Asymmetric Substitutions of O-Boc-Protected Morita-Baylis-Hillman Adducts with Pyrrole and Indole Derivatives

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Supporting Information

CONTENTS

General Remarks: ^{1}H NMR spectra were recorded on a Bruker AM-300 or AM-400 spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard; J-values are in Hz. Mass spectra were recorded with a HP-5989 instrument. All of the compounds reported in this paper gave satisfactory HRMS analytic data. Melting points were determined on a digital melting point apparatus and temperatures were uncorrected. Optical rotations were determined at 589 nm (sodium D line) by using a Perkin-Elmer-341 MC digital polarimeter; $[\alpha]_D$-values are given in unit of 10 deg^{-1} cm^2 g^{-1}. Infrared spectra were recorded on a Perkin-Elmer PE-983 spectrometer with absorption in cm^{-1}. Chiral HPLC was performed on a SHIMADZU SPD-10A vp series with chiral columns (Chiralpak AD-H, IC-H columns 4.6 × 250 mm, (Daicel Chemical Ind., Ltd.)). THF, toluene and Et_2O were distilled from sodium (Na) under argon (Ar) atmosphere. CH_3CN, 1,2-dichloroethane and dichloromethane were distilled from CaH_2 under argon (Ar) atmosphere.Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF254 silica gel coated plates. Flash column chromatography was carried out using 300-400 mesh silica gel at increased pressure. Cinchona alkaloids catalysts β-ICD[1] and catalysts **1a, 1b, 1c, 1d, 1e** were prepared according to the literature procedure.[2] Catalysts **3b** and **3c** were prepared based on Buchwald and Hartwig's Pd-catalyzed amination reaction.[3] O-Boc-Protected Morita-Baylis-Hillman products were prepared according to the literature procedure.[2]

(1) Iwabuchi, Y.; Nakatani, M.; Hatakeyama, S. *J. Am. Chem. Soc.* **1999**, *121*, 10219.

(2) Pei, C. –K.; Zhang, X. –C.; Shi, M. *Eur. J. Org. Chem*. **2011**, *23*, 4479.

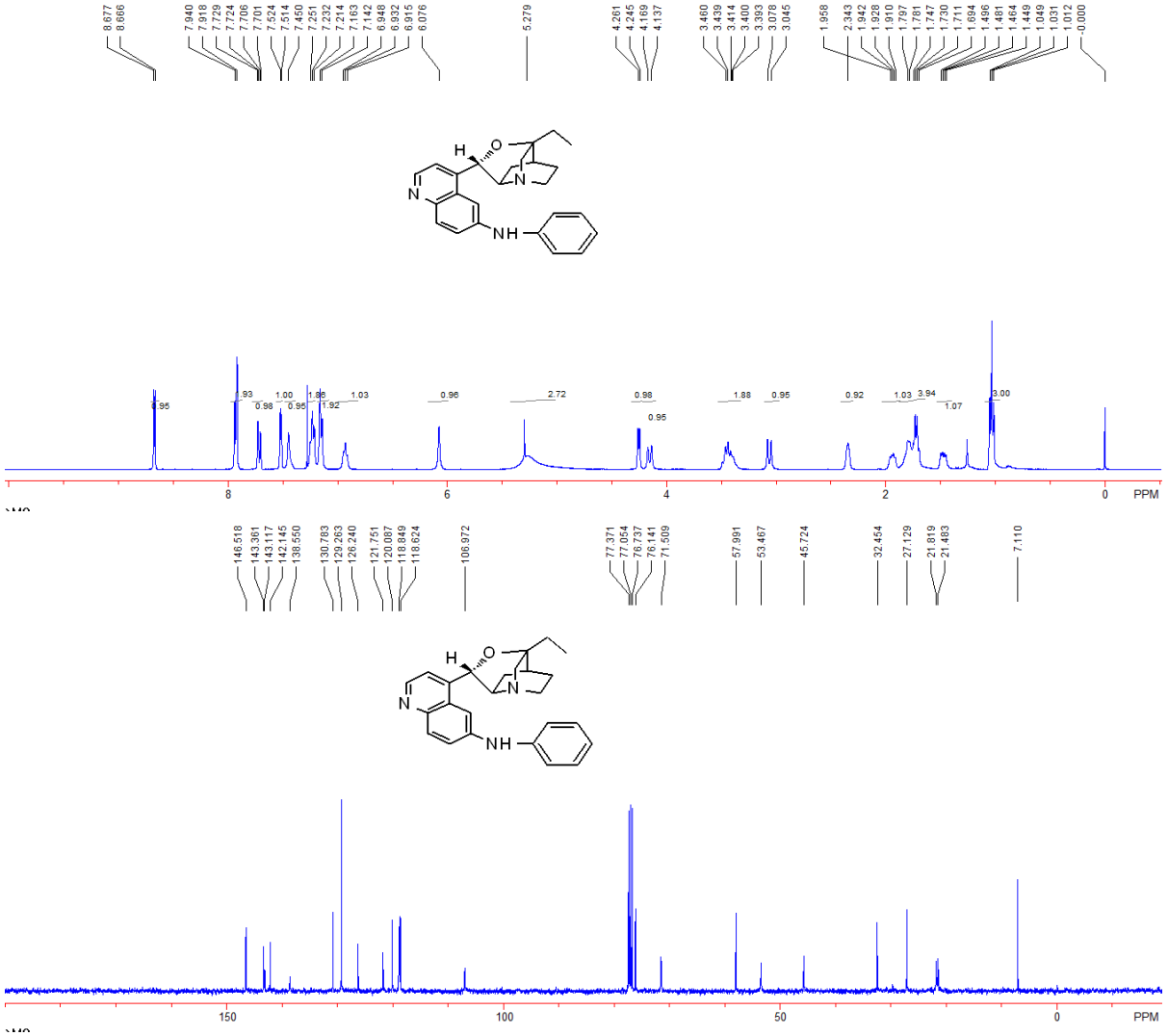
(3) (a) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **1997**, *62*, 1264. (b) Louie, J.; Driver, M. S.; Hamann, B. C.; Hartwig, J. F. *J. Org. Chem*. **1997**, *62*, 1268. (c) Watanabe, T.; Ueda, S.; Inuki, S.; Oishi, S.; Fujii, N.; Ohno, H. *Chem. Commum*. **2007**, *36*, 4516.

Preparation of Catalysts

To a tube charged with $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), BINAP (19 mg, 0.03 mmol), and cesium carbonate (77 mg, 0.24 mmol) was added a solution of **6** (91 mg, 0.2 mmol) and **7a** (21 μL, 0.22 mmol) in toluene (2 mL) via syringe at 100 ^{o}C for 16 h until **6** had been consumed by TLC analysis. After being cooled to room temperature, it was concentrated under reduced pressure. The red-brown residue was dissolved in 20 mL of EtOAc and washed with H_2O. The organic phase was dried over Na_2SO_4 and comcentrated under reduced pressure. The crude material was purified by silica gel column chromatography (elution with DCM/EtOH = 30/1), giving the corresponding catalyst in 92% yield (70 mg).

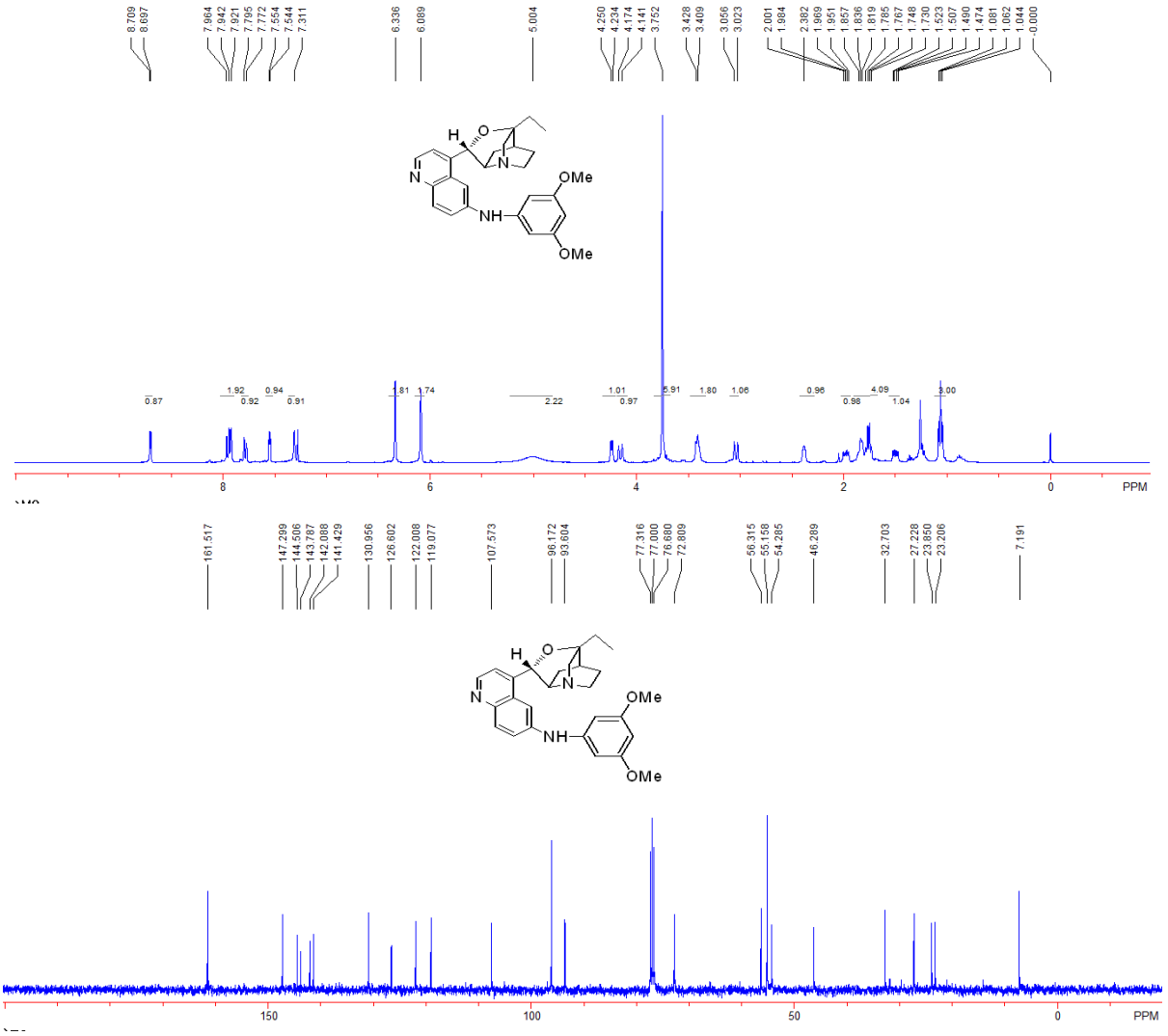
4-((1S,5S)-3-ethyl-4-oxa-1-azatricyclo[4.4.0.03,8]decan-5-yl)-N-phenylquinolin-6-amine cat. 3b: a yellow solid; $[\alpha]^{20}_{D}$ = +141.2 (c 0.72, $CHCl_3$); m.p. 166-168 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.03 (t, *J* = 7.5 Hz, 3H), 1.47 (dd, *J* = 12.8 Hz, 6.0 Hz, 1H), 1.69-1.80 (m, 4H), 1.94 (dd, *J* = 12.8 Hz, 6.0 Hz, 1H), 2.71 (d, *J* = 12.8 Hz, 1H), 3.40-3.46 (m, 2H), 4.15 (d, *J* = 12.8 Hz, 1H), 4.25 (d, *J* = 6.0 Hz, 1H), 5.28 (brs, 3H), 6.08 (s, 1H), 6.93 (t, *J* = 6.4 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 2H), 7.45 (s,1H), 7.52 (d, *J* = 4.0 Hz, 1H), 7.72 (dd, *J* = 9.2 Hz, 2.0 Hz, 1H), 7.92-7.94 (m, 2H), 8.68 (d, *J* = 4.0 Hz, 1H); ^{13}C NMR

(75 MHz, $CDCl_3$) δ 7.1, 21.5, 21.8, 27.1, 32.5, 45.7, 53.5, 58.0, 71.5, 76.1, 107.0, 118.6, 118.9, 120.1, 121.8, 126.2, 129.3, 130.8, 138.6, 142.2, 143.1, 143.4, 146.5; IR (neat) ν 3445, 2935, 2360, 2342, 1601,1508, 1593, 1480, 1458, 1279, 1203. 1152, 1069, 822 cm^{-1}; MS (%) m/e 385 (45), 328 (100), 346 (6), 285 (9), 233 (6), 166 (9); HRMS (EI) for $C_{25}H_{26}N_3O$: 385.2154; Found: 385.2158.



N-(3,5-dimethoxyphenyl)-4-((1S,5S)-3-ethyl-4-oxa-1-azatricyclo[4.4.0.03,8]decan-5-yl)quinolin-6-amine cat. 3c: a yellow solid; $[\alpha]^{20}_D$ = +63.6 (c 0.31, $CHCl_3$); m.p. 179-182 °C; ^1H

NMR (400 MHz, $CDCl_3$, TMS) δ 1.06 (t, *J* = 7.2 Hz, 3H), 1.50 (dd, *J* = 13.2 Hz, 6.8 Hz, 1H), 1.73-1.86 (m, 4H), 1.98 (dd, *J* = 13.2 Hz, 6.8 Hz, 1H), 2.38 (s, 1H), 3.04 (d, *J* = 13.2 Hz, 1H), 3.41-3.43 (m, 2H), 3.75 (s, 6H), 4.16 (d, *J* = 13.2 Hz, 1H), 4.24 (d, *J* = 6.4 Hz, 1H), 5.00 (brs, 2H), 6.09 (s, 2H), 6.34 (s, 2H), 7.31 (s, 1H), 7.55 (d, *J* = 4.0 Hz, 1H), 7.78 (d, *J* = 9.2 Hz, 1H), 7.92-7.96 (m, 2H), 8.70 (d, *J* = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.2, 23.2, 23.9, 27.2, 32.7, 46.3, 54.3, 55.2, 56.3, 72.8, 93.6, 96.2, 107.6, 119.1, 122.0, 126.6, 131.0, 141.4, 142.1, 143.8, 144.5, 147.3, 161.5; IR (neat) ν 3396, 2928, 2359, 1608, 1508, 1480, 1463, 1279, 1204, 1152, 1069, 1014, 860, 823 cm^{-1}; MS (%) m/e 445 (65), 388 (100), 346 (6), 223 (6), 166 (6); HRMS (EI) for $C_{27}H_{31}N_3O_3$: 445.2365; Found: 445.2371.



Typical procedure for the preparation of Boc-protected Morita-Baylis-Hillman adducts.

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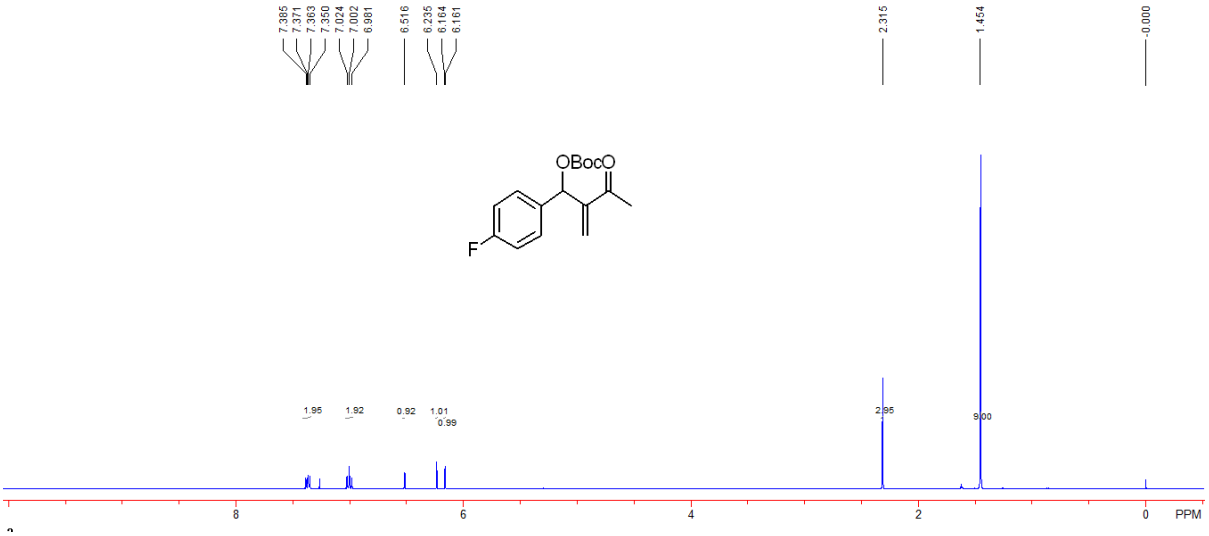
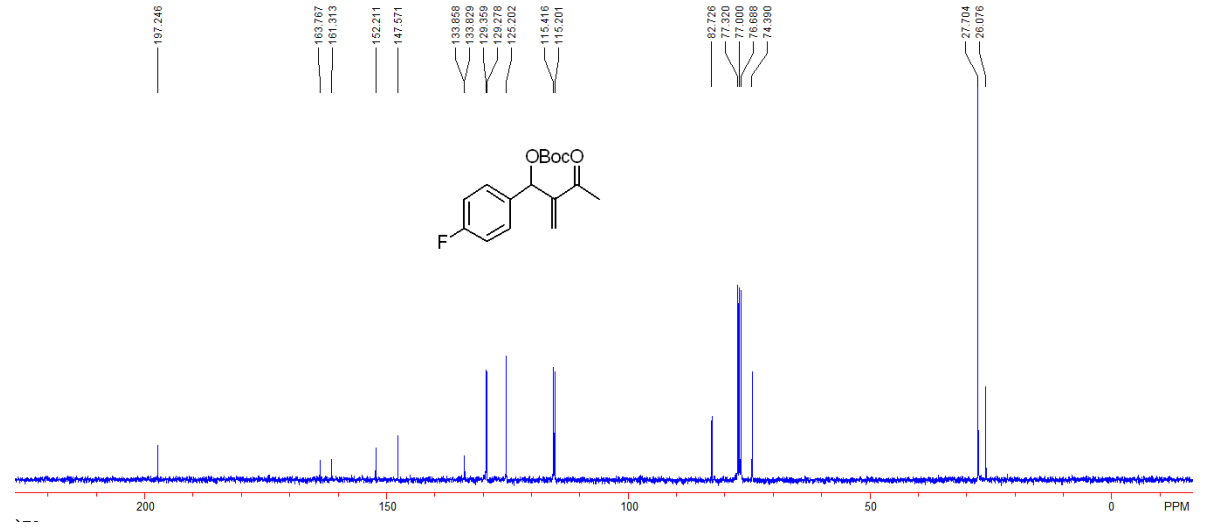
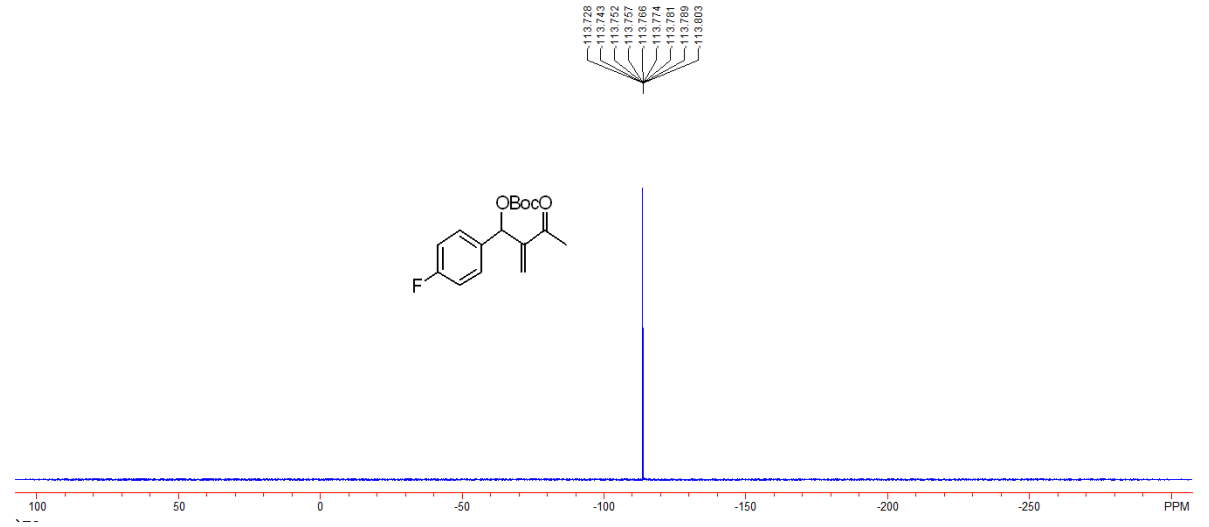
To an ice-water cooled solution of **A** (10.0 mmol) in dry CH_2Cl_2 (20 mL) was added Boc_2O (11.0 mmol) and DMAP (0.50 mmol) in dry CH_2Cl_2 (20 mL) over half an hour. The reaction mixture was stirred at room temperature overnight. The solution was washed with aqueous hydrochloric acid (15%, 20 mL), saturated sodium bicarbonate (20 mL), and brine (20 mL) sequentially, dried over anhydrous sodium sulfate, concentrated, and purified by column chromatography to get the product **2**.

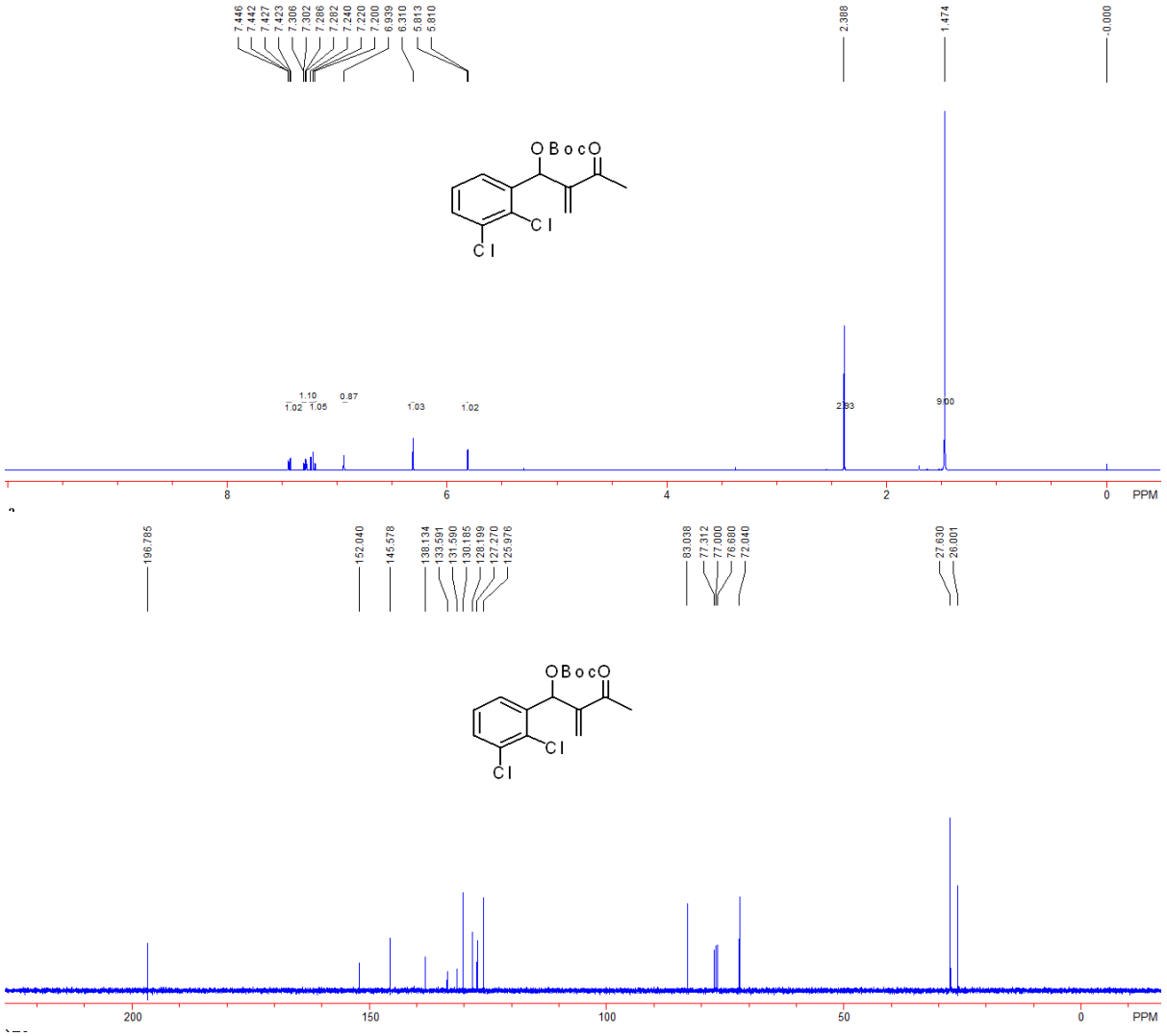
tert-butyl (1-(4-fluorophenyl)-2-methylene-3-oxobutyl) carbonate 2b: a white solid (2.99 g, 74% yield); m.p. 84-87 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.45 (s, 9H), 2.32 (s, 3H), 6.16 (d, *J* = 1.2 Hz, 1H), 6.24 (s, 1H), 6.52 (s, 1H), 7.00 (t, *J* = 8.4 Hz, 2H), 7.37 (dd, *J* = 5.2 Hz, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 27.7, 74.4, 82.7, 115.3 (d, J_{C-F} = 21.5 Hz), 125.2, 129.3 (d, J_{C-F} = 8.1 Hz), 133.8 (d, J_{C-F} = 2.9 Hz), 147.6, 152.2, 162.5 (d, J_{C-F} = 245.4 Hz), 197.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ -113.803--113.728 (m, 1F); IR (neat) ν 2982, 2935, 1747, 1682, 1606, 1510, 1082, 973, 839 cm^{-1}; MS (ESI) m/e 317.2 M+Na); HRMS (ESI) for $C_{16}H_{19}FNa_1O_4$ (M+Na): 317.1160; Found: 317.1173.







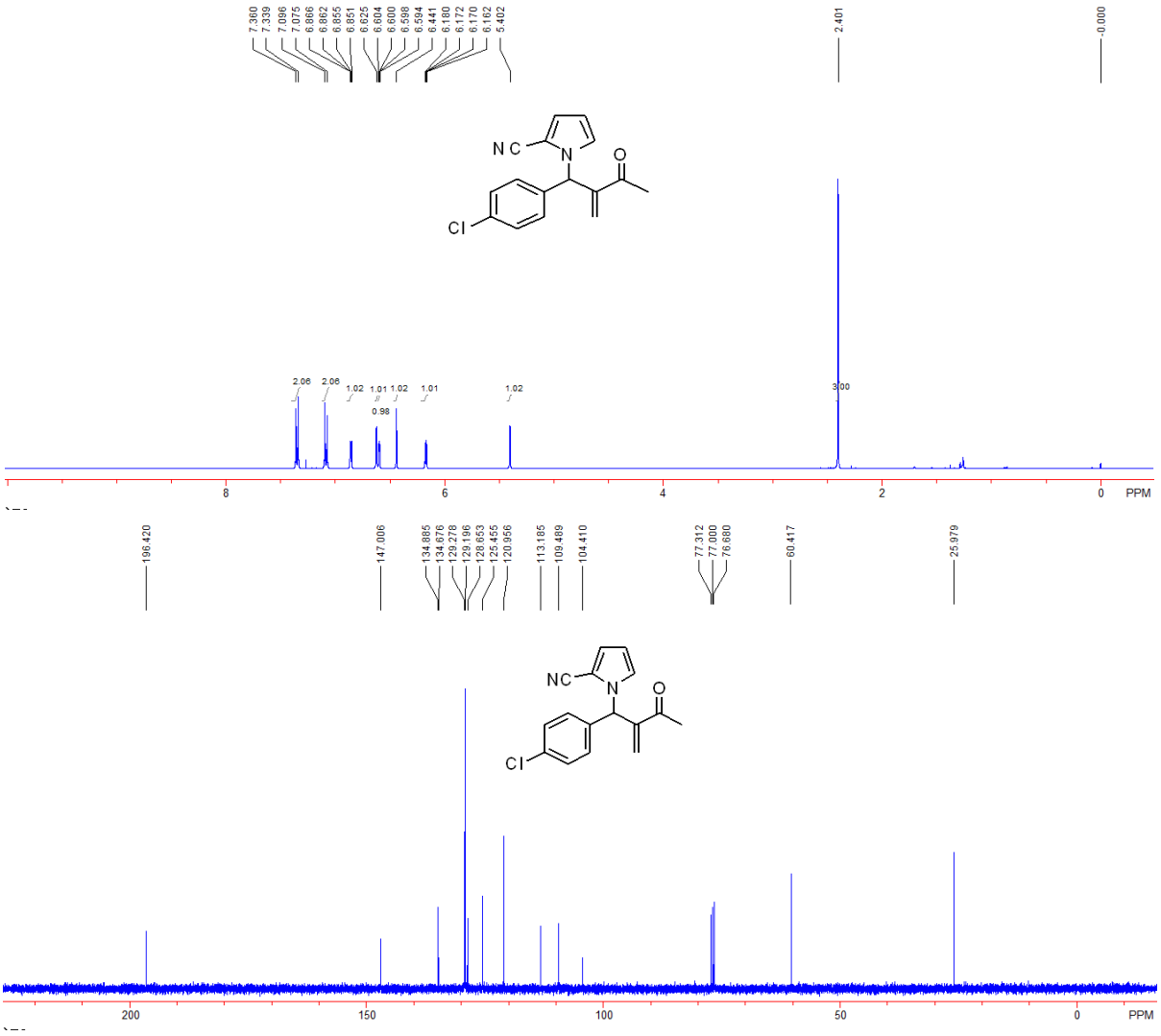
tert-butyl (1-(2,3-dichlorophenyl)-2-methylene-3-oxobutyl) carbonate 2g: a white solid (1.14g, 33% yield); m.p. 114-117 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.47 (s, 9H), 2.39 (s, 3H), 5.81 (d, *J* = 1.2 Hz, 1H), 6.31 (s, 1H), 6.94 (s, 1H), 7.22 (t, *J* = 8.0 Hz, 1H), 7.29 (dd, *J* = 1.6 Hz, *J* = 8.0 Hz, 1H), 7.43 (dd, *J* = 1.6 Hz, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.0, 27.6, 72.0, 83.0, 126.0, 127.3, 128.2, 130.2, 131.6, 133.6, 138.1, 145.6, 152.0, 196.8; IR (neat) ν 2979, 2920, 2351, 1744, 1670, 1566, 1414, 1279, 959, 847 cm^{-1}; MS (ESI) m/e 367.1 (M+Na); HRMS (ESI) for $C_{16}H_{18}Cl_2Na_1O_4$ (M+Na): 367.0474; Found: 367.0492.



