Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Enantioselective Electrophilic Cyanation of β-keto Amides Catalyzed by Cinchona Organocatalyst

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1. General information

All reactions were carried out with oven dried glassware under argon atmosphere, unless otherwise stated. All chemicals were purchased from Acros, Alfa, Aladdin, or InnoChem and used as it comes unless otherwise stated. TLC was performed on silica gel F254 TLC glass plates and visualized with UV light. Solvent of petroleum ether (PE) and ethyl acetate (EA) were used directly in column chromatography. Toluene, THF were dried over sodium (diphenyl ketone) and distilled; CH_2Cl_2, CH_3CN, $CHCl_3$ were distilled over CaH_2 before use. ^1H NMR spectra were recorded on a Brucker Avance400 (400 MHz) spectrometer in chloroform-d, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm as the standard. The data is reported as (s = singlet, d =doublet, t = triplet, m = multiplet or unresolved, coupling constant(s) in Hz, integration, assignment). ^{13}C NMR spectra were recorded with ^1H-decoupling on a Brucker Avance400 (100 MHz) spectrometer in chloroform-d, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm as the standard. Cinchona alkaloids (**A_6-A_{10}**) were prepared according to known literature procedure [1][2][3]. Other analyses were carried out on the following instruments.

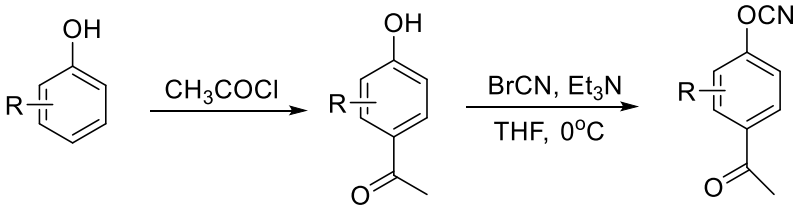
Infrared spectrometer: Bruker ALPHA FT-IR-Spectrometer.
High resolution mass spectrum: Bruker Apex IV FTMS.
Rotation polarity: Krüss P8000.
High Performance Liquid Chromatography: Shimadzu LC-20A.
Melting point detector： Binocular microscope XT4A melting point apparatus (without correct).

2. Preparation of reactants

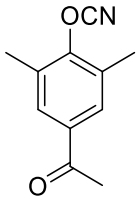
2.1 Synthesis of cyano reagents

Caution! All operations must be carried out in a well-ventilated fume food because cyanogen bromide is highly toxic and can generate hydrogen cyanide upon hydrolysis.

Following the reported procedure,[4] to a solution of cyanogen bromide (1.2 equiv) in THF (20 mL) was added slowly a solution of phenol (1.0 equiv) with triethylamine (3.0 equiv) in THF (20 mL) at 0 °C. The reaction mixture was stirred for 2 h at 0 °C and then at rt for 4 h. Filtered on a Celite pad and concentrated in vacuum, the residue was dissolved in ethyl acetate and petroleum ether (1:5) for recrystallization to get the colorless solid.

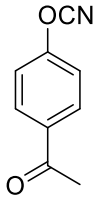


1-(4-cyanato-3,5-dimethylphenyl)ethan-1-one (2a)



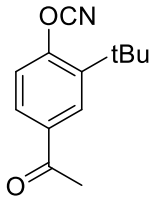
White solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (s, 2H, Ar-H), 2.58 (s, 3H, CH_3CO), 2.48 (s, 6H, CH_3-Ar) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.6, 154.0, 136.2, 130.0, 129.5, 109.6 (CN), 26.7, 16.0 ppm. IR (KBr) 3347, 2964, 2265, 1685, 1317, 1150, 1067, 886, 758 cm^{-1}. HRMS: calc. for $C_{11}H_{12}NO_2$ $[M+H]^+$: 190.0863, found: 190.0862

1-(4-cyanatophenyl)ethan-1-one (2b)



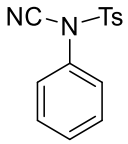
Colorless solid, 55% yield (after recrystallization), m.p. 60-62 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (dd, J = 6.8, 2.0 Hz, 2H, Ar-H), 7.40 (dd, J =7.2, 2.0 Hz, 2H, Ar-H), 2.62 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.2, 155.9, 136.1, 131.4, 115.9, 108.2 (CN), 27.0 ppm. IR (KBr) 3349, 3071, 2964, 2266, 1919, 1692, 1592, 1495, 1317, 1267, 1150, 1195, 1167, 962, 829 cm^{-1}. HRMS: calc. for $C_9H_8NO_2$ $[M+H]^+$: 161.0477, found: 161.0475.

1-(3-(tert-butyl)-4-cyanatophenyl)ethan-1-one (2c)



Colorless solid, 75% yield, m.p. 69-72 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.04 (d, J = 2 Hz, ^{1}H, Ar-H), 7.91(dd, J = 8.8, 2.4 Hz, 1H, Ar-H), 7.57(d, J = 8.4 Hz, 1H, Ar-H), 2.61(s, 3H, CH_3), 1.42(s, 9H, *t*Bu-H) ppm; ^{13}CNMR (100 MHz, $CDCl_3$): δ = 196.3, 154.8, 138.6, 135.5, 128.6, 128.5,115.7, 107.9 (CN), 34.5, 29.7, 26.6 ppm. IR (KBr) 3347, 2969, 2256, 1462, 1349, 1184, 961,836, 728 cm^{-1}. HRMS: calc. for $C_{13}H_{16}NO_2$ $[M+H]^+$: 218.1176, found: 218.1173.

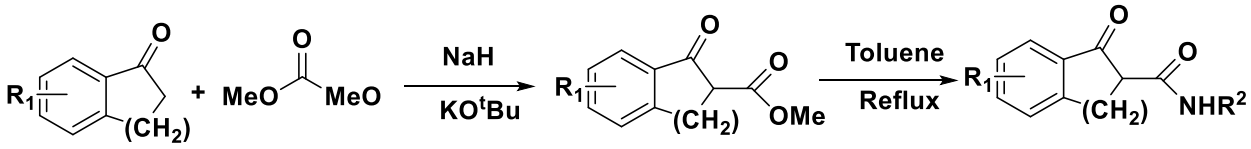
N-cyano-4-methyl-N-phenylbenzenesulfonamide (2d)[5]



Colorless solid, 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, J = 8.4, 2H), 7.46 – 7.32 (m, 5H), 7.21 – 7.17 (m, 2H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.7, 134.5, 132.3, 130.2, 129.9, 129.8, 128.4, 126.5, 108.6.

2.2 Synthesis of substrates

General procedure for preparation of β-keto amides (1a-1r)



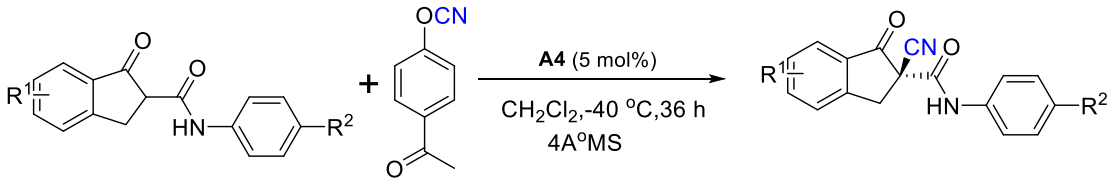
β-Keto esters were synthesized according to a slightly modified literature procedure.[6] To a dried three-necked flask equipped with a magnetic stirrer was added dimethyl carbonate (3.0 equiv)

andketone (1.0 equiv) at 0 ^{o}C, then sodium hydride (2.2 equiv) was added slowly. The reaction was stopped until the evolution of hydrogen ceased (15-20 min). Then chlorine hydride (1.0 M) was added dropwise, and a heavy, pasty solid appeared (about pH 4). Ice-water and ethyl acetate was added to dissolve the solid completely. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate three times. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate and concentrated *in vacuo* to get the crude product without further purification.

To a dried flask equipped with a reflux condenser was added β-keto methyl esters (1.0 mmol), amine (2.0 mmol) in toluene (10 mL). The mixture was heated to reflux. After completion, monitored by TLC, the mixture was concentrated under reduced pressure directly. The residue was purified by flash column chromatography to give the title compounds **1a-1r.**

3. Asymmetric cyanation reactions of *β*-keto carbonyls

3.1 General procedure for asymmetric cyanation reaction of *β*-keto amides



4-Acetylphenyl cyanate **2b** (5 equiv.) was added to a stirred solution of the corresponding β-ketoamides **1** and cinchonine (**A4**, 5mol %) with 4Å MS in dichloromethane (1 mL) at -40 ^{o}C temperature. The reaction mixture was stirred at this temperature for 36 h. The crude product was directly transferred to a silica-gel column and eluted with a gradient of PE and EtOAc to give the products **3** in the reported yields and enantiopurities.

3.2 The observed enantioselectivity with reaction time

We noticed the ee value increasing as the reaction proceeds which also observed in other catalytic process. After careful monitoring the ee vs reaction time, a plot was obtained as the following. We interpret this as some unknown reaction path ways with inferior enantioselectivity in competition with the desired asymmetric catalysis. As the reaction proceeding, either the product itself or any other byproduct could suppress the competition reactions and/or accelerate desired asymmetric catalysis. Similar phenomena were also recorded with higher equivalent of cyano reagent. It's interesting but looks a much complicate situation. To take advantages of these observations further optimization of the catalyst efficiency and the mechanism elucidation are underway. It would be presented in full length in near future.

Table S1 The observed enantioselectivity with reaction time.[a]

Entry	Time (h)	Yields (%)[b]	Ee (%)[c]
1	2	12	29
2	6	18	62
3	12	31	71
4	24	62	69
5	36	68	75

[a] Reaction Conditions: **1a** (0.1 mmol), **2b** (0.12 mmol, 1.2 equiv), catalyst (5 mol%), 4Å MS (5 mg), CH_2Cl_2 (1.0 mL) at -40 °C, argon atmosphere, unless otherwise indicated; [b] isolated yield; [c] Enantiomeric excess (ee) was determined by chiral HPLC analysis on Chiralpak AD-H.

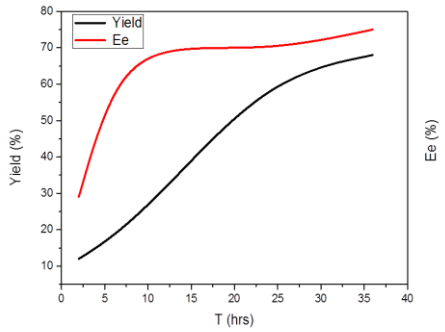
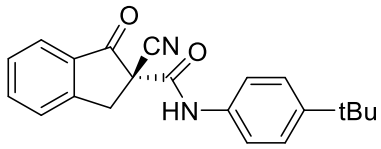
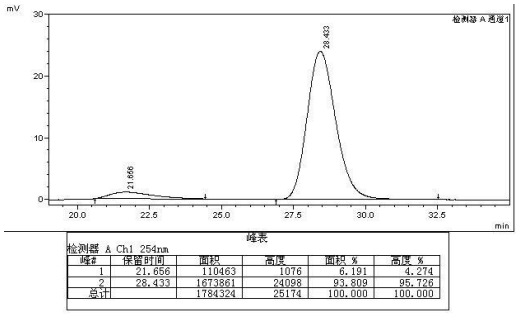


Figure S1 Plot of enantioselectivity and reaction time

4. Characterization for cyanation products



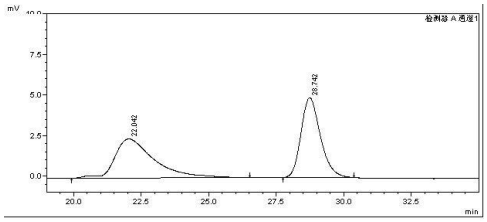
***N*-(4-(tert-butyl) phenyl)-2-cyano-1-oxo-2,3-dihydro-*1H*-indene-2-carboxamide** (**3a**)[7]
Colorless oil, 90% yield, 88% *ee*. Developing solvent PE/EA (10/1, V/V), $[\alpha]_D^{20}$= +45.71 (*c* 0.35, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42 (s, 1H), 7.84 (d, *J* = 7.7, 1H), 7.75 (t, *J* = 7.5 Hz, 1H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.50-7.45 (m, 3H), 7.37 (d, *J* = 8.5 Hz, 2H), 4.36 (d, *J* = 17.5 Hz, 1H), 3.64 (d, *J* = 17.5 Hz, 1H), 1.30 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.8, 158.1, 152.6, 148.7, 137.4, 134.1, 131.9, 128.8, 126.6, 126.1, 126.0, 120.0, 117.0, 54.1, 35.3, 34.5, 31.3 ppm. IR (neat): $\tilde{\nu}$ = 3341, 2962, 2252, 1725, 1598, 1523, 1271, 1202, 905, 832, 727 cm^{-1}. HRMS: calc. for $C_{21}H_{20}N_2NaO_2$ [*M*+Na]$^+$: 355.1414, found: 355.1417. HPLC on Chiralpak AD-H (*n*-hexane /*iso*-propanol 80:20, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	21.656	110463	1076	6.191	4.274
2	28.433	1673861	24098	93.809	95.726
总计		1784324	25174	100.000	100.000

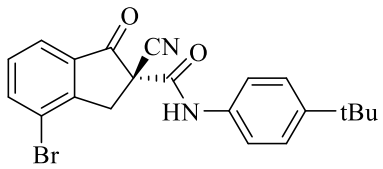


峰表

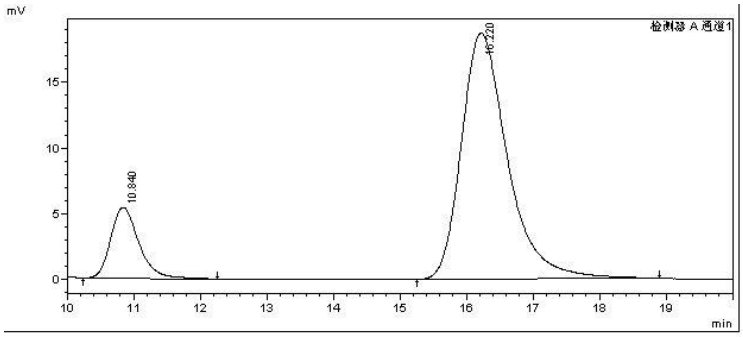
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	22.042	245458	2409	49.988	32.889
2	28.742	245580	4916	50.012	67.111
总计		491038	7326	100.000	100.000

4-Bromo-*N*-(4-(tert-butyl)phenyl)-2-cyano-1-oxo-2,3-dihydro-*1H*-indene-2-carboxamide (3b)



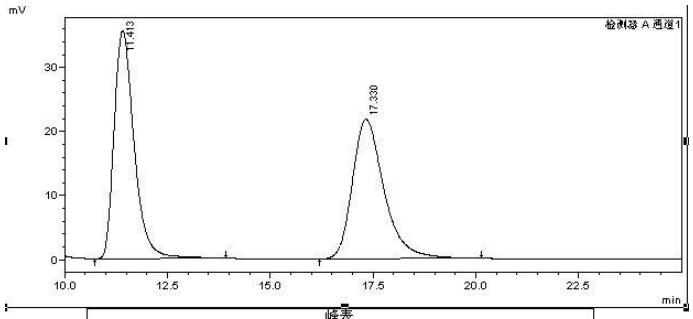
White solid, 69% yield, 71% *ee*, m.p. 293-295 °C. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$= +13.0 (*c* 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (s, 1H), 7.93 (t, *J* = 4.0 Hz, 1H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.68 – 7.61 (m, 3H), 7.41 (dd, *J* = 12.6, 8.8 Hz, 2H), 4.29 (d, *J* = 9.2 Hz, 1H), 3.57 (d, *J* = 8.8 Hz, 1H), 1.31(s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.2, 157.7, 141.9, 133.8, 130.9, 130.5, 128.8, 126.0, 124.8, 116.5, 65.5, 54.2, 36.5, 34.4, 31.3 ppm. IR (neat): $\tilde{\nu}$ = 3336, 2957, 2242, 1734, 1598, 1533, 1261, 1199, 904, 834, 749 cm^{-1}. HRMS: calc. for $C_{21}H_{20}BrN_2O_2[M+H]^+$: 411.0703, found: 411.0710. HPLC on Chiralpak OD-H (*n*-hexane /*iso*-propanol 90:10, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	10.840	157807	5395	14.826	22.324
2	16.220	906622	18772	85.174	77.676
总计		1064428	24168	100.000	100.000

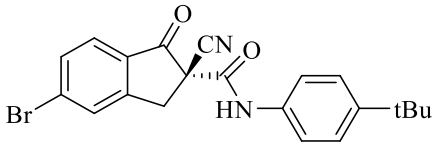


峰表

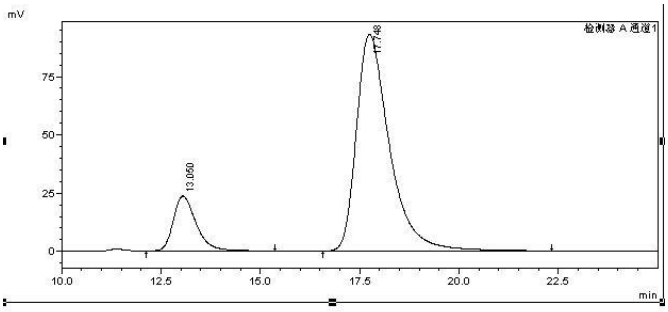
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	11.413	1212303	35564	50.959	62.005
2	17.330	1166686	21793	49.041	37.995
总计		2378989	57356	100.000	100.000

5-bromo-*N*-(4-(tert-butyl)phenyl)-2-cyano-1-oxo-2,3-dihydro-*1H*-indene-2-carboxamide (**3c**)



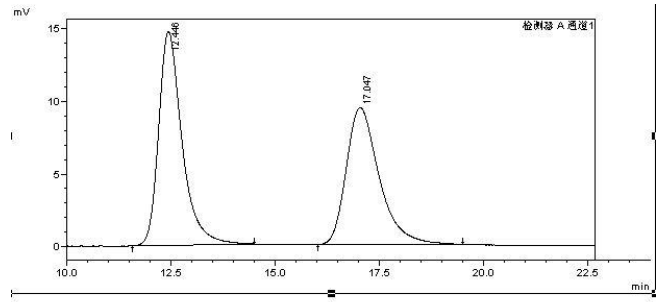
White solid, 88% yield, 71% *ee*, m.p. 171-173 °C. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$ = +12.2 (*c* 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (s, 1H), 7.77 (s, 1H), 7.66 (dd, *J* = 9.6, 7.2 Hz, 3H), 7.40 (dd, *J* = 12.0, 7.6 Hz, 5H), 4.33 (ab, *J* = 17.7 Hz, 1H), 3.61 (ab, *J* = 17.6 Hz, 1H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.6, 157.7, 153.9, 148.8, 133.9, 133.4, 132.7, 130.7, 130.0, 127.0, 126.0, 120.0, 116.6, 54.2, 34.9, 34.5, 31.3 ppm. IR (neat): $\tilde{\nu}$ = 3336, 2959, 2239, 1730, 1595, 1521, 1315, 1263, 1204, 905, 834, 749 cm^{-1}. HRMS: calc. for $C_{21}H_{20}BrN_2O_2$[*M*+H]$^+$: 411.0703, found 411.0712. HPLC on Chiralpak OD-H (*n*-hexane/*iso*-propanol 90:10, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

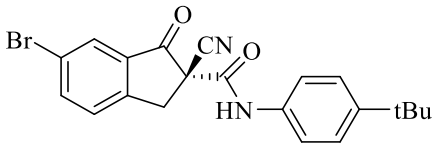
峰#	保留时间	面积	高度	面积 %	高度 %
1	13.050	936950	23491	14.817	20.180
2	17.748	5386327	92919	85.183	79.820
总计		6323276	116410	100.000	100.000



峰表

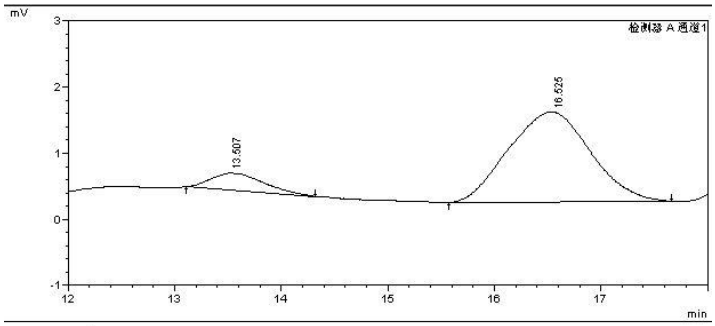
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	12.446	575599	14698	52.673	60.970
2	17.047	517176	9409	47.327	39.030
总计		1092775	24107	100.000	100.000



6-bromo-*N*-(4-tert-butylphenyl)-2-cyano-1-oxo-2,3-dihydro-*1H*-indene-2-carboxamide (**3d**)

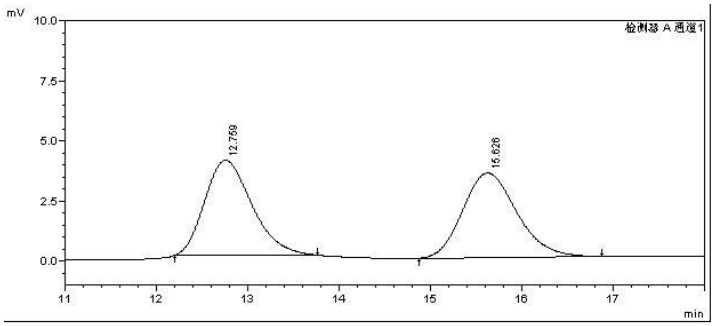
White solid, 78% yield, 79% *ee*, m.p. 79-83 ºC. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$ = +8.6 (*c* 0.2, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32 (s, 1H), 7.96 (s, 1H), 7.85 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.45 (t, *J* = 8.5 Hz, 3H), 7.37 (d, *J* = 8.4 Hz, 2H), 4.29 (ab, *J* = 16.9 Hz, 1H), 3.57 (ab, *J* = 17.6 Hz, 1H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.5, 157.6, 151.1,148.8, 140.1, 133.8, 133.6， 128.7, 128.0, 125.9, 123.0, 120.1, 116.5, 54.5, 35.1, 34.4, 31.2 ppm. IR (neat): $\tilde{\nu}$ = 3336, 2958, 2243, 1739, 1597, 1525, 1318, 1248, 1196, 913, 831, 748 cm^{-1}. HRMS: calc. for $C_{21}H_{20}BrN_2O_2[M+H]^+$: 411.0703, found 411.0712. HPLC on Chiralpak OD-H (*n*-hexane/*iso*-propanol 90:10, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

