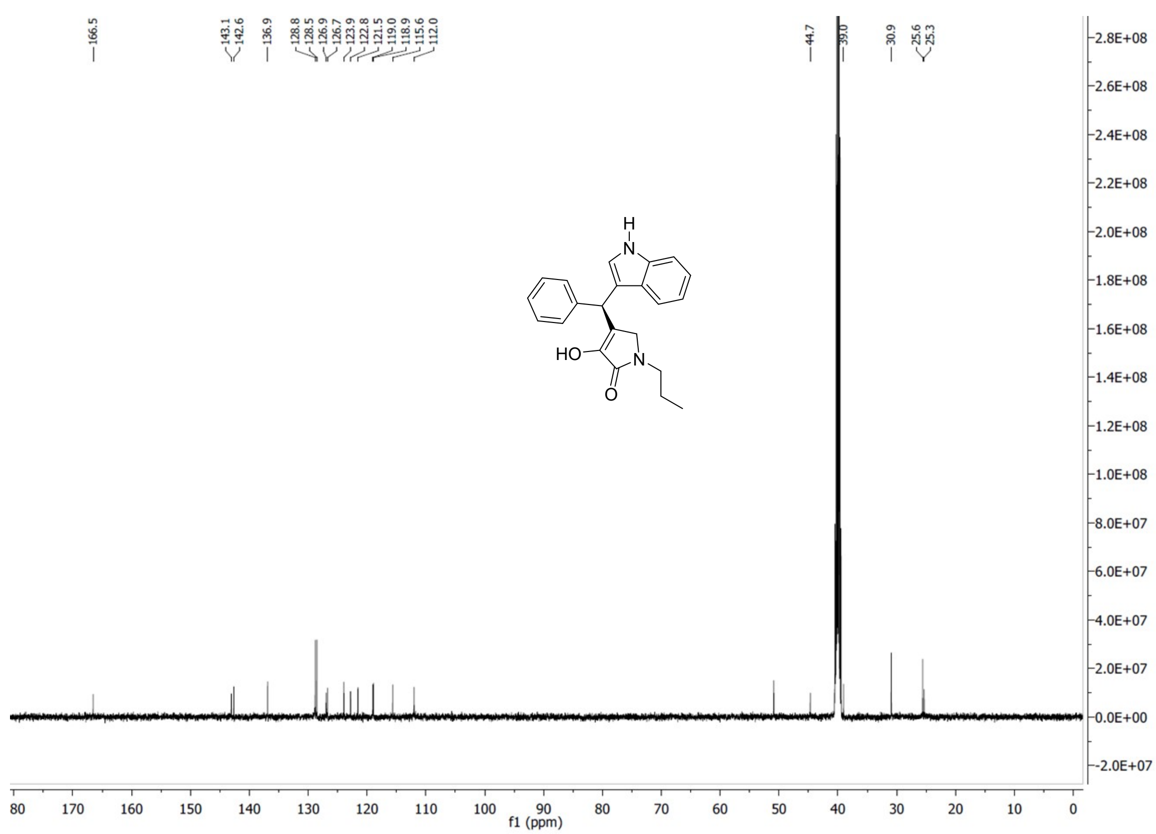
[1]H NMR and [13]C NMR of **3l**



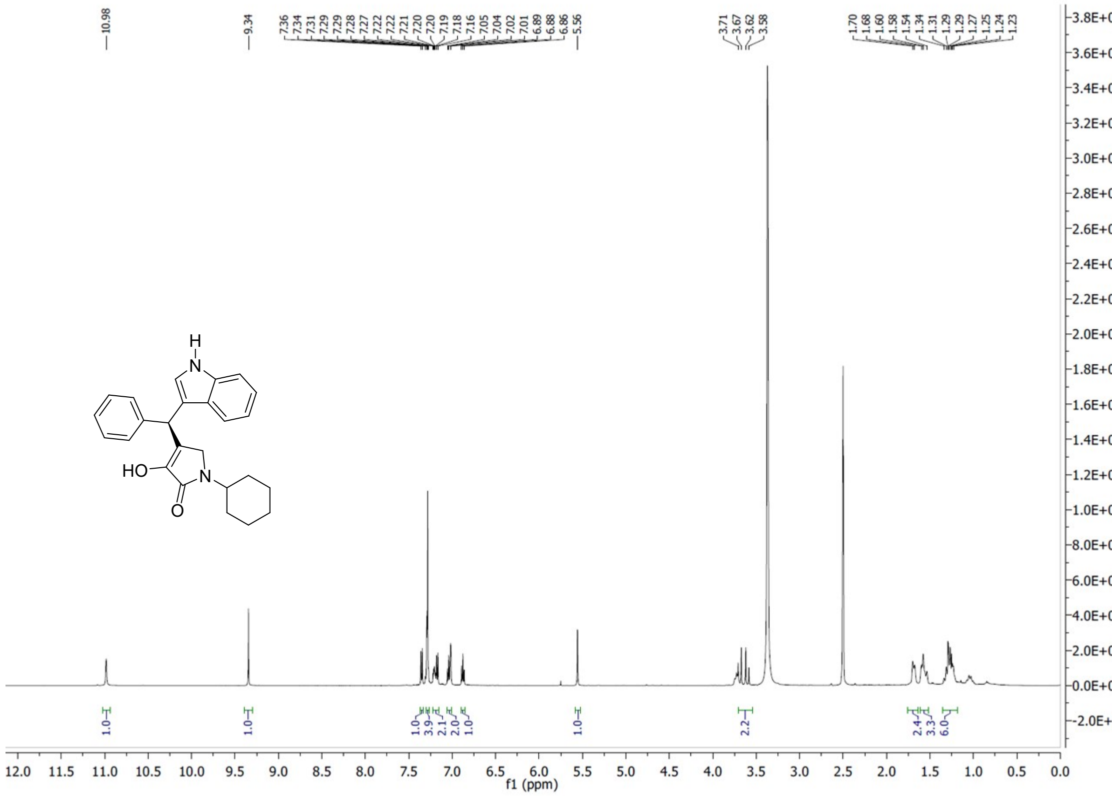


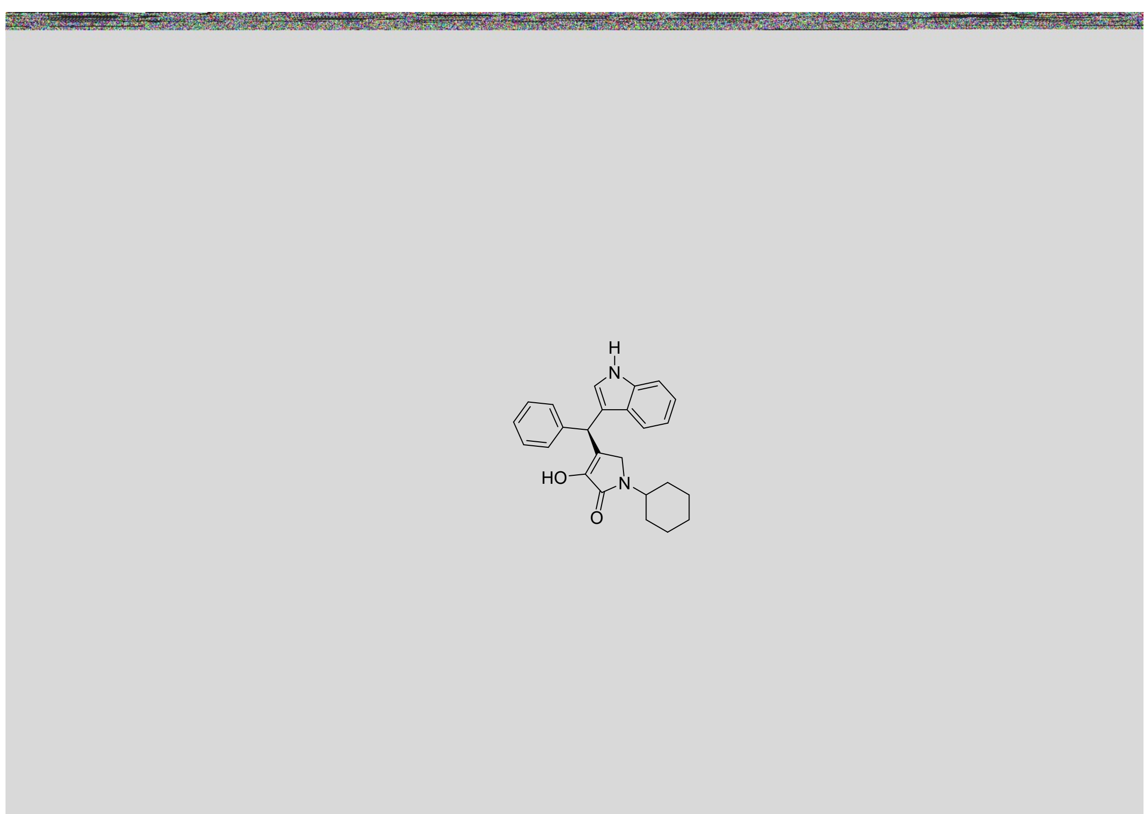
^{1}H NMR and ^{13}C NMR of **3m**



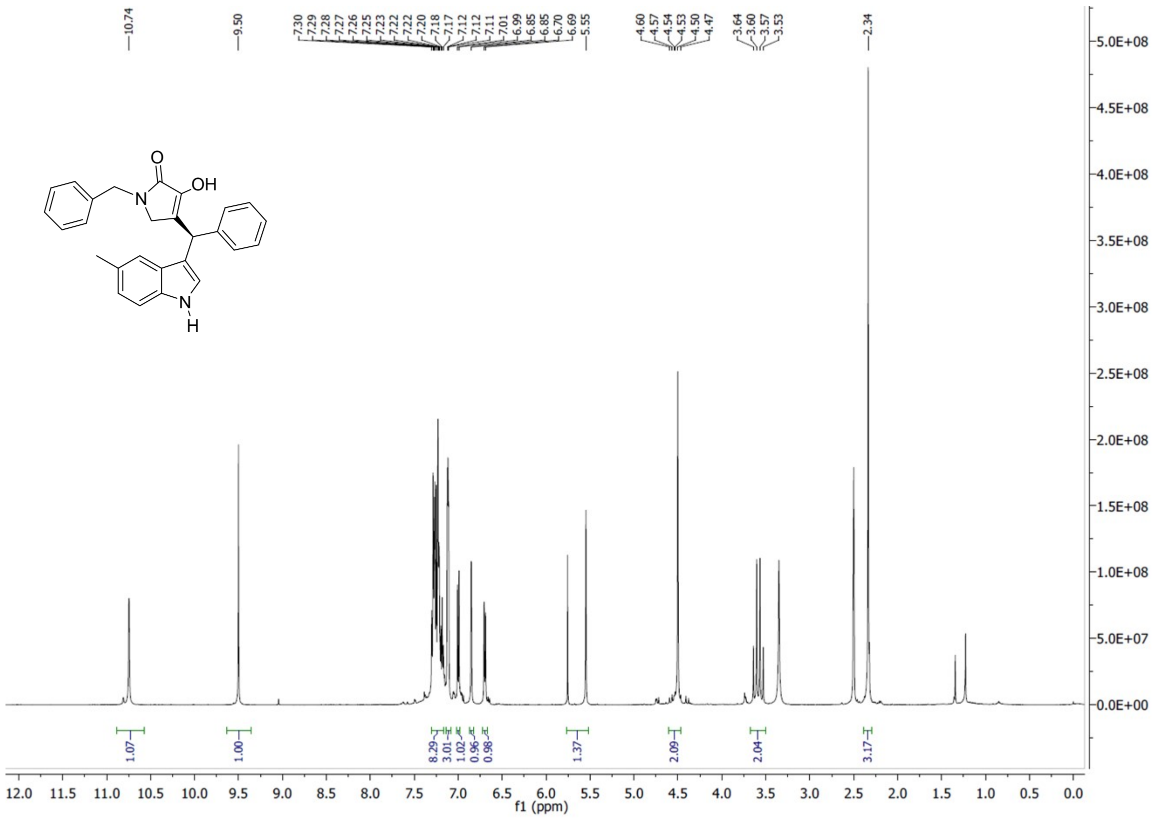


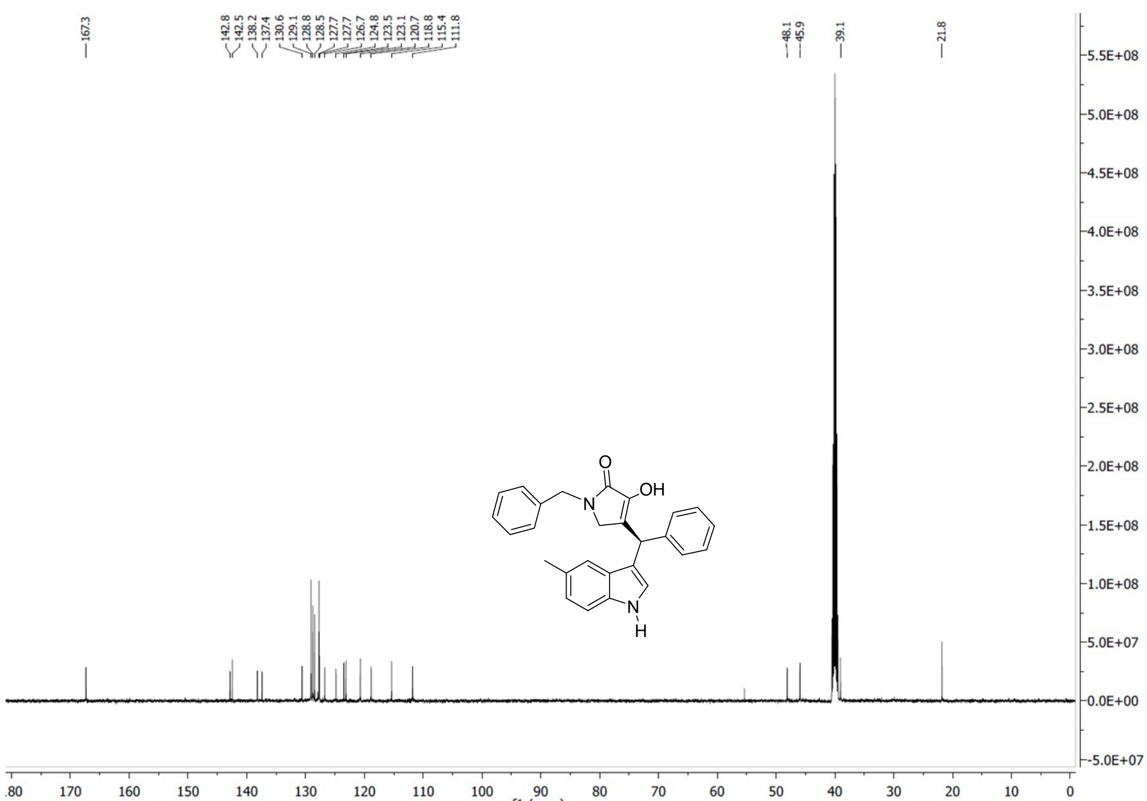
^{1}H NMR and ^{13}C NMR of **3n**



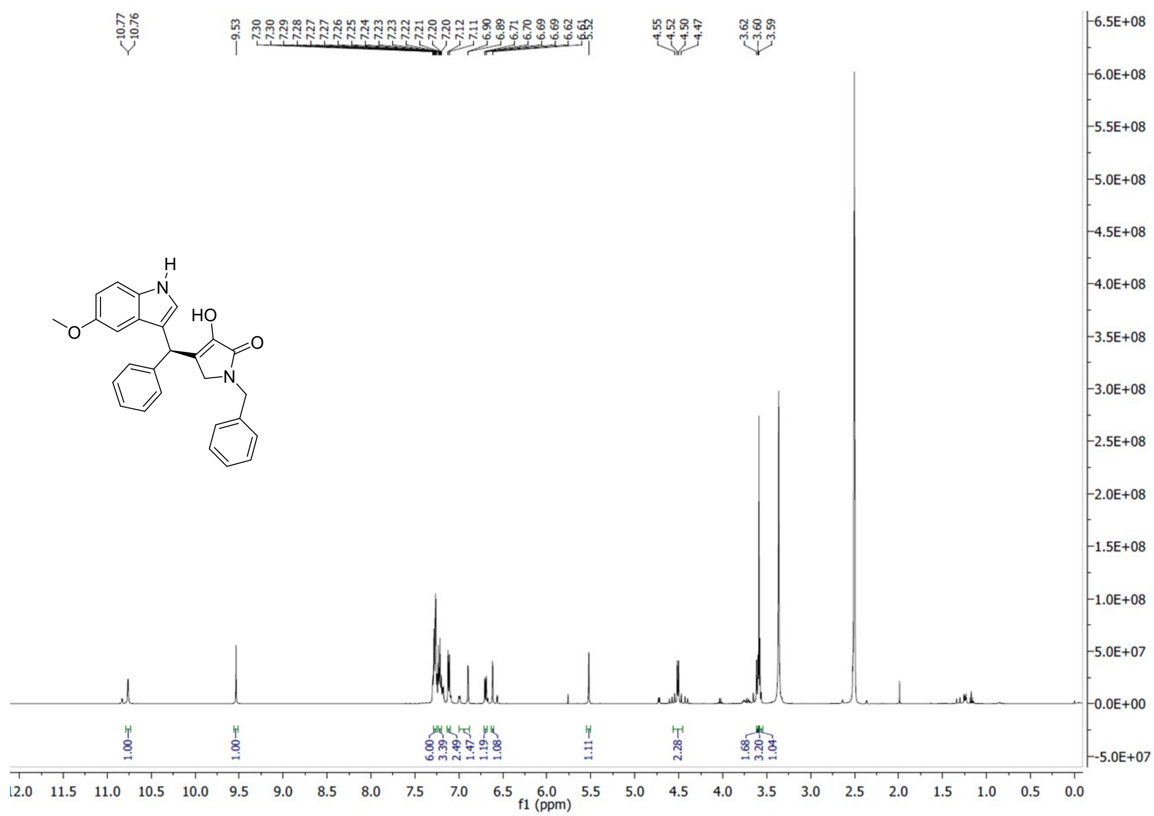


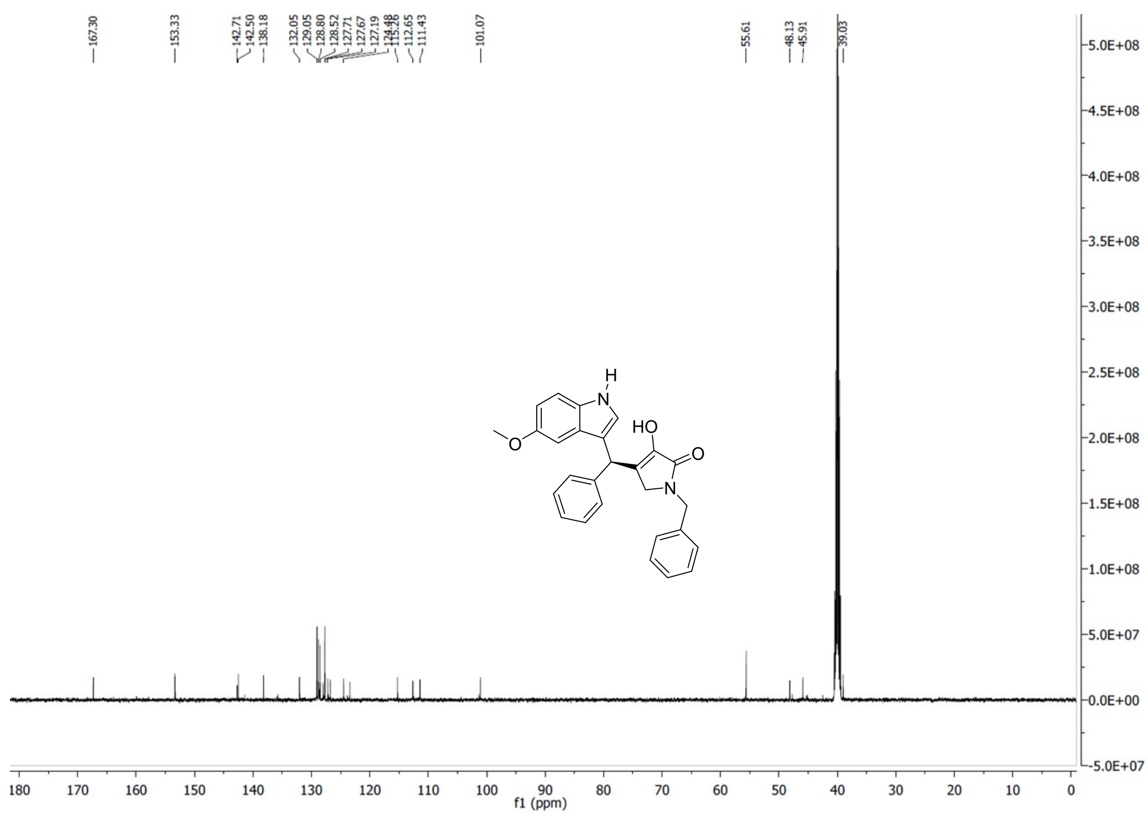
^{1}H NMR and ^{13}C NMR of **3o**



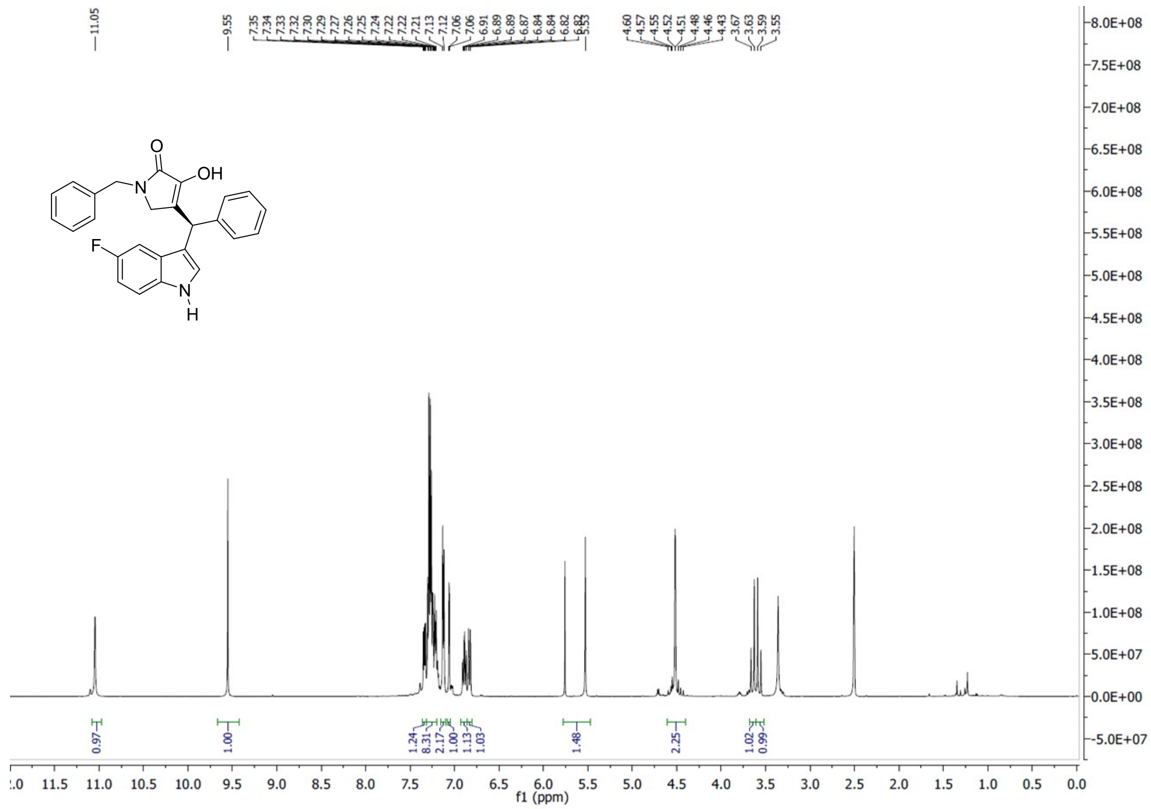