General procedure for the synthesis of 3

A solution of compound **1a** (0.2 mmol) and compound **2a** (0.1 mmol) in THF (0.5 mL) was stirred at -10 ^{o}C for 96 h in the presence of organocatalyst $(DHQD)_2PYR$ (15 mol%) under argon atmosphere. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (elution with petroleum ether/EtOAc = 16/1-8/1) to provide the corresponding product **3**.

(R)-1-(1-(4-chlorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3a: a white solid (23 mg, 81% yield); m.p. 91-92 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 5.40 (s, 1H), 6.17 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H), 6.44 (s, 1H), 6.60 (dd, *J* = 1.6 Hz, 2.4 Hz, 1H), 6.63 (s, 1H), 6.86 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.09 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.4, 104.4, 109.5, 113.2, 121.0, 125.5, 128.7, 129.2, 129.3, 134.7, 134.9, 147.0, 196.4; IR (neat) ν 2924, 2854, 2215, 1678, 1490, 1367, 1225, 1088, 1070, 969, 861, 815, 735 cm^{-1}; MS (%) m/e 284 (35), 242 (4), 193 (11), 149 (4), 115 (22), 89 (4), 57 (6), 43 (100); HRMS (EI) for $C_{16}H_{13}N_2OCl$: 284.0716; Found: 284.0718; $[\alpha]^{20}_{D}$ = -116.6 (c 0.35, $CHCl_3$) (92% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 12.10 min, t_{minor} = 9.65 min.



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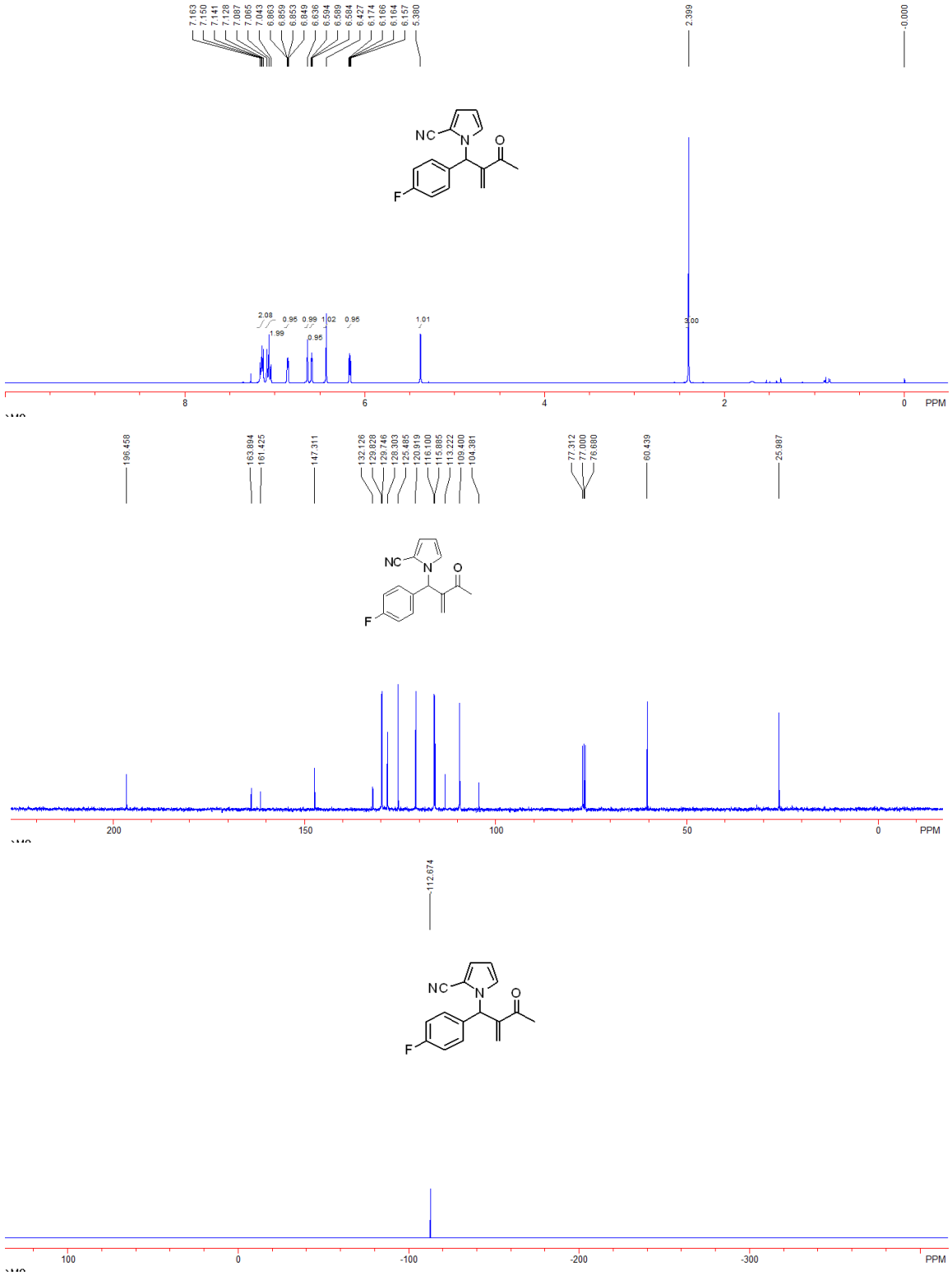
1	9.522	1803880	49.94	97143

2	12.054	1808551	50.06	78348

	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	9.645	90085	4.05	4690
2	12.098	2132447	95.95	93203

(R)-1-(1-(4-fluorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3b: a yellow oil (21 mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 5.38 (s, 1H), 6.16 (dd, *J* = 3.2 Hz, 4.0 Hz, 1H), 6.43 (s, 1H), 6.59 (t, *J* = 2.0 Hz, 1H), 6.64 (s, 1H), 6.86 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.07 (t, *J* = 8.8 Hz, 2H), 7.15 (dd, *J* = 5.2 Hz, 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.4, 104.4, 109.4, 113.2, 116.0 (d, $J_{C\text{-}F}$ = 21.5 Hz), 121.0, 125.5, 128.3, 129.8 (d, $J_{C\text{-}F}$ = 8.2 Hz), 132.1 (d, $J_{C\text{-}F}$ = 3.0 Hz), 147.3, 162.7 (d, $J_{C\text{-}F}$ = 246.9 Hz), 196.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ -112.674 (s, 1F); IR (neat) ν 2925, 2853, 2216, 1681, 1509, 1410, 1366, 1293, 1226, 1172, 977, 823, 739 cm^{-1}; MS (ESI) m/e 291.2 (M+Na); HRMS (ESI) for $C_{16}H_{13}FN_2NaO$ (M+Na): 291.0904; Found: 291.0914; $[\alpha]^{20}_{D}$ = -197.9 (c 0.60, $CHCl_3$) (82% ee); Chiralcel AD-H, hexane/^{i}PrOH = 70/30, 0.6 mL/min, 214 nm, t_{major} =

7.62 min, t_{minor} = 8.42 min.

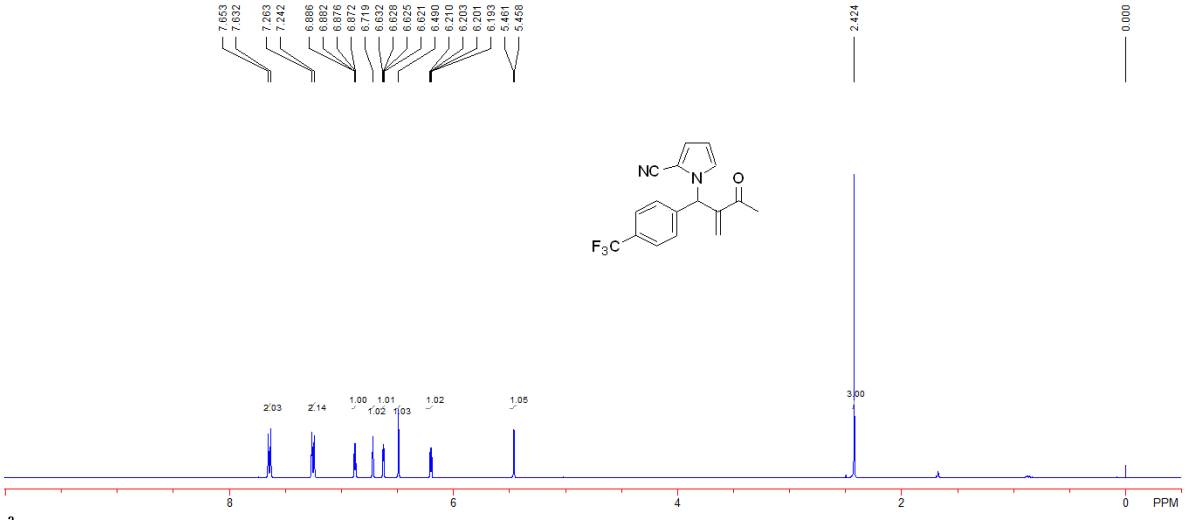


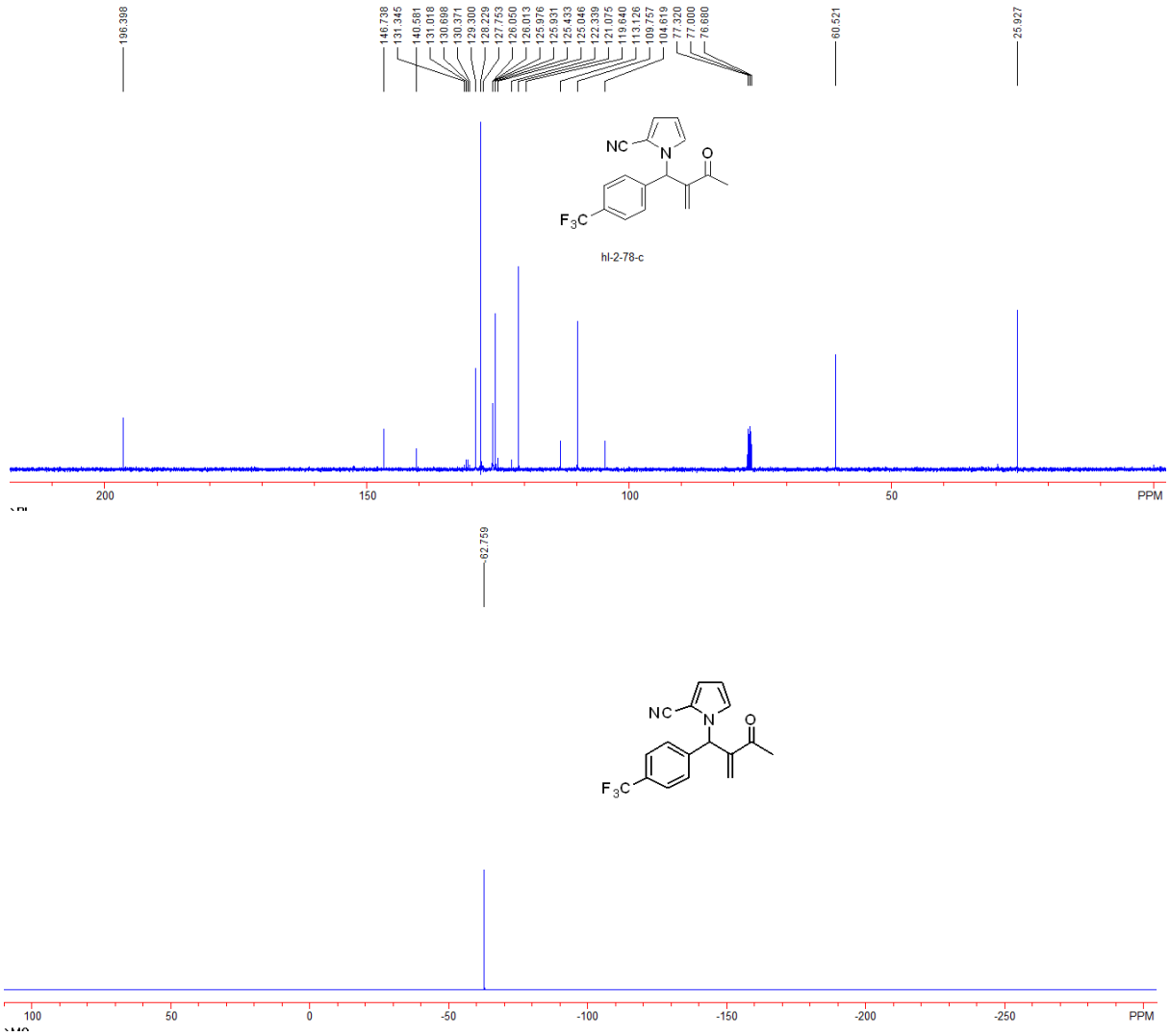
	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	7.613	3628381	49.70	326512
2	8.420	3672150	50.30	307993

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	7.622	4816904	90.90	433767
2	8.416	482027	9.10	39702

(R)-1-(2-methylene-3-oxo-1-(4-(trifluoromethyl)phenyl)butyl)-1H-pyrrole-2-carbonitrile

3c: a colorless oil (29 mg, 91% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.42 (s, 3H), 5.45 (d, J = 1.2 Hz, 1H), 6.20 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.49 (s, 1H), 6.63 (dd, *J* = 1.6 Hz, 2.8 Hz, 1H), 6.72 (s, 1H), 6.88 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.9, 60.5, 104.6, 109.8, 113.1, 121.1, 123.7 (q, $J_{C\text{-}F}$ = 270.7 Hz), 125.4, 126.0 (q, $J_{C\text{-}F}$ = 3.7 Hz), 128.2, 129.3, 130.5 (q, $J_{C\text{-}F}$ = 32.7 Hz), 140.6 , 146.7, 196.4; ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ -62.759 (s, 3F); IR (neat) ν 2925, 2218, 1740, 1682, 1621, 1523, 1418, 1323, 1264, 1166, 1114, 1068, 823, 738 cm^{-1}; MS (%) m/e 318 (11), 115 (8), 89 (4), 57 (7), 43 (100); HRMS (EI) for $C_{17}H_{13}N_2OF_3$: 318.0980; Found: 318.0981; $[\alpha]^{20}_{D}$ = -80.3 (c 1.50, $CHCl_3$) (88% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 11.20 min, t_{minor} = 8.56 min.



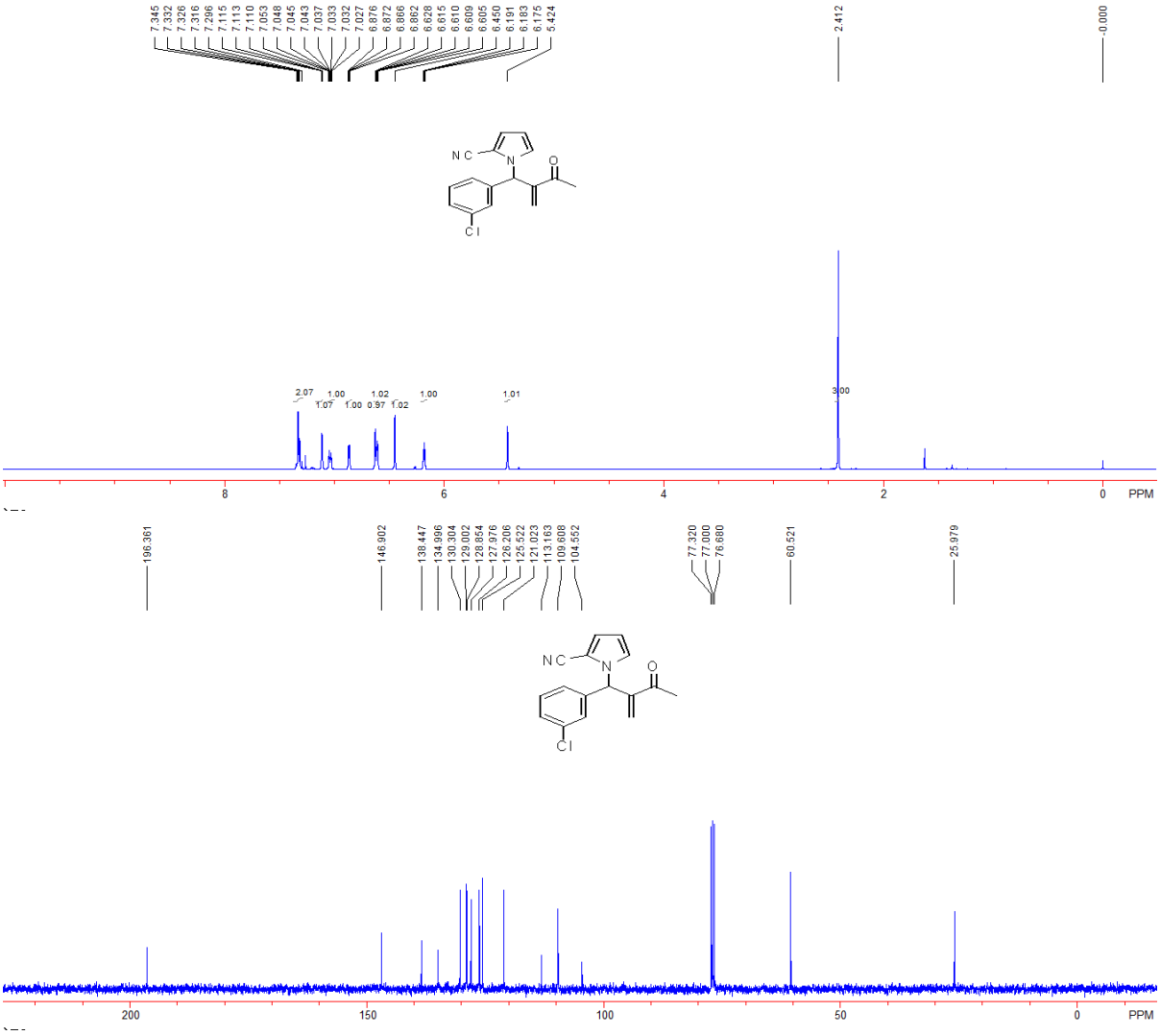


	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	8.469	2078363	49.96	127874

2	11.200	2081745	50.04	95444

	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	8.561	142119	6.15	6612
2	11.209	2169963	93.85	99973

(R)-1-(1-(3-chlorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3d: a yellow oil (25 mg, 88% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.41 (s, 3H), 5.42 (s, 1H), 6.18 (t, *J* = 3.2 Hz, 1H), 6.45 (s, 1H), 6.61 (t, *J* = 2.0 Hz, 1H), 6.63 (s, 1H), 6.87 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.03-7.05 (m, 1H), 7.11-7.12 (m, 1H), 7.30-7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 60.5, 104.5, 109.6, 113.2, 121.0, 125.5, 126.2, 128.0, 128.9, 129.0, 130.3, 135.0, 138.5, 146.9, 196.4; IR (neat) ν 2925, 2854, 2216, 1679, 1575, 1429, 1365, 1286, 1227, 1116, 1072, 977, 736 cm^{-1}; MS (%) m/e 284 (34), 242 (4), 193 (5), 115 (19), 89 (7), 57 (6), 43 (100); HRMS (EI) for $C_{16}H_{13}N_2OCl$: 284.0716; Found: 284.0719; $[\alpha]^{20}_D$ = -198.5 (c 0.80, $CHCl_3$) (85% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 12.20 min, t_{minor} = 10.92 min.

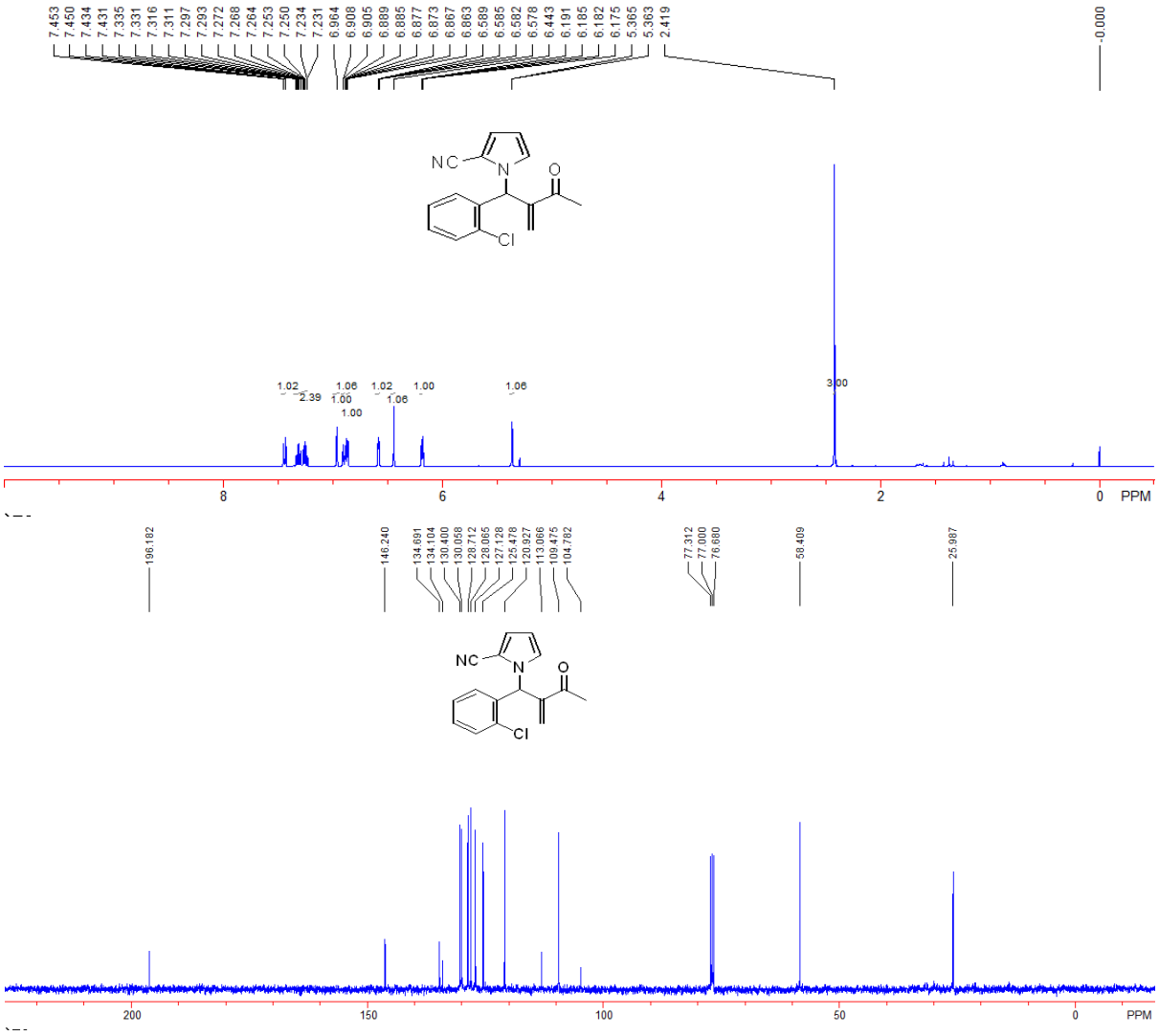


	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	10.870	4670908	49.90	232741

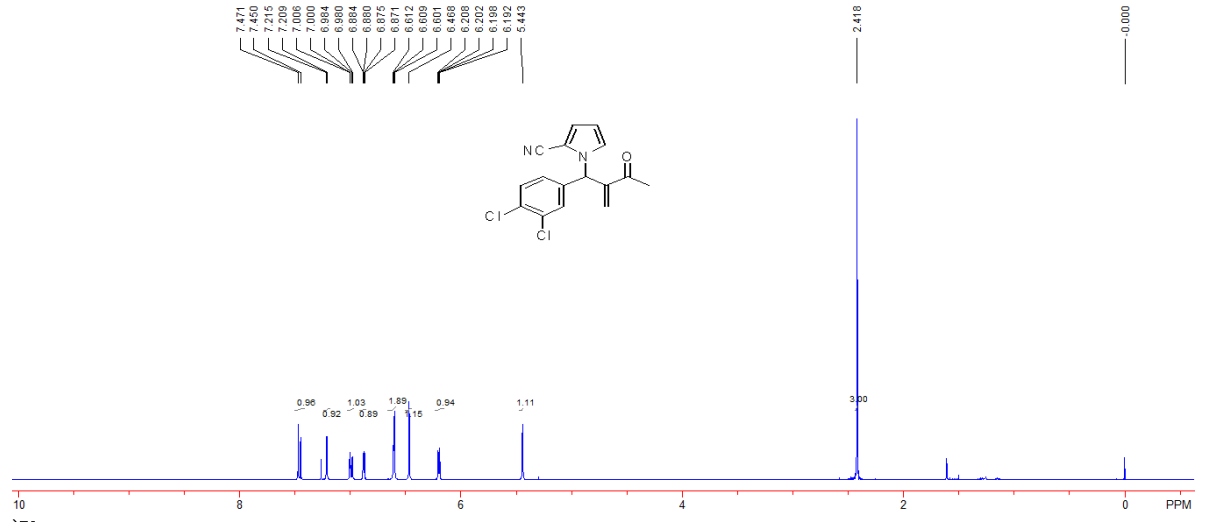
2	12.223	4690025	50.10	186323

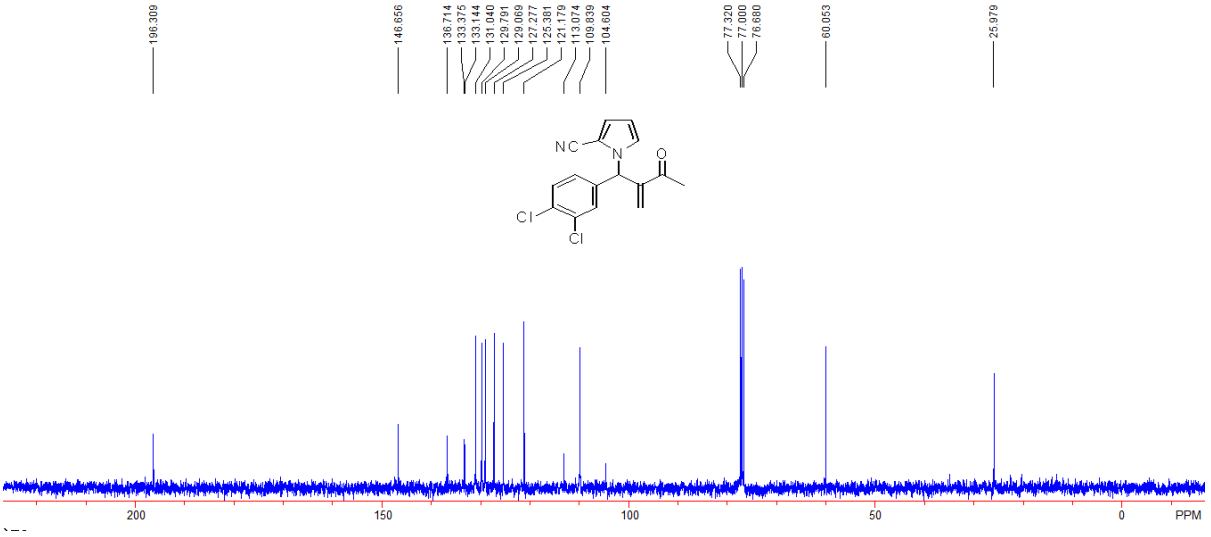
	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	10.921	503841	7.46	25597
2	12.198	6249329	92.54	245532

(S)-1-(1-(2-chlorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3e: a yellow oil (27 mg, 95% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.42 (s, 3H), 5.36 (d, *J* = 0.8 Hz, 1H), 6.18 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.44 (s, 1H), 6.58 (dd, *J* = 1.6 Hz, 2.8 Hz, 1H), 6.87 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.88-6.91 (m, 1H), 6.96 (s, 1H), 7.23-7.34 (m, 2H), 7.43-7.45 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 58.4, 104.8, 109.5, 113.1, 120.9, 125.5, 127.1 128.1, 128.7, 130.1, 130.4, 134.1, 134.7, 146.2, 196.2; IR (neat) ν 2924, 2854, 2216, 1679, 1469, 1409, 1365, 1290, 1116, 1052, 976, 855, 738 cm^{-1}; MS (%) m/e 284 (4), 249 (36), 193 (5), 115 (15), 84 (9), 57 (7), 43 (100); HRMS (EI) for $C_{16}H_{13}N_2OCl$: 284.0716; Found: 284.0715; $[\alpha]^{20}_{D}$ = -72.9 (c 1.35, $CHCl_3$) (90% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 13.61 min, t_{minor} = 12.34 min.



