Electronic Supplementary Information

Iridium (III) Catalyzed Regioselective Amidation of Indoles at C4 –Position Using Weak Coordinating Groups

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Contents

Experimental Section:

General experimental

NMR spectra were recorded on 400 MHZ spectrometer in $CDCl_3$, Tetramethylsilane (TMS; δ = 0.00 ppm) served as an internal standard for ^1H NMR. The corresponding residual non-deuterated solvent signal ($CDCl_3$; δ = 77.00 ppm) was used as internal standard for ^{13}C NMR. IR spectra were measured using a FT/IR spectrometer. Mass spectra were measured with uisng Q-Tof (ESI-HRMS) machine. Column chromatography was carried out on Silica gel 230-400 mesh (commercial suppliers) and thin-layer chromatography was carried out using SILICA GEL GF-254. Iridium catalyst has prepared based on reported procedure[1] and Silver catalysts are purchased from Alfa asera.

3-Formyl indole derivatives were prepared by Vilsmeier-Haack reaction according to a literature method.[2] and sulfonyl azides were synthesized from commercially available reagents.[3] Other reagents and solvents were purchased from commercial supplier and used without further purification.

NMR Yield calculation – After work up, 0.5 equiv of terephthaldehyde was added into the round bottom flask containing the combined organic layers from the work up. Either an aliquot from the round bottom flask was taken, evaporated and then submitted for NMR, or the organic layer was completely evaporated and the residue was dissolved in an appropriate amount of solvent to submit for NMR.

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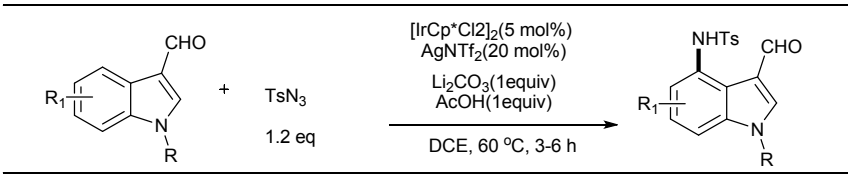
[1] C. White, A. Yates, P. M. Maitlis and D. M. Heinekey, (1992) (η^5-Pentamethylcyclopentadienyl)Rhodium and -Iridium Compounds, in Inorganic Syntheses, Volume 29 (ed R. N. Grimes), John Wiley & Sons, Inc., Hoboken, NJ, USA. **doi**: 10.1002/9780470132609.ch53.

[2] Bioorg. *Med. Chem. Lett*. 2005, **15**, 5039.

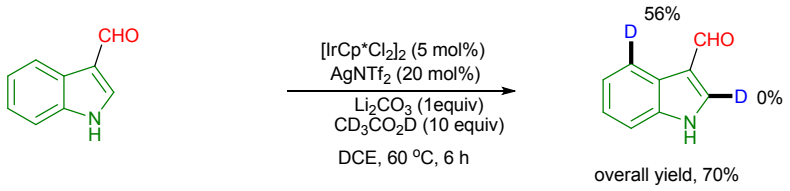
[3] J. Kim, J. Kim, S. Chang, *Chem.-Eur. J.,* 2013, **19**, 7328.

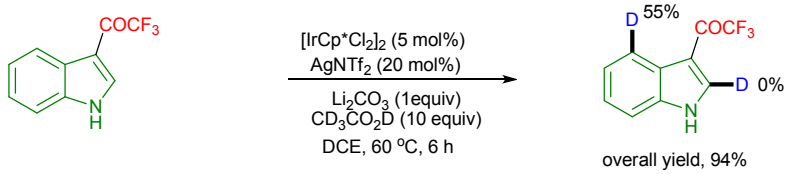
1. Typical experimental procedure for C4-amidation.



To a pre-dried 8mL screw cap vial was added indole-3-carbaldehyde derivative (**1**, 0.3 mmol, 1 equiv), tosyl azide derivative (**2**, 0.36 mmol, 1.2equiv), $[IrCp^*Cl_2]_2$ (5 mol %), $AgNTf_2$ (20 mol %) Li_2CO_3 (1 equiv) and AcOH (1 equiv) in open atmosphere in dichloroethane (2 mL). Then, the reaction mixture was stirred at 60 ^oC for 3-6 h (monitored by TLC). After the completion of the reaction, the reaction mixture was cooled to room temperature, and diluted with 50% EtOAc/hexane (5 mL), passed through a short silica gel (100-200 mesh size) bed, and washed with 50% EtOAc/ hexane (20 mL x 3 times). The combined organic layer was concentrated under reduced pressure and the crude product was purified on a silica gel column using EtOAc/hexane mixture.

2. **Deuterium incorporation studies:**

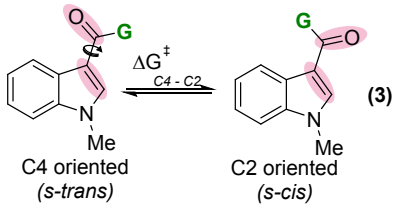




To a pre-dried 8mL screw cap vial was added 1H-indole-3-carbaldehyde(**1a**)/ 2,2,2-trifluoro-1-(1H-indol-3-yl)ethanone(**4a**)(0.2mmol, 1 equiv), $[IrCp^*Cl_2]_2$ (5mol %), $AgNTf_2$ (20mol %), Li_2CO_3 (1 equiv) and CD_3CO_2D (2 mmol,10 equiv) and dichloroethane (2 mL). The vial was placed in a pre-heated (60 °C) metal block. After 6h, the reaction mixture was cooled to room temperature, and diluted with diethyl ether and passed through a short silica gel (100-200 mesh size) bed, and repeatedly washed with diethyl ether (20 mL x 3 times). The combined organic layers were concentrated under reduced pressure and the crude product was submitted for NMR.

Preliminary DFT studies towards identification of probable reasons for regioselectivity [4]

1. *Preferred orientation of the directing group*

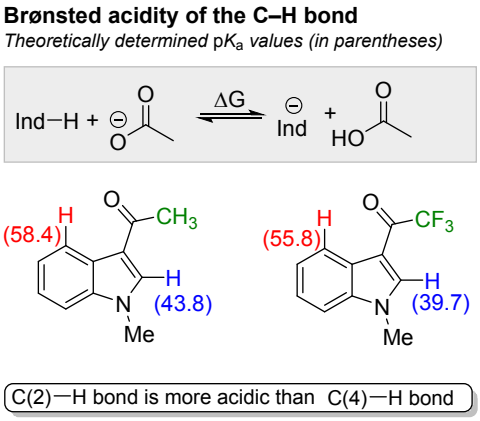


(3)

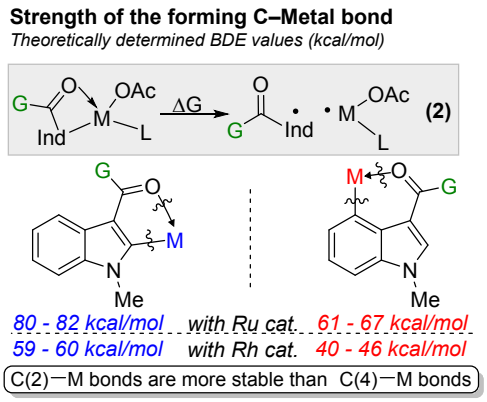
G	$\Delta G_{C4} - \Delta G_{C2}$	$\Delta G^{\ddagger}_{C4 \rightarrow C2}$
CF_3	-1.43	12.6
CH_3	-0.97	11.2
H	-1.42	14.0
Ph	-1.70	8.24
OMe	-0.16	10.6
NHMe	+0.08	6.38
OH	-0.68	7.99

[4] V. Lanke, K. R. Bettadapur, K. R. Prabhu, *Org. Lett*., 2016, **18**, 5496

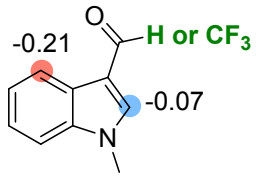
2. *Acidity of proton for C-H activation:*



3. *Strength of metallacycle*: Done with Ru(II) and Rh(III), expect same results with Iridium



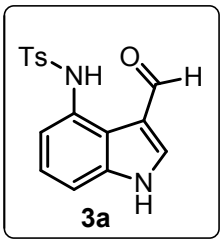
4. *Partial charge calculations on various positions of indole*



Since, no result is a clear cut support for C4 functionalization vs C2 functionalization, further work is needed and is currently ongoing in our laboratory.

Characterization data for the products

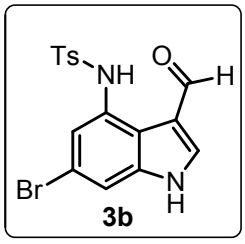
1. N-(3-formyl-1H-indol-4-yl)-4-methylbenzenesulfonamide (3a)



3a

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc, 6:4) to obtain the product as a yellow solid, **Yield** - 86 mg, (90%); $\mathbf{R_f}$- (40% EtOAc/Hexane) 0.3; **IR** (KBr, cm^{-1}): 3266, 1620,1141; ***mp:*** **205 - 208 °C;** ^{1}**H NMR** (400 MHz, DMSO-d_6) ppm 2.25 (s, 3 H) 7.11 - 7.21 (m, 2 H) 7.25 (d, *J*=7.33 Hz, 3 H) 7.62 (d, *J*=8.34 Hz, 2 H) 8.40 (d, *J*=3.03 Hz, 1 H) 9.61 (s, 1 H) 11.53 (s, 1 H) 12.48 (br. s., 1 H), ^{13}**C NMR** (100 MHz, DMSO-d_6) ppm 20.84, 108.23, 110.09, 115.79, 117.81, 125.04, 126.69, 129.63, 131.45, 136.36, 138.72, 142.19, 143.42, 186.78. **HRESI-MS***(m/z)*–Calculated for $C_{16}H_{14}N_2O_3SNa$ (M+Na): 337.0623, found (M+Na) 337.0628

2. N-(6-bromo-3-formyl-1H-indol-4-yl)-4-methylbenzenesulfonamide (3b)

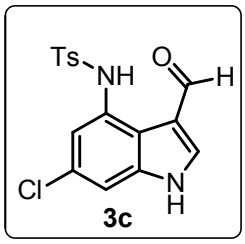


3b

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc, 6:4) to obtain the product as a yellow solid, **Yield** - 108 mg, (92%); $\mathbf{R_f}$- (40% EtOAc/Hexane) 0.3; **IR** (KBr, cm^{-1}): 3126, 1635, 1193; ***mp:*** **260 - 262 °C;** ^{1}**H NMR** (400 MHz, DMSO-d_6) ppm 2.27 (s, 3 H) 7.24 - 7.38 (m, 4 H) 7.64 (d, *J*=8.24 Hz, 2 H) 8.43 (d, *J*=3.05 Hz, 1 H) 9.62 (s, 1 H) 11.67 (s, 1 H) 12.56 (br. s., 1 H); ^{13}**C NMR** (100 MHz, DMSO-d_6) ppm 20.90 ,110.89 ,112.48 ,114.90 ,117.14 ,117.83

,126.64 ,129.89 ,132.58 ,135.98 ,139.25 ,142.84 ,143.90 ,187.23; **HRESI-MS***(m/z)*–Calculated for $C_{16}H_{13}BrN_2O_3SNa$ (M+Na): 414.9728, found (M+Na) 414.9729

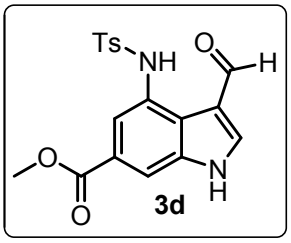
3. **N-(6-chloro-3-formyl-1H-indol-4-yl)-4-methylbenzenesulfonamide (3c)**



3c

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc, 6:4) to obtain the product as a yellow solid, **Yield** - 88 mg, (84%); **R_f-** (40% EtOAc/Hexane) 0.3; **IR** (KBr, cm^{-1}): 3221, 1712, 1127; ***mp:*** **255 - 258 °C** **^{1}H NMR** (400 MHz, DMSO-d_6) ppm 2.22 (s, 3 H) 7.12 - 7.33 (m, 4 H) 7.57 (d, *J*=8.10 Hz, 2 H) 8.24 (d, *J*=3.2 Hz, 1 H) 9.60 (s, 1 H) 11.71 (s, 1 H) 12.49 (br. s., 1 H); **^{13}C NMR** (100 MHz, DMSO-d_6) ppm 20.85 ,110.56 ,111.98 ,115.10 ,117.62 ,117.75 ,126.00 ,129.23 ,132.62 ,136.07 ,140.15 ,142.47 ,144.07 ,187.92; **HRESI-MS***(m/z)*–Calculated for $C_{16}H_{13}ClN_2O_3SNa$ (M+Na): 371.0233, found (M+Na) 371.0235

4. Methyl 3-formyl-4-((4-methylphenyl)sulfonamido)-1H-indole-6-carboxylate (3d)

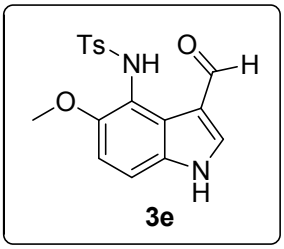


3d

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc, 5:5) to obtain the product as a yellow solid, **Yield** - 86 mg, (77%); **R_f-** (50% EtOAc/Hexane) 0.2; **IR** (KBr, cm^{-1}): 3190, 1620, 1141; ***mp:*** **253 - 255 °C;** **^{1}H NMR** (400 MHz, DMSO-d_6) ppm 2.23 (s, 3 H) 3.87 (s, 3 H) 7.26 (m, *J*=8.08 Hz, 2 H) 7.61 (m, *J*=8.08 Hz, 2 H) 7.78 (d, *J*=1.26 Hz, 1 H) 7.88 (d, *J*=1.26 Hz, 1 H) 8.58 (d, *J*=3.03 Hz, 1 H) 9.67 (s, 1 H) 11.55 (s, 1 H) 12.77 (br. s., 1 H).; **^{13}C NMR** (100 MHz, DMSO-d_6) ppm 20.86 ,52.34 ,110.09 ,110.25 ,117.74 ,119.35 ,126.18 ,126.65 ,129.78

,131.45 ,136.09 ,138.08 ,143.71 ,144.30 ,166.07 ,187.36.; **HRESI-MS***(m/z)*–Calculated for $C_{18}H_{16}N_2O_5SNa$ (M+Na): 395.0678, found (M+Na) 395.0679

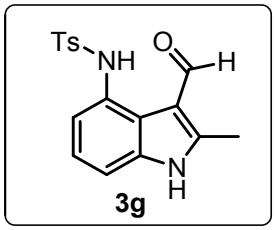
5. **N-(3-formyl-5-methoxy-1H-indol-4-yl)-4-methylbenzenesulfonamide (3e)**



3e

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc, 5:5) to obtain the product as a yellow solid, **Yield** - 53 mg, (48%); $\mathbf{R_f}$- (50% EtOAc/Hexane) 0.2; **IR** (KBr, cm^{-1}): 3214, 1625, 1209; ***mp:*** **232 - 234 °C;** ^{1}**H NMR** (400 MHz, DMSO-d_6) ppm 2.26 (s, 3 H) 3.38 (s, 3 H) 6.96 (m, *J*=8.4 Hz, 1 H) 7.30 (d, *J*=8.34 Hz, 3 H) 7.56 (d, *J*=8.04 Hz, 2 H) 8.28 (d, *J*=3.1 Hz, 1 H) 9.90 (s, 1 H) 10.2 (s, 1 H) 12.28 (br. s., 1 H).; ^{13}**C NMR** (100 MHz, DMSO-d_6) ppm 21.42, 56.40, 111.23, 111.36, 118.33, 118.86, 122.58, 126.99, 129.28, 133.47, 139.30, 142.70, 149.36, 186.34.; **HRESI-MS***(m/z)*–Calculated for $C_{17}H_{16}N_2NaO_4S$ (M+Na): 367.3747, found (M+Na) 367.3742

5. N-(3-formyl-2-methyl-1H-indol-4-yl)-4-methylbenzenesulfonamide (3g)

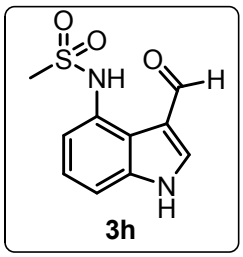


3g

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc, 6:4) to obtain the product as a yellow solid, **Yield** - 87 mg, (88%); $\mathbf{R_f}$- (40% EtOAc/Hexane) 0.2; **IR** (KBr, cm^{-1}): 3310, 1670, 1121; ***mp:*** **256 - 258 °C;** ^{1}**H NMR** (400 MHz, DMSO-d_6) ppm 2.24 (s, 3 H) 2.65 (s, 3 H) 6.99 - 7.04 (m, 1 H) 7.10 (t, *J*=7.96 Hz, 1 H) 7.18 - 7.27 (m, 3 H) 7.62 (d, *J*=8.08 Hz, 2 H) 9.69 (s, 1 H) 11.96 (s, 1 H) 12.37 (br. s., 1 H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm 11.64 ,20.85

,107.26 ,110.08 ,113.61 ,116.63 ,124.51 ,126.69 ,129.61 ,131.13 ,136.56 ,137.12 ,143.31 ,152.64 ,185.77.; **HRESI-MS***(m/z)*–Calculated for $C_{17}H_{16}N_2O_3SNa$ (M+Na): 351.0779, found (M+Na) 351.0777.

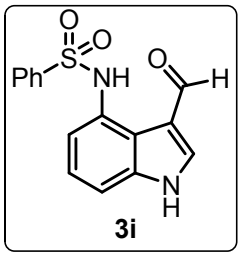
6. **10. N-(3-formyl-1H-indol-4-yl)methanesulfonamide (3h)**



3h

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc,6:4) to obtain the product as a light yellow solid, **Yield** - 41mg, (57%); $\mathbf{R_f}$- (40% EtOAc/Hexane) 0.2; **IR** (KBr, cm^{-1}): 3251, 1617, 1113; ***mp:* 175 - 177 °C; ^{1}H NMR** (400 MHz, DMSO-d_6) ppm 3.02 (s, 3 H) 7.20 - 7.32 (m, 3 H) 8.47 (d, *J*=3.28 Hz, 1 H) 9.65 (s, 1 H) 11.05 (s, 1 H) 12.56 (br. s., 1 H); **^{13}C NMR** (100 MHz, DMSO-d_6) ppm 39.06 ,108.01 ,109.71 ,115.59 ,118.08 ,125.27 ,132.17 ,138.96 ,142.13 ,186.64.; **HRESI-MS***(m/z)*–Calculated for $C_{10}H_{10}N_2O_3SNa$ (M+Na): 261.0310, found (M+Na) 261.0308.

7. N-(3-formyl-1H-indol-4-yl)benzenesulfonamide (3i)

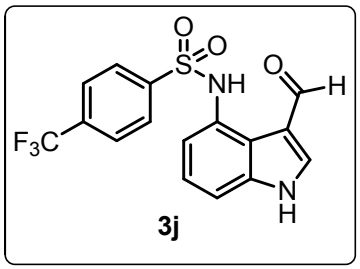


3i

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc,6:4) to obtain the product as a yellow solid, **Yield** - 63mg, (70%); $\mathbf{R_f}$- (40% EtOAc/Hexane) 0.2; **IR** (KBr, cm^{-1}): 3162, 1634, 1155; ***mp:* 203 - 205 °C; ^{1}H NMR** (400 MHz, DMSO-d_6) ppm 7.11 - 7.19 (m, 2 H) 7.24 (d, *J*=7.21 Hz, 1 H) 7.43 (t, *J*=7.21 Hz, 2 H) 7.55 (t, *J*=7.34 Hz, 1H) 7.71 (d, *J*=8.2 Hz, 1H) 8.40 (d,

J=3.03 Hz, 1 H) 9.60 (s, 1 H) 11.56 (s, 1 H) 12.48 (br. s., 1 H), **^{13}C NMR** (100 MHz, DMSO-d_6) ppm 108.23, 110.09, 115.79, 117.81, 125.04, 126.69, 129.63, 131.45, 136.36, 138.72, 142.19, 143.42, 186.78. **HRESI-MS***(m/z)*–Calculated for $C_{15}H_{12}N_2O_3SNa$ (M+Na): 323.0466, found (M+Na) 323.0467.

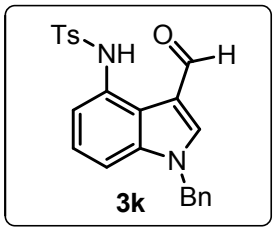
8. N-(3-formyl-1H-indol-4-yl)-4-(trifluoromethyl)benzenesulfonamide (3j)



3j

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc,6:4) to obtain the product as a light yellow solid, **Yield** - 75mg, (67%); **R_f-** (40% EtOAc/Hexane) 0.2; **IR** (KBr, cm^{-1}): 3266, 1674, 1145; ***mp:* 209 - 211 °C; ^{1}H NMR** (400 MHz, DMSO-d_6) ppm 7.18 - 7.23 (m, 2 H) 7.27 (dd, *J*=6.19, 2.40 Hz, 1 H) 7.85 (d, *J*=8.34 Hz, 2 H) 7.94 (d, *J*=8.34 Hz, 2 H) 8.42 (d, *J*=3.03 Hz, 1 H) 9.60 (s, 1 H) 11.79 (s, 1 H) 12.54 (br. s., 1 H); **^{13}C NMR** (100 MHz, DMSO-d_6) ppm 108.87 ,110.52 ,116.05, 117.68, 123.23 (d, *J*= 271Hz) 125.16, 126.50, (d, *J*= 4Hz) 127.70, 130.74,132.72 (d, *J*= 33Hz) 138.78, 142.39, 143.02, 187.00.; **HRESI-MS***(m/z)*–Calculated for $C_{16}H_{11}F_3N_2O_3SNa$ (M+Na): 391.0340, found (M+Na) 391.0339

9. N-(1-benzyl-3-formyl-1H-indol-4-yl)-4-methylbenzenesulfonamide (3k)

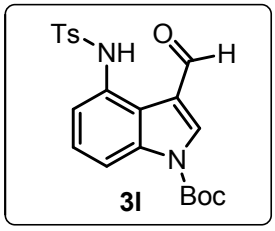


3k

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc, 6:4) to obtain the product as a yellow solid, **Yield** - 100mg, (82%); **R_f-** (40% EtOAc/Hexane) 0.4; **IR** (KBr, cm^{-1}): 3217,

1632, 1181; ***mp:* 165 - 167 °C; ^{1}H NMR** (400 MHz, CHLOROFORM-*d*) ppm 2.29 (s, 3 H) 5.27 (s, 2 H) 6.94 (d, *J*=8.24 Hz, 1 H) 7.08 - 7.20 (m, 5 H) 7.31 - 7.37 (m, 3 H) 7.44 (d, *J*=7.93 Hz, 1 H) 7.63 (s, 1 H) 7.73 (d, *J*=7.93 Hz, 2 H) 9.47 (s, 1 H) 11.35 (s, 1 H); **^{13}C NMR** (100 MHz, CHLOROFORM-*d*) ppm 21.42 ,51.14 ,105.71 ,111.41 ,116.81 ,118.25 ,125.72 ,127.22 ,127.37 ,128.59 ,129.16 ,129.30 ,132.87 ,134.49 ,137.13 ,139.13 ,141.39 ,143.13 ,185.00.; **HRESI-MS***(m/z)*–Calculated for $C_{23}H_{20}N_2O_3SNa$ (M+Na): 427.1092, found (M+Na) 427.1090.

