**Electronic supplementary materials** *Mendeleev Commun.*, 2020, **30**, 347-349

# Synthesis of new physiologically active (2-oxoimidazolidin-5-yl)indoles

**Lyudmila A. Sviridova, Polina S. Protopopova, Mikhail G. Akimov, Polina V. Dudina, Elizaveta K. Melnikova and Konstantin A. Kochetkov**

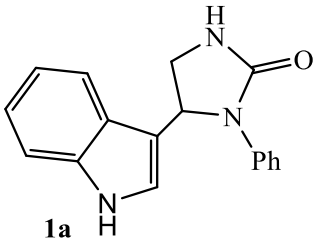
**Synthesis and the target compounds and characterization.**

$^1$H NMR spectra of the obtained compounds were recorded on a "BrukerAvance 400" instrument (working frequency 400 MHz), "Agilent 400-MR" (working frequency 400 MHz) in DMSO-$d_6$, and "BrukerAvance$^{TM}$600" for $^{13}$C NMR (150.93 MHz). Elemental analysis was performed in the laboratory of elemental analysis of INEOS RAS. Melting points were determined on an Electrothermal IA 9100 instrument. The progress of the reactions and the purity of the products were monitored by thin layer chromatography (TLC) on Silufol UV254 plates with a fixed layer of silica gel, eluent $CHCl_3$/MeOH (10:1) manifestation by iodine vapor and Kovac's reagent. Solvents were purified by standard methods.

**5-Hydroxy-1-phenylimidozolidin-2-one (3)** was prepared by $LiAlH_4$ reduction of the corresponding hydantoin derivative [S. Cortes and H. Kohn, *J. Org. Chem.*, 1983, **48** (13), 2247]. Yield 66%; Mp 112-114 ° C. IR spectrum, *v*, cm$^{-1}$: 1700 (C = O). $^1$H NMR spectrum (DMSO-$d_6$, δ, ppm, *J*, Hz): 3.08 (1H, d, 4-H, *J* = 10.1), 3.58-3.62 (1H, m, 4-H'), 5.58-5.62 (1H, dd, 5-H, *J* = 7.0, *J* = 7.2), 6.42 (1H, d, OH, *J* = 8.2), 6.95-7.05 (2H, d, Ph, *J* = 7.2), 7.24-7.30 (2H, m, Ph), 7.35 (1H, s, NH), 7.60 (2H, d, Ph, *J* = 8.8)

**General method for the amidoalkylation of indoles.** 5-Hydroxy-1-phenylimidosolidin-2-one (1 mmol) and indole (1 mmol) in of dry THF (10 ml) were dissolved. A few drops (1-10 mol%) of boron trifluoride etherate were added with stirring. The mixture was stirred for 30 min to several hours, then left overnight at room temperature (TLC control). In case of precipitation, the solid was filtered off, washed successively with chloroform, alcohol, ether and dried. Otherwise, the resulting solution with a small amount of a light, colorless precipitate was passed through a thin layer of silica gel to separate it from salt-like impurities (eluent chloroform). After this, the solvent was distilled off, ether (~5 ml) was added to the resulting oil, and triturated to a fine crystalline precipitate. The precipitate was filtered off and recrystallized from ethanol.

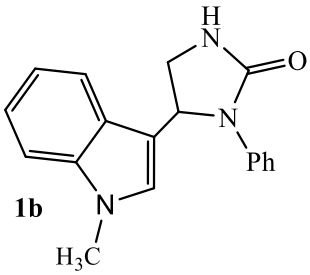
**5-(1*H*-Indol-3-yl)-1-phenylimidozolidin-2-one (1a)**




**1a**

Yield 30%. Mp 244°C. IR spectrum (ν, $cm^{-1}$): 1680 (C = O); 3350 (NH) Found,%: C (71.41), H (5.46), N (14.23). $2C_{17}H_{15}N_3O \times H_2O$. Calculated, %: C (71.31), H (5.63), N (14.68). Mass spectrum, m / z: 277 $[M]^+$. $^1$H NMR spectrum (DMSO-$d_6$, δ, ppm *J*, Hz): 3.35-3.37 (1H, m, 4-H), 3.84-3.88 (1H, m, 4-H '), 5.72 (1H, dd, 5-H, *J* = 6.2, *J* = 9.2), 6.87 (1H, t, N-Ph, *J* = 7.3), 6.95 (1H, s, $NH_{imid}$), 6.97-7.00 (1H, m, Ar), 7.06-7.08 (1H, m, Ar), 7.13-7.15 (2H, m, Ar), 7.31 (1H, s, 2-Ind), 7.33-7.34 (1H, d., Ar, *J* = 7.66,), 7.46-7.47 ( 2H, d, Ar, *J* = 8.0), 7.62-7.63 (1H, d, Ar, *J* = 7.6), 10.87 (1H, s, $NH_{ind}$). $^{13}$C NMR spectrum (DMSO-$d_6$, δ, ppm): 45.80 (4-C), 53.86 (5-C), 112.25, 114.58, 119.15, 119.34, 120.88 (2C), 121.70, 122.67, 124.57, 125.46, 128.42 (2C), 137.28, 140.22 (14 C, Ar), 159.62 (C = O)

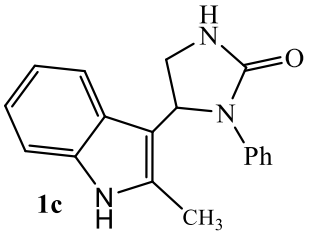
**5-(1-Methylindol-3-yl)-1-phenylimidozolidin-2-one (1b)**




**1b**

Yield 25%. Mp 233°C. IR spectrum (ν, $cm^{-1}$): 1695 (C = O); Found,%: C (71.77), H (5.72), N (13.63). $2C_{18}H_{17}N_3O \times H_2O$. Calculated,%: C (71.98), H (6.04), N (13.99). Mass spectrum, m / z: 291 $[M]^+$. $^1$H NMR spectrum (DMSO-$d_6$, δ, ppm *J*, Hz): 3.30 (1H, m, 4-H), 3.68 (3H, s, N-$CH_3$), 3.82 (1H, t., 4-H ', J = 9.0), 5.71 (1H, dd, 5-H, *J* = 6.1, *J* = 9.2), 6.87 (1H, t, *p*-Ph, *J* = 7.36), 7.01-7.03 (1H, m, Ind), 7.11-7.16 (1H, m, Ind; 2H, m, *μ*-Ph), 7.33 (1H, s, 2-Ind), 7.35-7.37 (1H, d, Ind, *J* = 7.7), 7.46-7.47 (2H, d, *o*-Ph, *J* = 8.0), 7.61-7.62 (1H, d., Ind, *J* = 7.7) $^{13}$C NMR spectrum (DMSO-$d_6$, δ, ppm): 32.79 (N-$CH_3$), 45.63 (4-C), 53.17 (5-C), 110.51, 113.47, 119.34, 119.51, 120.60 (2C), 121.86 , 122.68, 125.59, 128.52 (2C), 128.83, 137.50, 139.86 (14 C, Ar), 159.50 (C = O)

**5-(2-Methyl-1*H*-indol-3-yl)-1-phenylimidozolidin-2-one (1c)**

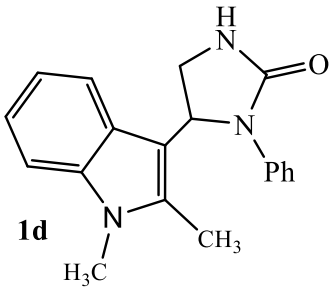



**1c**

Yield 28%. Mp 275°C. IR spectrum (ν, $cm^{-1}$): 1681 (C = O); 3240 (NH); Found,%: C (74.51), H (6.27), N (14.32). $C_{18}H_{17}N_3O$. Calculated,%: C (74.20), H (5.88), N (14.32). Mass spectrum, m /

z: 291 $[M]^+$. $^1H$ NMR spectrum (DMSO-$d_6$, δ, ppm *J*, Hz): 2.41 (3H, s, 2'-$CH_3$), 3.34 (1H, m, 4-H), 3.76 (1H, m, 4-H '), 5.72 (1H, m, 5-H), 6.84-6.87 (1H, m, *p*-Ph), 6.90-6.92 (1H, m, Ind), 6.95 (1H, m, Ind), 7.11-7.16 (2H, t, *μ*-Ph, *J* = 7.8), 7.19-7.20 (1H, d, Ind, *J* = 7.9), 7.33-7.34 (2H, d, *o*-Ph, *J* = 8.0), 7.48-7.50 (1H, d, Ind, *J* = 7.9), 10.88 (1H, s, $NH_{ind}$). $^{13}C$ NMR spectrum (DMSO-$d_6$, δ, ppm): 11.71 (2'-$CH_3$), 44.86 (4-C), 52.53 (5-C), 109.21, 111.13, 118.28, 119.12, 120.81, 120.86, 122.81 , 128.39 (4C), 133.79, 135.62, 139.74 (14 C, Ar), 159.52 (C = O).

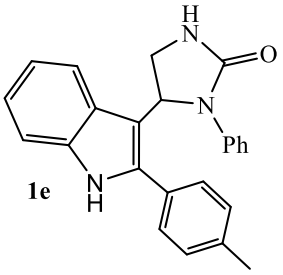
**5-(1,2-Dimethylindol-3-yl)-1-phenylimidozolidin-2-one (1d)**




**1d**

Yield 19%. Mp 278°C. IR spectrum (ν, $cm^{-1}$): 1699 (C = O); Found,%: C (73.18), H (6.07), N (13.32). $2C_{19}H_{19}N_3O \times H2O$. Calculated,%: C (72.59), H (4.41), N (13.37) Mass spectrum, m / z: 305 $[M]^+$. $^1H$ NMR spectrum (DMSO-$d_6$, δ, ppm, *J*, Hz): 2.45 (3H, s, 2'-$CH_3$), 3.30-3.34 (1H, m, 4-H), 3.58 (3H, s, N-$CH_3$), 3.78-3.82 (1H, m, 4-H '), 5.76-5.80 (1H, m, 5-H), 6.84-6.86 (1H, m, *p*-Ph), 6.94-6.96 (1H, m, Ind), 7.02-7.04 (1H m, Ind), 7.11-7.13 (2H, m, *μ*-Ph), 7.30-7.33 (1H, m, Ind; 2H, *o*-Ph), 7.51 (1H, d, Ind, *J* = 7.9). $^{13}C$ NMR spectrum (DMSO-$d_6$, δ, ppm): 10.33 (2'-$CH_3$), 29.67 (N-$CH_3$), 44.97 (4-C), 52.80 (5-C), 109.30, 109.84, 118.42, 119.41 (2C), 120.91 (2C), 122.85, 128.83 (3C), 135.54, 137.01, 139.74 (14 C, Ar), 159.89 (C = O).

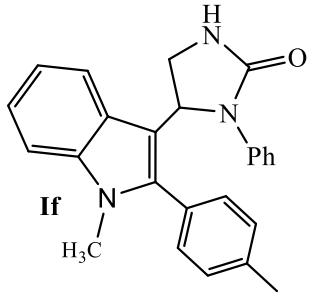
**1-Phenyl-5-(2-*p*-tolyl-1*H*-indol-3-yl)imidozolidin-2-one (1e)**




**1e**

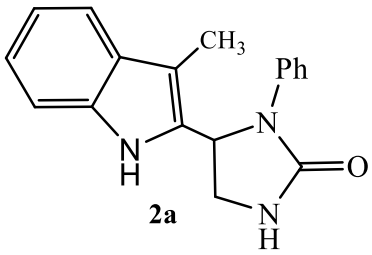
Yield 32%. Mp 317°C. IR spectrum (ν, $cm^{-1}$): 1684 (C = O); 3282 (NH); Found,%: C (74.27), H (5.69), N (10.70). $C_{24}H_{23}N_3O$. Calculated,%: C (74.78), H (6.01), N (10.90). Mass spectrum, m / z: 367 $[M]^+$. $^1H$ NMR spectrum (DMSO-$d_6$, δ, ppm, *J*, Hz): 2.42 (3H, s, Tol $CH_3$), 3.54-3.58, (1H, m, 4-H), 4.01-4.06 (1H, m, 4-H '), 5.59-5.63 (1H, m, 5-H), 6.77-6.79 (1H, m, *p*-Ph), 6.94-7.08 (4H, m, Ph; 1H, m, Ind), 7.02-7.04 (1H, m, Ind), 7.21 (1H, s, $NH_{imid}$), 7.28-7.31 (1H, m, Ind), 7.38-7.46 (4H, m, Tol), 7.57-7.59 (1H, m, Ind), 11.32 (1H, s, $NH_{ind}$). $^{13}C$ NMR spectrum (DMSO-$d_6$, δ, ppm): 21.34 (Tol-$CH_3$), 44.93 (4-C), 52.85 (5-C), 109.79, 111.96, 119.47, 119.65, 120.32 (2C), 121.95, 122.60, 128.26 (3C), 129.03 (2C), 129.42 129.93 (2C), 136.59, 137.59, 138.13, 139.63 (20 C, Ar), 159.40 (C = O).

