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

OrganocatalyticAsymmetricMannich reaction for the Synthesis of 3,3-Disubstituted 3,4-Dihydro-2-quinolones

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Table of contents

A.General information:

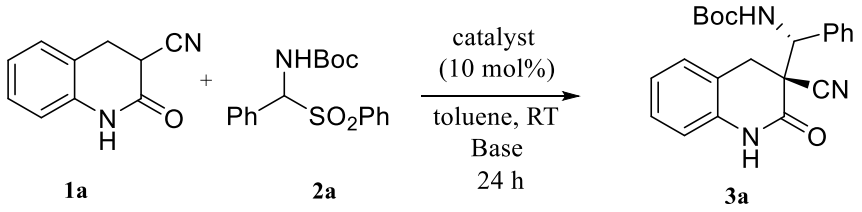
All the reagents used are of commercial grade and used without purification. Organic solvents that are used for reactions were dried using standard methods. Reactions were monitored by silica gel 60 F254 (0.25mm). NMR spectra were recorded in $CDCl_3$ and tetramethylsilane as the internal standard for ^1H NMR (600 MHz) and $CDCl_3$ solvent as the internal standard for ^{13}C NMR (150 MHz). Chemical shifts are reported in ppm tetramethylsilane ($CDCl_3$: δ 7.26, for ^1H NMR and $CDCl_3$: δ 77.23, for ^{13}C NMR). For ^1H NMR, datareported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = double doublet, t =triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz) and integration. HRMS spectra were recorded using APCI and ESI mode. HPLC data were recorded using Dionex (Ultimate 3000) HPLC Instruments.

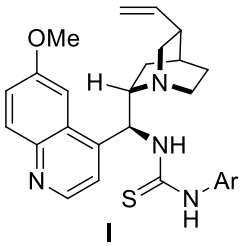
Amidosulfones and N-Boc imines were prepared according to literature procedures.[1]Dihydroquinolones**1a-e** were prepared according to the literature procedure.[2]Thiourea catalysts were prepared according to the reported procedures.[3]Squaramide catalyst was prepared according to the reported procedure.[4]

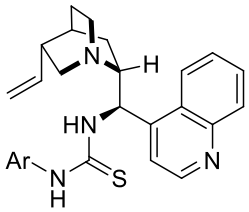
B. General procedure for the synthesis of compound 3:

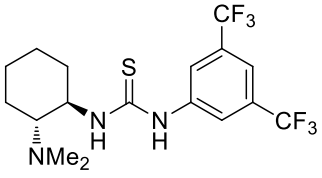
Under argon atmosphere, compound **1** dihydro-3-cyano-2-quinolone (0.15 mmole), amidosulfone**2** (0.23 mmole) and catalyst **V** (10 mol %) were placed in a round bottom flask, benzene (2.5 ml) and 75 µl saturated Na_2CO_3 solution were added to it. Then the reaction mixture stirred at room temperature under argon atmosphere. After the reaction was completed monitored by TLC. The reaction mixture was filtered through a sinter funnel and the filtrate was evaporated. the crude reaction mixture was subjected to column chromatography on silica gel (100-200 mesh) and (230-400 mesh) using 15-20% ethyl acetate in hexane to afford the corresponding productswith both diastereomer separated.

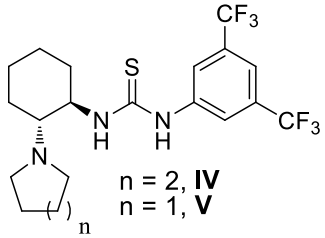
C. Optimization of reaction condition of Mannich reaction of activated carbonyl compounds with in situ generated *N*-Boc imines from amidosulfones:

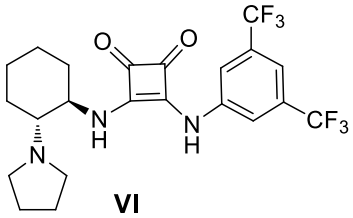


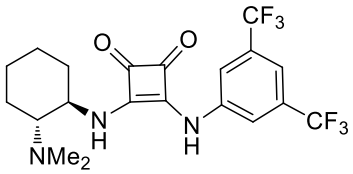


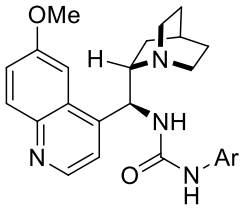




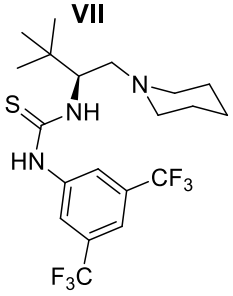








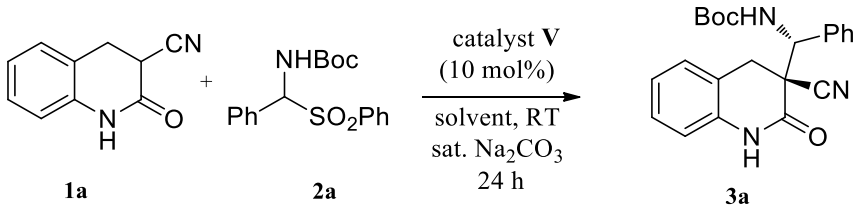
Ar = 3,5-$(CF3)_2C_6H_3$



Entry[a]	catalyst	Yield(%)[b]	d.r[c]	ee(%)[d]
1	**I**	60	3:1	36
2	**II**	62	1.5:1	34
3	**III**	70	4:1	56
4	**IV**	70	4:1	75
5	**V**	72	5:1	79
6	**VI**	68	4:1	77
7	**VII**	61	3:1	40
8	**VIII**	65	3:1	50
9	**IX**	55	3:1	30

[a] Reaction condition: 0.15 mmol of **1a** with 0.23 mmol of **2a** in 2.5 ml solvent using 10 mol% catalyst and 75 µL sat. sodium carbonate. [b]Isolated combined yield after silica gel column chromatography.[c]Determined by ^{1}H NMR.[d]Determined by chiral HPLCand of the major diastereomer.

Solvent screening:



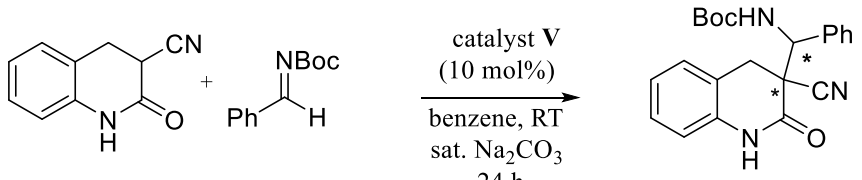
1a **2a** **3a**

Entry[a]	Solvent	Yield(%)[b]	dr[c]	ee(%)[d]
1	Toluene	72	5:1	79
2	$PhCF_3$	71	5:1	73
3	DCM	70	5:1	65
4	*o*-xylene	70	5:1	75
5	mesitylene	68	5:1	65
6	Benzene	75	5:1	98
7[e]	Benzene	73	5:1	96
8[f]	Benzene	75	5:1	97

9[g]	Benzene	74	5:1	91
10[h]	Benzene	70	5:1	85

[a] Reaction condition:0.15 mmol of **1a** with 0.23 mmol of **2a** in 2.5 ml solvent using 10 mol% catalyst and 75 uL sat. sodium carbonate. [b]Isolated combined yield after silica gel column chromatography.[c]Determined by ^{1}H NMR.[d]Determined by chiral HPLCand of the major diastereomer.[e]Reaction carried out 5 mol% catalyst. [f]Reaction carried out with 20 mol% catalyst. [g]Reaction was performed with sat. Potassium carbonate solution. [h]Reaction was performed with sat. Sodium bicarbonate solution.

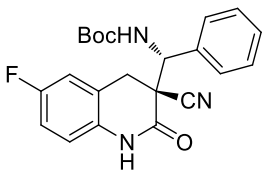
D. General procedure for the synthesis of compound 3a with preformed N-Boc imine:

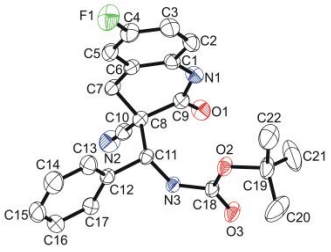


1a

3a
yield= 50%,
dr= 3:1,
ee= 86%

E. Crystal data and structure refinement for chiral compound (CCDC No. 1831432) (3v):



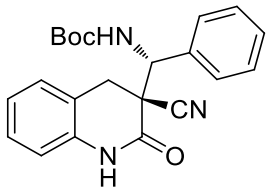


Empirical formula	$C_{22}H_{22}FN_3O_3$
Formula weight	395.4
CCDC Number	1831432
Crystal habit, colour	Needle, White
Crystal size, mm^3	0.18 × 0.12 ×0.08
Temperature, *T*	293(2)
Wavelength, λ(Å)	0.71073
Crystal system	monoclinic
Space group	P2(1)/c
Unit cell dimensions	*a* = 11.8968(11)Å

	b = 18.4254(17)Å c = 10.7033(8)Å α = 90.00°, β= 103.556(8)° γ = 90.00°
Volume, V (Å^3)	2280.8(3)
Z	4
Calculated density, Mg·m^{-3}	1.242
Absorption coefficient, μ (mm^{-1})	0.091
F(000)	900.0
θ range for data collection	2.95 to 25°
Limiting indices	–14 ≤ h ≤ 10, –14≤ k ≤ 21, –11 ≤ l ≤ 12
Reflection collected/unique	8912/ 4015[R(int)=0.0329]
Completeness to θ	99.81% (θ = 25.00°)
Max. and min. transmission	0.993/0.987
Refinement method	'SHELXL–97(Sheldrick, 1997)'
Data/restraints/parameters	4015/0/285
Goodness–of–fit on F^2	1.051
Final R indices [I>2sigma(I)]	R_1= 0.0567, wR_2= 0.1208
R indices (all data)	R1 = 0.0982, wR2 = 0.1468
Largest diff. peak and hole	0.44 and –0.21e·Å^{-3}

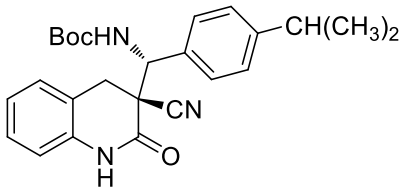
F. Characterization data for compounds (3a-3y):

Tert-butyl ((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(phenyl)methyl)carbamat (3a)



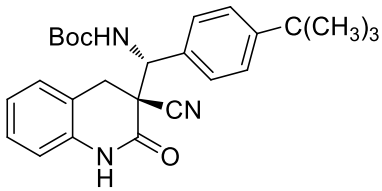
White sticky solid (42.4 mg, yield: 75%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (600 MHz, $CDCl_3$)**: δ 8.43 (s, 1H), 7.45 – 7.35 (m, 3H), 7.32 (t, *J* = 7.7 Hz, 1H), 7.26 (d, *J* = 6.3 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.03 (d, *J* = 7.2 Hz, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 5.64 (d, *J* = 9.0 Hz, 1H), 4.94 (d, *J* = 7.4 Hz, 1H), 3.35 (d, *J* = 16.1 Hz, 1H), 2.72 (d, *J* = 16.1 Hz, 1H), 1.35 (s, 9H);**^{13}C NMR(125 MHz, $CDCl_3$)**: δ 164.4, 154.9, 136.0, 135.7, 129.4, 129.3, 129.1, 128.9, 127.7, 124.6, 118.3, 117.5, 116.4, 80.8, 54.8, 51.0, 33.8, 28.3;**HRMS (+ESI):** Calc for $C_{22}H_{24}N_3O_3$ $[M+H]^+$ 378.1812; found378.1817; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (90:10 *n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 13.5 min, τ_{major} = 24.0 min); Enatiomeric excess: 98%;

Tert-butyl ((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(4-isopropylphenyl)methyl)carbamate (3b)



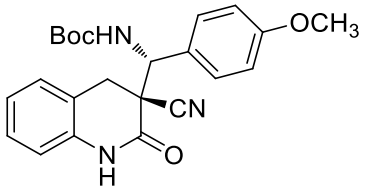
White sticky solid (46.5 mg, yield: 74%);**Diastereomeric ratio**: 5:1; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 8.67 (s, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.29 – 7.26 (m, 2H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.07 (d, *J* = 7.1 Hz, 1H), 7.01 (d, *J* = 7.9 Hz, 1H), 5.63 (d, *J* = 8.8 Hz, 1H), 4.96 (d, *J* = 8.4 Hz, 1H), 3.37 (d, *J* = 16.1 Hz, 1H), 2.95 (dt, *J* = 13.8, 6.9 Hz, 1H), 2.78 (d, *J* = 16.1 Hz, 1H), 1.36 (s, 9H), 1.28 (d, *J* = 6.8 Hz, 6H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 164.6, 154.9, 150.1, 136.1, 133.0, 129.2, 128.9, 127.7, 127.1, 124.5, 118.4, 116.4, 80.6, 54.6, 51.3, 34.0, 33.8, 28.3, 24.1, 24.0; **HRMS (+ESI):** Calc for $C_{22}H_{30}N_3O_3$ $[M+H]^+$ 420.2282; found 420.2280; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 7.1 min, τ_{major} = 18.4 min); Enatiomeric excess: 94%;

Tert-butyl ((R)-(4-(tert-butyl)phenyl)((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)methyl)carbamate (3c)



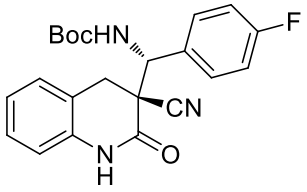
White sticky solid (46.8 mg, yield: 72%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.51 (s, 1H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.31 (t, *J* = 7.7 Hz, 1H), 7.19 (d, *J* = 8.2 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.06 (d, *J* = 7.0 Hz, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 5.62 (d, *J* = 8.7 Hz, 1H), 4.95 (d, *J* = 8.3 Hz, 1H), 3.35 (d, *J* = 16.1 Hz, 1H), 2.76 (d, *J* = 16.2 Hz, 1H), 1.36 (s, 9H), 1.33 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$):** δ 164.4, 155.0, 152.4, 136.1, 132.6, 129.2, 128.9, 127.4, 126.0, 124.5, 118.5, 117.7, 116.3, 80.7, 54.5, 51.3, 34.9, 33.9, 31.5, 28.4;**HRMS (+ESI):** Calc for $C_{26}H_{32}N_3O_3$ $[M+H]^+$ 434.2438; found 434.2435; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 6.7 min, τ_{major} = 12.4 min);Enatiomeric excess: 96%;

Tert-butyl ((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(4-methoxyphenyl)methyl)carbamate (3d)



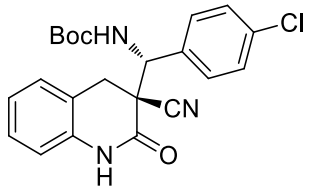
White sticky solid (42.1 mg, yield: 69%);**Diastereomeric ratio**: 5:1; **^{1}H NMR (600 MHz, $CDCl_3$)**: δ 7.31 (t, *J* = 7.7 Hz, 1H), 7.17 (d, *J* = 8.6 Hz, 2H), 7.11 (t, *J* = 7.4 Hz, 1H), 7.02 (d, *J* = 7.4 Hz, 1H), 6.91 (t, *J* = 7.1 Hz, 3H), 5.55 (d, *J* = 8.6 Hz, 1H), 4.88 (d, *J* = 8.3 Hz, 1H), 3.83 (s, 3H), 3.35 (d, *J* = 16.1 Hz, 1H), 2.73 (d, *J* = 16.2 Hz, 1H), 1.37 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$)**: δ 164.1, 160.3, 154.9, 135.9, 129.3, 128.9, 128.9, 127.8, 124.6, 118.4, 117.6, 116.1, 114.4, 80.7, 55.6, 54.3, 51.3, 33.8, 28.4; **HRMS (+ESI):** Calc for $C_{23}H_{26}N_3O_4$ $[M+H]^+$ 408.1918; found 408.1921; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 11.0 min, τ_{major}= 17.6 min)Enatiomeric excess: 86%;

Tert-butyl ((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(4-fluorophenyl)methyl)carbamate (3e)



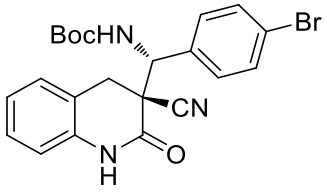
White sticky solid (45.6 mg, yield: 77%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 8.43 (s, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.30 – 7.26 (m, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 8.5 Hz, 2H), 7.05 (d, *J* = 7.3 Hz, 1H), 6.99 (d, *J* = 7.9 Hz, 1H), 5.67 (d, *J* = 8.1 Hz, 1H), 4.93 (d, *J* = 7.6 Hz, 1H), 3.39 (d, *J* = 16.2 Hz, 1H), 2.73 (d, *J* = 16.2 Hz, 1H), 1.37 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$)**: δ 164.1 (d, *J* = 16.5), 162.4, 154.9, 135.9, 131.8, 129.6 (d, *J* = 9), 129.4, 128.8, 124.8, 118.2, 117.3, 116.4, 116.1 (d, *J* = 21), 80.9, 54.3, 50.9, 33.8, 28.3; **HRMS (+ESI):** Calc for $C_{22}H_{23}FN_3O_3$ $[M+H]^+$ 396.1718; found 396.1722; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 9.3 min, τ_{major} = 14.5 min); Enatiomeric excess: 92%.

Tert-butyl ((R)-(4-chlorophenyl)((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)methyl)carbamate(3f)



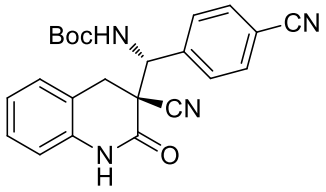
White sticky solid (46.3 mg, yield: 75%);**Diastereomeric ratio**: 5:1; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.23 (s, 1H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.21 (d, *J* = 8.5 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.04 (d, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 5.66 (d, *J* = 8.4 Hz, 1H), 4.89 (d, *J* = 8.4 Hz, 1H), 3.37 (d, *J* = 16.2 Hz, 1H), 2.73 (d, *J* = 16.3 Hz, 1H), 1.36 (s, 9H); **^{13}C NMR(100 MHz, $CDCl_3$):**δ 163.7, 154.6, 135.6, 135.2, 134.2, 129.2, 129.1, 128.9, 128.7, 124.6, 118.0, 116.9, 116.1, 80.8, 54.2, 50.5, 33.6, 28.2; **HRMS (+ESI):** Calc for $C_{22}H_{23}ClN_3O_3$ $[M+H]^+$ 412.1422; found 412.1422; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm,τ_{minor} = 9.4 min, τ_{major} = 16.2 min); Enatiomeric excess: 79%.

Tert-butyl ((R)-(4-bromophenyl)((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)methyl)carbamate (3g)



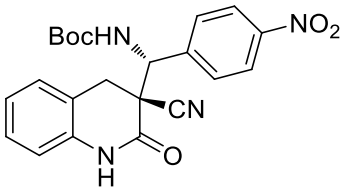
White sticky solid (49.9 mg, yield: 73%);**Diastereomeric ratio**: 5:1; **^{1}H NMR (600 MHz, $CDCl_3$)**: δ 8.35 (s, 1H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.14 (dd, *J* = 14.0, 7.9 Hz, 3H), 7.04 (d, *J* = 7.3 Hz, 1H), 6.96 (d, *J* = 7.9 Hz, 1H), 5.65 (d, *J* = 8.1 Hz, 1H), 4.88 (d, *J* = 7.4 Hz, 1H), 3.37 (d, *J* = 16.2 Hz, 1H), 2.72 (d, *J* = 16.3 Hz, 1H), 1.35 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$):** δ 164.1, 154.9, 135.8, 134.9, 132.2, 129.5, 129.4, 128.8, 124.8, 123.6, 118.2, 117.1, 116.4, 81.0, 54.4, 50.7, 33.8, 28.3; **HRMS (+ESI):** Calc for $C_{22}H_{23}BrN_3O_3$ $[M+H]^+$ 456.0917; found 456.0908; The enantiomeric ratio was determined by HPLC analysis using Daicel ChiralpakIA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 10.0 min, τ_{major} = 17.0 min); Enatiomeric excess: 81%;

Tert-butyl ((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(4-cyanophenyl)methyl)carbamate (3h)



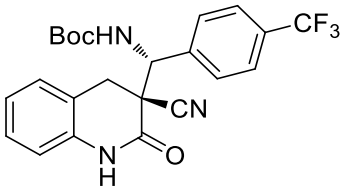
White sticky solid (40.4 mg, yield: 67%);**Diastereomeric ratio**: 4:1; **^{1}H NMR (600 MHz, $CDCl_3$)**: δ 7.91 (s, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.42 (d, *J* = 8.3 Hz, 2H), 7.36 (t, *J* = 7.7 Hz, 1H), 7.16 (t, *J* = 7.3 Hz, 1H), 7.06 (d, *J* = 7.4 Hz, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 5.73 (d, *J* = 8.1 Hz, 1H), 4.94 (d, *J* = 7.4 Hz, 1H), 3.41 (d, *J* = 16.3 Hz, 1H), 2.72 (d, *J* = 16.3 Hz, 1H), 1.36 (s, 9H); **^{13}C NMR(150 MHz, $CDCl_3$):** δ 163.3, 154.8, 141.1, 135.6, 132.8, 129.7, 128.8, 128.7, 125.1, 118.4, 118.0, 116.7, 116.4, 113.4, 81.4, 54.7, 50.2, 33.8, 28.3; **HRMS (+ESI):** Calc for $C_{23}H_{22}N_4NaO_4$ $[M+Na]^+$ 425.1584; found 425.1594; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 14.6 min, τ_{major} = 26.0 min); Enatiomeric excess: 84%.

Tert-butyl ((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(4-nitrophenyl)methyl)carbamate (3i)



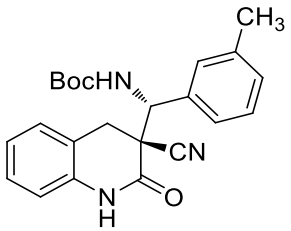
White sticky solid (44.3 mg, yield: 70%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.47 (s, 1H), 8.27 (d, *J* = 8.6 Hz, 2H), 7.51 (d, *J* = 8.7 Hz, 2H), 7.36 (t, *J* = 7.7 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.09 (s, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 5.87 (d, *J*= 4.0 Hz, 1H), 5.01 (d, *J* = 7.9 Hz, 1H), 3.42 (d, *J* = 16.3 Hz, 1H), 2.75 (d, *J* = 16.4 Hz, 1H), 1.35 (s, 9H); **^{13}C NMR (100 MHz,$CDCl_3$):** δ 163.6, 154.8, 148.5, 143.1, 135.6, 129.7, 129.0, 128.8, 125.2, 124.2, 118.1, 116.6, 116.5, 81.4, 54.6, 50.1, 33.8, 28.3; **HRMS (+ESI):** Calc for $C_{22}H_{23}N_4O_5$ $[M+H]^+$ 423.1663; found 423.1662; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15 *n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 14.8 min, τ_{major} = 23.8 min); Enatiomeric excess: 89%;

Tert-butyl((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(4-(trifluoromethyl)phenyl)methyl)carbamate (3j)



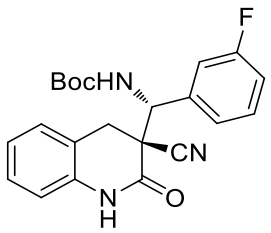
White sticky solid (52.1 mg, yield: 78%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.25 (s, 1H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.42 (d, *J* = 8.1 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.07 (d, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 5.75 (d, *J* = 4.5 Hz, 1H), 4.98 (d, *J* = 7.8 Hz, 1H), 3.40 (d, *J* = 16.3 Hz, 1H), 2.73 (d, *J* = 16.3 Hz, 1H), 1.36 (s, 10H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 163.8, 154.8, 139.9, 135.7, 131.8, 129.6, 128.9 (q, J_{C-F} = 251.2 Hz), 128.8, 128.3, 126.9, 126.0 (q, J_{C-F} = 10.5 Hz), 125.0, 118.2, 116.9, 116.4, 81.2, 54.6, 50.5, 33.8, 28.4; **HRMS (+ESI):** Calc for $C_{23}H_{23}F_3N_3O_3$ $[M+H]^+$ 446.1686; found 446.1689; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 7.9 min, τ_{major} = 12.4 min); Enatiomeric excess: 93%;

Tert-butyl ((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(m-tolyl)methyl)carbamate (3k)



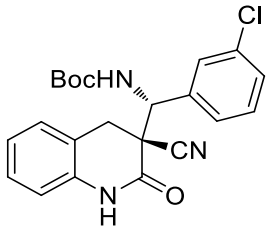
White sticky solid (44.6 mg, yield: 76%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.10 (s, 1H), 7.30 (dd, *J* = 15.2, 7.7 Hz, 2H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.04 (s, 2H), 7.02 – 6.96 (m, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 5.58 (d, *J* = 9.1 Hz, 1H), 4.90 (d, *J* = 8.7 Hz, 1H), 3.35 (d, *J* = 16.1 Hz, 1H), 2.72 (d, *J* = 16.1 Hz, 1H), 2.36 (s, 3H), 1.37 (s, 9H); **^{13}C NMR(150 MHz, $CDCl_3$):** δ 164.4, 154.9, 138.8, 136.0, 135.6, 130.2, 129.3, 129.0, 128.9, 128.4, 124.8, 124.5, 118.4, 117.5, 116.3, 80.7, 54.8, 51.1, 33.9, 28.4, 21.7; **HRMS (+ESI):** Calcfor $C_{23}H_{26}N_3O_3$ $[M+H]^+$ 392.1963; found 392.1962; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (90:10 *n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 10.4 min, τ_{major} = 18.7 min);Enatiomeric excess: 98%;

Tert-butyl ((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(3-fluorophenyl)methyl)carbamate (3l)



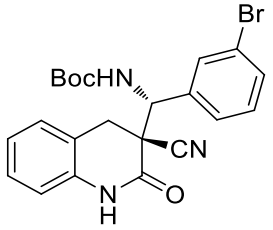
White sticky solid (45.6 mg, yield: 77%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.18 (s, 1H), 7.36 (dt, *J* = 15.1, 7.8 Hz, 2H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.12 – 7.03 (m, 3H), 6.99 (d, *J* = 9.5 Hz, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 5.66 (d, *J* = 8.5 Hz, 1H), 4.91 (d, *J* = 8.2 Hz, 1H), 3.38 (d, *J* = 16.2 Hz, 1H), 2.76 (d, *J* = 16.3 Hz, 1H), 1.37 (s, 9H); **^{13}C NMR (100 MHz,$CDCl_3$):** δ 164..0 (d, *J* = 46.5), 161.7, 154.9, 135.8, 130.7 (d, *J* = 12), 129.5, 128.9, 124.9, 123.5, 123.5, 118.3, 116.6, 116.3, 115.0 (d, *J* = 33), 81.1, 54.5, 50.7, 33.8, 28.4; **HRMS (+ESI):** Calc for $C_{22}H_{23}FN_3O_3[M+H]^+$ 396.1718; found 396.1718; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15 *n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{major} = 11.3 min, τ_{minor} = 13.7 min);Enatiomeric excess: 89%;

Tert-butyl ((R)-(3-chlorophenyl)((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)methyl)carbamate (3m)



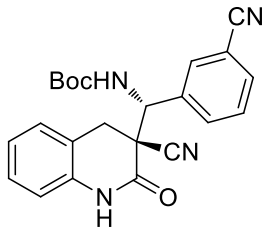
White sticky solid (45.7 mg, yield: 74%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.54 (s, 1H), 7.39 – 7.30 (m, 3H), 7.22 (d, *J* = 7.2 Hz, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 7.4 Hz, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 5.70 (d, *J* = 7.7 Hz, 1H), 4.90 (d, *J* = 8.2 Hz, 1H), 3.38 (d, *J* = 16.2 Hz, 1H), 2.75 (d, *J* = 16.3 Hz, 1H), 1.36 (s, 9H);**^{13}C NMR (100 MHz, $CDCl_3$)**: δ 164.1, 154.8, 137.9, 135.8, 134.9, 130.4, 129.6, 129.5, 128.9, 128.2, 125.8, 124.9, 118.2, 117.0, 116.5, 81.1, 54.6, 50.6, 33.9, 28.4; **HRMS (+ESI):** Calc for $C_{22}H_{23}ClN_3O_3$ $[M+H]^+$412.1422; found 412.1428; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 8.0 min, τ_{major} = 15.2 min);Enatiomeric excess: 87%;

Tert-butyl ((R)-(3-bromophenyl)((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)methyl)carbamate (3n)



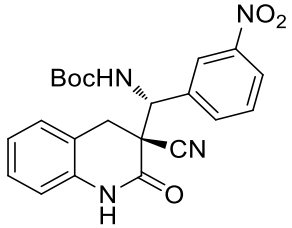
White sticky solid (49.2 mg, yield: 72%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.21 (s, 1H), 7.53 (d, *J* = 7.0 Hz, 1H), 7.33 (d, *J* = 11.5 Hz, 2H), 7.28 (d, *J* = 7.3 Hz, 2H), 7.16 (t, *J* = 7.4 Hz, 1H), 7.06 (d, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 5.65 (d, *J* = 8.5 Hz, 1H), 4.88 (d, *J* = 8.2 Hz, 1H), 3.38 (d, *J* = 16.2 Hz, 1H), 2.74 (d, *J* = 16.3 Hz, 1H), 1.37 (s, 9H); **^{13}C NMR(100 MHz, $CDCl_3$):** δ 163.9, 154.8, 138.1, 135.8, 132.5, 131.2, 130.7, 129.5, 128.9, 126.1, 124.9, 123.0, 118.2, 117.0, 116.4, 81.1, 54.5, 50.7, 33.9, 28.4; **HRMS (+ESI):** Calc for $C_{22}H_{23}BrN_3O_3$ $[M+H]^+$456.0917; found 456.0916; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 8.1 min, τ_{major} = 15.8 min);Enatiomeric excess: 87%;

Tert-butyl ((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(3-cyanophenyl)methyl)carbamate (3o)



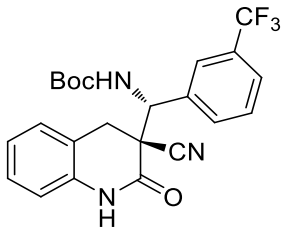
White sticky solid (39.2 mg, yield: 65%); **Diastereomeric ratio**: 4:1; **^{1}H NMR (600 MHz, $CDCl_3$)**: δ 8.42 (s, 1H), 7.70 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.62 (d, *J* = 6.9 Hz, 1H), 7.59 – 7.47 (m, 2H), 7.36 (t, *J* = 7.7 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 7.3 Hz, 1H), 6.96 (d, *J* = 7.8 Hz, 1H), 5.79 (d, *J* = 6.4 Hz, 1H), 4.95 (d, *J* = 7.5 Hz, 1H), 3.42 (d, *J* = 16.3 Hz, 1H), 2.74 (d, *J* = 16.3 Hz, 1H), 1.36 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$):**δ 163.7, 154.8, 137.8, 135.6, 133.0, 132.1, 131.6, 130.0, 129.7, 128.7, 125.3, 118.3, 118.1, 116.7, 116.5, 113.2, 81.4, 54.5, 50.2, 33.9, 28.3; **HRMS (+ESI):** Calc for $C_{23}H_{22}N_4NaO_4$ $[M+H]^+$ 403.1765; found 403.1781; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{major} = 12.4 min, τ_{minor} = 19.0 min); Enatiomeric excess: 93%;

Tert-butyl ((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(3-nitrophenyl)methyl)carbamate (3p)



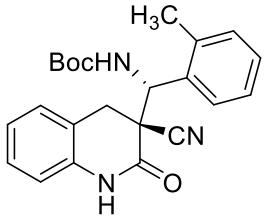
White sticky solid (41.8 mg, yield: 66%); **Diastereomeric ratio**: 4:1; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 8.43 (s, 1H), 8.27 (d, *J* = 8.1 Hz, 1H), 8.12 (s, 1H), 7.76 (d, *J* = 6.2 Hz, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.13 (d, *J* = 7.1 Hz, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 5.89 (s, 1H), 5.04 (d, *J* = 7.9 Hz, 1H), 3.43 (d, *J* = 16.3 Hz, 1H), 2.79 (d, *J* = 16.2 Hz, 1H), 1.37 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$):**δ 163.7, 154.9, 148.3, 138.2, 135.5, 133.5, 130.3, 129.7, 128.9, 125.3, 124.3, 123.3, 118.1, 116.6, 81.4, 54.6, 50.2, 33.9, 28.3; **HRMS (+ESI):** Calc for $C_{22}H_{23}N_4O_5$ $[M+H]^+$423.1662; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm,τ_{minor} = 13.1 min, τ_{major} = 20.6 min);Enatiomeric excess: 90%;

tert-butyl ((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(3-(trifluoromethyl)phenyl)methyl)carbamate (3q)



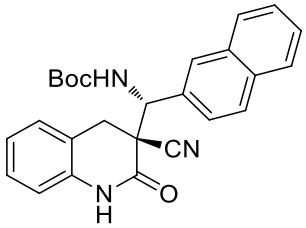
White sticky solid (52.7 mg, yield: 79%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.24 (s, 1H), 7.64 (dd, *J* = 36.2, 6.0 Hz, 3H), 7.38 (dd, *J* = 17.1, 9.5 Hz, 2H), 7.24 – 7.12 (m, 1H), 7.06 (s, 1H), 7.02 – 6.90 (m, 1H), 5.75 (d, *J* = 7.5 Hz, 1H), 5.00 (d, *J* = 2.8 Hz, 1H), 3.41 (d, *J* = 16.2 Hz, 1H), 2.69 (d, *J* = 16.5 Hz, 1H), 1.38 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$):** δ 163.8, 154.9, 136.9, 135.8, 131.3, 131.1, 130.7, 129.8, 129.6, 128.9, 126.2 (q, $J_{C\text{-}F}$ = 6 Hz), 125.7 (q, $J_{C\text{-}F}$ = 262.5 Hz), 125.3 (q, $J_{C\text{-}F}$ = 3 Hz), 118.1, 116.9, 116.4, 81.2, 54.7, 50.7, 33.9, 28.3; **HRMS (+ESI):** Calc for $C_{23}H_{23}F_3N_3O_3$ $[M+H]^+$ 446.1686; found 446.1687; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15 *n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 6.4 min, τ_{major} = 10.4 min); Enatiomeric excess: 90%;

Tert-butyl ((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(o-tolyl)methyl)carbamate (3r)



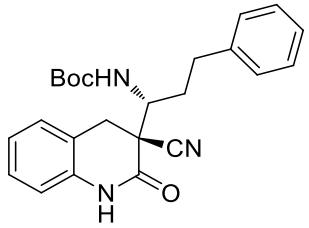
White sticky solid (32.3 mg, yield: 55%); **Diastereomeric ratio**: 3:1; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 8.10 (s, 1H), 7.83 (d, *J* = 7.7 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.26 – 7.23 (m, 2H), 7.11 (d, *J* = 7.7 Hz, 1H), 7.00 (t, *J* = 7.4 Hz, 1H), 6.93 (t, *J* = 8.2 Hz, 1H), 6.78 (d, *J* = 7.3 Hz, 1H), 5.37 (dd, *J* = 45.3, 8.3 Hz, 2H), 3.40 (d, *J* = 16.1 Hz, 1H), 2.79 (d, *J* = 16.1 Hz, 1H), 1.65 (s, 3H), 1.38 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$):** δ 164.5, 155.0, 136.0, 134.9, 131.5, 129.2, 129.0, 128.8, 127.3, 125.8, 124.4, 118.7, 118.6, 116.1, 80.7, 50.7, 34.1, 28.4, 18.9; **HRMS (+ESI):** Calcfor $C_{23}H_{26}N_3O_3$ $[M+H]^+$ 392.1963; found 392.1968; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15 *n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 8.2 min, τ_{major} = 10.5 min); Enatiomeric excess: 48%;

Tert-butyl ((R)-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(naphthalen-2-yl)methyl)carbamate (3s)



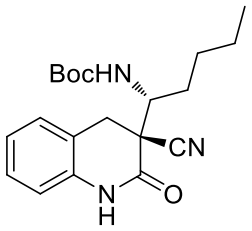
White sticky solid (49.9 mg, yield: 78%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.22 (s, 1H), 7.88 (dd, *J* = 12.2, 7.0 Hz, 2H), 7.84 – 7.78 (m, 1H), 7.65 (s, 1H), 7.57 – 7.47 (m, 2H), 7.45 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 7.06 – 6.93 (m, 2H), 5.76 (d, *J* = 8.9 Hz, 1H), 5.11 (d, *J* = 8.8 Hz, 1H), 3.36 (d, *J* = 16.2 Hz, 1H), 2.73 (d, *J* = 16.2 Hz, 1H), 1.37 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)**:δ 164.2, 155.0, 136.0, 133.7, 133.1, 129.4, 129.1, 129.0, 128.4, 128.0, 127.6, 127.0, 126.9, 124.6, 118.5, 117.5, 116.3, 80.9, 55.2, 53.6, 33.9, 28.4; **HRMS (+ESI):** Calc for $C_{26}H_{26}N_3O_3$ $[M+H]^+$428.1969; found 412.19.70; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 10.3 min, τ_{major} = 16.8 min); Enatiomeric excess: 98%;

Tert-butyl ((R)-1-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-3-phenylpropyl)carbamate (3t)



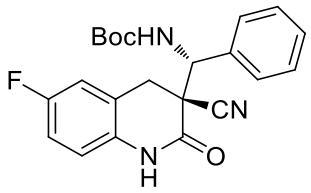
White sticky solid (33.4 mg, yield: 55%); **Diastereomeric ratio**: 3:1; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.79 (s, 1H), 7.24 (d, *J* = 7.5 Hz, 3H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.11 (dd, *J* = 13.9, 7.4 Hz, 3H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 4.90 (d, *J* = 10.4 Hz, 1H), 4.11 – 3.99 (m, 1H), 3.35 – 3.21 (m, 2H), 2.78 (dd, *J* = 21.0, 7.1 Hz, 1H), 2.60 – 2.48 (m, 1H), 2.20 (dd, *J* = 14.6, 7.3 Hz, 2H), 1.42 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 163.9, 155.8, 140.7, 135.5, 129.0, 128.7, 128.6, 128.5, 126.4, 124.6, 119.7, 117.5, 115.8, 80.5, 52.2, 49.4, 34.5, 33.8, 32.5, 28.5; **HRMS (+ESI):** Calc for $C_{24}H_{28}N_3O_3$$[M+H]^+$406.2125; found 406.2127; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak ID column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{major} = 22.3 min, τ_{minor} = 30.0 min);Enatiomeric excess: 71%;

Tert-butyl ((R)-1-((R)-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)pentyl)carbamate (3u)



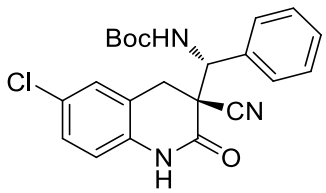
Brown sticky solid (28.9 mg, yield: 54%); **Diastereomeric ratio**: 3:1; **^{1}H NMR (400 MHz, $CDCl_3$)**:δ 8.02 (s, 1H), 7.28 – 7.24 (m, 2H), 7.20 (d, *J* = 7.3 Hz, 1H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.85 (d, *J* = 7.8 Hz, 1H), 4.81 (d, *J*= 10.4 Hz, 1H), 4.07 – 3.94 (m, 1H), 3.33 (q, *J*= 16.0 Hz, 2H), 1.91 – 1.78 (m, 2H), 1.43 (dd, *J* = 7.9, 6.3 Hz, 2H), 1.40 (s, 9H), 1.29 (d, *J* = 4.7 Hz, 2H), 0.87 (d, *J* = 4.4 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 164.2, 156.0, 135.7, 129.1, 128.5, 124.5, 119.8, 117.7, 115.9, 80.3, 52.6, 49.5, 34.6, 31.5, 28.4, 28.3, 22.3, 14.1; **HRMS (+ESI):** Calc for $C_{20}H_{28}N_3O_3$ $[M+H]^+$ 358.2125; found 358.2129; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IE column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{major} = 20.9 min, τ_{minor} = 24.4 min); Enatiomeric excess: 67%;

Tert-butyl ((R)-((R)-3-cyano-6-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(phenyl)methyl)carbamate (3v)



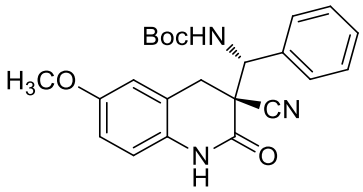
White sticky solid (44.4 mg, yield: 75%);**Diastereomeric ratio**: 5:1; **^{1}H NMR (600 MHz, $CDCl_3$)**: δ 8.35 (s, 1H), 7.51 – 7.33 (m, 3H), 7.29 – 7.26 (m, 2H), 7.04 (t, *J* = 8.4 Hz, 1H), 6.94 (dt, *J* = 8.7, 4.4 Hz, 1H), 6.76 (d, *J* = 7.2 Hz, 1H), 5.60 (d, *J* = 8.9 Hz, 1H), 4.94 (d, *J* = 7.3 Hz, 1H), 3.34 (d, *J* = 16.3 Hz, 1H), 2.70 (d, *J* = 16.3 Hz, 1H), 1.36 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$)**: δ 163.9 (d, *J* = 9 Hz), 160.2, 158.6, 155.0, 135.5, 132.3, 129.6, 129.2, 127.7, 120.2 (d, *J* = 7.5 Hz), 117.6 (d, *J* = 7.5 Hz), 116.2, 116.0, 115.9, 115.8, 80.9, 54.9, 50.8, 33.8, 28.4; **HRMS (+ESI):** Calc for $C_{22}H_{23}FN_3O_3$ $[M+H]^+$ 396.1718; found 396.1724; The enantiomeric ratio was determined by HPLC analysis using Phenomenex Lux C1 column (90:10 *n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{major} = 10.6 min, τ_{minor} = 13.3 min); Enatiomeric excess: 92%;

Tert-butyl ((R)-((R)-6-chloro-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(phenyl)methyl)carbamate (3w)



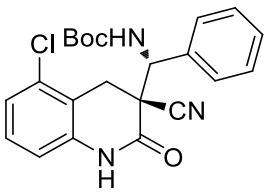
White sticky solid (43.7 mg, yield: 71%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.08 (s, 1H), 7.42 (dd, *J* = 5.0, 1.7 Hz, 3H), 7.30 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.27 (s, 2H), 7.02 (s, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 5.56 (d, *J* = 9.2 Hz, 1H), 4.94 (d, *J* = 7.9 Hz, 1H), 3.33 (d, *J* = 16.3 Hz, 1H), 2.70 (d, *J* = 16.3 Hz, 1H), 1.36 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$)**:δ 163.8, 155.0, 135.4, 134.7, 129.6, 129.3, 129.3, 128.8, 127.7, 120.1, 117.4, 117.2, 80.9, 55.0, 50.9, 33.7, 28.4; **HRMS (+ESI):** Calc for $C_{22}H_{23}ClN_3O_3$ $[M+H]^+$ 412.1422; found 412.1426; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (88:12*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 10.8 min, τ_{major} = 23.5 min) Enatiomeric excess: 93%.