(R)-1-(1-(3,4-dichlorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3f: a yellow oil (29 mg, 91% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.42 (s, 3H), 5.44(s, 1H), 6.20 (dd, *J* = 2.4 Hz, 4.0 Hz, 1H), 6.47 (s, 1H), 6.60-6.61 (m, 2H), 6.88 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.99 (dd, *J* = 2.4Hz, 8.0 Hz, 1H), 7.21 (d, *J* = 2.4 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.1, 104.6, 109.8, 113.1, 121.2, 125.4, 127.3, 129.1, 129.8, 131.0, 133.1, 133.4, 136.7, 146.7, 196.3; IR (neat) ν 2925, 2855, 2216, 1677, 1523, 1470, 1365, 1285, 1115, 1073, 961, 879, 817, 737 cm^{-1}; MS (%) m/e 318 (17), 227 (4), 149 (10), 57 (3), 43 (100); HRMS (EI) for $C_{16}H_{12}N_2OCl_2$: 318.0327; Found: 318.0323; $[\alpha]^{20}_D$ = -154.5 (c 1.20, $CHCl_3$) (90% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 13.01 min, t_{minor} = 9.69 min.





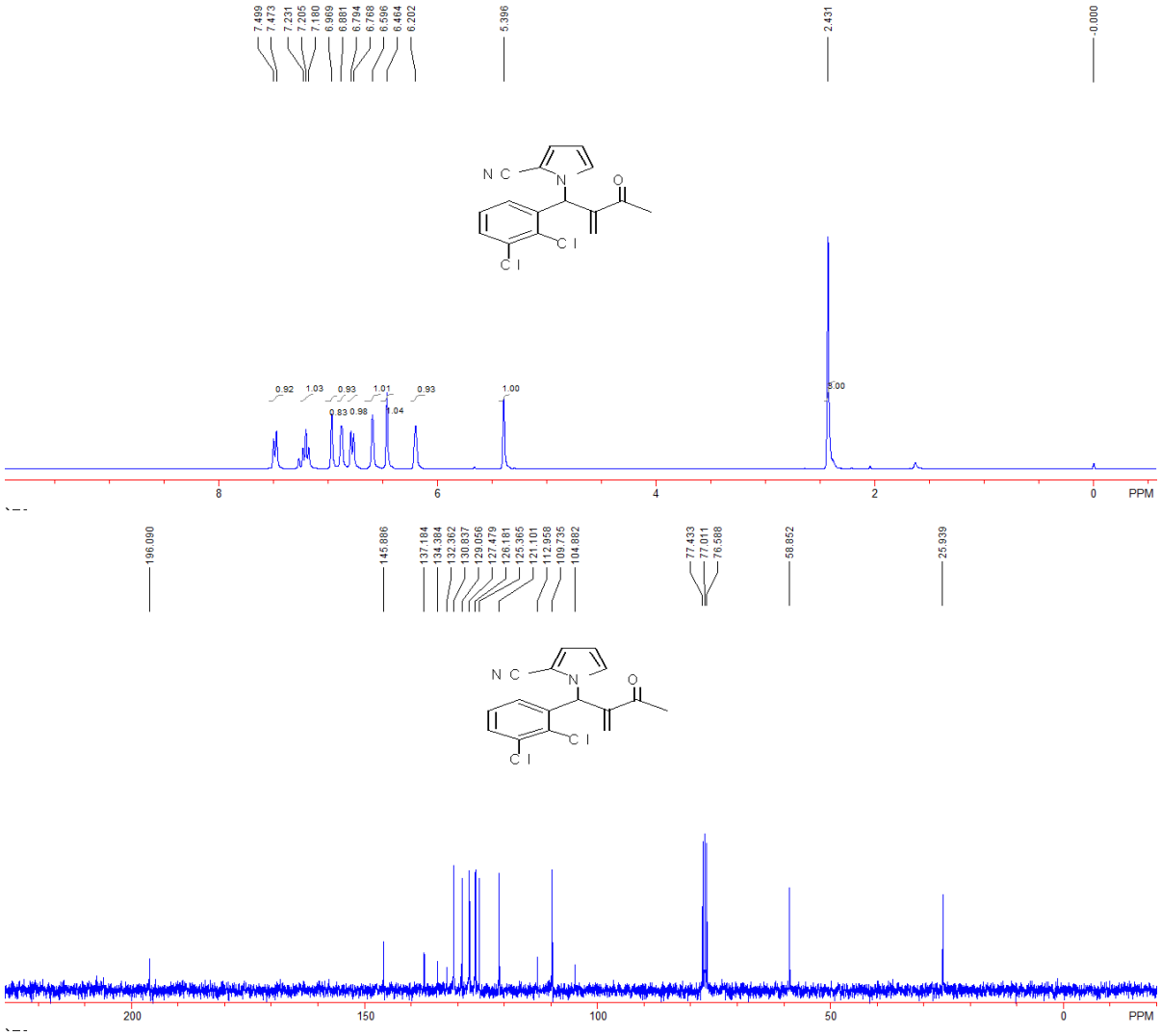
	RT	Area	% Area	Height

	(min)	（μV*sec)		(μV)
1	9.660	1072922	49.92	54547
2	13.047	1076285	50.08	41205

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	9.687	143025	5.10	5215
2	13.006	2663559	94.90	102647

(S)-1-(1-(2,3-dichlorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3g: a white solid (29 mg, 91% yield); m.p. 124-126 ^{o}C ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 5.40 (s, 1H), 6.20 (s, 1H), 6.46 (s, 1H), 6.60 (s, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 6.88 (s, 1H), 6.97 (s, 1H), 7.21 (t, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.9, 58.9, 104.8, 109.7, 113.0, 121.1, 125.4, 126.2, 127.5, 129.1, 130.8, 132.4,

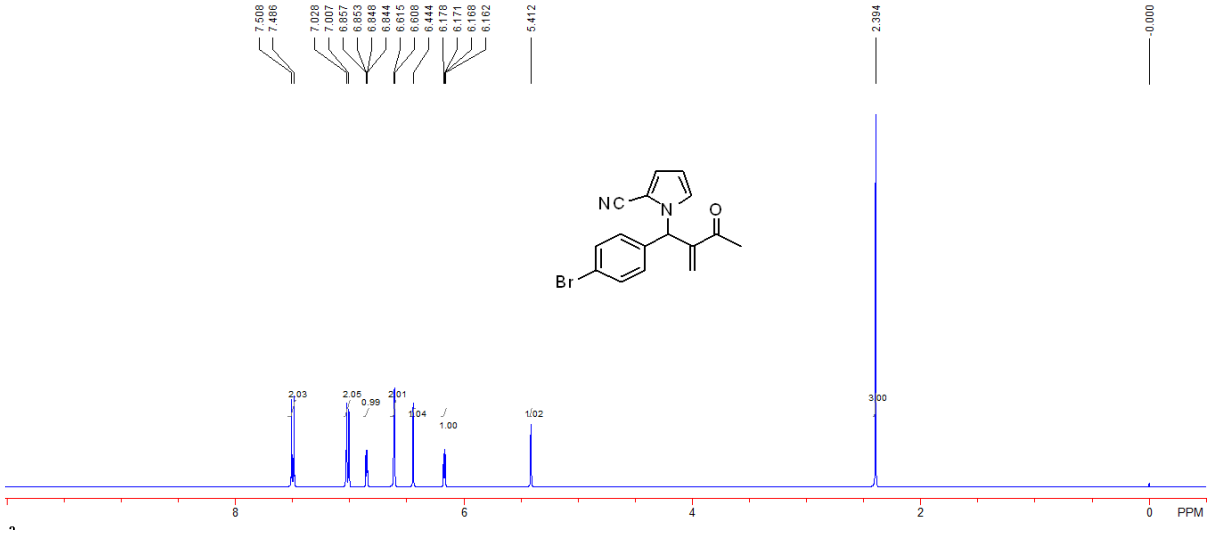
134.4, 137.2, 145.9, 196.1; IR (neat) ν 2923, 2850, 2214, 1676, 1447, 1411, 1365, 1290, 1177, 1121, 1047, 963, 876, 745 cm^{-1}; MS (%) m/e 318 (4), 283 (37), 149 (11), 113 (5), 43 (100); HRMS (EI) for $C_{16}H_{12}N_2OCl_2$: 318.0327; Found: 318.0325; $[\alpha]^{20}_D$ = -119.5 (c 0.90, $CHCl_3$) (91% ee); Chiralcel AD-H, hexane/^{i}PrOH = 90/10, 0.7 mL/min, 230 nm, t_{major} = 11.88 min, t_{minor} = 10.92 min.

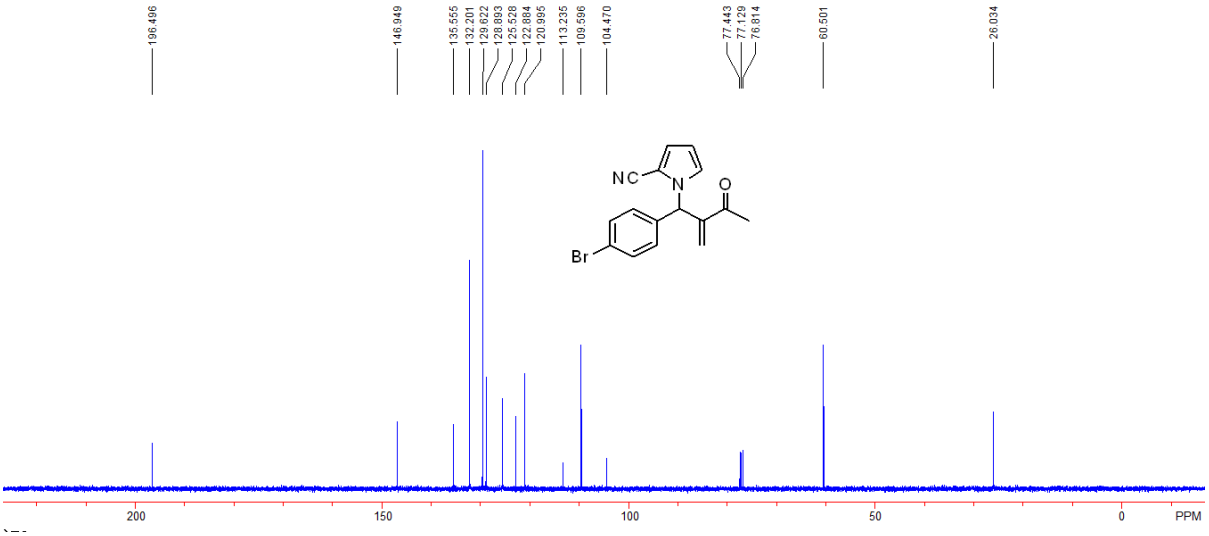


	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	10.895	1197022	49.96	70789
2	11.853	1199144	50.04	64720

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	10.917	38097	4.71	2407
2	11.875	771154	95.29	42573

(R)-1-(1-(4-bromophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3h: a white solid (27 mg, 82% yield); m.p. 87-89 ^{o}C ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 5.41 (s, 1H), 6.17 (dd, *J* = 2.4 Hz, 3.6 Hz, 1H), 6.44 (s, 1H), 6.60-6.62 (m, 1H), 6.85 (dd, *J* = 1.6 Hz, 3.6 Hz, 1H), 7.01 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.5, 104.5, 109.6, 113.2, 121.0, 122.9, 125.5, 128.9, 129.6, 132.2, 135.6, 146.9, 196.5; IR (neat) ν 2925, 2215, 1940, 1680, 1521, 1367, 1440, 1350, 1224, 1170, 1069, 818, 737 cm^{-1}; MS (%) m/e 328 (8), 237 (4), 158 (13), 115 (17), 89 (4), 84 (4), 63 (4), 43 (100); HRMS (EI) for $C_{16}H_{13}N_2OBr$: 328.0211; Found: 328.0209; $[\alpha]^{20}_{D}$ = -177.0 (c 0.25, $CHCl_3$) (91% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 12.42 min, t_{minor} = 9.91 min.

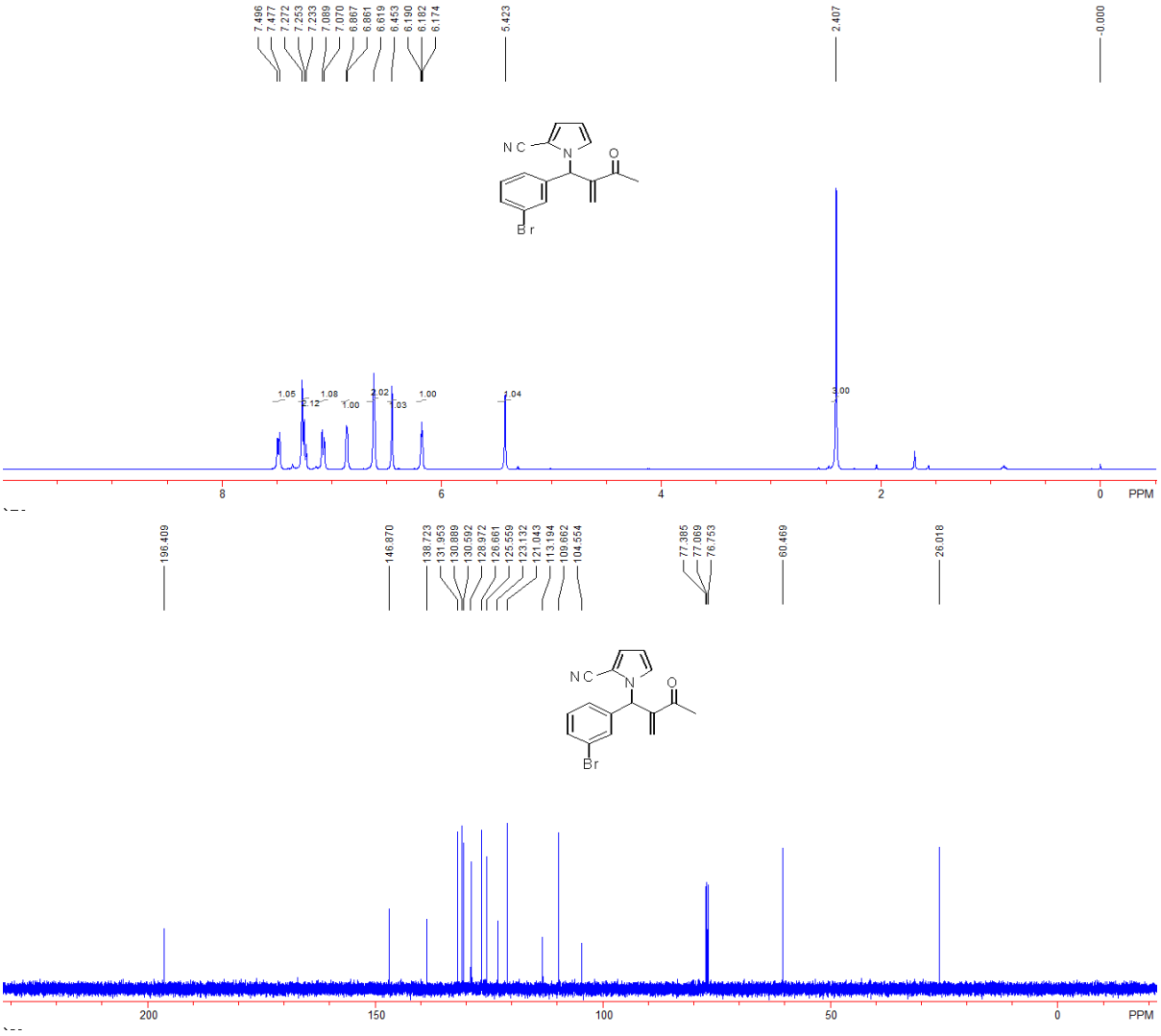




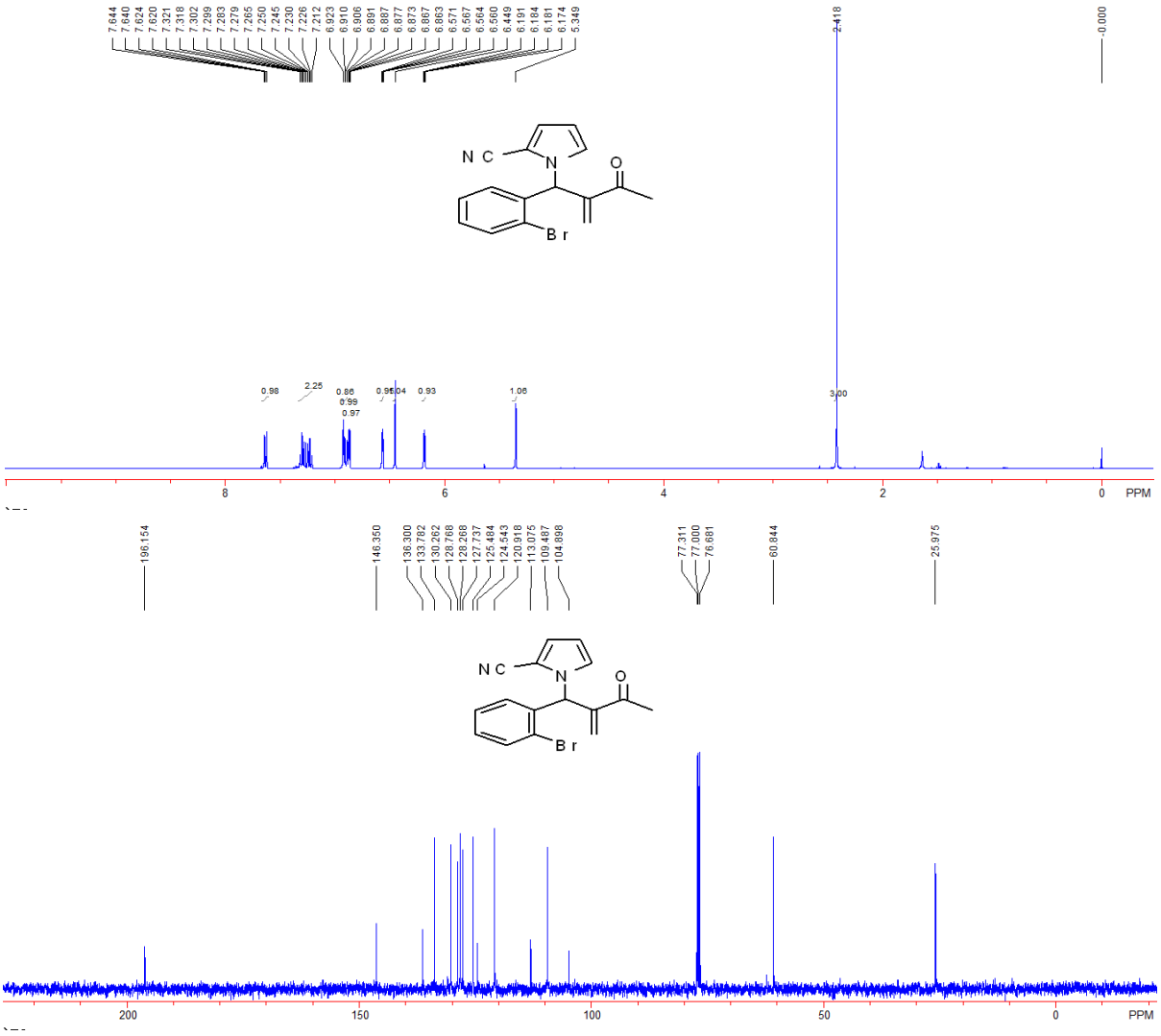
	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	9.907	2583294	50.12	133951
2	12.479	2571015	49.88	109011

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	9.912	196061	4.11	9579
2	12.422	4570169	95.89	192418

(R)-1-(1-(3-bromophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3i: a yellow oil (32 mg, 97% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.41 (s, 3H), 5.42 (s, 1H), 6.18 (t, *J* = 2.8 Hz, 1H), 6.45 (s, 1H), 6.62 (s, 2H), 6.86 (d, *J* = 2.8 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 7.23-7.27 (m, 2H), 7.49 (d, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.5, 104.6, 109.7, 113.2, 121.0, 123.1, 125.6, 126.7, 129.0, 130.6, 130.9, 132.0, 138.7, 146.9, 196.4; IR (neat) ν 2925, 2853, 2216, 1679, 1570, 1456, 1409, 1365, 1286, 1226, 1116, 1072, 976, 738, 688 cm^{-1}; MS (%) m/e 328 (6), 253 (4), 207 (1), 158 (8), 115 (15), 84 (8), 57 (5), 43 (100); HRMS (EI) for $C_{16}H_{13}N_2OBr$: 328.0211; Found: 328.0215; $[\alpha]^{20}_{D}$ = -107.1 (c 1.50, $CHCl_3$) (84% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 16.58 min, t_{minor} = 15.28 min.



(S)-1-(1-(2-bromophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3j: a yellow oil (31 mg, 94% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.42 (s, 3H), 5.35 (s, 1H), 6.18 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.45 (s, 1H), 6.57 (dd, *J* = 1.6 Hz, 2.8 Hz, 1H), 6.87 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.88-6.91 (m, 1H), 6.92 (s, 1H), 7.21-7.32 (m, 2H), 7.62-7.64 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.8, 104.9, 109.5, 113.0, 120.9, 124.5, 125.5, 127.7, 128.3, 128.8, 130.2, 133.8, 136.3, 146.4, 196.2; IR (neat) ν 2367, 2218, 1678, 1521, 1406, 1281, 1220, 1111, 1074, 978, 751 cm^{-1}; MS (ESI) m/e 351.2 (M+Na); HRMS (ESI) for $C_{16}H_{13}BrN_2NaO$ (M+Na): 351.0104; Found: 351.0116; $[\alpha]^{20}_{D}$ = -84.2 (c 0.67, $CHCl_3$) (84% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 11.07 min, t_{minor} = 9.88 min.

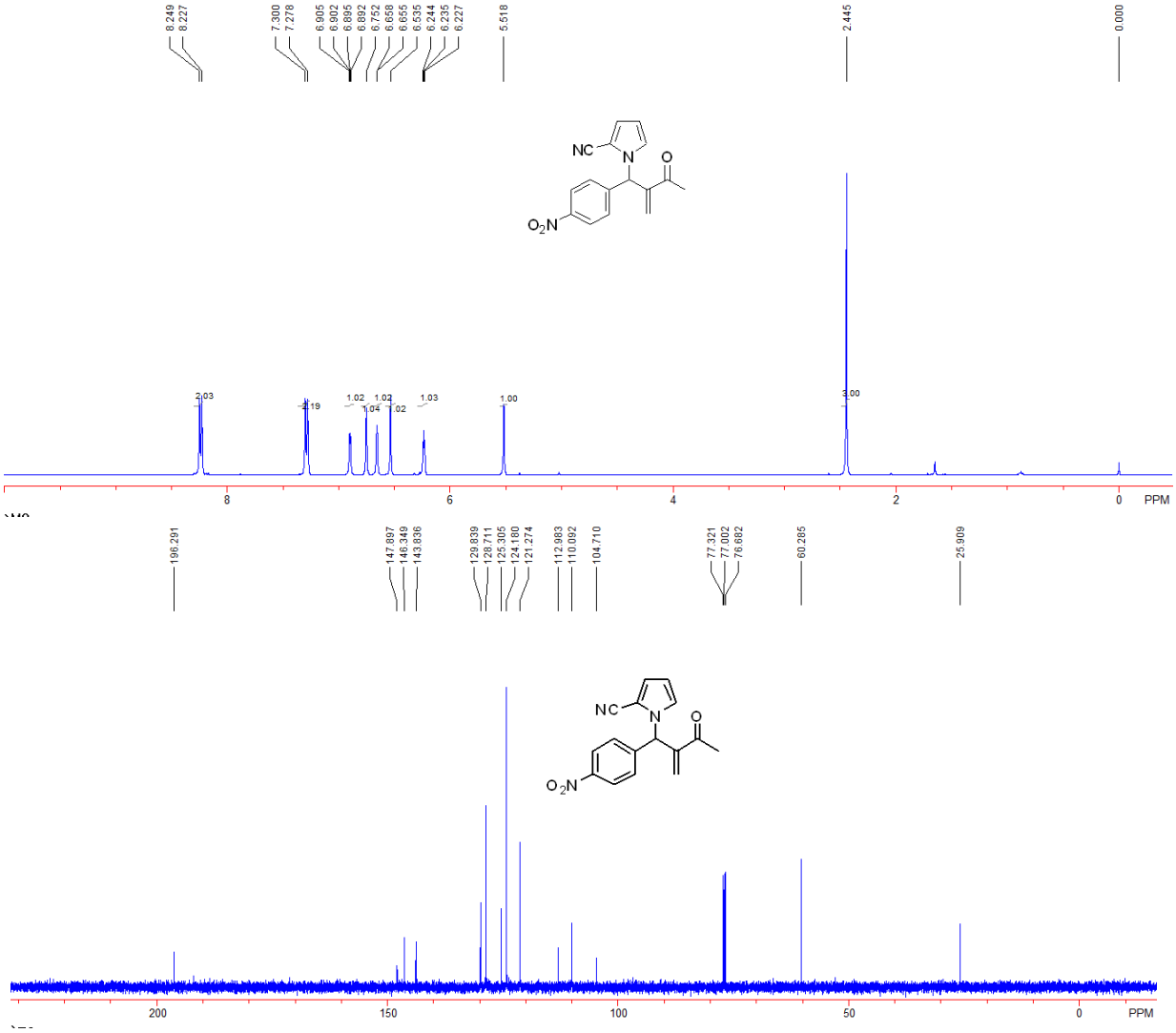


	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	9.722	3014875	50.00	172340
2	10.840	3015281	50.00	155133

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	9.876	268834	8.46	14831
2	11.067	2907256	91.54	142822

(R)-1-(2-methylene-1-(4-nitrophenyl)-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3k: a yellow oil (30 mg, 99% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.45 (s, 3H), 5.52 (s, 1H), 6.24 (t, *J* = 2.8 Hz, 3.6 Hz, 1H), 6.54 (s, 1H), 6.66 (d, *J* = 1.2 Hz, 1H), 6.75 (s, 1H), 6.90 (dd, *J* = 1.2 Hz, 4.0 Hz, 1H), 7.29 (d, *J* = 8.8 Hz, 2H), 8.24 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.3, 104.7, 110.1, 113.0, 121.3, 124.2, 125.3, 128.7, 129.8, 143.8, 146.3, 147.9, 196.3; IR (neat) ν 2923, 2853, 2216, 1679, 1605, 1520, 1440, 1346, 1227, 1173, 976,

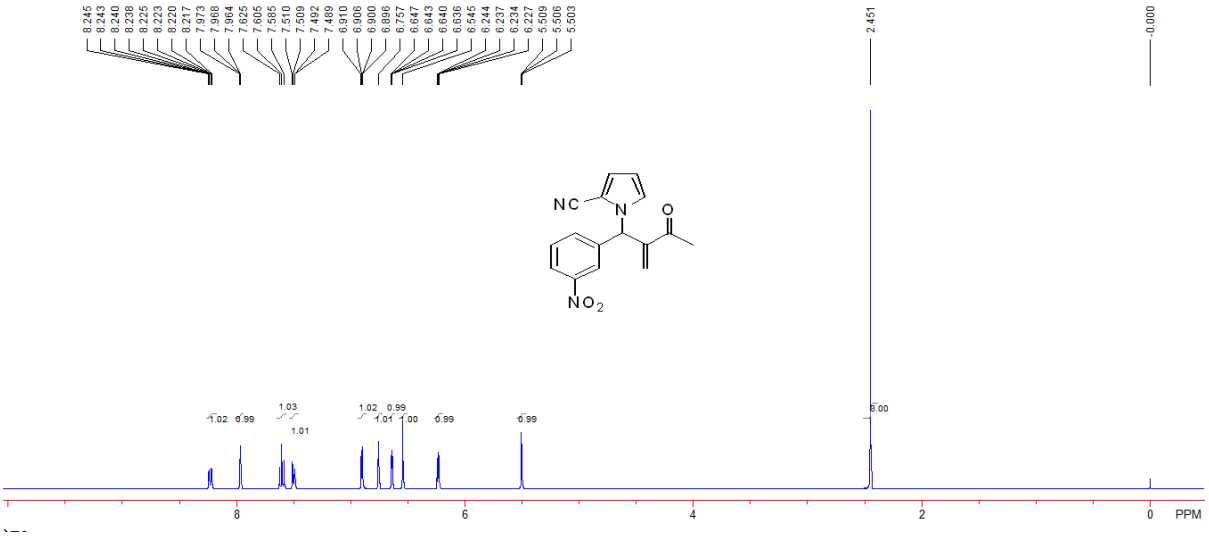
856, 735 cm^{-1}; MS (%) m/e 295 (465), 278 (49), 236 (15), 162 (18), 115 (9), 92 (11), 43 (100); HRMS (EI) for $C_{16}H_{13}N_3O_3$: 295.0957; Found: 295.0956; $[\alpha]^{20}_D$ = -87.9 (c 1.50, $CHCl_3$) (93% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 31.61 min, t_{minor} = 22.63 min.