**5-(1-Methyl-2-*p*-tolylindol-3-yl)-1-phenylimidozolidin-2-one (1f)**



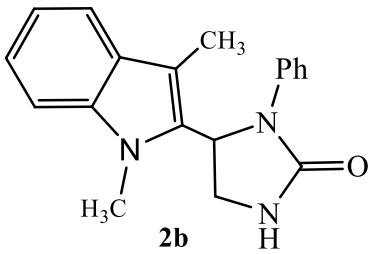

Yield 28%. Mp 183°C. IR spectrum (ν, $cm^{-1}$): 1701 (C = O); Found,%: C (78.44), H (6.02), N (10.65). $C_{25}H_{23}N_3O$. Calculated,%: C (78.71), H (6.08), N (11.02); Mass spectrum, m / z: 381 $[M]^+$. $^1H$ NMR spectrum (DMSO-$d_6$, δ, ppm, *J*, Hz): 2.45 (3H, s, Tol-$CH_3$), 3.43-3.45, (1H, m, 4-H), 3.49 (3H, s, N-$CH_3$), 3.88-3.91 (1H, m, 4-H '), 5.19 (1H, m, 5-H), 6.80-6.82 (1H, m, *p*-Ph), 7.00-7.06 (2H, m, Ph; 2H, m, Tol ; 1H, m, Ind), 7.13-7.16 (1H, m, Ind), 7.31-7.33 (2H, m, Ph), 7.41-7.45 (1H, m, Ind; 2H m, Tol) , 7.60-7.62 (1H, m, Ind). $^{13}C$ NMR spectrum (DMSO-$d_6$, δ, ppm): 21.40 (Tol-$CH_3$), 30.57 (N-$CH_3$), 45.30 (4-C), 54.45 (5-C), 109.57, 110.16, 119.75, 119.99, 122.01, 122.39, 123.83, 125.12, 127.70, 128.20 (4C), 129.34 (2C), 130.39, 137.36, 138.38, 138.91, 140.09 (20 C, Ar), 160.17 (C = O).

**1-Phenyl-5-(3-methyl-1H-indol-2-yl)imidozolidin-2-one (2a)**




Yield 11%; Mp 201°C. IR spectrum (ν, $cm^{-1}$): 1700 (C = O). $^1H$ NMR spectrum ($CDCl_3$, δ, ppm, *J*, Hz): 2.32 (3H, s, 3'-$CH_3$), 3.87-3.91 (1H, t, H-4, *J* = 8.2), 4.22 (1H, t, H-4 ', *J* = 9.2 ), 5.04 (1H, s, $NH_{imid}$), 5.24 (1H, dd, 5-H, *J* = 7.8, *J* = 9.5), 7.09 (1H, t, Ar, *J* = 7.8), 7.14 ( 1H, m, Ar, *J* = 7.5), 7.22 (1H, dd, Ar, *J* = 7.0, *J* = 8.0), 7.31-7.37 (3H, m, Ar), 7.52-7.55 (3H, m, Ar), 8.46 (1H, s, $NH_{ind}$). Mass spectrum of high resolution. Found: m / z $[M + H]^+$ 292.3551. Calculated: 292.3551 $C_{18}H_{17}N_3O$

**5-(1,3-Dimethylindol-2-yl)-1-phenylimidozolidin-2-one (2b)**




Yield 19%. Mp 211°C. IR spectrum (ν, $cm^{-1}$): 1702 (C = O); Mass spectrum, m / z: 305 $[M]^+$ $^1H$ NMR spectrum ($CDCl_3$, δ, ppm, *J*, Hz): 2.38 (3H, s, 3'-$CH_3$), 3.83 (3H, s, N-$CH_3$), 4.05 (1H, t, H-4, *J* = 9.0), 4.29 (1H, t, H-4 ', *J* = 9.8), 4.95 (1H, s, $NH_{imid}$), 5.43 (1H, dd, 5-H, *J* = 8.6, *J* = 9.7), 7.09-7.14 (2H, m, Ar), 7.25-7.32 (2H, m, Ar), 7.38 (2H, t, Ph, *J* = 7.8), 7.56 (1H, d, Ar, *J* =

7.8), 7.60 (1H, d, Ar, *J* = 8.1). Mass spectrum of high resolution. Found: m/z $[M + H]^+$ 306.3822. Calculated: 306.3817 $C_{19}H_{19}N_3O$

**Determination of cytotoxicity and anti-inflammatory action for compounds 1a-f**

Nutrient medium DMEM, L-glutamine, penicillin, streptamycin, amphotericin B, MTT, trypsin solution in EDTA, Earl solution, glucose, Versen solution from Paneko, Russia. DMSO, lipopolysaccharide, sulfonamide, naphthylethylenediamine and TritonX-100 from Sigma-Aldrich, USA. Isopropyl alcohol and HCl company Himmed, Russia. Fetal cow serum from BioSera, France.

The experiments were performed on cells of mouse microglia of the BV-2 line (CVCL_0182) and human neuroblastoma of the SH-SY5Y line (ATCCCRL-2266). Cells were cultured in DMEM supplemented with 4 mML-glutamine, 10% fetal bovine serum, 100 units / ml penicillin, 100 μg $ml^{-1}$ streptamycin and 2.5 μg $ml^{-1}$ amphotericin B. All cell lines were cultured at 37 °C and 5% $CO_2$.

To assess cytotoxicity, cells were scattered at a density of 15 thousand per well in 96-well plates on the eve of addition of substances. Stock solutions of substances were prepared in DMSO and added to the cells in triplicate as a solution in a culture medium without removing the old culture medium, so that the final solution contained 50% conditioned medium and not more than 0.5% DMSO. The control contained only DMSO, the positive control - 0.5% TritonX-100. Cells were incubated with substances for 24 hours. Cell viability was evaluated using the MTT test. For this, the medium was removed and replaced with a 0.5 mg / ml MTT solution in Earle solution with the addition of 1 g $dm^{-3}$ D-glucose and incubated for 1.5 h in a $CO_2$ incubator. After that, an equal volume of 0.04 *M* HCl in isopropanol was added to the wells and incubated with stirring at 37 °C for 30 min. The optical density of the solution was evaluated at wavelengths of 594 and 620 nm using an Efos 9304 apparatus (MZ Sapphire, Russia). Each experiment was repeated at least two times.

To evaluate the anti-inflammatory effect, on the eve of the experiment, the cells were plated in a 96-well plate with a density of 15 thousand per well. Inflammation was induced by 1 μg $ml^{-1}$ bacterial lipopolysaccharide (LPS), added simultaneously with the substances. Substances were dissolved in DMSO and added as a DMSO solution in cell culture medium (final concentration of DMSO 0.5% by volume); fresh medium (100 μl) with substances and LPS was added to old medium (100 μl) in the wells. Cells were incubated with substances for 18 h, after which the inflammatory response was assessed by the accumulation in the medium of the product of the metabolism of nitric oxide $NO_2$. The concentration of nitrite anion was measured by the Gris method. To do this, an aqueous solution of 0.04% sulfanilamide (12.5 μl) was added to the analyzed mixture (75 μl), kept at room temperature for 10 min with protection from light, then 2% solution of naphthylethylenediamine in 3M HCl (12.5 μl) was added, kept for another 10 min at room temperature with protection from light, after which the optical absorption was determined at a wavelength of 540 nm. As a control, samples were only with culture medium and with culture medium supplemented with LPS.

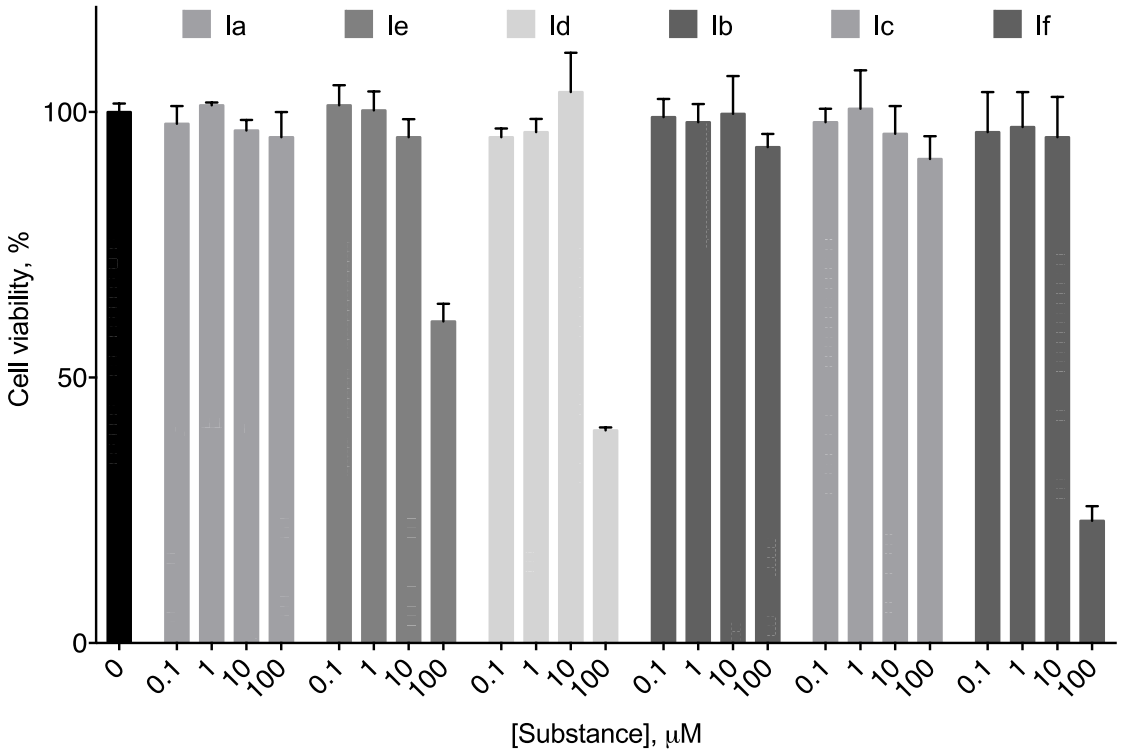



**Figure S1.** The results of determining the toxicity of compounds **1a-f** on cells of human neuroblastoma SH-SY5Y (24 hours incubation), MTT test, mean ± standard deviation (N = 3 experiments).