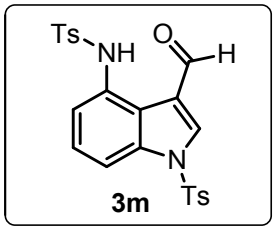
10. *Tert*-butyl 3-formyl-4-((4-methylphenyl)sulfonamido)-1H-indole-1-carboxylate (3l)



3l

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc,7:3) to obtain the product as a light brown solid, **Yield** - 84mg, (67%); **R_f-** (40% EtOAc/Hexane) 0.4; **IR** (KBr, cm^{-1}): 3174, 1672, 1099; ***mp:* 132 - 135 °C; ^{1}H NMR** (400 MHz, CHLOROFORM-*d*) ppm 1.68 (s, 9 H) 2.30 (s, 3 H) 7.12 (m, *J*=7.83 Hz, 2 H) 7.31 (t, *J*=8.21 Hz, 1 H) 7.57 (d, *J*=8.08 Hz, 1 H) 7.70 (m, *J*=8.34 Hz, 2 H) 7.81 (d, *J*=8.34 Hz, 1 H) 8.22 (s, 1 H) 9.68 (s, 1 H) 10.91 (s, 1 H); **^{13}C NMR** (100 MHz, CHLOROFORM-*d*) ppm 21.42 ,27.95 ,86.60 ,110.55 ,113.88 ,117.06 ,121.33 ,127.18 ,127.52 ,129.36 ,132.49 ,136.81 ,137.41 ,140.01 ,143.34 ,147.98 ,186.61.;**HRESI-MS***(m/z)*–Calculated for $C_{21}H_{22}N_2O_5SNa$ (M+Na): 437.1147, found (M+Na) 437.1150.

11. N-(3-formyl-1-tosyl-1H-indol-4-yl)-4-methylbenzenesulfonamide (3m)

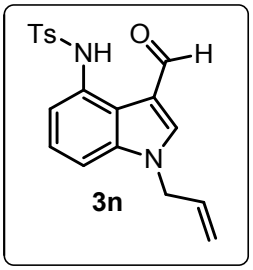


3m

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc,7:3) to obtain the product as

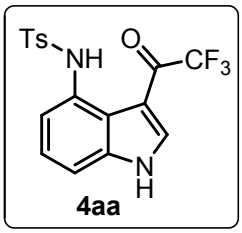
a light brown solid, **Yield** - 90mg, (64%); $\mathbf{R_f}$- (30% EtOAc/Hexane) 0.3; **IR** (KBr, cm^{-1}): 3214, 1635, 1134; ***mp:*** **171 - 173 °C;** **^{1}H NMR** (400 MHz, CHLOROFORM-*d*) ppm 2.30 (s, 3 H) 2.38 (s, 3 H) 7.12 (m, *J*=8.34 Hz, 2 H) 7.30 (d, *J*=8.59 Hz, 3 H) 7.55 (d, *J*=8.34 Hz, 1 H) 7.52 (d, *J*=8.08 Hz, 1 H) 7.69 (m, *J*=8.08 Hz, 2 H) 7.82 (d, *J*=8.34 Hz, 2 H) 8.25 (s, 1 H) 9.70 (s, 1 H) 10.84 (s, 1 H); **^{13}C NMR** (100 MHz, CHLOROFORM-*d*) ppm 21.42 ,21.66 ,108.27 ,113.70 ,117.10 ,122.04 ,127.17 ,127.39 ,127.74 ,129.42 ,130.44 ,132.96 ,133.54 ,136.49 ,136.68 ,139.47 ,143.54 ,146.72 ,186.40.; **HRESI-MS***(m/z)***–**Calculated for $C_{23}H_{20}N_2O_5S_2Na$ (M+Na): 491.0711, found (M+Na) 491.0712.

12. N-(1-allyl-3-formyl-1H-indol-4-yl)-4-methylbenzenesulfonamide (3n)



Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc,7:3) to obtain the product as a light brown solid, **Yield** - 36mg, (34%); $\mathbf{R_f}$- (30% EtOAc/Hexane) 0.3; **IR** (KBr, cm^{-1}): 3194, 1671, 1177; ***mp:*** **140 - 143 °C;** **^{1}H NMR** (400 MHz, CHLOROFORM-*d*) ppm 2.29 (s, 3 H) 5.16 (dd, *J*=16.93, 0.76 Hz, 1 H) 5.33 (dd, *J*=10.36, 0.76 Hz, 1 H) 5.91 - 6.02 (m, 1 H) 6.96 (d, *J*=8.34 Hz, 1 H) 7.13 (d, *J*=8.34 Hz, 2 H) 7.21 (t, *J*=8.08 Hz, 1 H) 7.46 (d, *J*=7.83 Hz, 1 H) 7.68 (s, 1 H) 7.75 (d, *J*=8.08 Hz, 2 H) 9.52 (s, 1 H) 11.34 (s, 1 H); **^{13}C NMR** (100 MHz, CHLOROFORM-*d*) ppm 21.43 ,49.74 ,105.59 ,111.46 ,116.79 ,118.21 ,119.67 ,125.66 ,127.25 ,129.31 ,130.99,138.95 ,141.09 ,143.11 ,184.94.; **HRESI-MS***(m/z)***–**Calculated for $C_{19}H_{18}N_2O_3SNa$ (M+Na): 377.0936, found (M+Na) 377.0933.

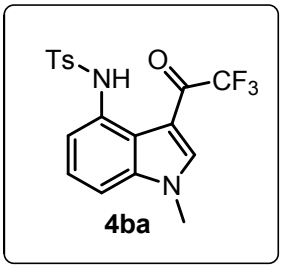
13. 4-methyl-N-(3-(2,2,2-trifluoroacetyl)-1H-indol-4-yl)benzenesulfonamide (4aa)



4aa

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc,6:4) to obtain the product as a light brown solid, **Yield** - 69mg, (60%); $\mathbf{R_f}$- (40% EtOAc/Hexane) 0.3; **IR** (KBr, cm^{-1}): 3184, 1677, 1191; ***mp:* 215 - 218 °C; ^{1}H NMR** (400 MHz, DMSO-d_6) ppm 2.25 (s, 3 H) 7.19 - 7.36 (m, 5 H) 7.55 (d, *J*=8.24 Hz, 2 H) 8.56 (d, *J*=1.53 Hz, 1 H) 10.86 (s, 1 H) 13.09 (br. s., 1 H); ^{13}**C NMR** (100 MHz, DMSO-d_6) ppm 20.84 ,109.02 ,109.36 ,113.14 ,115.99 ,117.87 (d, *J*= 200 MHz),125.98 ,126.75 ,129.60 ,131.34 ,135.88 ,138.61 ,141.13 ,143.66 ,175.19 (d, *J*= 34 MHz).; **HRESI-MS***(m/z)*–Calculated for $C_{17}H_{13}F_3N_2O_3SNa$ (M+Na): 405.0497, found (M+Na) 405.0500.

14. 4-methyl-N-(1-methyl-3-(2,2,2-trifluoroacetyl)-1H-indol-4-yl)benzenesulfonamide (4ba)

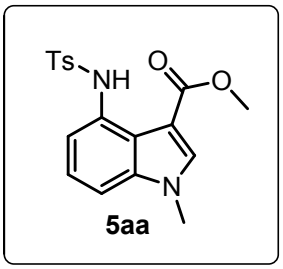


4ba

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc,7:3) to obtain the product as a light yellow solid, **Yield** - 47mg, (40%); $\mathbf{R_f}$- (40% EtOAc/Hexane) 0.4; **IR** (KBr, cm^{-1}): 3196, 1680, 1133; ***mp:* 161 - 163 °C; ^{1}H NMR** (400 MHz, DMSO-d_6) ppm 2.24 (s, 3 H) 3.88 (s, 3 H) 7.23 (m, *J*=7.83 Hz, 2 H) 7.31 - 7.41 (m, 3 H) 7.57 (m, *J*=8.08 Hz, 2 H) 8.64 (s, 1 H) 10.99 (s, 1 H); ^{13}**C NMR** (101 MHz, DMSO-d_6) ppm 20.89 ,34.23 ,107.85 ,113.29 ,118.85-115.98 (m) ,125.66 ,126.08 ,126.81 ,129.71 ,131.52 ,135.89 ,139.36 ,143.79 ,144.48 (d, *J*= 4 MHz), 174.64

(d, *J*= 34 MHz).; **HRESI-MS***(m/z)*–Calculated for $C_{18}H_{15}F_3N_2O_3SNa$ (M+Na): 419.0653, found (M+Na) 419.0655.

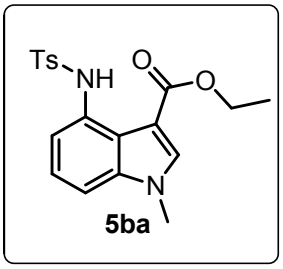
15. Methyl 1-methyl-4-((4-methylphenyl)sulfonamido)-1H-indole-3-carboxylate (5aa)



5aa

Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc,7:3) to obtain the product as a brown solid, **Yield** - 70mg, (65%); $\mathbf{R_f}$- (40% EtOAc/Hexane) 0.4; **IR** (KBr, cm^{-1}): 3211, 1735, 1152; ***mp:* 160 - 163 °C; ^{1}H NMR** (400 MHz, CHLOROFORM-*d*) ppm 2.30 (s, 3 H) 3.74 (s, 3 H) 3.91 (s, 3 H) 6.96 (d, *J*=8.34 Hz, 1 H) 7.10 - 7.21 (m, 3 H) 7.40 (d, *J*=8.08 Hz, 1 H) 7.68 (s, 1 H) 7.77 (d, *J*=8.34 Hz, 2 H) 11.63 (s, 1 H); **^{13}C NMR** (100 MHz, CHLOROFORM-*d*) ppm 21.43 ,33.68 ,52.13 ,105.22 ,105.56 ,110.72 ,117.20 ,124.24 ,127.30 ,129.26 ,131.93 ,136.11 ,137.16 ,138.58 ,143.02 ,167.24 .; **HRESI-MS***(m/z)*–Calculated for $C_{18}H_{18}N_2O_4SNa$ (M+Na): 381.0885, found (M+Na) 381.0691.

16. Ethyl 1-methyl-4-((4-methylphenyl)sulfonamido)-1H-indole-3-carboxylate (5ba)



5ba

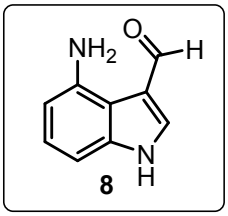
Prepared according to the general procedure. Crude reaction mixture was purified on flash column using silica (230-400) with a suitable eluent (Hexane/EtOAc,7:3) to obtain the product as a brown solid, **Yield** - 77mg, (69%); $\mathbf{R_f}$- (40% EtOAc/Hexane) 0.4; **IR** (KBr, cm^{-1}): 3219, 1715, 1141; ***mp:* 164 - 166 °C; ^{1}H NMR** (400 MHz, CHLOROFORM-*d*) ppm 1.39 (t, *J*=7.07 Hz, 3 H) 2.29 (s, 3 H) 3.72 (s, 3 H) 4.38 (q, *J*=7.07 Hz, 2 H) 6.95 (d, *J*=8.34 Hz, 1 H) 7.08 - 7.18 (m, 3

H) 7.40 (d, *J*=7.83 Hz, 1 H) 7.69 (s, 1 H) 7.75 (d, *J*=8.08 Hz, 2 H) 11.70 (s, 1 H); **^{13}C NMR** (100 MHz, CHLOROFORM-*d*) ppm 14.37 ,21.37 ,33.59 ,60.94 ,105.28 ,110.71 ,117.24 ,124.06 ,126.34 ,127.21 ,129.21 ,131.78 ,136.13 ,137.07 ,138.52 ,142.98 ,166.84.; **HRESI-MS***(m/z)*– Calculated for $C_{19}H_{20}N_2O_4SNa$ (M+Na): 395.1041, found (M+Na) 395.1042.

Experimental section for deprotection of tosyl group

The C4-amidated product, **3aa** (0.5 mmol) was added to the cold conc H_2SO_4 (1 mL) at 0 ^oC. The mixture was stirred at rt for 2 h. Upon completion, the reaction mixture was quenched with $NaHCO_3$ solution and the resulting mixture was extracted with EtOAc(3 x 20mL). The organic layers were collected, dried over Na_2SO_4, and concentrated in vacuum to give 4-amino-1H-indole-3-carbaldehyde as a 52% yield.

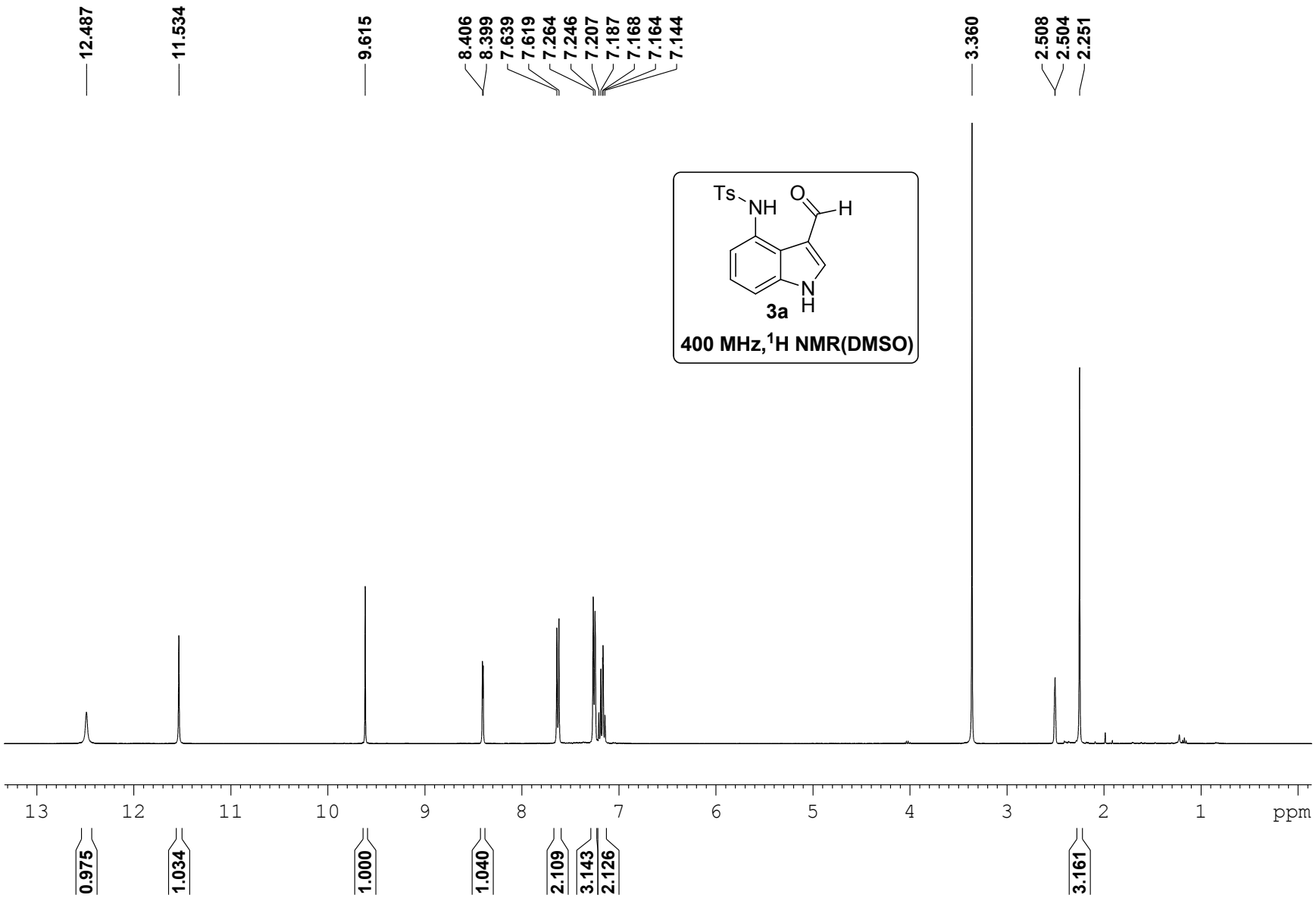
17. 4-amino-1H-indole-3-carbaldehyde

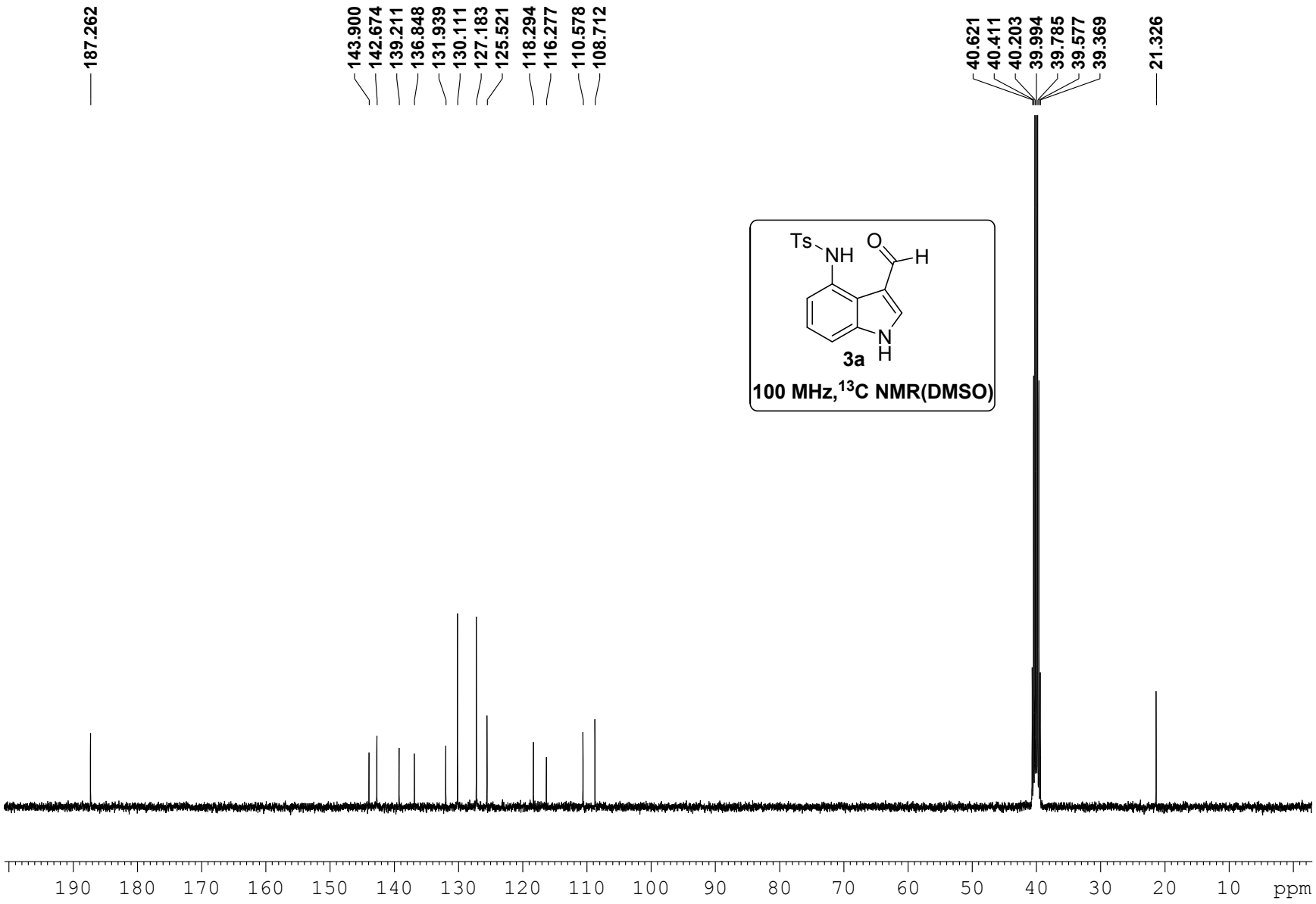


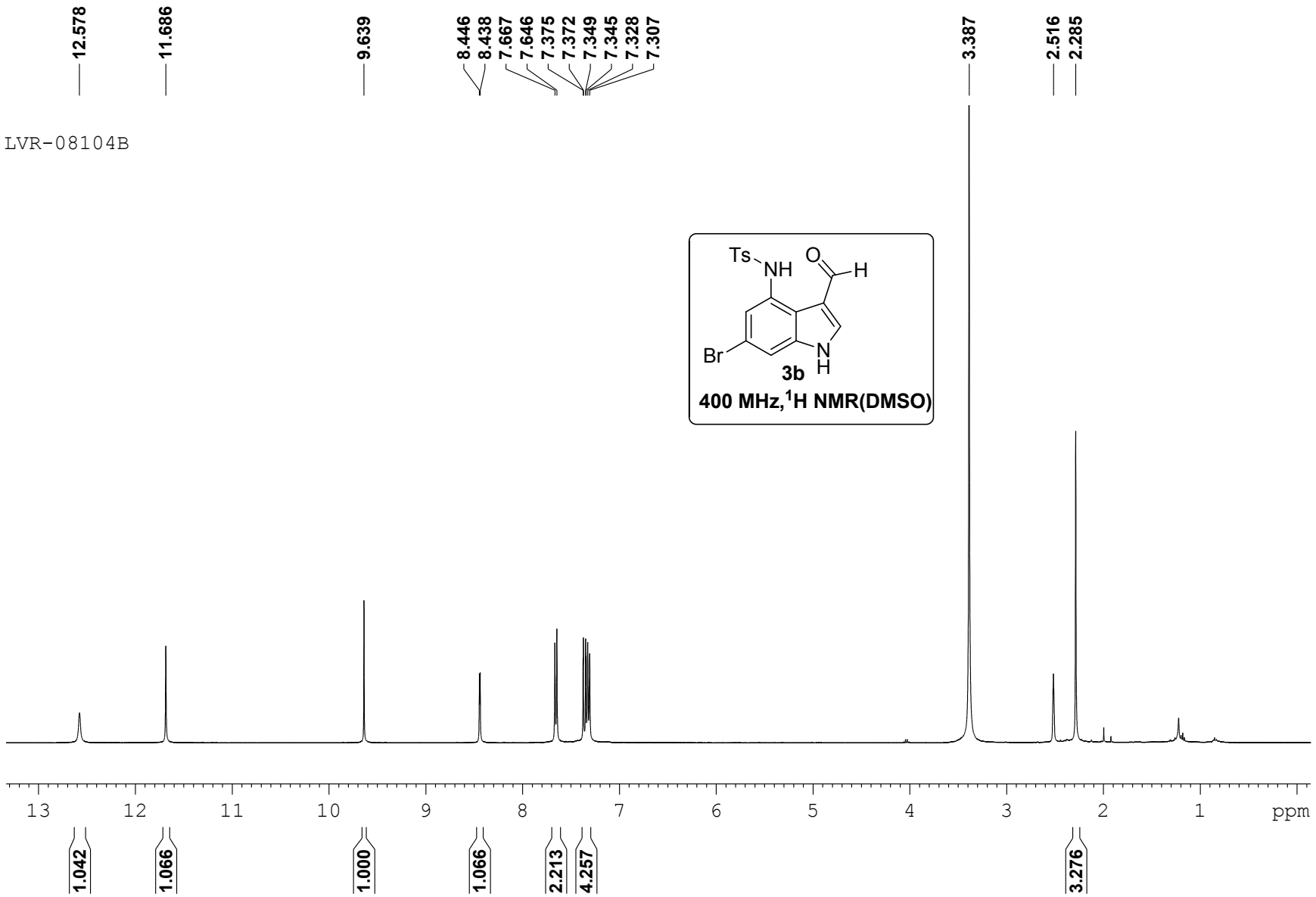
8

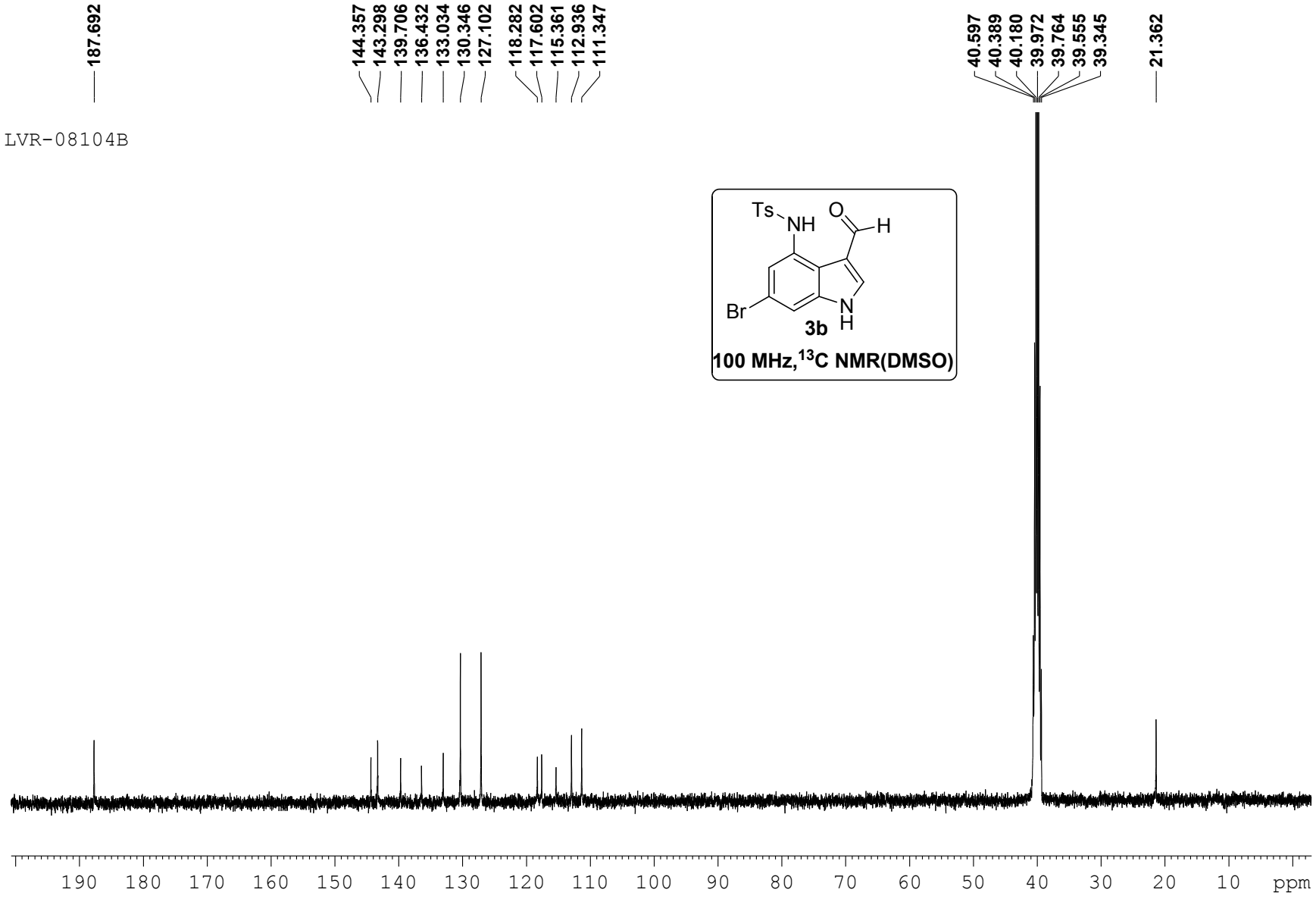
Yield - 42mg, (52%); **R_f-** (40% EtOAc/Hexane) 0.3; **IR** (KBr, cm^{-1}): 3302, 1732, 1209;

