Electronic Supplementary Information (ESI)

Co(III)(salen)-catalyzed Phenolic Kinetic Resolution of two stereocentered benzyloxy and azido epoxides: its application in the synthesis of ICI-118,551, an *anti*-hypertensive agent

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General Description: Solvents were purified and dried by standard procedures before use; petroleum ether of boiling range 60-80 °C was used. Melting points are uncorrected and recorded on a Buchi B-542 instrument. Optical rotations were measured using sodium D line on a JASCO-181 digital polarimeter. ^{1}H NMR and ^{13}C NMR spectra were recorded on Brucker AC-200 spectrometer unless mentioned otherwise. Infrared spectra were recorded on Shimadzu FTIR-8400 spectrometer and absorption is expressed in cm^{-1}. HPLC was performed on Agilent chromatogram with variable wavelength detector. HRMS data were recorded on a Thermo Scientific Q-Exactive, Accela 1250 pump. XRD studies were performed on BRUKERAXS, data refined by apex 2. Purification was done using column chromatography (230-400 mesh).

(4*S*, 5*S*)-5-Azido-2,2-dimethyl-4-[(7-methylindan-4-yloxy)methyl]-1,3-dioxane (9)

To a stirred solution of silyl ether **1o** (1.8 g, 4.6 mmol) in THF (20 mL) was added TBAF (10 mL, 1 M solution in THF) at 0 ^{o}C. The reaction mixture was stirred for 1 h at the same temperature and then quenched with water. It was extracted with ethyl acetate and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to obtain the crude azido diol, which was purified by column chromatography using pet. ether/ethyl acetate (70:30) to obtain pure azido diol (90 % yield).

Yield: 90%, gum; $[\alpha]_D^{25}$ +12 (c 1, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): 778, 837, 1095, 1243, 1492, 2100, 2858, 2929, 2953, 3446; ^{1}H NMR (200 MHz, $CDCl_3$) 2.01-2.16 (appt. quintet, *J* = 7.9 Hz, 2H), 2.20 (s, 3H), 2.68 (d, *J* = 5.2 Hz, 1H), 2.85 (q, *J* = 8.0 Hz, 4H), 3.63-3.71 (m, 1H), 3.87-4.17 (m, 5H), 6.59 (d, *J* = 8.0 Hz, 1H), 6.89 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): 18.4, 24.5, 29.7, 31.9, 62.7, 63.8, 69.0, 70.3, 109.6, 126.9, 128.0, 131.5, 145.0, 152.6; HRMS (ESI) m/z Calcd for $C_{14}H_{19}N_3O_3Na$ $[M + Na]^+$, 300.1319; found, 300.1314.

To a stirred mixture of the above azido diol (1 g, 3.6 mmol), 2, 2-dimethoxypropane (1.8 mL, 14.4 mmol) in dry CH_2Cl_2 (25 mL) was added camphor sulfonic acid (0.080 g, 10 mol %). The reaction mixture was stirred at 25 ^{o}C for 12 h. After completion of the reaction (as monitored by TLC), it was neutralized with triethylamine, concentrated and the crude was purified by column chromatography using pet. ether/EtOAc (9:1) as eluent to produce protected azide **9** as gum (89%).

Yield: 89% gum; $[\alpha]_D^{25}$ +15 (c 1, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): 778, 837, 1095, 1243, 1492, 2100, 2858, 2929, 2953, 3446; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.41 (s, 3H), 1.47 (s, 3H), 2.00-2.14 (appt. quintet, *J* = 7.9 Hz, 2H), 2.19 (s, 3H), 2.82 (t, *J* = 7.4 Hz, 2H), 2.92 (t, *J* = 7.4 Hz, 2H), 3.67-3.77 (m, 2H), 3.88-3.96 (m, 1H), 3.98- 4.04 (m, 1H), 4.11 (d, *J* = 3.5 Hz, 2H), 6.58 (d, *J* = 8.2 Hz, 1H), 6.87 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): 18.4, 19.2, 24.5, 28.3, 29.7, 31.9, 55.1, 62.2, 68.4, 71.4, 99.1, 109.7, 126.3, 127.7, 131.9, 144.7, 153.2; HRMS (ESI) m/z Calcd for $C_{17}H_{23}N_3O_3Na$ $[M + Na]^+$, 340.1632; found, 340.1630.

(4*S*, 5*S*)-*N*-Isopropyl-2,2-dimethyl-4-[(7-methylindan-4-yloxy)methyl]-1,3-dioxan-5-amine (10)

To a stirred solution of **9** (0.5 g, 1.5 mmol) in methanol (5 mL), was added 10% Pd/C (10 mg) at 25 ^{o}C. The reaction mixture was stirred under hydrogen atmosphere (60 psi) for 20 h. After completion of reaction (as monitored by TLC), it was filtered through a celite pad and washed with EtOAc (3 x 20 mL). The combined organic phase was concentrated under reduced pressure to give the crude amino compound.

To a stirred suspension containing activated powdered 4 Å molecular sieves (1.6 g) in anhydrous DMF (30 mL), KOH powder (63 mg, 1.14 mmol), 18-crown-6 (300 mg, 1.14 mmol) was added, and the mixture was vigorously stirred for 10 min. The crude amine compound (332 mg, 1.14 mmol) obtained above was added and the mixture was stirred for an additional 30 min followed by the addition of 2-bromopropane (0.12 mL, 1.34 mmol), and the whole reaction mixture was allowed to stir at room temperature for 20 h. It was filtered to remove insoluble solids and washed several times with ethyl acetate. The filtrate was concentrated, the residue basified with 1 N NaOH, and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated. The resulting crude mixture was purified by column chromatography using ethyl acetate/methanol (9:1 v/v) as the eluting solvent to afford the *N*-alkylated acetonide **10** as a colorless oil (65%).

Yield: 65%, gum; $[\alpha]_D^{25}$ +25 (*c* 1, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): 778, 837, 1095, 1243, 1492, 2100, 2858, 2929, 2953, 3446; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.42 (s, 3H), 1.49 (s, 3H), 1.54 (s, 6H), 2.03-2.10 (appt. quintet, *J* = 7.6 Hz, 2H), 2.19 (s, 3H), 2.83 (t, *J* = 7.2 Hz, 2H), 2.89 (t, *J* = 7.4 Hz, 2H), 2.95-3.04 (m, 2H), 3.51-3.57 (m, 1H), 3.66-3.68 (m, 1H), 3.82-3.89 (m, 1H), 4.07-4.18 (m, 2H), 6.62 (d, *J* = 8.0 Hz, 1H), 6.91 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): 18.7, 19.5, 24.7, 29.1, 30.1, 32.2, 48.5, 66.1, 70.5, 74.3, 98.8, 109.7, 126.7, 128.1, 131.9, 145.2, 153.5; HRMS (ESI) m/z Calcd for $C_{20}H_{31}NO_3Na$ $[M + Na]^+$, 356.2196; found, 356.2190.

(2*S*, 3*S*)-3-Isopropylamino-1-(7-methylindan-4-yloxy)-butan-1,3-diol (11)

To a stirred solution of acetonide **10** (0.180 g, 0.54 mmol) in CH_2Cl_2 (6 mL), was added trifluoroacetic acid (0.162 mL, 2.12 mmol). The reaction mixture was stirred at 25 ^{o}C (monitored

by TLC). The organic layer was washed with saturated aq. $NaHCO_3$ followed by brine and dried over anhyd. Na_2SO_4 and concentrated to give the crude product **11**, which was then purified by column chromatography over silica gel using pet. ether/EtOAc (20:80) as an eluent to give colorless oil (65%).

Yield: 65%, gum; $[\alpha]_D^{25}$ +35 (c 1, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): 785, 1160, 1125, 1250, 1280, 1513, 1605, 2915, 3358, 3556; ^1H NMR (200 MHz, $CDCl_3$) δ 1.41 (s, 6H), 2.03 (m, 2H), 2.15 (m, 2H), 2.30-2.32 (m, 1H), 2.44-2.84 (m, 7H), 3.62-3.69 (m, 2H), 4.02-4.16 (m, 2H), 4.90-4.99 (dd, *J* = 10.1 and 16.8 Hz, 2H) 5.76-5.82 (m, 1H), 6.58 (d, *J* = 8.1 Hz, 1H), 6.87 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): 18.4, 24.4, 25.6, 30.1, 30.4, 50.0, 62.1, 63.5, 69.9, 109.4, 126.9, 128.0, 131.3, 145.0, 152.4; HRMS (ESI) m/z Calcd $C_{17}H_{27}NO_3Na$ $[M + Na]^+$, 316.1883; found, 316.1880.

(2*S*, 3*S*)-3-Isopropylamino-1-(7-methylindan-4-yloxy)-butan-2-ol (4)

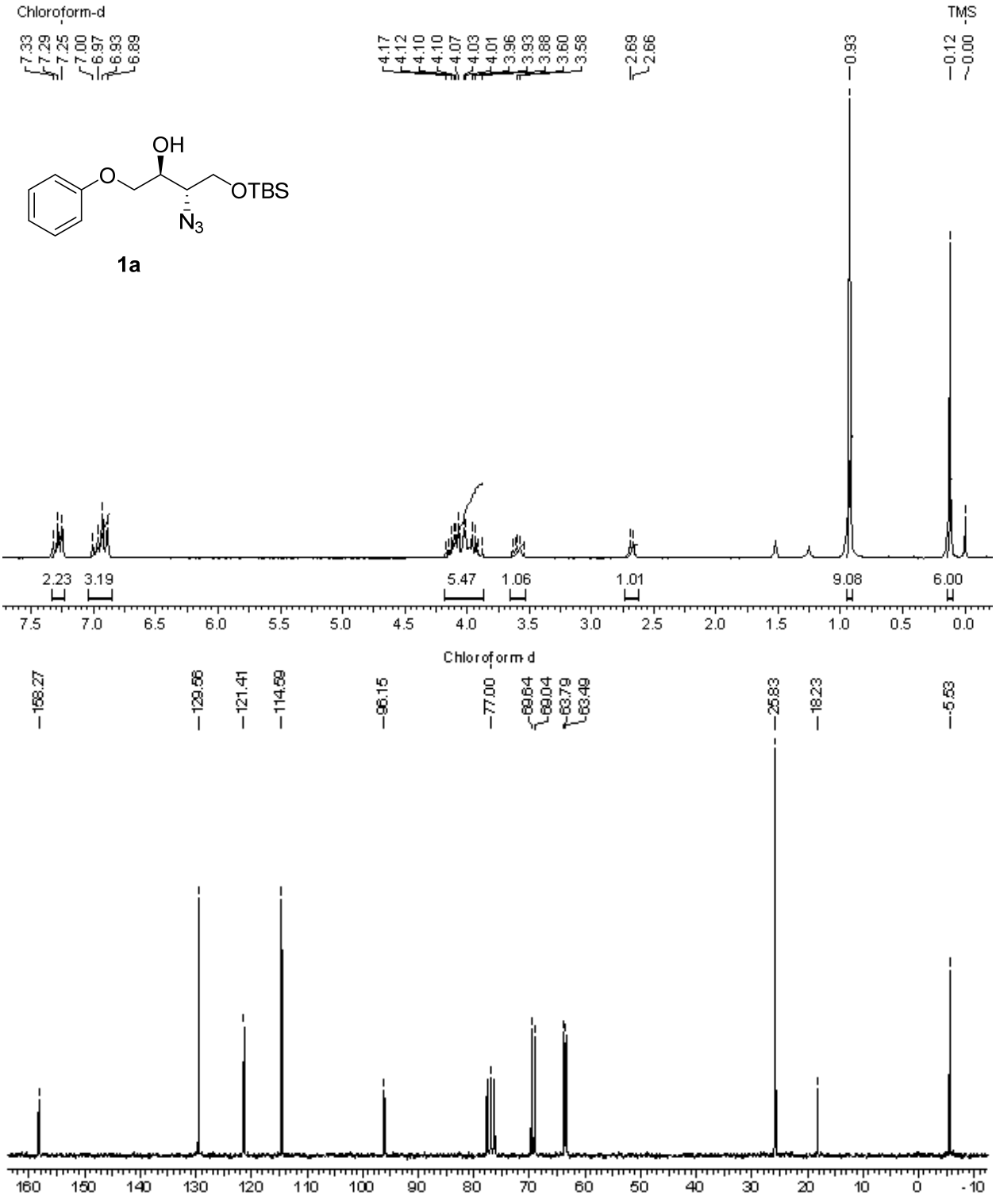
To a stirred solution of amino diol **11** (50 mg, 0.17 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added Et_3N (0.45 mL, 0.18 mmol) and *p*-toluenesulfonyl chloride (36 mg, 0.187 mmol). The reaction mixture was stirred at 0 °C for 1 h. After complete conversion, (monitored by TLC), it was quenched with 10% aq. $NaHCO_3$ solution and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated under reduced pressure to give the crude tosylate, which was directly taken up for the next step.

A solution of the above tosylate (76 mg, 0.17 mmol) in THF (5 mL) was added drop-wise to a stirred suspension of $LiAlH_4$ (20 mg, 0.53 mmol) in THF (10 mL) at 0 ^oC. It was refluxed for 4 h and then cooled to 0 °C and the excess $LiAlH_4$ was quenched with EtOAc (2 mL). Then it was treated with 20% NaOH (0.5 mL), the formed white precipitate was filtered off and the residue was washed with EtOAc (3 x 10 mL). The combined ethyl acetate layers were dried over anhyd. Na_2SO_4, and solvent concentrated under reduced pressure. The crude product was purified by column chromatography using ethyl acetate/methanol (9:1) to obtain pure **4** as gummy liquid (65% yield over two steps).

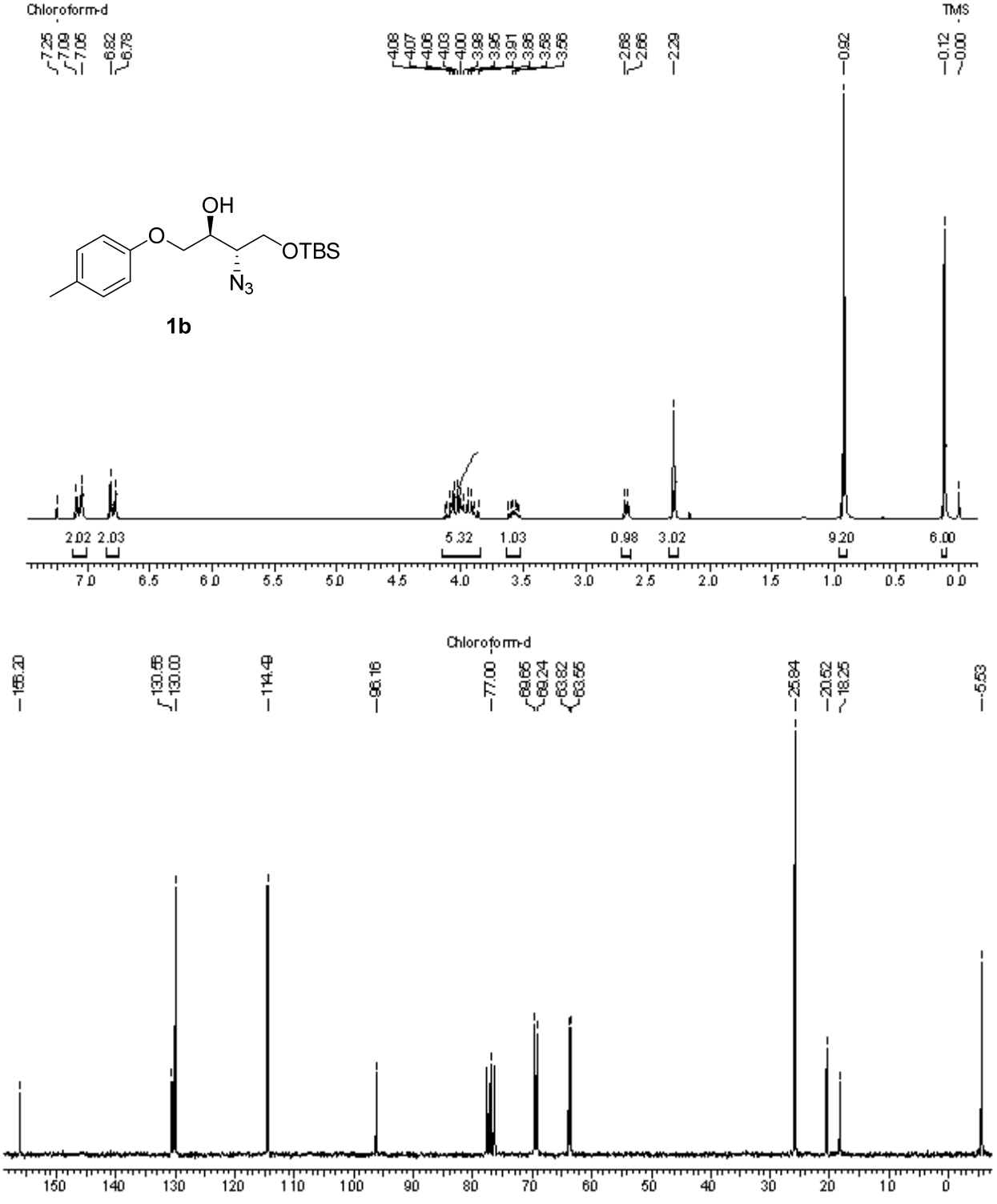
Yield: 65% gum; $[\alpha]_D^{25}$ +38.4 (c 1, CD_3OD); IR ($CHCl_3$, cm^{-1}):778, 837, 1095, 1243, 1492, 2932, 2953, 3343, 3446; ^1H NMR (200 MHz, $CDCl_3$) δ 1.24-1.30 (m, 9H), 1.98-2.14 (appt. quintet, *J* = 7.9 Hz, 2H), 2.17 (s, 3H), 2.85 (q, *J* = 8.0 Hz, 4H), 3.37-3.50 (m, 2H), 3.90-4.11 (m,

2H), 4.01-4.25 (m, 1H), 6.62-6.66 (d, J = 8.0 Hz, 1H) 6.89 (d, J = 8.2 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): 11.9, 18.6, 20.3, 23.6, 25.7, 30.8, 32.8, 48.1, 53.7, 69.4, 70.0, 110.6, 127.6, 129.2, 132.4, 145.9, 154.4; HRMS (ESI) m/z Calcd $C_{17}H_{27}NO_2Na$ $[M + Na]^+$, 300.1934; found, 300.1940.