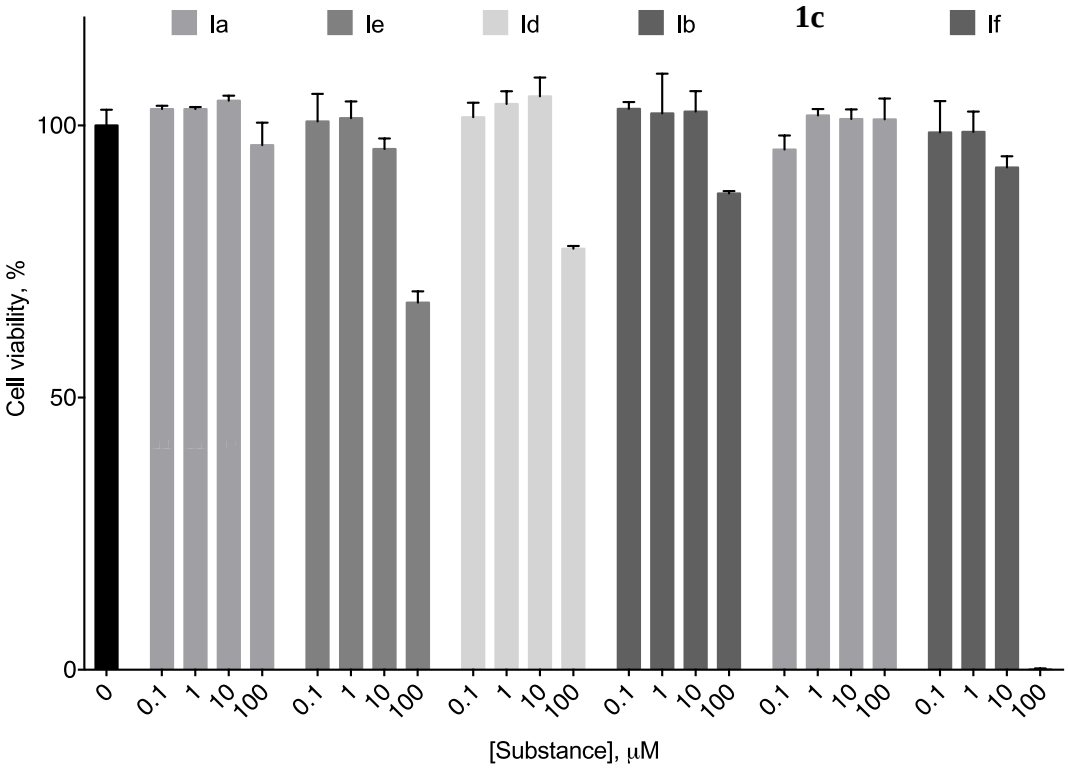



**Figure S2.** The results of determining the toxicity of compounds **1a-f** on cells of mouse microglia of the BV-2 line (24 hours), MTT test, mean ± standard deviation (N = 3 experiments).

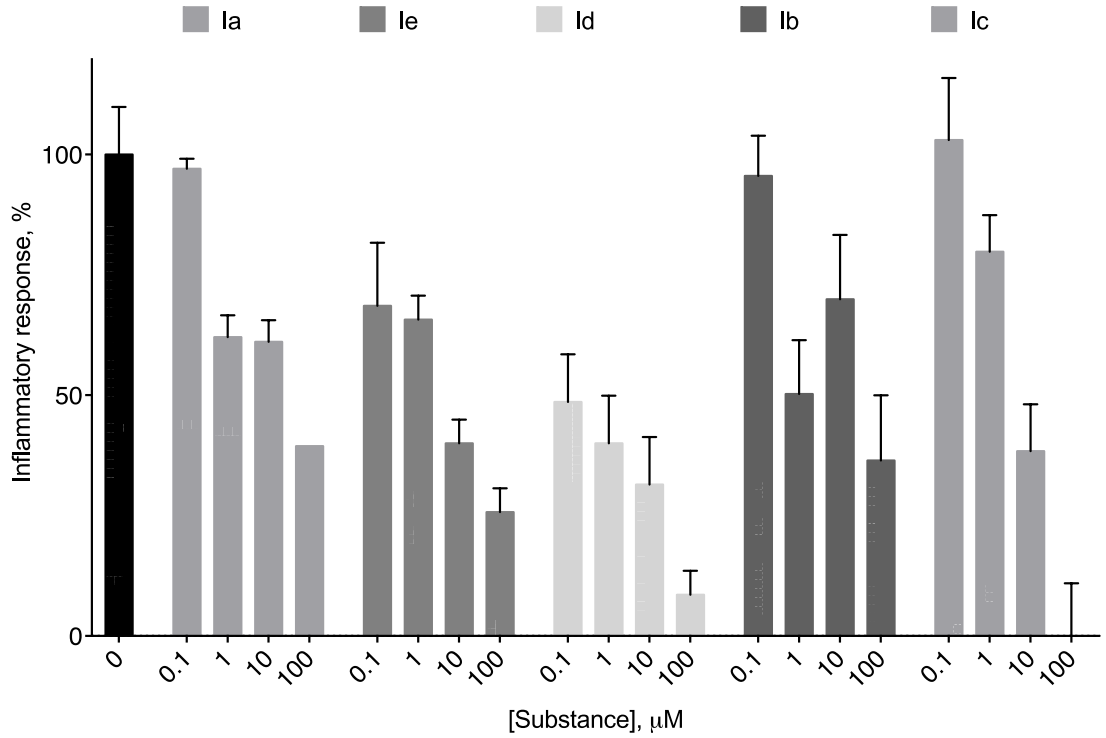
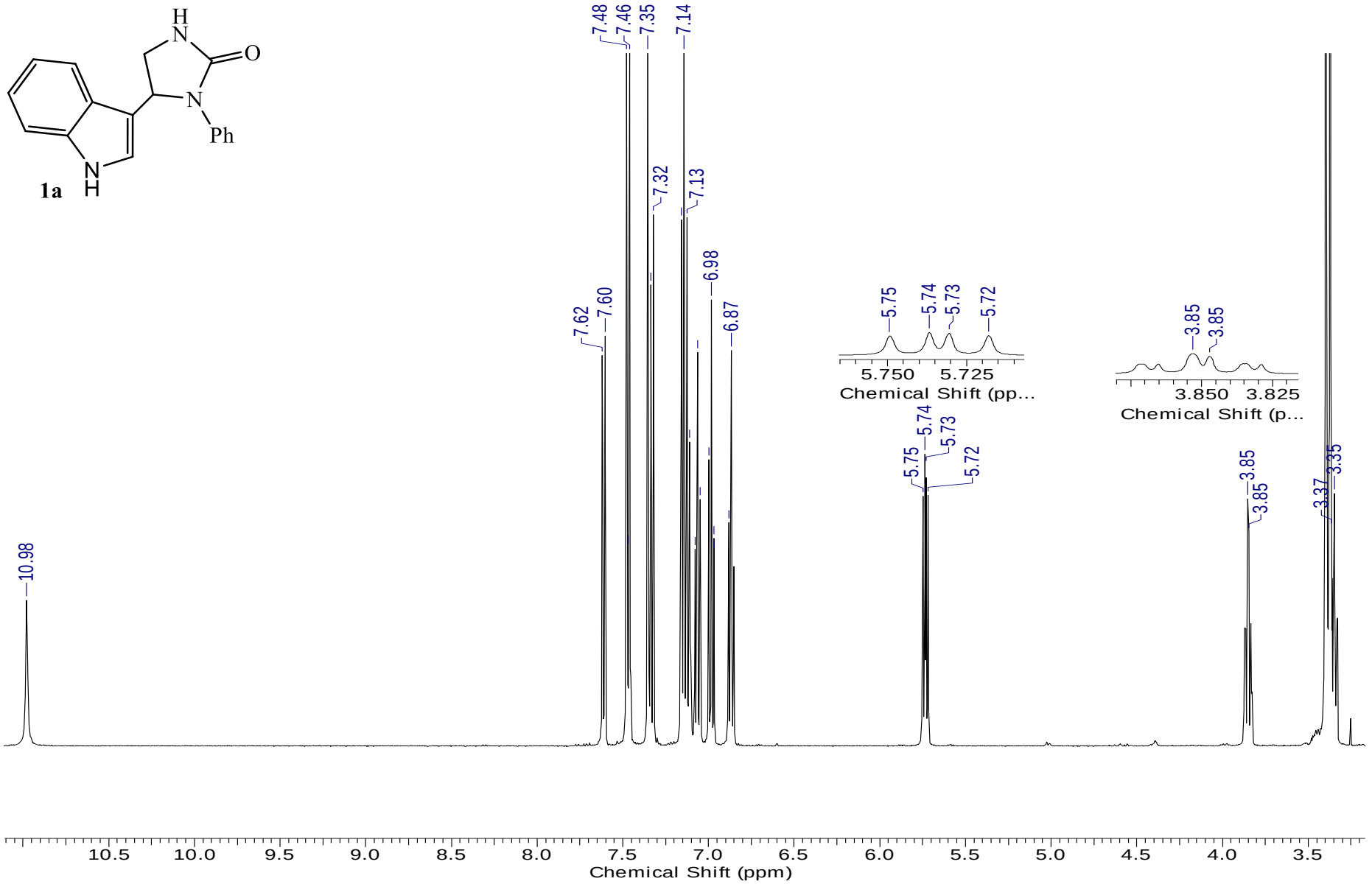



**Figure S3.** Results of the anti-inflammatory effect of compounds **1a-f** on a BV-2 cell line treated with 1 μg $ml^{-1}$ bacterial lipopolysaccharide, 18 hr incubation, Gris reaction, mean ± standard deviation (N = 3 experiments).