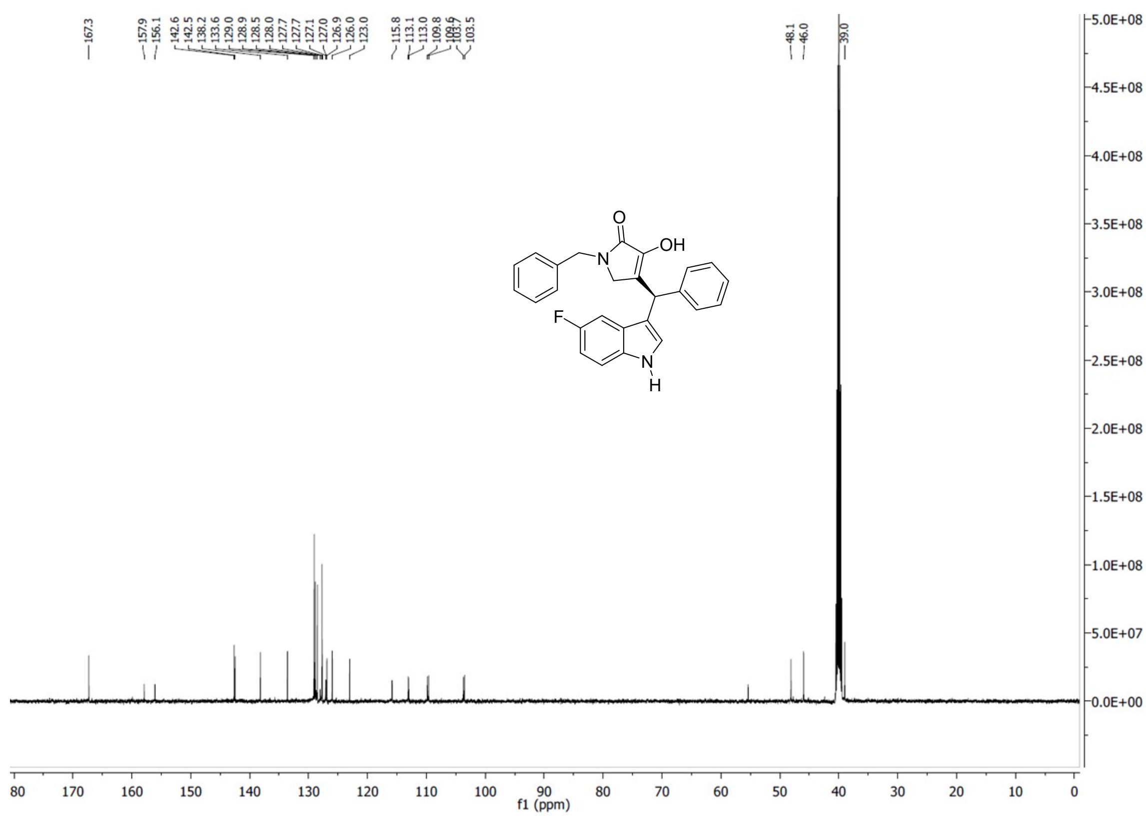
^{1}H NMR and ^{13}C NMR of **3p**



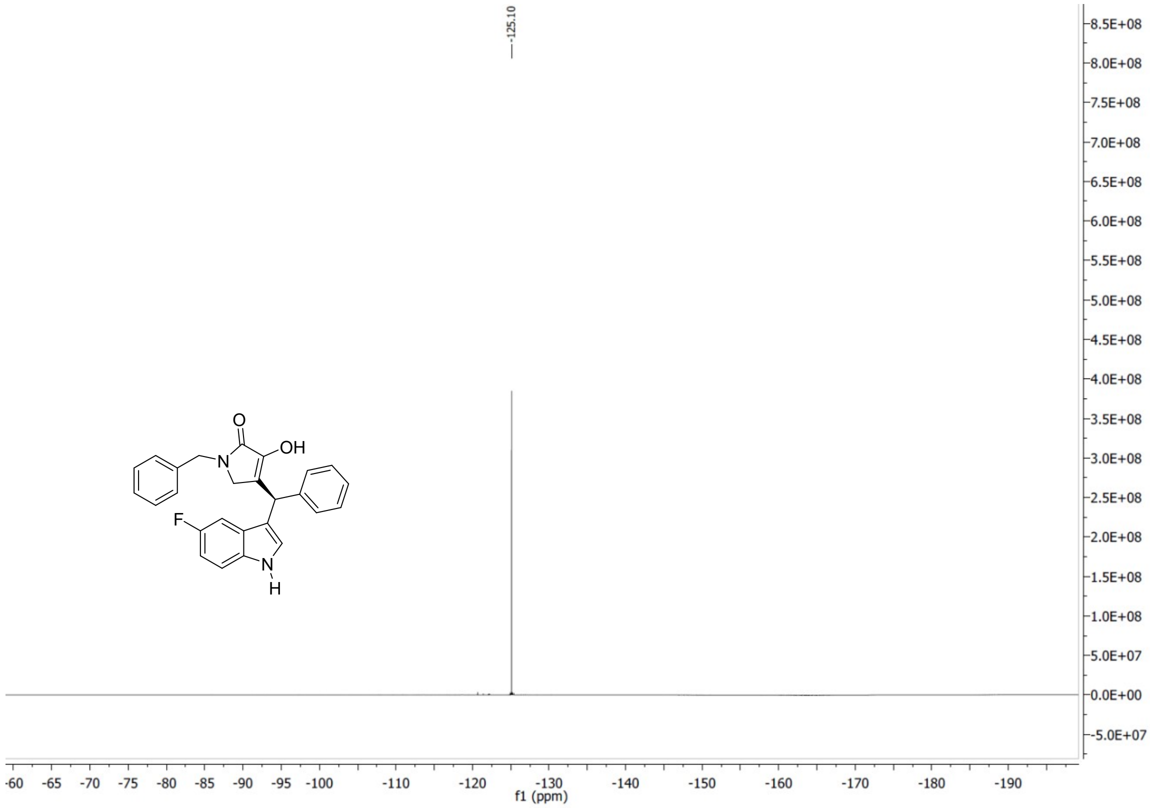


^{1}H NMR and ^{13}C NMR of **3q**



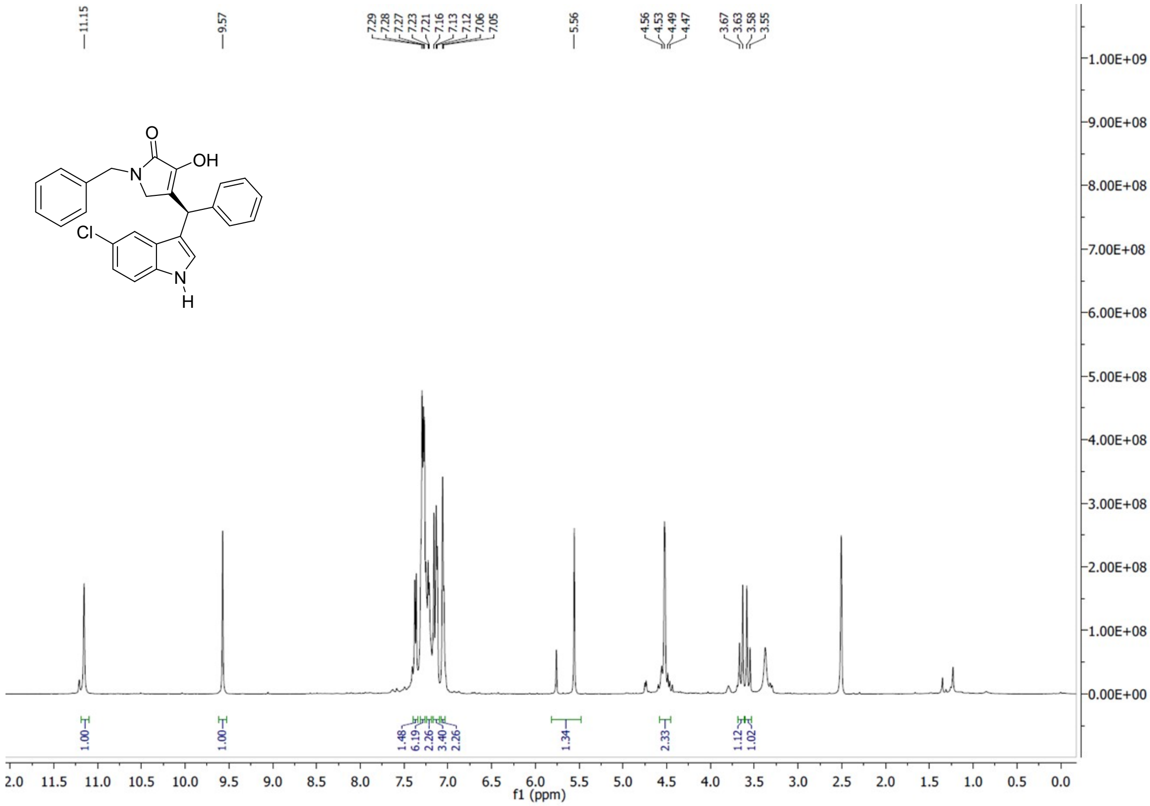


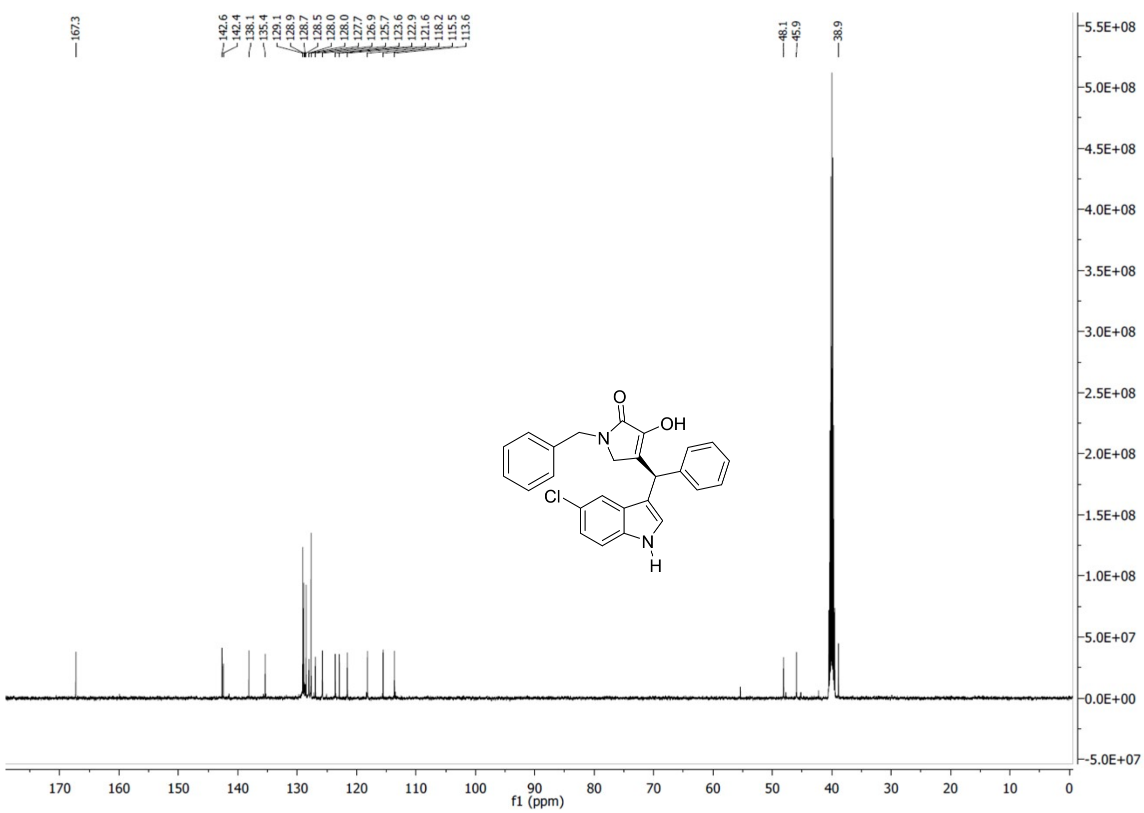
^{19}F NMR of **3q**



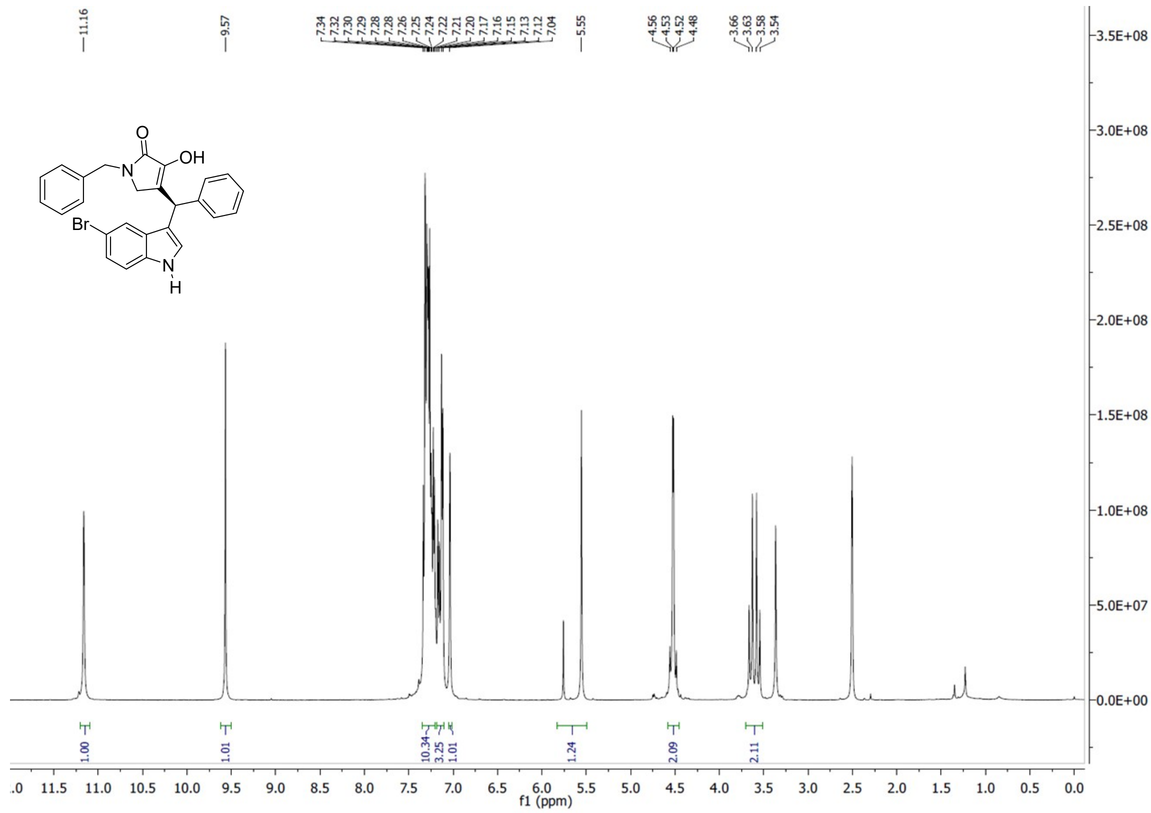
-125.10
8.5E+08
8.0E+08
7.5E+08
7.0E+08
6.5E+08
6.0E+08
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
-60 -65 -70 -75 -80 -85 -90 -95 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)
O
OH
N
F
N
H