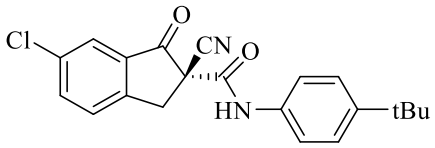
峰#	保留时间	面积	高度	面积 %	高度 %
1	13.507	8930	255	10.936	15.771
2	16.525	72728	1362	89.064	84.229
总计		81658	1617	100.000	100.000



峰表

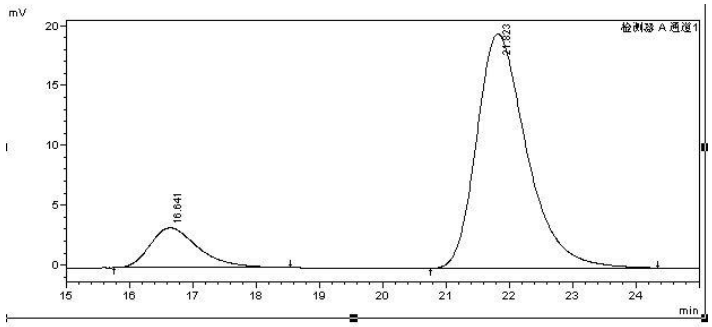
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	12.759	142220	3955	49.638	52.941
2	15.626	144295	3516	50.362	47.059
总计		286515	7471	100.000	100.000



***N*-(4-(tert-butyl)phenyl)-6-chloro-2-cyano-1-oxo-2,3-dihydro-*1H*-indene-2-carboxamide** (**3e**)

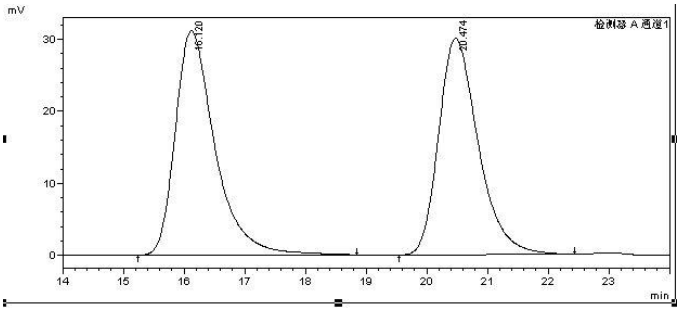
White solid, 84% yield, 71% *ee*, m.p. 155-158 °C. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$ = +30.48 (*c* 0.25, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.31 (s, 1H), 7.80 (s, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* =8.0 Hz, 3H), 7.38 (d, *J* = 8.0 Hz, 2H), 4.32 (ab, *J* = 17.6 Hz, 1H), 3.60 (ab, *J* = 17.6 Hz, 1H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.6, 157.7, 150.7, 148.8, 137.3, 135.4, 133.8, 133.3, 127.7, 126.0,125.6, 120.1, 116.5, 54.7, 35.0, 34.4, 31.2 ppm. IR (neat): $\tilde{\nu}$ = 3351, 2959, 2241, 1735, 1600, 1533, 1317, 1249, 1197, 907, 833, 720 cm^{-1}. HRMS: calc. for $C_{21}H_{20}ClN_2O_2$ [*M*+H]$^+$: 367.1208, found 367.1214. HPLC on Chiralpak AD-H (*n*-hexane/*iso*-propanol 80:20, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

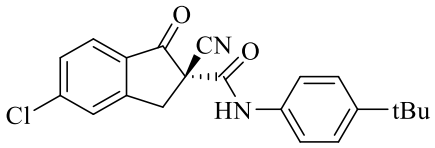
峰#	保留时间	面积	高度	面积 %	高度 %
1	16.641	177327	3326	14.136	14.521
2	21.823	1077127	19576	85.864	85.479
总计		1254454	22902	100.000	100.000



峰表

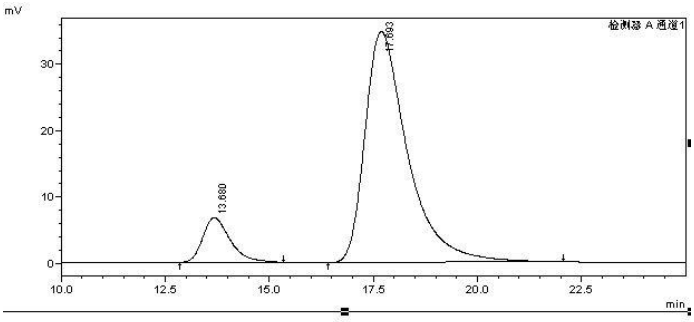
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	16.120	1415418	31158	50.884	50.900
2	20.474	1366233	30056	49.116	49.100
总计		2781651	61214	100.000	100.000



***N*-(4-(tert-butyl)phenyl)-5-chloro-2-cyano-1-oxo-2,3-dihydro-*1H*-indene-2-carboxamide** (**3f**)

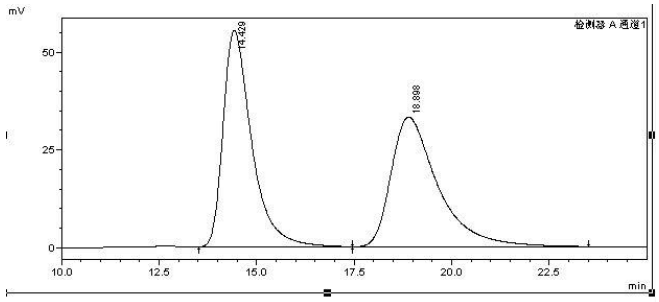
White solid, 92% yield, 79% *ee*, m.p. 114-118 ºC. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$ = +84.5 (*c* 0.4, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (s, 1H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.59 (s, 1H), 7.45 (t, *J* = 11.2 Hz, 3H), 7.37 (dd, *J* = 8.6, 1.4 Hz, 2H), 4.33 (ab, *J* = 17.6 Hz, 1H), 3.60 (ab, *J* = 17.6 Hz, 1H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.3, 157.8, 153.9, 148.8, 144.4, 133.9, 120.3, 129.8, 127.1, 126.9, 126.0, 120.1, 116.6, 54.4, 35.0, 34.5, 31.3 ppm. IR (neat): $\tilde{\nu}$ = 3340, 2959, 2241, 1730, 1598, 1528, 1316, 1265, 1204, 907, 834, 749 cm^{-1}. HRMS: calc. for $C_{21}H_{20}ClN_2O_2$ [*M*+H]$^+$: 367.1208, found 367.1217. HPLC on Chiralpak OD-H (*n*-hexane/*iso*-propanol 90:10, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

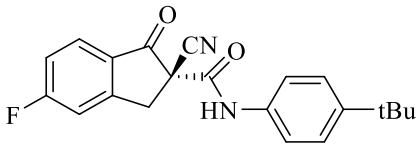
峰#	保留时间	面积	高度	面积 %	高度 %
1	13.680	305239	6699	10.937	16.142
2	17.693	2485722	34803	89.063	83.858
总计		2790961	41503	100.000	100.000



峰表

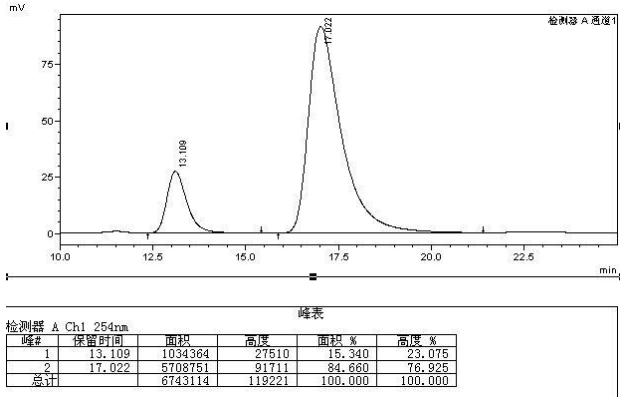
检测器 A Ch1 254nm

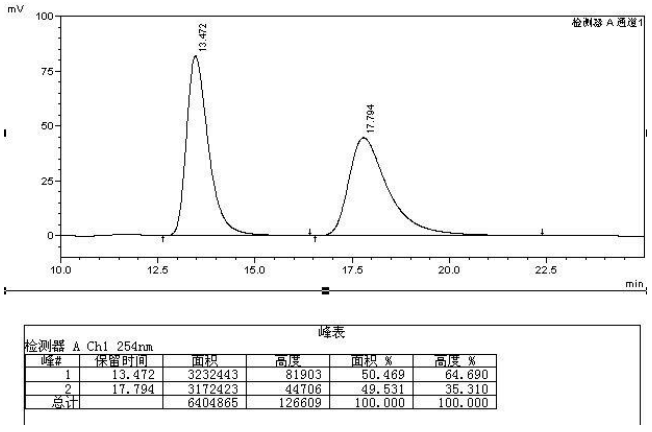
峰#	保留时间	面积	高度	面积 %	高度 %
1	14.429	2814176	55152	50.443	62.539
2	18.898	2764721	33036	49.557	37.461
总计		5578897	88188	100.000	100.000

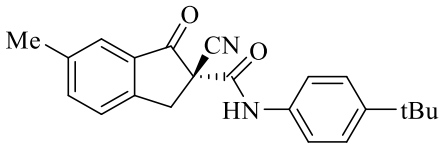


***N*-(4-(tert-butyl)phenyl)-2-cyano-5-fluoro-1-oxo-2,3-dihydro-*1H*-indene-2-carboxamide (3g)**

White solid, 92% yield, 70% *ee*, m.p. 268-271 ºC. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$ = +70.4 (*c* 0.25, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.37 (s, 1H), 7.86 (dd, *J* = 8.6, 5.1 Hz, 1H), 7.67 – 7.54 (m, 1H), 7.44 (t, *J* = 9.1 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 4.35 (ab, *J* = 17.7 Hz, 1H), 3.61 (ab, *J* = 17.7 Hz, 1H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.8, 169.9, 167.3, 157.8, 155.7, 148.8, 133.9, 128.7, 128.6, 126.0, 120.0, 117.7, 117.4, 116.7, 113.7, 113.5, 54.4, 35.1, 34.5, 31.3 ppm. IR (neat): $\tilde{\nu}$ = 3336, 2962, 2239, 1726, 1595, 1527, 1318, 1258, 1202, 913, 833, 743 cm^{-1}. HRMS: calc. for $C_{21}H_{20}FN_2O_2[M+H]^+$: 351.1503, found 351.1509. HPLC on Chiralpak OD-H (*n*-hexane/*iso*-propanol 90:10, 1.0 mL min^{-1}, 254 nm).

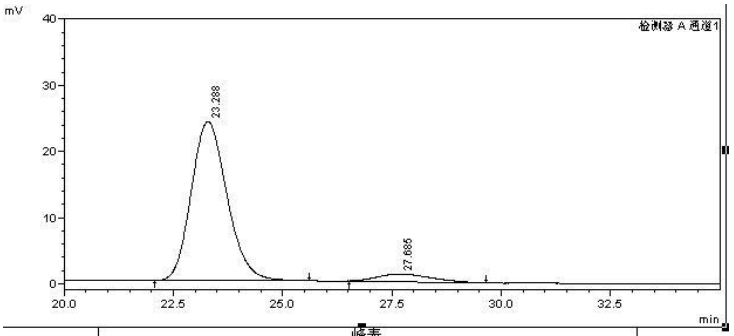






_N_-(4-(tert-butyl)phenyl)-2-cyano-6-methyl-1-oxo-2,3-dihydro-_1H_-indene-2-carboxamide (3h)

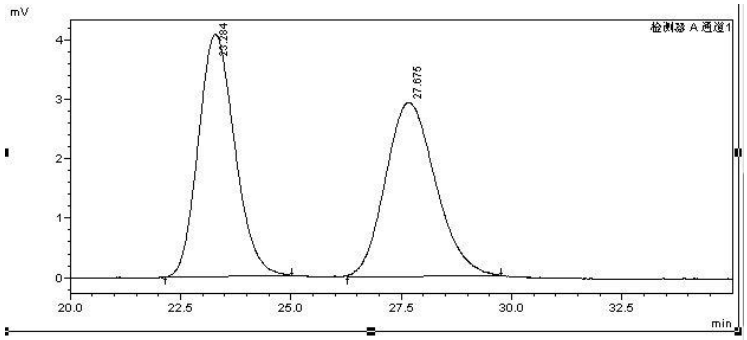
White solid, 83% yield, 86% *ee*, m.p. 133-135 ºC. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$ = +56.93 (*c* 0.3, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.44 (s, 1H), 7.63 (s, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.51 – 7.41 (m, 3H), 7.36 (dd, *J* = 8.6, 1.5 Hz, 2H), 4.30 (ab, *J* = 17.4 Hz, 1H), 3.58 (ab, *J* = 17.4 Hz, 1H), 2.43 (s, 3H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.9, 158.2, 150.1, 148.6, 139.2, 138.8, 134.1, 132.0, 126.3, 125.9, 125.8, 120.0, 117.1, 54.4, 35.0, 34.5, 31.3, 21.0 ppm. IR (neat): $\tilde{\nu}$ = 3324, 2957, 2239, 1721, 1599, 1521, 1318, 1277, 1196, 904, 831, 750 cm^{-1}. HRMS: calc. for $C_{22}H_{23}N_2O_2[M+H]^+$: 347.1754, found 347.1758. HPLC on Chiralpak AD-H (*n*-hexane/*iso*-propanol 80:20, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

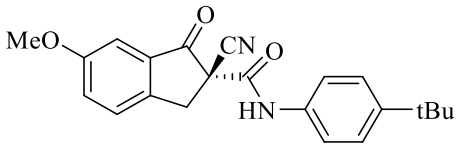
峰#	保留时间	面积	高度	面积 %	高度 %
1	23.288	1371892	24075	93.095	95.324
2	27.685	101749	1181	6.905	4.676
总计		1473641	25256	100.000	100.000



峰表

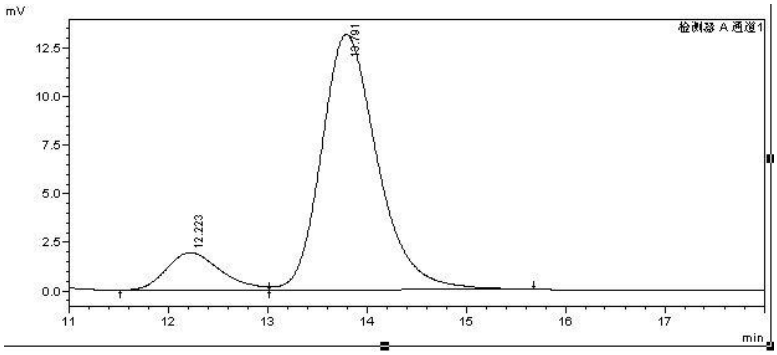
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	23.284	233737	4076	50.322	58.204
2	27.675	230742	2927	49.678	41.796
总计		464479	7003	100.000	100.000



***N*-(4-(*t*-butyl)phenyl)-2-cyano-6-methoxy-1-oxo-2,3-dihydro-*1H*-indene-2-carboxamide (3i)**

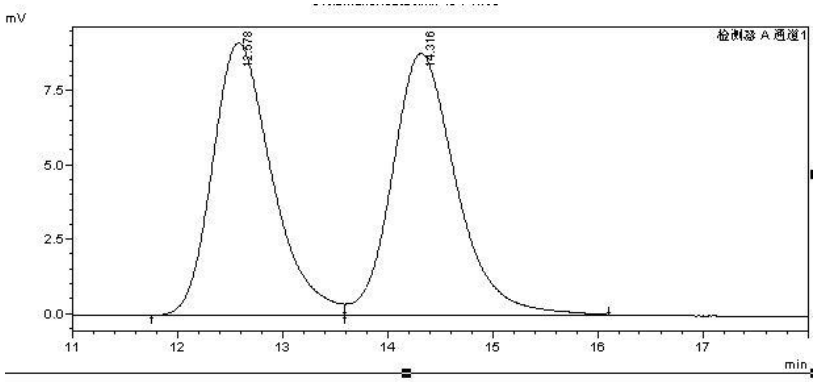
White solid, 70% yield, 75% *ee*, m.p. 83-85 °C. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$ = +44.93 (*c* 0.15, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.39 (s, 1H), 7.45 (d, *J* = 8.0 Hz, 3H), 7.38–7.32 (m, 3H), 7.21 (s, 1H), 4.25 (ab, *J* = 17.2 Hz, 1H), 3.85 (s, 3H), 3.56 (ab, *J* = 17.2 Hz, 1H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.7, 160.3, 158.1, 148.6, 145.7, 134.0, 133.0, 127.2, 125.9, 120.0, 117.0, 106.6, 55.7, 54.8, 34.7, 34.4, 31.2 ppm. IR (neat): $\tilde{\nu}$ = 3348, 2957, 2924, 2239, 1718, 1600, 1521, 1278, 1197, 913, 834, 749 cm^{-1}. HRMS: calc. for $C_{22}H_{23}N_2O_3$ [*M*+H]$^+$: 363.1703, found 363.1708. HPLC on Chiralpak OD-H (*n*-hexane/*iso*-propanol 90:10, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

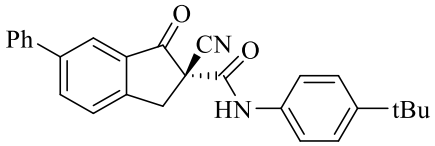
峰#	保留时间	面积	高度	面积 %	高度 %
1	12.223	73071	1931	12.459	12.810
2	13.791	513406	13141	87.541	87.190
总计		586478	15072	100.000	100.000



峰表

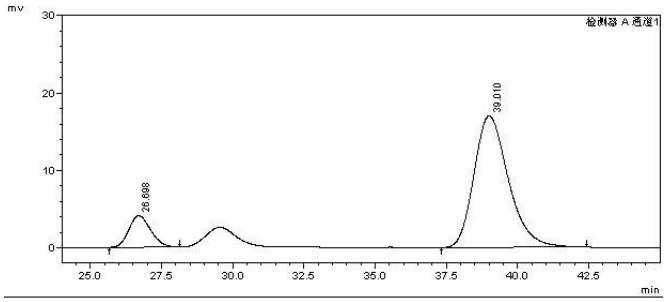
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	12.578	360332	9179	49.218	51.037
2	14.316	371788	8806	50.782	48.963
总计		732120	17984	100.000	100.000



_N_-(4-(tert-butyl)phenyl)-2-cyano-1-oxo-6-phenyl-2,3-dihydro-_1H_-indene-2-carboxamide (**3j**)

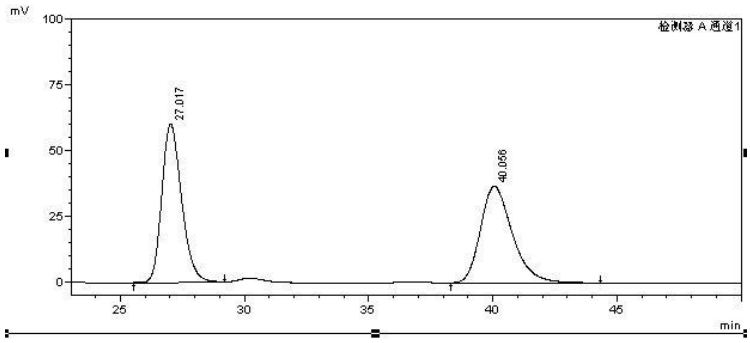
White solid, 80% yield, 74% *ee*, m.p. 182-185 ºC. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$ = +13.72 (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.44 (s, 1H), 8.03 (s, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.65 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.58 (d, *J* = 7.3 Hz, 2H), 7.54 – 7.45 (m, 4H), 7.44 – 7.35 (m, 3H), 4.39 (ab, *J* = 17.5 Hz, 1H), 3.67 (ab, *J* = 17.5 Hz, 1H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.8, 158.1, 151.4, 148.7, 142.5, 138.9, 136.6, 134.0, 132.5, 129.1, 128.3, 127.1, 126.9, 126.0, 124.0, 120.0, 117.0, 54.6, 35.2, 34.5, 31.3 ppm. IR (neat): $\tilde{\nu}$ = 3343, 2958, 2241, 1734, 1600, 1527, 1376, 1246, 1184, 1051, 835, 761cm^{-1}. HRMS: calc. for $C_{27}H_{25}N_2O_2$ $[M+H]^+$: 409.1911, found: 409.1907. HPLC on Chiralpak AD-H (*n*-hexane/*iso*-propanol 80:20, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

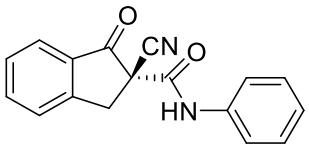
峰#	保留时间	面积	高度	面积 %	高度 %
1	26.698	218145	4089	13.173	19.333
2	39.010	1437801	17059	86.827	80.667
总计		1655945	21147	100.000	100.000



峰表

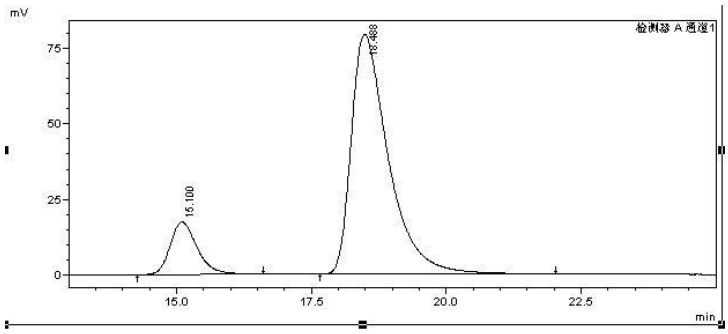
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	27.017	3328617	60089	50.346	62.109
2	40.056	3282884	36659	49.654	37.891
总计		6611502	96748	100.000	100.000



2-Cyano-*N*-Phenyl-1-oxo-2,3-dihydro-*1H*-indene-2-carboxamide (3m)[7]