**X-ray diffraction**

Crystals of **1a** ($C_{17}H_{15}N_3O$, M = 277.32) are monoclinic, space group *C* 2/*c*, at 120 K: *a* = 31.1999(15) Å, *b* = 9.6008(5) Å, *c* = 18.1218(9) Å, β = 90.234(2)°, *V* = 5428.2(5) $Å^3$, Z = 16 (Z' = 2), $d_{calc}$ = 1.357 g $cm^{-3}$, μ(CuKα) = 6.96 $cm^{-1}$, F(000) = 2336. Crystals of **1f** ($C_{26}H_{27}N_3O_2$, M = 413.50) are triclinic, space group *P -1*, at 120 K: *a* = 10.3813(13) Å, *b* = 10.4643(14) Å, *c* = 10.9767(14) Å, α = 69.775(3)°, β = 77.091(3)°, γ = 88.883(3)°, *V* = 1088.5(2) $Å^3$, Z = 2 (Z' = 1), $d_{calc}$ = 1.262 g $cm^{-3}$, μ(MoKα) = 0.81 $cm^{-1}$, F(000) = 440. Intensities of 38005 and 15081 reflections were measured for **1a** and **1f** with a Bruker APEX2 DUO CCD diffractometer using graphite monochromated Cu-Kα (λ = 0.71073 Å, ω-scans, 2θ<68°) and Mo-Kα (λ = 0.71073 Å, ω-scans, 2θ<58°) radiation, respectively; 4890 and 5778 independent reflections [$R_{int}$ 0.0214 and 0.0657] were used in further refinement. Using Olex2 [O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann, *J. Appl. Cryst.*, 2009, **42**, 339], the structures were solved with the ShelXT structure solution program [G. M. Sheldrick, *Acta Cryst., Sect. A: Found. Crystallogr.*, 2015, **71**, 3] using Intrinsic Phasing and refined against $F^2$ with the SHELXTL PLUS 5.0 refinement package [G. M. Sheldrick, *Acta Cryst., Sect. A: Found. Crystallogr.