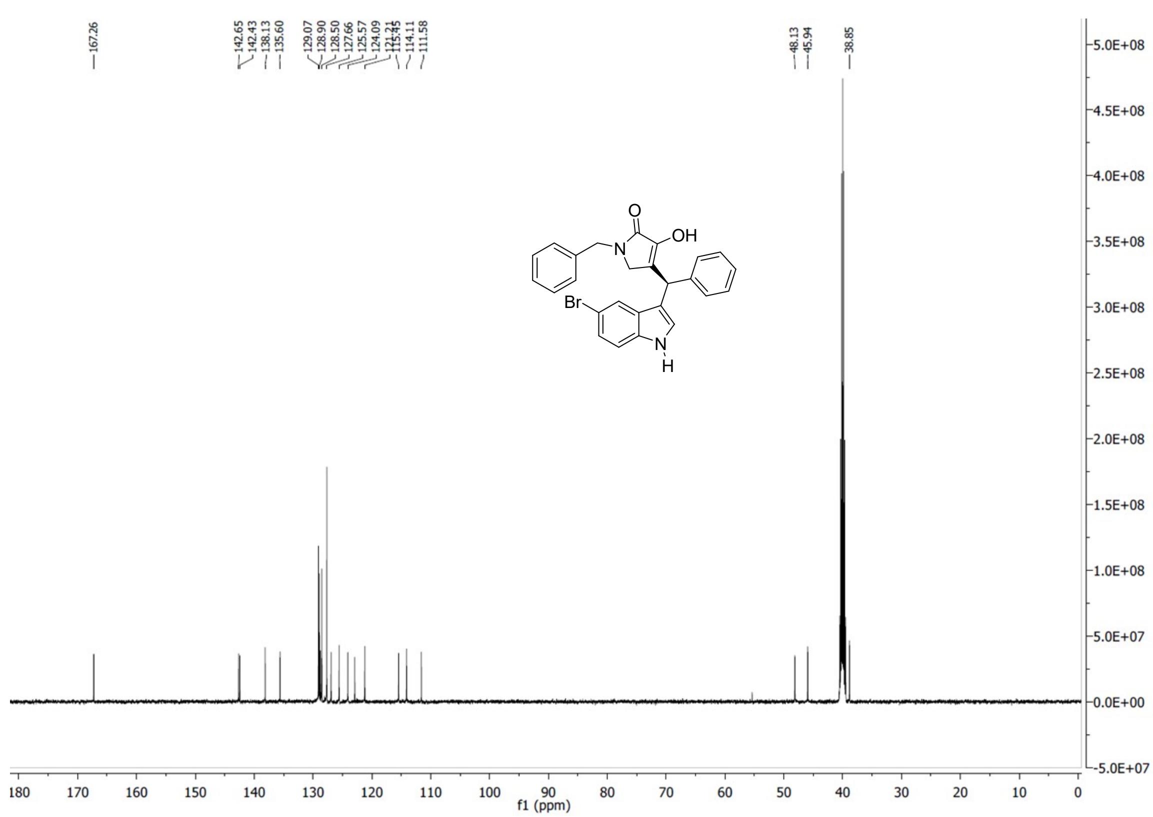
[1]H NMR and [13]C NMR of **3r**



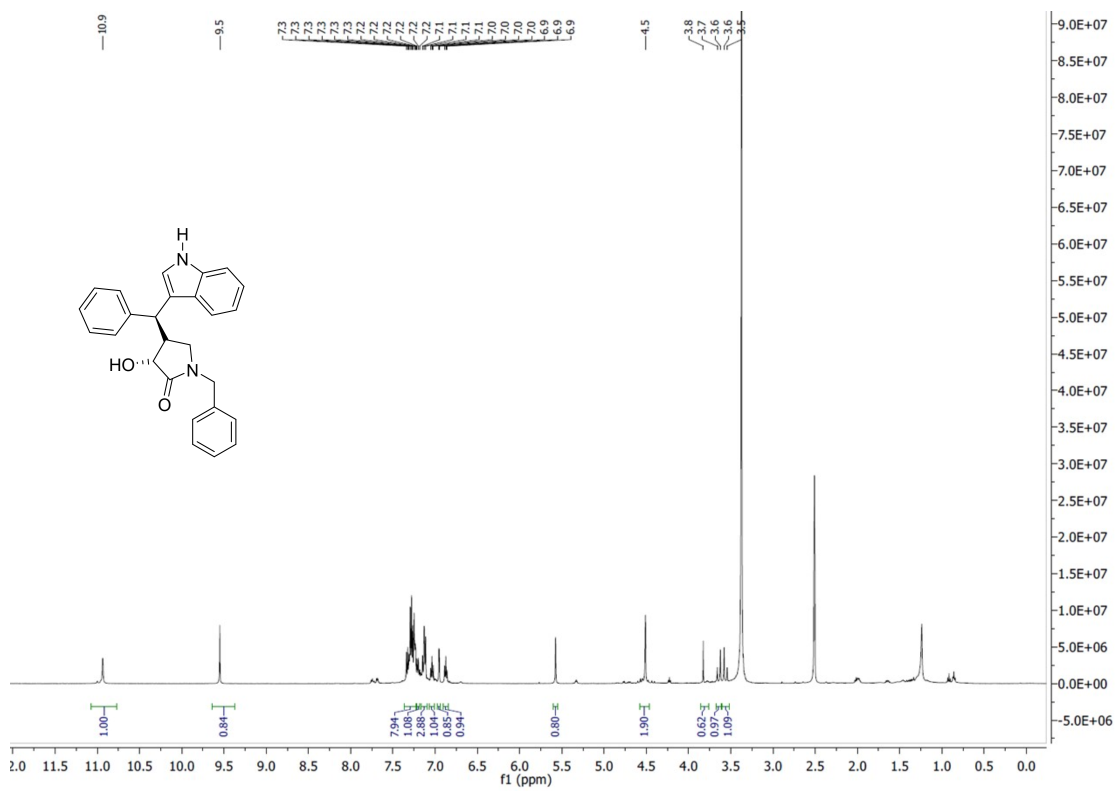


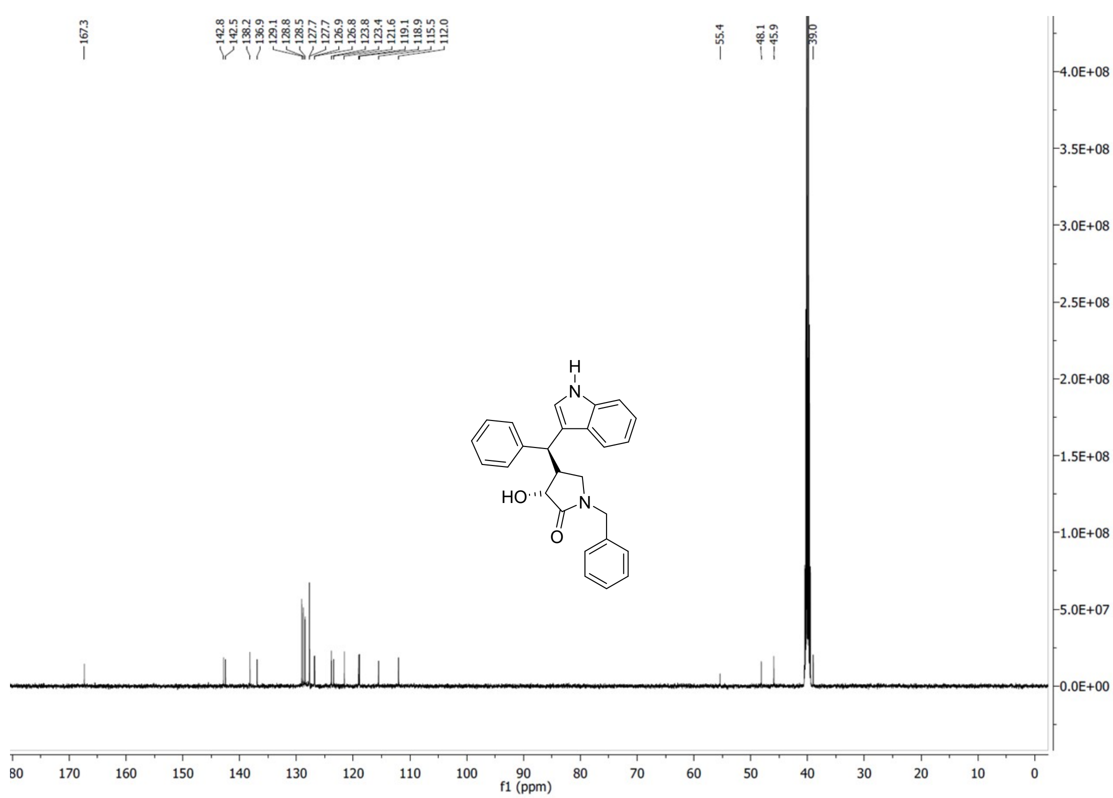
[1]H NMR and [13]C NMR of **3s**





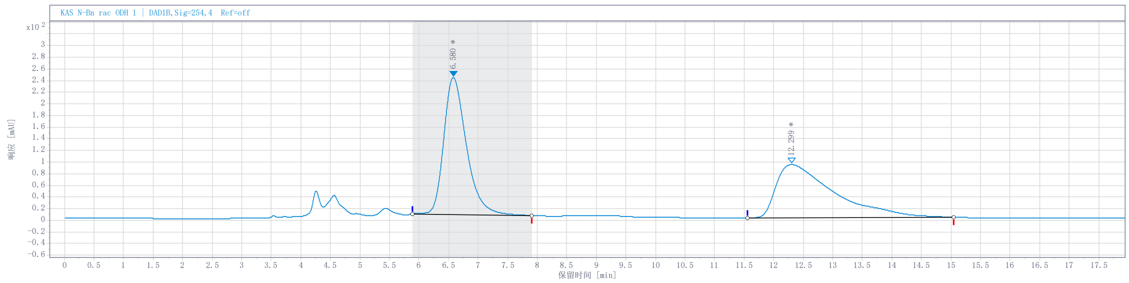
^{1}H NMR and ^{13}C NMR of **4a**





Part 4: HPLC Spectra

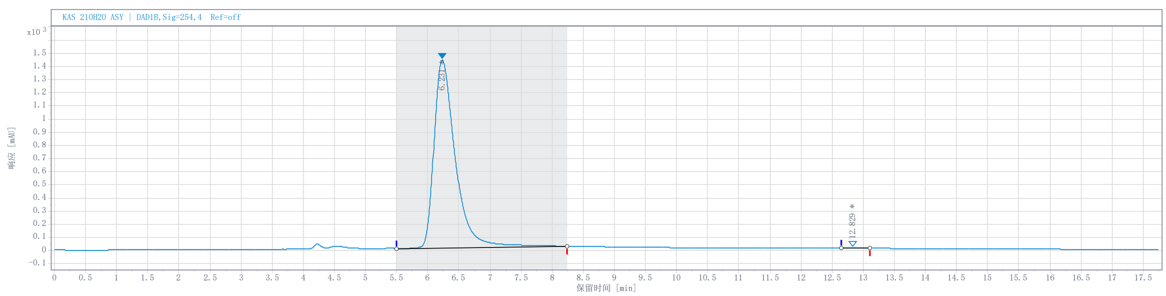
3a Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
6. 58	2. 02	6259. 26	235. 27	50. 19
12. 3	3. 49	6211. 40	91. 29	49. 81

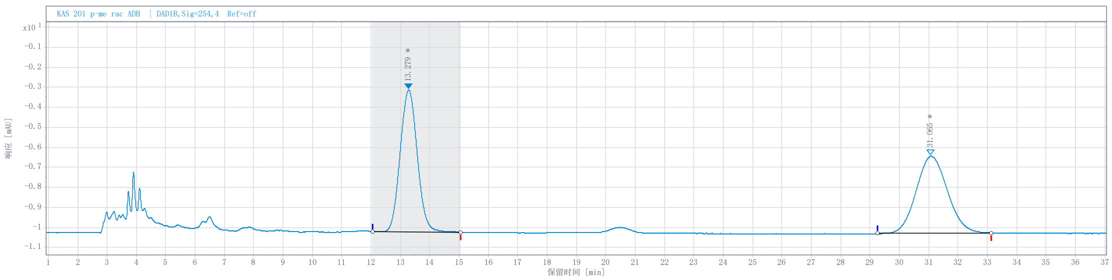
3a



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
6. 23	2. 74	33985. 92	1428. 30	99. 89
12. 8	0. 46	36. 68	2. 10	0. 11

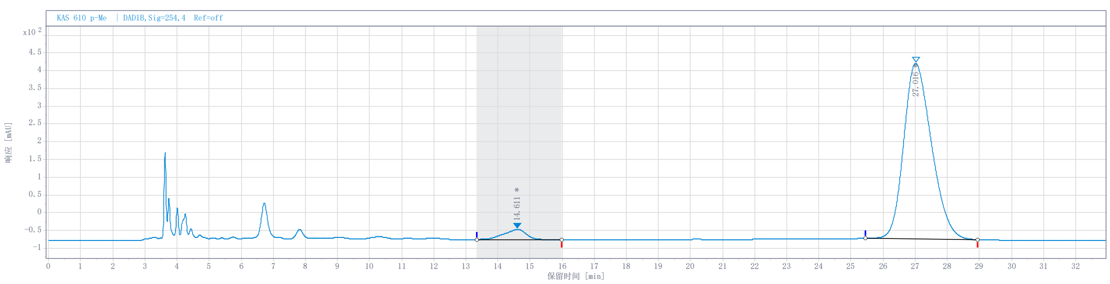
3b Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
13. 3	3. 02	284. 62	7. 08	50. 12
31. 1	3. 87	283. 21	3. 84	49. 88

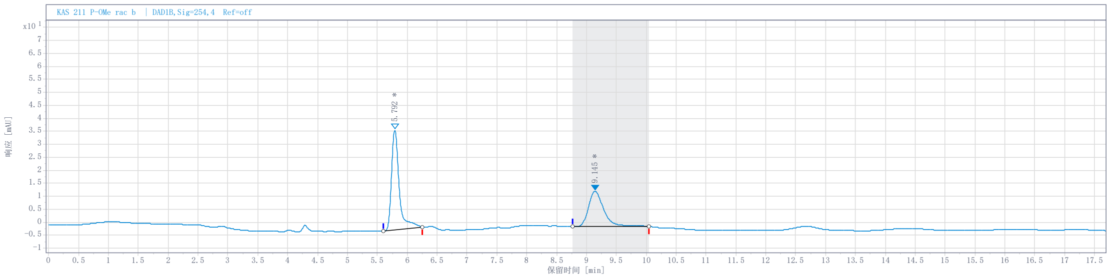
3b



Signal: DAD1B, Sig=254, 4 Ref=off

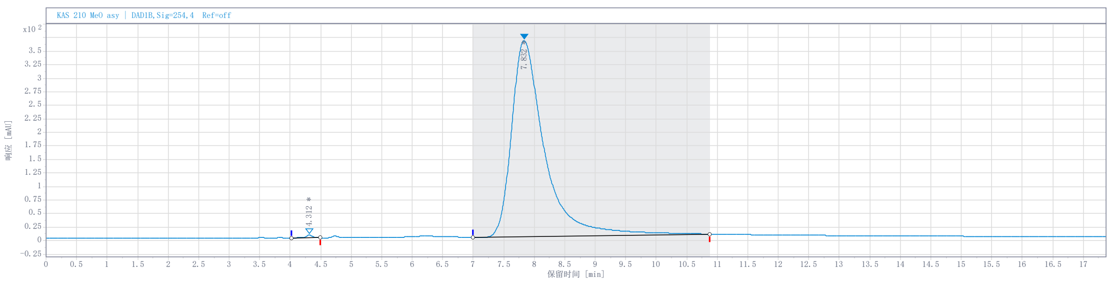
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
14. 6	2. 67	1352. 95	28. 51	4. 32
27. 0	4. 49	29993. 50	495. 26	95. 68

3c Racemic Mixture



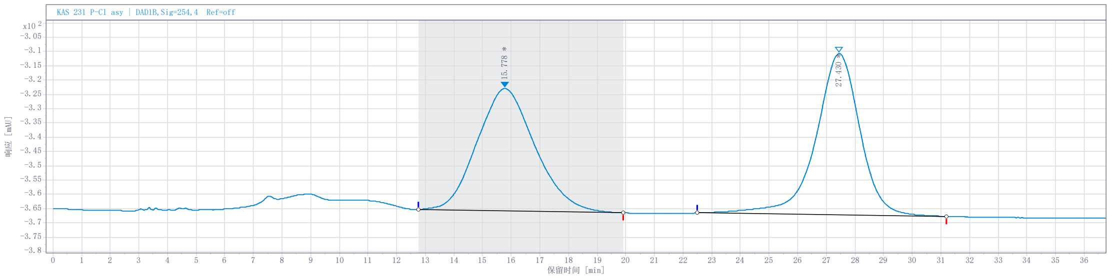
Signal:	DAD1B, Sig=254, 4 Ref=off			
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
5.79	0.65	334.83	38.33	58.24
9.15	1.28	240.04	13.63	41.76

3c



Signal:	DAD1B, Sig=254, 4 Ref=off			
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
4.31	0.48	41.75	5.16	0.31
7.83	3.88	13620.97	362.10	99.69

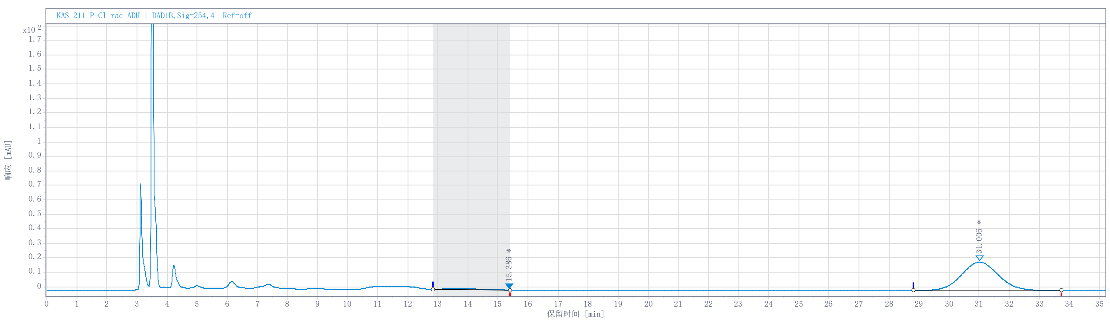
3d Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
15. 8	7. 15	6032. 17	42. 84	49. 93
27. 4	8. 69	6047. 91	56. 45	50. 07

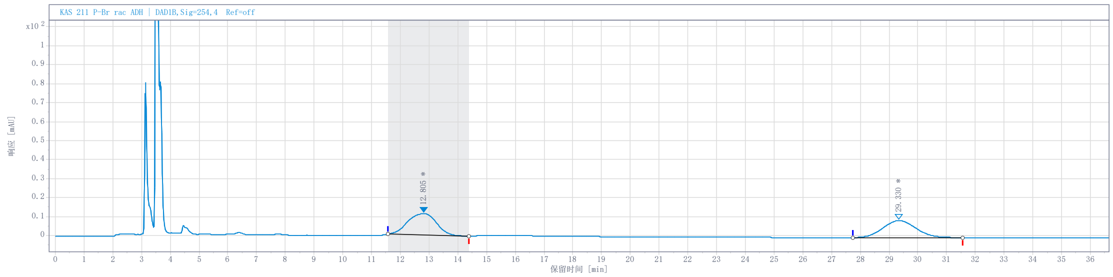
3d



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
15. 4	2. 55	34. 86	0. 00	2. 12
31. 0	4. 91	1610. 05	19. 23	97. 88

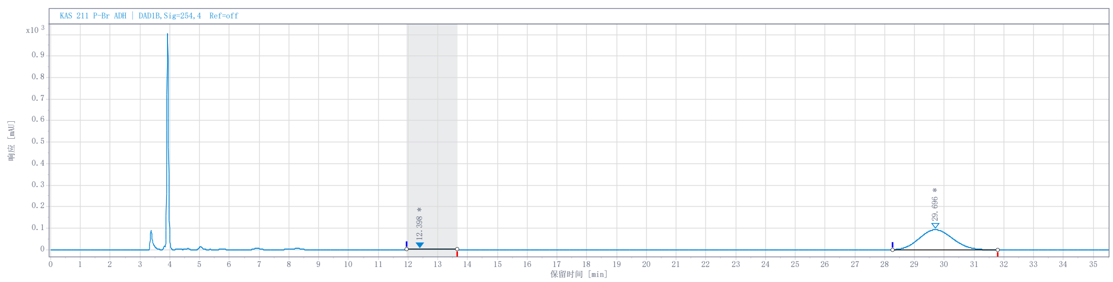
3e Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
12. 8	2. 83	775. 58	11. 23	52. 03
29. 3	3. 82	715. 16	8. 93	47. 97

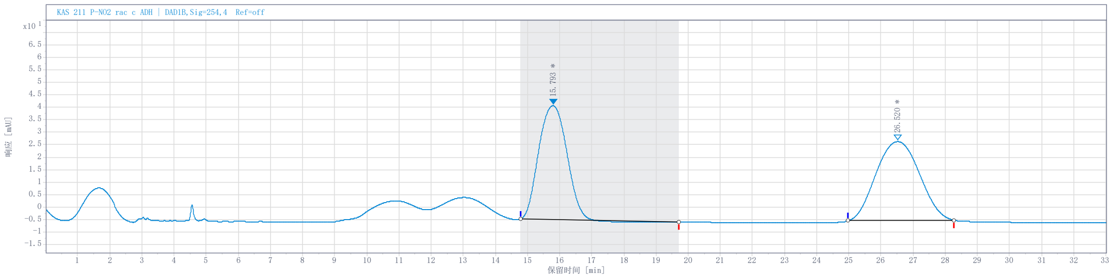
3e



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
12. 4	1. 69	145. 53	2. 05	1. 95
29. 7	3. 53	7327. 08	93. 30	98. 05

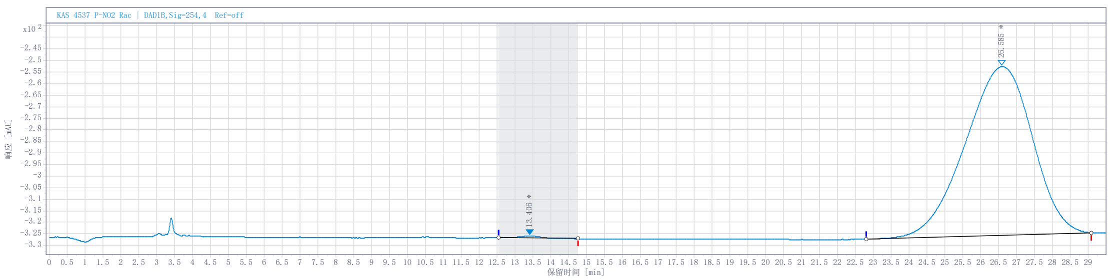
3f Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
15.8	4.92	2760.25	45.73	48.11
26.5	3.28	2977.15	31.71	51.89

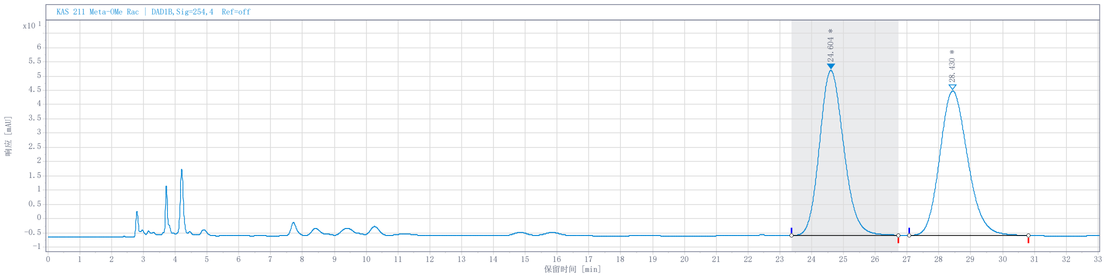
3f



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
13.4	2.22	38.50	0.92	0.40
26.6	6.28	9526.95	72.97	99.60

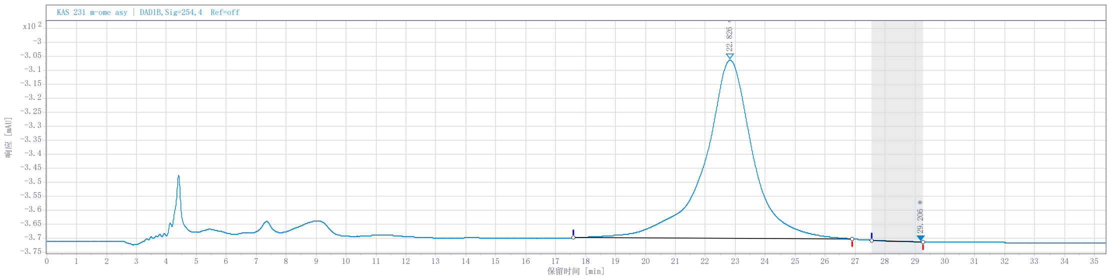
3g Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
24. 6	2. 74	3024. 41	57. 67	49. 78
28. 4	3. 33	3051. 61	50. 49	50. 22