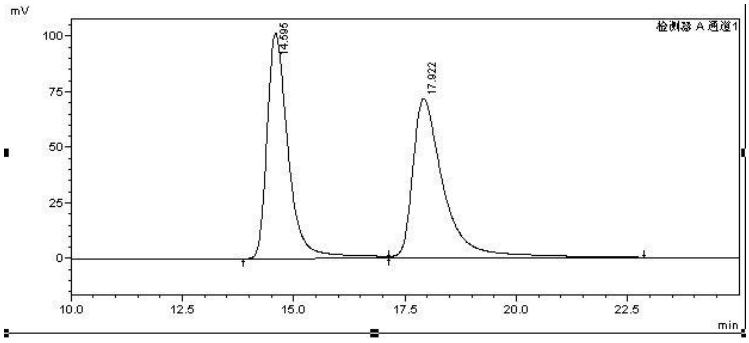
White solid, 74% yield, 73% *ee*, m.p. 136-139 ºC. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$ = +41.13 (*c* 0.3, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.49 (s, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.80-7.70 (m, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 2H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 2H), 7.18 (t, *J* = 7.43 Hz, 1H), 4.36 (ab, *J* = 17.5 Hz, 1H), 3.64 (ab, *J* = 17.7 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.8, 158.1, 152.6, 137.4, 136.6, 131.8, 129.1, 128.9, 126.6, 126.1, 125.5, 120.3, 116.9, 54.1, 35.3 ppm. IR (neat): $\tilde{\nu}$ = 3331, 2250, 1718, 1598, 1535, 1272, 905, 753, 690 cm^{-1}. HRMS: calc. for $C_{17}H_{12}N_2O_2$ [*M*+H]$^+$: 277.0972, found: 277.0970. HPLC on Chiralpak OD-H (*n*-hexane/*iso*-propanol 90:10, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

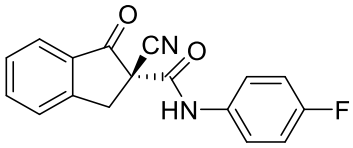
峰#	保留时间	面积	高度	面积 %	高度 %
1	15.100	603515	17389	13.639	17.951
2	18.488	3821272	79476	86.361	82.049
总计		4424787	96864	100.000	100.000



峰表

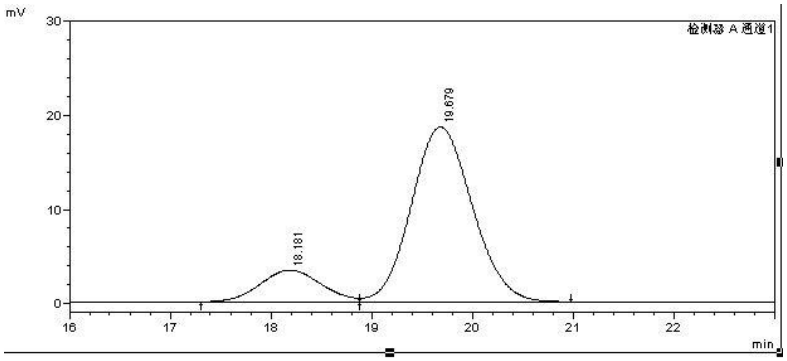
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	14.595	3371961	101341	49.255	58.573
2	17.922	3473916	71676	50.745	41.427
总计		6845877	173017	100.000	100.000



2-Cyano-*N*-(4-fluorophenyl)-1-oxo-2,3-dihydro-*1H*-indene-2-carboxamide (3n)[7]

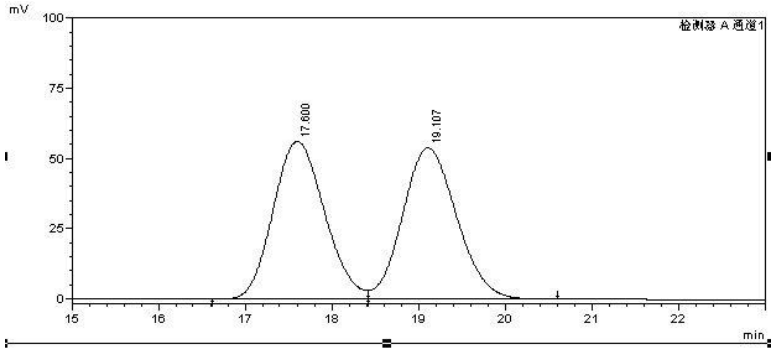
White solid, 83% yield, 70% *ee*, m.p. 138-141 ºC. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$ = +20.67 (*c* 0.3, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.47 (s, 1H), 7.85 (d, *J* = 7.7 Hz, 1H), 7.76 (t, *J* = 7.12, 1H), 7.58 (d, *J* = 7.7 Hz, 1H), 7.52-7.47(m, 3H), 7.05 (t, *J* = 8.6 Hz, 2H), 4,35 (ab, *J* = 17.6 Hz, 1H), 3.65 (ab, *J* = 17.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.6, 154.6 (d, $^1J_{C\text{-}F}$ = 290.2 Hz), 147.4, 132.3, 127.4 (d, $^4J_{C\text{-}F}$ = 2.8 Hz), 126.6, 123.7, 121.5, 121.0, 117.1 (d, $^3J_{C\text{-}F}$ = 8.0 Hz),111.7, 110.7 (d, $^2J_{C\text{-}F}$ = 22.6 Hz), 104.5, 48.8, 30.1 ppm. IR (neat): $\tilde{\nu}$ = 3341, 2923, 2239, 1723, 1606, 1508, 1272, 1213, 906, 832 cm^{-1}. HRMS: calc. for $C_{17}H_{12}FN_2O_2$ [*M*+H]$^+$: 295.0877, found: 295.0877. HPLC on Chiralpak AD-H (*n*-hexane/*iso*-propanol 80:20, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

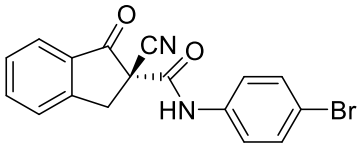
峰#	保留时间	面积	高度	面积 %	高度 %
1	18.181	141803	3368	15.313	15.331
2	19.679	784248	18599	84.687	84.669
总计		926050	21966	100.000	100.000



峰表

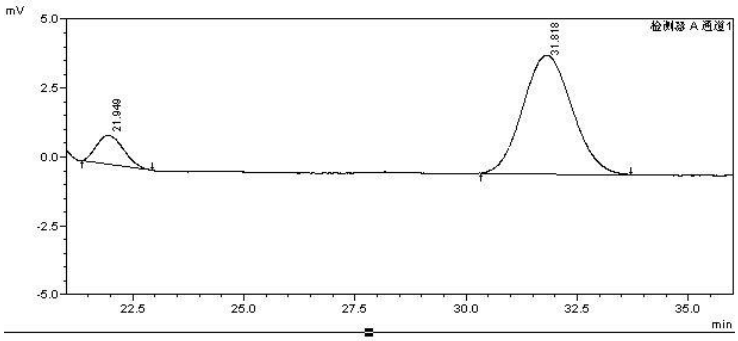
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	17.600	2320376	56244	49.825	51.048
2	19.107	2336710	53934	50.175	48.952
总计		4657086	110178	100.000	100.000



_N_-(4-Bromophenyl)-2-cyano-1-oxo-2,3-dihydro-_1H_-indene-2-carboxamide (3o)[7]

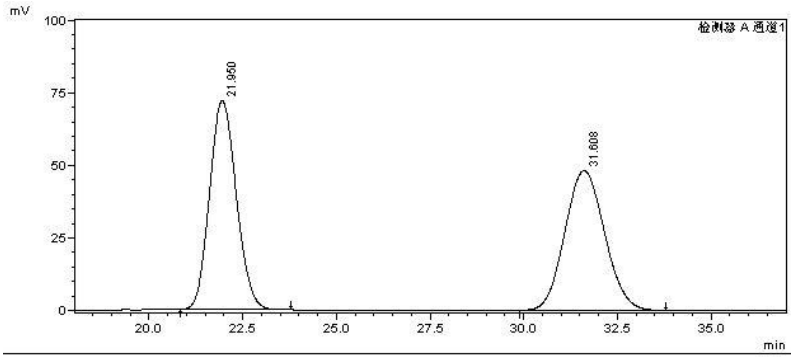
White solid, 60% yield, 77% *ee*, m.p. 135-140 ºC. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$ = +15.4 (*c* 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.50 (s, 1H), 7.85 (d, *J* = 7.1 Hz, 1H), 7.76 (t, *J* = 7.2 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.51-7.43 (m, 5H), 4.35 (ab, *J* = 17.6 Hz, 1H), 3.65 (ab, *J* = 17.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.7, 158.3, 152.6, 137.6, 135.7,132.1, 131.7, 129.0, 126.7, 126.2, 121.9, 118.4, 116.7, 54.1, 35.2 ppm. IR (neat): $\tilde{\nu}$ = 3336, 2926, 2239, 1726, 1595, 1527, 1488, 1395, 1727, 1073, 906, 824 cm^{-1}. HRMS: calc. for $C_{17}H_{11}BrN_2NaO_2$ $[M+Na]^+$: 376.9896, found: 376.9894. HPLC on Chiralpak AD-H (*n*-hexane/*iso*-propanol 80:20, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

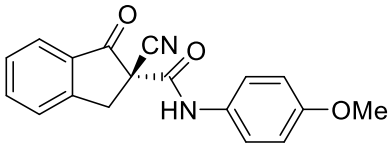
峰#	保留时间	面积	高度	面积 %	高度 %
1	21.949	45078	1048	11.900	19.509
2	31.818	333724	4322	88.100	80.491
总计		378802	5370	100.000	100.000



峰表

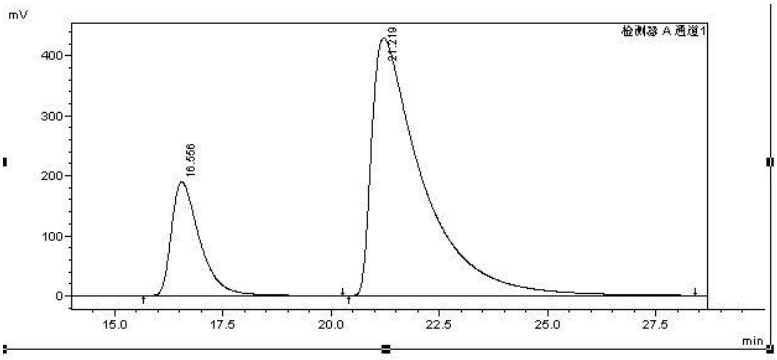
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	21.950	3569884	71773	50.183	59.914
2	31.608	3543853	48020	49.817	40.086
总计		7113736	119794	100.000	100.000



2-Cyano-*N*-(4-methoxyphenyl)-1-oxo-2,3-dihydro-*1H*-indene-2-carboxamide (3p)[7]

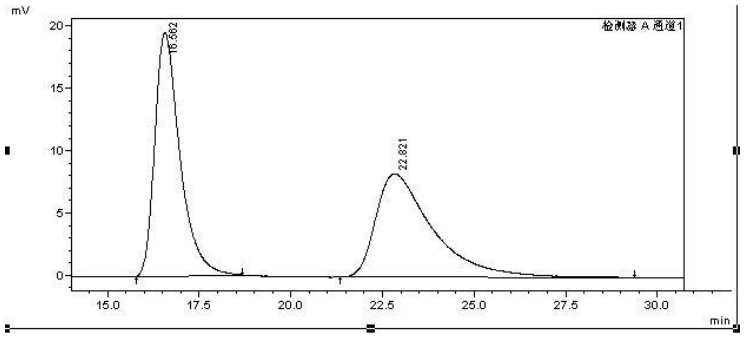
White solid, 84% yield, 61% *ee*, m.p. 109-113 ºC. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$ = +52.2 (*c* 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40 (s, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.74 (t, *J* = 7.1 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.50-7.42 (m, 3H), 6.87 (d, *J* = 9.0 Hz, 2H), 4.35 (ab, *J* = 17.5 Hz, 1H), 3.79 (s, 3H), 3.63 (ab, *J* = 17.53 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ =193.9, 157.2, 152.7, 141.8, 137.4, 131.9, 129.7, 128.8, 126.6, 126.1, 122.2, 117.0, 114.2, 55.4, 54.0, 35.4 ppm. IR (neat): $\tilde{\nu}$ = 3350, 2923, 2237, 1711, 1531, 1230, 1176, 994, 826, 739 cm^{-1}. HRMS: calc.for $C_{18}H_{15}N_2O_3$ $[M+H]^+$: 307.1077, found: 307.1075. HPLC on Chiralpak OD-H (*n*-hexane/*iso*-propanol 80:20, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

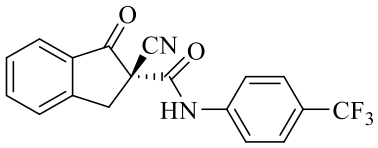
峰#	保留时间	面积	高度	面积 %	高度 %
1	16.556	8653876	189263	19.807	30.614
2	21.219	35038134	428954	80.193	69.386
总计		43692010	618217	100.000	100.000



峰表

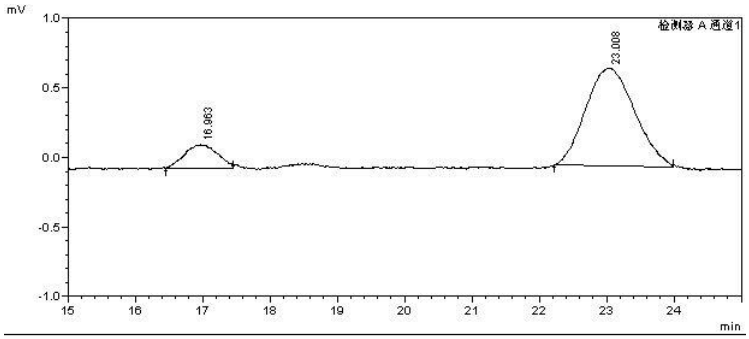
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	16.562	931249	19525	50.974	70.185
2	22.821	895663	8294	49.026	29.815
总计		1826913	27819	100.000	100.000



2-cyano-1-oxo-*N*-(4-(trifluoromethyl)phenyl)-2,3-dihydro-*1H*-indene-2-carboxamide (**3q**)

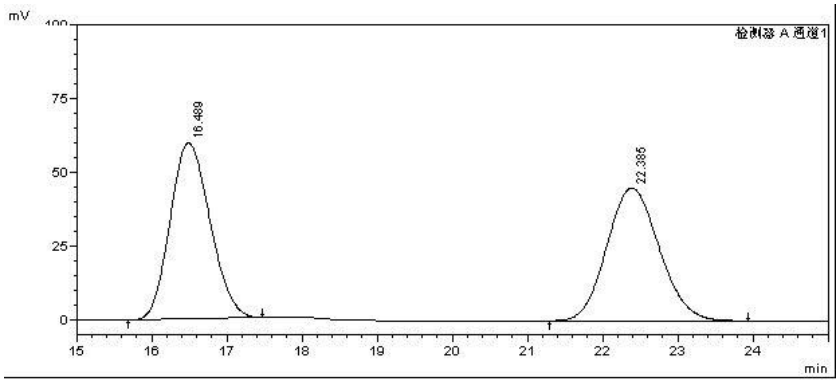
White solid, 73% yield, 73% *ee*, m.p. 107-109 ºC. Developing solvent PE/EA (10/1, V/V), $[\alpha]^{20}_{D}$ = +69.6 (*c* 0.25, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.65 (s, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.78 (t, *J* = 7.5 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 3H), 7.61 (t, *J* = 8.0 Hz 4H), 7.51 (t, *J* = 7.5 Hz, 1H), 4.37 (ab, *J* = 17.6 Hz, 1H), 3.67 (ab, *J* = 17.6 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.6, 158.5, 152.6, 139.6, 137.7, 131.6, 129.0, 126.7, 126.5, 126.4, 126.4, 126.4, 126.3, 120.0, 116.6, 54.1, 35.1 ppm. IR (neat): $\tilde{\nu}$ = 3336, 2926, 2241, 1734, 1605, 1533, 1325, 1272, 1166, 1068, 906, 841, 745, 692 cm^{-1}. HRMS: calc. for $C_{18}H_{11}F_3N_2O_2$ $[M+H]^+$: 345.0845, found: 345.0841. HPLC on Chiralpak AD-H (*n*-hexane/*iso*-propanol 80:20, 1.0 mL min^{-1}, 254 nm).



峰表

检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	16.963	5762	168	13.890	19.263
2	23.008	35720	704	86.110	80.737
总计		41482	872	100.000	100.000



峰表

检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	16.489	2210652	59671	50.367	57.028
2	22.385	2178465	44964	49.633	42.972
总计		4389118	104634	100.000	100.000

5. X-ray Structure

Product **3c** (CCDC 1563576)

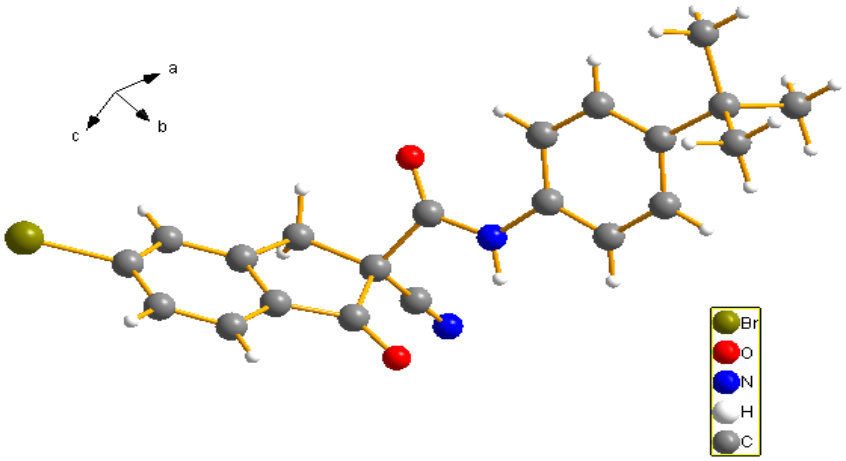


Table S2. Crystal data and structure refinement for **3c**.

Empirical Formula	C21H19BrN2O2
Formula weight	410.28 *g/mol*
Crystal system	Monoclinic
Space-group	C 2
Unit cell dimensions	*a*=20.509(7) *Å b*=7.053(2) *Å c*=15.828(6) *Å*
Cell ratio	α=90.00° , β=120.784(15)°, γ=90.00°
Cell volume	1966.9(12) *Å3*
Z	*4*
Density	2.491*g/cm3*
Temperature	296(2) K
Wavelength	0.71073Å
F_000	836
Absorption coefficient	12.280
Data completeness	1.81/0.99
Theta range for data collection	1.50 to 22.970
Refinement method	Full-matrix least-squares on F2
Data/ restraints/ parameters	2708/1/228
Goodness of fit ref	0.897
R factor all	0.1175
R factor gt	0.0704
wR factor ref	0.2111
wR factor gt	0.1811
Absolute structure parameter	0.91(3)

Table S3. Atomic coordinates and equivalent isotropic displacement parameters (Å2) for **3c**.
U (eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U (eq)
C13 C	0.8094(5)	0.928(3)	0.0173(7)	0.070(3)
C18 C	1.0821(6)	0.908(2)	0.1463(7)	0.068(3)
H18 H	1.0956	0.7814	0.1509	0.081
C15 C	0.9112(7)	1.1807(16)	0.0942(8)	0.062(3)
H15A H	0.8799	1.2337	0.0289	0.074
H15B H	0.9091	1.2638	0.1416	0.074
C4 C	0.8813(6)	0.435(3)	0.5546(7)	0.079(3)
C16 C	1.0096(5)	0.9576(19)	0.1234(7)	0.063(3)
C17 C	0.9904(6)	1.1555(14)	0.1176(7)	0.050(3)
N2 N	0.8716(6)	0.7698(13)	0.2154(7)	0.064(3)
H2 H	0.8613	0.6898	0.1692	0.076
C11 C	0.8838(5)	0.947(2)	0.1988(6)	0.060(3)
C14 C	0.9461(6)	0.8437(17)	0.1028(7)	0.064(3)
O1 O	0.8937(8)	1.0804(14)	0.2500(7)	0.114(5)
C7 C	0.8597(6)	0.430(2)	0.3805(7)	0.072(3)
H7 H	0.8486	0.3018	0.3790	0.087
O2 O	0.9381(6)	0.6750(13)	0.0917(7)	0.089(3)
C12 C	0.8841(5)	0.9770(13)	0.0998(7)	0.055(3)
C21 C	1.1146(5)	1.2393(16)	0.1558(7)	0.060(3)
C5 C	0.8792(6)	0.5332(17)	0.4650(7)	0.065(3)
N1 N	0.7512(6)	0.899(2)	0.0468(7)	0.096(4)
C20 C	1.1348(6)	1.0491(17)	0.1626(8)	0.067(3)
H20 H	1.1836	1.0160	0.1781	0.080
C10 C	0.8735(6)	0.6959(15)	0.3003(7)	0.060(3)
C9 C	0.8563(7)	0.5099(15)	0.2987(8)	0.068(3)
H9 H	0.8422	0.4369	0.2430	0.082
C6 C	0.8937(7)	0.7217(16)	0.4620(7)	0.077(4)
H6 H	0.9053	0.7967	0.5162	0.092
C8 C	0.8920(7)	0.8053(17)	0.3821(8)	0.086(4)
H8 H	0.9030	0.9335	0.3832	0.103
C19 C	1.0423(6)	1.2931(14)	0.1317(7)	0.056(3)
H19 H	1.0290	1.4206	0.1251	0.067
Br1 Br	1.18664(6)	1.4261(3)	0.17477(10)	0.0940(6)
C2 C	0.9312(13)	0.276(3)	0.5833(15)	0.212(13)
H2A H	0.9546	0.2569	0.6529	0.319
H2B H	0.9698	0.2998	0.5673	0.319
H2C H	0.9030	0.1651	0.5491	0.319
C1 C	0.8035(8)	0.382(3)	0.5287(10)	0.125(6)
H1A H	0.7834	0.2906	0.4763	0.188
H1B H	0.7719	0.4927	0.5079	0.188
H1C H	0.8047	0.3279	0.5851	0.188
C3 C	0.9078(10)	0.584(3)	0.6389(12)	0.133(6)
H3A H	0.9184	0.5215	0.6984	0.200
H3B H	0.8685	0.6763	0.6210	0.200
H3C H	0.9529	0.6462	0.6489	0.200

Table S4 Bond lengths [Å] and angles [°] for **3c**.