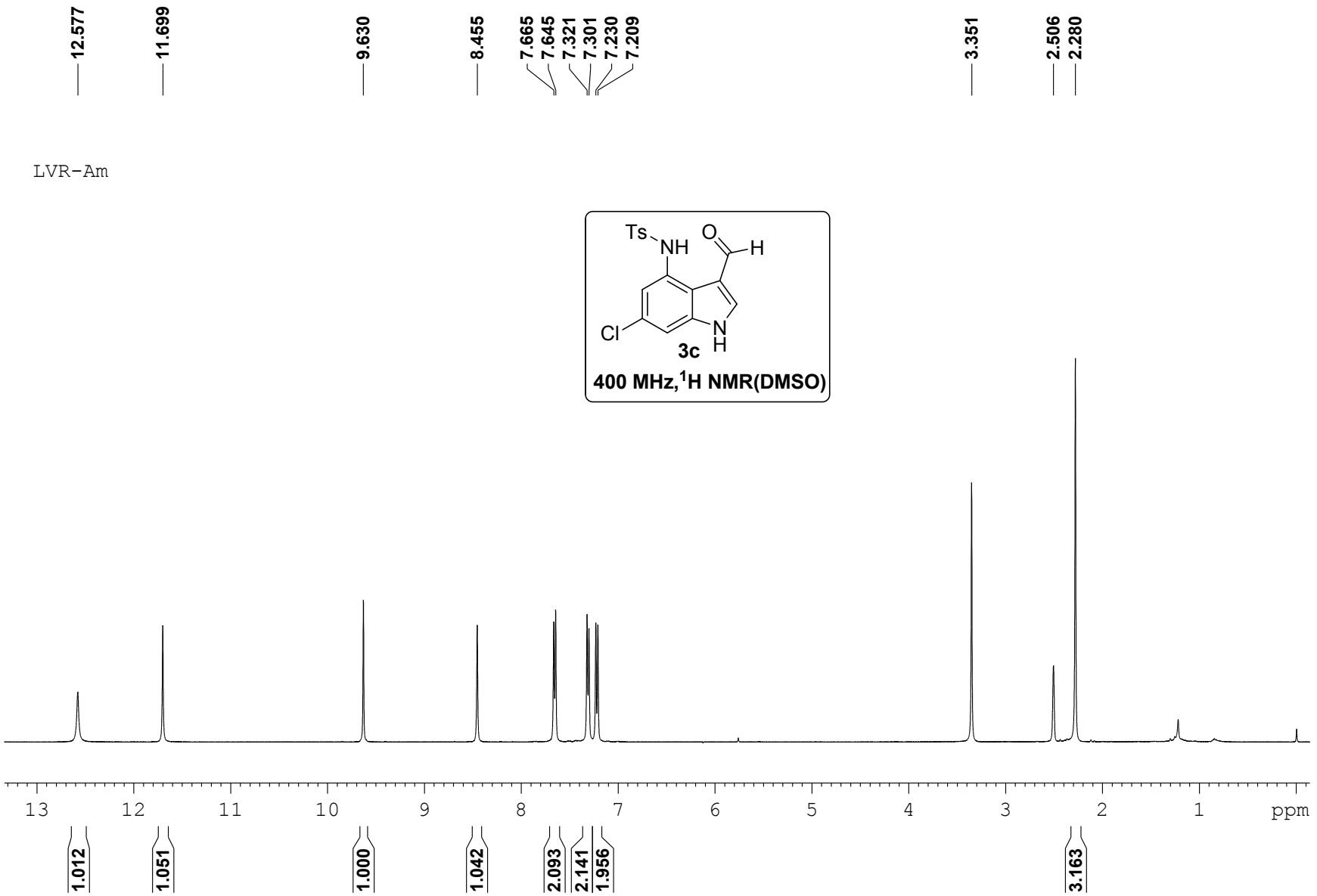
^{1}H NMR (400 MHz, DMSO-d_6) ppm 6.25 (br. s., 2 H) 6.26 - 6.30 (m, 1 H) 6.55 - 6.62 (m, 1 H) 6.92 (t, *J*=7.83 Hz, 1 H) 8.14 (d, *J*=3.28 Hz, 1 H) 9.58 (s, 1 H) 11.98 (br. s., 1 H); **^{13}C NMR** (100 MHz, DMSO-d_6) ppm 99.45 ,105.04 ,111.84 ,119.79 ,125.41 ,139.36 ,140.08 ,143.10 ,184.82 (s, 1 C).; **HRESI-MS***(m/z)*–Calculated for $C_9H_8N_2ONa$ (M+Na): 183.0534, found (M+Na) 183.0537.

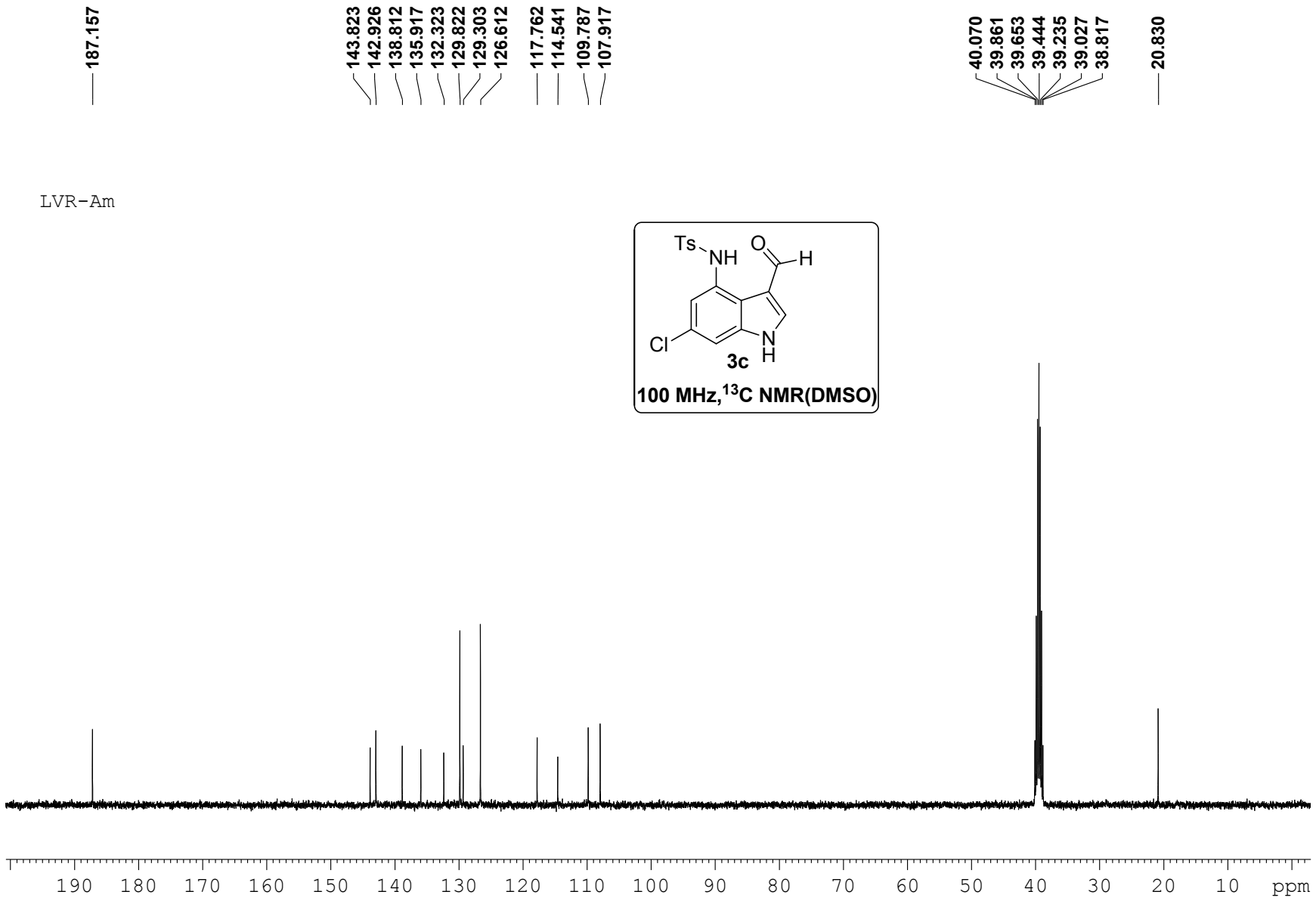

12.487
11.534
9.615
8.406
8.399
7.639
7.619
7.264
7.246
7.207
7.187
7.168
7.164
7.144
3.360
2.508
2.504
2.251
Ts
NH
O
H
N
H
3a
400 MHz,1H NMR(DMSO)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.975
1.034
1.000
1.040
2.109
3.143
2.126
3.161

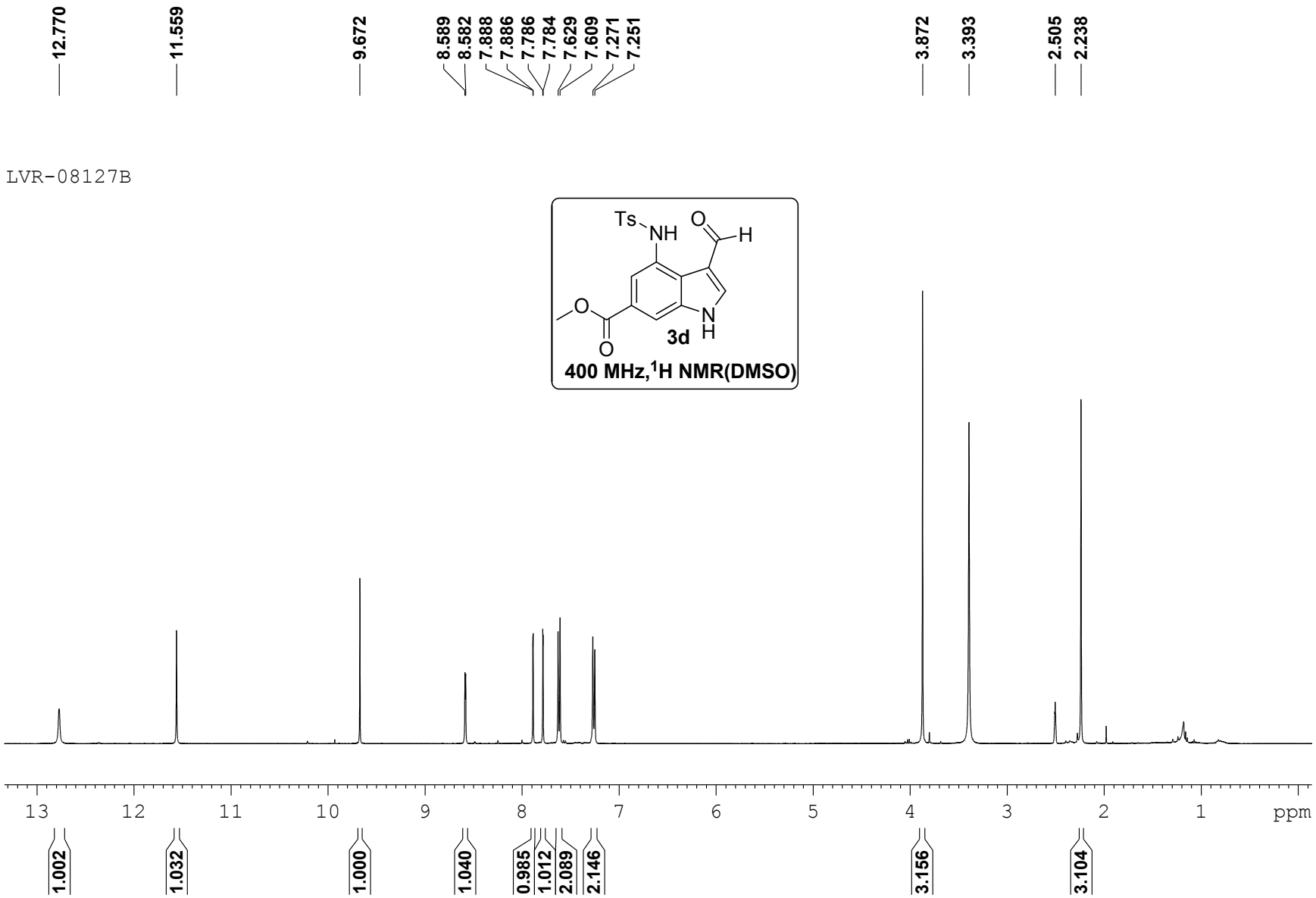

187.262
143.900
142.674
139.211
136.848
131.939
130.111
127.183
125.521
118.294
116.277
110.578
108.712
40.621
40.411
40.203
39.994
39.785
39.577
39.369
21.326
Ts
NH
O
H
N
H
3a
100 MHz, 13C NMR(DMSO)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

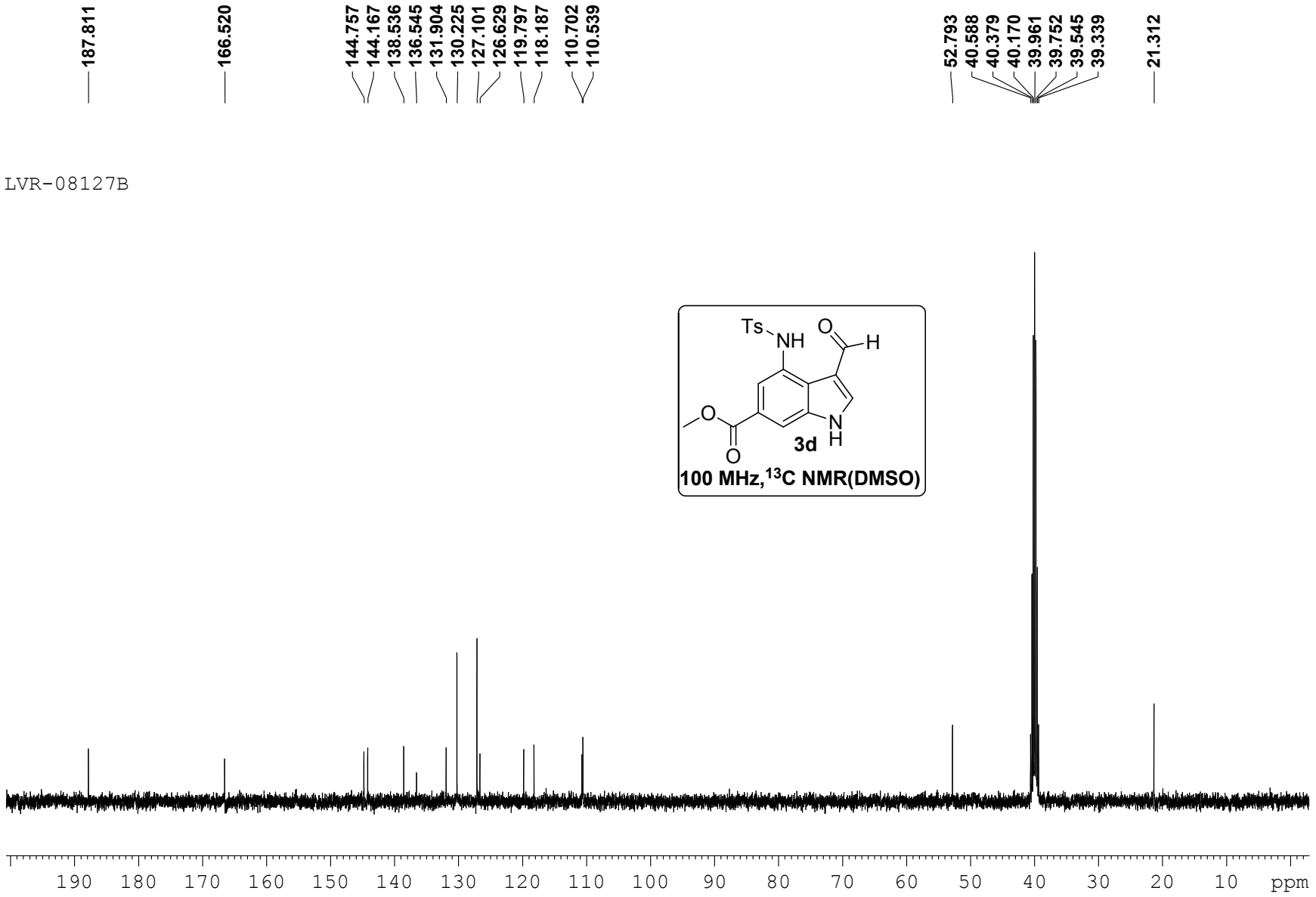

12.578
11.686
9.639
8.446
8.438
7.667
7.646
7.375
7.372
7.349
7.345
7.328
7.307
3.387
2.516
2.285
LVR-08104B
Ts
NH
O
H
Br
N
H
3b
400 MHz, 1H NMR(DMSO)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.042
1.066
1.000
1.066
2.213
4.257
3.276

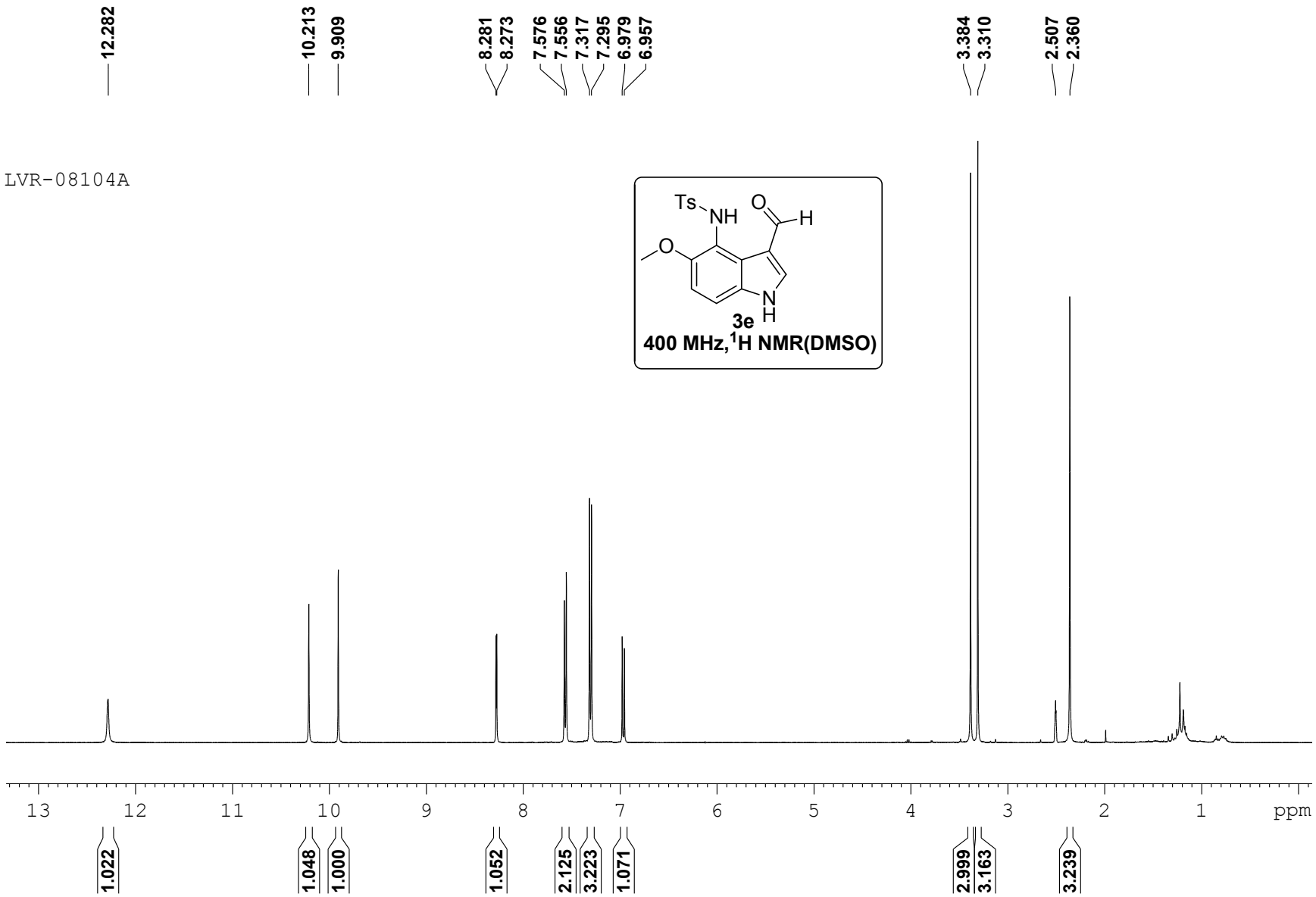

187.692
144.357
143.298
139.706
136.432
133.034
130.346
127.102
118.282
117.602
115.361
112.936
111.347
40.597
40.389
40.180
39.972
39.764
39.555
39.345
21.362
LVR-08104B
Ts
NH
O
H
Br
N
H
3b
100 MHz, 13C NMR(DMSO)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