Tert-butyl ((R)-((R)-3-cyano-6-methoxy-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(phenyl)methyl)carbamate (3x)



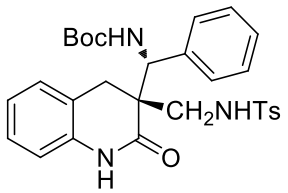
White sticky solid (47.6 mg, yield: 78%); **Diastereomeric ratio**: 6:1; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.65 (s, 1H), 7.48 – 7.35 (m, 3H), 7.29 (dd, *J* = 6.6, 2.8 Hz, 2H), 6.93 (dd, *J* = 13.1, 8.7 Hz, 1H), 6.85 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.58 (s, 1H), 5.70 (d, *J* = 8.6 Hz, 1H), 4.94 (d, *J* = 8.0 Hz, 1H), 3.81 (s, 3H), 3.32 (d, *J* = 16.2 Hz, 1H), 2.69 (d, *J* = 16.3 Hz, 1H), 1.35 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 164.1, 156.7, 154.9, 135.9, 129.4, 129.0, 127.8, 119.8, 117.5, 117.4, 114.8, 114.0, 80.7, 55.9, 54.9, 50.9, 34.1, 28.4; **HRMS (+ESI):** Calc for $C_{23}H_{26}N_3O_4$ $[M+H]^+$408.1918; found 408.1926; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{major} = 10.6 min, τ_{minor} = 17.5 min);Enatiomeric excess: 92%.

Tert-butyl ((R)-((R)-5-chloro-3-cyano-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(phenyl)methyl)carbamate (3y)



White sticky solid (43.1 mg, yield: 70%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (600 MHz, $CDCl_3$)**: δ 8.26 (d, *J* = 22.6 Hz, 1H), 7.41 (dd, *J* = 5.0, 1.7 Hz, 2H), 7.29 – 7.24 (m, 2H), 7.22 (dd, *J* = 6.6, 2.8 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 1H), 6.91 – 6.85 (m, 1H), 5.59 (d, *J* = 9.2 Hz, 1H), 4.95 (d, *J* = 8.6 Hz, 1H), 3.16 (s, 2H), 1.37 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$)**: δ 164.0, 155.0, 137.4, 135.1, 134.1, 130.0, 129.5, 129.4, 127.7, 125.4, 117.1, 116.9, 114.8, 80.9, 55.2, 51.4, 31.1, 28.4; **HRMS (+ESI):** Calc for $C_{22}H_{23}ClN_3O_3$ $[M+H]^+$ 412.1422; found 412.1418; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (85:15*n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm,τ_{minor} = 7.2 min, τ_{major} = 10.7 min);Enatiomeric excess: 84%.

G.*Tert-butyl((R)-((S)-3-((4-methylphenylsulfonamido)methyl)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)(phenyl)methyl)carbamate(5)*



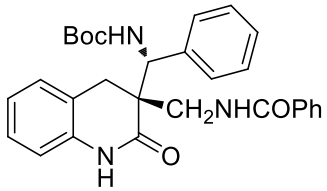
General procedure for the synthesis of compound 5:

Under argon atmosphere, 3a (0.15 mmol) in Et_2O (1.5 ml) was added suspension solution $LiAlH_4$(0.9 mmol) in 1 ml Et_2O at 0 ^oC. The mixture was allowed to warm at ambient temperature and stirred for 4h. Next water (20 µl), 15% aqueous NaOH (20 µl) and water (60 µl) were sequentially added dropwise at 0 ^oC, the mixture was allowed stirred at room temperature for 15 min. Then the reaction mixture was filtered through a celite pad, the celite pad was washed with ether. The filtrate concentrated in vacuo and the corresponding amine was used for the next step without further purification.

To a round-bottom flask were added sequentially amine (0.1 mmol), CH_2Cl_2 (3 ml), Et_3N (0.1 mmol) and TsCl (0.1 mmol). the reaction was stirred for 24 h at room temperature. Then the mixture was poured into water (2 ml) and the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 twice. The combined organic layers were dried over Na_2SO_4 and evaporated. The crude product was purified by column chromatography using 30% ethyl acetate in hexane.

White sticky solid (36.1 mg, yield: 45%);**Diastereomeric ratio**: 5:1; **^{1}H NMR (600 MHz, $CDCl_3$)**: δ 9.03 (s, 1H), 7.69 (d, *J* = 8.1 Hz, 2H), 7.32 (dd, *J* = 15.2, 7.2 Hz, 5H), 7.18 (t, *J* = 6.9 Hz, 2H), 7.07 (t, *J* = 6.7 Hz, 3H), 6.79 (d, *J* = 8.0 Hz, 1H), 5.73 (s, 1H), 4.77 (s, 1H), 3.43 (d, *J* = 17.3 Hz, 2H), 2.67 (dd, *J* = 12.8, 9.2 Hz, 1H), 2.58 (d, *J* = 16.9 Hz, 1H), 2.45 (s, 3H), 1.34 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$)**: δ 172.8, 155.1, 149.2, 143.7, 136.8, 135.7, 130.1, 129.3, 129.0, 128.9, 128.5, 128.3, 128.0, 127.9, 127.2, 124.5, 116.1, 79.9, 60.6, 55.2, 49.0, 44.9, 28.5, 21.8; **HRMS (+ESI):** Calc for $C_{29}H_{33}N_2O_5S$ $[M+H]^+$ 536.2214; found 536.2222; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (70:30 *n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 18.3min,τ_{major} = 28.5 min); Enatiomeric excess: 98%.

H. *Tert-butyl((R)-((S)-2-oxo-3-(2-oxo-2-phenylethyl)-1,2,3,4-tetrahydroquinolin-3-yl)(phenyl)methyl)carbamate(6)*



General procedure for the synthesis of compound 6:

Under argon atmosphere, 3a (0.15 mmol) in Et_2O (1.5 ml) was added suspension solution $LiAlH_4$(0.9 mmol) in 1 ml Et_2O at 0 ^oC. The mixture was allowed to warm at ambient temperature and stirred for 4h. Next water (20 µl), 15% aqueous NaOH (20 µl) and water (60 µl) were sequentially added dropwise at 0 ^oC, the mixture was allowed stirred at room temperature for 15 min. Then the reaction mixture was filtered through a celite pad, the celite pad was washed with ether. The filtrate concentrated in vacuo and the corresponding amine was used for the next step without further purification.

To a round-bottom flask were added sequentially amine (0.1 mmol), CH_2Cl_2 (3 ml), Et_3N (0.1 mmol) and PhCOCl (0.1 mmol). the reaction was stirred for 24 h at room temperature. Then the mixture was poured into water (2 ml) and the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 twice. The combined organic layers were dried over Na_2SO_4 and evaporated. The crude product was purified by column chromatography using 30% ethyl acetate in hexane.

White sticky solid (30.5 mg, yield: 42%); **Diastereomeric ratio**: 5:1; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 8.17 (s, 1H), 8.11 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 2H), 7.29 (d, *J* = 7.1 Hz, 1H), 7.20 (dd, *J* = 17.1, 8.7 Hz, 3H), 7.15 (d, *J* = 7.2 Hz, 1H), 7.05 (t, *J* = 7.3 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 5.59 (s, 1H), 5.11 (s, 1H), 3.99 – 3.86 (m, 1H), 3.65 (d, *J* = 6.4 Hz, 1H), 2.95 (d, *J* = 15.6 Hz, 1H), 2.81 (d, *J* = 16.6 Hz, 1H), 1.37 (s, 9H); **^{13}C NMR (150 MHz, $CDCl_3$):** δ 172.6, 167.9, 155.6, 135.9, 134.2, 133.5, 131.8, 130.3, 129.0, 128.7, 128.7, 128.6, 128.3, 128.2, 127.2, 124.2, 115.4, 80.4, 55.3, 50.1, 40.9, 31.8, 28.5; **HRMS (+ESI):** Calc for $C_{29}H_{32}N_3O_4$ $[M+H]^+$ 486.2387; found 486.2388; The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (70:30 *n*-Hexane/2-PrOH, 1.0 mL/min, 25 °C, 254 nm, τ_{minor} = 10.8 min, τ_{major} = 27.3 min); Enatiomeric excess: 98%.

I. References:

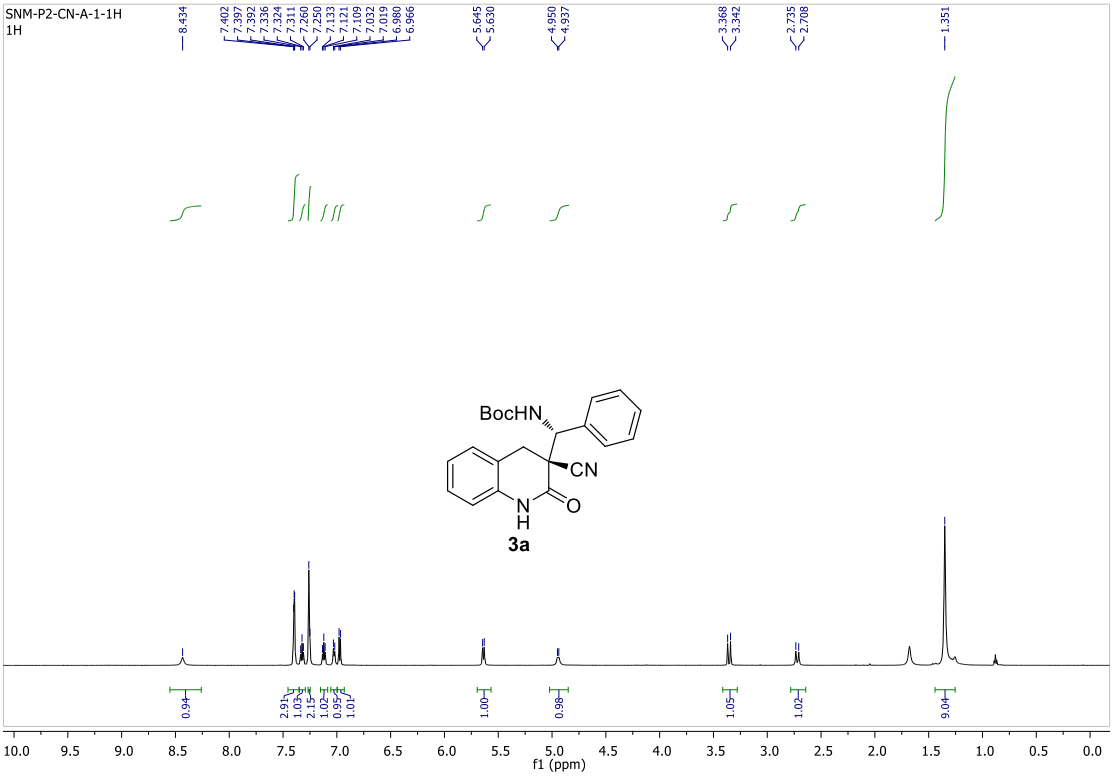
1 (*a*) A. G. Wenzel, E. N. Jacobsen, *J. Am. Chem. Soc.*,2002, **124**, 12964; (*b*) J. W. Yang, S. C. Pan, B. List, *Org. Synth.*,2009, **86**, 11; (*c*) A. S. Tsai, M. E. Tauchert, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc*.,2011, **133**, 1248.

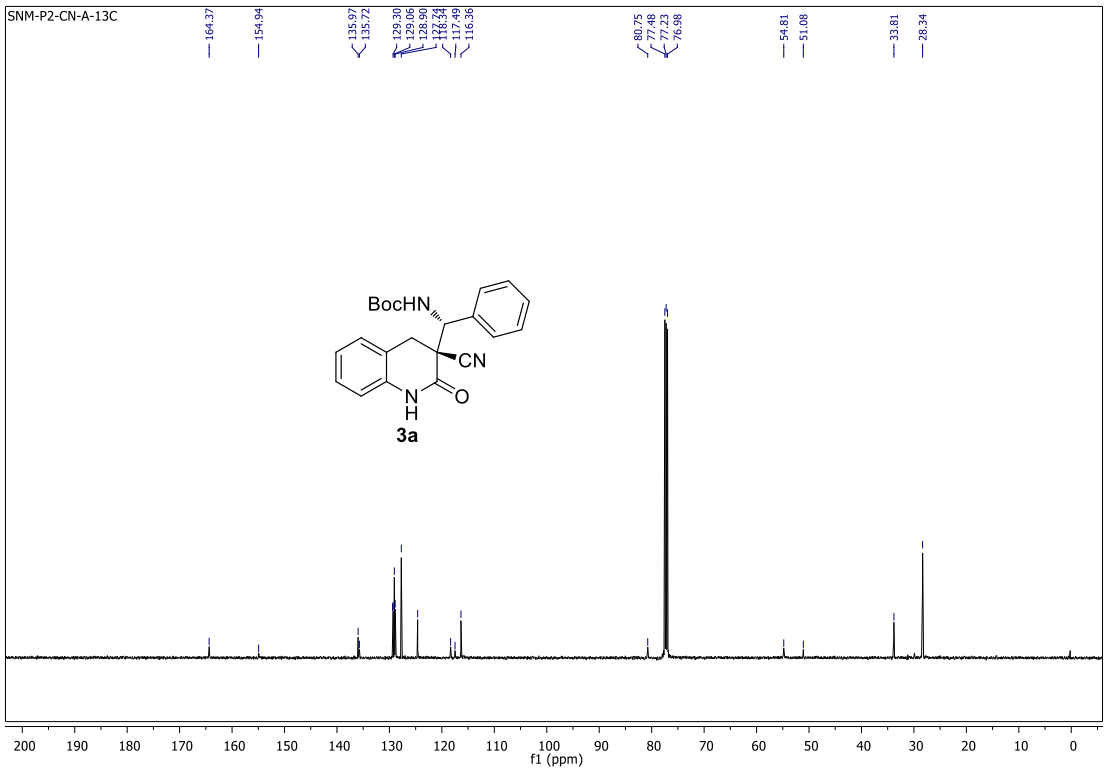
2 B. Nammalwar, R. A. Bunce, J. T. Hiett, *Org. Prep. Proc. Int*.,2015, **47**, 338.

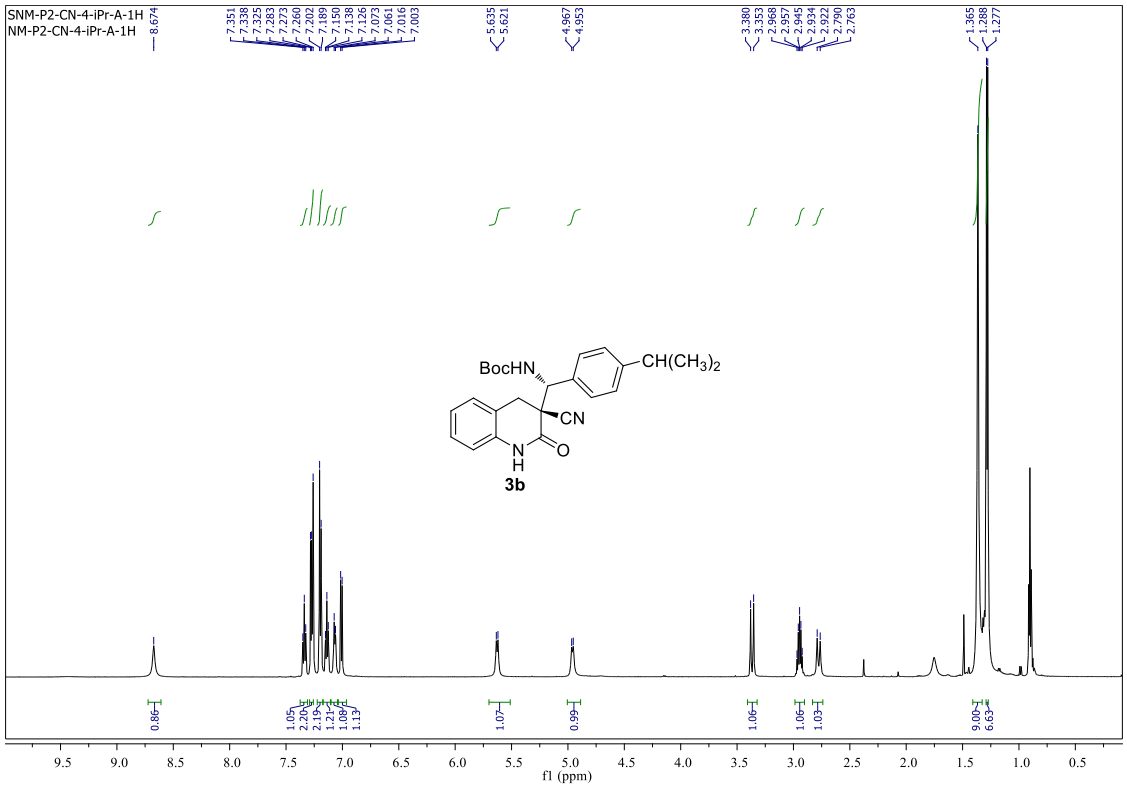
3 (*a*) A. Berkessel, S. Mukherjee, T. N. Muller, F. Cleemann, K. Roland, M. Brandenburg, J.-M. Neudorfl, J. Lex, *Org. Biomol. Chem*.,2006, **4**, 4319; (*b*) B. Vakulya, S. Varga, A. Csámpai, T. Soós, *Org. Lett*.,**2005**, *7*, 1967; (*c*) M. S. Manna, V. Kumar, S. Mukherjee, *Chem. Commun*.,**2012**, *48*, 5193; (*d*) C. B. Tripathi, S. Kayal, and S. Mukherjee, *Org. Lett*.,**2012**, *14*, 3296; (*e*) Y. Gao, Q. Ren, L. Wang and J. Wang, *Chem. Eur. J.*, **2010**, *16*, 13068.

4 K. S. Yang, A. E. Nibbs, Y. E. Turkmen and V. H. Rawal, *J. Am. Chem. Soc*.,2013, **135**, 16.

J. NMR Spectra of compounds (3a-3x):



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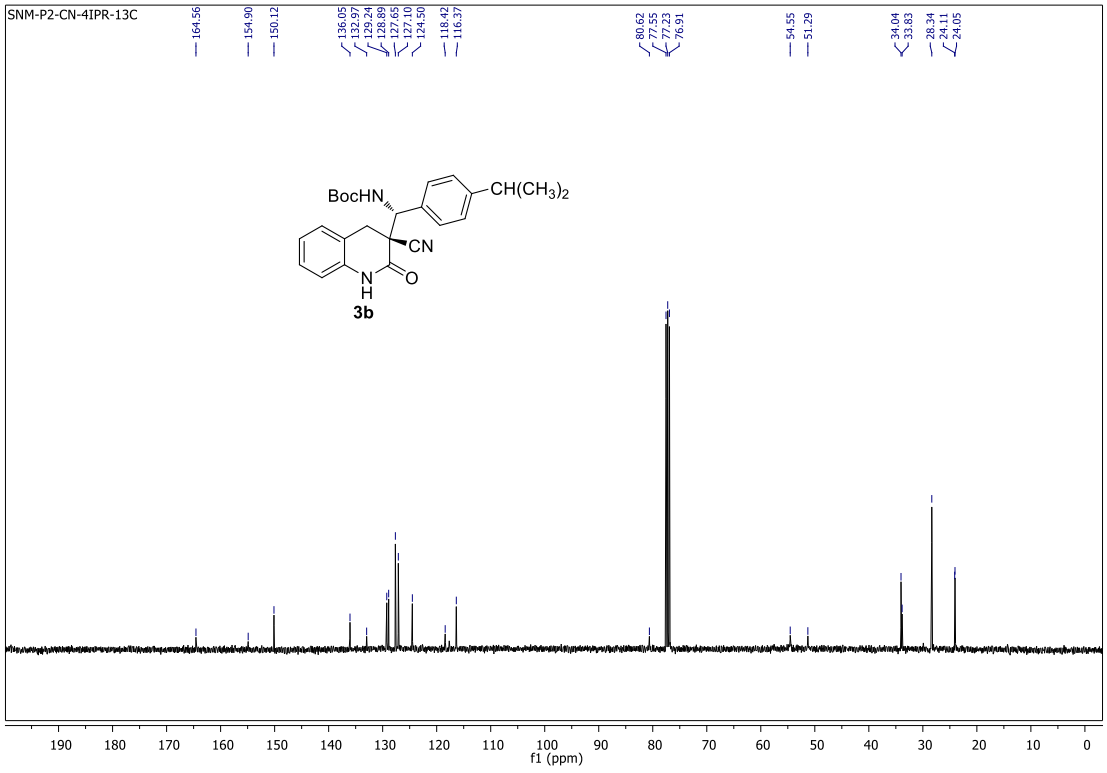
CN
N
H
O
3b
f1 (ppm)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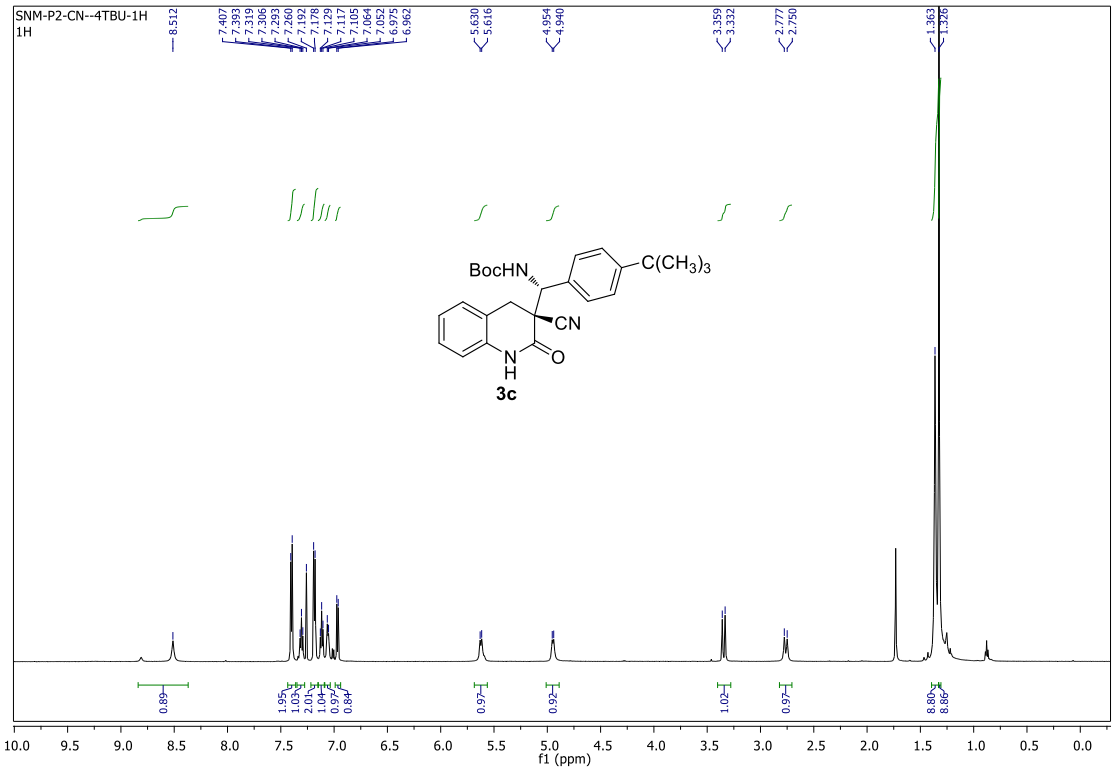
CN
N
H
O
3b
f1 (ppm)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7.393
7.319
7.306
7.293
7.260
7.192
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4.954
4.940
3.359
3.332
2.777
2.750
1.363
1.326
BocHN
C(CH3)3
CN
N
H
O
3c
0.89
1.95
1.03
2.01
1.04
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0.97
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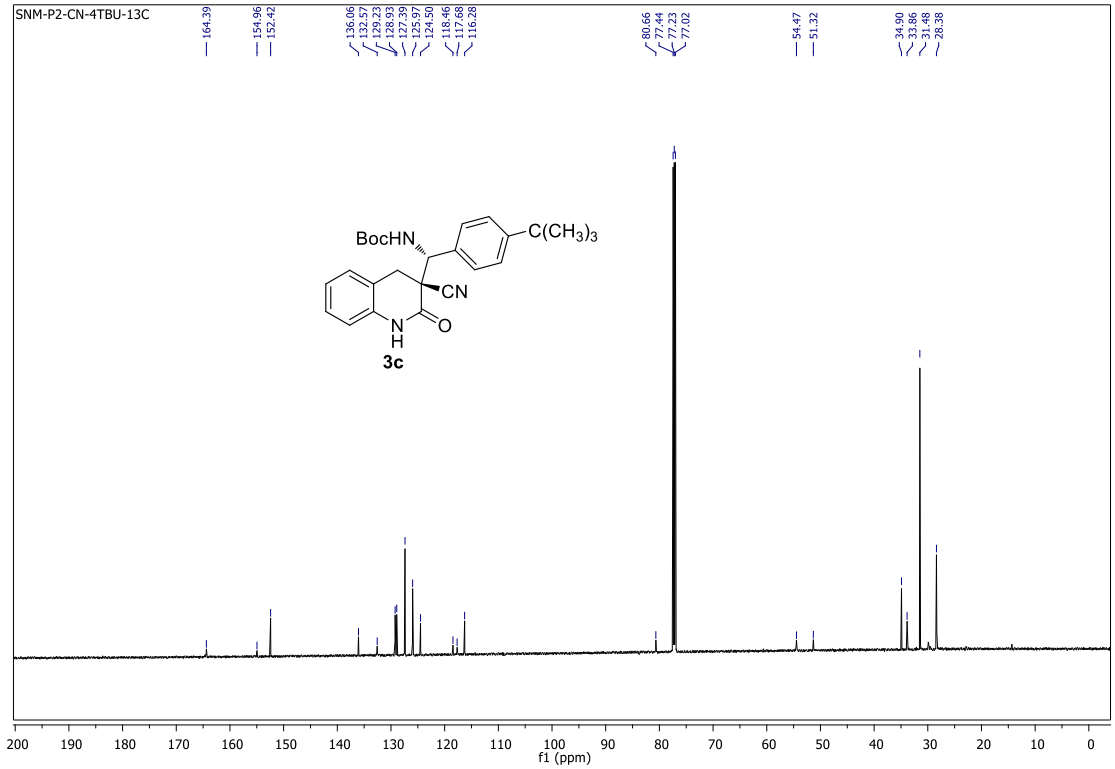
0.97
8.80
8.86
f1 (ppm)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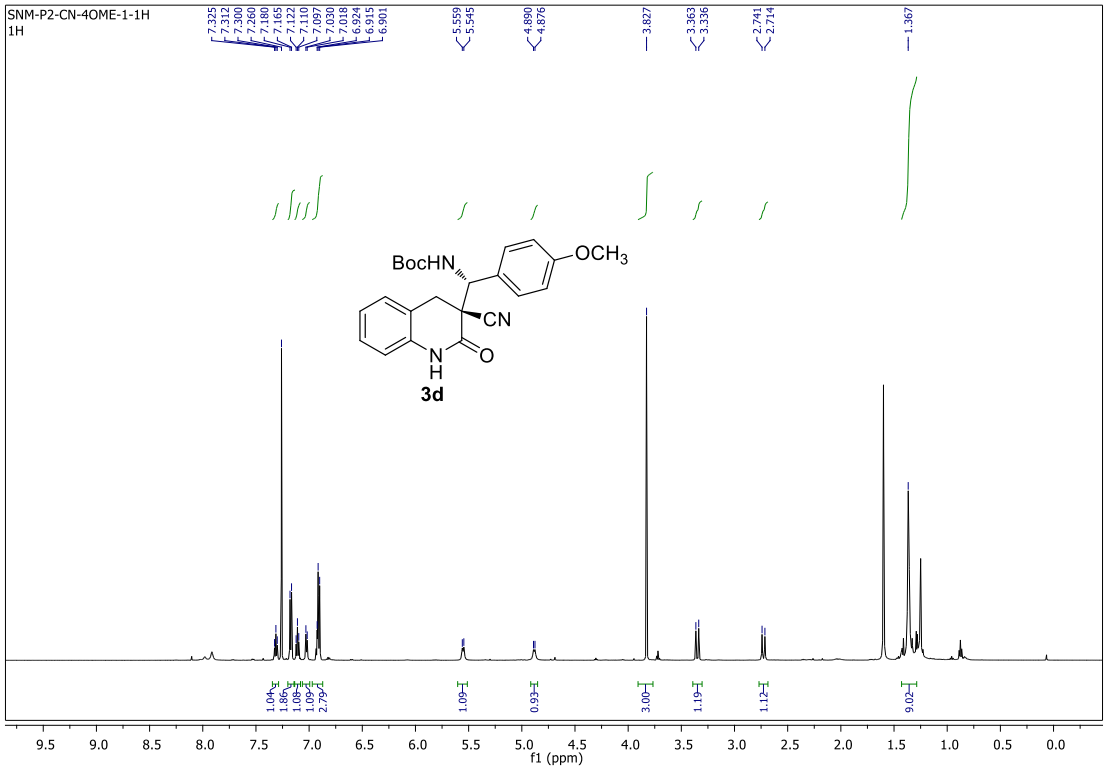
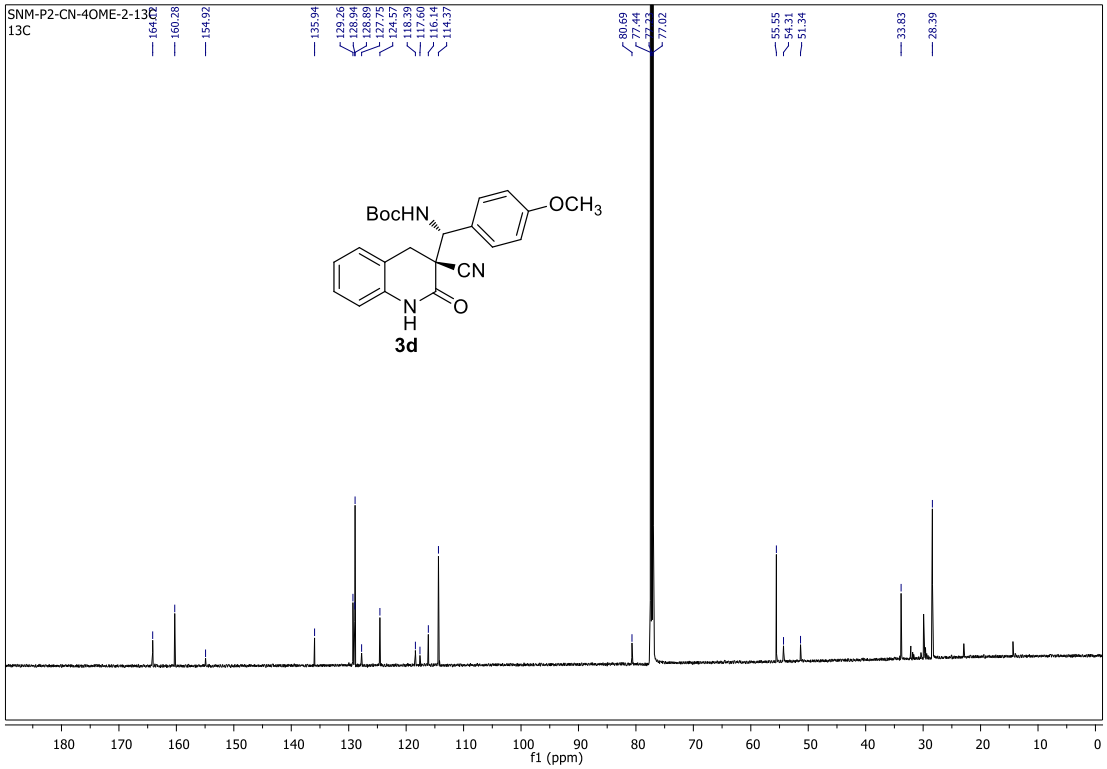
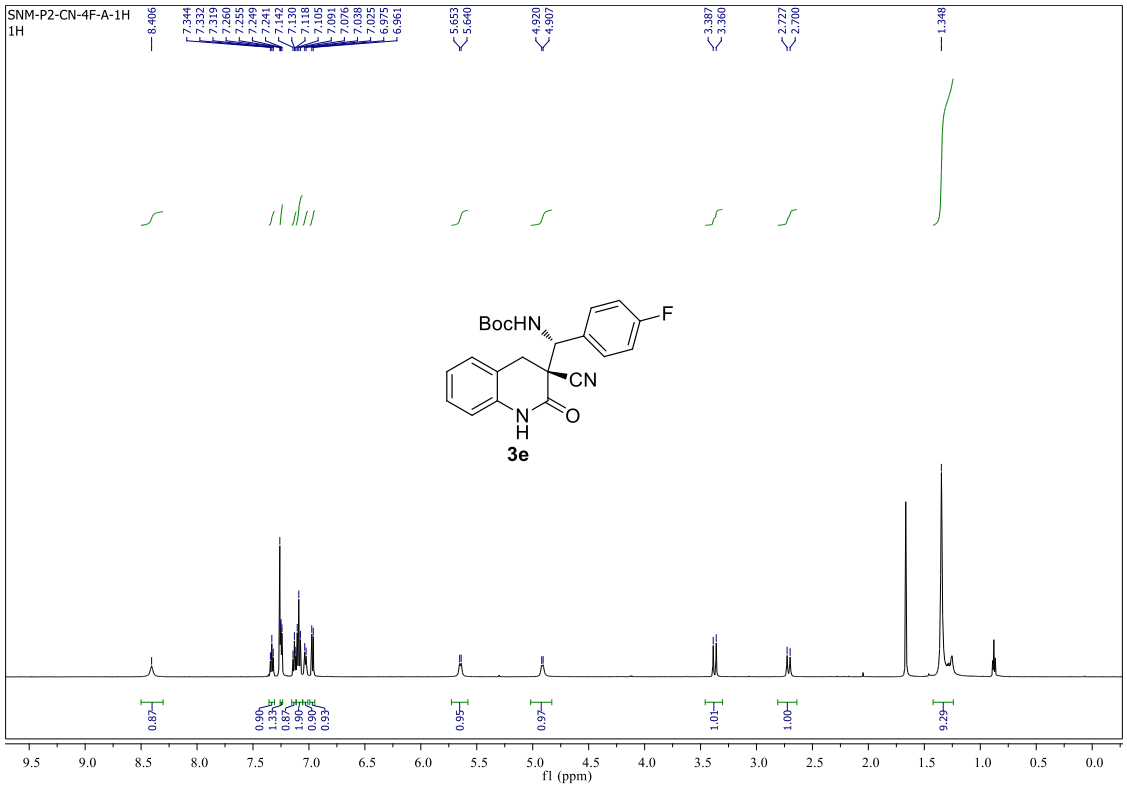
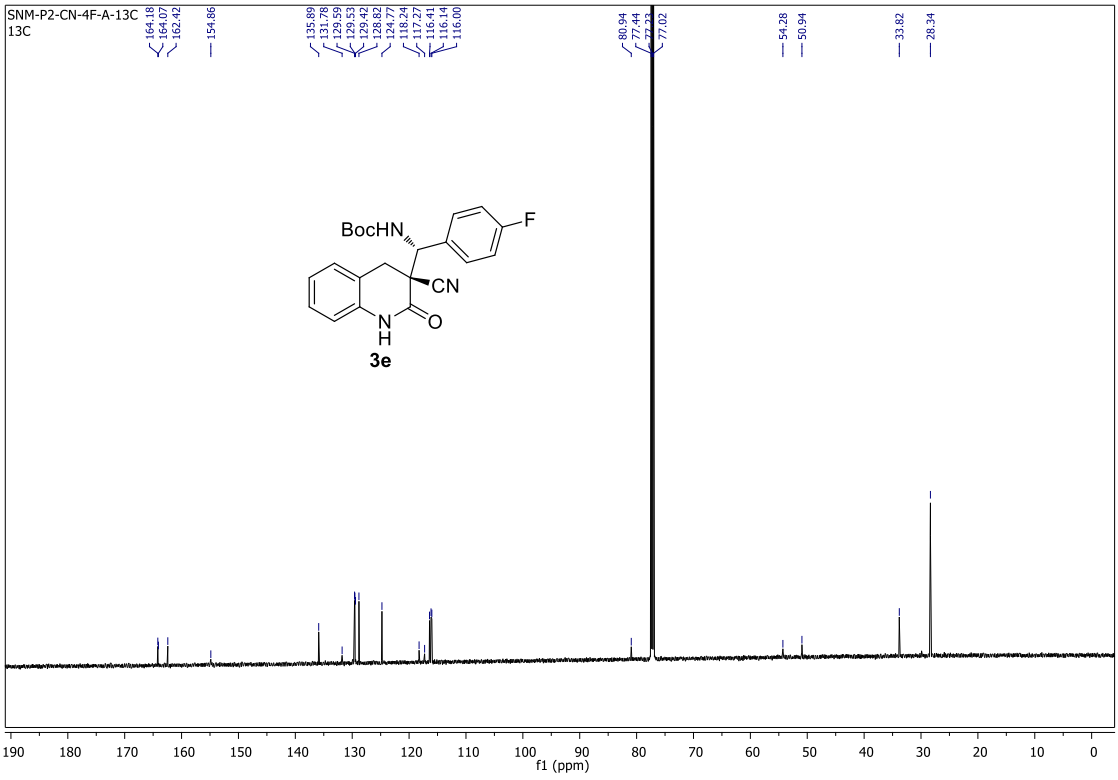
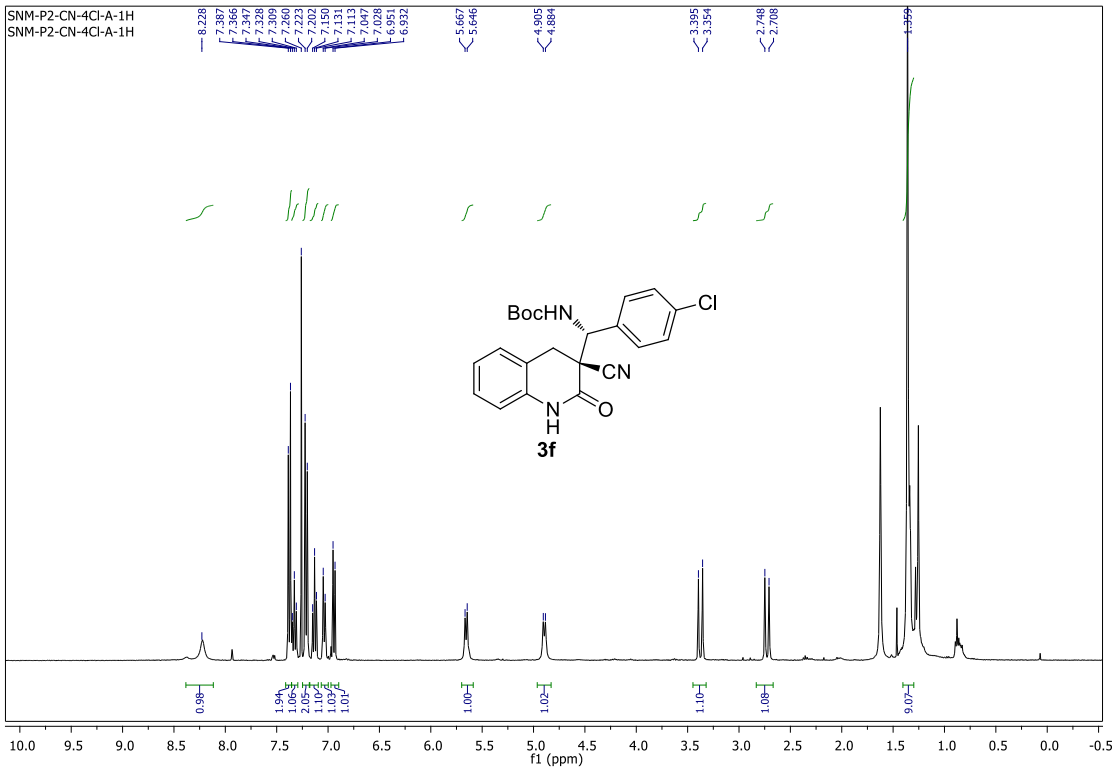
77.44
77.23
77.02
54.47
51.32
34.90
33.86
31.48
28.38
BocHN
C(CH3)3
CN
N
H
O
3c
f1 (ppm)