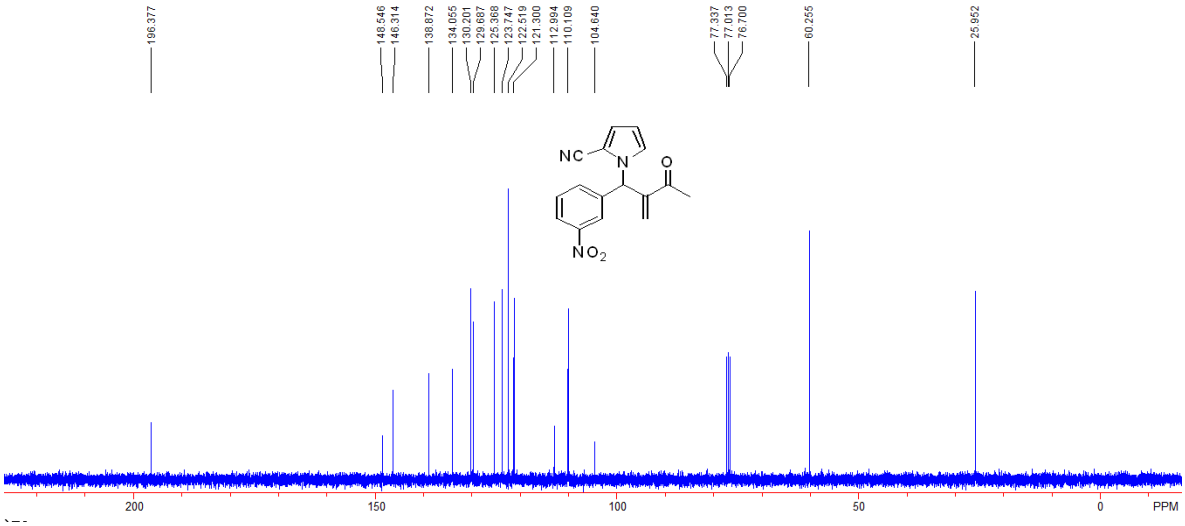


	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	22.715	544679	49.85	9989
2	32.333	547973	50.15	7293

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	22.630	39215	3.25	788
2	31.608	1166188	96.75	16033

(R)-1-(2-methylene-1-(3-nitrophenyl)-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3l: a yellow oil (25 mg, 84% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.45 (s, 3H), 5.51 (t, *J* = 1.2 Hz, 1H), 6.24 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.55 (s, 1H), 6.64 (dd, *J* = 1.6 Hz, 2.8 Hz, 1H), 6.76 (s, 1H), 6.90 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.49-7.51 (m, 1H), 7.59-7.63 (m, 1H), 7.96-7.97 (m, 1H), 8.22-8.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 60.3, 104.6, 110.1, 113.0, 121.3, 122.5, 123.7, 125.4, 129.7, 130.2, 134.1, 138.9, 146.3, 148.6, 196.4; IR (neat) ν 2926, 2855, 2216, 1679, 1529, 1456, 1409, 1349, 1291, 1073, 967, 808, 730 cm^{-1}; MS (%) m/e 295 (14), 278 (32), 162 (6), 115 (14), 92 (11), 43 (100); HRMS (EI) for $C_{16}H_{13}N_3O_3$: 295.0957; Found: 295.0953; $[\alpha]^{20}_{D}$ = -122.5 (c 1.10, $CHCl_3$) (78% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 23.20 min, t_{minor} = 18.43 min.

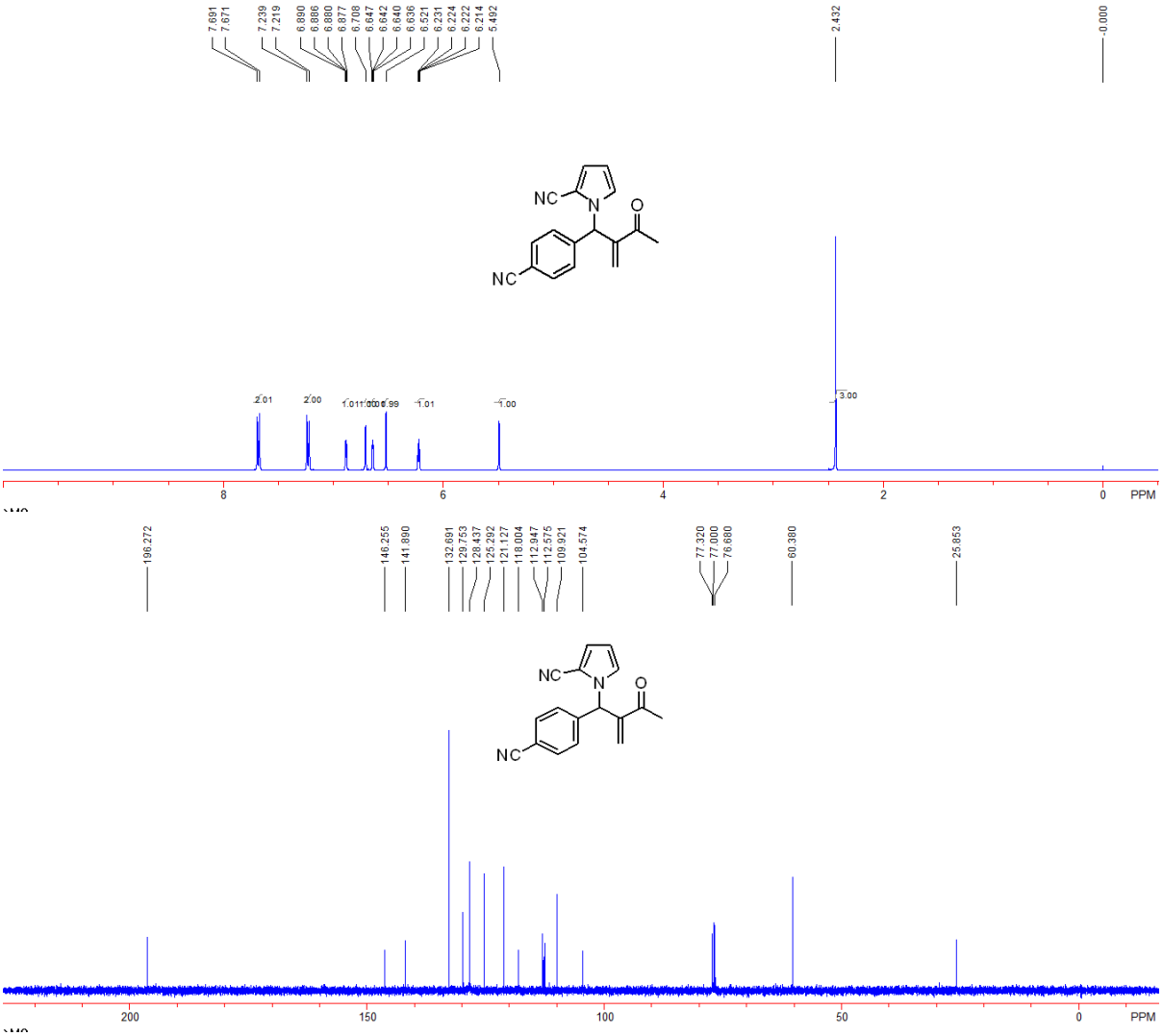




	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	18.156	2820953	50.38	71635
2	23.207	2778859	49.62	53101

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	18.427	741901	10.76	18694
2	23.199	6154655	89.24	107732

(R)-1-(1-(4-cyanophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3m: a colorless oil (27.3 mg, 99% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 5.49 (s, 1H), 6.22 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.52 (s, 1H), 6.64 (dd, *J* = 1.6 Hz, 2.8 Hz, 1H), 6.71 (s, 1H), 6.88 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 60.4, 104.6, 110.0, 112.6, 113.0, 118.0, 121.1, 125.3, 128.4, 129.8, 132.7, 141.9, 146.3, 196.3; IR (neat) ν 2925, 2854, 2216, 1678, 1454, 1410, 1366, 1295, 1115, 1073, 976, 818, 740 cm^{-1}; MS (%) m/e 275 (85), 260 (12), 232 (11), 184 (15), 142 (51), 92 (11), 43 (100); HRMS (EI) for $C_{17}H_{13}N_3O$: 275.1059; Found: 275.1055; $[\alpha]^{20}_{D}$ = -121.1 (c 1.50, $CHCl_3$) (88% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 26.84 min, t_{minor} = 19.98 min.

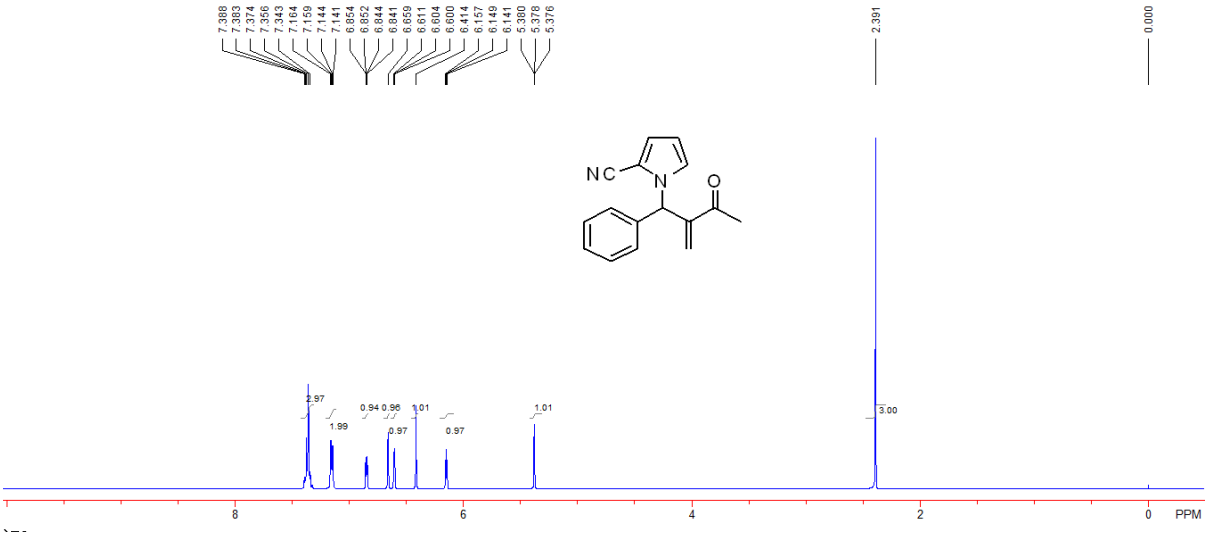


	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	19.410	10150611	50.11	206907

2	26.799	10105392	49.89	146062

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	19.983	968111	6.08	14482
2	26.835	14947145	93.92	213471

(R)-1-(2-methylene-3-oxo-1-phenylbutyl)-1H-pyrrole-2-carbonitrile 3n: a yellow oil (17 mg, 68% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.39 (s, 3H), 5.38 (t, *J* = 0.8 Hz, 1H), 6.15 (t, *J* = 3.2 Hz, 1H), 6.41 (s, 1H), 6.60-6.61 (m, 1H), 6.66 (s, 1H), 6.85 (dd, *J* = 1.2 Hz, 3.2 Hz, 1H), 7.14-7.16 (m, 2H), 7.34-7.39 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 61.2, 104.4, 109.3, 113.4, 120.9, 125.7, 128.0, 128.3, 128.8, 129.0, 136.3, 147.4, 196.6; IR (neat) ν 3124, 2216, 1740, 1680, 1598, 1451, 1365, 1292, 1171, 976, 734, 699 cm^{-1}; MS (%) m/e 250 (18), 235 (4), 207 (3), 159 (7), 115 (14), 91 (4), 57 (8), 43 (100); HRMS (EI) for $C_{16}H_{14}N_2O$: 250.1106; Found: 250.1103; $[\alpha]^{20}_{D}$ = -165.6 (c 0.75, $CHCl_3$) (82% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 16.49 min, t_{minor} = 14.90 min.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5.378
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N
O
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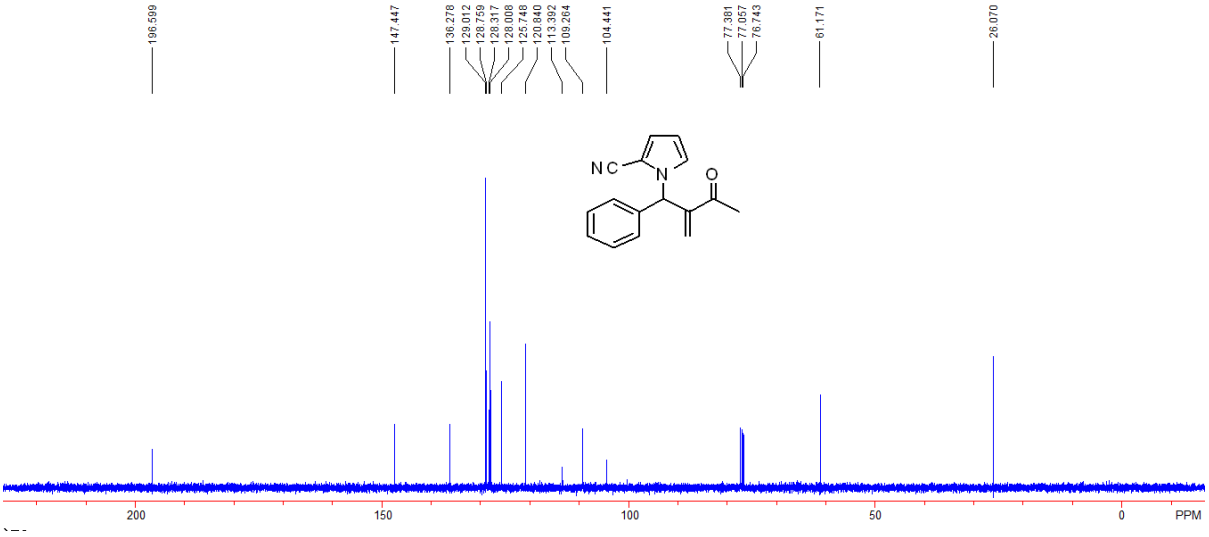
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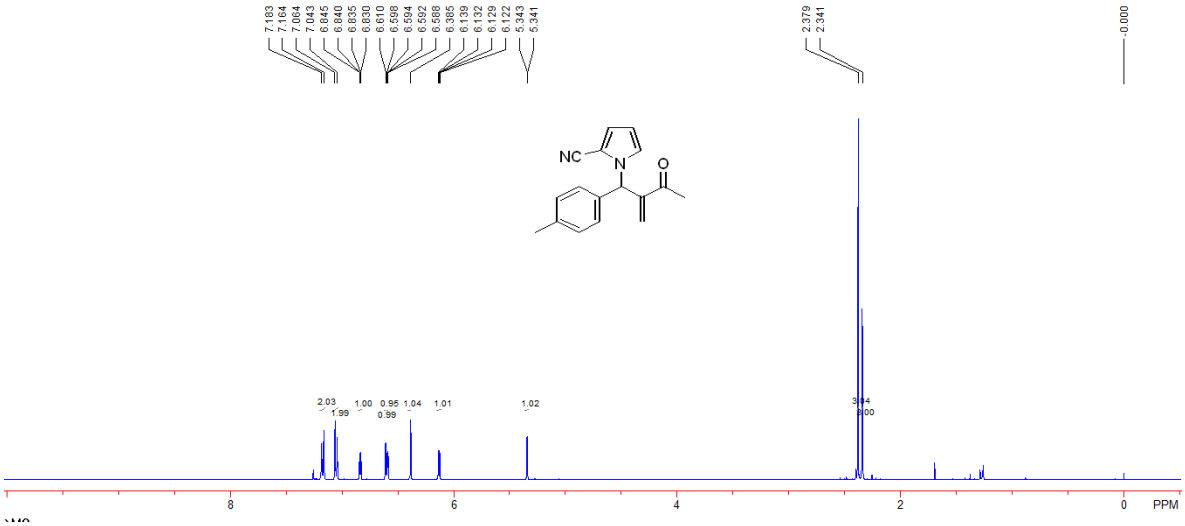
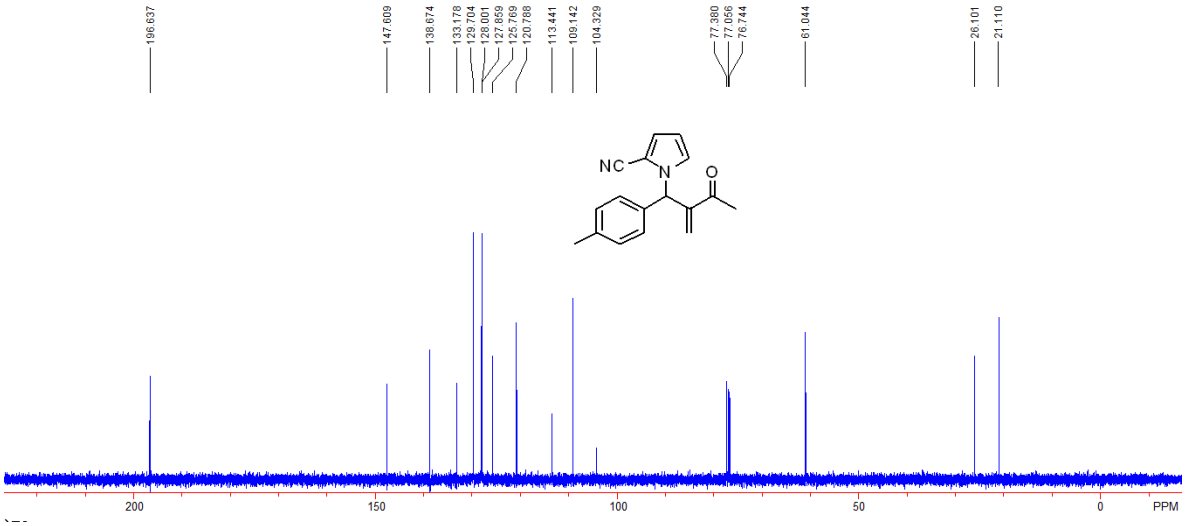
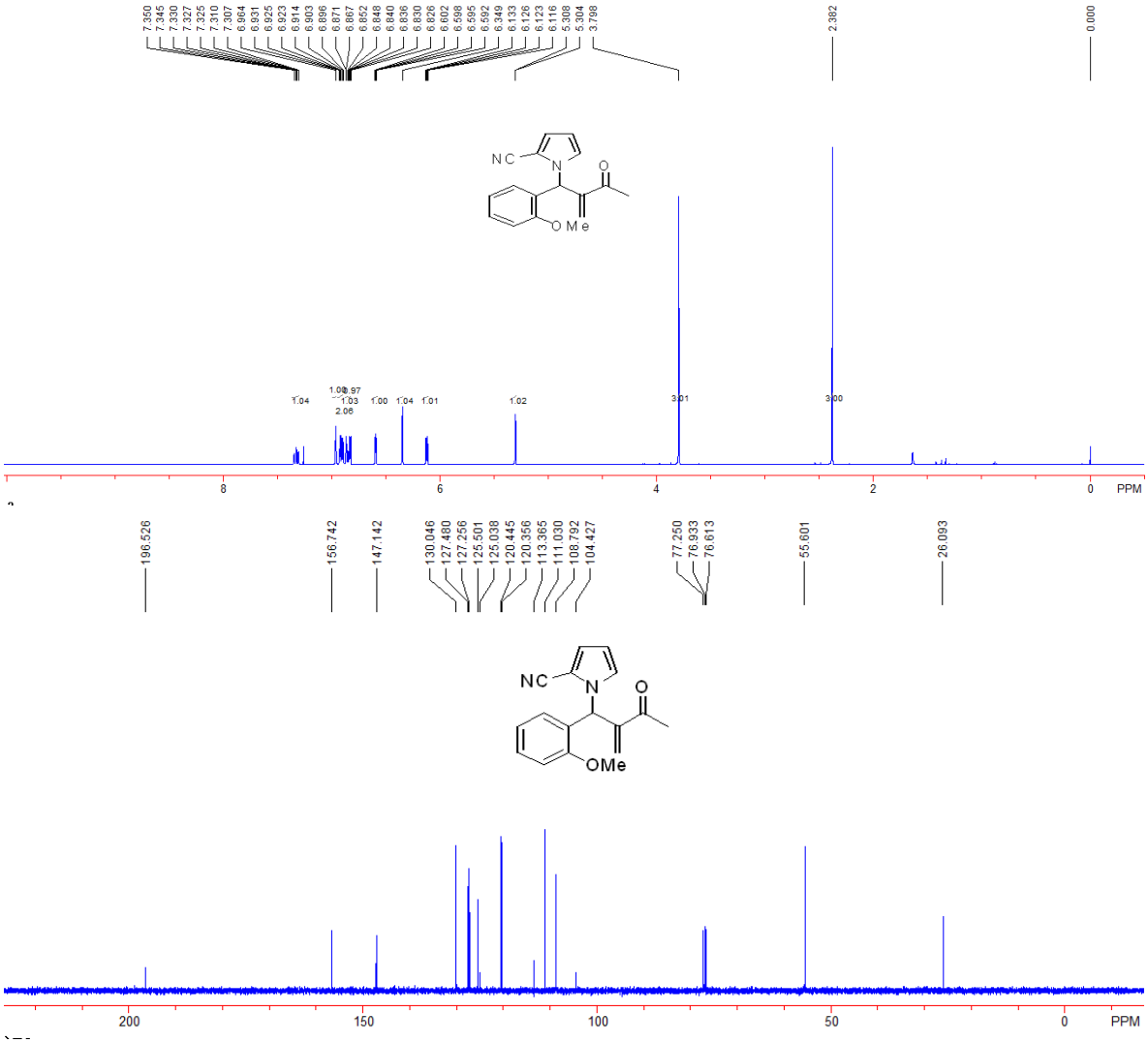
100
50
0
PPM

(R)-1-(2-methylene-3-oxo-1-(p-tolyl)butyl)-1H-pyrrole-2-carbonitrile 3o: a white solid (21 mg, 80% yield); m.p. 63-65 ^{o}C ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.34 (s, 3H), 2.38 (s, 3H), 5.34 (d, *J* = 1.2 Hz, 1H), 6.13 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.39 (s, 1H), 6.59 (dd, *J* = 1.6 Hz, 2.8 Hz, 1H), 6.61 (s, 1H), 6.84 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 26.1, 61.0, 104.3, 109.1, 113.4, 120.8, 125.8, 127.9, 128.0, 129.7, 133.2, 138.7, 147.6, 196.6; IR (neat) ν 2925, 2854, 1718, 1622, 1560, 1467, 1380, 1259, 1186, 1082, 965, 763 cm^{-1}; MS (%) m/e 264 (20), 249 (7), 173 (10), 131 (7), 115 (7), 91 (3), 84 (3), 43 (100); HRMS (EI) for $C_{17}H_{16}N_2O$: 264.1263; Found: 264.1267; $[\alpha]^{20}_{D}$ = -142.1 (c 1.00, $CHCl_3$) (76% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 13.81 min, t_{minor} = 10.92 min.

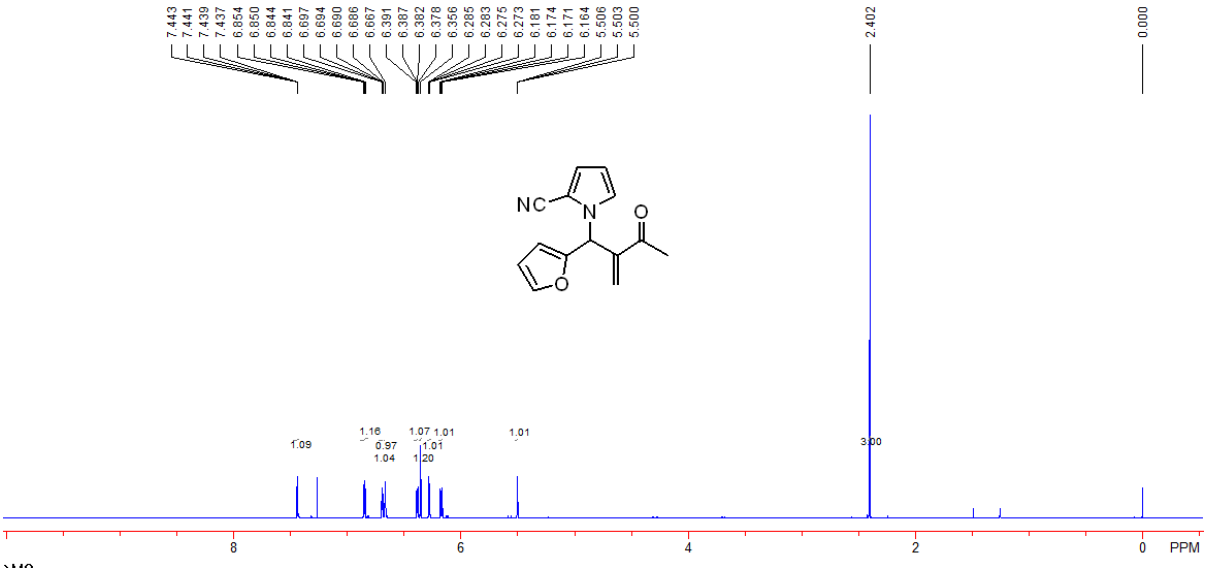


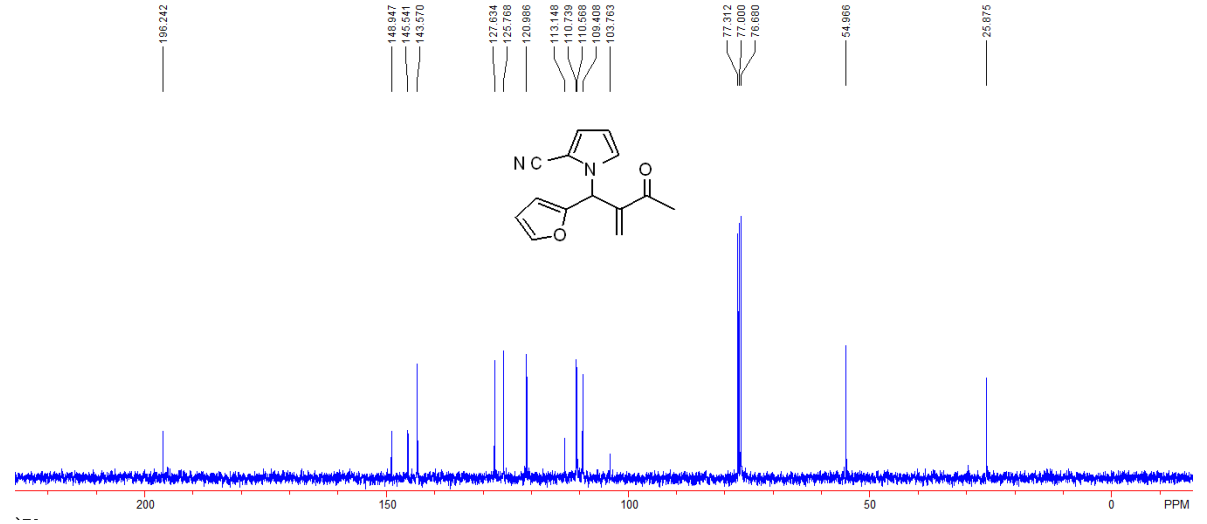


(R)-1-(1-(2-methoxyphenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3p: a white solid (26 mg, 93% yield); m.p. 95-97 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.38 (s, 3H), 3.80 (s, 3H), 5.31 (d, *J* = 1.2 Hz, 1H), 6.12 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.35 (s, 1H), 6.60 (dd, *J* = 1.6 Hz, 2.8 Hz, 1H), 6.83 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.85-6.87 (m, 1H), 6.90-6.93 (m, 2H), 6.96 (s, 1H), 7.31-7.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 55.6, 104.4, 108.8, 113.4, 120.4, 120.5, 125.0, 125.5, 127.3, 127.5, 130.1, 147.1, 156.7, 196.5; IR (neat) ν 2924, 2854, 1713, 1671, 1598, 1490, 1463, 1361, 1250, 1111, 1022, 970, 745 cm^{-1}; MS (%) m/e 280 (19), 189 (12), 147 (14), 115 (7), 91 (7), 71 (13), 57 (17), 43 (100); HRMS (EI) for $C_{17}H_{16}N_2O_2$: 280.1212; Found: 280.1210; $[\alpha]^{20}_{D}$ = -183.1 (c 0.50, $CHCl_3$) (89% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 12.91 min, t_{minor} = 11.29 min.


7.350
7.345
7.330
7.327
7.325
7.310
7.307
6.964
6.931
6.925
6.923
6.914
6.903
6.896
6.871
6.867
6.852
6.848
6.840
6.836
6.830
6.826
6.602
6.598
6.595
6.592
6.349
6.133
6.126
6.123
6.116
5.308
5.304
3.798
2.382
0.000
NC
N
O
O Me
1.04
1.08
0.97
1.03
2.06
1.00
1.04
1.01
1.02
3.01
3.00
8
6
4
2
0
PPM
196.526
156.742
147.142
130.046
127.480
127.256
125.501
125.038
120.445
120.356
113.365
111.030
108.792
104.427
77.250
76.933
76.613
55.601
26.093
NC
N
O
OMe
200
150
100
50
0
PPM

(S)-1-(1-(furan-2-yl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3q: a yellow oil (18 mg, 75% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 5.50 (t, *J* = 1.2 Hz, 1H), 6.17 (dd, *J* = 2.8 Hz, *J* = 4.0 Hz, 1H), 6.28 (dd, *J* = 0.8 Hz, *J* = 4.0 Hz, 1H), 6.36 (s, 1H), 6.38 (dd, *J* = 1.6 Hz, *J* = 4.0 Hz, 1H), 6.67 (s, 1H), 6.69 (dd, *J* = 1.6 Hz, *J* = 2.8 Hz, 1H), 6.85 (dd, *J* = 1.6 Hz, *J* = 4.0 Hz, 1H), 7.44 (dd, *J* = 0.8 Hz, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 55.0, 103.8, 109.4, 110.6, 110.7, 113.1, 121.0, 125.8, 127.6, 143.6, 145.5, 149.0, 196.2; IR (neat) ν 2924, 2855, 2217, 1680, 1454, 1409, 1366, 1286, 1142, 1116, 1071, 1015, 961, 808, 815 cm^{-1}; MS (ESI) m/e 263.1 (M+Na); HRMS (ESI) for $C_{20}H_{20}N_2NaO_7S$ (M+Na): 263.0791; Found: 263.0801; $[\alpha]^{20}_{D}$ = +134 (c 0.17, $CHCl_3$) (62% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 17.58 min, t_{minor} = 24.15 min.