^{1}H and ^{13}C-NMR Charts of New Compounds



^{1}H and ^{13}C NMR Spectra of 1a



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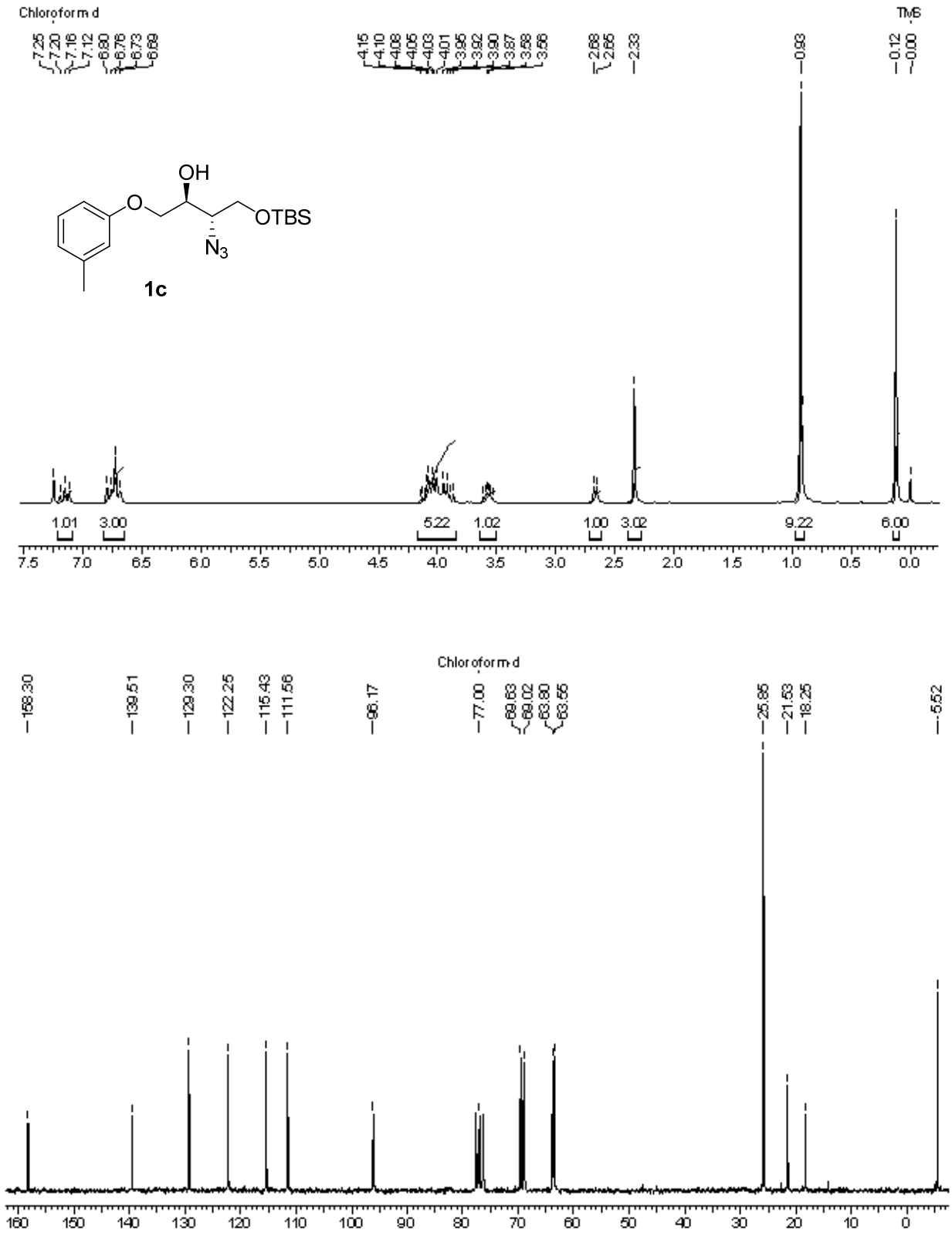

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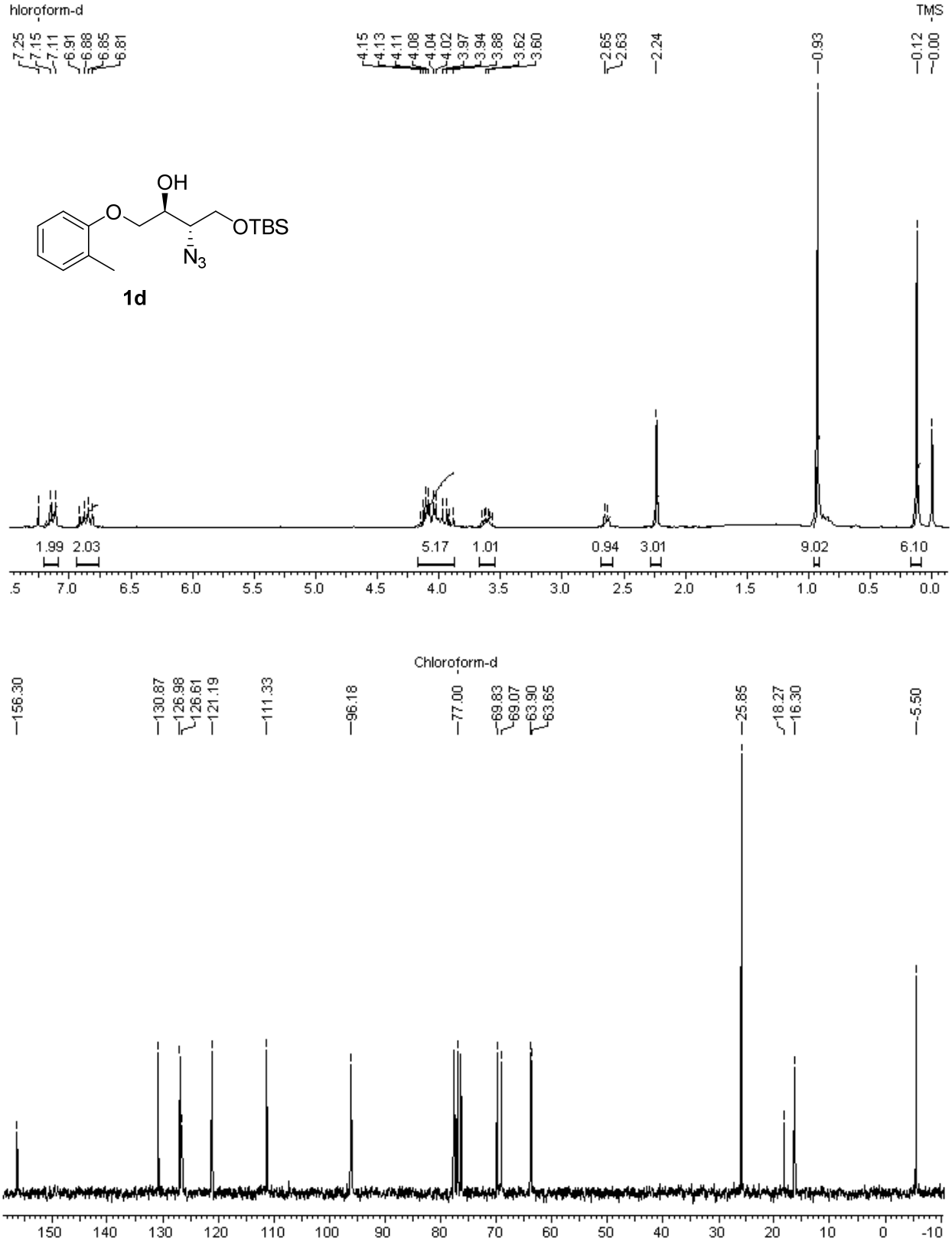

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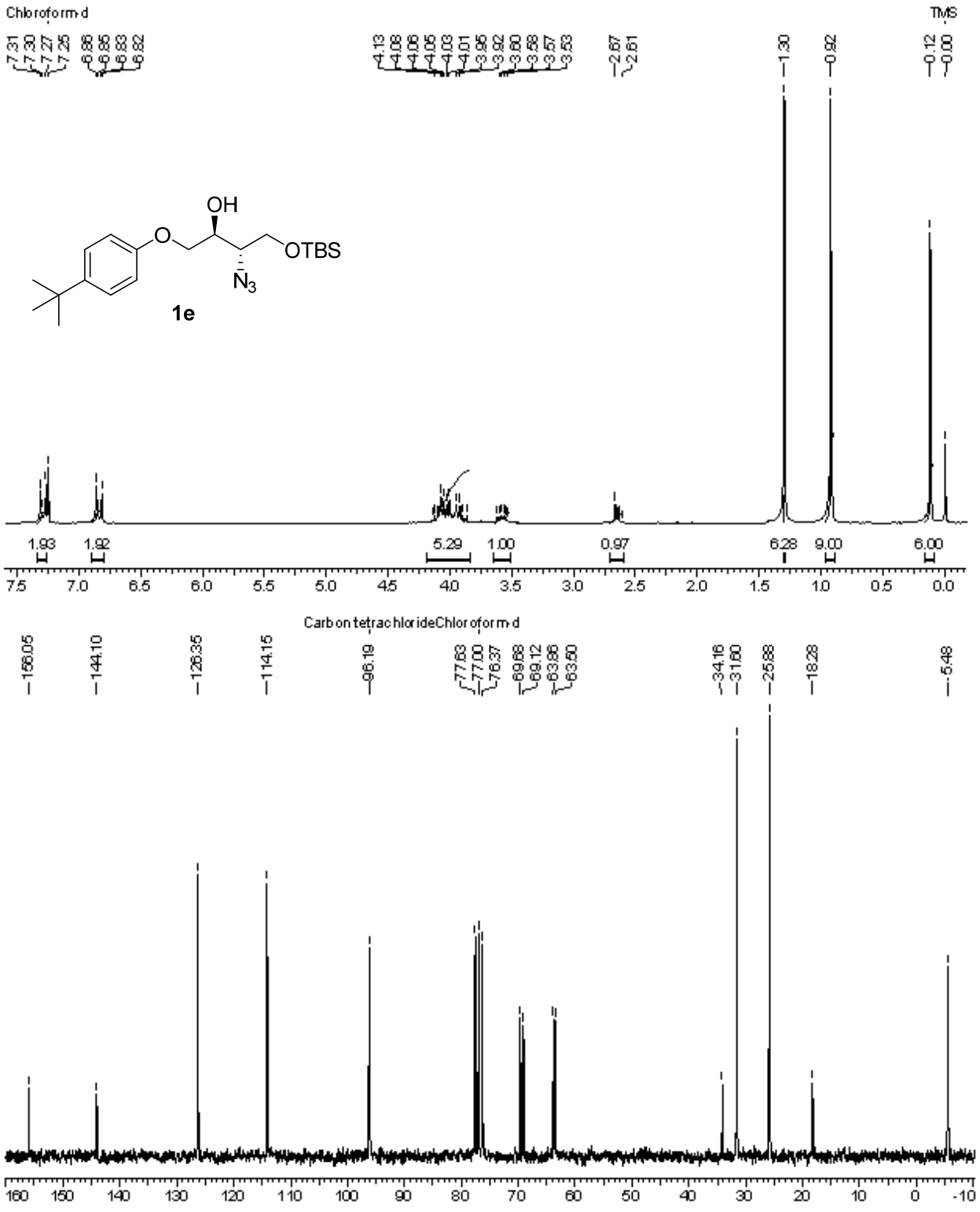

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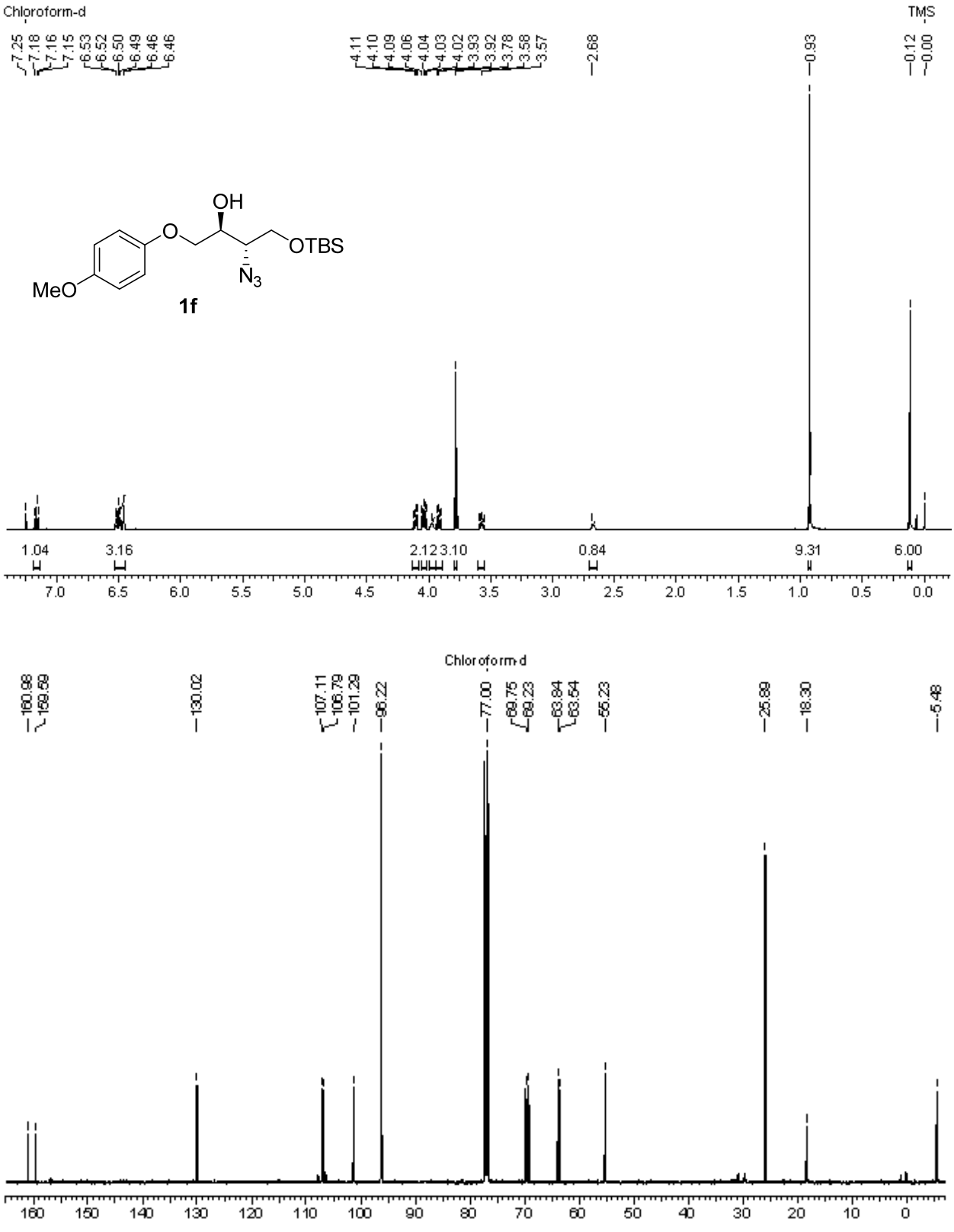