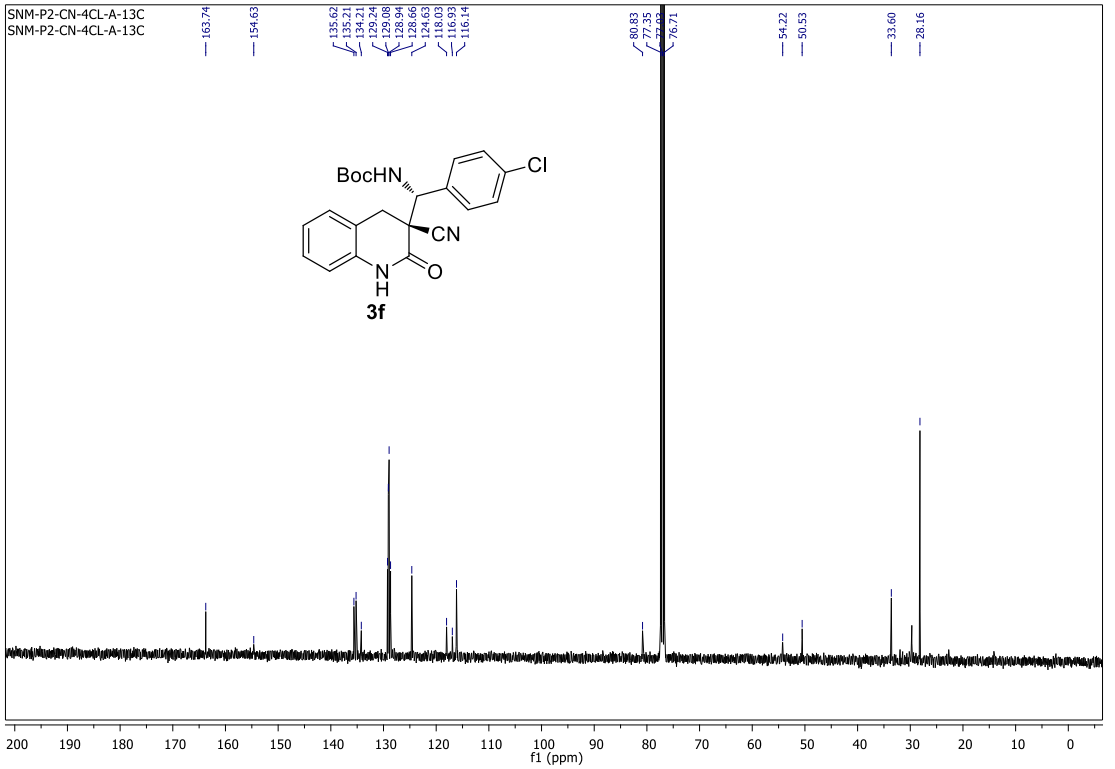

SNM-P2-CN-4OME-1-1H
1H
BocHN
OCH3
CN
N
H
O
3d
f1 (ppm)

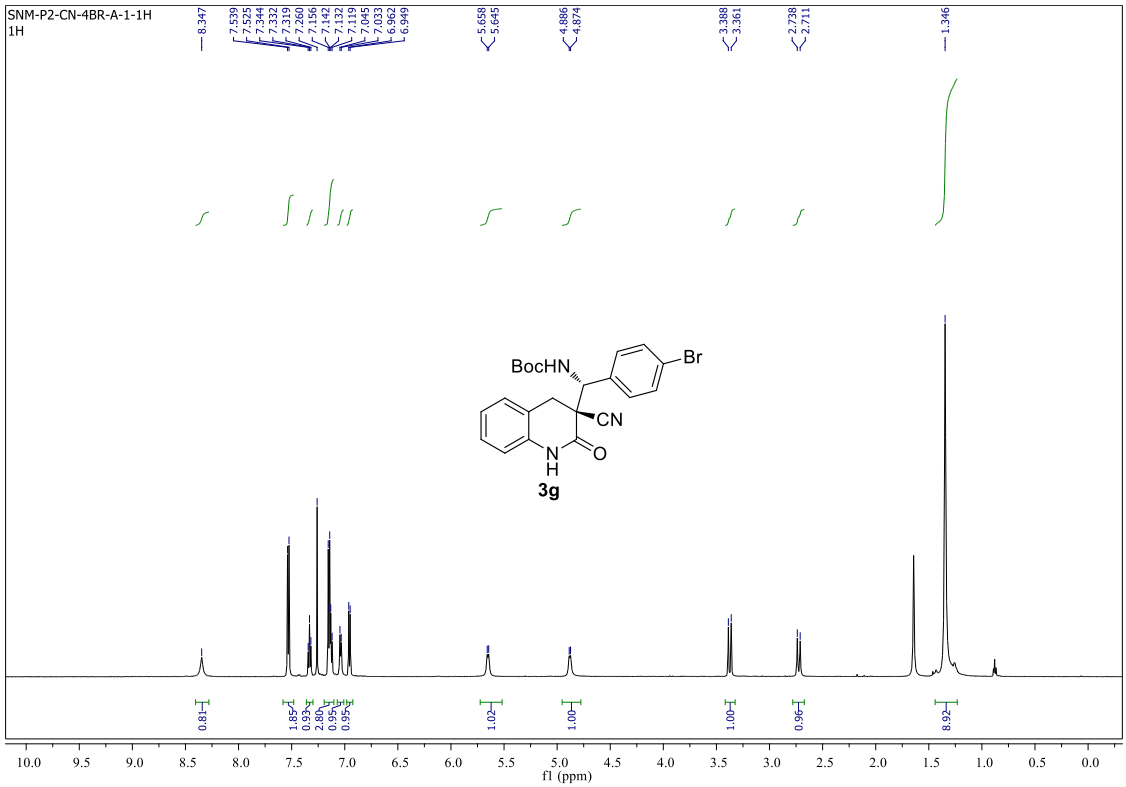

SNM-P2-CN-4OME-2-13C
13C
BocHN
OCH3
CN
N
H
O
3d
f1 (ppm)

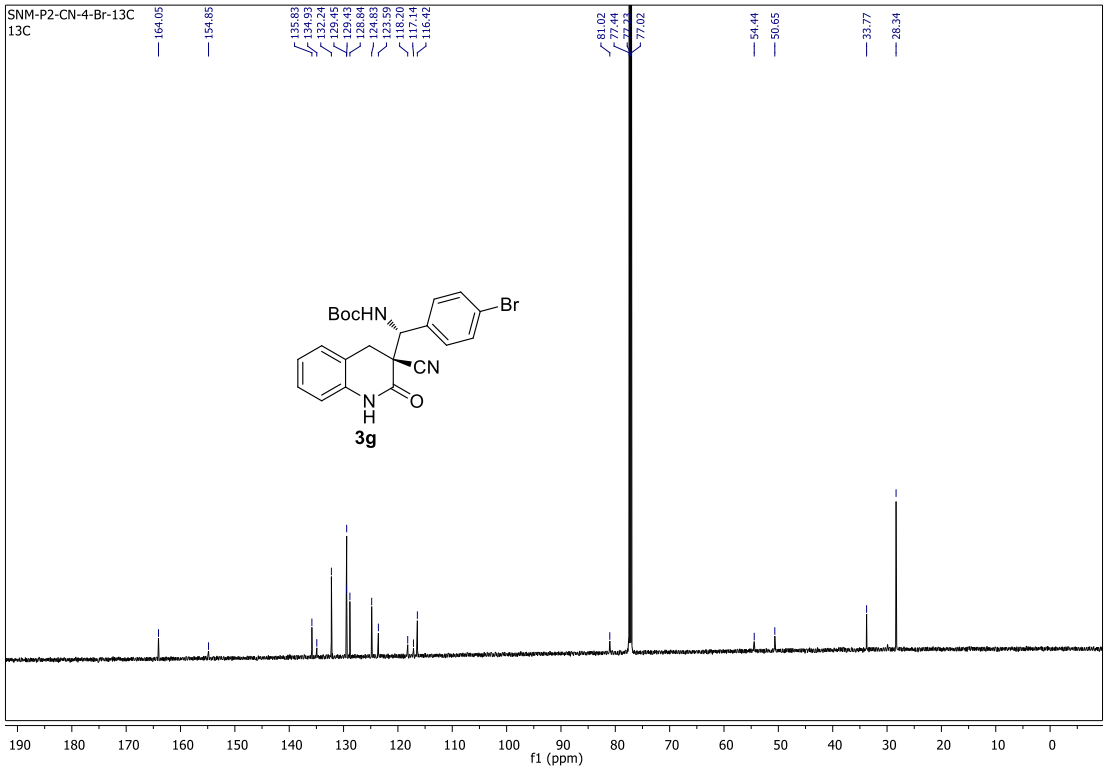

SNM-P2-CN-4F-A-1H
1H
8.406
7.344
7.332
7.319
7.260
7.255
7.249
7.241
7.143
7.130
7.118
7.105
7.091
7.076
7.038
7.025
6.975
6.961
5.653
5.640
4.920
4.907
3.387
3.360
2.727
2.700
1.348
BocHN
F
CN
N
H
O
3e
0.87
0.90
1.33
0.87
1.90
0.90
0.93
0.95
0.97
1.01
1.00
9.29
f1 (ppm)

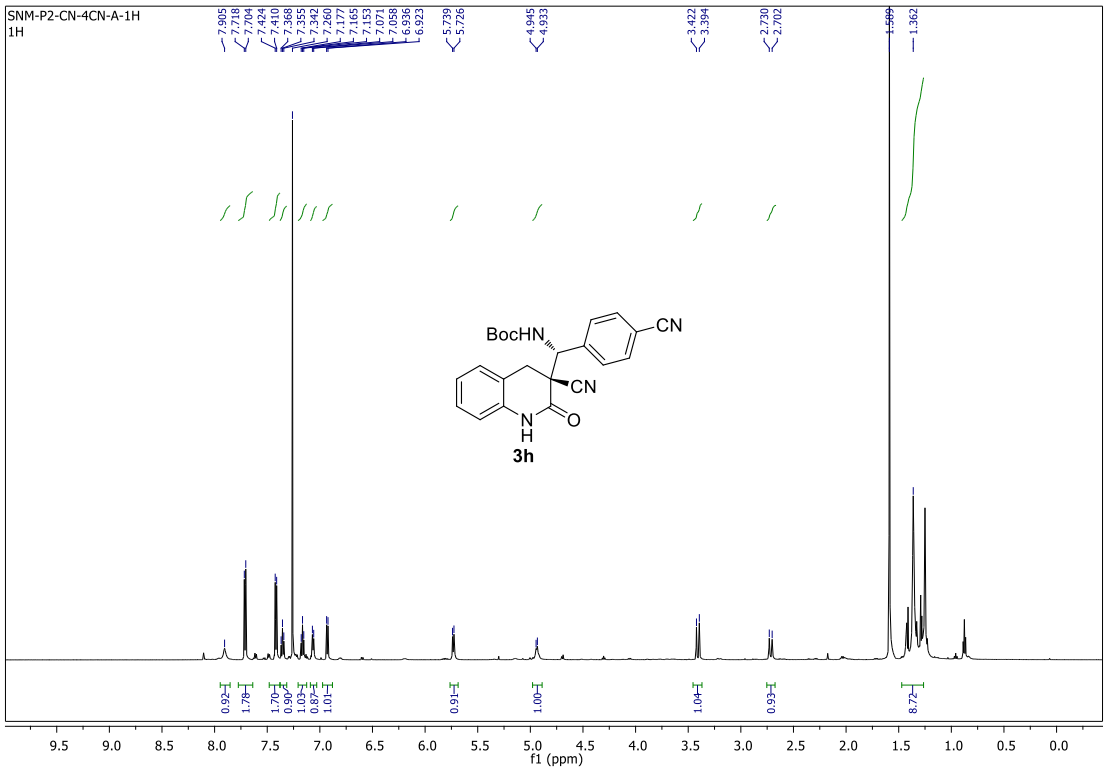

SNM-P2-CN-4F-A-13C
13C
164.18
164.07
162.42
154.86
135.89
131.78
129.59
129.53
129.42
128.82
124.77
118.24
117.27
116.41
116.14
116.00
80.94
77.44
77.23
77.02
54.28
50.94
33.82
28.34
BocHN
F
CN
N
H
O
3e
f1 (ppm)

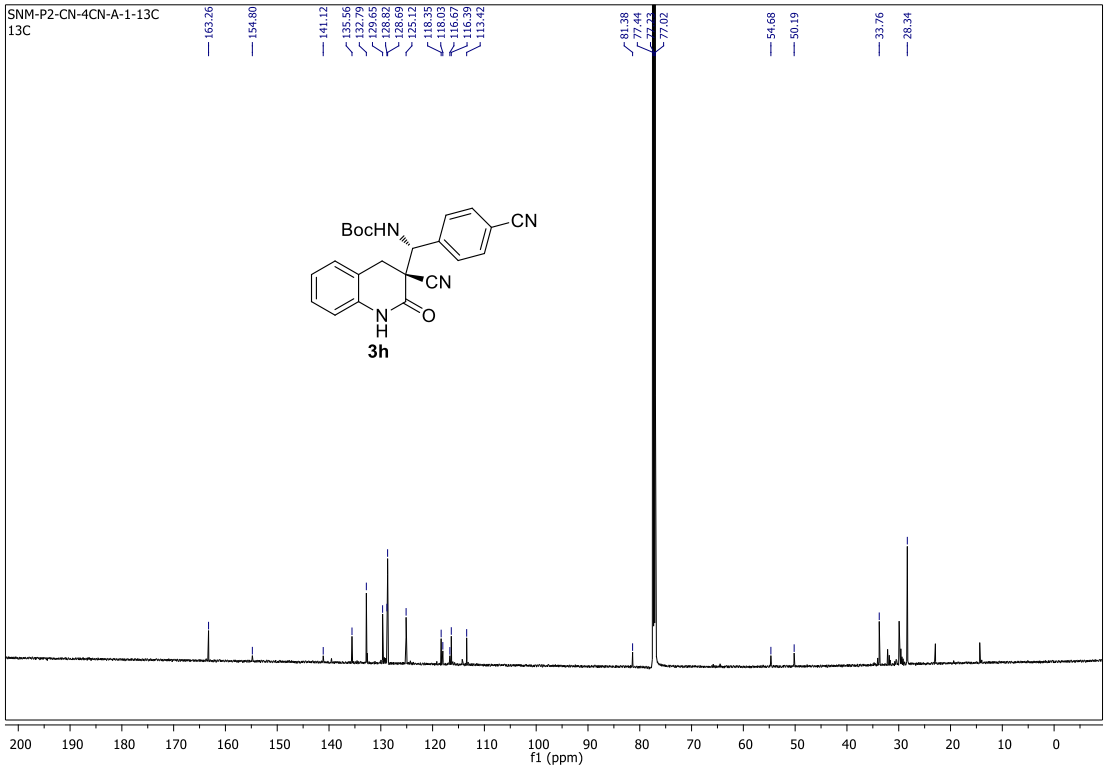

SNM-P2-CN-4Cl-A-1H
SNM-P2-CN-4Cl-A-1H
BocHN
Cl
CN
N
H
O
3f
f1 (ppm)

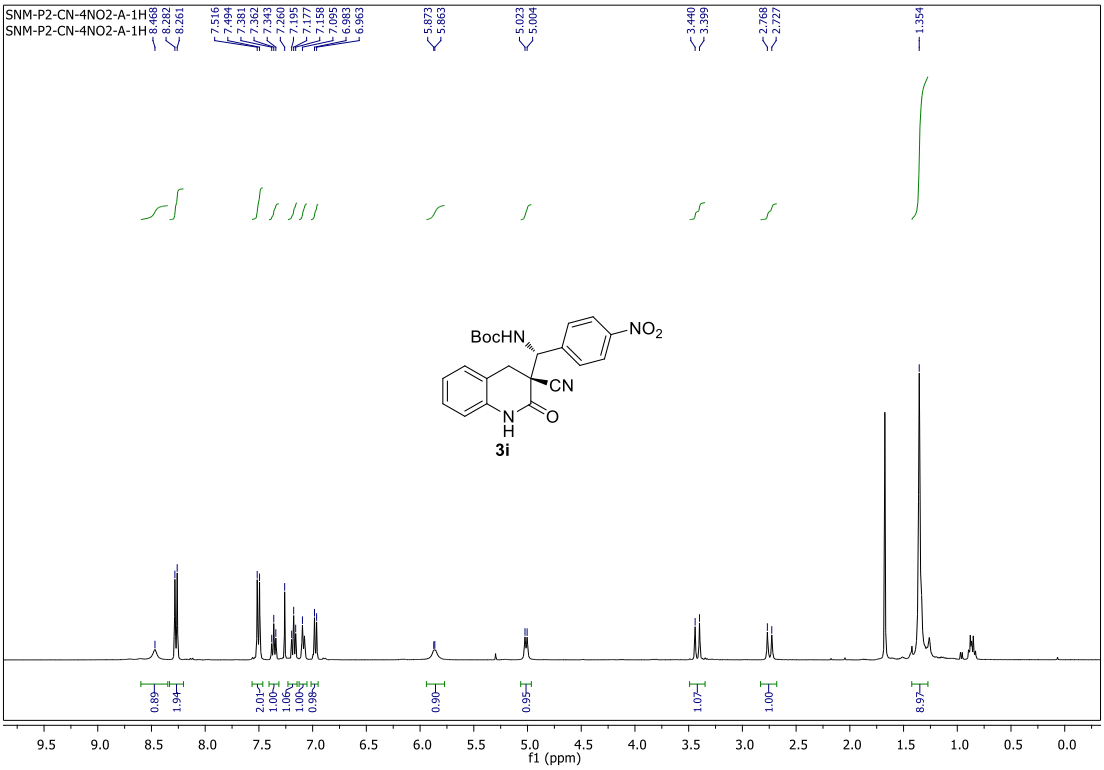

SNM-P2-CN-4CL-A-13C
SNM-P2-CN-4CL-A-13C
BocHN
Cl
CN
N
H
O
3f
f1 (ppm)

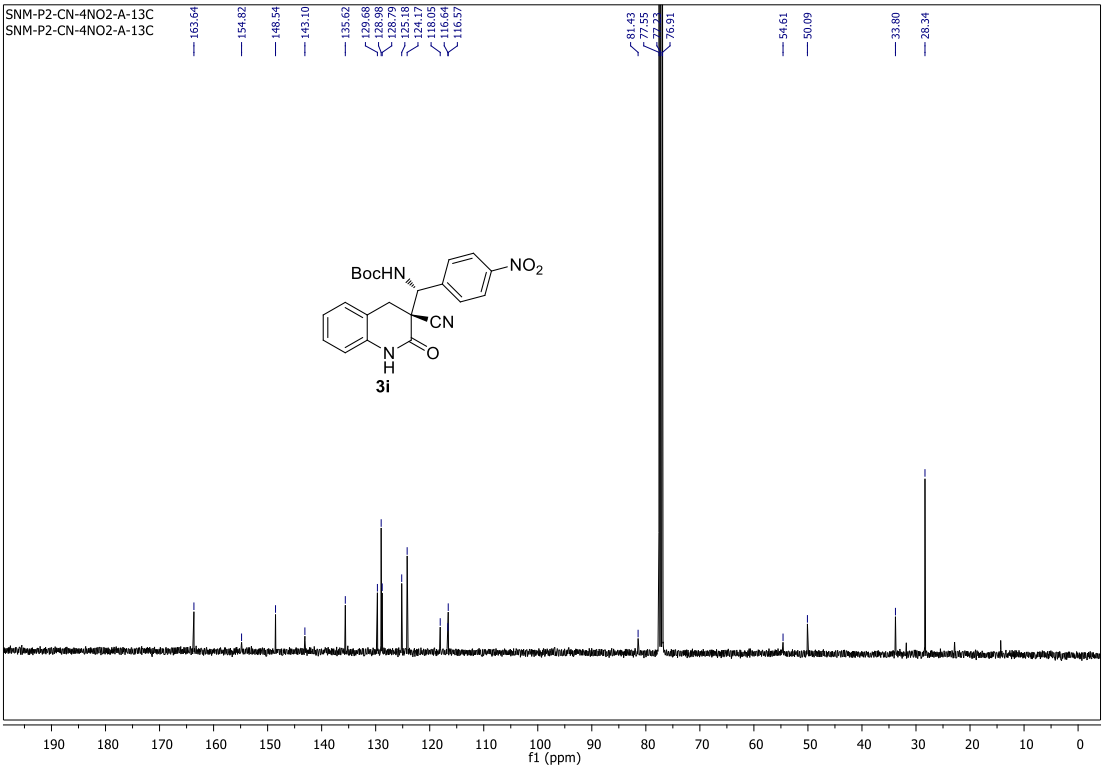

SNM-P2-CN-4BR-A-1-1H
1H
BocHN
Br
CN
O
N
H
3g
f1 (ppm)

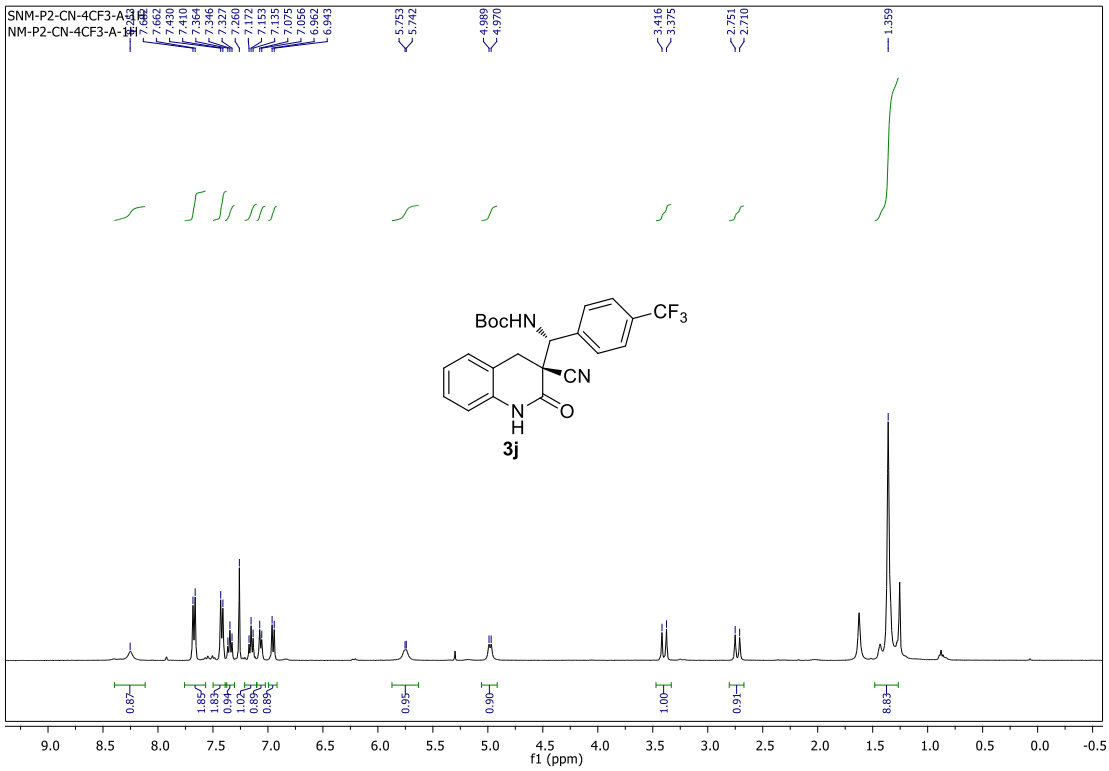

SNM-P2-CN-4-Br-13C
13C
BocHN
Br
CN
O
N
H
3g
f1 (ppm)

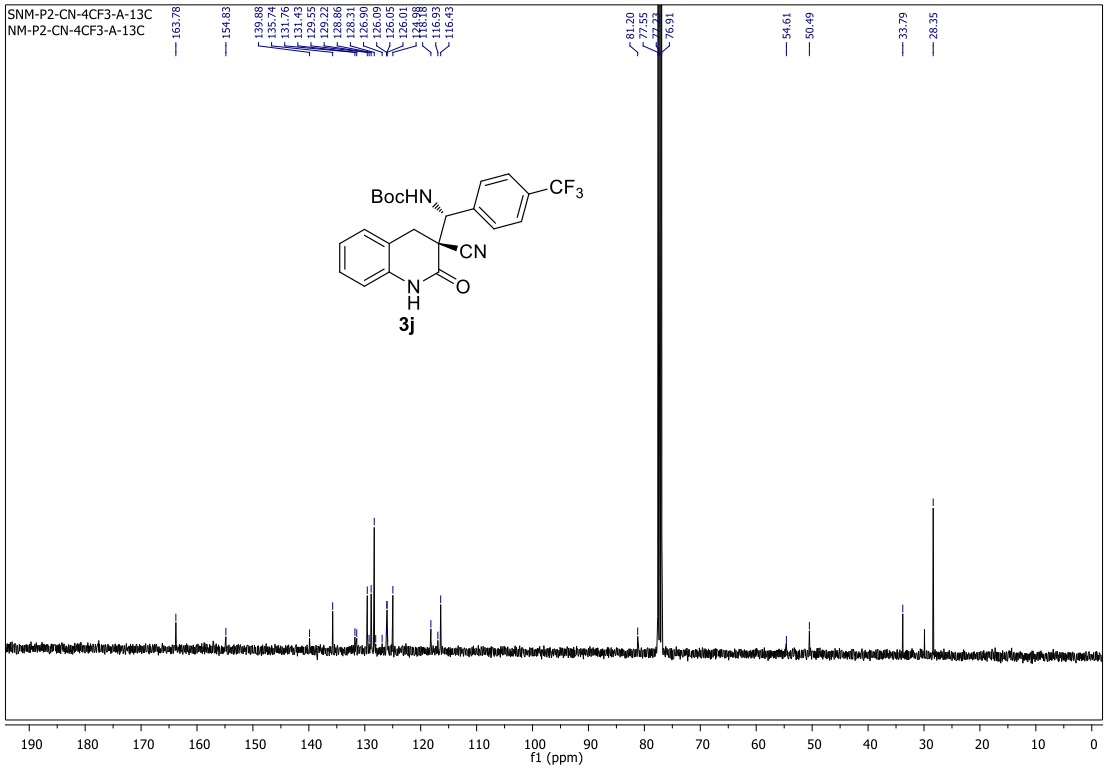

SNM-P2-CN-4CN-A-1H
1H
7.905
7.718
7.704
7.424
7.410
7.368
7.355
7.342
7.260
7.177
7.165
7.153
7.071
7.058
6.936
6.923
5.739
5.726
4.945
4.933
3.422
3.394
2.730
2.702
1.589
1.362
BocHN
CN
CN
N
H
O
3h
0.92
1.78
1.70
0.90
1.03
0.87
1.01
0.91
1.00
1.04
0.93
8.72
f1 (ppm)

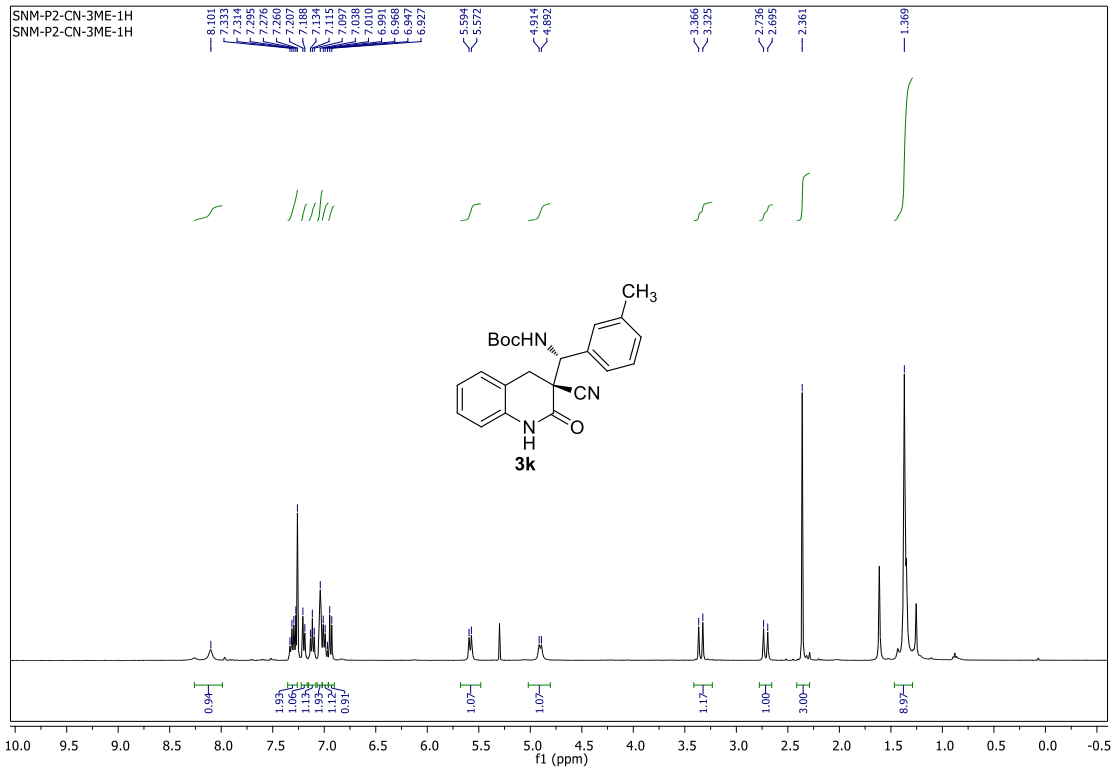

SNM-P2-CN-4CN-A-1-13C
13C
163.26
154.80
141.12
135.56
132.79
129.65
128.82
128.69
125.12
118.35
118.03
116.67
116.39
113.42
81.38
77.44
77.22
77.02
54.68
50.19
33.76
28.34
BocHN
CN
CN
N
H
O
3h
f1 (ppm)

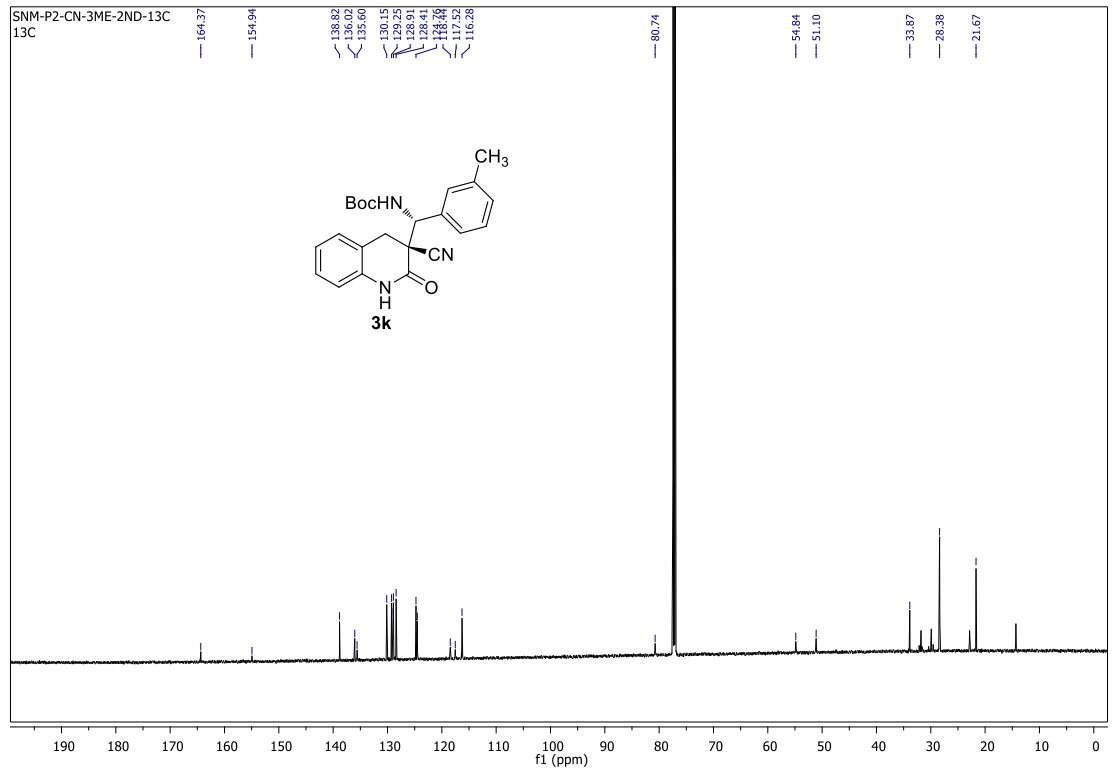

SNM-P2-CN-4NO2-A-1H
SNM-P2-CN-4NO2-A-1H
8.468
8.282
8.261
7.516
7.494
7.381
7.362
7.343
7.260
7.195
7.177
7.158
7.095
6.983
6.963
5.873
5.863
5.023
5.004
3.440
3.399
2.768
2.727
1.354
BocHN
NO2
CN
O
N
H
3i
0.89
1.94
2.01
1.00
1.06
1.00
0.98
0.90
0.95
1.07
1.00
8.97
f1 (ppm)

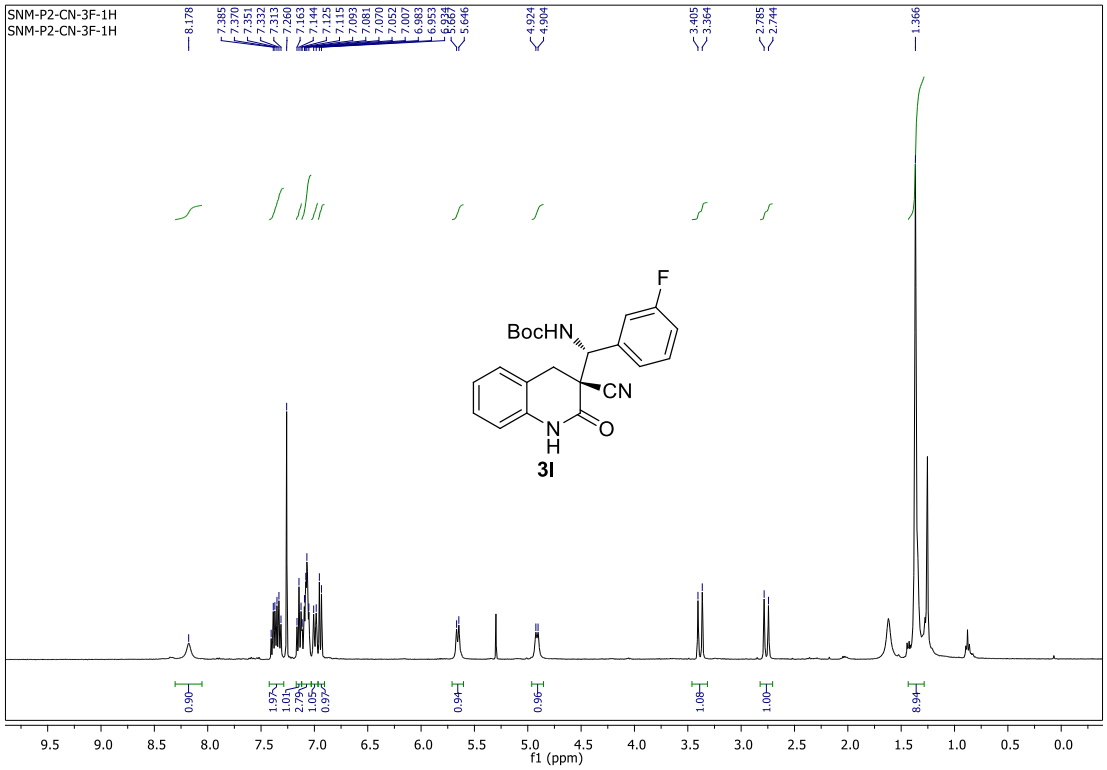

SNM-P2-CN-4NO2-A-13C
SNM-P2-CN-4NO2-A-13C
163.64
154.82
148.54
143.10
135.62
129.68
128.98
128.79
125.18
124.17
118.05
116.64
116.57
81.43
77.55
77.23
76.91
54.61
50.09
33.80
28.34
BocHN
NO2
CN
O
N
H
3i
f1 (ppm)