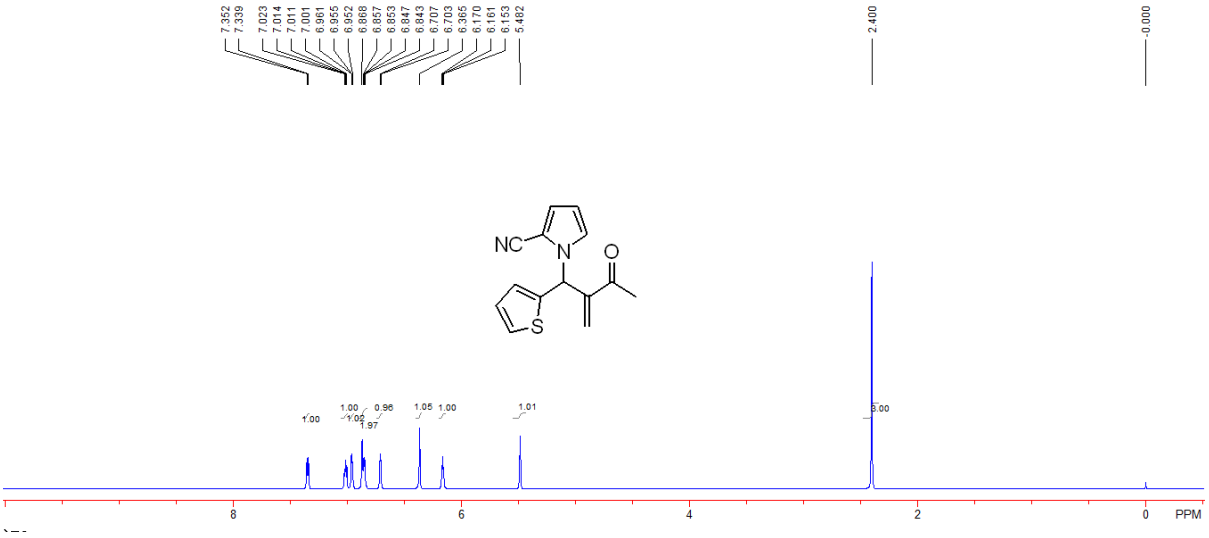


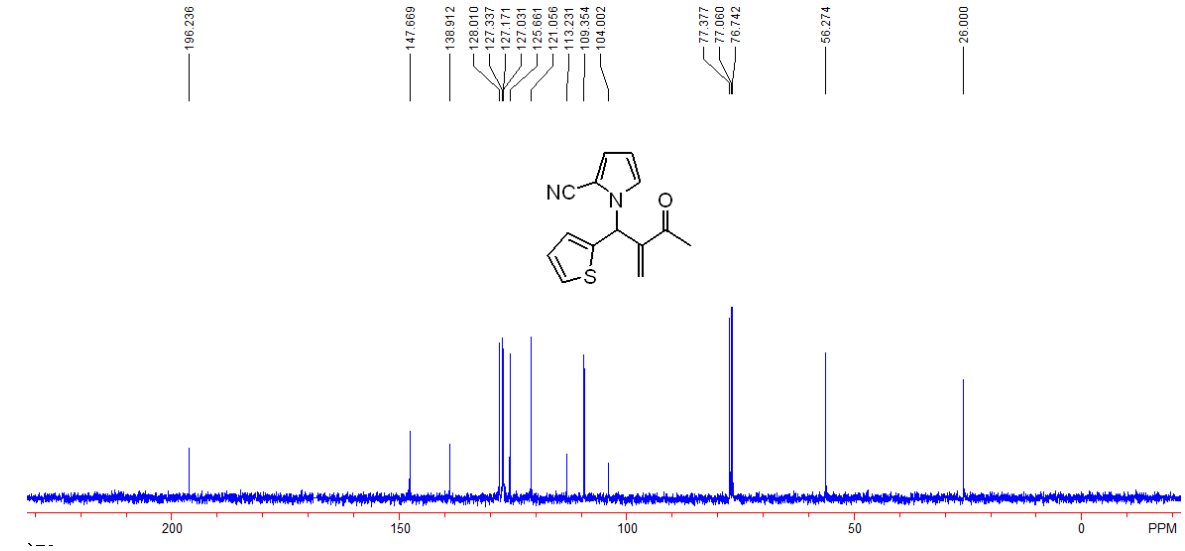
	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	17.481	12146411	49.97	552044

2	23.876	12159831	50.03	383570

	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	17.584	1182241	81.04	55832
2	24.152	276620	18.96	9378

(S)-1-(2-methylene-3-oxo-1-(thiophen-2-yl)butyl)-1H-pyrrole-2-carbonitrile 3r: a yellow oil (23 mg, 89% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 5.48 (s, 1H), 6.16 (t, *J* = 3.2 Hz, 1H), 6.37 (s, 1H), 6.71 (d, *J* = 1.6 Hz, 1H), 6.85 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 6.87 (s, 1H), 6.95-6.96 (m, 1H), 7.00-7.02 (m, 1H), 7.34-7.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 56.3, 104.0, 109.4, 113.2, 121.1, 125.7, 127.0, 127.2, 127.3, 128.0, 138.9, 147.7, 196.2; IR (neat) ν 2925, 2854, 2216, 1669, 1574, 1468, 1359, 1254, 1082, 1065, 972, 851, 760 cm^{-1}; MS (ESI) m/e 279.1 (M+Na); HRMS (ESI) for $C_{20}H_{20}N_2NaO_7S$ (M+Na): 279.0563; Found: 279.0576; $[\alpha]^{20}_{D}$ = +84.4 (c 1.1, $CHCl_3$) (39% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 10.47 min, t_{minor} = 12.70 min.



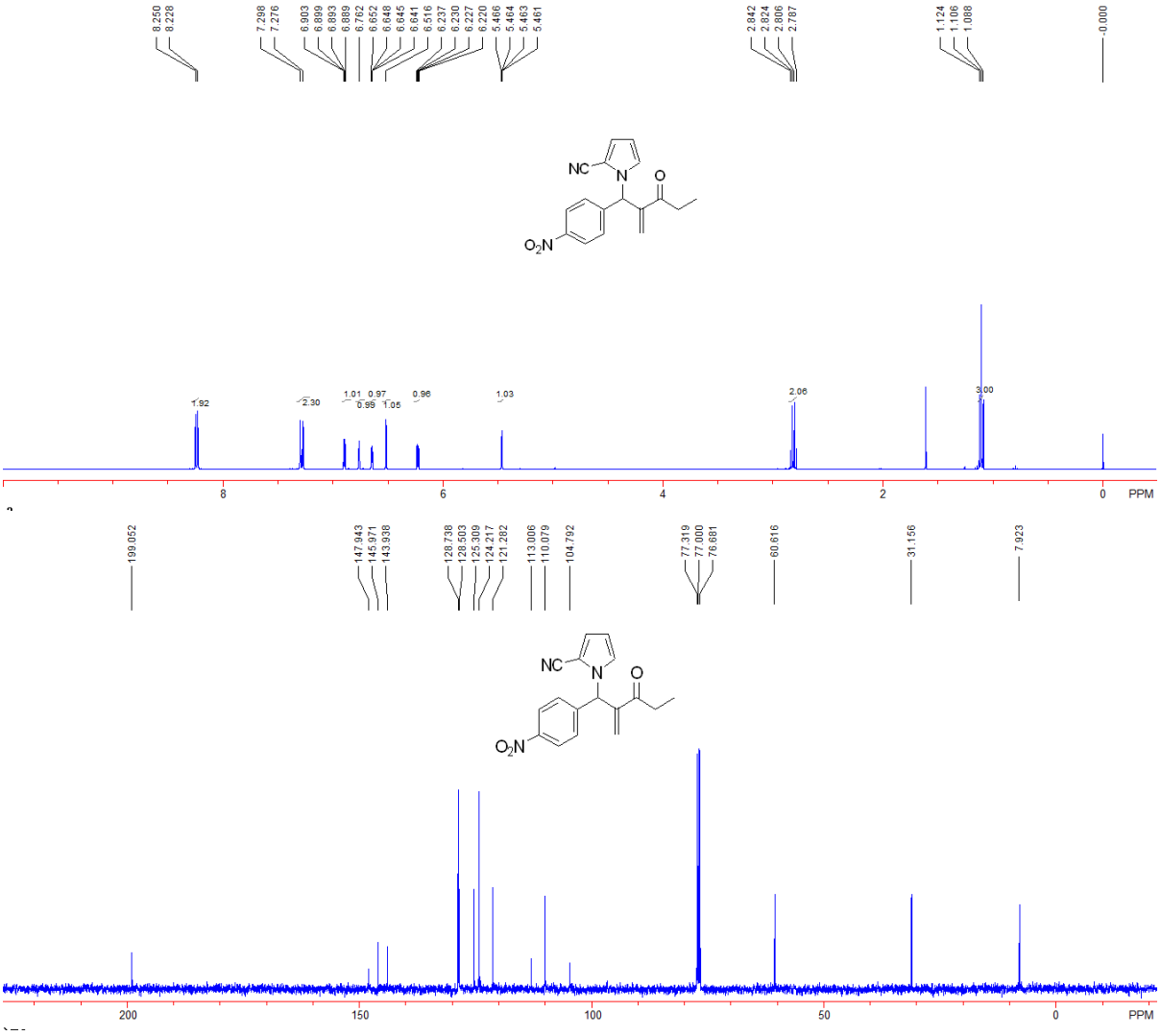


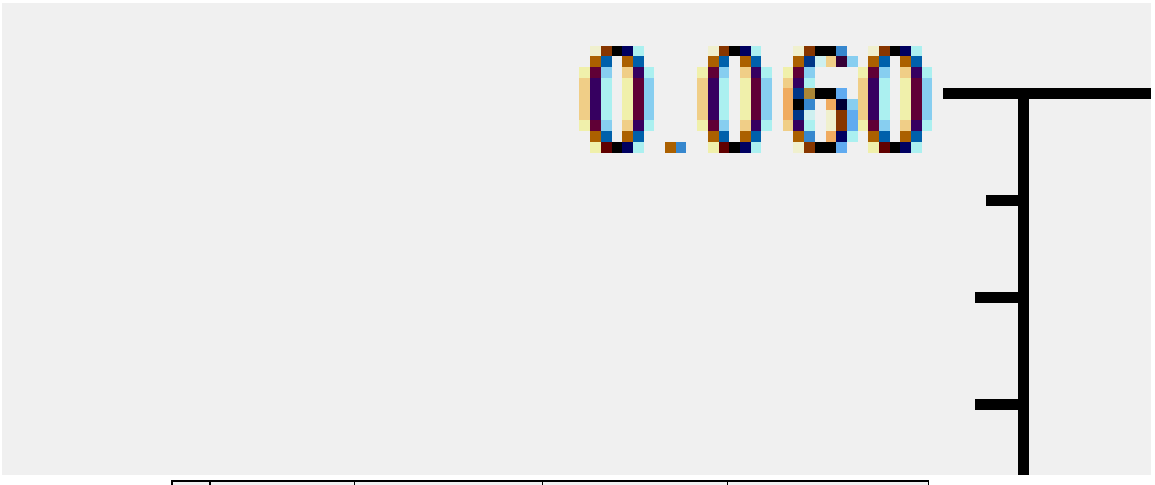
	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	10.602	483796	50.39	25112

2	12.824	476384	49.61	20409

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	10.471	2207243	69.34	113897
2	12.702	975912	30.66	41964

(R)-1-(2-methylene-1-(4-nitrophenyl)-3-oxobutyl)-1H-pyrrole-2-carbonitrile 3s: a yellow oil (19 mg, 61% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.11 (t, *J* = 7.2 Hz, 3H), 2.81 (q, *J* = 7.2 Hz, 2H), 5.46 (dd, *J* = 0.8 Hz, 1.2 Hz, 1H), 6.23 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.52 (s, 1H), 6.65 (dd, *J* = 1.6 Hz, 2.8 Hz, 1H), 6.76 (s, 1H), 6.90 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.29 (d, *J* = 8.8 Hz, 2H), 8.24 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.9, 31.2, 60.6, 104.8, 110.1, 113.0, 121.3, 124.2, 125.3, 128.5, 128.7, 143.9, 146.0, 147.9, 199.1; IR (neat) ν 2981, 2940, 2218, 1682, 1607, 1522, 1456, 1345, 1225, 1073, 979, 839, 739 cm^{-1}; MS (ESI) m/e 332.3 (M+Na); HRMS (ESI) for $C_{17}H_{15}N_3NaO_3S$ (M+Na): 332.1006; Found: 332.1015; $[\alpha]^{20}_{D}$ = -116.3 (c 1.00, $CHCl_3$) (93% ee); Chiralcel OD-H, hexane/^{i}PrOH = 90/10, 0.7 mL/min, 230 nm, t_{major} = 32.22 min, t_{minor} = 29.03min.





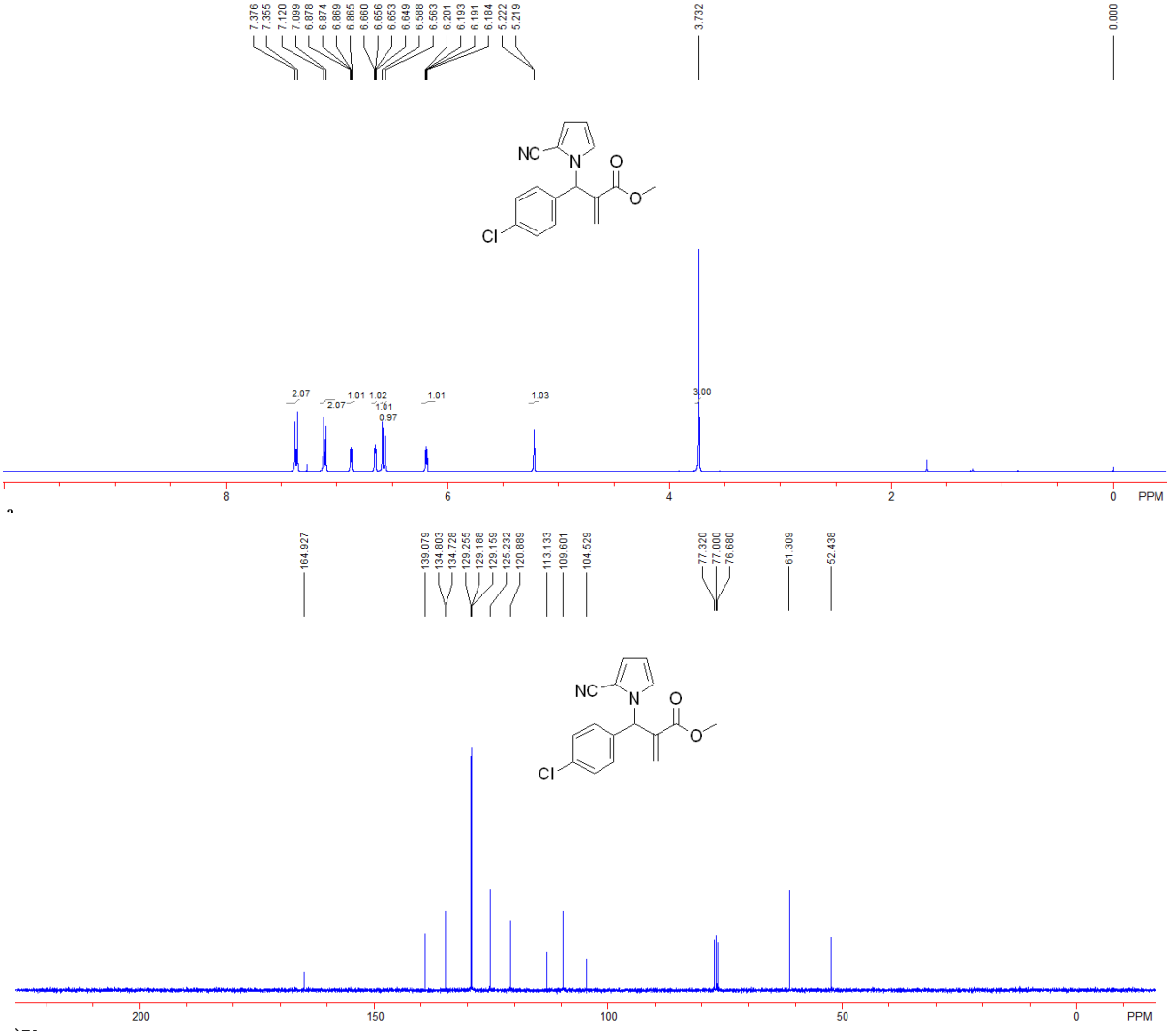
	RT	Area	% Area	Height

	(min)	（μV*sec)		(μV)
1	28.721	1203462	49.99	19334
2	32.214	1204083	50.01	17452

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	29.034	103651	3.68	1795
2	32.215	2711353	96.32	37791

(R)-methyl 2-((4-chlorophenyl)(2-cyano-1H-pyrrol-1-yl)methyl)acrylate 3t: a colorless oil (22 mg, 73% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.73 (s, 3H), 5.22 (d, *J* = 1.2 Hz, 1H), 6.19 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.56 (s, 1H), 6.59 (s, 1H), 6.65 (dd, *J* = 1.6 Hz, 2.8 Hz, 1H), 6.87 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.11 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.4, 61.3, 104.5, 109.6, 113.1, 120.9, 125.2, 129.1, 129.2, 129.3, 134.7, 134.8, 139.1, 164.9; IR (neat) ν 2923, 2853, 2216, 1679, 1605, 1520, 1440, 1346, 1227,

1173, 976, 856, 735 cm^{-1}; MS (%) m/e 300 (58), 209 (47), 177 (16), 149 (69), 130 (27), 115 (100), 91 (15), 59 (50), 49 (15); HRMS (EI) for $C_{16}H_{13}N_2O_2Cl$: 300.0666; Found: 300.0663; $[\alpha]^{20}_D$ = -110.0 (c 1.00, $CHCl_3$) (83% ee); Chiralcel AD, hexane/^{i}PrOH = 70/30, 0.6 mL/min, 214 nm, t_{major} = 7.37 min, t_{minor} = 8.31 min.



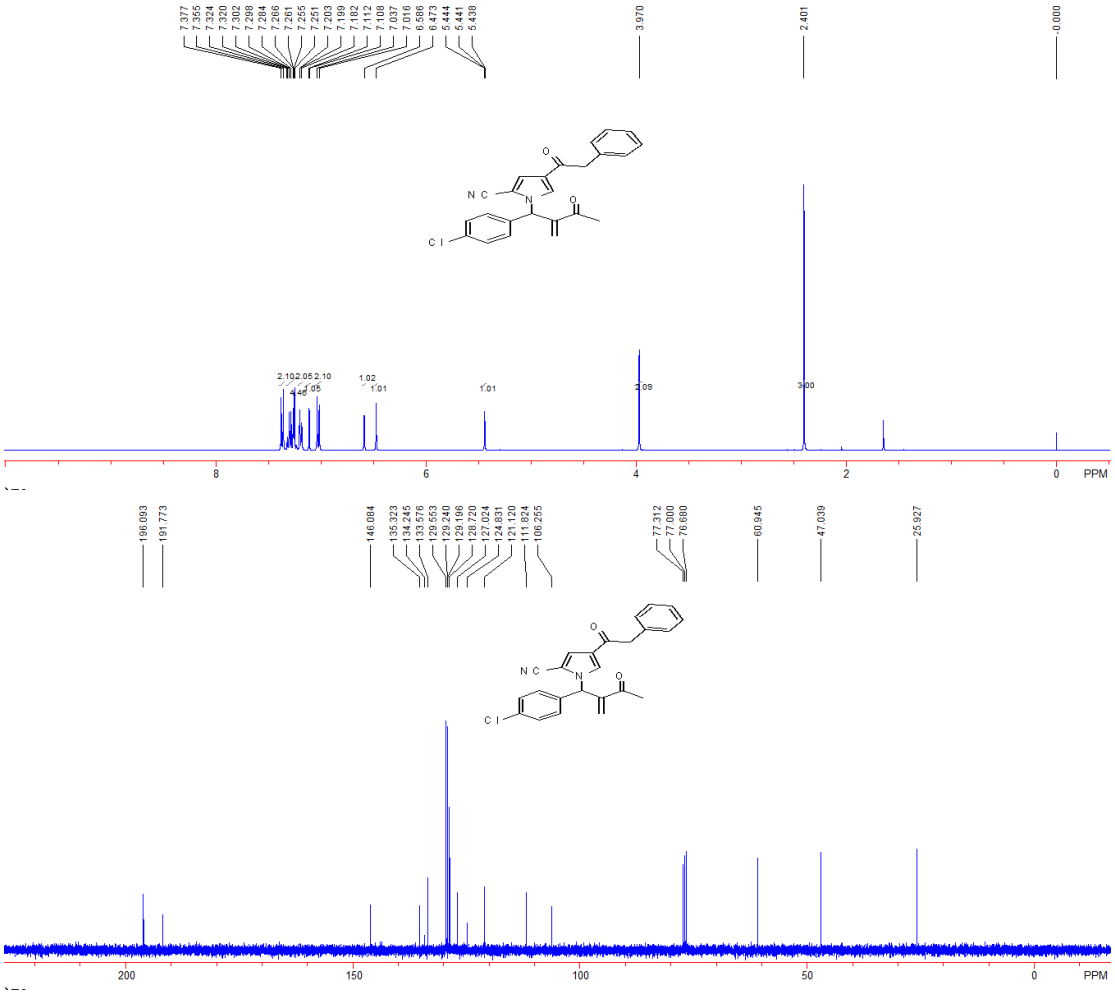
	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	7.416	3411361	49.98	303093
2	8.363	3413827	50.02	287501

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	7.368	2445284	91.58	219623
2	8.309	224865	8.42	19460

General procedure for the synthesis of 4

A solution of compound **1** (0.2 mmol) and compound **2** (0.1 mmol) in THF (0.5 mL) was stirred at 0 ^{o}C in the presence of organocatalyst $(DHQD)_2PYR$ (15 mol%) under argon atmosphere. The reaction solution was monitored by TLC. After the reaction complete, the solvent was removed under reduced pressure and the residue was chromatographed on silica gel (elution with petroleum ether/EtOAc = 4/1-2/1) to provide the corresponding product **4**.

(R)-1-(1-(4-chlorophenyl)-2-methylene-3-oxobutyl)-4-(2-phenylacetyl)-1H-pyrrole-2-carbonitrile 4a: a white oil (30 mg, 75% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 3.97 (s, 2H), 5.44 (t, *J* = 1.2 Hz, 1H), 6.47 (s, 1H), 6.59 (s, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 1.6 Hz, 1H), 7.18-7.20 (m, 2H), 7.25-7.32 (m, 4H), 7.37 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 47.0, 60.9, 106.3, 111.8, 121.1, 124.8, 127.0, 128.7, 129.2, 129.3, 129.6, 133.6, 134.2, 135.3, 146.1, 191.8, 196.1; IR (neat) ν 2925, 2855, 2222, 1674, 1538, 1491, 1367, 1277, 1216, 1157, 1068, 977, 931, 863, 835, 724, 637 cm^{-1}; MS (%) m/e 311 (48), 193 (28), 115 (13), 91 (31), 65 (8), 43 (100); HRMS (EI) for $C_{24}H_{19}N_2O_2Cl$: 402.1135; Found: 402.1138; $[\alpha]^{20}_{D}$ = -10.1 (c 0.60, $CHCl_3$) (96% ee); Chiralcel IC, hexane/^{i}PrOH = 70/30, 0.7 mL/min, 214 nm, t_{major} = 36.70 min, t_{minor} = 32.15 min.



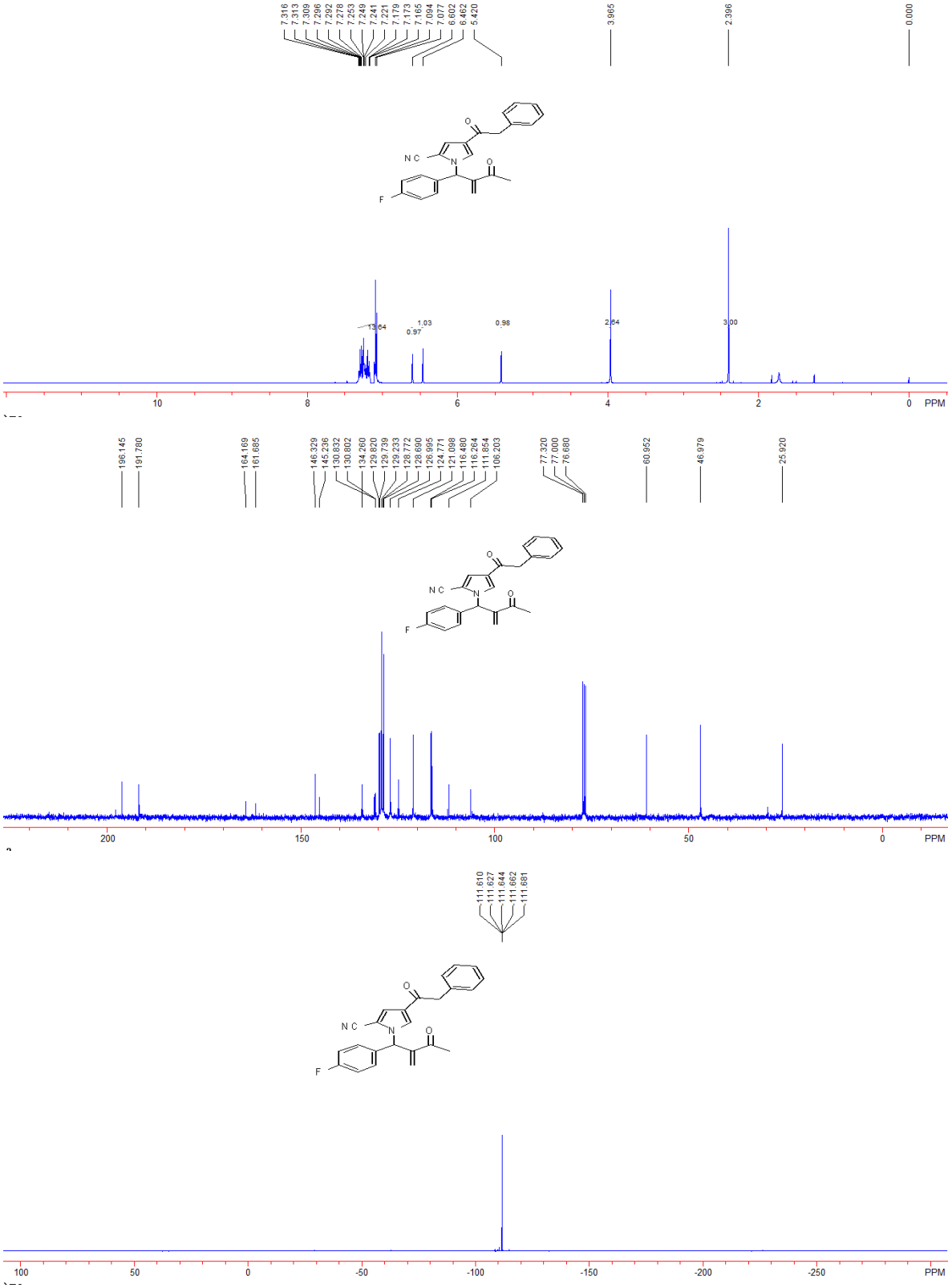
	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	32.247	3768002	49.93	61655

2	37.249	3777934	50.07	53251

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	32.150	130016	2.18	2161
2	36.700	5820724	97.82	84118

(R)-1-(1-(4-fluorophenyl)-2-methylene-3-oxobutyl)-4-(2-phenylacetyl)-1H-pyrrole-2-carbonitrile 4b: a white oil (27 mg, 70% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 3.97 (s, 2H), 5.42 (s, 1H), 6.46 (s, 1H), 6.60 (s, 1H) 7.08-7.32 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 47.0, 61.0, 106.2, 111.9, 116.4 (d, $J_{C\text{-}F}$ = 21.6 Hz), 121.1, 124.8, 127.0, 128.7, 128.8, 129.2, 129.8 (d, $J_{C\text{-}F}$ = 8.1 Hz), 130.8 (d, $J_{C\text{-}F}$ = 3.0 Hz), 145.2, 146.3, 162.9 (d, $J_{C\text{-}F}$ = 248.4 Hz), 191.8, 196.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ -111.681- -111.610 (m, 1F); IR (neat) ν 2925, 2854, 2222, 1674, 1538, 1510, 1367, 1319, 1224, 1158, 978, 931, 868, 832, 764, 724,

637 cm^{-1}; MS (ESI) m/e 409.3 (M+Na); HRMS (ESI) for $C_{24}H_{19}FN_2NaO_2$ (M+Na): 409.1323; Found: 409.1341; $[\alpha]^{20}_D$ = -11.1 (c 0.50, $CHCl_3$) (91% ee); Chiralcel IC, hexane/^{i}PrOH = 70/30, 0.7 mL/min, 214 nm, t_{major} = 33.90 min, t_{minor} = 33.29 min.



