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Supplementary Information

C-H Activation Enables a Rapid Structure-Activity Relationship Study of Arylcyclopropyl Amines for Potent and Selective LSD1 Inhibitors

Shin Miyamura,[a] Misaho Araki,[a] Yosuke Ota,[b] Yukihiro Itoh,[b] Shusuke Yasuda,[b] Mitsuharu Masuda,[b] Tomoyuki Taniguchi,[b] Yoshihiro Sowa,[b] Toshiyuki Sakai,[b,c] Takayoshi Suzuki,*[,b,c] Kenichiro Itami,*[,a, d] and Junichiro Yamaguchi*[e ¶]

[a]*Institute of Transformative Bio-Molecules (WPI-ITbM) and Graduate School of Science, Nagoya University, Chikusa, Nagoya, 464-8602, Japan*

[b]*Graduate School of Medical Science, Kyoto Prefectural University of Medicine, 1-5 Shimogamo-hangi-Cho, Sakyo-ku, Kyoto, 603-0823, Japan*

[c]*CREST, Japan Science and Technology Agency (JST), 4-1-8 Honcho Kawaguchi, Saitama 332-0012, Japan*

[d]*JST, ERATO, Itami Molecular Nanocarbon Project, Nagoya University, Chikusa, Nagoya 464-8602, Japan*

[e]*Department of Applied Chemistry, Waseda University 3-4-1 Ohkubo, Shinjuku, Tokyo 169-8555, Japan.*

E-mail: *suzukit@koto.kpu-m.ac.jp, itami@chem.nagoya-u.ac.jp, junyamaguchi@waseda.jp*

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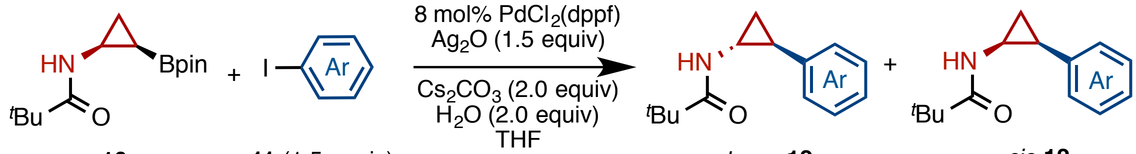
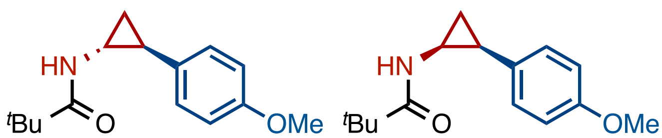
1. Suzuki–Miyaura Coupling of Boronate 10



General Procedure: A mixture of boronate **10** (1.0 equiv), aryl iodide **11** (1.5 equiv), $PdCl_2(dppf)\cdot CH_2Cl_2$ (8.0 mol%), Ag_2O (1.5 equiv), Cs_2CO_3 (2.0 equiv), water (2.0 equiv) in THF (0.1 M) was put into a 20-mL glass vessel tube equipped with J. Young® O-ring tap containing a stir bar. The mixture was heated at 70 °C for 6 h in a heating block under the indicated atmosphere. After cooling to room temperature, the mixture was diluted with ethyl acetate. The insolubles were filtered off through Celite® and the filtrate was concentrated *in vacuo*. The resultant residue was purified by flash column chromatography or MPLC to afford both coupling products *trans*-**12** and *cis*-**12**. PTLC was also carried out as a further purification if needed.

trans-**12a** *cis*-**12a**

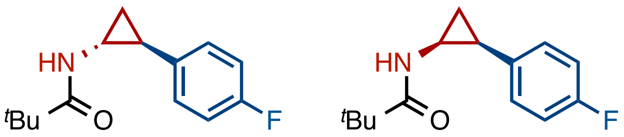
***trans*-*N*-(2-Phenylcyclopropyl)pivalamide (*trans*-12a) and *cis*-*N*-(2-phenylcyclopropyl)pivalamide (*cis*-12a):** Boronate **10** (50.0 mg, 0.19 mmol) was used. Purification was performed by MPLC (hexane/ethyl acetate = 3:1 to 3:7) to afford *trans*-**12a** as a white solid (21.7 mg, 53% yield) and *cis*-**12a** as a white solid (7.1 mg, 18% yield). *trans*-**12a**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28–7.25 (m, 2H), 7.19–7.16 (m, 3H), 5.85 (brs, 1H), 2.88–2.85 (m, 1H), 2.02 (ddd, J = 9.6, 6.0, 3.6 Hz, 1H), 1.24 (dt, J = 7.2, 6.0 Hz, 1H), 1.20 (s, 9H), 1.12 (ddd, J = 10.8, 6.0, 4.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.6, 140.5, 128.3, 126.6, 126.1, 38.5, 32.1, 27.5, 24.8, 16.1; HRMS (ESI) *m/z* calcd for $C_{14}H_{20}NO$ $[M+H]^+$: 218.1539 found 218.1531. *cis*-**12a**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (t, J = 7.8 Hz, 2H), 7.23–7.19 (m, 3H), 5.20 (brs, 1H), 3.10 (m, 1H), 2.34 (q, J = 7.8 Hz, 1H), 1.35 (ddd, J = 9.0, 7.8, 6.6 Hz, 1H), 1.01 (td, J = 6.6, 4.8 Hz, 1H), 0.93 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.5, 136.3, 128.9, 128.3, 126.6, 38.5, 28.2, 27.2, 21.8, 11.5; HRMS (ESI) *m/z* calcd for $C_{14}H_{20}NO$ $[M+H]^+$: 218.1539 found 218.1534.



trans-**12b** *cis*-**12b**

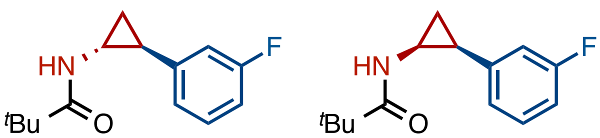
***trans*-*N*-(2-(4-Methoxyphenyl)cyclopropyl)pivalamide (*trans*-12b) and**

***cis*-*N*-(2-(4-methoxyphenyl)cyclopropyl)pivalamide (*cis*-12b):** Boronate **10** (50.0 mg, 0.19 mmol) was used. Purification was performed by MPLC (hexane/ethyl acetate = 3:1 to 1:3) to afford *trans*-**12b** as a white solid (17.9 mg, 41% yield) and *cis*-**12b** as a yellow solid (14.0 mg, 30% yield). *trans*-**12b**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.4 Hz, 2H), 6.81 (d, *J* = 8.4 Hz, 2H), 5.88 (brs, 1H), 3.77 (s, 3H), 2.80–2.76 (m, 1H), 1.97 (ddd, *J* = 9.6, 6.6, 3.6 Hz, 1H), 1.20 (s, 9H), 1.17 (dt, *J* = 7.8, 6.0 Hz, 1H), 1.05 (ddd, *J* = 9.6, 6.0, 4.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.6, 158.0, 132.5, 128.0, 113,7, 55.3, 38.5, 31.7, 27.5, 24.2, 15.6; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{22}NO_2$ $[M+H]^+$: 248.1645 found 248.1638. *cis*-**12b**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 5.18 (brs, 1H), 3.80 (s, 3H), 3.08–3.04 (m, 1H), 2.27 (q, *J* = 7.8 Hz, 1H), 1.32 (ddd, *J* = 9.0, 7.8, 6.6 Hz, 1H), 0.95 (s, 9H), 0.91 (td, *J* = 6.6, 4.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.5, 158.3, 130.0, 128.2, 113.7, 55.3, 38.4, 27.9, 27.3, 20.9, 11.5; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{22}NO_2$ $[M+H]^+$: 248.1645 found 248.1636.



trans-**12c** *cis*-**12c**

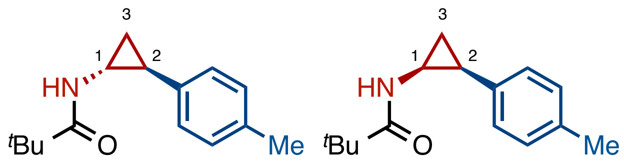
***trans*-*N*-(2-(4-Fluorophenyl)cyclopropyl)pivalamide (*trans*-12c) and *cis*-*N*-(2-(4-fluorophenyl)cyclopropyl)pivalamide (*cis*-12c):** Boronate **10** (150.0 mg, 0.19 mmol) was used. Purification was performed by MPLC (hexane/ethyl acetate = 4:1 to 1:3) to afford *trans*-**12c** as a white solid (35.3 mg, 27% yield) and *cis*-**12c** as a white solid (55.4 mg, 42% yield). *trans*-**12c**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21–7.18 (m, 2H), 6.97–6.93 (m, 2H), 5.90 (brs, 1H), 2.79–2.76 (m, 1H), 1.99 (ddd, *J* = 9.6, 6.0, 3.6 Hz, 1H), 1.20 (s, 9H), 1.18 (dt, *J* = 7.8, 6.0 Hz, 1H), 1.10 (ddd, *J* = 9.6, 6.0, 4.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.8, 161.4 (d, J_{CF} = 246.3 Hz), 136.1, 128.5 (d, J_{CF} = 8.7 Hz), 115.0 (d, J_{CF} = 21.6 Hz), 38.5, 31.8, 27.5, 24.4, 15.4; HRMS (DART) *m*/*z* calcd for $C_{14}H_{19}FNO$ $[M+H]^+$: 236.1445 found 236.1455. *cis*-**12c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19–7.15 (m, 2H), 7.02–6.96 (m, 2H), 5.20 (brs, 1H), 3.11–3.04 (m, 1H), 2.30 (q, *J* = 7.6 Hz, 1H), 1.35 (ddd, *J* = 8.8, 7.6, 6.4 Hz, 1H), 0.98–0.92 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.5, 161.6 (d, J_{CF} = 243.4 Hz), 132.1 (d, J_{CF} = 3.0 Hz), 130.5 (d, J_{CF} = 11.7 Hz), 114.9 (d, J_{CF} = 21.2 Hz), 38.4, 28.2, 27.2, 21.3, 11.3; HRMS (DART) *m*/*z* calcd for $C_{14}H_{19}FNO$ $[M+H]^+$: 236.1445 found 236.1448.



trans-**12d** *cis*-**12d**

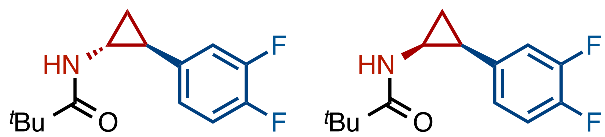
***trans*-*N*-(2-(3-Fluorophenyl)cyclopropyl)pivalamide (*trans*-12d) and *cis*-*N*-(2-(3-fluorophenyl)cyclopropyl)pivalamide (*cis*-12d):** Boronate **10** (50.0 mg, 0.19 mmol) was used. Purification was performed by MPLC (hexane/ethyl acetate = 3:1 to 2:3) to afford *trans*-**12d** as a white solid

(26.5 mg, 60% yield) and *cis*-**12d** as a light yellow solid (5.7 mg, 13% yield). *trans*-**12d**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (td, J = 7.8, 6.0 Hz, 1H), 6.98 (d, J = 7.8 Hz, 1H), 6.89–6.84 (m, 2H), 5.91 (brs, 1H), 2.85–2.82 (m, 1H), 2.01 (ddd, J = 9.6, 6.0, 3.6 Hz, 1H), 1.22 (dt, J = 7.8, 6.0 Hz, 1H), 1.20 (s, 9H), 1.15 (ddd, J = 9.6, 6.0, 4.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.7, 162.9 (d, J_{CF} = 246.3 Hz), 143.2 (d, J_{CF} = 8.6 Hz), 129.7 (d, J_{CF} = 8.6 Hz), 122.4 (d, J_{CF} = 2.9 Hz), 113.5 (d, J_{CF} = 21.6 Hz), 112.9 (d, J_{CF} = 20.3 Hz), 38.5, 32.2, 27.5, 24.8, 16.1; HRMS (ESI) *m/z* calcd for $C_{14}H_{19}FNO$ $[M+H]^+$: 236.1445 found 236.1435. *cis*-**12d**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (td, J = 9.6, 7.2 Hz, 1H), 7.00 (d, J = 9.6 Hz, 1H), 6.93–6.87 (m, 2H), 5.26 (brs, 1H), 3.13–3.08 (m, 1H), 2.33 (q, J = 9.4 Hz, 1H), 1.38 (ddd, J = 10.2, 9.0, 7.2 Hz, 1H), 1.01 (td, J = 7.2, 5.4 Hz, 1H), 0.95 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.6, 162.7 (d, J_{CF} = 244.1 Hz), 139.3 (d, J_{CF} = 7.2 Hz), 129.6 (d, J_{CF} = 8.7 Hz), 124.7, 115.6 (d, J_{CF} = 21.6 Hz), 113.4 (d, J_{CF} = 20.1 Hz), 38.5, 28.6, 27.3, 21.9, 11.6; HRMS (ESI) *m/z* calcd for $C_{14}H_{19}FNO$ $[M+H]^+$: 236.1445 found 236.1434.



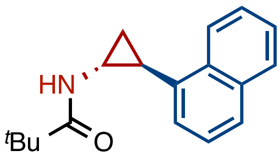
trans-**12e** *cis*-**12e**

***trans*-*N*-(2-(*p*-Tolyl)cyclopropyl)pivalamide (*trans*-12e) and *cis*-*N*-(2-(*p*-tolyl)cyclopropyl)pivalamide (*cis*-12e):** Boronate **10** (50.0 mg, 0.19 mmol) was used. Purification was performed by flash column chromatography (hexane/ethyl acetate = 3:1 to 2:1) to afford *trans*-**12e** as a white solid (28.8 mg, 67% yield) and *cis*-**12e** as a white solid (8.7 mg, 20% yield). *trans*-**12e**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.10–7.06 (m, 4H, Ar-*H*), 5.83 (brs, 1H, N*H*), 2.84–2.81 (m, 1H, 1-H), 2.30 (s, 3H, ArC*H₃*), 1.98 (ddd, J = 9.6, 6.6, 3.6 Hz, 1H, 2-H), 1.22–1.19 (m, 10H, 3-H_b and *t*Bu), 1.08 (ddd, J = 10.2, 6.0, 4.8 Hz, 1H, 3-H_a); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.6 (*C*O), 137.4, 135.6, 129.0, 126.7 (Ar-*C*), 38.5 (*C*(CH_3)$_3$), 31.9 (C-1), 27.5 (C(*C*H_3)$_3$), 24.5 (C-2), 21.0 (Ar*C*H_3), 16.0 (C-3); HRMS (ESI) *m/z* calcd for $C_{15}H_{22}NO$ $[M+H]^+$: 232.1696 found 232.1689; m.p.: 108.7–111.8 °C; IR (film): 3318, 2957, 1636, 1509, 1452, 1364, 1288, 1228, 1185, 882, 794 cm^{-1}. *cis*-**12e**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.11 (d, J = 8.4 Hz, 2H, Ar-H^2), 7.07 (d, J = 8.4 Hz, 2H, Ar-H^3), 5.21 (brs, 1H, N*H*), 3.09–3.05 (m, 1H, 1-H), 2.32 (s, 3H, Ar-C*H₃*), 2.29 (q, J = 7.8 Hz, 1H, 2-H), 1.32 (ddd, J = 9.0, 7.8, 6.6 Hz, 1H, 3-H_a), 0.97–0.93 (m, 10H, 3-H_b); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.6 (*C*O), 136.1, 133.1, 129.0, 128.7 (Ar-*C*), 38.5 (*C*(CH_3)$_3$), 28.0 (C-1), 27.3 (C(*C*H_3)$_3$), 21.2 (Ar*C*H_3), 21.0 (C-2), 11.6 (C-3); HRMS (ESI) *m/z* calcd for $C_{15}H_{22}NO$ $[M+H]^+$: 232.1696 found 232.1690; m.p.: 120.4–122.1 °C; IR (film): 3291, 2968, 1632, 1528, 1477, 1457, 1300, 1242, 1053, 809, 684 cm^{-1}.

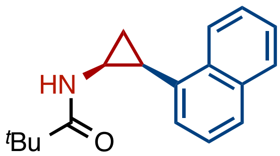


trans-**12f** *cis*-**12f**

***trans-N*-(2-(3,4-Difluorophenyl)cyclopropyl)pivalamide (*trans*-12f) and *cis-N*-(2-(3,4-difluorophenyl)cyclopropyl)pivalamide (*cis*-12f):** Boronate **10** (50.0 mg, 0.19 mmol) was used. Purification was performed by flash column chromatography (hexane/ethyl acetate = 2:1 to 1:1) to afford *trans*-**12f** as a light yellow solid (28.0 mg, 59% yield) and *cis*-**12f** as a white solid (7.8 mg, 16% yield). *trans*-**12f**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.06–7.01 (m, 2H), 6.98–6.96 (m, 1H), 5.90 (brs, 1H), 2.77–2.74 (m, 1H), 1.98 (ddd, J = 9.6, 6.0, 3.6 Hz, 1H), 1.20 (s, 9H), 1.17 (dt, J = 7.2, 6.0 Hz, 1H), 1.13 (ddd, J = 9.6, 6.0, 4.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.9, 150.1 (dd, J_{CF} = 249.2, 12.9 Hz), 148.9 (dd, J_{CF} = 247.7, 13.1 Hz), 137.5 (q, J_{CF} = 2.9 Hz), 123.0 (q, J_{CF} = 2.9 Hz), 116.9 (d, J_{CF} = 17.3 Hz), 116.0 (d, J_{CF} = 17.3 Hz), 38.5, 31.9, 27.5, 24.5, 15.3; HRMS (ESI) *m*/*z* calcd for $C_{14}H_{18}F_2NO$ [M+H]$^+$: 254.1351 found 254.1341. *cis*-**12f**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.07 (dt, J = 10.2, 8.4 Hz, 1H), 7.02–6.99 (m, 1H), 6.95–6.93 (m, 1H), 5.30 (brs, 1H), 3.10–3.06 (m, 1H), 2.28 (q, J = 7.8 Hz, 1H), 1.38 (ddd, J = 9.0, 7.8, 6.6 Hz, 1H), 0.97–0.94 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.6, 149.9 (dd, J_{CF} = 249.2, 12.9 Hz), 149.1 (dd, J_{CF} = 249.2, 13.1 Hz), 133.7 (t, J_{CF} = 5.0 Hz), 125.1 (d, J_{CF} = 5.7 Hz), 117.8 (d, J_{CF} = 17.3 Hz), 116.7 (d, J_{CF} = 17.3 Hz), 38.4, 28.6, 27.3, 21.6, 11.5; HRMS (ESI) *m*/*z* calcd for $C_{14}H_{18}F_2NO$ [M+H]$^+$: 254.1351 found 254.1342.

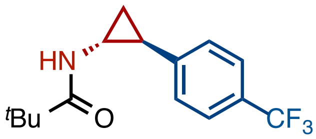


trans-**12g**

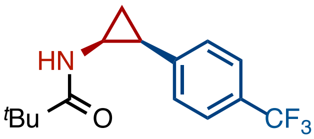


cis-**12g**

***trans-N*-(2-(Naphthalen-1-yl)cyclopropyl)pivalamide (*trans*-12g) and *cis-N*-(2-(naphthalen-1-yl)cyclopropyl)pivalamide (*cis*-12g):** Boronate **10** (150.0 mg, 0.56 mmol) was used. Purification was performed by MPLC (hexane/ethyl acetate = 4:1 to 1:3) to afford *trans*-**12g** as a pale yellow solid (73.5 mg, 49% yield) and *cis*-**12g** as a pale yellow solid (48.3 mg, 32% yield). *trans*-**12g**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (d, J = 7.8 Hz,1H), 7.84 (d, J = 7.8 Hz,1H), 7.72 (d, J = 8.4 Hz,1H), 7.56–7.52 (m, 2H), 7.48 (ddd, J = 7.8, 6.6, 1.2 Hz, 1H), 7.39 (dd, J = 7.2, 1.2 Hz,1H), 5.99 (brs, 1H), 3.20–3.17 (m, 1H), 2.41 (ddd, J = 10.2, 6.6, 3.6 Hz, 1H), 1.29 (dt, J = 10.2, 5.4, 1.2 Hz, 1H), 1.25 (s, 9H), 1.20 (ddd, J = 7.8, 6.6, 5.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.9, 136.0, 133.5, 132.9, 128.5, 127.1, 125.8, 125.6, 125.5, 125.1, 124.1, 38.6, 30.4, 27.6, 22.7, 15.3; HRMS (DART) *m*/*z* calcd for $C_{18}H_{22}NO$ [M+H]$^+$: 268.1696 found 268.1705. *cis*-**12g**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.59–7.50 (m, 2H), 7.44 (t, J = 7.6 Hz, 1H), 7.36 (d, J = 7.2 Hz, 1H), 4.84 (brs, 1H), 3.57–3.50 (m, 1H), 2.66 (q, J = 7.8 Hz, 1H), 1.55 (ddd, J = 8.8, 7.2, 6.0 Hz, 1H), 1.14 (td, J = 6.4, 4.0 Hz, 1H), 0.63 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.2, 133.5, 133.3, 132.9, 128.5, 127.6, 126.9, 126.4, 126.0, 125.4, 123.9, 38.2, 27.6, 26.8, 19.3, 11.8; HRMS (DART) *m*/*z* calcd for $C_{18}H_{22}NO$ [M+H]$^+$: 268.1696 found 268.1700.

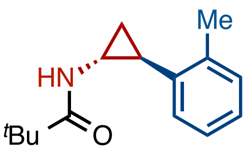


trans-**12h**

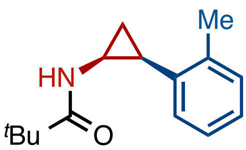


cis-**12h**

***trans*-*N*-(2-(4-(Trifluoromethyl)phenyl)cyclopropyl)pivalamide (*trans*-12h) and *cis*-*N*-(2-(4-(trifluoromethyl)phenyl)cyclopropyl)pivalamide (*cis*-12h):** Boronate **10** (100 mg, 0.37 mmol) was used. Purification was performed by flash column chromatography (hexane/ethyl acetate = 3:1 to 1:1) to afford *trans*-**12h** as a light yellow solid (60.6 mg, 57% yield) and *cis*-**12h** as a light brown solid (16.8 mg, 16% yield). *trans*-**12h**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 5.89 (brs, 1H), 2.87–2.84 (m, 1H), 2.06 (ddd, *J* = 9.6, 6.6, 3.6 Hz, 1H), 1.28 (dt, *J* = 7.8, 6.6 Hz, 1H), 1.22–1.18 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.8, 144.7, 128.3 (q, J_{CF} = 32.7 Hz), 127.0, 125.2 (d, J_{CF} = 4.4 Hz), 124.3 (q, J_{CF} = 272.1 Hz), 38.6, 32.4, 27.5, 25.0, 16.1; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{19}F_3NO$ $[M+H]^+$: 286.1413 found 286.1400. *cis*-**12h**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 5.30 (brs, 1H), 3.15–3.11 (m, 1H), 2.39 (q, *J* = 7.6 Hz, 1H), 1.42 (ddd, *J* = 9.0, 7.8, 6.6 Hz, 1H), 1.10 (td, *J* = 6.6, 4.8 Hz, 1H), 0.92 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.6, 140.9, 129.2, 128.7 (q, J_{CF} = 31.5 Hz), 124.9 (q, J_{CF} = 3.6 Hz), 124.2 (q, J_{CF} = 270.5 Hz), 38.4, 29.0, 27.2, 22.3, 11.4; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{19}F_3NO$ $[M+H]^+$: 286.1413 found 286.1401.

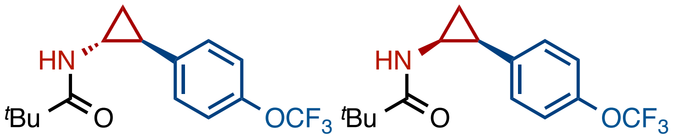


trans-**12i**

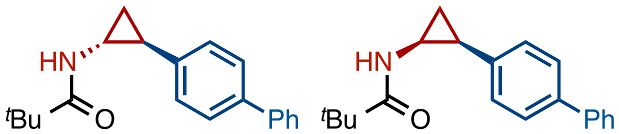


cis-**12i**

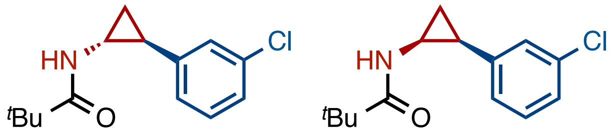
***trans*-*N*-(2-(*o*-Tolyl)cyclopropyl)pivalamide (*trans*-12i) and *cis*-*N*-(2-(*o*-tolyl)cyclopropyl)pivalamide (*cis*-12i):** Boronate **10** (50.0 mg, 0.19 mmol) was used. Purification was performed by MPLC (hexane/ethyl acetate = 4:1 to 1:1) to afford *trans*-**12i** as a colorless oil (13.0 mg, 30% yield) and *cis*-**12i** as a white solid (23.6 mg, 55% yield). *trans*-**12i**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17–7.10 (m, 4H), 5.86 (brs, 1H), 3.02–2.99 (m, 1H), 2.40 (s, 3H), 1.96 (ddd, *J* = 9.6, 6.0, 3.6 Hz, 1H), 1.20 (s, 9H), 1.15–1.10 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.6, 138.1, 137.7, 129.6, 126.4, 126.3, 125.9, 38.5, 30.8, 27.5, 23.1, 19.6, 15.0; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{22}NO$ $[M+H]^+$: 232.1696 found 232.1688. *cis*-**12i**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21–7.14 (m, 3H), 7.07–7.06 (m, 1H), 4.91 (brs, 1H), 3.36–3.32 (m, 1H), 2.38 (s, 3H), 2.23 (q, *J* = 7.8 Hz, 1H), 1.35 (dt, *J* = 9.0, 7.2 Hz, 1H), 1.02 (td, *J* = 6.6, 4.2 Hz, 1H), 0.87 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.3, 138.9, 134.4, 130.0, 127.8, 126.9, 125.8, 38.4, 27.3, 27.1, 20.0, 19.4, 11.1; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{22}NO$ $[M+H]^+$: 232.1696 found 232.1687.



***trans*-*N*-(2-(4-(Trifluoromethoxy)phenyl)cyclopropyl)pivalamide (*trans*-12j) and *cis*-*N*-(2-(4-(trifluoromethoxy)phenyl)cyclopropyl)pivalamide (*cis*-12j):** Boronate **10** (50.0 mg, 0.19 mmol) was used. Purification was performed by MPLC (hexane/ethyl acetate = 3:1 to 3:7) to afford *trans*-**12j** as a white solid (31.2 mg, 55% yield) and *cis*-**12j** as a white solid (6.7 mg, 12% yield). *trans*-**12j**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 (d, J = 8.4 Hz, 2H), 7.11 (d, J = 8.4 Hz, 2H), 5.90 (brs, 1H), 2.81–2.78 (m, 1H), 2.02 (ddd, J = 9.6, 6.6, 3.6 Hz, 1H), 1.23–1.20 (m, 10H), 1.15 (ddd, J = 9.6, 6.0, 4.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.8, 147.5, 139.3, 128.2, 120.9, 120.4 (q, J_{CF} = 257.8 Hz), 38.5, 32.1, 27.5, 24.5, 15.6; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{19}F_3NO_2$ $[M+H]^+$: 302.1362 found 302.1349. *cis*-**12j**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 8.4 Hz, 2H), 5.23 (brs, 1H), 3.12–3.08 (m, 1H), 2.34 (dt, J = 9.0, 7.8 Hz, 1H), 1.37 (ddd, J = 9.0, 7.8, 6.6 Hz, 1H), 1.02 (td, J = 6.6, 4.8 Hz, 1H), 0.91 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.6, 147.8, 135.4, 130.3, 120.7, 120.5 (q, J_{CF} = 255.2 Hz), 38.4, 28.5, 27.2, 21.7, 11.2; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{19}F_3NO_2$ $[M+H]^+$: 302.1362 found 302.1350.

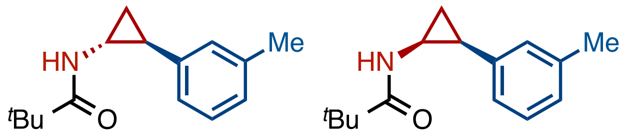


***trans*-*N*-(2-[1,1'-Biphanyl]-4-yl)cyclopropyl)pivalamide (*trans*-12k) and *cis*-*N*-(2-[1,1'-biphanyl]-4-yl)cyclopropyl)pivalamide (*cis*-12k):** Boronate **10** (50.0 mg, 0.19 mmol) was used. Purification was performed by MPLC (hexane/ethyl acetate = 3:1 to 1:4) to afford *trans*-**12k** as a light yellow solid (27.9 mg, 51% yield) and *cis*-**12k** as a yellow solid (11.5 mg, 32% yield). *trans*-**12k**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.42 (t, J = 7.8 Hz, 2H), 7.32 (t, J = 7.8 Hz, 1H), 7.26 (d, J = 8.4 Hz, 2H), 5.90 (brs, 1H), 2.91–2.88 (m, 1H), 2.06 (ddd, J = 9.6, 6.0, 3.6 Hz, 1H), 1.28 (dt, J = 7.2, 6.0 Hz, 1H), 1.21 (s, 9H), 1.15 (ddd, J = 9.6, 6.0, 4.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.6, 141.0, 139.7, 139.1, 128.7, 127.10, 127.05, 127.03, 126.95, 38.5, 32.2, 27.6, 24.6, 16.2; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{24}NO$ $[M+H]^+$: 294.1852 found 294.1839. *cis*-**12k**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, J = 7.8 Hz, 2H), 7.54 (d, J = 7.8 Hz, 2H), 7.43 (t, J = 7.8 Hz, 2H), 7.34 (t, J = 7.8 Hz, 1H), 7.26 (d, J = 7.8 Hz, 2H), 5.30 (brs, 1H), 3.14–3.10 (m, 1H), 2.37 (q, J = 7.8 Hz, 1H), 1.38 (ddd, J = 9.0, 7.2, 6.0 Hz, 1H), 1.06 (td, J = 7.2, 4.8 Hz, 1H), 0.94 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.6, 140.7, 139.4, 135.5, 129.2, 128.7, 127.2, 126.9, 126.8, 38.4, 28.4, 27.2, 21.6, 11.6; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{24}NO$ $[M+H]^+$: 294.1852 found 294.1839.



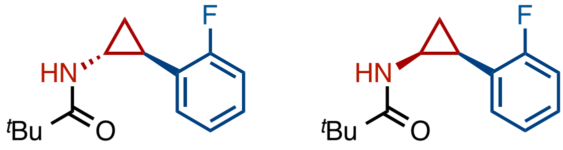
trans-**12l** *cis*-**12l**

***trans*-*N*-(2-(3-Chlorophenyl)cyclopropyl)pivalamide (*trans*-12l) and *cis*-*N*-(2-(3-chlorophenyl)cyclopropyl)pivalamide (*cis*-12l):** Boronate **10** (100 mg, 0.37 mmol) was used. Purification was performed by flash column chromatography (hexane/ethyl acetate = 3:1 to 2:1) to afford *trans*-**12l** as a light yellow solid (54.7 mg, 58% yield) and *cis*-**12l** as a light yellow solid (14.3 mg, 15% yield). *trans*-**12l**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20–7.13 (m, 3H), 7.09 (d, *J* = 7.2 Hz, 1H), 5.92 (brs, 1H), 2.84–2.81 (m, 1H), 1.99 (ddd, *J* = 9.6, 6.6, 3.6 Hz, 1H), 1.22 (dt, *J* = 7.8, 6.0 Hz, 1H), 1.20 (s, 9H), 1.14 (ddd, *J* = 9.6, 6.0, 4.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.7, 142.6, 134.1, 129.5, 126.9, 126.2, 125.0, 38.5, 32.1, 27.5, 24.7, 15.9; HRMS (ESI) *m*/*z* calcd for $C_{14}H_{19}{}^{35}ClNO$ $[M+H]^+$: 252.1150 found 252.1141. *cis*-**12l**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23–7.18 (m, 2H), 7.15 (t, *J* = 1.8 Hz, 1H), 7.11 (dd, *J* = 7.2, 1.8 Hz, 1H), 5.28 (brs, 1H), 3.12–3.08 (m, 1H), 2.31 (dt, *J* = 9.0, 7.8 Hz, 1H), 1.38 (ddd, *J* = 9.0, 7.8, 6.6 Hz, 1H), 1.02 (td, *J* = 6.6, 4.2 Hz, 1H), 0.96 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.6, 138.8, 134.0, 129.3, 128.7, 127.4, 126.6, 38.5, 28.6, 27.3, 21.9, 11.5; HRMS (ESI) *m*/*z* calcd for $C_{14}H_{19}{}^{35}ClNO$ $[M+H]^+$: 252.1150 found 252.1141.



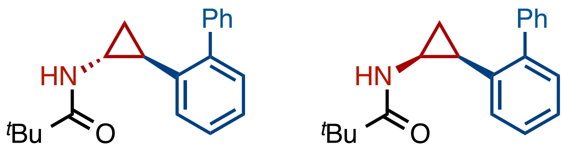
trans-**12m** *cis*-**12m**

***trans*-*N*-(2-(*m*-Tolyl)cyclopropyl)pivalamide (*trans*-12m) and *cis*-*N*-(2-(*m*-tolyl)cyclopropyl)pivalamide (*cis*-12m):** Boronate **10** (50.0 mg, 0.19 mmol) was used. Purification was performed by MPLC (hexane/ethyl acetate = 3:1 to 3:7) to afford *trans*-**12m** as a colorless oil (27.1 mg, 63% yield) and *cis*-**12m** as a white solid (7.3 mg, 17% yield). *trans*-**12m**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (t, *J* = 7.8 Hz, 1H), 7.00–6.95 (m, 3H), 5.90 (brs, 1H), 2.88–2.85 (m, 1H), 2.31 (s, 3H), 1.98 (ddd, *J* = 9.6, 6.0, 3.6 Hz, 1H), 1.22 (dt, *J* = 7.8, 6.0 Hz, 1H), 1.19 (s, 9H), 1.09 (ddd, *J* = 9.6, 6.0, 4.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.6, 140.4, 137.8, 128.2, 127.4, 126.8, 123.6, 38.5, 32.0, 27.5, 24.7, 21.3, 16.2; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{22}NO$ $[M+H]^+$: 232.1696 found 232.1686. *cis*-**12m**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 (t, *J* = 7.8 Hz, 1H), 7.03 (d, *J* = 7.8 Hz, 1H), 7.00 (s, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 5.21 (brs, 1H), 3.10–3.06 (m, 1H), 2.33 (s, 3H), 2.29 (q, *J* = 7.8 Hz, 1H), 1.34 (ddd, *J* = 9.0, 7.2, 6.0 Hz, 1H), 0.99 (td, *J* = 7.2, 4.8 Hz, 1H), 0.94 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.5, 137.8, 136.2, 129.6, 128.2, 127.3, 125.8, 38.5, 28.1, 27.2, 21.6, 21.3, 11.6; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{22}NO$ $[M+H]^+$: 232.1696 found 232.1687.



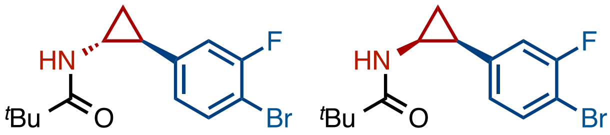
trans-**12n** *cis*-**12n**

***trans*-*N*-(2-(2-Fluorophenyl)cyclopropyl)pivalamide (*trans*-12n) and *cis*-*N*-(2-(2-fluorophenyl)cyclopropyl)pivalamide (*cis*-12n):** Boronate **10** (100 mg, 0.37 mmol) was used. Purification was performed by flash column chromatography (hexane/ethyl acetate = 3:1 to 2:1), then PTLC (hexane/ethyl acetate = 3:2) to afford *trans*-**12n** as a light yellow solid (33.6 mg, 38% yield) and *cis*-**12n** as a white solid (6.6 mg, 7% yield). *trans*-**12n**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17–7.12 (m, 1H), 7.09–6.98 (m, 3H), 5.89 (brs, 1H), 3.01–2.97 (m, 1H), 2.14 (ddd, *J* = 10.5, 6.5, 4.0 Hz, 1H), 1.26 (dt, *J* = 7.5, 6.0 Hz, 1 H), 1.20–1.16 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.7, 161.6 (d, J_{CF} = 246.3 Hz), 127.5, 127.4 (d, J_{CF} = 7.2 Hz), 127.2 (d, J_{CF} = 2.9 Hz), 124.0 (d, J_{CF} = 2.9 Hz), 115.0 (d, J_{CF} = 21.6 Hz), 38.5, 31.2, 27.5, 18.1 (d, J_{CF} = 4.2 Hz), 15.9; HRMS (ESI) *m*/*z* calcd for $C_{14}H_{19}FNO$ $[M+H]^+$: 236.1445 found 236.1434. *cis*-**12n**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23–7.20 (m, 1H), 7.08–7.04 (m, 3H), 5.29 (brs, 1H), 3.17–3.13 (m, 1H), 2.36 (dt, *J* = 9.0, 7.8 Hz, 1H), 1.41 (ddd, *J* = 9.0, 7.2, 6.6 Hz, 1 H), 1.10 (td, *J* = 6.6, 4.8 Hz, 1H), 0.95 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.5, 162.4 (d, J_{CF} = 244.2 Hz), 129.9 (d, J_{CF} = 4.4 Hz), 128.2 (d, J_{CF} = 7.2 Hz), 123.8, 123.7 (d, J_{CF} = 4.4 Hz), 115.3 (d, J_{CF} = 23.1 Hz), 38.5, 27.9, 27.2, 16.2 (d, J_{CF} = 4.4 Hz), 11.5; HRMS (ESI) *m*/*z* calcd for $C_{14}H_{19}FNO$ $[M+H]^+$: 236.1445 found 236.1434.



trans-**12o** *cis*-**12o**

***trans*-*N*-(2-[1,1'-Biphanyl]-2-yl)cyclopropyl)pivalamide (*trans*-12o) and *cis*-*N*-(2-[1,1'-biphanyl]-2-yl)cyclopropyl)pivalamide (*cis*-12o):** Boronate **10** (50.0 mg, 0.19 mmol) was used. Purification was performed by MPLC (hexane/ethyl acetate = 4:1 to 1:1), then PTLC (hexane/ethyl acetate = 3:2) to afford *trans*-**12o** as a white solid (22.1 mg, 40% yield) and *cis*-**12o** as a white solid (4.0 mg, 8% yield). *trans*-**12o**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43–7.41 (m, 4H), 7.38–7.35 (m, 1H), 7.31–7.24 (m, 3H), 7.15 (d, *J* = 8.4 Hz, 1H), 5.44 (brs, 1H), 2.78–2.74 (m, 1H), 1.92 (ddd, *J* = 9.6, 6.0, 3.6 Hz, 1H), 1.23 (dt, *J* = 7.2, 6.6 Hz, 1H), 1.12 (s, 9H), 0.96 (ddd, *J* = 10.2, 6.0, 4.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.4, 142.7, 141.8, 137.5, 129.6, 129.5, 128.0, 127.6, 126.9, 126.2, 125.9, 38.4, 32.6, 27.5, 23.3, 16.1; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{24}NO$ $[M+H]^+$: 294.1852 found 294.1839. *cis*-**12o**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48–7.42 (m, 4H), 7.37–7.29 (m, 4H), 7.12–7.10 (m, 1H), 5.23 (brs, 1H), 2.98–2.93 (m, 1H), 2.29 (dt, *J* = 10.8, 9.0 Hz, 1H), 1.26 (dt, *J* = 10.8, 7.8 Hz, 1H), 0.96 (s, 9H), 0.92 (td, *J* = 7.8, 4.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.5, 143.7, 141.1, 133.4, 130.3, 129.4, 128.2, 127.6, 127.11, 127.08, 126.69, 38.5, 29.1, 27.3, 20.7, 13.0; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{24}NO$ $[M+H]^+$: 294.1852 found 294.1839.



trans-**12p** *cis*-**12p**

***trans-N*-(2-(4-Bromo-3-fluorophenyl)cyclopropyl)pivalamide (*trans*-12p) and *cis-N*-(2-(4-bromo-3-fluorophenyl)cyclopropyl)pivalamide (*cis*-12p):** Boronate **10** (150.0 mg, 0.19 mmol) was used. Purification was performed by MPLC (hexane/ethyl acetate = 4:1 to 1:1), then PTLC (hexane/ethyl acetate = 4:1 to 1:3) to afford *trans*-**12p** as a pale yellow solid (87.0 mg, 49% yield) and *cis*-**12p** as a pale yellow solid (21.0 mg, 12% yield). *trans*-**12p**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (dd, J = 7.2, 1.2 Hz, 1H), 6.98 (dd, J = 8.4, 2.0 Hz, 1H), 6.91 (dd, J = 6.4, 2.4 Hz, 1H), 5.85 (brs, 1H), 2.81–2.76 (m, 1H), 2.00–1.95 (m, 1H), 1.19 (s, 9H), 1.19–1.13 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.8, 158.9 (d, J_{CF} = 245.7 Hz), 142.5 (d, J_{CF} = 7.2 Hz), 133.1, 124.0 (d, J_{CF} = 2.9 Hz), 115.1 (d, J_{CF} = 21.5 Hz), 106.2 (d, J_{CF} = 20.1 Hz), 38.9, 32.2, 27.5, 24.7, 15.7; HRMS (DART) *m*/*z* calcd for $C_{14}H_{18}BrFNO$ $[M+H]^+$: 314.0550 found 314.0551. *cis*-**12p**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (dd, J = 8.4, 7.6 Hz, 1H), 6.95 (dd, J = 9.6, 2.0 Hz, 1H), 6.90 (dd, J = 8.4, 2.0 Hz, 1H), 5.35 (brs, 1H), 3.13–3.06 (m, 1H), 2.28 (q, J = 7.7 Hz, 1H), 1.40 (ddd, J = 9.2, 7.6, 6.8 Hz, 1H), 1.02–0.94 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.7, 158.7 (d, J_{CF} = 245.6 Hz), 138.8 (d, J_{CF} = 6.8 Hz), 132.9, 126.0 (d, J_{CF} = 3.4 Hz), 116.8 (d, J_{CF} = 22.1 Hz), 106.5 (d, J_{CF} = 20.9 Hz), 38.4, 28.9, 27.3, 21.9, 11.7; HRMS (DART) *m*/*z* calcd for $C_{14}H_{18}BrFNO$ $[M+H]^+$: 314.0550 found 314.0557.

2. General Procedure for Deprotection of Pivalamide 12

To a mixture of *trans*-**12** in 1-PrOH (2 mL) was added conc. HCl (1 mL). The mixture was heated at 100 °C for 60 h in a test tube in oil bath. After cooling to room temperature, the reaction mixture was poured into water (5 mL). The aqueous phase was washed with ethyl acetate (5 mL x 2) and basified with 5N NaOH. The basic aqueous phase was extracted with ethyl acetate (5 mL x 2). The combined organic layers were washed with water (10 mL x 1) and brine (5 mL x 2), dried over Na_2SO_4, and concentrated *in vacuo* to afford arylcyclopropylamine **1**. The obtained arylcyclopropylamine **1** was dissolved into 0.5 M HCl-EtOH (1 mL). Then, the volatiles were evaporated *in vacuo*. The resultant residue was washed with ethyl acetate to afford HCl salt of **1**.