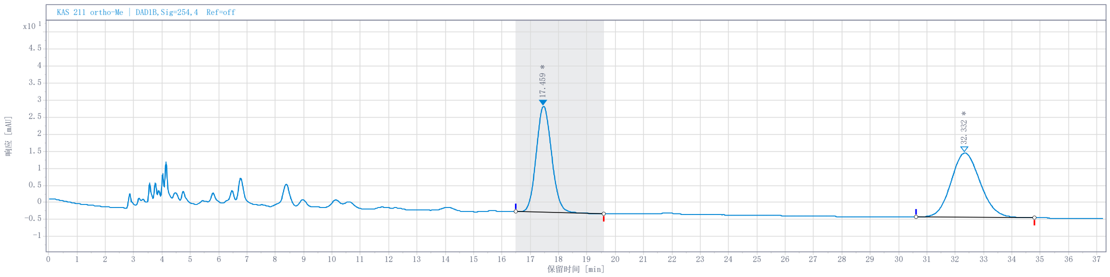
3g



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
22. 8	9. 30	7155. 99	63. 72	99. 91
29. 2	1. 70	6. 67	0. 03	0. 09

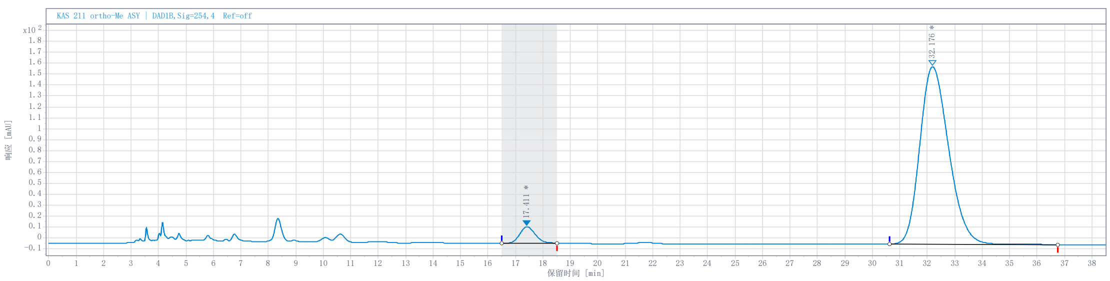
3h Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
17.5	3.10	1165.86	31.04	46.44
32.3	4.17	1344.69	18.81	53.56

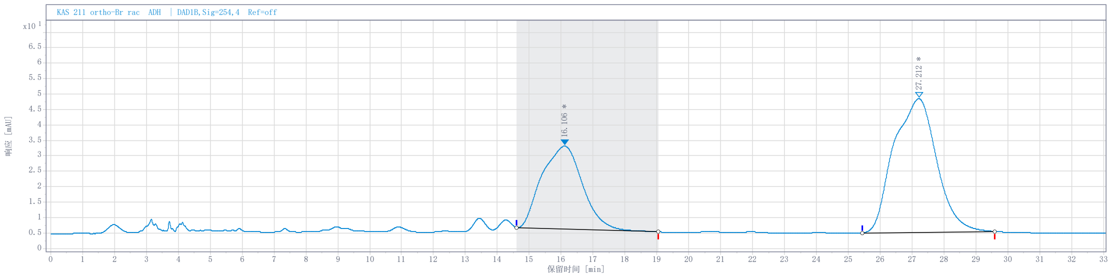
3h



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
17.4	1.99	589.15	15.07	4.73
32.2	6.10	11875.07	162.67	95.27

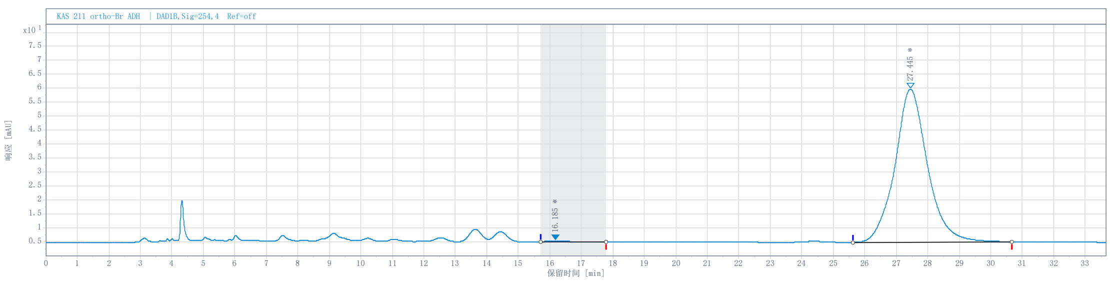
3i Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
16. 1	4. 43	2392. 00	26. 88	37. 16
27. 2	4. 15	4045. 42	43. 28	62. 84

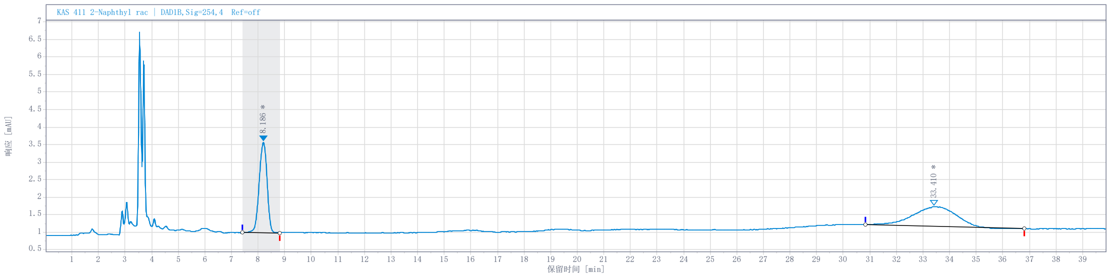
3i



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
16. 2	2. 06	13. 52	0. 32	0. 34
27. 4	5. 05	3922. 73	54. 66	99. 66

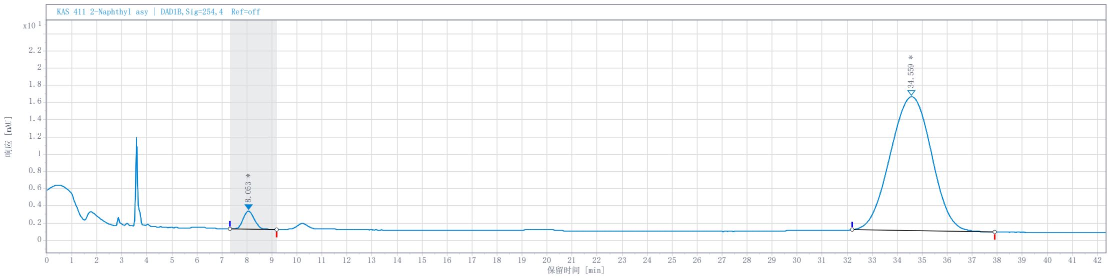
3j Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
8. 19	1. 38	53. 29	2. 58	46. 13
33. 4	5. 97	62. 24	0. 55	53. 87

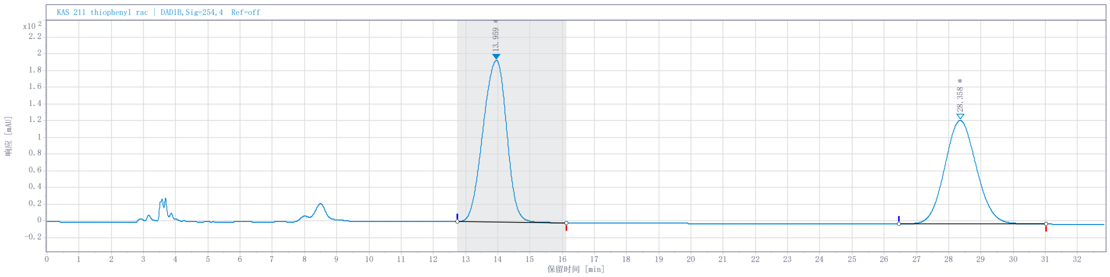
3j



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
8. 05	1. 85	63. 14	2. 09	3. 42
34. 6	5. 70	1782. 60	15. 55	96. 58

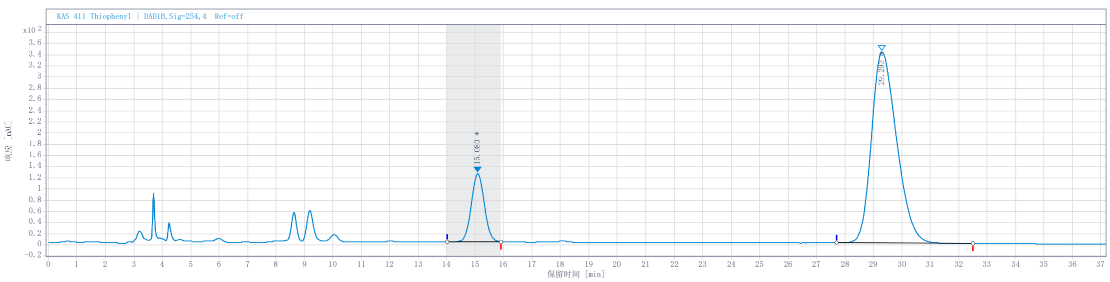
3k Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
14. 0	3. 37	9851. 66	193. 48	53. 82
28. 4	4. 55	8451. 79	123. 89	46. 18

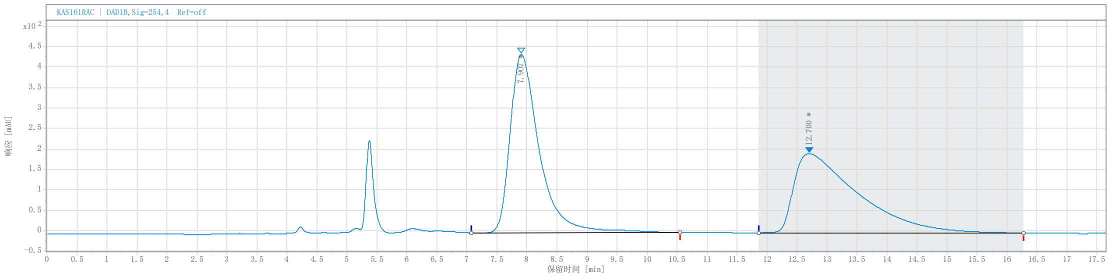
3k



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
15. 1	1. 91	3864. 54	122. 25	15. 52
29. 3	4. 79	21038. 83	341. 97	84. 48

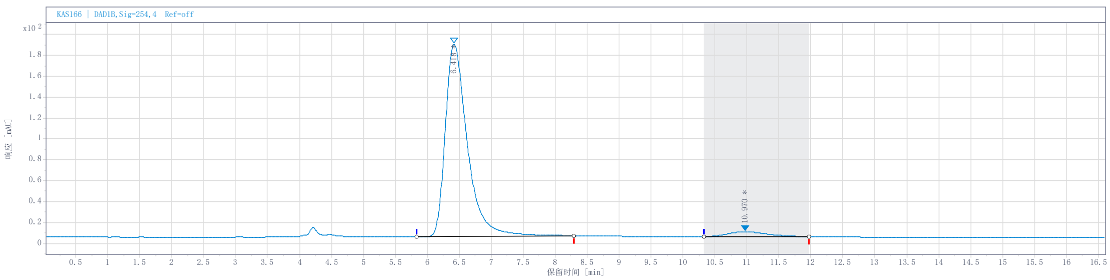
3l Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
7.91	3.48	14712.66	435.63	50.69
12.7	4.41	14309.37	193.51	49.31

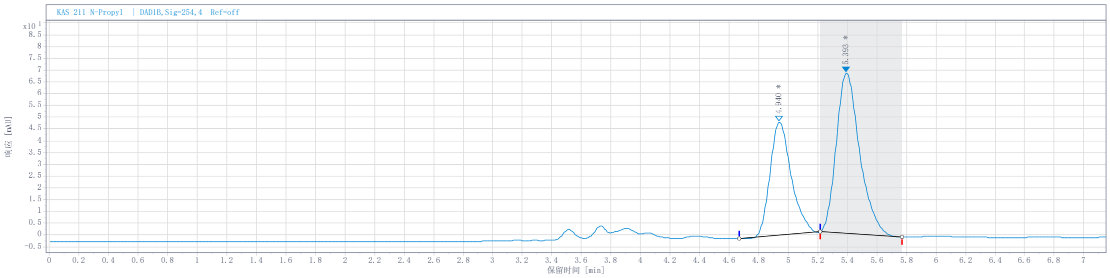
3l



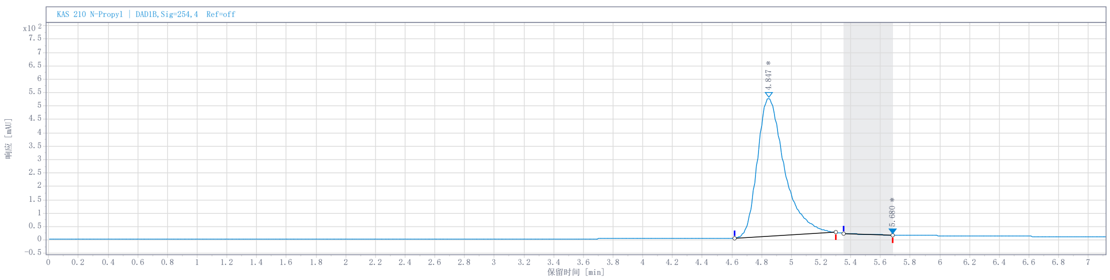
Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
6.42	2.45	4435.41	184.46	95.66
11.0	1.64	201.08	4.64	4.34

3m Racemic Mixture

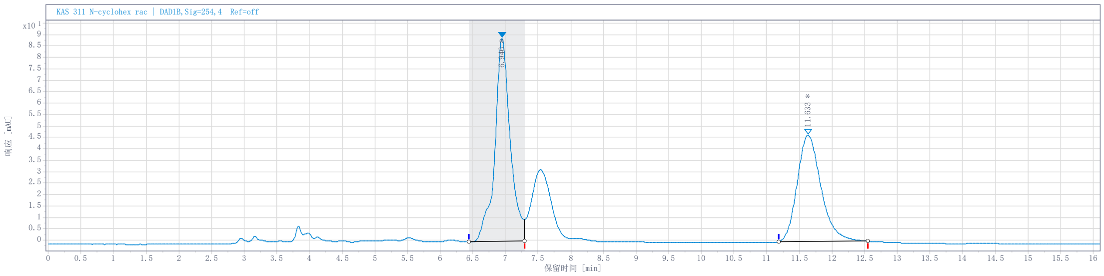


Signal:	DAD1B, Sig=254, 4 Ref=off			
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
4.94	0.55	473.21	47.90	38.68
5.39	0.55	750.22	68.09	61.32



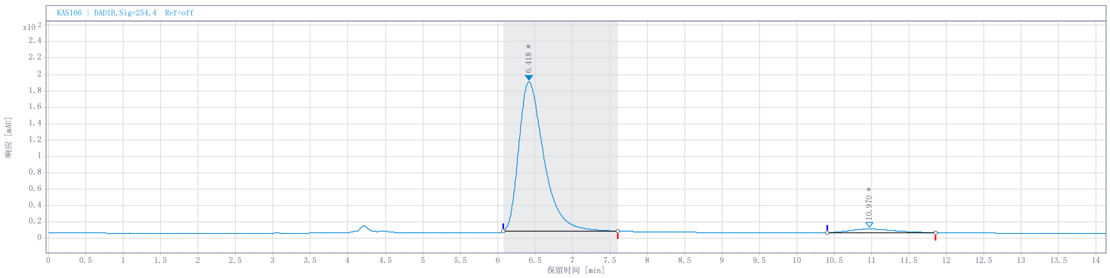
Signal:	DAD1B, Sig=254, 4 Ref=off			
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
4.85	0.68	6548.93	513.89	99.78
5.68	0.33	14.17	0.00	0.22

3n Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

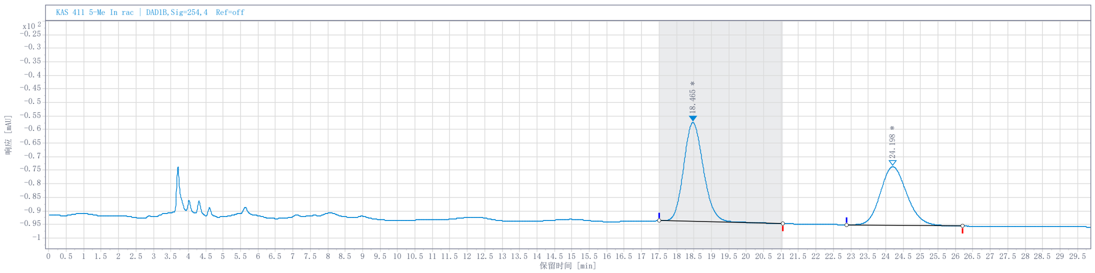
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
6. 95	0. 86	1465. 38	88. 86	55. 45
11. 6	1. 36	1177. 54	46. 48	44. 55



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
6. 42	1. 52	4254. 20	182. 66	95. 84
11. 0	1. 45	184. 53	4. 46	4. 16

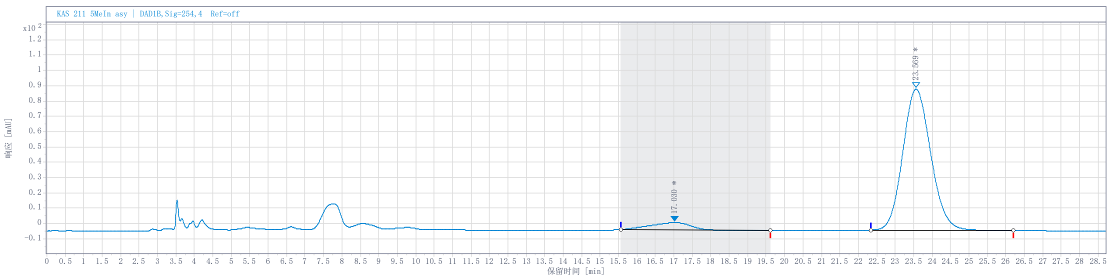
3o Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
18. 5	3. 56	1442. 01	36. 51	55. 81
24. 2	3. 32	1141. 78	21. 61	44. 19

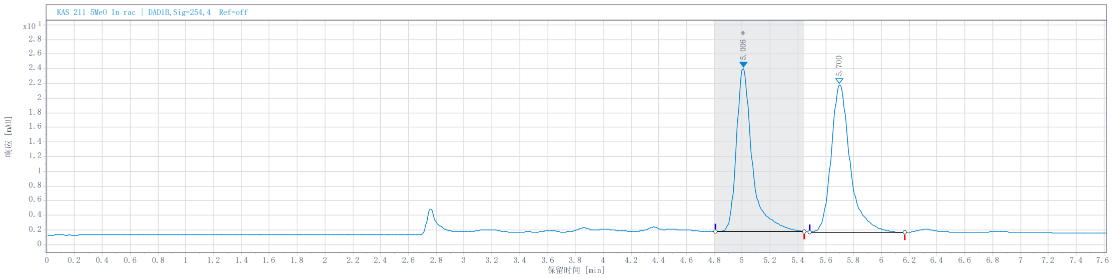
3o



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
17. 0	4. 05	348. 42	4. 73	6. 71
23. 6	3. 86	4846. 80	92. 10	93. 29

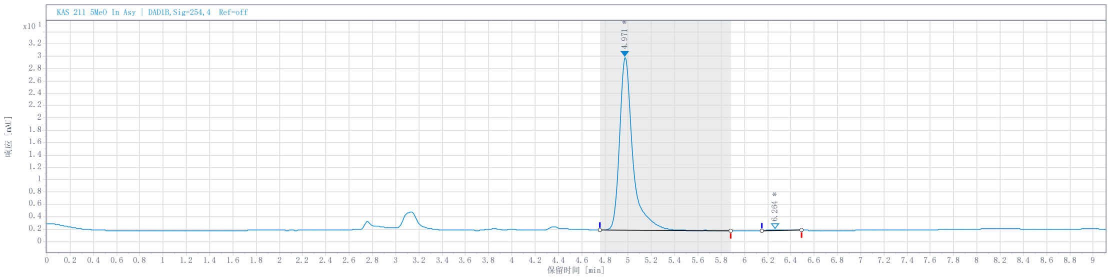
3p Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
5.01	0.64	177.19	22.21	48.18
5.70	0.68	190.59	20.05	51.82

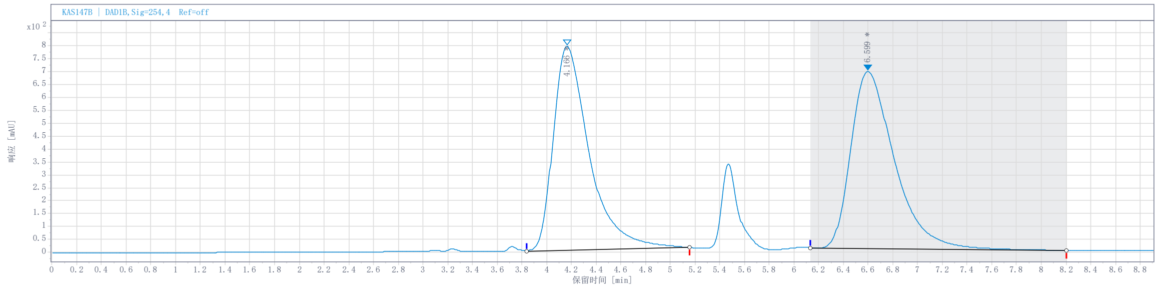
3p



Signal: DAD1B, Sig=254, 4 Ref=off

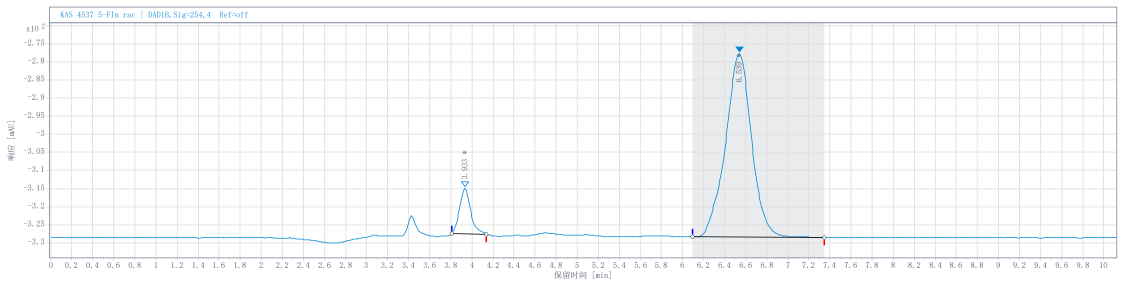
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
4.97	1.13	220.78	27.98	99.51
6.26	0.34	1.09	0.14	0.49