C13 N1	1.121(11)
C13 C12	1.458(14)
C18 C16	1.382(14)
C18 C20	1.390(17)
C15 C17	1.481(15)
C15 C12	1.558(14)
C4 C2	1.42(2)
C4 C1	1.479(17)
C4 C5	1.559(15)
C4 C3	1.56(2)
C16 C14	1.418(15)
C16 C17	1.440(16)
C17 C19	1.371(14)
N2 C11	1.324(16)
N2 C10	1.423(13)
C11 O1	1.192(15)
C11 C12	1.585(13)
C14 O2	1.202(13)
C14 C12	1.563(14)
C7 C5	1.389(16)
C7 C9	1.380(15)
C21 C19	1.383(13)
C21 C20	1.392(15)
C21 Br1	1.885(10)
C5 C6	1.368(16)
C10 C9	1.356(15)
C10 C8	1.383(14)
C6 C8	1.380(15)
N1 C13 C12	177.0(19)
C16 C18 C20	120.0(13)
C17 C15 C12	104.6(8)
C2 C4 C1	112.8(18)
C2 C4 C5	108.8(12)
C1 C4 C5	109.7(10)
C2 C4 C3	112.2(13)
C1 C4 C3	105.1(12)
C5 C4 C3	108.2(14)
C18 C16 C14	131.0(13)
C18 C16 C17	118.8(12)
C14 C16 C17	110.2(9)
C19 C17 C16	120.8(9)
C19 C17 C15	128.1(9)

C16 C17 C15	111.1(9)
C11 N2 C10	128.0(9)
O1 C11 N2	126.5(9)
O1 C11 C12	118.6(12)
N2 C11 C12	114.9(10)
O2 C14 C16	129.5(12)
O2 C14 C12	122.9(11)
C16 C14 C12	107.7(10)
C5 C7 C9	122.7(14)
C13 C12 C15	114.1(10)
C13 C12 C11	108.6(8)
C15 C12 C11	111.3(9)
C13 C12 C14	110.6(9)
C15 C12 C14	104.4(8)
C11 C12 C14	107.7(8)
C19 C21 C20	121.3(10)
C19 C21 Br1	119.7(9)
C20 C21 Br1	118.9(8)
C6 C5 C7	115.9(10)
C6 C5 C4	124.0(11)
C7 C5 C4	120.1(12)
C21 C20 C18	120.1(10)
C9 C10 C8	120.0(10)
C9 C10 N2	117.2(9)
C8 C10 N2	122.8(10)
C10 C9 C7	119.4(11)
C5 C6 C8	122.9(10)
C10 C8 C6	119.1(11)
C17 C19 C21	119.0(9)

Symmetry transformations used to generate equivalent atoms:

Table S5. Anisotropic displacement parameters ($Å^2$ x10^3) for **3c**.
The anisotropic displacement factor exponent takes the form: -2π2[h2 a*2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C13	0.043(5)	0.101(8)	0.052(6)	0.012(8)	0.014(5)	0.023(10)
C18	0.072(6)	0.054(6)	0.088(7)	-0.005(7)	0.048(6)	0.003(8)
C15	0.070(8)	0.056(7)	0.058(6)	0.010(5)	0.032(6)	0.008(6)
C4	0.073(6)	0.099(8)	0.064(6)	0.016(9)	0.034(5)	-0.009(11)
C16	0.056(6)	0.083(10)	0.056(5)	0.002(6)	0.035(5)	0.013(7)
C17	0.058(7)	0.037(6)	0.054(6)	0.005(4)	0.029(5)	0.008(6)
N2	0.097(7)	0.037(5)	0.067(6)	0.001(4)	0.049(6)	-0.007(5)
C11	0.066(6)	0.068(8)	0.044(5)	-0.002(7)	0.028(4)	0.002(8)
C14	0.070(8)	0.062(8)	0.058(7)	0.001(5)	0.032(6)	0.002(6)
O1	0.215(14)	0.065(6)	0.085(7)	-0.014(5)	0.093(8)	-0.039(7)
C7	0.087(7)	0.061(6)	0.072(7)	0.002(8)	0.043(6)	0.003(9)
O2	0.114(8)	0.048(6)	0.118(7)	-0.005(5)	0.070(7)	0.007(5)
C12	0.047(5)	0.060(8)	0.065(6)	0.000(5)	0.034(5)	0.008(5)
C21	0.042(6)	0.067(7)	0.063(6)	-0.017(5)	0.022(5)	-0.008(5)
C5	0.057(6)	0.077(8)	0.058(7)	0.016(6)	0.028(5)	0.015(6)
N1	0.081(7)	0.126(11)	0.076(6)	0.020(8)	0.036(6)	-0.016(9)
C20	0.049(6)	0.079(8)	0.078(8)	0.003(6)	0.037(6)	0.007(6)
C10	0.066(7)	0.060(7)	0.045(6)	0.004(5)	0.023(5)	0.009(6)
C9	0.093(9)	0.057(7)	0.054(7)	-0.003(5)	0.037(6)	0.005(6)
C6	0.121(11)	0.061(7)	0.051(7)	-0.002(6)	0.046(7)	-0.006(7)
C8	0.128(12)	0.068(8)	0.069(8)	-0.009(6)	0.055(8)	-0.011(8)
C19	0.063(7)	0.046(6)	0.062(6)	-0.005(5)	0.034(5)	0.009(6)
Br1	0.0679(7)	0.0924(9)	0.1343(11)	-0.0254(10)	0.0609(7)	-0.0133(10)
C2	0.26(3)	0.24(3)	0.19(2)	0.17(2)	0.15(2)	0.16(2)

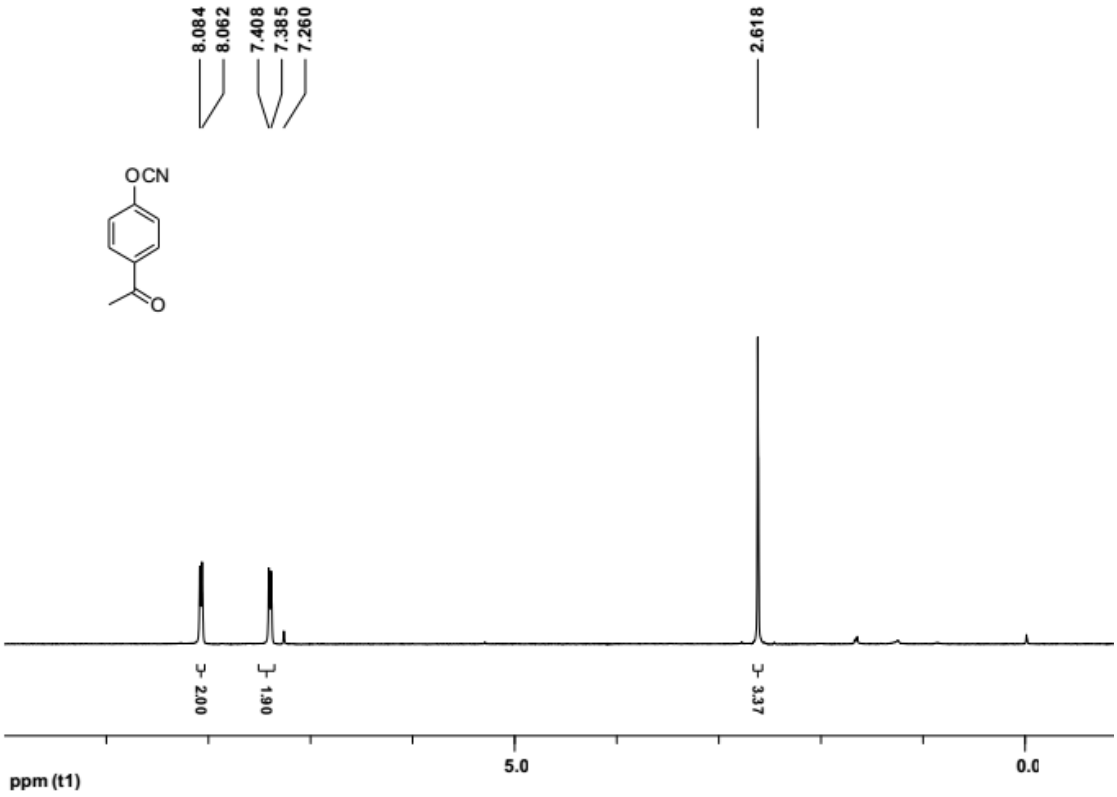
Table S6. Hydrogen bonds for **3c** [Å and º]

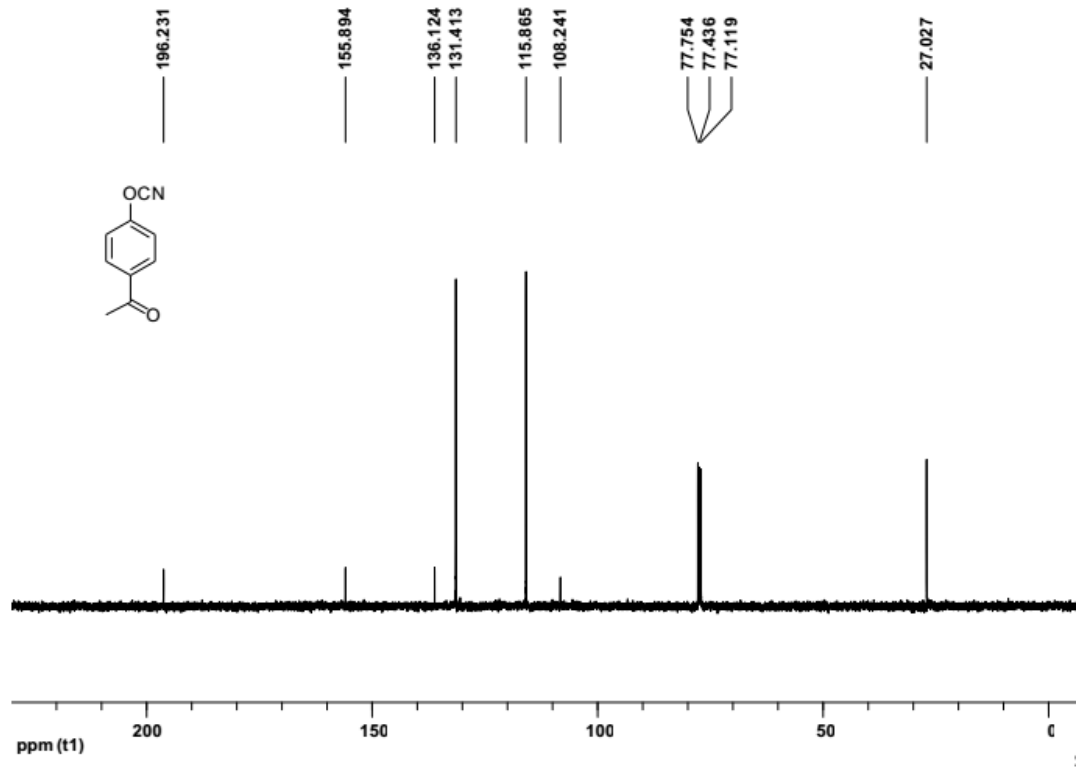
D-H…A	d (D-H)	d (H….A)	d (D…A)	<(DHA)

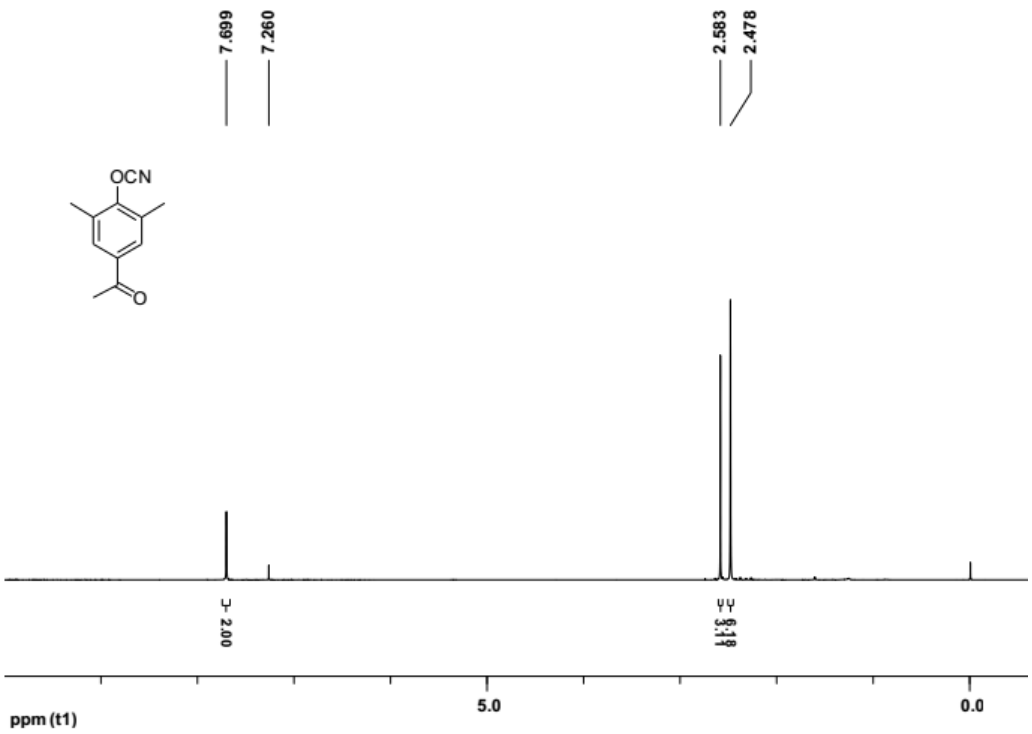
6, References

[1] Amberg, W.; Bennani, Y.; Chadha, R. K.; Crispino, G. A.; Davis, W. D.; Hartung, J.; Jeong, K.; Ogino, Y.; Shibata, T.; Sharpless, K. B. *J. Org. Chem.* **1993**, *58*, 844-849.
[2] Smith, A. B.; Schow, S. R.; Bloom, J. D.; Thompson, A. S.; Winzenberg, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 4015-4018.
[3] Matoba, K.; Kawai, H.; Furukawa, T.; Kusuda, A.; Tokunaga, E.; Nakamura, S.; Shiro, M.; Shibata, N. *Angew. Chem.* **2010**, *122*, 5898-5902; *Angew, Chem. Int. Ed*. **2010**, *49*, 5762-5766.
[4] R. E. Murray, G. Zweifel. *Synthesis*, **1980**, 150-151.
[5] Kurzer F. 221. Cyanamides. Part I. The Synthesis of Substituted Aryl sulphonyl cyanamides. *J. Chem. Soc.* (Resumed), **1949**, (0): 1034-1038.
[6]. Wang, X. Q.; Yang, T.; Shen, Q. L. *Angew. Chem. Int. Ed*. **2013**, *52*, 12860-12864.
[7] Wang, Y.; Qiu, J.; Gao, Y.; Lu, F.; Karmaker, P. G.; Chen, F.-X. *Org. Biochem. Lett.* **2015**, *13*, 365-368.