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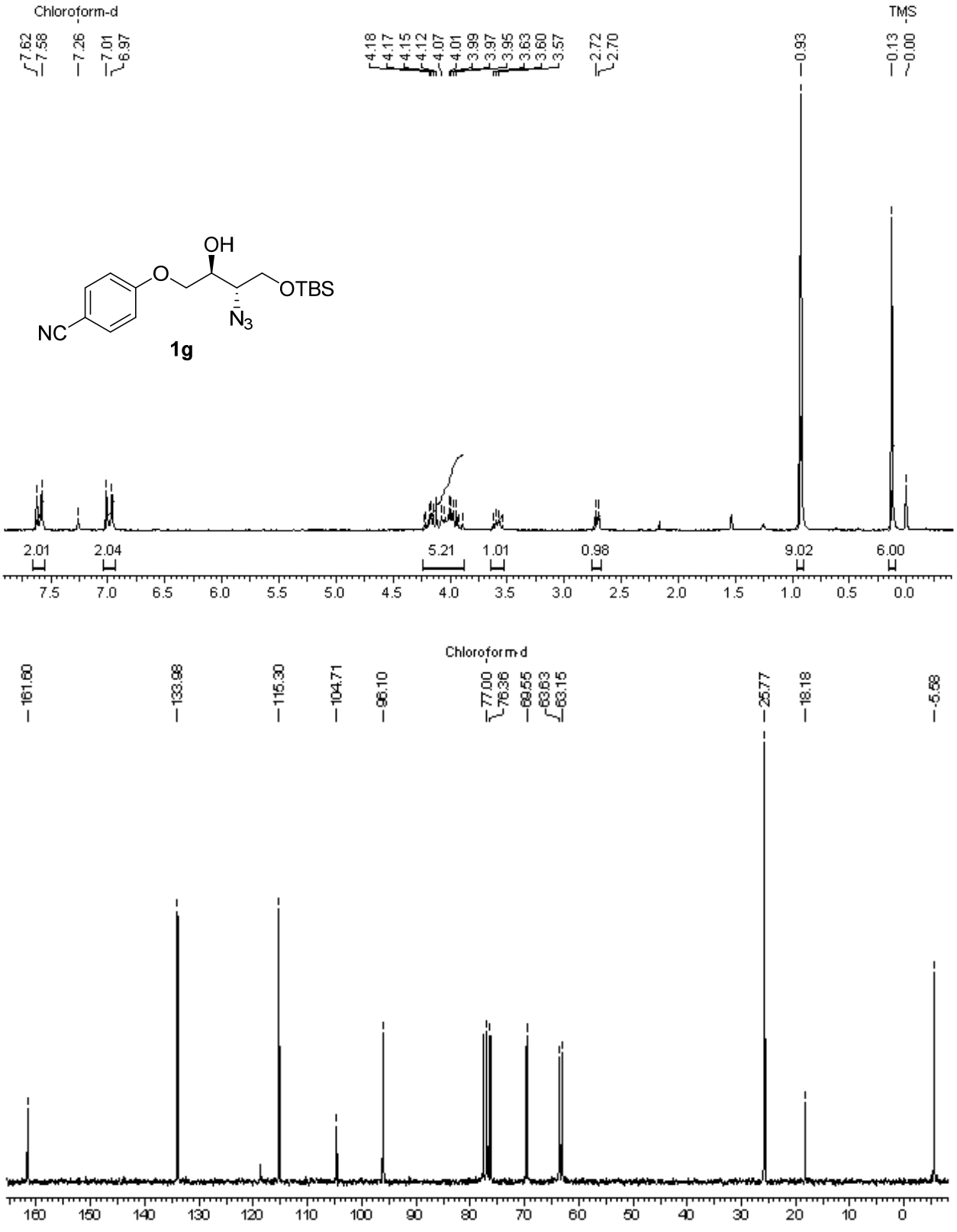

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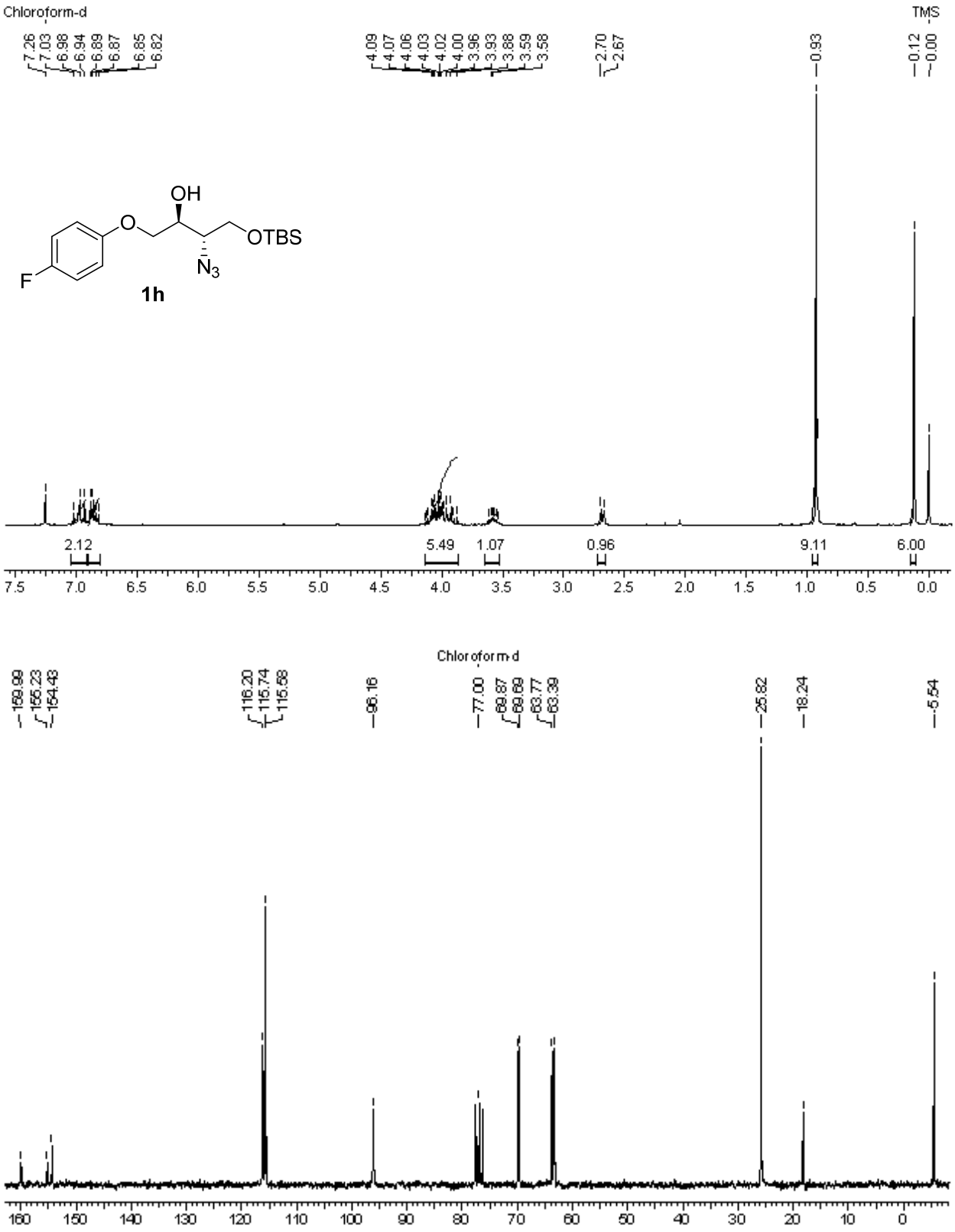

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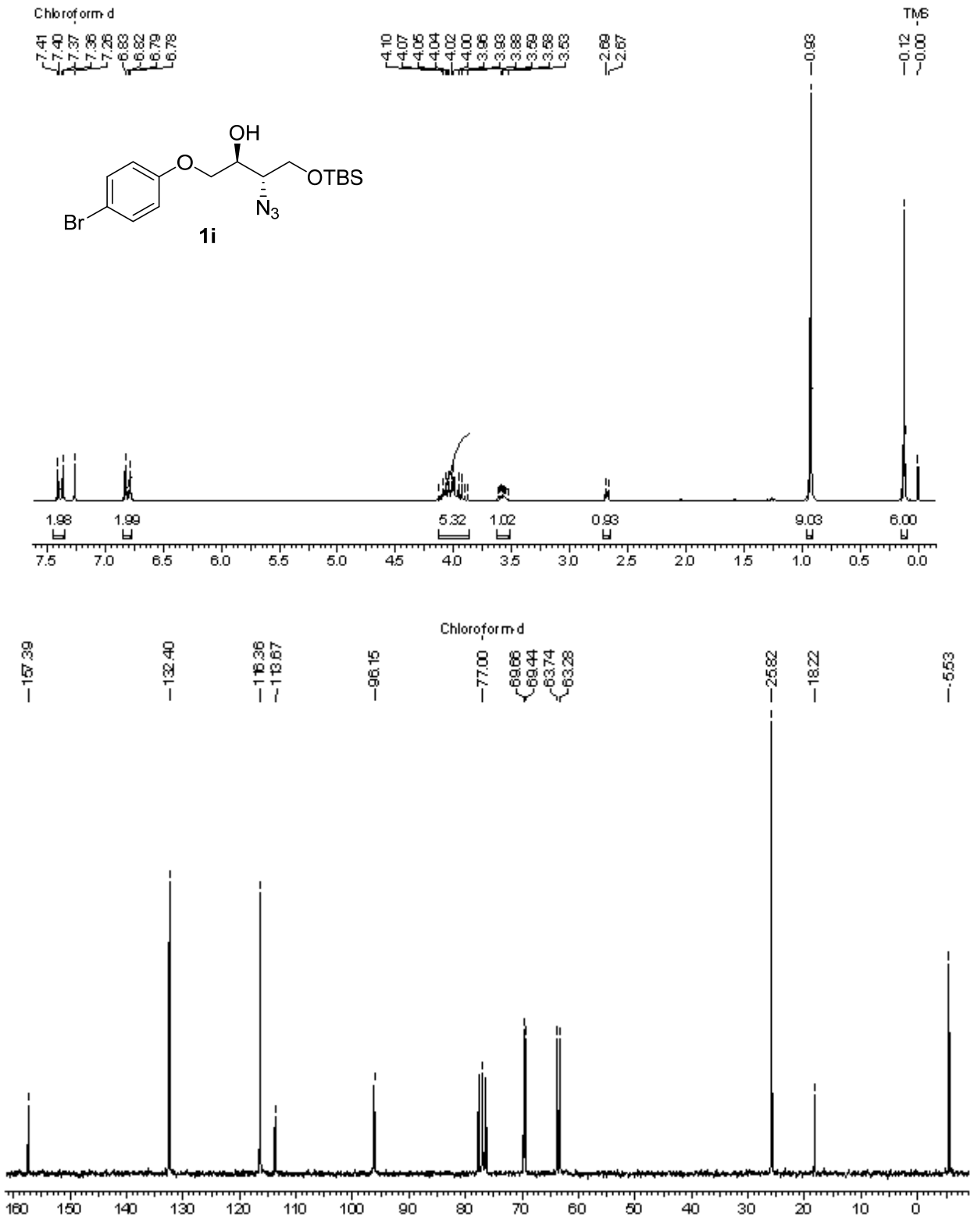

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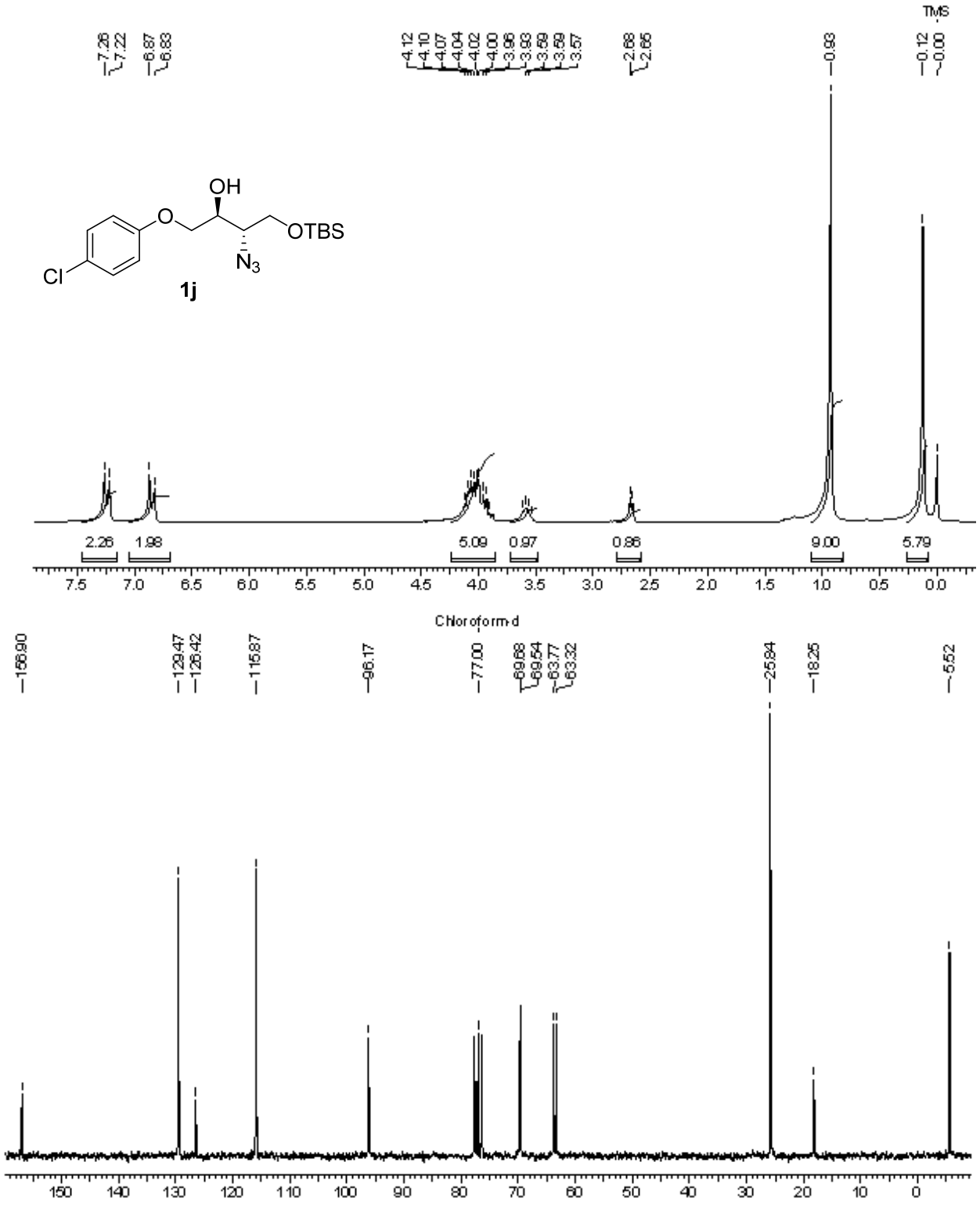

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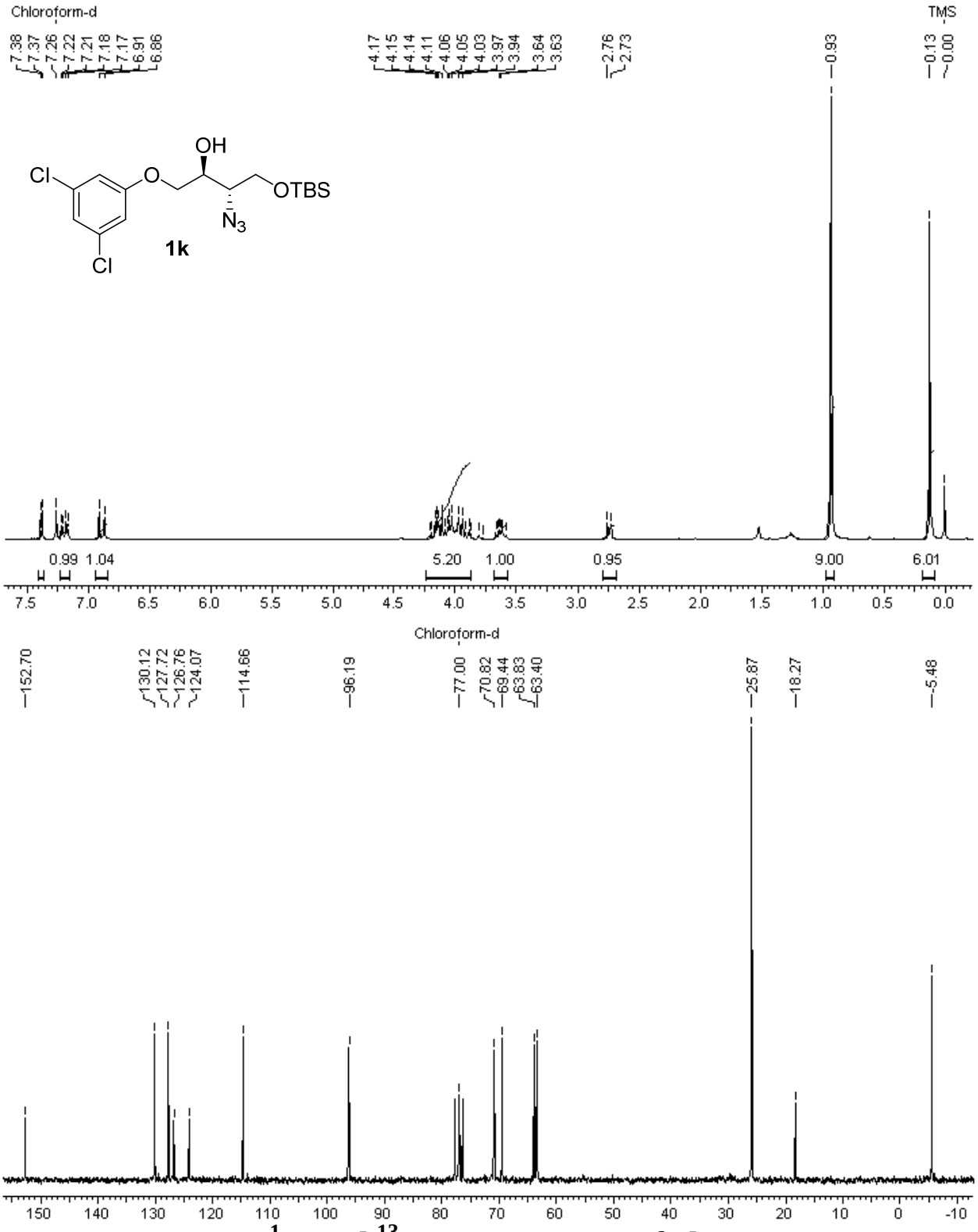