*, 2008, **64**, 112] using full-matrix least-squares technique. Hydrogen atoms of NH groups in both compounds and those of solvent ethanol molecule in **1f** were found in difference Fourier synthesis. Positions of other hydrogen atoms were calculated, and they all were refined in isotropic approximation in riding model. For **1a**, the refinement converged to wR2 = 0.0803 and GOF = 1.032 for all the independent reflections (R1 = 0.0304 was calculated against F for 4661 observed reflections with I>2σ(I)). For **1f**, the refinement converged to wR2 = 0.1887 and GOF = 1.024 for all the independent reflections (R1 = 0.0687 was calculated against F for 3342 observed reflections with I>2σ(I)). CCDC 1979556 and 1979557 contain the supplementary crystallographic data for **1a** and **1f**.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7.62
7.60
7.48
7.46
7.35
7.32
7.14
7.13
6.98
6.87
5.75
5.74
5.73
5.72
3.85
3.85
3.37
3.35
5.750 5.725
Chemical Shift (pp...
3.850 3.825
Chemical Shift (p...
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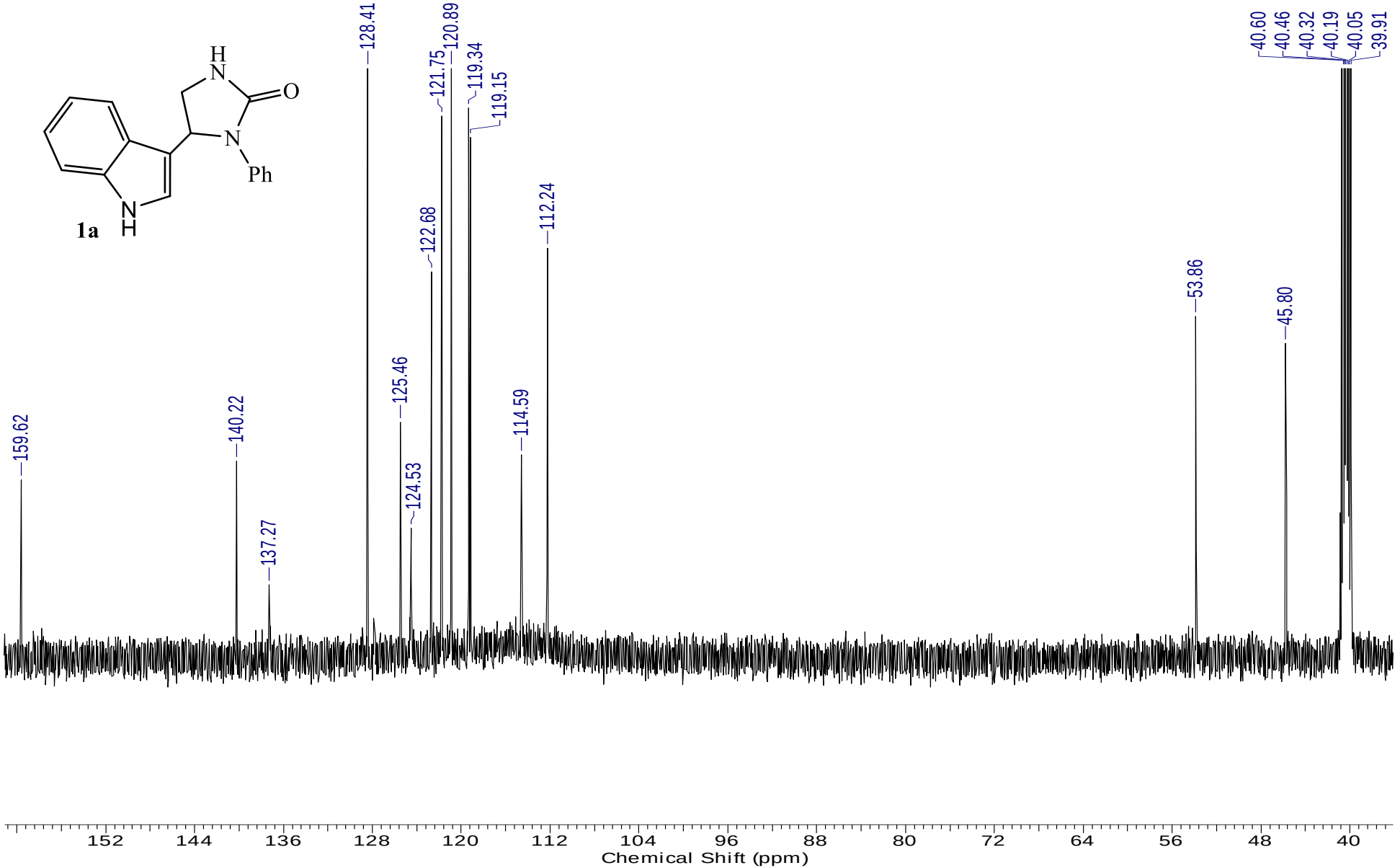
Chemical Shift (ppm)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122.68
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119.34
119.15
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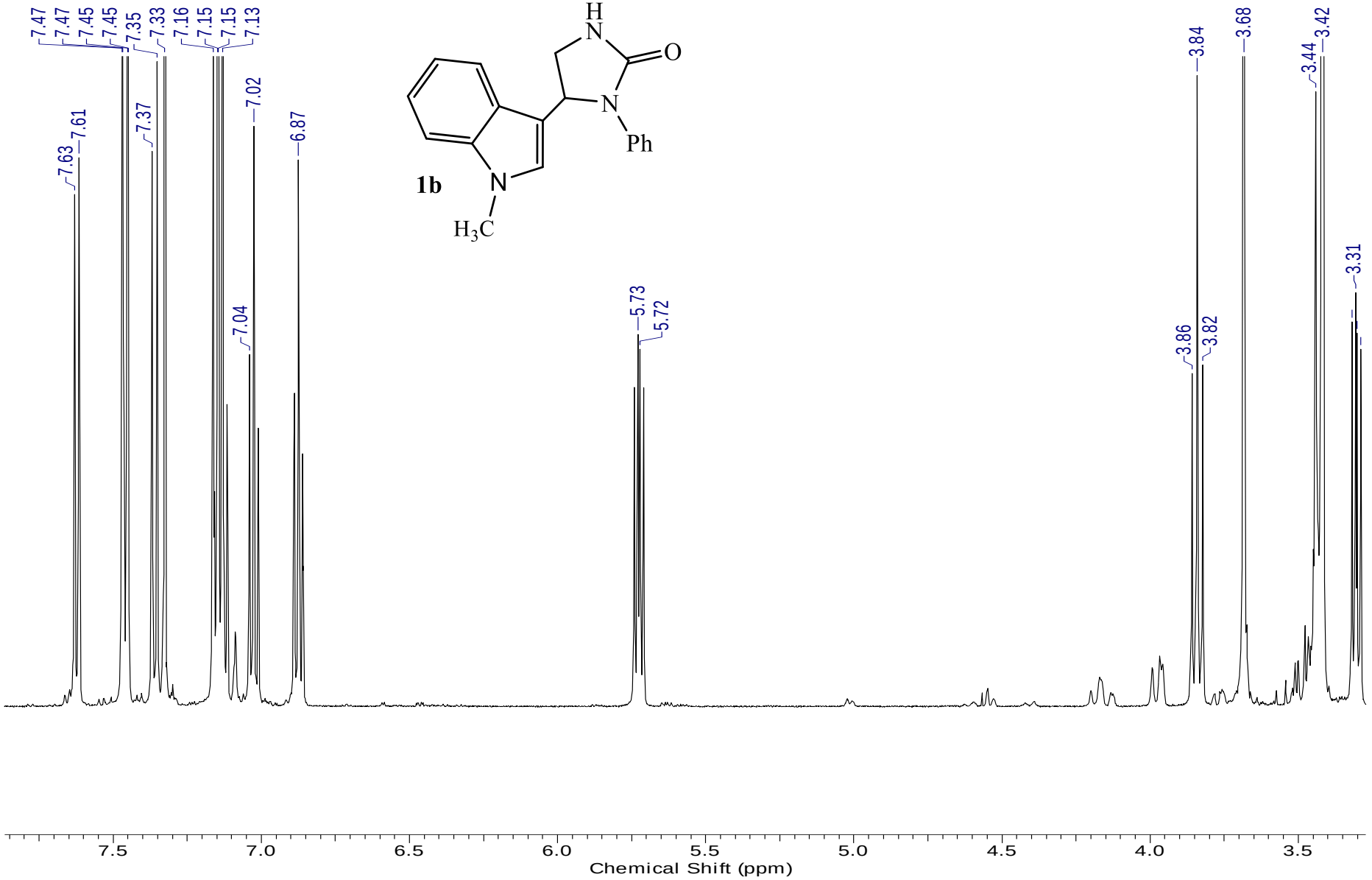
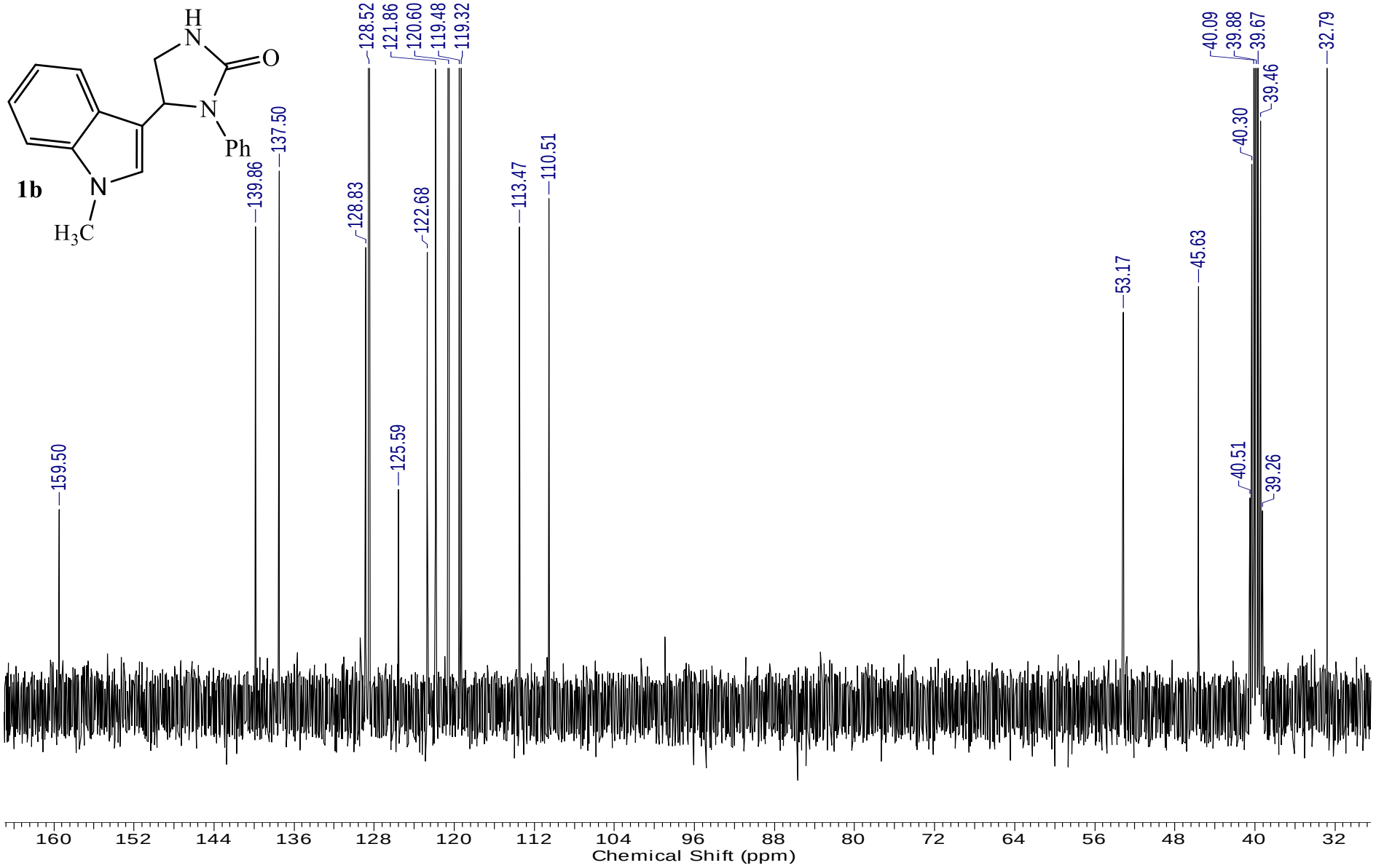
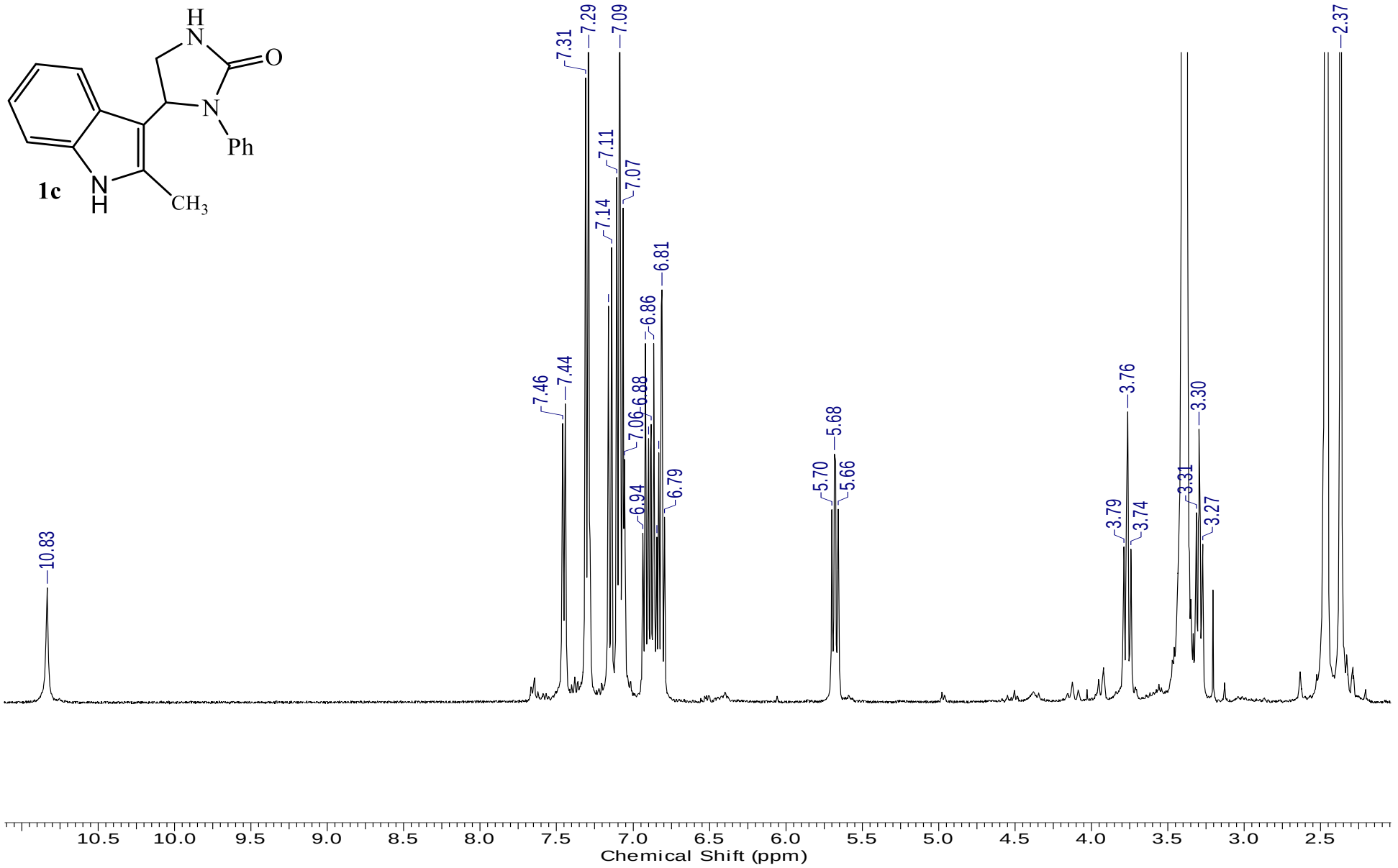
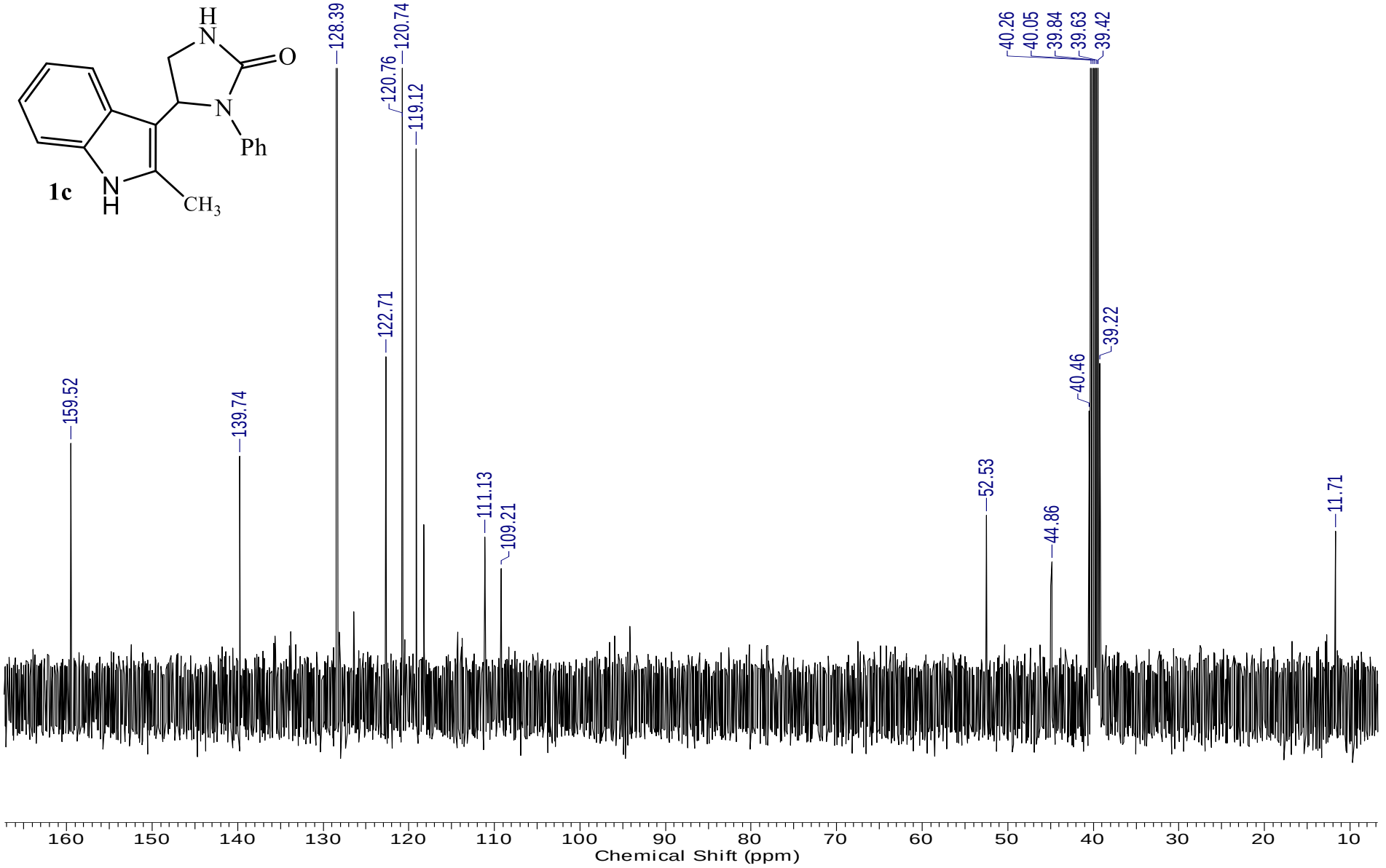
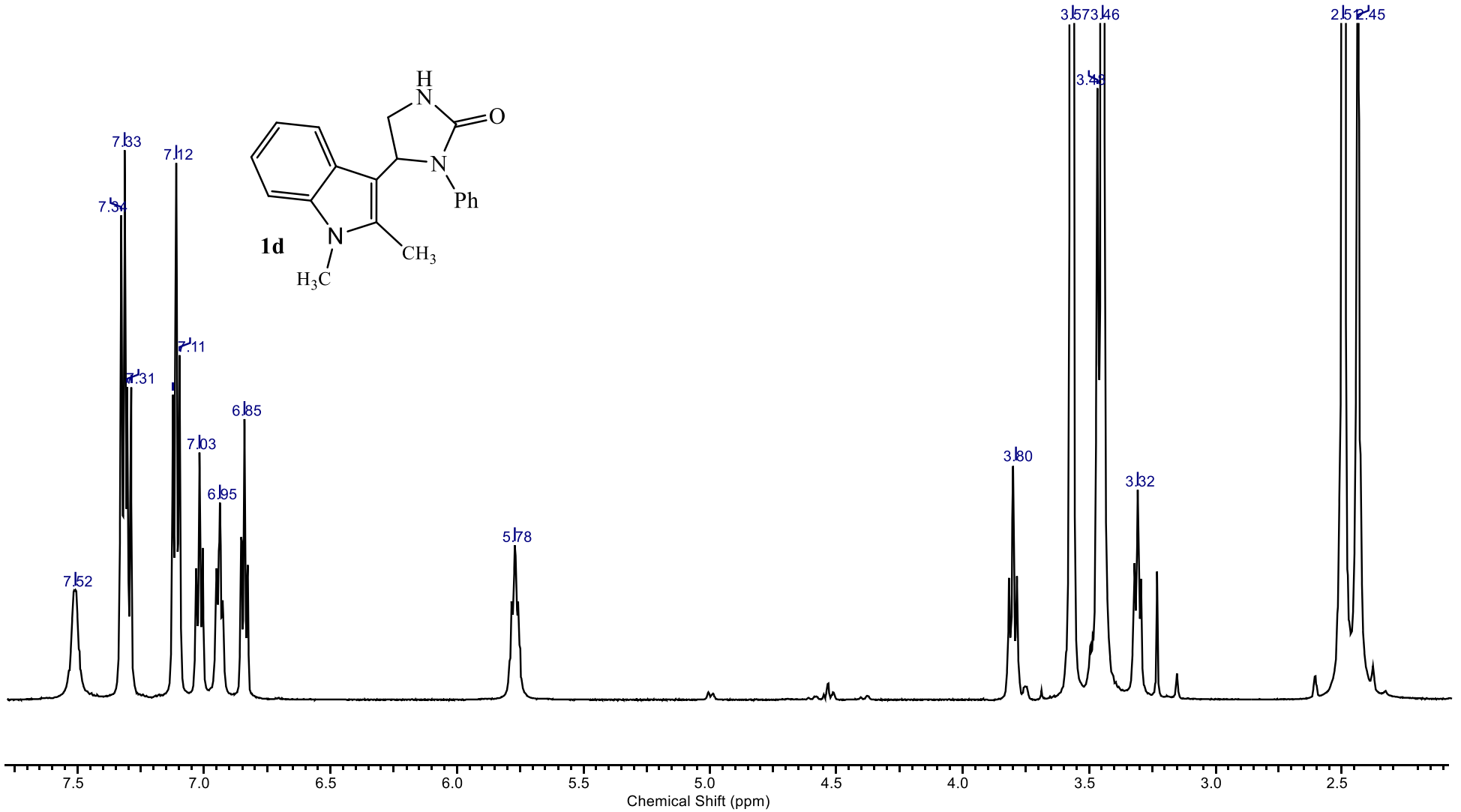
112.24
53.86
45.80
40.60
40.46
40.32
40.19
40.05
39.91
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
Chemical Shift (ppm)