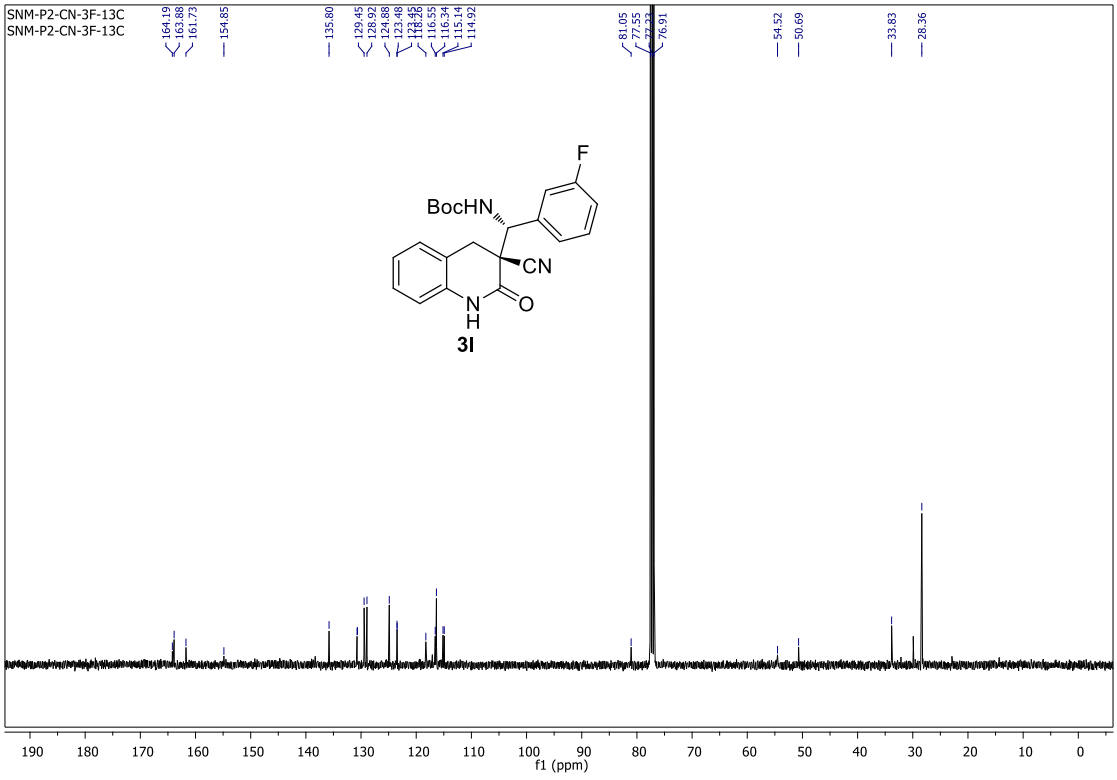

SNM-P2-CN-4CF3-A-1H
NM-P2-CN-4CF3-A-1H
BocHN
CF3
CN
N
H
O
3j
f1 (ppm)

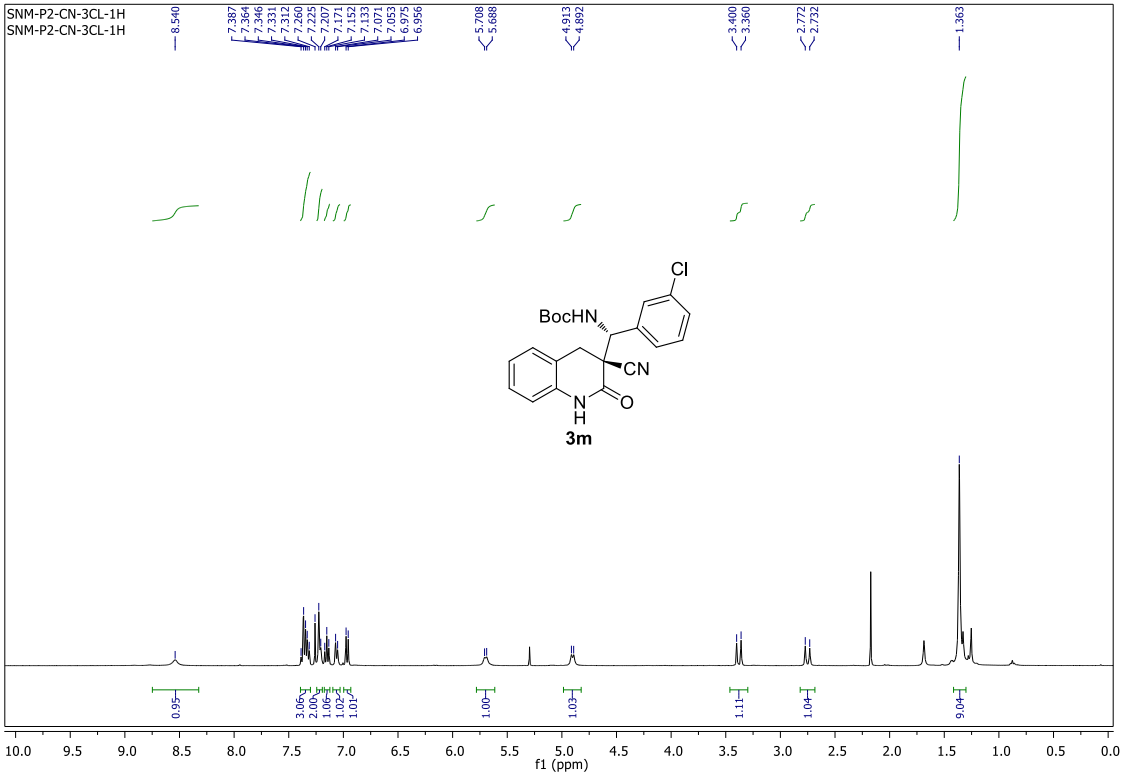

SNM-P2-CN-4CF3-A-13C
NM-P2-CN-4CF3-A-13C
BocHN
CF3
CN
N
H
O
3j
f1 (ppm)

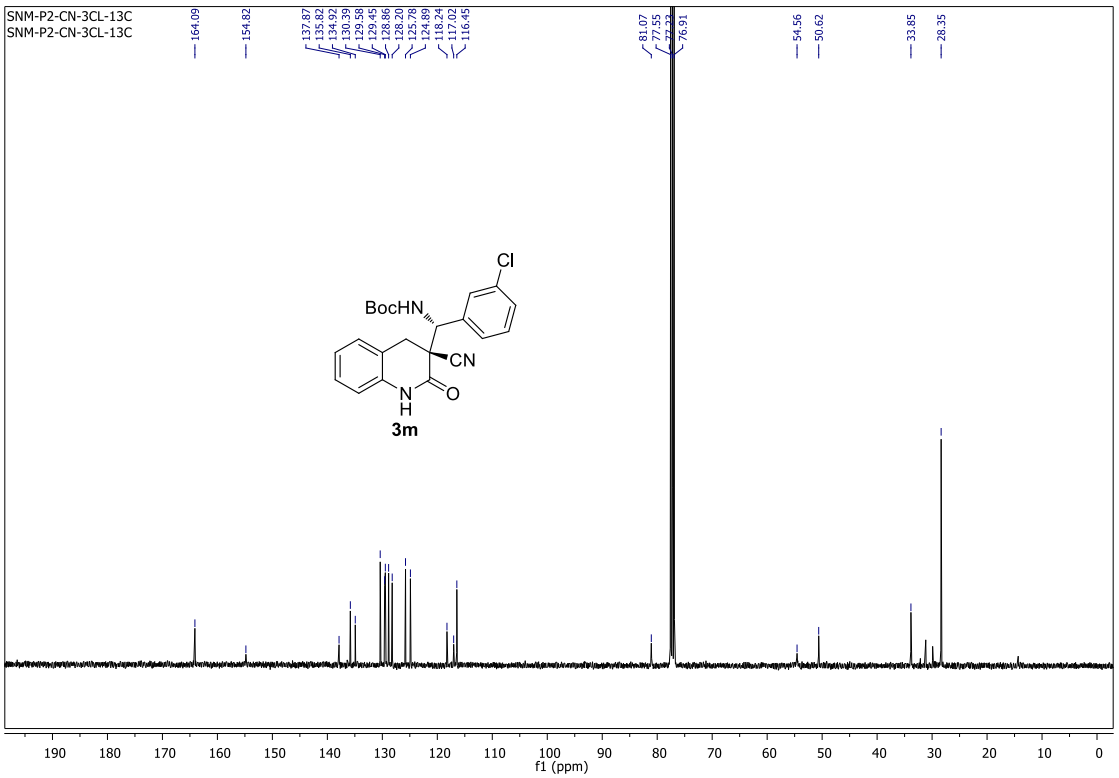

SNM-P2-CN-3ME-1H
SNM-P2-CN-3ME-1H
8.101
7.333
7.314
7.295
7.276
7.260
7.207
7.198
7.194
7.115
7.097
7.038
7.010
6.991
6.968
6.947
6.927
5.594
5.572
4.914
4.892
3.366
3.325
2.736
2.695
2.361
1.369
CH3
BocHN
CN
N
H
O
3k
0.94
1.93
1.06
1.13
1.93
1.12
0.91
1.07
1.07
1.17
1.00
3.00
8.97
f1 (ppm)

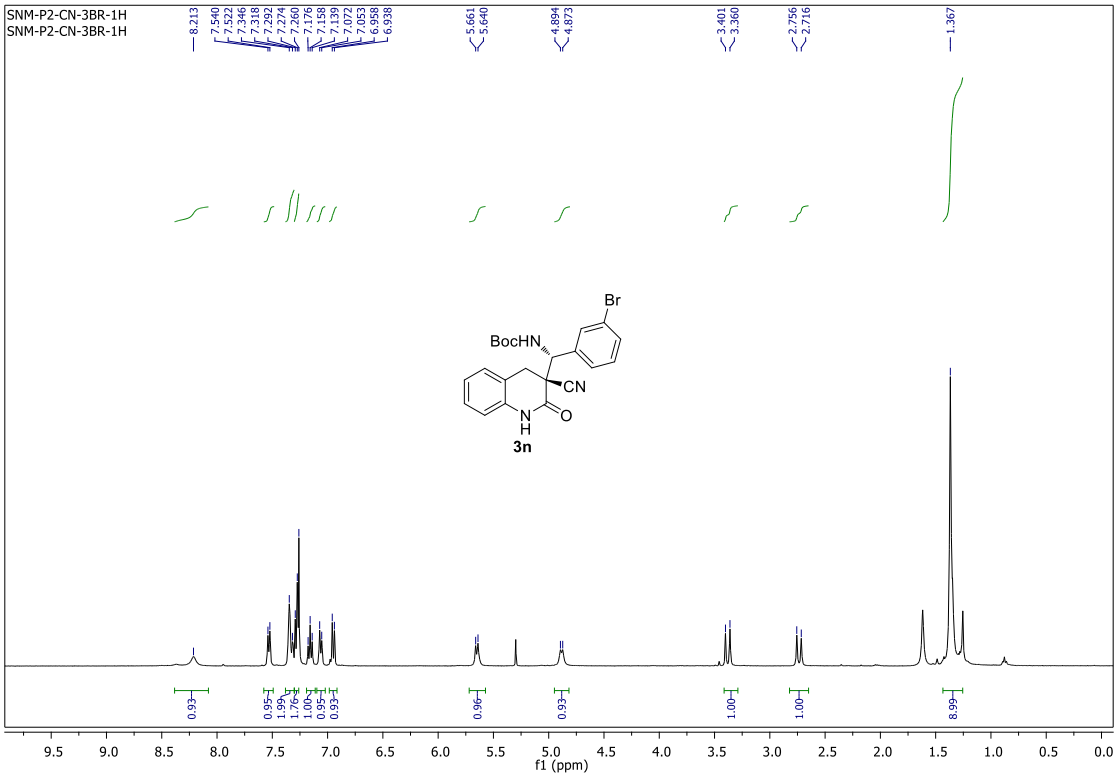

SNM-P2-CN-3ME-2ND-13C
13C
164.37
154.94
138.82
136.02
135.60
130.15
129.25
128.91
128.41
117.52
116.28
80.74
54.84
51.10
33.87
28.38
21.67
CH3
BocHN
CN
N
H
O
3k
f1 (ppm)

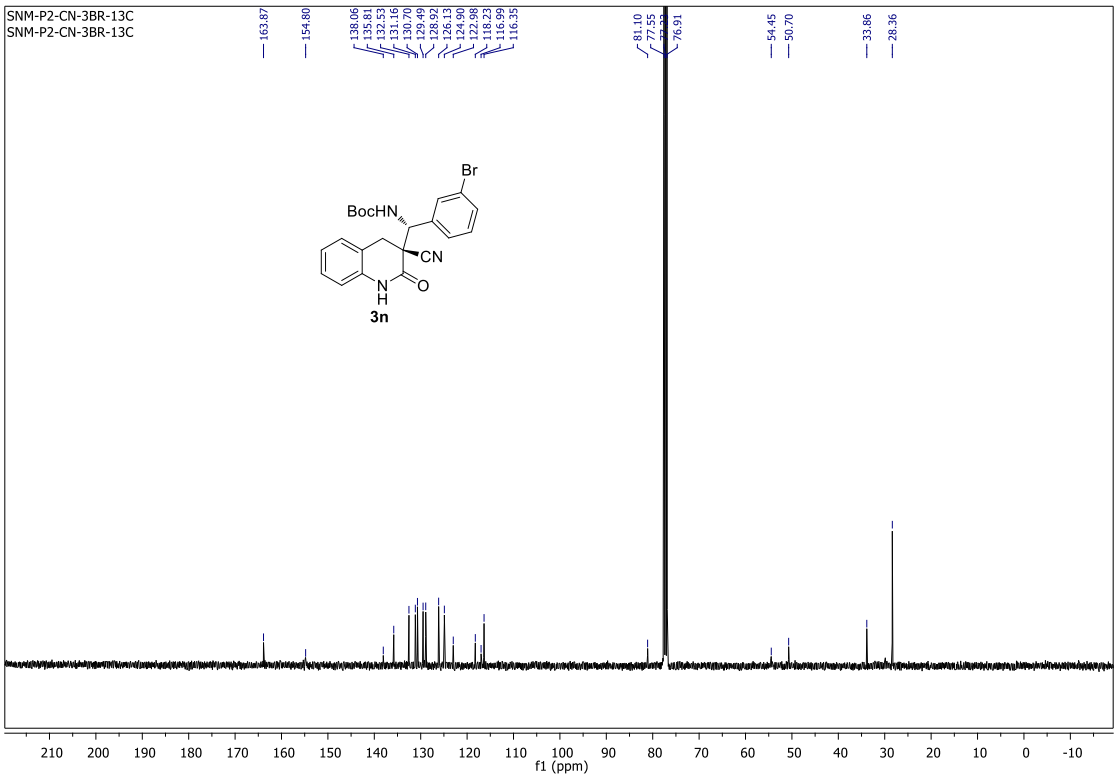

SNM-P2-CN-3F-1H
SNM-P2-CN-3F-1H
8.178
7.385
7.370
7.351
7.332
7.313
7.260
7.163
7.144
7.125
7.115
7.093
7.081
7.070
7.052
7.007
6.983
6.953
5.646
4.924
4.904
3.405
3.364
2.785
2.744
1.366
F
BocHN
CN
N
H
O
3l
0.90
1.97
1.01
2.79
1.05
0.97
0.94
0.96
1.08
1.00
8.94
f1 (ppm)

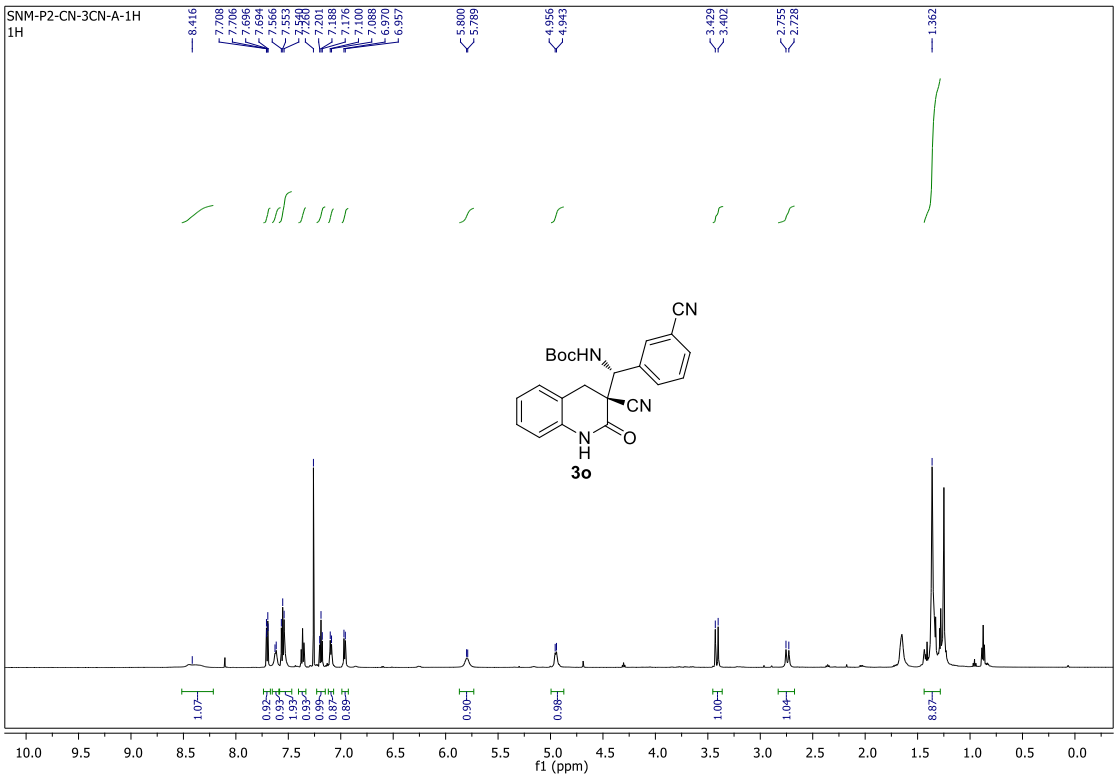

SNM-P2-CN-3F-13C
SNM-P2-CN-3F-13C
164.19
163.88
161.73
154.85
135.80
129.45
128.92
124.88
123.48
116.55
116.34
115.14
114.92
81.05
77.55
76.91
54.52
50.69
33.83
28.36
F
BocHN
CN
N
H
O
3l
f1 (ppm)

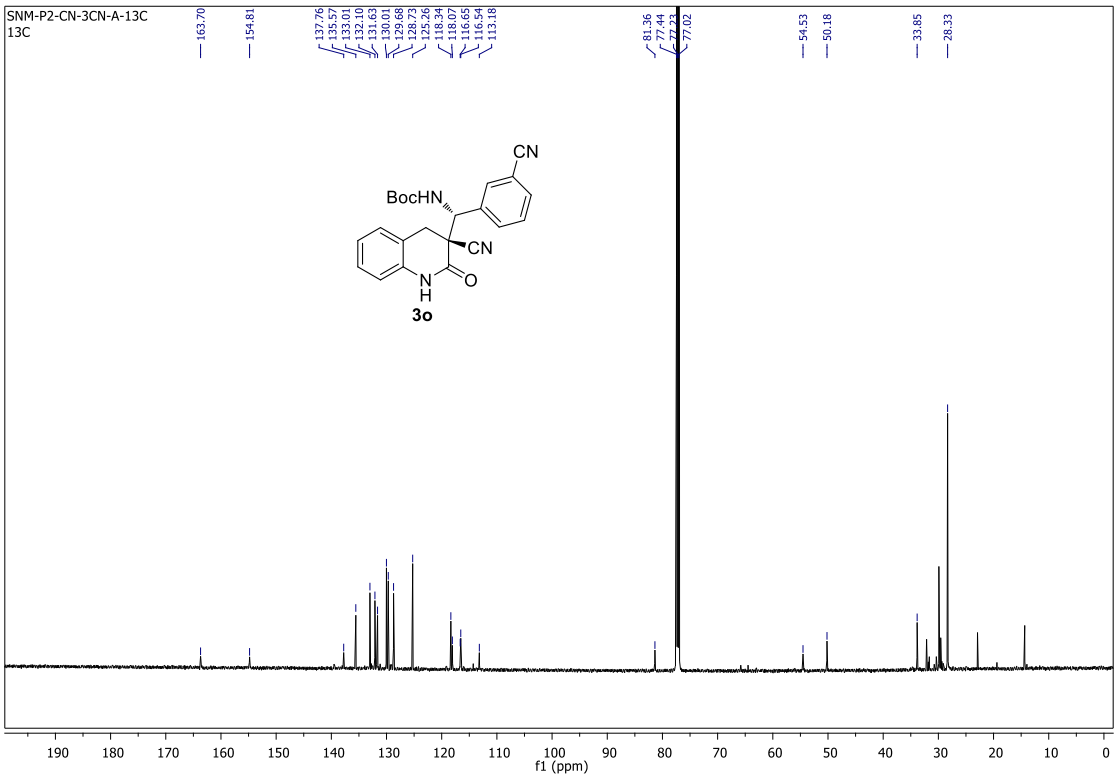

SNM-P2-CN-3CL-1H
SNM-P2-CN-3CL-1H
8.540
7.387
7.364
7.346
7.331
7.312
7.260
7.225
7.207
7.171
7.152
7.133
7.071
7.053
6.975
6.956
5.708
5.688
4.913
4.892
3.400
3.360
2.772
2.732
1.363
Cl
BocHN
CN
N
H
O
3m
0.95
3.06
2.00
1.06
1.02
1.01
1.00
1.03
1.11
1.04
9.04
f1 (ppm)

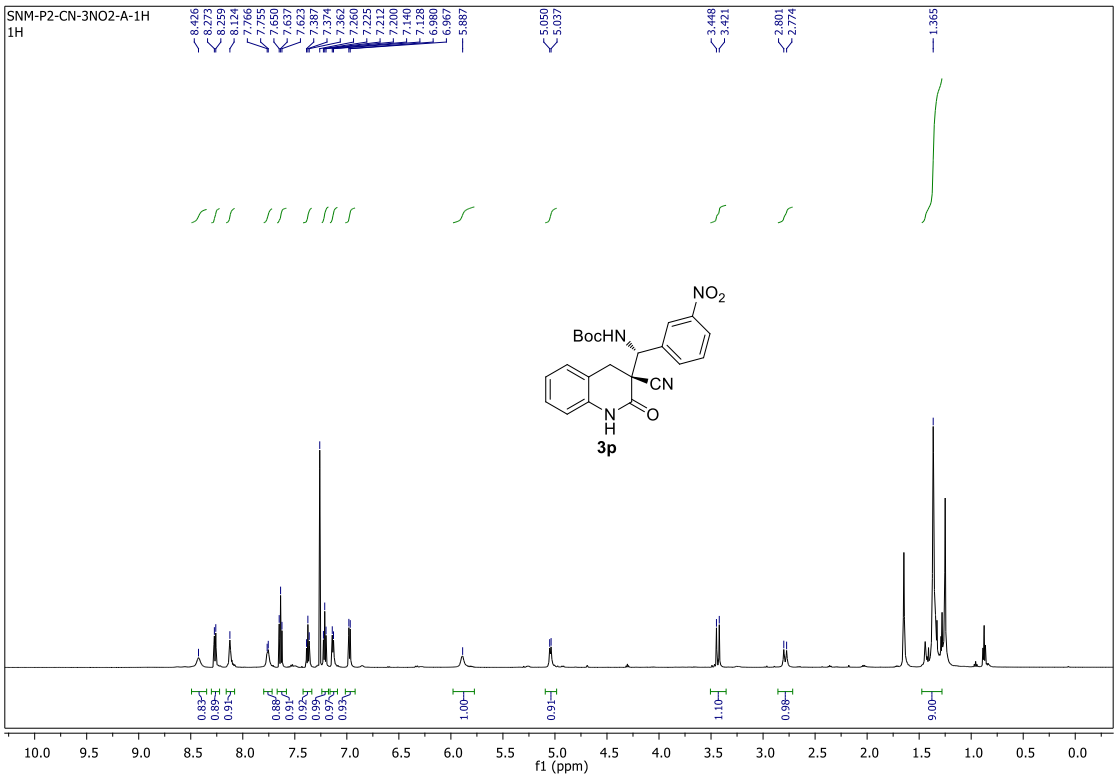

SNM-P2-CN-3CL-13C
SNM-P2-CN-3CL-13C
164.09
154.82
137.87
135.82
134.92
130.39
129.58
129.45
128.86
128.20
125.78
124.89
118.24
117.02
116.45
81.07
77.55
77.22
76.91
54.56
50.62
33.85
28.35
Cl
BocHN
CN
N
H
O
3m
f1 (ppm)

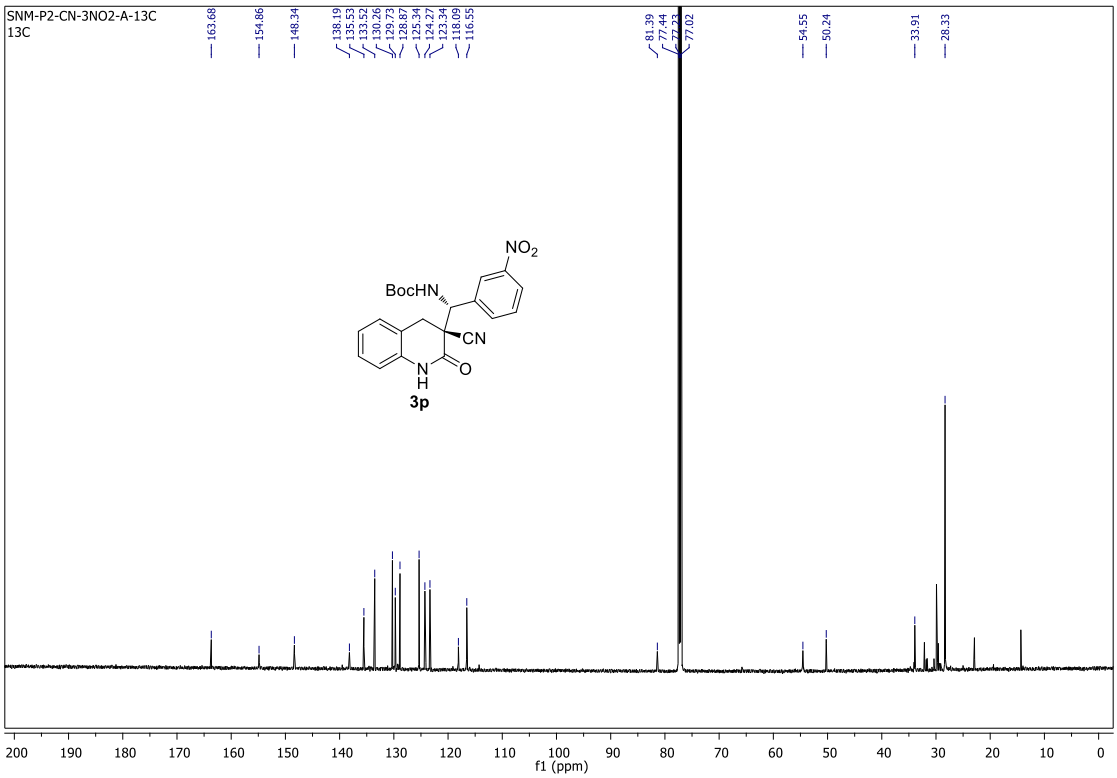

SNM-P2-CN-3BR-1H
SNM-P2-CN-3BR-1H
8.213
7.540
7.522
7.346
7.318
7.292
7.274
7.260
7.176
7.158
7.139
7.072
7.053
6.958
6.938
5.661
5.640
4.894
4.873
3.401
3.360
2.756
2.716
1.367
Br
BocHN
CN
N
H
O
3n
0.93
0.95
1.99
1.76
1.00
0.95
0.93
0.96
0.93
1.00
1.00
8.99
f1 (ppm)

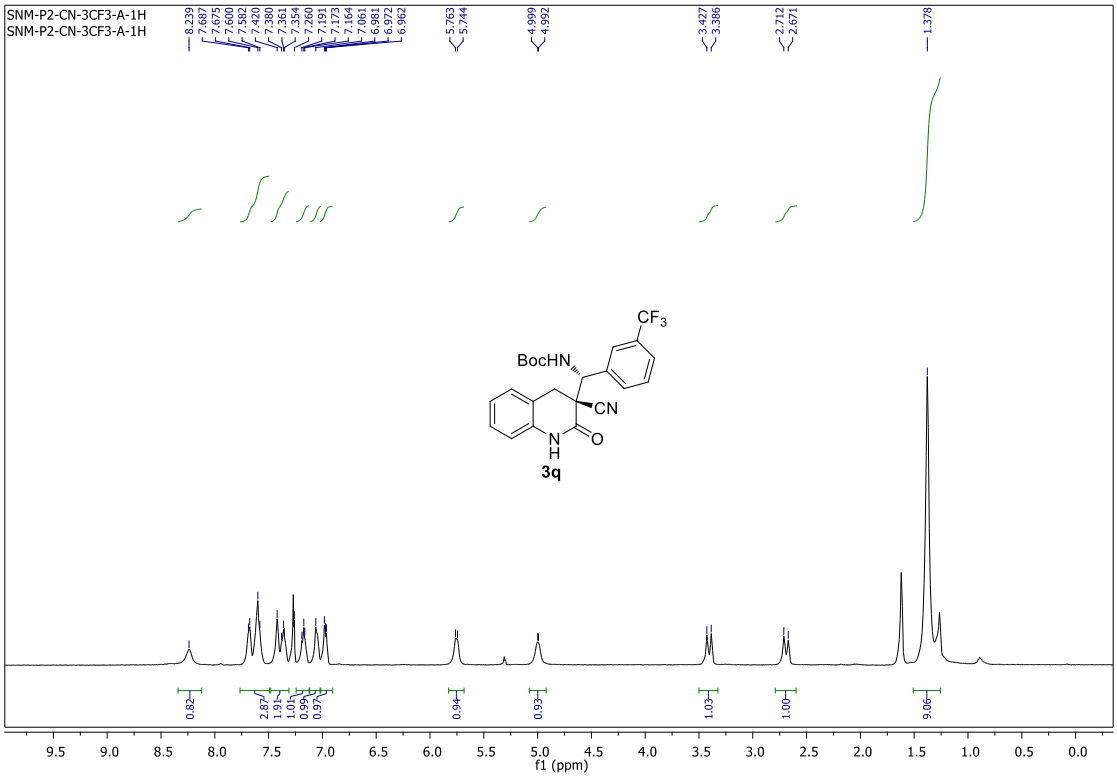

SNM-P2-CN-3BR-13C
SNM-P2-CN-3BR-13C
163.87
154.80
138.06
135.81
132.53
131.16
130.70
129.49
128.92
126.13
124.90
122.98
118.23
116.99
116.35
81.10
77.55
76.91
54.45
50.70
33.86
28.36
Br
BocHN
CN
N
H
O
3n
f1 (ppm)

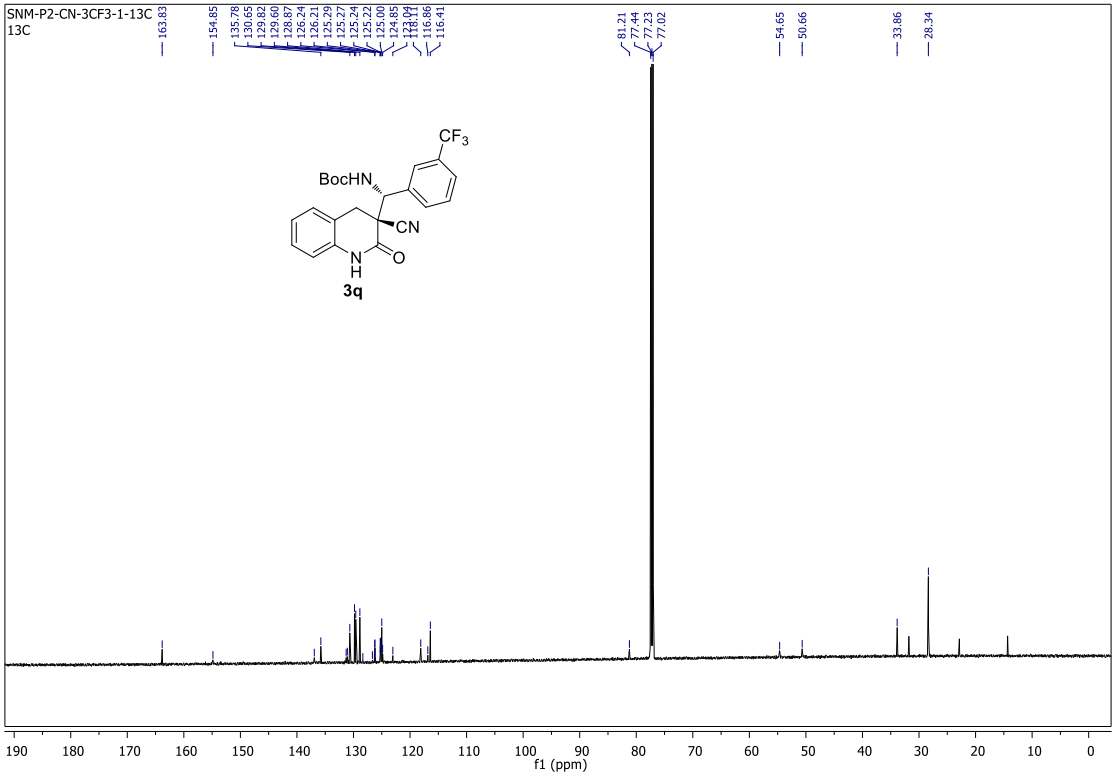

SNM-P2-CN-3CN-A-1H
1H
8.416
7.708
7.706
7.696
7.694
7.566
7.553
7.549
7.201
7.188
7.176
7.100
7.088
6.970
6.957
5.800
5.789
4.956
4.943
3.429
3.402
2.755
2.728
1.362
CN
BocHN
CN
N
H
O
3o
1.07
0.92
0.92
1.93
0.93
0.99
0.87
0.89
0.90
0.98
1.00
1.04
8.87
f1 (ppm)

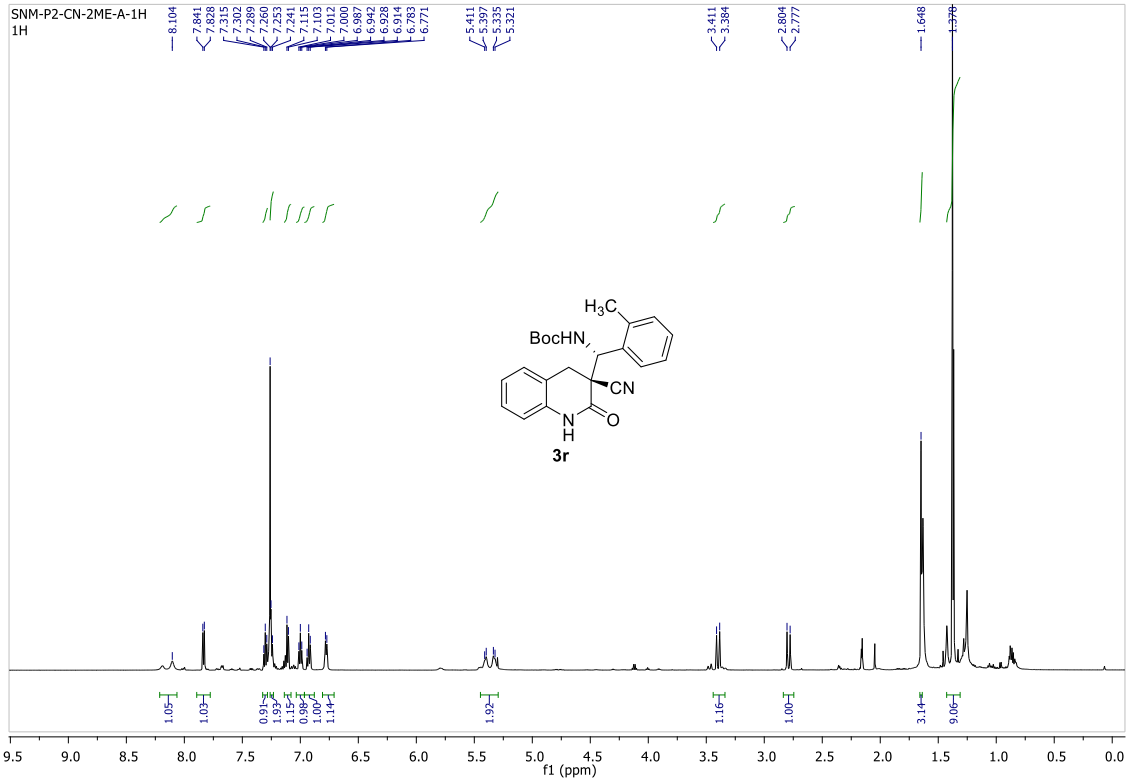

SNM-P2-CN-3CN-A-13C
13C
163.70
154.81
137.76
135.57
133.01
132.10
131.63
130.01
129.68
128.73
125.26
118.34
118.07
116.65
116.54
113.18
81.36
77.44
77.23
77.02
54.53
50.18
33.85
28.33
CN
BocHN
CN
N
H
O
3o
f1 (ppm)

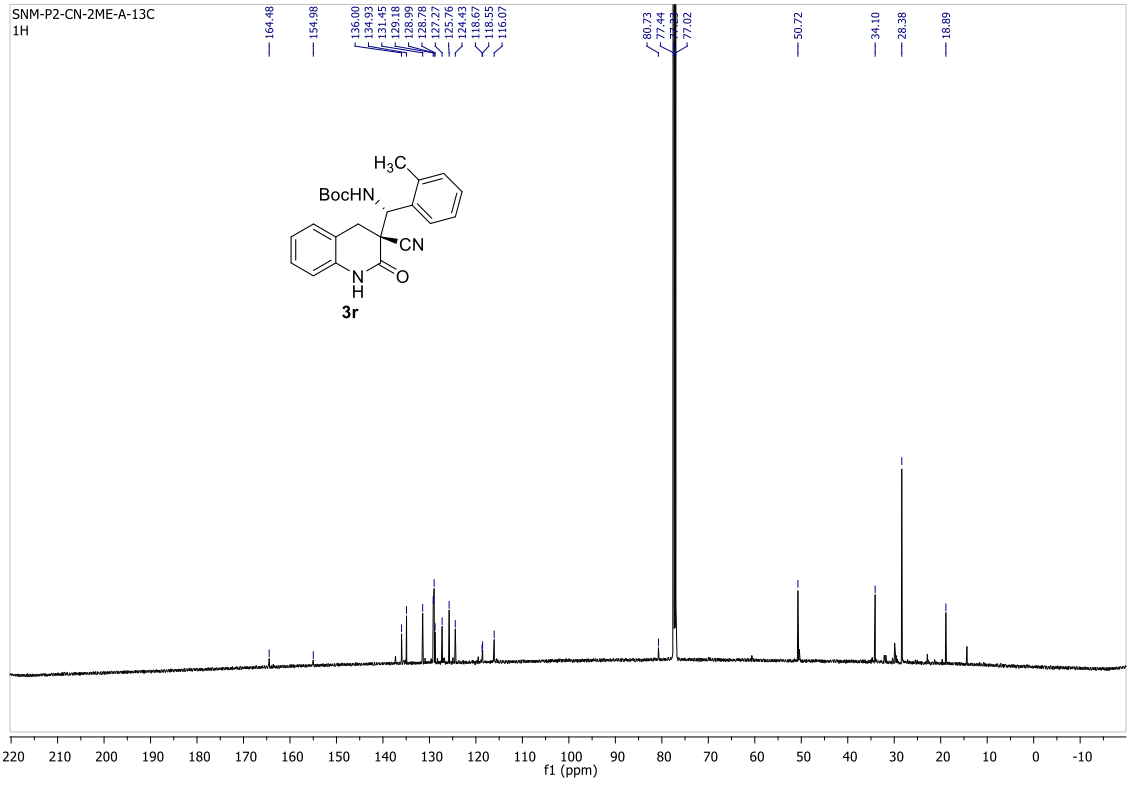

SNM-P2-CN-3NO2-A-1H
1H
8.426
8.273
8.259
8.124
7.766
7.755
7.650
7.637
7.623
7.387
7.374
7.362
7.260
7.225
7.212
7.200
7.140
7.128
6.980
6.967
5.887
5.050
5.037
3.448
3.421
2.801
2.774
1.365
NO2
BocHN
CN
N
H
O
3p
0.83
0.89
0.91
0.89
0.91
0.95
0.98
0.97
0.93
1.00
0.91
1.10
0.98
9.00
f1 (ppm)