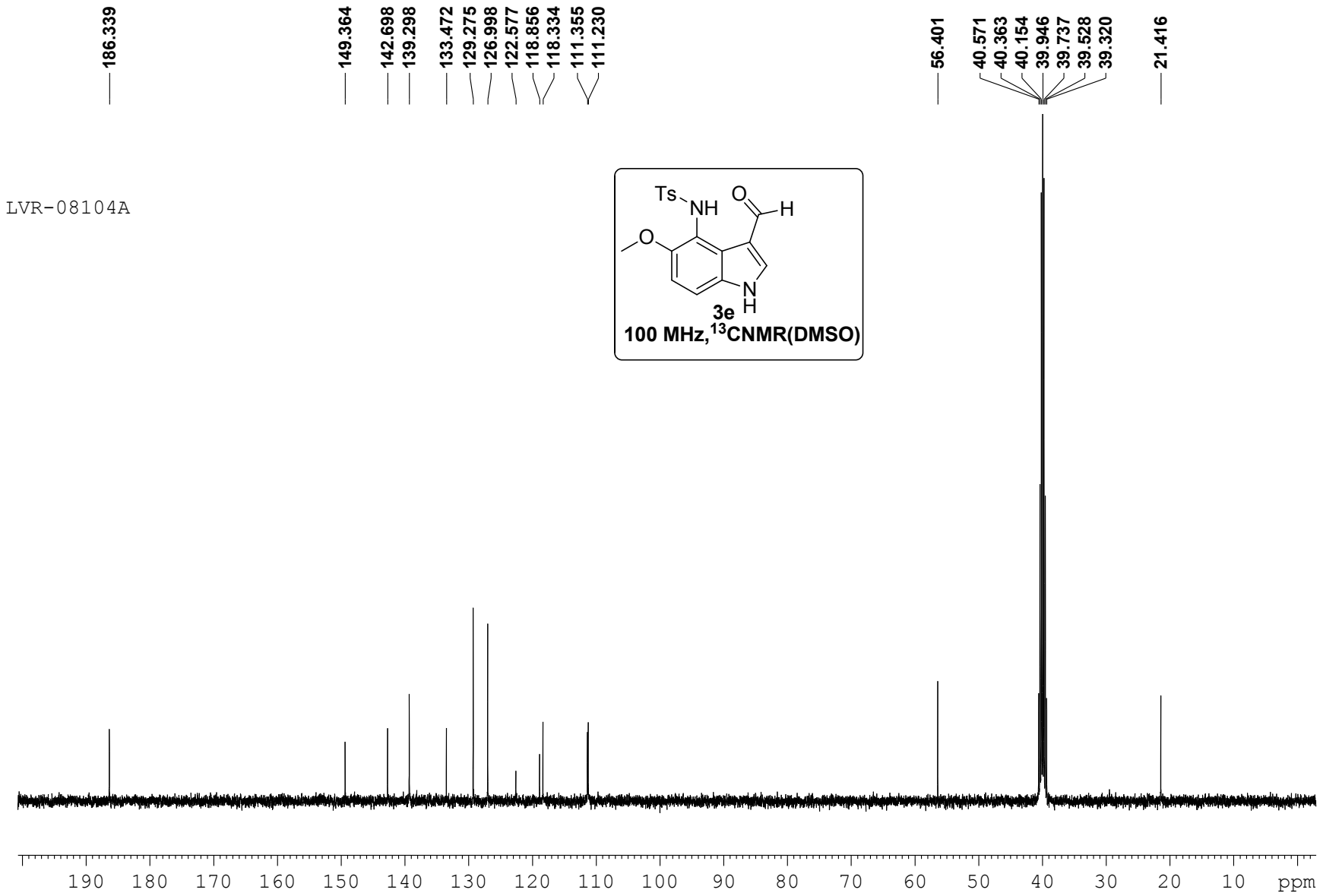

12.577
11.699
9.630
8.455
7.665
7.645
7.321
7.301
7.230
7.209
3.351
2.506
2.280
LVR-Am
Ts
NH
O
H
Cl
N
H
3c
400 MHz, 1H NMR(DMSO)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.012
1.051
1.000
1.042
2.093
2.141
1.956
3.163

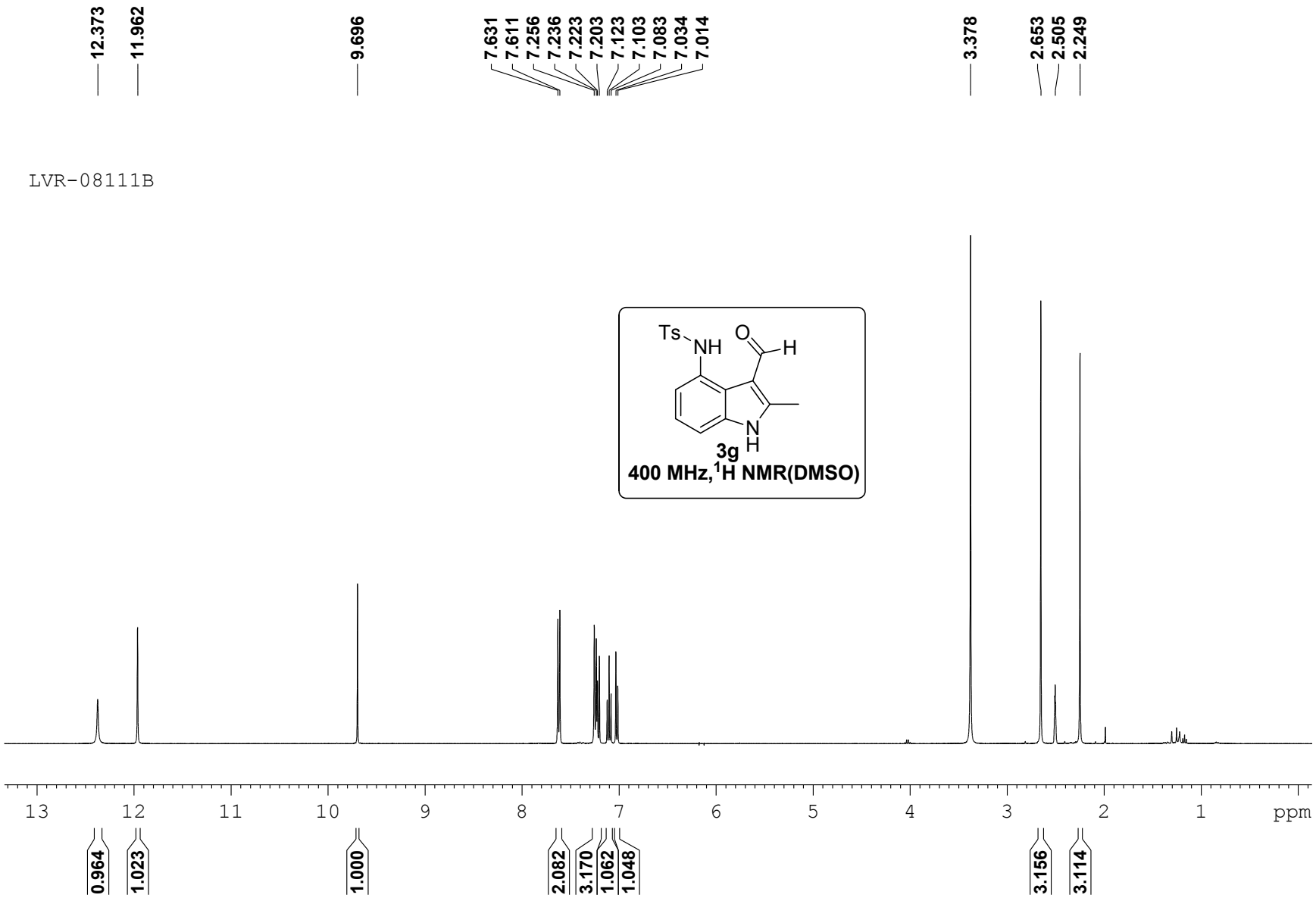

187.157
143.823
142.926
138.812
135.917
132.323
129.822
129.303
126.612
117.762
114.541
109.787
107.917
40.070
39.861
39.653
39.444
39.235
39.027
38.817
20.830
LVR-Am
Ts
NH
O
H
Cl
N
H
3c
100 MHz, 13C NMR(DMSO)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

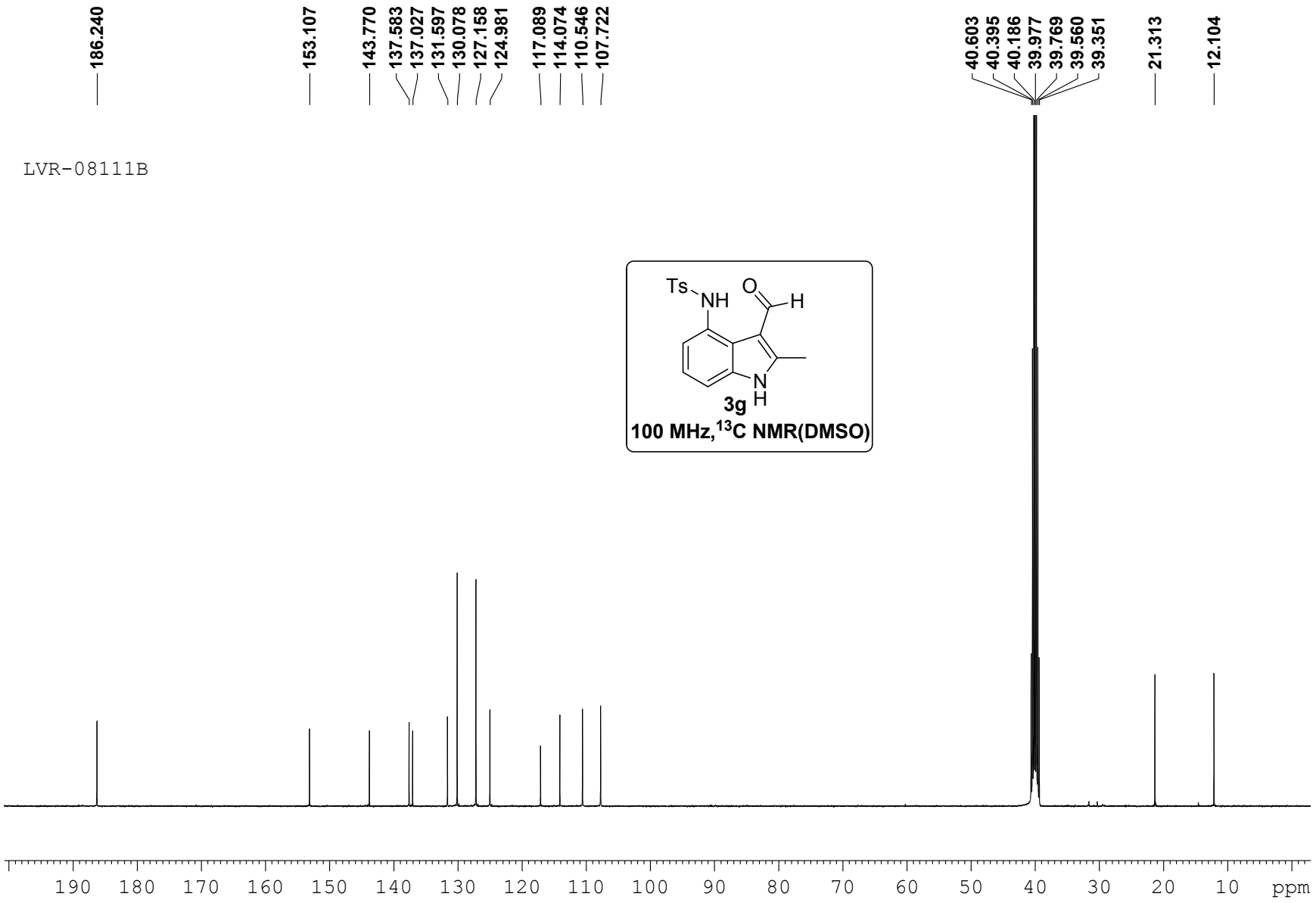

12.770
11.559
9.672
8.589
8.582
7.888
7.886
7.786
7.784
7.629
7.609
7.271
7.251
3.872
3.393
2.505
2.238
LVR-08127B
Ts
NH
O
H
O
N
H
O
3d
400 MHz,1H NMR(DMSO)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.002
1.032
1.000
1.040
0.985
1.012
2.089
2.146
3.156
3.104

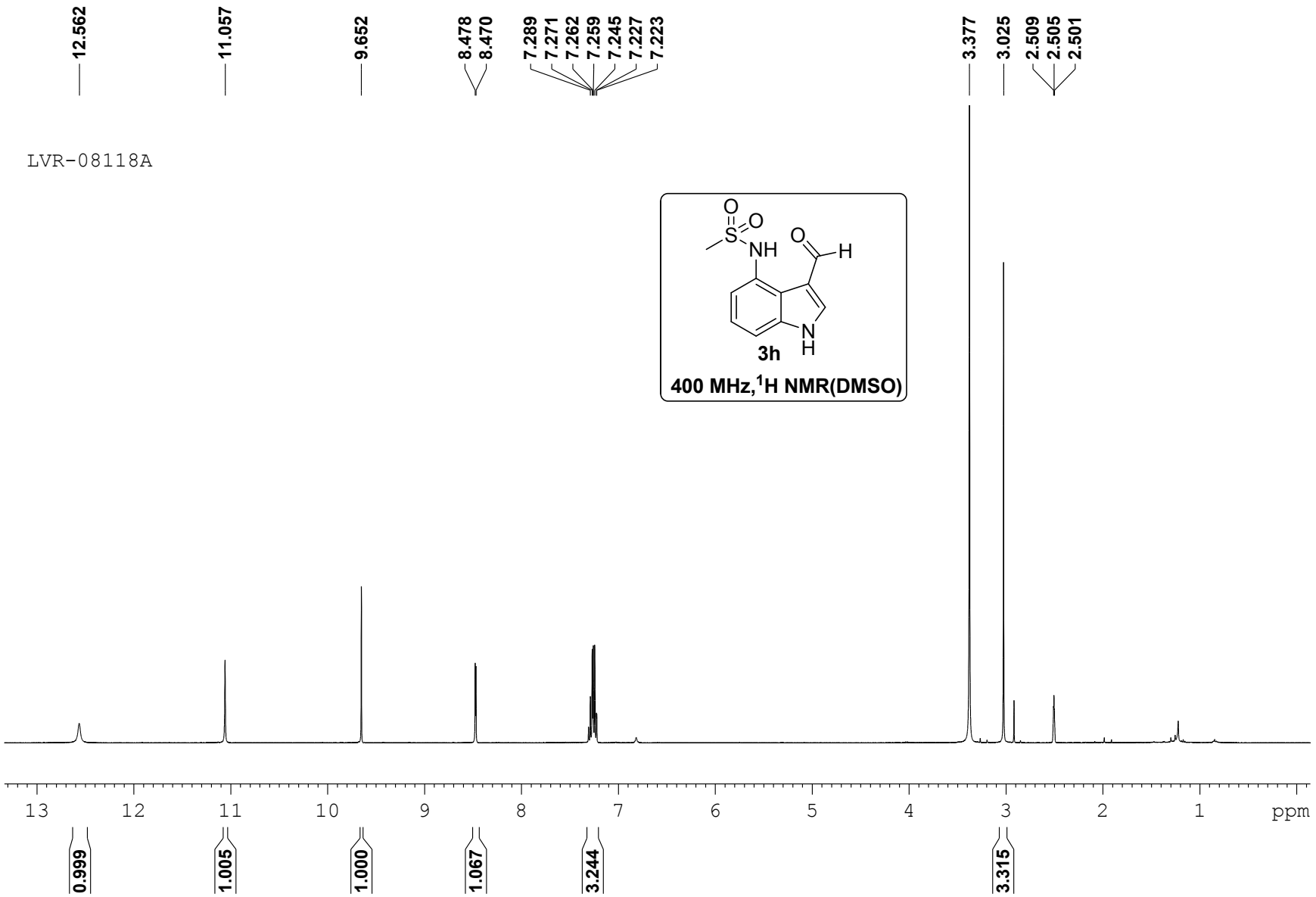

187.811
166.520
144.757
144.167
138.536
136.545
131.904
130.225
127.101
126.629
119.797
118.187
110.702
110.539
52.793
40.588
40.379
40.170
39.961
39.752
39.545
39.339
21.312
LVR-08127B
Ts
NH
O
H
O
N
H
O
3d
100 MHz,13C NMR(DMSO)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

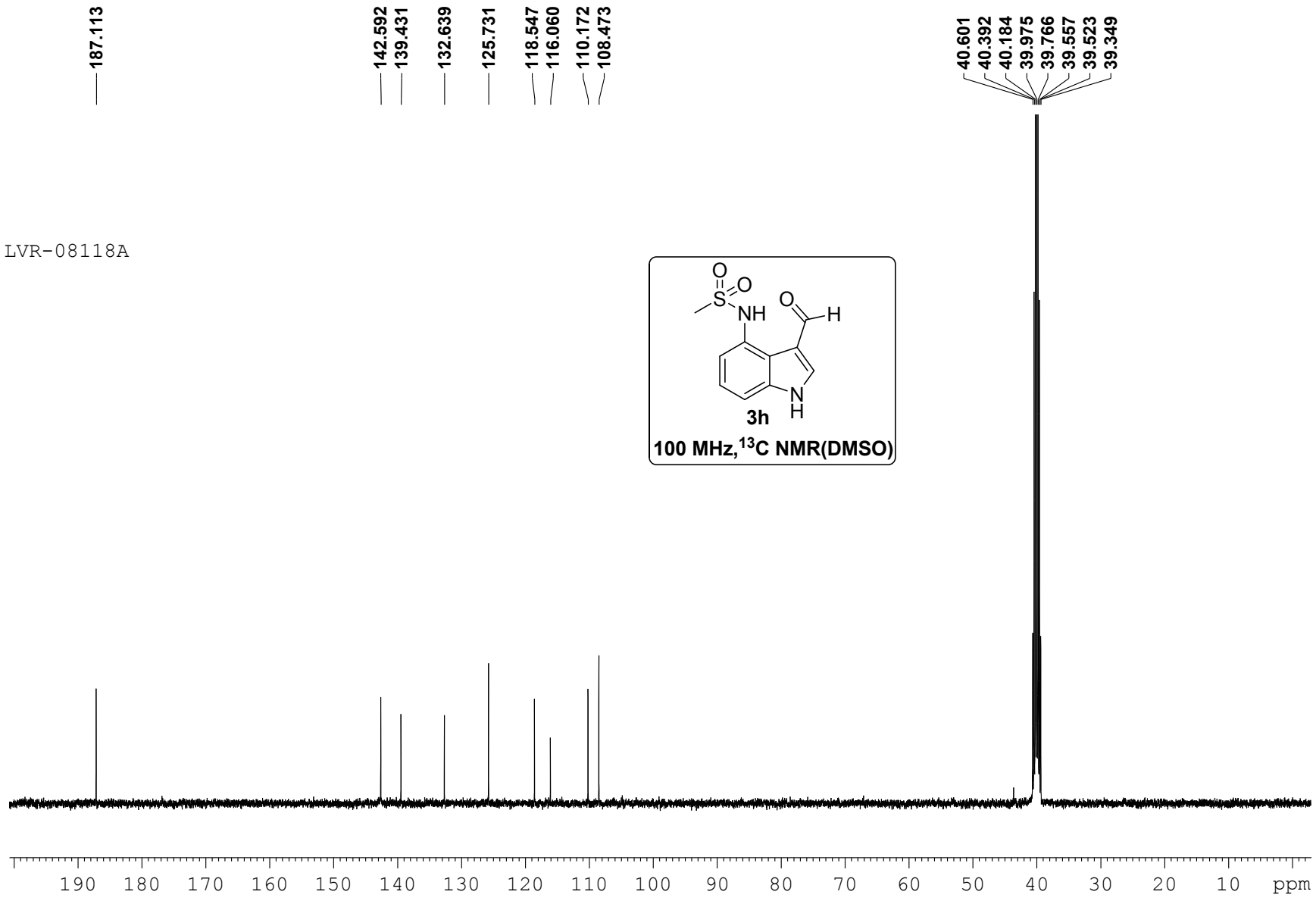

12.282
10.213
9.909
8.281
8.273
7.576
7.556
7.317
7.295
6.979
6.957
3.384
3.310
2.507
2.360
LVR-08104A
Ts
NH
O
H
O
N
H
3e
400 MHz, 1H NMR(DMSO)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.022
1.048
1.000
1.052
2.125
3.223
1.071
2.999
3.163
3.239

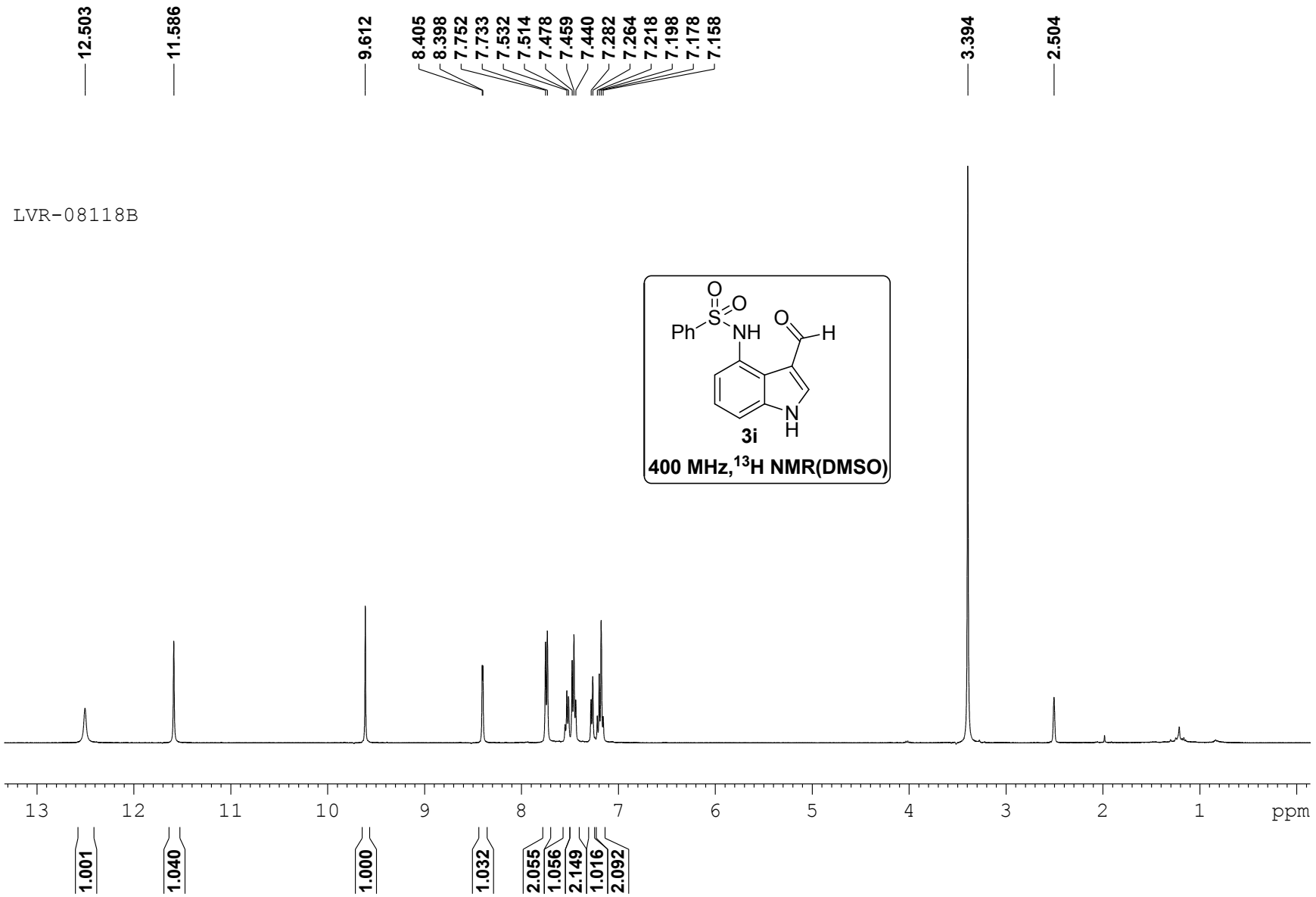

186.339
149.364
142.698
139.298
133.472
129.275
126.998
122.577
118.856
118.334
111.355
111.230
56.401
40.571
40.363
40.154
39.946
39.737
39.528
39.320
21.416
LVR-08104A
Ts
NH
O
H
O
N
H
3e
100 MHz, 13CNMR(DMSO)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