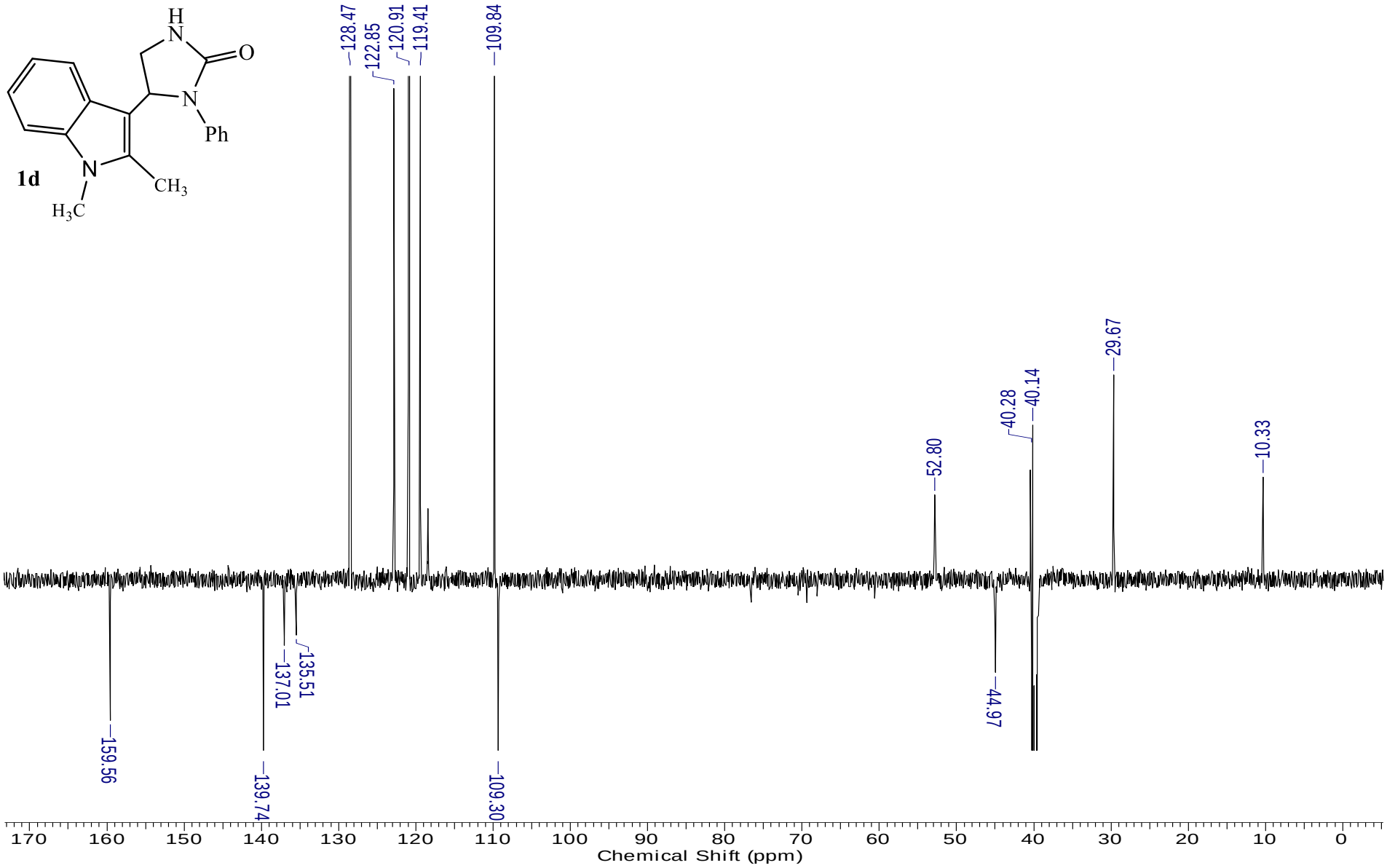

7.47
7.47
7.45
7.45
7.35
7.33
7.16
7.15
7.15
7.13
7.63
7.61
7.37
7.02
6.87
7.04
5.73
5.72
3.84
3.68
3.44
3.42
3.86
3.82
3.31
H
N
O
N
Ph
1b
N
H3C
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
Chemical Shift (ppm)

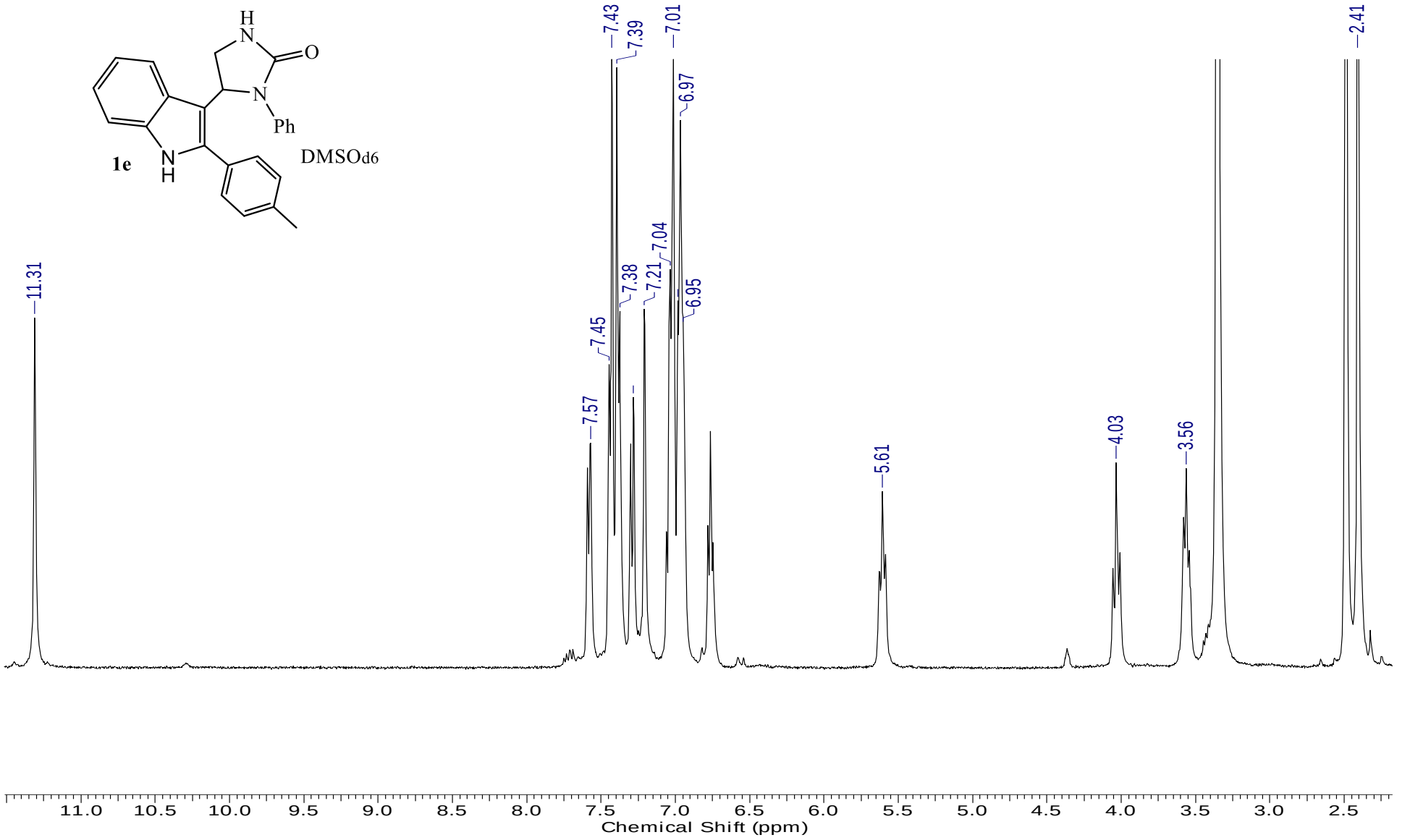

1b
H
N
O
N
Ph
N
H3C
159.50
139.86
137.50
128.83
128.52
125.59
122.68
121.86
120.60
119.48
119.32
113.47
110.51
53.17
45.63
40.51
40.30
40.09
39.88
39.67
39.46
39.26
32.79
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
Chemical Shift (ppm)

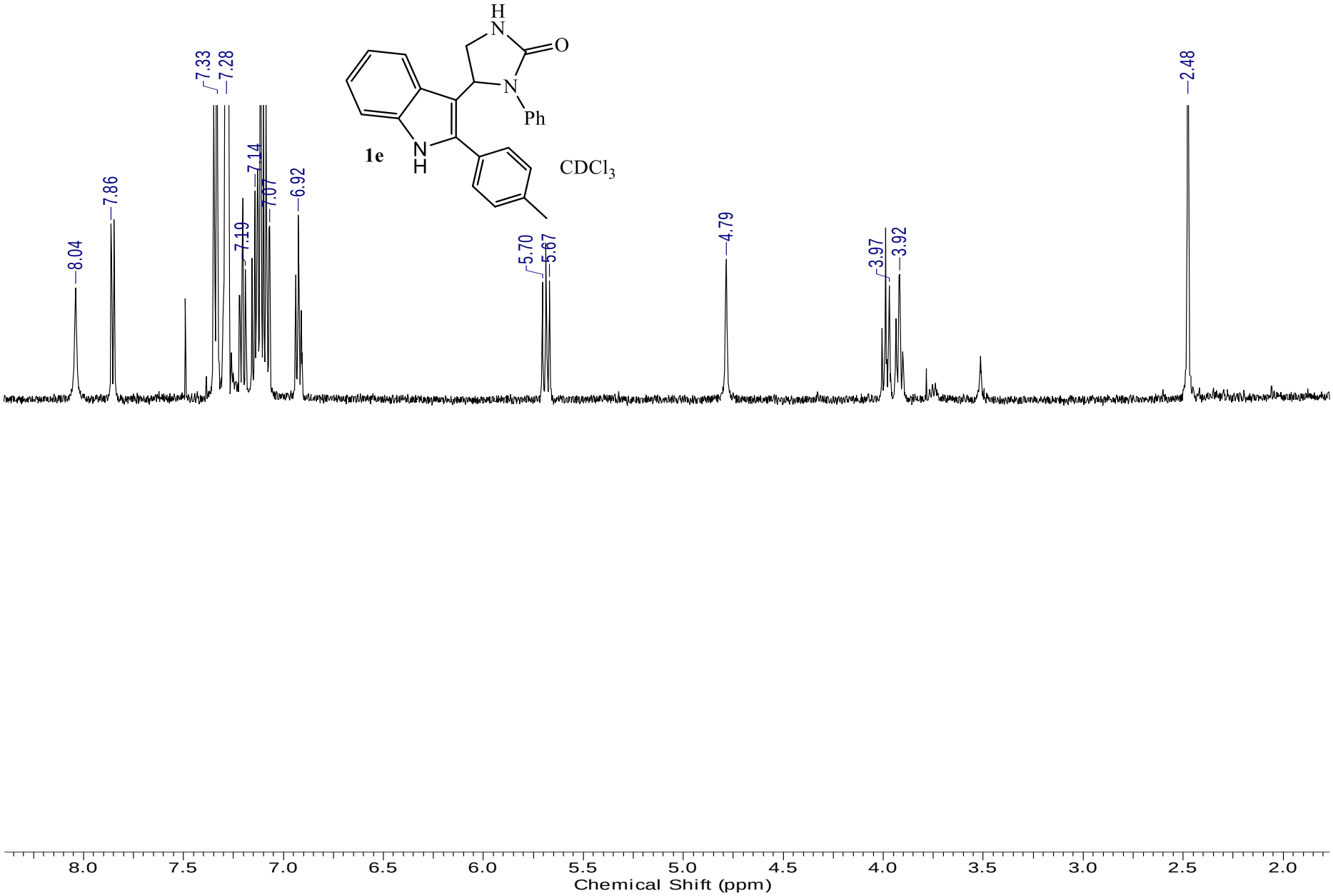

1c
H
N
O
N
Ph
N
H
CH3
10.83
7.46
7.44
7.31
7.29
7.14
7.11
7.09
7.07
7.06
6.94
6.88
6.86
6.81
6.79
5.70
5.68
5.66
3.79
3.76
3.74
3.31
3.30
3.27
2.37
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
Chemical Shift (ppm)