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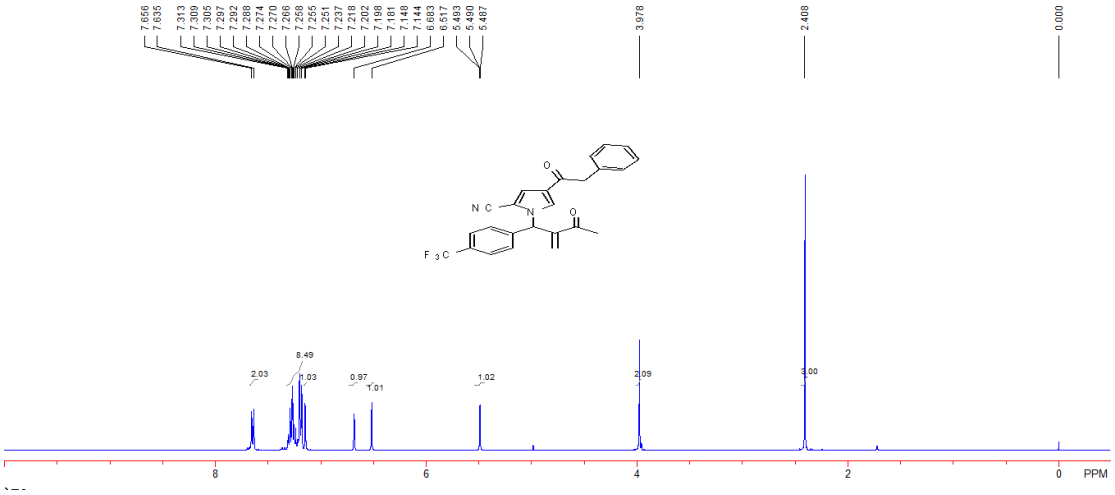
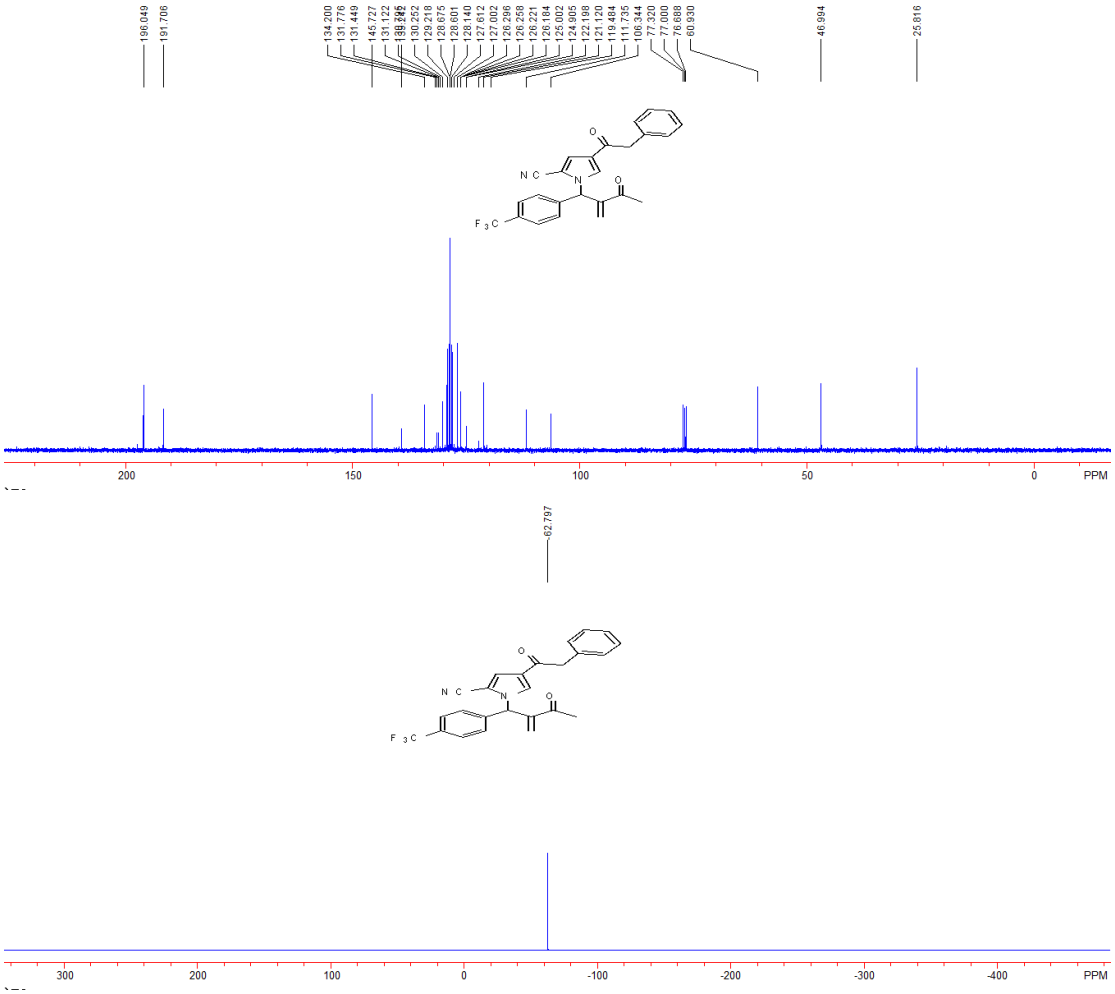
1	30.229	7476989	49.95	140036
2	34.056	7493142	50.05	122438

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	30.287	90257	4.36	1748
2	33.904	1980217	95.64	32735

(R)-1-(2-methylene-3-oxo-1-(4-(trifluoromethyl)phenyl)butyl)-4-(2-phenylacetyl)-1H-pyrrole-2-carbonitrile 4c: a white oil (27 mg, 46% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.41 (s, 3H), 3.98 (s, 2H), 5.49 (t, J = 1.2 Hz, 1H), 6.52 (s, 1H), 6.68 (s, 1H), 7.14 (d, J = 1.6 Hz, 1H), 7.14-7.31 (m, 8H), 7.64 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.8, 47.0, 60.9, 106.3, 111.7, 119.5, 123.1 (q, $J_{C\text{-}F}$ = 270.7 Hz), 125.0, 126.2 (q, $J_{C\text{-}F}$ = 3.7 Hz), 127.0, 128.1, 128.6, 128.7, 129.2, 130.3, 131.3 (q, $J_{C\text{-}F}$ = 32.7 Hz), 134.2, 139.2, 145.7, 191.7, 196.1; ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.797 (s, 3F); IR (neat) ν 3121, 2223, 1676, 1539, 1510, 1367, 1319, 1224, 1161, 1112, 1068, 978, 931, 863, 827, 722, 637 cm^{-1}; MS (ESI) m/e 459.3 (M+Na); HRMS (ESI) for $C_{25}H_{19}F_3N_2NaO_2$ (M+Na): 459.1291; Found: 459.1307; $[\alpha]^{20}_{D}$ = +21.1 (c 0.90, $CHCl_3$) (91% ee); Chiralcel IC, hexane/^{i}PrOH = 70/30, 0.7 mL/min, 214 nm, t_{major} = 16.26 min, t_{minor} = 14.73 min.





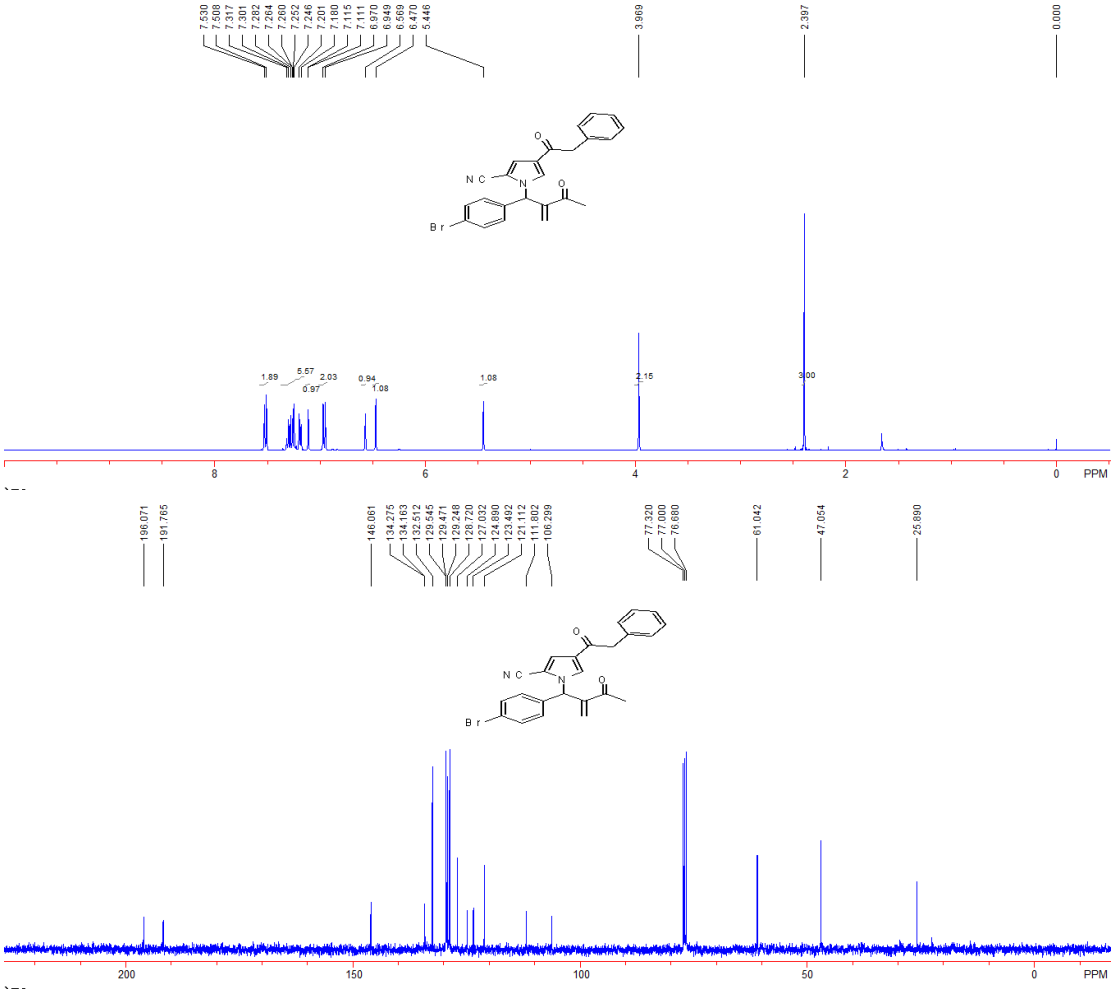
	RT (min)	Area (μV*sec)	% Area	Height (μV)

1	14.775	3929622	49.94	163906
2	16.331	3938416	50.06	144185

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	14.733	105769	4.19	4686
2	16.259	2416585	95.81	88304

(R)-1-(1-(4-bromophenyl)-2-methylene-3-oxobutyl)-4-(2-phenylacetyl)-1H-pyrrole-2-carbonitrile 4d: a white oil (34 mg, 76% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 3.97 (s, 2H), 5.45 (s, 1H), 6.47 (s, 1H), 6.57 (s, 1H), 6.96 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 1.6 Hz, 1H), 7.18-7.32 (m, 6H), 7.52 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 47.1, 61.0, 106.3, 111.8, 121.1, 123.5, 124.9, 127.0, 128.7, 129.2, 129.5, 129.6, 132.5, 134.2,

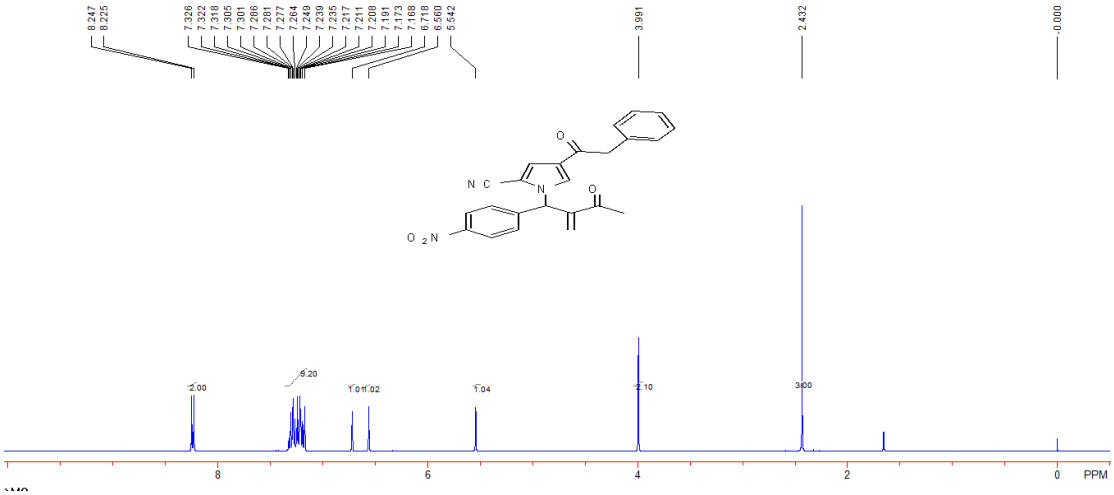
134.3, 146.1, 191.8, 196.1; IR (neat) ν 2925, 2855, 2222, 1673, 1538, 1489, 1387, 1367, 1217, 1158, 1072, 1011, 978, 931, 859, 723, 637 cm^{-1}; MS (%) m/e 355 (27), 237 (14), 158 (17), 115 (12), 91 (21), 65 (8), 43 (100); HRMS (EI) for $C_{24}H_{19}N_2O_2Br$: 446.0630; Found: 446.0633; $[\alpha]^{20}_D$ = -4.8 (c 0.90, $CHCl_3$) (94% ee); Chiralcel IC, hexane/^{i}PrOH = 70/30, 0.7 mL/min, 214 nm, t_{major} = 38.74 min, t_{minor} = 33.76 min.

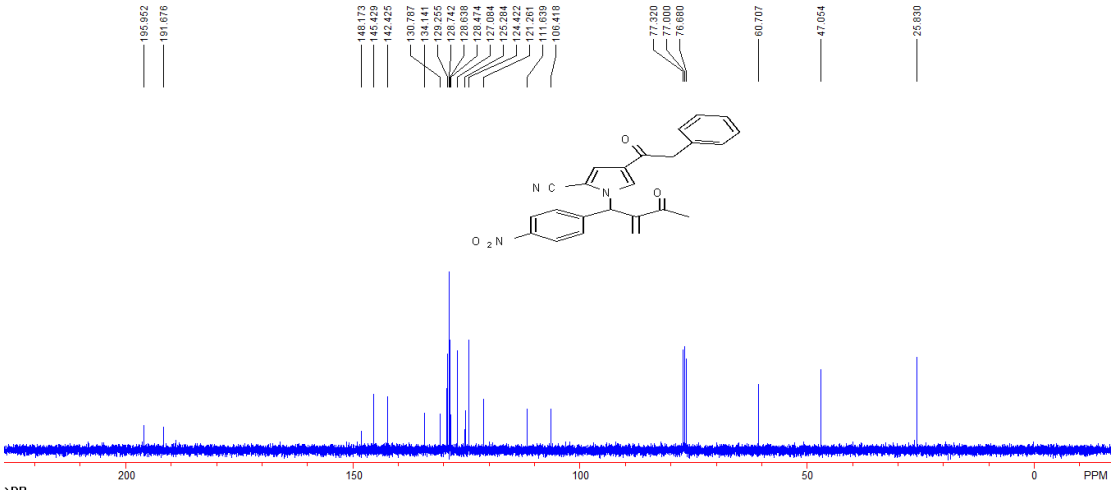


	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	33.145	1511977	50.05	23776
2	38.148	1508784	49.95	20626

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	33.755	39548	3.01	599
2	38.743	1274016	96.99	16675

(R)-1-(2-methylene-1-(4-nitrophenyl)-3-oxobutyl)-4-(2-phenylacetyl)-1H-pyrrole-2-carbonitrile 4e: a white solid (26 mg, 63% yield); m.p. 150-152 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 3.99 (s, 2H), 5.54 (s, 1H), 6.56 (s, 1H), 6.72 (s, 1H), 7.17-7.33 (m, 9H), 8.24 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.8, 47.1, 60.7, 106.4, 111.6, 124.4, 125.3, 127.1, 128.5, 128.6, 128.7, 129.3, 130.8, 134.1, 142.4, 145.4, 148.2, 191.7, 196.0; IR (neat) ν 2925, 2855, 2221, 1679, 1538, 1493, 1462, 1376, 1325, 1278, 1197, 1161, 979, 932, 853, 764,750, 637 cm^{-1}; MS (%) m/e 322 (72), 158 (13), 119 (42), 115 (9), 91 (46), 71 (14), 57 (20), 43 (100); HRMS (EI) for $C_{24}H_{19}N_3O_4$: 413.1376; Found: 413.1371; $[\alpha]^{20}_{D}$ = +22.4 (c 0.55, $CHCl_3$) (93% ee); Chiralcel OD-H, hexane/^{i}PrOH = 70/30, 0.7 mL/min, 214 nm, t_{major} = 47.40 min, t_{minor} = 35.17 min.

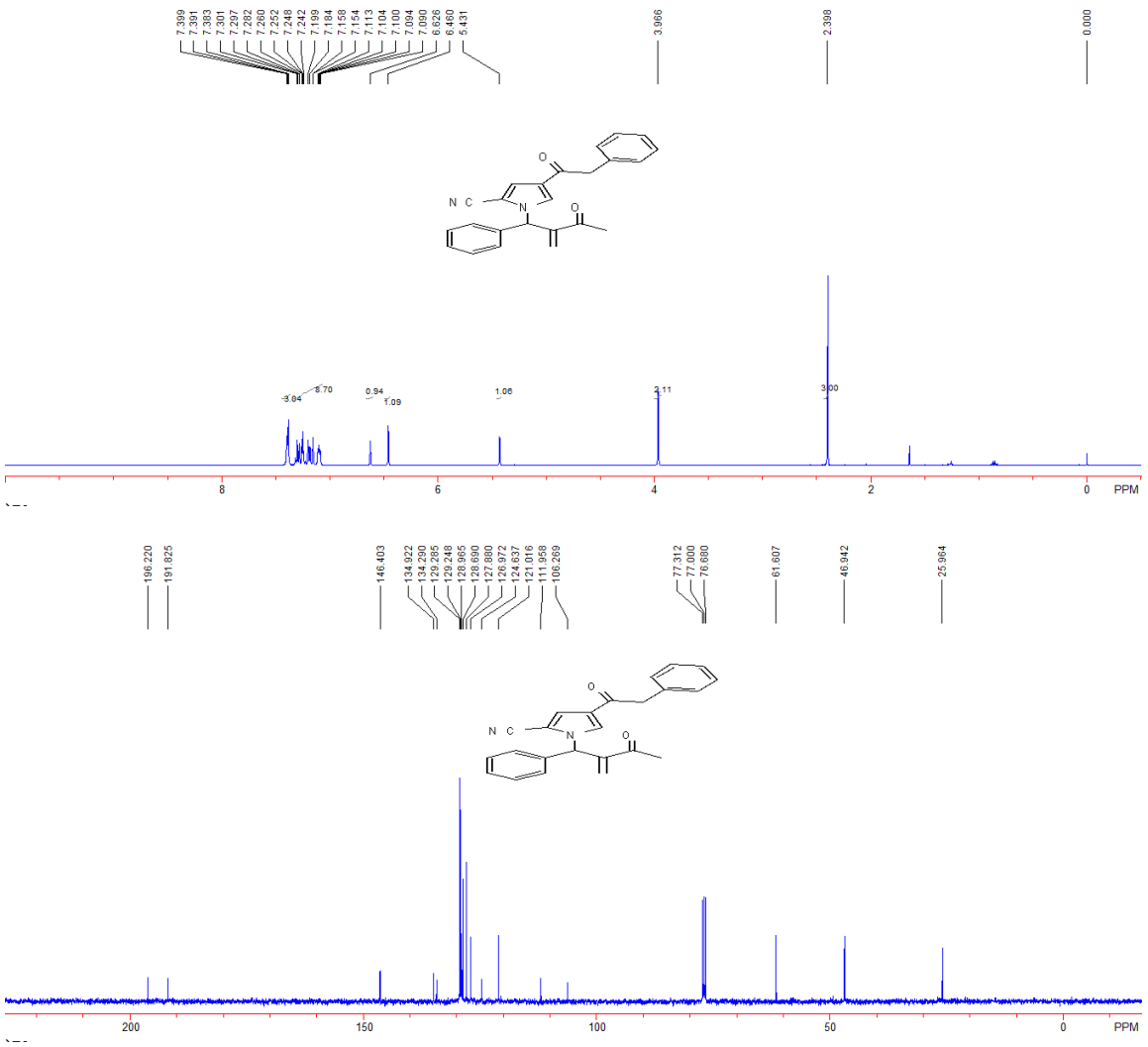




	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	35.619	1261596	50.02	6499
2	50.799	1260791	49.98	4741

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	35.167	238583	3.54	1558
2	47.400	6494770	96.46	30682

(R)-1-(2-methylene-3-oxo-1-phenylbutyl)-4-(2-phenylacetyl)-1H-pyrrole-2-carbonitrile 4f: a yellow oil (23 mg, 58% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 3.97 (s, 2H), 5.43 (s, 1H), 6.46 (s, 1H), 6.63 (s, 1H), 7.09-7.30 (m, 9H), 7.38-7.40 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 46.9, 61.6, 106.3, 112.0, 121.0, 124.6, 127.0, 127.9, 128.7, 129.0, 129.2, 129.3, 130.8, 134.3, 134.9, 146.4, 191.8, 196.2; IR (neat) ν 2924, 2854, 2223, 1666, 1537, 1455, 1379, 1276, 1215, 1158, 978, 955, 931, 859, 749, 696 cm^{-1}; MS (%) m/e 277 (84), 159 (46), 119 (15), 115 (14), 91 (18), 71 (4), 57 (7), 43 (100); HRMS (EI) for $C_{24}H_{20}N_2O_2$: 368.1525; Found: 368.1523; $[\alpha]^{20}_{D}$ = -4.1 (c 1.00, $CHCl_3$) (89% ee); Chiralcel OD-H, hexane/^{i}PrOH = 70/30, 0.6 mL/min, 214 nm, t_{major} = 27.99 min, t_{minor} = 24.04 min.



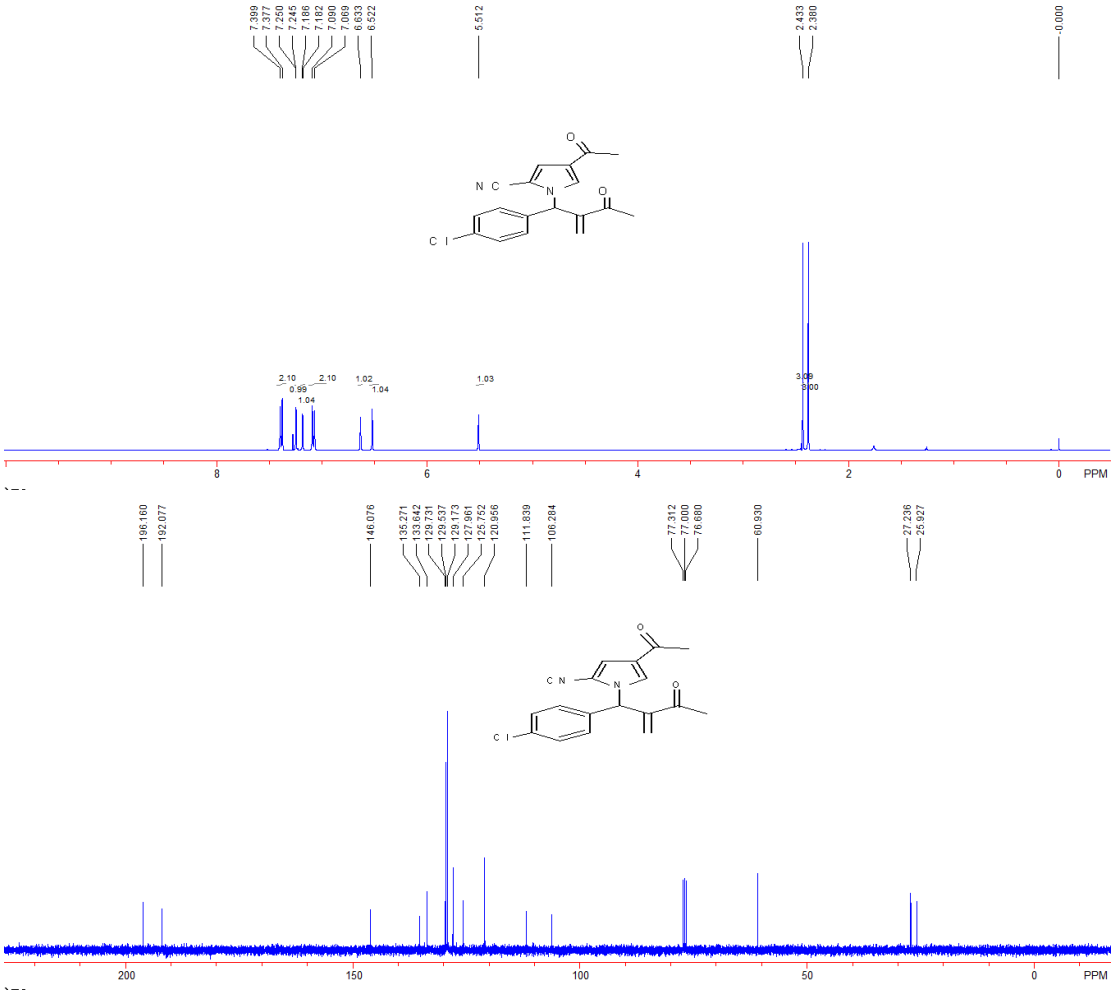
	RT	Area	% Area	Height

	(min)	（μV*sec)		(μV)
1	24.387	2089428	49.96	30818
2	28.791	2092746	50.04	25019

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	24.039	270775	5.60	4205
2	27.985	4567578	94.40	56208

(R)-4-acetyl-1-(1-(4-chlorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbonitrile 4g: a white solid (25 mg, 76% yield); m.p. = 122-124 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.38 (s, 3H), 2.43 (s, 3H), 5.51 (s, 1H), 6.52 (s, 1H), 6.63 (s, 1H), 7.08 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 1.6 Hz, 1H), 7.25 (d, *J* = 1.6 Hz, 1H), 7.39 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 27.2, 60.9, 106.3, 111.8, 121.0, 125.8, 128.0, 129.2, 129.5, 129.7, 133.6, 135.3, 146.1, 192.1, 196.2; IR (neat) ν 3114, 2924, 2223, 1669, 1538, 1489, 1391, 1372, 1205,

1118, 1092, 1014, 974, 936, 809, 780, 659, 643 cm^{-1}; MS (%) m/e 326 (45), 193 (16), 115 (8), 85 (13), 71 (13), 57 (14), 43 (100); HRMS (EI) for $C_{18}H_{15}N_2O_2Cl$: 326.0822; Found: 326.0820; $[\alpha]^{20}_D$ = -2.1 (c 1.00, $CHCl_3$) (94% ee); Chiralcel AD-H, hexane/^{i}PrOH = 70/30, 0.6 mL/min, 214 nm, t_{major} = 10.39 min, t_{minor} = 14.88 min.