***trans*-2-Phenylcyclopropan-1-amine hydrochloride (1a, commercially available):** A white solid in 68% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.69 (brs, 3H), 7.32–7.27 (m, 2H), 7.23–7.18 (m, 1H), 7.17–7.13 (m, 2H), 3.72 (s, 3H), 2.79–2.74 (m, 1H), 2.41–2.35 (m, 1H), 1.44 (ddd, J = 10.4, 6.0, 4.4 Hz, 1H), 1.19 (dt, J = 7.6, 6.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 139.3, 128.3, 126.3, 126.2, 30.5, 20.7, 13.2; HRMS (ESI) *m*/*z* calcd for $C_{21}H_{20}N$ $[M+H]^+$: 286.1590 found 286.1590.

***trans*-2-(4-Methoxyphenyl)cyclopropan-1-amine hydrochloride (1b):** A pale brown solid in 41% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.43 (brs, 3H), 7.08 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 8.8 Hz, 2H), 3.72 (s, 3H), 2.74–2.66 (m, 1H), 2.30–2.25 (m, 1H), 1.35–1.30 (m, 1H), 1.13 (dt, J = 8.0, 6.4 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 157.7, 130.9, 127.3, 113.7, 55.0, 30.1, 19.9, 12.7; HRMS (ESI) m/z calcd for $C_{10}H_{14}NO$ $[M+H]^+$: 164.1070 found 164.1068.

***trans*-2-(4-Fluorophenyl)cyclopropan-1-amine hydrochloride (1c):** A pale yellow solid in 37% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.60 (brs, 3H), 7.23–7.19 (m, 2H), 7.12 (t, J = 8.8 Hz, 2H), 2.82–2.72 (m, 1H), 2.39–2.34 (m, 1H), 1.40 (ddd, J = 6.4, 4.8, 1.6 Hz, 1H), 1.18 (dt, J = 8.0, 6.4 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 160.8 (d, J_{CF} = 240.0 Hz), 135.3, 128.1 (d, J_{CF} = 7.2 Hz), 115.0 (d, J_{CF} = 21.6 Hz), 30.3, 19.9, 13.0; HRMS (ESI) m/z calcd for $C_9H_{11}FN$ $[M+H]^+$: 152.0870 found 152.0868.

***trans*-2-(3-Fluorophenyl)cyclopropan-1-amine hydrochloride (1d):** A pale brown solid in 41% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.55 (brs, 3H), 7.36–7.30 (m, 1H), 7.06–7.00 (m, 3H), 2.86–2.84 (m, 1H), 2.40–2.35 (m, 1H), 1.46–1.41 (m, 1H), 1.25 (dt, J = 7.6, 6.4 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 162.2 (d, J_{CF} = 241.4 Hz), 142.3 (d, J_{CF} = 8.7 Hz), 130.1 (d, J_{CF} = 8.6 Hz), 122.6, 113.0 (d, J_{CF} = 21.6 Hz), 112.7 (d, J_{CF} = 21.5 Hz), 30.6, 20.4, 13.5; HRMS (ESI) m/z calcd for $C_9H_{11}FN$ $[M+H]^+$: 152.0870 found 152.0869.

***trans*-2-(*p*-Tolyl)cyclopropan-1-amine hydrochlorid (1e):** An off-white solid in 44% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.55 (brs, 3H), 7.10 (d, J = 7.8 Hz, 2H), 7.03 (d, J = 7.8 Hz, 2H), 2.75–2.72 (m, 1H), 2.31 (ddd, J = 10.2, 6.6, 3.6 Hz, 1H), 1.37 (ddd, J = 10.2, 6.0, 4.2 Hz, 1H), 1.14 (dt, J = 8.4, 6.6 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 136.2, 135.3, 128.9, 126.1, 30.4, 20.6, 20.4, 13.0; HRMS (ESI) m/z calcd for $C_{10}H_{14}N$ $[M+H]^+$: 148.1121 found 148.1119.

***trans*-2-(3,4-Difluorophenyl)cyclopropan-1-amine hydrochloride (1f):** A pale brown solid in 33% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.54 (brs, 3H), 7.36 (dt, J = 10.8, 8.4 Hz, 1H), 7.29–7.25 (m, 1H), 7.08–7.05 (m, 1H), 2.84–2.81 (m, 1H), 2.36 (ddd, J = 10.2, 6.6, 4.2 Hz, 1H), 1.42 (ddd, J = 10.2, 5.4, 4.8 Hz, 1H), 1.24 (dt, J = 8.4, 6.6 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 149.5 (dd, J_{CF} = 246.3, 12.9 Hz), 147.9 (dd, J_{CF} = 244.8, 11.6 Hz), 137.2, 123.4, 117.3 (d, J_{CF} = 17.3 Hz), 115.2 (d, J_{CF} = 17.3 Hz), 30.6, 20.0, 13.4; HRMS (ESI) m/z calcd for $C_9H_{10}F_2N$ $[M+H]^+$: 170.0776 found 170.0772.

***trans*-2-(Naphthalen-1-yl)cyclopropan-1-amine hydrochloride (1g):** A brown solid in 28% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.65 (brs, 3H), 8.32 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 7.65–7.62 (m, 1H), 7.59–7.56 (m, 1H), 7.45 (t, J = 7.8 Hz, 1H), 7.31 (d, J = 6.6 Hz, 1H), 2.91–2.84 (m, 2H), 1.53–1.50 (m, 1H), 1.35 (q, J = 7.2 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 134.5, 133.1, 132.3, 128.5, 127.3, 126.3, 126.0, 125.5, 124.1, 124.0, 29.4, 18.7, 11.2; HRMS (ESI) *m*/*z* calcd for $C_{13}H_{14}N$ $[M+H]^+$: 184.1121 found 184.1118.

***trans*-2-(4-(Trifluoromethyl)phenyl)cyclopropan-1-amine hydrochloride (1h):** A pale brown solid in 11% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.52 (brs, 3H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 2.92–2.89 (m, 1H), 2.45 (ddd, *J* = 9.8, 6.3, 3.5 Hz, 1H), 1.48 (ddd, *J* = 10.3, 6.3, 4.6 Hz, 1H), 1.31 (dt, *J* = 7.5, 6.3 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 144.3, 126.9, 126.8 (q, J_{CF} = 31.7 Hz), 125.1 (d, J_{CF} = 4.4 Hz), 124.1 (q, J_{CF} = 231.3 Hz), 39.0, 20.5, 13.7; HRMS (ESI) *m*/*z* calcd for $C_{10}H_{11}ClF_3N$ $[M+H]^+$: 202.0838 found 202.0835.

***trans*-2-(*o*-Tolyl)cyclopropan-1-amine hydrochloride (1i):** A white powder in 46% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.64 (brs, 3H), 7.18–7.17 (m, 1H), 7.14–7.10 (m, 2H), 6.99–6.98 (m, 1H), 2.72–2.69 (m, 1H), 2.41 (ddd, *J* = 10.2, 7.8, 4.2 Hz, 1H), 2.39 (s, 3H), 1.36 (ddd, *J* = 10.8, 6.6, 4.8 Hz, 1H), 1.19 (dt, *J* = 7.8, 6.0 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 137.2, 136.8, 129.6, 126.5, 125.9, 125.6, 29.6, 19.5, 18.9, 11.4; HRMS (ESI) *m*/*z* calcd for $C_{10}H_{14}N$ $[M+H]^+$: 148.1121 found 148.1119.

***trans*-2-(4-(Trifluoromethoxy)phenyl)cyclopropan-1-amine hydrochloride (1j):** A white powder in 48% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.51 (brs, 3H), 7.30 (s, 4H), 2.85–2.81 (m, 1H), 2.42–2.35 (m, 1H), 1.45–1.39 (m, 1H), 1.25 (dt, *J* = 8.0, 6.4 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 146.8, 138.8, 128.1, 121.0, 120.0 (q, J_{CF} = 254.3 Hz), 30.6, 20.2, 13.4; HRMS (ESI) *m*/*z* calcd for $C_{10}H_{11}ClF_3NO$ $[M+H]^+$: 218.0787 found 218.0784.

***trans*-2-([1,1'-Biphenyl]-4-yl)cyclopropan-1-amine hydrochloride (1k):** A pale yellow solid in 78% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.52 (brs, 3H), 7.64 (d, *J* = 7.2 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 2H), 2.86–2.82 (m, 1H), 2.39 (ddd, *J* = 10.2, 7.8, 3.6 Hz, 1H), 1.45–1.41 (m, 1H), 1.26 (dt, *J* = 7.8, 6.0 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 139.7, 138.6, 138.2, 128.9, 127.3, 126.8, 126.6, 126.5, 30.6, 20.5, 13.3; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{16}N$ $[M+H]^+$: 210.1277 found 210.1275.

***trans*-2-(3-Chlorophenyl)cyclopropan-1-amine hydrochloride (1l):** A white solid in 36% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.52 (brs, 3H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.28–7.26 (m, 2H), 7.15 (d, *J* = 7.8 Hz, 1H), 2.88–2.83 (m, 1H), 2.36 (ddd, *J* = 10.2, 6.6, 4.2 Hz, 1H), 1.44–1.40 (m, 1H), 1.27 (q, *J* = 6.6 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 142.0, 133.2, 130.2, 126.3, 126.1, 125.2, 30.6, 20.4, 13.4; HRMS (ESI) *m*/*z* calcd for $C_9H_{11}Cl_1N$ $[M+H]^+$: 168.0575 found 168.0571.

***trans*-2-(*m*-Tolyl)cyclopropan-1-amine hydrochloride (1m):** A pale brown solid in 22% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.51 (brs, 3H), 7.17 (t, J = 7.8 Hz, 1H), 7.02 (d, J = 7.2 Hz, 1H), 6.96–6.93 (m, 1H), 2.78–2.76 (m, 1H), 2.30 (ddd, J = 10.2, 6.6, 3.6 Hz, 1H), 2.27 (s, 3H), 1.37 (ddd, J = 10.2, 6.0, 4.2 Hz, 1H), 1.18 (dt, J = 7.8, 6.0 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 139.1, 137.5, 128.3, 127.0, 126.8, 123.3, 30.4, 20.9, 20.6, 13.1; HRMS (ESI) *m*/*z* calcd for $C_{10}H_{14}N$ $[M+H]^+$: 148.1121 found 148.1119.

***trans*-2-(2-Fluorophenyl)cyclopropan-1-amine hydrochloride (1n):** A white solid in 48% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.61 (brs, 3H), 7.29–7.25 (m, 1H), 7.20–7.17 (m, 1H), 7.14 (t, J = 7.8 Hz, 1H), 7.09 (dt, J = 7.8, 4.2 Hz, 1H), 2.91–2.89 (m, 1H), 2.53–2.48 (m, 1H), 1.48–1.42 (m, 1H), 1.26 (q, J = 6.6 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 160.8 (d, J_{CF} = 244.8 Hz), 128.2 (d, J_{CF} = 8.7 Hz), 127.0 (d, J_{CF} = 2.9 Hz), 125.9 (d, J_{CF} = 14.4 Hz), 124.5, 115.1 (d, J_{CF} = 21.6 Hz), 29.7, 14.3, 12.4; HRMS (ESI) *m*/*z* calcd for $C_9H_{11}FN$ $[M+H]^+$: 152.0870 found 152.0868.

***trans*-2-([1,1'-Biphenyl]-2-yl)cyclopropan-1-amine hydrochloride (1o):** A pale yellow solid in 31% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.38 (brs, 3H), 7.51–7.48 (m, 2H), 7.46–7.44 (m, 2H), 7.41 (t, J = 7.2 Hz, 1H), 7.34–7.28 (m, 2H), 7.24 (dd, J = 7.2, 1.8 Hz, 1H), 7.03 (dd, J = 7.2, 1.8 Hz, 1H), 2.95–2.92 (m, 1H), 2.26 (ddd, J = 10.2, 6.6, 3.6 Hz, 1H), 1.23–1.20 (m, 1H), 1.16 (q, J = 6.6 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 141.6, 140.5, 136.1, 129.7, 129.4, 128.4, 127.7, 127.1, 126.3, 124.4, 31.0, 18.9, 14.3; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{16}N$ $[M+H]^+$: 210.1277 found 210.1275.

***trans*-2-(4-Bromo-3-fluorophenyl)cyclopropan-1-amine hydrochloride (1p):** A white solid in 68% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.48 (brs, 3H), 7.61 (t, J = 7.8 Hz, 1H), 7.22 (d, J = 10.8 Hz, 1H), 7.03 (d, J = 8.4 Hz, 1H), 2.88–2.86 (m, 1H), 2.38–2.36 (m, 1H), 1.47–1.42 (m, 1H), 1.29–1.26 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.3 (d, J_{CF} = 242.7 Hz), 142.2 (d, J_{CF} = 7.2 Hz), 133.3, 124.5, 114.5 (d, J_{CF} = 21.5 Hz), 105.4 (d, J_{CF} = 20.1 Hz), 30.9, 20.3, 13.8; HRMS (ESI) *m*/*z* calcd for $C_9H_{10}BrFN$ $[M+H]^+$: 229.9975 found 229.9967.

3. General Procedure for Preparation of Biphenyl Derivatives

To a solution of **1q** (299 mg, 1.41 mmol, 1.0 equiv) in CH_2Cl_2 (7.1 mL) was slowly added $(Boc)_2O$ (0.98 mL, 4.23 mmol, 3.0 equiv) at 0 °C. The reaction mixture was stirred for 3 h at room temperature. The volatiles were evaporated *in vacuo*. The resultant residue was purified by silica gel column chromatography (hexane/ethyl acetate = 5:1 to 3:1) to give 327 mg of **13** as a white solid in a 74% yield. Then, a 20-mL glass vessel equipped with J. Young® O-ring tap containing a magnetic stirring bar was flame-dried under vacuum and filled with nitrogen after cooling to room temperature. A mixture of the protected amine **13** (60 mg, 0.19 mmol, 1.0 equiv), $Pd(PPh_3)_4$ (43.9 mg, 0.04 mmol, 20 mol%), Na_2CO_3 (40.3 mg, 0.38 mmol, 2.0 equiv), and arylboronic acid **14** (0.76 mmol, 4.0 equiv) were added to this tube and dissolved into water (0.01 mL) and toluene/MeOH (0.54 mL/0.12 mL). The mixture was heated at 80 °C for 18 h in oil bath under N_2. After cooling to room temperature, the mixture was diluted with ethyl acetate. The insolubles were filtered off through Celite® and the filtrate was concentrated *in vacuo*. The resultant residue was purified by flash column chromatography (hexane/ethyl acetate = 3:1 to 2:1) to afford the coupling product **15**. The obtained coupling product was dissolved into THF (1.0 mL) and added 12 N HCl aq. (1.0 mL). The reaction mixture was stirred for 12 h at room temperature. The volatiles were evaporated *in vacuo* and washed with ethyl acetate to afford HCl salt of **16**.

***trans-tert*-Butyl (2-(4-bromophenyl)cyclopropyl)carbamate (13):** A white solid in 74% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.4 Hz, 2H), 7.02 (d, *J* = 8.4 Hz, 2H), 4.83 (brs, 1H), 2.68 (s, 1H), 2.03–1.98 (m, 1H), 1.45 (s, 9H), 1.16–1.12 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.2, 139.8, 131.3, 128.4, 119.7, 79.7, 32.4, 28.4, 24.7, 16.1.

***trans*-2-(4-(Anthracen-9-yl)phenyl)cyclopropan-1-amine hydrochloride (16a):** An orange solid in 54% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.72 (brs, 3H), 8.68 (s, 1H), 8.15 (d, *J* = 8.4 Hz, 2H), 7.52–7.50 (m, 4H), 7.43–7.41 (m, 4H), 7.34 (d, *J* = 8.4 Hz, 2H), 2.97 (brs, 1H), 2.49–2.46 (m, 1H), 1.55 (brs, 1H), 1.39–1.36 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 138.9, 136.1, 135.9, 130.91, 130.88, 129.5, 128.4, 126.5, 126.4, 126.0, 125.8, 125.3, 30.8, 20.7, 13.6; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{20}N$ $[M+H]^+$: 310.1590 found 310.1586.

***trans*-2-(4-(Thiophen-3-yl)phenyl)cyclopropan-1-amine hydrochloride (16b):** A white solid in 73% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.43 (brs, 3H), 7.94–7.83 (m, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.62–7.61 (m, 1H), 7.53 (d, *J* = 4.8 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 2.83 (brs, 1H), 2.36–2.32 (m, 1H), 1.41–1.37 (m, 1H), 1.25–1.21 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 141.1, 138.1, 133.3, 127.1, 126.8, 126.1 (2 peaks overlapped), 120.7, 30.6, 20.6, 13.4; HRMS (ESI) *m*/*z* calcd for $C_{13}H_{14}NS$ $[M+H]^+$: 216.0841 found 216.0835.

***trans*-2-(3'-Chloro-(1,1'-biphenyl)-4-yl)cyclopropan-1-amine hydrochloride (16c):** A light yellow solid in 57% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.39 (brs, 3H), 7.70 (s, 1H), 7.64 (t, *J* = 8.4 Hz, 3H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 7.2 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 2H), 2.88–2.86 (m, 1H), 2.38–2.36 (m, 1H), 1.43–1.39 (m, 1H), 1.29–1.26 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 141.8, 139.3, 136.5, 133.6, 130.7, 127.0, 126.8, 126.7, 126.1, 125.1, 30.5, 20.4, 13.3; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{15}Cl_1N$ $[M+H]^+$: 244.0888 found 244.0880.

***trans*-2-(2'-Methyl-(1,1'-biphenyl)-4-yl)cyclopropan-1-amine hydrochloride (16d):** A white solid in 69% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.43 (brs, 3H), 7.29–7.20 (m, 7H), 7.16 (d, *J* = 7.2 Hz, 1H), 2.85

(brs, 1H), 2.38–2.36 (m, 1H), 2.21 (s, 3H), 1.43–1.40 (m, 1H), 1.28–1.25 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 140.9, 139.3, 137.9, 134.6, 130.3, 129.4, 128.9, 127.2, 126.1, 125.9, 30.6, 20.5, 20.1, 13.2; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{18}N$ $[M+H]^+$: 224.1434 found 224.1427.

***trans*-2-(4-(Pyridin-4-yl)phenyl)cyclopropan-1-amine hydrochloride (16e):** A dark orange solid in 97% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.88 (brs, 2H), 8.64 (brs, 3H), 8.29 (brs, 2H), 7.96 (d, J = 4.2 Hz, 2H), 7.41 (d, J = 4.2 Hz, 2H), 2.93 (brs, 1H), 2.48 (brs, 1H), 1.53–1.50 (m, 1H), 1.34–1.31 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 153.4, 143.5, 143.2, 132.5, 127.7, 127.3, 122.9, 30.9, 20.6, 13.8; HRMS (ESI) *m*/*z* calcd for $C_{14}H_{15}N_2$ $[M+H]^+$: 211.1230 found 211.1225.

***trans*-4'-(2-Aminocyclopropyl)-(1,1'-biphenyl)-2-carbonitrile hydrochloride (16f):** A pale yellow solid in 69% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.48 (brs, 3H), 7.94 (d, J = 8.4 Hz, 1H), 7.79 (t, J = 7.8 Hz, 1H), 7.61–7.57 (m, 2H), 7.52 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 2.90–2.88 (m, 1H), 2.44–2.38 (m, 1H), 1.48–1.44 (m, 1H), 1.33–1.30 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 144.2, 140.1, 135.8, 133.8, 133.5, 130.0, 128.7, 128.1, 126.6, 118.6, 110.1, 30.8, 20.6, 13.5; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{15}N_2$ $[M+H]^+$: 235.1230 found 235.1223.

***trans*-2-(3'-Fluoro-(1,1'-biphenyl)-4-yl)cyclopropan-1-amine hydrochloride (16g):** A light yellow solid in 32% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.40 (brs, 3H), 7.65 (d, J = 7.2 Hz, 2H), 7.51–7.50 (m, 3H), 7.27 (d, J = 7.2 Hz, 2H), 7.18–7.17 (m, 1H), 2.87 (brs, 1H), 2.38–2.37 (m, 1H), 1.42–1.41 (m, 1H), 1.28–1.27 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 162.7 (d, J_{CF} = 242.7 Hz), 142.2 (d, J_{CF} = 7.2 Hz), 139.3, 136.8, 130.9 (d, J_{CF} = 8.6 Hz), 126.9, 126.8, 122.5, 114.1 (d, J_{CF} = 21.6 Hz), 113.1 (d, J_{CF} = 23.0 Hz), 30.7, 20.5, 13.4; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{15}FN$ $[M+H]^+$: 228.1183 found 228.1174.

***trans*-2-(2-Fluoro-(1,1'-biphenyl)-4-yl)cyclopropan-1-amine hydrochloride (16h):** Starting from **1p**. A white solid in 62% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.54 (brs, 3H), 7.52 (d, J = 7.2 Hz, 2H), 7.49–7.44 (m, 3H), 7.40 (t, J = 7.8 Hz, 1H), 7.15–7.13 (m, 2H), 2.91–2.88 (m, 1H), 2.43–2.40 (m, 1H), 1.47–1.44 (m, 1H), 1.32–1.29 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 159.0 (d, J_{CF} = 244.2 Hz), 152.1, 141.6, 134.7, 130.4, 128.5, 127.6, 126.0 (d, J_{CF} = 12.9 Hz), 122.5, 113.6 (d, J_{CF} = 23.1 Hz), 30.8, 20.4, 13.7; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{15}FN$ $[M+H]^+$: 228.1183 found 228.1174.

***trans*-2-(3',5'-Difluoro-(1,1'-biphenyl)-4-yl)cyclopropan-1-amine hydrochloride (16i):** A white solid in 7% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.32, (brs, 3H), 7.69 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 9.0 Hz, 2H), 7.27 (d, J = 7.8 Hz, 2H), 7.20 (t, J = 9.6 Hz, 1H), 2.87 (brs, 1H), 2.36 (brs, 1H), 1.41–1.40 (m, 1H), 1.28–1.26 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 162.8 (dd, J_{CF} = 244.2, 14.4 Hz), 143.2, 139.9, 135.4, 126.8, 126.7, 109.4 (dd, J_{CF} = 20.2, 4.4 Hz), 102.5 (t, J_{CF} = 25.8 Hz), 30.6, 20.4, 13.4; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{14}F_2N$ $[M+H]^+$: 246.1089 found 246.1080.

***trans*-2-(3'-(Methylsulfonyl)-(1,1'-biphenyl)-4-yl)cyclopropan-1-amine hydrochloride (16j):** A white solid in 59% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.44 (brs, 3H), 8.13 (s, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.75–7.71 (m, 3H), 7.31 (d, *J* = 8.4 Hz, 2H), 3.30 (s, 3H), 2.89–2.88 (m, 1H), 2.40–2.39 (m, 1H), 1.45–1.42 (m, 1H), 1.30–1.27 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 141.5, 140.8, 139.6, 136.3, 131.4, 130.0, 126.93, 126.88, 125.5, 124.6, 43.3, 30.6, 20.4, 13.3; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{18}NO_2S$ $[M+H]^+$: 288.1053 found 288.1042.

***trans*-2-(4'-(Trifluoromethyl)-(1,1'-biphenyl)-4-yl)cyclopropan-1-amine hydrochloride (16k):** A white solid in 41% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.40 (brs, 3H), 7.88 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 7.8 Hz, 2H), 7.69 (d, *J* = 7.2 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 2.88 (brs, 1H), 2.39 (brs, 1H), 1.43–1.42 (m, 1H), 1.30–1.28 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 143.7, 139.8, 136.6, 127.7 (q, J_{CF} = 31.6 Hz), 127.2, 127.0 (2 peaks overlapped), 126.2 (q, J_{CF} = 270.0 Hz), 125.8 (d, J_{CF} = 4.4 Hz), 30.7, 20.5, 13.5; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{15}ClF_3N$ $[M+H]^+$: 278.1151 found 278.1140.

***trans*-1-(4'-(2-Aminocyclopropyl)-(1,1'-biphenyl)-3-yl)ethan-1-one hydrochloride (16l):** A pale yellow solid in 21% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.34 (brs, 3H), 8.15 (s, 1H), 7.95–7.92 (m, 2H), 7.68 (d, *J* = 7.8 Hz, 2H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 2.88 (brs, 1H), 2.65 (s, 3H), 2.38–2.37 (m, 1H), 1.44–1.39 (m, 1H), 1.29–1.26 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 198.0, 140.1, 139.1, 137.5, 137.3, 131.1, 129.4, 127.1, 126.9, 126.8, 126.0, 30.7, 26.9, 20.5, 13.4; HRMS (ESI) *m*/*z* calcd for $C_{17}H_{18}NO$ $[M+H]^+$: 252.1383 found 252.1374.

***trans*-2-(3'-Methoxy-(1,1'-biphenyl)-4-yl)cyclopropan-1-amine hydrochloride (16m):** A light yellow solid in 46% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.44 (brs, 3H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.36 (t, *J* = 8.4 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 2H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.16 (s, 1H), 6.93 (dd, *J* = 5.4, 3.0 Hz, 1H), 3.82 (s, 3H), 2.85 (brs, 1H), 2.38–2.35 (m, 1H), 1.43–1.40 (m, 1H), 1.27–1.24 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 159.7, 141.2, 138.6, 138.1, 130.0, 126.8, 126.7, 118.8, 112.8, 112.0, 55.1, 30.6, 20.5, 13.3; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{18}NO$ $[M+H]^+$: 240.1383 found 240.1383.

***trans*-4'-(2-Aminocyclopropyl)-(1,1'-biphenyl)-3-ol hydrochloride (16n):** An orange solid in 59% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.53 (brs, 1H), 8.40 (brs, 3H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 7.2 Hz, 2H), 7.04 (d, *J* = 7.2 Hz, 2H), 7.00 (s, 1H), 6.75 (dd, *J* = 7.8, 2.4 Hz, 1H), 2.84 (brs, 1H), 2.35 (brs, 1H), 1.42–1.38 (m, 1H), 1.27–1.24 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 157.8, 141.1, 138.40, 138.37, 129.9, 126.8, 126.5, 117.2, 114.3, 113.3, 30.6, 20.5, 13.3; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{16}NO$ $[M+H]^+$: 226.1226 found 226.1222.

***trans*-2-((1,1':4',1''-Terphenyl)-4-yl)cyclopropan-1-amine hydrochloride (16o):** A light yellow solid in 16% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.33 (brs, 3H), 7.76 (s, 4H), 7.72 (d, J = 7.2 Hz, 2H), 7.67 (d, J = 8.4 Hz, 2H), 7.49 (t, J = 7.8 Hz, 2H), 7.39 (t, J = 7.8 Hz, 1H), 7.28 (d, J = 8.4 Hz, 2H), 2.88 (brs, 1H), 2.37–2.34 (m, 1H), 1.42–1.38 (m, 1H), 1.30–1.27 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 139.6, 139.0, 138.7, 137.6, 129.0, 127.5, 127.2, 126.95, 126.90, 126.45, 126.50, 30.6, 20.5, 13.3 (1 aromatic peak overlapped somewhere); HRMS (ESI) *m/z* calcd for $C_{21}H_{20}N$ $[M+H]^+$: 286.1590 found 286.1590.

***trans*-*N*-(4'-(-2-Aminocyclopropyl)-(1,1'-biphenyl)-4-yl)acetamide hydrochloride (16p):** A dark orange solid in 32% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.05 (brs, 1H), 8.37 (brs, 3H), 7.66–7.58 (m, 6H), 7.24–7.22 (m, 2H), 2.85 (brs, 1H), 2.35 (brs, 1H), 2.07 (s, 3H), 1.42–1.37 (m, 1H), 1.27–1.22 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.3, 138.7, 137.8, 134.2, 126.8, 126.8, 126.6, 126.1, 119.3, 30.6, 24.0, 20.5, 13.3; HRMS (ESI) *m/z* calcd for $C_{17}H_{19}N_2O$ $[M+H]^+$: 267.1492 found 267.1485.

***trans*-2-(4'-Nitro-[1,1'-biphenyl]-4-yl)cyclopropan-1-amine hydrochloride (16q):** A pale brown solid in 77% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.49 (brs, 3H), 8.30 (d, J = 9.0 Hz, 2H), 8.96 (d, J = 9.0 Hz, 2H), 7.74 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 2.89 (brs, 1H), 2.43–2.39 (m, 1H), 1.47–1.44 (m, 1H), 1.31–1.28 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 146.5, 146.1, 140.5, 135.7, 127.5, 127.2, 127.1, 124.0, 30.6, 20.5, 13.5; HRMS (ESI) *m/z* calcd for $C_{15}H_{15}ClN_2O_2$ $[M+H]^+$: 255.1128 found 255.1124.

***trans*-2-(4-(1*H*-Indol-5-yl)phenyl)cyclopropan-1-amine hydrochloride (16r):** An orange solid in 88% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.50 (brs, 3H), 7.99 (d, J = 9.0 Hz, 2H), 7.93 (d, J = 8.4 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 9.0 Hz, 2H), 3.25 (s, 3H), 2.88 (brs, 1H), 2.42–2.39 (m, 1H), 1.47–1.43 (m, 1H), 1.30–1.27 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 144.6, 140.0, 139.4, 136.3, 127.6, 127.3, 127.1, 127.0, 43.6, 30.7, 20.5, 13.5; HRMS (ESI) *m/z* calcd for $C_{16}H_{18}NO_2S$ $[M+H]^+$: 288.1053 found 288.1051.

***N*-(4'-(*trans*-2-Aminocyclopropyl)-[1,1'-biphenyl]-3-yl)methanesulfonamide hydrochloride (16s):** A pale yellow solid in 89% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.18 (s, 1H), 9.15 (s, 2H), 8.67 (brs, 3H), 7.76 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 8.2 Hz, 2H), 2.88–2.85 (m, 1H), 2.46–2.43 (m, 1H), 1.51–1.47 (m, 1H), 1.30–1.26 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 157.0, 154.5, 140.4, 132.9, 131.7, 127.2, 126.9, 30.7, 20.5, 13.5; HRMS (ESI) *m/z* calcd for $C_{13}H_{14}N_3$ $[M+H]^+$: 212.1182 found 212.1178.

***N*-(4'-(*trans*-2-Aminocyclopropyl)-[1,1'-biphenyl]-3-yl)methanesulfonamide hydrochloride (16t):** A pale yellow solid in 69% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.85 (s, 1H), 8.46 (brs, 3H), 7.54 (d, J = 8.2 Hz, 2H), 7.45–7.44 (m, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.37 (dt, J = 7.9, 1.4 Hz, 1H), 7.27 (d, J = 8.3 Hz, 2H), 7.21–7.19 (m, 1H), 3.03 (s, 3H), 2.86 (brs, 1H), 2.39–2.37 (m, 1H), 1.44–1.41 (m, 1H), 1.28–1.24 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 141.0, 139.0, 138.9, 137.8, 129.9, 126.9, 126.7, 122.1, 118.6, 117.7, 40.0, 30.6, 20.5, 13.4; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{19}N_2O_2S$ [M+H]$^+$: 303.1162 found 303.156.

***N*-(4'-(*trans*-2-Aminocyclopropyl)-[1,1'-biphenyl]-4-yl)methanesulfonamide hydrochloride (16u):** A pale yellow solid in 70% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.85 (s, 1H), 8.46 (brs, 3H), 7.63 (d, *J* = 8.6 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.29 (dd, *J* = 8.9, 2.0 Hz, 2H), 7.23 (d, *J* = 8.3 Hz, 2H), 3.01 (s, 3H), 2.84 (brs, 1H), 2.38–2.35 (m, 1H), 1.43–1.39 (m, 1H), 1.26–1.23 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 138.2, 137.7, 137.5, 135.1, 127.3, 126.8, 126.3, 120.0, 40.0, 30.6, 20.5, 13.3; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{19}N_2O_2S$ [M+H]$^+$: 303.1162 found 303.1154.

***trans*-2-(3'-(Trifluoromethyl)-[1,1'-biphenyl]-4-yl)cyclopropan-1-amine hydrochloride (16v):** A pale yellow solid in 64% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.54 (brs, 3H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.94 (s, 1H), 7.73–7.68 (m, 4H), 7.29 (d, *J* = 7.8 Hz, 2H), 2.87–2.86 (m, 1H), 2.42–2.40 (m, 1H), 1.47–1.44 (m, 1H), 1.29−1.26 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 140.8, 139.6, 136.5, 130.6, 130.1, 129.8 (q, J_{CF} = 31.5 Hz), 127.01, 126.96, 124.2 (q, J_{CF} = 270.0 Hz), 123.9 (d, J_{CF} = 4.4 Hz), 122.8 (d, J_{CF} = 4.4 Hz), 30.7, 20.5, 13.4; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{15}ClF_3N$ [M+H]$^+$: 228.1151 found 228.1144.

***trans*-2-(2'-Fluoro-[1,1'-biphenyl]-4-yl)cyclopropan-1-amine hydrochloride (16w):** A white solid in 96% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.56 (brs, 3H), 7.51 (td, *J* = 7.9, 1.7 Hz, 1H), 7.48 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.43–7.39 (m, 1H), 7.32–7.27 (m, 4H), 2.86–2.85 (m, 1H), 2.42–2.39 (m, 1H), 1.47–1.43 (m, 1H), 1.28–1.25 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 159.1 (d, J_{CF} = 244.2 Hz), 139.1, 133.1, 130.6 (d, J_{CF} = 2.9 Hz), 129.5 (d, J_{CF} = 7.2 Hz), 128.8 (d, J_{CF} = 2.9 Hz), 127.9 (d, J_{CF} = 13.1 Hz), 126.5, 124.9 (d, J_{CF} = 4.2 Hz), 116.1 (d, J_{CF} = 21.6 Hz), 30.6, 20.5, 13.4; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{15}FN$ [M+H]$^+$: 228.1183 found 228.1179.

***trans*-2-(4'-Fluoro-[1,1'-biphenyl]-4-yl)cyclopropan-1-amine hydrochloride (16x):** A white solid in 70% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.53 (brs, 3H), 7.70–7.67 (m, 2H), 7.58 (d, *J* = 8.3 Hz, 2H), 7.30–7.27 (m, 2H), 7.25 (d, *J* = 8.3 Hz, 2H), 2.87–2.81 (m, 1H), 2.40–2.37 (m, 1H), 1.45–1.42 (m, 1H), 1.27–1.23 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 161.8 (d, J_{CF} = 242.9 Hz), 138.6, 137.2, 136.2, 128.4 (d, J_{CF} = 8.6 Hz), 126.9, 126.6, 115.7 (d, J_{CF} = 21.6 Hz), 30.6, 20.5, 13.3; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{15}FN$ [M+H]$^+$: 228.1183 found 228.1179.

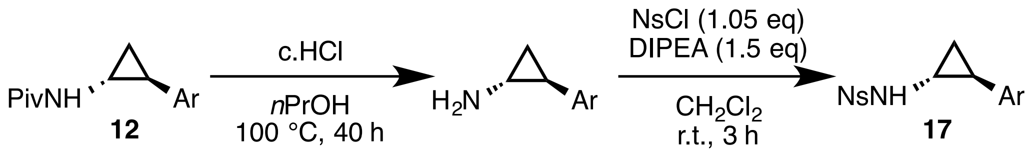
***trans*-2-(2'-Methoxy-[1,1'-biphenyl]-4-yl)cyclopropan-1-amine hydrochloride (16y):** A yellow solid in 72% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.51 (brs, 3H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.33 (td, *J* = 7.7, 1.7 Hz, 1H), 7.25 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 2H), 7.10 (d, *J* = 7.8 Hz, 1H), 7.02 (td, *J* = 8.1, 1.1 Hz, 1H), 3.75 (s, 3H), 2.83 (brs, 1H), 2.36 (brs, 1H), 1.42–1.41 (m, 1H), 1.26–1.23 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 156.1, 137.8, 136.2, 130.2, 129.4, 129.2, 128.8, 125.9, 120.8, 111.7, 55.5, 30.5, 20.5, 13.2; HRMS (ESI) *m/z* calcd for $C_{16}H_{18}NO$ $[M+H]^+$: 240.1383 found 240.1378.

***trans*-2-(4'-Methoxy-[1,1'-biphenyl]-4-yl)cyclopropan-1-amine hydrochloride (16z):** A pale yellow in 81% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.50 (brs, 3H), 7.58 (d, *J* = 9.0 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 3.79 (s, 3H), 2.83 (brs, 1H), 2.38–2.35 (m, 1H), 1.43–1.40 (m, 1H), 1.25–1.22 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 158.7, 137.8, 137.6, 132.0, 127.4, 126.7, 126.0, 114.2, 55.1, 30.4, 20.4, 13.2; HRMS (ESI) *m/z* calcd for $C_{16}H_{18}NO$ $[M+H]^+$: 240.1383 found 240.1378.

***trans*-2-(2'-(Trifluoromethyl)-[1,1'-biphenyl]-4-yl)cyclopropan-1-amine hydrochloride (16aa):** A pale yellow solid in 49% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.29 (brs, 3H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.71 (t, *J* = 7.8 Hz, 1H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.37 (d, *J* = 7.2 Hz, 1H), 7.26–7.22 (m, 4H), 2.90 (brs, 1H), 2.34 (brs, 1H), 1.42–1.38 (m, 1H), 1.32–1.28 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 140.5, 138.9, 137.5, 132.4, 132.2, 128.9, 128.2, 126.9 (q, J_{CF} = 30.2 Hz), 126.2 (d, J_{CF} = 5.7 Hz), 125.8, 124.3 (q, J_{CF} = 271.4 Hz), 30.9, 20.7, 13.6; HRMS (ESI) *m/z* calcd for $C_{16}H_{15}F_3N$ $[M+H]^+$: 278.1151 found 278.1144.

***trans*-2-(4'-(Methylthio)-[1,1'-biphenyl]-4-yl)cyclopropan-1-amine hydrochloride (16ab):** A yellow solid in 65% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.46 (brs, 3H), 7.61–7.58 (m, 4H), 7.33 (d, *J* = 9.0 Hz, 2H), 7.24 (d, *J* = 7.8 Hz, 2H), 2.84 (brs, 1H), 2.50 (s, 3H), 2.38–2.35 (m, 1H), 1.43–1.40 (m, 1H), 1.27–1.23 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 138.4, 137.6, 137.4, 136.2 126.9 (2 peaks overlapped), 126.4, 126.3, 30.6, 20.5, 14.7, 13.4; HRMS (ESI) *m/z* calcd for $C_{16}H_{18}NS$ $[M+H]^+$: 256.1154 found 256.1149.

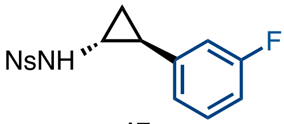
4. Synthesis of *trans*-2-nitro-*N*-(2-arylcyclopropyl)benzenesulfonamide 17



General procedure

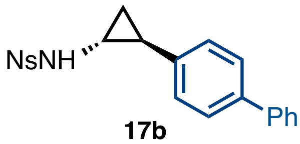
To a solution of *trans*-*N*-(2-arylcyclopropyl)pivalamide (1 equiv, ref. *Angew. Chem. Int. Ed.* **2015**, *54*, 846) in *n*PrOH was added conc.HCl (excess). The mixture was heated at 100 °C for 40 h in a screw vial. After cooling to room temperature, the reaction mixture was diluted with water and washed with AcOEt (back-extraction). The aqueous phase was basified with 5M NaOH and extracted with AcOEt. The organic layers were washed with water and brine, dried over Na_2SO_4, filtered off and concentrated *in vacuo* to give the crude primary amine. To a solution of the obtained amine (1 eqiuv.) and Hünig's base (1.5 equiv) in CH_2Cl_2 was slowly added 2-nitrobenzenesulfonyl chloride (1.05 equiv). The reaction mixture was stirred for

3 h at room temperature. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtered off and concentrated *in vacuo*. The resultant residue was purified by MPLC to give the desired nosylate **17**.



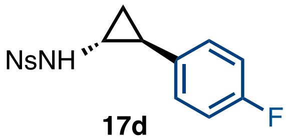
17a

***trans*-*N*-(2-(3-Fluorophenyl)cyclopropyl)-2-nitrobenzenesulfonamide (17a):** 185 mg of the pivalate was used to obtain 108 mg of the desired product as a light brown oil in 41% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.0 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.74–7.68 (m, 2H), 7.22–7.19 (m, 1H), 6.91–6.82 (m, 2H), 6.67 (d, *J* = 7.6 Hz, 2H), 5.79 (brs, 1H), 2.49–2.45 (m, 1H), 2.31–2.26 (m, 1H), 1.44–1.39 (m, 1H), 1.28–1.19 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.9 (d, J_{CF} = 244.2 Hz), 148.2, 142.1, 133.9, 132.9, 132.8, 131.7, 129.9 (d, J_{CF} = 8.7 Hz), 125.4, 122.0 (d, J_{CF} = 2.9 Hz), 113.4 (d, J_{CF} = 21.5 Hz), 113.0 (d, J_{CF} = 21.6 Hz), 34.3, 24.3, 15.4.



17b

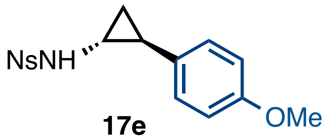
***trans*-*N*-(2-([1,1'-Biphenyl]-4-yl)cyclopropyl)-2-nitrobenzenesulfonamide (17b):** 320 mg of the pivalate was used to obtain 282 mg of the desired product as a yellow solid in 66% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.86 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.74 (td, *J* = 7.8, 1.8 Hz, 1H), 7.68 (td, *J* = 7.8, 1.2 Hz, 1H), 7.55 (dd, *J* = 7.8, 1.2 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.43 (t, *J* = 8.4 Hz, 2H), 7.34 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.09 (d, *J* = 7.8 Hz, 2H), 5.79 (brs, 1H), 2.53–2.51 (m, 1H), 2.32 (ddd, *J* = 9.6, 6.6, 3.0 Hz, 1H), 1.42 (ddd, *J* = 10.2, 6.0, 4.2 Hz, 1H), 1.27 (q, *J* = 6.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.3, 140.6, 139.4, 138.5, 133.8, 133.1, 132.7, 131.8, 128.8, 127.3, 127.1, 126.9, 126.7, 125.3, 34.3, 24.2, 15.3; HRMS (ESI) *m/z* calcd for $C_{21}H_{17}N_2O_4S$ $[M-H]^-$: 393.0915 found 393.0901.



17d

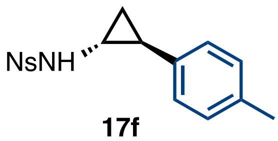
***trans*-*N*-(2-(4-Fluorophenyl)cyclopropyl)-2-nitrobenzenesulfonamide (17d):** 210 mg of the pivalate was used to obtain 114 mg of the desired product as a yellow oil in 38% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.87 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.75 (td, *J* = 7.8, 1.2 Hz, 1H), 7.69 (td, *J* = 7.2, 1.2 Hz, 1H), 7.02–6.99 (m, 2H), 6.97–6.93 (m, 2H), 5.76 (brs, 1H), 2.43–2.40 (m, 1H), 2.30 (ddd, *J* = 9.6, 6.6, 3.0 Hz, 1H), 1.37 (ddd, *J* = 9.6, 6.0, 3.6 Hz, 1H), 1.18 (ddd, *J* = 7.2, 6.6, 6.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.5 (d, J_{CF} = 242.7 Hz), 148.2, 135.0 (d, J_{CF} = 2.9 Hz), 133.9, 133.0, 132.7, 131.6, 127.8

(d, J_{CF} = 7.2 Hz), 125.3, 115.2 (d, J_{CF} = 21.6 Hz), 34.0, 23.8, 14.9; HRMS (ESI) *m/z* calcd for $C_{15}H_{12}N_2O_4S$ $[M-H]^-$: 335.0507 found 335.0496.