7, Copies of ^{1}H NMR and ^{13}C NMR Spectra



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2.583
2.478
OCN
O
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3.19
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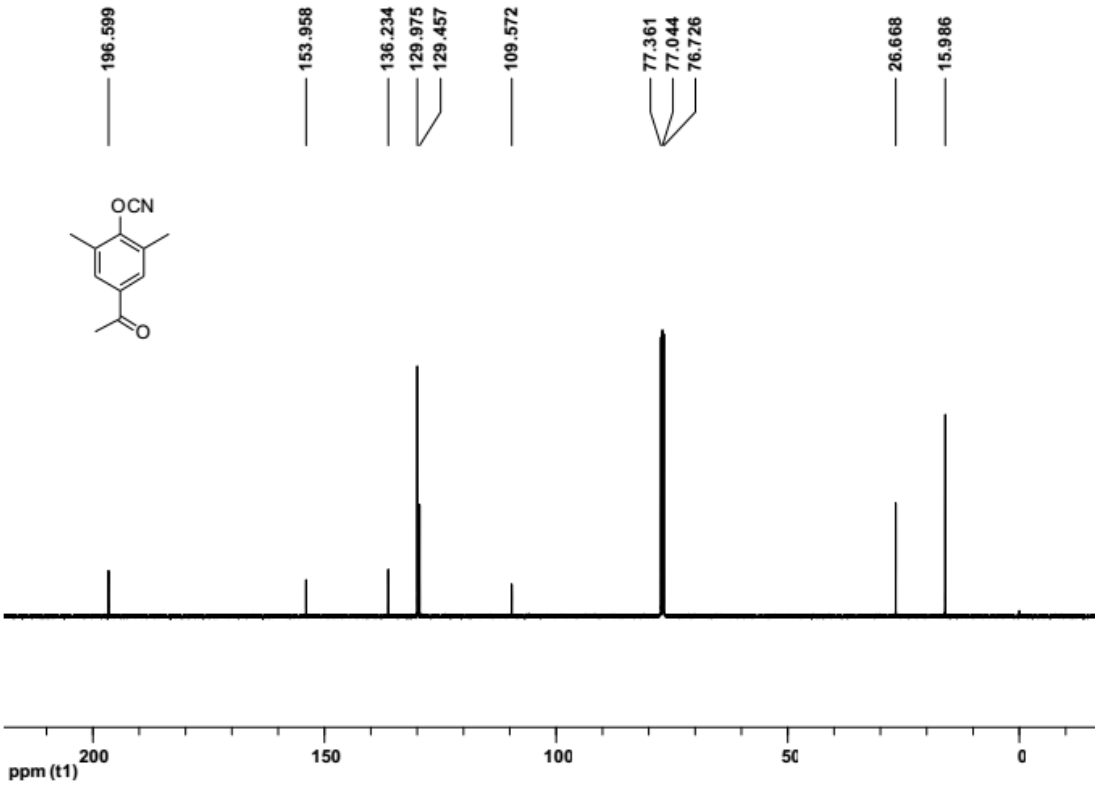
0.0
ppm (t1)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153.958
136.234
129.975
129.457
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77.361
77.044
76.726
26.668
15.986
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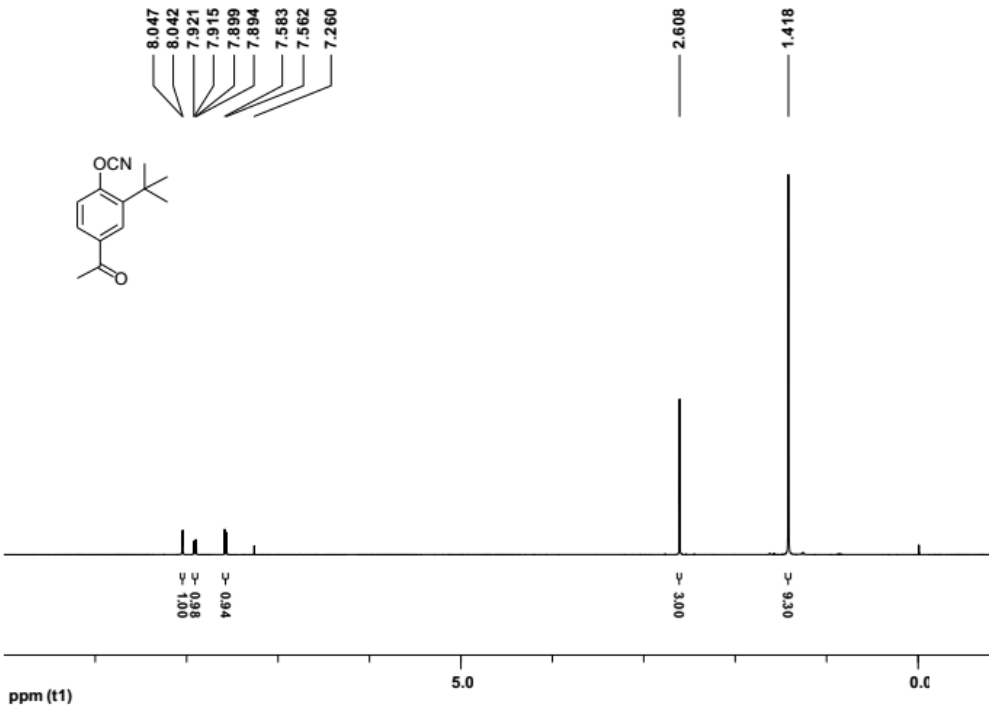
100
50
0
ppm (t1)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7.921
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7.583
7.562
7.260
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OCN
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1.00
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3.00
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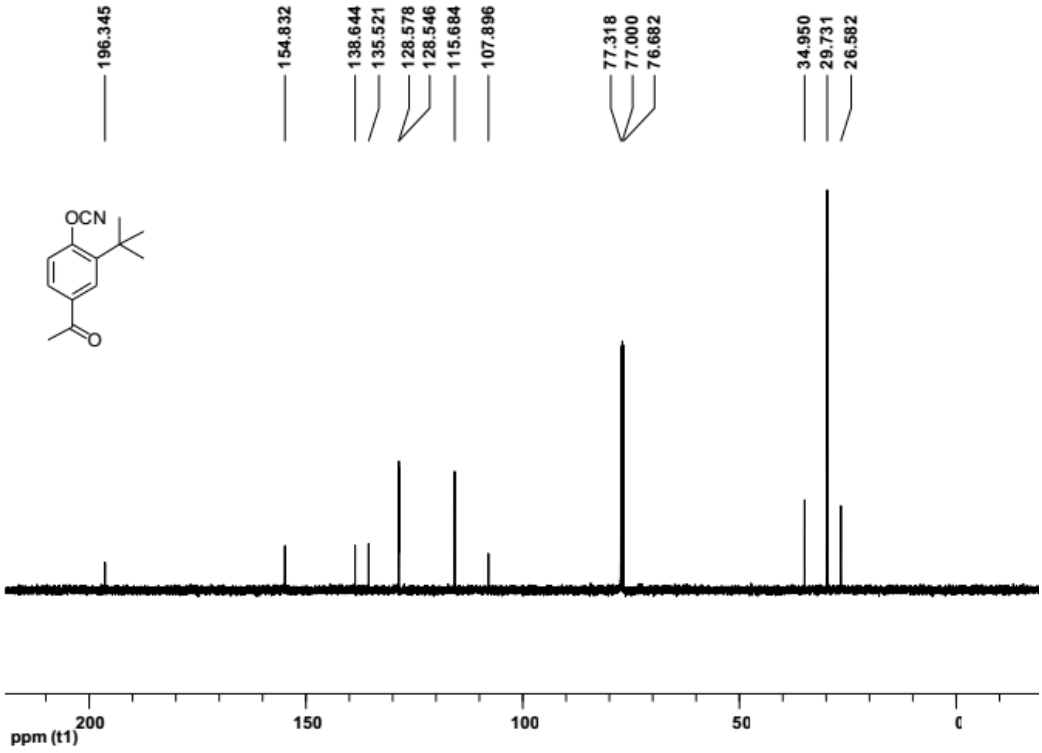
ppm (t1)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138.644
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128.546
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77.000
76.682
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OCN
O
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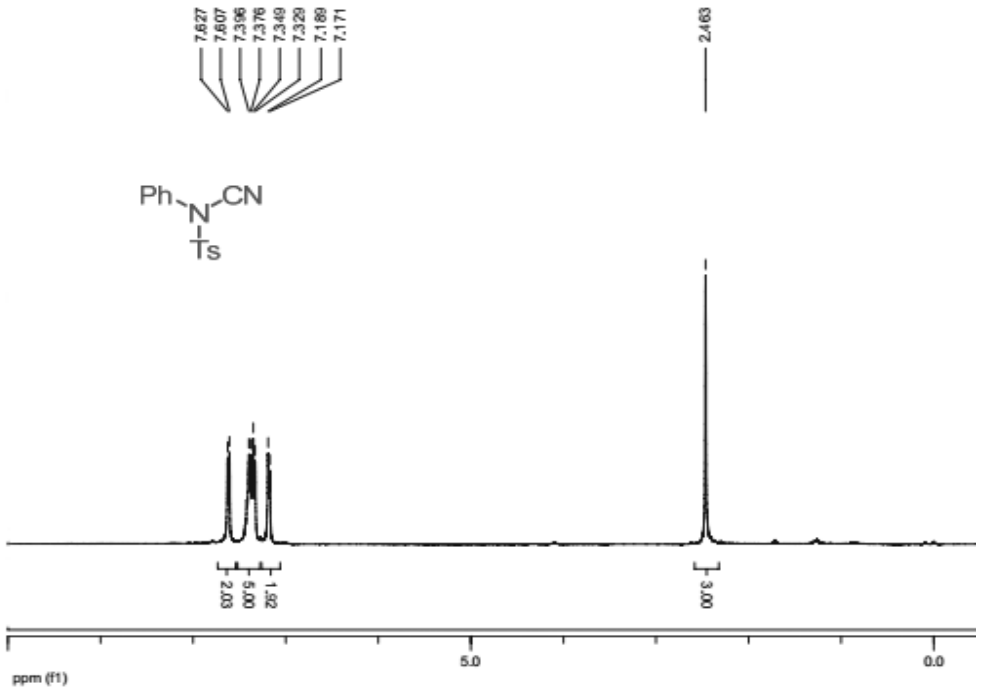
150
100
50
ppm (t1)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7.376
7.349
7.329
7.189
7.171
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Ph
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CN
Ts
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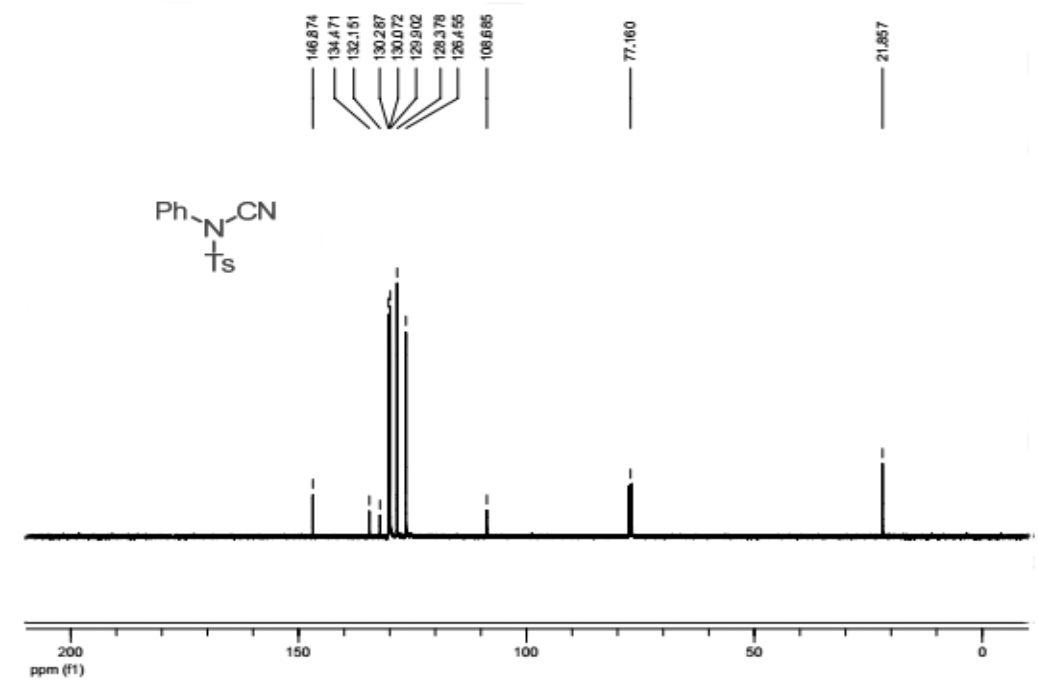
1.52
3.00
5.0
0.0
ppm (f1)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Ph
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CN
Ts
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150
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50
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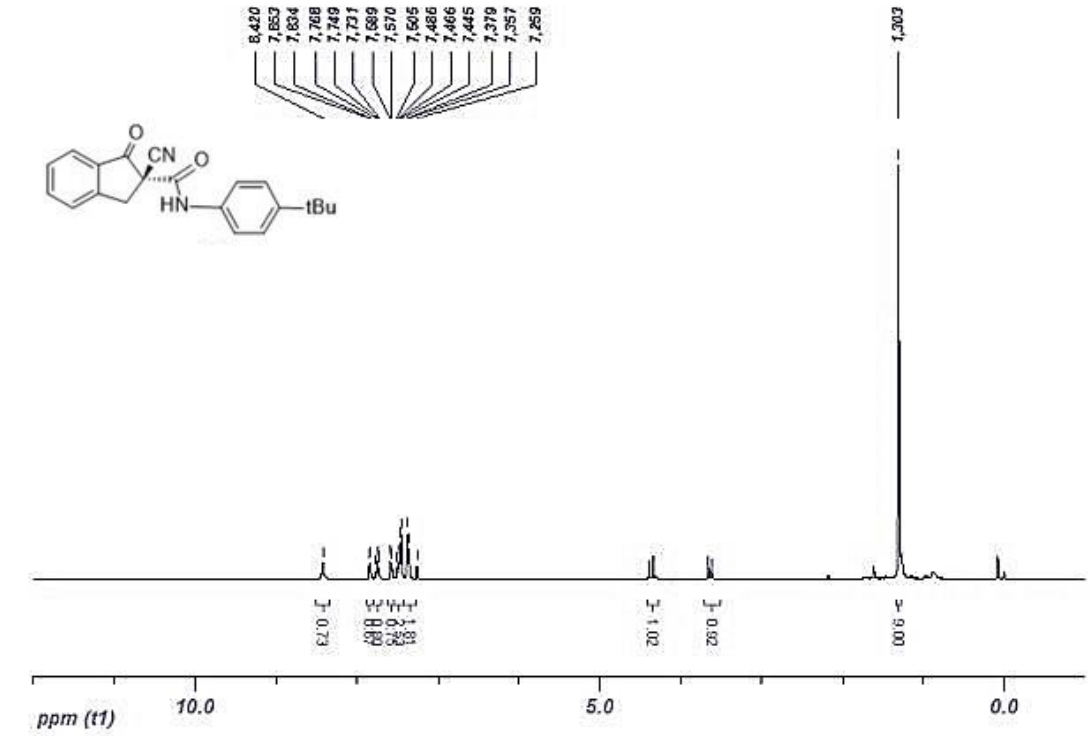
ppm (f1)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7.379
7.357
7.259
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O
HN
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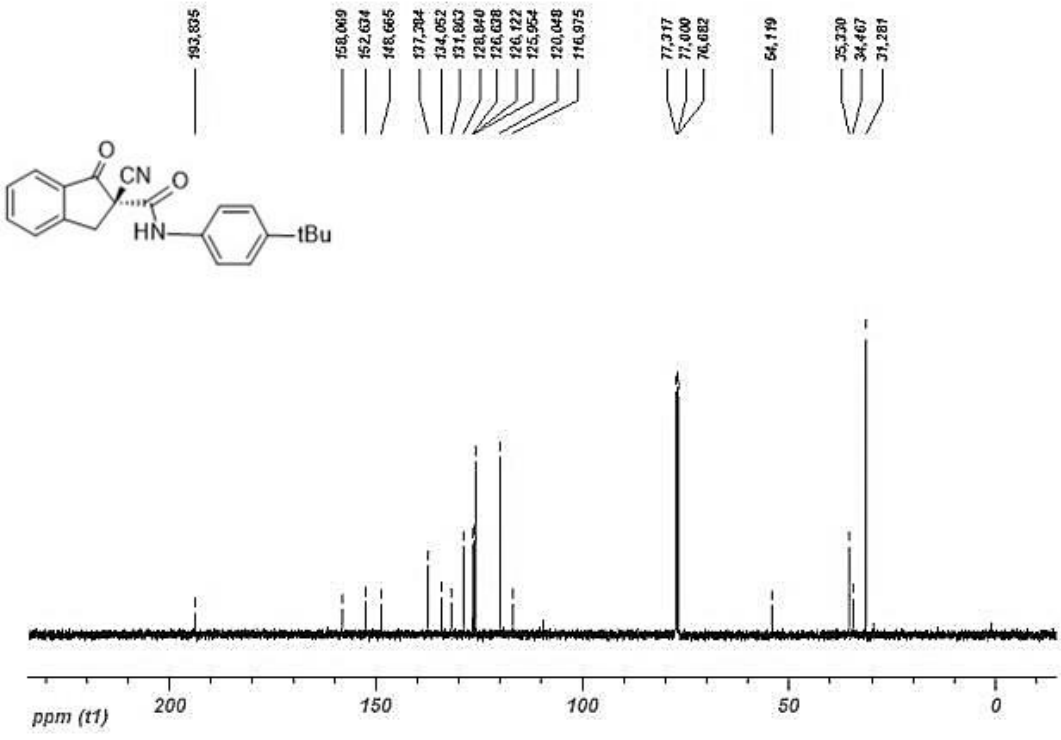
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77.317
77.000
76.682
54.119
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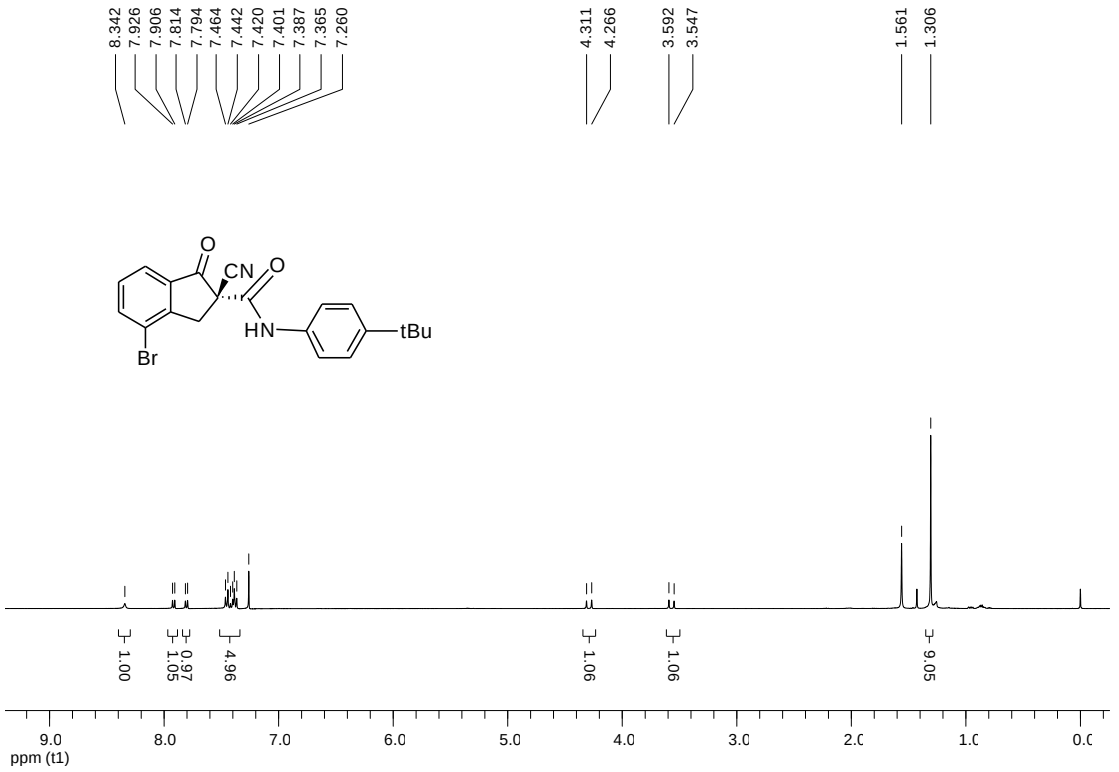