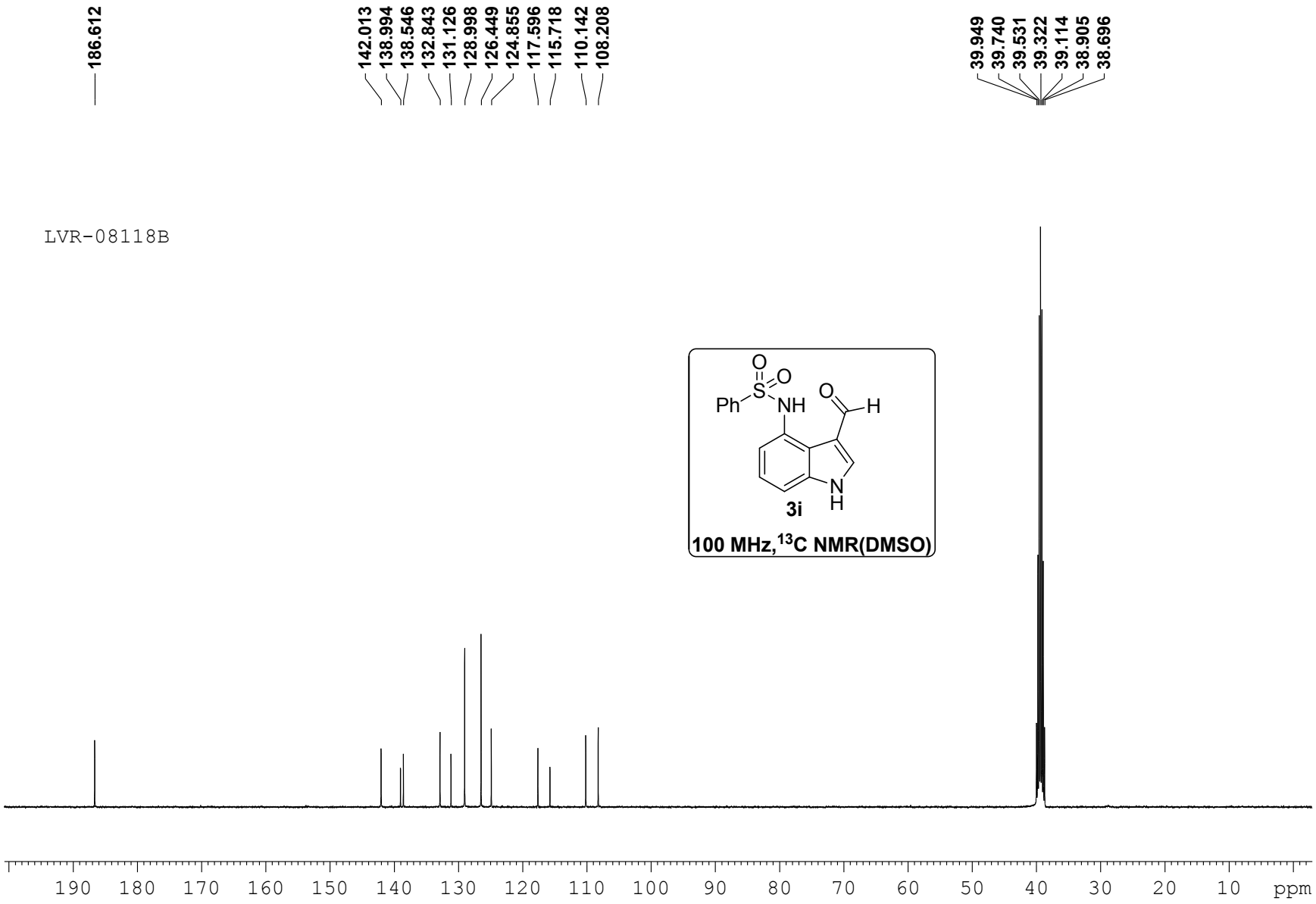

12.373
11.962
9.696
7.631
7.611
7.256
7.236
7.223
7.203
7.123
7.103
7.083
7.034
7.014
3.378
2.653
2.505
2.249
LVR-08111B
Ts
NH
O
H
N
H
3g
400 MHz,1H NMR(DMSO)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.964
1.023
1.000
2.082
3.170
1.062
1.048
3.156
3.114

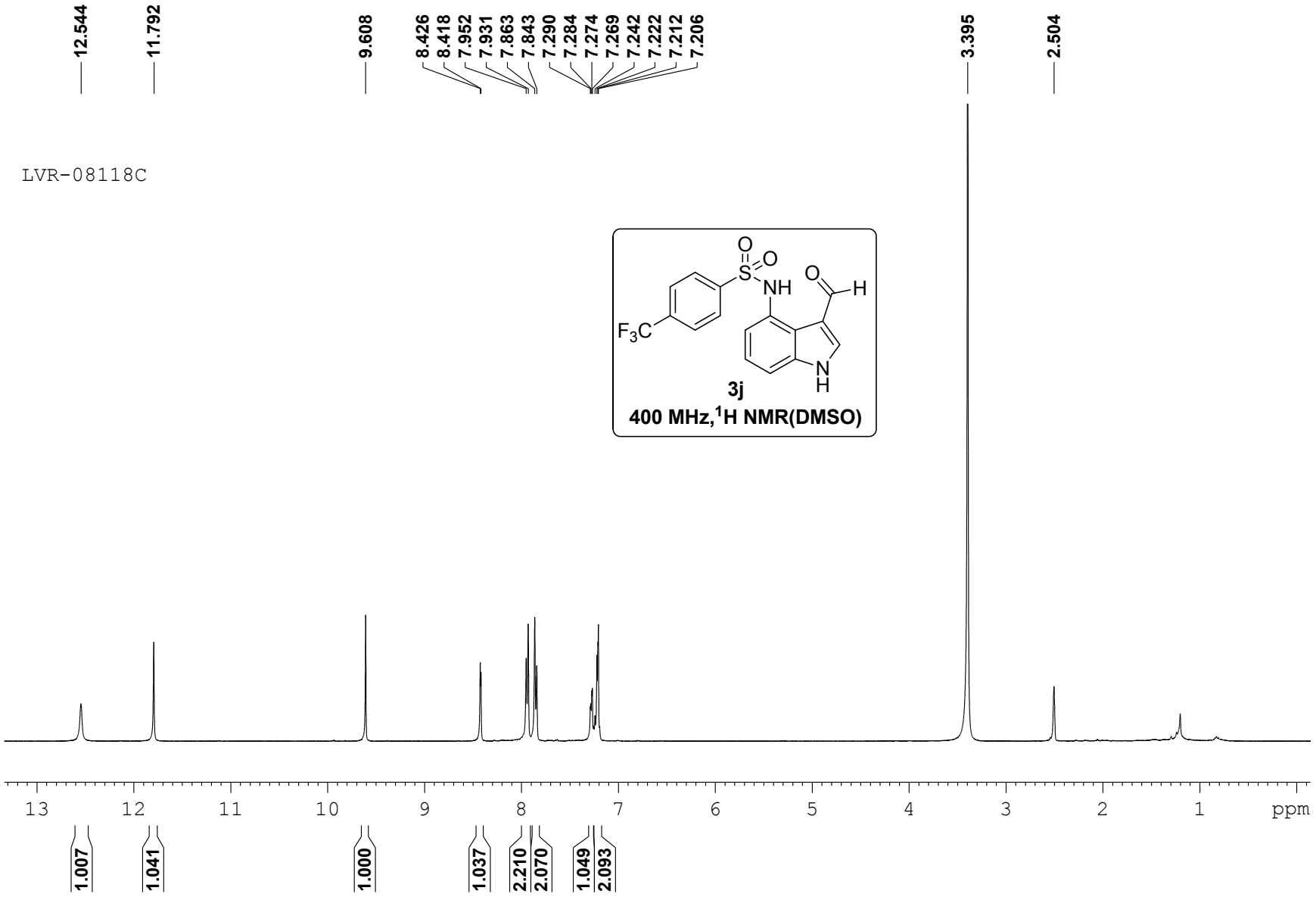

186.240
153.107
143.770
137.583
137.027
131.597
130.078
127.158
124.981
117.089
114.074
110.546
107.722
40.603
40.395
40.186
39.977
39.769
39.560
39.351
21.313
12.104
LVR-08111B
Ts
NH
O
H
N
H
3g
100 MHz, 13C NMR(DMSO)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

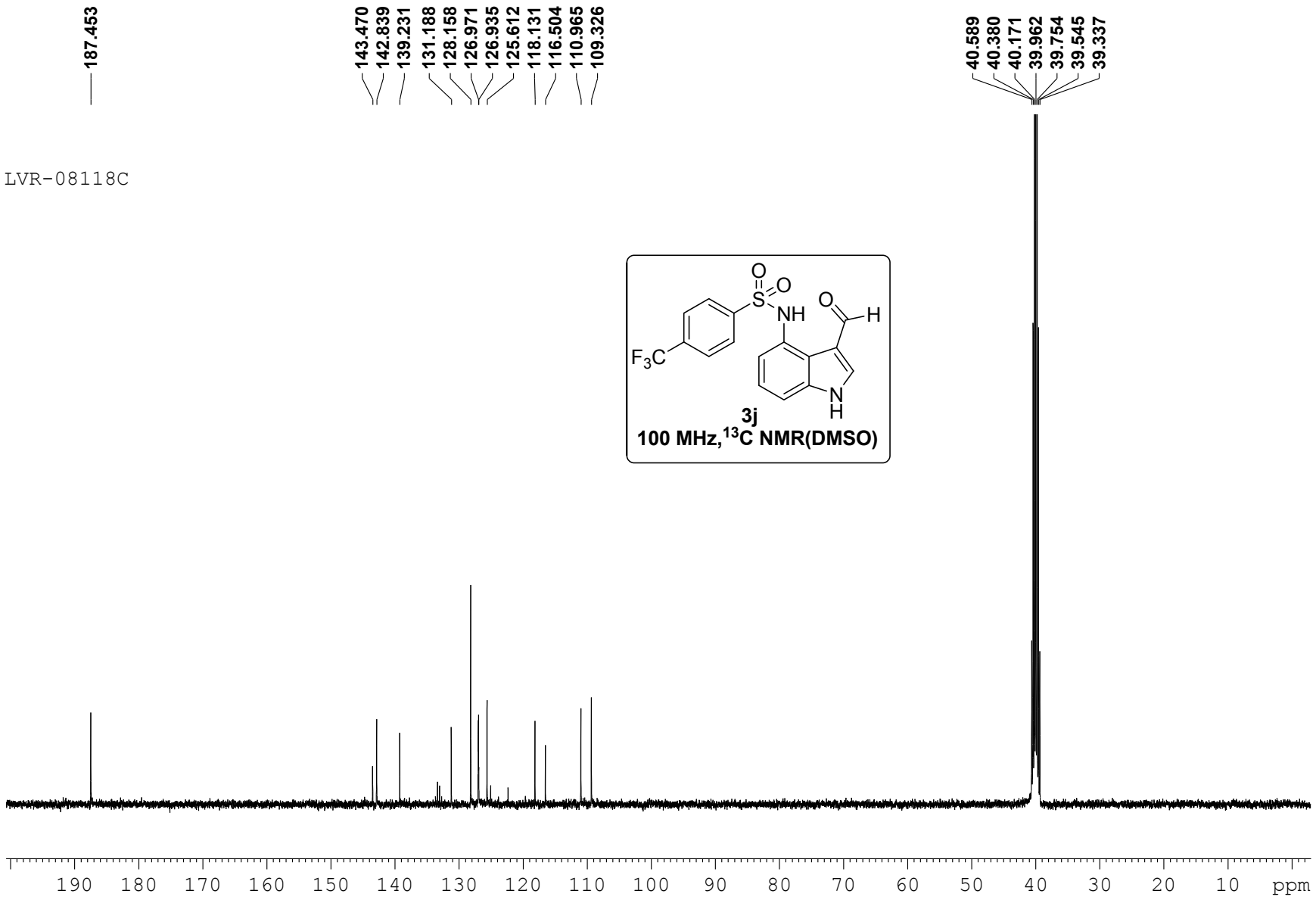

12.562
11.057
9.652
8.478
8.470
7.289
7.271
7.262
7.259
7.245
7.227
7.223
3.377
3.025
2.509
2.505
2.501
LVR-08118A
O
O
S
NH
O
H
N
H
3h
400 MHz,1H NMR(DMSO)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.999
1.005
1.000
1.067
3.244
3.315

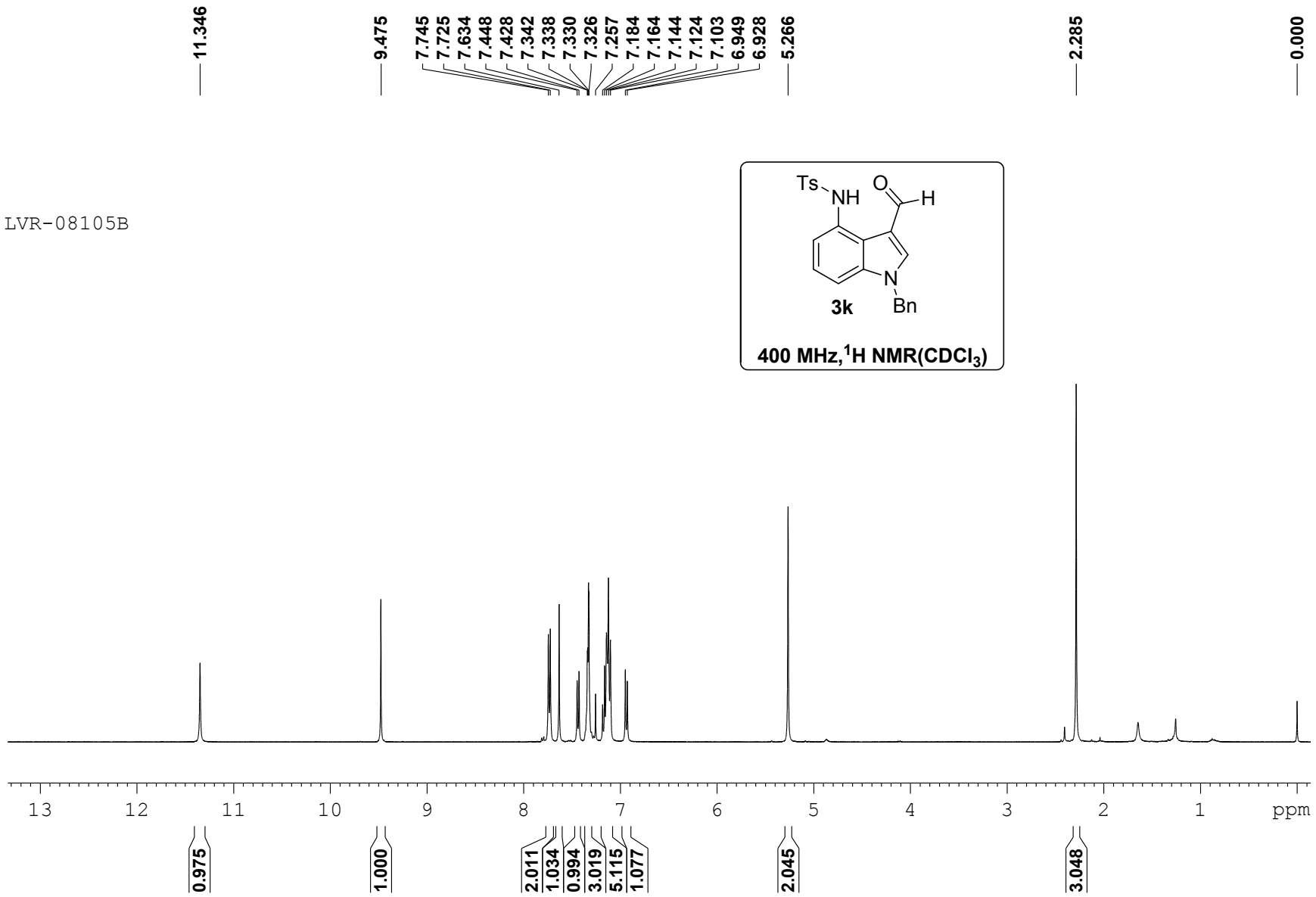

187.113
142.592
139.431
132.639
125.731
118.547
116.060
110.172
108.473
40.601
40.392
40.184
39.975
39.766
39.557
39.523
39.349
LVR-08118A
O
S
O
NH
O
H
N
H
3h
100 MHz, 13C NMR(DMSO)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

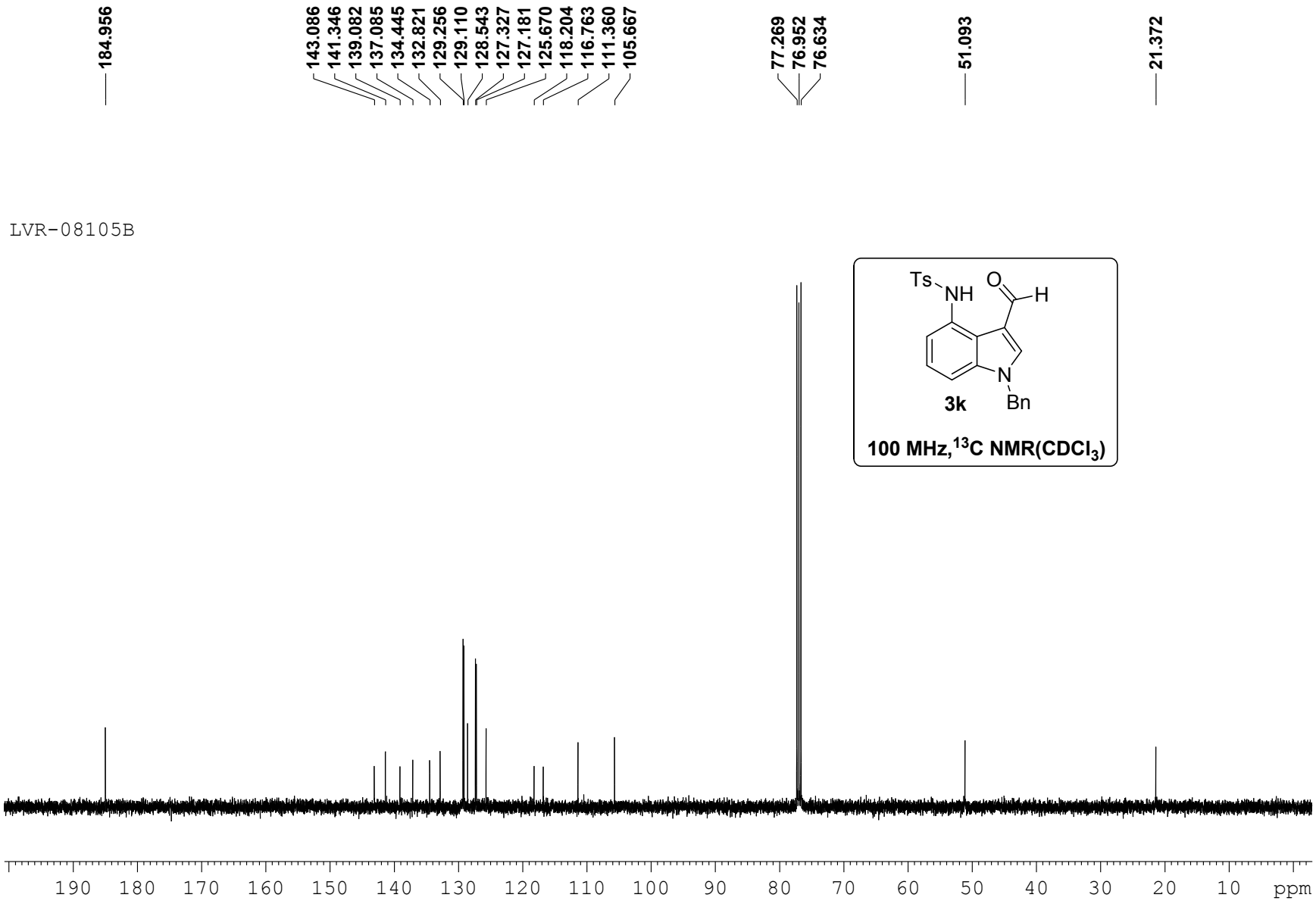

12.503
11.586
9.612
8.405
8.398
7.752
7.733
7.532
7.514
7.478
7.459
7.440
7.282
7.264
7.218
7.198
7.178
7.158
3.394
2.504
LVR-08118B
3i
400 MHz,13H NMR(DMSO)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.001
1.040
1.000
1.032
2.055
1.056
2.149
1.016
2.092

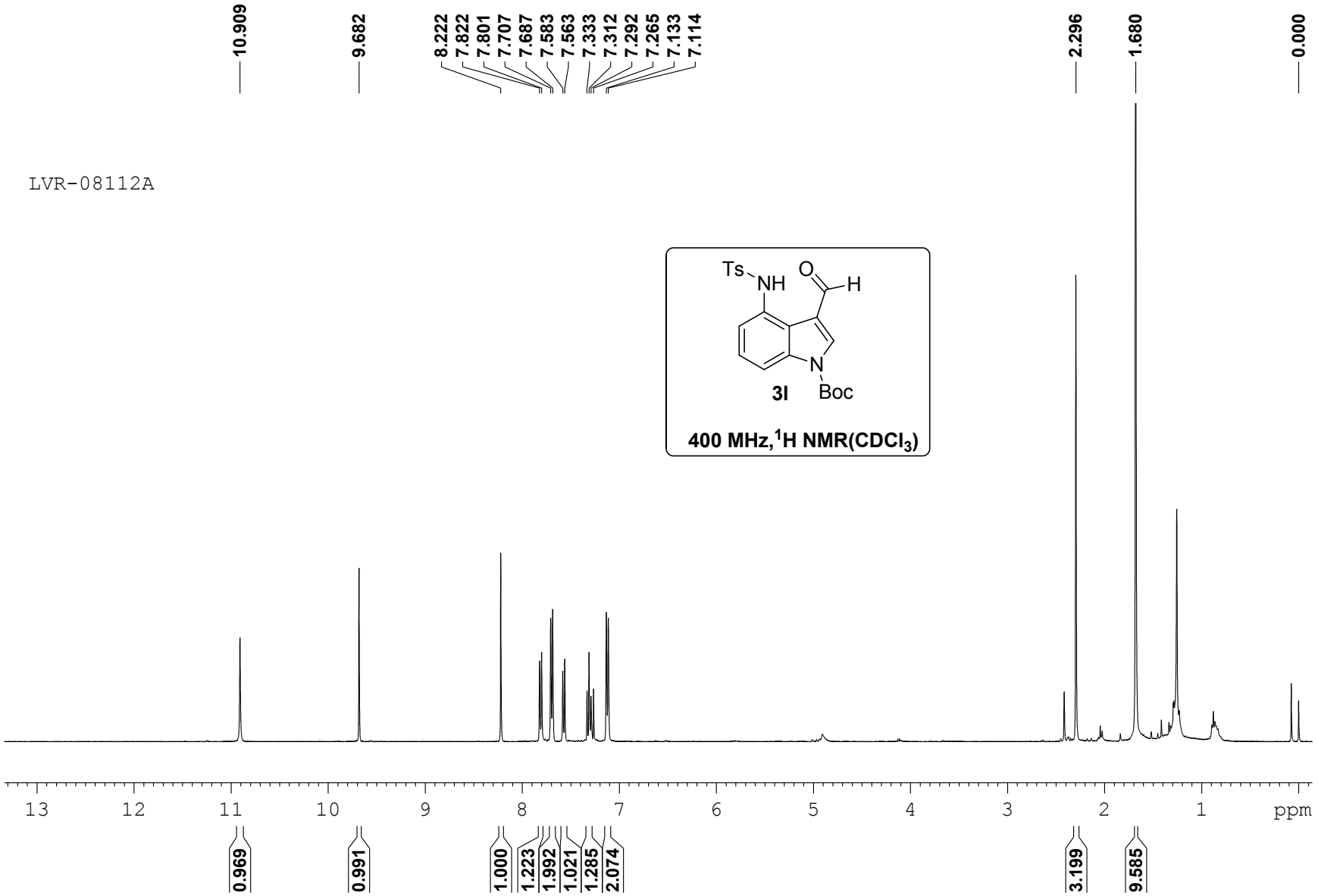

186.612
142.013
138.994
138.546
132.843
131.126
128.998
126.449
124.855
117.596
115.718
110.142
108.208
39.949
39.740
39.531
39.322
39.114
38.905
38.696
LVR-08118B
Ph
NH
O
H
N
H
3i
100 MHz, 13C NMR(DMSO)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