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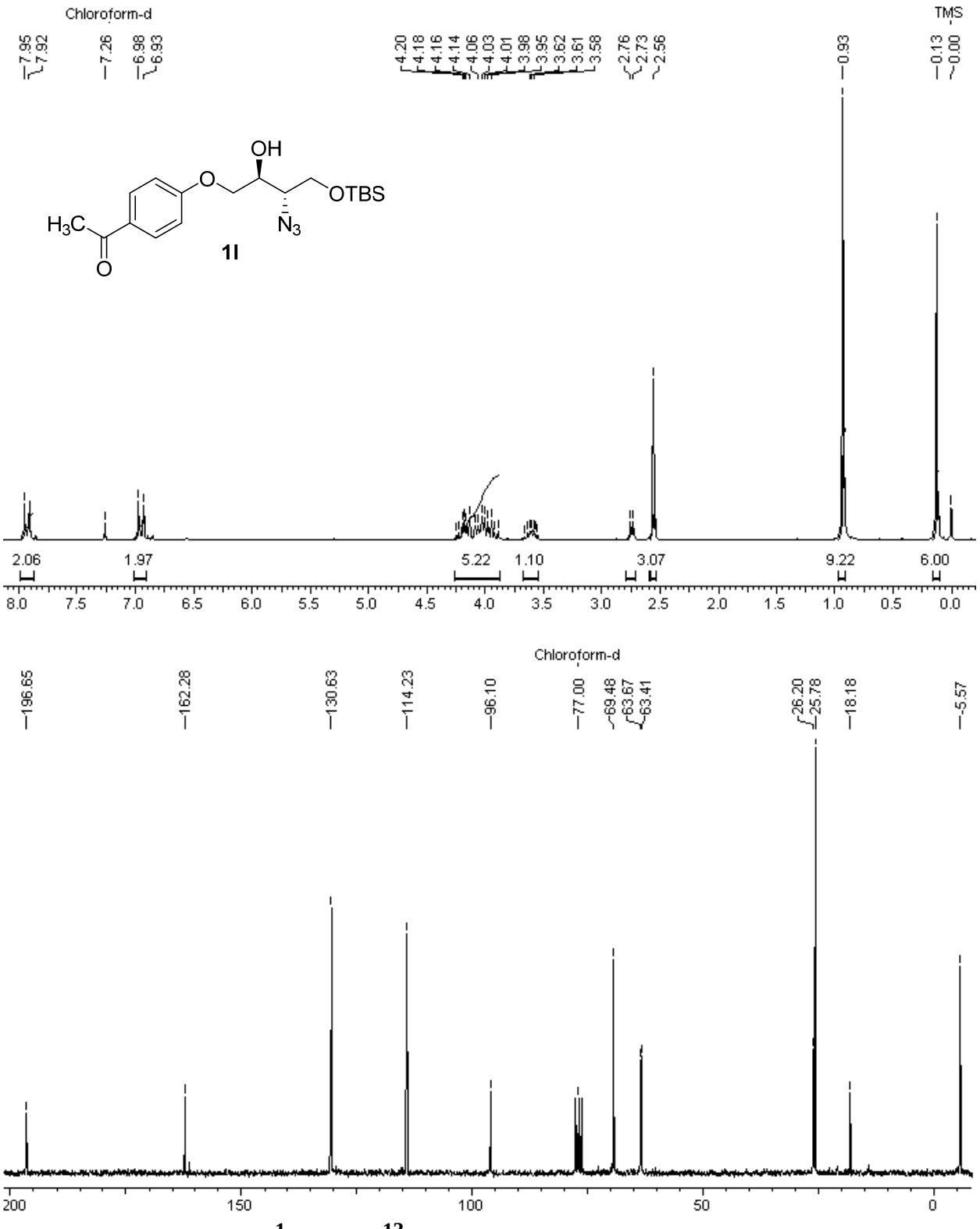

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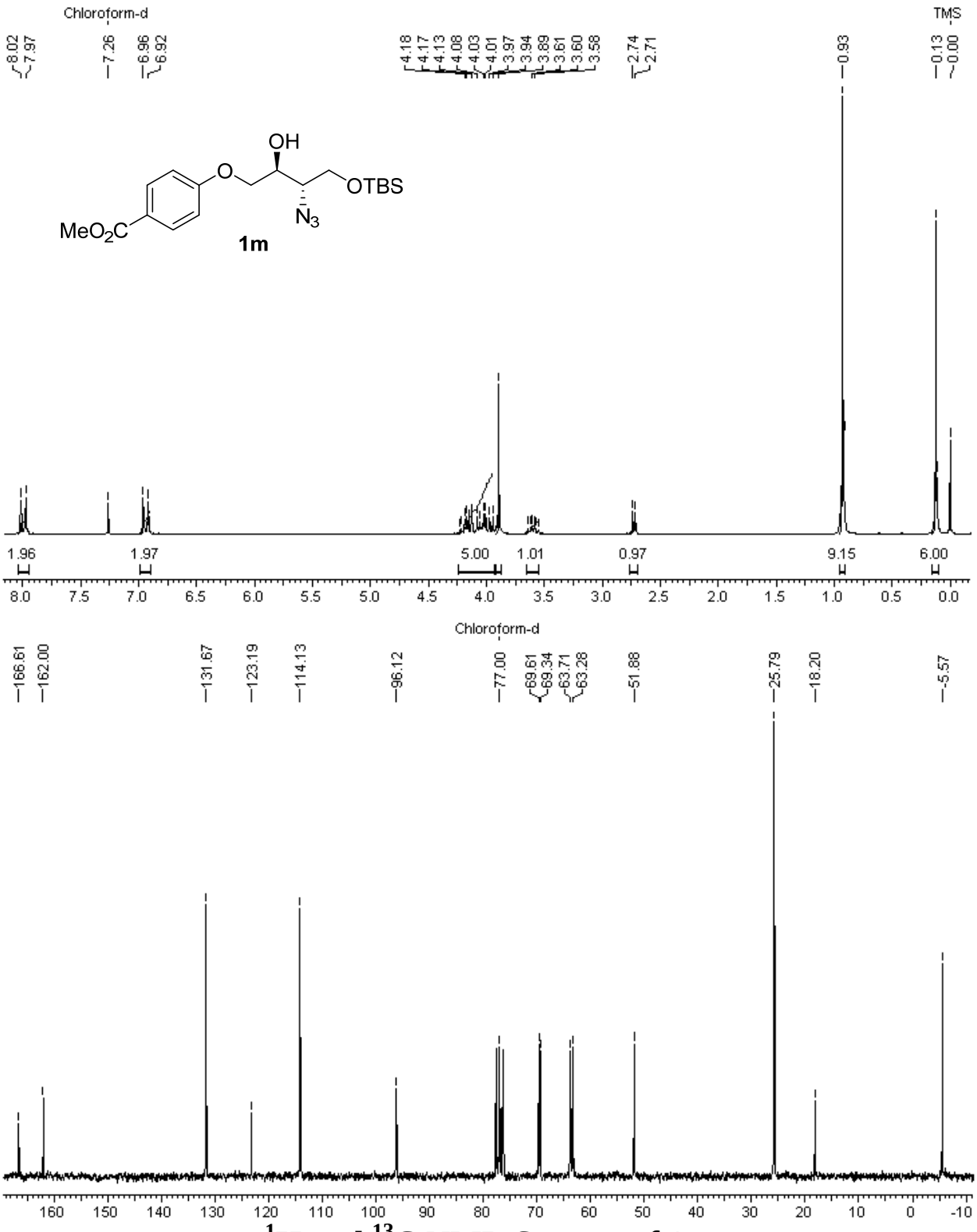

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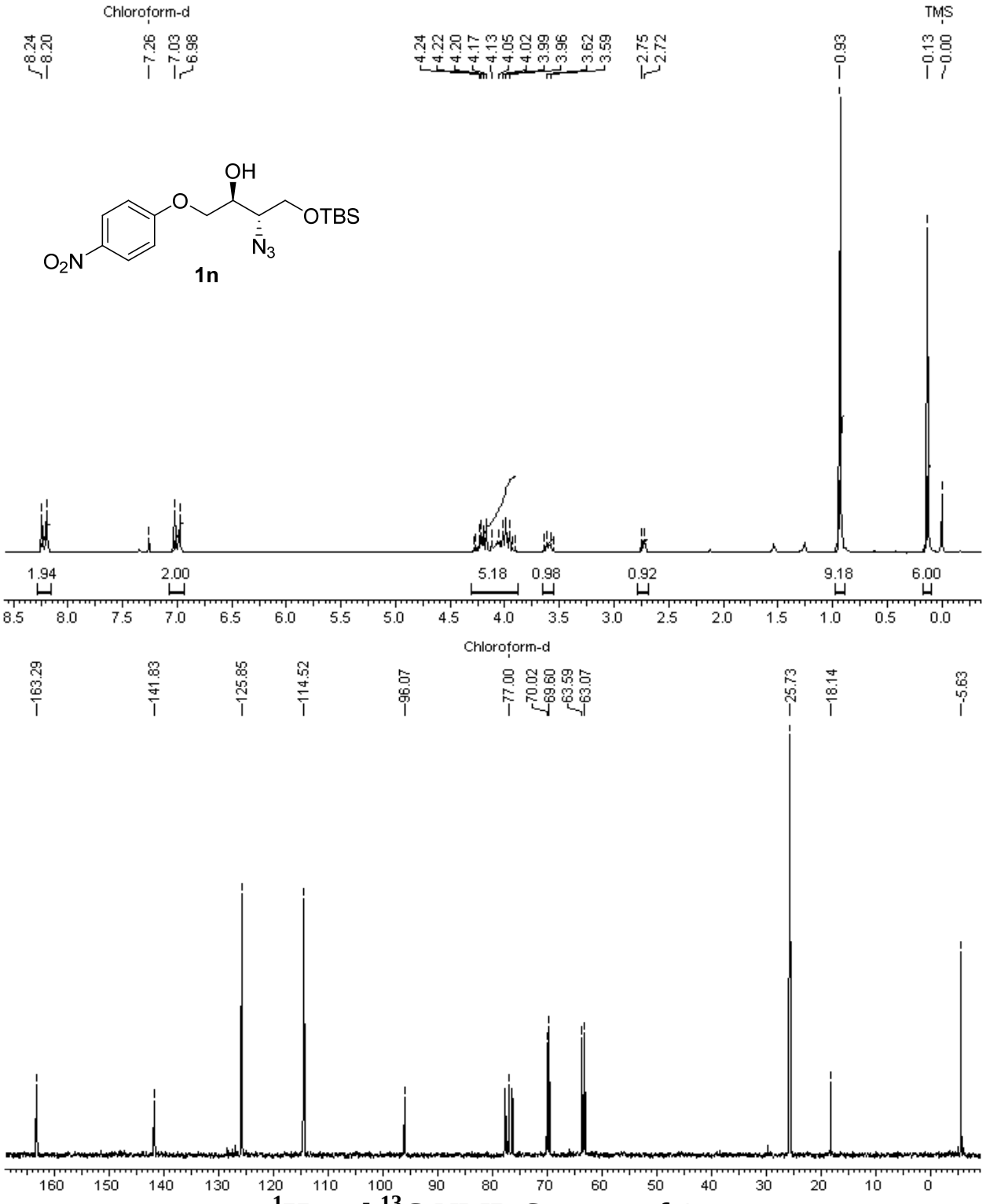

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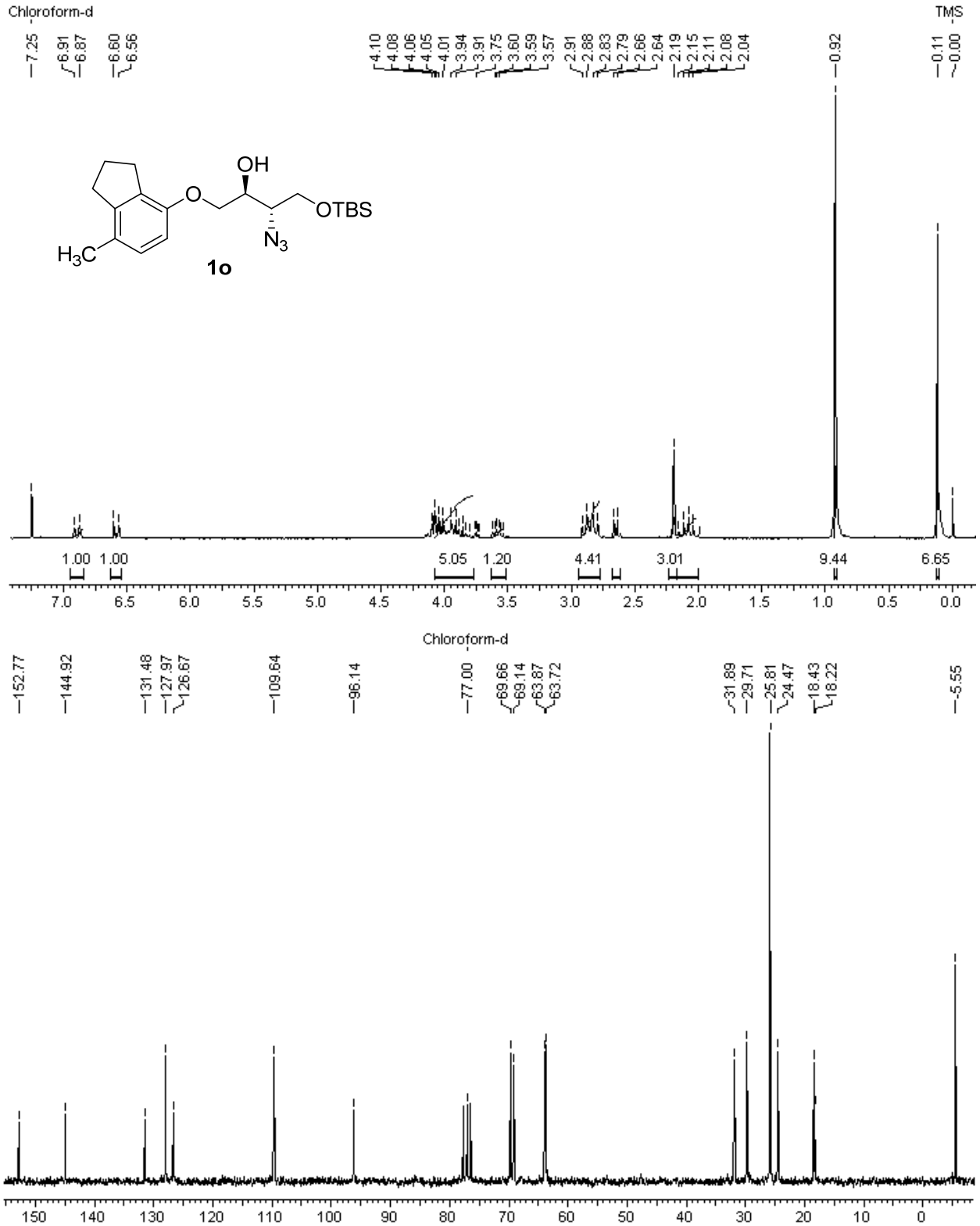