34.467
31.281
O
CN
O
HN
tBu
ppm (t1)
200
150
100
50
0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7.365
7.260
4.311
4.266
3.592
3.547
1.561
1.306
O
CN
O
HN
tBu
Br
1.00
0.97
1.05
4.96
1.06
1.06
9.05
9.0
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7.0
6.0
5.0
4.0
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2.0
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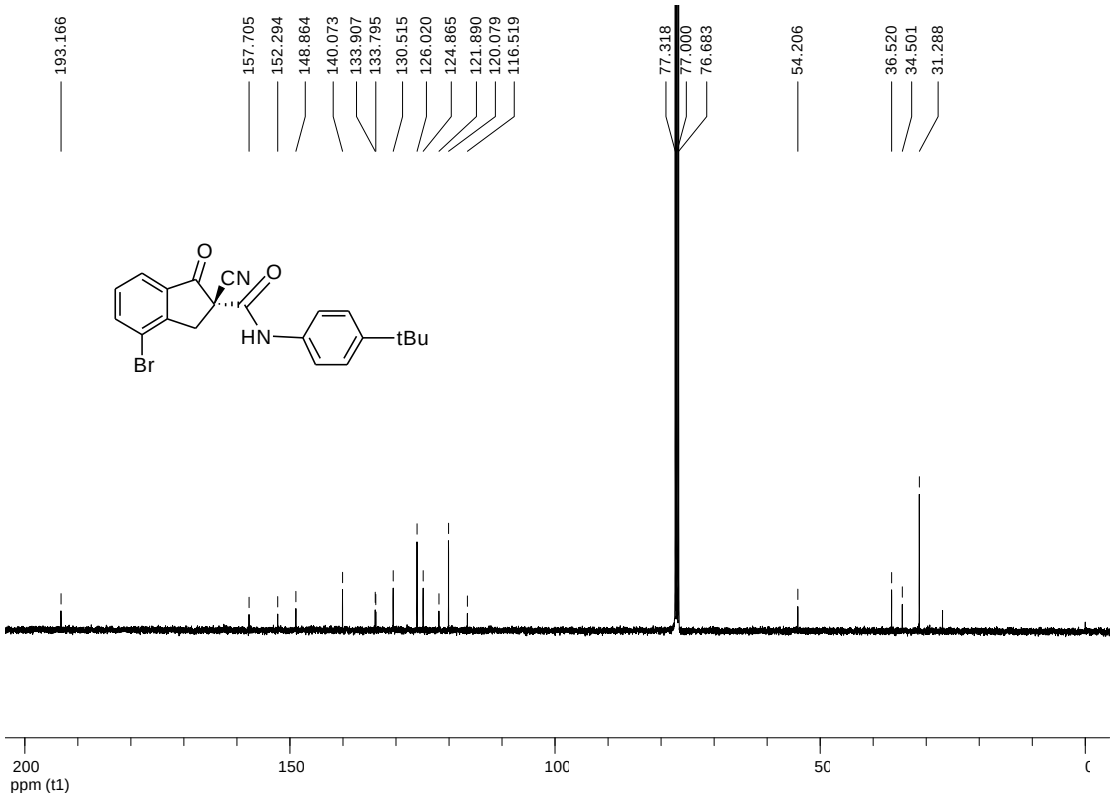
ppm (t1)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124.865
121.890
120.079
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77.000
76.683
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Br
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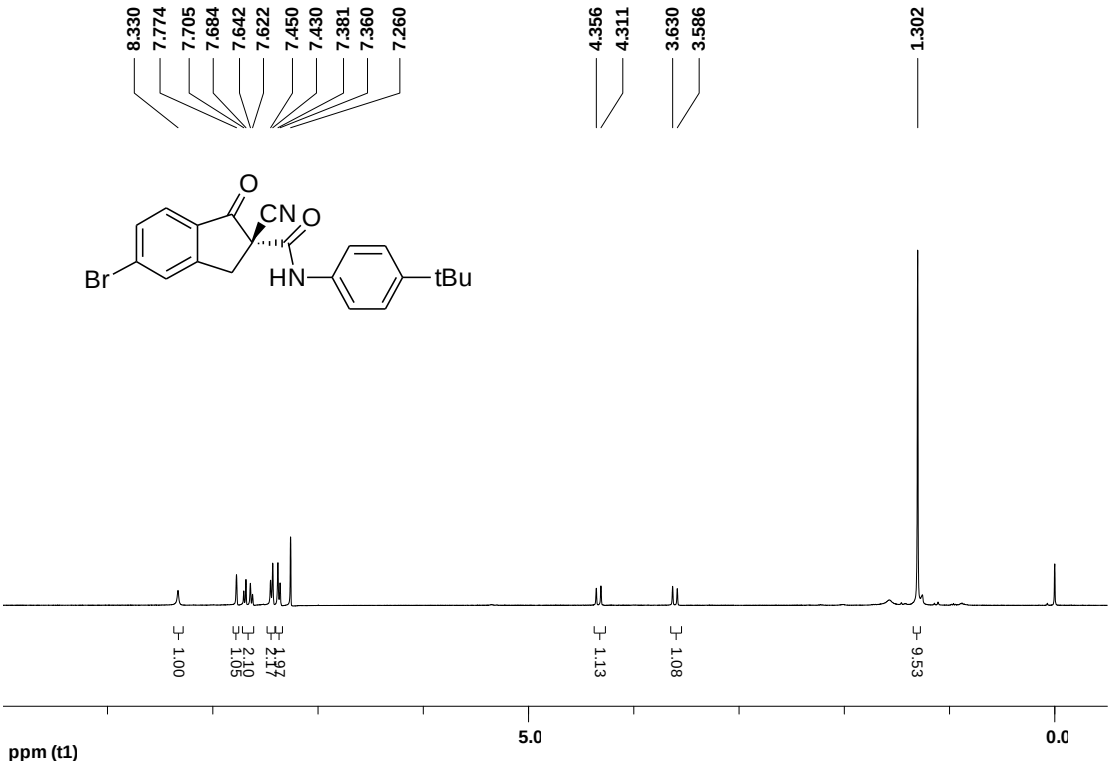
ppm (t1)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4.311
3.630
3.586
1.302
O
CN
O
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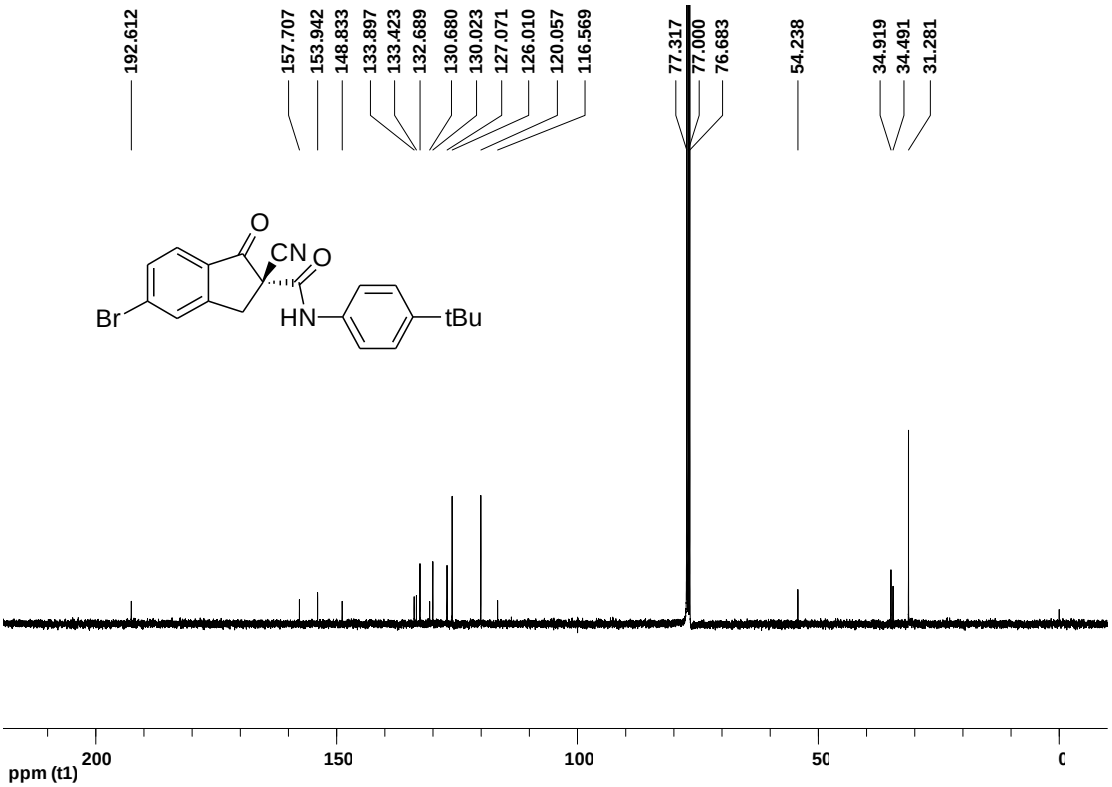
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77.000
76.683
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CN
O
Br
HN
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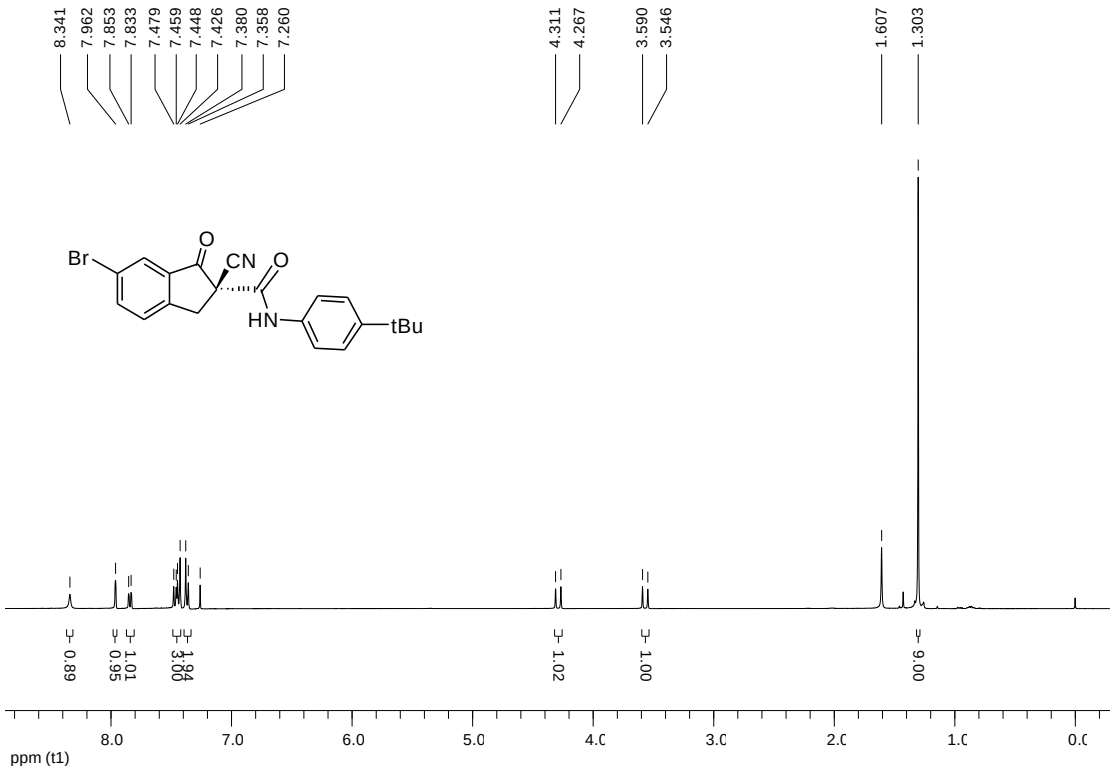
200
150
100
50
0
ppm (t1)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3.546
1.607
1.303
Br
O
CN
O
HN
tBu
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0.95
1.01
3.00
1.04
1.02
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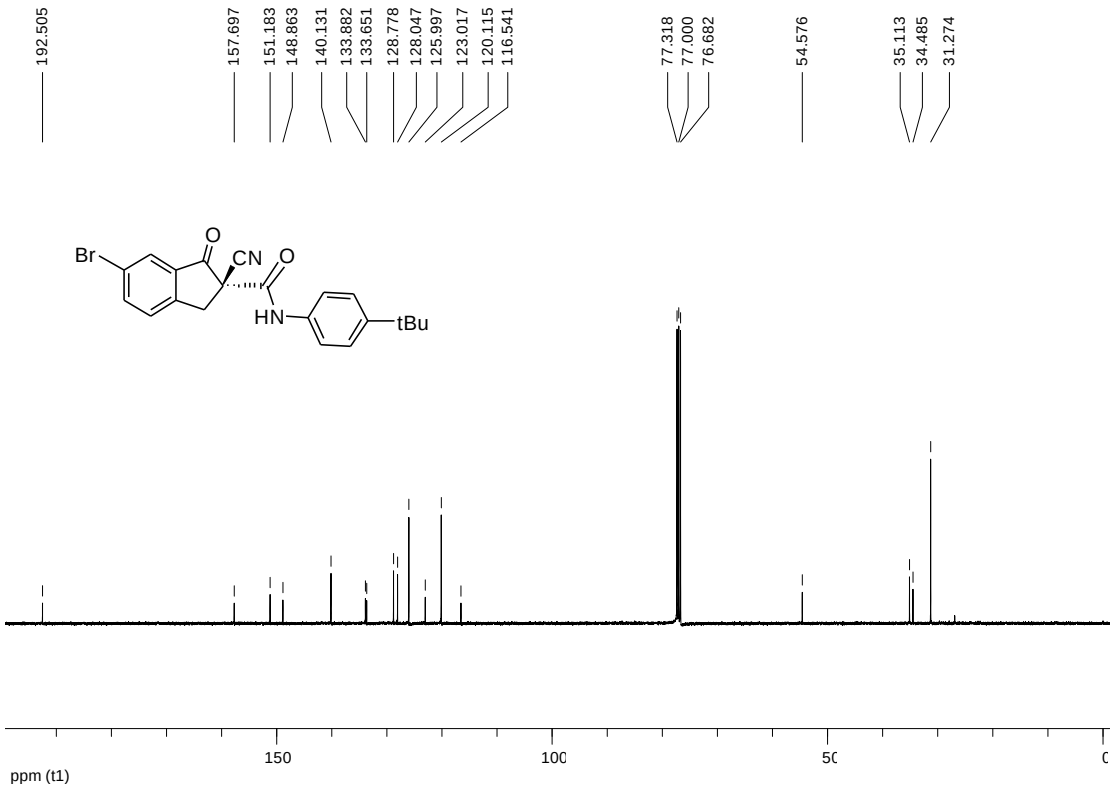
ppm (t1)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77.000
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tBu
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50
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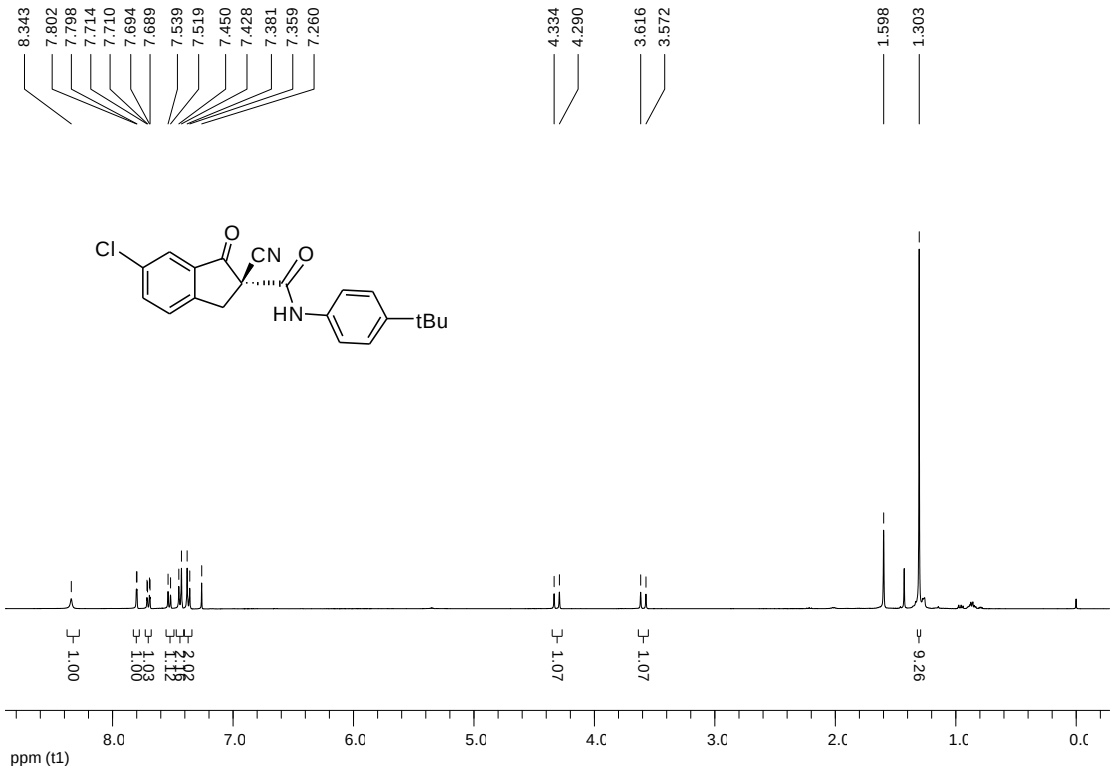
ppm (t1)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4.290
3.616
3.572
1.598
1.303
Cl
O
CN
O
HN
tBu
1.00
1.03
1.00
1.13
2.02
1.07
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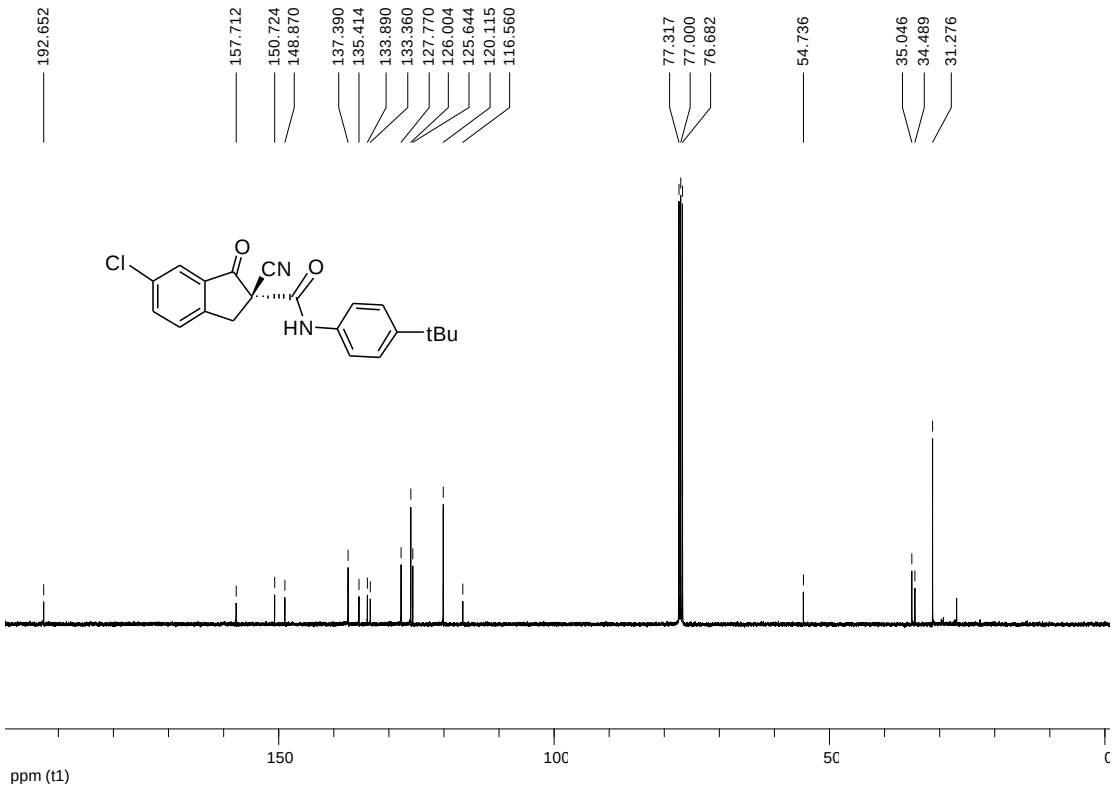
ppm (t1)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77.000
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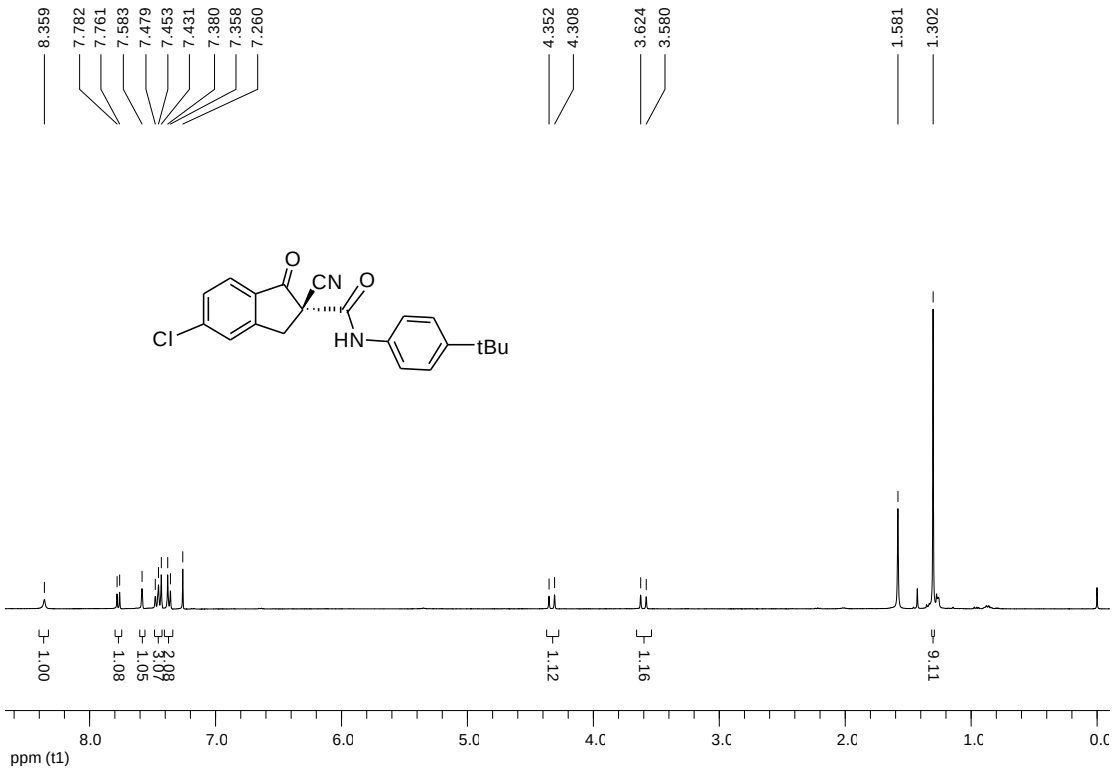
ppm (t1)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3.624
3.580
1.581
1.302
O
CN
O
Cl
HN
tBu
1.00
1.08
1.05
2.08
1.12
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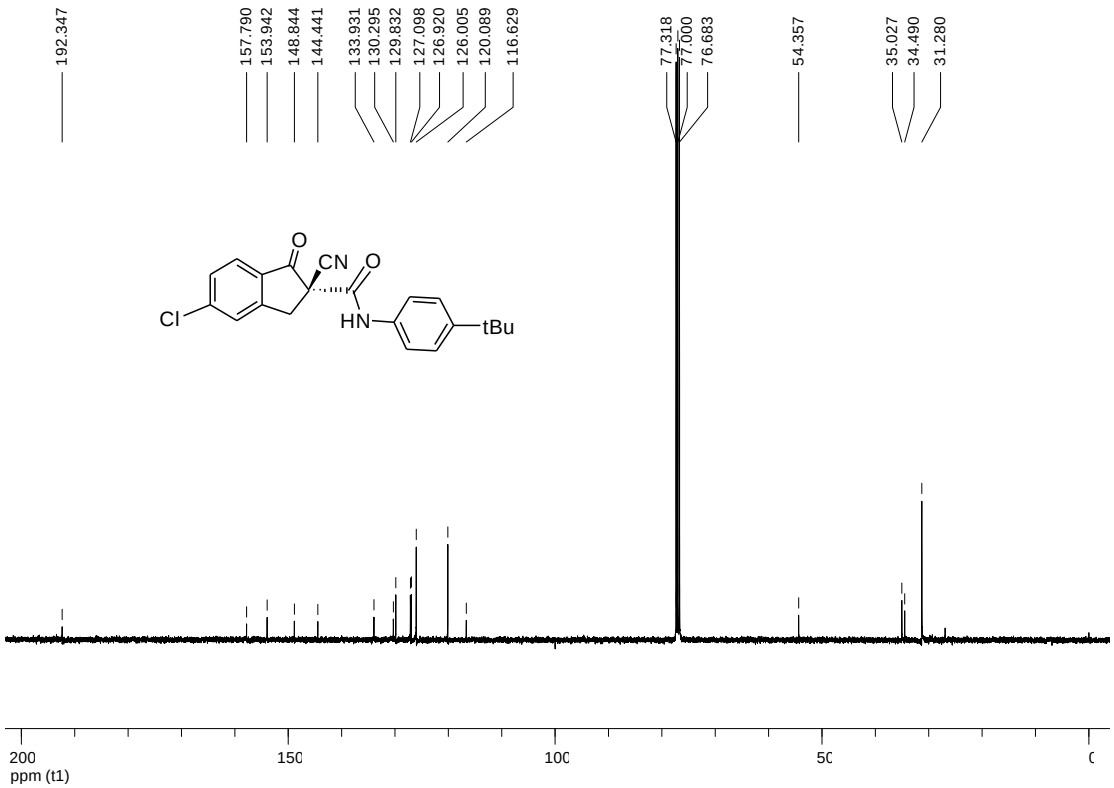
ppm (t1)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120.089