3q Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

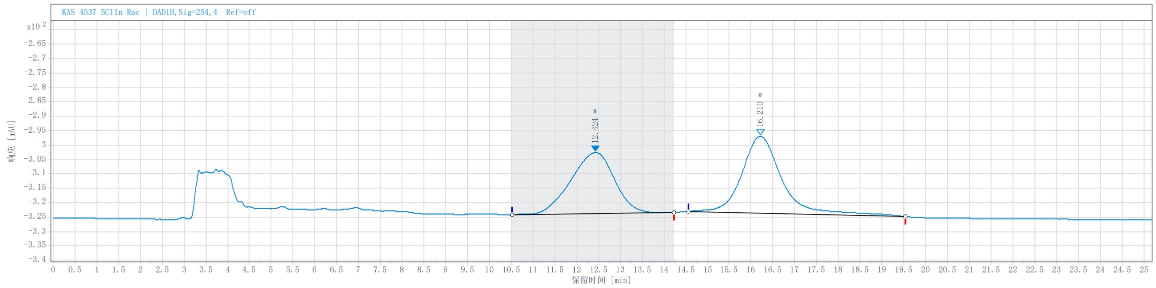
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
4. 17	1. 32	15995. 57	788. 16	48. 88
6. 60	2. 08	16728. 67	682. 79	51. 12



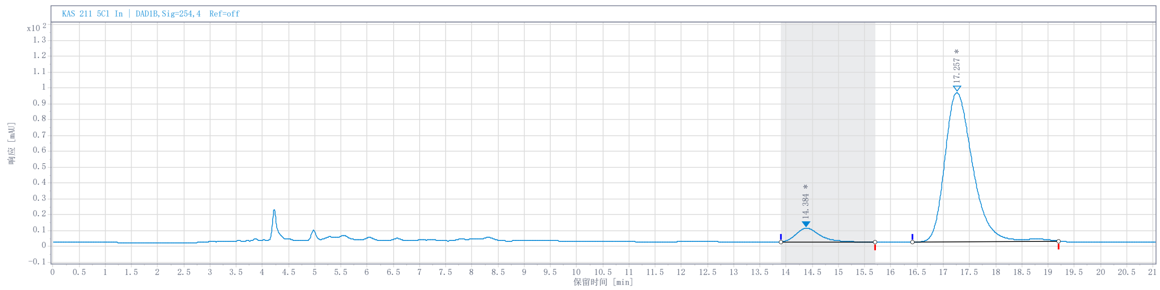
Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
3. 93	0. 33	91. 37	12. 50	9. 48
6. 54	1. 25	872. 34	50. 69	90. 52

3r Racemic Mixture

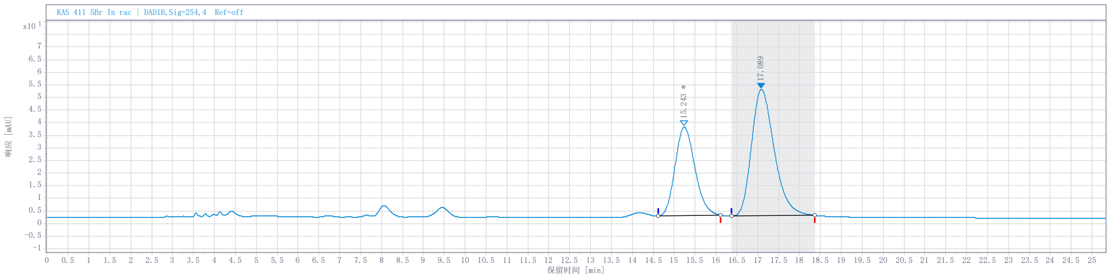


Signal:	DAD1B, Sig=254, 4 Ref=off			
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
12.4	3.71	1462.46	21.15	46.31
16.2	4.97	1695.31	26.69	53.69



Signal:	DAD1B, Sig=254, 4 Ref=off			
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
14.4	1.80	270.83	8.59	7.23
17.3	2.79	3474.15	93.93	92.77

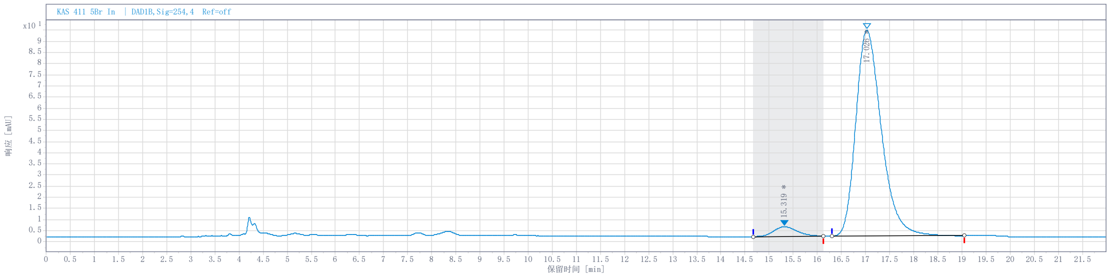
3s Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
15. 2	1. 50	1158. 84	35. 12	37. 91
17. 1	2. 00	1898. 01	50. 24	62. 09

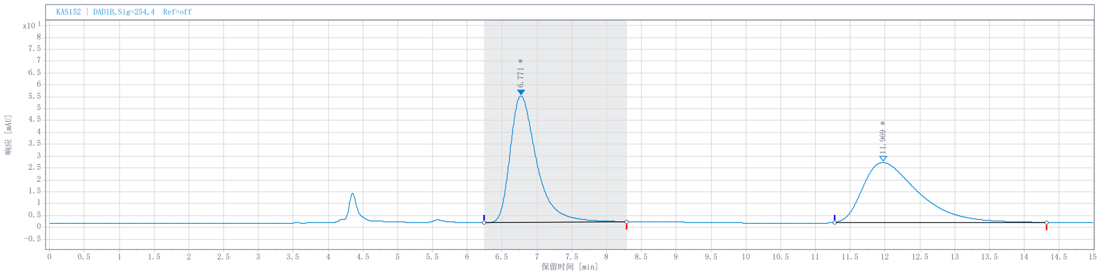
3s



Signal: DAD1B, Sig=254, 4 Ref=off

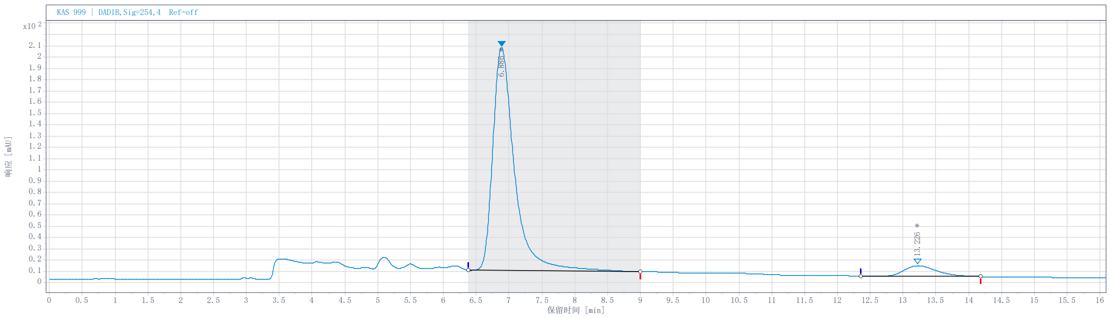
RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
15. 3	1. 46	144. 96	4. 33	4. 08
17. 0	2. 74	3412. 22	92. 40	95. 92

4a Racemic Mixture



Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
6.77	2.05	1409.73	53.34	50.29
12.0	3.04	1393.62	25.20	49.71

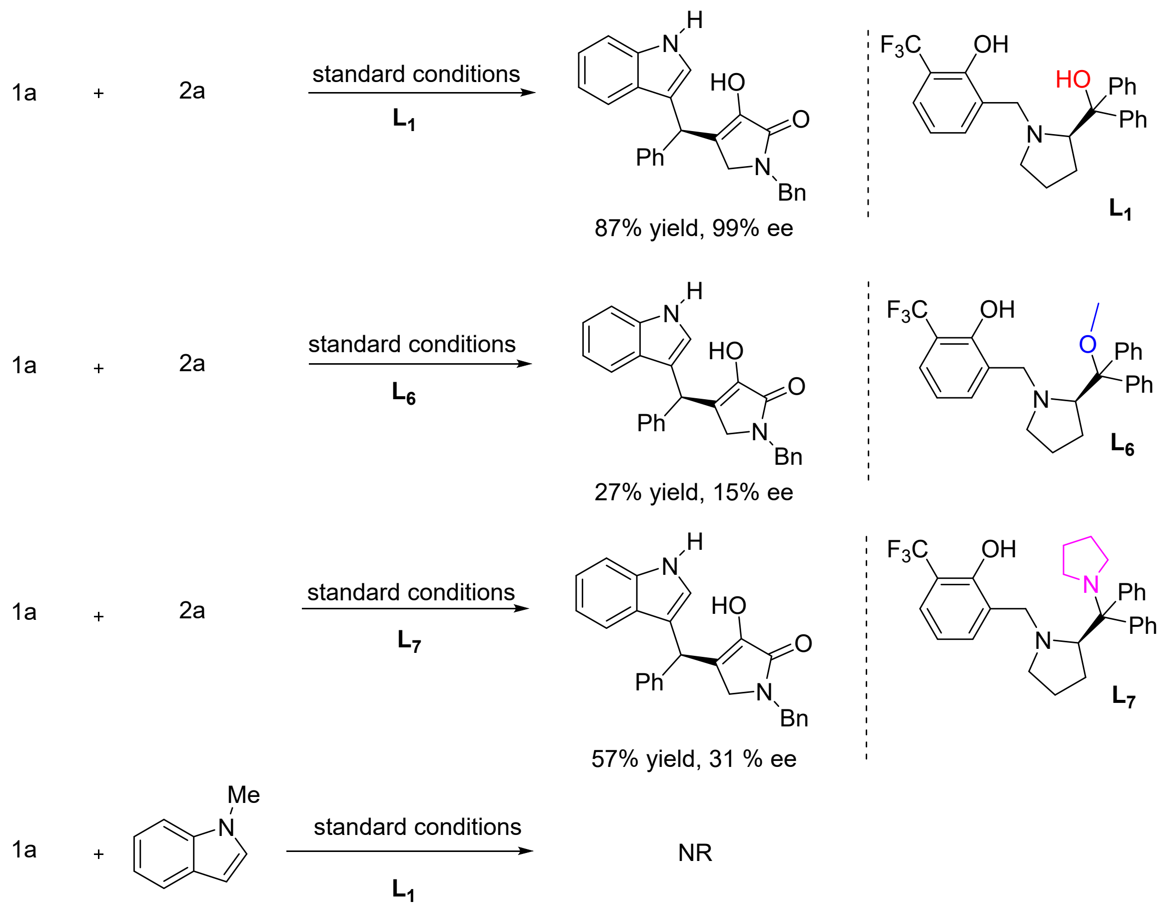


Signal: DAD1B, Sig=254, 4 Ref=off

RetTime [min]	width [min]	Arer [mAU*s]	Height [mAU]	Area%
6.89	2.62	4552.64	197.89	93.46
13.2	1.82	318.44	9.36	6.54

Part 5: Mechanistic Study

5.1 Control Experiments



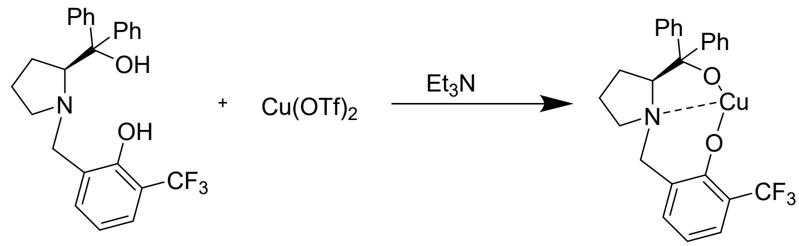
Scheme S1: Control Experiments

5.2 XPS analyses

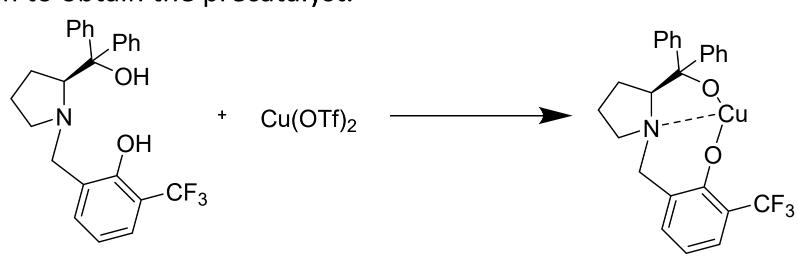
a) Preparation of samples

Sample 1: $Cu(OTf)_2$

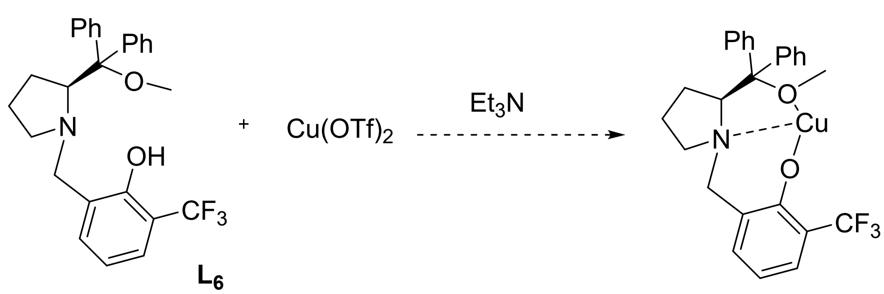
Sample 2: The pre-catalyst was prepared by mixing **L_1** (10 mol %), $Cu(OTf)_2$ (10 mol %) and Et_3N (20 mol %) in H_2O/Tol (0.9/0.1)mL and stirred for two hours at ambient atmosphere, then evaporated in vacuum. Extract with DCM dry by anhydrous MgSO4 and evaporated in vacuum to obtain the precatalyst.



Sample 3: The pre-catalyst was prepared by mixing **L_1** (10 mol %), and $Cu(OTf)_2$ (20 mol %) in H_2O/Tol (0.9/0.1) mL and stirred for two hours at ambient atmosphere, then evaporated in vacuum. Extract with DCM dry by anhydrous $MgSO_4$ and evaporated in vacuum to obtain the precatalyst.



Sample 4: the pre-catalyst was prepared by mixing **L_6** (10 mol %), $Cu(OTf)_2$ (10 mol %) and Et_3N (20 mol %) in H_2O/Tol (0.9/0.1) mL and stirred for two hours at ambient atmosphere, then evaporated in vacuum. Extract with DCM dry by anhydrous $MgSO_4$ and evaporated in vacuum to obtain the precatalyst.



Sample 5: the pre-catalyst was prepared by mixing **L_7** (10 mol %), $Cu(OTf)_2$ (10 mol %) and Et_3N (20 mol %) in H_2O/Tol (0.9/0.1) mL and stirred for two hours at ambient atmosphere, then evaporated in vacuum. Extract with DCM, dry by anhydrous $MgSO_4$ and evaporated in vacuum to obtain the precatalyst.

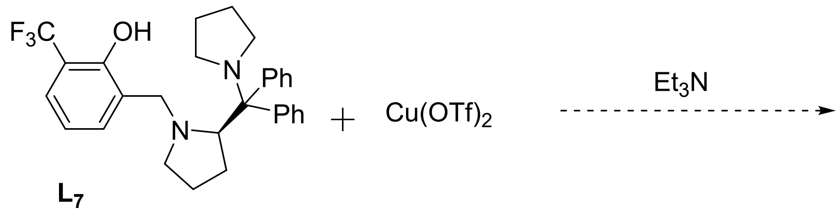


Table S3: Spectra of XPS

		Sample 1	Sample 2	Sample 3	Sample 4	Sample 5
1st Bend	Binding Energy (eV)	952.90	953.45	953.25	952.92	952.78
	Intensity (a.u)	18108.06	5679.07	3543.11	3156.75	4068.87
2nd Bend	Binding Energy (eV)	933.00	933.65	933.15	932.72	932.99
	Intensity (a.u)	22602.80	6354.11	3821.91	3334.56	4301.56

Cu 2P

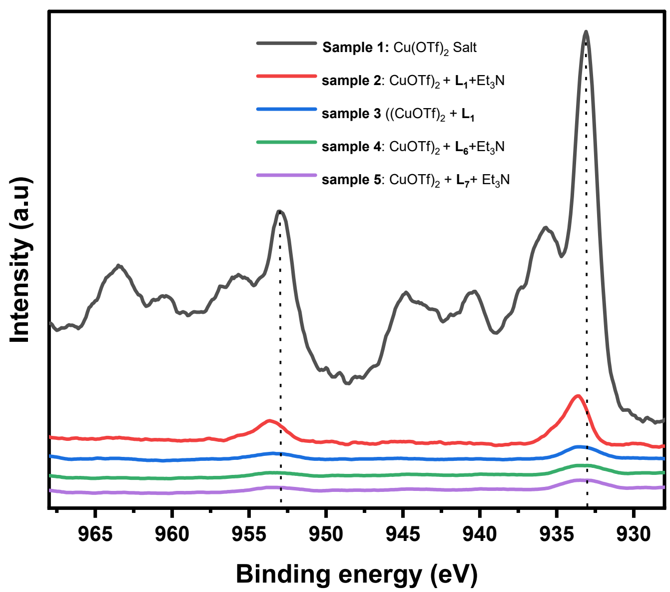


Figure S1: Grey line- sample 1 (Pure $Cu(OTf)_2$ Salt), Red Line-sample 2 ($Cu(OTf)_2$ + $\mathbf{L_1}$ +Et_3N), Blue Line-sample 3 ($Cu(OTf)_2$ + $\mathbf{L_1}$), Green Line-sample 4 ($Cu(OTf)_2$ + $\mathbf{L_6}$+Et_3N), Mauve Line-sample 5 ($Cu(OTf)_2$ + $\mathbf{L_7}$+Et_3N).

To further understand the reaction mechanism with regards the coordination environment around the copper center , we empolyed XPS analysis to investigate five samples as shown above, from the spectra of the XPS, it was observed that the binding energy increased considerably when **L_1** with aliphatic OH group is added to the Cu salts in the presence of the base (sample 2, Red line) Compared to the binding energy of the pure copper salt (sample 1, grey line), only a slight increase was also observed when a base was not used (sample 3, blue line). We suppose the excess base could accelerate the rate of this reaction, perhaps due to the dehydro-alkenylation of indole. On the contrary the binding energy was observed to decrease when the copper is coordinated with ligand **L_6** and **L_7** respectively even in the presence of a base. The increase in binding energy of the Cu **2P** of the precatalyst indicate decrease in electronic density which should come as a result of the coordination with the hydroxyl group of **L_1**. Binding energy difference of +0.5-0.6 ev (0.55 eV in our study with sample 1&2) for **2p** confirm complete chelation for Oxygen of the ligands in the copper metal complex. Our result appears reasonable and in keeping with the donor-acceptor concept of the Feltham-Brant possibly of empty S3d orbitals with respect to oxygen ligands.[1] The decrease in binding energy of the Cu **2P** of precatalyst ligand **L_6** and **L_7** indicated increase in electronic density which should come as a result of poor coordination with the methoxy and pyrrolidine groups of the ligand.

The catalyst is a complex of copper ion with the ligand, which was confirmed by the XPS experimental results. The copper ion of this complex should take a tri-dentate model, leaving the vacant to coordinate with the electron rich group. In comparison with water, the oxygen atom of 2,3-dioxopyrrolidine (**1a**) has a higher nucleophilicity than the oxygen in water since the O=C double bond at the 2,3-dioxopyrrolidine ring can conjugate with the neighboring sterene group, which assists the oxygen to bind the copper ions. On the other hand, NH at the indol ring (**2a**) has a higher than the oxygen. As a result, the indole (**2a**) occupies the other vacant of the copper ion. More importantly, the addition between **1a** and **2a** occurs once **1a** and **2a** coordinate with the copper ion to give the stable adduct, which promote the **1a** and **2a** coordination with the copper ions. When water binds to the center ions, in contrast, no adduct can be obtained. In other words, the nucleophile addition also assists the coordination of **1a** and **2a** with the copper ions.

Table S4: XPS DATA Binding Energy and Counts per second (Intensity).