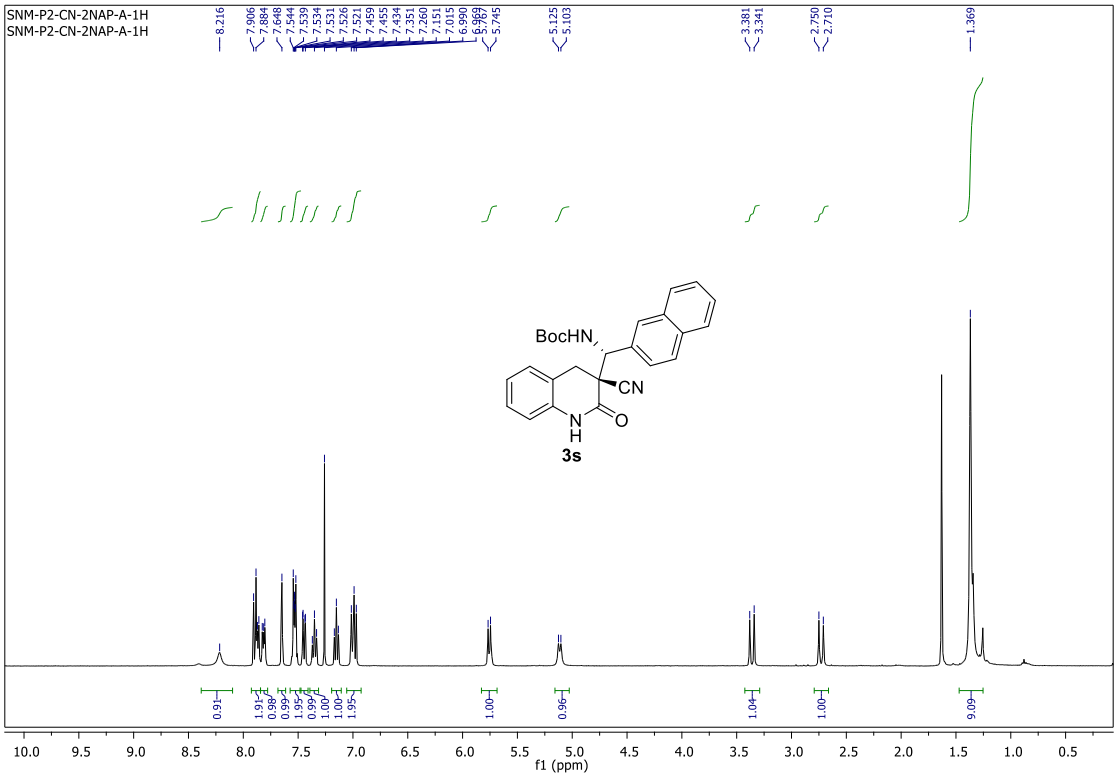

SNM-P2-CN-3NO2-A-13C
13C
163.68
154.86
148.34
138.19
135.53
133.52
130.26
129.73
128.87
125.34
124.27
123.34
118.09
116.55
81.39
77.44
77.23
77.02
54.55
50.24
33.91
28.33
NO2
BocHN
CN
N
H
O
3p
f1 (ppm)

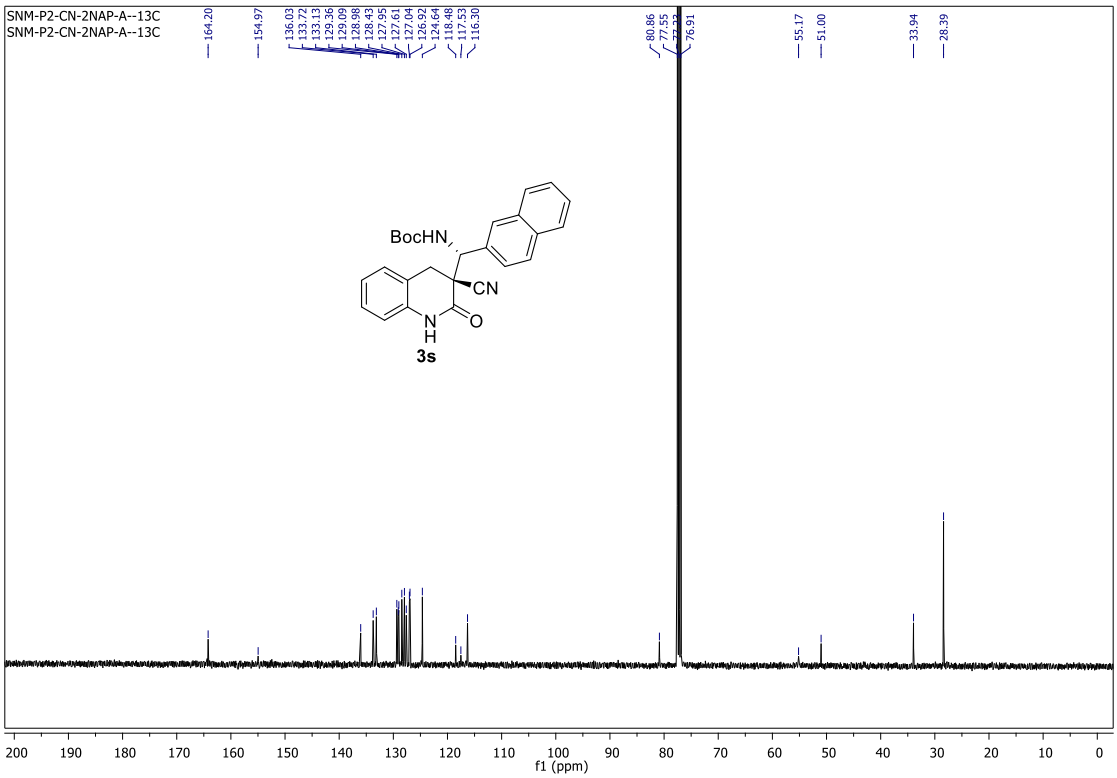

SNM-P2-CN-3CF3-A-1H
SNM-P2-CN-3CF3-A-1H
8.239
7.687
7.675
7.600
7.582
7.420
7.380
7.361
7.354
7.260
7.191
7.173
7.164
7.061
6.981
6.972
6.962
5.763
5.744
4.999
4.992
3.427
3.386
2.712
2.671
1.378
CF3
BocHN
CN
N
H
O
3q
0.82
2.87
1.91
1.01
0.99
0.97
0.94
0.93
1.03
1.00
9.06
f1 (ppm)

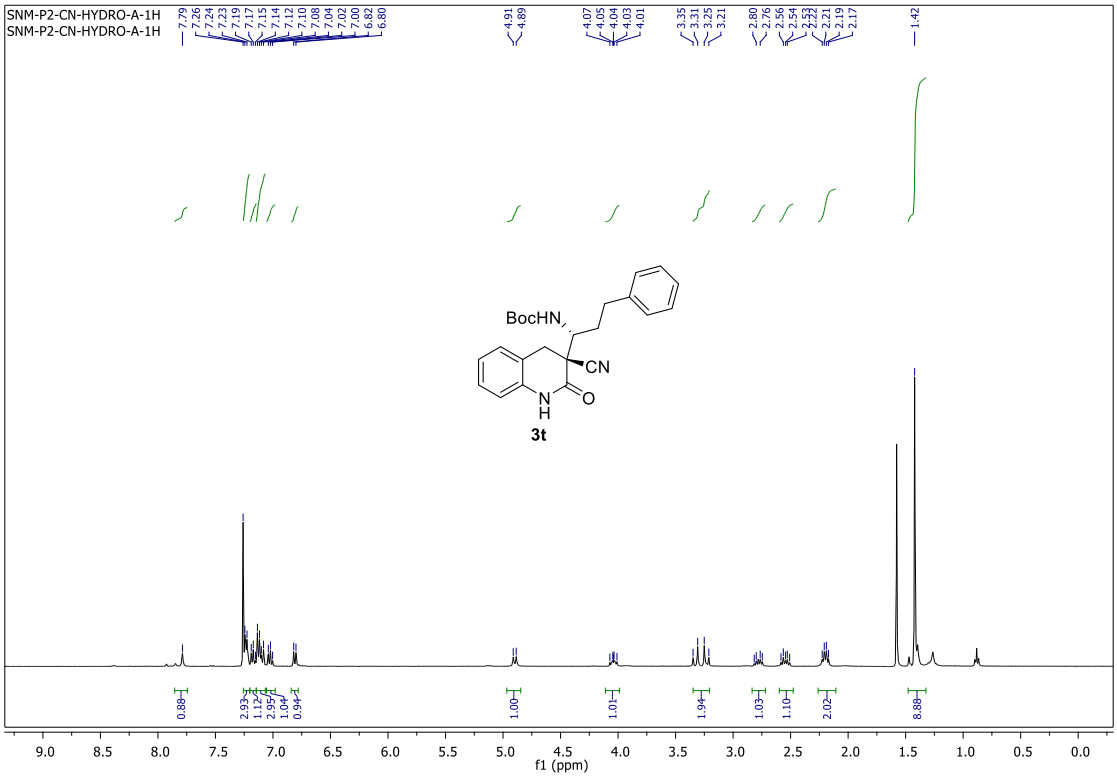

SNM-P2-CN-3CF3-1-13C
13C
163.83
154.85
135.78
130.65
129.82
129.60
128.87
126.24
126.21
125.29
125.27
125.24
125.22
125.00
124.85
123.04
118.11
116.86
116.41
81.21
77.44
77.23
77.02
54.65
50.66
33.86
28.34
CF3
BocHN
CN
N
H
O
3q
f1 (ppm)

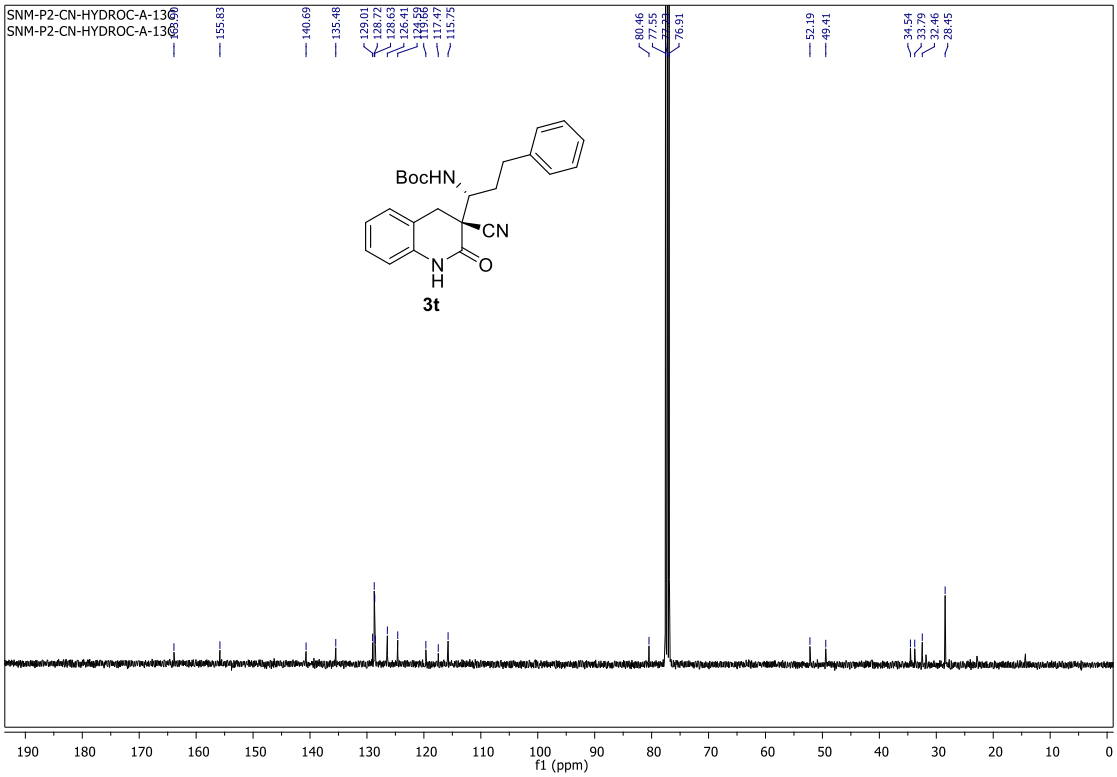

SNM-P2-CN-2ME-A-1H
1H
8.104
7.841
7.828
7.315
7.302
7.289
7.260
7.253
7.241
7.115
7.103
7.012
7.000
6.987
6.942
6.928
6.914
6.783
6.771
5.411
5.397
5.335
5.321
3.411
3.384
2.804
2.777
1.648
1.378
1.05
1.03
0.91
1.93
1.15
0.98
1.00
1.14
1.92
1.16
1.00
3.14
9.06
f1 (ppm)
H3C
BocHN
CN
N
H
O
3r

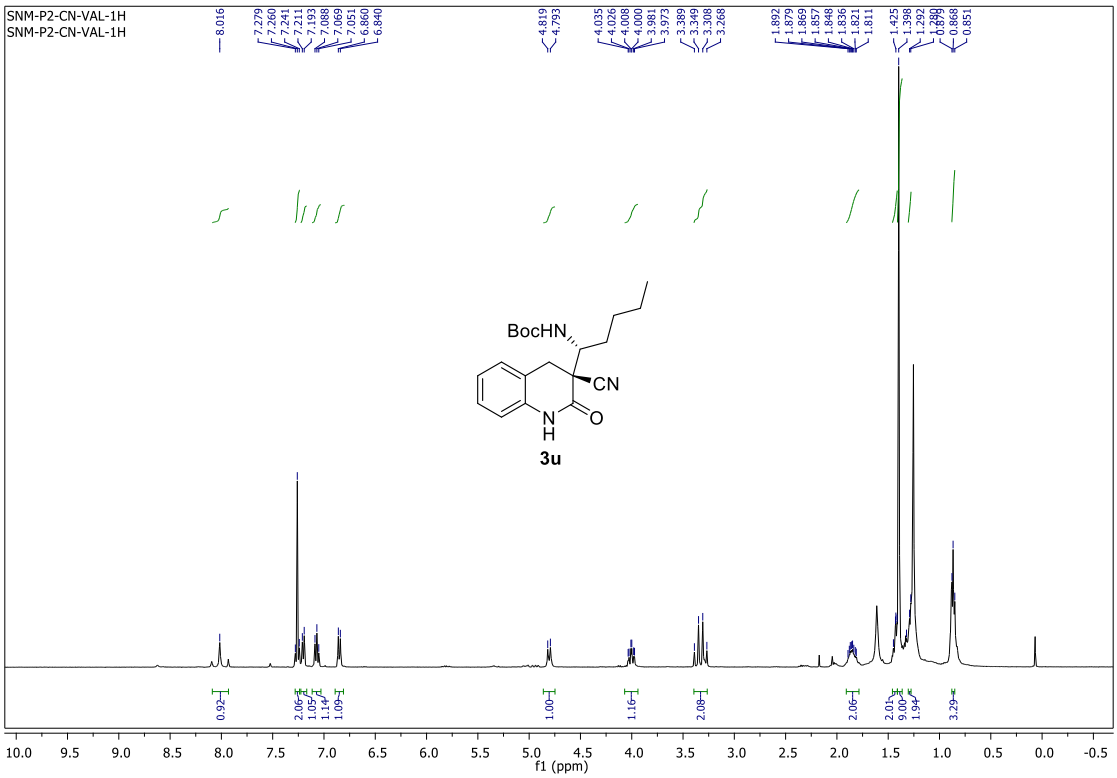

SNM-P2-CN-2ME-A-13C
1H
164.48
154.98
136.00
134.93
134.45
131.18
128.99
128.78
127.27
125.76
124.43
118.67
118.55
116.07
80.73
77.44
77.02
50.72
34.10
28.38
18.89
f1 (ppm)
H3C
BocHN
CN
N
H
O
3r

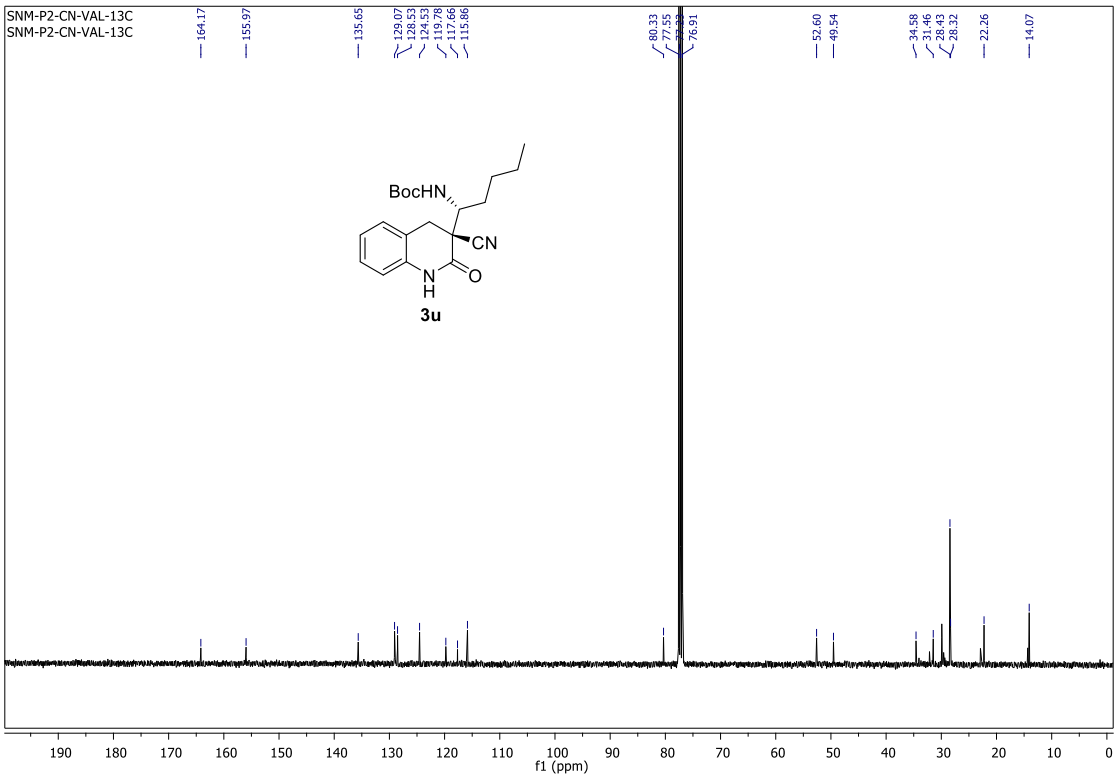

SNM-P2-CN-2NAP-A-1H
SNM-P2-CN-2NAP-A-1H
8.216
7.906
7.884
7.648
7.544
7.539
7.534
7.531
7.526
7.521
7.459
7.455
7.434
7.351
7.260
7.151
7.015
6.990
5.745
5.125
5.103
3.381
3.341
2.750
2.710
1.369
BocHN
CN
N
H
O
3s
0.91
1.91
0.98
0.99
1.95
0.99
1.00
1.00
1.95
1.00
0.96
1.04
1.00
9.09
f1 (ppm)

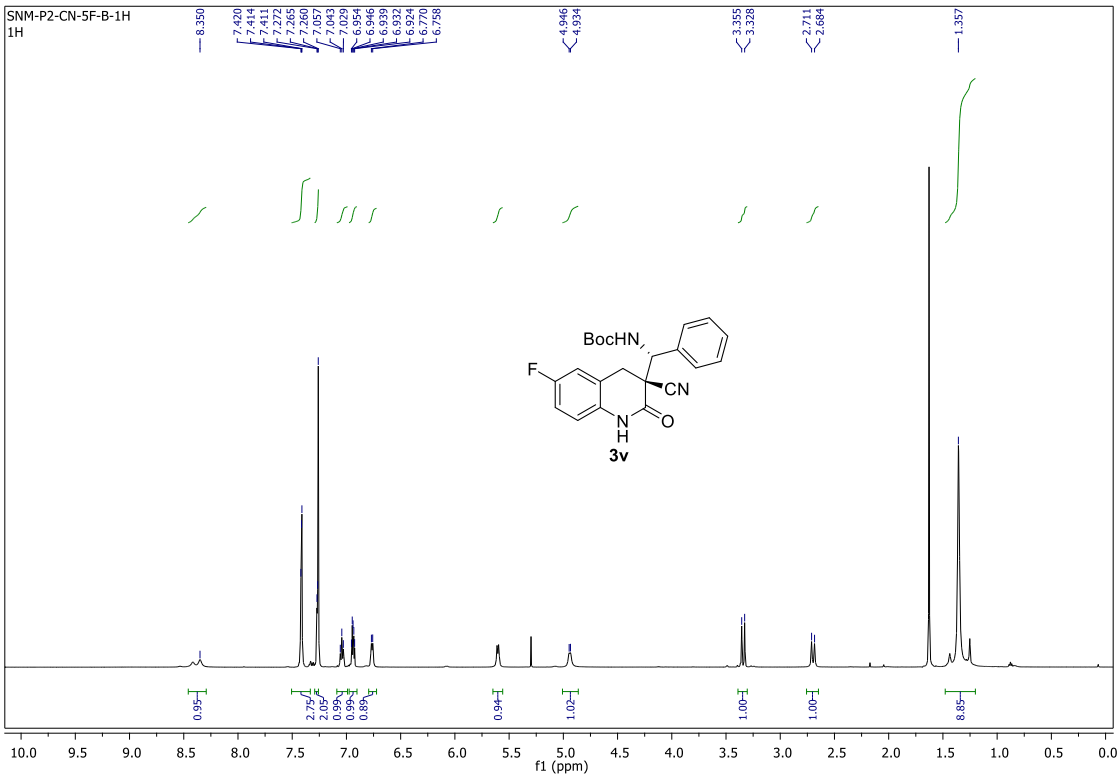

SNM-P2-CN-2NAP-A--13C
SNM-P2-CN-2NAP-A--13C
164.20
154.97
136.03
133.72
133.13
129.36
129.09
128.98
128.43
127.95
127.61
127.04
126.92
124.64
118.48
117.53
116.30
80.86
77.55
77.33
76.91
55.17
51.00
33.94
28.39
BocHN
CN
N
H
O
3s
f1 (ppm)

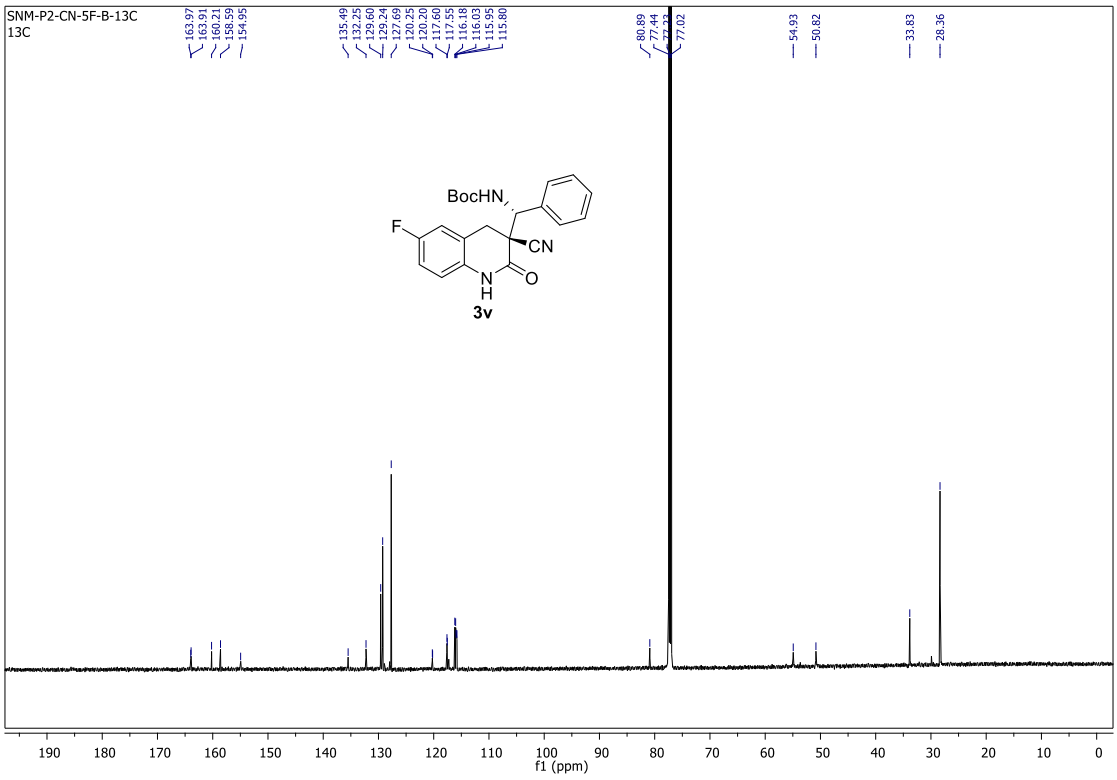

SNM-P2-CN-HYDRO-A-1H
SNM-P2-CN-HYDRO-A-1H
BocHN
CN
N
H
O
3t
f1 (ppm)

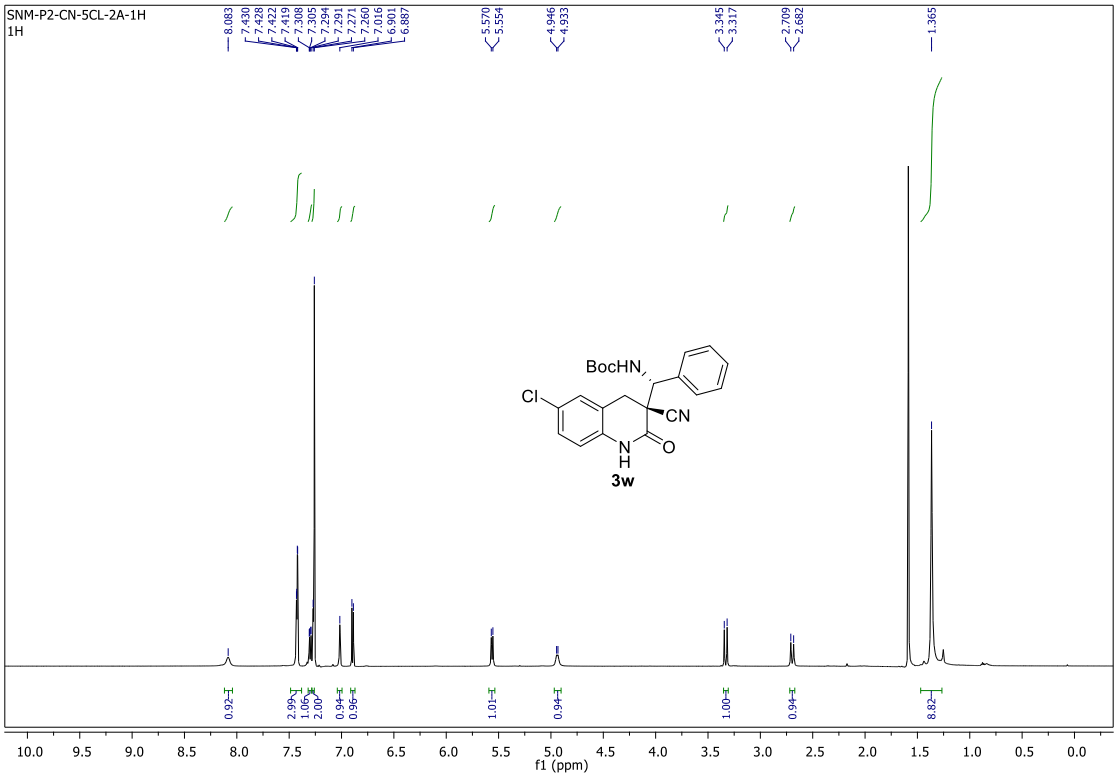

SNM-P2-CN-HYDROC-A-13C
SNM-P2-CN-HYDROC-A-13C
BocHN
CN
N
H
O
3t
f1 (ppm)

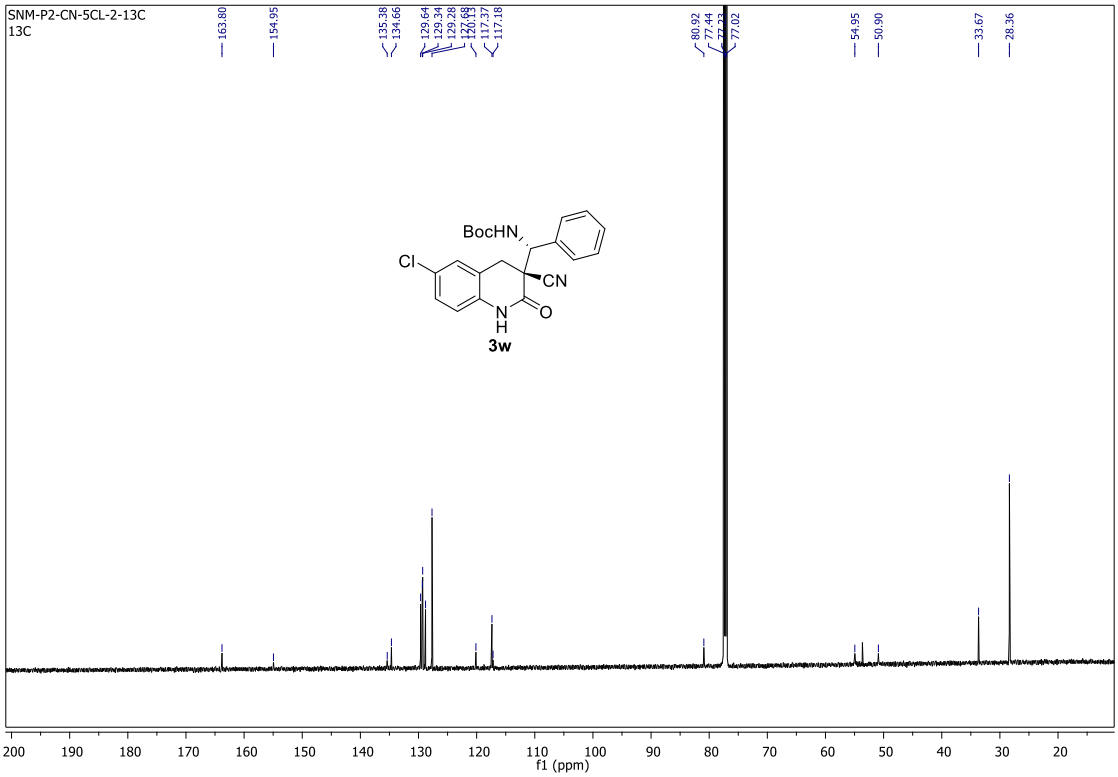

SNM-P2-CN-VAL-1H
SNM-P2-CN-VAL-1H
BocHN
CN
N
H
O
3u
f1 (ppm)

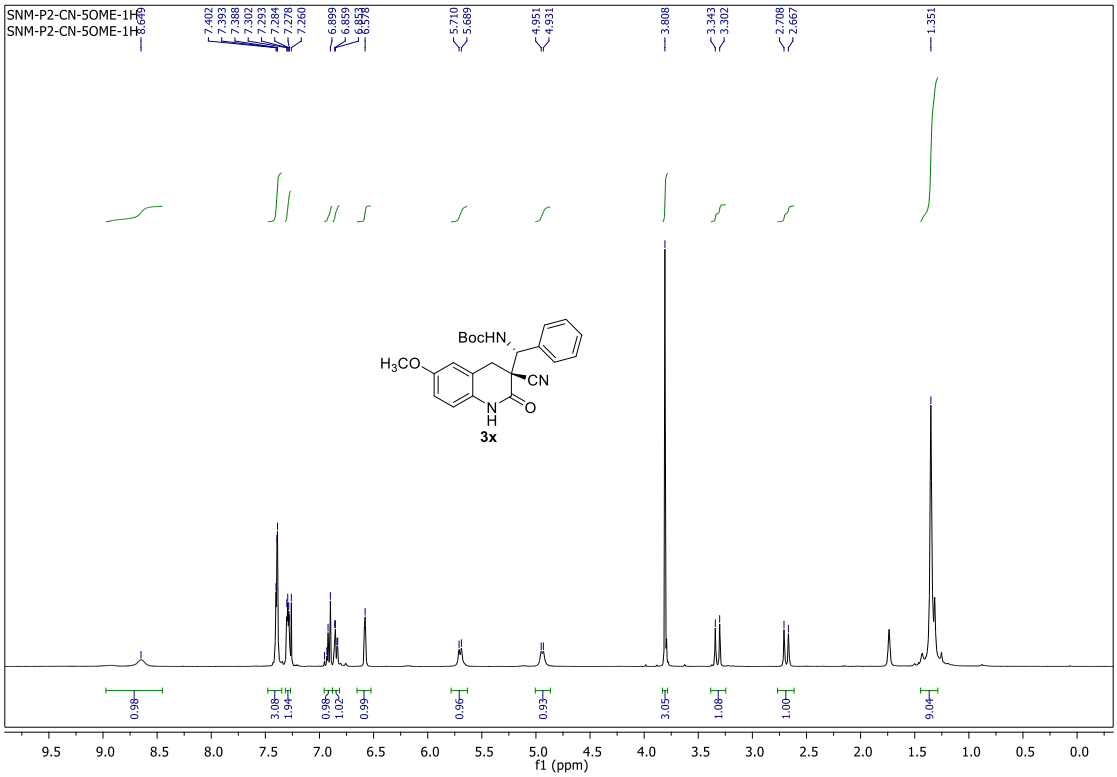

SNM-P2-CN-VAL-13C
SNM-P2-CN-VAL-13C
BocHN
CN
N
H
O
3u
f1 (ppm)

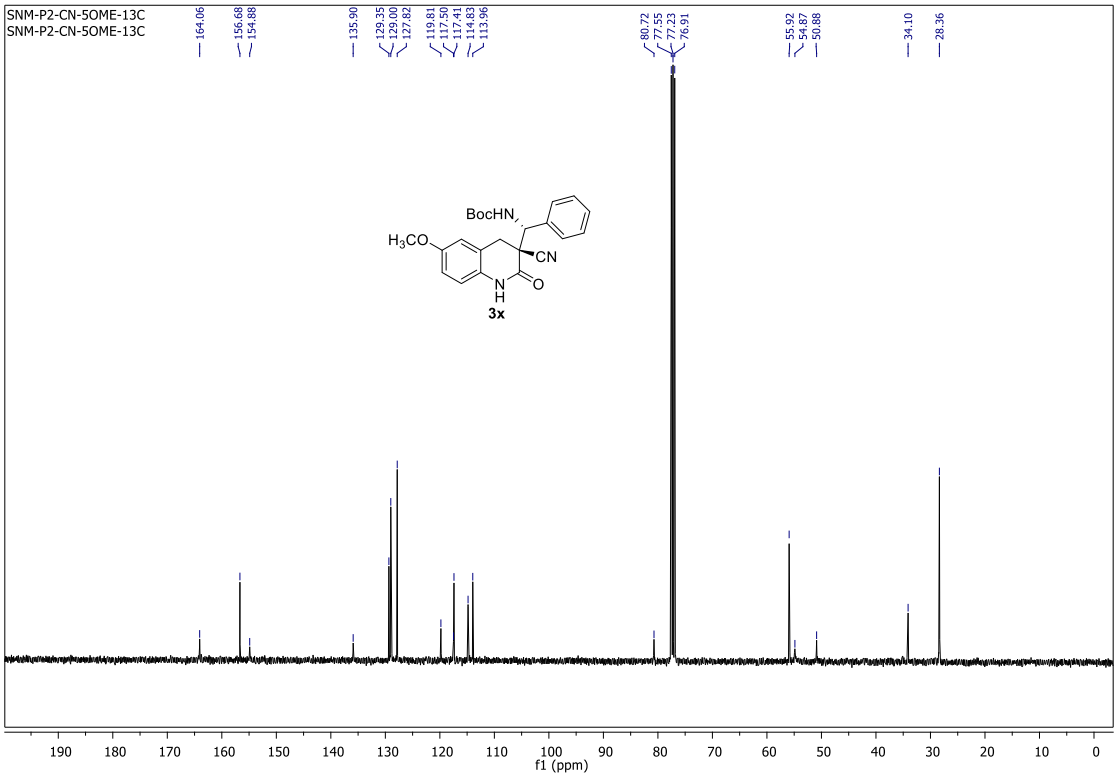

SNM-P2-CN-5F-B-1H
1H
8.350
7.420
7.414
7.411
7.272
7.265
7.260
7.057
7.049
7.029
6.954
6.946
6.939
6.932
6.924
6.770
6.758
4.946
4.934
3.355
3.328
2.711
2.684
1.357
BocHN
F
CN
N
H
O
3v
0.95
2.75
2.05
0.99
0.99
0.89
0.94
1.02
1.00
1.00
8.85
f1 (ppm)

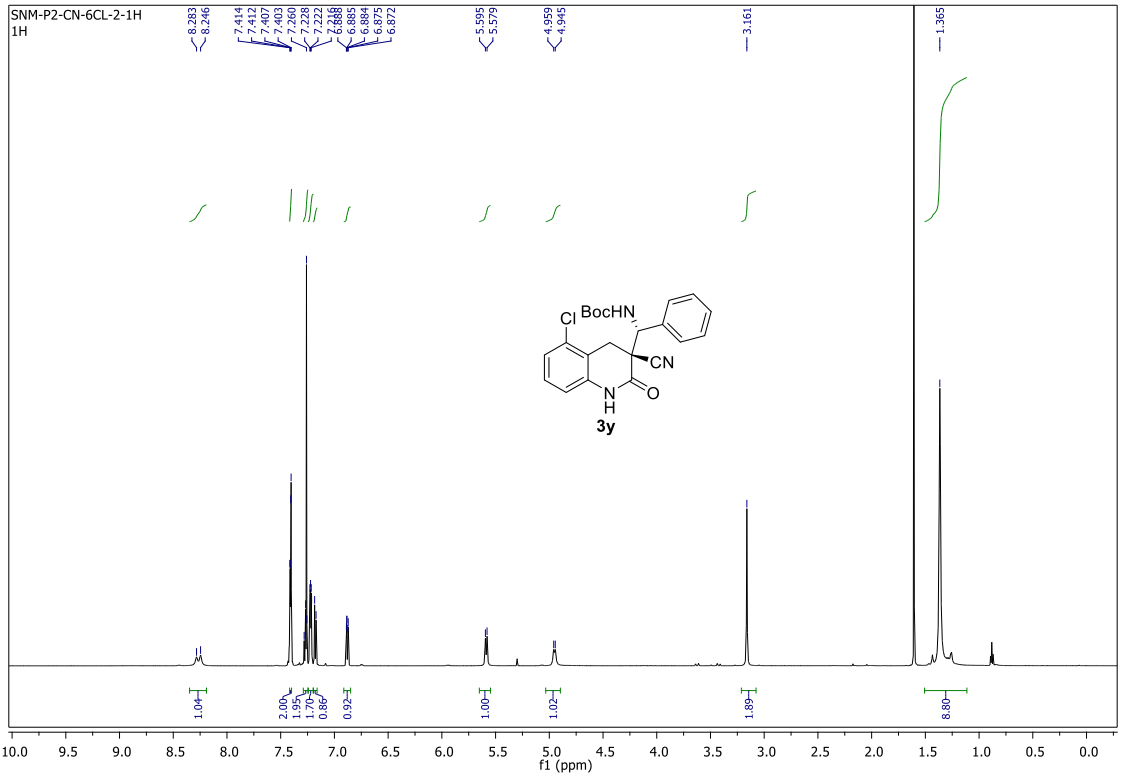

SNM-P2-CN-5F-B-13C
13C
163.97
163.91
160.21
158.59
154.95
135.49
132.25
129.60
129.24
127.69
120.25
120.20
117.60
117.55
116.18
116.03
115.95
115.80
80.89
77.44
77.23
77.02
54.93
50.82
33.83
28.36
BocHN
F
CN
N
H
O
3v
f1 (ppm)