116.629
77.318
77.000
76.683
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Cl
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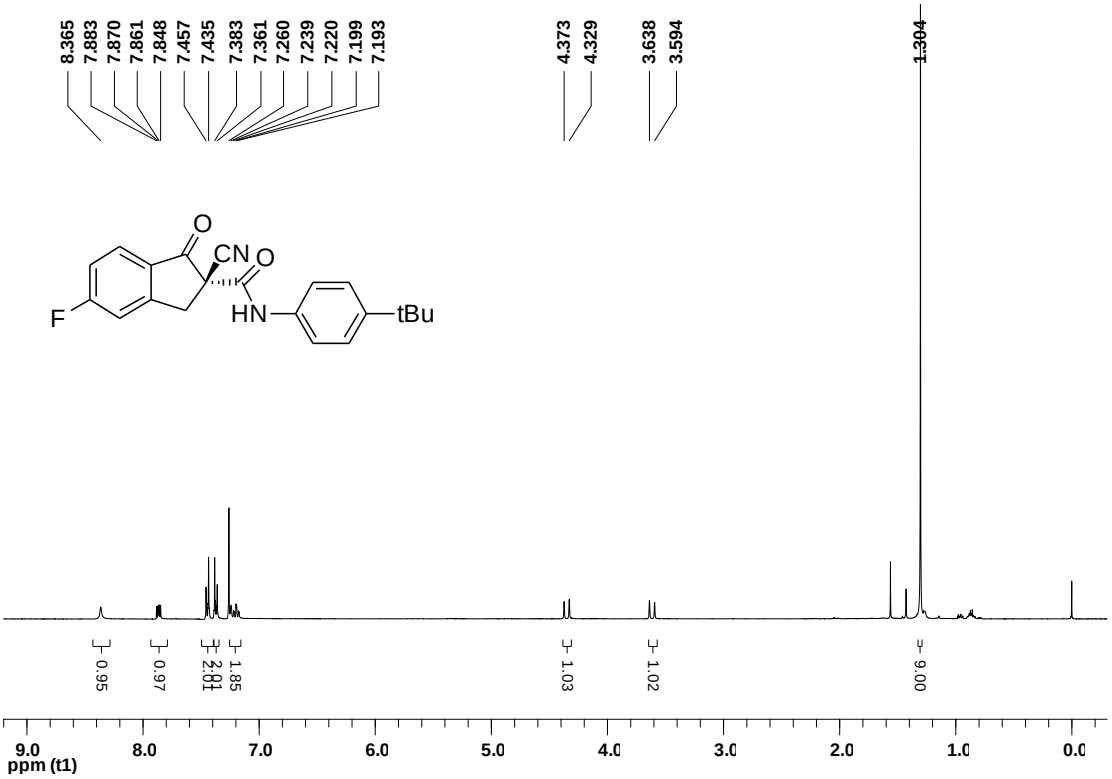
ppm (t1)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7.199
7.193
4.373
4.329
3.638
3.594
1.304
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CN
O
F
HN
tBu
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0.97
2.01
1.85
1.03
1.02
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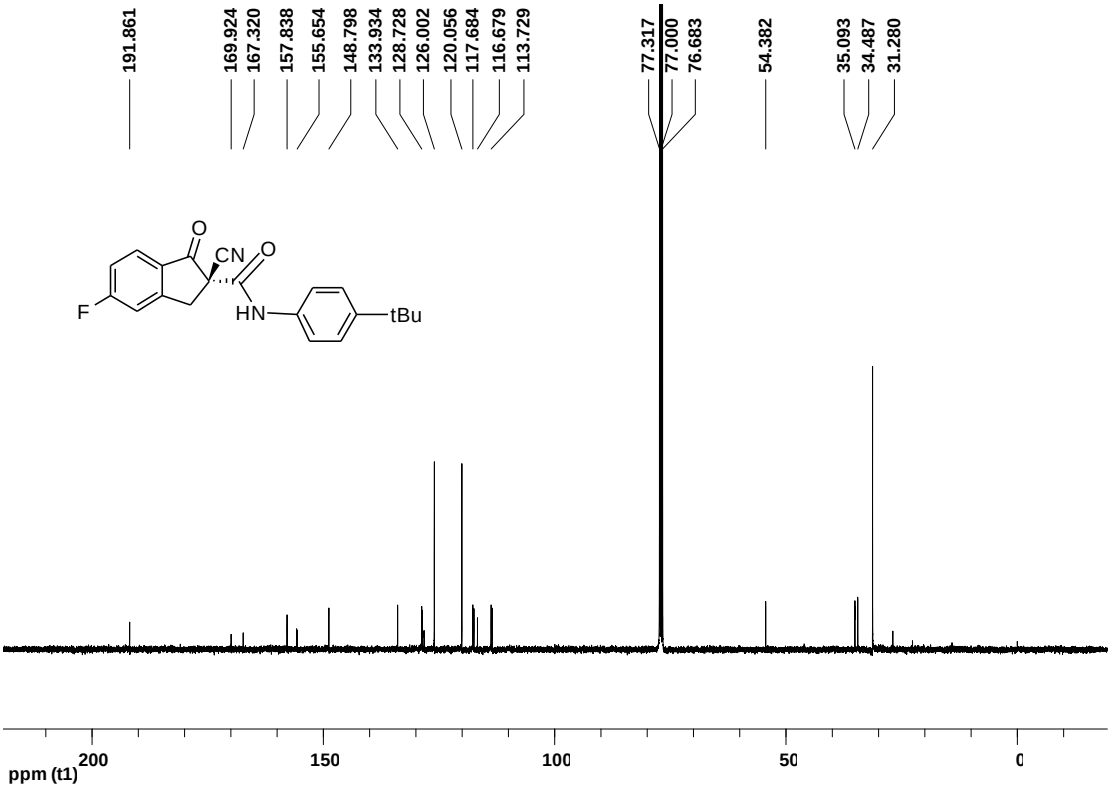
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77.000
76.683
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F
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50
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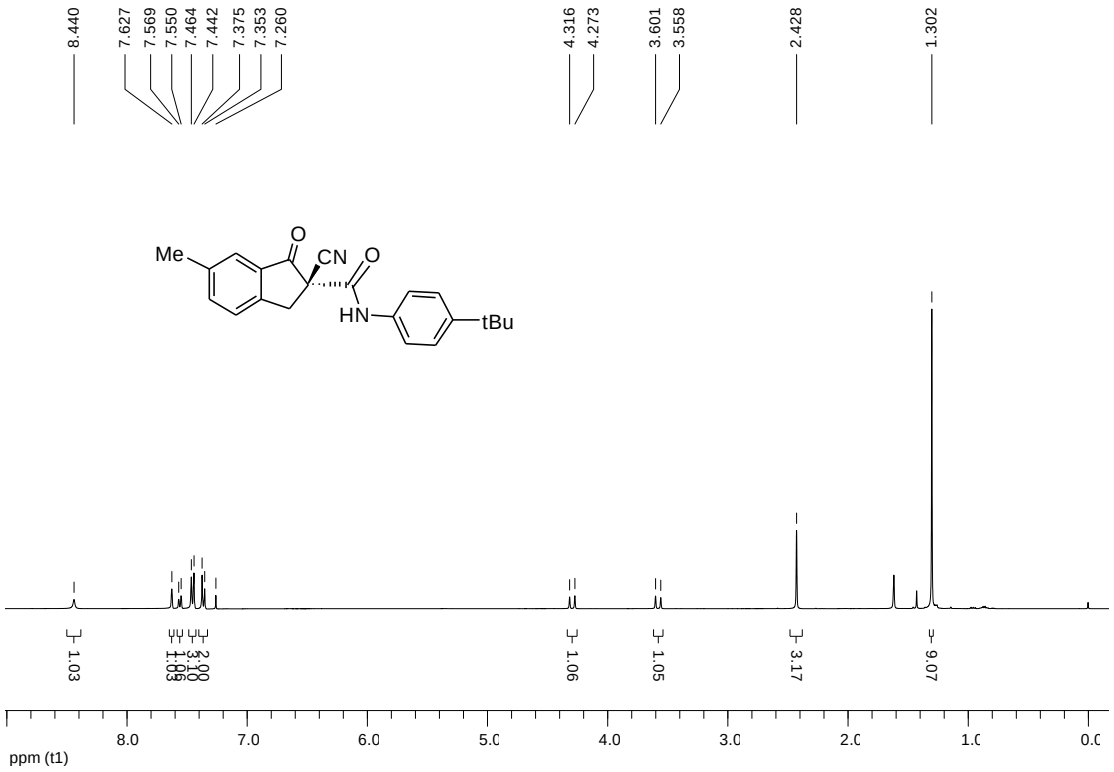
ppm (t1)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2.428
1.302
Me
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CN
O
HN
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2.00
1.06
1.06
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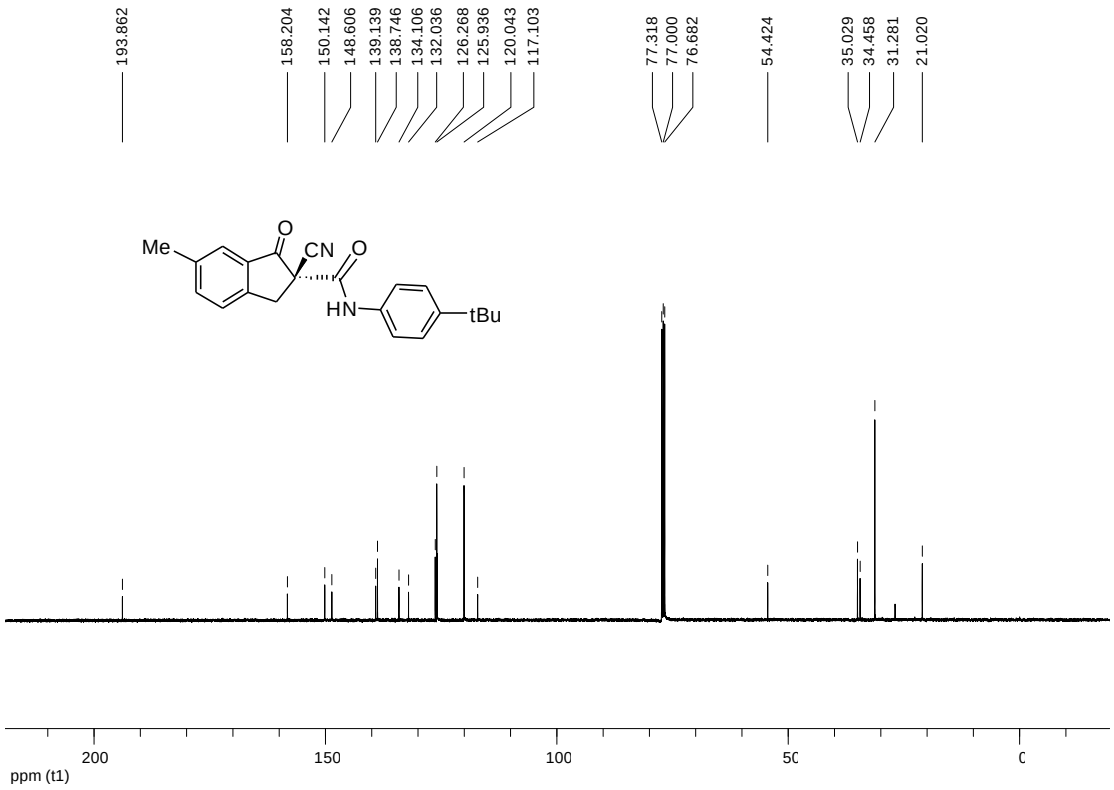
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77.000
76.682
54.424
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tBu
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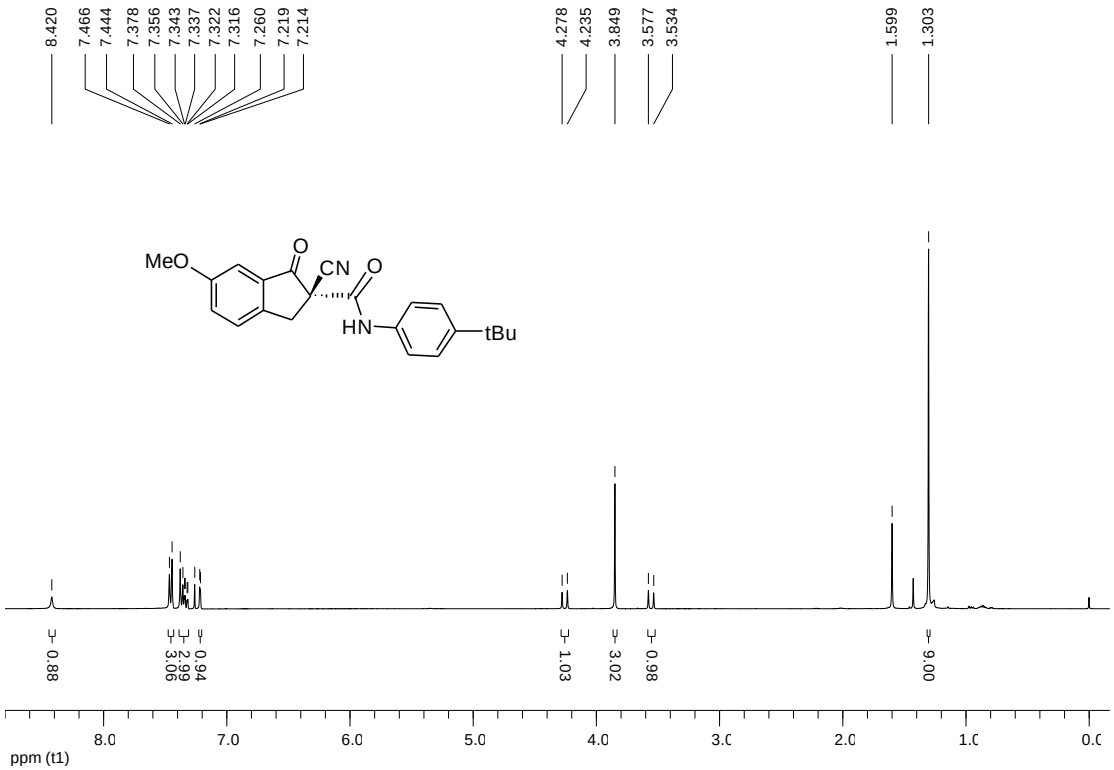
150
100
50
0
ppm (t1)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4.278
4.235
3.849
3.577
3.534
1.599
1.303
MeO
O
CN
O
HN
tBu
0.88
3.06
2.99
0.94
1.03
3.02
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4.0
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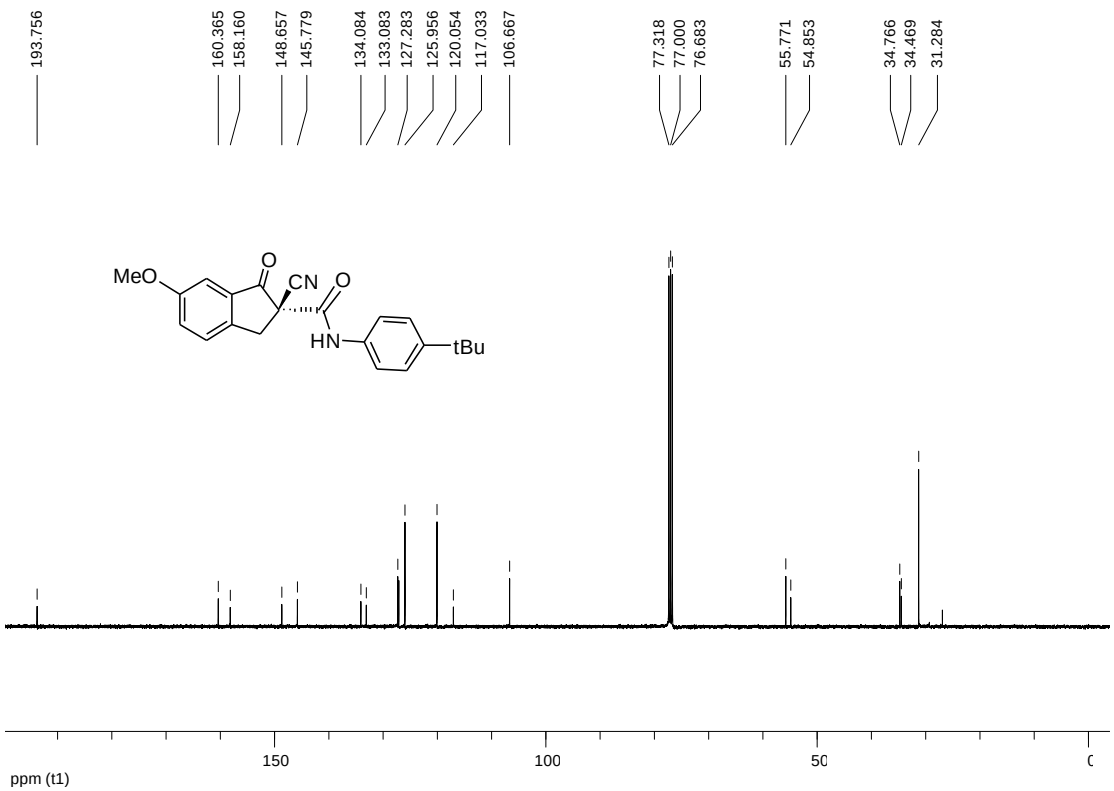
ppm (t1)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77.000
76.683
55.771
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tBu
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50
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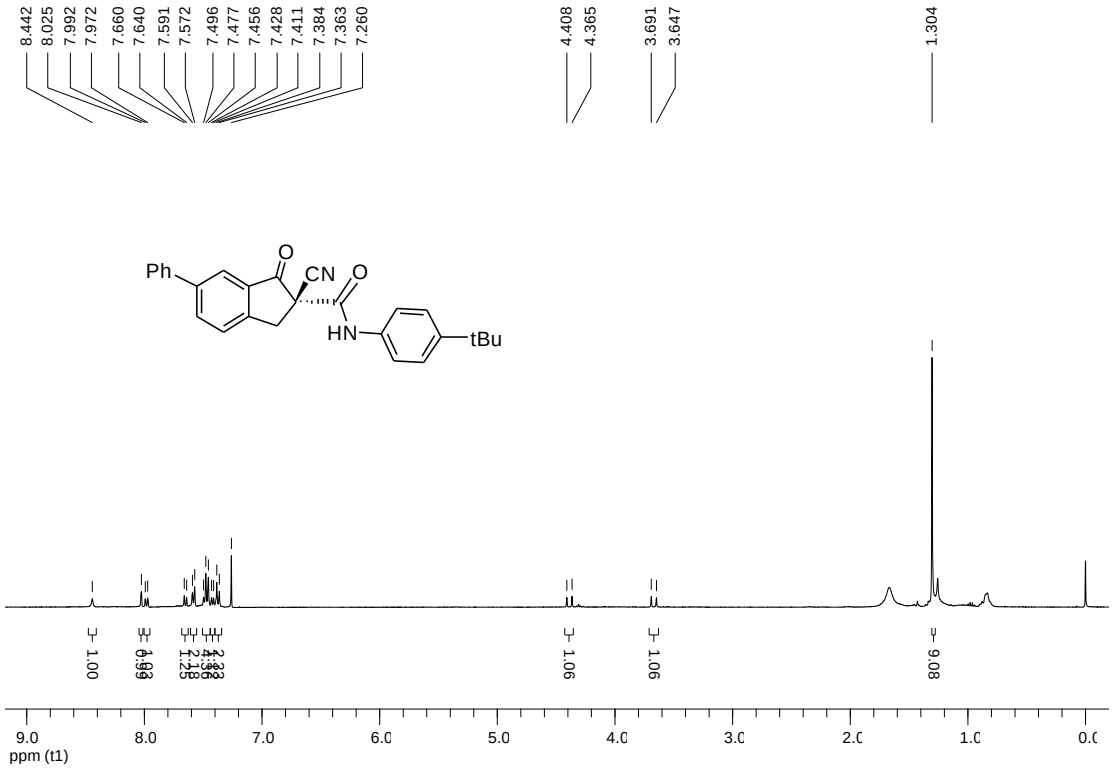
ppm (t1)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7.411
7.384
7.363
7.260
4.408
4.365
3.691
3.647
1.304
Ph
O
CN
O
HN
tBu
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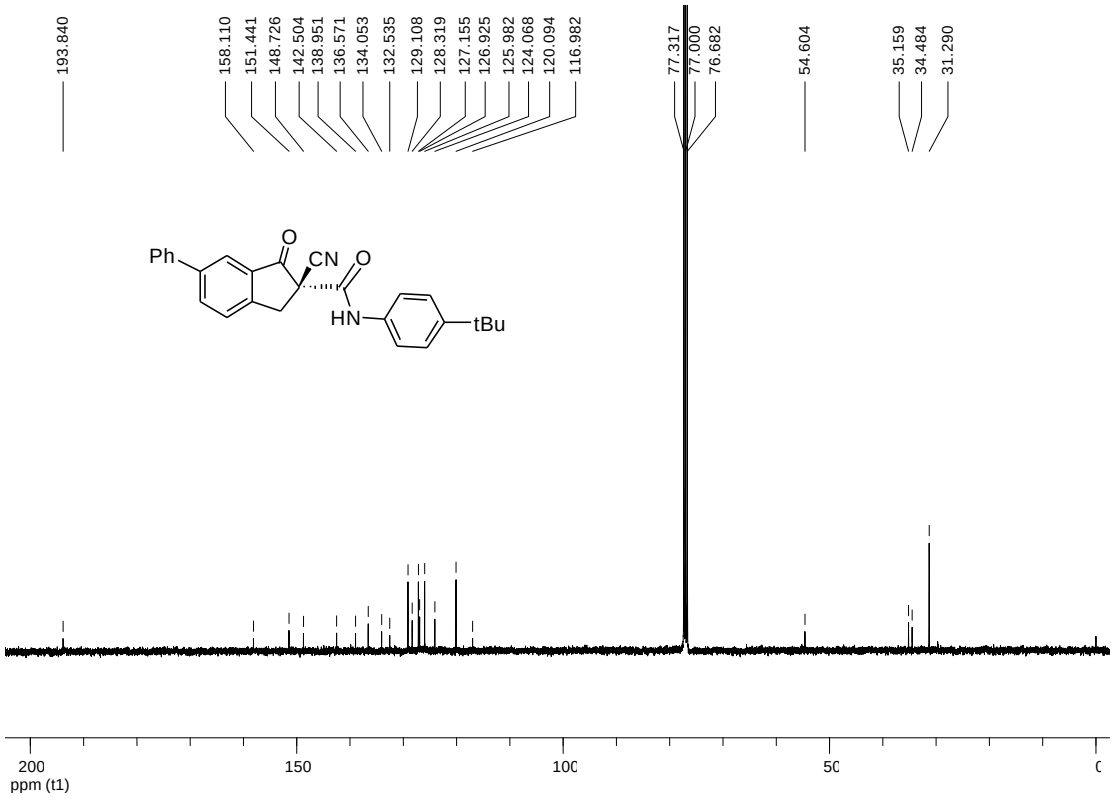
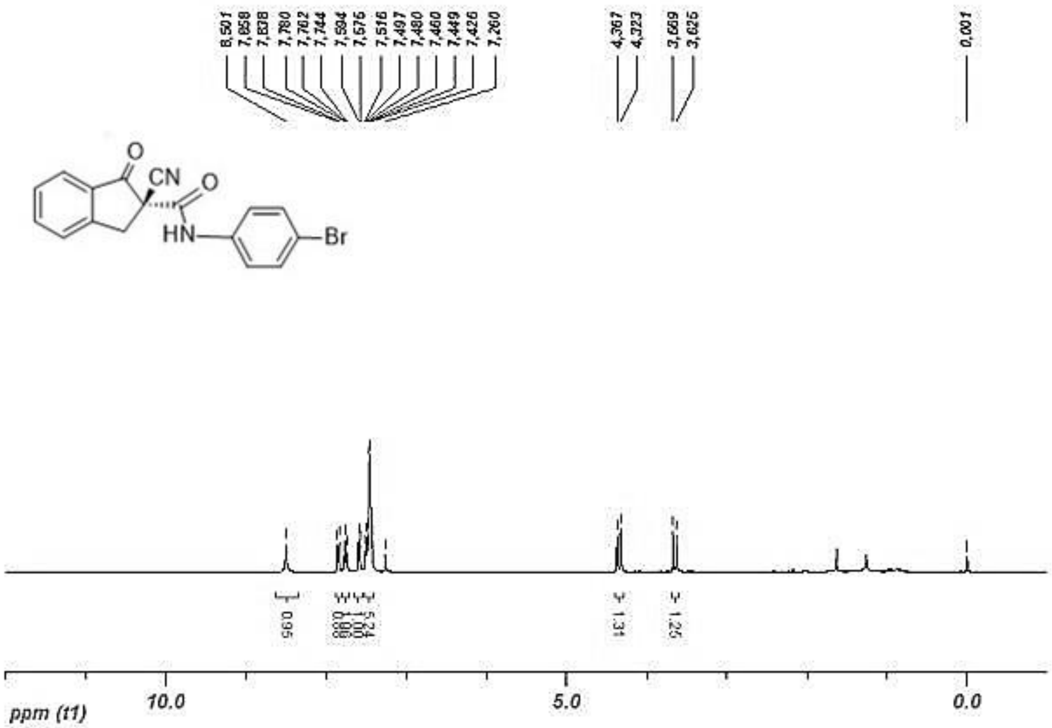
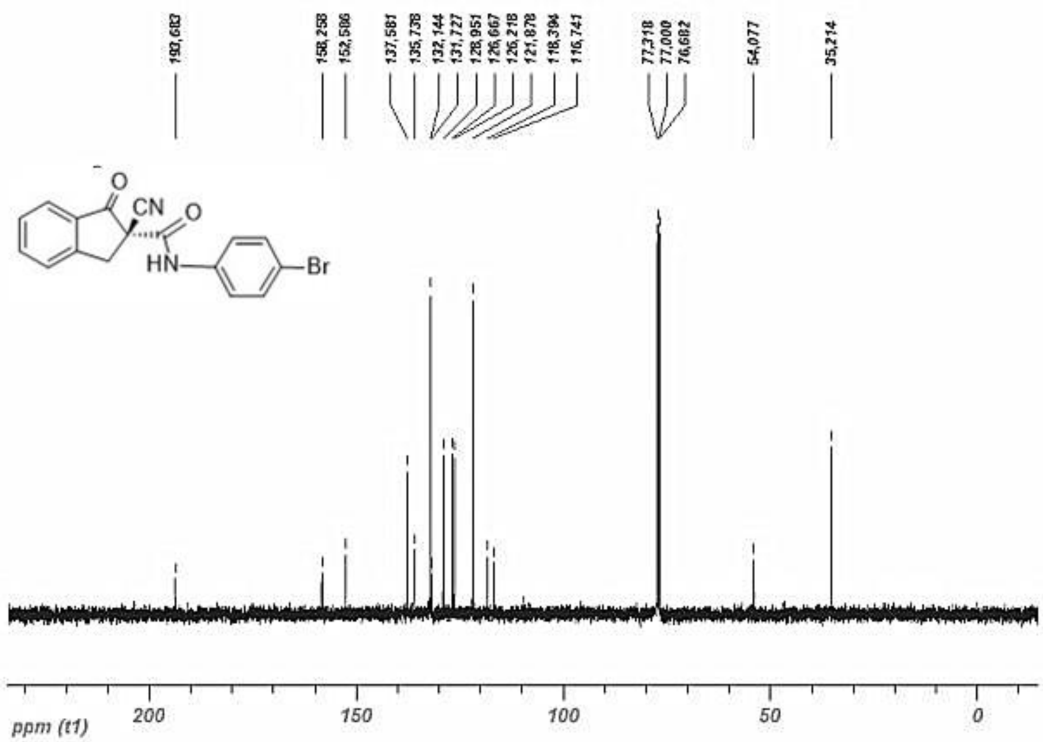
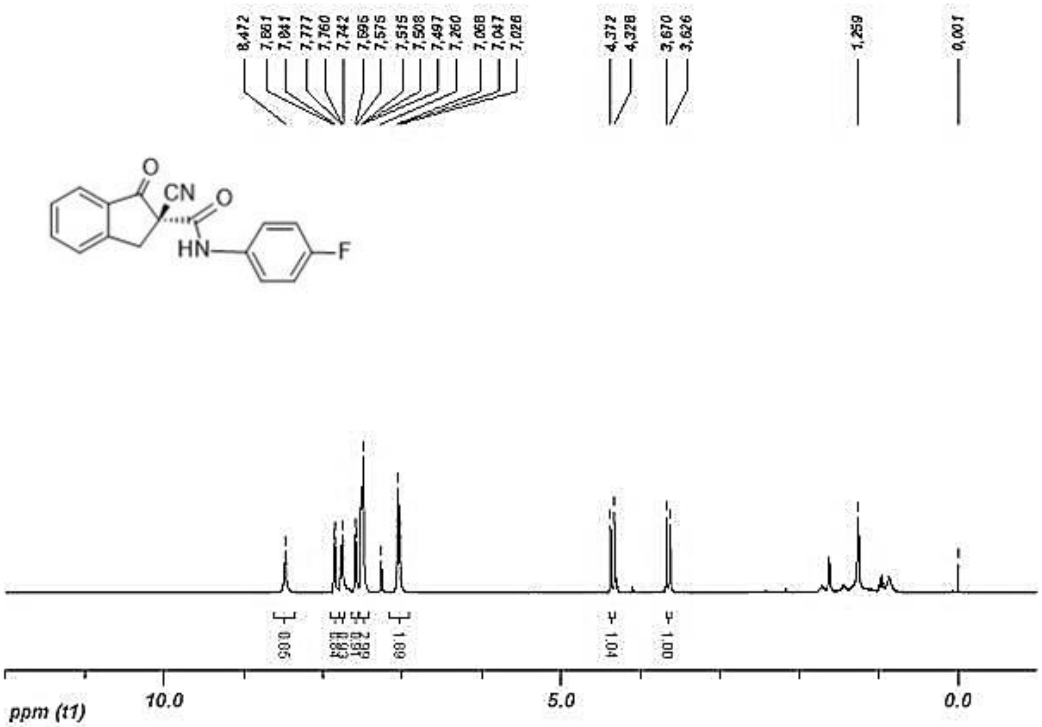
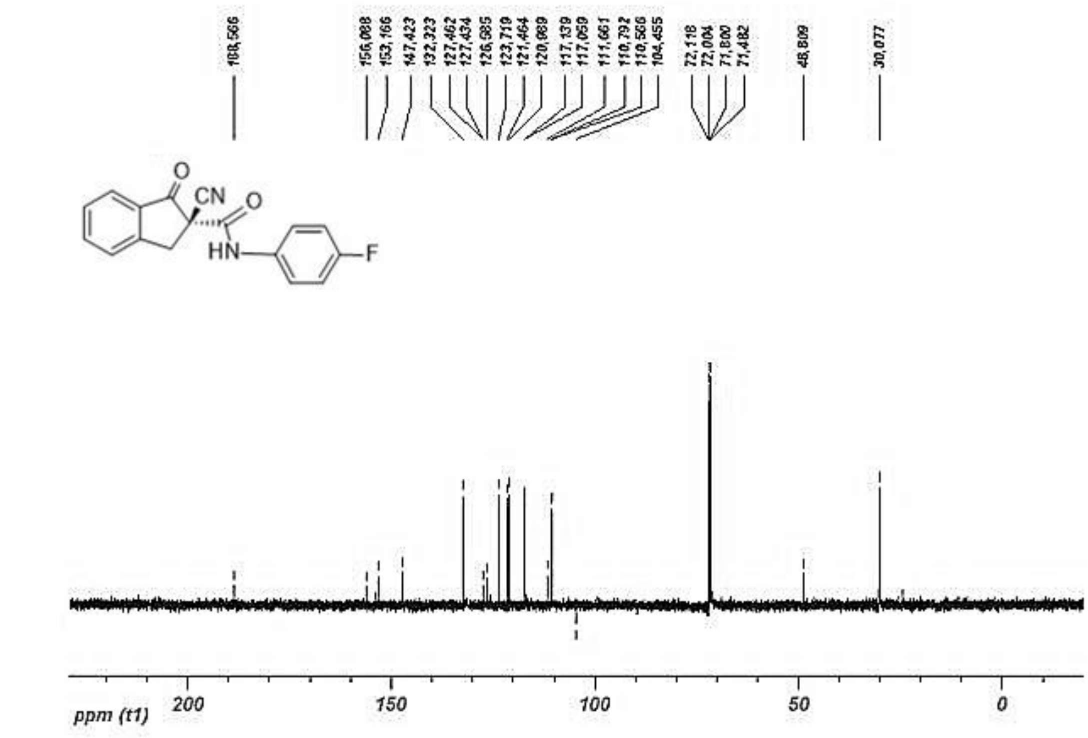
1.06
9.08
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