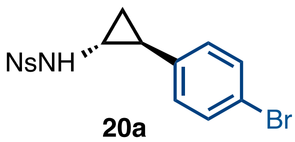
17e

***trans*-*N*-(2-(4-Methoxyphenyl)cyclopropyl)-2-nitrobenzenesulfonamide (17e):** 180 mg of the pivalate was used to obtain 73.3 mg of the desired product as a yellow oil in 29% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.83 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.73 (td, *J* = 7.8, 1.2 Hz, 1H), 7.67 (td, *J* = 7.8, 1.2 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 2H), 5.78 (brs, 1H), 3.77 (s, 3H), 2.43–2.40 (m, 1H), 2.22 (ddd, *J* = 10.2, 7.2, 3.0 Hz, 1H), 1.31 (ddd, *J* = 10.2, 6.0, 4.2 Hz, 1H), 1.15 (q, *J* = 6.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.2, 148.1, 133.8, 132.9, 132.7, 131.6, 131.2, 127.4, 125.2, 113.8, 55.2, 33.8, 23.6, 14.7; HRMS (ESI) *m/z* calcd for $C_{16}H_{16}N_2NaO_5S$ $[M+Na]^+$: 371.0672 found 371.0663.



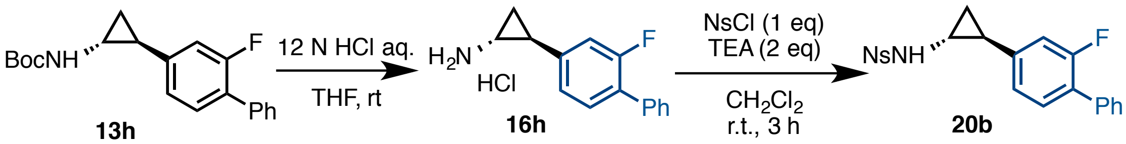
17f

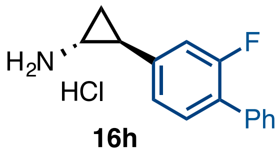
***trans*-2-Nitro-*N*-(2-(*p*-tolyl)cyclopropyl)benzenesulfonamide (17f):** 150 mg of the pivalate was used to obtain 96.9 mg of the desired product as a colorless oil in 45% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.84 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.73 (td, *J* = 7.5, 1.5 Hz, 1H), 7.67 (td, *J* = 8.0, 1.0 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 8.0 Hz, 2H), 5.76 (brs, 1H), 2.46–2.44 (m, 1H), 2.29 (s, 3H), 2.22 (ddd, *J* = 10.0, 6.5, 3.5 Hz, 1H), 1.34 (ddd, *J* = 10.0, 6.0, 4.0 Hz, 1H), 1.18 (q, *J* = 7.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.1, 136.2, 136.0, 133.8, 132.9, 132.7, 131.7, 129.1, 126.1, 125.2, 34.0, 24.0, 20.9, 15.0; HRMS (ESI) *m/z* calcd for $C_{16}H_{16}N_2NaO_4S$ $[M+Na]^+$: 355.0723 found 355.0699.



20a

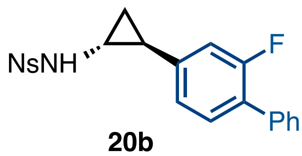
***trans*-*N*-(2-(4-Bromophenyl)cyclopropyl)-2-nitrobenzenesulfonamide (19a):** A yellow amorphous in 73% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.85 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.75 (td, *J* = 7.8, 1.8 Hz, 1H), 7.69 (td, *J* = 7.8, 1.2 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 5.81 (brs, 1H), 2.45–2.42 (m, 1H), 2.25 (ddd, *J* = 9.6, 6.6, 3.0 Hz, 1H), 1.39 (ddd, *J* = 9.6, 6.0, 4.2 Hz, 1H), 1.19 (q, *J* = 6.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.1, 138.5, 133.9, 132.8, 132.7, 131.6, 131.4, 128.0, 125.3, 120.1, 34.1, 24.1, 15.1; HRMS (ESI) *m/z* calcd for $C_{15}H_{13}N_2NaO_4S$ $[M+Na]^+$: 418.9672 found 418.9670.





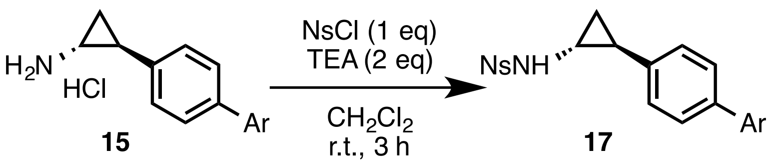
16h

***trans*-2-(2-Fluoro-(1,1'-biphenyl)-4-yl)cyclopropan-1-amine hydrochloride (16h):** A white solid in 62% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.54 (brs, 3H), 7.52 (d, J = 7.2 Hz, 2H), 7.49–7.44 (m, 3H), 7.40 (t, J = 7.8 Hz, 1H), 7.15–7.13 (m, 2H), 2.91–2.88 (m, 1H), 2.43–2.40 (m, 1H), 1.47–1.44 (m, 1H), 1.32–1.29 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 159.0 (d, J_{CF} = 244.2 Hz), 152.1, 141.6, 134.7, 130.4, 128.5, 127.6, 126.0 (d, J_{CF} = 12.9 Hz), 122.5, 113.6 (d, J_{CF} = 23.1 Hz), 30.8, 20.4, 13.7; HRMS (ESI) *m/z* calcd for $C_{15}H_{15}FN$ $[M+H]^+$: 228.1183 found 228.1174.

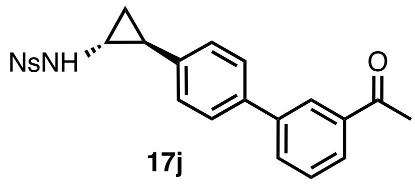


20b

***trans*-*N*-(2-(2-Fluoro-(1,1'-biphenyl)-4-yl)cyclopropyl)-2-nitrobenzenesulfonamide (19b):** A white solid in 69% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, J = 9.6, 1.6 Hz, 1H), 7.87 (d, J = 9.6, 1.6 Hz, 1H), 7.79–7.69 (m, 2H), 6.91 (dd, J = 10.0, 2.0 Hz, 1H), 6.77 (dd, J = 14.0, 2.0 Hz, 1H), 5.80 (brs, 1H), 2.53–2.49 (m, 1H), 2.35–2.30 (m, 1H), 1.49–1.44 (m, 1H), 1.29–1.23 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.5, 158.9, 132.8, 141.1 (d, J_{CF} = 8.6 Hz), 135.2, 134.0, 132.8, 131.7, 130.7 (d, J_{CF} = 4.4 Hz), 128.85, 128.83, 128.5, 127.1 (d, J_{CF} = 12.9 Hz), 125.4, 122.5, 113.7 (d, J_{CF} = 24.5 Hz), 34.4, 24.1, 15.5.

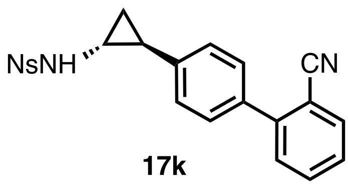


General procedure: To a solution of **15** (1 equiv) and triethylamine (2 equiv) in dichloromethane was slowly added a solution of 2-nitrobenzenesulfonyl chloride (1 equiv) in CH_2Cl_2 at 0 °C. The reaction mixture was raised at room temperature and stirred for 2 h. 1N HCl was added to the reaction mixture and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The resultant residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 1:1) to afford the nosylate **17**.



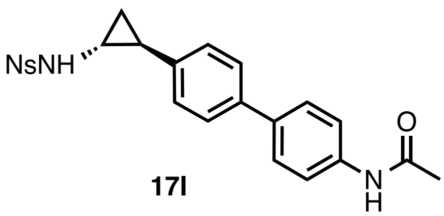
17j

trans-N**-(2-(3'-Acetyl-(1,1'-biphenyl)-4-yl)cyclopropyl)-2-nitrobenzenesulfonamide (17j):** A pale yellow solid in 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15–7.93 (m, 2H), 7.93–7.86 (m, 2H), 7.77–7.75 (m, 2H), 7.69 (t, J = 7.6 Hz, 1H), 7.52 (d, J = 8.4 Hz, 3H), 7.11 (d, J = 8.0 Hz, 2H), 5.84 (brs, 1H), 2.65 (s, 3H), 2.55–2.52 (m, 1H), 2.36–2.31 (m, 1H), 1.46–1.41 (m, 1H), 1.30–1.25 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.1, 148.2, 141.1, 139.2, 138.3, 137.6, 133.9, 133.0, 132.7, 131.7, 131.5, 129.1, 127.3, 127.2, 126.8, 126.6, 125.4, 34.3, 26.8, 24.3, 15.4.



17k

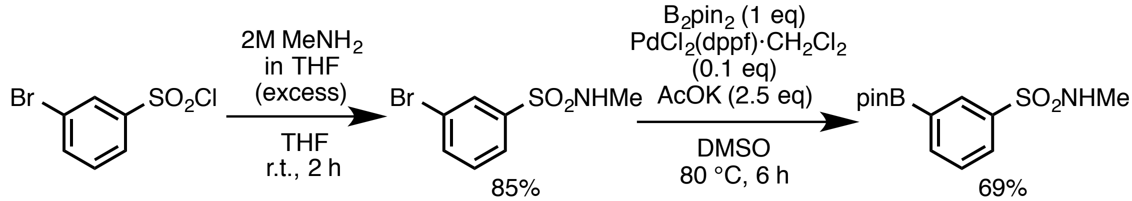
trans-N**-(2-(2'-Cyano-(1,1'-biphenyl)-4-yl)cyclopropyl)-2-nitrobenzenesulfonamide (17k):** A white solid in 50% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 10.8 Hz, 1H), 7.87 (d, J = 10.8 Hz, 1H), 7.76–7.62 (m, 5H), 7.52–7.41 (m, 3H), 7.12 (d, J = 8.4 Hz, 2H), 5.81 (brs, 1H), 2.52–2.49 (m, 1H), 2.39–2.34 (m, 1H), 1.49–1.43 (m, 1H), 1.32–1.25 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.1, 145.1, 140.2, 136.3, 134.0, 133.7, 132.9, 132.7, 131.9, 129.9, 128.9, 127.6, 126.5, 125.3, 119.0, 111.2, 34.6, 24.3, 15.4 (1 peak overlapped somewhere).

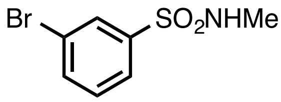


17l

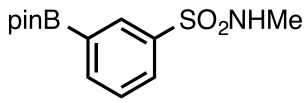
trans-N**-(4'-(2-((2-Nitrophenyl)sulfonamido)cyclopropyl)-(1,1'-biphenyl)-4-yl)acetamide (17l):** An yellow oil in 23% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, J = 8.0, 1.2 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 8.4 Hz, 1H), 7.69 (t, J = 7.6 Hz, 1H), 7.56 (d, J = 8.8 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.4 Hz, 2H), 5.80 (brs, 1H), 2.53–2.49 (m, 1H), 2.34–2.29 (m, 1H), 2.21 (s, 3H), 1.45–1.39 (m, 1H), 1.27 (dd, J = 7.2, 6.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.3, 148.2, 138.7, 138.4, 137.1, 136.6, 133.9, 133.1, 132.7, 131.8, 127.8, 127.4, 126.8, 126.7, 125.3, 120.2, 34.3, 24.7, 24.2, 15.3.

5. Synthesis of boronate intermediates

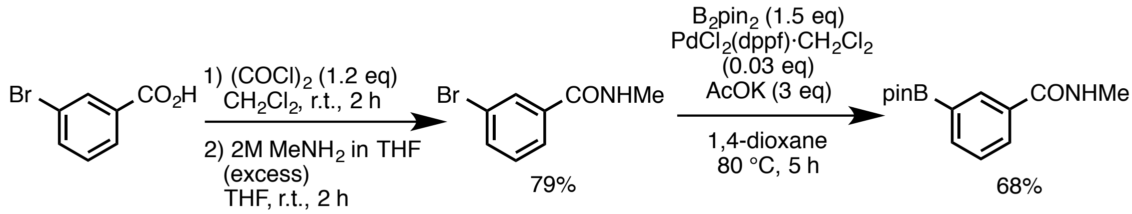


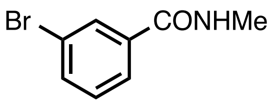


3-Bromo-*N*-methylbenzenesulfonamide: To a solution of 2 M $MeNH_2$ in THF solution (8.67 mL, 17 mmol) in THF 10 mL was slowly added *m*-bromobenzenesufonyl chloride (0.50 mL, 3.5 mmol). The reaction mixture was stirred for 2 h at room temperature. The reaction mixture was diluted with water (20 mL) and extracted with AcOEt (15 mL x 2). The combined organic layers were washed with water (15 mL x 1) and brine (15 mL x 1), dried over Na_2SO_4, filtered off and concentrated *in vacuo*. The resultant residue was purified by MPLC (hexane/ethyl acetate = 3:1 to 2:3) to give 734 mg of the desired product as a white solid in an 85% yield. ^1H NMR (600 MHz, $CDCl_3$) δ 8.02 (t, *J* = 1.8 Hz, 1H), 7.81–7.79 (m, 1H), 7.73–7.71 (m, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 4.42 (brs, 1H), 2.70 (d, *J* = 5.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.8, 135.8, 130.6, 130.1, 125.7, 123.2, 29.4; HRMS (ESI) *m*/*z* calcd for $C_7H_7{}^{79}BrNO_2S$ $[M-H]^-$: 247.9386 found 247.9383.

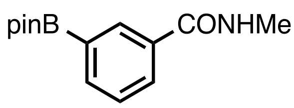


***N*-Methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenesulfonamide:** A suspension of 3-Bromo-*N*-methylbenzenesulfonamide (730 mg, 2.9 mmol), AcOK (716 mg, 7.3 mmol), $PdCl_2(dppf){\cdot}CH_2Cl_2$ (238 mg, 0.29 mmol), B_2pin_2 (741 mg, 2.9 mmol) in DMSO (10 mL) was heated at 80 °C for 6 h. After cooling to room temperature, the reaction mixture was diluted with water (20 mL) and AcOEt (20 mL). The insolubles were filtered through Celite. The filtrate was extracted with AcOEt (15 mL x 2). The combined organic layers were washed with water (20 mL x 1) and brine (20 mL x 1), dried over Na_2SO_4, filtered off and concentrated *in vacuo*. The resultant residue was purified by MPLC (hexane/ethyl acetate = 3:1 to 15:85) to give 602 mg of the product as a white solid in a 69% yield. ^1H NMR (600 MHz, $CDCl_3$) δ 8.29 (s, 1H), 8.00 (d, *J* = 7.2 Hz, 1H), 7.96–7.94 (m, 1H), 7.53 (t, *J* = 7.2 Hz, 1H), 4.54 (brs, 1H), 2.66 (d, *J* = 5.4 Hz, 3H), 1.35 (s, 12H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.8, 138.2, 133.2, 129.8, 128.4, 84.4, 29.3, 24.8 (B ipso carbon not observed); HRMS (ESI) *m*/*z* calcd for $C_{13}H_{20}BNNaO_4S$ $[M+Na]^+$: 320.1098 found 320.1096.





3-Bromo-*N*-methylbenzamide: To a mixture of 3-bromobenzoic acid (1.0 g, 5.0 mmol) and NMP (3 drops) in CH_2Cl_2 (10 mL) was added oxalyl chloride (0.51 mL, 6.0 mmol). After being stirred for 2 h at room temperature, the volatiles were evaporated *in vacuo*. The resultant residue was dissolved in CH_2Cl_2 (20 mL). Then, 2M NH_3 in THF (8.0 mL, 16 mmol) was slowly added to the solution at 0 °C. The reaction mixture was stirred for 2 h at room temperature. The volatiles were evaporated *in vacuo*. Water (20 mL) was added to the resultant residue and extracted with AcOEt (15 mL x 2). The combined organic layers were washed with brine (20 mL x 1), dried over Na_2SO_4, filtered off and concentrated *in vacuo*. The resultant residue was purified by MPLC (hexane/ethyl acetate = 3:1 to 1:4) to give 845 mg of the product as a white solid in a 79% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (t, *J* = 2.0 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 6.11 (brs, 1H), 3.02 (d, *J* = 4.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.7, 136.6, 134.3, 130.14, 130.09, 125.4, 122.7, 26.9; HRMS (ESI) *m/z* calcd for $C_8H_9{}^{79}BrNO$ $[M+H]^+$: 213.9862 found 213.9860.



***N*-Methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide:** A suspension of 3-Bromo-*N*-methylbenzamide (400 mg, 1.9 mmol), AcOK (550 mg, 5.6 mmol), $PdCl_2(dppf){\cdot}CH_2Cl_2$ (45.8 mg, 56 μmol), B_2pin_2 (712 mg, 2.8 mmol) in 1,4-dioxane (10 mL) was heated at 80 °C for 5 h. After cooling to room temperature, the reaction mixture was diluted with water (20 mL) and extracted with AcOEt (15 mL x 2). The combined organic layers were washed with water (20 mL x 1) and brine (20 mL x 1), dried over Na_2SO_4, filtered off and concentrated *in vacuo*. The resultant residue was purified by MPLC ($CHCl_3$/acetone = 99:1 to 93:7) to give 330 mg of the product as a pale brown solid in a 68% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.98–7.96 (m, 1H), 7.92 (dt, *J* = 7.2, 1.2 Hz, 1H), 7.45 (t, *J* = 7.2 Hz, 1H), 6.31 (brs, 1H), 3.01 (d, *J* = 4.8 Hz, 3H), 1.35 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 137.6, 133.9, 132.1, 130.5, 128.2, 84.1, 26.7, 24.8 (B ipso carbon not observed); HRMS (ESI) *m/z* calcd for $C_{14}H_{20}{}^{11}BNNaO_3$ $[M+Na]^+$: 284.1428 found 284.1423.

6. Synthesis of NCD derivatives

General procedure for Synthesis of NCD derivatives, M1206, M1291, and M1304. A suspension of (*S*)-5-([1,1'-biphenyl]-4-carboxamido)-6-(3-chlorobenzyl)amino)-6-oxohexyl methanesulfonate **18a**[14] (1.0 equiv), *trans*-*N*-(2-(4-bromophenyl)cyclopropyl)-2-nitrobenzenesulfonamide **19a** (3.0 equiv.) and K_2CO_3 (5.0 equiv) in DMF (0.04 M) was heated at 70 ºC overnight. After cooling to room temperature, the reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The resultant residue was purified by MPLC (hexane/ethyl acetate = 7:3 to 0:1) to give the crude product **20** as a yellow amorphous. HRMS (ESI) *m*/*z* calcd for $C_{41}H_{38}{}^{79}Br^{35}ClN_4NaO_6S$ $[M+Na]^+$: 851.1276 found 851.1262. A suspension of the obtained crude nosylate **20** (1.0 equiv), the boronic acid or boronate (3.0 equiv), Na_2CO_3 (3.0 equiv) and $Pd(PPh_3)_4$ (0.1 equiv) in toluene/MeOH/H_2O (25:5:1 mL) was heated at 70 ºC overnight under N_2 atmosphere. After cooling to room temperature, the reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine dried over Na_2SO_4, and concentrated *in vacuo*. The resultant residue was purified by MPLC (ethyl acetate/MeOH = 99:1 to 97:3) to give the crude product. To a suspension of the obtained crude nosylate (1.0 equiv) and K_2CO_3 (4.0 equiv) in CH_3CN or DMF was added PhSH (3.0 equiv). The reaction mixture was stirred overnight at 60 ºC. After cooling to room temperature, the reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The resultant residue was purified by NH-MPLC (hexane/ethyl acetate = 1:1 to 0:1) to give the desired NCD38 derivatives.

***trans*-*N*-(6-((2-(3'-Chloro-[1,1'-biphenyl]-4-yl)cyclopropyl)amino)-1-((3-chlorobenzyl)amino)-1-oxohexan-2-yl)-[1,1'-biphenyl]-4-carboxamide (M1206):** A light yellow amorphous in 53% yield. ^1H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.66–7.53 (m, 5H), 7.51 (t, *J* = 2.4 Hz, 1H), 7.45–7.37 (m, 6H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.28–7.22 (m, 3H), 7.18–7.15 (m, 2H), 7.11–7.08 (m, 1H), 7.05 (d, *J* = 7.8 Hz, 2H), 4.77 (q, *J* = 7.2 Hz, 1H), 4.44 (dd, *J* = 15.0, 6.6 Hz, 1H), 4.35 (dt, *J* = 15.0, 6.0 Hz, 1H), 2.75 (t, *J* = 7.2 Hz, 2H), 2.35–2.32 (m, 1H), 2.04–2.01 (m, 1H), 1.91–1.86 (m, 2H), 1.61–1.56 (m, 2H), 1.51–1.46 (m, 2H), 1.09–1.06 (m, 1H), 0.99–0.95 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.9, 167.3, 144.6, 142.7, 142.2, 140.1, 139.8, 136.9, 134.6, 134.4, 132.1, 129.91, 129.88, 128.9, 128.1, 127.6, 127.5, 127.18, 127.14, 126.95, 126.93, 126.88, 126.2, 125.6, 125.0, 53.5, 49.1, 42.8, 41.7, 32.6, 29.5, 24.8, 23.3, 17.2 (1 aromatic carbon peak overlapped somewhere); HRMS (ESI) m/z calcd for $C_{41}H_{40}{}^{35}Cl_2N_3O_2$ $[M+H]^+$: 676.2492 found 676.2473.

***trans*-*N*-(1-((3-Chlorobenzyl)amino)-6-((2-(3'-(*N*-methylsulfamoyl)-[1,1'-biphenyl]-4-yl)cyclopropyl)amino)-1-oxohexan-2-yl)-[1,1'-biphenyl]-4-carboxamide (M1291):** An orange amorphous in 13% yield. ^1H NMR (600 MHz, $CDCl_3$) δ 8.04 (q, *J* = 1.8 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 2H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.46–7.43 (m, 4H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.24–7.17 (m, 4H), 7.13–7.11 (m, 1H), 7.08 (dd, *J* = 8.4, 1.8 Hz, 2H), 7.04 (dd, *J* = 7.8, 3.6 Hz, 1H), 4.77–4.73 (m, 2H), 4.45 (dd, *J* = 15.0, 6.0 Hz, 1H), 4.38–4.33 (m, 1H), 2.78–2.73 (m, 2H), 2.67 (s, 3H), 2.35–2.32 (m, 1H), 2.05–2.01 (m, 1H), 1.91–1.82 (m, 2H), 1.59–1.55 (m, 2H), 1.50–1.45 (m, 2H), 1.10–1.06 (m, 1H), 1.01–0.98 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.8, 167.3, 144.7, 142.8, 142.2, 140.0, 139.8, 139.4, 136.4, 134.5, 132.2, 130.9, 129.9, 129.5, 128.9, 128.1, 127.6, 127.3, 127.2, 127.0, 126.4, 125.7, 125.5, 125.3, 53.5, 49.1, 42.9, 42.0, 32.4, 29.6, 29.4, 24.9, 23.3, 17.3 (1 aromatic carbon peak overlapped somewhere); HRMS (ESI) m/z calcd for $C_{42}H_{44}{}^{35}ClN_4O_4S$ $[M+H]^+$: 735.2766 found 735.2759.

***trans*-4'-(2-((5-([1,1'-Biphenyl]-4-carboxamido)-6-((3-chlorobenzyl)amino)-6-oxohexyl)amino)cyclopropyl)-*N*-methyl-[1,1'-biphenyl]-3-carboxamide (M1304):** A white amorphous in 13% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.69–7.62 (m, 4H), 7.59 (d, *J* = 7.2 Hz, 2H), 7.48–7.44 (m, 5H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.24–7.10 (m, 5H), 7.07 (d, *J* = 7.2 Hz, 2H), 6.99 (t, *J* = 8.4 Hz, 1H), 6.32 (dd, *J* = 17.4, 4.2 Hz, 1H), 4.75–4.70 (m, 1H), 4.45 (ddd, *J* = 15.0, 6.0, 3.0 Hz, 1H), 4.39–4.32 (m, 1H), 3.01 (dd, *J* = 7.8, 5.4 Hz, 3H), 2.79–2.72 (m, 2H), 2.35–2.31 (m, 1H), 2.04–1.99 (m, 1H), 1.91–1.80 (m, 2H), 1.61–1.55 (m, 2H), 1.50–1.45 (m, 2H), 1.09–1.05 (m, 1H), 1.01–0.97 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.7, 168.2, 167.3, 144.7, 142.1, 141.3, 140.0, 139.8, 137.4, 135.2, 134.5, 132.2, 129.9, 129.7, 129.0, 128.9, 128.1, 127.63, 127.60, 127.3, 127.2, 127.0, 126.2, 125.7, 125.39, 125.31, 125.26, 53.5, 49.1, 42.9, 41.8, 32.4, 29.6, 26.9, 25.0, 23.3, 17.1; HRMS (ESI) m/z calcd for $C_{43}H_{44}{}^{35}ClN_4O_3$ $[M+H]^+$: 699.3096 found 699.3092.

General procedure for Synthesis of NCD derivatives, M1302, M1284, and M1310. To a solution of **18b** (1.0 equiv), the nosylate **17** (1.1 equiv) and PPh_3 (3.0 equiv) in THF (0.03 M) was slowly added 40% DEAD in toluene (3.0 equiv). The reaction mixture was stirred at room temperature overnight. The volatiles were evaporated *in vacuo*. The resultant residue was purified by MPLC (hexane/ethyl acetate = 1:1 to 0:1) to give the crude product. The ^{1}H NMR spectrum of this compound was consistent with the desired product though some impurities were included. To a suspension of the obtained crude nosylate (1.0 equiv) and K_2CO_3 (4.0 equiv) in CH_3CN (0.04 M) was added PhSH (3 equiv.). The reaction mixture was stirred overnight at 60 ºC. After cooling to room temperature, the reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The resultant residue was purified by NH-MPLC (hexane/ethyl acetate = 1:1 to 0:1) to give the desired product.

***trans*-*N*-(1-((3-Chlorobenzyl)amino)-6-((2-(4-fluorophenyl)cyclopropyl)amino)-1-oxohexan-2-yl)-[1,1'-biphenyl]-4-carboxamide (M1302):** A white amorphous in 40% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.59–7.54 (m, 5H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.22–7.09 (m, 5H), 6.97–6.88 (m, 4H), 4.82 (q, *J* = 7.2 Hz, 1H), 4.45 (dd, *J* = 15.2, 6.0 Hz, 1H), 4.31 (dd, *J* = 15.2, 6.0 Hz, 1H), 2.73–2.70 (m, 2H), 2.25–2.21 (m, 1H), 2.05–1.99 (m, 1H), 1.91–1.78 (m, 2H), 1.58–1.45 (m, 4H), 1.02–0.96 (m, 1H), 0.89–0.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 167.3, 161.0 (d, J_{CF} = 244.3 Hz), 144.6, 140.1, 139.8, 137.8 (d, J_{CF} = 2.8 Hz), 134.4, 132.1, 129.9, 128.9, 128.1, 127.61, 127.56, 127.20 (d, J_{CF} = 8.6 Hz), 127.15, 125.6, 114.9 (d, J_{CF} = 21.1 Hz), 53.5, 49.1, 42.8, 41.3, 32.6, 29.7, 24.3, 23.3, 16.8 (2 aromatic carbon peaks overlapped somewhere); HRMS (ESI) m/z calcd for $C_{35}H_{36}{}^{35}ClFN_3O_2$ $[M+H]^+$: 584.2475 found 584.2468.

***trans*-*N*-(1-((3-Chlorobenzyl)amino)-6-((2-(4-methoxyphenyl)cyclopropyl)amino)-1-oxohexan-2-yl)-[1,1'-biphenyl]-4-carboxamide (M1284):** A white amorphous in 42% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, J = 8.4 Hz, 2H), 7.59–7.52 (m, 5H), 7.45 (t, J = 7.8 Hz, 2H), 7.39 (tt, J = 7.2, 1.2 Hz, 1H), 7.22 (brs, 1H), 7.19–7.15 (m, 3H), 7.11–7.10 (m, 1H), 6.94 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 4.82 (q, J = 6.6 Hz, 1H), 4.44 (dd, J = 15.0, 6.0 Hz, 1H), 4.32 (dt, J = 15.0, 5.4 Hz, 1H), 3.75 (s, 3H), 2.75–2.70 (m, 2H), 2.23–2.21 (m, 1H), 2.05–1.99 (m, 1H), 1.89–1.84 (m, 1H), 1.82–1.78 (m, 1H), 1.59–1.53 (m, 2H), 1.50–1.45 (m, 2H), 0.97–0.93 (m, 1H), 0.87–0.84 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.9, 167.2, 157.6, 144.6, 140.1, 139.8, 134.4, 134.2, 132.2, 129.9, 128.9, 128.1, 127.6, 127.5, 127.18, 127.16, 126.9, 125.6, 113.7, 55.3, 53.5, 49.1, 42.8, 41.0, 32.6, 29.6, 24.2, 23.3, 16.4 (1 aromatic carbon peak overlapped somewhere); HRMS (ESI) m/z calcd for $C_{36}H_{39}{}^{35}ClN_3O_3$ $[M+H]^+$: 596.2674 found 596.2672.

***trans*-*N*-(1-((3-Chlorobenzyl)amino)-1-oxo-6-((2-(p-tolyl)cyclopropyl)amino)hexan-2-yl)-[1,1'-biphenyl]-4-carboxamide (M1310):** A white amorphous in 60% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 (d, J = 7.8 Hz, 2H), 7.68 (dt, J = 15.0, 6.0 Hz, 1H), 7.56 (d, J = 8.4 Hz, 4H), 7.44 (t, J = 7.8 Hz, 2H), 7.38 (t, J = 7.8 Hz, 1H), 7.26 (d, J = 7.8 Hz, 1H), 7.21 (brs, 1H), 7.18–7.14 (m, 2H), 7.10–7.09 (m, 1H), 7.03 (d, J = 7.8 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 4.84 (q, J = 6.6 Hz, 1H), 4.43 (dd, J = 15.0, 6.0 Hz, 1H), 4.29 (dt, J = 15.0, 5.4 Hz, 1H), 2.74–2.69 (m, 2H), 2.28 (s, 3H), 2.26–2.24 (m, 1H), 2.04–2.00 (m, 1H), 1.89–1.79 (m, 2H), 1.58–1.45 (m, 4H), 0.99–0.95 (m, 1H), 0.90–0.86 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.0, 167.2, 144.5, 140.2, 139.8, 139.1, 134.9, 134.4, 132.1, 129.8, 128.0, 127.62, 127.59, 127.5, 127.1, 125.7, 125.6, 113.7, 53.5, 49.1, 42.8, 41.3, 32.6, 29.6, 24.6, 23.3, 20.9, 16.8 (2 aromatic carbon peaks overlapped somewhere); HRMS (ESI) m/z calcd for $C_{36}H_{39}{}^{35}ClN_3O_2$ $[M+H]^+$: 580.2725 found 580.2718.

General procedure for Synthesis of NCD derivatives, M585, M1194, M608, M626, M607, M634, and M1304. A suspension of **18a** (1.0 equiv), nosylate (3.0 equiv) and K_2CO_3 (5.0 equiv.) in DMF (0.03 M) was heated at 70 ºC overnight. If the starting mesylate **17** remained, nosylate **17** and K_2CO_3 were added again and heated until the starting material was consumed. After cooling to room temperature, the reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The resultant residue was purified by MPLC (hexane/ethyl acetate = 3:1 to 1:4) to give the crude product. To a suspension of the obtained crude nosylate

(1.0 equiv) and K_2CO_3 (4.0 equiv) in CH_3CN or DMF (0.02 M) was added PhSH (3.0 equiv). The reaction mixture was stirred overnight at 60 ºC. After cooling to room temperature, the reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The resultant residue was purified by NH-MPLC (hexane/ethyl acetate = 1:1 to 0:1) to give the desired product.

***trans*-*N*-(1-((3-Chlorobenzyl)amino)-6-((2-(3-fluorophenyl)cyclopropyl)amino)-1-oxohexan-2-yl)-[1,1'-biphenyl]-4-carboxamide (M585):** A pale brown amorphous in 10% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84 (d, J = 7.8 Hz, 2H), 7.65 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 7.8 Hz, 2H), 7.47 (t, J = 7.8 Hz, 2H), 7.40 (t, J = 7.2 Hz, 1H), 7.27–7.24 (m, 1H), 7.23–7.21 (m, 2H), 7.18 (q, J = 8.4 Hz, 1H), 7.15–7.13 (m, 1H), 6.92–6.89 (m, 1H), 6.87 (d, J = 7.8 Hz, 1H), 6.84–6.80 (m, 2H), 6.69–6.66 (m, 1H), 4.69 (q, J = 7.2 Hz, 1H), 4.47 (dd, J = 15.0, 6.0 Hz, 1H), 4.40 (dt, J = 15.0, 6.0 Hz, 1H), 2.77–2.70 (m, 2H), 2.31–2.28 (m, 1H), 2.05–2.00 (m, 1H), 1.86–1.79 (m, 2H), 1.58–1.53 (m, 2H), 1.50–1.45 (m, 2H), 1.07–1.03 (m, 1H), 0.96–0.92 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.6, 167.2, 163.0 (d, J_{CF} = 242.7 Hz), 145.1 (d, J_{CF} = 7.1 Hz), 144.8, 140.0, 139.9, 134.5, 132.2, 130.0, 129.6 (d, J_{CF} = 8.6 Hz), 129.0, 128.1, 127.7 (d, J_{CF} = 10.1 Hz), 127.6, 127.3 (d, J_{CF} = 14.4 Hz), 125.7, 121.6, 112.5 (d, J_{CF} = 4.4 Hz), 112.38, 112.35, 112.2, 53.5, 49.1, 43.0, 41.9, 32.3, 29.6, 25.0, 23.3, 17.3; HRMS (ESI) m/z calcd for $C_{35}H_{36}{}^{35}ClFN_3O_2$ $[M+H]^+$: 584.2475 found 584.2468.

***trans*-*N*-(6-((-2-([1,1'-Biphenyl]-4-yl)cyclopropyl)amino)-1-((3-chlorobenzyl)amino)-1-oxohexan-2-yl)-[1,1'-biphenyl]-4-carboxamide (M1194):** An off-white solid in 23% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (d, J = 8.4 Hz, 2H), 7.62–7.57 (m, 4H), 7.54 (d, J = 8.4 Hz, 2H), 7.47–7.30 (m, 9H), 7.24–7.23 (m, 1H), 7.20–7.17 (m, 2H), 7.13–7.11 (m, 1H), 7.08–7.06 (m, 3H), 4.77 (q, J = 6.6 Hz, 1H), 4.45 (dd, J = 15.0, 6.0 Hz, 1H), 4.35 (ddd, J = 15.0, 9.0, 6.0 Hz, 1H), 2.78–2.74 (m, 2H), 2.36–2.33 (m, 1H), 2.05–1.84 (m, 3H), 1.60–1.57 (m, 2H), 1.51–1.47 (m, 2H), 1.08–1.05 (m, 1H), 1.00–0.97 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.8, 167.3, 144.7, 141.5, 141.0, 140.1, 139.8, 138.5, 134.5, 132.2, 129.9, 128.9, 128.7, 128.1, 127.65, 127.62, 127.25, 127.18, 127.0, 126.9, 126.2, 125.7, 53.5, 49.1, 42.9, 41.7, 32.5, 29.6, 24.9, 23.3, 17.1 (2 aromatic carbon peaks overlapped somewhere); HRMS (ESI) m/z calcd for $C_{41}H_{41}{}^{35}ClN_3O_2$ $[M+H]^+$: 642.2882 found 642.2870.

***trans*-*N*-(1-((3-Chlorobenzyl)amino)-6-((2-(2-fluoro-[1,1'-biphenyl]-4-yl)cyclopropyl)amino)-1-oxohexan-2-yl)-[1,1'-biphenyl]-4-carboxamide (M608):** A white amorphous in 13% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 2H), 7.63–7.57 (m, 4H), 7.50 (d, J = 8.2 Hz, 2H), 7.47–7.24 (m, 9H), 7.21–7.19 (m, 2H), 7.14–7.11 (m, 1H), 7.06 (d, J = 8.0 Hz, 1H), 6.87 (dd, J = 8.0, 1.6 Hz, 1H), 6.77 (dt, J = 12.0, 1.2 Hz, 1H), 4.77 (q, J = 7.2 Hz, 1H), 4.46 (dd, J = 15.0, 6.0 Hz, 1H), 4.36 (ddd, J = 15.0, 6.0, 2.0 Hz, 1H), 2.78–2.73 (m, 2H), 2.36–2.32 (m, 1H), 2.07–1.82 (m, 3H), 1.60–1.42 (m, 4H), 1.12–1.06 (m, 1H), 1.00–0.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 167.3, 159.7 (d, J_{CF} = 246.0 Hz), 144.7, 144.2 (d, J_{CF} = 7.8

Hz), 140.1, 139.8, 135.7, 134.5, 132.2, 130.4 (d, J_{CF} = 4.2 Hz), 129.9, 128.9, 128.8 (d, J_{CF} = 2.9 Hz), 128.4, 128.1, 127.63, 127.61, 127.4, 127.25, 127.18, 126.0 (d, J_{CF} = 13.6 Hz), 125.7, 121.9 (d, J_{CF} = 2.9 Hz), 113.1 (d, J_{CF} = 23.2 Hz), 53.5, 49.0, 42.9, 41.9, 32.5, 29.6, 24.7, 23.3, 17.3 (1 aromatic carbon peak overlapped somewhere); HRMS (ESI) m/z calcd for $C_{41}H_{40}{}^{35}ClFN_3O_2$ $[M+H]^+$: 660.2788 found 660.2788.

***trans-N*-(6-((-2-(3'-Acetyl-[1,1'-biphenyl]-4-yl)cyclopropyl)amino)-1-((3-chlorobenzyl)amino)-1-oxohexan-2-yl)-[1,1'-biphenyl]-4-carboxamide (M626):** A pale yellow amorphous in 8% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (t, *J* = 1.6 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 7.6 Hz, 2H), 7.53–7.44 (m, 5H), 7.41–7.37 (m, 1H), 7.26–7.22 (m, 3H), 7.15–7.09 (m, 3H), 6.92–6.84 (m, 2H), 4.69 (q, *J* = 7.2 Hz, 1H), 4.50–4.37 (m, 2H), 2.81–2.75 (m, 2H), 2.65 (s, 3H), 2.38–2.33 (m, 1H), 2.07–2.02 (m, 1H), 1.93–1.78 (m, 2H), 1.63–1.54 (m, 2H), 1.52–1.45 (m, 2H), 1.11–1.05 (m, 1H), 1.04–0.98 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.1, 171.6, 167.2, 144.8, 142.2, 141.4, 140.0, 139.9, 137.6, 137.4, 134.6, 132.2, 131.5, 130.0, 129.0, 128.9, 128.1, 127.72, 127.65, 127.6, 127.3, 127.2, 127.0, 126.9, 126.7, 126.3, 125.7, 53.5, 49.1, 43.0, 41.9, 32.3, 29.6, 26.8, 25.0, 23.3, 17.3. HRMS (ESI) m/z calcd for $C_{43}H_{43}{}^{35}ClN_3O_3$ $[M+H]^+$: 684.2987 found 684.2978.

***trans-N*-(1-((3-Chlorobenzyl)amino)-6-((2-(2'-cyano-[1,1'-biphenyl]-4-yl)cyclopropyl)amino)-1-oxohexan-2-yl)-[1,1'-biphenyl]-4-carboxamide (M607):** A pale yellow amorphous in 24% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.66 (dd, *J* = 8.4, 1.8 Hz, 2H), 7.64–7.58 (m, 3H), 7.51–7.38 (m, 7H), 7.33–7.21 (m, 5H), 7.17–7.11 (m, 2H), 6.85–6.81 (m, 1H), 4.67 (q, *J* = 7.2 Hz, 1H), 4.49–4.41 (m, 2H), 2.91–2.73 (m, 2H), 2.38–2.34 (m, 1H), 2.07–2.02 (m, 1H), 1.93–1.79 (m, 2H), 1.64–1.55 (m, 2H), 1.51–1.43 (m, 2H), 1.12–1.07 (m, 1H), 1.05–1.01 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7, 167.2, 145.4, 144.7, 143.2, 140.0, 139.9, 135.3, 134.5, 133.7, 132.8, 132.2, 130.0, 129.9, 128.9, 128.8, 128.6, 128.1, 127.65, 127.62, 127.3, 127.2, 126.0, 125.7, 118.9, 111.1, 53.5, 49.1, 42.9, 42.0, 32.4, 29.5, 25.0, 23.2, 17.2 (1 aromatic carbon peak overlapped somewhere). HRMS (ESI) m/z calcd for $C_{42}H_{39}{}^{35}Cl_2N_4O_2$ $[M+Cl]^-$: 701.2456 found 701.2442.

***trans-N*-(6-((2-(4'-Acetamido-[1,1'-biphenyl]-4-yl)cyclopropyl)amino)-1-((3-chlorobenzyl)amino)-1-oxohexan-2-yl)-[1,1'-biphenyl]-4-carboxamide (M634):** A white amorphous in 42% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.8 Hz, 2H), 7.63–7.58 (m, 4H), 7.53–7.38 (m, 9H), 7.31 (brs, 1H), 7.24 (d, *J* = 5.4 Hz, 1H), 7.20 (d, *J* = 4.8 Hz, 2H), 7.14–7.11 (m, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 7.8 Hz, 1H), 4.74 (q, *J* = 7.0 Hz, 1H), 4.45 (dd, *J* = 15.0, 6.0 Hz, 1H), 4.40–4.34 (m, 1H), 2.79–2.72 (m, 2H), 2.34–2.32 (m, 1H), 2.19 (s, 3H), 2.06–2.00 (m, 1H), 1.88–1.80 (m, 2H), 1.59–1.54 (m, 2H), 1.51–1.46 (m, 2H), 1.07–1.02 (m, 1H), 0.99–0.95 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.7, 168.3, 167.2, 144.7, 141.4, 140.1, 139.8, 137.7, 136.9, 134.5, 132.2, 130.0, 128.9, 128.1, 127.7, 127.6, 127.31, 127.28, 127.2, 126.6, 126.2, 125.7, 120.2, 53.5, 49.1, 42.9, 41.8, 32.4, 29.7, 24.9, 24.6, 23.3, 17.1 (2 aromatic carbon peaks overlapped somewhere). HRMS (ESI) m/z calcd for $C_{43}H_{44}{}^{35}ClN_4O_3$ $[M+H]^+$: 699.3096 found 699.3101.