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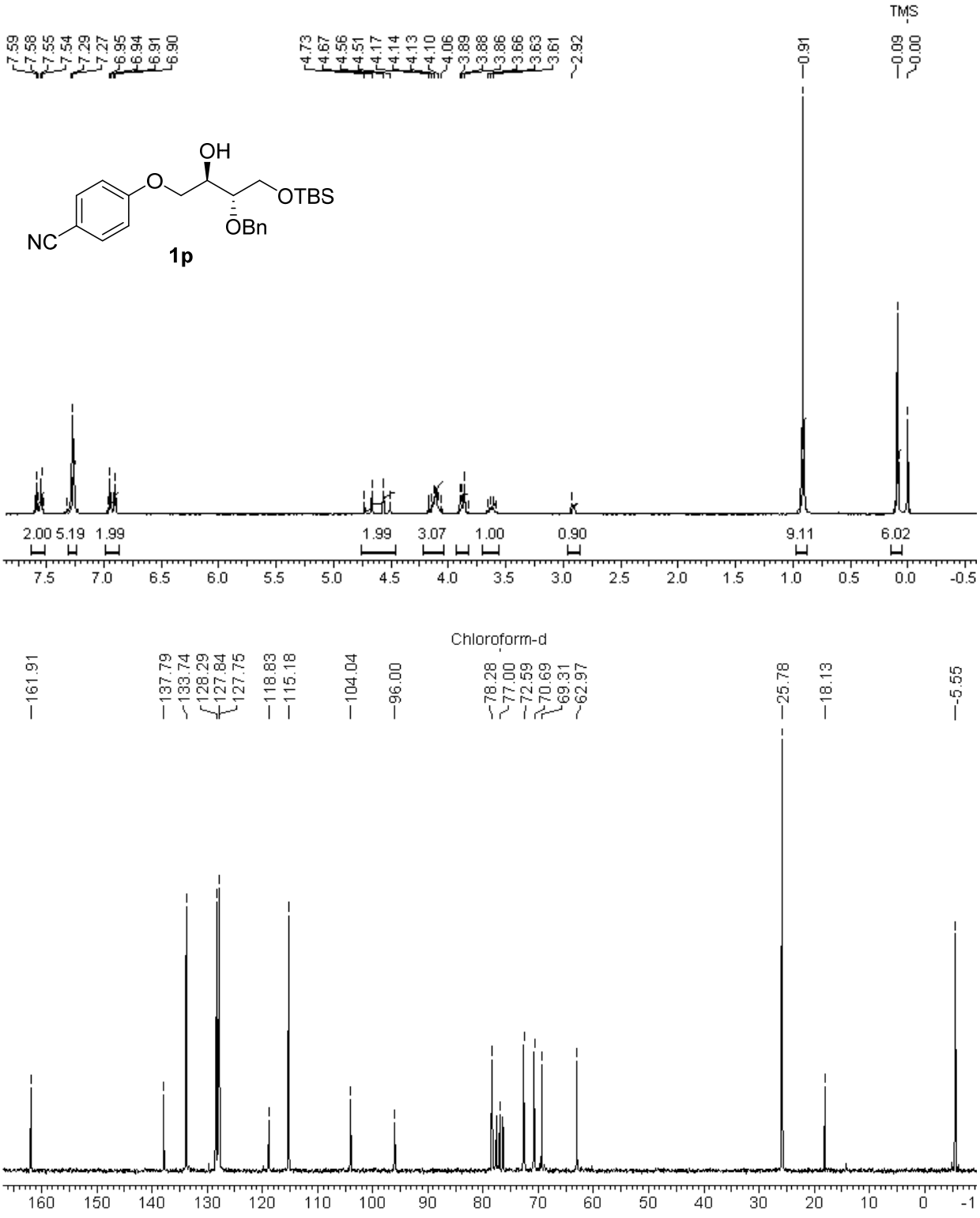

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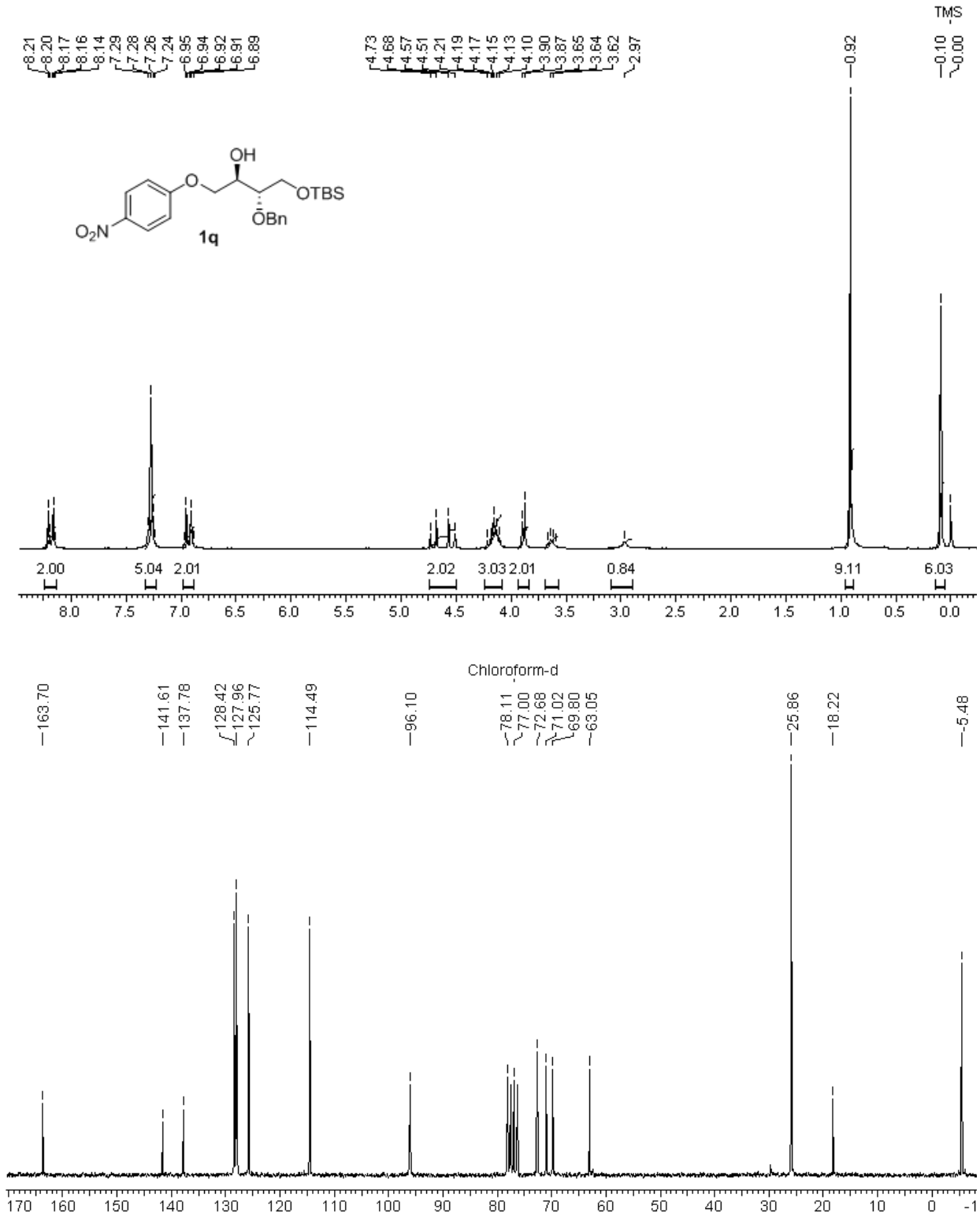

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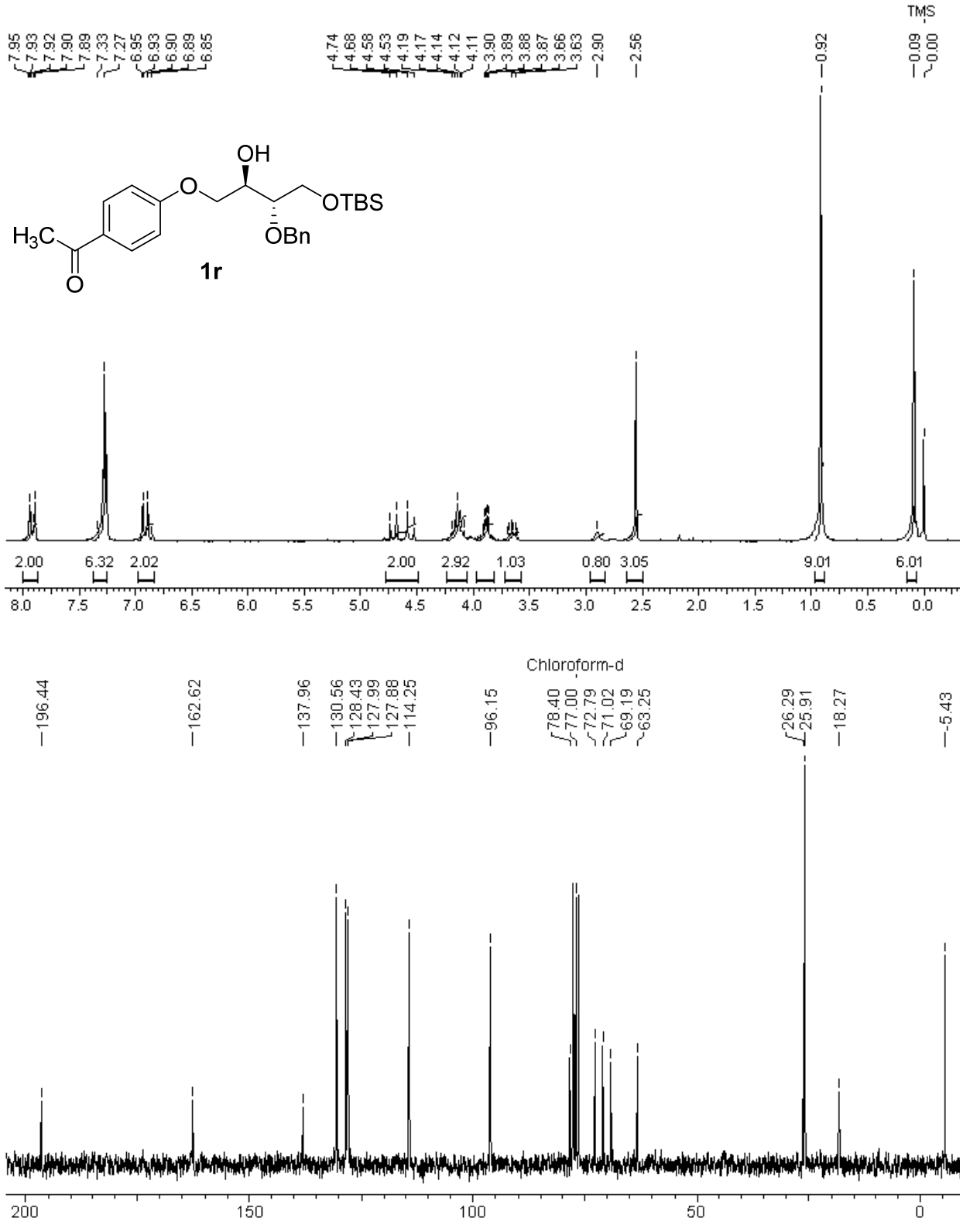

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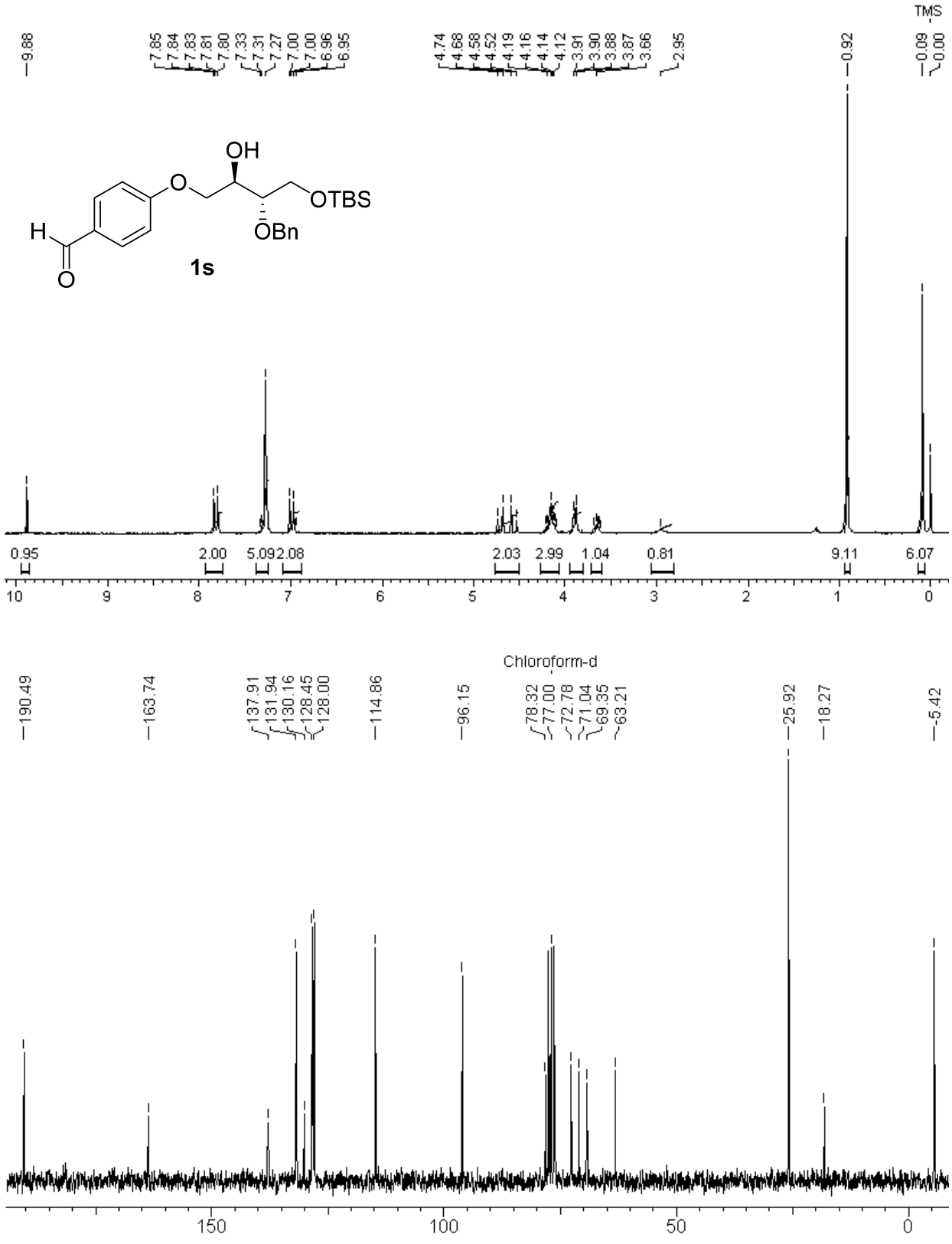

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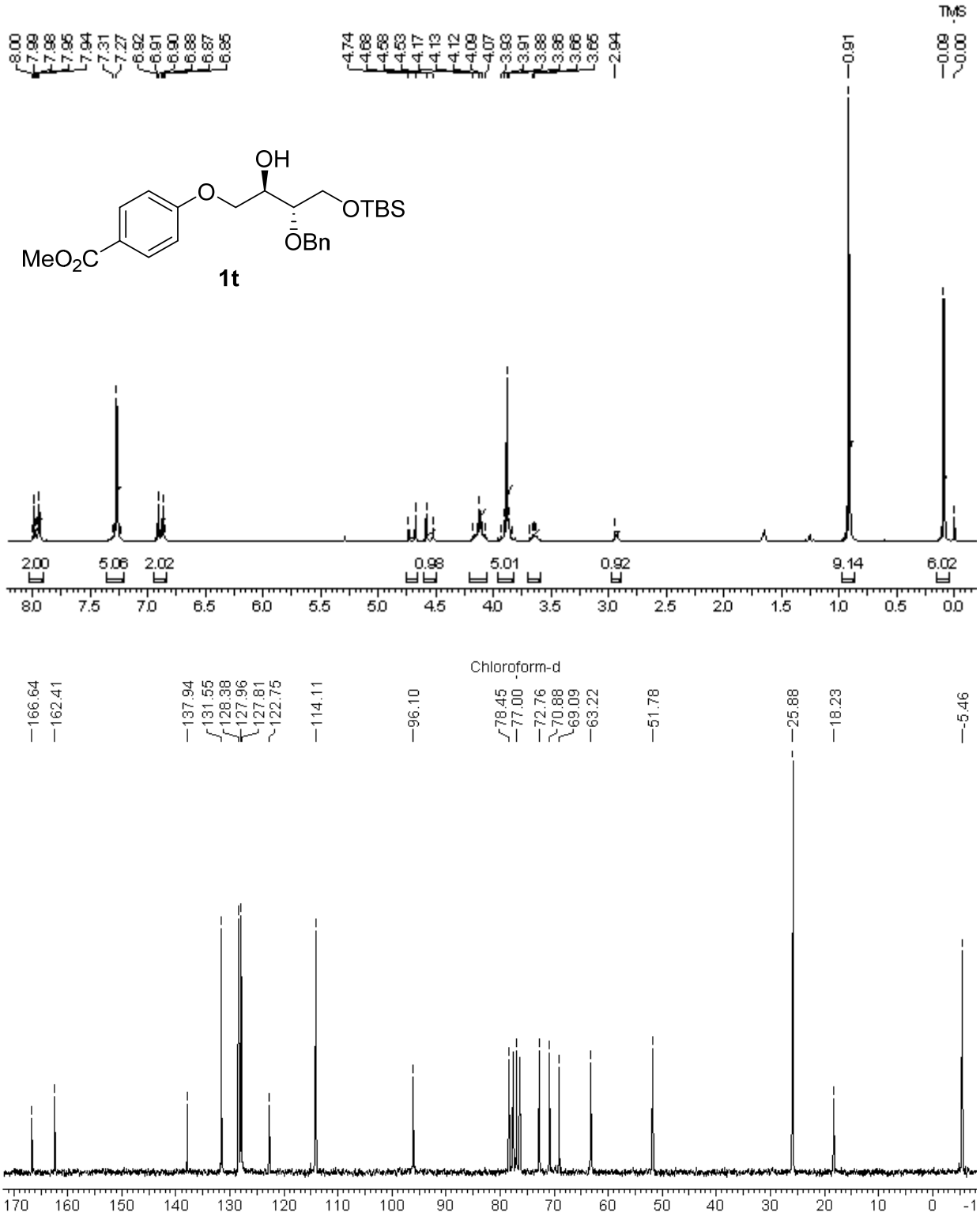