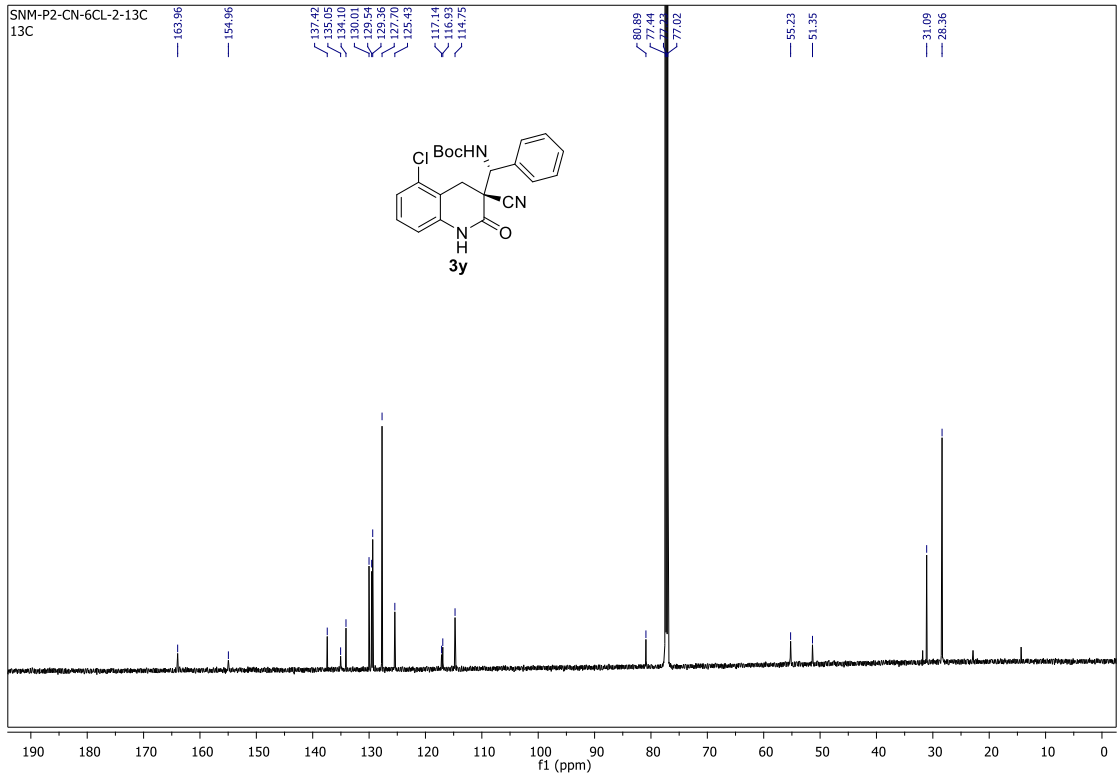

SNM-P2-CN-5CL-2A-1H
1H
8.083
7.430
7.428
7.422
7.419
7.308
7.305
7.294
7.291
7.271
7.260
7.016
6.901
6.887
5.570
5.554
4.946
4.933
3.345
3.317
2.709
2.682
1.365
BocHN
Cl
CN
N
H
O
3w
0.92
2.99
1.06
2.00
0.94
0.96
1.01
0.94
1.00
0.94
8.82
f1 (ppm)


SNM-P2-CN-5CL-2-13C
13C
163.80
154.95
135.38
134.66
129.64
129.34
129.28
117.37
117.18
80.92
77.44
77.23
77.02
54.95
50.90
33.67
28.36
BocHN
Cl
CN
N
H
O
3w
f1 (ppm)

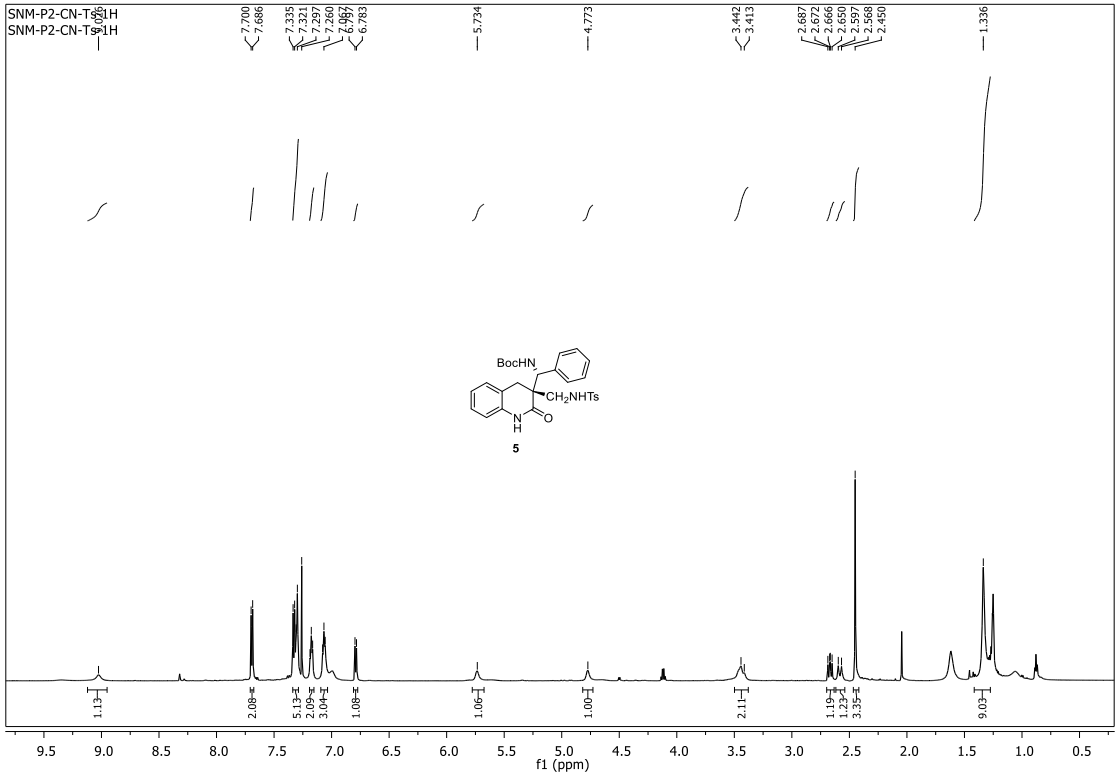

SNM-P2-CN-5OME-1H
SNM-P2-CN-5OME-1H
8.647
7.402
7.393
7.388
7.302
7.293
7.284
7.278
7.260
6.899
6.859
6.578
5.710
5.689
4.951
4.931
3.808
3.343
3.302
2.708
2.667
1.351
BocHN
H3CO
CN
N
H
O
3x
0.98
3.08
1.94
0.98
1.02
0.99
0.96
0.93
3.05
1.09
1.00
9.04
f1 (ppm)

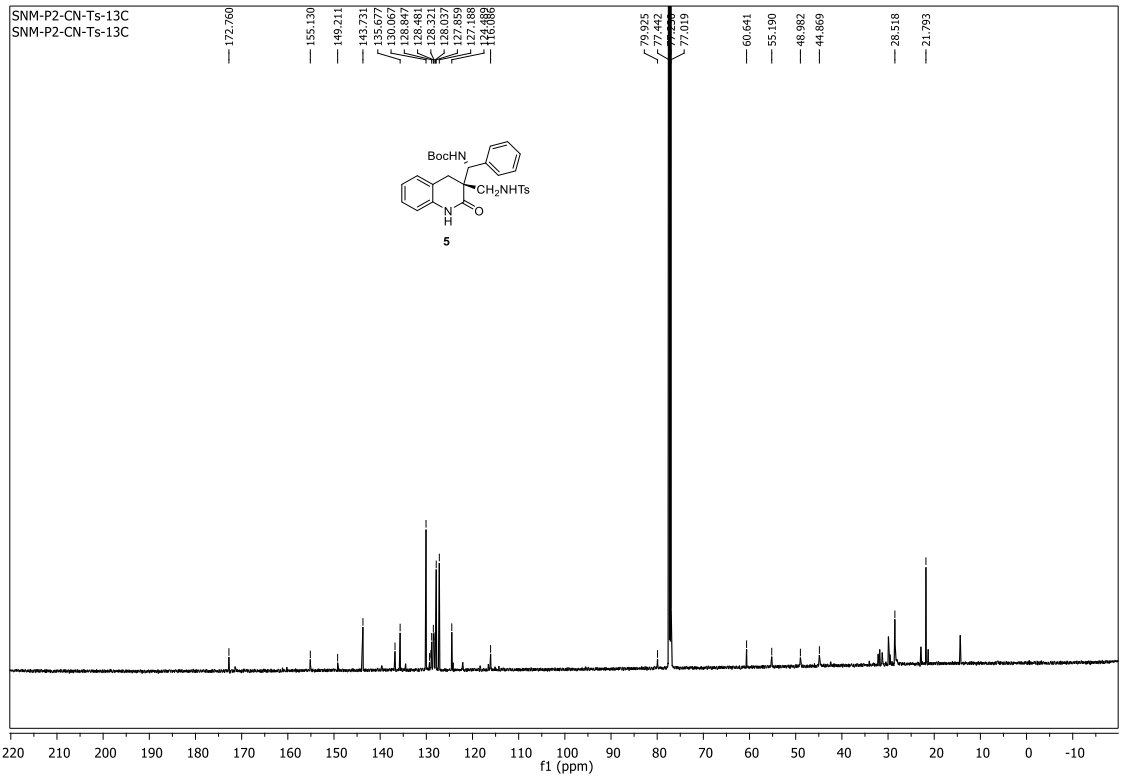

SNM-P2-CN-5OME-13C
SNM-P2-CN-5OME-13C
164.06
156.68
154.88
135.90
129.35
129.00
127.82
119.81
117.50
117.41
114.83
113.96
80.72
77.55
77.23
76.91
55.92
54.87
50.88
34.10
28.36
BocHN
H3CO
CN
N
H
O
3x
f1 (ppm)

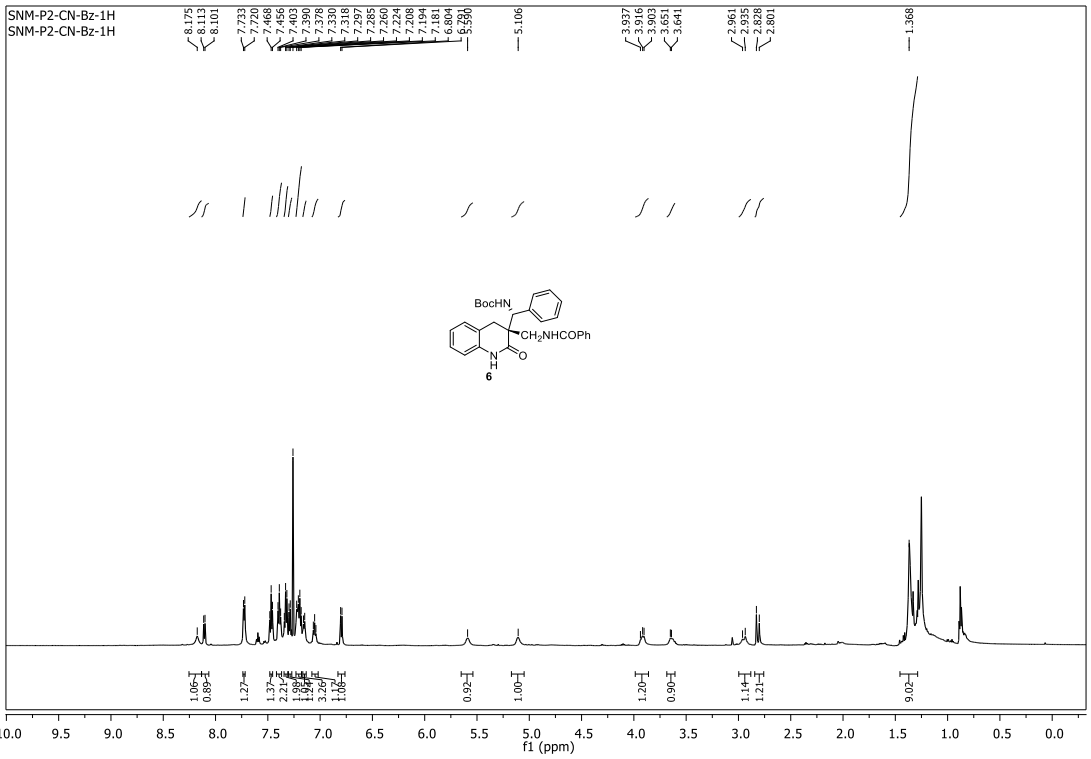

SNM-P2-CN-6CL-2-1H
1H
8.283
8.246
7.414
7.412
7.407
7.403
7.260
7.228
7.222
7.216
6.888
6.885
6.884
6.875
6.872
5.595
5.579
4.959
4.945
3.161
1.365
Cl
BocHN
CN
N
H
O
3y
1.04
2.00
1.95
1.70
0.86
0.92
1.00
1.02
1.89
8.80
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

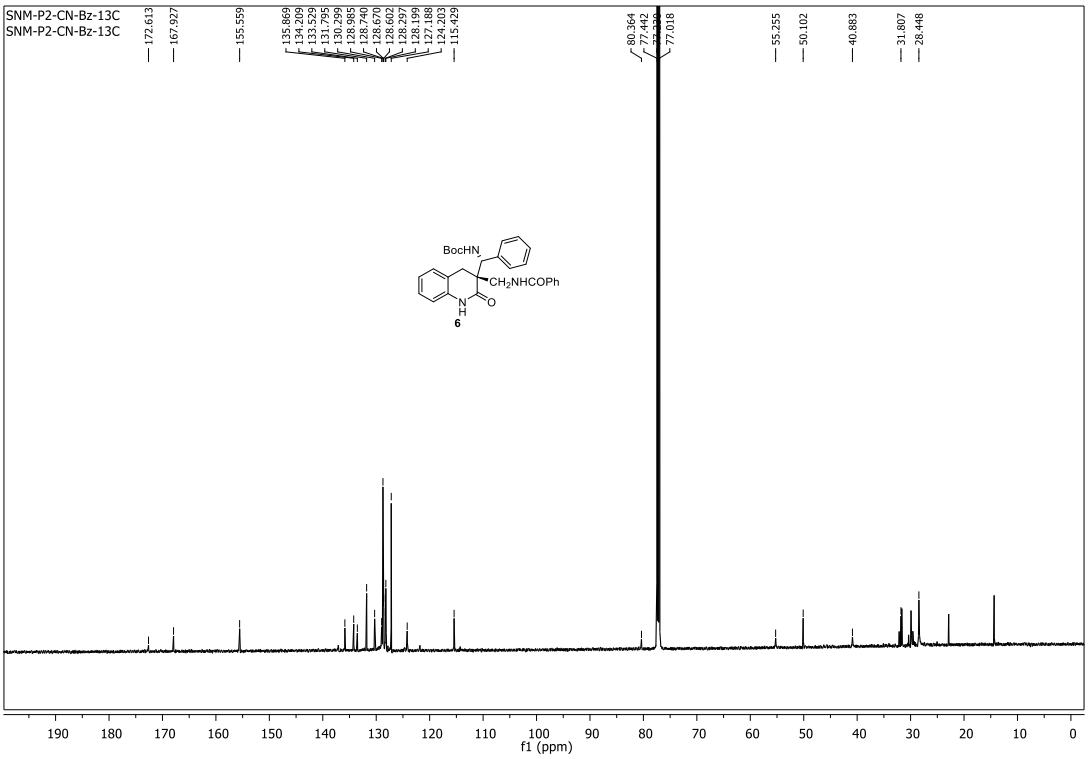

SNM-P2-CN-6CL-2-13C
13C
163.96
154.96
137.42
135.05
134.10
130.01
129.54
129.36
127.70
125.43
117.14
116.93
114.75
80.89
77.44
77.23
77.02
55.23
51.35
31.09
28.36
Cl
BocHN
CN
N
H
O
3y
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

K. **NMR spectra for compounds 5 and 6**.

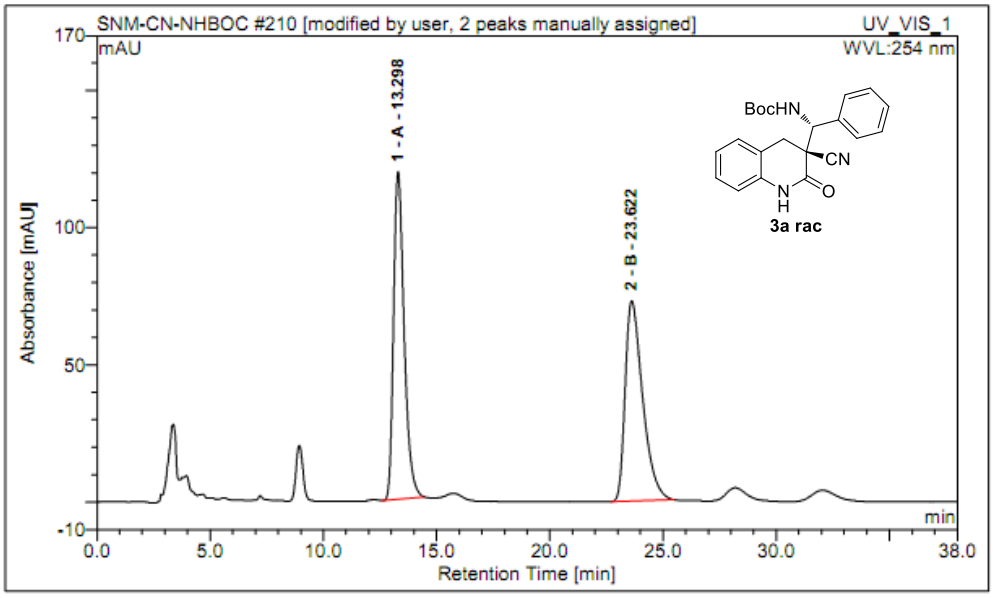




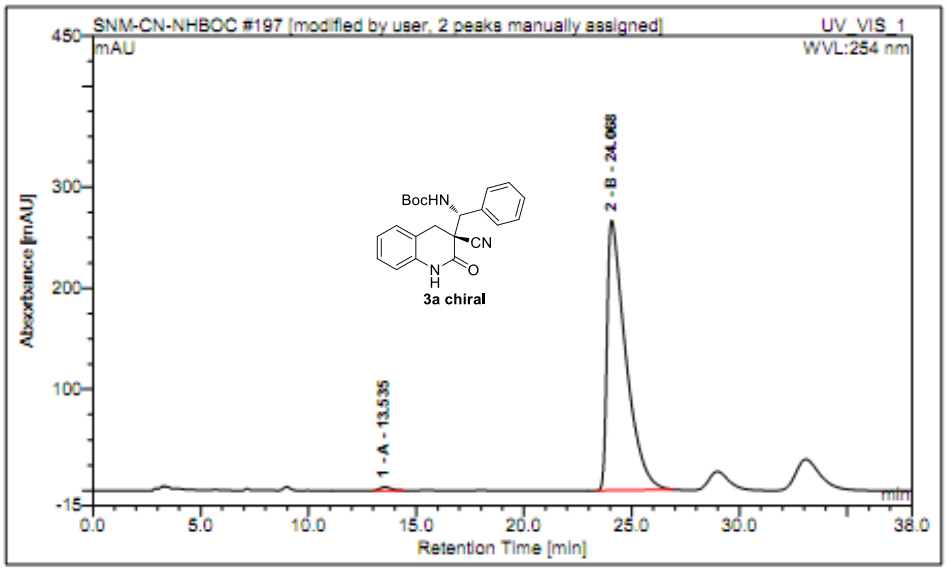

SNM-P2-CN-Bz-1H
SNM-P2-CN-Bz-1H
8.175
8.113
8.101
7.733
7.720
7.468
7.456
7.403
7.390
7.378
7.330
7.318
7.297
7.285
7.260
7.224
7.208
7.194
7.181
6.804
5.490
5.106
3.937
3.916
3.903
3.651
2.961
2.935
2.828
2.801
1.368
BocHN
CH2NHCOPh
N
H
O
6
1.06
0.89
1.27
1.37
2.21
3.26
1.05
0.92
1.00
1.20
0.96
1.14
1.21
9.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


SNM-P2-CN-Bz-13C
SNM-P2-CN-Bz-13C
172.613
167.927
155.559
135.869
134.209
133.529
131.795
130.299
128.985
128.740
128.670
128.602
128.297
128.199
127.188
124.203
115.429
80.364
77.442
77.018
55.255
50.102
40.883
31.807
28.448
BocHN
CH2NHCOPh
N
H
O
6
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

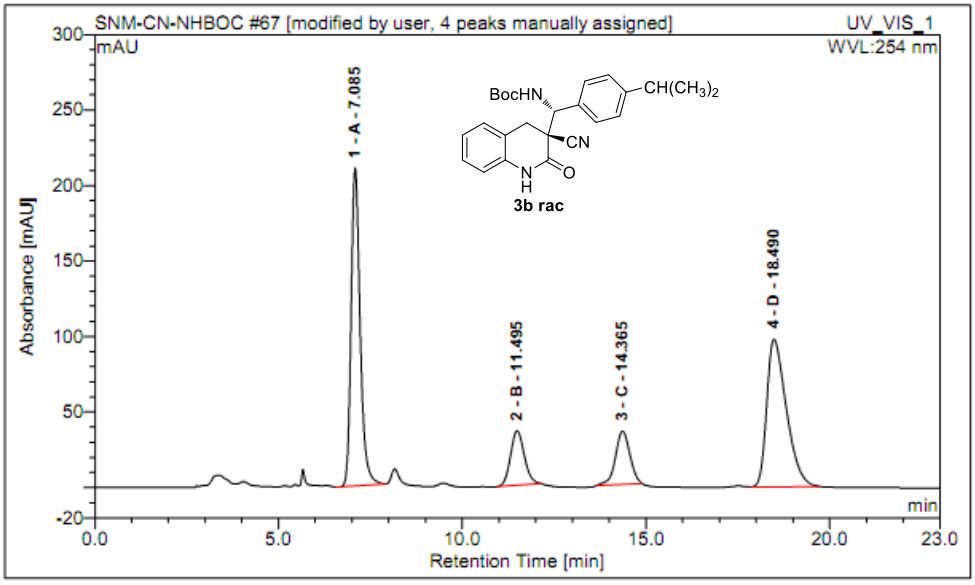
L. HPLC chromatogram of (3a-3x):



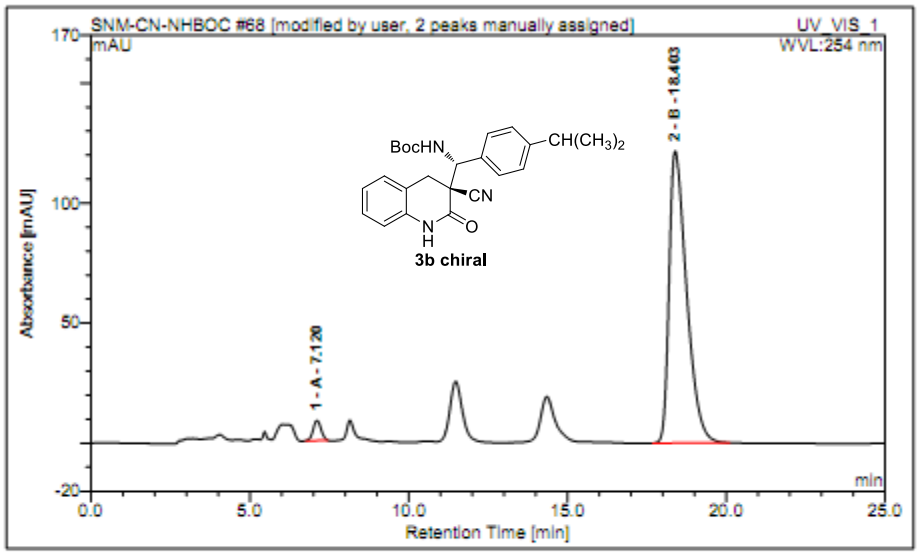
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	13.30	64.46922	49.67792177	119.3821	n.a.
2	B	23.62	65.305	50.32207823	73.072	n.a.



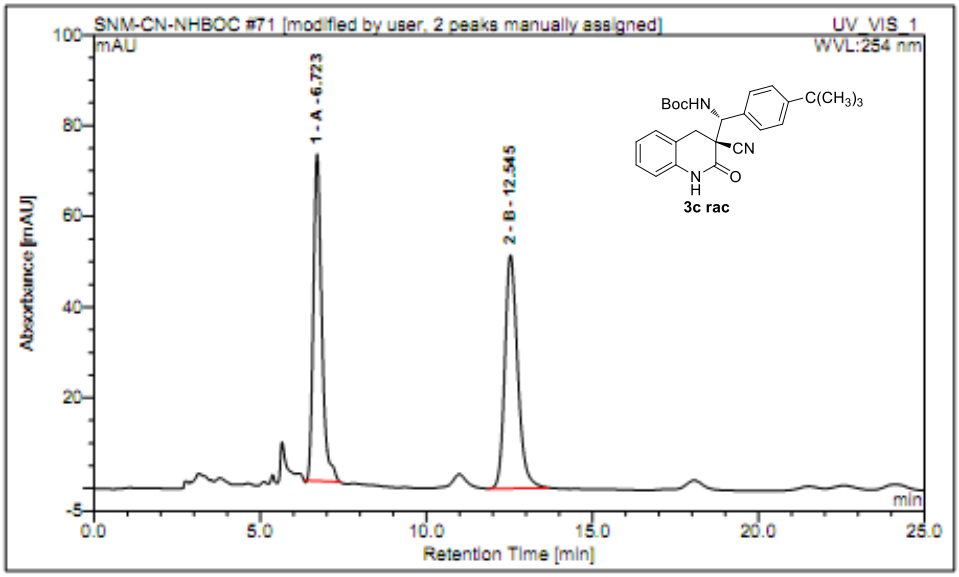
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	13.54	1.958975	0.7249404456	3.48584	n.a.
2	B	24.07	268.267	99.27505955	267.162	n.a.



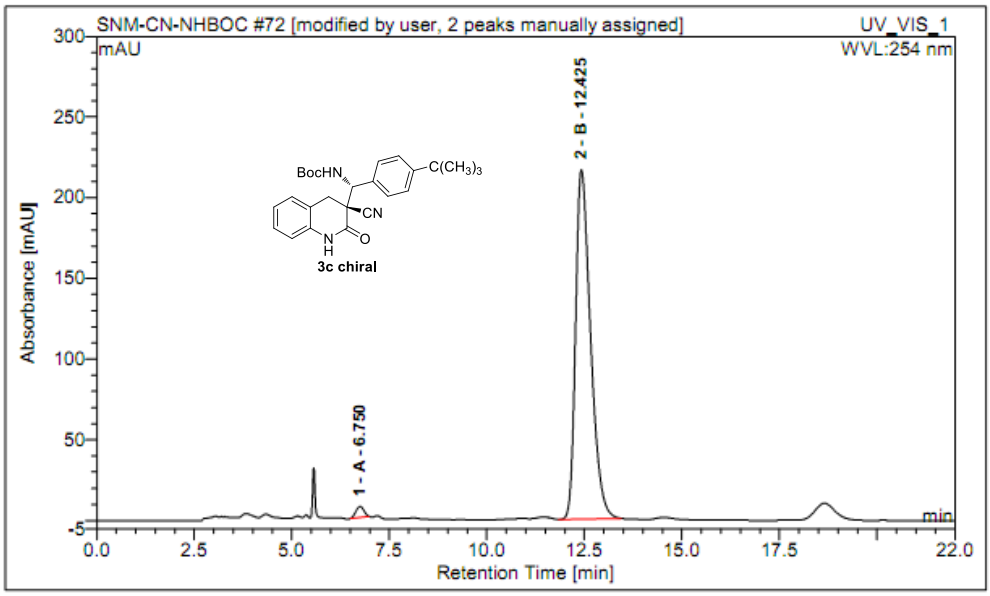
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	7.09	59.74332	39.3100704	210.4476	n.a.
2	B	11.50	15.74025	10.35681341	36.13066	n.a.
3	C	14.37	16.11928	10.60620663	35.33223	n.a.
4	D	18.49	60.377	39.72690957	97.716	n.a.



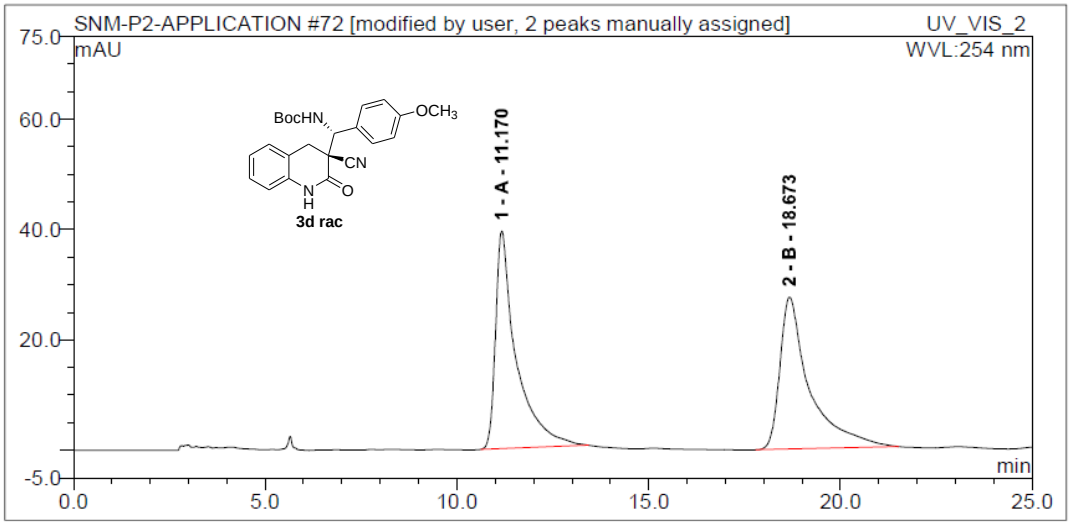
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	7.12	2.375762	2.995406368	8.29824	n.a.
2	B	18.40	76.938	97.00459363	121.483	n.a.



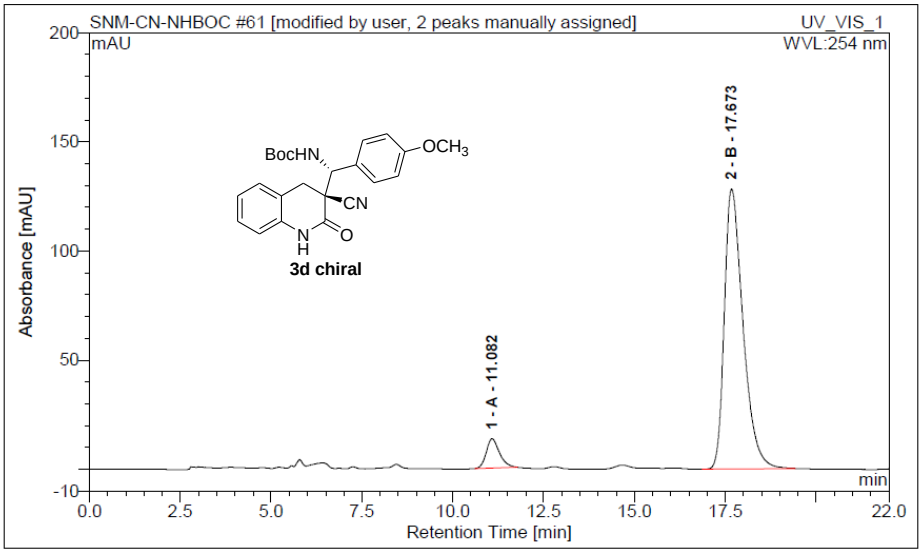
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	6.72	21.04102	47.87106647	72.11329	n.a.
2	B	12.55	22.913	52.12893353	51.419	n.a.



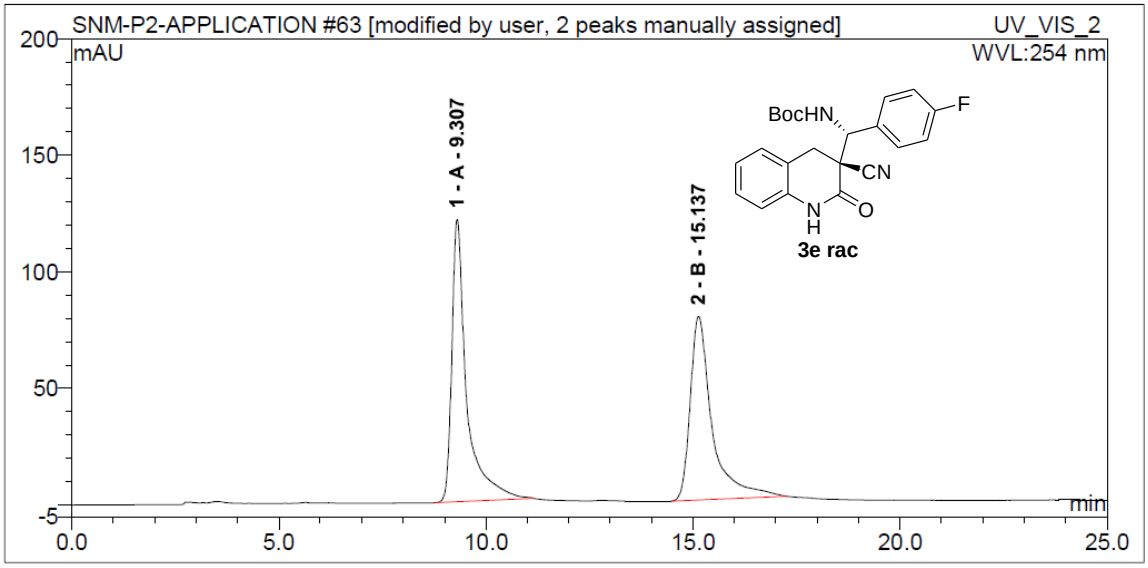
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	6.75	1.628575	1.669745436	6.82761	n.a.
2	B	12.43	95.906	98.33025456	216.476	n.a.



No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	11.17	24.64335	49.98869234	39.39663	n.a.
2	B	18.67	24.654	50.01130766	27.507	n.a.

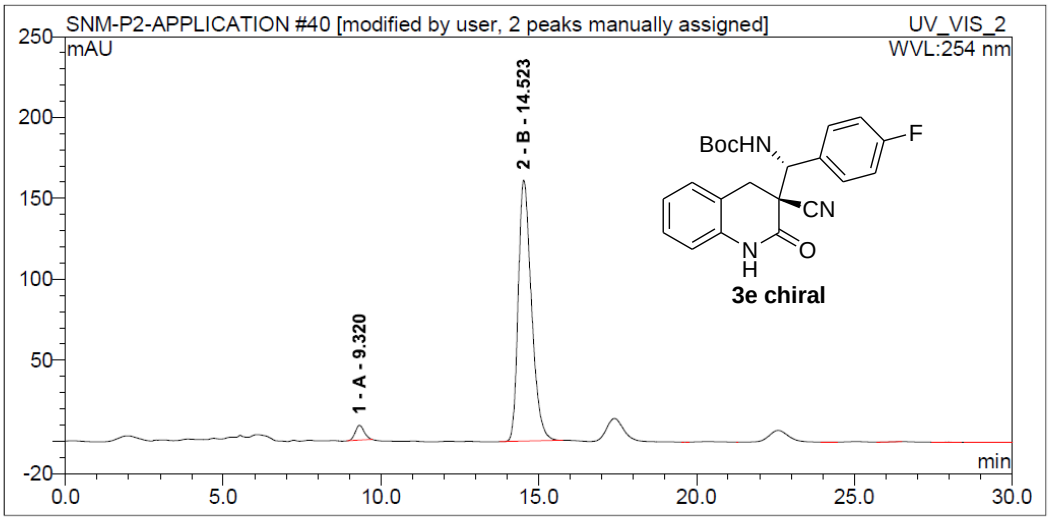


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	11.08	5.639742	6.873293241	13.4057	n.a.
2	B	17.67	76.413	93.12670676	128.277	n.a.

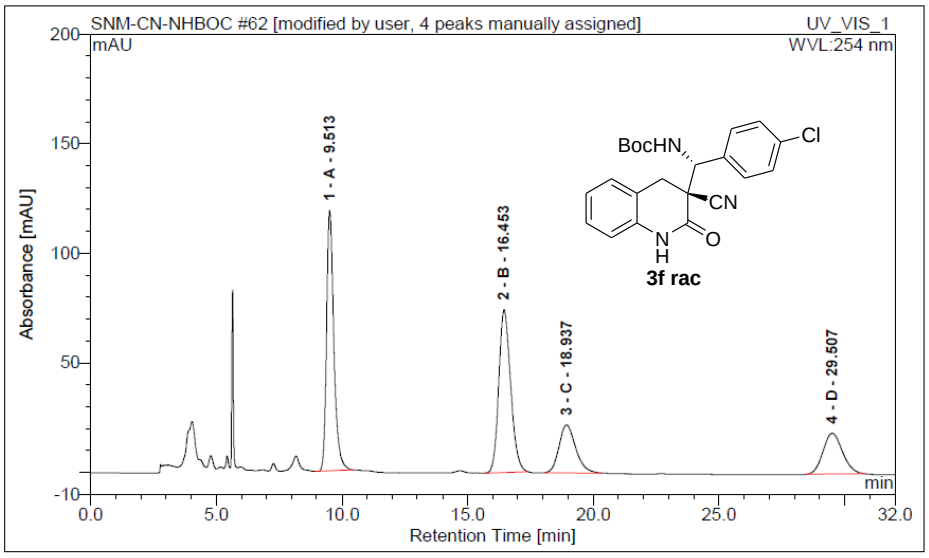


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	9.31	50.16329	50.94421387	120.9652	n.a.
2	B	15.14	48.304	49.05578613	78.630	n.a.

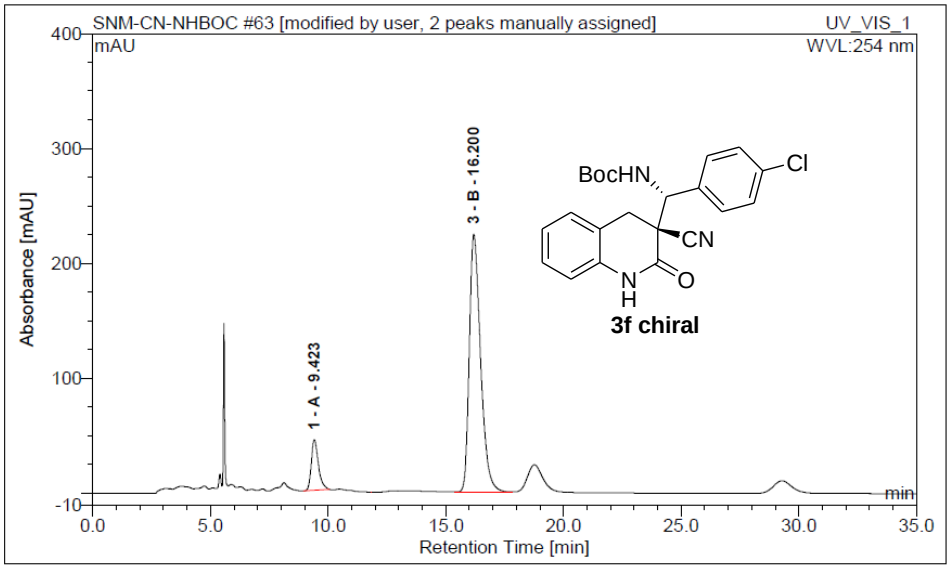
AMS-2-11C



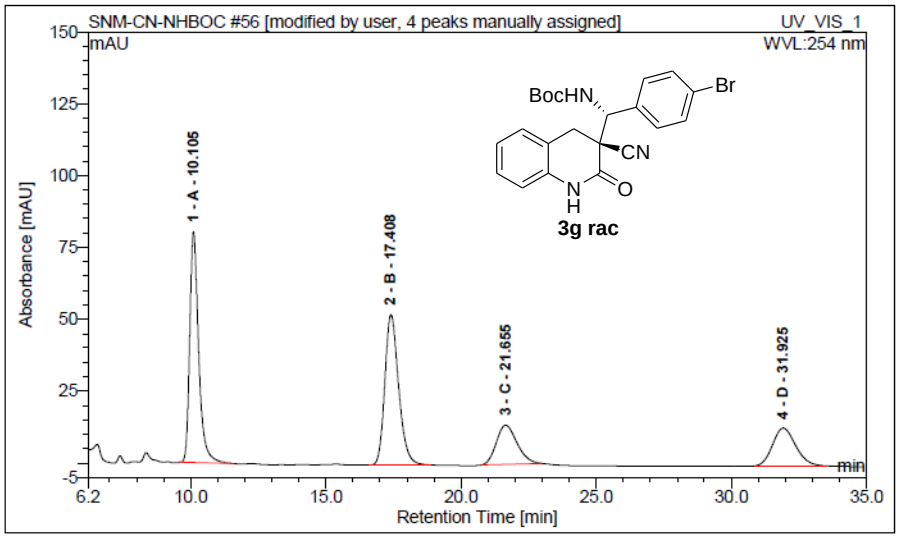
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	9.32	2.974208	3.659658508	9.14231	n.a.
2	B	14.52	78.296	96.34034149	161.373	n.a.