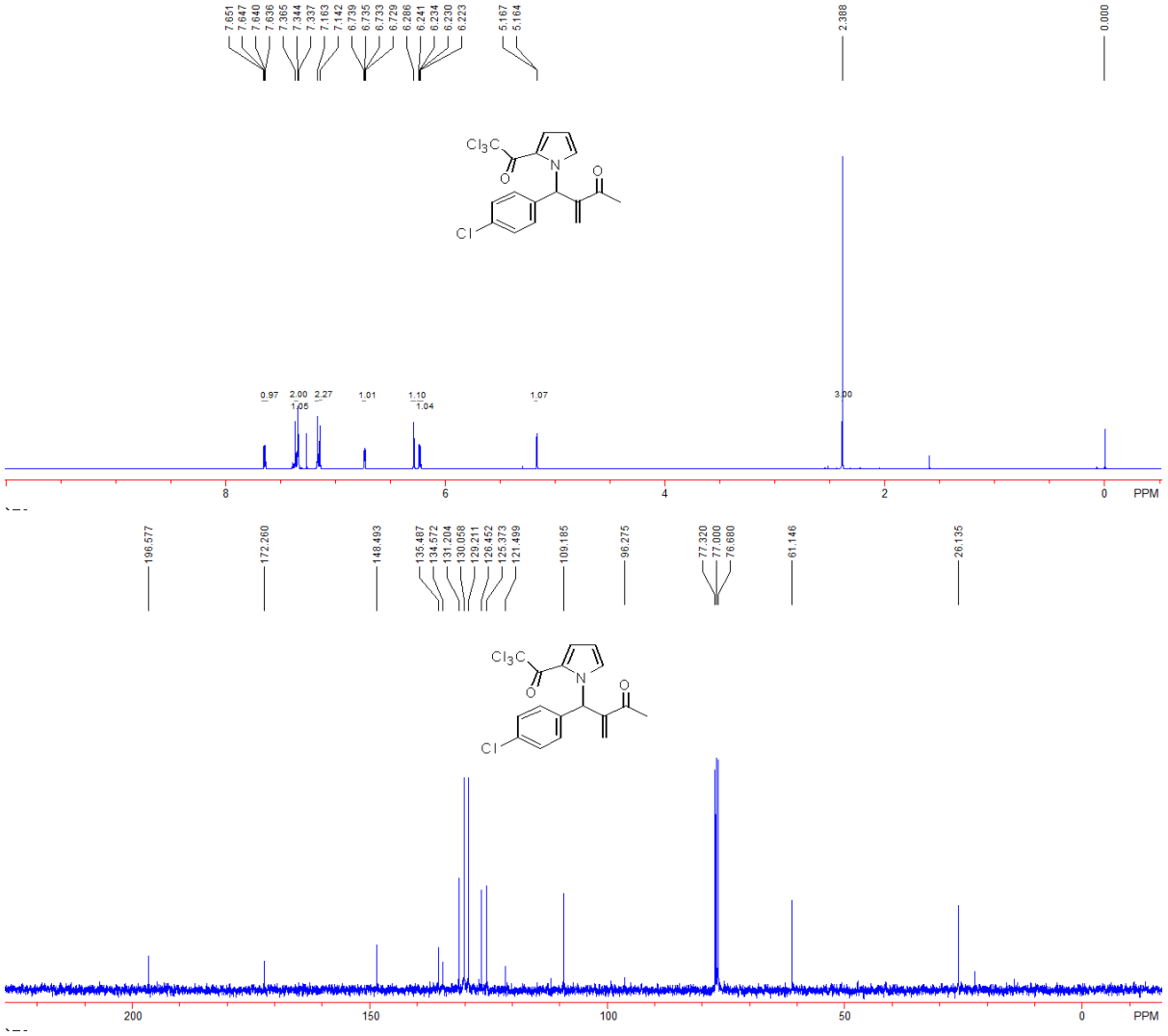
	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	10.377	2362483	50.00	152934
2	14.702	2362055	50.00	90076

	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	10.389	5585969	97.02	360961
2	14.883	171720	2.98	7831

(R)-3-((4-chlorophenyl)(3-(2,2,2-trichloroacetyl)-1H-pyrrol-1-yl)methyl)but-3-en-2-one

4h: a white solid (33.6 mg, 83% yield); m.p. = 152-124 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.39 (s, 3H), 5.17 (d, *J* = 1.2 Hz, 1H), 6.23 (dd, *J* = 2.8 Hz, 4.4 Hz, 1H), 6.29 (s, 1H), 6.73 (dd, *J* = 1.6 Hz, 2.8 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 2H), 7.33 (s, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.64 (dd, *J* = 1.6 Hz, 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 61.2, 96.3, 109.2, 121.5, 125.4, 126.4, 129.2, 129.5, 130.1, 131.2, 134.6, 135.5, 148.5, 172.3, 196.6; IR (neat) ν 2925, 2855, 2224, 1677, 1538, 1489, 1408, 1373, 1326, 1230, 1168, 1132, 1068, 979, 946, 865, 851, 765, 726, 689 cm^{-1}; MS (%) m/e 286 (24), 258 (9), 244 (9), 193 (5), 115 (10), 84 (11), 71

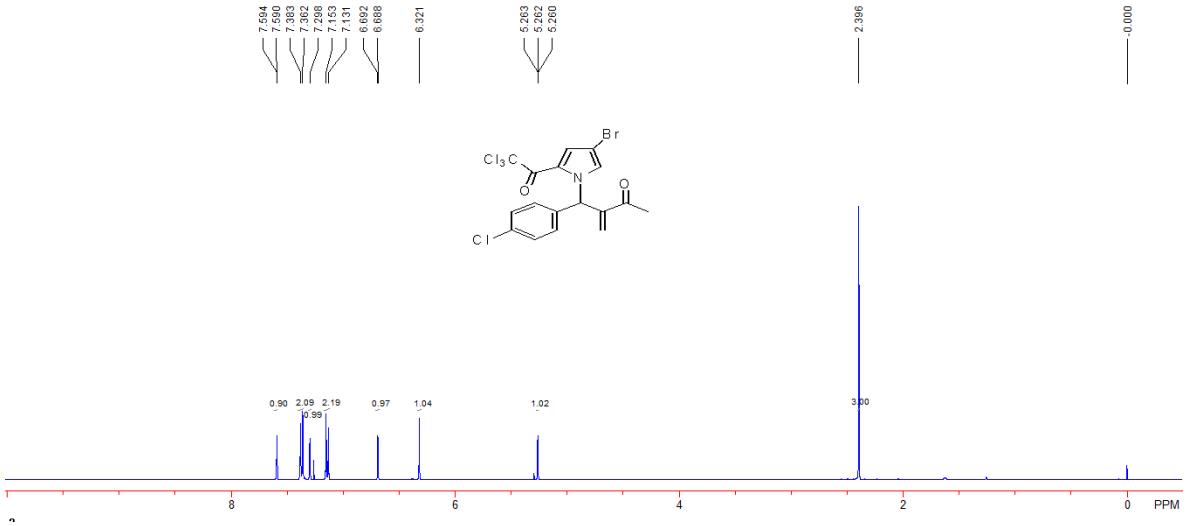
(13), 57 (5), 43 (100); HRMS (EI) for $C_{17}H_{13}NO_2Cl_4$: 402.9700; Found: 402.9705; $[\alpha]^{20}_D$ = -216.4 (c 0.65, $CHCl_3$) (90% ee); Chiralcel IC, hexane/^{i}PrOH = 70/30, 0.5 mL/min, 214 nm, t_{major} = 11.17 min, t_{minor} = 14.50 min.

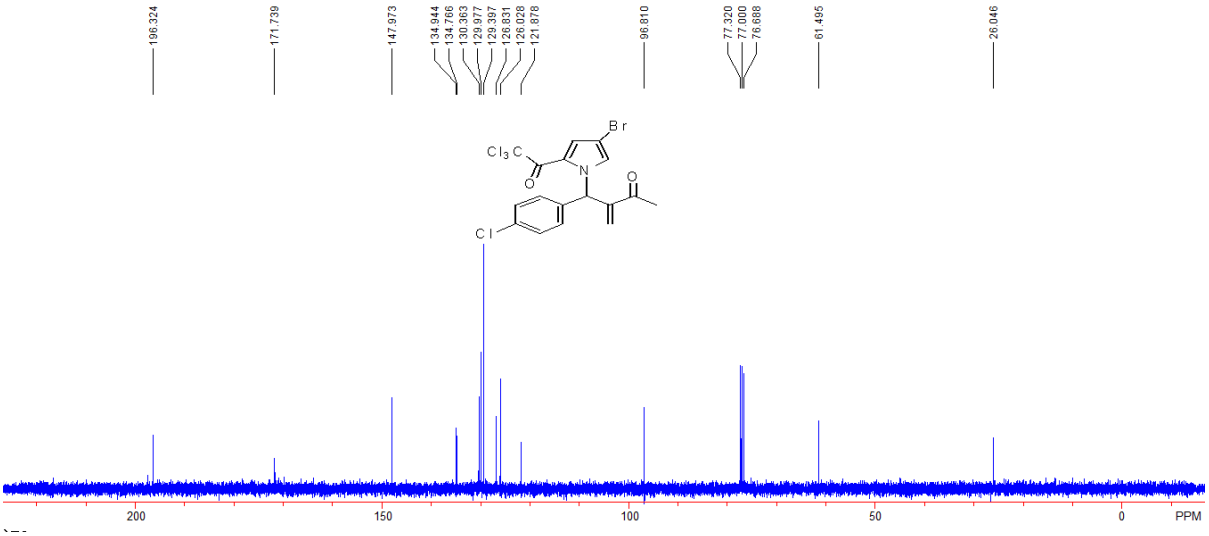


	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	11.147	1942401	49.84	138250
2	14.433	1955163	50.16	105131

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	11.171	7786896	95.15	560450
2	14.498	396751	4.85	21944

(R)-3-((2-bromo-4-(2,2,2-trichloroacetyl)-1H-pyrrol-1-yl)(4-chlorophenyl)methyl)but-3-en-2-one 4i: a white solid (34.0 mg, 71% yield); m.p. = 168-170 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.40 (s, 3H), 5.26 (t, *J* = 0.8 Hz, 1H), 6.32 (s, 1H), 6.69 (d, *J* = 1.6 Hz, 1H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.30 (s, 1H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 61.5, 96.8, 121.9, 126.0, 126.8, 129.4, 130.0, 130.4, 134.8, 134.9, 148.0, 171.7, 196.3; IR (neat) ν 2925, 2855, 2224, 1679, 1366, 1326, 1191, 1169, 1068, 979, 955, 922, 861, 836, 765, 732, 683 cm^{-1}; MS (%) m/e 364 (5), 193 (5), 115 (8), 84 (12), 43 (100); HRMS (EI) for $C_{17}H_{12}NO_2Cl_4Br$: 480.8806; Found: 480.8802; $[\alpha]^{20}_{D}$ = -111.3 (c 0.50, $CHCl_3$) (84% ee); Chiralcel IC, hexane/^{i}PrOH = 70/30, 0.5 mL/min, 214 nm, t_{major} = 9.07 min, t_{minor} = 10.65 min.

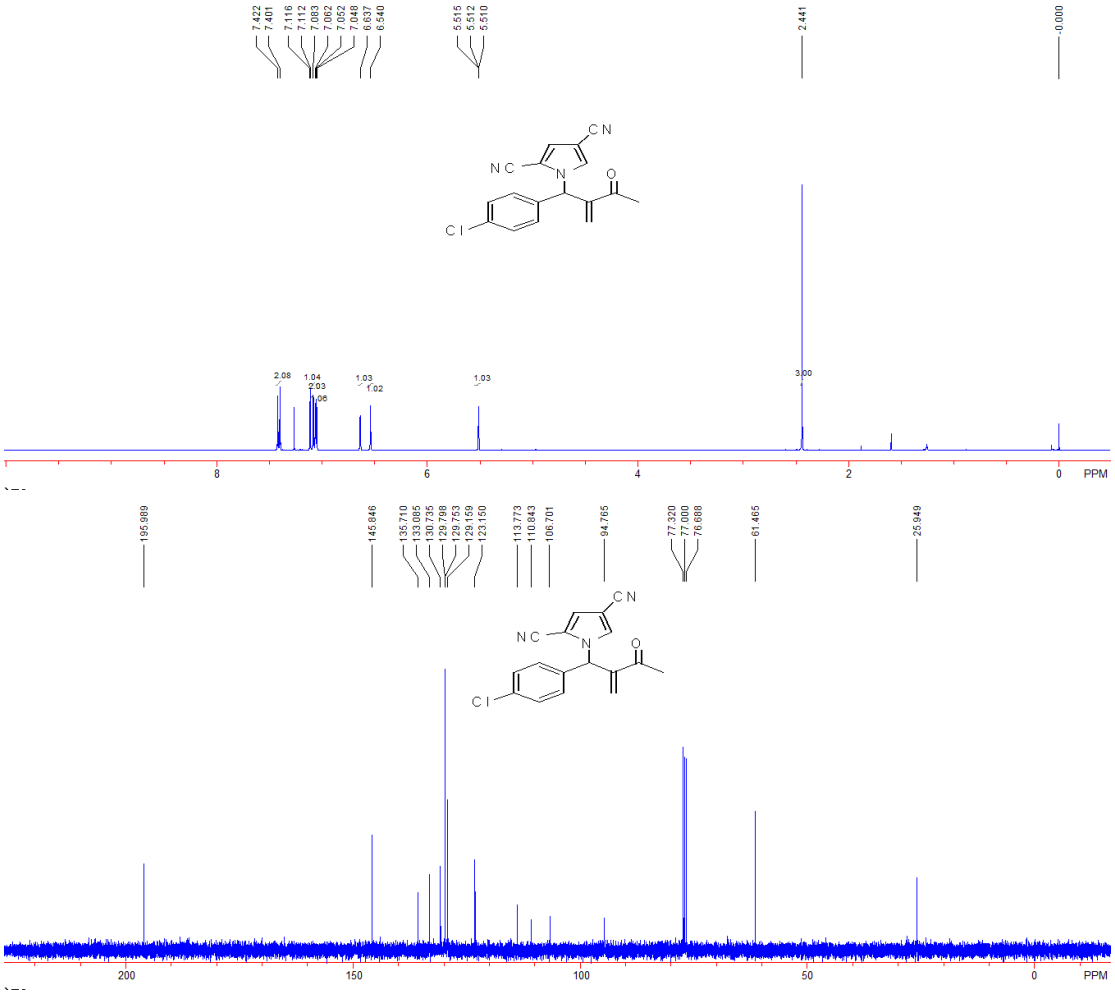




	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	9.051	1497435	49.95	127572
2	9.879	1500440	50.05	122944

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	9.065	2032576	91.86	171473
2	10.646	180215	8.14	14152

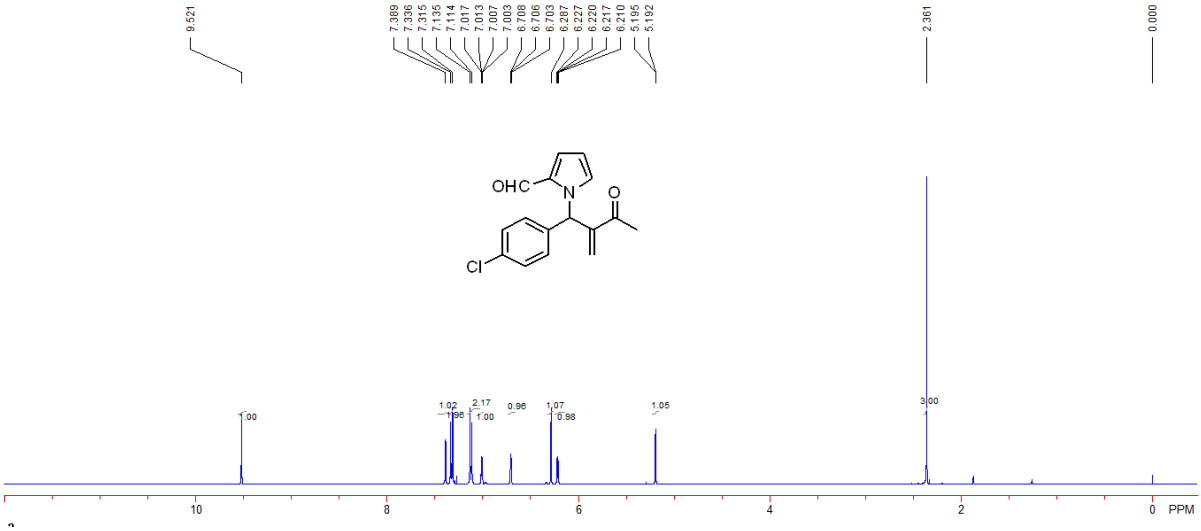
(R)-1-(1-(4-chlorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2,4-dicarbonitrile 4j: a white solid (26 mg, 84% yield); m.p. = 117-119 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.44 (s, 3H), 5.51 (t, *J* = 0.8 Hz, 1H), 6.54 (s, 1H), 6.64 (s, 1H), 7.05 (d, *J* = 1.6 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 1.6 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 61.5, 94.8, 106.7, 110.8, 113.8, 123.2, 129.2, 129.7, 129.8, 130.7, 133.1, 135.7, 145.9, 196.0; IR (neat) ν 2930, 2859, 2222, 1669, 1263, 1112, 1022, 910, 803, 662 cm^{-1}; MS (%) m/e 309 (36), 274 (8), 193 (11), 115 (18), 85 (11), 71 (14), 57 (25), 43 (100); HRMS (EI) for $C_{17}H_{12}N_3OCl$: 309.0669; Found: 309.0668; $[\alpha]^{20}_{D}$ = -1.3 (c 0.50, $CHCl_3$) (85% ee); Chiralcel IC, hexane/^{i}PrOH = 70/30, 0.7 mL/min, 214 nm, t_{major} = 30.62 min, t_{minor} = 25.64 min.

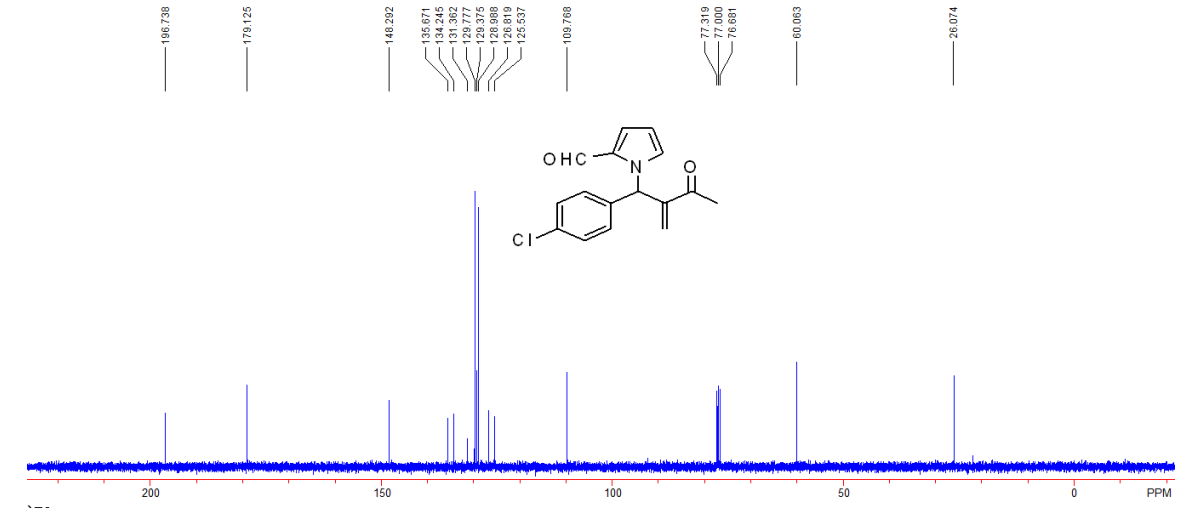


	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	25.668	1279561	50.21	29364
2	31.009	1268651	49.79	24321

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	25.635	1296312	7.40	31004
2	30.621	16228255	92.60	316483

(R)-1-(1-(4-chlorophenyl)-2-methylene-3-oxobutyl)-1H-pyrrole-2-carbaldehyde 4k: a white solid (20.0 mg, 70% yield); m.p. = 140-143 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.36 (s, 3H), 5.19 (d, *J* = 1.2 Hz, 1H), 6.22 (dd, *J* = 2.8 Hz, 4.0 Hz, 1H), 6.29 (s, 1H), 6.71 (t, *J* = 0.8 Hz, 1H), 7.01 (dd, *J* = 1.6 Hz, 4.0 Hz, 1H), 7.12 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.39 (s, 1H), 9.52 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 60.1, 109.8, 125.5, 126.8, 129.0, 129.4, 129.8, 131.4, 134.3, 135.7, 148.3, 179.1, 196.7; IR (neat) ν 2803, 2346, 1675, 1651, 1460, 1327, 1220, 1058, 956, 861, 741 cm^{-1}; MS (%) m/e 287 (6), 258 (9), 244 (25), 115 (15), 43 (100); HRMS (EI) for $C_{16}H_{14}NO_2Cl$: 287.0713; Found: 287.0716; $[\alpha]^{20}_{D}$ = -193.1 (c 0.75, $CHCl_3$) (92% ee); Chiralcel OD, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 30.62 min, t_{minor} = 25.64 min.





	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	10.009	1651478	49.73	83194

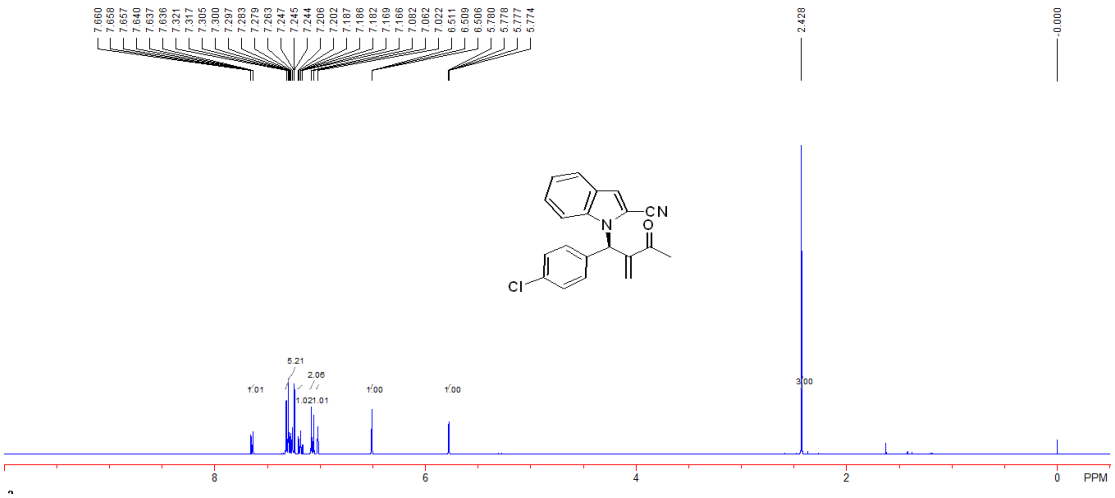
2	12.632	1669636	50.27	67237

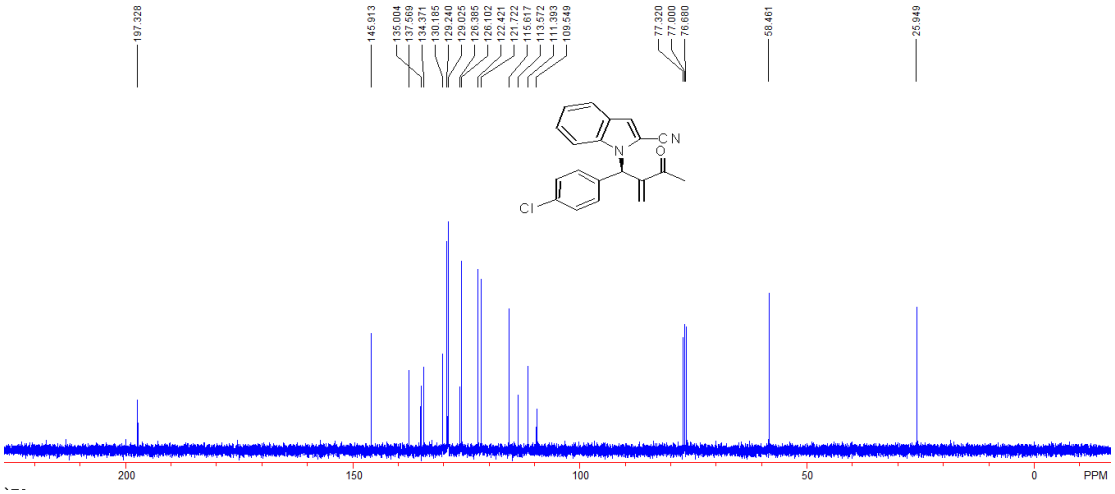
	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	10.082	82294	3.98	4399
2	12.653	1987742	96.02	80882

General Procedure for the synthesis of 5

A solution of compound **1h** (0.2 mmol) and compound **2** (0.1 mmol) in THF (0.5 mL) was stirred at -10 ^{o}C for 96 h in the presence of organocatalyst $(DHQD)_2PYR$ (15 mol%) under argon atmosphere. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (elution with petroleum ether/EtOAc = 16/1-8/1) to provide the corresponding product **5**.

1-(1-(4-chlorophenyl)-2-methylene-3-oxobutyl)-1H-indole-2-carbonitrile 5a: a white solid (33 mg, 99% yield); m.p. 144-146 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 5.78 (dd, *J* = 0.8 Hz, 1.2 Hz, 1H), 6.51 (t, *J* = 0.8 Hz, 1H), 7.02 (s, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 7.17-7.21 (m, 1H), 7.24-7.32 (m, 5H), 7.64-7.66 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 58.5, 109.6, 111.4, 113.6, 115.6, 121.7, 122.4, 126.1, 126.4, 129.0, 129.2, 130.2, 134.4, 135.0, 137.6, 145.9, 197.3; IR (neat) ν 2925, 2855, 2221, 1680, 1444, 1406, 1343, 1320, 1277, 1226, 1164, 948, 853, 750 cm^{-1}; MS (%) m/e 334 (50), 299 (4), 193 (13), 142 (8), 115 (13), 84 (5), 71 (2), 57 (3), 43 (100); HRMS (EI) for $C_{20}H_{15}N_2OCl$: 334.0873; Found: 334.0874; $[\alpha]^{20}_{D}$ = -49.6 (c 1.10, $CHCl_3$) (95% ee); Chiralcel AD-H, hexane/^{i}PrOH = 70/30, 0.6 mL/min, 214 nm, t_{major} = 9.10 min, t_{minor} = 10.07 min.



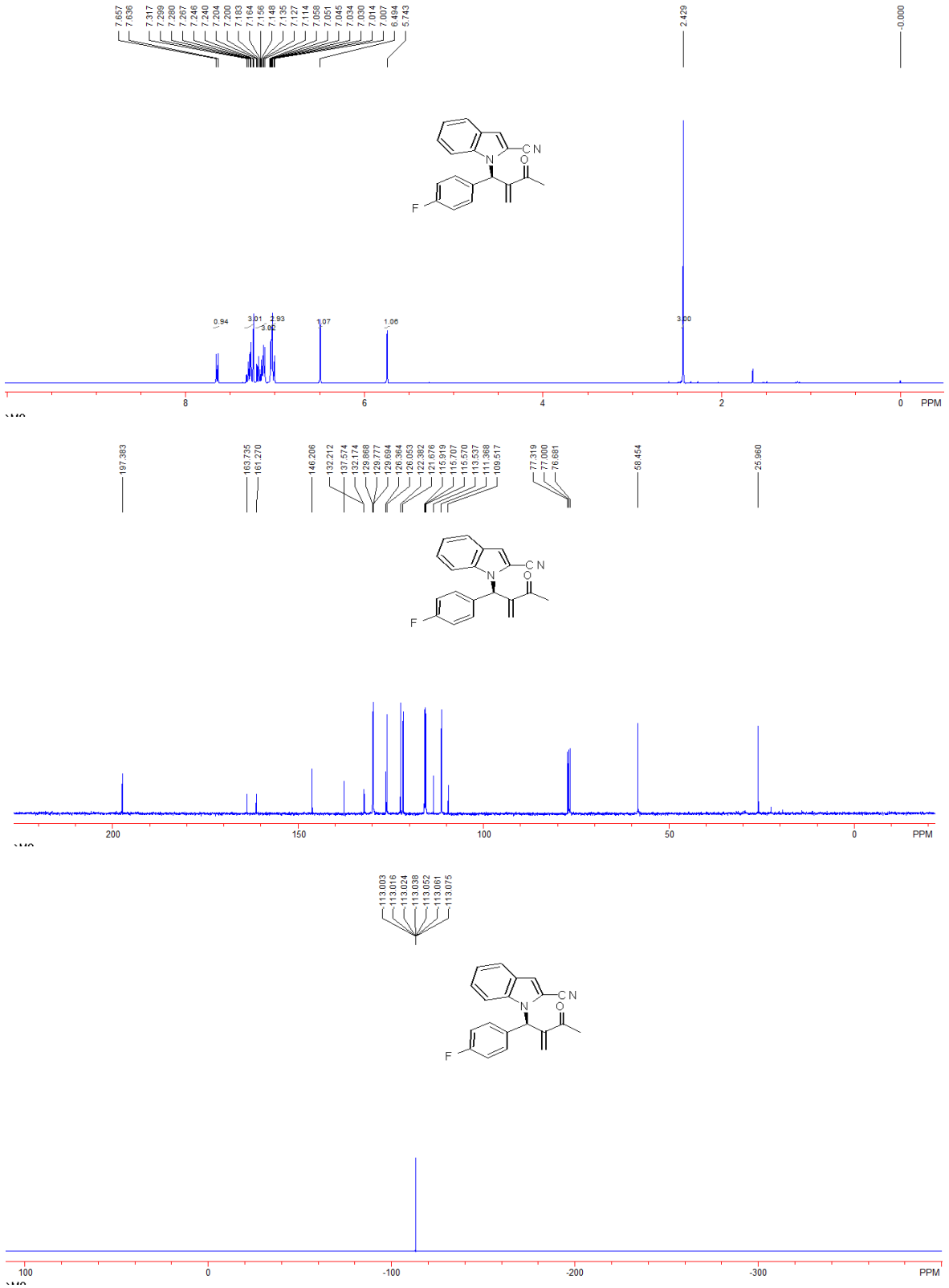


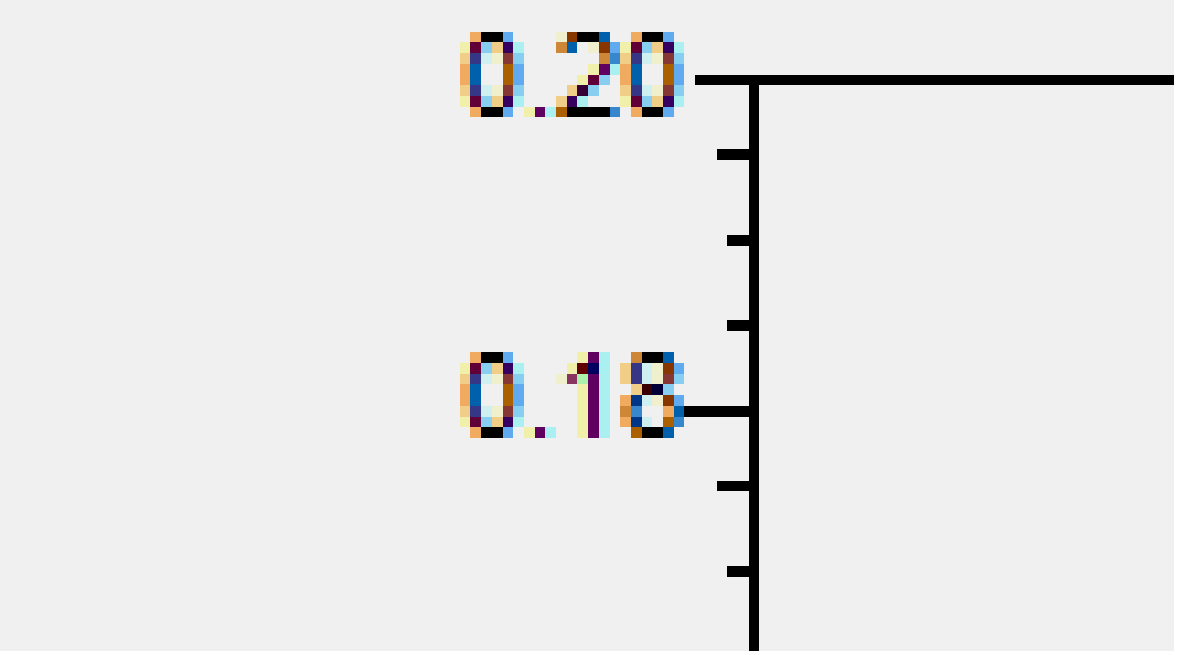
	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	9.077	2065755	49.99	160963
2	10.041	2066655	50.01	144525

	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	9.099	7410329	97.63	579429
2	10.065	179652	2.37	12917

1-(1-(4-fluorophenyl)-2-methylene-3-oxobutyl)-1H-indole-2-carbonitrile 5b: a white foam (32 mg, 99% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 5.74 (s, 1H), 6.49 (s, 1H), 7.01-7.05 (m, 3H), 7.11-7.18 (m, 3H), 7.20-7.32 (m, 3H), 7.65 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 58.5, 109.5, 111.4, 113.5, 115.6 (d, $J_{C\text{-}F}$ = 3.7 Hz), 115.9, 121.7, 122.4, 126.1, 126.4, 129.7 (d, $J_{C\text{-}F}$ = 8.3 Hz), 129.9, 132.2 (d, $J_{C\text{-}F}$ = 3.8 Hz), 137.6, 146.2, 162.5 (d, $J_{C\text{-}F}$ = 246.5 Hz), 197.4; ^{19}F NMR (376 MHz, $CDCl_3$): δ -113.075- -113.003 (m, 1F); IR (neat) ν 2923, 2855, 2219, 1675, 1510, 1365, 1319, 1226, 1160, 972, 846, 750 cm^{-1}; MS (%) m/e 318 (35), 275 (4), 177 (21), 142 (8), 133 (13), 115 (5), 84 (5), 57 (3), 43 (100); HRMS (EI) for $C_{20}H_{15}N_2OF$: 318.1168; Found: 318.1171; $[\alpha]^{20}_D$ = -82.0 (c 0.50,

$CHCl_3$) (96% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 13.97 min, t_{minor} = 9.40 min.