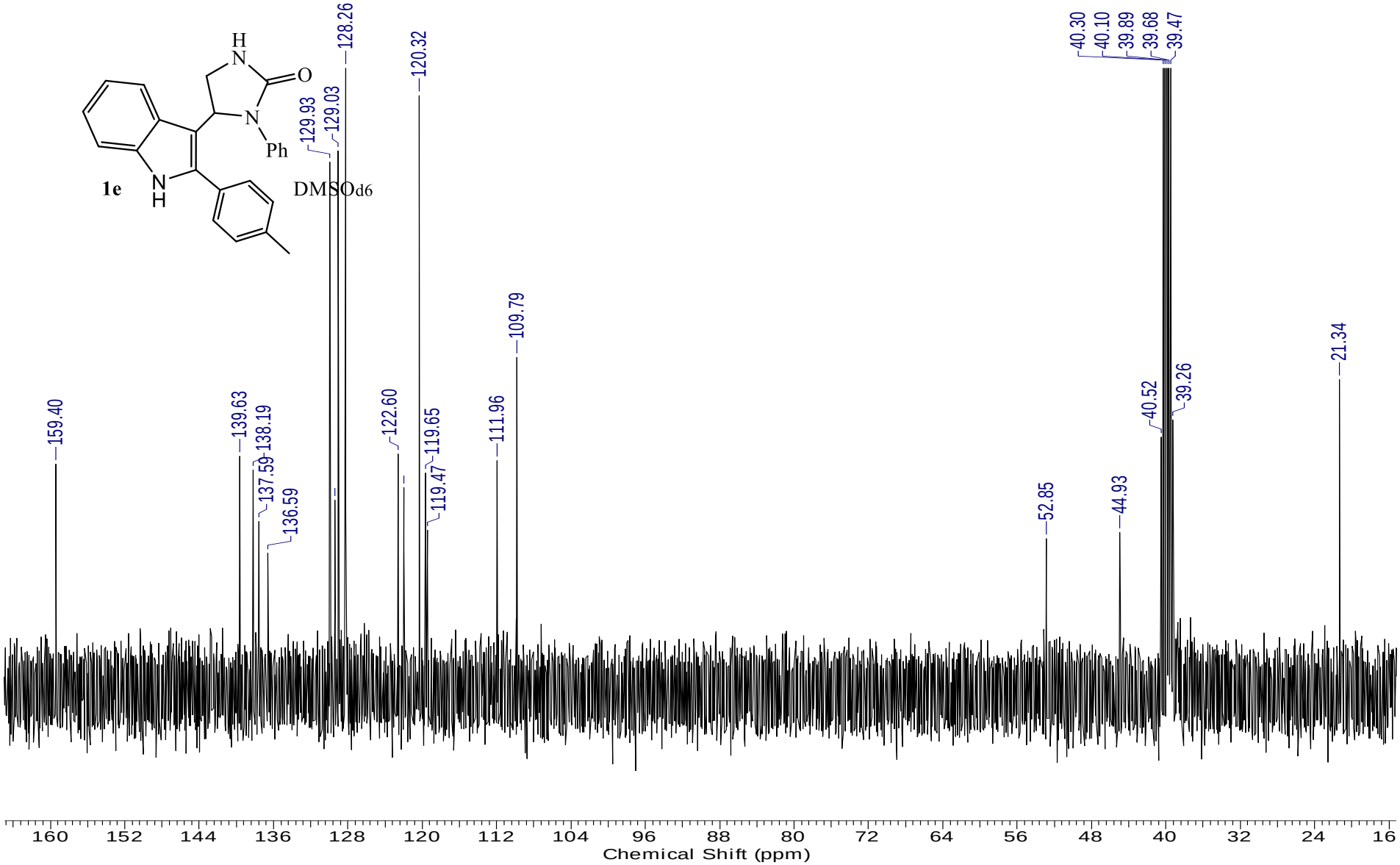

1c
H
N
O
N
Ph
N
H
CH3
159.52
139.74
128.39
122.71
120.76
120.74
119.12
111.13
109.21
52.53
44.86
40.46
40.26
40.05
39.84
39.63
39.42
39.22
11.71
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
Chemical Shift (ppm)

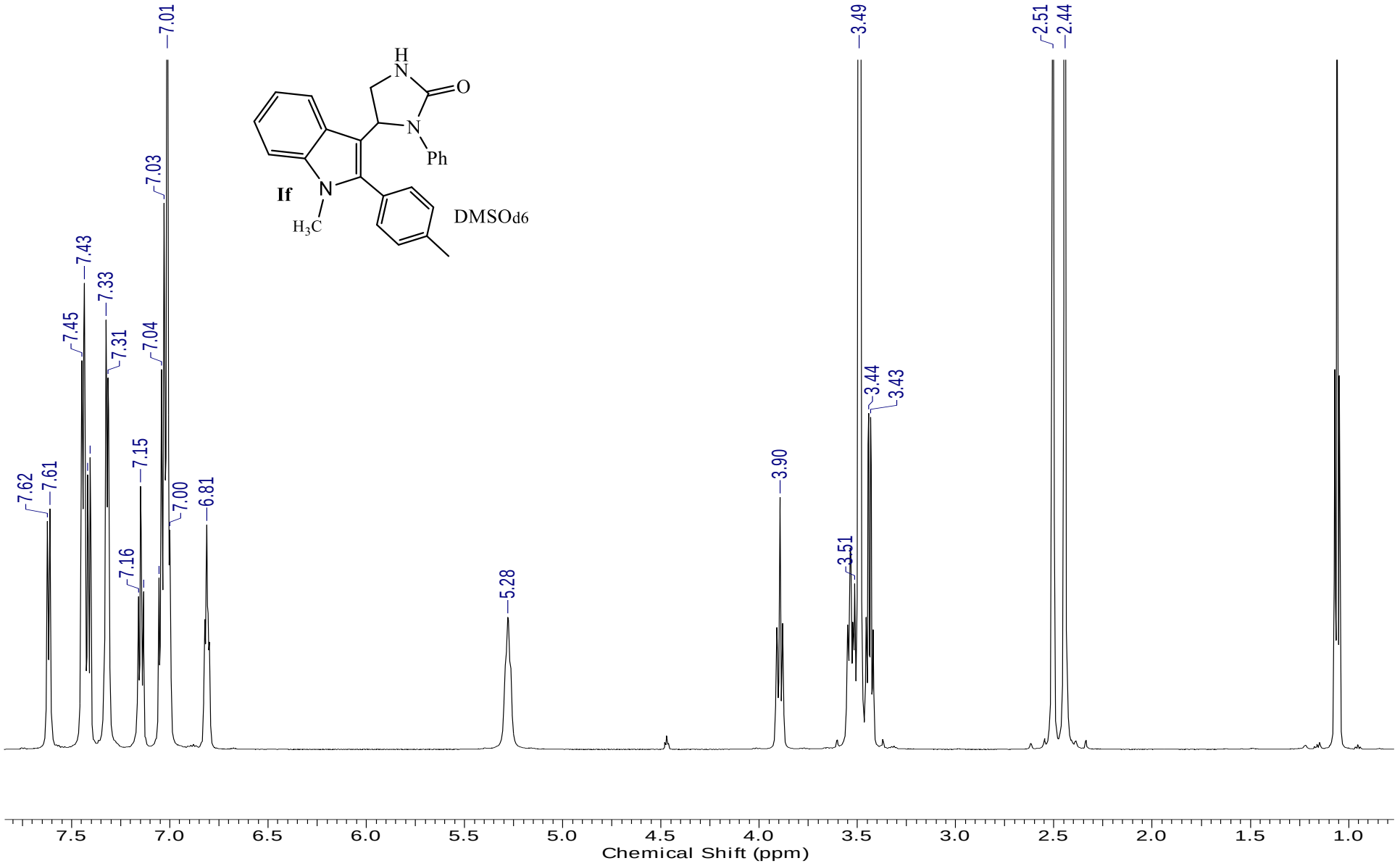

1d
Chemical Shift (ppm)

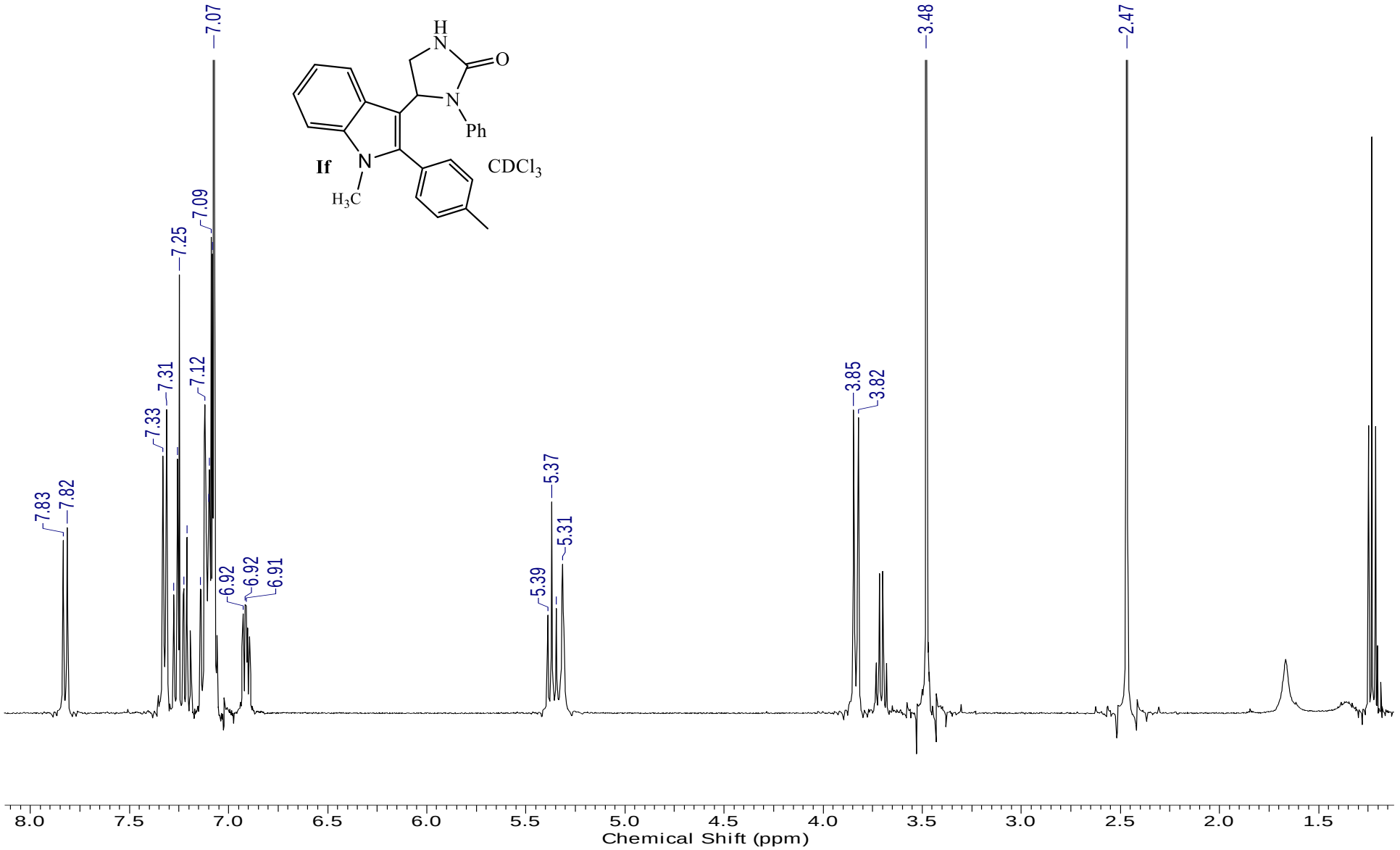

1d
H
N
O
N
Ph
N
CH3
H3C
128.47
122.85
120.91
119.41
109.84
52.80
40.28
40.14
29.67
10.33
159.56
139.74
137.01
135.51
109.30
44.97
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)