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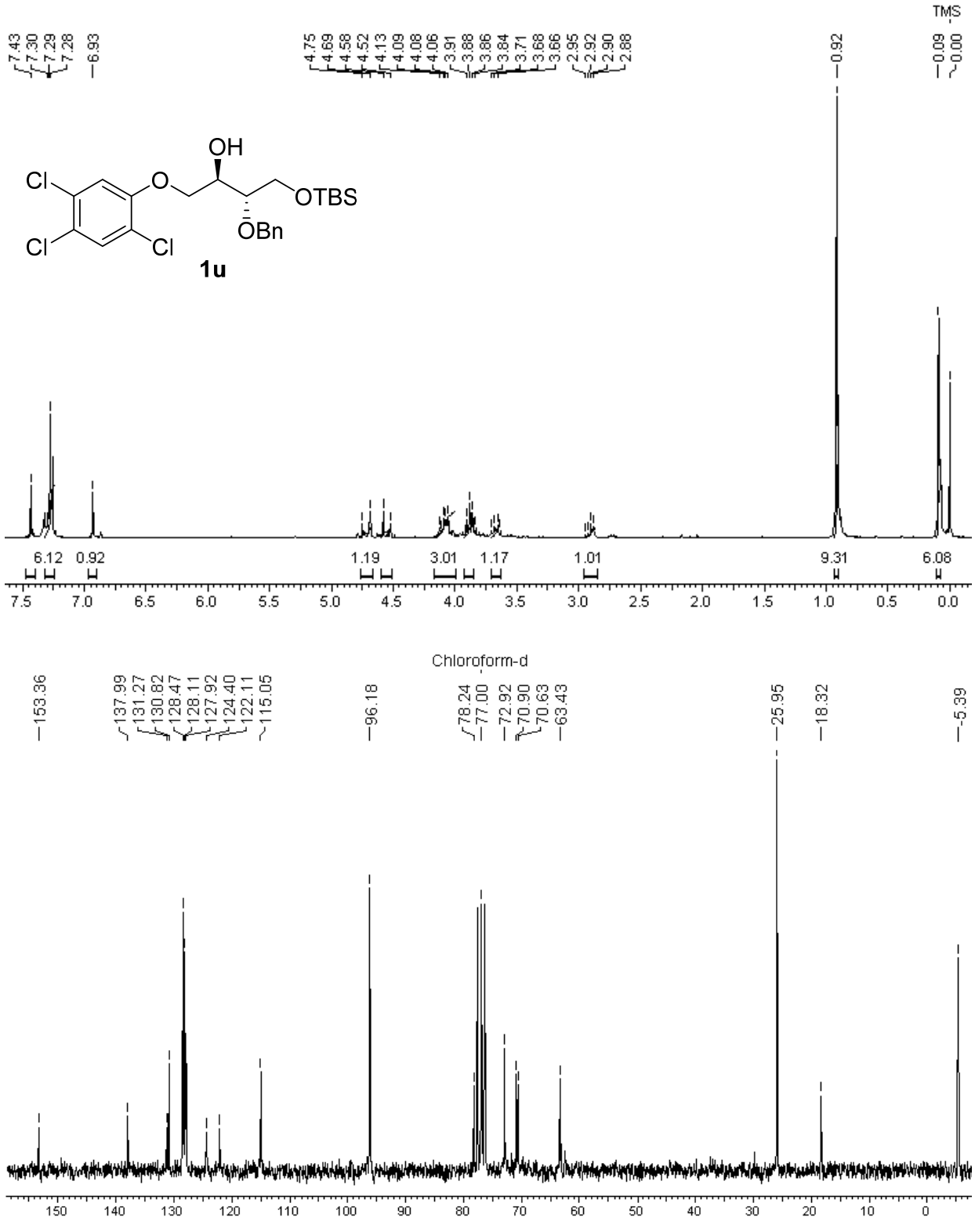

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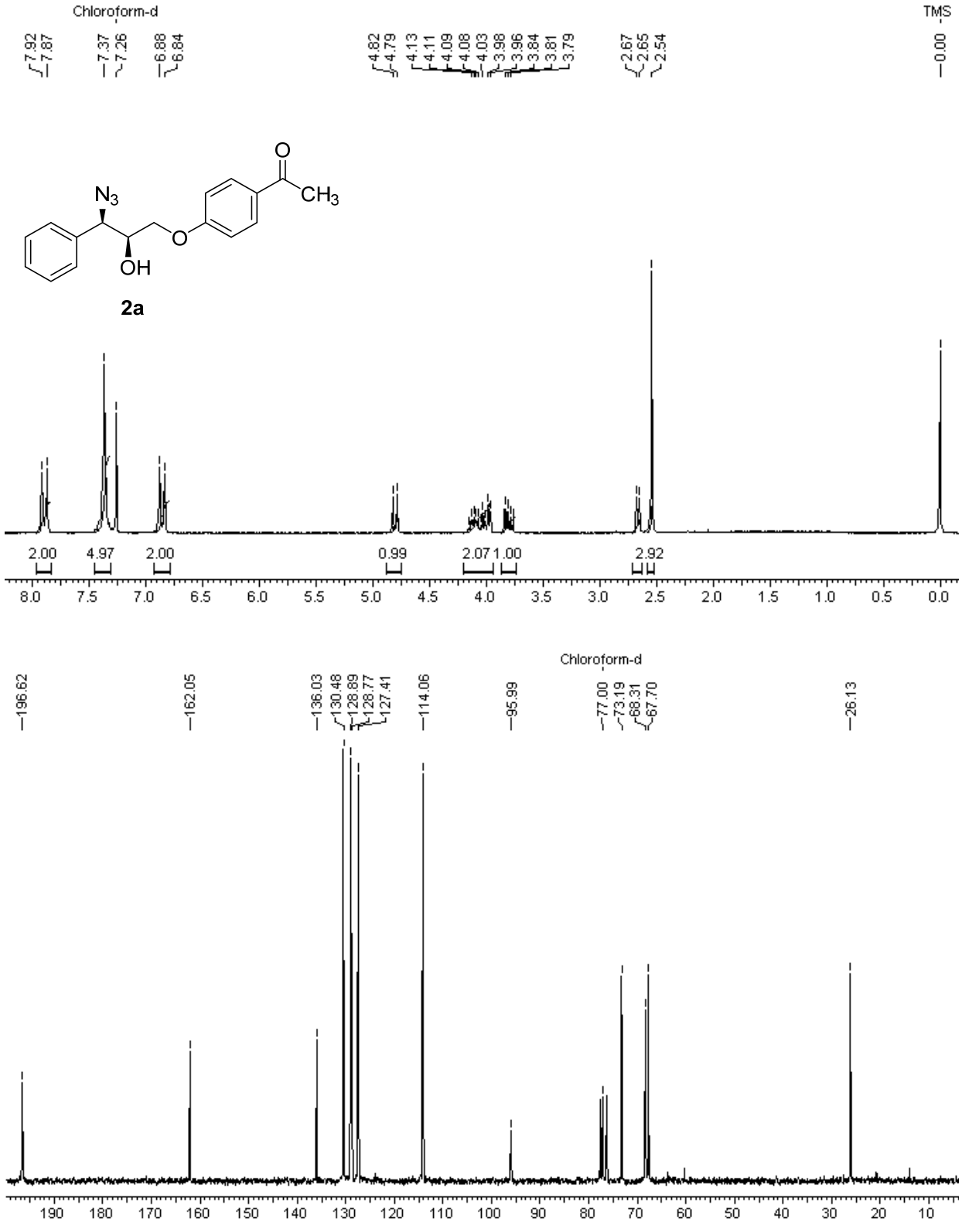

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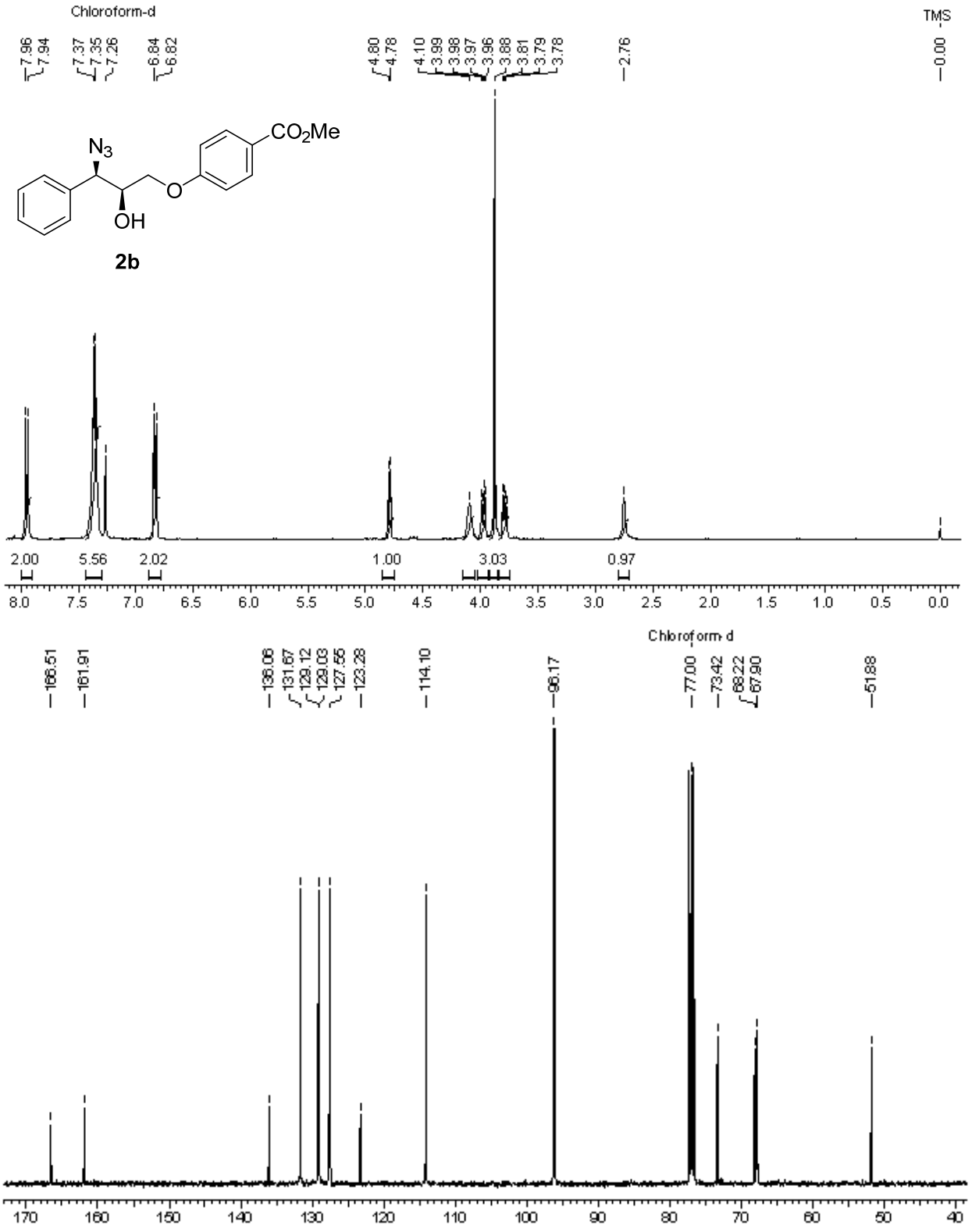

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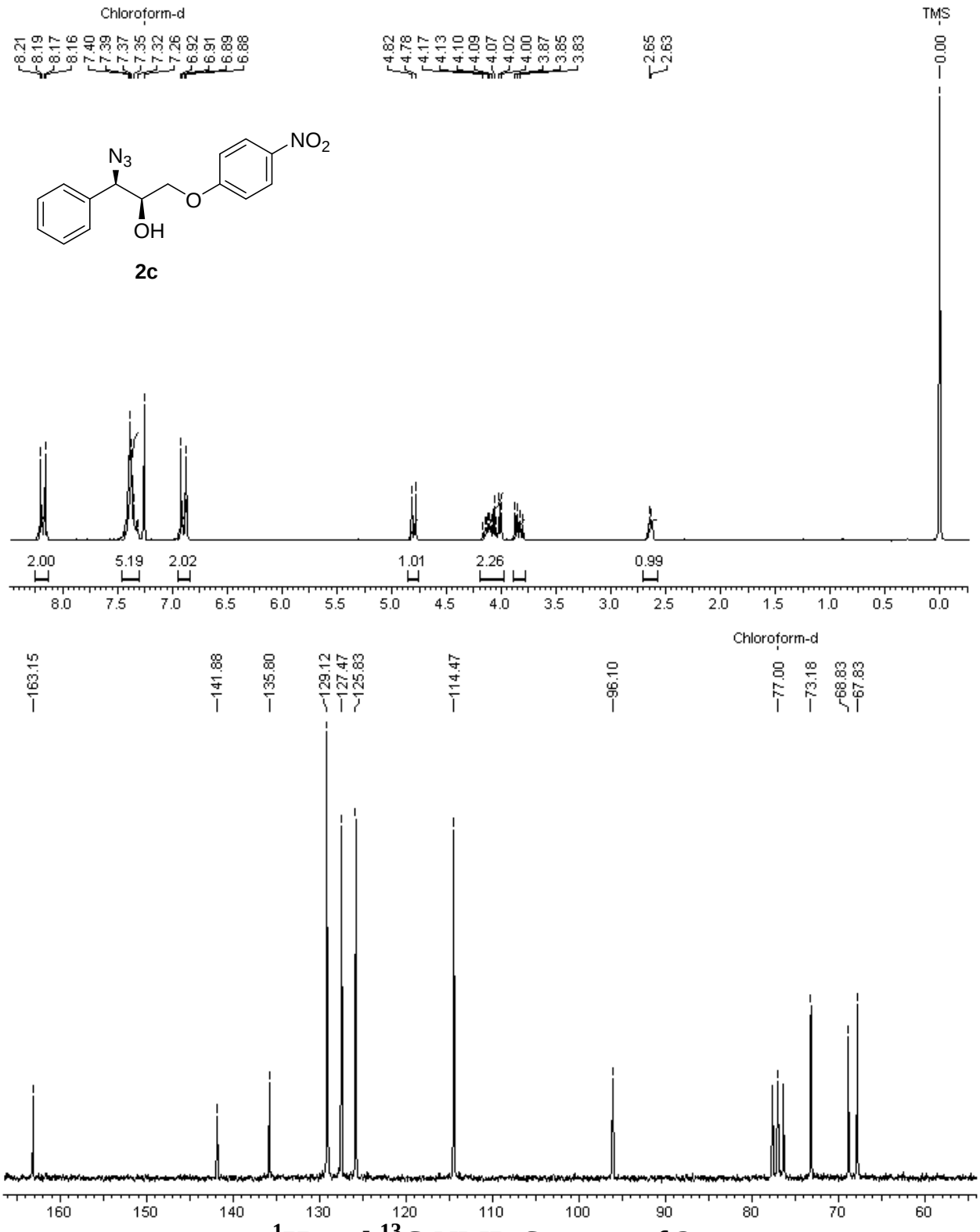