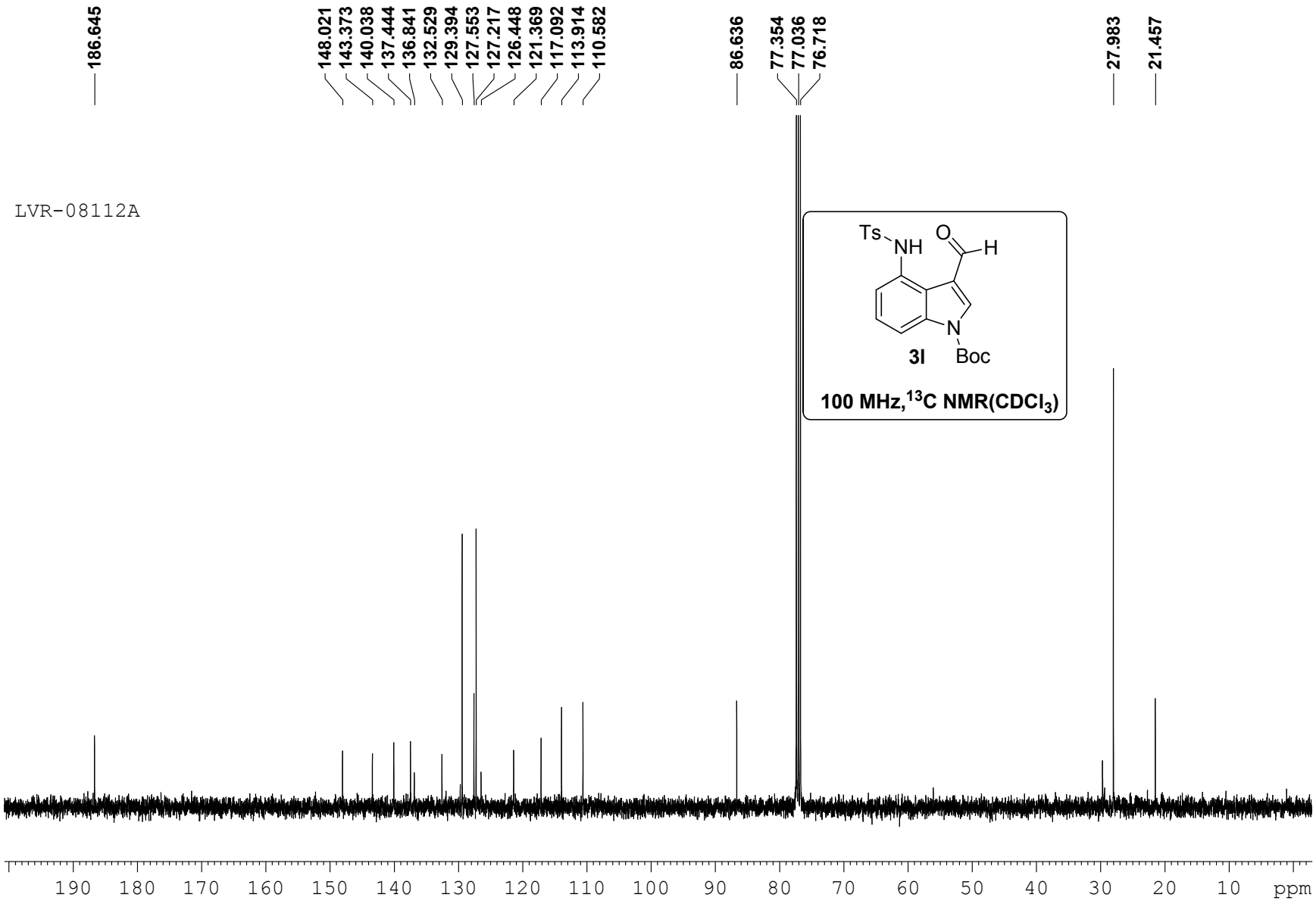

12.544
11.792
9.608
8.426
8.418
7.952
7.931
7.863
7.843
7.290
7.284
7.274
7.269
7.242
7.222
7.212
7.206
3.395
2.504
LVR-08118C
3j
400 MHz,1H NMR(DMSO)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.007
1.041
1.000
1.037
2.210
2.070
1.049
2.093

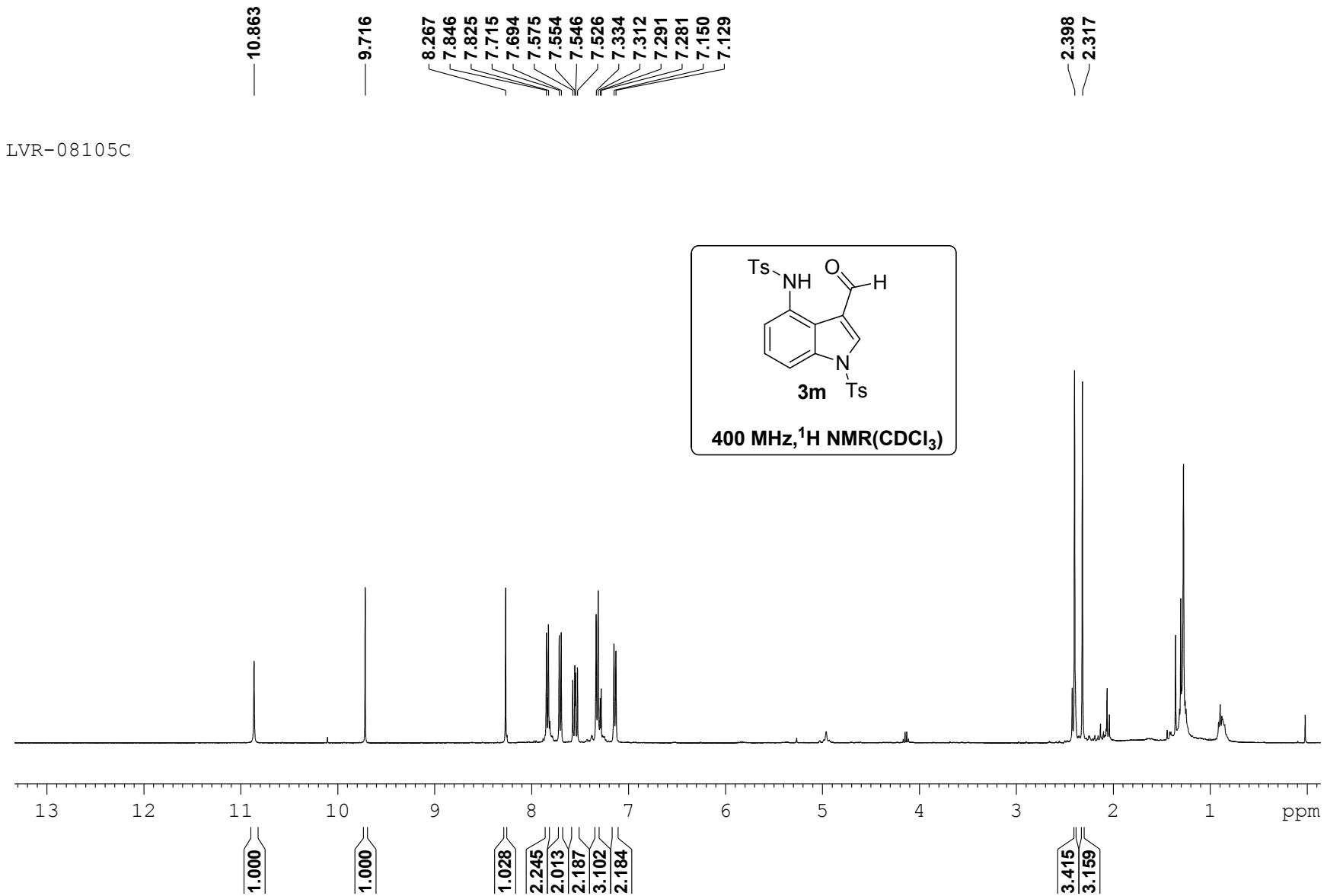

187.453
143.470
142.839
139.231
131.188
128.158
126.971
126.935
125.612
118.131
116.504
110.965
109.326
40.589
40.380
40.171
39.962
39.754
39.545
39.337
LVR-08118C
3j
100 MHz, 13C NMR(DMSO)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

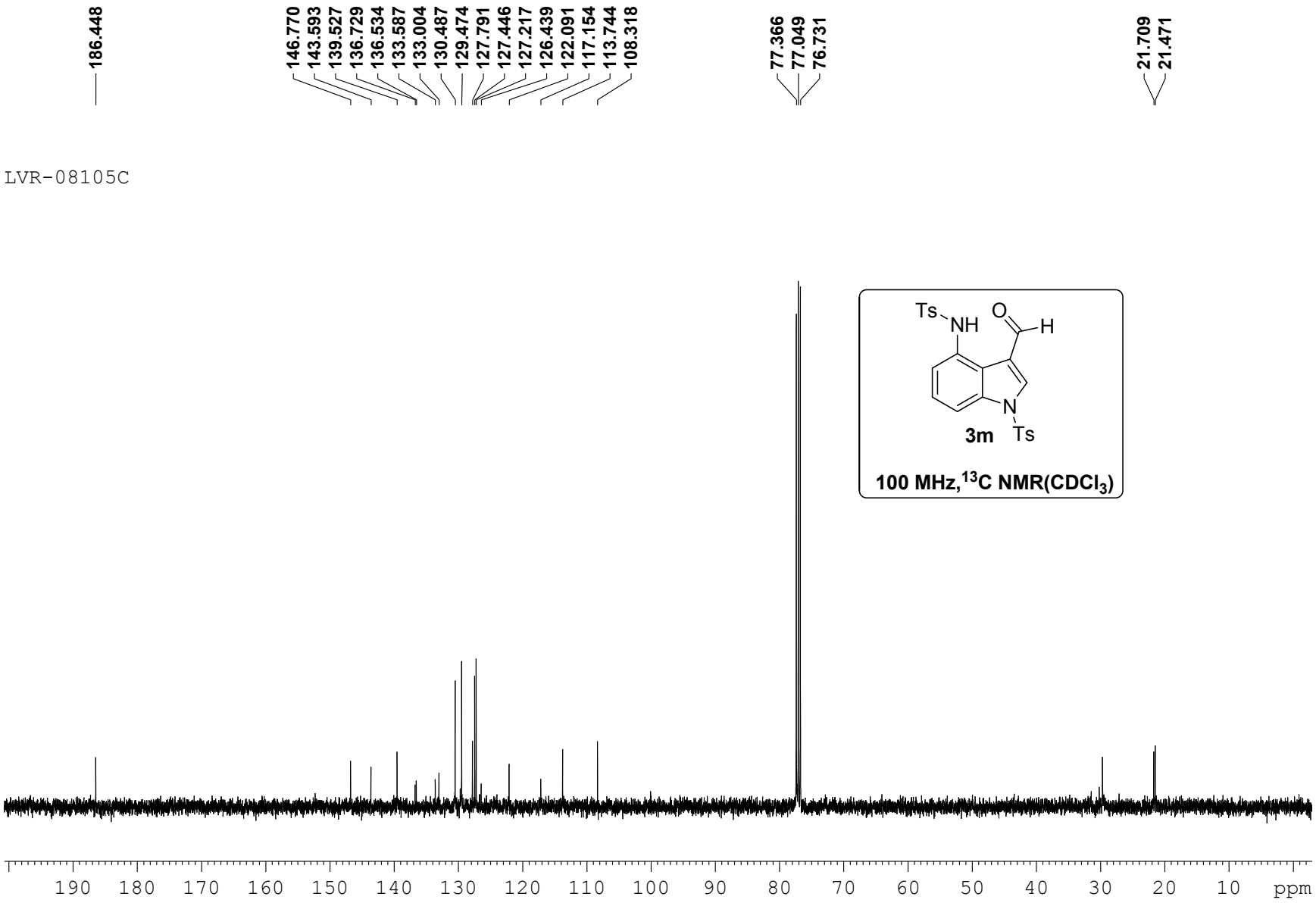

11.346
9.475
7.745
7.725
7.634
7.448
7.428
7.342
7.338
7.330
7.326
7.257
7.184
7.164
7.144
7.124
7.103
6.949
6.928
5.266
2.285
0.000
LVR-08105B
Ts
NH
O
H
N
Bn
3k
400 MHz,1H NMR(CDCl3)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.975
1.000
2.011
1.034
0.994
3.019
5.115
1.077
2.045
3.048

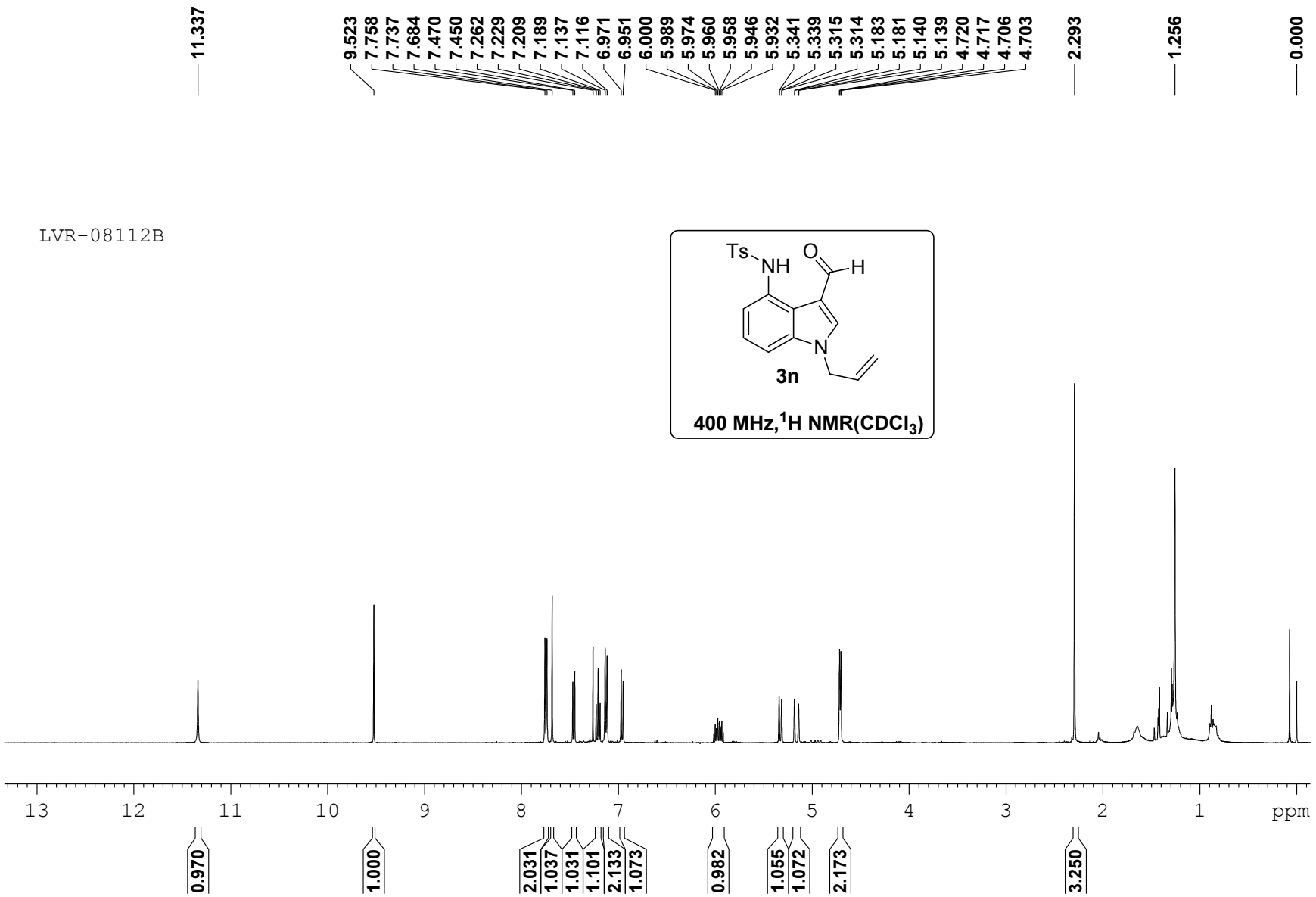

184.956
143.086
141.346
139.082
137.085
134.445
132.821
129.256
129.110
128.543
127.327
127.181
125.670
118.204
116.763
111.360
105.667
77.269
76.952
76.634
51.093
21.372
LVR-08105B
Ts
NH
O
H
N
Bn
3k
100 MHz, 13C NMR(CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

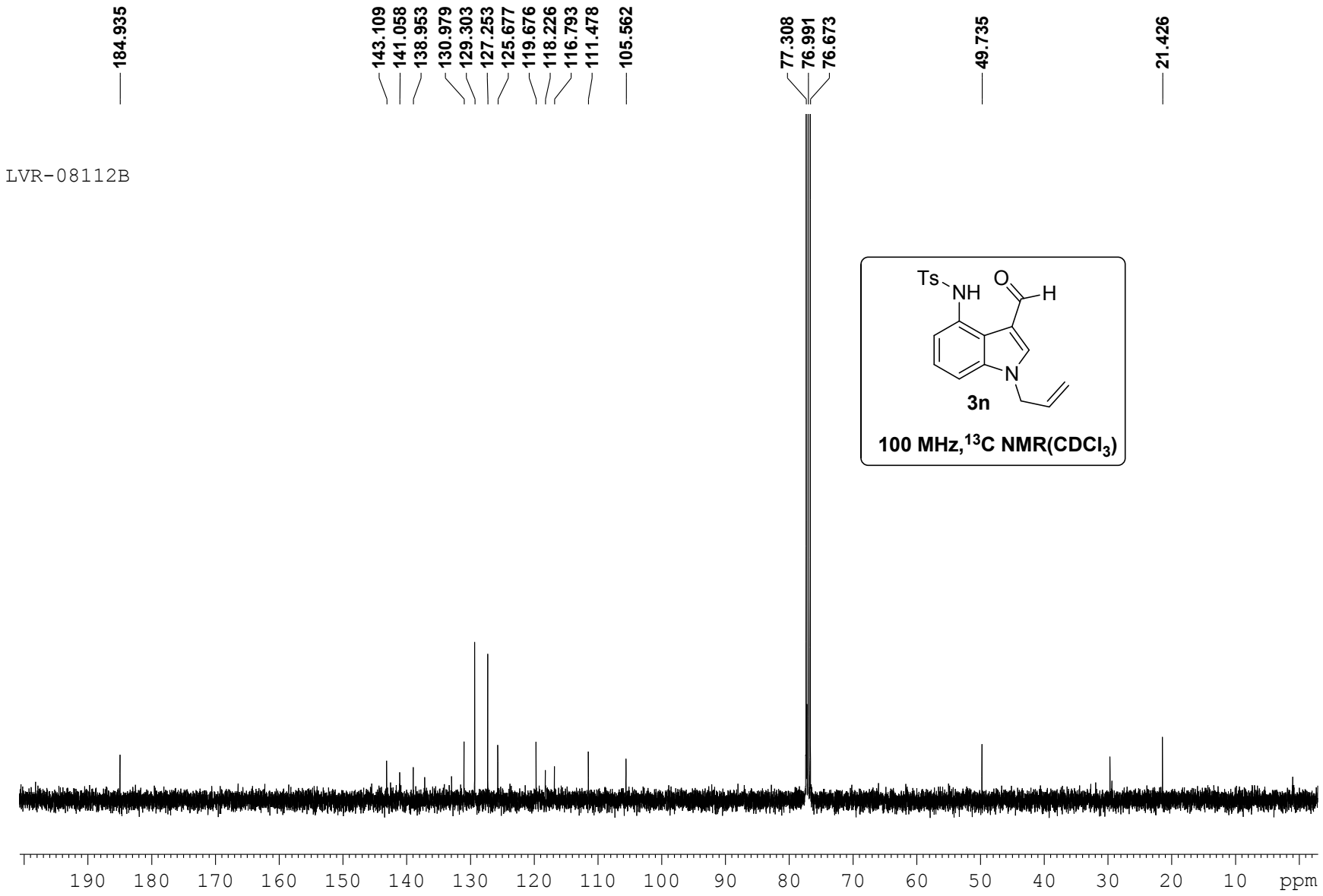

10.909
9.682
8.222
7.822
7.801
7.707
7.687
7.583
7.563
7.333
7.312
7.292
7.265
7.133
7.114
2.296
1.680
0.000
LVR-08112A
Ts
NH
O
H
N
Boc
3l
400 MHz,1H NMR(CDCl3)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.969
0.991
1.000
1.223
1.992
1.021
1.285
2.074
3.199
9.585

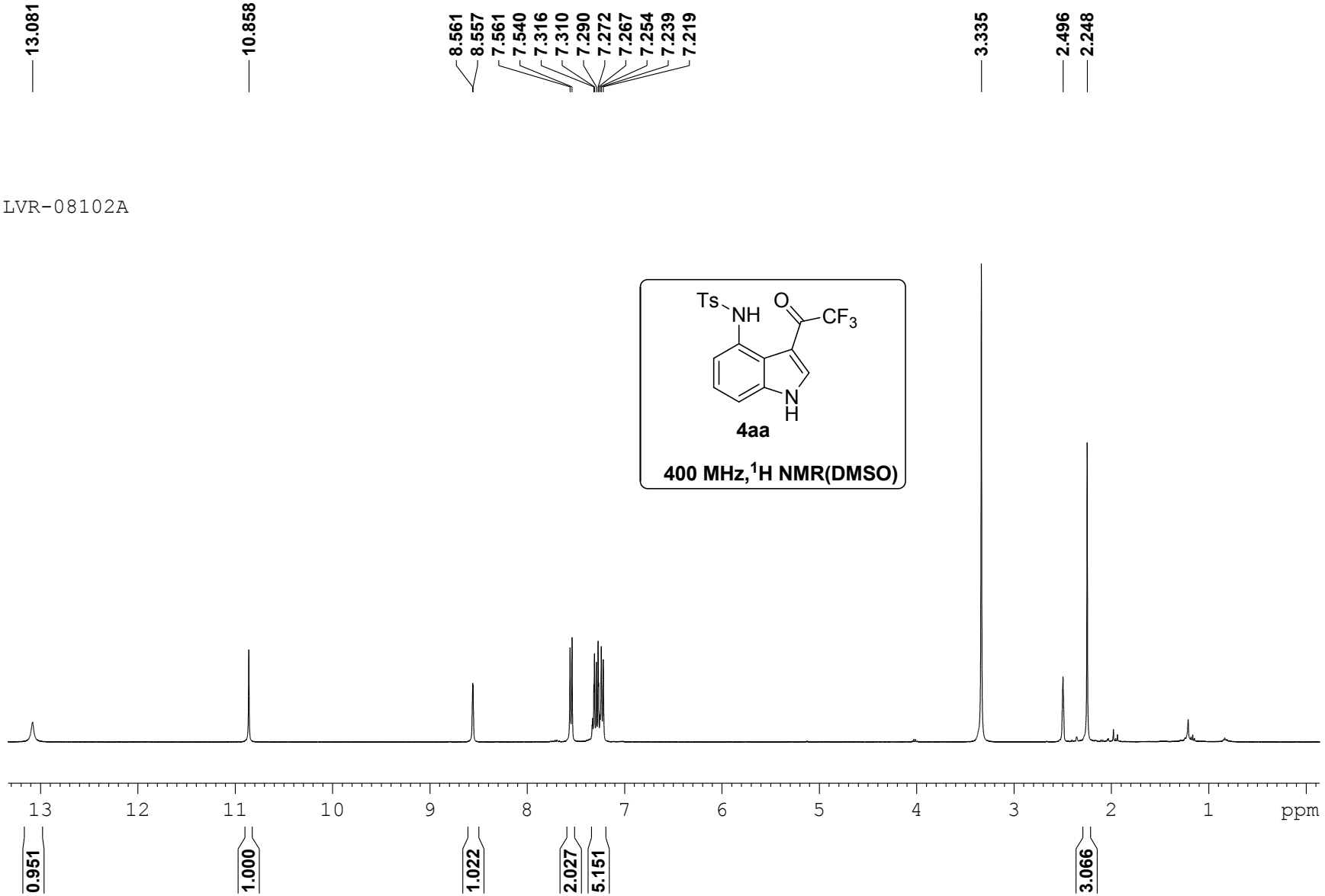

186.645
148.021
143.373
140.038
137.444
136.841
132.529
129.394
127.553
127.217
126.448
121.369
117.092
113.914
110.582
86.636
77.354
77.036
76.718
27.983
21.457
LVR-08112A
Ts
NH
O
H
N
Boc
3l
100 MHz,13C NMR(CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