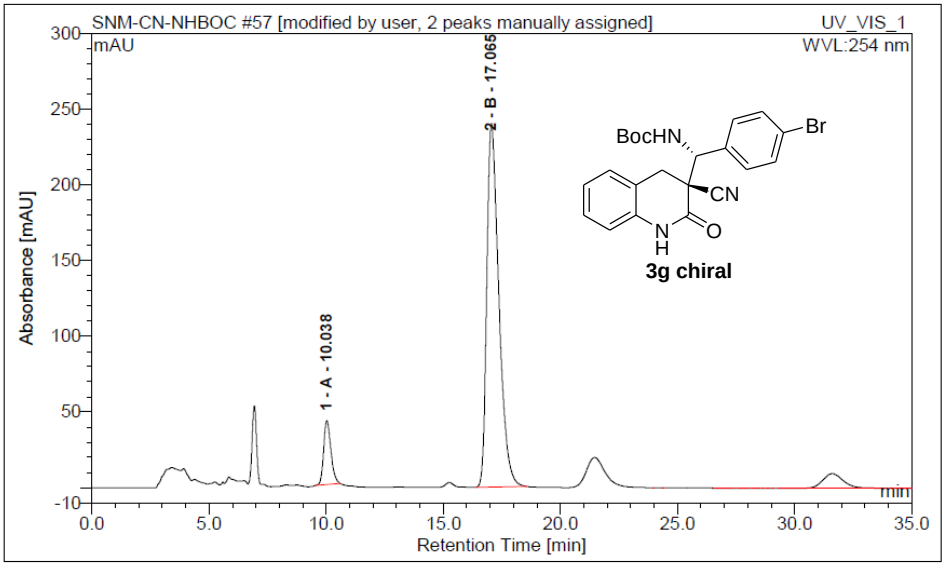
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	9.51	39.81493	34.93880522	118.688	n.a.
2	B	16.45	40.69044	35.70708627	74.23365	n.a.
3	C	18.94	16.66013	14.61976984	21.76877	n.a.
4	D	29.51	16.791	14.73433867	18.680	n.a.



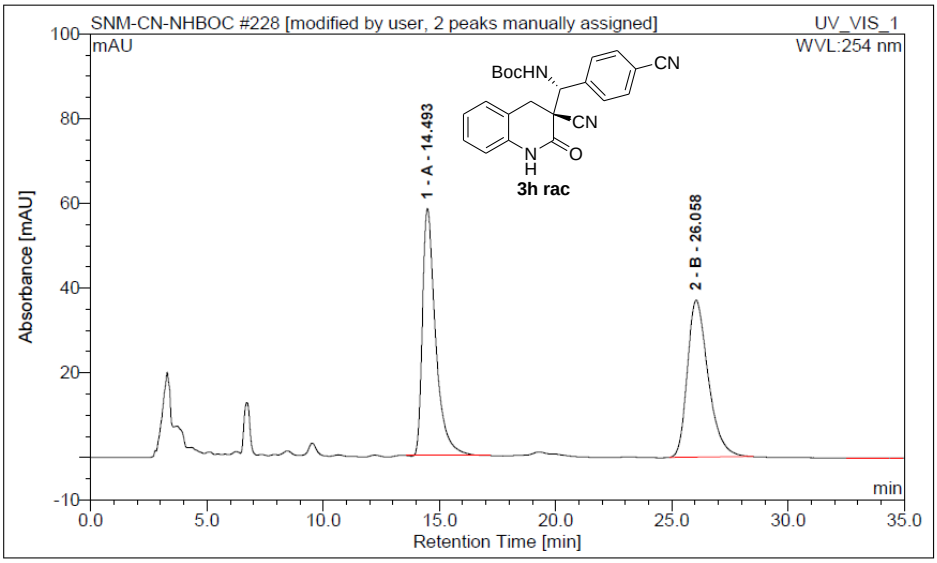
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	9.42	15.32218	10.9308055	44.01151	n.a.
3	B	16.20	124.852	89.0691945	224.408	n.a.



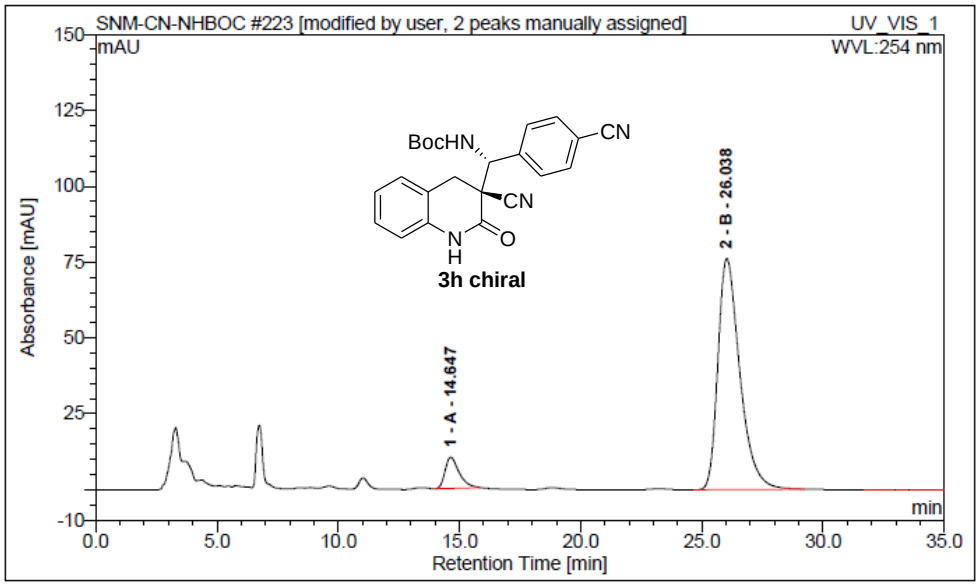
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.11	30.64083	35.29685367	80.30374	n.a.
2	B	17.41	31.06313	35.78332561	52.42863	n.a.
3	C	21.66	12.03251	13.86090761	13.61745	n.a.
4	D	31.93	13.072	15.05891312	13.195	n.a.



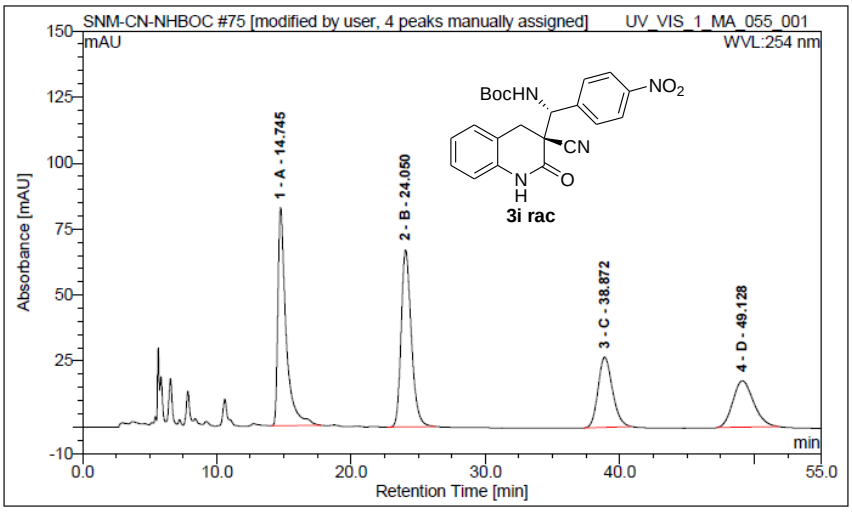
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.04	15.204	9.616497016	42.20298	n.a.
2	B	17.07	142.899	90.38350298	239.903	n.a.



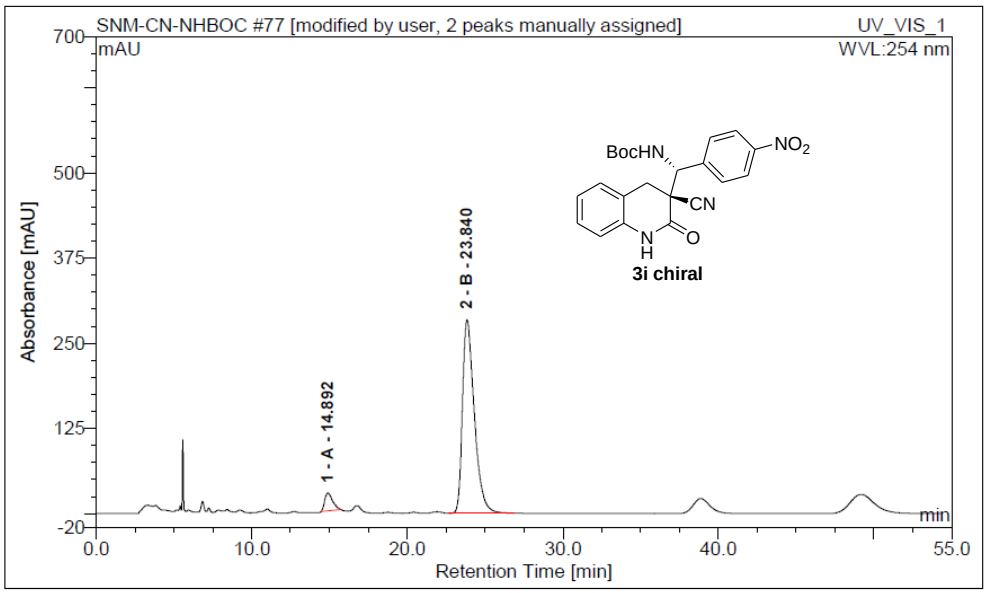
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	14.49	38.36162	49.90884617	58.3193	n.a.
2	B	26.06	38.502	50.09115383	37.019	n.a.



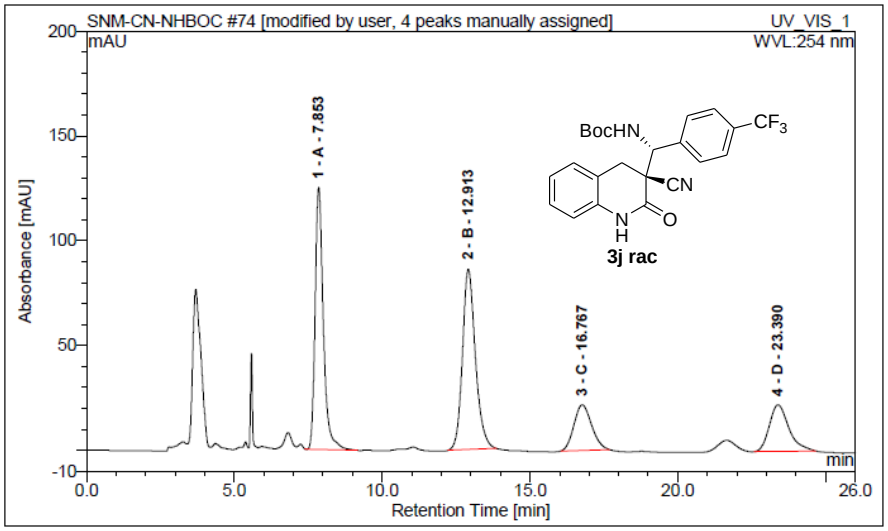
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	14.65	6.838047	7.889626137	10.24163	n.a.
2	B	26.04	79.833	92.11037386	76.114	n.a.



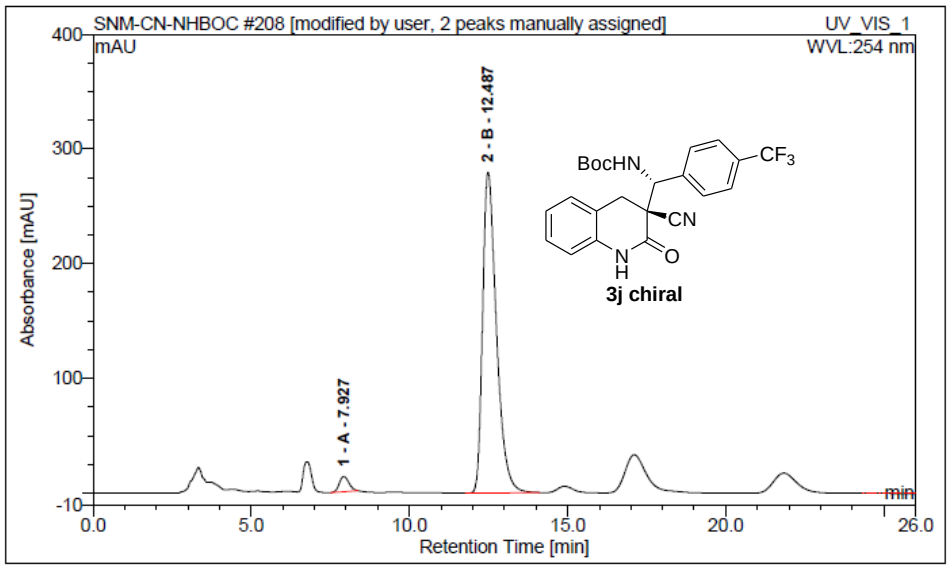
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	14.75	58.37699	32.13962175	82.68809	n.a.
2	B	24.05	58.90589	32.43080831	67.01871	n.a.
3	C	38.87	32.9835	18.15916249	26.58437	n.a.
4	D	49.13	31.369	17.27040745	17.534	n.a.



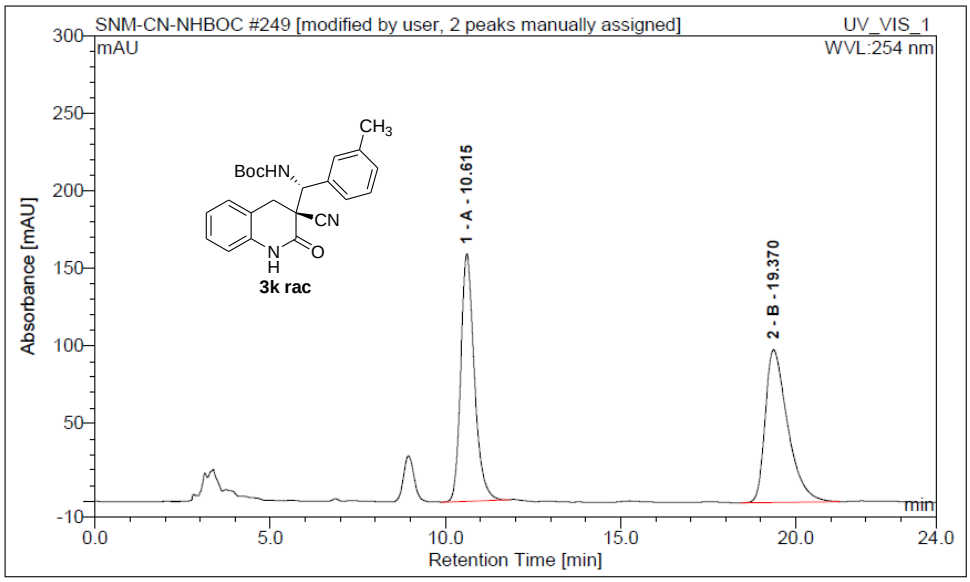
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	14.89	15.15808	5.696434244	25.79444	n.a.
2	B	23.84	250.940	94.30356576	283.865	n.a.



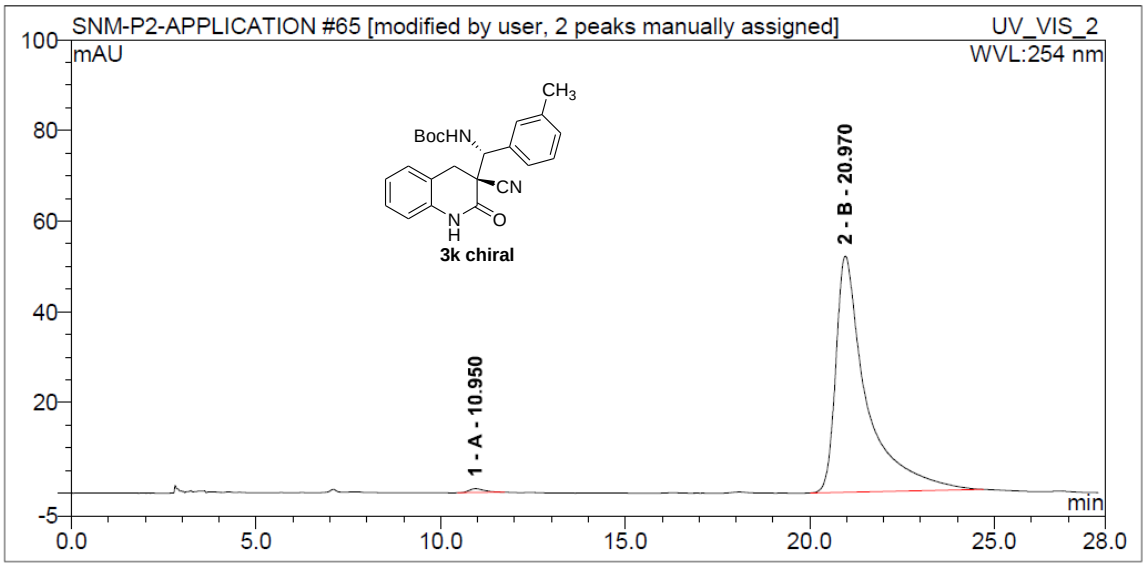
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	7.85	40.28421	34.73902805	124.9848	n.a.
2	B	12.91	43.6674	37.6565091	86.13129	n.a.
3	C	16.77	15.04645	12.97528148	21.70995	n.a.
4	D	23.39	16.964	14.62918137	22.215	n.a.



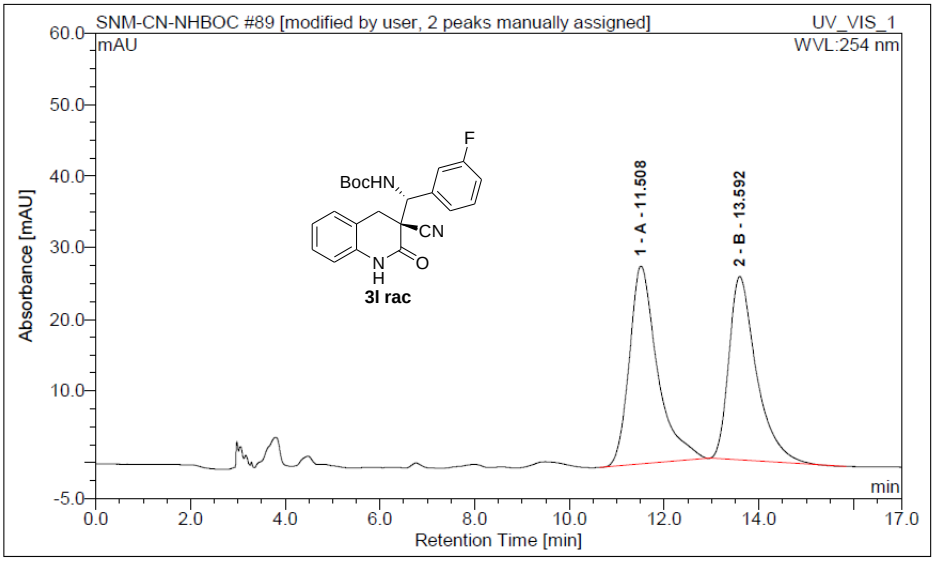
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	7.93	4.629399	3.168950292	13.25405	n.a.
2	B	12.49	141.457	96.83104971	279.469	n.a.



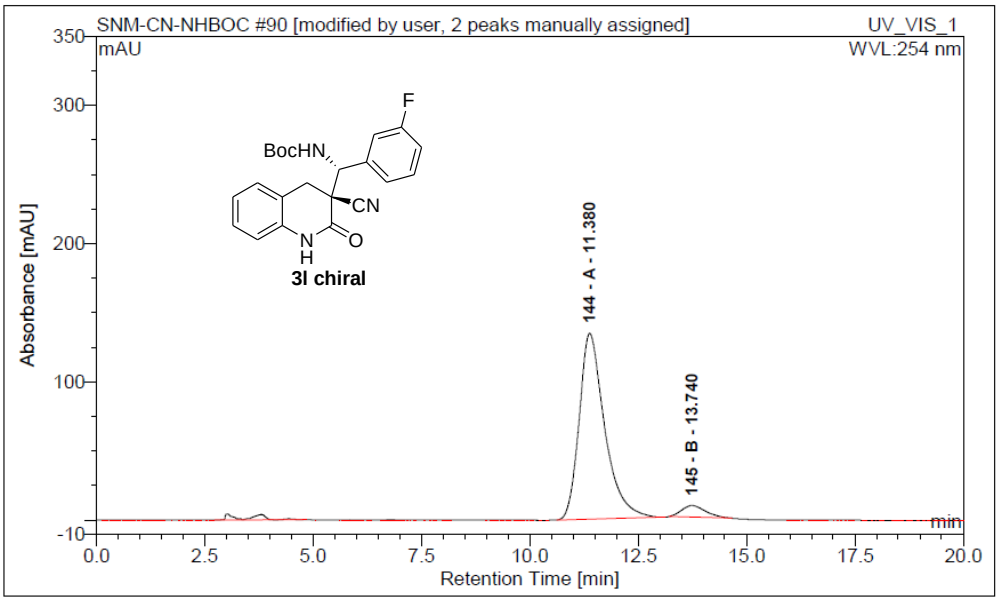
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.62	71.56518	49.54853841	159.3418	n.a.
2	B	19.37	72.869	50.45146159	98.340	n.a.



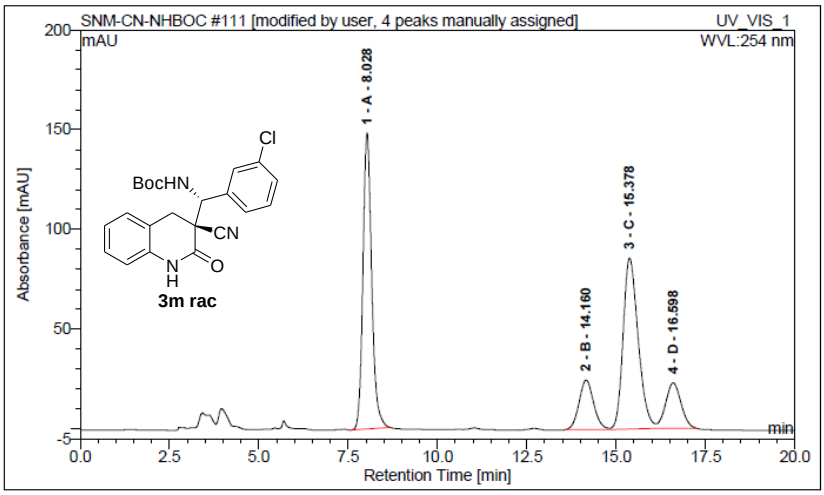
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.95	0.419681	0.8294113961	0.88436	n.a.
2	B	20.97	50.180	99.1705886	52.078	n.a.



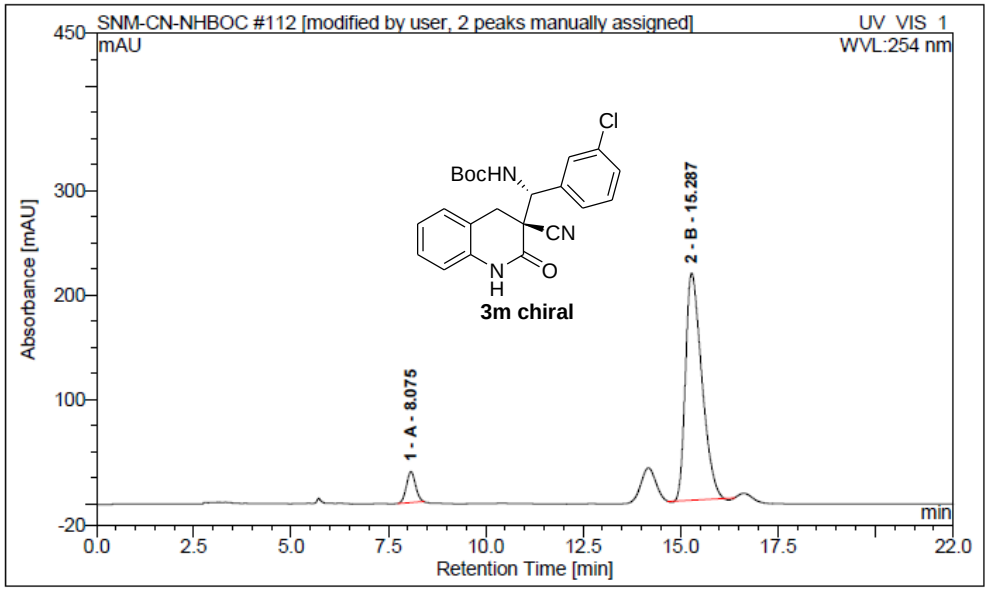
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	11.51	18.97842	52.39895874	27.64896	n.a.
2	B	13.59	17.241	47.60104126	25.632	n.a.



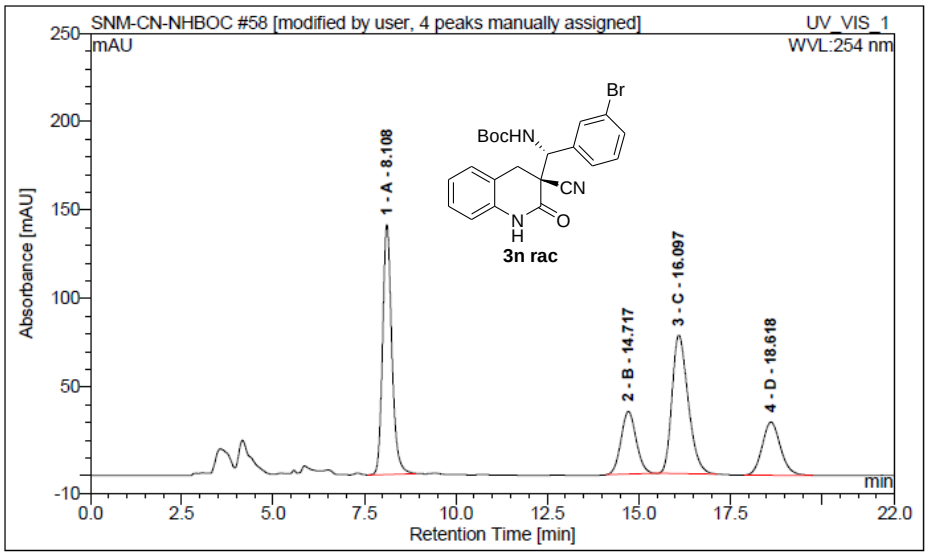
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
144	A	11.38	91.62073	94.40659037	134.3572	n.a.
145	B	13.74	5.428	5.593409631	8.398	n.a.



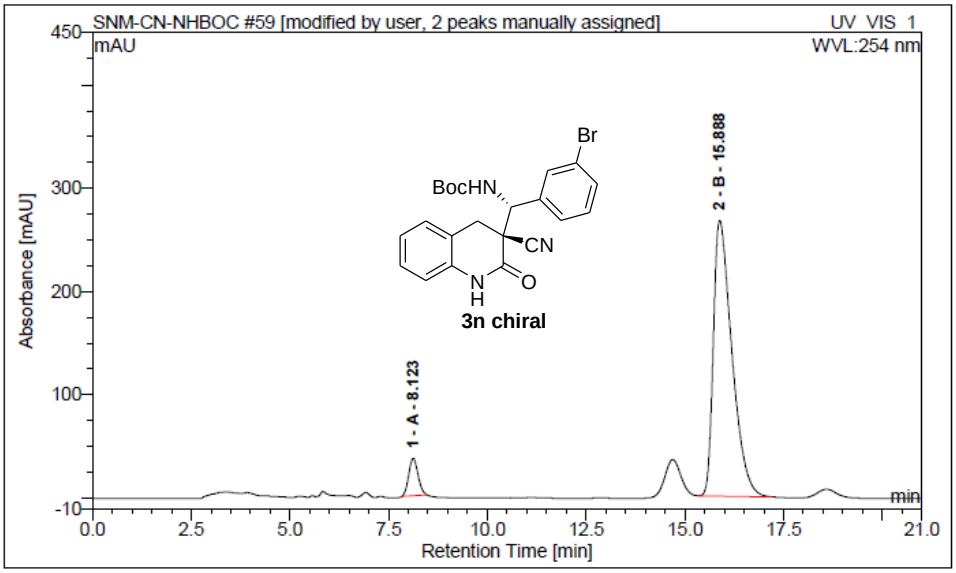
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	8.03	41.99742	39.19883782	148.3711	n.a.
2	B	14.16	11.78208	10.99695735	24.91815	n.a.
3	C	15.38	41.91837	39.12505283	85.7863	n.a.
4	D	16.60	11.442	10.679152	22.832	n.a.



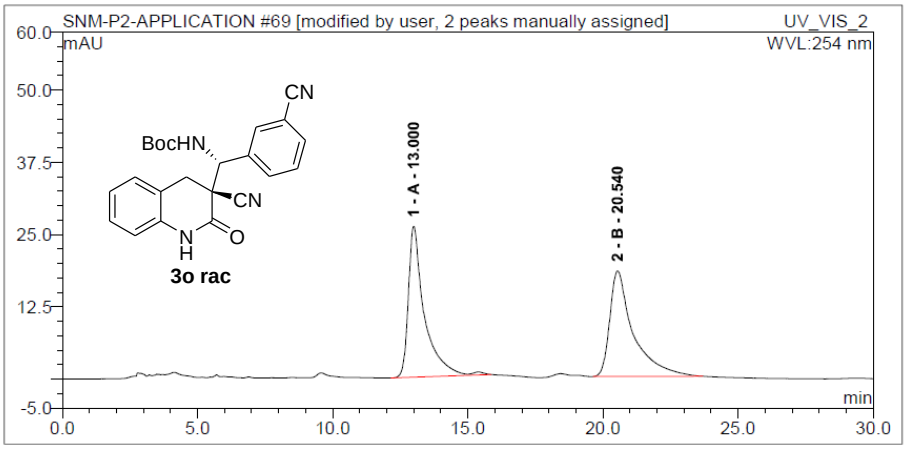
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	8.08	7.933325	7.00414999	29.35516	n.a.
2	B	15.29	105.333	92.99585001	217.205	n.a.



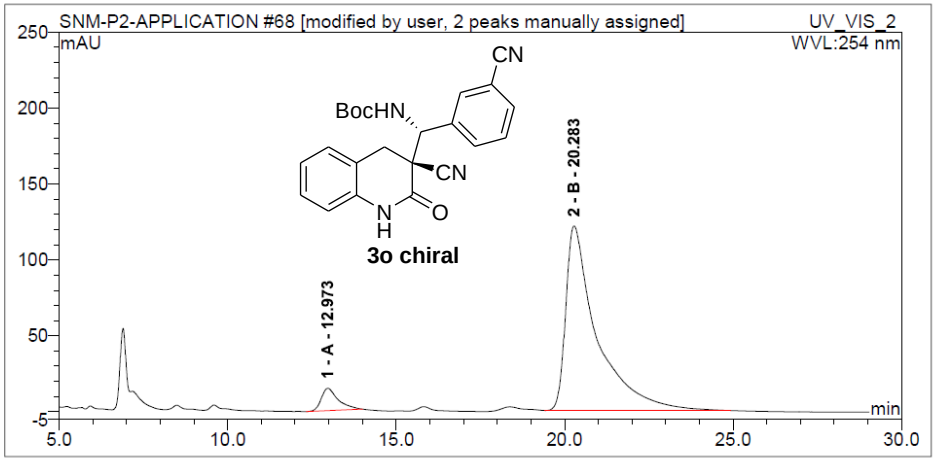
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	8.11	41.33693	35.65109068	141.0964	n.a.
2	B	14.72	17.14856	14.78979819	35.46796	n.a.
3	C	16.10	40.01417	34.51027181	78.08548	n.a.
4	D	18.62	17.449	15.04883932	30.030	n.a.



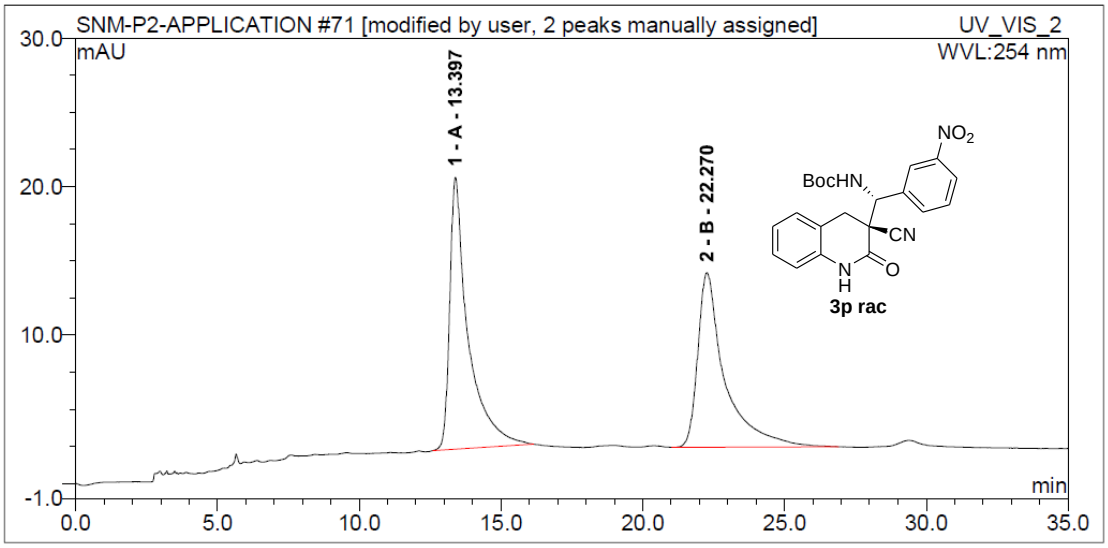
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	8.12	9.878258	6.386007989	36.26539	n.a.
2	B	15.89	144.808	93.61399201	266.852	n.a.



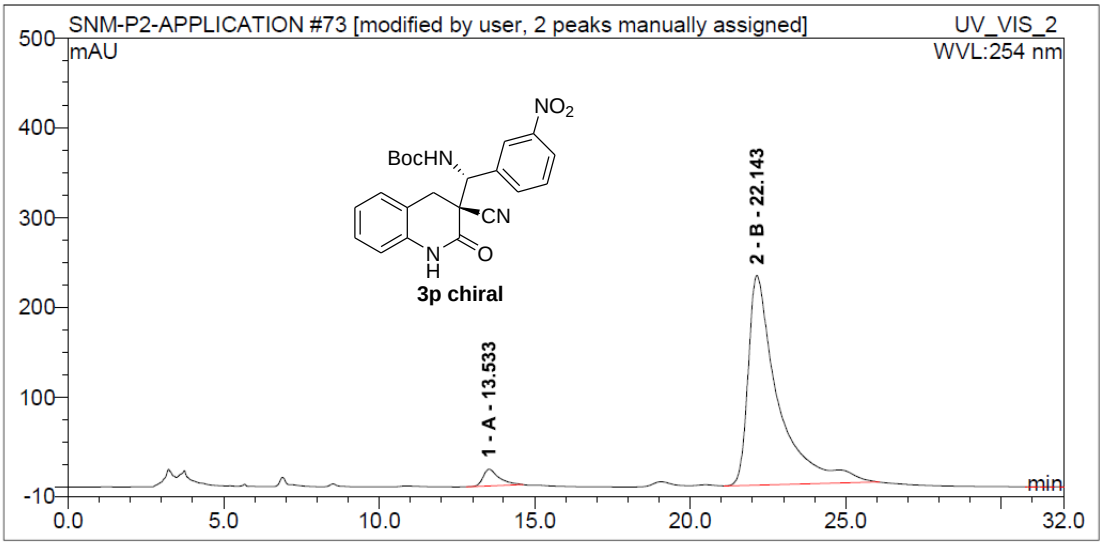
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	13.00	18.00653	49.46412902	26.09284	n.a.
2	B	20.54	18.397	50.53587098	18.262	n.a.



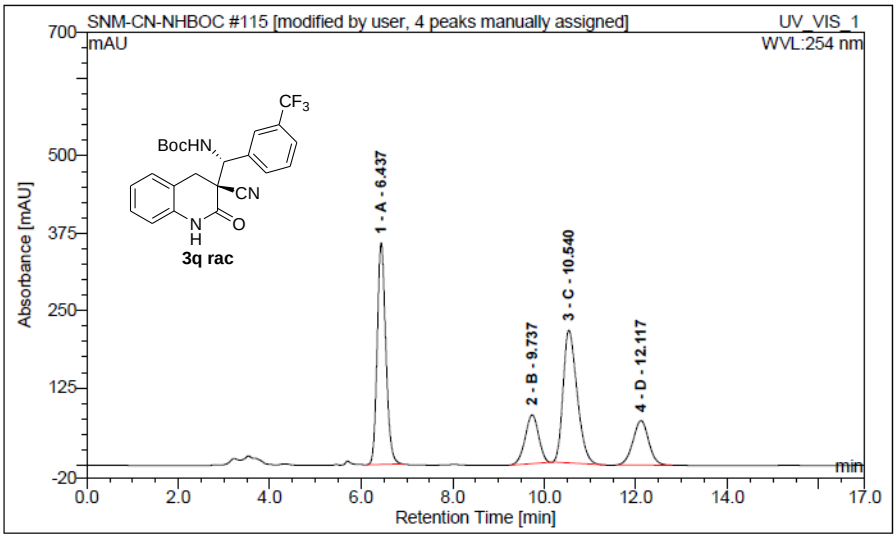
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	12.97	8.476404	6.126382643	14.67749	n.a.
2	B	20.28	129.883	93.87361736	121.406	n.a.



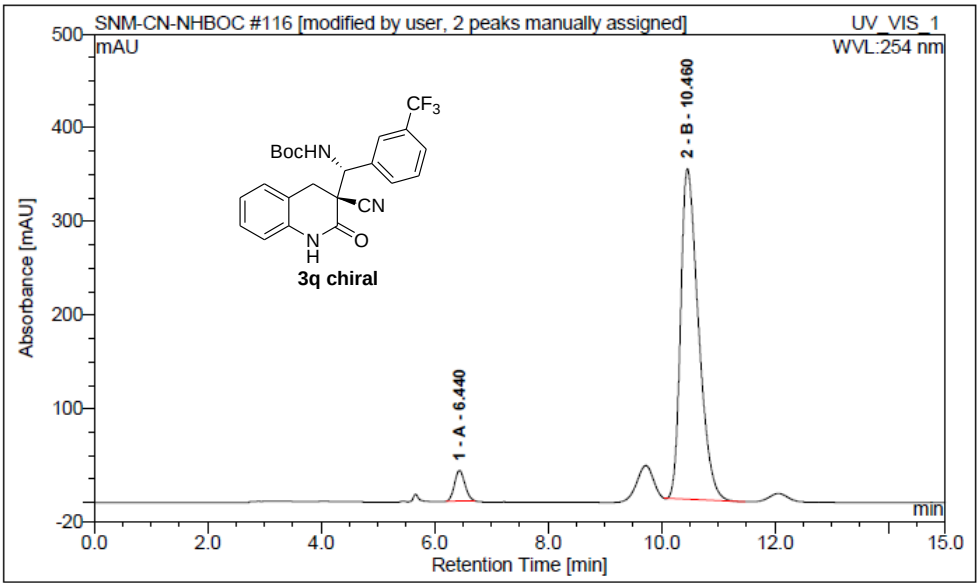
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	13.40	13.80261	51.5090966	18.30333	n.a.
2	B	22.27	12.994	48.4909034	11.751	n.a.