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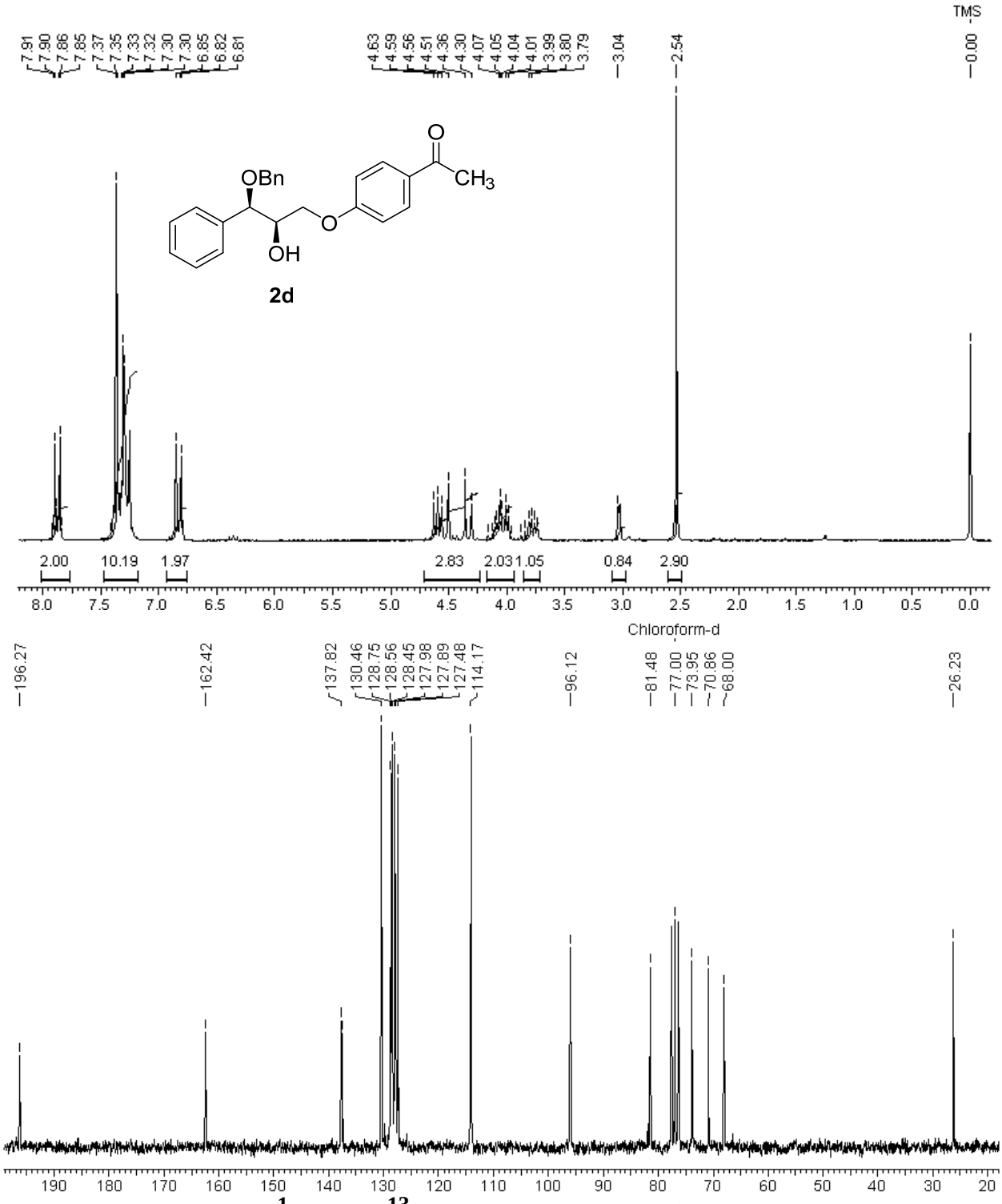

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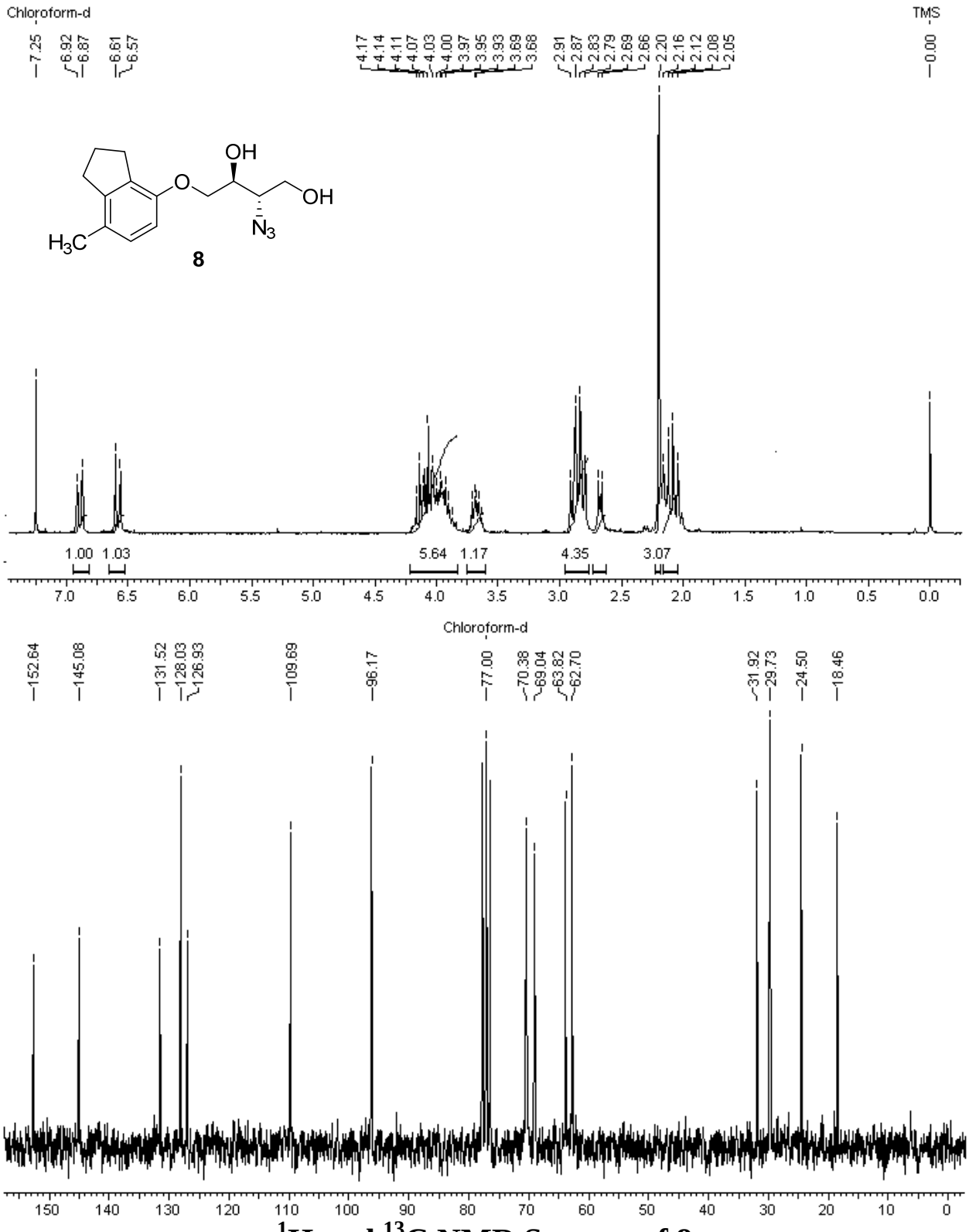

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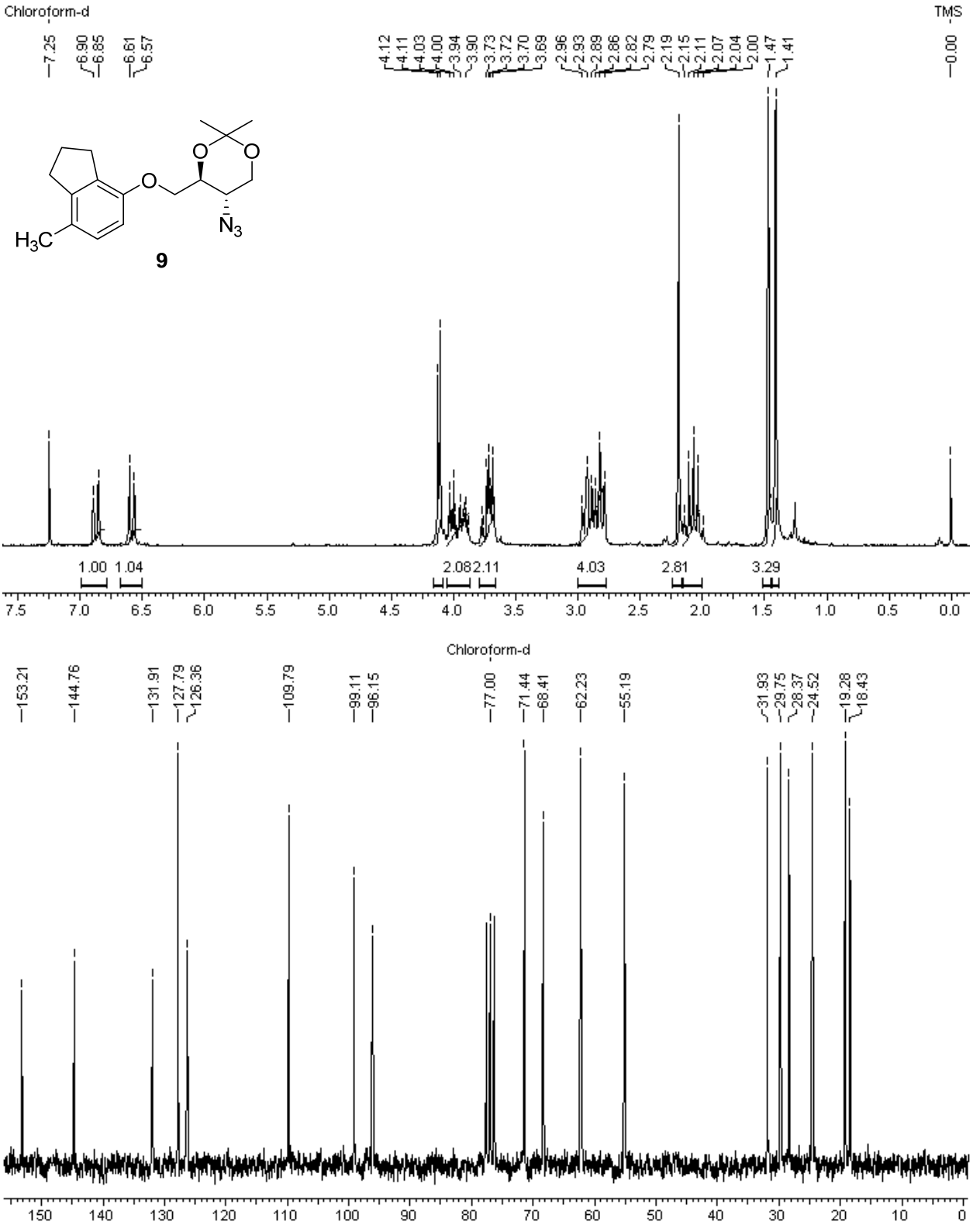

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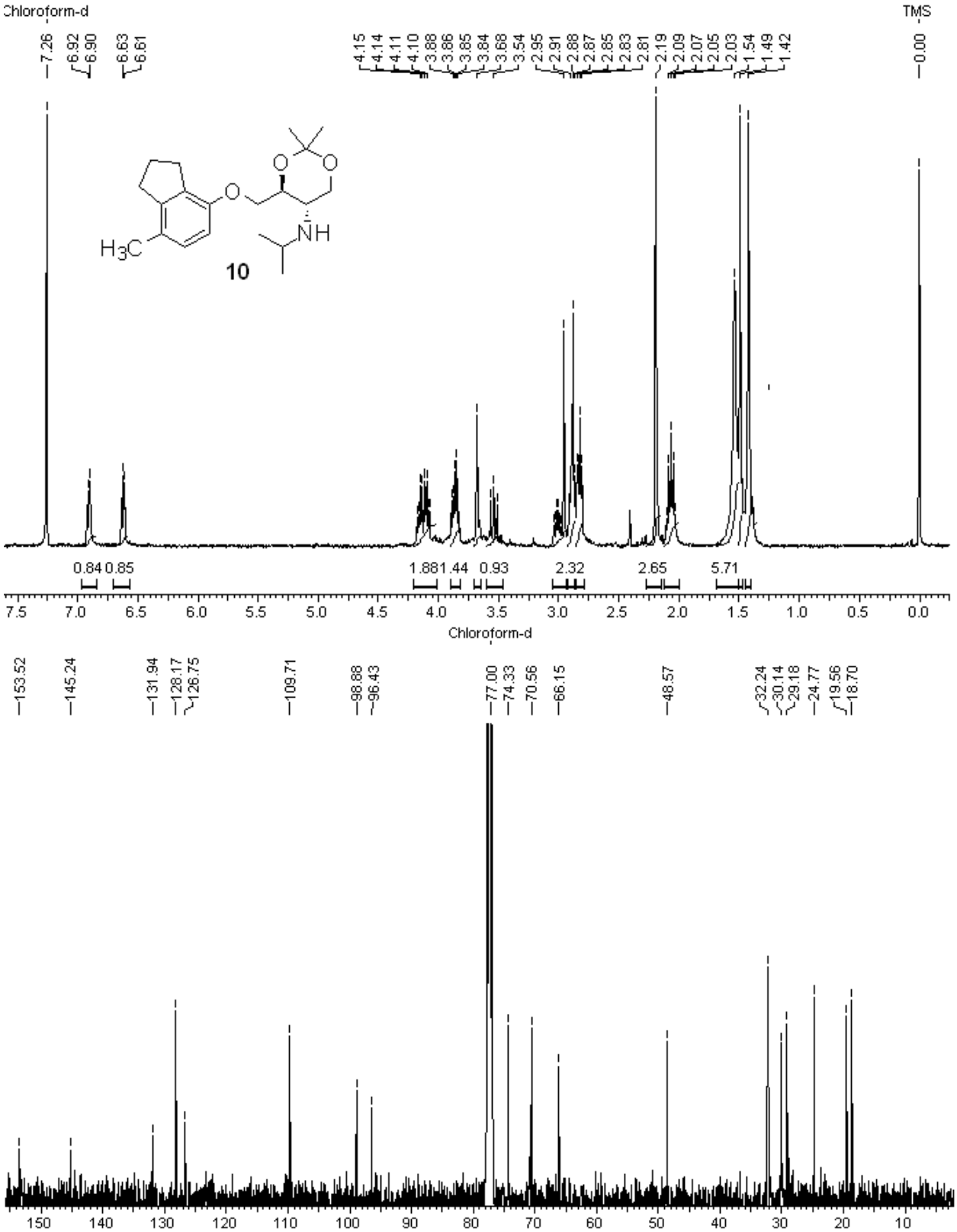

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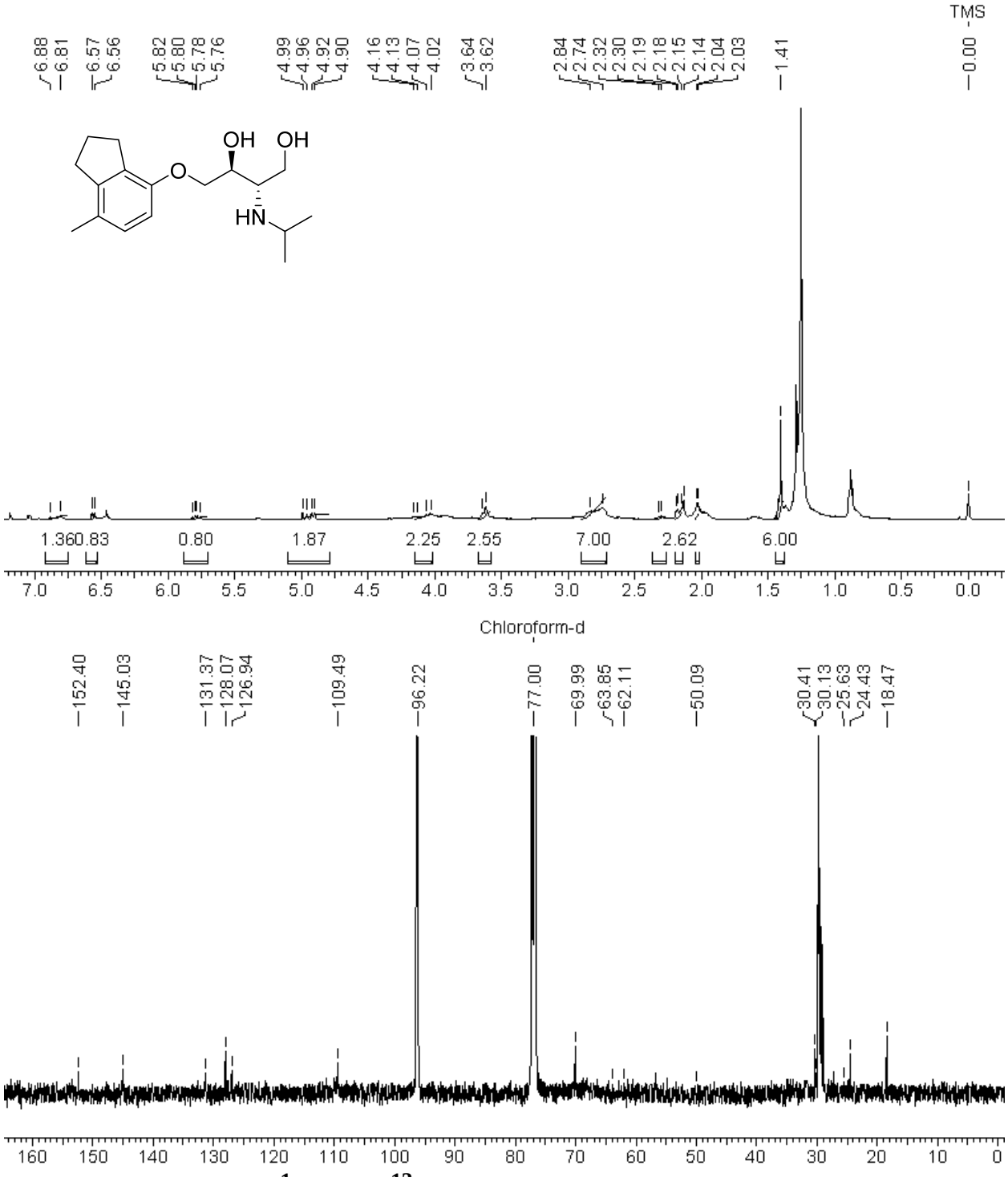