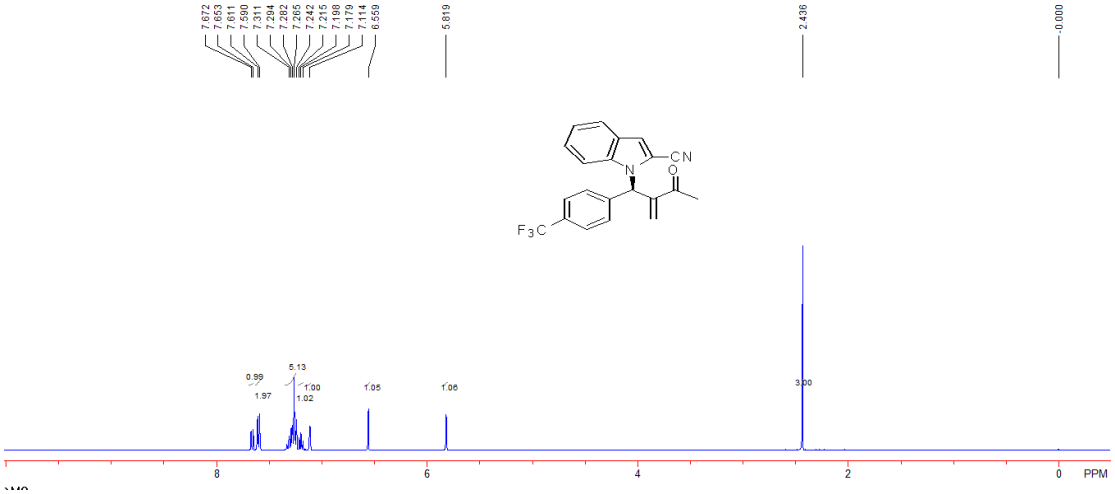


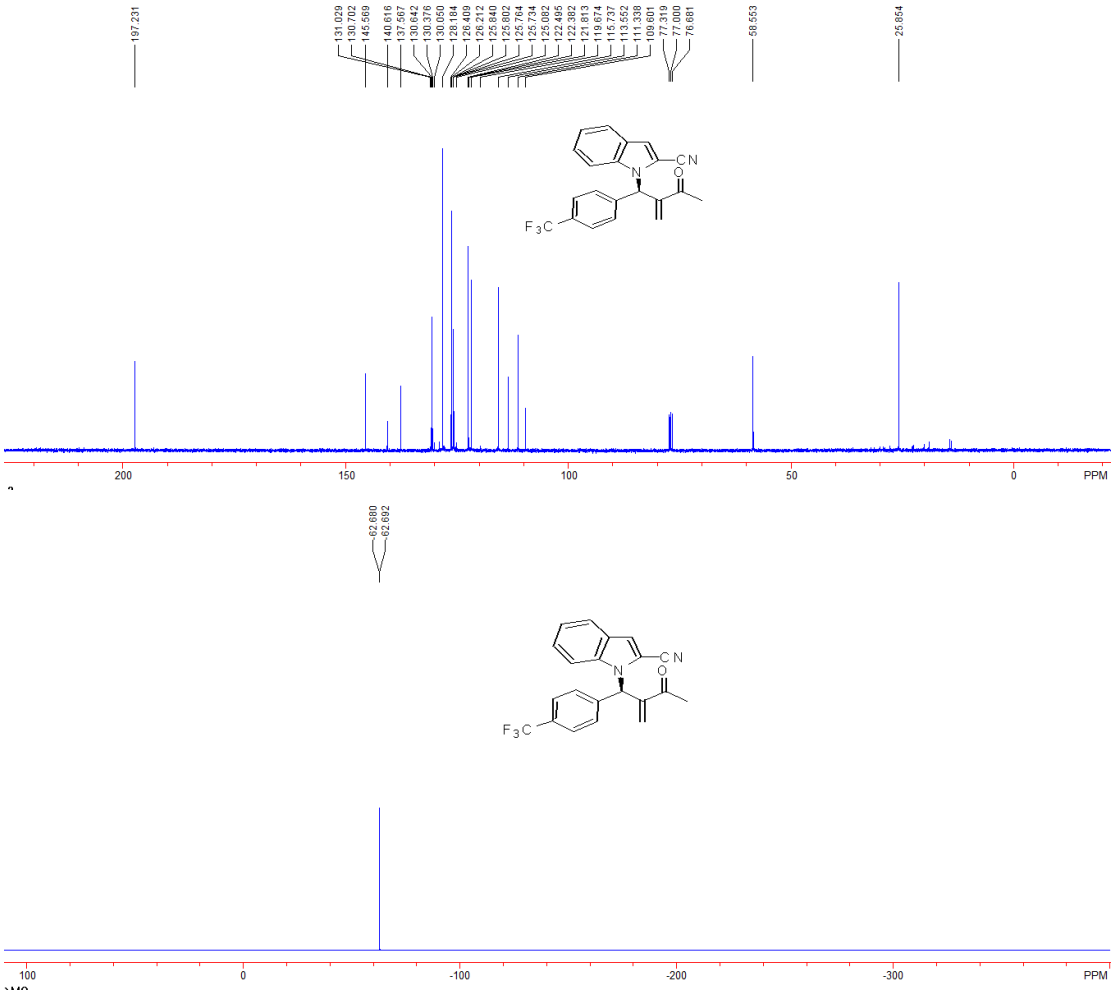
	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	9.400	1829583	50.07	92459
2	14.099	1824395	49.93	60925

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	9.395	73039	2.24	3703

2	13.971	3192880	97.76	107628

1-(2-methylene-3-oxo-1-(4-(trifluoromethyl)phenyl)butyl)-1H-indole-2-carbonitrile 5c: a white foam (25 mg, 68% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.44 (s, 3H), 5.82 (s, 1H), 6.56 (s, 1H), 7.11 (s, 1H), 7.18-7.22 (m, 1H), 7.24-7.31 (m, 5H), 7.60 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 58.6, 109.6, 111.3, 113.6, 115.7, 121.8, 122.5, 123.8 (q, $J_{C\text{-}F}$ = 270.7 Hz), 125.8 (q, $J_{C\text{-}F}$ = 2.9 Hz), 126.2, 126.4, 128.2, 130.6 (q, $J_{C\text{-}F}$ = 32.6 Hz), 130.7, 137.6, 140.6, 145.6, 197.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.692--62.680 (m, 3F); IR (neat) ν 2925, 2854, 2221, 1681, 1618, 1445, 1321, 1247, 1165, 1120, 1168, 977, 877, 750 cm^{-1}; MS (%) m/e 368 (44), 349 (3), 325 (7), 299 (3), 227 (8), 142 (20), 133 (2), 115 (14), 84 (2), 63 (3), 43 (100); HRMS (EI) for $C_{21}H_{15}N_2OF_3$: 368.1136; Found: 368.1141; $[\alpha]^{20}_D$ = -36.4 (c 0.50, $CHCl_3$) (92% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 9.75 min, t_{minor} = 8.35 min.





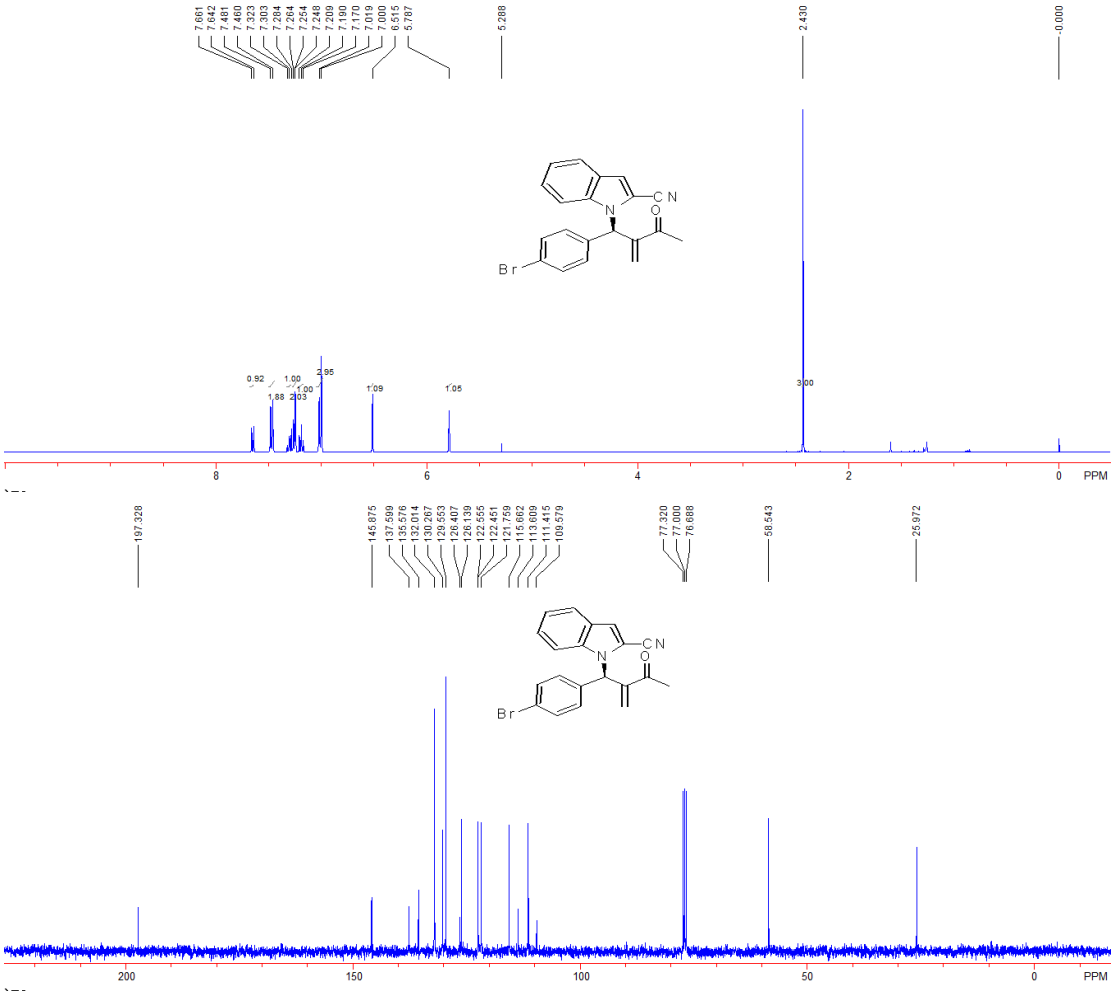
	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	8.349	1519354	49.99	84768

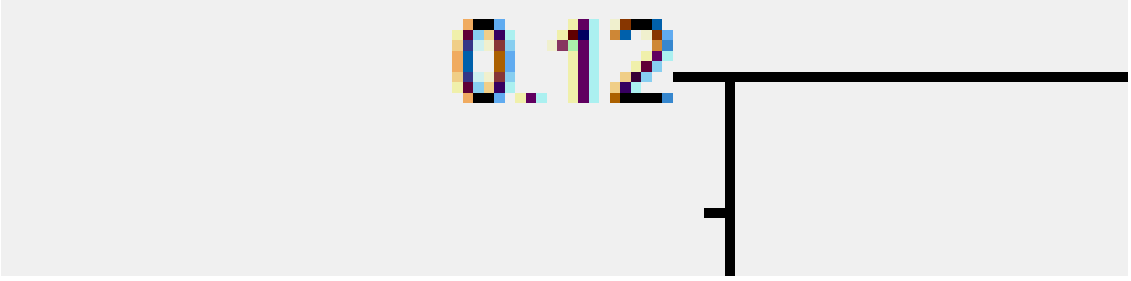
2	9.808	1519864	50.01	72987

	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	8.349	243702	3.55	14147
2	9.747	6612696	96.45	316160

1-(1-(4-bromophenyl)-2-methylene-3-oxobutyl)-1H-indole-2-carbonitrile 5d: a white solid (38 mg, 99% yield); m.p. 151-153 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.43 (s, 3H), 5.79 (s, 1H), 6.52 (s, 1H), 7.00-7.02 (m, 3H), 7.17-7.21 (m, 1H), 7.25-7.32 (m, 3H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 58.5, 109.6, 111.4, 113.6, 115.7, 121.8, 122.5, 122.6, 126.1, 126.4, 129.6, 130.3, 132.0, 135.6, 137.6, 145.9, 197.3; IR (neat) ν 2925, 2854, 2221, 1680, 1444, 1402, 1346, 1319, 1278, 1225, 1163, 1070, 948, 852, 749 cm^{-1}; MS (%) m/e 378 (28), 299 (5), 237 (8), 158 (22), 142 (9), 115 (47), 89 (6), 63 (7), 43 (100); HRMS (EI) for $C_{20}H_{15}N_2OBr$: 378.0368; Found: 378.0363; $[\alpha]^{20}_{D}$ = -38.6 (c

1.10, $CHCl_3$) (96% ee); Chiralcel OD-H, hexane/^{i}PrOH = 80/20, 0.7 mL/min, 230 nm, t_{major} = 10.20 min, t_{minor} = 12.25 min.



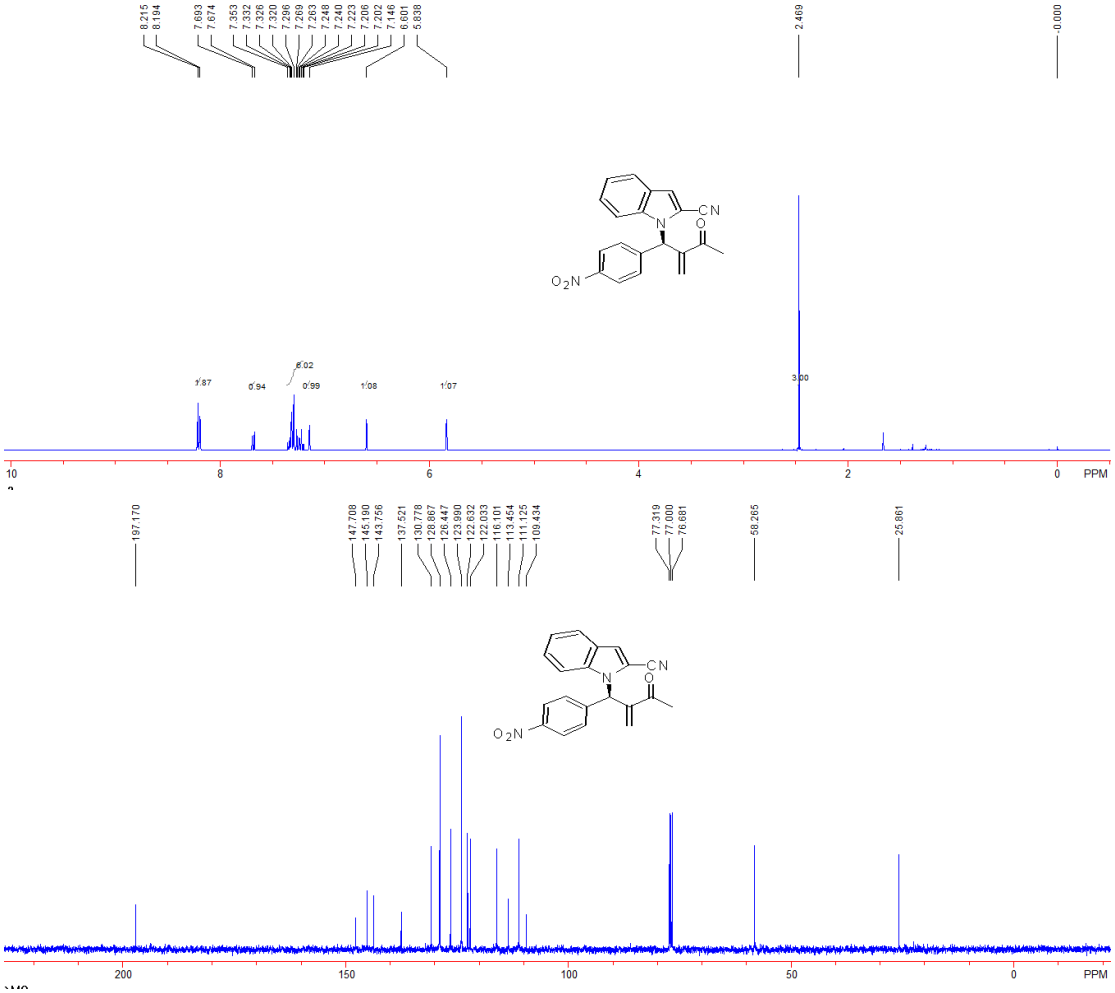


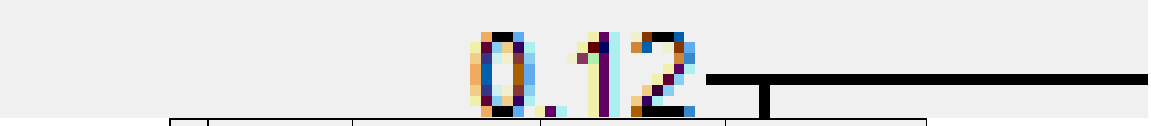
	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	10.203	1368533	49.97	61456
2	12.331	1370133	50.03	51214

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	10.198	111018	1.92	5130
2	12.254	5656719	98.08	215228

1-(2-methylene-1-(4-nitrophenyl)-3-oxobutyl)-1H-indole-2-carbonitrile 5e: a yellow solid (32 mg, 93% yield); m.p. 90-93 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.47 (s, 3H), 5.84 (s, 1H), 6.60 (s, 1H), 7.15 (s, 1H), 7.20-7.35 (m, 6H), 7.68 (d, *J* = 7.6 Hz, 2H), 8.20 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 58.3, 109.4, 111.1, 113.5, 116.1, 122.0, 122.6, 124.0, 126.5, 128.9, 130.8, 137.5, 143.8, 145.2, 147.7, 197.2; IR (neat) ν 2925, 2855, 2221, 1680,

1517, 1446, 1344, 1318, 1279, 1228, 1192, 1165, 964, 850, 750 cm^{-1}; MS (%) m/e 345 (56), 328 (15), 299 (5), 256 (8), 162 (15), 142 (31), 115 (28), 89 (7), 63 (8), 43 (100); HRMS (EI) for $C_{20}H_{15}N_3O_3$: 345.1113; Found: 345.1111; $[\alpha]^{20}_D$ = -69.5 (c 1.40, $CHCl_3$) (95% ee); Chiralcel AD-H, hexane/^{i}PrOH = 70/30, 0.6 mL/min, 214 nm, t_{major} = 13.69 min, t_{minor} = 18.09 min.



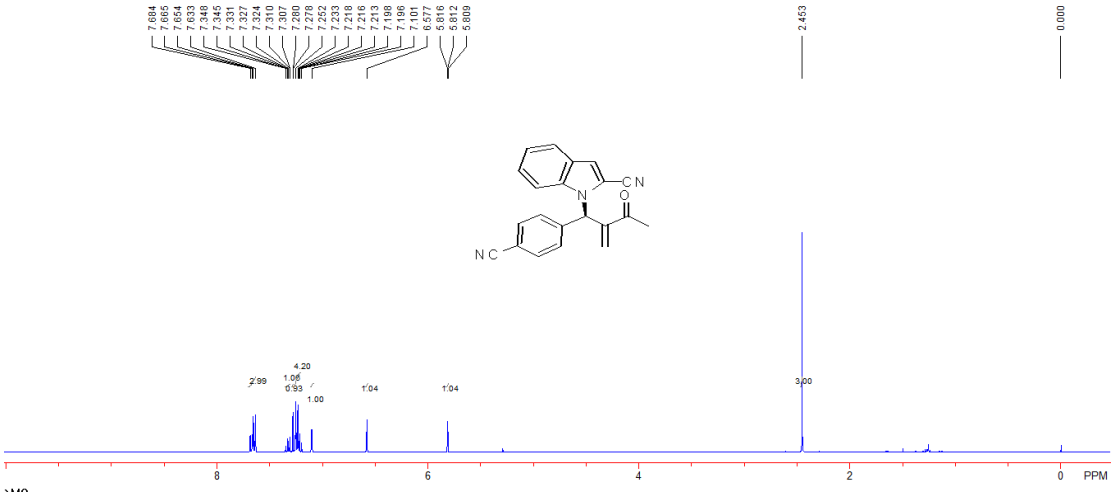


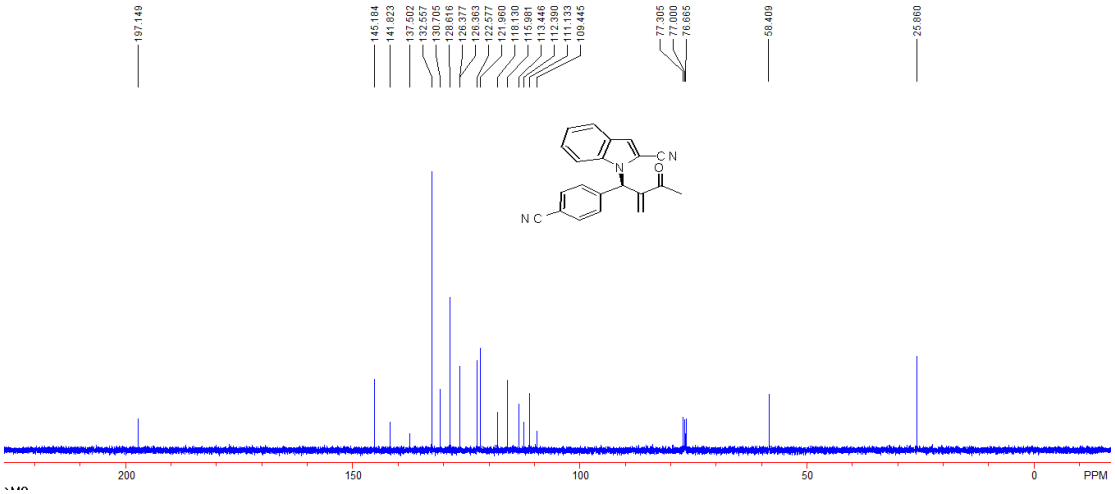
	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	13.755	1296048	50.05	68140
2	18.296	1293220	49.95	49723

	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	13.691	7510697	97.43	399136

2	18.097	197864	2.57	7970

1-(2-methylene-1-(4-nitrophenyl)-3-oxobutyl)-1H-indole-2-carbonitrile 5f: a colorless oil (32 mg, 98% yield); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.45 (s, 3H), 5.81 (t, *J* = 1.2 Hz, 1H), 6.58 (s, 1H), 7.10 (s, 1H), 7.20-7.35 (m, 7H), 7.63-7.68 (m, 3H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 58.4, 109.5, 111.1, 112.4, 113.5, 116.0, 118.1, 122.0, 122.6, 126.3, 126.4, 128.6, 130.7, 132.6, 137.5, 141.8, 145.2, 197.2; IR (neat) ν 2924, 2854, 2221, 1680, 1446, 1401, 1363, 1345, 1317, 1278, 1229, 1194, 967, 851, 750 cm^{-1}; MS (%) m/e 325 (40), 310 (5), 282 (7), 184 (6), 142 (51), 115 (9), 84 (4), 63 (4), 43 (100); HRMS (EI) for $C_{21}H_{15}N_3O$: 325.1215; Found: 325.1214; $[\alpha]^{20}_{D}$ = -51.8 (c 1.60, $CHCl_3$) (93% ee); Chiralcel AD-H, hexane/^{i}PrOH = 70/30, 0.6 mL/min, 214 nm, t_{major} = 12.94 min, t_{minor} = 15.17 min.

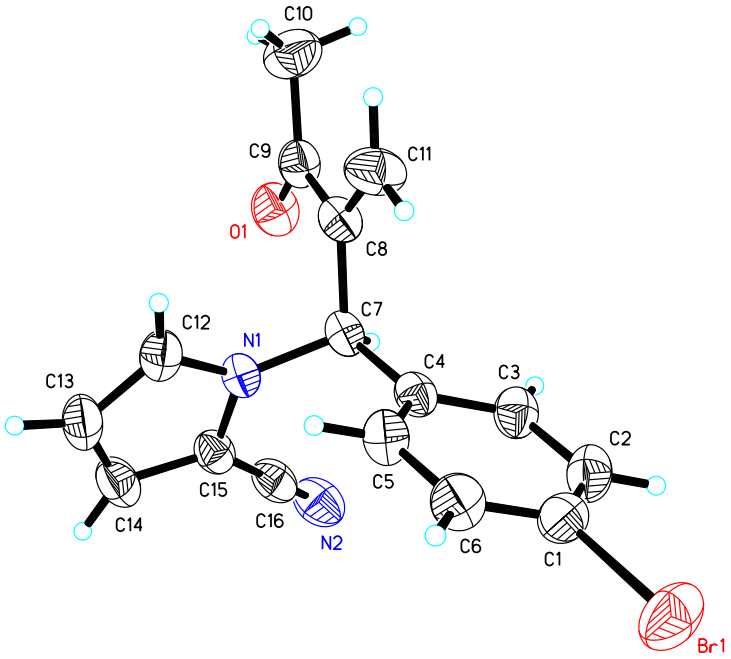




	RT (min)	Area (μV*sec)	% Area	Height (μV)
1	13.826	2471754	49.90	103638
2	16.563	2481735	50.10	81293

	RT (min)	Area （μV*sec)	% Area	Height (μV)
1	12.941	2595449	96.51	121308
2	15.165	93730	3.49	3009

X-ray crystal data of 3h



The crystal data of **3h** have been deposited in CCDC with number 812598. Empirical Formula: $C_{16}H_{13}BrN_2O$; Formula Weight: 329.19; Crystal Color, Habit: colorless, Crystal Dimensions: 0.26 x 0.18 x 0.13 mm; Crystal System: Orthorhombic; Lattice Parameters: a = 8.5810(18)Å, b = 9.4511(19)Å, c = 18.265(4)Å, $\alpha = 90^o$, $\beta = 90^o$, $\gamma = 90^o$, V = 1481.3(5)Å^3; Space group: P2(1)2(1)2(1); Z = 4; D_{calc}= 1.476 g/cm^3; F_{000} = 664; Final R induces [I>2sigma(I)]: R1 = 0.0407; wR2 = 0.1105.