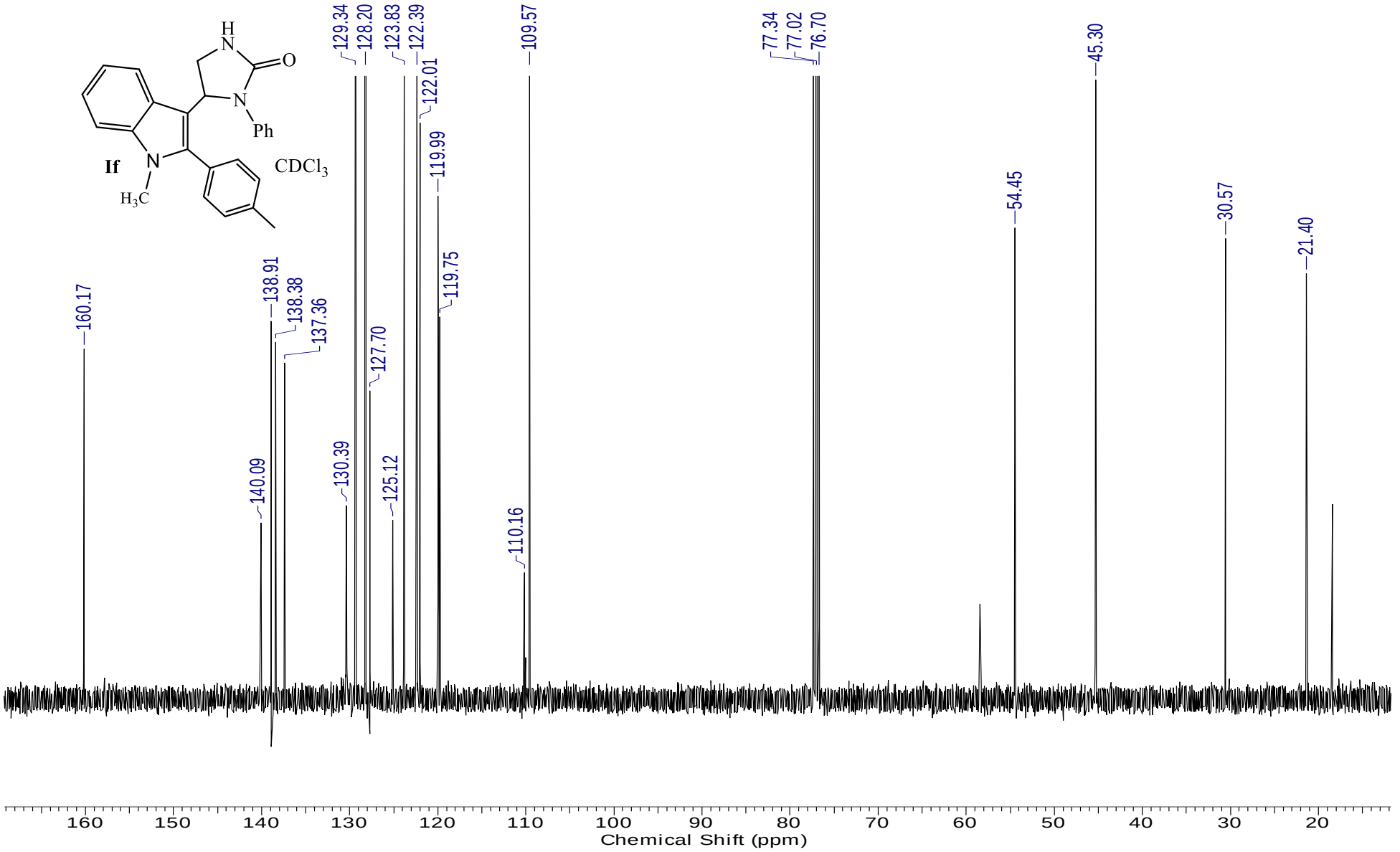

1e
DMSOd6
11.31
7.57
7.45
7.43
7.39
7.38
7.21
7.04
7.01
6.97
6.95
5.61
4.03
3.56
2.41
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
Chemical Shift (ppm)

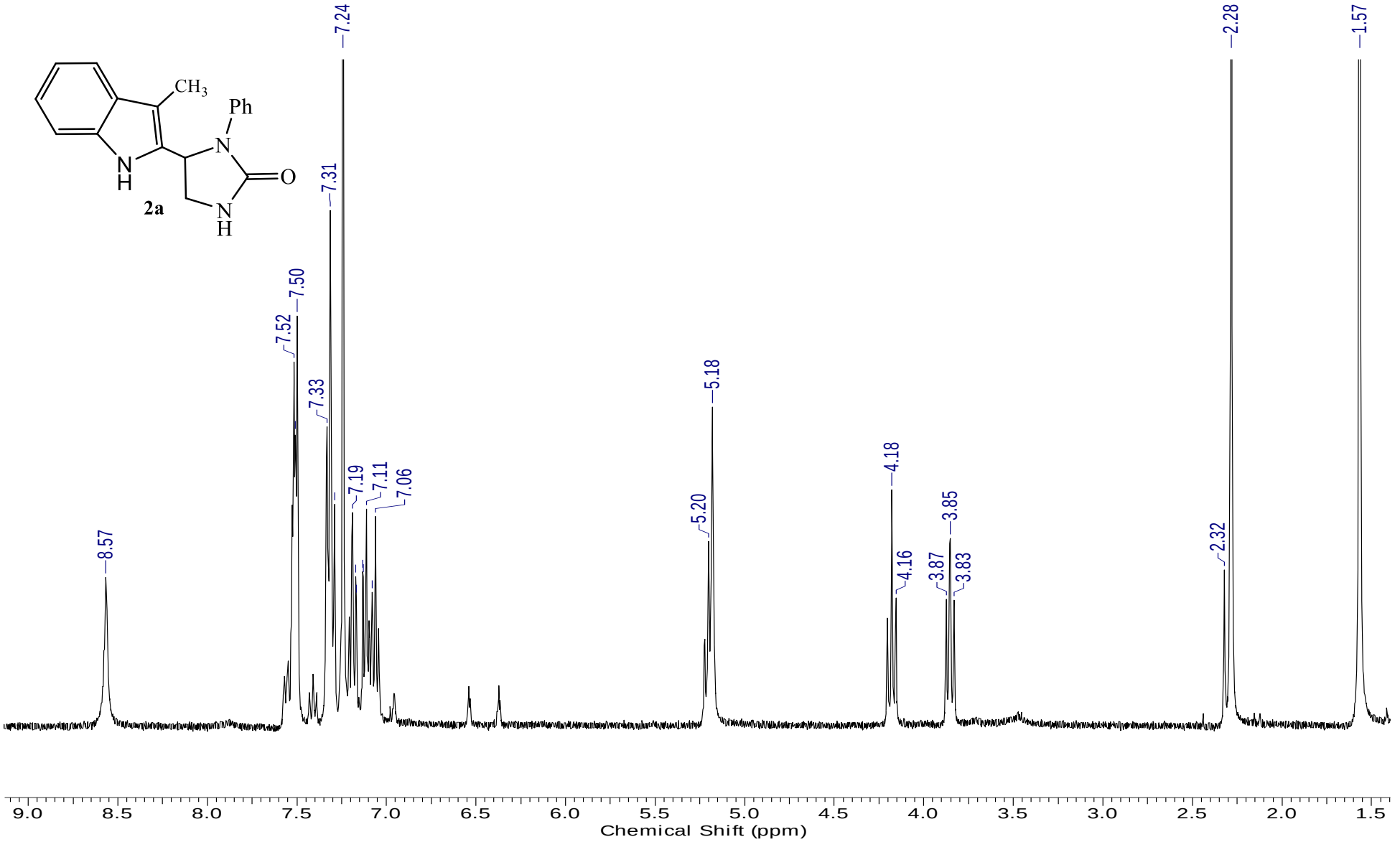

H
N
O
N
Ph
N
H
1e
CDCl3
8.04
7.86
7.33
7.28
7.19
7.14
7.07
6.92
5.70
5.67
4.79
3.97
3.92
2.48
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
Chemical Shift (ppm)

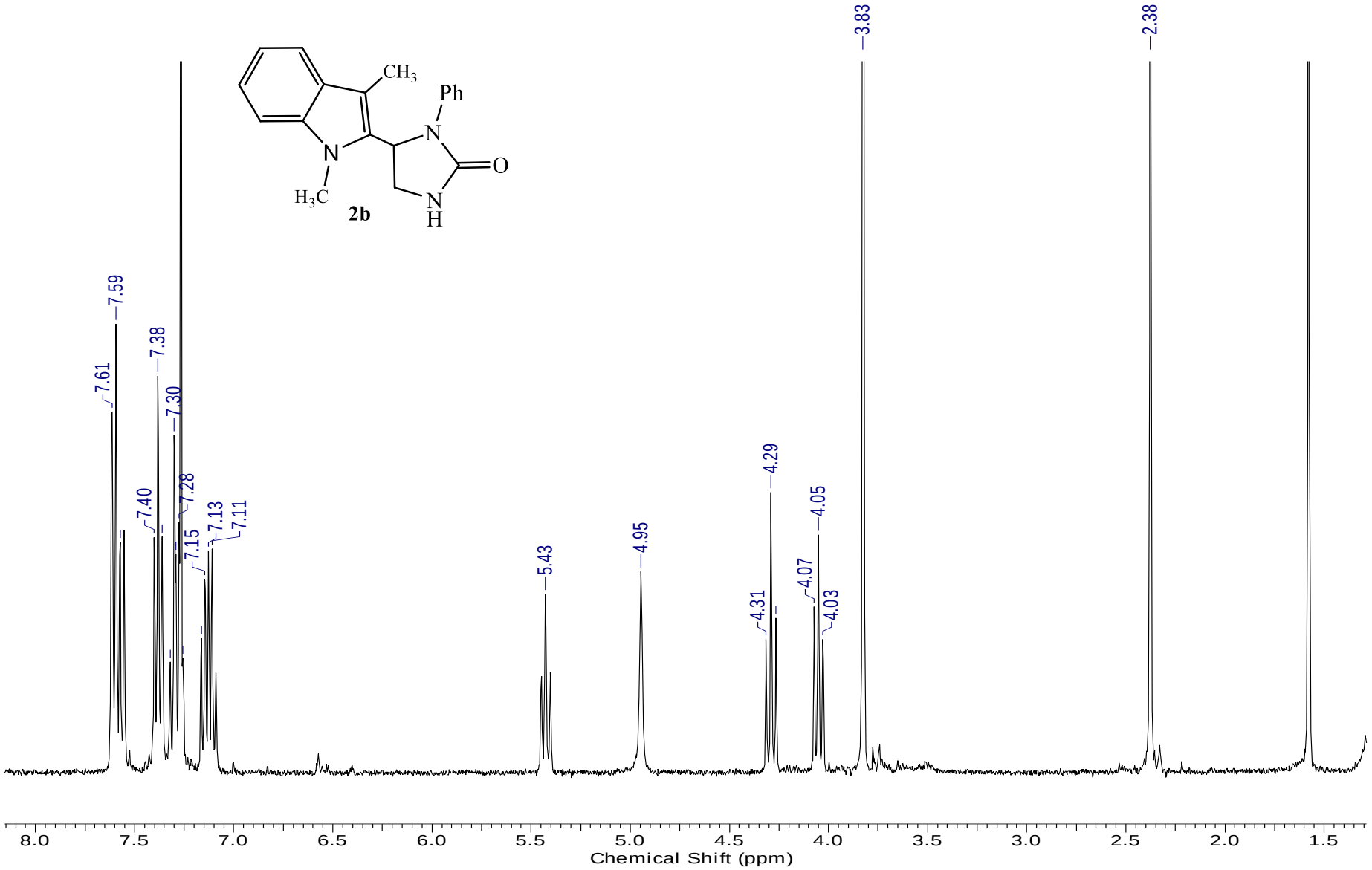

1e
DMSOd6
159.40
139.63
138.19
137.59
136.59
128.26
129.93
129.03
122.60
120.32
119.65
119.47
111.96
109.79
52.85
44.93
40.52
40.30
40.10
39.89
39.68
39.47
39.26
21.34
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)


7.01
7.03
7.43
7.45
7.33
7.31
7.04
7.15
7.62
7.61
7.00
6.81
7.16
5.28
3.90
3.49
3.51
3.44
3.43
2.51
2.44
If
DMSOd6
Chemical Shift (ppm)


7.83
7.82
7.33
7.31
7.25
7.09
7.07
7.12
6.92
6.92
6.91
5.39
5.37
5.31
3.85
3.82
3.48
2.47
H
N
O
N
Ph
If
N
H3C
CDCl3
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
Chemical Shift (ppm)


H
N
O
N
Ph
If
N
$H_3C$
$CDCl_3$
160.17
140.09
138.91
138.38
137.36
130.39
129.34
128.20
127.70
125.12
123.83
122.39
122.01
119.99
119.75
110.16
109.57
77.34
77.02
76.70
54.45
45.30
30.57
21.40
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
Chemical Shift (ppm)


CH3
Ph
N
N
H
O
N
H
2a
8.57
7.52
7.50
7.33
7.24
7.31
7.19
7.11
7.06
5.20
5.18
4.18
4.16
3.87
3.85
3.83
2.32
2.28
1.57
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
Chemical Shift (ppm)


CH3
Ph
N
N
O
H3C
N
H
2b
7.61
7.59
7.40
7.38
7.30
7.28
7.15
7.13
7.11
5.43
4.95
4.31
4.29
4.07
4.05
4.03
3.83
2.38
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
Chemical Shift (ppm)