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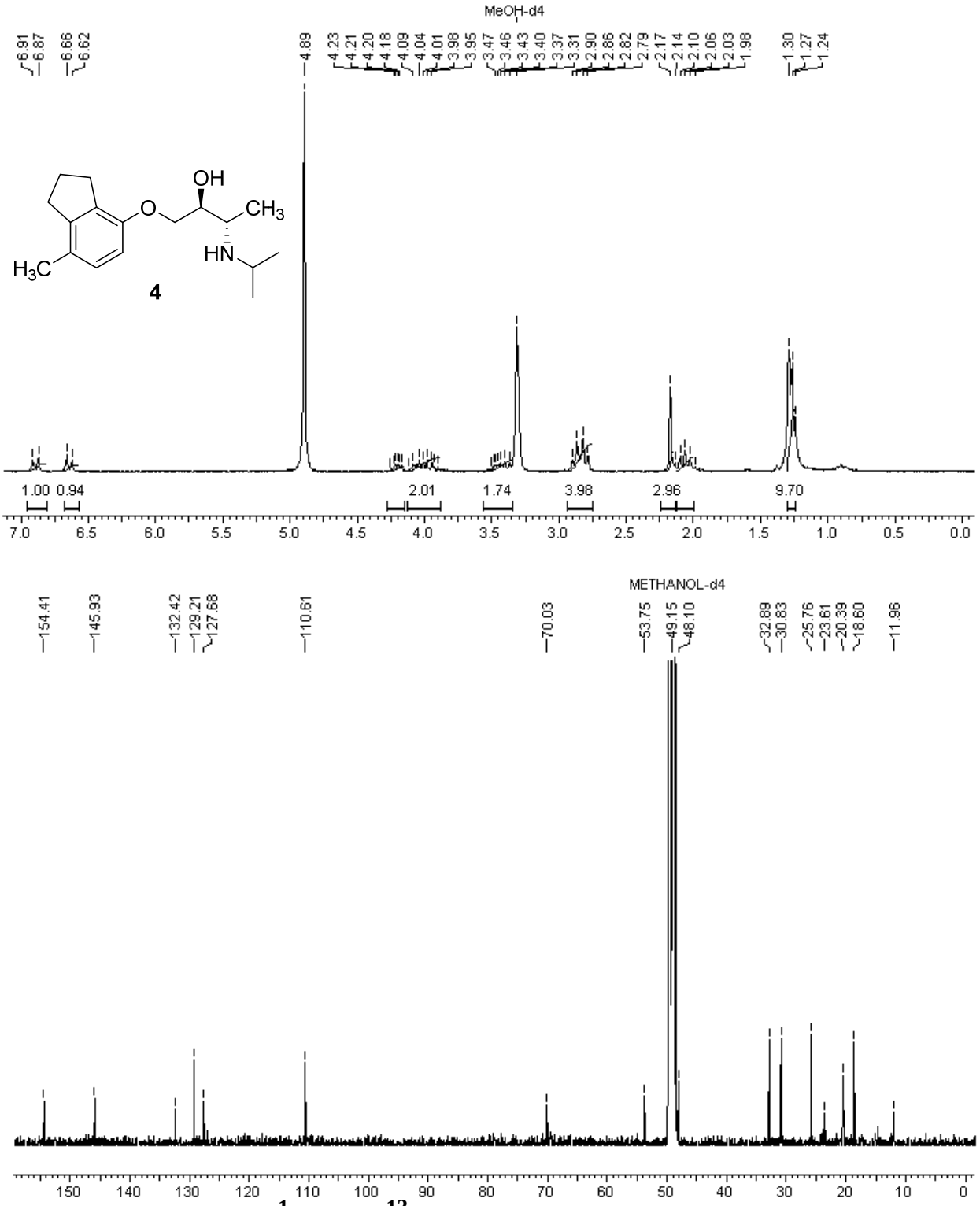
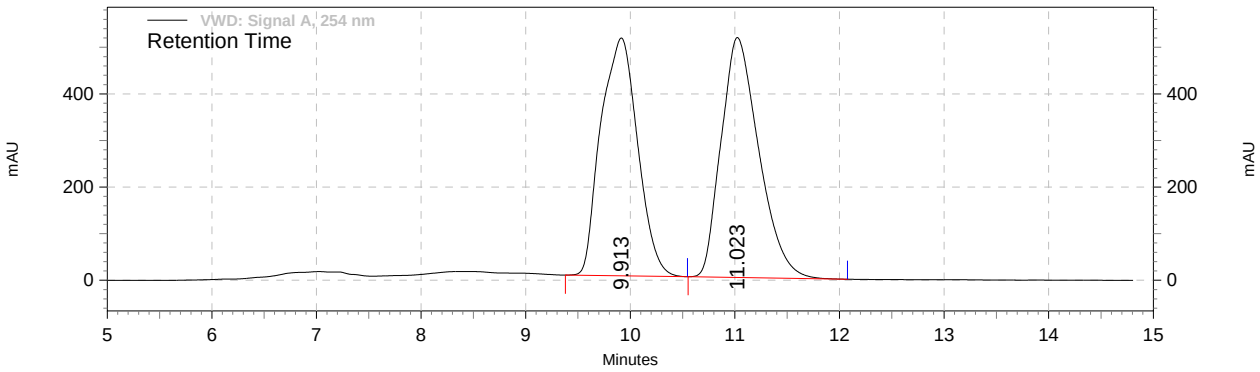
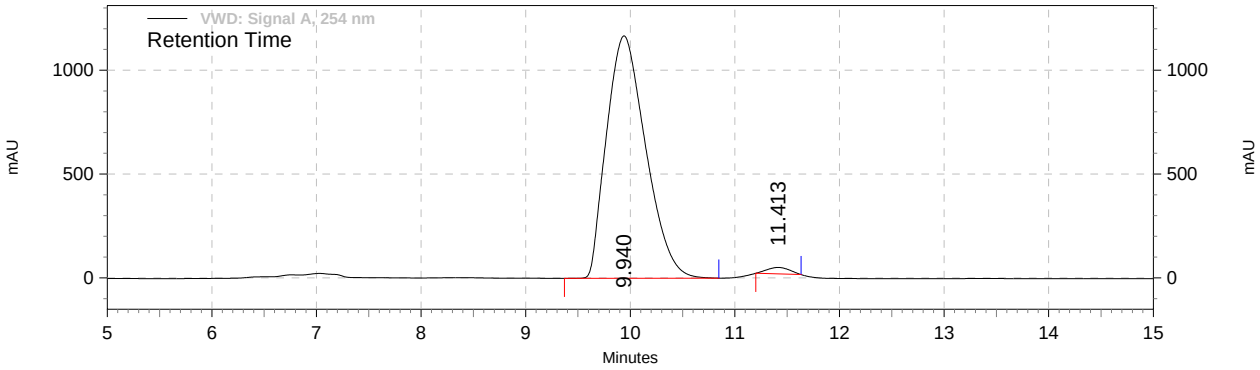


^{1}H and ^{13}C NMR Spectra of 4

HPLC Chromatograms





VWD: Signal A, 254 nm Results

Retention Time	Area	Area %	Height	Height %
9.940	514024562	99.35	19588723	99.40
11.413	3102764	0.65	522812	0.60
Totals	517127326	100.00	20111535	100.00

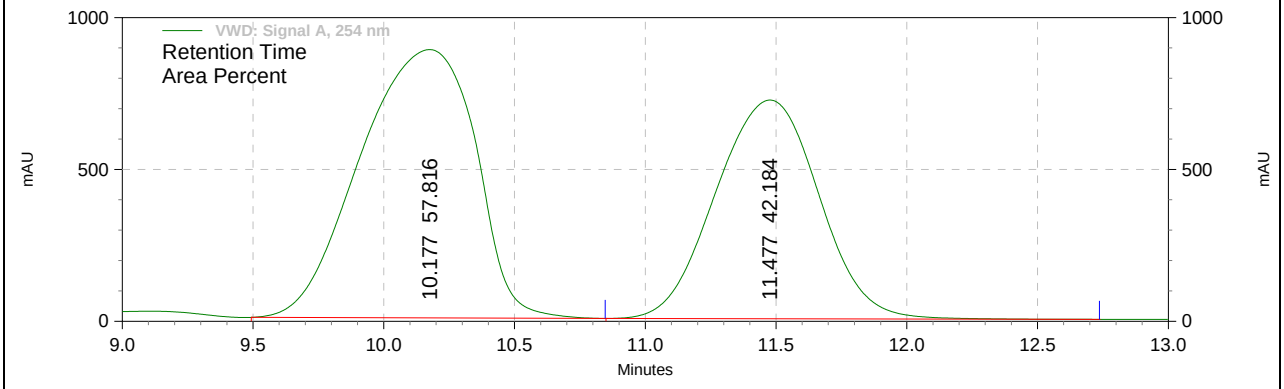
Column :Chiracel OD-H (4.6X250 nm)

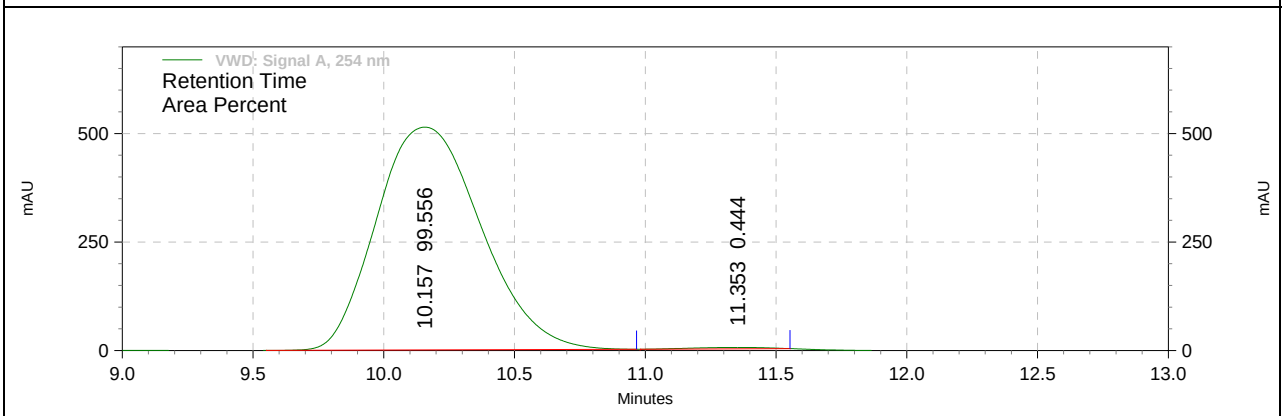
Mobile Phase :IPA:n-Hexane(5:95)

Wavelength :254 nm

Flow rate :0.5ml/min

(2*S*,3*S*)-3-azido-4-((*tert*-butyldimethylsilyl)oxy)-1-((7-methyl-2,3-dihydro-1H-inden-4-yl)oxy)butan-2-ol (1o)





VWD: Signal A, 254 nm

Results

Retention Time	Area	Area %	Height	Height %
10.157	239861276	99.56	8617320	99.39
11.353	1070458	0.44	52774	0.61
Totals	240931734	100.00	8670094	100.00

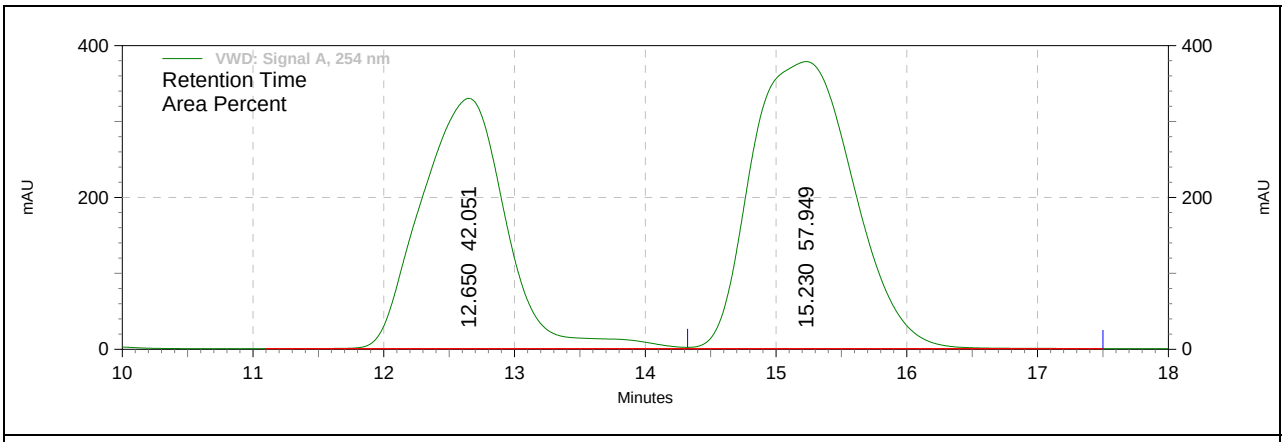
Column : Chiracel OD-H (4.6X250 nm)

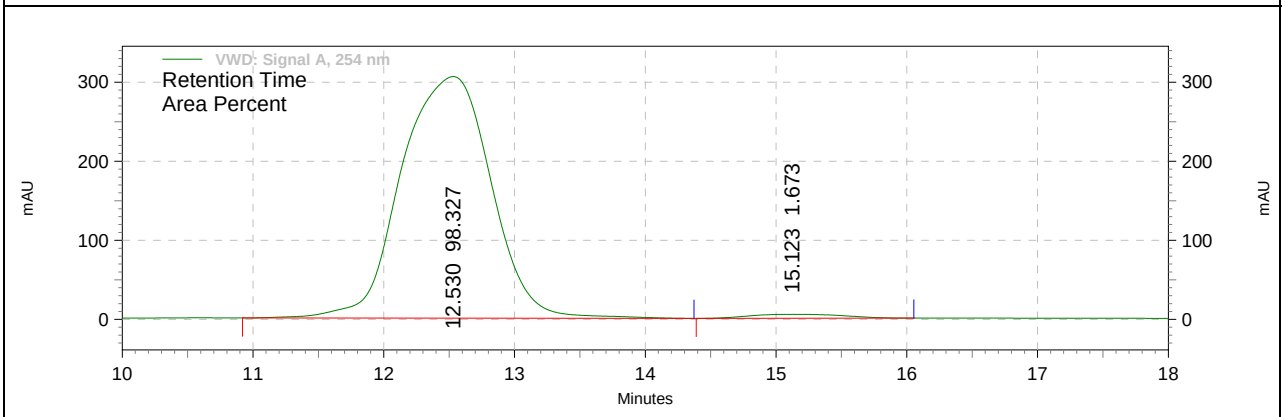
Mobile Phase : IPA:n-Hexane(20:80)

Wavelength : 210nm

Flow rate : 0.5ml/min

4-((2*R*,3*S*)-4-(*tert*-butyl dimethylsiloxy)-3-(benzyloxy)-2-hydroxybutoxy)benzonitrile(1p)





VWD: Signal A, 254 nm Results

Retention Time	Area	Area %	Height	Height %
12.530	244951558	98.33	5128098	98.40
15.123	4168475	1.67	83636	1.60
Totals	249120033	100.00	5211734	100.00

Column : Chiracel OJ-H (4.6X250 nm)

Mobile Phase : IPA:n-Hexane(20:80)

Wavelength : 210nm

Flow rate : 0.5ml/min

(2*R*,3*S*)-4-(*tert*-butyldimethylsiloxy)-1-(4-nitrophenoxy)-3-(benzyloxy)butan-2-ol (1q)