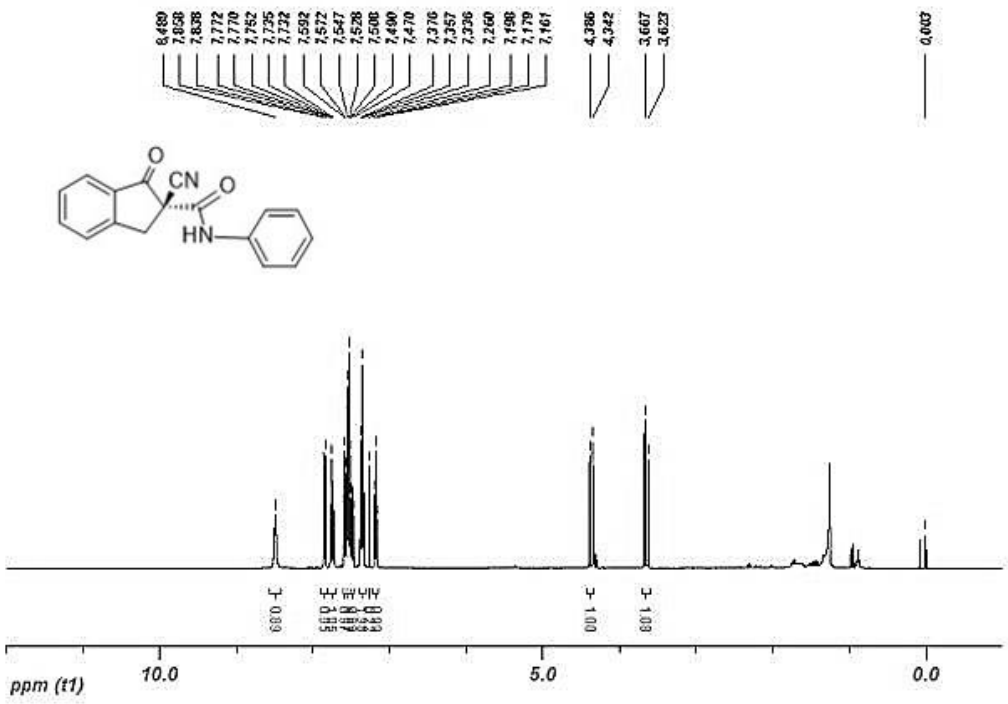

193.840
158.110
151.441
148.726
142.504
138.951
136.571
134.053
132.535
129.108
128.319
127.155
126.925
125.982
124.068
120.094
116.982
77.317
77.000
76.682
54.604
35.159
34.484
31.290
Ph
O
CN
O
HN
tBu
200
150
100
50
0
ppm (t1)

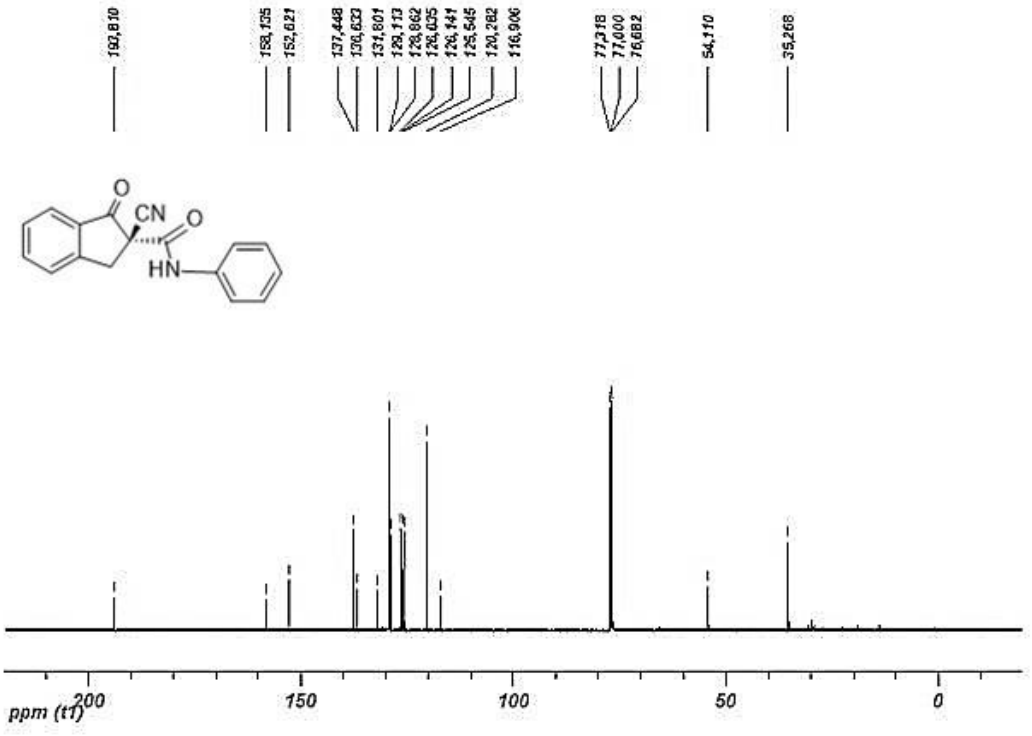

8.501
7.858
7.838
7.780
7.762
7.744
7.594
7.576
7.516
7.497
7.480
7.460
7.449
7.426
7.260
4.367
4.323
3.669
3.625
0.001
CN
HN
Br
0.95
0.98
1.00
5.24
1.31
1.25
10.0
5.0
0.0
ppm (t1)

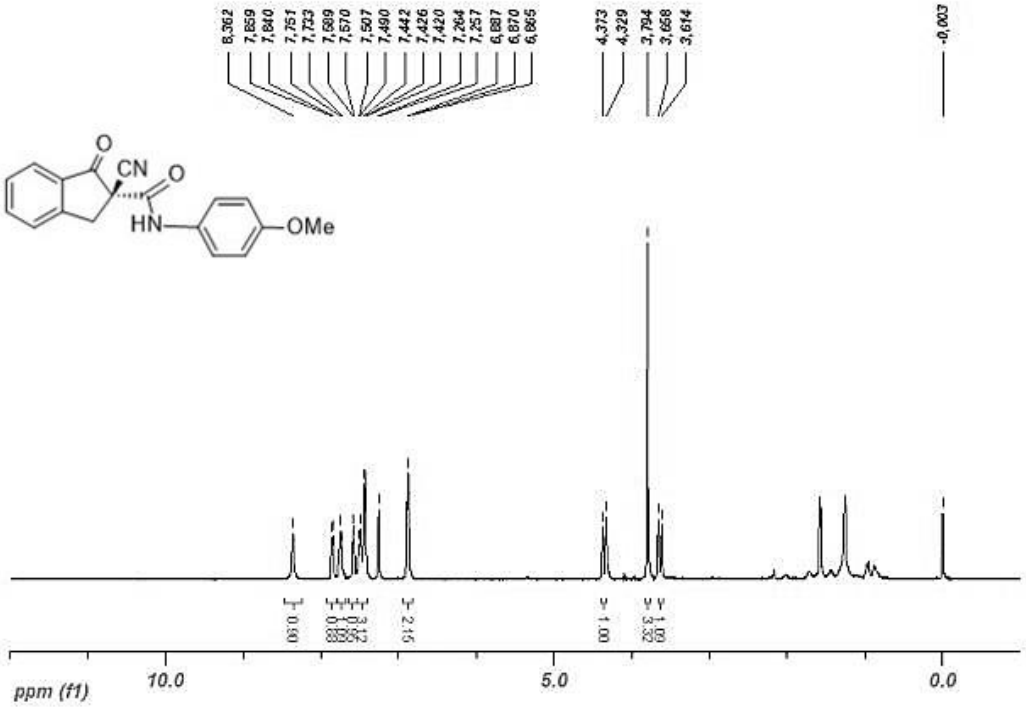

193.683
158.258
152.586
137.581
135.736
132.144
131.727
128.951
126.667
126.218
121.878
118.394
116.741
77.318
77.000
76.682
54.077
35.214
CN
HN
Br
200
150
100
50
0
ppm (t1)

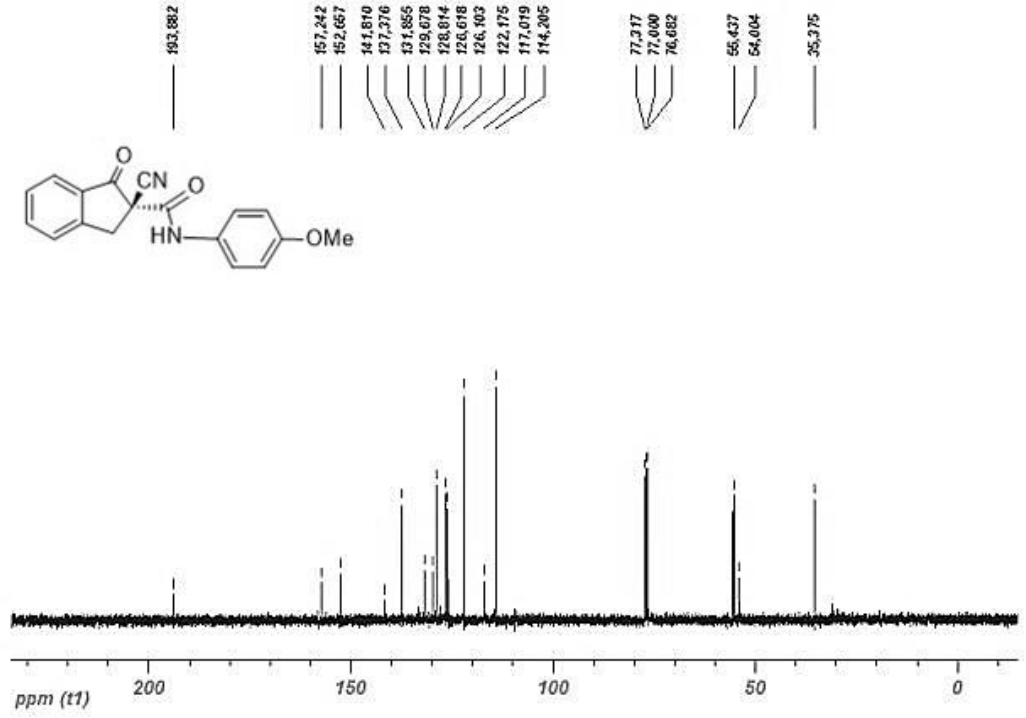


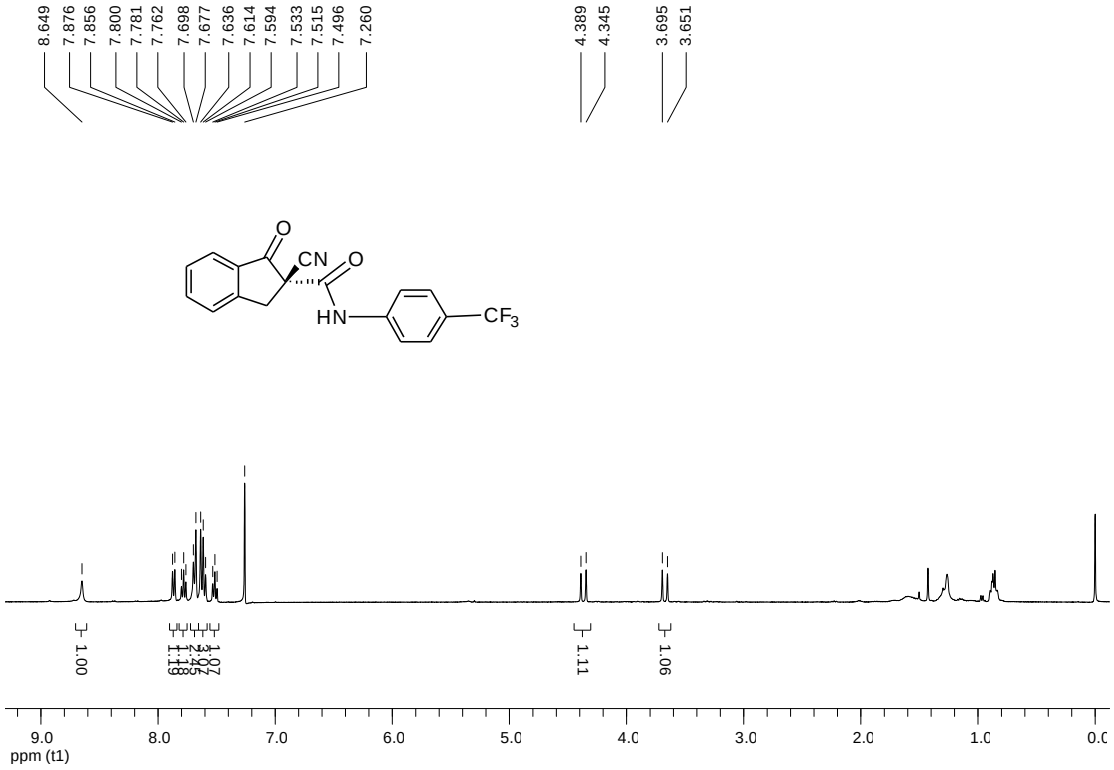


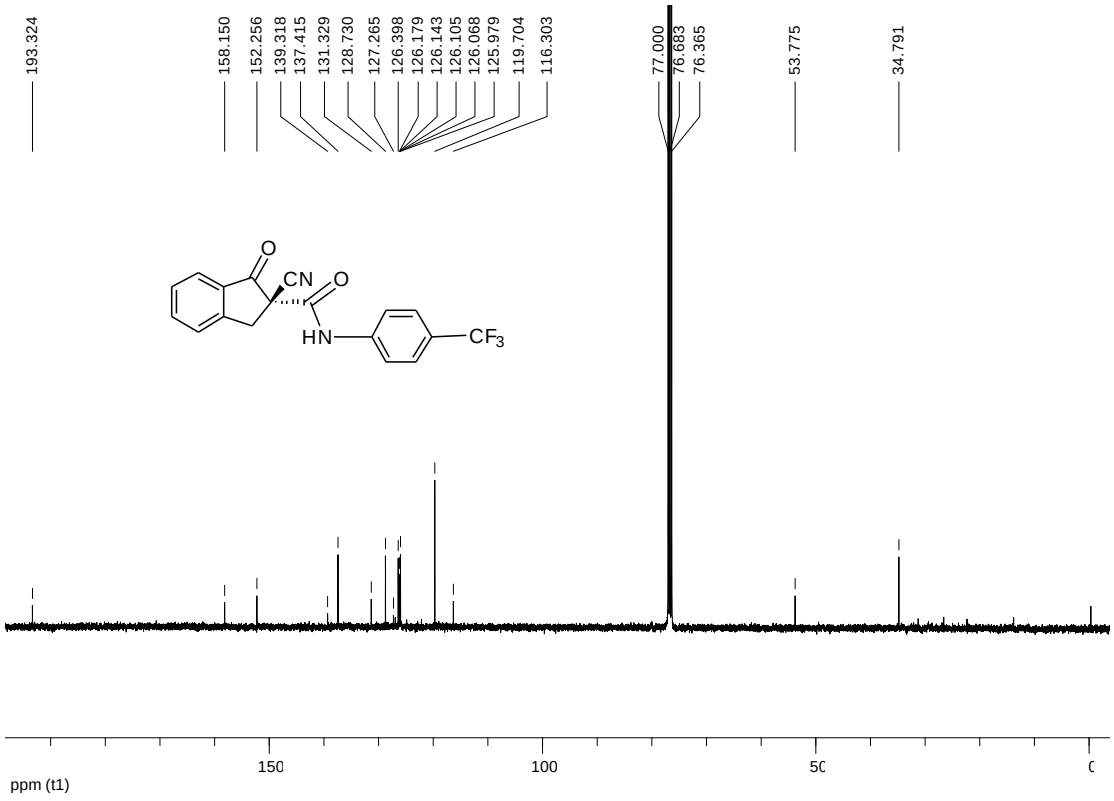

8.489
7.838
7.772
7.770
7.752
7.735
7.732
7.592
7.572
7.547
7.528
7.506
7.490
7.470
7.376
7.357
7.336
7.260
7.198
7.179
7.161
4.386
4.342
3.667
3.623
0.000
O
CN
O
HN
3.089
3.100
3.108
ppm (t1)
10.0
5.0
0.0


193.810
153.135
152.621
137.448
136.633
131.801
129.113
128.862
128.625
126.141
125.545
120.282
116.906
77.318
77.000
76.682
54.110
35.268
O
CN
O
HN
ppm (t1)
200
150
100
50
0


8,362
7,859
7,840
7,751
7,733
7,589
7,570
7,507
7,490
7,442
7,426
7,420
7,264
7,257
6,887
6,870
6,865
4,373
4,329
3,794
3,668
3,614
-0,003
O
CN
O
HN
OMe
0,90
2,15
1,00
3,32
ppm (f1)
10.0
5.0
0.0


193,882
157,242
152,657
141,810
137,376
131,855
129,678
128,814
126,618
126,103
122,175
117,019
114,205
77,317
77,000
76,682
55,437
54,004
35,375
O
CN
O
HN
OMe
ppm (t1)
200
150
100
50
0


8.649
7.876
7.856
7.800
7.781
7.762
7.698
7.677
7.636
7.614
7.594
7.533
7.515
7.496
7.260
4.389
4.345
3.695
3.651
O
CN
O
HN
CF3
1.00
1.19
1.11
1.06
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


193.324
158.150
152.256
139.318
137.415
131.329
128.730
127.265
126.398
126.179
126.143
126.105
126.068
125.979
119.704
116.303
77.000
76.683
76.365
53.775
34.791
O
CN
O
HN
CF3
150
100
50
0
ppm (t1)