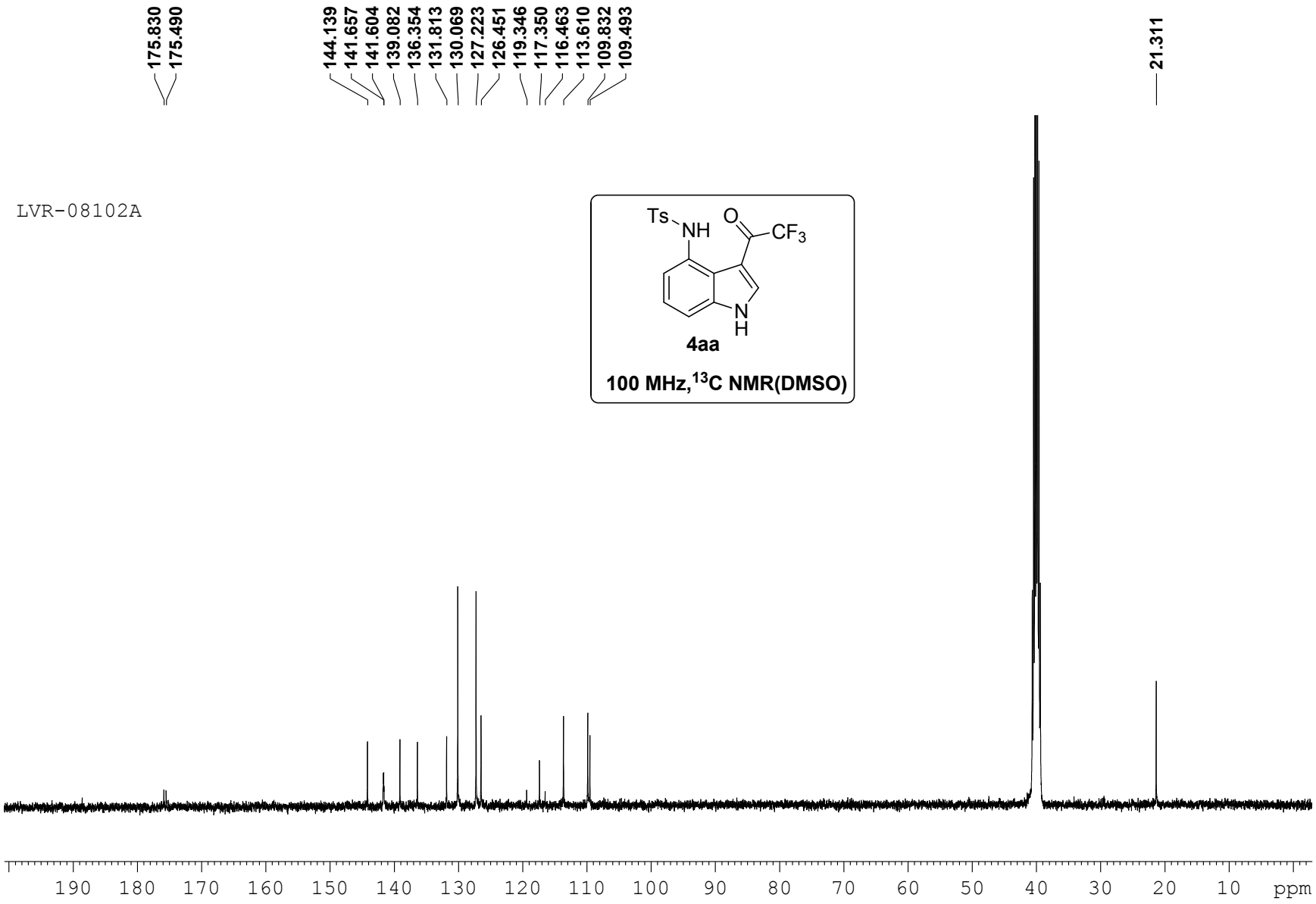

10.863
9.716
8.267
7.846
7.825
7.715
7.694
7.575
7.554
7.546
7.526
7.334
7.312
7.291
7.281
7.150
7.129
2.398
2.317
LVR-08105C
Ts
NH
O
H
N
Ts
3m
400 MHz,1H NMR(CDCl3)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.000
1.000
1.028
2.245
2.013
2.187
3.102
2.184
3.415
3.159

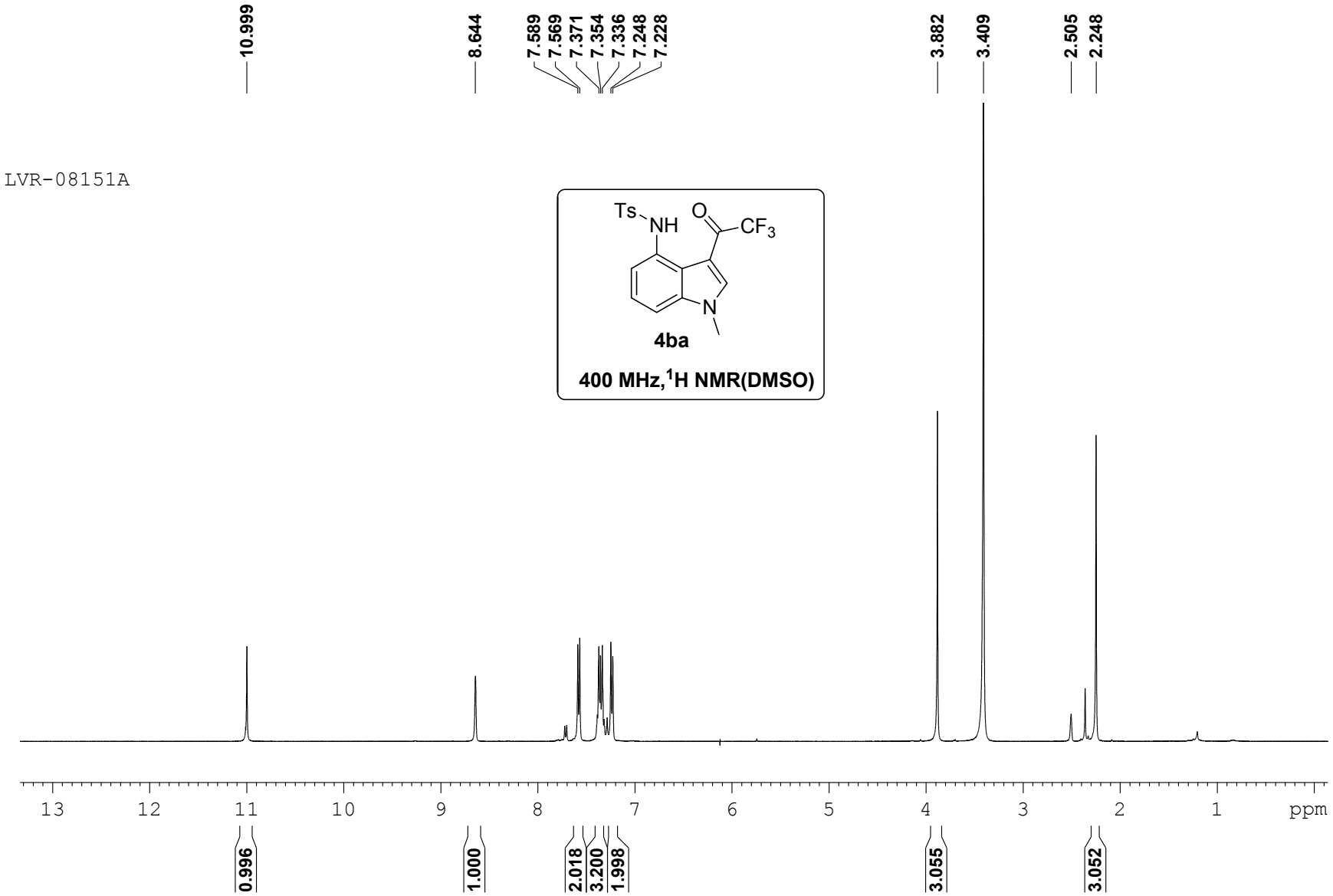

186.448
146.770
143.593
139.527
136.729
136.534
133.587
133.004
130.487
129.474
127.791
127.446
127.217
126.439
122.091
117.154
113.744
108.318
77.366
77.049
76.731
21.709
21.471
LVR-08105C
Ts
NH
O
H
N
Ts
3m
100 MHz, 13C NMR(CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

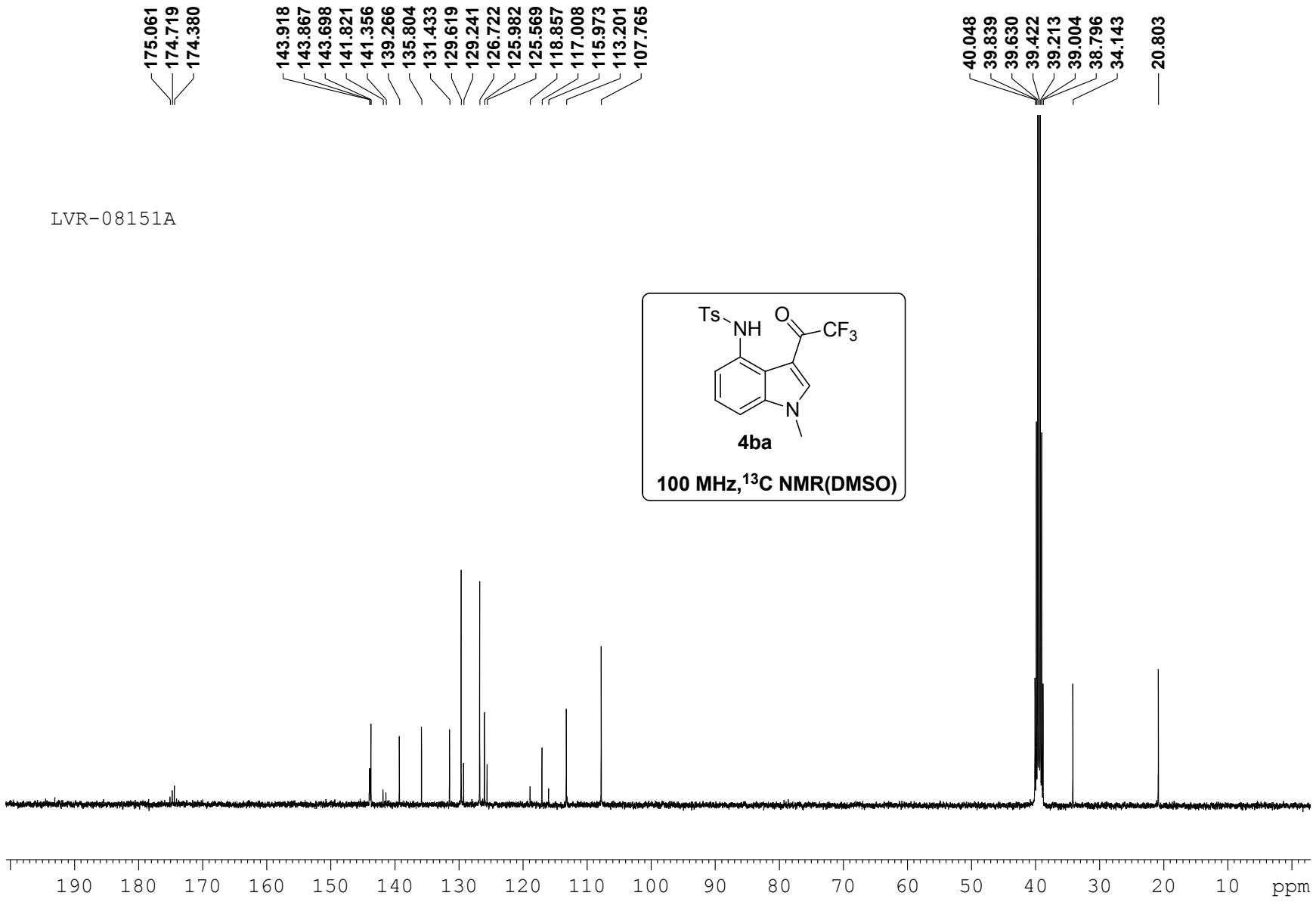

11.337
9.523
7.758
7.737
7.684
7.470
7.450
7.262
7.229
7.209
7.189
7.137
7.116
6.971
6.951
6.000
5.989
5.974
5.960
5.958
5.946
5.932
5.341
5.339
5.315
5.314
5.183
5.181
5.140
5.139
4.720
4.717
4.706
4.703
2.293
1.256
0.000
LVR-08112B
Ts
NH
O
H
N
3n
400 MHz,1H NMR(CDCl3)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.970
1.000
2.031
1.037
1.031
1.101
2.133
1.073
0.982
1.055
1.072
2.173
3.250

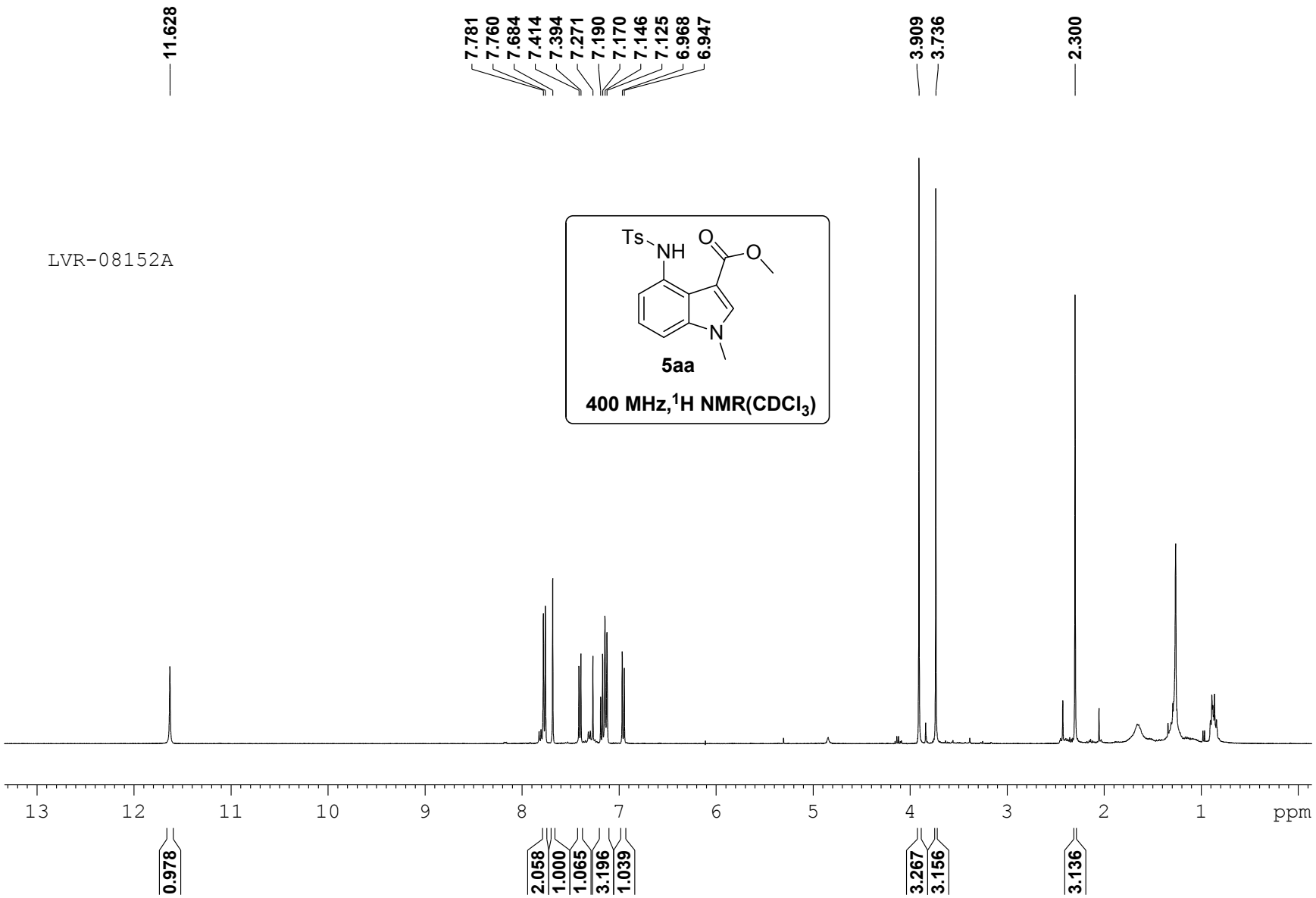

184.935
143.109
141.058
138.953
130.979
129.303
127.253
125.677
119.676
118.226
116.793
111.478
105.562
77.308
76.991
76.673
49.735
21.426
LVR-08112B
Ts
NH
O
H
N
3n
100 MHz,13C NMR(CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

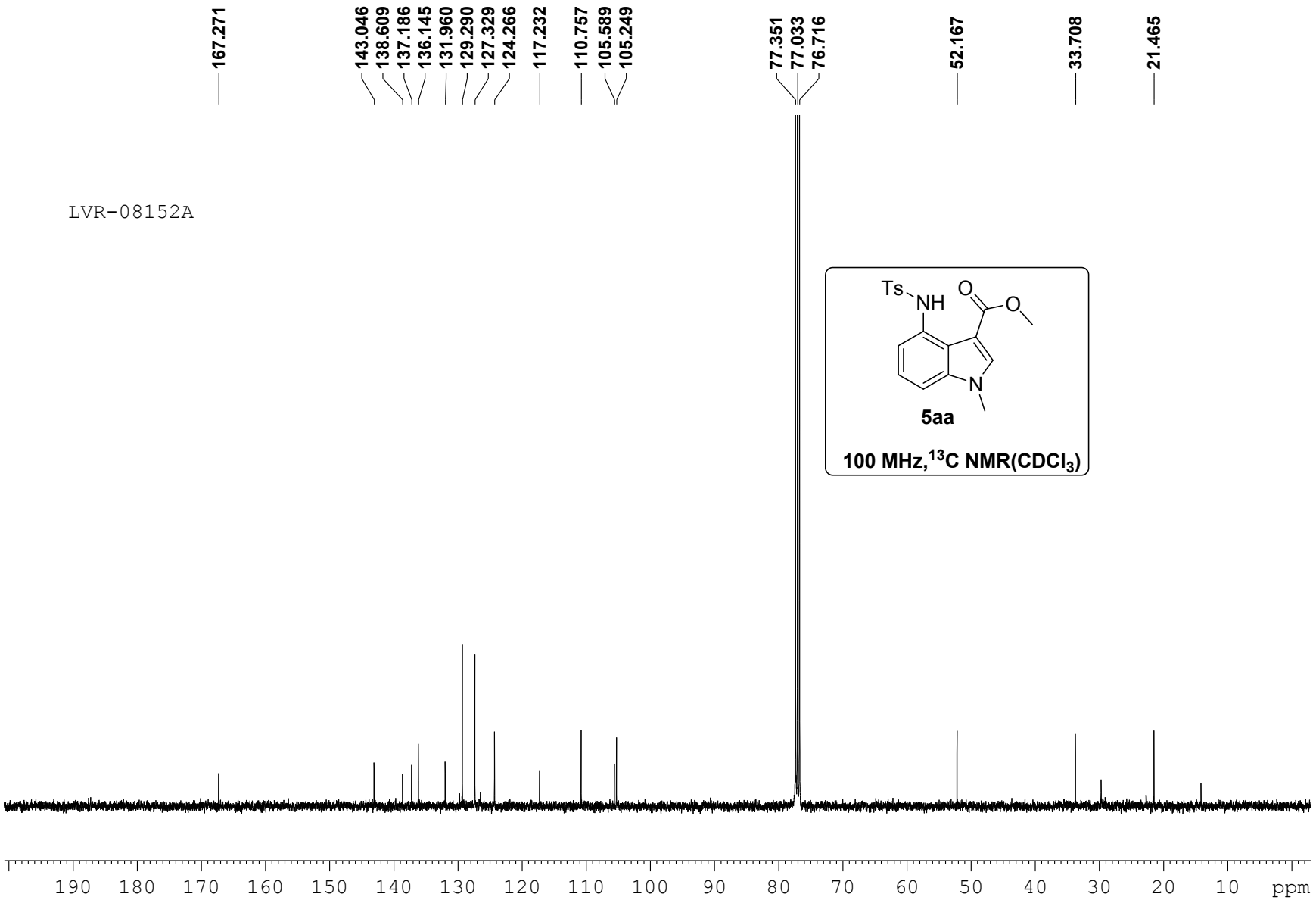

13.081
10.858
8.561
8.557
7.561
7.540
7.316
7.310
7.290
7.272
7.267
7.254
7.239
7.219
3.335
2.496
2.248
LVR-08102A
Ts
NH
O
CF3
N
H
4aa
400 MHz,1H NMR(DMSO)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.951
1.000
1.022
2.027
5.151
3.066

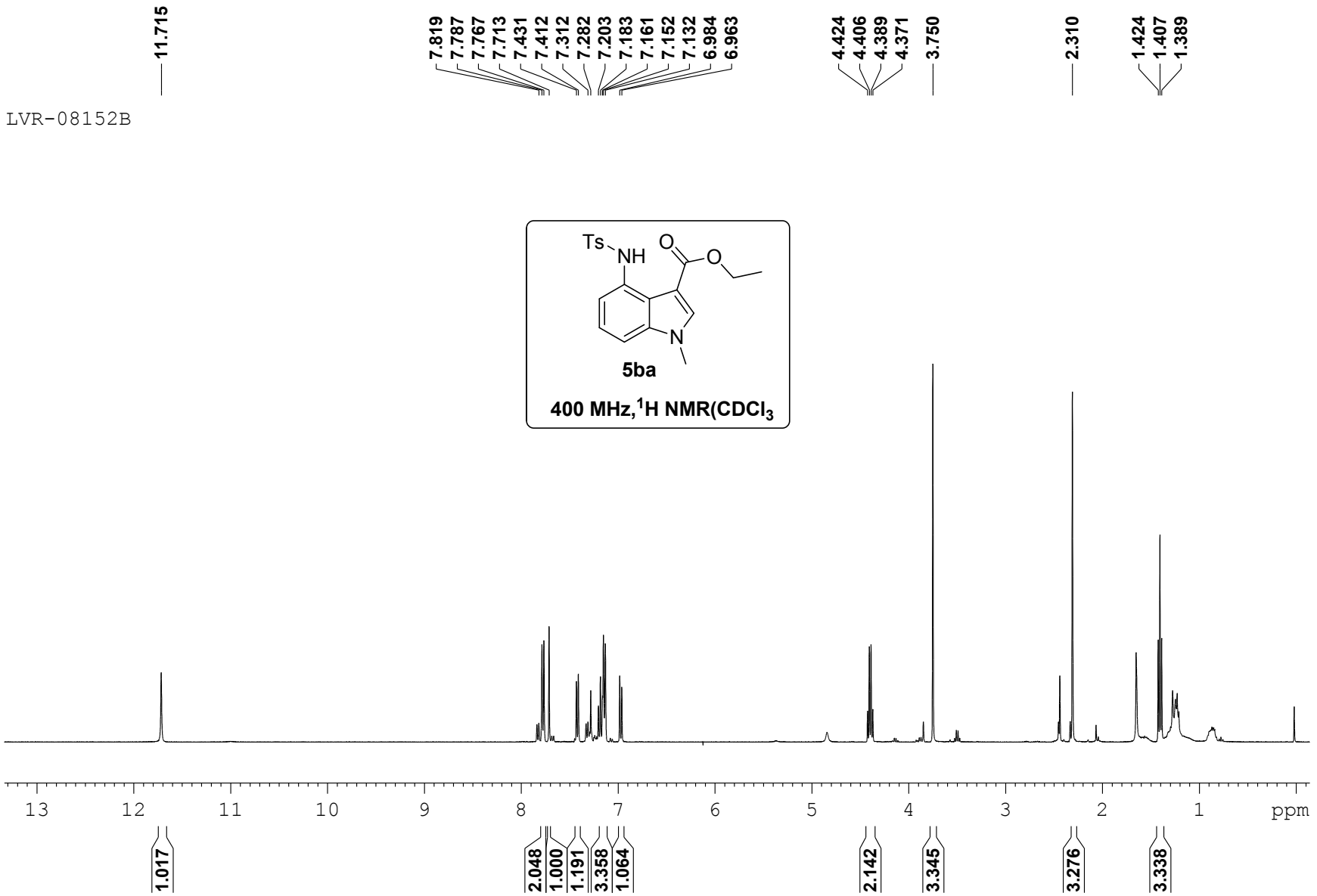

175.830
175.490
144.139
141.657
141.604
139.082
136.354
131.813
130.069
127.223
126.451
119.346
117.350
116.463
113.610
109.832
109.493
21.311
LVR-08102A
Ts
NH
O
CF3
N
H
4aa
100 MHz,13C NMR(DMSO)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