Sample1: Cu(OTf)$_2$ 2Sp		**Sample2: Base Cu 2Sp**		**Sample3 Without Base Cu 2p**		**Sample 4 OMe Cu 2p**		**Sample 5 Py; Cu2sp**	
Binding energy (eV)	Counts per second	Binding energy (eV)	Counts per second	Binding energy (eV)	Counts per second	Binding energy (eV)	Counts per second	Binding energy (eV)	Counts per second
955.9017	15990.53	955.9525	5201.61	955.9454	3386.151	955.9186	3071.134	955.9808	3824.1

955.8017	16018.19	955.8525	5094.044	955.8454	3357.613	955.8186	2989.911	955.8808	3848.248
955.7017	15879.89	955.7525	5176.365	955.7454	3378.467	955.7186	3059.061	955.7808	3813.124
955.6017	16250.23	955.6525	5263.077	955.6454	3385.053	955.6186	3150.163	955.6808	3850.443
955.5017	15932.14	955.5525	5197.22	955.5454	3389.444	955.5186	3143.577	955.5808	3814.222
955.4017	16058.15	955.4525	5168.682	955.4454	3259.925	955.4186	3102.965	955.4808	3923.983
955.3017	15732.37	955.3525	5090.751	955.3454	3330.172	955.3186	3006.375	955.3808	3920.69
955.2017	15965.95	955.2525	5207.098	955.2454	3437.739	955.2186	3028.327	955.2808	3847.15
955.1017	15987.46	955.1525	5201.61	955.1454	3392.736	955.1186	3037.108	955.1808	3948.131
955.0017	16095.03	955.0525	5261.979	955.0454	3433.348	955.0186	3053.572	955.0808	3943.74
954.9017	15776.94	954.9525	5348.691	954.9454	3472.862	954.9186	3042.596	954.9808	3899.836
954.8017	15629.42	954.8525	5216.977	954.8454	3371.882	954.8186	3121.625	954.8808	3869.102
954.7017	15753.89	954.7525	5283.932	954.7454	3424.567	954.7186	3123.82	954.7808	3911.91
954.6017	15812.28	954.6525	5332.227	954.6454	3379.565	954.6186	3045.889	954.6808	3833.979
954.5017	15867.6	954.5525	5312.47	954.5454	3486.034	954.5186	3073.33	954.5808	3910.812
954.4017	15899.87	954.4525	5389.303	954.4454	3499.205	954.4186	3084.306	954.4808	3937.155
954.3017	16004.36	954.3525	5433.208	954.3454	3465.179	954.3186	3038.206	954.3808	3925.081
954.2017	15915.24	954.2525	5439.793	954.2454	3433.348	954.2186	3098.575	954.2808	4010.695
954.1017	16041.24	954.1525	5406.865	954.1454	3443.227	954.1186	3108.453	954.1808	3922.886
954.0017	16150.35	954.0525	5435.403	954.0454	3422.372	954.0186	3042.596	954.0808	3917.398
953.9017	16084.27	953.9525	5539.677	953.9454	3434.446	953.9186	3100.77	953.9808	3992.036
953.8017	16293.26	953.8525	5614.315	953.8454	3532.134	953.8186	3046.987	953.8808	3897.641
953.7017	16546.81	953.7525	5562.727	953.7454	3478.351	953.7186	3039.303	953.7808	3877.883
953.6017	16834.16	953.6525	5524.31	953.6454	3454.203	953.6186	3023.937	953.6808	3897.641
953.5017	16918.68	953.5525	5660.415	953.5454	3460.789	953.5186	3022.839	953.5808	3917.398
953.4017	17350.48	953.4525	5679.074	953.4454	3447.617	953.4186	3018.449	953.4808	3933.862
953.3017	17576.37	953.3525	5616.51	953.3454	3437.739	953.3186	3049.182	953.3808	4022.769
953.2017	17631.69	953.2525	5405.767	953.2454	3543.11	953.2186	3088.696	953.2808	4033.745
953.1017	17756.16	953.1525	5493.577	953.1454	3505.791	953.1186	3149.065	953.1808	3996.426
953.0017	17510.3	953.0525	5454.062	953.0454	3533.231	953.0186	3139.187	953.0808	3994.231
952.9017	18108.06	952.9525	5433.208	952.9454	3532.134	952.9186	3156.749	952.9808	3982.157
952.8017	17605.57	952.8525	5369.546	952.8454	3424.567	952.8186	3147.968	952.8808	3989.84
952.7017	17508.76	952.7525	5277.346	952.7454	3539.817	952.7186	3020.644	952.7808	4068.869
952.6017	17459.59	952.6525	5251.003	952.6454	3502.498	952.6186	3120.527	952.6808	4052.405
952.5017	17368.92	952.5525	5400.279	952.5454	3476.155	952.5186	3099.672	952.5808	3954.717
952.4017	16957.1	952.4525	5285.029	952.4454	3393.834	952.4186	3133.699	952.4808	4013.988
952.3017	16743.5	952.3525	5286.127	952.3454	3486.034	952.3186	3064.549	952.3808	4004.109
952.2017	16294.79	952.2525	5208.196	952.2454	3443.227	952.2186	3062.353	952.2808	3959.107
952.1017	15781.55	952.1525	5201.61	952.1454	3367.491	952.1186	3023.937	952.1808	3892.152
952.0017	15752.35	952.0525	5128.07	952.0454	3407.005	952.0186	2995.399	952.0808	3857.029
951.9017	15535.68	951.9525	5155.51	951.9454	3410.298	951.9186	3042.596	951.9808	3865.81
951.8017	14937.92	951.8525	4955.744	951.8454	3462.984	951.8186	3010.765	951.8808	3883.371
951.7017	15016.29	951.7525	4989.77	951.7454	3344.441	951.7186	3097.477	951.7808	3850.443
951.6017	14879.53	951.6525	5088.556	951.6454	3380.663	951.6186	3129.308	951.6808	3964.595

951.5017	14698.2	951.5525	5056.725	951.5454	3355.417	951.5186	3062.353	951.5808	3882.274
951.4017	14407.77	951.4525	4928.304	951.4454	3343.344	951.4186	3136.991	951.4808	3786.781
951.3017	13943.7	951.3525	4988.673	951.3454	3370.784	951.3186	3104.063	951.3808	3852.638
951.2017	14134.24	951.2525	5097.337	951.2454	3419.079	951.2186	3030.523	951.2808	3839.467
951.1017	14188.03	951.1525	5049.041	951.1454	3322.489	951.1186	3017.351	951.1808	3906.421
951.0017	13876.08	951.0525	5078.677	951.0454	3278.584	951.0186	3073.33	951.0808	3891.055
950.9017	13785.42	950.9525	5055.627	950.9454	3344.441	950.9186	3108.453	950.9808	3894.348
950.8017	13770.05	950.8525	5060.018	950.8454	3326.879	950.8186	3141.382	950.8808	3960.205
950.7017	13542.63	950.7525	5069.896	950.7454	3282.975	950.7186	3117.234	950.7808	3876.786
950.6017	13591.8	950.6525	4994.161	950.6454	3311.513	950.6186	3021.742	950.6808	3917.398
950.5017	13647.12	950.5525	4930.499	950.5454	3354.32	950.5186	3051.377	950.5808	3848.248
950.4017	13368.98	950.4525	4909.644	950.4454	3277.486	950.4186	3053.572	950.4808	3839.467
950.3017	13249.12	950.3525	4950.256	950.3454	3377.37	950.3186	3121.625	950.3808	3833.979
950.2017	13550.31	950.2525	4983.184	950.2454	3378.467	950.2186	3104.063	950.2808	3817.514
950.1017	13553.38	950.1525	5020.503	950.1454	3371.882	950.1186	3111.746	950.1808	3819.71
950.0017	13562.6	950.0525	5018.308	950.0454	3312.61	950.0186	3056.865	950.0808	3904.226
935.9017	17241.38	935.9525	5083.068	935.9454	3362.003	935.9186	3098.575	935.9808	3880.079
935.8017	17287.48	935.8525	5182.951	935.8454	3321.391	935.8186	3055.768	935.8808	3868.005
935.7017	17218.33	935.7525	5184.048	935.7454	3262.12	935.7186	3040.401	935.7808	4003.012
935.6017	17318.21	935.6525	5210.391	935.6454	3343.344	935.6186	3118.332	935.6808	4042.526
935.5017	17442.68	935.5525	5320.153	935.5454	3324.684	935.5186	3205.044	935.5808	3909.714
935.4017	17103.08	935.4525	5306.982	935.4454	3367.491	935.4186	3100.77	935.4808	3936.057
935.3017	16960.17	935.3525	5279.541	935.3454	3363.101	935.3186	3161.139	935.3808	3885.567
935.2017	17156.86	935.2525	5400.279	935.2454	3402.615	935.2186	3126.015	935.2808	3873.493
935.1017	17202.96	935.1525	5467.234	935.1454	3453.105	935.1186	3179.799	935.1808	3919.593
935.0017	16821.87	935.0525	5492.479	935.0454	3479.448	935.0186	3168.822	935.0808	4056.795
934.9017	16706.62	934.9525	5519.919	934.9454	3436.641	934.9186	3134.796	934.9808	3977.767
934.8017	16746.57	934.8525	5667	934.8454	3393.834	934.8186	3084.306	934.8808	3943.74
934.7017	16543.73	934.7525	5645.048	934.7454	3495.912	934.7186	3104.063	934.7808	3943.74
934.6017	16460.75	934.6525	5632.974	934.6454	3458.593	934.6186	3172.115	934.6808	3995.328
934.5017	16654.37	934.5525	5519.919	934.5454	3542.012	934.5186	3195.165	934.5808	4133.628
934.4017	16835.7	934.4525	5690.05	934.4454	3551.891	934.4186	3140.284	934.4808	4073.259
934.3017	17136.89	934.3525	5747.126	934.3454	3490.424	934.3186	3119.43	934.3808	4051.307
934.2017	17212.18	934.2525	5910.671	934.2454	3509.084	934.2186	3180.896	934.2808	4142.409
934.1017	17688.55	934.1525	6037.995	934.1454	3618.846	934.1186	3192.97	934.1808	4134.726
934.0017	18103.45	934.0525	6186.173	934.0454	3604.577	934.0186	3246.753	934.0808	4095.212
933.9017	18698.14	933.9525	6128	933.9454	3742.876	933.9186	3304.927	933.9808	4091.919
933.8017	19581.72	933.8525	6216.907	933.8454	3608.967	933.8186	3176.506	933.8808	4141.312
933.7017	20201	933.7525	6114.828	933.7454	3668.238	933.7186	3123.82	933.7808	4112.774
933.6017	20981.62	933.6525	6354.109	933.6454	3704.46	933.6186	3258.827	933.6808	4186.314
933.5017	21227.49	933.5525	6349.718	933.5454	3741.779	933.5186	3198.458	933.5808	4266.44
933.4017	21892.86	933.4525	6272.885	933.4454	3709.948	933.4186	3226.996	933.4808	4271.928
933.3017	22272.42	933.3525	6258.616	933.3454	3662.75	933.3186	3192.97	933.3808	4254.366

933.2017	22673.49	933.2525	6130.195	933.2454	3719.826	933.2186	3248.948	933.2808	4243.39
933.1017	22544.41	933.1525	6010.555	933.1454	3821.905	933.1186	3220.41	933.1808	4318.028
933.0017	22602.8	933.0525	5782.25	933.0454	3712.143	933.0186	3239.07	933.0808	4243.39
932.9017	22229.39	932.9525	5660.415	932.9454	3622.138	932.9186	3184.189	932.9808	4301.564
932.8017	21703.85	932.8525	5572.605	932.8454	3646.286	932.8186	3190.775	932.8808	4224.731
932.7017	21046.16	932.7525	5521.017	932.7454	3692.386	932.7186	3334.563	932.7808	4207.169
932.6017	20492.96	932.6525	5366.253	932.6454	3547.5	932.6186	3217.118	932.6808	4204.973
932.5017	19819.9	932.5525	5188.439	932.5454	3641.896	932.5186	3095.282	932.5808	4110.578
932.4017	18782.65	932.4525	5241.125	932.4454	3491.522	932.4186	3200.653	932.4808	4031.55
932.3017	17768.46	932.3525	5189.537	932.3454	3528.841	932.3186	3154.553	932.3808	4097.407
932.2017	17090.79	932.2525	5054.53	932.2454	3549.696	932.2186	3222.606	932.2808	3973.376
932.1017	16383.92	932.1525	5034.772	932.1454	3477.253	932.1186	3226.996	932.1808	4114.969
932.0017	15895.26	932.0525	4968.915	932.0454	3415.786	932.0186	3189.677	932.0808	4083.138
931.9017	15206.83	931.9525	5031.48	931.9454	3338.953	931.9186	3190.775	931.9808	4038.136
931.8017	14587.56	931.8525	4999.649	931.8454	3417.982	931.8186	3207.239	931.8808	3920.69
931.7017	13900.67	931.7525	4987.575	931.7454	3362.003	931.7186	3206.141	931.7808	3990.938
931.6017	13708.59	931.6525	5036.968	931.6454	3419.079	931.6186	3174.31	931.6808	3973.376
931.5017	13310.59	931.5525	4884.399	931.5454	3495.912	931.5186	3138.089	931.5808	3949.229
931.4017	13310.59	931.4525	4829.518	931.4454	3405.908	931.4186	3186.384	931.4808	3854.833
931.3017	13150.78	931.3525	4957.939	931.3454	3388.346	931.3186	3214.922	931.3808	4001.914
931.2017	12780.44	931.2525	4932.694	931.2454	3386.151	931.2186	3181.994	931.2808	3949.229
931.1017	12880.32	931.1525	4954.646	931.1454	3347.734	931.1186	3176.506	931.1808	4027.159
931.0017	12553.01	931.0525	4921.718	931.0454	3393.834	931.0186	3213.825	931.0808	3993.133
930.9017	12466.96	930.9525	4892.082	930.9454	3488.229	930.9186	3267.608	930.9808	3999.719
930.8017	12423.93	930.8525	4908.546	930.8454	3389.444	930.8186	3202.848	930.8808	4007.402
930.7017	12301	930.7525	5024.894	930.7454	3293.951	930.7186	3210.532	930.7808	4056.795
930.6017	12383.98	930.6525	4839.397	930.6454	3412.493	930.6186	3190.775	930.6808	3945.936
930.5017	12402.42	930.5525	4926.108	930.5454	3368.589	930.5186	3194.068	930.5808	4023.867
930.4017	12396.27	930.4525	5008.43	930.4454	3367.491	930.4186	3188.579	930.4808	3915.202
930.3017	12313.3	930.3525	4914.035	930.3454	3443.227	930.3186	3192.97	930.3808	3929.471
930.2017	12328.66	930.2525	4942.573	930.2454	3345.539	930.2186	3116.137	930.2808	3928.374
930.1017	12271.81	930.1525	4949.158	930.1454	3323.586	930.1186	3093.087	930.1808	3847.15
930.0017	12161.17	930.0525	4909.644	930.0454	3347.734	930.0186	3048.084	930.0808	3992.036

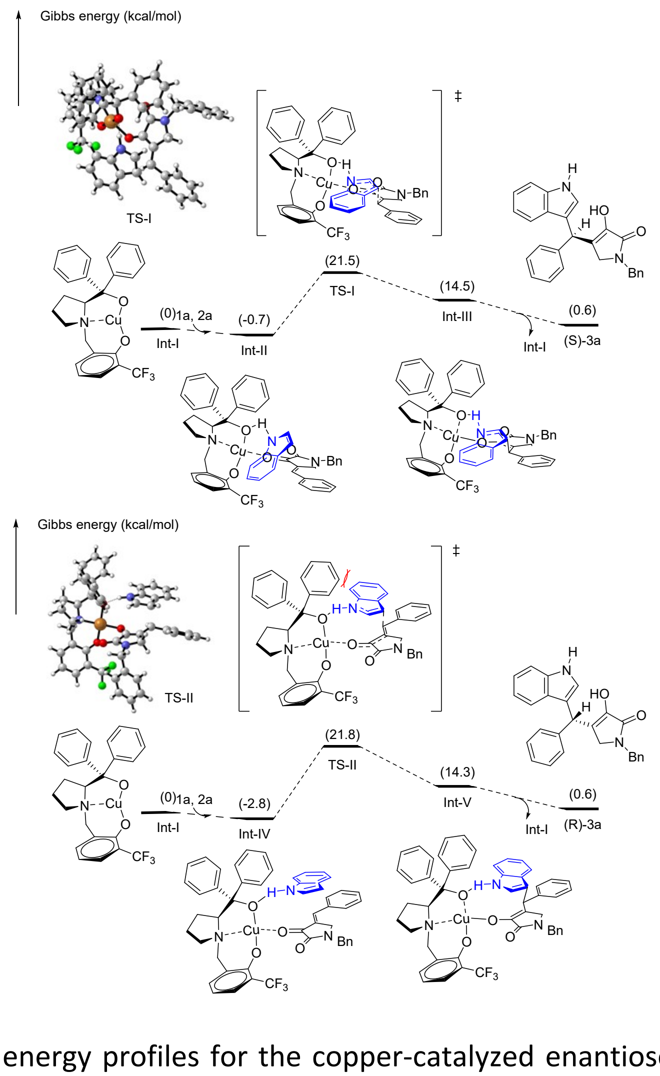
5.3 DFT calculations

All the calculations were performed using Gaussian 16 software packages.[2] The geometry of all reactants and transition states were optimized using the (U)B3LYP[3]-D3(Becke-Johnson damping function)[4] in water (using SMD solvation model[5]). In these geometry optimizations, a basis set of SDD[6] for Cu, while 6-31G(d)[7] for all the other atoms was used. Vibrational frequency analysis was calculated at the same level of theory to validate each structure as either a minimum or a transition state and to evaluate its zero-point energy and thermal corrections at 298 K. For each transition state, the intrinsic reaction coordinate (IRC) analysis was conducted to ensure that it connects the right reactant and product.[8] To obtain more accurate energies, solution-phase single point energy calculations were performed at the (U)B3LYP-D3(BJ)/6-311+G(d,p)-SDD level.

Table S5: Thermal correction of Gibbs free energy (TCG, hartree) and single point energies (SP, hartree) in water for all species involved in this study

Compounds	TCG	SP	Compounds	TCG	SP
Int-I	0.365206	-1668.601983	**(*S*)-3a**	0.363582	1264.461732
1a	0.241559	-900.488349	**Int-IV**	0.753729	2933.093944
2a	0.099816	-363.952075	**TS-II**	0.757059	2933.058156

Int-II	0.754124	-2933.090446	**Int-V**	0.757316	2933.070396
TS-I	0.755729	-2933.057242	**(*R*)-3a**	0.363578	1264.461732
Int-III	0.756902	-2933.069683			



Scheme S2: Gibbs energy profiles for the copper-catalyzed enantioselective of **1a** with **2a**. Gibbs energies in solution (in kcal/mol).