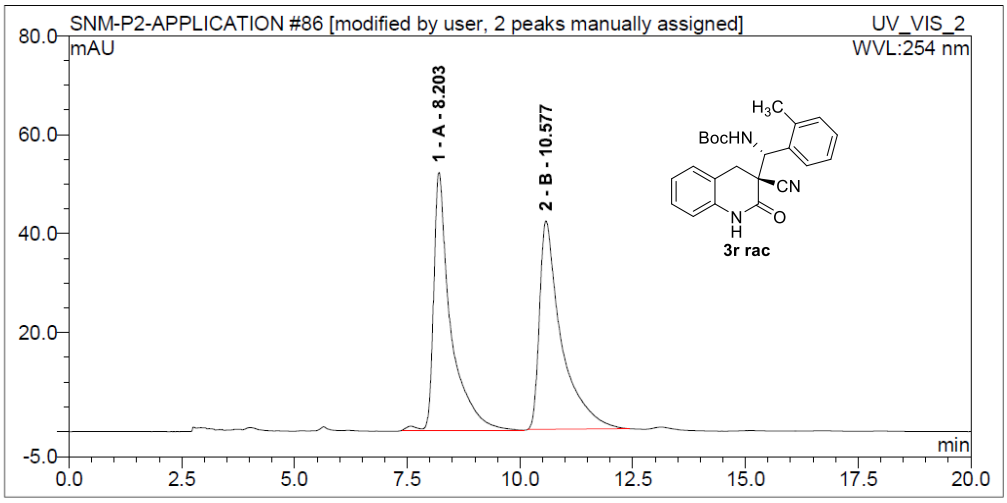
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	13.53	11.05259	4.087419083	18.57838	n.a.
2	B	22.14	259.353	95.91258092	233.160	n.a.



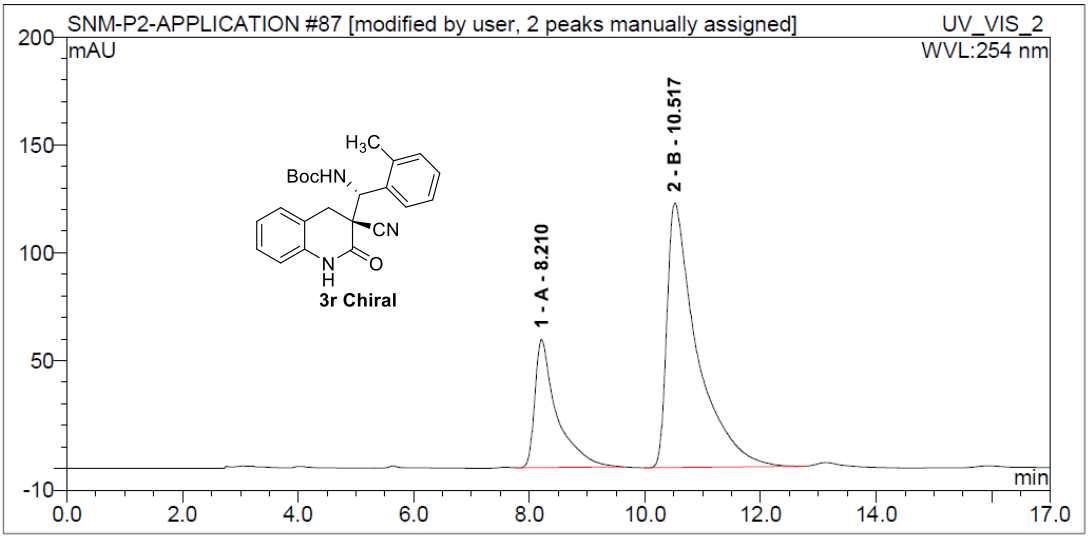
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	6.44	78.08648	37.35313338	358.4304	n.a.
2	B	9.74	26.69917	12.77170553	78.63542	n.a.
3	C	10.54	75.97264	36.34196408	214.3655	n.a.
4	D	12.12	28.291	13.53319701	71.593	n.a.



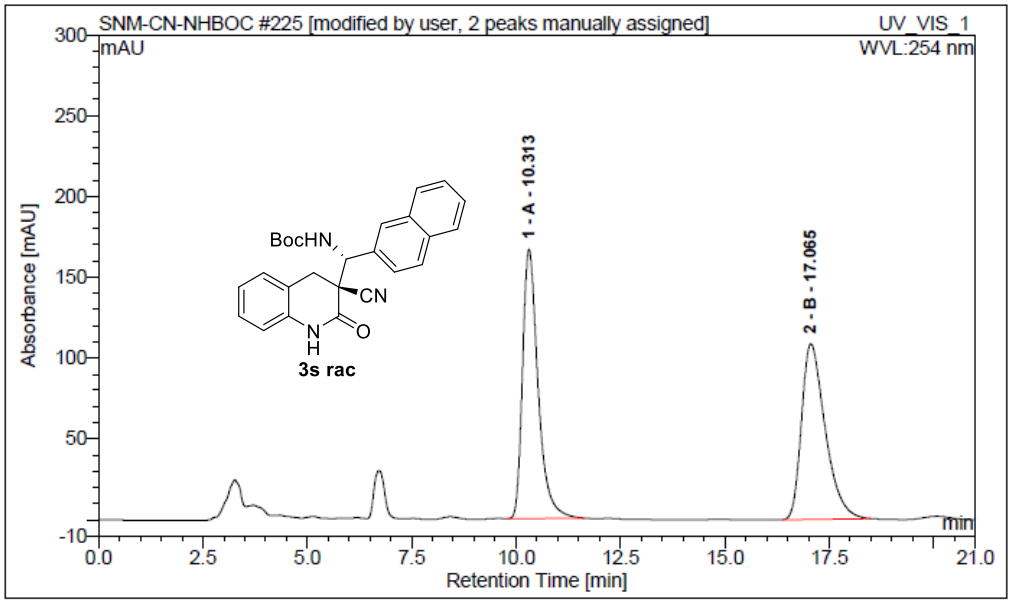
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	6.44	6.883532	5.078912396	32.58087	n.a.
2	B	10.46	128.648	94.9210876	353.070	n.a.



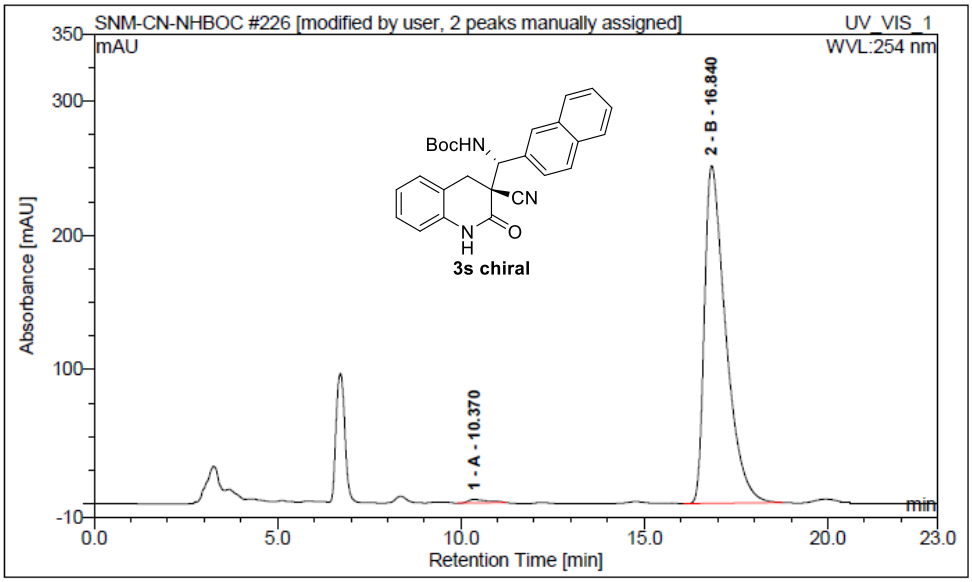
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	8.20	22.7404	49.03843212	52.00156	n.a.
2	B	10.58	23.632	50.96156788	42.062	n.a.



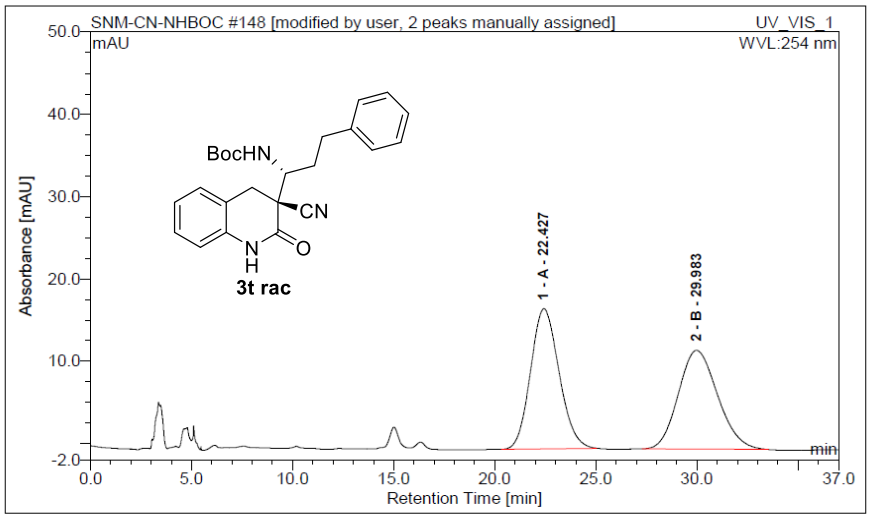
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	8.21	25.94806	26.02499672	59.30465	n.a.
2	B	10.52	73.756	73.97500328	122.536	n.a.



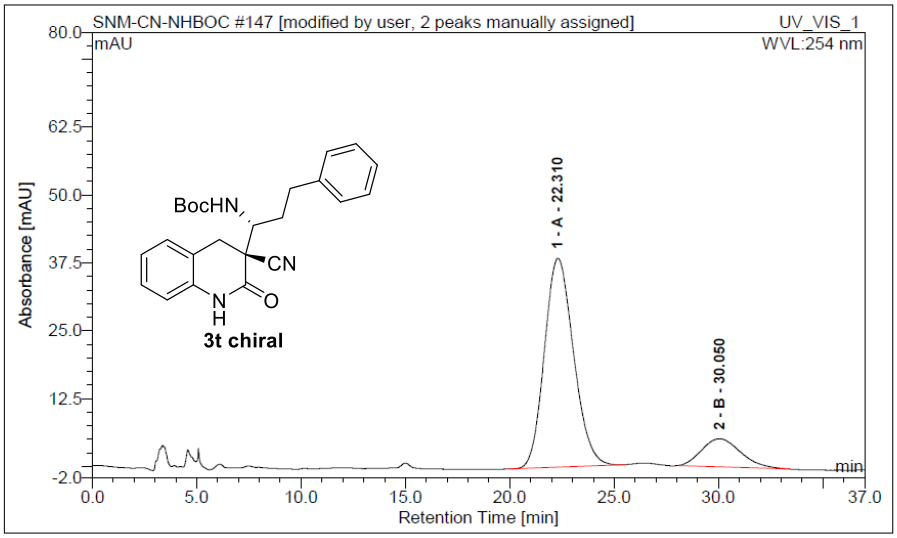
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.31	71.7199	50.08119109	166.7285	n.a.
2	B	17.07	71.487	49.91880891	108.571	n.a.



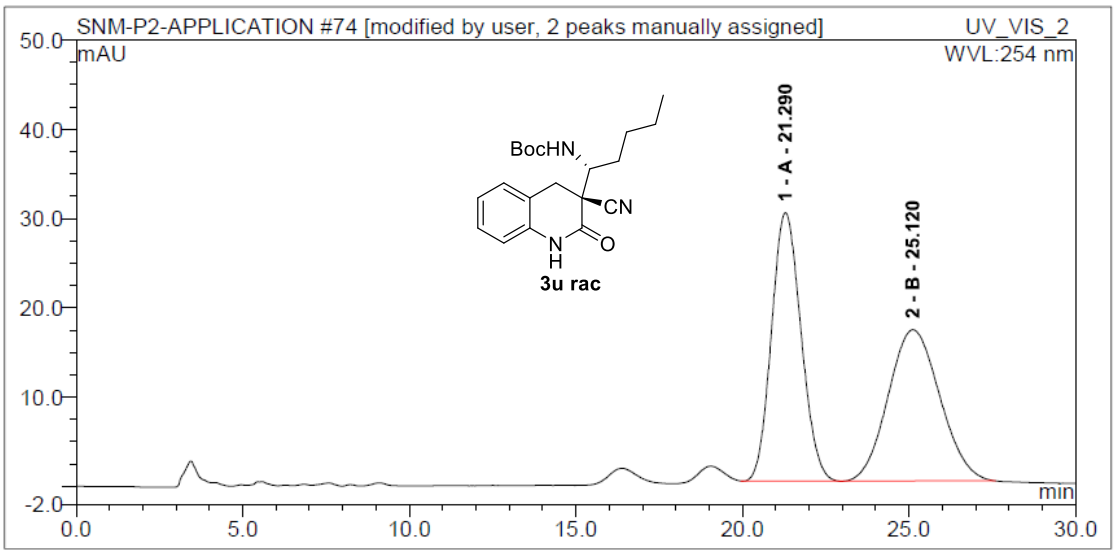
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.37	1.628998	0.9546322419	2.57398	n.a.
2	B	16.84	169.012	99.04536776	251.429	n.a.



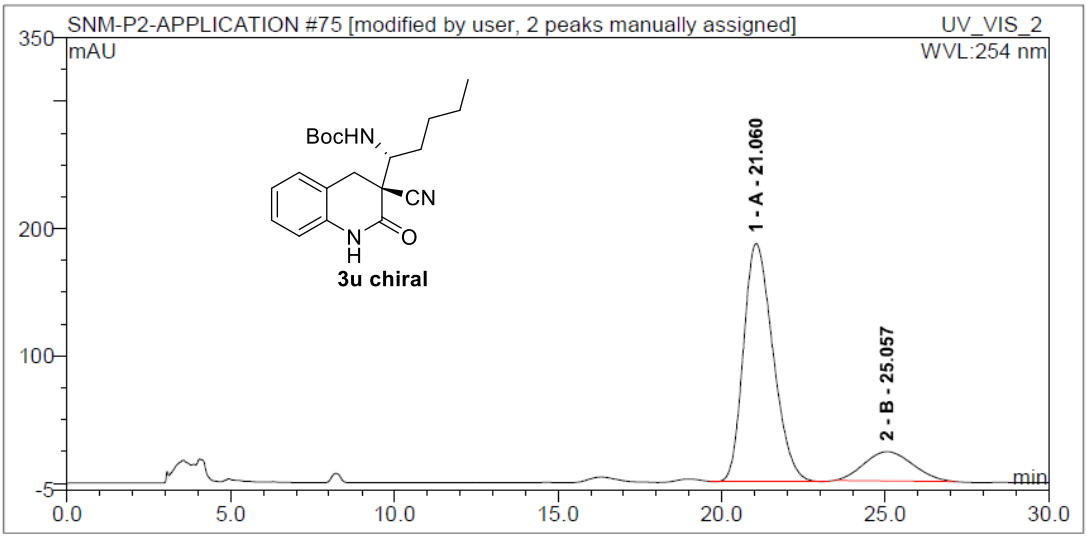
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	22.43	27.86222	50.73268163	17.04704	n.a.
2	B	29.98	27.057	49.26731837	12.019	n.a.



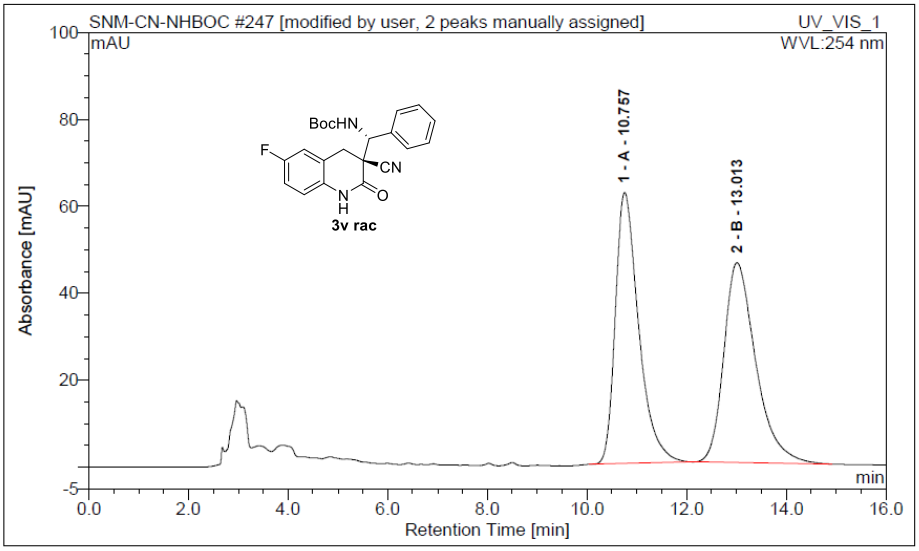
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	22.31	62.25753	84.74694349	38.4897	n.a.
2	B	30.05	11.205	15.25305651	5.172	n.a.



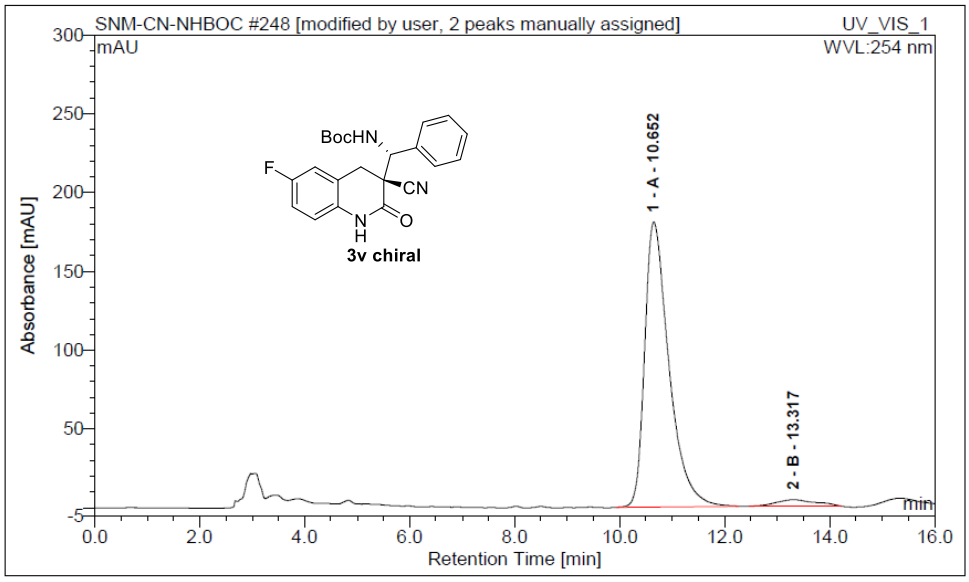
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	21.29	30.86896	50.37087474	30.04578	n.a.
2	B	25.12	30.414	49.62912526	16.935	n.a.



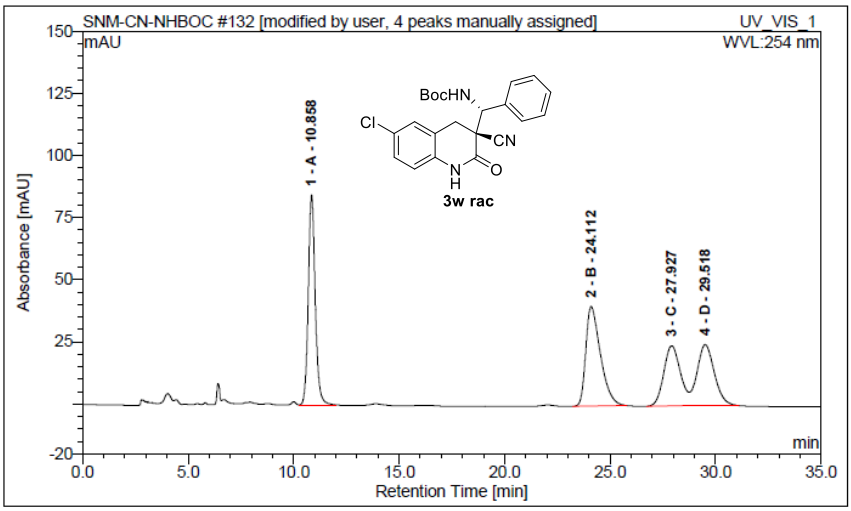
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	21.06	194.4983	83.12295792	186.7552	n.a.
2	B	25.06	39.490	16.87704208	22.867	n.a.



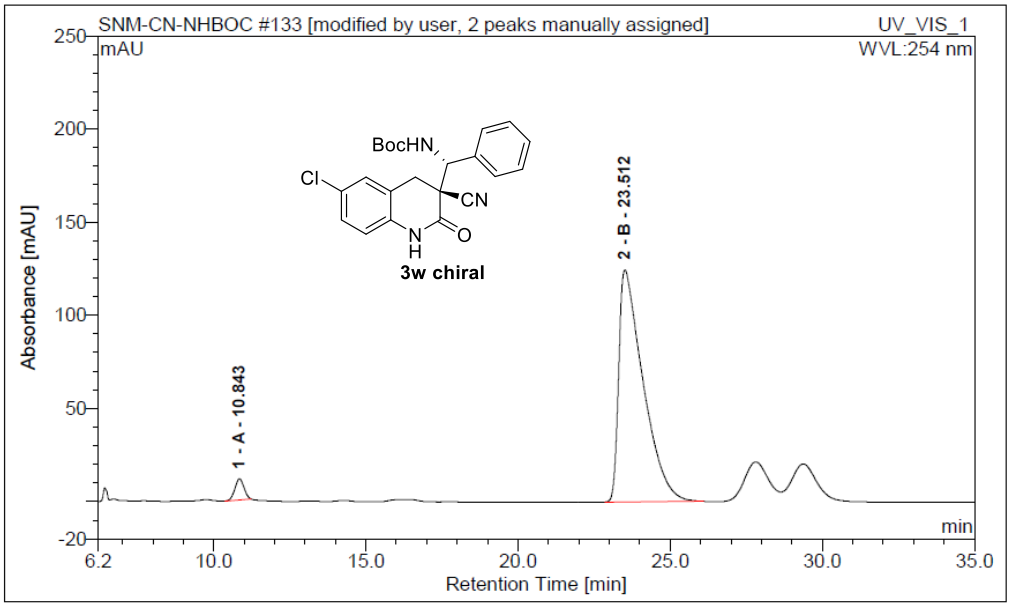
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.76	33.85185	49.77898691	62.34965	n.a.
2	B	13.01	34.152	50.22101309	45.978	n.a.



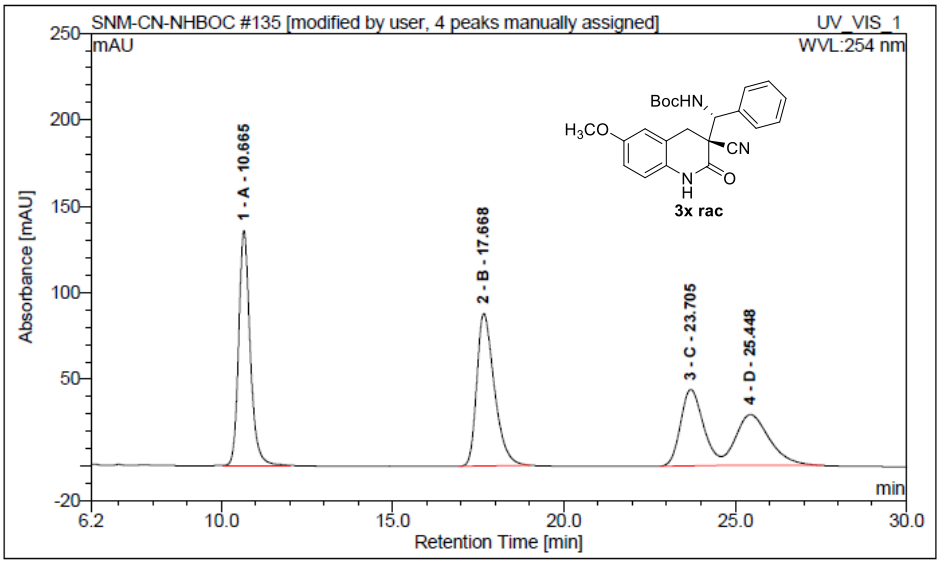
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.65	96.99013	96.32680253	180.8534	n.a.
2	B	13.32	3.698	3.673197474	4.071	n.a.



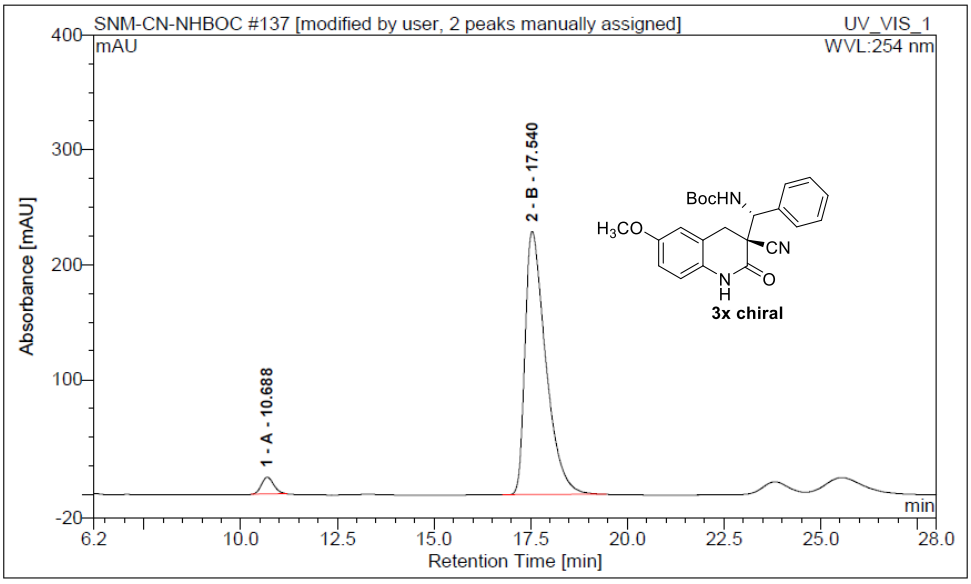
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.86	32.28392	29.3185486	84.50904	n.a.
2	B	24.11	32.23458	29.2737406	40.06417	n.a.
3	C	27.93	22.42861	20.36847479	24.20182	n.a.
4	D	29.52	23.167	21.03923601	24.568	n.a.



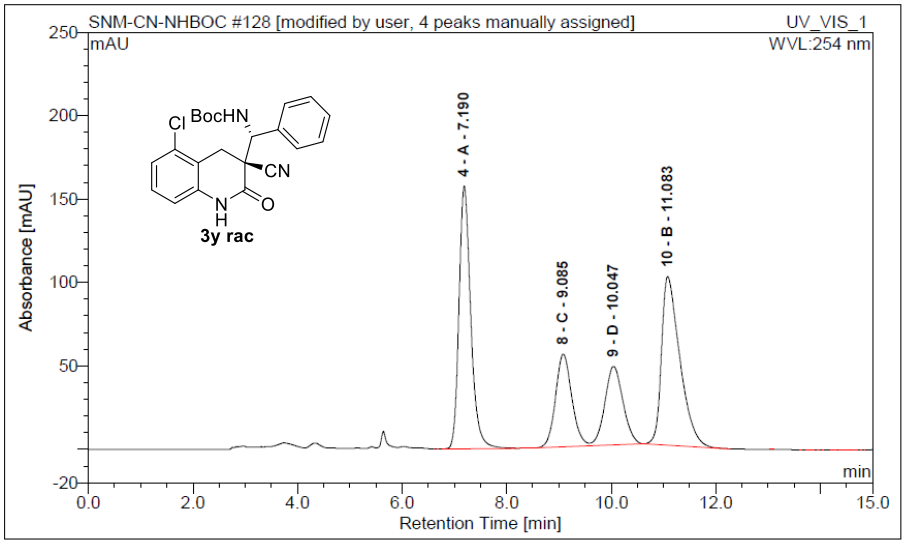
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.84	3.919813	3.289448757	11.27861	n.a.
2	B	23.51	115.243	96.71055124	124.473	n.a.



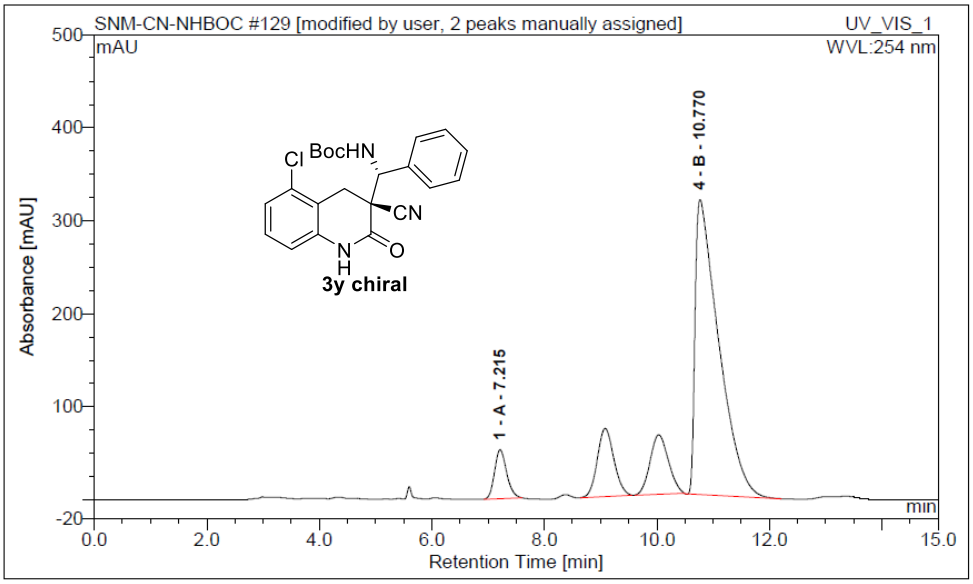
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.67	52.48322	30.41939122	135.7668	n.a.
2	B	17.67	52.32263	30.32631509	88.02782	n.a.
3	C	23.71	34.59746	20.05276238	44.1098	n.a.
4	D	25.45	33.129	19.20153131	29.425	n.a.



No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.69	5.42617	3.677921219	14.63836	n.a.
2	B	17.54	142.107	96.32207878	228.993	n.a.

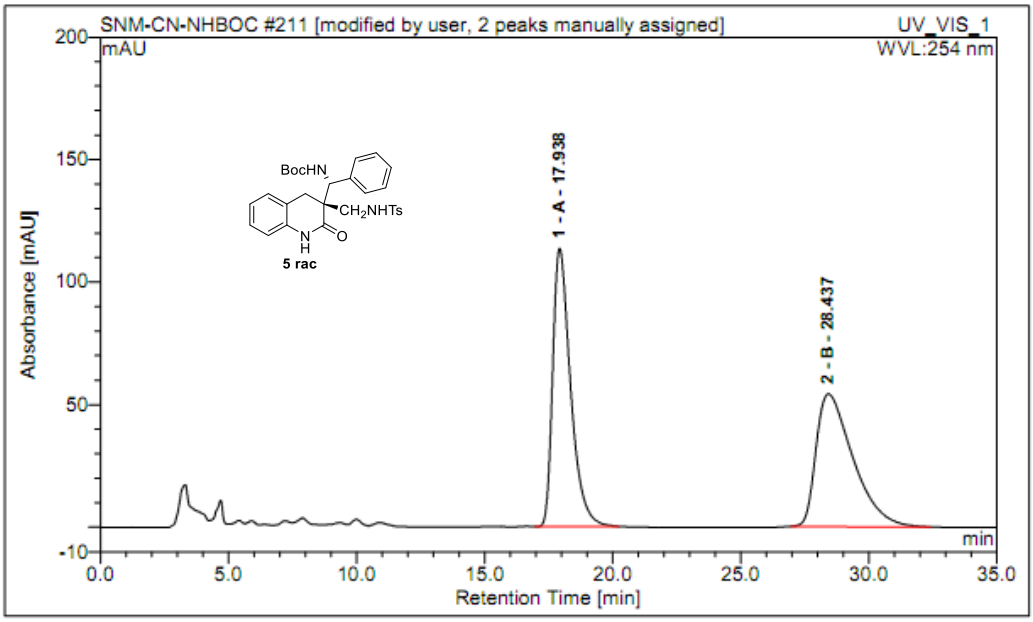


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
4	A	7.19	41.01699	33.79748663	157.4912	n.a.
8	C	9.09	20.1149	16.57442373	55.62952	n.a.
9	D	10.05	19.04609	15.69374012	47.19043	n.a.
10	B	11.08	41.183	33.93434952	101.095	n.a.

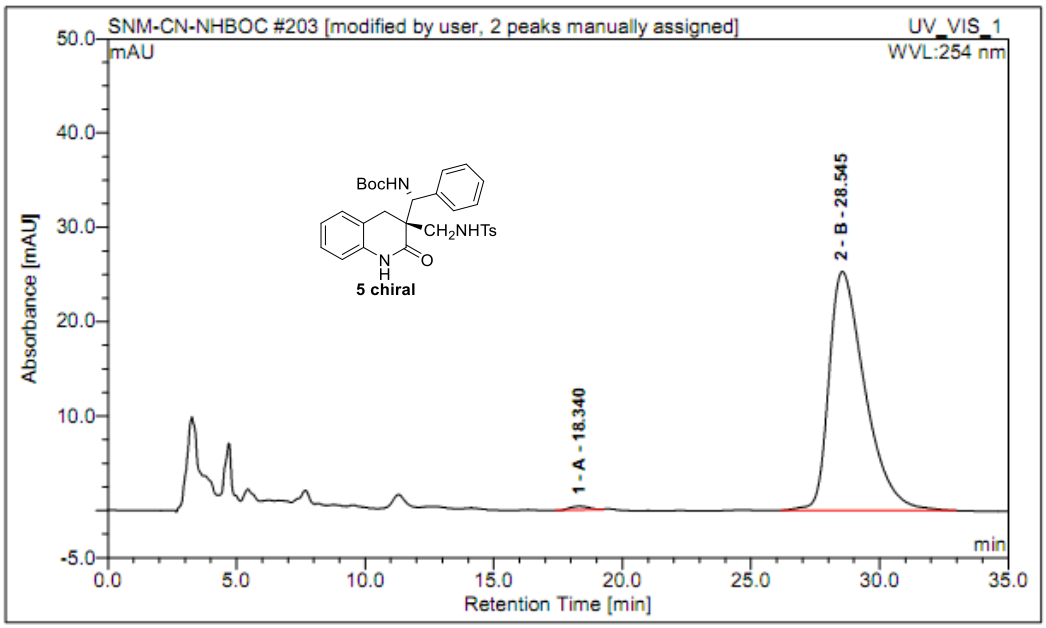


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	7.22	13.04918	7.838527622	52.58909	n.a.
4	B	10.77	153.426	92.16147238	316.909	n.a.

M.HPLC chromatograms of product 5 and 6:

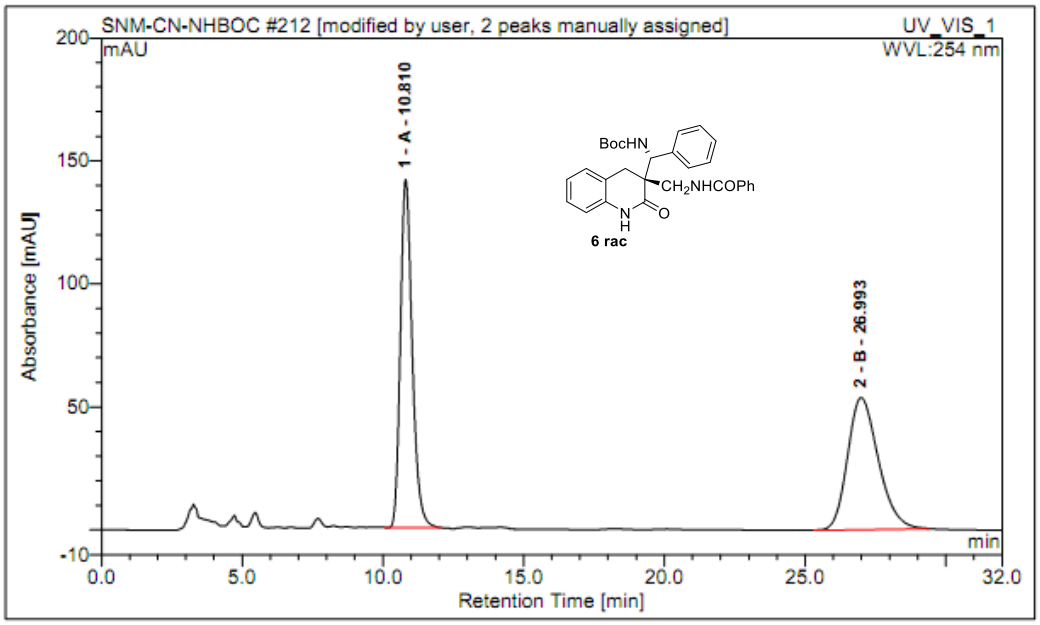


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	17.94	91.62296	50.32049977	113.5988	n.a.
2	B	28.44	90.456	49.67950023	54.086	n.a.

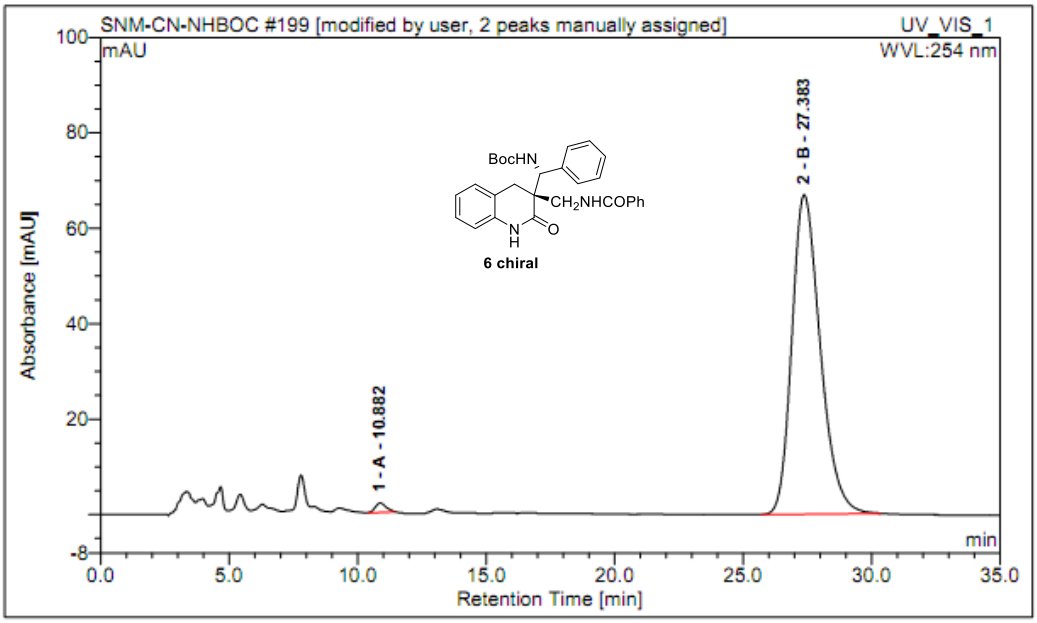


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	18.34	0.305987	0.7407735219	0.38036	n.a.
2	B	28.55	41.000	99.25922648	25.308	n.a.

HPLC chromatograms of product 9:



No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.81	68.64028	50.26092549	141.4346	n.a.
2	B	26.99	67.928	49.73907451	53.610	n.a.



No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	A	10.88	0.948717	1.094703394	1.94094	n.a.
2	B	27.38	85.716	98.90529661	66.913	n.a.