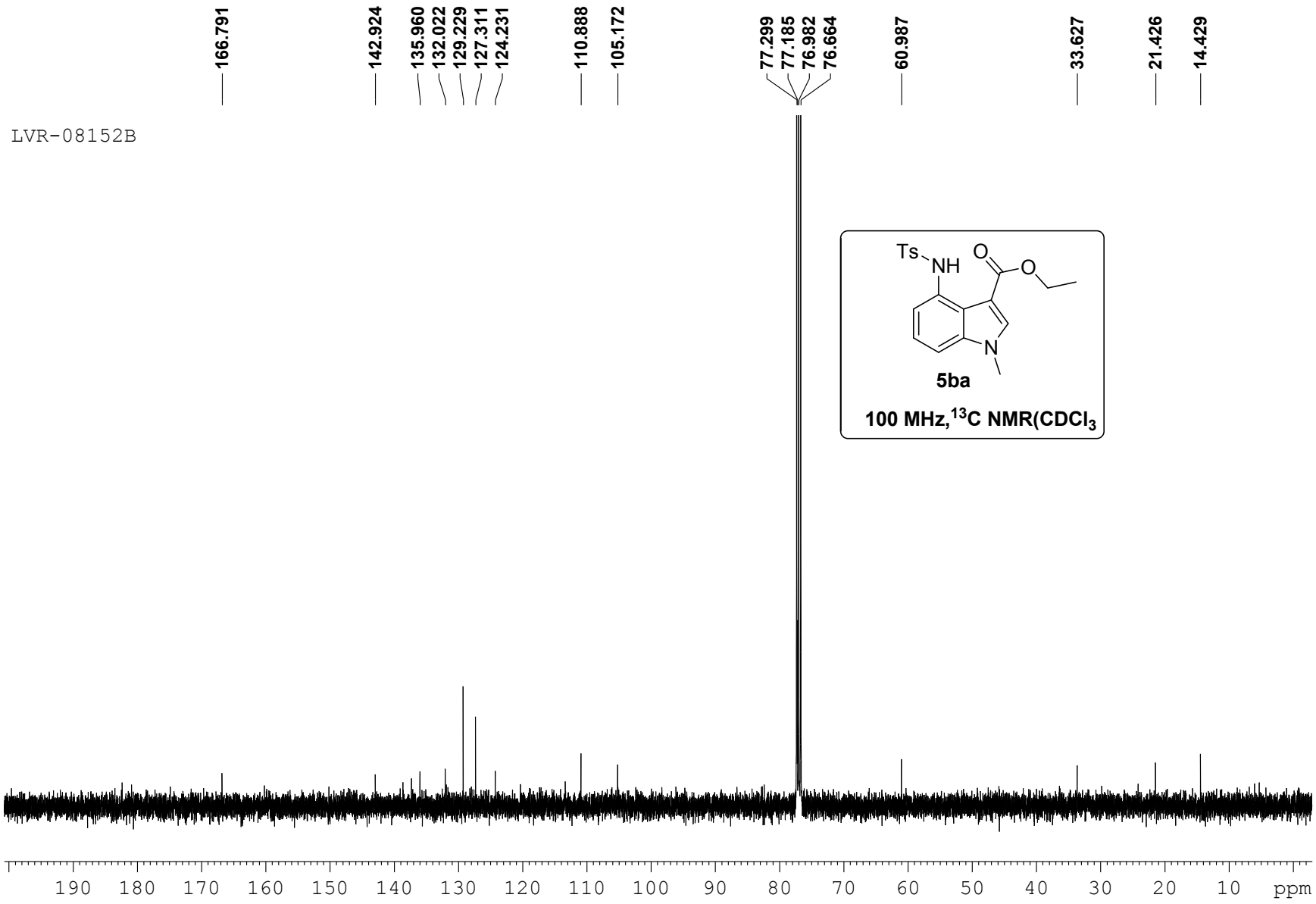

10.999
8.644
7.589
7.569
7.371
7.354
7.336
7.248
7.228
3.882
3.409
2.505
2.248
LVR-08151A
Ts
NH
O
CF3
N
4ba
400 MHz,1H NMR(DMSO)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.996
1.000
2.018
3.200
1.998
3.055
3.052

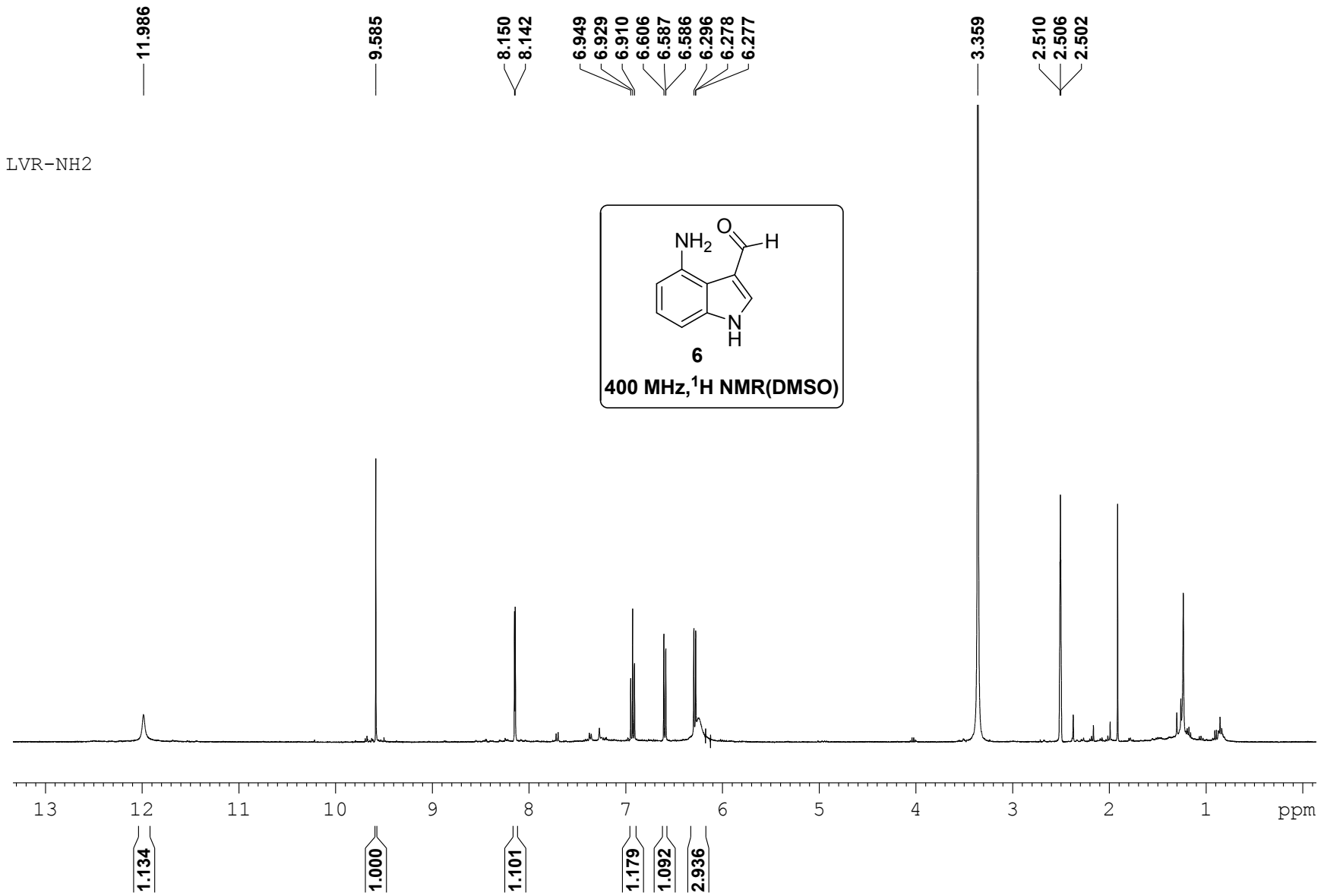

175.061
174.719
174.380
143.918
143.867
143.698
141.821
141.356
139.266
135.804
131.433
129.619
129.241
126.722
125.982
125.569
118.857
117.008
115.973
113.201
107.765
40.048
39.839
39.630
39.422
39.213
39.004
38.796
34.143
20.803
LVR-08151A
Ts
NH
O
CF3
N
4ba
100 MHz, 13C NMR(DMSO)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

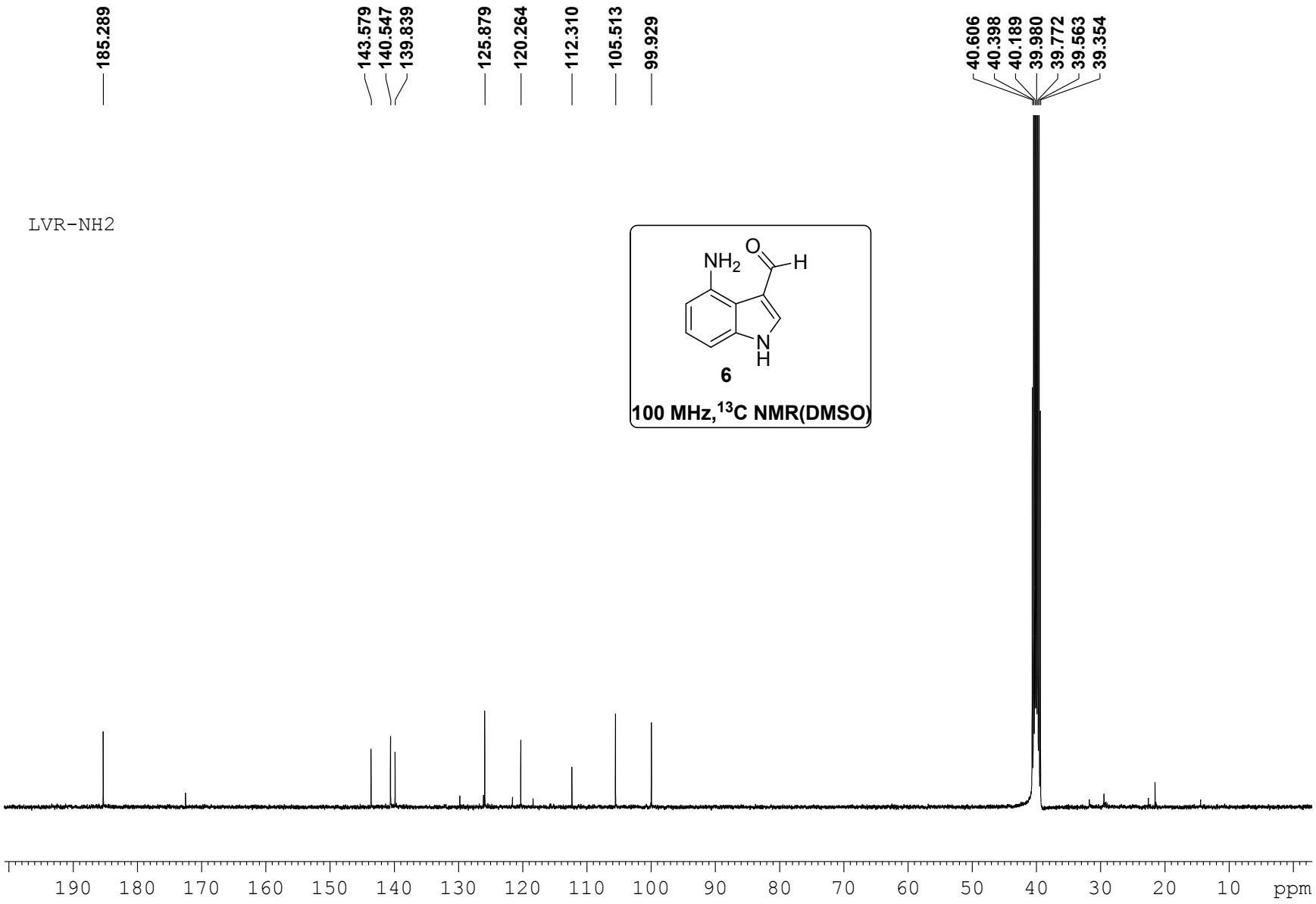

11.628
7.781
7.760
7.684
7.414
7.394
7.271
7.190
7.170
7.146
7.125
6.968
6.947
3.909
3.736
2.300
LVR-08152A
Ts
NH
O
O
N
5aa
400 MHz,1H NMR(CDCl3)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.978
2.058
1.000
1.065
3.196
1.039
3.267
3.156
3.136

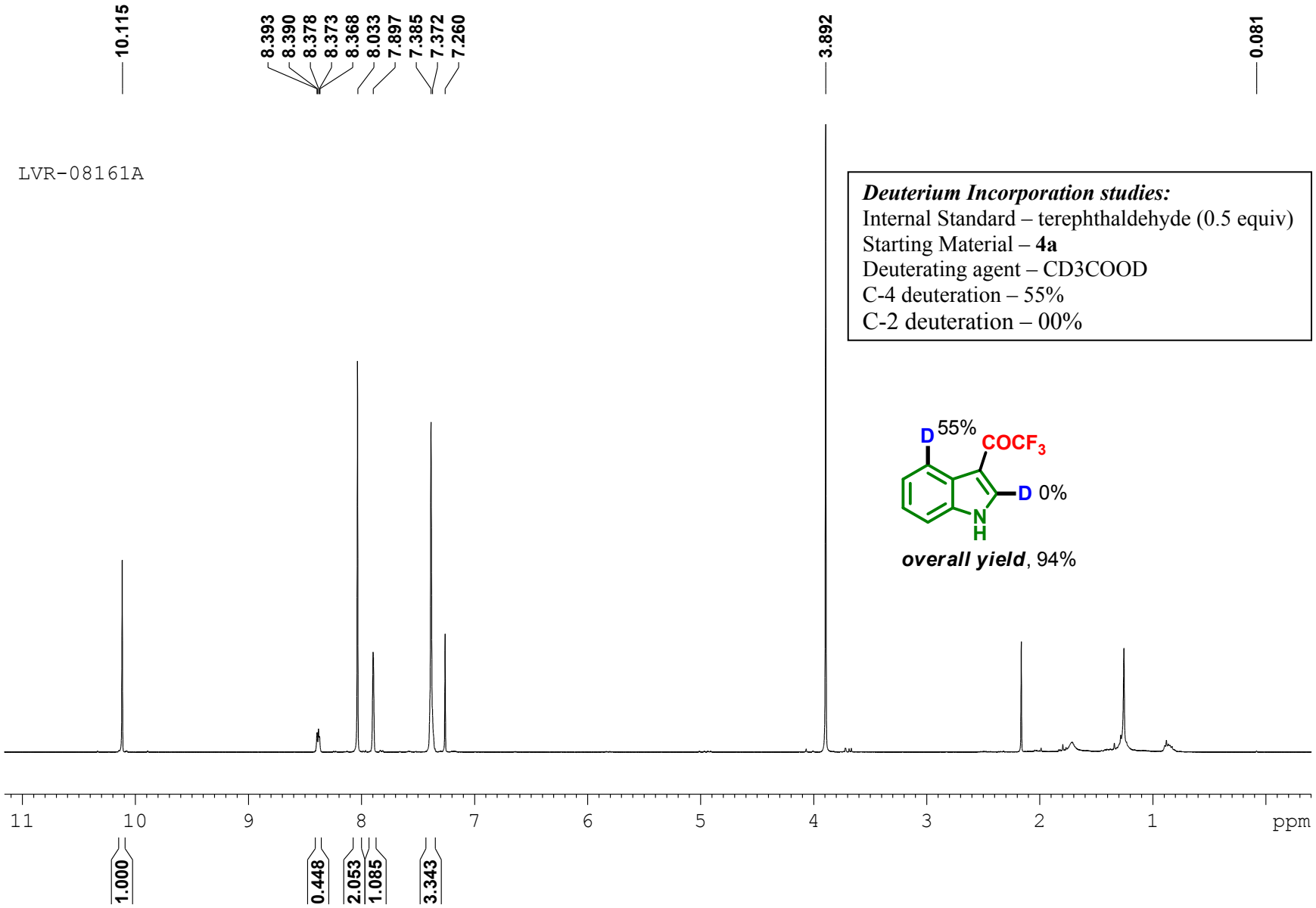

167.271
143.046
138.609
137.186
136.145
131.960
129.290
127.329
124.266
117.232
110.757
105.589
105.249
77.351
77.033
76.716
52.167
33.708
21.465
LVR-08152A
Ts
NH
O
O
N
5aa
100 MHz,13C NMR(CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

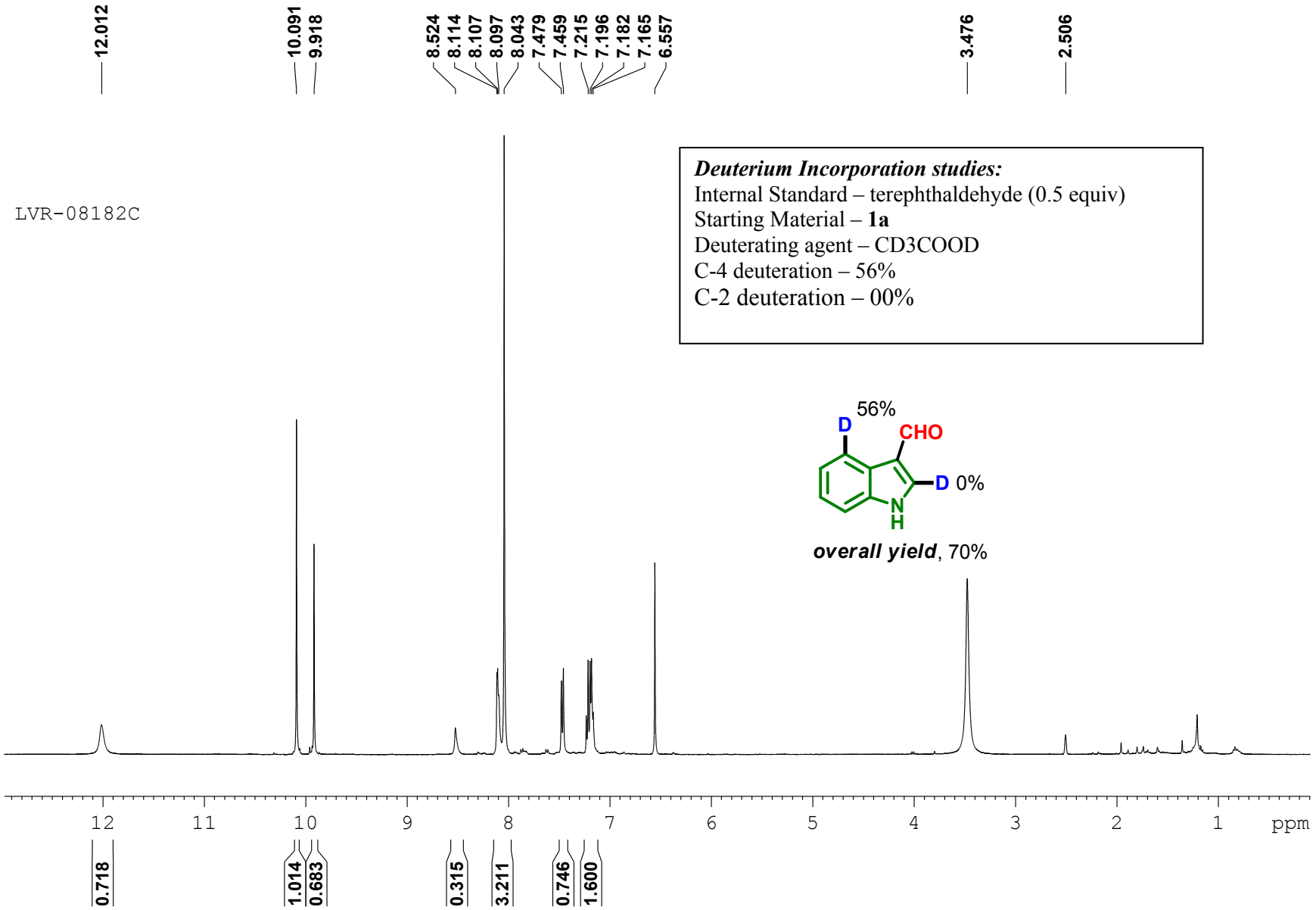

11.715
7.819
7.787
7.767
7.713
7.431
7.412
7.312
7.282
7.203
7.183
7.161
7.152
7.132
6.984
6.963
4.424
4.406
4.389
4.371
3.750
2.310
1.424
1.407
1.389
LVR-08152B
Ts
NH
O
O
N
5ba
400 MHz,1H NMR(CDCl3
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.017
2.048
1.000
1.191
3.358
1.064
2.142
3.345
3.276
3.338


166.791
142.924
135.960
132.022
129.229
127.311
124.231
110.888
105.172
77.299
77.185
76.982
76.664
60.987
33.627
21.426
14.429
LVR-08152B
Ts
NH
O
O
N
5ba
100 MHz, 13C NMR(CDCl3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


11.986
9.585
8.150
8.142
6.949
6.929
6.910
6.606
6.587
6.586
6.296
6.278
6.277
3.359
2.510
2.506
2.502
LVR-NH2
NH2
O
H
N
H
6
400 MHz, 1H NMR(DMSO)
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.134
1.000
1.101
1.179
1.092
2.936


185.289
143.579
140.547
139.839
125.879
120.264
112.310
105.513
99.929
40.606
40.398
40.189
39.980
39.772
39.563
39.354
LVR-NH2
NH2
O
H
N
H
6
100 MHz,13C NMR(DMSO)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


10.115
8.393
8.390
8.378
8.373
8.368
8.033
7.897
7.385
7.372
7.260
3.892
0.081
LVR-08161A
Deuterium Incorporation studies:
Internal Standard – terephthaldehyde (0.5 equiv)
Starting Material – 4a
Deuterating agent – CD3COOD
C-4 deuteration – 55%
C-2 deuteration – 00%
D 55%
COCF3
D 0%
N
H
overall yield, 94%
11
10
9
8
7
6
5
4
3
2
1
ppm
1.000
0.448
2.053
1.085
3.343


12.012
10.091
9.918
8.524
8.114
8.107
8.097
8.043
7.479
7.459
7.215
7.196
7.182
7.165
6.557
3.476
2.506
LVR-08182C
Deuterium Incorporation studies:
Internal Standard – terephthaldehyde (0.5 equiv)
Starting Material – 1a
Deuterating agent – CD3COOD
C-4 deuteration – 56%
C-2 deuteration – 00%
56%
D
CHO
D 0%
N
H
overall yield, 70%
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.718
1.014
0.683
0.315
3.211
0.746
1.600