1a

C	0.03581200	0.28220200	-0.76126900
H	0.43145400	-0.00466900	-1.74211700
H	-0.17040700	-0.63579500	-0.19839200
C	0.18507000	2.44657300	0.26287000
C	-1.21314200	2.24840100	-0.32049900
O	0.53025400	3.46654700	0.85342000
O	-2.14796900	3.05275400	-0.23812000
C	0.93993500	1.22773500	-0.01594900
C	2.23107400	1.09600400	0.37192400
H	2.64116200	1.96066000	0.89259800
C	3.15873400	-0.00567700	0.19908500
C	4.48095000	0.18125000	0.65549300
C	2.82067800	-1.24155500	-0.39344900
C	5.43438100	-0.82180100	0.51882700
H	4.74798200	1.12801300	1.11628500
C	3.77662100	-2.24280600	-0.52581600
H	1.81449900	-1.42837600	-0.74493900
C	5.08424200	-2.03766300	-0.07383000
H	6.44736600	-0.65853800	0.87355900
H	3.50237500	-3.18875700	-0.98267500
H	5.82542500	-2.82388000	-0.18186000
N	-1.20580700	1.04520700	-0.92997300
C	-2.39614400	0.41717100	-1.49608400
H	-3.10104300	1.22221800	-1.71481800
H	-2.11312500	-0.06149400	-2.43772900
C	-3.00141900	-0.59470500	-0.54766000
C	-3.65233600	-0.16224900	0.61587000

C	-2.88557600	-1.96526500	-0.79737000
C	-4.18340500	-1.08914100	1.51147600
H	-3.73749700	0.90273900	0.81438100
C	-3.41895900	-2.89563100	0.09845600
H	-2.37749800	-2.30278900	-1.69694100
C	-4.06824800	-2.45893500	1.25392900
H	-4.68954000	-0.74490800	2.40886100
H	-3.32485300	-3.95822600	-0.10639800
H	-4.48352800	-3.18050300	1.95156100

2a

C	0.25011100	-0.67172200	0.00035300
C	0.24889200	0.75533300	0.00029200
C	-0.98566000	1.43062900	0.00012600
C	-2.16139100	0.68920200	-0.00016000
C	-2.13454200	-0.72250900	-0.00018000
C	-0.93148000	-1.42067000	0.00009800
C	2.38882100	0.02965400	-0.00022800
C	1.62518100	1.17082500	-0.00015500
H	-1.01659000	2.51705000	0.00024600
H	-3.11950400	1.20136600	-0.00044500
H	-3.07045200	-1.27386900	-0.00054600
H	-0.90607200	-2.50653100	0.00019600
H	1.88223800	-2.03989500	-0.00077200
H	3.46291300	-0.09077900	-0.00061300
H	1.99725700	2.18629600	0.00002200
N	1.56723100	-1.07972600	0.00014700

Int-I

C	0.20976800	0.42030700	1.82506700

C	-1.37037600	-1.03397300	0.74890400
C	-1.78919600	-0.96396900	2.22684200
C	-0.89185600	0.12138100	2.86568700
H	1.21855300	0.36910700	2.23500100
H	0.07503400	1.40430700	1.37967200
H	-1.39043600	-2.05592500	0.36721300
H	-2.85104700	-0.74767800	2.34600800
H	-1.60179500	-1.93621700	2.69186300
H	-1.45828700	1.03062300	3.07963400
H	-0.46067100	-0.23323700	3.80527200
N	0.07074500	-0.61131500	0.75234800
C	0.99048000	-1.77013500	0.96341500
H	0.75129400	-2.26529700	1.91202600
H	0.78126000	-2.48022400	0.15586800
C	2.44306400	-1.36401800	0.96494800
C	3.00067300	-0.58678000	-0.08987600
C	3.25667400	-1.76971000	2.02421100
C	4.37974700	-0.26044000	-0.00791800
C	4.61597000	-1.45491200	2.08044600
H	2.80684800	-2.35038000	2.82575100
C	5.17215000	-0.69387100	1.05696200
H	5.22544200	-1.78855600	2.91364100
H	6.22226400	-0.42521800	1.08351400
O	2.30539100	-0.15663600	-1.13748800
C	4.97316800	0.58250200	-1.09015100
F	4.37655500	1.80136200	-1.19111400
F	4.87482000	0.01415700	-2.32071500
F	6.29189100	0.82469300	-0.89107100

C	-2.16125500	-0.17655400	-0.29827600
C	-2.42414100	1.26134100	0.19951800
C	-1.62170200	2.32406500	-0.23194400
C	-3.47396600	1.54325200	1.08660700
C	-1.83196700	3.62287700	0.23715800
H	-0.81829000	2.13173700	-0.93481900
C	-3.68756900	2.83840800	1.55979100
H	-4.14065800	0.74726500	1.40129900
C	-2.86231800	3.88534400	1.14121200
H	-1.19092200	4.42901400	-0.10928800
H	-4.50544000	3.03017400	2.24874700
H	-3.02909600	4.89487200	1.50580400
C	-3.51260600	-0.82586400	-0.64079500
C	-4.27409700	-0.21874300	-1.65317600
C	-4.01704200	-1.98034000	-0.03354000
C	-5.49628400	-0.75188800	-2.05323000
H	-3.89953600	0.68398600	-2.12619000
C	-5.24869100	-2.51600400	-0.42943700
H	-3.46819100	-2.47974700	0.75640600
C	-5.99145700	-1.90763100	-1.43938700
H	-6.06532400	-0.26536400	-2.84064500
H	-5.62201400	-3.41200700	0.05851600
H	-6.94648500	-2.32456000	-1.74587200
O	-1.39874800	-0.16674300	-1.48937000
Cu	0.42781700	-0.09655900	-1.16252200

Int-II

C	-4.15800000	-1.25649500	-0.46776200
C	-2.29580500	-2.59990800	0.15288000

C	-3.42146700	-3.59042700	-0.18093500
C	-4.55114200	-2.71912800	-0.78317800
H	-4.96561600	-0.67562700	-0.02340400
H	-3.82127900	-0.73564800	-1.36131700
H	-1.74350800	-2.88034000	1.04979100
H	-3.09407100	-4.38019100	-0.85716000
H	-3.75795500	-4.07277500	0.74125300
H	-4.63100200	-2.86015600	-1.86372900
H	-5.51761000	-2.97215400	-0.33974800
N	-3.01916100	-1.33200100	0.49534400
C	-3.51201700	-1.34734700	1.91177900
H	-4.15975000	-2.21528300	2.07839500
H	-2.62655400	-1.46237900	2.54625000
C	-4.26838100	-0.08714400	2.23884700
C	-3.65150300	1.17739800	2.03631800
C	-5.58536100	-0.14726100	2.69263400
C	-4.43220900	2.34032900	2.26308700
C	-6.32682700	1.00808200	2.95935700
H	-6.04130800	-1.12434100	2.83388800
C	-5.74676100	2.25236100	2.72740900
H	-7.34781200	0.93628900	3.31922900
H	-6.31502700	3.16067800	2.89586300
O	-2.39269200	1.30533300	1.65564200
C	-3.82395500	3.66757500	1.94657100
F	-3.44098900	3.76314500	0.63950700
F	-2.71371000	3.94185500	2.67982100
F	-4.68152100	4.69423100	2.16122200
C	-1.22139700	-2.32964900	-0.96329600

C	-1.81128600	-2.32780400	-2.39031900
C	-2.05189900	-3.52258100	-3.08445000
C	-2.09616700	-1.11924300	-3.03652300
C	-2.60274500	-3.51120000	-4.36663000
H	-1.79380700	-4.47193700	-2.62677500
C	-2.64297800	-1.10183200	-4.32132800
H	-1.89082000	-0.18472400	-2.52930300
H	-2.78422200	-4.45056900	-4.88151400
H	-2.85781400	-0.15007400	-4.79972000
C	-0.10519700	-3.39488700	-0.91066500
C	0.99643100	-3.20603800	-1.76254900
C	-0.10178100	-4.50883100	-0.06584100
C	2.07419100	-4.08693200	-1.75630100
H	1.00160500	-2.36160100	-2.44418500
C	0.97959600	-5.39932000	-0.05787800
H	-0.93713800	-4.71033300	0.59484000
H	2.91519000	-3.91428300	-2.42218900
H	0.95832900	-6.25701900	0.60864200
O	-0.61816000	-1.08672200	-0.69187700
Cu	-1.51927600	0.03951300	0.52602200
C	3.61562700	-0.02192900	0.32452400
H	3.93578300	-0.21877500	-0.70454700
H	4.50769700	0.15625500	0.93542400
C	1.37244800	0.54353300	0.88844500
C	1.63162400	-0.90719300	1.26623900
O	0.27288300	1.10762800	1.02007400
O	0.86024900	-1.65508000	1.87960000
C	2.61139400	1.09825900	0.40501400

C	2.71744900	2.42030200	0.09926700
H	1.81347900	3.00125600	0.27051200
C	3.84359300	3.18352800	-0.39024800
C	3.67078500	4.57892900	-0.51703900
C	5.08042800	2.61840500	-0.77067900
C	4.69529500	5.38415700	-1.00316700
H	2.71822900	5.01661300	-0.23584300
C	6.10043300	3.42682700	-1.25870300
H	5.24476800	1.55131600	-0.70018000
C	5.91285000	4.80911400	-1.37674800
H	4.54550900	6.45539600	-1.09499400
H	7.04542200	2.98042600	-1.55237400
H	6.71409200	5.43365500	-1.76026100
N	2.88232000	-1.17953200	0.84625400
C	0.46996800	1.86325700	-2.25074200
C	1.51319700	2.63337300	-2.85140800
C	1.38345000	4.03354800	-2.89326200
C	0.25559500	4.62489900	-2.33245200
C	-0.76429900	3.84506000	-1.74079900
C	-0.67633800	2.45730700	-1.70309700
C	2.08717900	0.44776500	-2.88651700
C	2.52981600	1.69841100	-3.25335500
H	2.16444400	4.64528400	-3.33627600
H	0.15358700	5.70652000	-2.34770300
H	-1.62976800	4.33399200	-1.30233800
H	-1.46161400	1.85609900	-1.25289400
H	0.32750800	-0.21253200	-1.81491800
H	2.56086200	-0.51810700	-2.99795600

H	3.47247900	1.93003700	-3.73015100
N	0.84053400	0.54050200	-2.30564300
C	2.07225200	-5.19145800	-0.89705900
H	2.91172900	-5.88055800	-0.88734500
C	-2.90620400	-2.29844700	-4.99035800
H	-3.32998400	-2.28703300	-5.99045500
C	3.54190000	-2.46435000	1.05893000
H	2.75152400	-3.20362600	1.19985400
H	4.08806300	-2.71541900	0.14592600
C	4.47513200	-2.42592200	2.24864200
C	3.95355600	-2.44579500	3.54961100
C	5.85856800	-2.33104200	2.06729600
C	4.80559500	-2.37613200	4.65132900
H	2.87843000	-2.51399300	3.69100000
C	6.71388500	-2.26188600	3.17028400
H	6.26432700	-2.31410900	1.05917000
C	6.18857000	-2.28430300	4.46351500
H	4.39304300	-2.39635500	5.65598600
H	7.78704800	-2.19052600	3.01830000
H	6.85188600	-2.23199000	5.32204300

TS-I

C	3.98713600	1.50403400	-0.14252700
C	1.97764100	2.58012500	0.52329100
C	3.04052000	3.69064300	0.47380400
C	4.27858900	3.02319300	-0.17311700
H	4.80542400	0.91171000	0.26694300
H	3.76255100	1.12421100	-1.13757800
H	1.33087500	2.66123400	1.39689800

H	2.70414400	4.56852100	-0.07716900
H	3.26677800	4.01512600	1.49356000
H	4.41846600	3.35799100	-1.20411600
H	5.18822100	3.26376500	0.38324100
N	2.77746900	1.32795000	0.71191400
C	3.14624000	1.15079100	2.15284700
H	3.66665400	2.04032600	2.52525500
H	2.20160900	1.06343600	2.70098100
C	4.01423200	-0.05910600	2.36764000
C	3.58604700	-1.33330100	1.90075600
C	5.24514300	0.06592300	3.01011400
C	4.45943700	-2.43570200	2.10590100
C	6.08150400	-1.03352400	3.22662900
H	5.55481300	1.05230500	3.34757100
C	5.68233300	-2.28418900	2.76397300
H	7.03223000	-0.91188600	3.73501800
H	6.32222100	-3.14852900	2.90457800
O	2.42623300	-1.52687200	1.30512300
C	4.04828700	-3.76871300	1.57390400
F	3.87198200	-3.76045400	0.22149000
F	2.87707800	-4.21859300	2.09709300
F	4.96755400	-4.73311300	1.82495700
C	1.02418100	2.44591900	-0.72484200
C	1.69578300	2.87494500	-2.04995300
C	1.78063700	4.22372000	-2.42731800
C	2.22446800	1.91538000	-2.92026100
C	2.41104100	4.60148300	-3.61356700
H	1.34140300	4.98858000	-1.79554800

C	2.85155000	2.28612500	-4.11147700
H	2.15218400	0.86797500	-2.66047900
H	2.46758100	5.65347300	-3.87916900
H	3.25651700	1.51855300	-4.76537600
C	-0.22384800	3.33417000	-0.53405300
C	-1.31472900	3.11055800	-1.38956700
C	-0.32343500	4.36605500	0.40510500
C	-2.46746800	3.88771400	-1.30863400
H	-1.25391900	2.32506000	-2.13509400
C	-1.48056300	5.15026300	0.49017900
H	0.49865600	4.58510000	1.07710300
H	-3.29696200	3.69220700	-1.98268100
H	-1.53220400	5.94637600	1.22767400
O	0.59896400	1.10910400	-0.81250300
Cu	1.43085500	-0.16970100	0.36012200
C	-3.49212400	0.05361700	0.01357400
H	-3.71957400	0.61674100	-0.90231900
H	-4.44446900	-0.29231800	0.43361000
C	-1.33701000	-0.76573100	0.47367200
C	-1.58105200	0.48689000	1.28194000
O	-0.20408700	-1.38967600	0.53111100
O	-0.80136300	0.99951800	2.10616400
C	-2.49642300	-1.05547300	-0.21589600
C	-2.69760000	-2.21162400	-1.06482000
H	-2.00248900	-3.00723100	-0.81144000
C	-4.07825200	-2.72609400	-1.28258100
C	-4.34807900	-4.06732400	-0.97223500
C	-5.11642700	-1.92408600	-1.78443600

C	-5.63320400	-4.58878200	-1.12792800
H	-3.54621400	-4.69749500	-0.59770800
C	-6.39749800	-2.44763000	-1.94658600
H	-4.91590400	-0.89726600	-2.07260300
C	-6.66221100	-3.77973000	-1.61330300
H	-5.82744100	-5.62681100	-0.87432800
H	-7.19012300	-1.81657700	-2.33775300
H	-7.66205300	-4.18448100	-1.73920300
N	-2.81399900	0.92980400	0.96004300
C	0.24312100	-1.71193100	-2.61447200
C	-0.72740000	-2.69996000	-2.86926600
C	-0.35351100	-4.04276300	-2.88315900
C	0.98724900	-4.35910900	-2.63932300
C	1.93628800	-3.35967400	-2.37216100
C	1.57626300	-2.00908700	-2.35503100
C	-1.69137400	-0.61424700	-2.88627600
C	-2.02823600	-2.00879200	-2.91878900
H	-1.08534400	-4.82365800	-3.06517300
H	1.30022800	-5.39871500	-2.64974600
H	2.96483700	-3.63814600	-2.17041400
H	2.30180800	-1.23306100	-2.13665600
H	0.01706800	0.37633300	-2.13204400
H	-2.36434700	0.23260700	-2.89299900
H	-2.87138900	-2.37805800	-3.48636600
N	-0.40397200	-0.45872200	-2.63121700
C	-2.55583300	4.91660500	-0.36480400
H	-3.45317800	5.52489600	-0.29851400
C	2.95473300	3.63328300	-4.46138700

H	3.44197900	3.92519700	-5.38727000
C	-3.47437700	2.06967600	1.57800600
H	-2.68747200	2.70759800	1.98685900
H	-3.99068000	2.63073000	0.79540500
C	-4.44730700	1.64598100	2.65716600
C	-3.96965900	1.14679100	3.87708900
C	-5.82719800	1.70882800	2.43966800
C	-4.85943500	0.72133000	4.86280500
H	-2.89742700	1.09231600	4.04580400
C	-6.72126400	1.28371400	3.42646000
H	-6.20073700	2.09342800	1.49407500
C	-6.23875500	0.78938600	4.63944900
H	-4.47932100	0.33931400	5.80605200
H	-7.79116800	1.33789600	3.24620900
H	-6.93151200	0.45872600	5.40796500

Int-III

C	4.05741300	1.37930000	0.02942000
C	2.10584500	2.47906700	0.79520200
C	3.22610900	3.52690200	0.89791800
C	4.43975800	2.86997700	0.19452200
H	4.83515000	0.68952700	0.35745200
H	3.81428100	1.14507500	-1.00558200
H	1.44048300	2.49437200	1.65824600
H	2.94962600	4.48171100	0.45176300
H	3.44636600	3.71431800	1.95268900
H	4.62658000	3.32101300	-0.78338000
H	5.34695100	2.98230600	0.79389600
N	2.83354200	1.17167900	0.85477900

C	3.18273900	0.83134800	2.27086800
H	3.74920100	1.64788500	2.73186600
H	2.23100300	0.74130900	2.80652900
C	3.98101900	-0.43926600	2.36259200
C	3.46817400	-1.63731700	1.79182900
C	5.22525700	-0.44537200	2.99073600
C	4.27414400	-2.80474400	1.88361000
C	5.99531700	-1.60817300	3.09268400
H	5.59896800	0.48612100	3.40956100
C	5.51268300	-2.78619900	2.52980500
H	6.95830700	-1.59056800	3.59215600
H	6.09933000	-3.69692200	2.58217800
O	2.29001800	-1.70030600	1.20456700
C	3.77279700	-4.06006700	1.25044200
F	3.56176000	-3.92376500	-0.08900500
F	2.59113900	-4.48721100	1.77004200
F	4.63998700	-5.09337500	1.38929400
C	1.18557300	2.54203500	-0.48793900
C	1.88974300	3.16132400	-1.71615300
C	1.99455100	4.55105800	-1.87729300
C	2.42947300	2.34145800	-2.71373700
C	2.65465400	5.10086900	-2.97683100
H	1.54816500	5.21362800	-1.14311400
C	3.08611900	2.88572500	-3.81942600
H	2.34143100	1.26652700	-2.62279900
H	2.72637000	6.18056900	-3.07428700
H	3.49924000	2.22439500	-4.57616700
C	-0.07130100	3.38944400	-0.19319100

C	-1.15862500	3.26143200	-1.07156300
C	-0.18592500	4.28707400	0.87352700
C	-2.33086600	3.98907600	-0.87974800
H	-1.08162300	2.58371400	-1.91523000
C	-1.36248900	5.01956800	1.07127700
H	0.63706000	4.43519700	1.56394000
H	-3.16011900	3.86658400	-1.57109800
H	-1.42863200	5.70650200	1.91038400
O	0.77055900	1.23535200	-0.79020200
Cu	1.41083700	-0.20096500	0.33565800
C	-3.62838500	-0.10290800	-0.01060000
H	-4.01333200	0.48934900	-0.85164500
H	-4.49118700	-0.59545100	0.45721700
C	-1.40485400	-0.78756600	0.27461200
C	-1.69065600	0.37413400	1.18737700
O	-0.22728200	-1.35535300	0.24149700
O	-0.90756700	0.87768200	2.01611500
C	-2.54757100	-1.06890000	-0.41867500
C	-2.74700400	-2.13594900	-1.48788800
H	-2.34661500	-3.08214900	-1.10949300
C	-4.21906600	-2.34368000	-1.79147200
C	-4.91650300	-3.36237400	-1.13099000
C	-4.92096300	-1.50545400	-2.66783800
C	-6.28422600	-3.54529400	-1.34298700
H	-4.38109000	-4.01566600	-0.44687100
C	-6.28842900	-1.68655300	-2.88294700
H	-4.40259900	-0.70297900	-3.18509700
C	-6.97498700	-2.70710100	-2.22111400

H	-6.80760200	-4.34434600	-0.82570900
H	-6.81641600	-1.02856900	-3.56725900
H	-8.03849000	-2.84896600	-2.38986500
N	-2.96351300	0.76748400	0.94875700
C	0.44217400	-1.48785700	-2.70486400
C	-0.54931100	-2.46720400	-2.82204800
C	-0.18328900	-3.80286400	-2.89714900
C	1.18322700	-4.12119500	-2.85079900
C	2.15683300	-3.12279400	-2.73326800
C	1.79785600	-1.77073100	-2.65749400
C	-1.48721800	-0.34188500	-2.65777000
C	-1.89889900	-1.78303400	-2.77379800
H	-0.93226600	-4.58479000	-2.97636300
H	1.48981800	-5.16120700	-2.90353400
H	3.20531700	-3.39721700	-2.69110000
H	2.54244100	-0.98892200	-2.55458400
H	0.27781700	0.61402400	-2.11833700
H	-2.13869700	0.51834600	-2.57832300
H	-2.48579000	-1.96622500	-3.67996600
N	-0.19724900	-0.21900200	-2.60625600
C	-2.44027900	4.87221400	0.19958500
H	-3.35443300	5.43752100	0.35571200
C	3.20919700	4.26949800	-3.95302300
H	3.71988700	4.69595600	-4.81160000
C	-3.66460000	1.79973300	1.69594800
H	-2.89792300	2.43780100	2.14221700
H	-4.24029900	2.40714800	0.99171700
C	-4.57269500	1.21663700	2.75724300

C	-4.02171200	0.60488800	3.89211100
C	-5.96206600	1.23958100	2.60251700
C	-4.84877500	0.03031500	4.85653800
H	-2.94170000	0.58058600	4.01116200
C	-6.79359800	0.66511500	3.56825300
H	-6.39286400	1.70925500	1.72190700
C	-6.23831200	0.05957900	4.69667900
H	-4.41186600	-0.43853600	5.73373500
H	-7.87168300	0.68930100	3.43674900
H	-6.88241900	-0.38770100	5.44834000

(S)-3a

C	1.00894300	-0.76458600	-0.67063300
H	0.44135500	-0.93063100	-1.59339000
H	1.42223400	0.24958100	-0.71607900
C	0.78717100	-1.90958300	1.31784200
C	2.03452400	-2.36297100	0.66525200
O	2.85107700	-3.16047900	1.15479200
C	0.17829900	-0.97475900	0.56998700
C	-1.10782900	-0.24342200	0.85034200
H	-1.34747100	-0.41389900	1.90763600
C	-0.89530300	1.26145400	0.68149700
C	-0.54594300	2.04076900	1.78927200
C	-0.99611100	1.87447900	-0.57302100
C	-0.30369700	3.40876000	1.65006600
H	-0.46429000	1.57037100	2.76600500
C	-0.74944100	3.24032100	-0.71671200
H	-1.27602300	1.27883300	-1.43694900
C	-0.40354100	4.01269900	0.39491600

H	-0.03910200	4.00137600	2.52132400
H	-0.83222300	3.70233100	-1.69653100
H	-0.21679700	5.07697500	0.28403100
N	2.08909600	-1.74242400	-0.54440600
C	-4.34208200	-1.05554900	-0.91590700
C	-3.59309400	-0.23951400	-0.01872000
C	-4.23429200	0.83976700	0.61569900
C	-5.57828600	1.07562800	0.34888400
C	-6.30012400	0.25492300	-0.54441300
C	-5.69373000	-0.81921600	-1.18778800
C	-2.23834800	-1.85135600	-0.83584500
C	-2.25082400	-0.76991200	0.01303700
H	-3.68555000	1.47957600	1.30023000
H	-6.08400800	1.90625100	0.83308500
H	-7.34876100	0.46583100	-0.73366800
H	-6.24529200	-1.45306400	-1.87600400
H	-3.73797500	-2.75450200	-2.05053200
H	-1.43202800	-2.52639700	-1.08306800
N	-3.48932200	-2.02733400	-1.39463800
C	3.31528800	-1.63531700	-1.33212800
H	3.89882700	-2.53575100	-1.12663900
H	3.04464900	-1.63936800	-2.39133300
C	4.10414800	-0.38836600	-0.99409600
C	4.79534300	-0.29922900	0.22214200
C	4.10973400	0.70797600	-1.86227100
C	5.48281000	0.86591700	0.55958900
H	4.78926200	-1.14621900	0.90251900
C	4.79823100	1.87645100	-1.52637900

H	3.57101700	0.64417200	-2.80424700
C	5.48532900	1.95746500	-0.31437900
H	6.01841200	0.92312000	1.50295700
H	4.79493900	2.72114900	-2.20939000
H	6.02140200	2.86470400	-0.05089500
O	0.42182700	-2.42190900	2.52369800
H	1.12272100	-3.05402700	2.77893300

Int-IV

C	-2.94567500	-2.48614000	0.85921100
C	-3.98067000	-0.84018100	-0.51312000
C	-5.12993800	-1.53320900	0.23909800
C	-4.43389100	-2.44800200	1.27557400
H	-2.53413900	-3.49336700	0.80344200
H	-2.32959400	-1.91163000	1.54551500
H	-4.21565400	-0.66758600	-1.56460200
H	-5.81216300	-0.82258000	0.70552500
H	-5.71371300	-2.12801500	-0.46939800
H	-4.52812200	-2.04584400	2.28742200
H	-4.87291100	-3.44896200	1.27093400
N	-2.87359500	-1.85146400	-0.49267500
C	-3.05201900	-2.88593700	-1.56634100
H	-4.00501500	-3.40913400	-1.43036600
H	-3.09362100	-2.34381800	-2.51612800
C	-1.91932000	-3.87624400	-1.55150600
C	-0.59896700	-3.40066300	-1.77180100
C	-2.13330300	-5.22692200	-1.28554500
C	0.46900800	-4.32803300	-1.67624000
C	-1.07280100	-6.13844600	-1.22734100

H	-3.15081900	-5.57050500	-1.11458600
C	0.22859900	-5.68046300	-1.41675000
H	-1.26003700	-7.18738100	-1.02267300
H	1.06415500	-6.36939500	-1.35541300
O	-0.35903100	-2.13277100	-2.05665200
C	1.86074500	-3.82378700	-1.87578100
F	2.18127700	-2.79437900	-1.04320300
F	2.07904500	-3.35833300	-3.13452600
F	2.79438500	-4.78476600	-1.65940400
C	-3.48413200	0.54102400	0.06142800
C	-3.55348700	0.61517800	1.60416200
C	-4.73887100	0.95488200	2.27228600
C	-2.41314900	0.36046900	2.37531100
C	-4.79009000	1.00660900	3.66659000
H	-5.62967200	1.19488700	1.70120100
C	-2.45722300	0.41464800	3.76948000
H	-1.48303300	0.10606700	1.88364900
H	-5.72166700	1.27047100	4.15956800
H	-1.55624300	0.20894000	4.34132300
C	-4.34667400	1.68630900	-0.50746500
C	-3.86932800	2.99746100	-0.34598200
C	-5.57133300	1.50520800	-1.15954500
C	-4.58043800	4.08929900	-0.83756100
H	-2.93147600	3.16168400	0.17230200
C	-6.29165500	2.60096300	-1.65016400
H	-5.98879100	0.51384600	-1.29266300
H	-4.18402600	5.09233700	-0.70555600
H	-7.23976500	2.43322000	-2.15358200

O	-2.15863100	0.75474400	-0.37030700
Cu	-1.21113500	-0.78379600	-0.95951700
C	3.29774800	0.70845100	1.12949400
H	4.29399500	0.29485500	0.93805000
H	3.39122300	1.52382400	1.85488400
C	1.38555700	0.35903300	-0.24538900
C	1.31651200	-0.56822300	0.95822900
O	0.53416800	0.37884000	-1.15167500
O	0.41559800	-1.38680000	1.19075000
C	2.59022400	1.13549000	-0.12967500
C	2.88258600	2.10030200	-1.04478600
H	2.16860900	2.17930200	-1.86168500
C	3.97423900	3.04235000	-1.10611600
C	4.00412500	3.92137300	-2.21113000
C	4.97686500	3.16175300	-0.11883500
C	4.99753700	4.88670300	-2.32859100
H	3.22955000	3.83926100	-2.96702900
C	5.96474500	4.13194300	-0.23804400
H	4.98591000	2.50527500	0.74134200
C	5.97854500	4.99612600	-1.33953900
H	5.00551700	5.55580200	-3.18328000
H	6.72841700	4.21838000	0.52858800
H	6.75353500	5.75196200	-1.42458700
N	2.42408300	-0.33214900	1.68164900
C	0.10276500	3.56904700	0.06712100
C	1.12690300	4.23736400	0.80897600
C	1.78044000	5.33666000	0.22271700
C	1.41874100	5.72972400	-1.06034700

C	0.41173200	5.04698300	-1.78071700
C	-0.25928300	3.96055400	-1.22914600
C	0.31067700	2.52647100	2.04117000
C	1.23610700	3.54594700	2.06415100
H	2.56853700	5.85874900	0.75864700
H	1.92538900	6.56973300	-1.52663400
H	0.15708400	5.37857700	-2.78333200
H	-1.04134700	3.43738700	-1.77085500
H	-1.08232300	1.85740700	0.52495400
H	0.07183400	1.79062800	2.79533000
H	1.90991600	3.77721100	2.87801600
N	-0.38442100	2.54833900	0.84867300
C	-5.79926400	3.89552300	-1.49609900
H	-6.35709400	4.74482300	-1.87999000
C	-3.64861300	0.73354200	4.42373900
H	-3.68551200	0.77882500	5.50840400
C	2.83269300	-1.14133700	2.82954400
H	3.26329500	-0.47017800	3.57710500
H	1.92507800	-1.58673300	3.24246600
C	3.82910300	-2.20389500	2.41861700
C	5.19374900	-2.04133900	2.67862800
C	3.39438200	-3.33525900	1.71487600
C	6.11471300	-2.99818900	2.24388800
H	5.53292100	-1.16352100	3.22235700
C	4.31304500	-4.28585900	1.27151600
H	2.33742700	-3.45988200	1.50303800
C	5.67575900	-4.11990700	1.53754300
H	7.17220000	-2.86442700	2.45297700

H	3.96567600	-5.14919600	0.71254900
H	6.39139700	-4.86121800	1.19377100

TS-II

C	-1.83306200	-3.20201300	1.12887200
C	-3.48443000	-2.10512100	-0.20667800
C	-4.25478100	-3.09738100	0.68040300
C	-3.20722000	-3.65254300	1.67447700
H	-1.11230200	-4.01498100	1.04569600
H	-1.39332300	-2.43203100	1.75639700
H	-3.82902700	-2.11932200	-1.24124300
H	-5.09964500	-2.62733700	1.18539600
H	-4.65615400	-3.90057500	0.05576600
H	-3.35942700	-3.24931400	2.67858200
H	-3.26968300	-4.74192600	1.73943700
N	-2.08139700	-2.63341100	-0.23405100
C	-1.94816800	-3.71306900	-1.26999400
H	-2.64019700	-4.53238800	-1.04405700
H	-2.25009800	-3.26656900	-2.22236800
C	-0.54295800	-4.24009200	-1.35193300
C	0.48981100	-3.34386000	-1.73895400
C	-0.23989800	-5.56656600	-1.05578300
C	1.81541700	-3.84643300	-1.80542400
C	1.07069400	-6.05163600	-1.13528000
H	-1.04635400	-6.23244100	-0.75729400
C	2.09350200	-5.18503700	-1.51189800
H	1.28887300	-7.08899900	-0.90392300
H	3.11537000	-5.54304600	-1.57481900
O	0.22530600	-2.08520000	-2.03276000

C	2.90833200	-2.92197200	-2.23230400
F	3.01214100	-1.80773900	-1.45802600
F	2.74564300	-2.46997700	-3.50513000
F	4.12953900	-3.51640900	-2.19631200
C	-3.50808300	-0.59993400	0.23089200
C	-3.30660000	-0.42610800	1.75075400
C	-4.37680200	-0.50698000	2.65259900
C	-2.02748200	-0.18649600	2.26647300
C	-4.16913200	-0.37755000	4.02750900
H	-5.38424700	-0.66147300	2.28064800
C	-1.81271400	-0.05388600	3.63886100
H	-1.18783800	-0.12496800	1.58615500
H	-5.01484000	-0.44540900	4.70611600
H	-0.80663700	0.12636200	4.00810700
C	-4.84180400	0.05833100	-0.17879300
C	-5.00207400	1.42789500	0.09355300
C	-5.88293500	-0.60426000	-0.83851500
C	-6.14393900	2.11806700	-0.30455600
H	-4.22750200	1.95858400	0.63565200
C	-7.03781800	0.08312500	-1.23137100
H	-5.82174600	-1.66421900	-1.05460000
H	-6.23493100	3.17834400	-0.08579900
H	-7.83113800	-0.45704800	-1.74041900
O	-2.48070000	0.06121300	-0.48006800
Cu	-0.91574300	-1.05151400	-0.80188200
C	2.89066800	1.46431400	1.59546100
H	3.95347100	1.58771500	1.35194500
H	2.68073800	2.08014000	2.47880700

C	1.27779900	0.60313200	0.11486500
C	1.70068700	-0.48647600	1.05869000
O	0.36457300	0.46478700	-0.78638200
O	1.28222900	-1.65685800	1.09016000
C	1.97167800	1.75183100	0.43994600
C	1.64775400	3.00882900	-0.18912200
H	1.13805800	2.84701200	-1.13567900
C	2.60111900	4.14163600	-0.25417600
C	2.72746800	4.83658700	-1.46857200
C	3.37151800	4.55723300	0.84570100
C	3.61596800	5.90533600	-1.58915700
H	2.12804500	4.52828600	-2.31966900
C	4.25527500	5.62684500	0.72519000
H	3.26214100	4.06251000	1.80414500
C	4.38327900	6.30273700	-0.49271200
H	3.70596200	6.42706900	-2.53727700
H	4.84252600	5.93751000	1.58425700
H	5.07326100	7.13652400	-0.58258300
N	2.60390500	0.06368000	1.90901000
C	-1.72358500	3.69501000	-0.76145100
C	-0.66598100	4.55411400	-0.37812000
C	-0.47546800	5.74912600	-1.07378200
C	-1.34209600	6.04836800	-2.12996900
C	-2.38012100	5.17572300	-2.49587300
C	-2.58970800	3.97515200	-1.81153500
C	-0.72243200	2.70921400	0.97246600
C	0.06815400	3.87210700	0.69793900
H	0.32511300	6.42919100	-0.80335100

H	-1.21145100	6.97635000	-2.67842600
H	-3.03572200	5.44036600	-3.31960200
H	-3.39808800	3.29897900	-2.07089500
H	-2.17888500	1.65169600	-0.07785700
H	-0.53061200	1.94372200	1.70796600
H	0.59390200	4.38977500	1.49016800
N	-1.71082400	2.58443000	0.10308300
C	-7.17163500	1.44579300	-0.97430000
H	-8.06602300	1.97873200	-1.28374200
C	-2.88469400	-0.15245900	4.52824700
H	-2.72333500	-0.04772400	5.59727400
C	3.47361200	-0.72774900	2.77572300
H	3.68184200	-0.14192600	3.67488600
H	2.90786300	-1.61552800	3.06763400
C	4.76195900	-1.11183300	2.07855100
C	5.95168500	-0.42762900	2.34998800
C	4.76136400	-2.12028700	1.10442900
C	7.12545600	-0.74416700	1.66066400
H	5.95638200	0.35535800	3.10402100
C	5.92929200	-2.43167600	0.40897900
H	3.84132400	-2.65144100	0.88468100
C	7.11530900	-1.74528500	0.68737600
H	8.04360700	-0.20729600	1.88179100
H	5.90968800	-3.20432500	-0.35325600
H	8.02555800	-1.98938600	0.14709600

Int-V

C	-2.27185000	-2.82195600	1.17721100
C	-3.76263200	-1.47267200	-0.09750900

C	-4.65758500	-2.33909400	0.80685100
C	-3.68312200	-3.09352600	1.74318000
H	-1.65896100	-3.71804800	1.08527600
H	-1.73148500	-2.11095400	1.79577500
H	-4.14071000	-1.41312500	-1.11876500
H	-5.38656300	-1.74388000	1.35727900
H	-5.21904800	-3.04334400	0.18652800
H	-3.75088000	-2.72655400	2.77031800
H	-3.90520700	-4.16380100	1.75559400
N	-2.46881600	-2.22275300	-0.17987000
C	-2.56390000	-3.30651100	-1.21583900
H	-3.39554700	-3.97877200	-0.97687000
H	-2.79227600	-2.80744300	-2.16274500
C	-1.28747500	-4.09135200	-1.31760300
C	-0.10810700	-3.40431400	-1.71342100
C	-1.23860500	-5.45088800	-1.02078400
C	1.10037200	-4.14709300	-1.77812100
C	-0.04315600	-6.17395000	-1.10534700
H	-2.15420200	-5.95255100	-0.71583500
C	1.12304500	-5.51387100	-1.48355400
H	-0.02258700	-7.23371300	-0.87356300
H	2.05998600	-6.05675500	-1.54597100
O	-0.13513200	-2.12110700	-2.01492900
C	2.34767600	-3.44524200	-2.20448900
F	2.63926500	-2.35354700	-1.44743800
F	2.28602000	-2.99722800	-3.48765600
F	3.44225100	-4.24809800	-2.13631100
C	-3.52530400	0.00690300	0.35494200

C	-3.24117100	0.14438400	1.86433100
C	-4.27856400	0.19856100	2.80569600
C	-1.92301900	0.23114400	2.32845500
C	-4.00423700	0.30642500	4.17043800
H	-5.31090800	0.17267700	2.47314600
C	-1.64256800	0.34471300	3.69097400
H	-1.10788400	0.18939200	1.61822600
H	-4.82551600	0.34452700	4.88057400
H	-0.60981700	0.40668200	4.02213000
C	-4.74323600	0.88215000	-0.00549700
C	-4.65852300	2.25967100	0.25950600
C	-5.91161700	0.40046100	-0.60648200
C	-5.68918200	3.12893500	-0.08840700
H	-3.77921500	2.65695500	0.75488300
C	-6.95481800	1.26928600	-0.94789500
H	-6.03762900	-0.65504500	-0.81573800
H	-5.59141900	4.19019700	0.12223900
H	-7.85139000	0.86743300	-1.41140000
O	-2.42366300	0.48565900	-0.39506100
Cu	-1.04589200	-0.87091500	-0.78464000
C	2.84796200	1.26889200	1.64544600
H	3.93170400	1.23005000	1.47495800
H	2.67430100	1.98668700	2.45764000
C	1.28409100	0.52950500	0.05808200
C	1.48049100	-0.53656000	1.09476700
O	0.45778200	0.40857400	-0.95539700
O	0.94062800	-1.65829800	1.12796100
C	2.07443400	1.58895800	0.40160300

C	2.05404900	2.92322500	-0.30614900
H	1.87140100	2.69793400	-1.35990500
C	3.35106300	3.69907100	-0.21788100
C	4.17247100	3.79946200	-1.34704800
C	3.77147800	4.30007300	0.97740200
C	5.39194400	4.47784300	-1.28543500
H	3.85295600	3.34055500	-2.27886800
C	4.98974800	4.97624700	1.04255900
H	3.14284500	4.24234800	1.86169200
C	5.80517900	5.06666200	-0.08914500
H	6.01538100	4.54718700	-2.17227900
H	5.30142600	5.43469900	1.97670700
H	6.75208700	5.59620700	-0.03862000
N	2.34805700	-0.05057500	2.02868700
C	-1.11927500	3.53860700	-1.17604300
C	0.05596700	4.29524600	-1.07088800
C	0.37681000	5.20105500	-2.07127100
C	-0.51146000	5.33754600	-3.14995800
C	-1.68295400	4.57535300	-3.22993900
C	-2.01040900	3.64810300	-2.23156800
C	-0.20724700	2.87539200	0.75499700
C	0.80201500	3.80839300	0.14855600
H	1.29061000	5.78492700	-2.02589600
H	-0.28396300	6.04761500	-3.93902600
H	-2.35047300	4.70424500	-4.07596300
H	-2.91770800	3.05490000	-2.27070800
H	-1.86815000	1.79366000	-0.03630100
H	-0.11961500	2.34722600	1.69335200

H	1.11490400	4.58890200	0.84509700
N	-1.21751300	2.69325900	-0.03434700
C	-6.84728400	2.63560700	-0.69783200
H	-7.65562100	3.30914300	-0.96715700
C	-2.68384800	0.37863100	4.62040900
H	-2.47033400	0.46861900	5.68157400
C	3.12440100	-0.93184300	2.90277100
H	3.39561500	-0.36925000	3.79969400
H	2.46306300	-1.74914700	3.19943200
C	4.36267500	-1.46025100	2.20791000
C	5.62800000	-0.94030400	2.50135200
C	4.24217700	-2.42976600	1.20177800
C	6.75577900	-1.37949300	1.80183000
H	5.72827600	-0.18661600	3.27832700
C	5.36326200	-2.85992600	0.49318300
H	3.26511500	-2.83402100	0.96358700
C	6.62485400	-2.33704400	0.79389700
H	7.73284800	-0.96868400	2.04008800
H	5.24627200	-3.59539100	-0.29731700
H	7.49956800	-2.67249800	0.24399200

(*R*)-3a

C	-1.00901600	-0.76451600	-0.67075300
H	-1.42245200	0.24959200	-0.71613100
H	-0.44139900	-0.93043400	-1.59351700
C	-0.78708100	-1.90965600	1.31763700
C	-2.03436900	-2.36316900	0.66501100
O	-2.85080300	-3.16084400	1.15447900
C	-0.17837300	-0.97466300	0.56985000

C	1.10770400	-0.24326900	0.85033100
H	1.34722700	-0.41373700	1.90765500
C	0.89519400	1.26159300	0.68142600
C	0.54590600	2.04100300	1.78915400
C	0.99598000	1.87454100	-0.57313800
C	0.30370300	3.40899500	1.64986300
H	0.46427100	1.57068400	2.76592600
C	0.74935200	3.24038000	-0.71691500
H	1.27584400	1.27884300	-1.43704700
C	0.40351800	4.01284900	0.39467300
H	0.03916700	4.00166700	2.52110100
H	0.83212100	3.70231200	-1.69677100
H	0.21680100	5.07712200	0.28371800
N	-2.08904300	-1.74253500	-0.54461400
C	4.34206800	-1.05570300	-0.91559300
C	3.59301600	-0.23943100	-0.01866900
C	4.23418300	0.84003900	0.61548100
C	5.57816500	1.07586900	0.34862000
C	6.30005900	0.25494000	-0.54443900
C	5.69372000	-0.81940700	-1.18750400
C	2.23833900	-1.85150100	-0.83545400
C	2.25074600	-0.76979200	0.01309900
H	3.68539400	1.48000600	1.29982600
H	6.08385200	1.90664300	0.83259800
H	7.34869000	0.46584100	-0.73373100
H	6.24530000	-1.45342600	-1.87554900
H	3.73792700	-2.75465400	-2.05016300
H	1.43203800	-2.52661200	-1.08253500

N	3.48937500	-2.02767200	-1.39404100
C	-3.31536400	-1.63534200	-1.33215800
H	-3.04484600	-1.63933900	-2.39139100
H	-3.89889300	-2.53578300	-1.12665700
C	-4.10415100	-0.38838100	-0.99397300
C	-4.10982300	0.70799400	-1.86211300
C	-4.79522800	-0.29927400	0.22233700
C	-4.79825300	1.87647400	-1.52610200
H	-3.57121700	0.64420300	-2.80415300
C	-5.48262800	0.86587700	0.55990100
H	-4.78912800	-1.14629800	0.90266700
C	-5.48521000	1.95746100	-0.31402100
H	-4.79502000	2.72119600	-2.20908400
H	-6.01813400	0.92305700	1.50332500
H	-6.02123200	2.86470200	-0.05044000
O	-0.42160000	-2.42206400	2.52340000
H	-1.12236500	-3.05433100	2.77859900

References:

1. (a) R. Feltham and I. Brant. *J. Am. chem. Soc.*,**1982**, *104*, 641. (b) M. Bressan, C. Furlam and G. Polzonett .*Polyhedron*, **1983**, *2*, 523.
2. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Jr. Montgomery, J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian 16, Revision C.01, Gaussian, Inc., Wallingford CT, **2016**.
3. (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C. T.; Yang, W. T.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.
4. (a) Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. *J. Chem. Phys.* **2010**, *132*, 154104; (b) Grimme, S.; Ehrlich, S.; Goerigk, L. *J. Comput. Chem.* **2011**, *32*, 1456.
5. Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2009**, *113*, 6378.
6. Andrae, D.; Häußermann, U.; Dolg, M.; Stoll, H.; Preuß, H. *Theor. Chim. Acta* **1990**, *77*, 123.
7. Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople. J. A, *Ab Initio Molecular Orbital Theory*; Wiley: New York, **1986**.
8. (a) Fukui, K. *Acc. Chem. Res.* **1981**, 14, 363. (b) Fukui, K. *J. Phys. Chem.* **1970**, *74*, 4161.
9. Legault, C. Y. CYLview, 1.0b; Université de Sherbrooke, **2009**; http://www.cylview.org.

10. Lindström, U. M. *Chem. Rev.* 2002, **102**, 2751.
11. Otto, S.; Engberts, J. B. F. N. *Pure and Applied Chemistry*, 2000, 72, 1365.
12. Cortes-Clerget, M.; Yu, J.; Kincaid, J. R. A.; Walde, P.; Gallou, F.; , Lipshutz, B. H. *Chem. Sci.,* 2021, **12**, 4237.