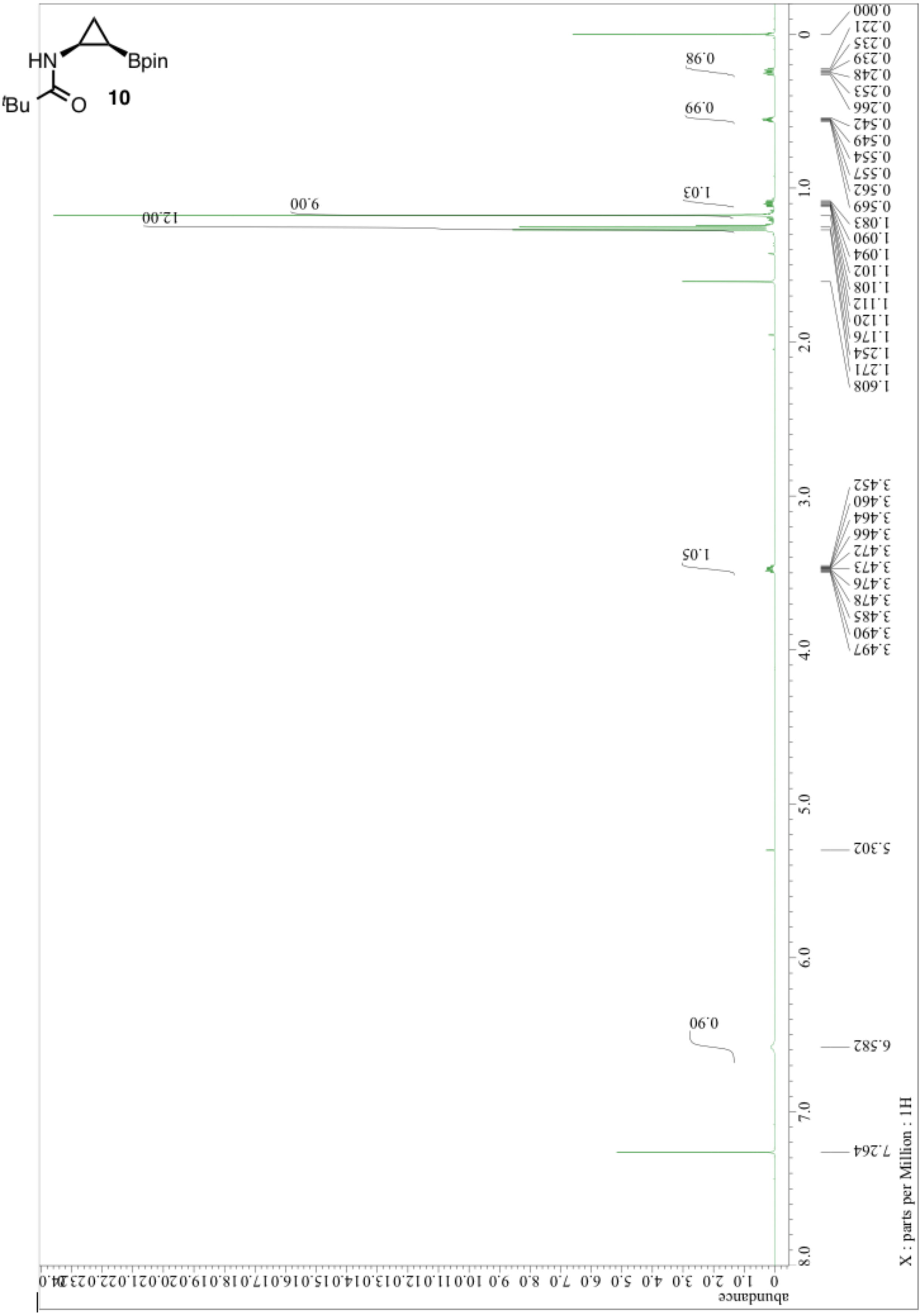
7. Purity of Tested Compounds

Table S1

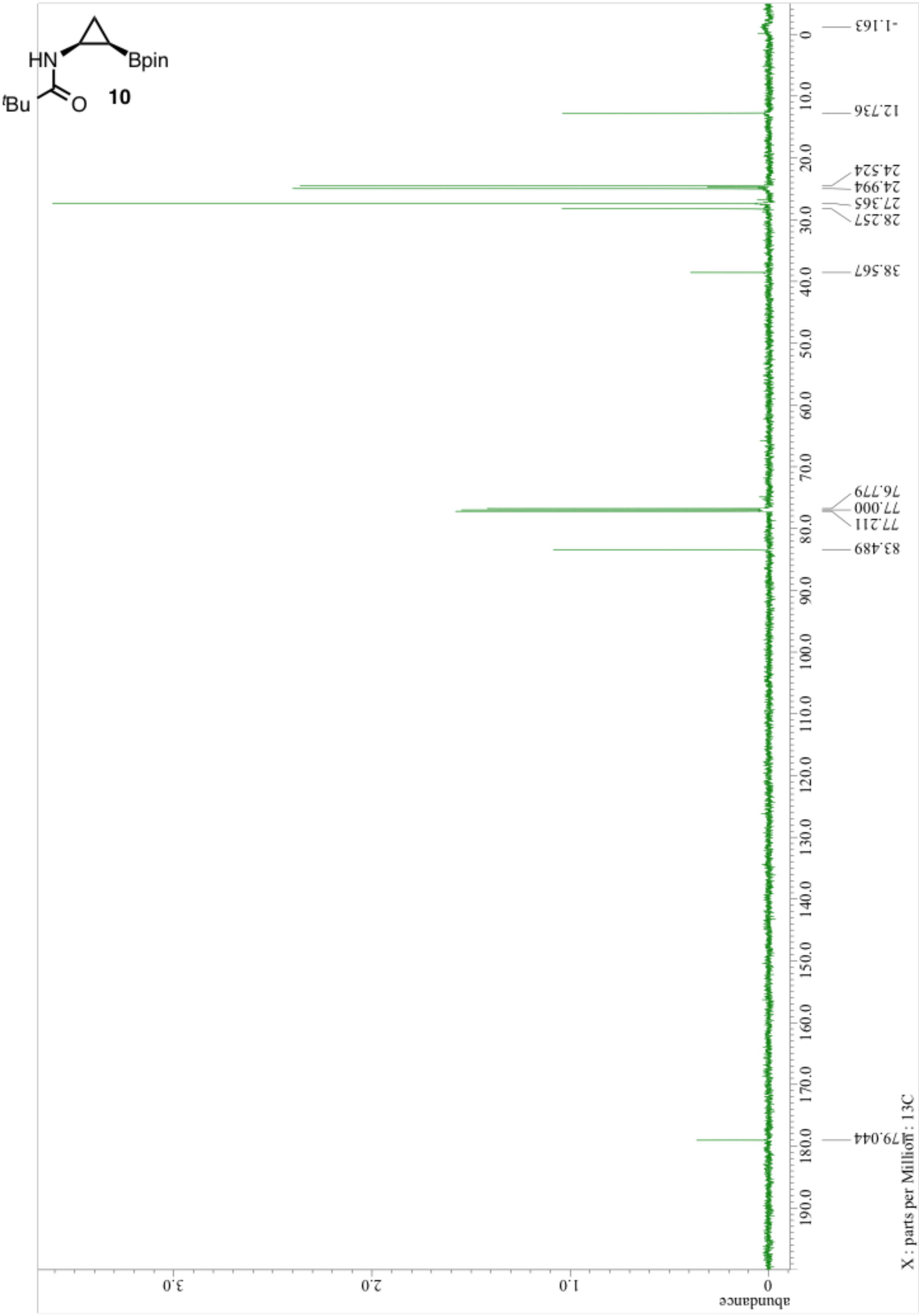
Cpd #	Exact MS	UV/nm	Purity/%	Cpd #	Exact MS	UV/nm	Purity/%
1b	163.1	220	100	**16n**	225.12	254	100
1c	151.08	220	100	**16o**	285.15	254	97.9
1d	151.08	220	98.9	**16p**	2661.4	254	100
1e	147.1	220	100	**16q**	254.11	254	95.4
1f	169.07	220	97.3	**16r**	287.1	254	95.7
1g	183.1	220	100	**16s**	211.11	254	99.8
1h	201.08	220	100	**16t**	302.11	254	100
1i	147.1	220	100	**16u**	302.11	254	98.5
1j	217.07	220	100	**16v**	277.11	254	98.6
1k	209.12	220	100	**16w**	227.11	254	98.8
1l	167.05	220	100	**16x**	227.11	254	100
1m	147.1	220	100	**16y**	239.13	254	100
1n	151.08	220	98.9	**16z**	239.13	254	100
1o	209.12	220	100	**16aa**	277.11	254	100
1p	228.99	220	98.2	**16ab**	255.11	254	100
16a	309.15	254	100	**M585**	583.24	254	96.2
16b	215.08	254	98.5	**M1194**	641.28	254	98.3
16c	243.08	254	100	**M608**	659.27	254	96.9
16d	223.14	254	100	**M1302**	583.24	254	98.9
16e	210.12	254	95.1	**M1284**	595.26	254	95.6
16f	234.12	254	100	**M1310**	579.27	254	97.2
16g	227.11	254	99.2	**M1206**	675.24	254	98.9
16h	227.11	254	100	**M1291**	734.27	254	95.1
16i	245.1	254	97	**M1304**	698.3	254	98.6
16j	287.1	254	98.7	**M626**	683.29	254	97.7
16k	277.11	254	100	**M607**	666.28	254	98.2
16l	251.13	254	100	**M634**	698.3	254	96.3
16m	239.13	254	98.7				

8. ^{1}H and ^{13}C NMR Spectra

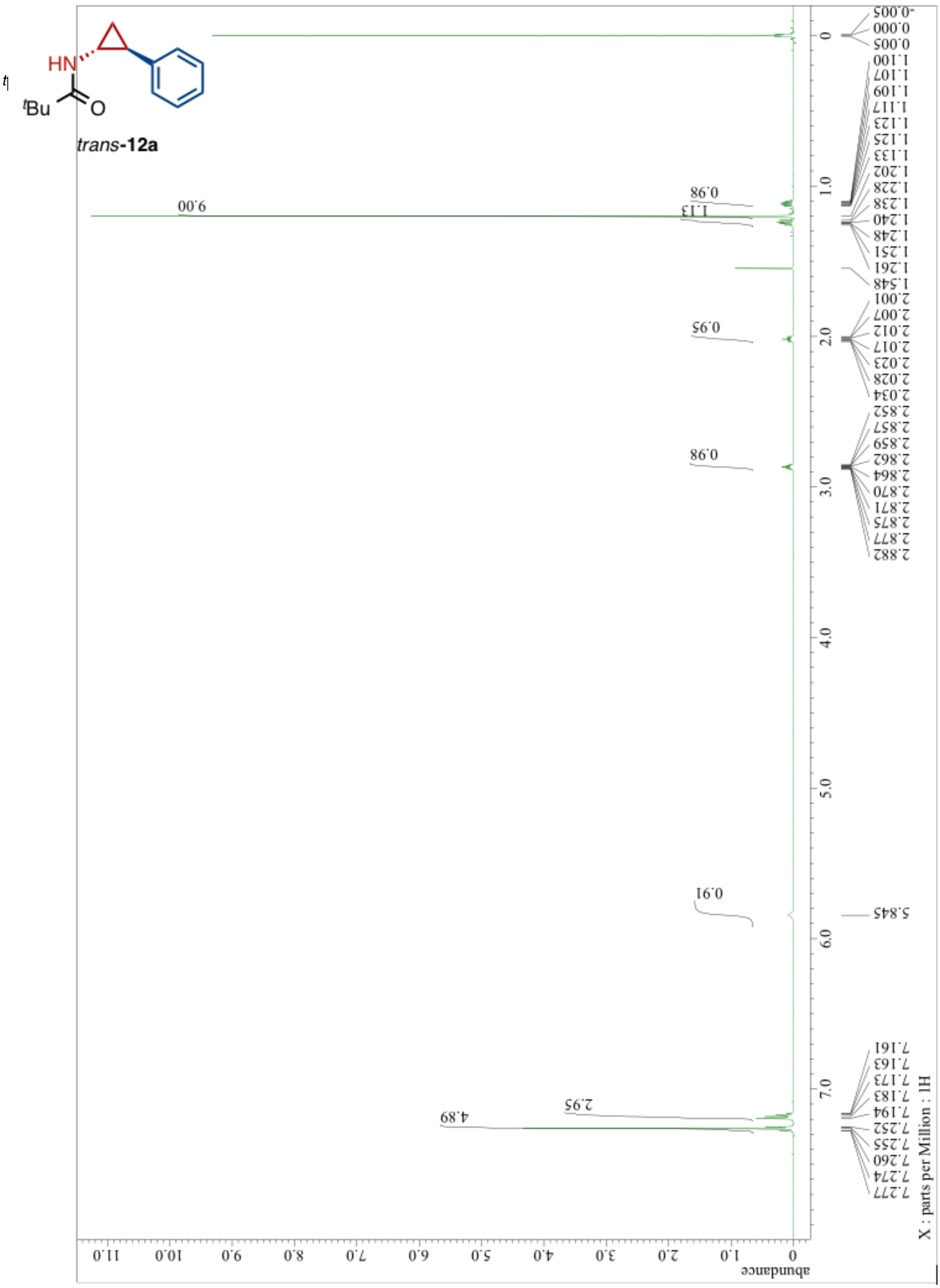
^{1}H NMR (600 MHz, $CDCl_3$) of 10:



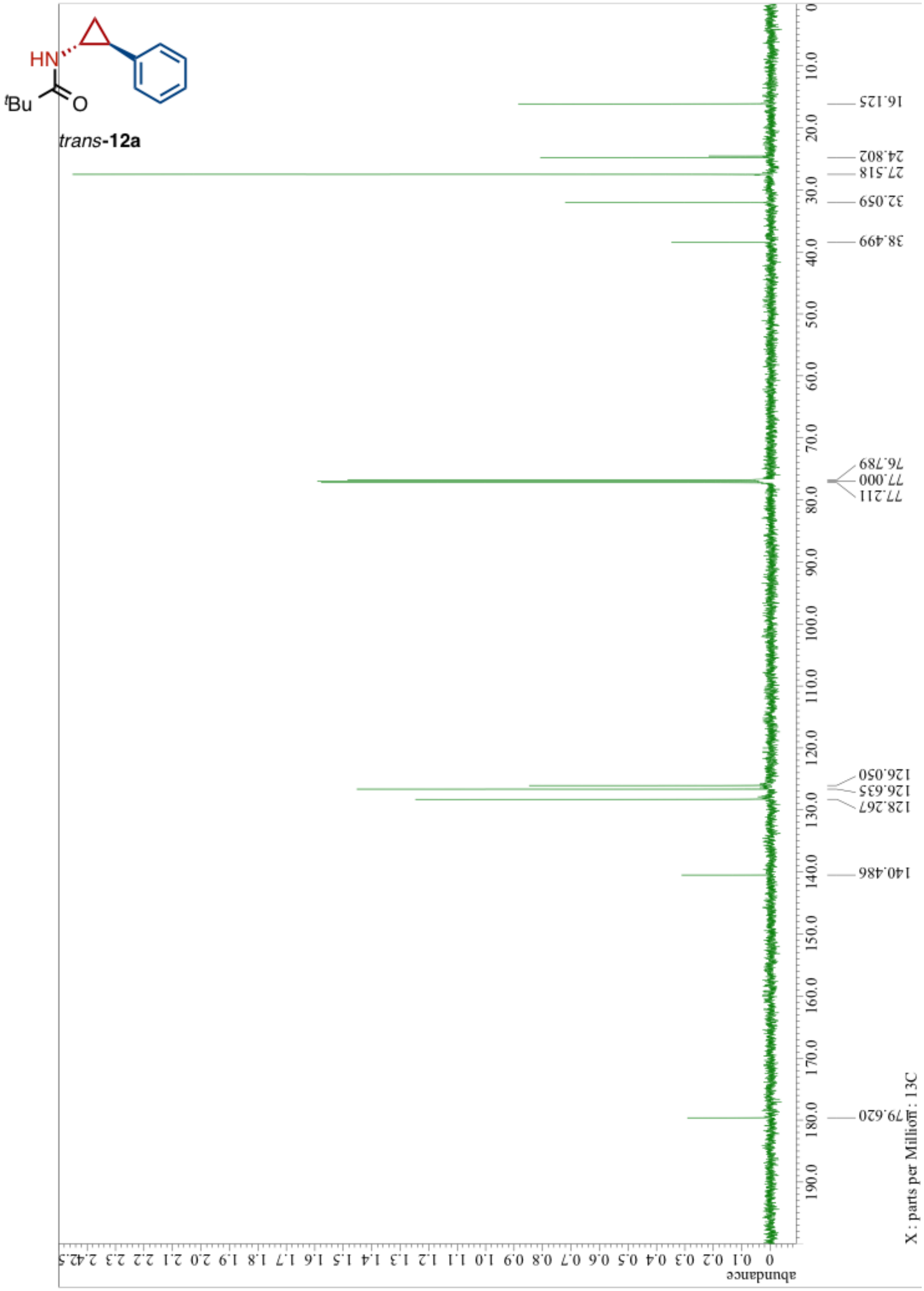
^{13}C NMR (150 MHz, $CDCl_3$) of 10:



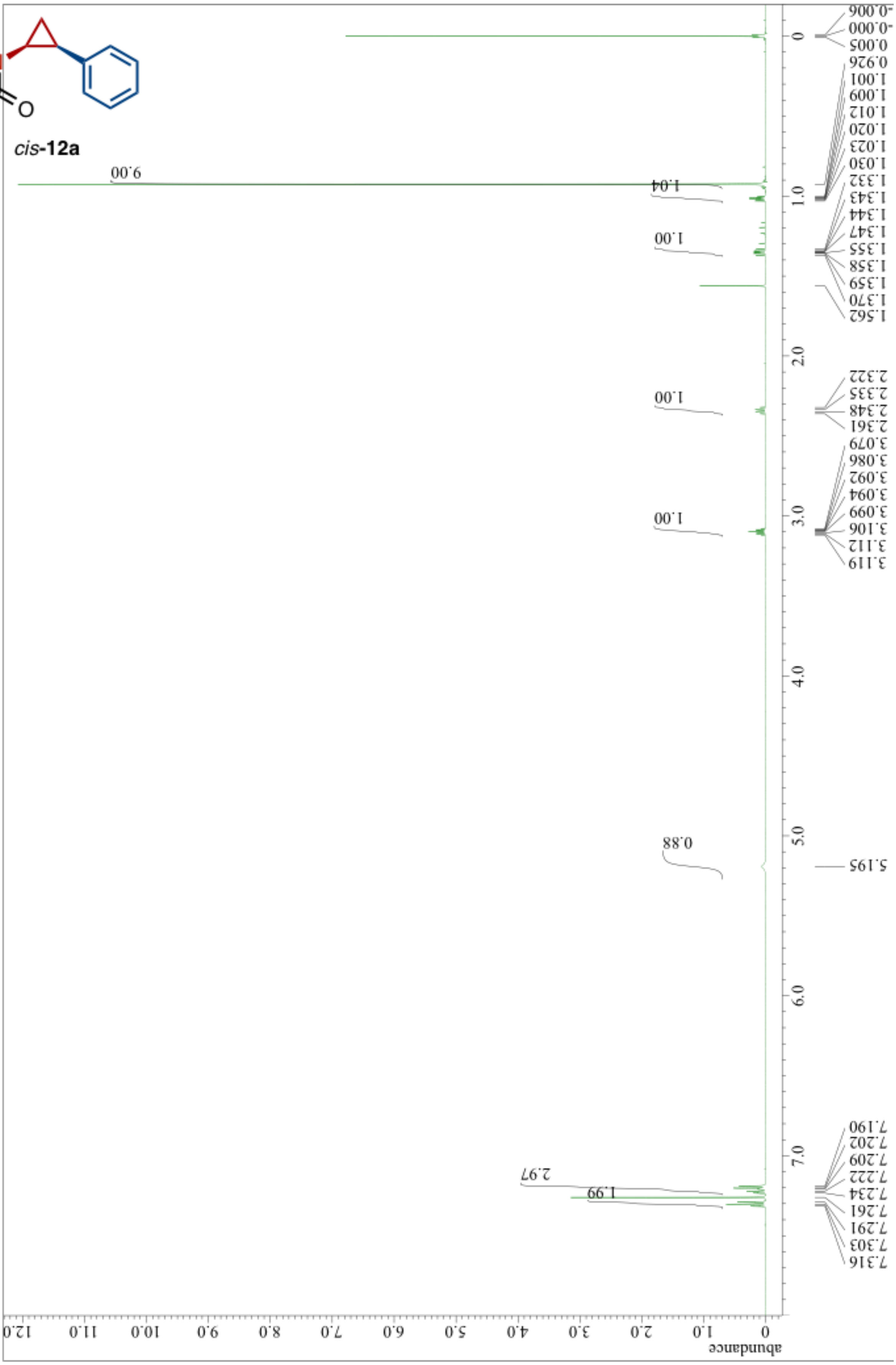
^{1}H NMR (600 MHz, $CDCl_3$) of *trans*-12a:



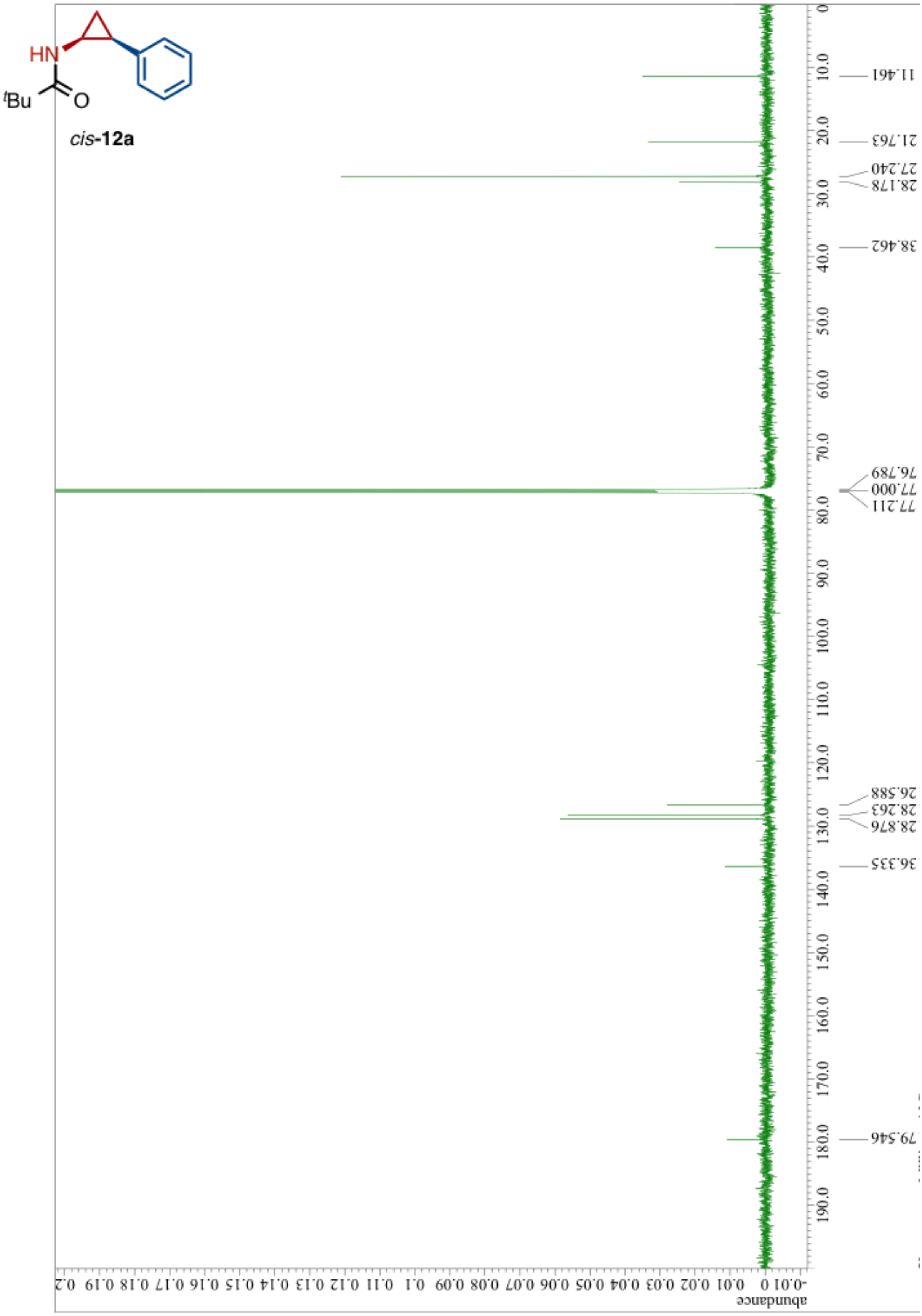
[13]C NMR (150 MHz, $CDCl_3$) of *trans*-12a:



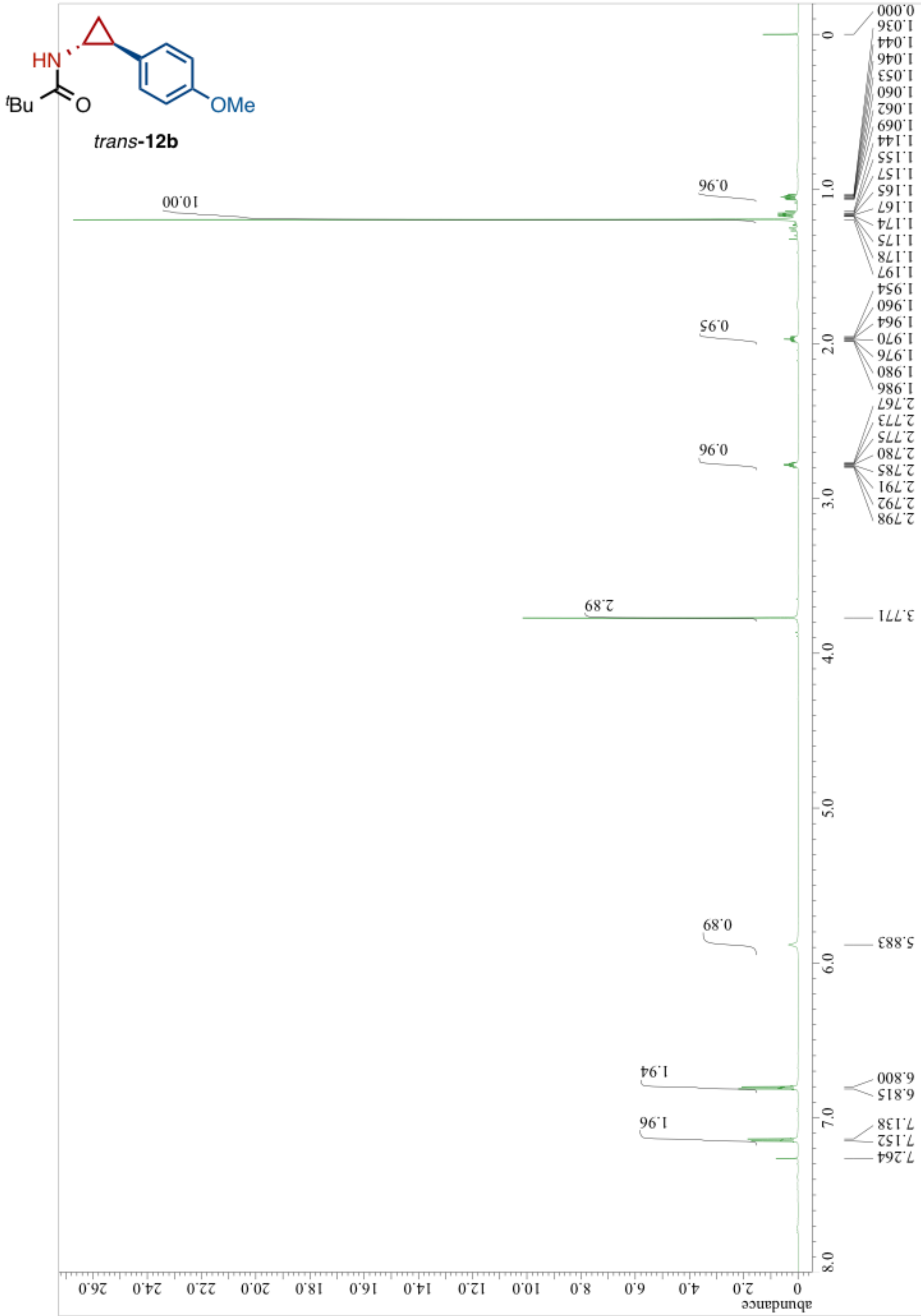
[1]H NMR (600 MHz, $CDCl_3$) of *cis*-12a:



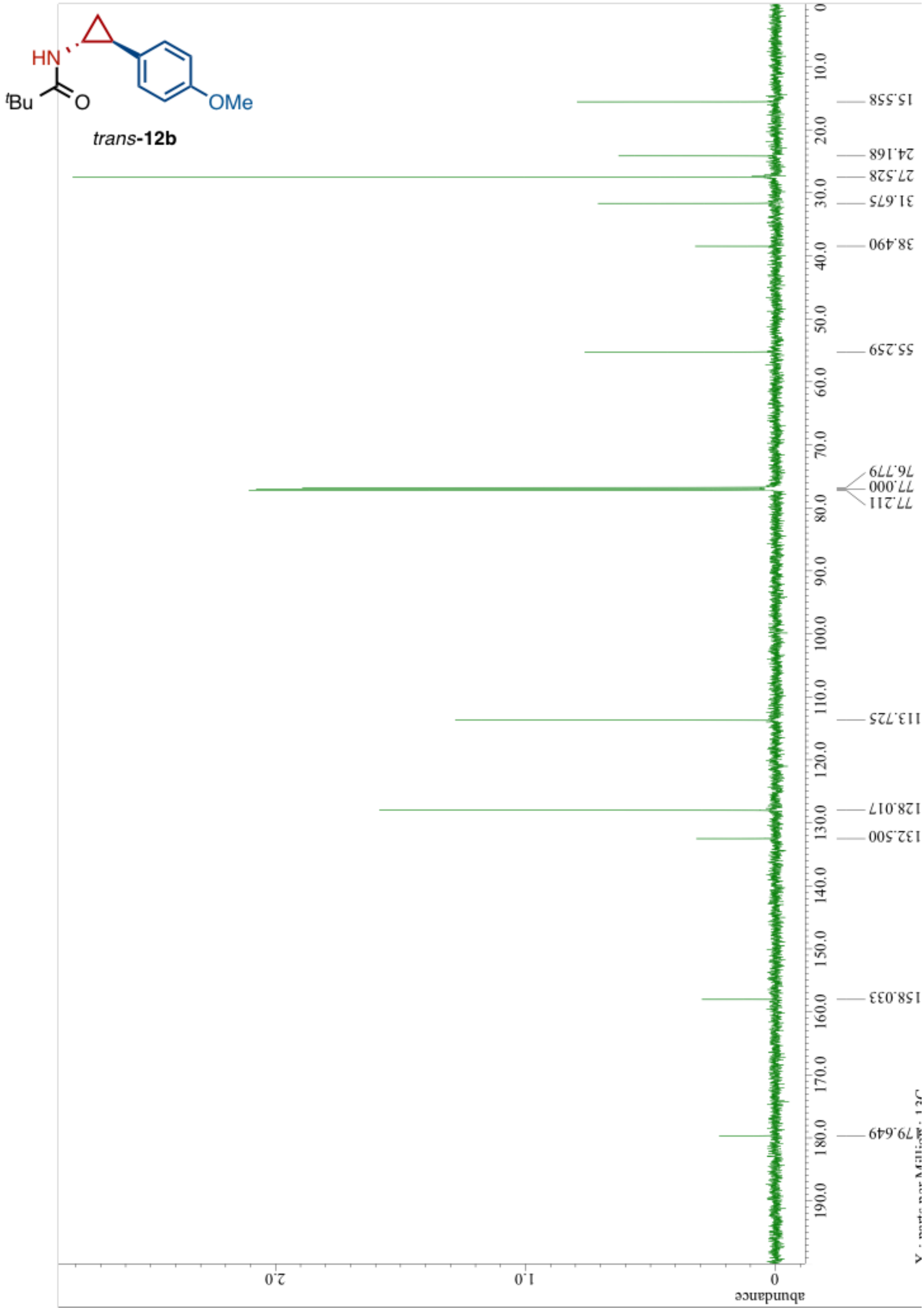
^{13}C NMR (150 MHz, $CDCl_3$) of *cis*-12a:



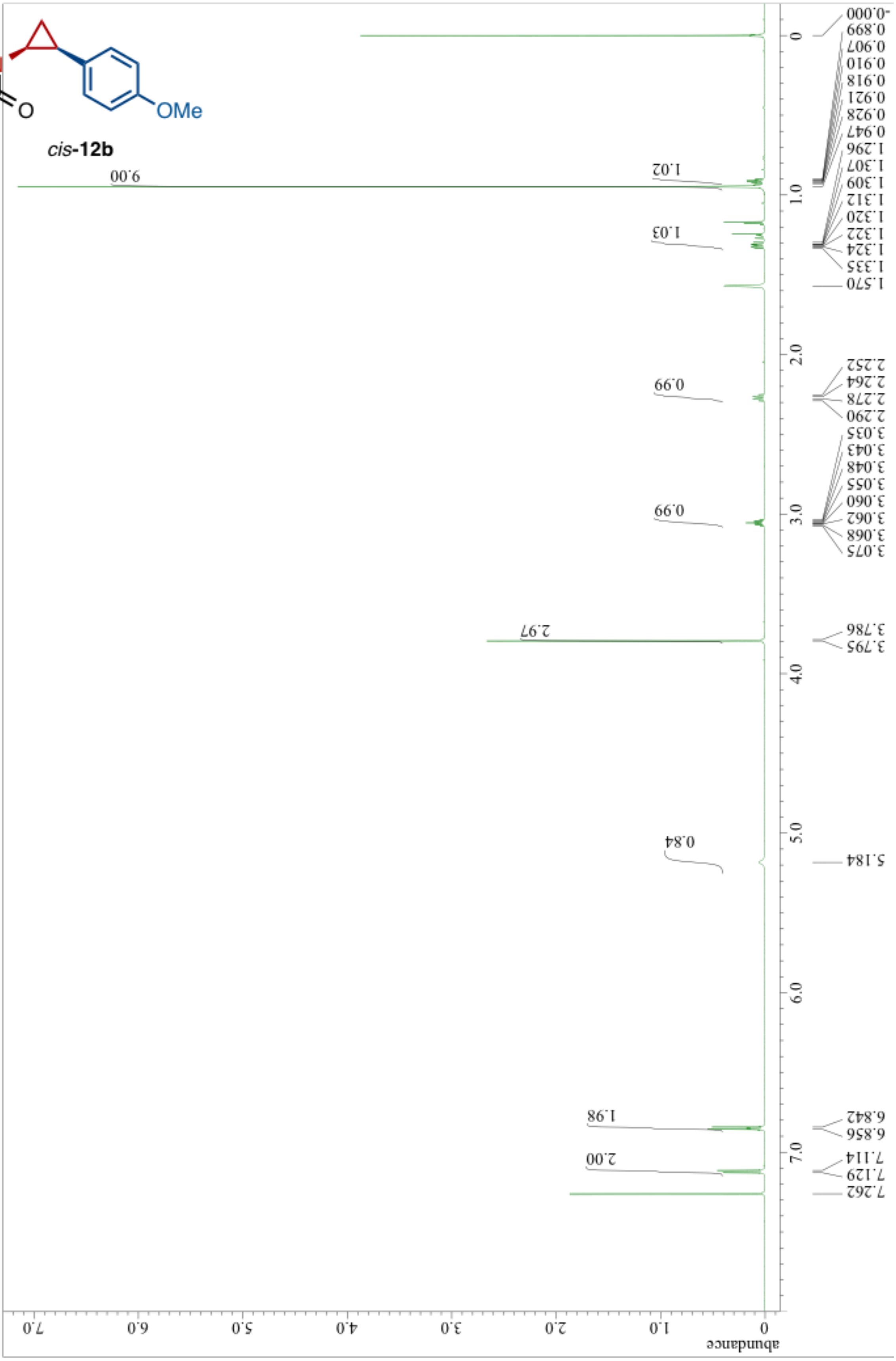
[1]H NMR (600 MHz, $CDCl_3$) of *trans*-12b:



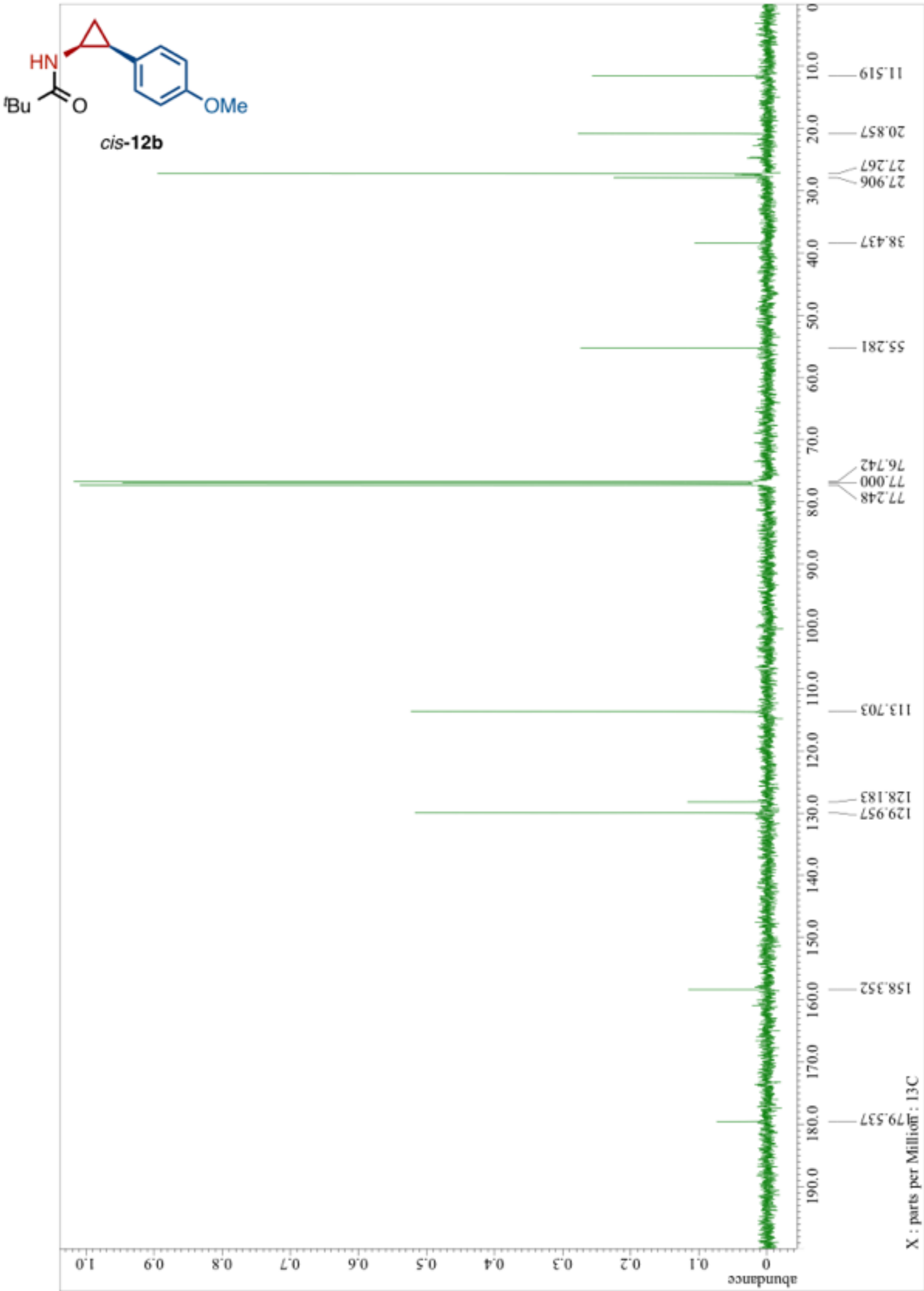
^{13}C NMR (150 MHz, CDCl$_3$) of *trans*-12b:



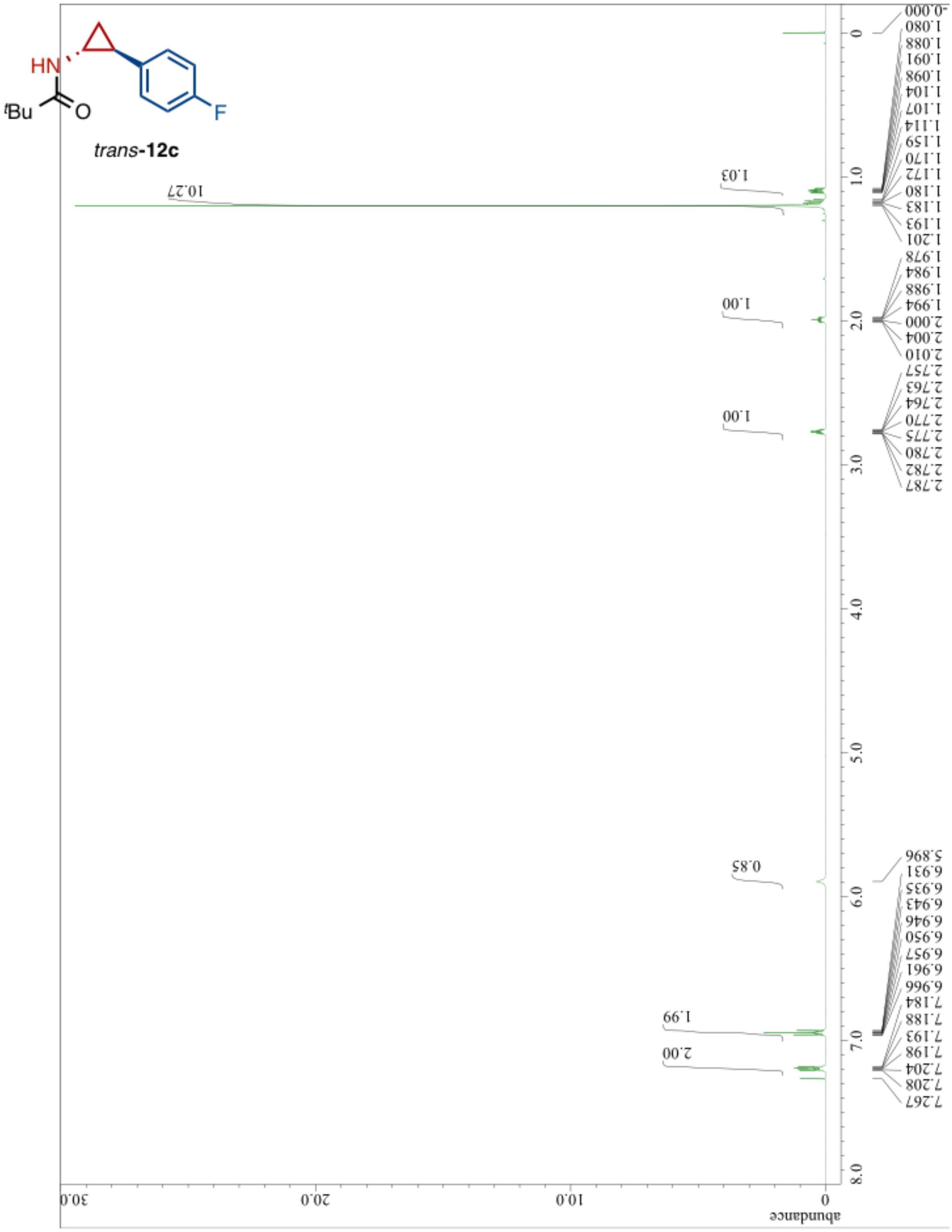
^{1}H NMR (600 MHz, CDCl$_3$) of *cis*-12b:



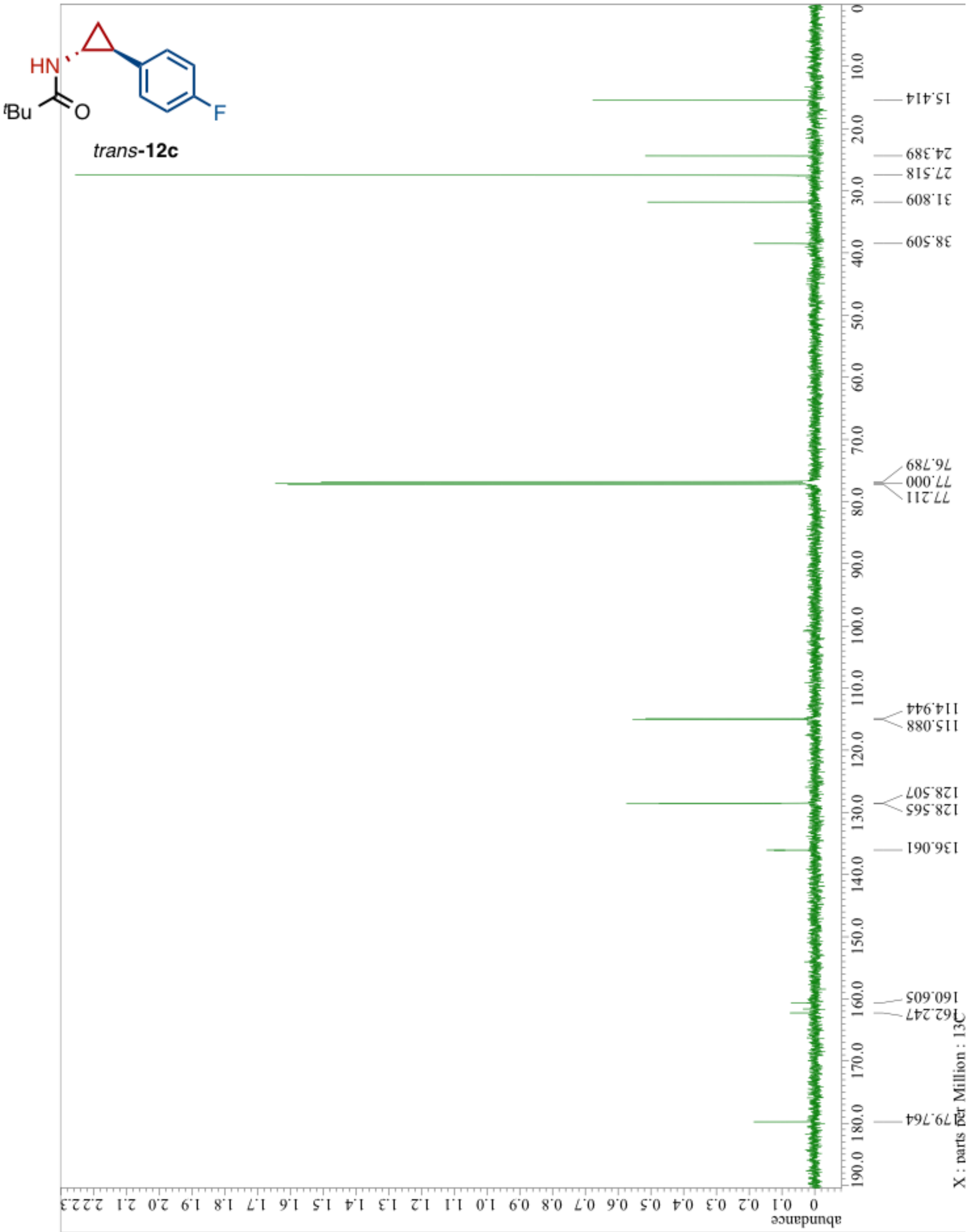
[13]C NMR (125 MHz, CDCl$_3$) of *cis*-12b:



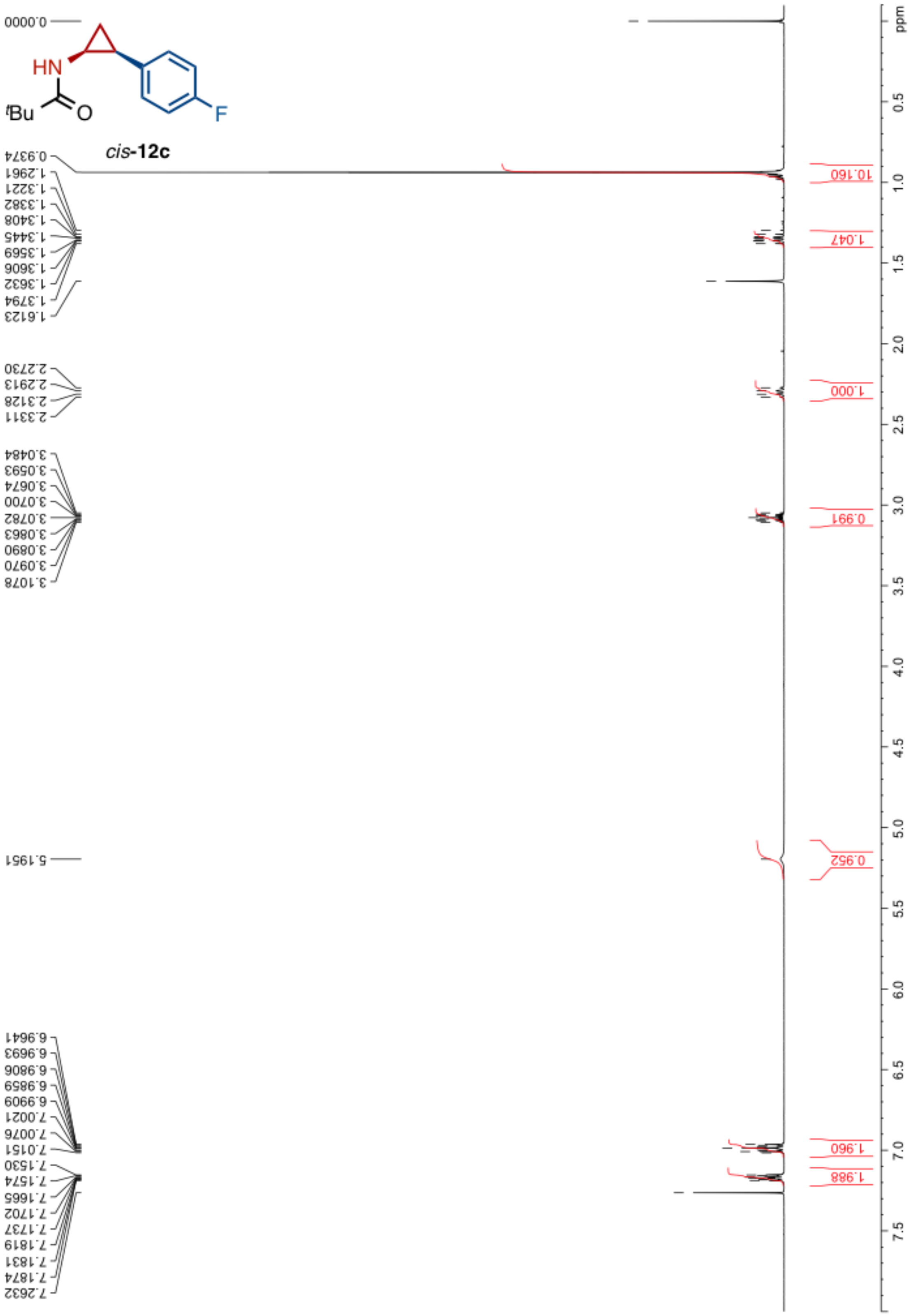
^{1}H NMR (600 MHz, $CDCl_3$) of *trans*-12c:



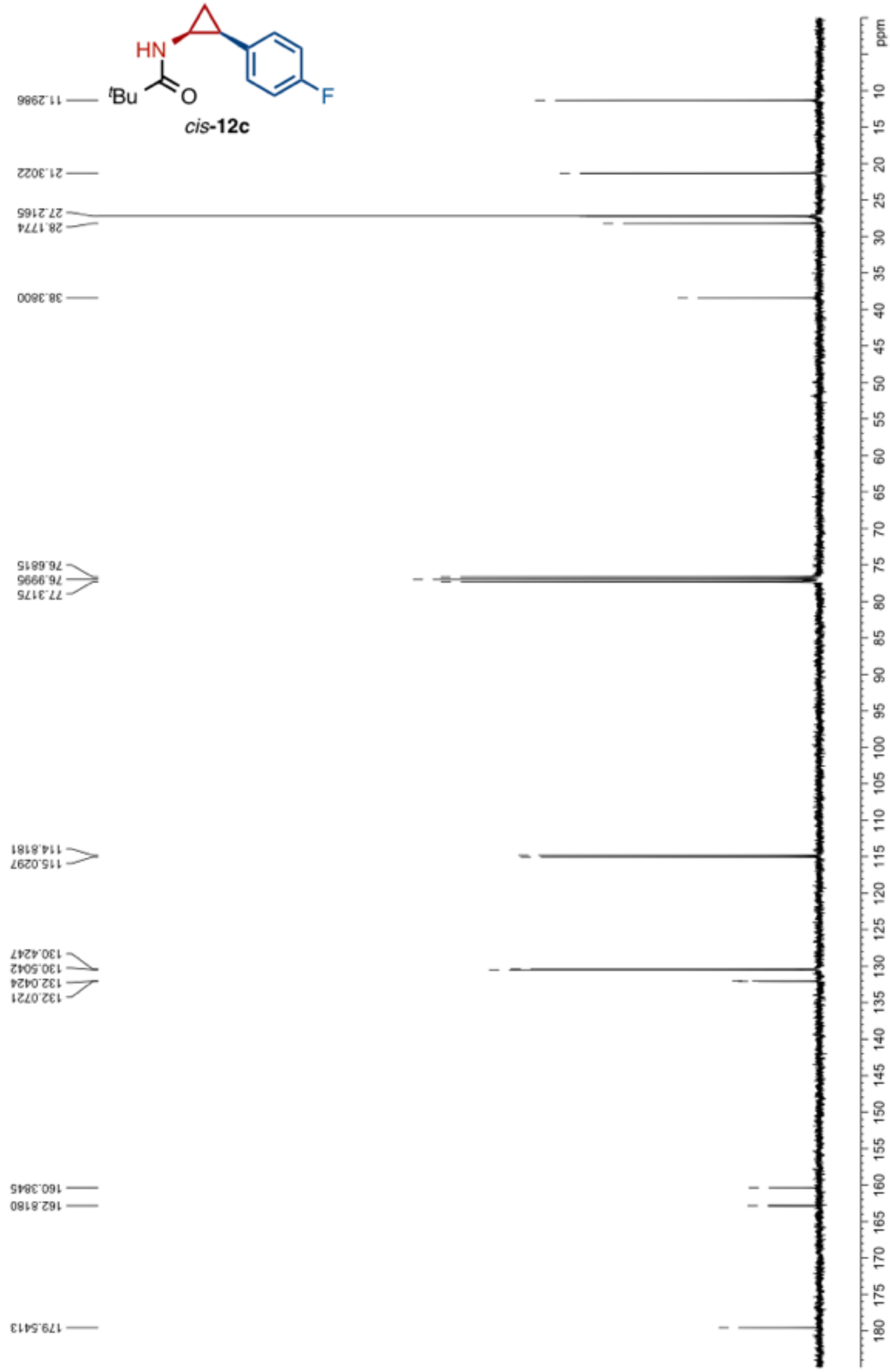
^{13}C NMR (125 MHz, CDCl$_3$) of *trans*-12c:



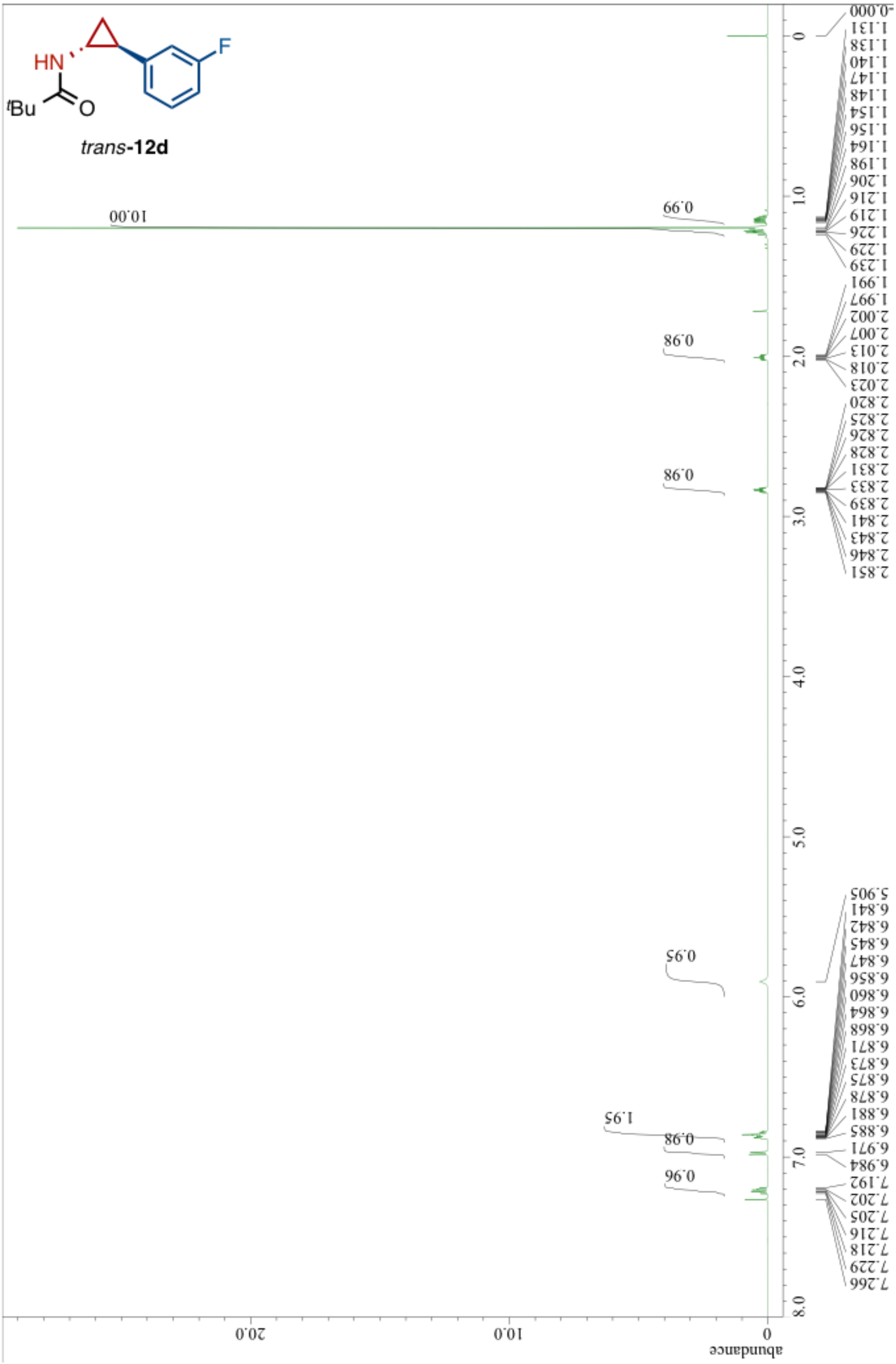
^{1}H NMR (400 MHz, $CDCl_3$) of *cis*-12c:



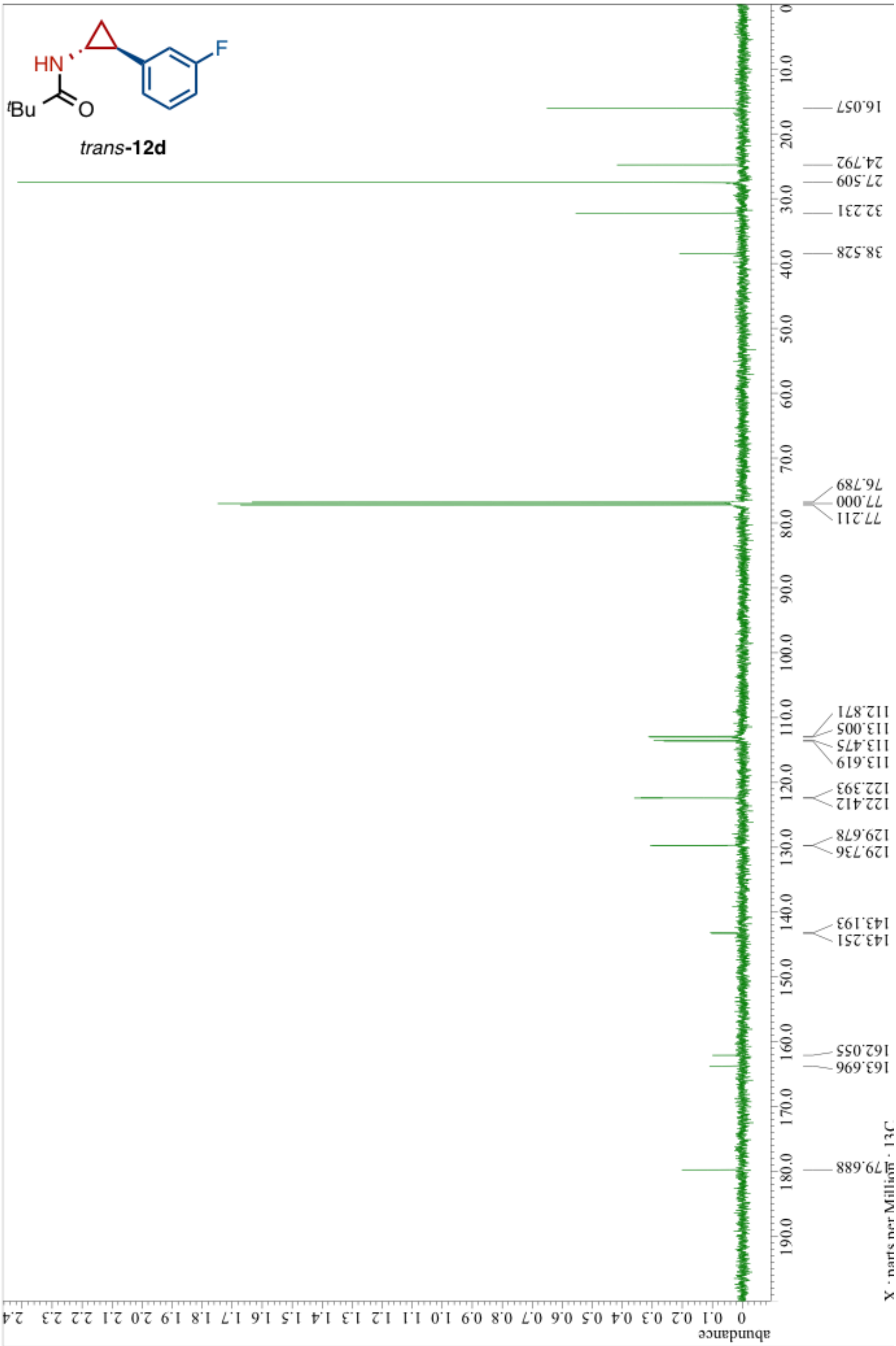
^{13}C NMR (100 MHz, CDCl$_3$) of *cis*-12c:



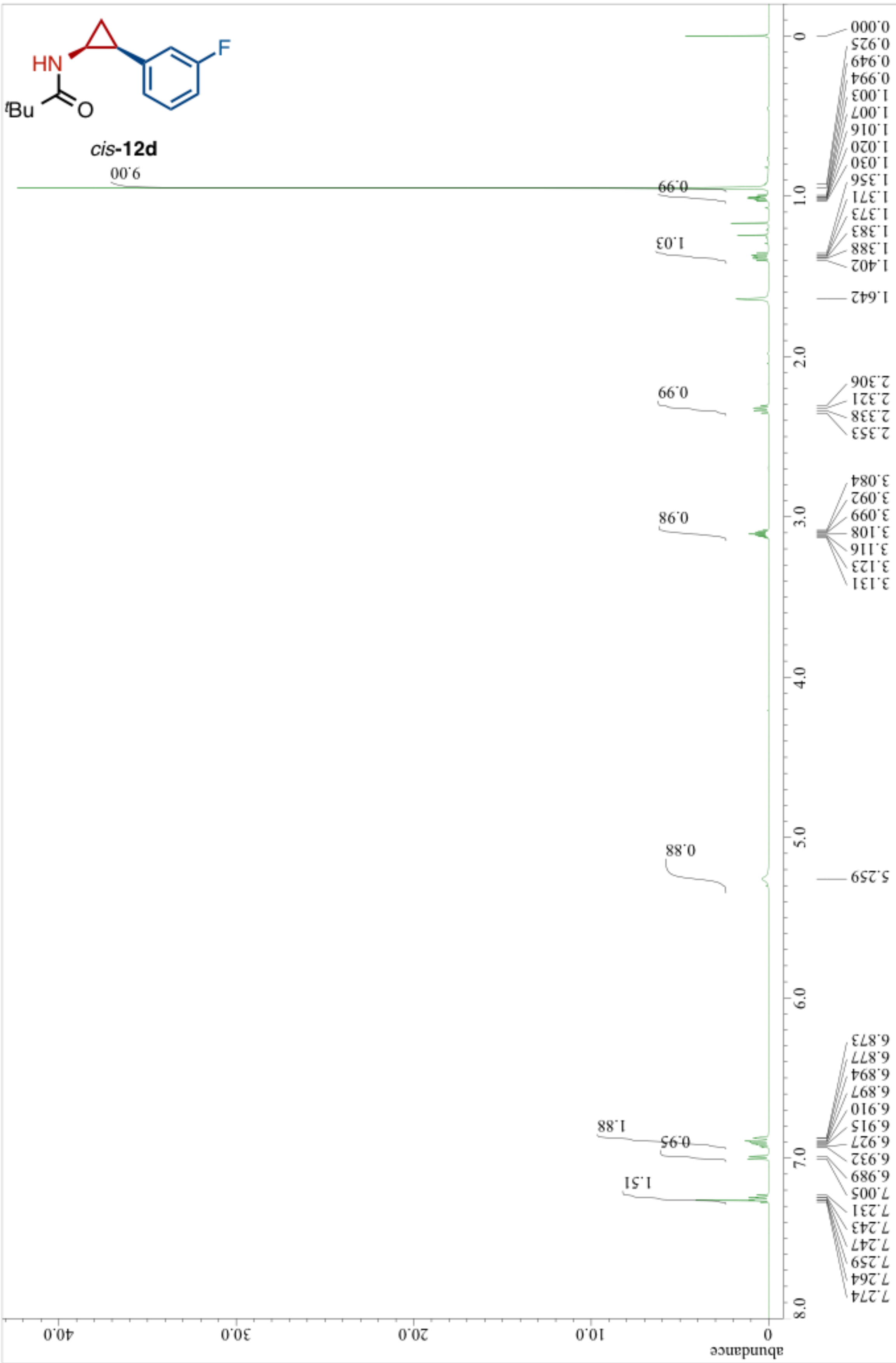
^{1}H NMR (600 MHz, $CDCl_3$) of *trans*-12d:



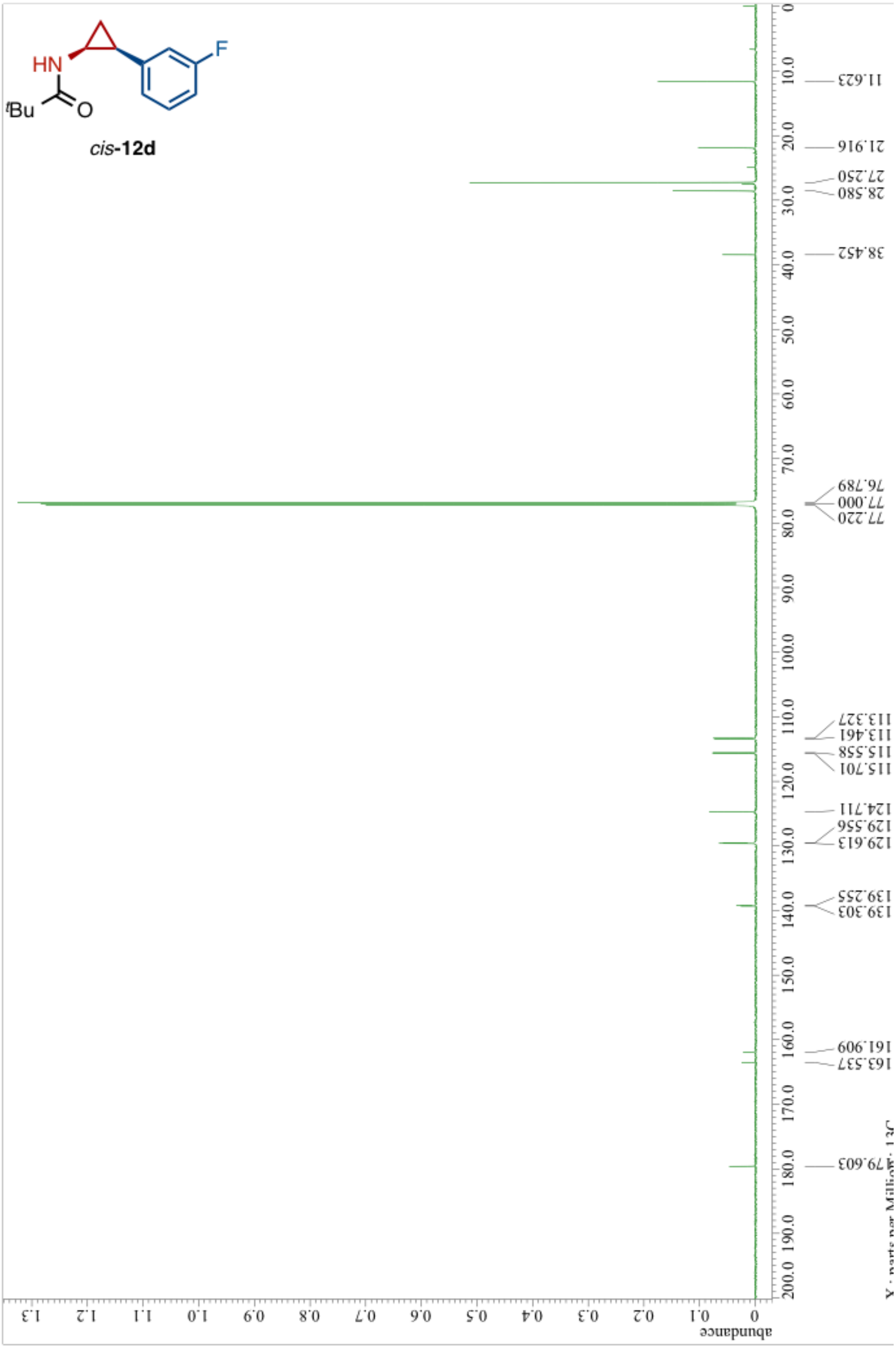
^{13}C NMR (150 MHz, $CDCl_3$) of *trans*-12d:



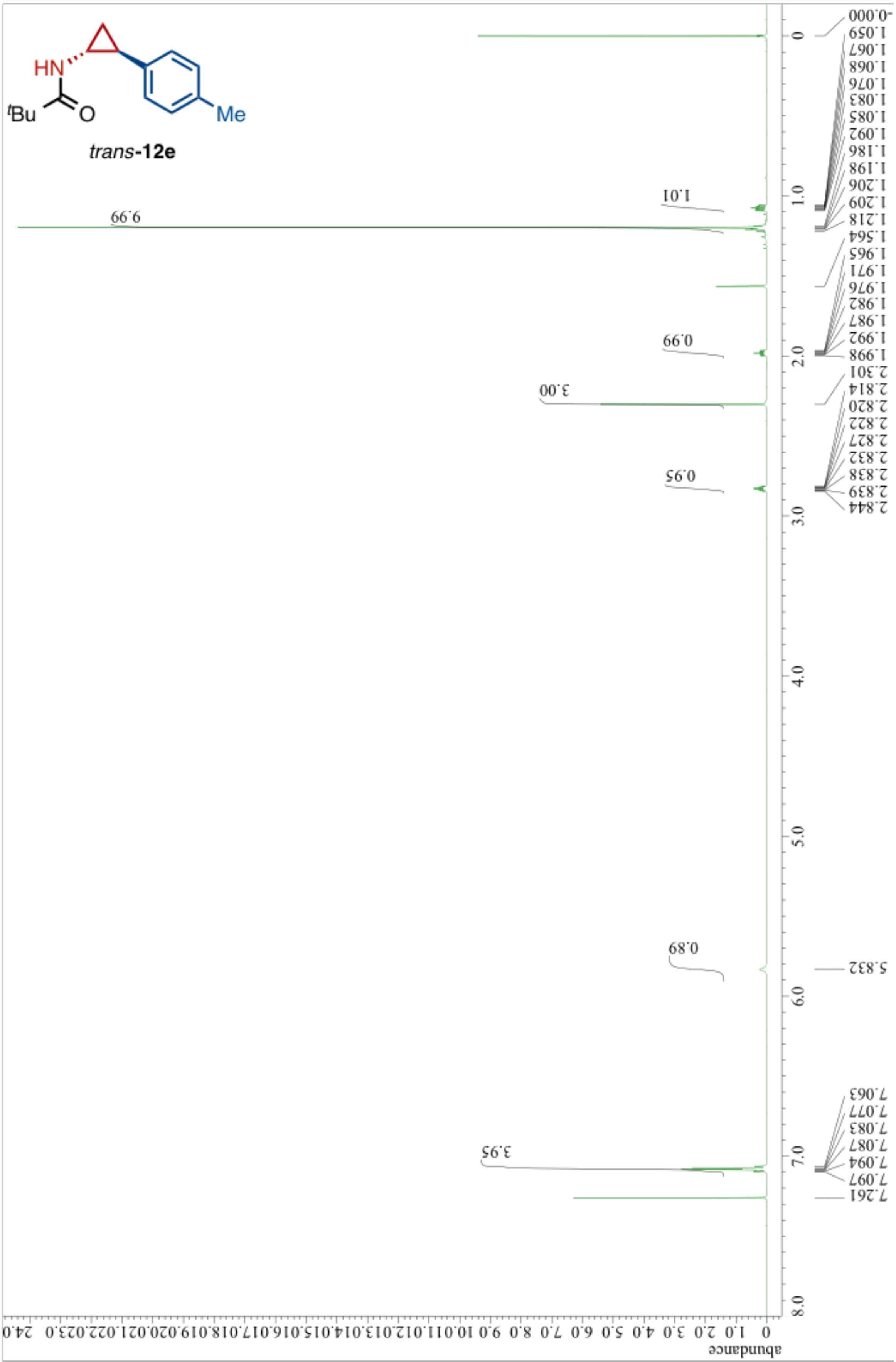
^{1}H NMR (600 MHz, $CDCl_3$) of *cis*-12d:



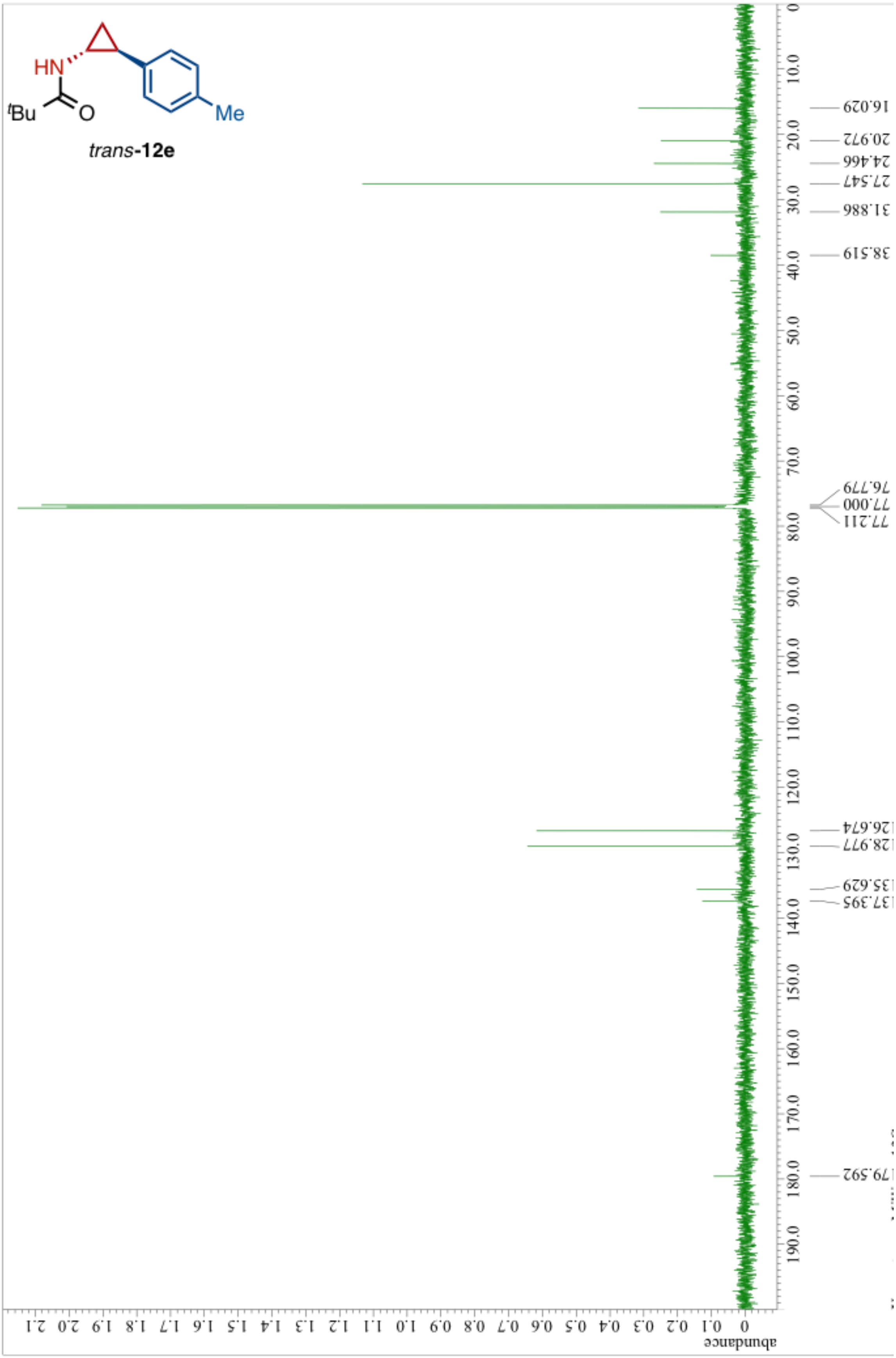
^{13}C NMR (150 MHz, CDCl$_3$) of *cis*-12d:



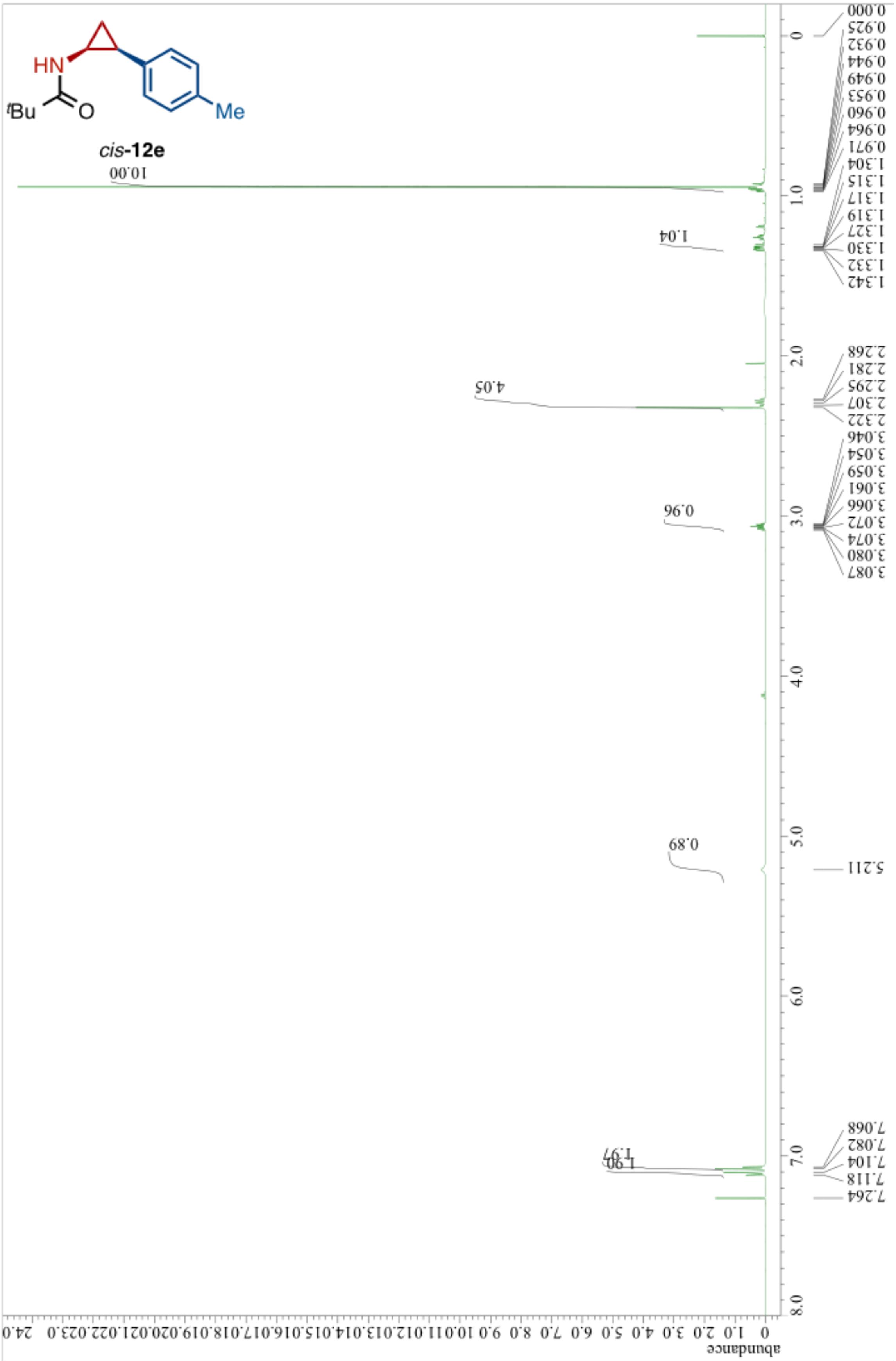
[1]H NMR (600 MHz, $CDCl_3$) of *trans*-12e:



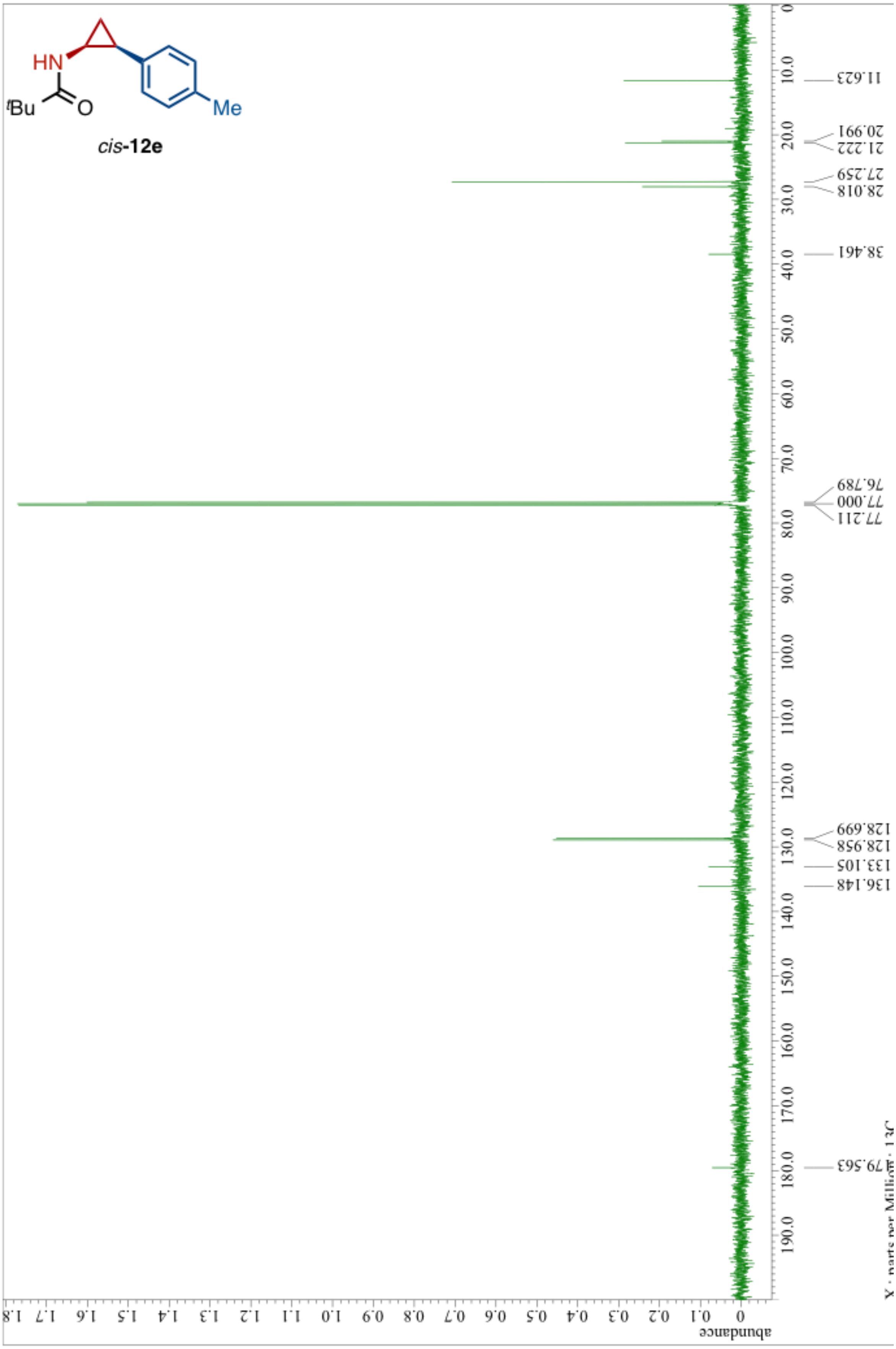
^{13}C NMR (150 MHz, CDCl$_3$) of *trans*-12e:



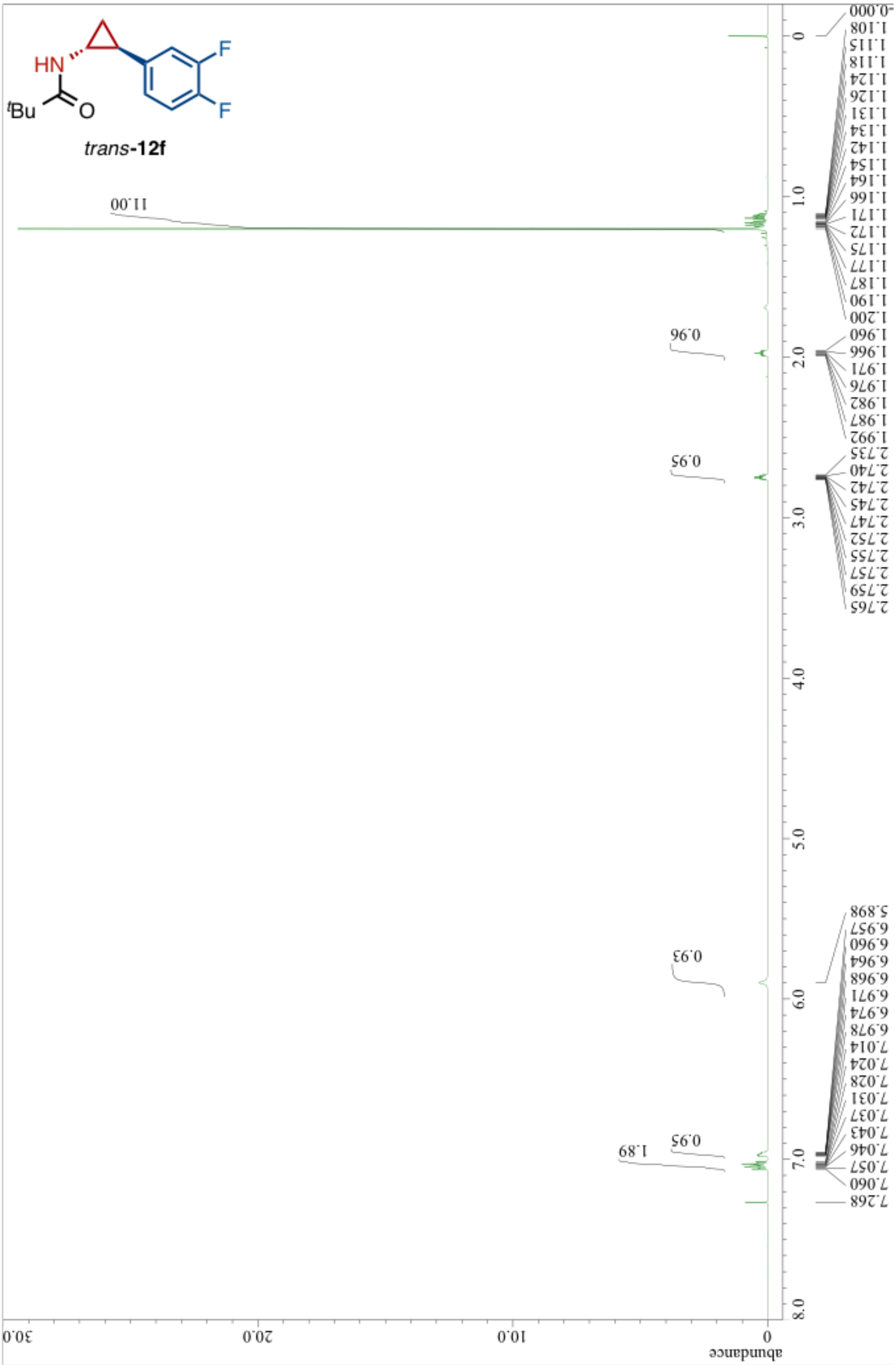
[1]H NMR (600 MHz, $CDCl_3$) of *cis*-12e:



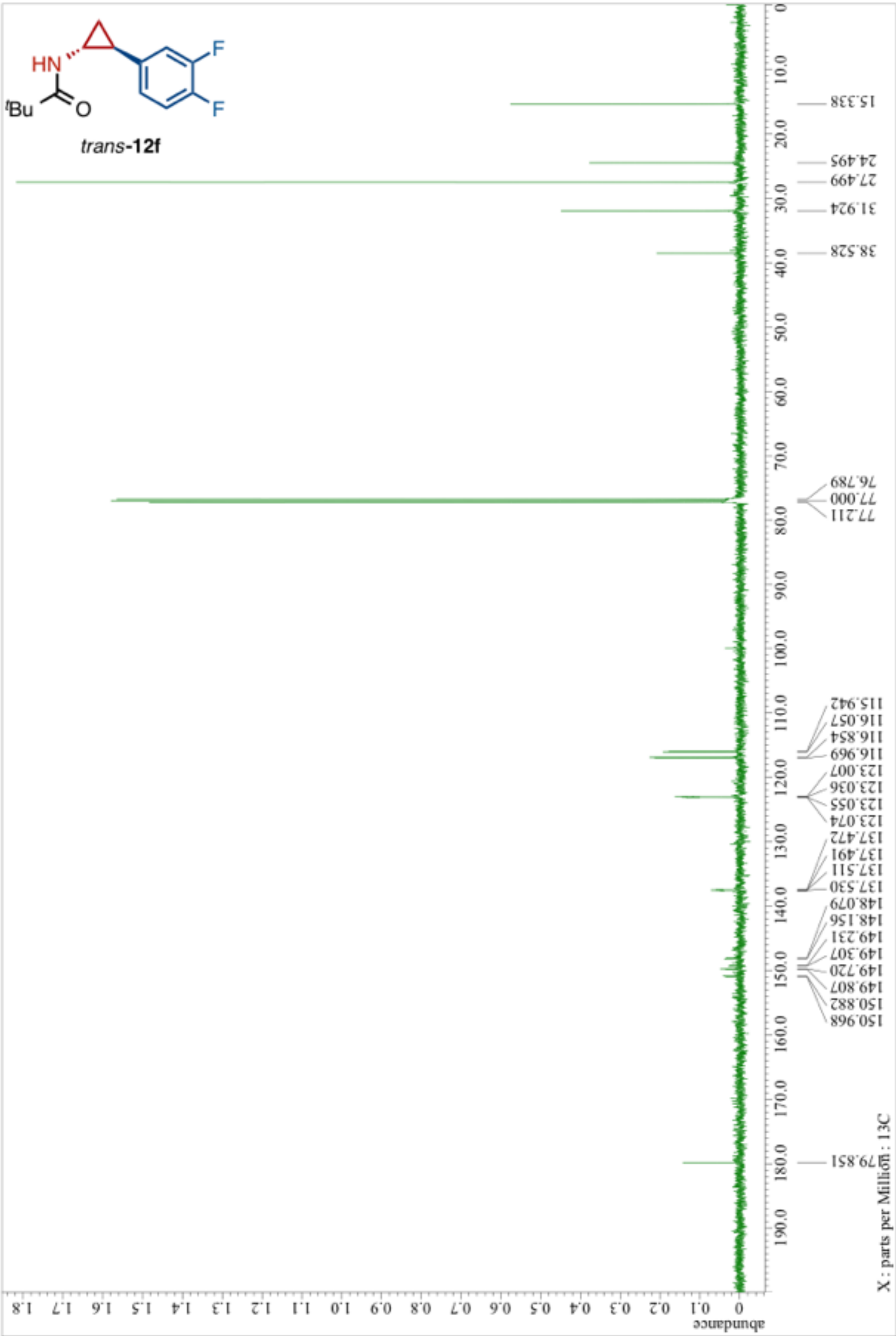
[13]C NMR (150 MHz, $CDCl_3$) of *cis*-12e:



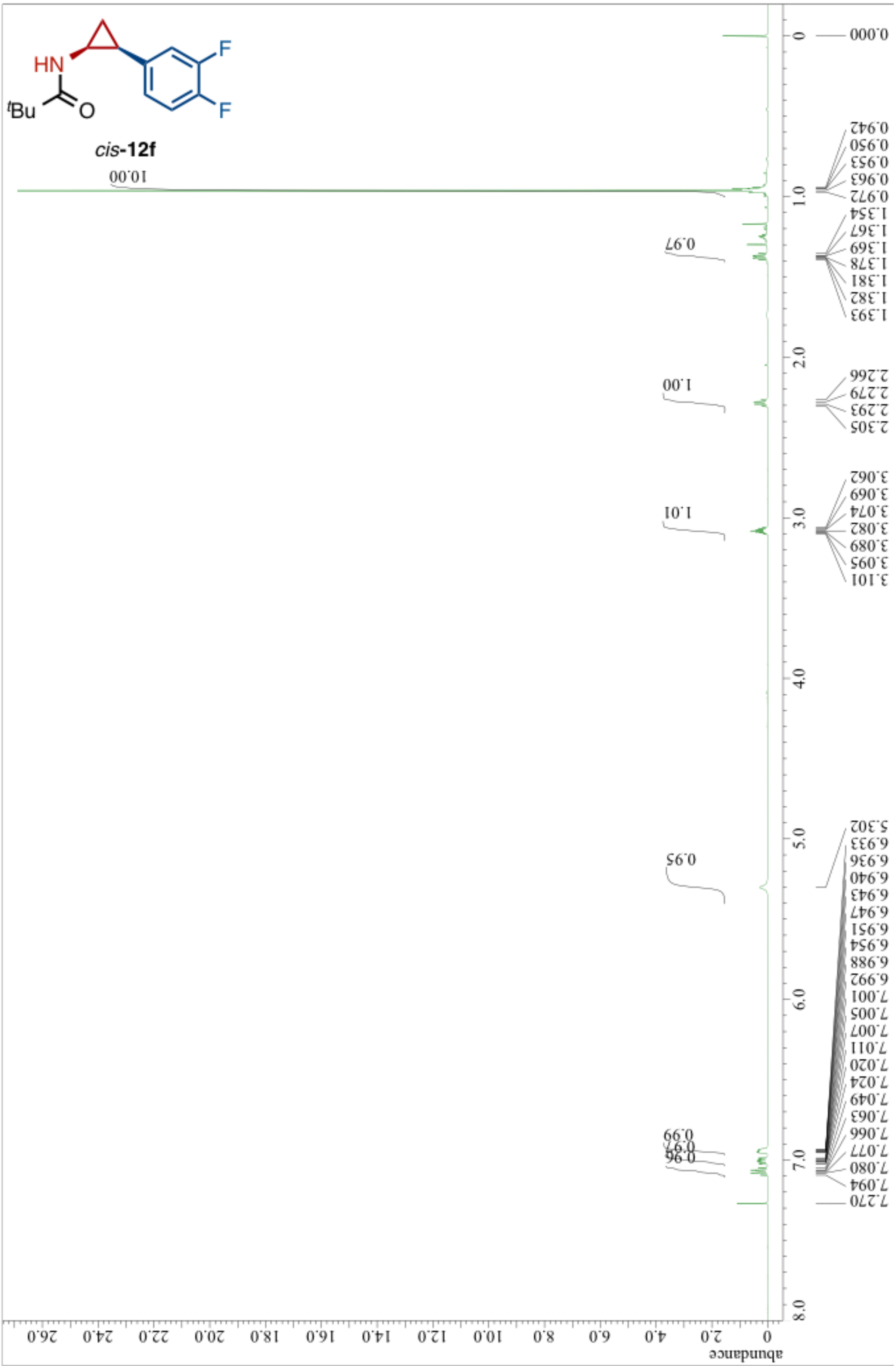
^{1}H NMR (600 MHz, $CDCl_3$) of *trans*-12f:



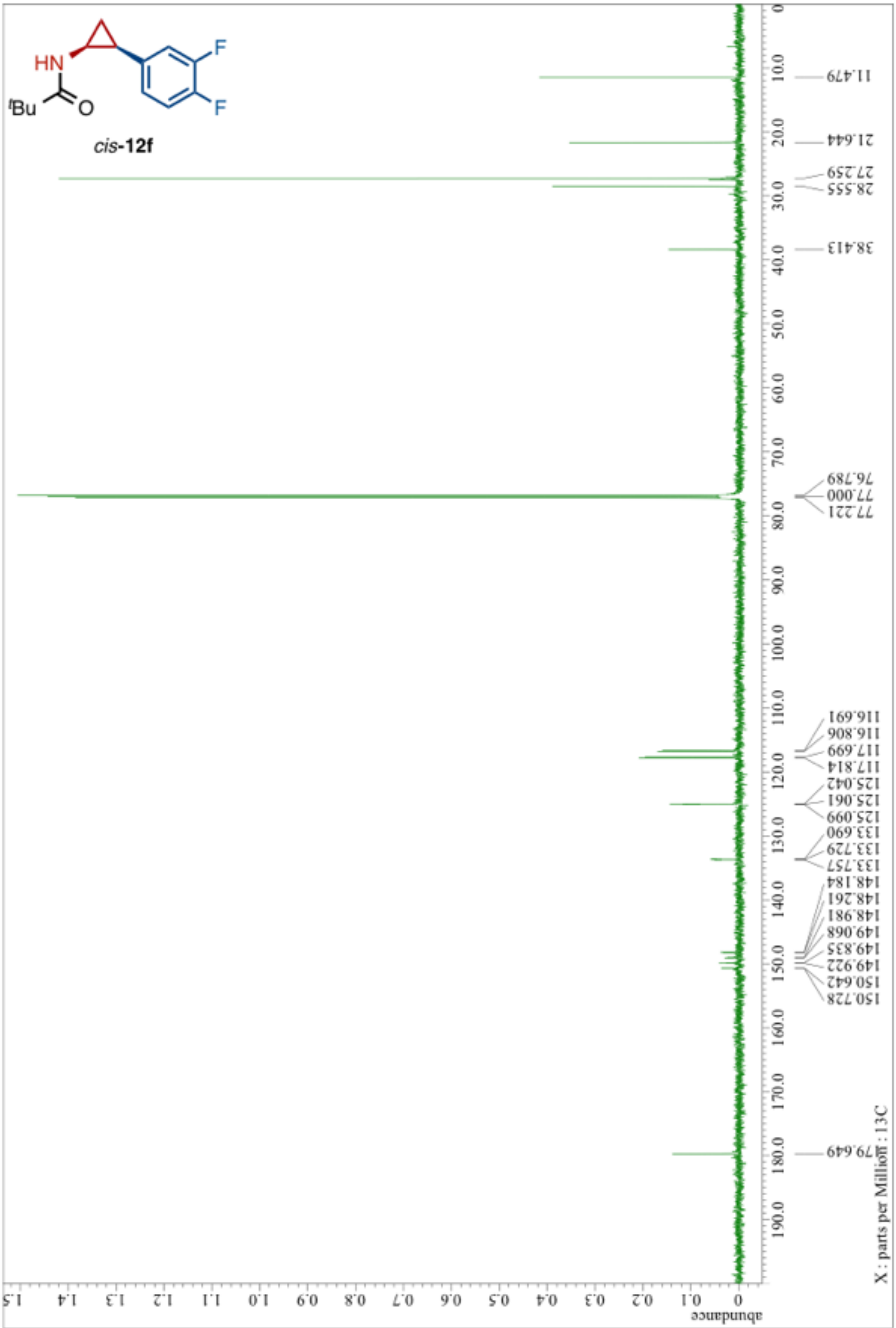
^{13}C NMR (150 MHz, $CDCl_3$) of *trans*-12f:



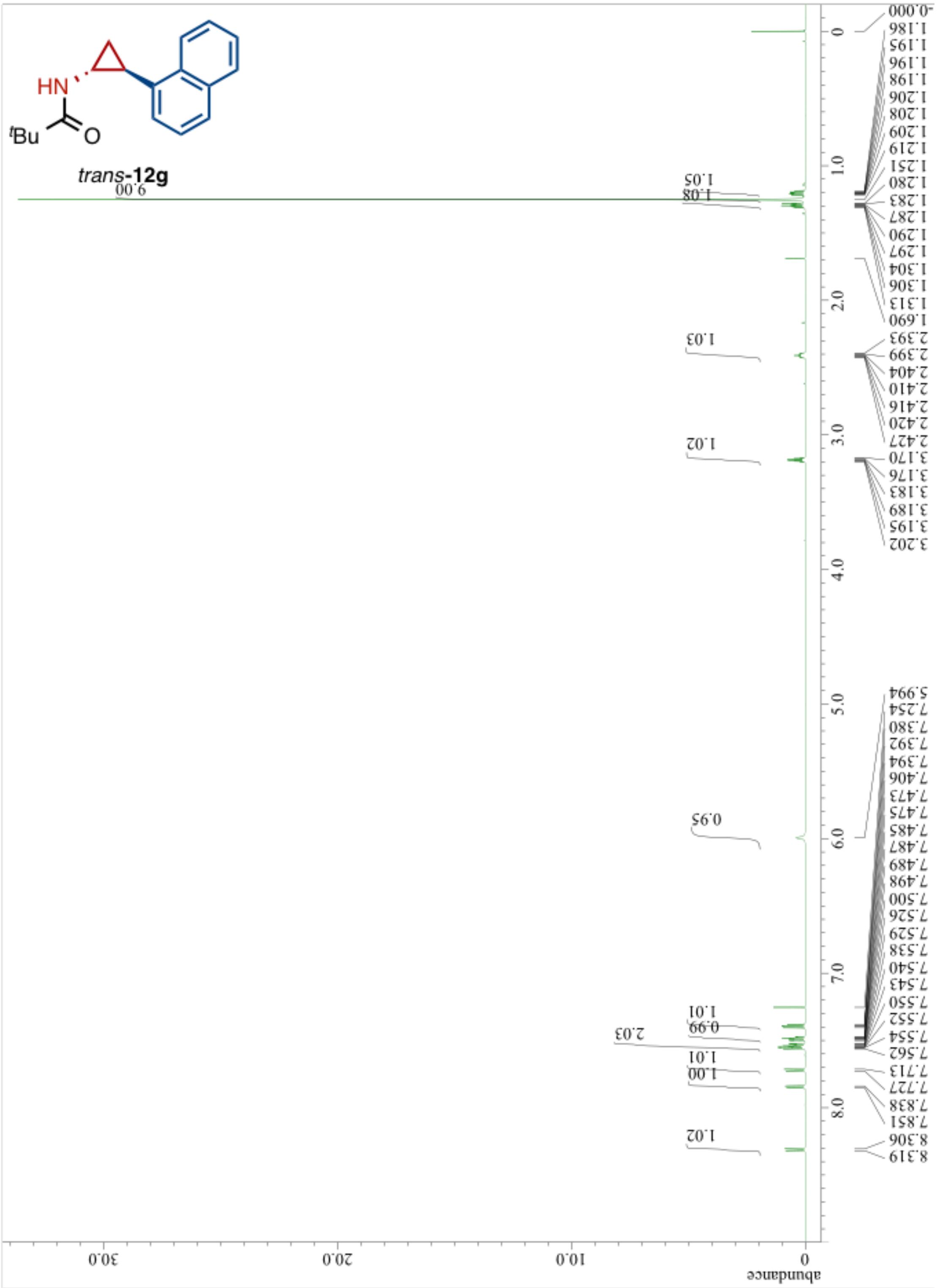
^{1}H NMR (600 MHz, $CDCl_3$) of *cis*-12f:



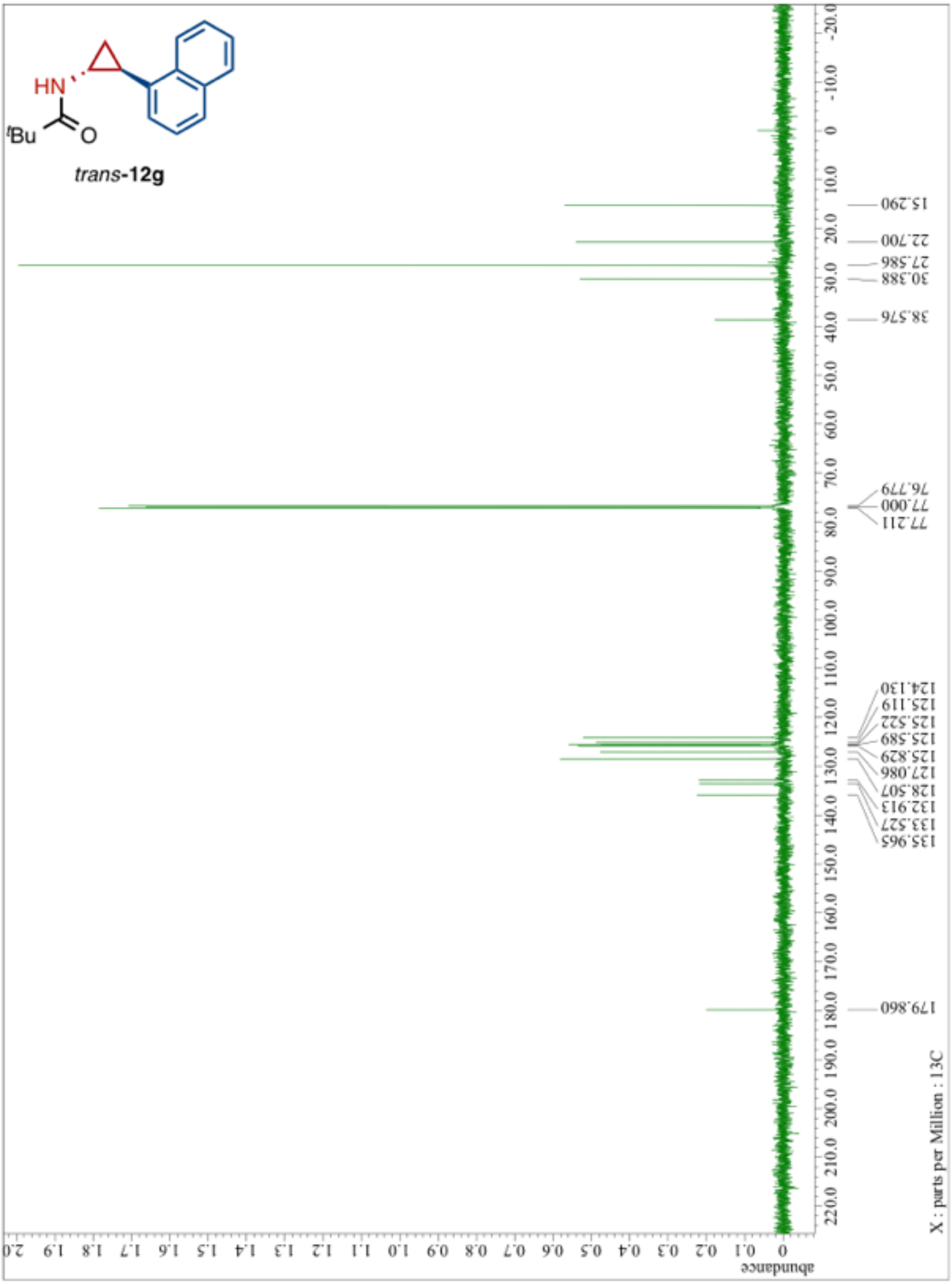
^{13}C NMR (150 MHz, $CDCl_3$) of *cis*-12f:



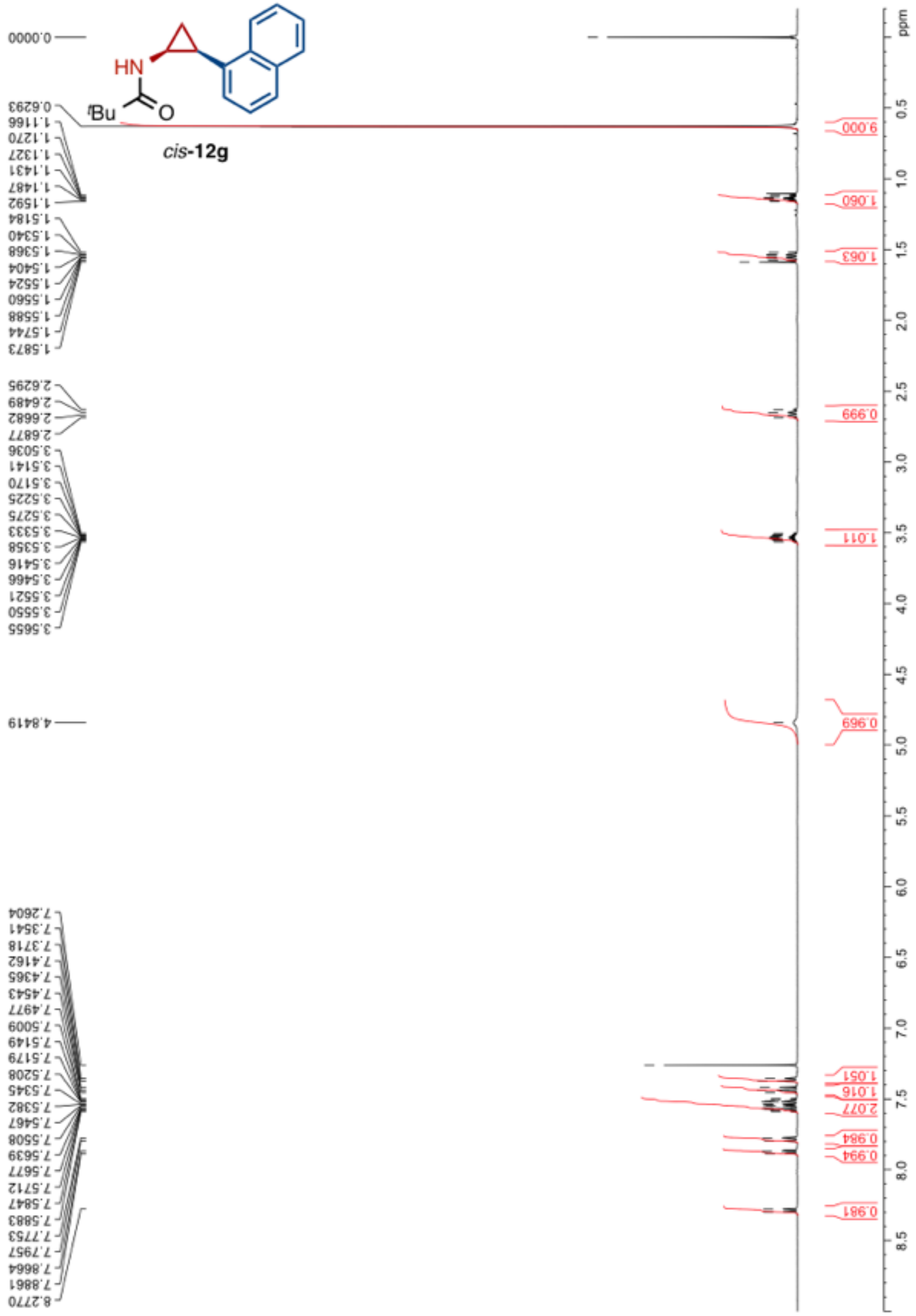
^{1}H NMR (600 MHz, $CDCl_3$) of *trans*-12g:



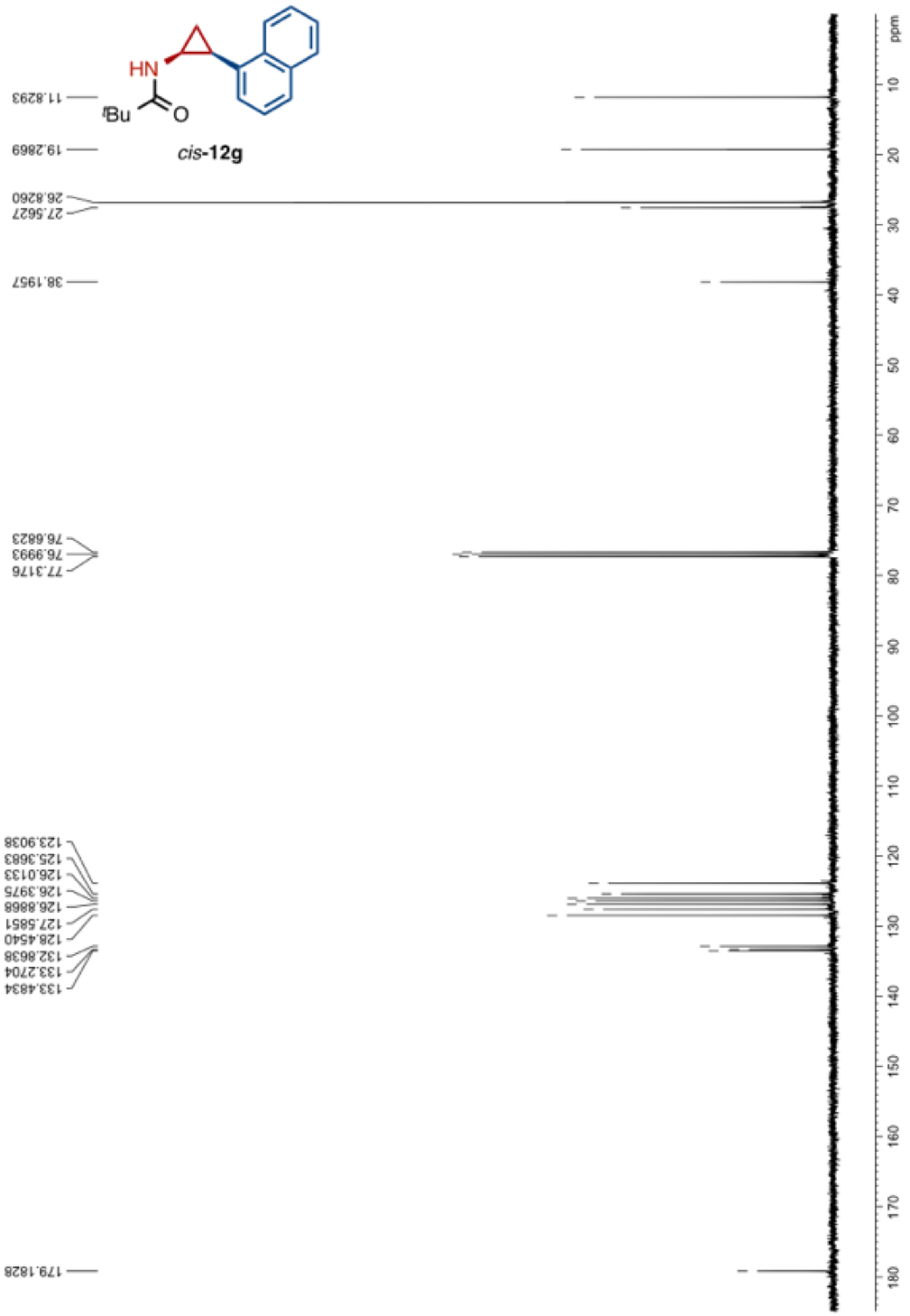
^{13}C NMR (150 MHz, CDCl$_3$) of *trans*-12g:



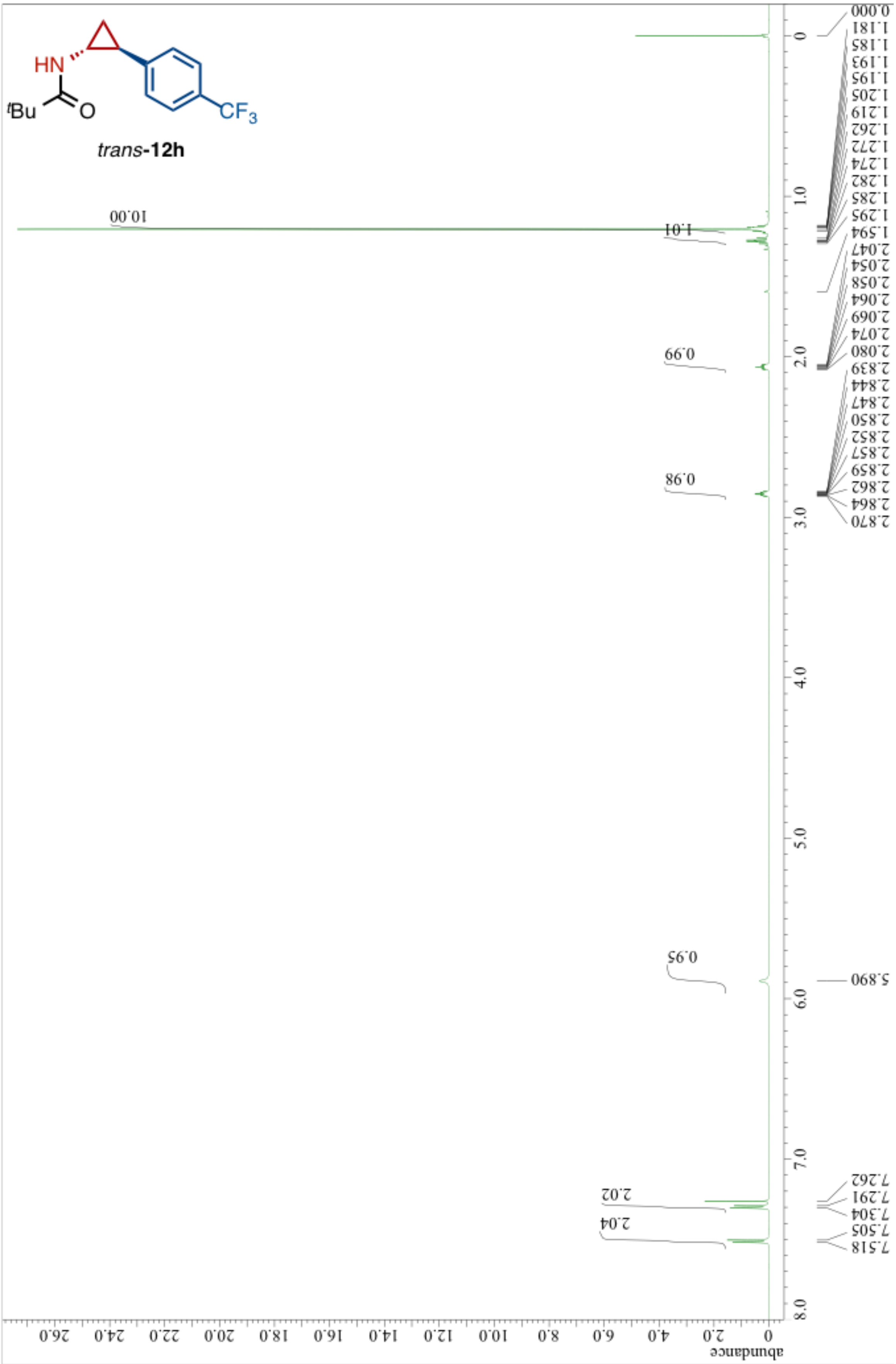
[1]H NMR (400 MHz, $CDCl_3$) of *cis*-12g:



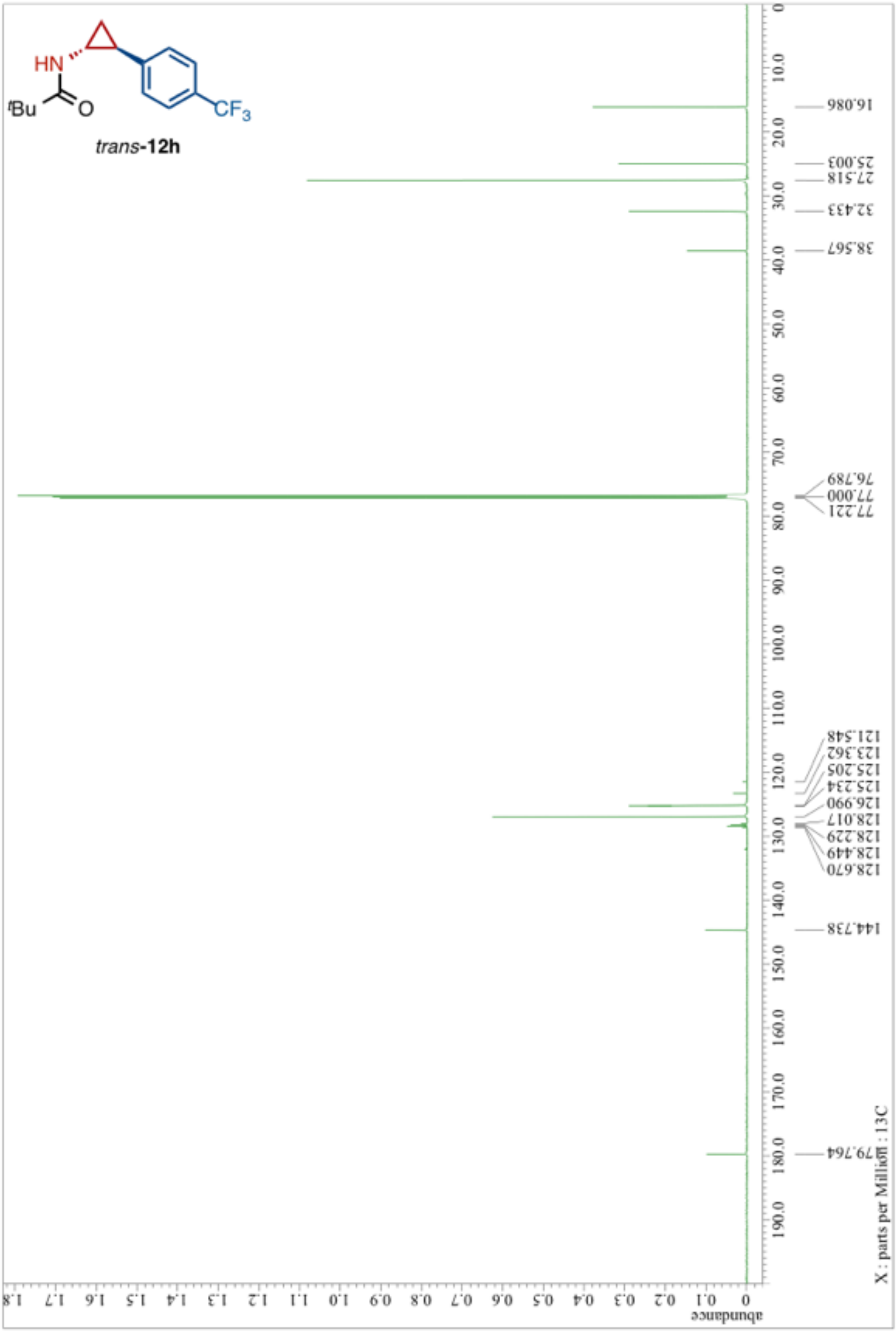
^{13}C NMR (100 MHz, $CDCl_3$) of *cis*-12g:



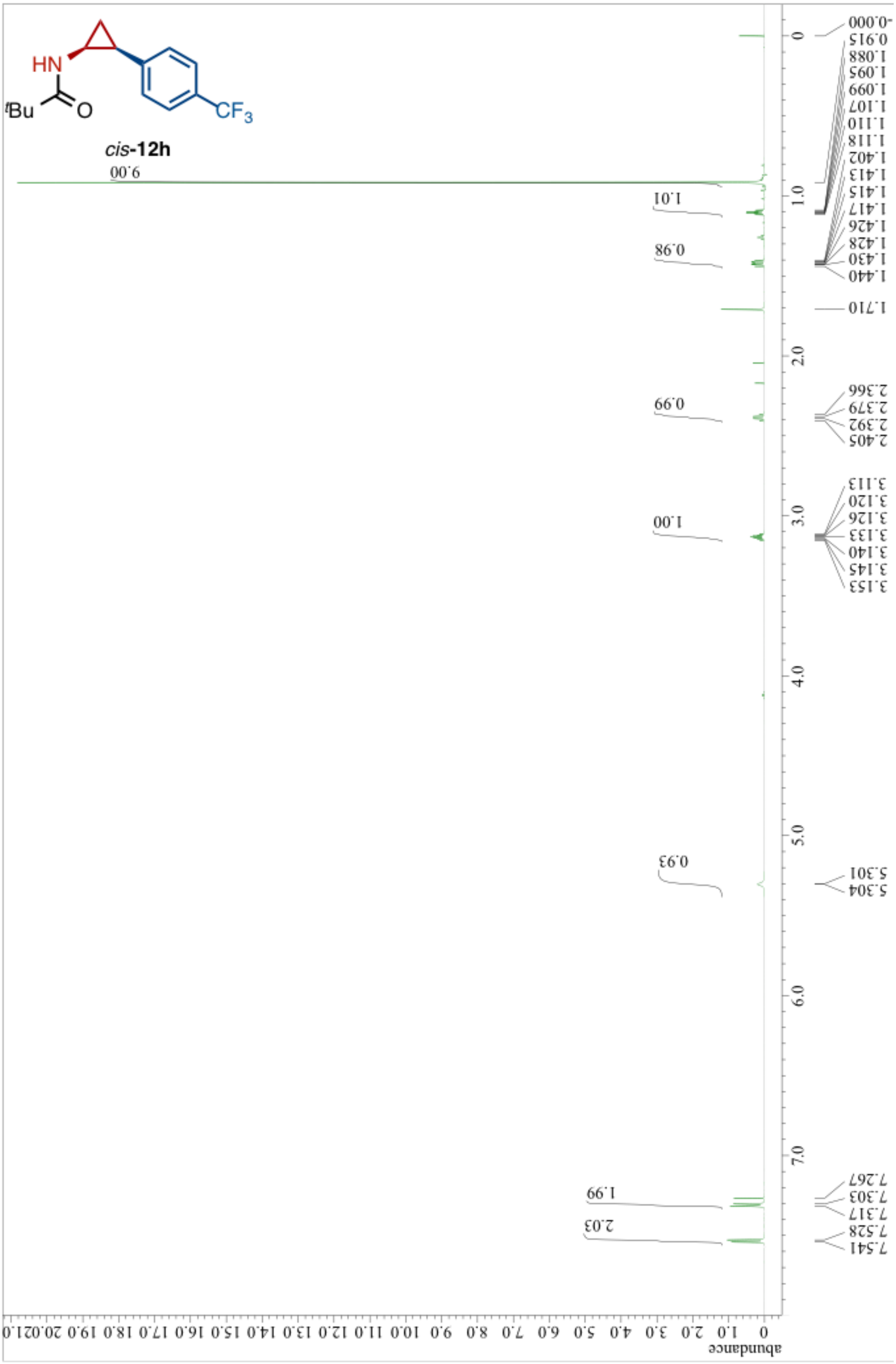
^{1}H NMR (600 MHz, $CDCl_3$) of *trans*-12h:



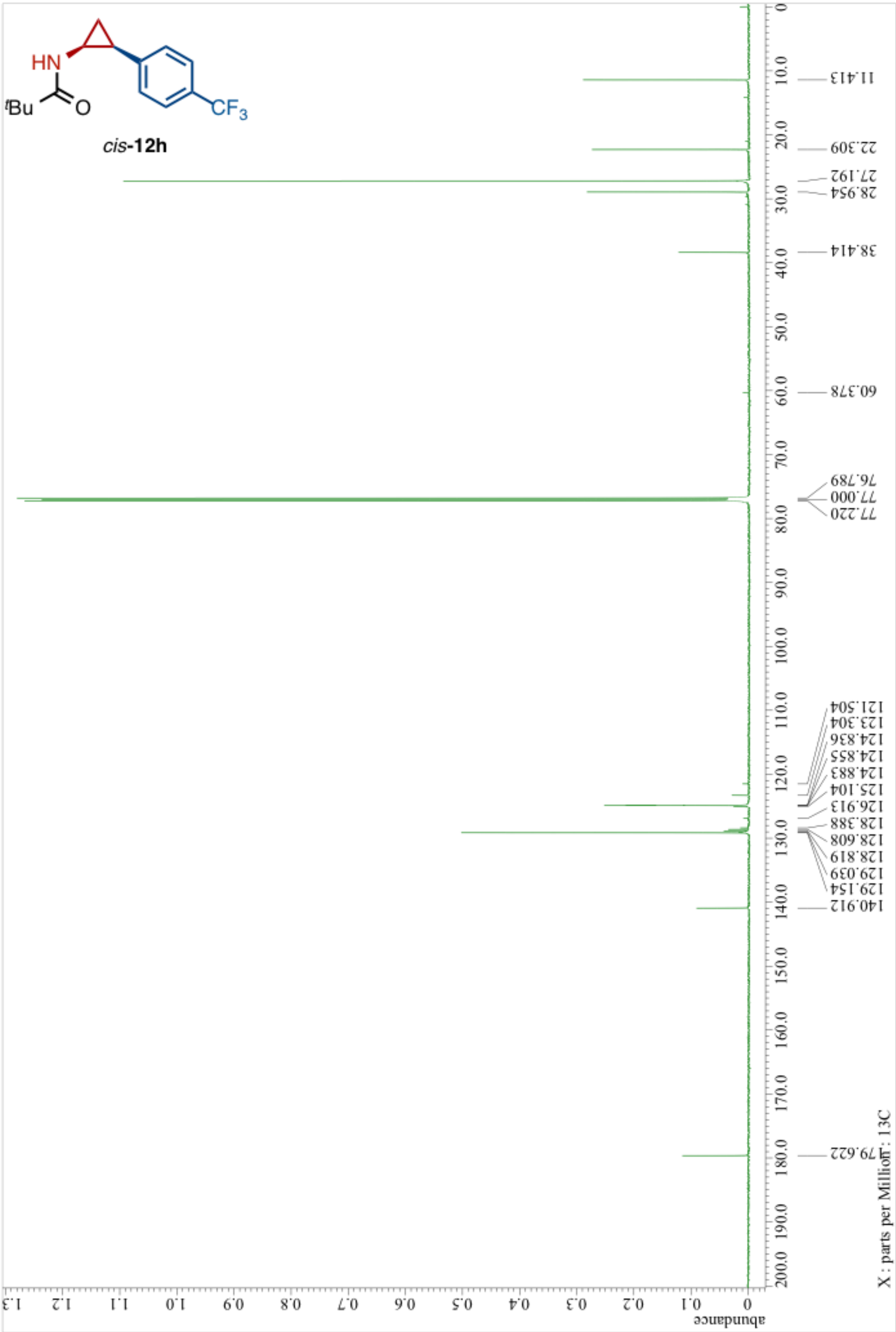
^{13}C NMR (150 MHz, $CDCl_3$) of *trans*-12h:



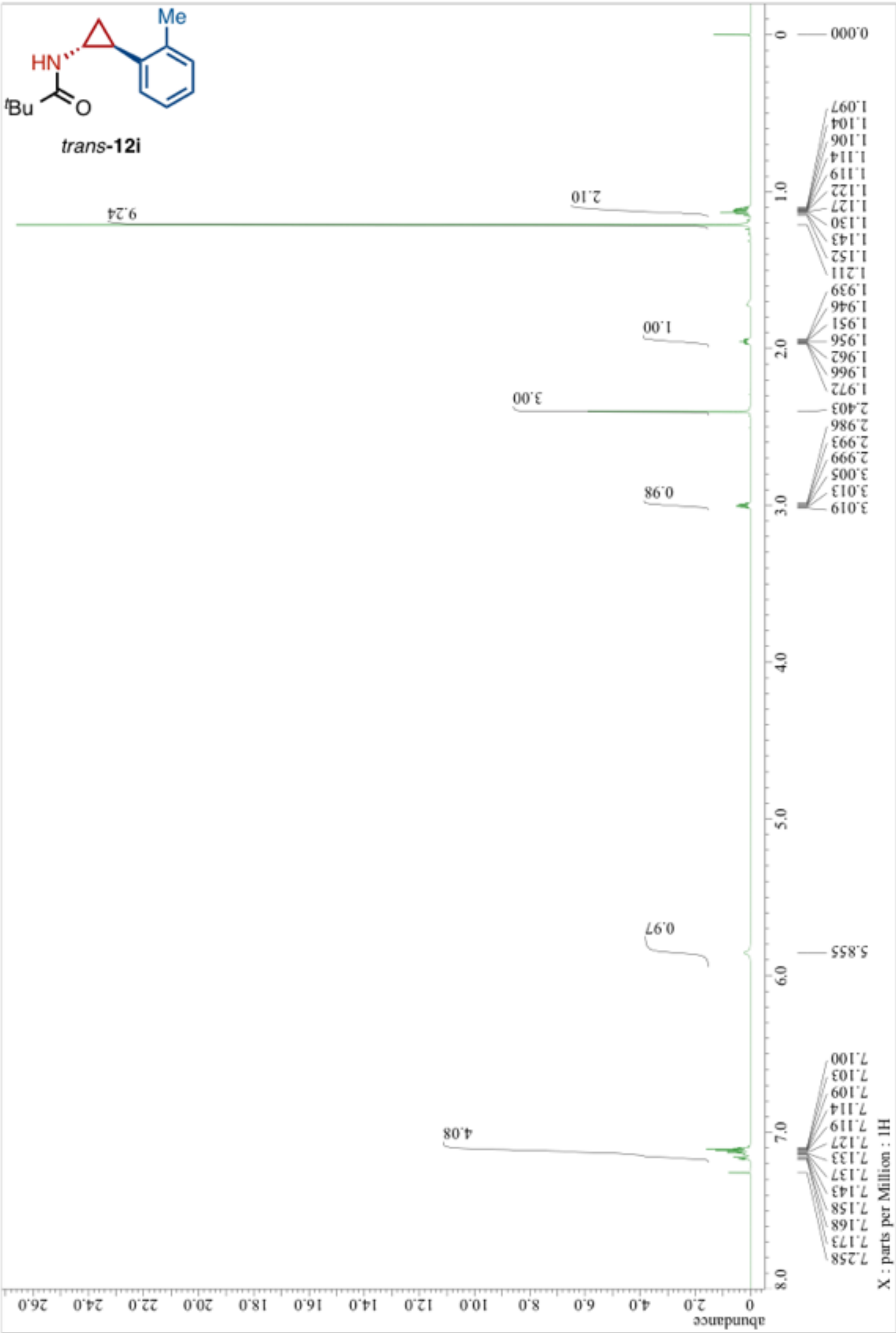
^{1}H NMR (600 MHz, CDCl$_3$) of *cis*-12h:



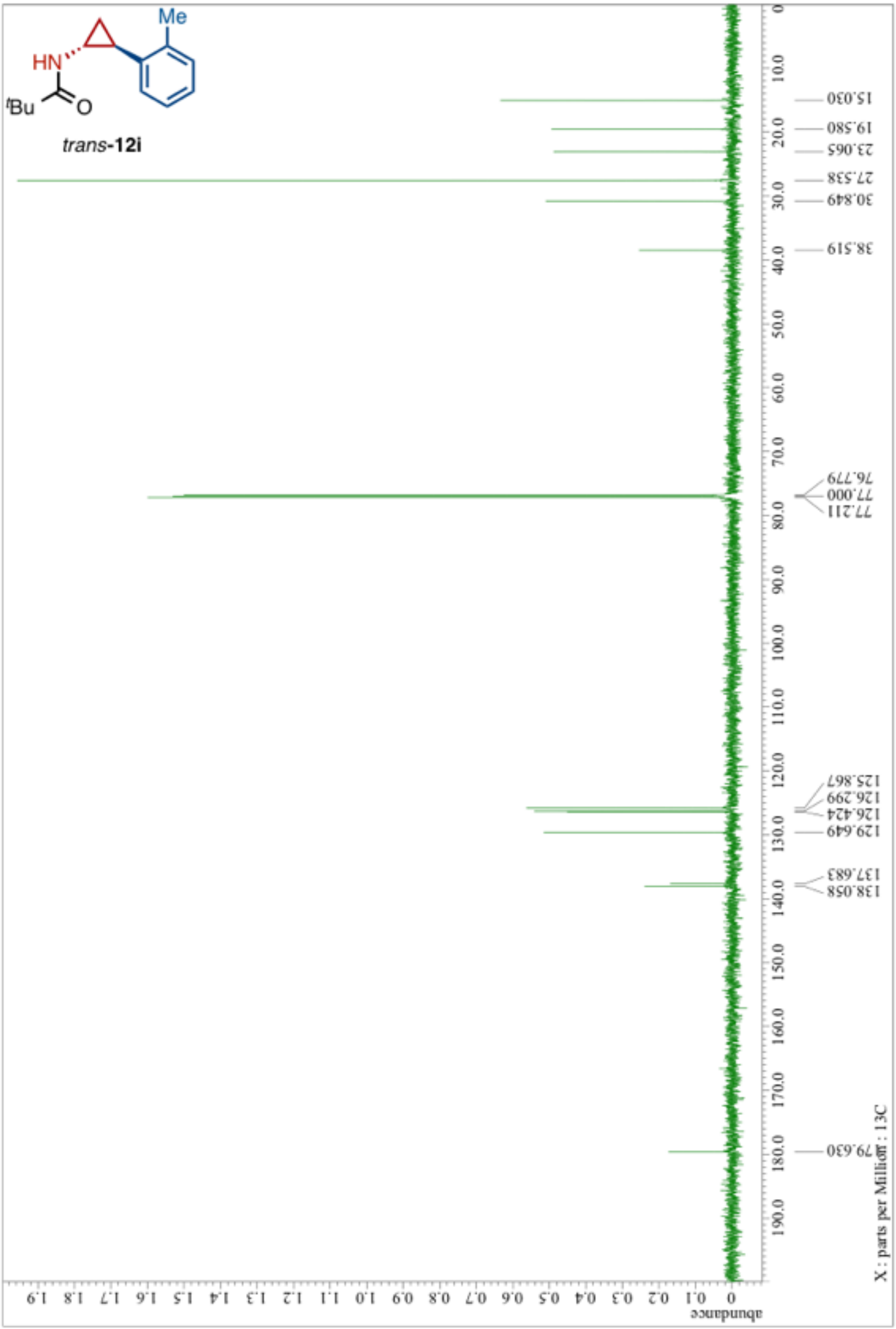
^{13}C NMR (150 MHz, $CDCl_3$) of *cis*-12h:



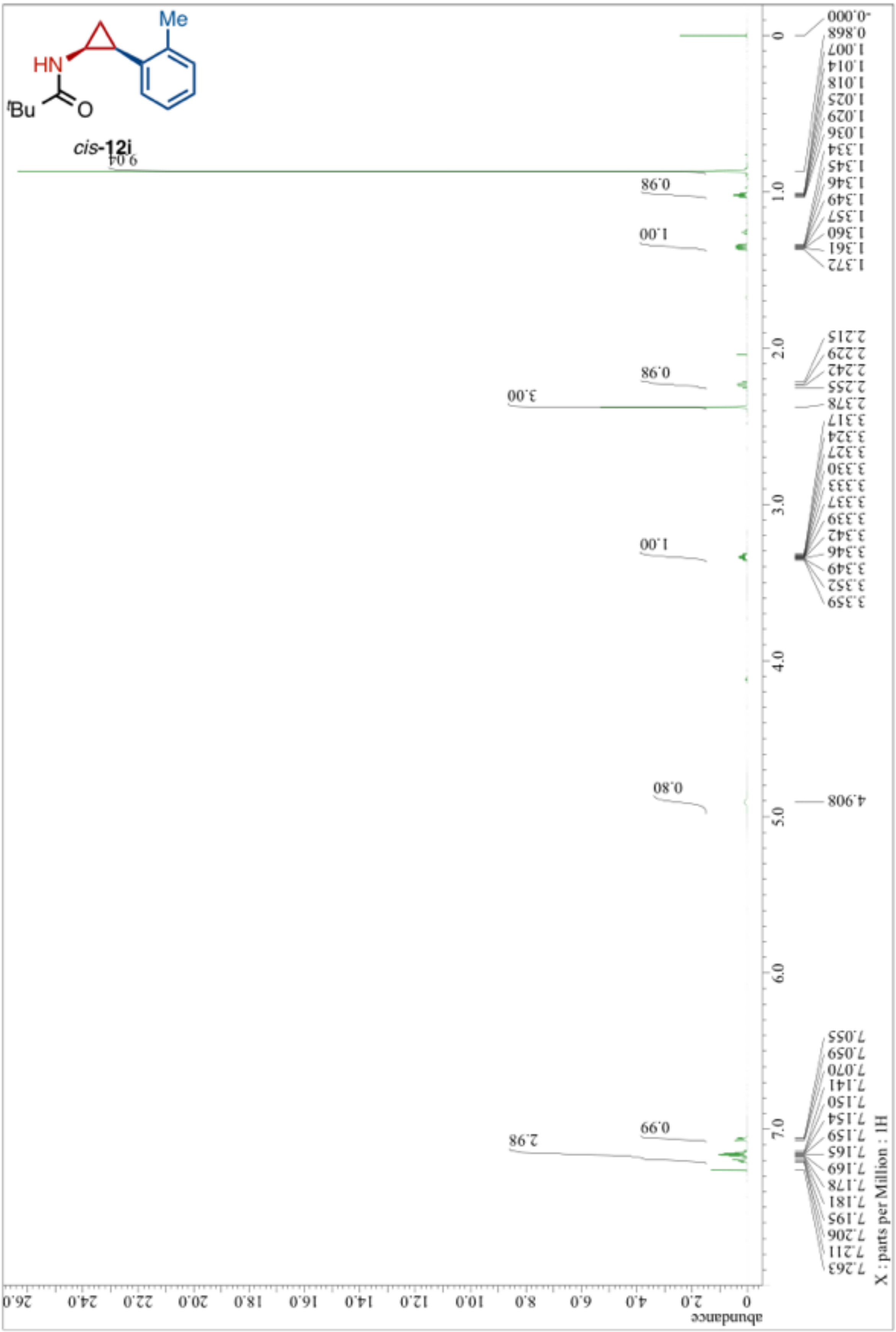
[1]H NMR (600 MHz, $CDCl_3$) of *trans*-12i:



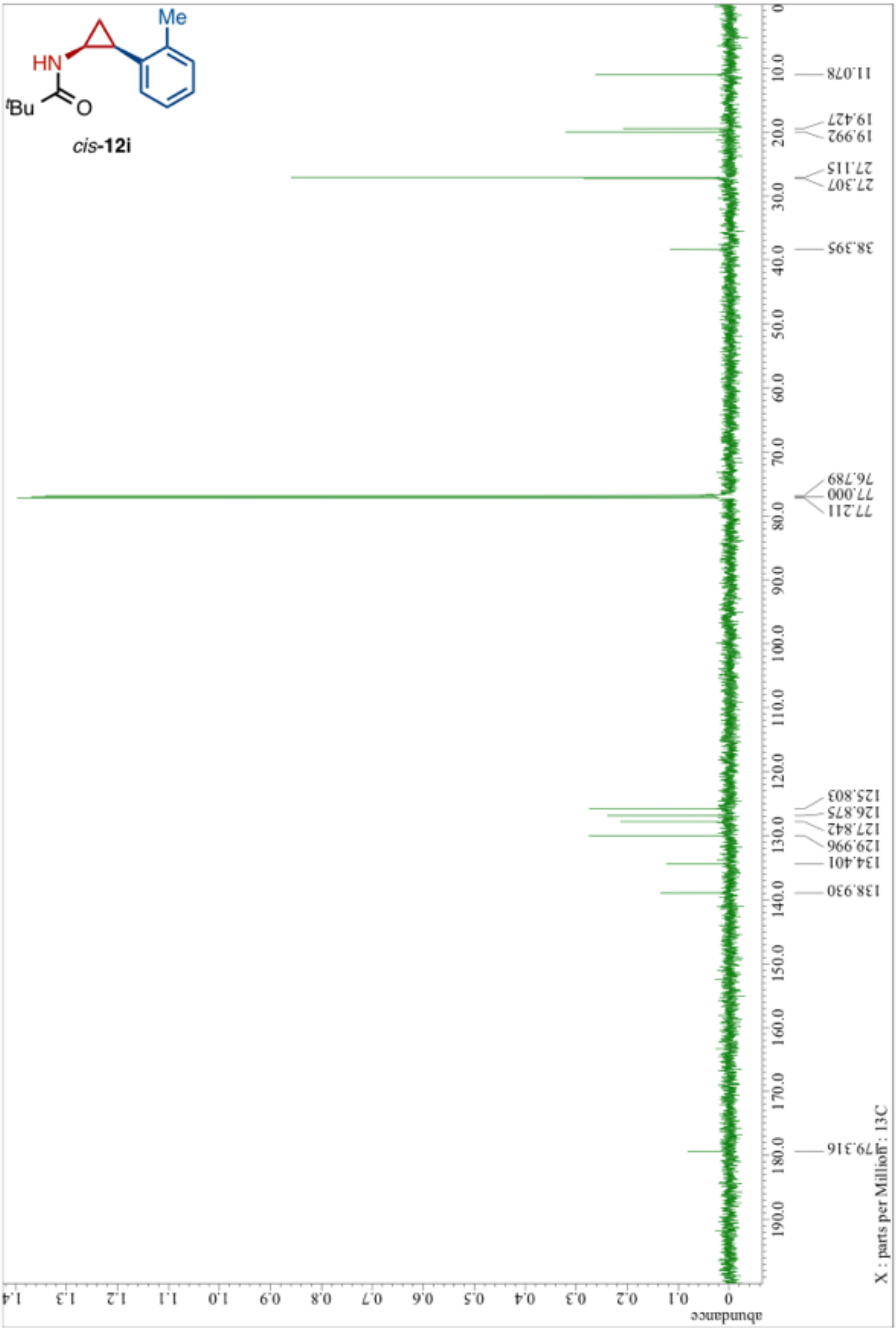
^{13}C NMR (150 MHz, CDCl$_3$) of *trans*-12i:



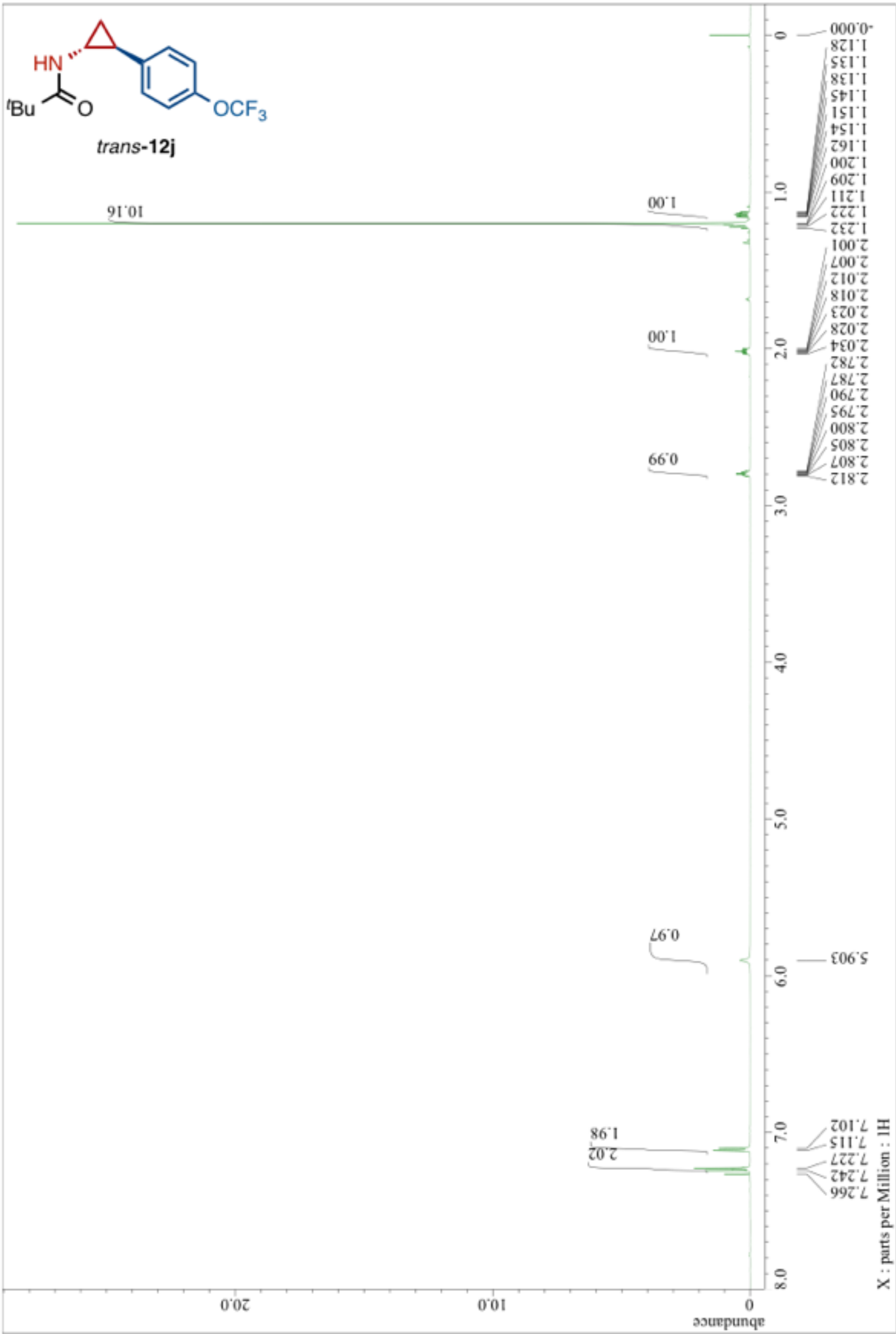
[1]H NMR (600 MHz, $CDCl_3$) of *cis*-12i:



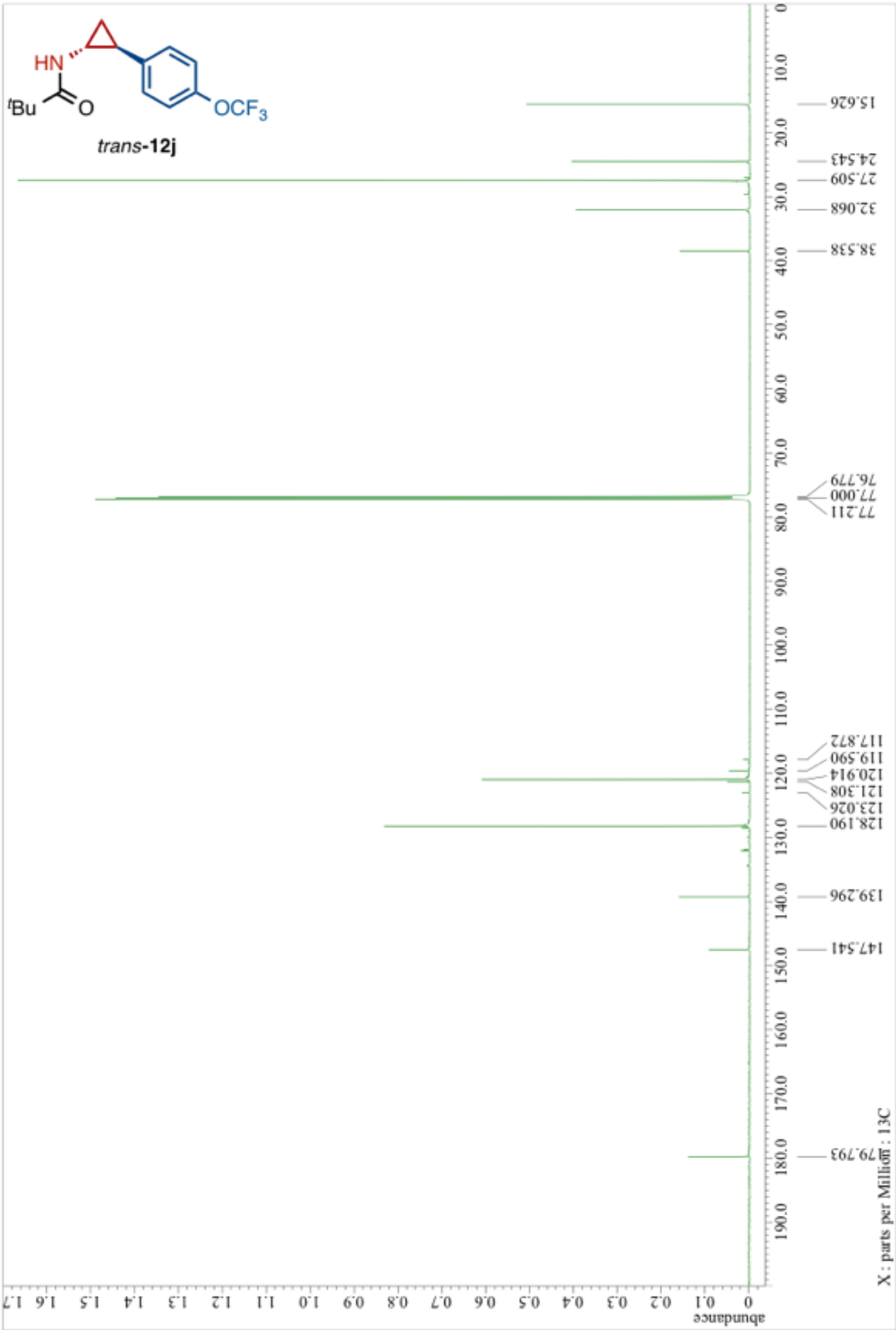
[13]C NMR (150 MHz, CDCl$_3$) of *cis*-12i:



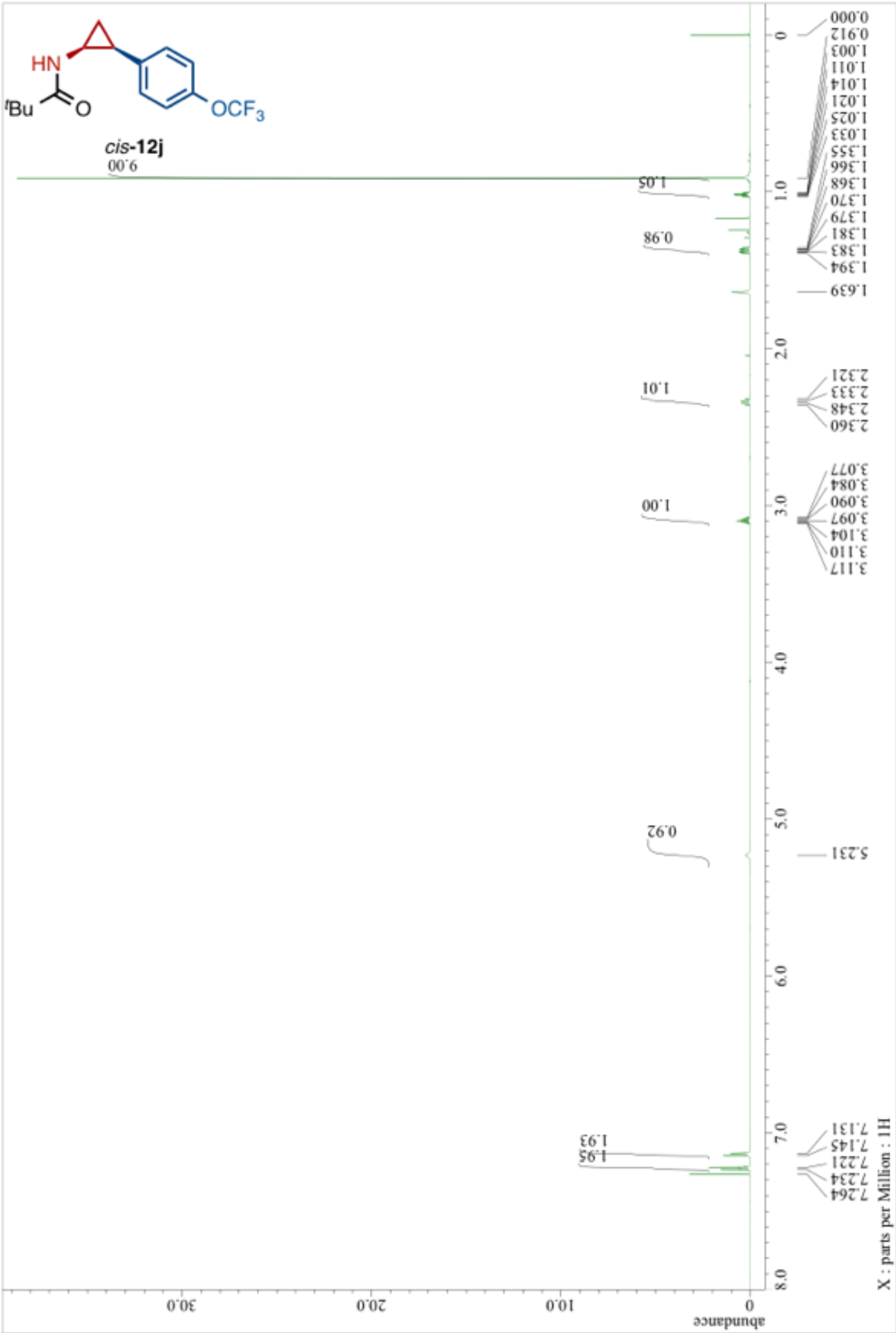
^{1}H NMR (600 MHz, $CDCl_3$) of *trans*-12j:



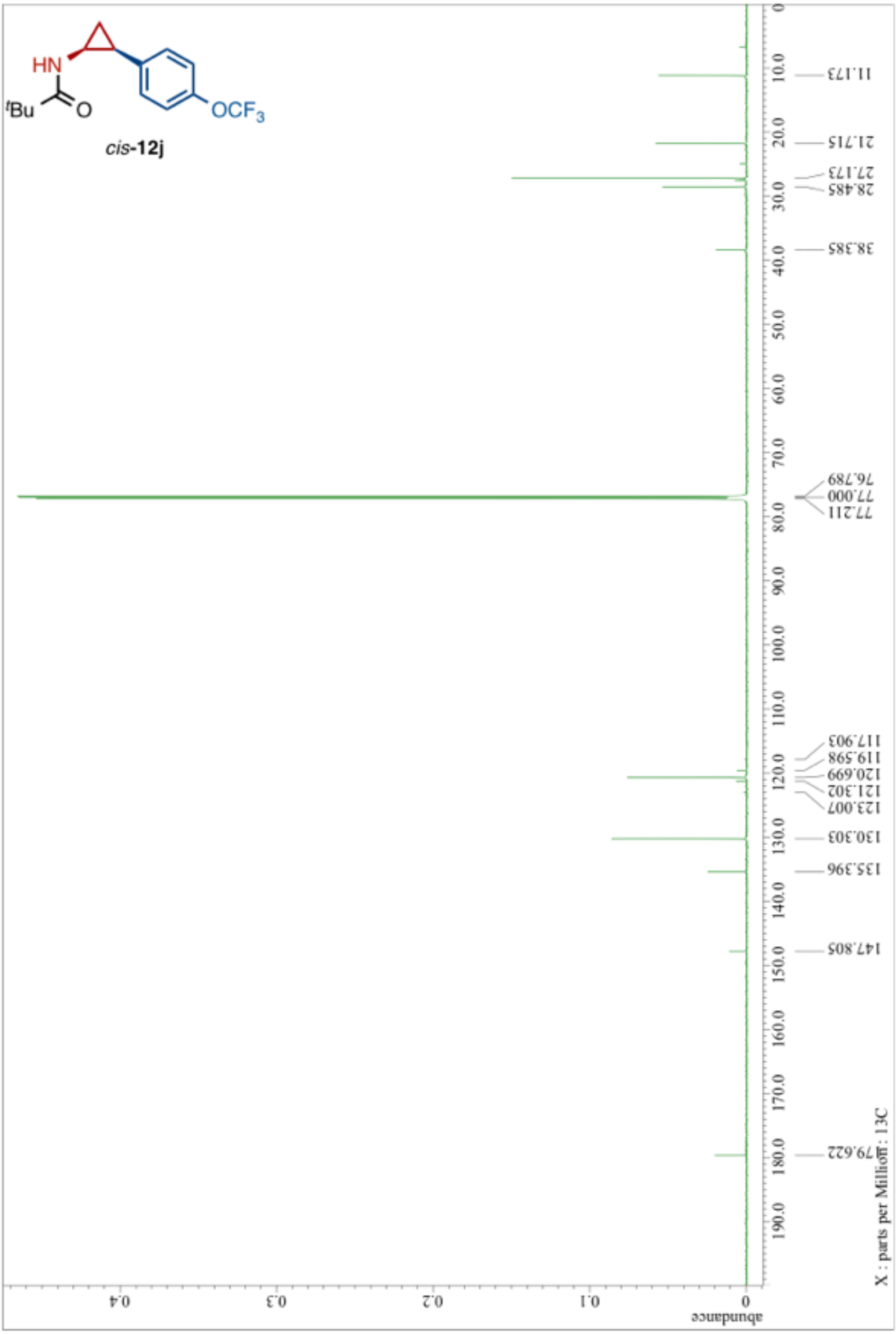
^{13}C NMR (150 MHz, CDCl$_3$) of *trans*-12j:



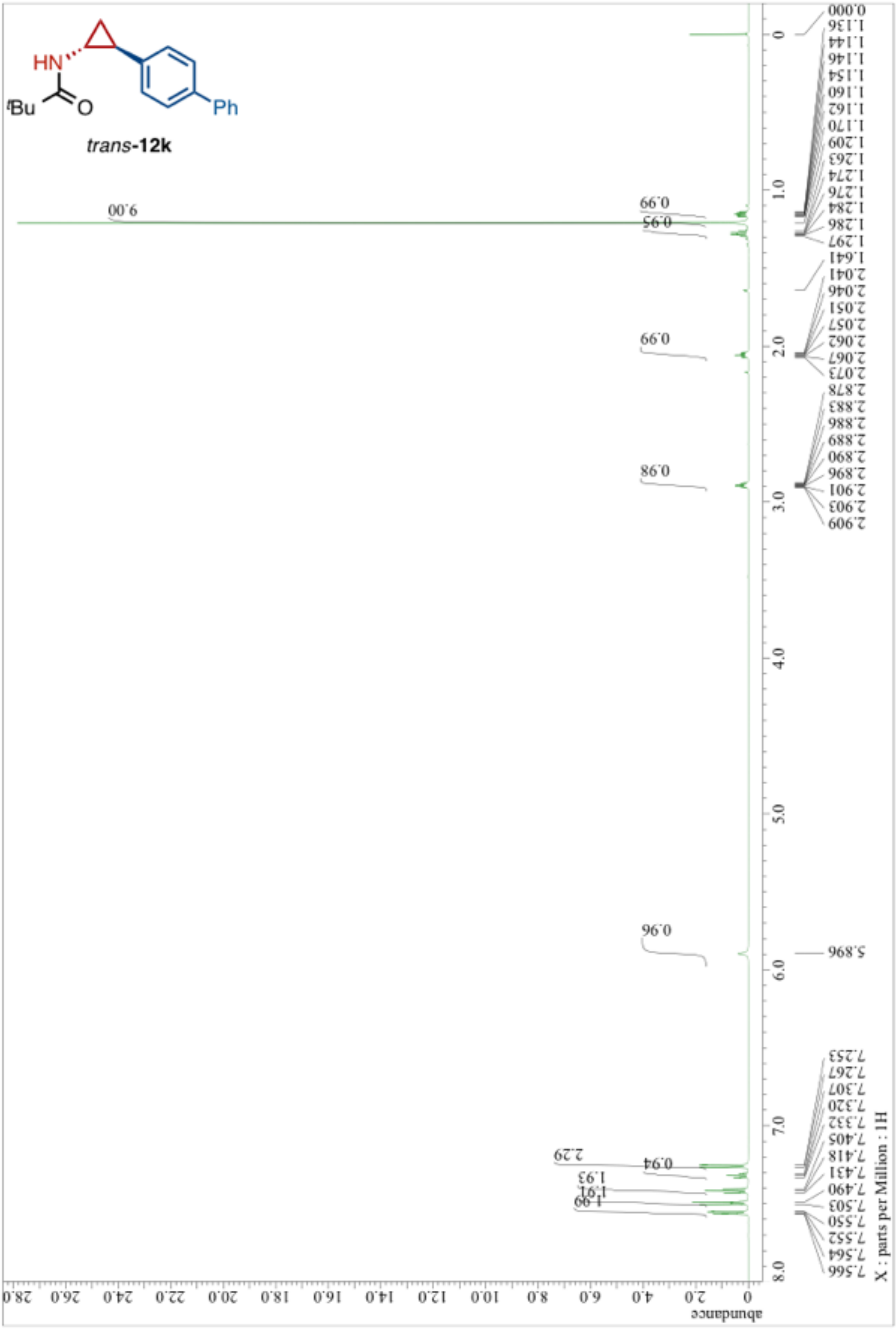
^{1}H NMR (600 MHz, $CDCl_3$) of *cis*-**12j**:



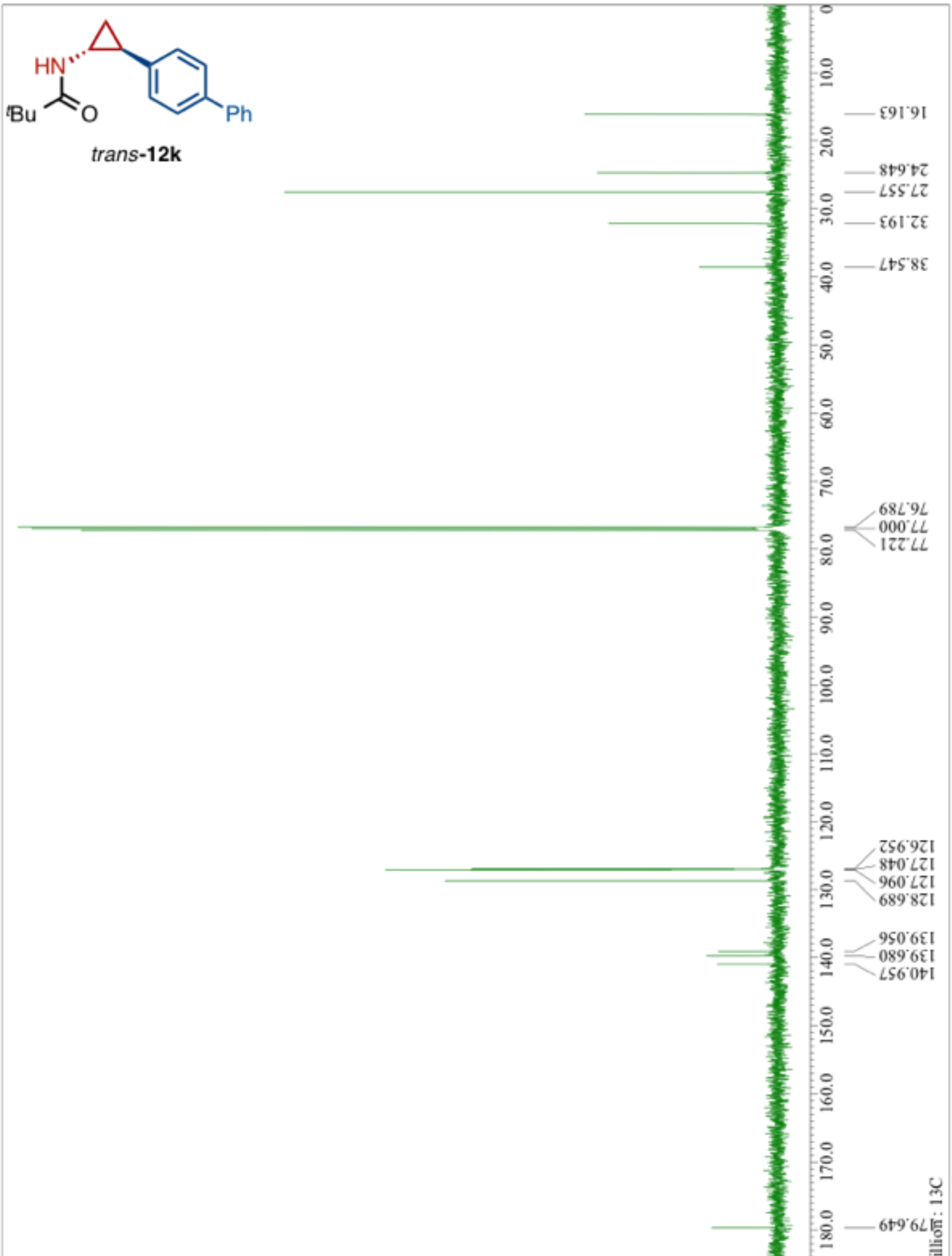
^{13}C NMR (150 MHz, $CDCl_3$) of *cis*-12j:



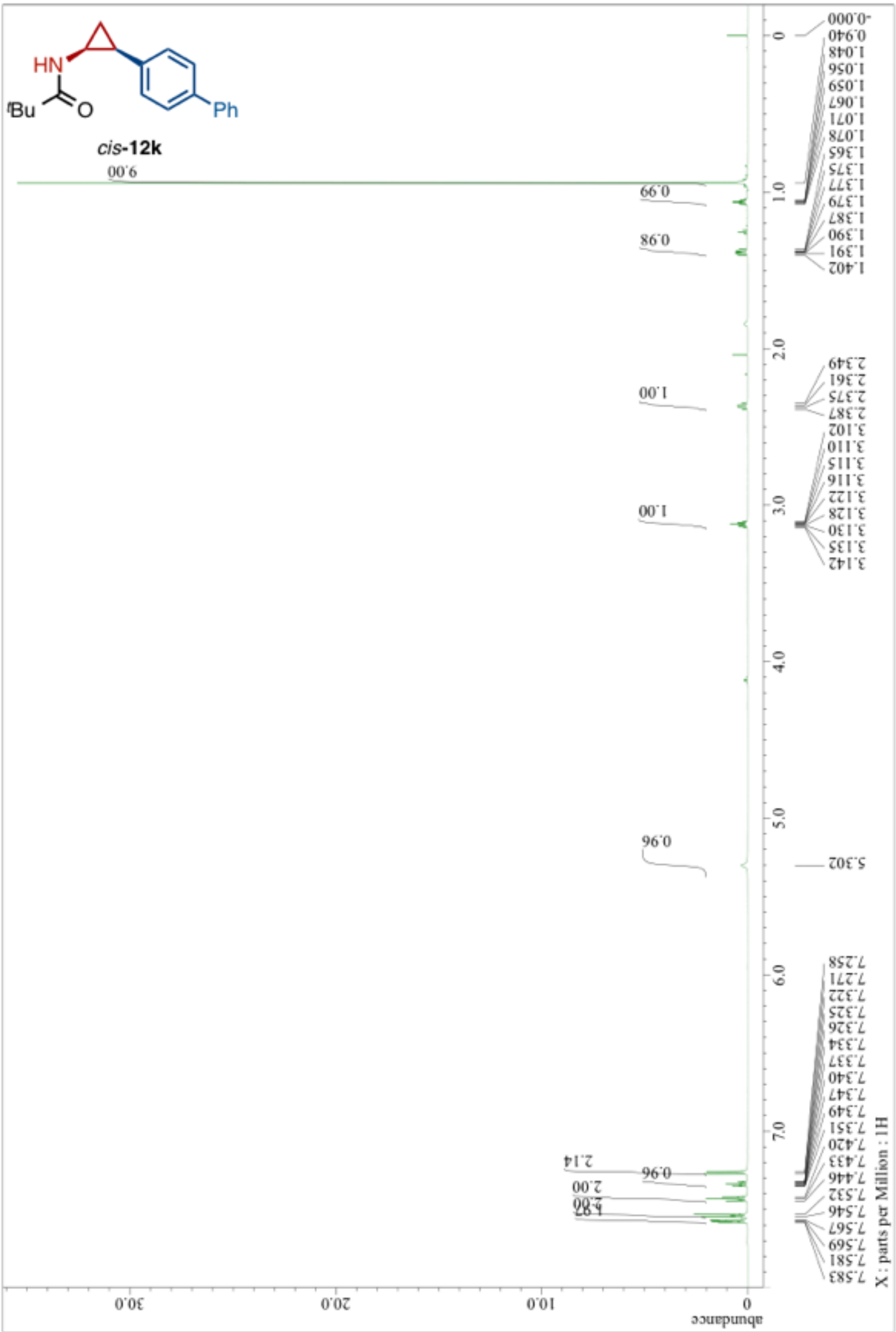
^{1}H NMR (600 MHz, CDCl$_3$) of *trans*-12k:



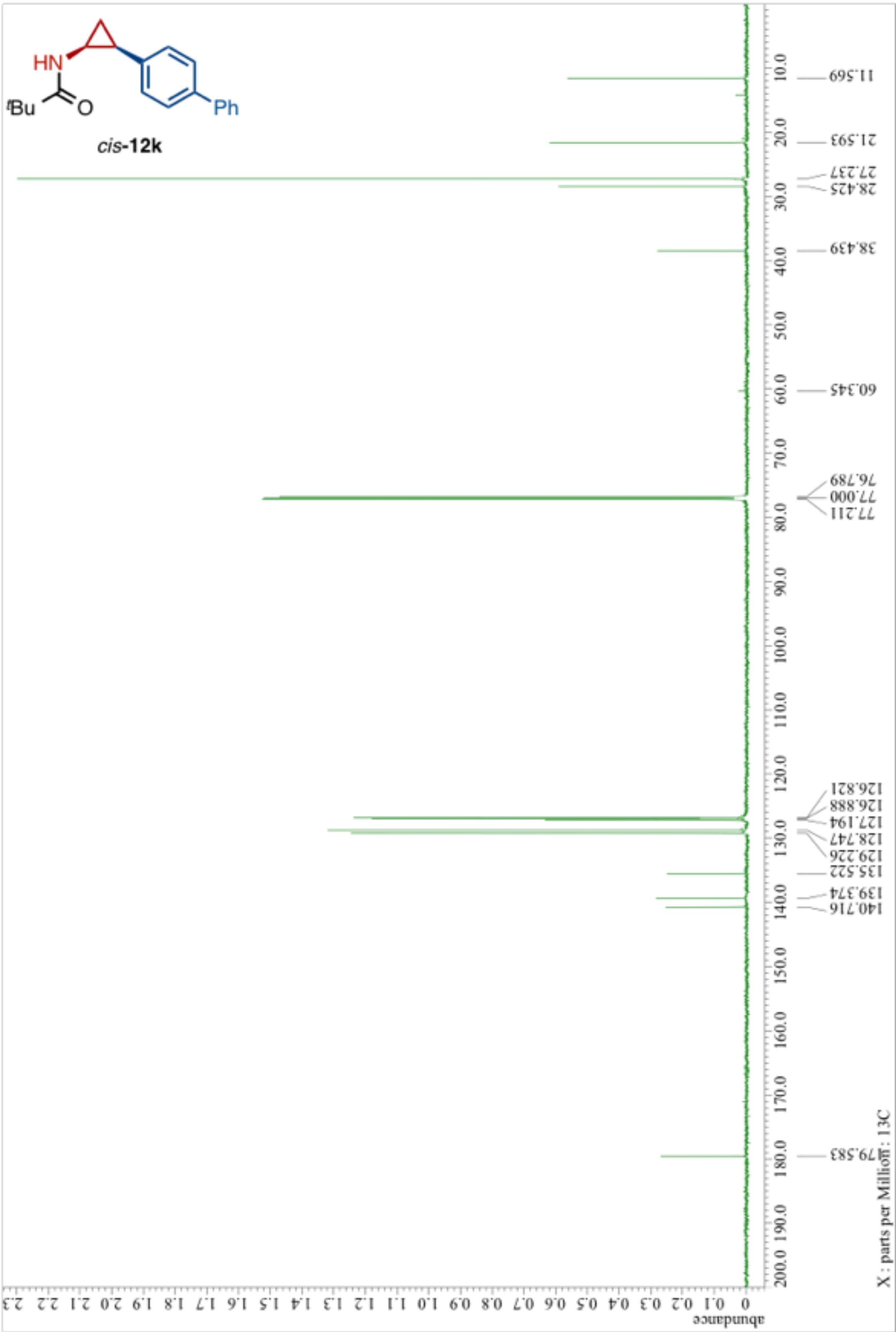
[13]C NMR (150 MHz, $CDCl_3$) of *trans*-12k:



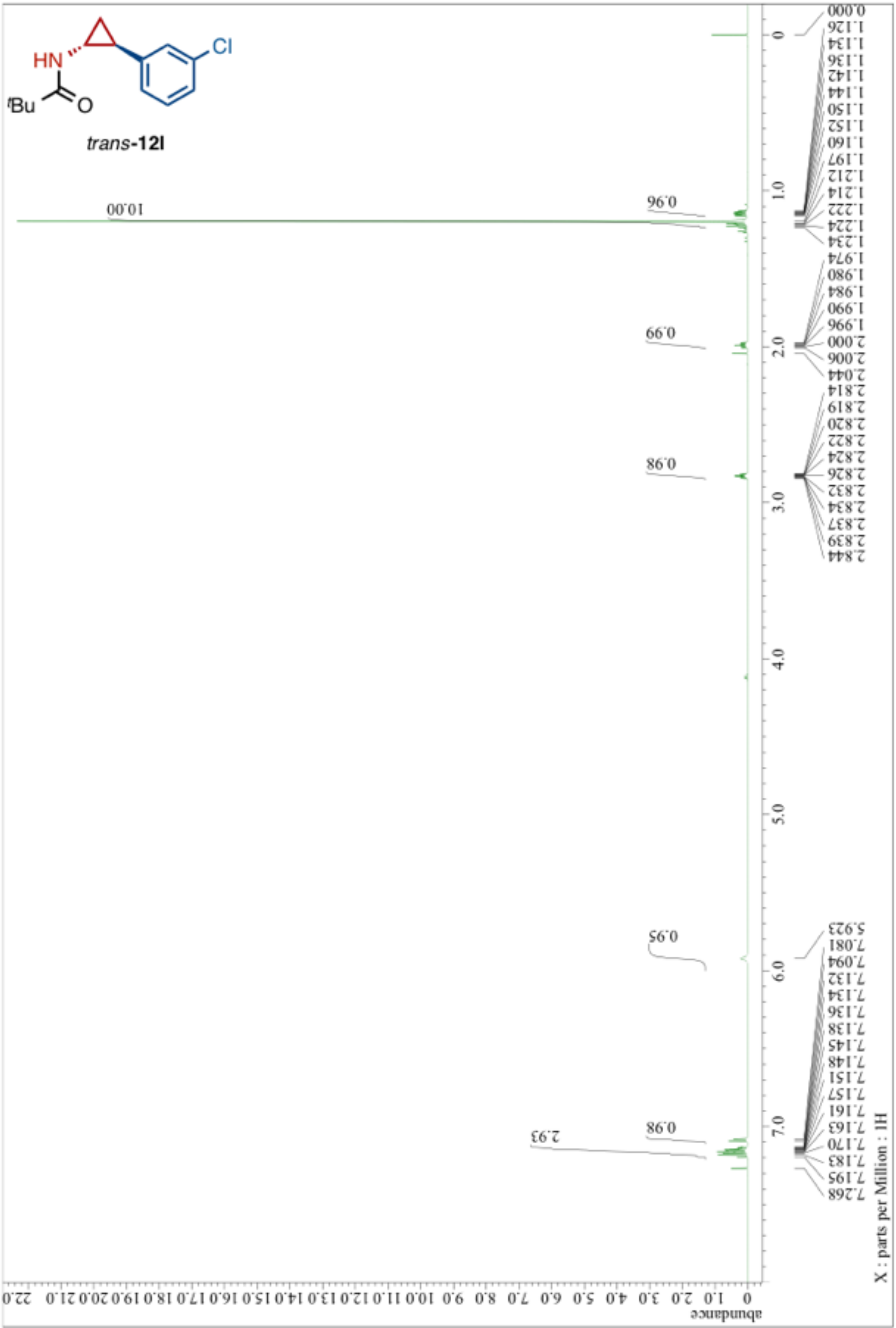
[1]H NMR (600 MHz, CDCl$_3$) of *cis*-12k:



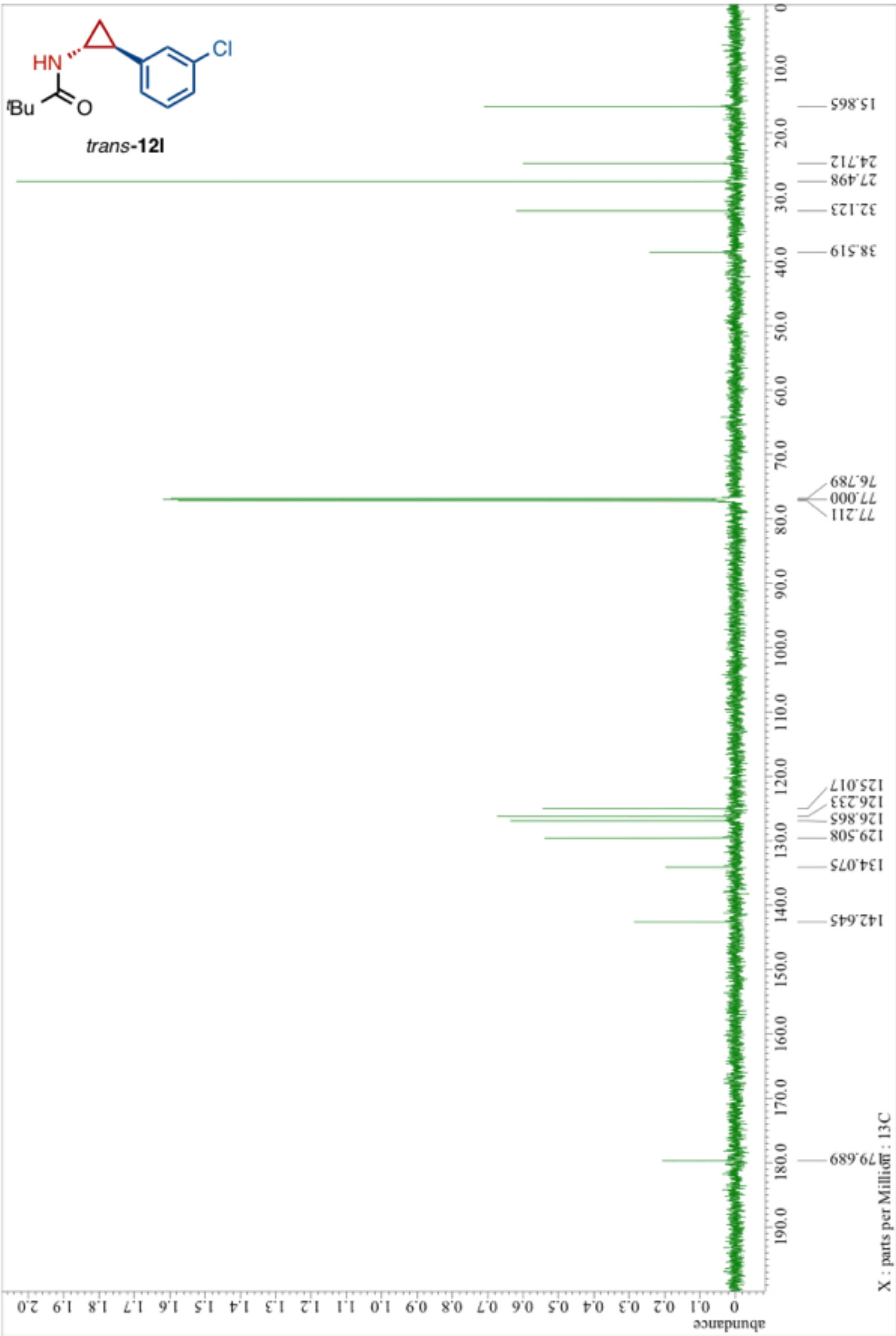
^{13}C NMR (150 MHz, $CDCl_3$) of *cis*-12k:



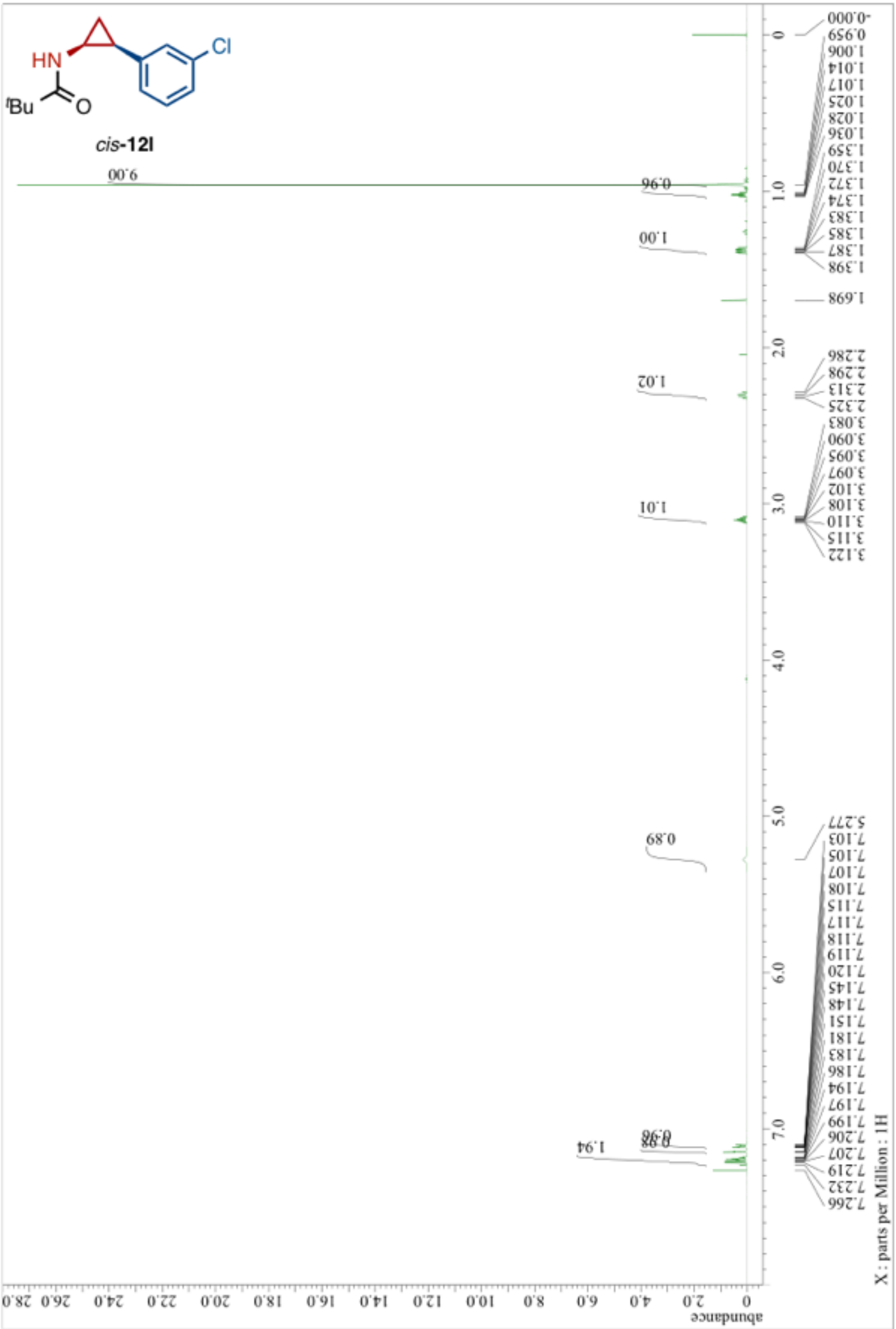
^{1}**H NMR (600 MHz, $CDCl_3$) of *trans*-12l:**



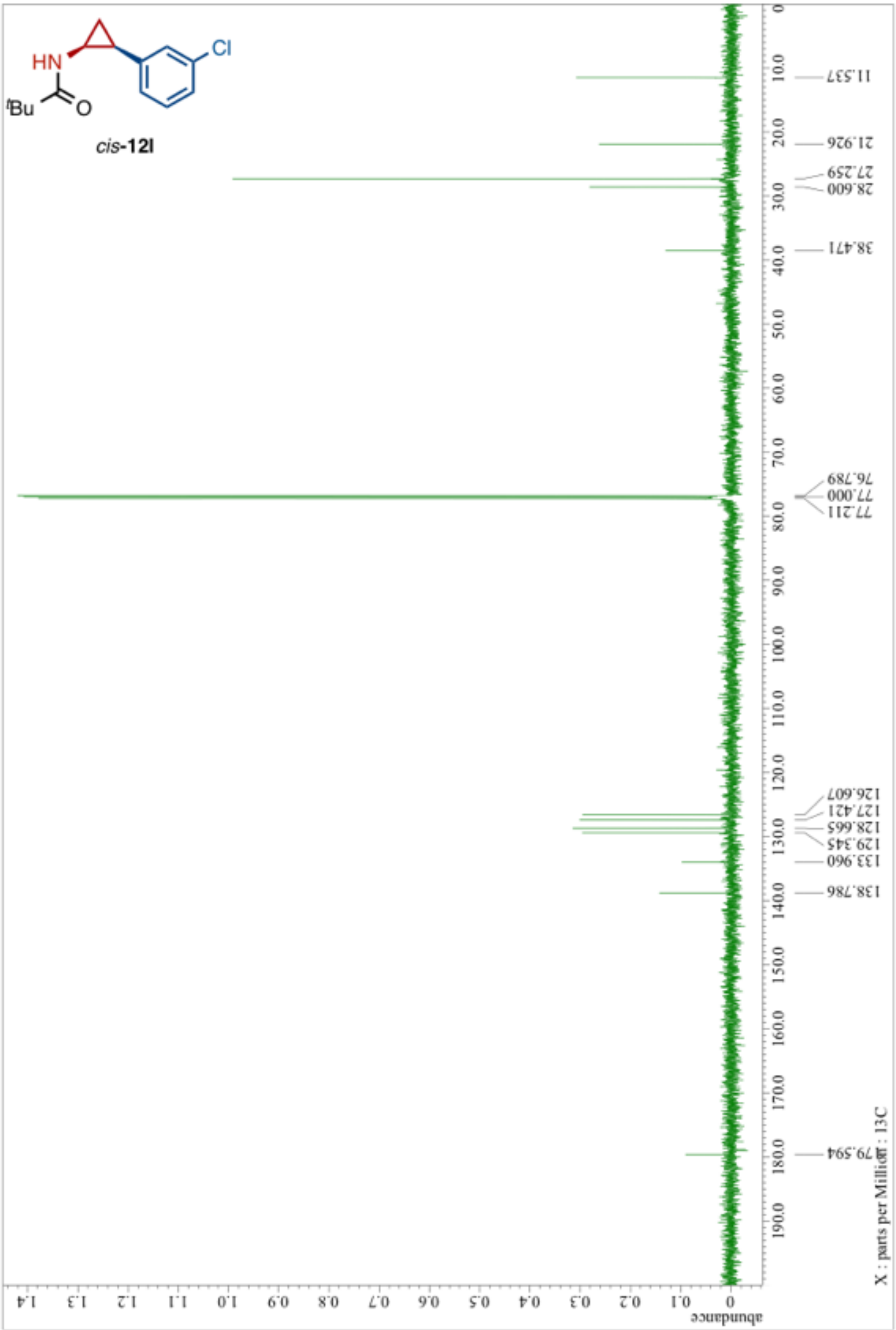
^{13}C NMR (150 MHz, $CDCl_3$) of *trans*-12l:



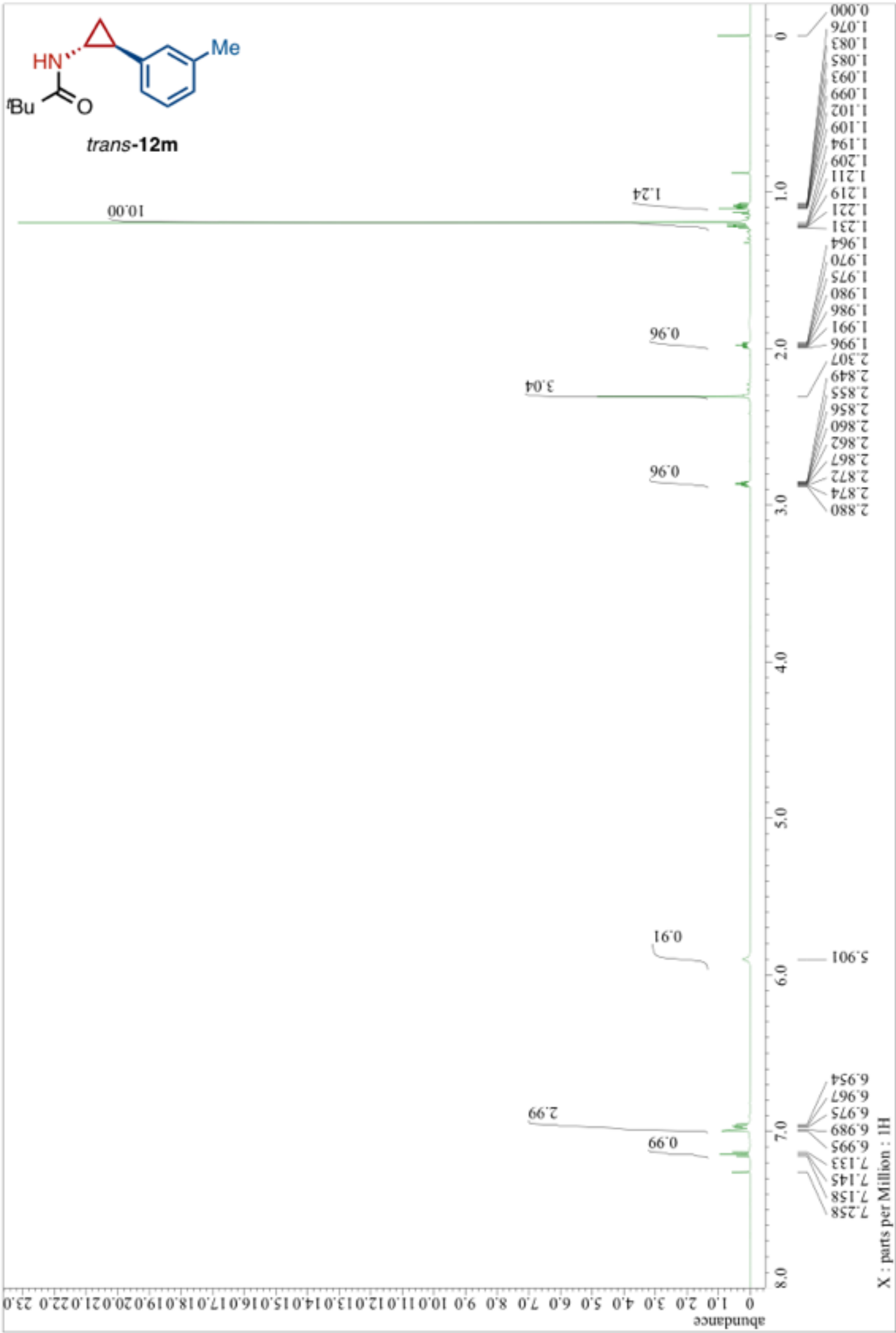
[1]H NMR (600 MHz, $CDCl_3$) of *cis*-12l:



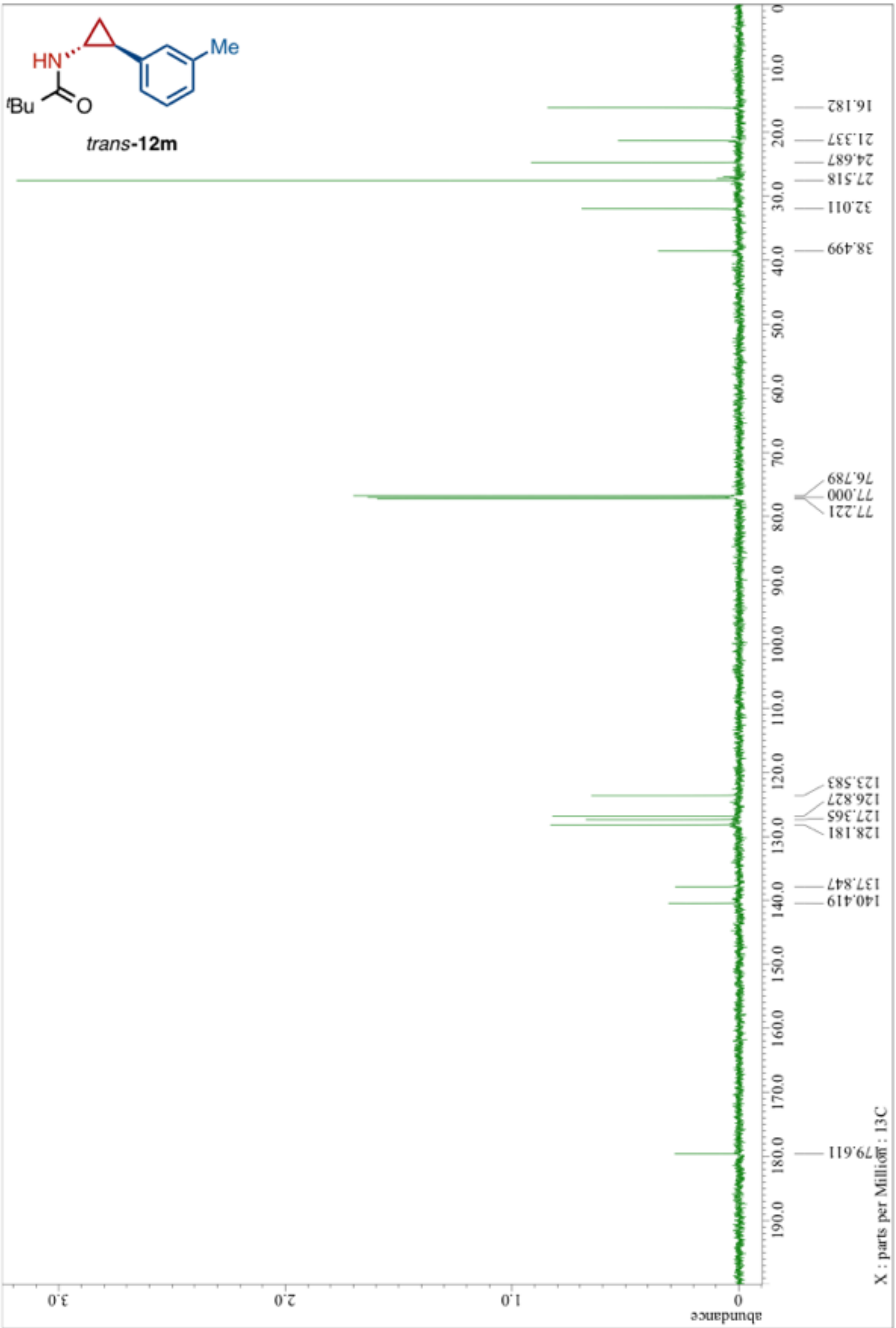
[13]C NMR (150 MHz, CDCl3) of *cis*-12l:



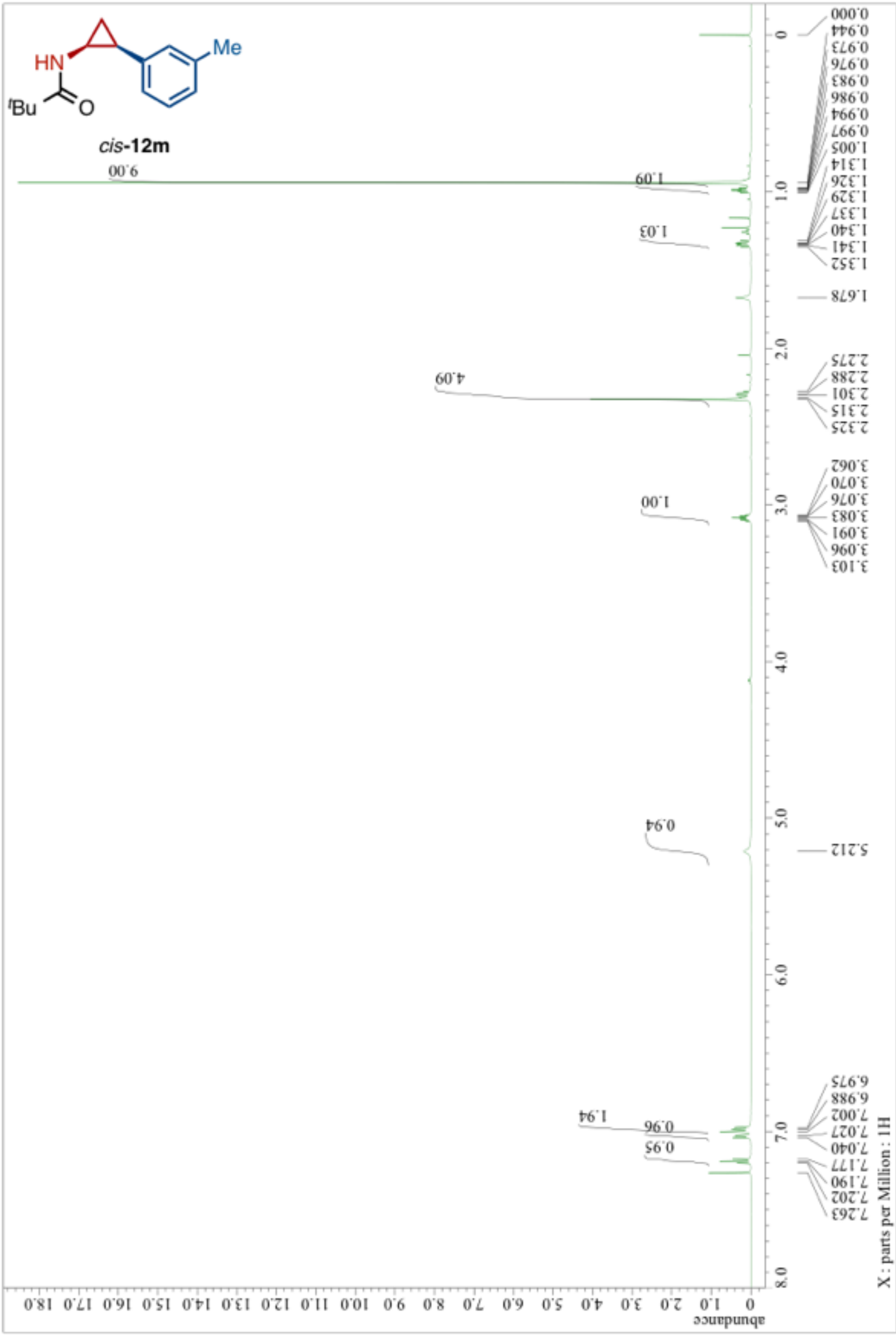
^{1}H NMR (600 MHz, $CDCl_3$) of *trans*-12m:



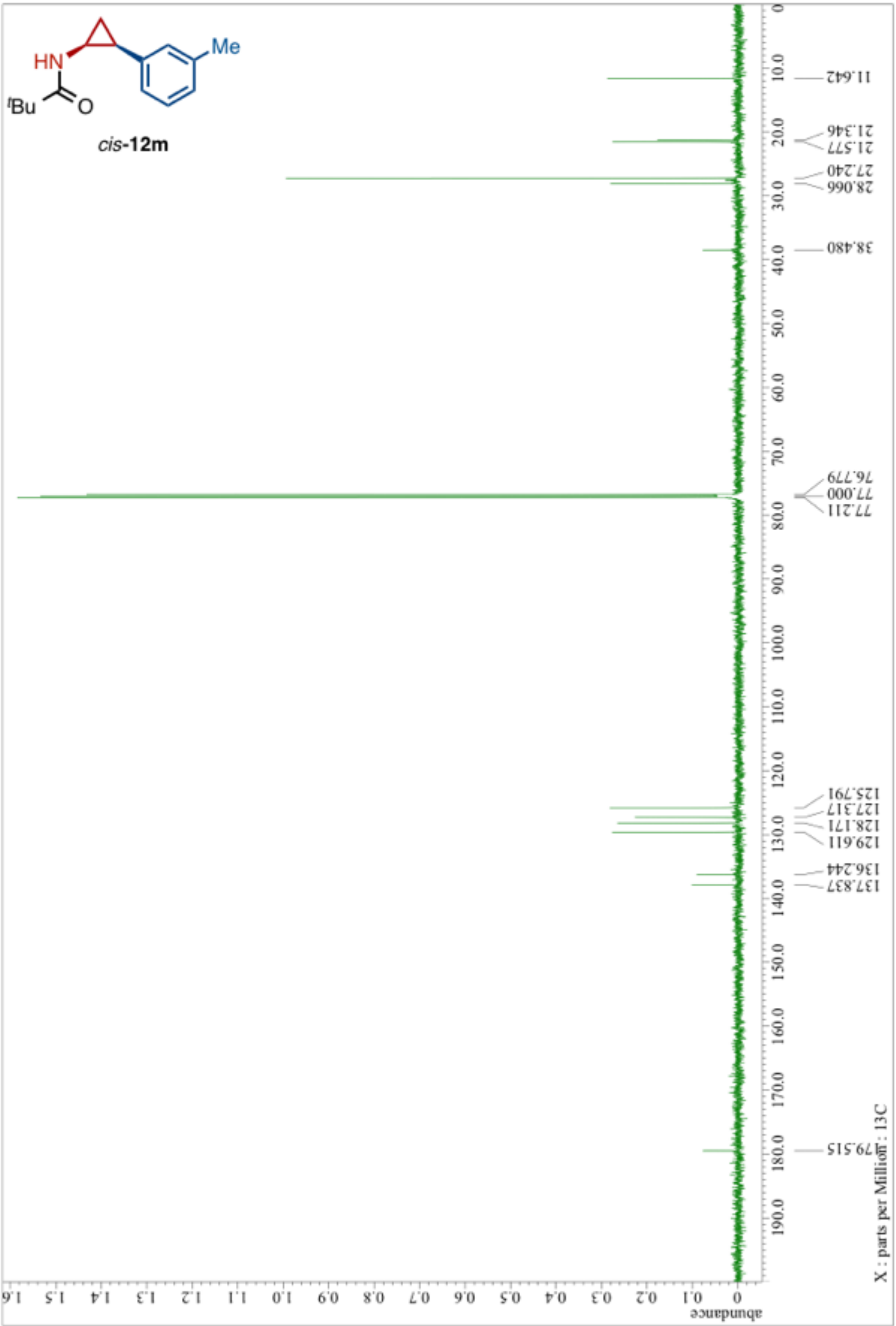
^{13}C NMR (150 MHz, $CDCl_3$) of *trans*-12m:



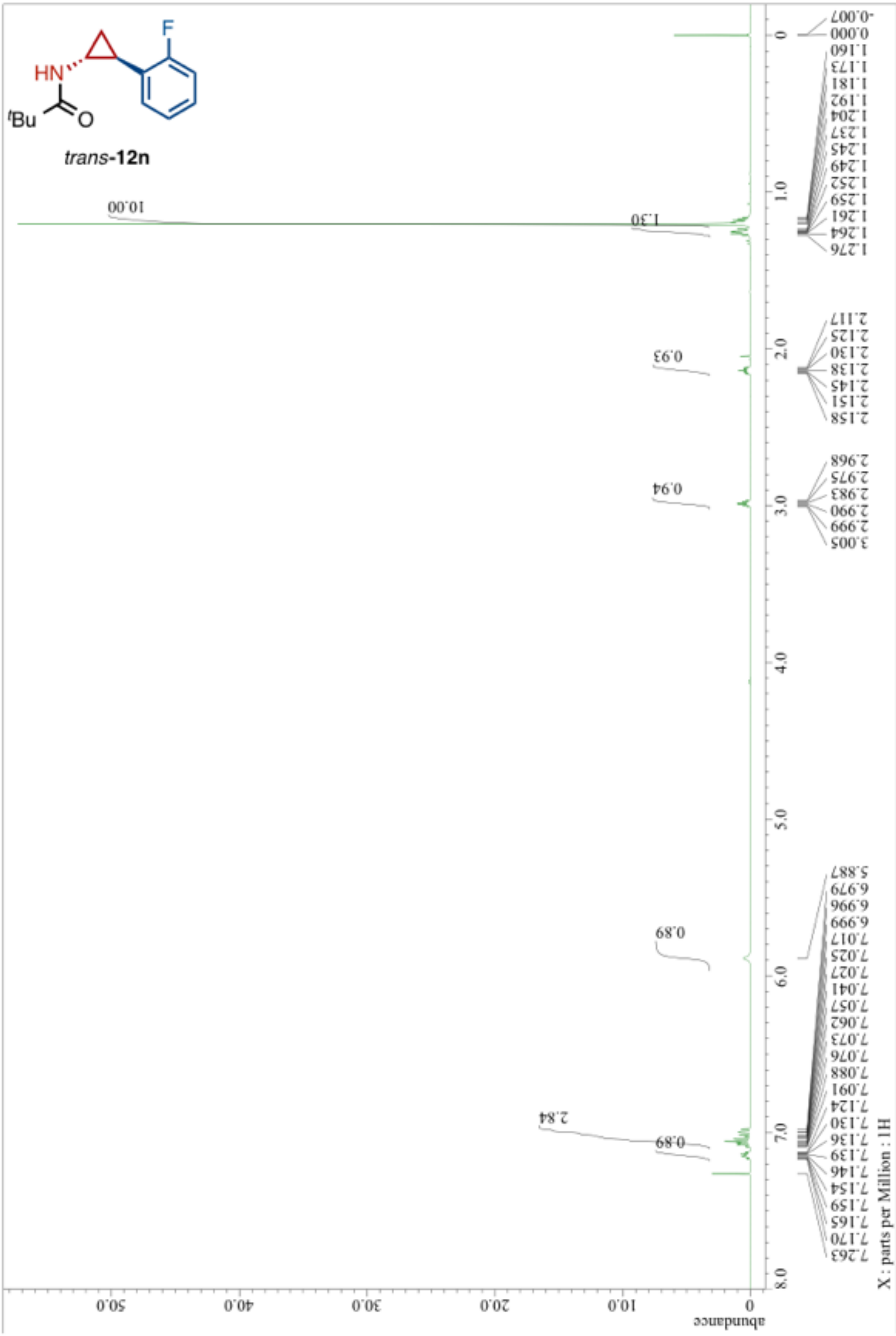
[1]H NMR (600 MHz, $CDCl_3$) of *cis*-12m:



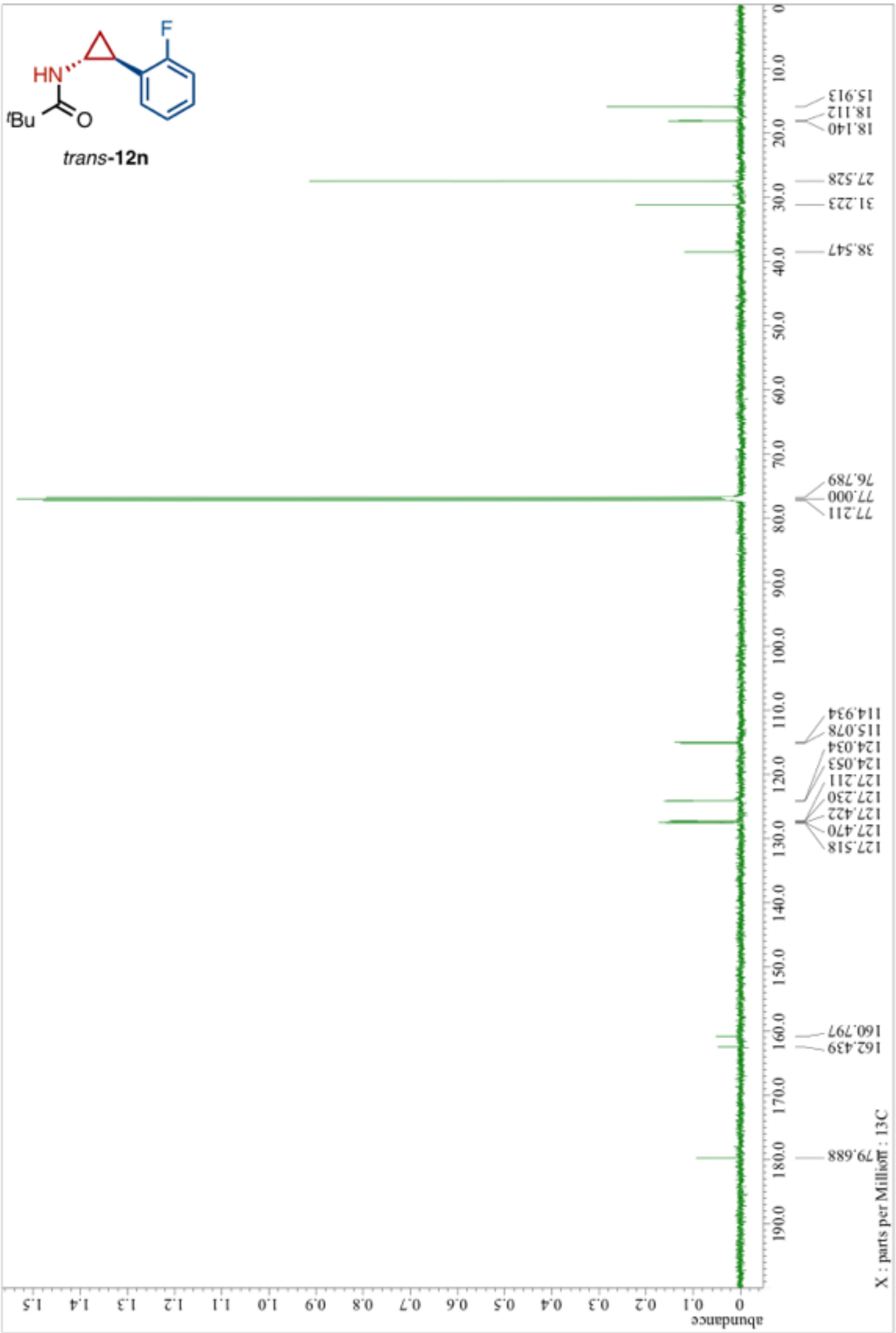
^{13}C NMR (150 MHz, $CDCl_3$) of *cis*-12m:



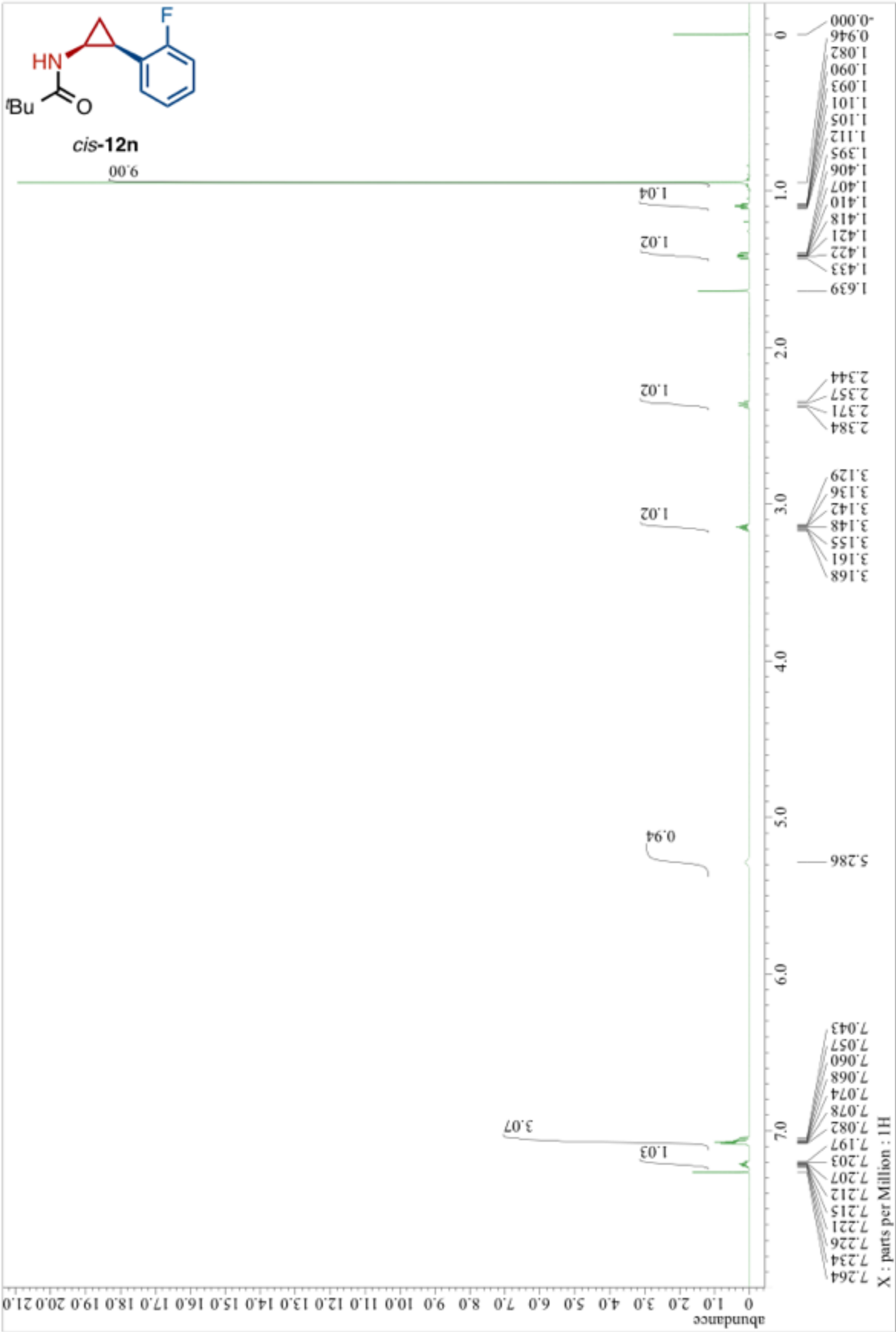
[1]H NMR (600 MHz, $CDCl_3$) of *trans*-12n:



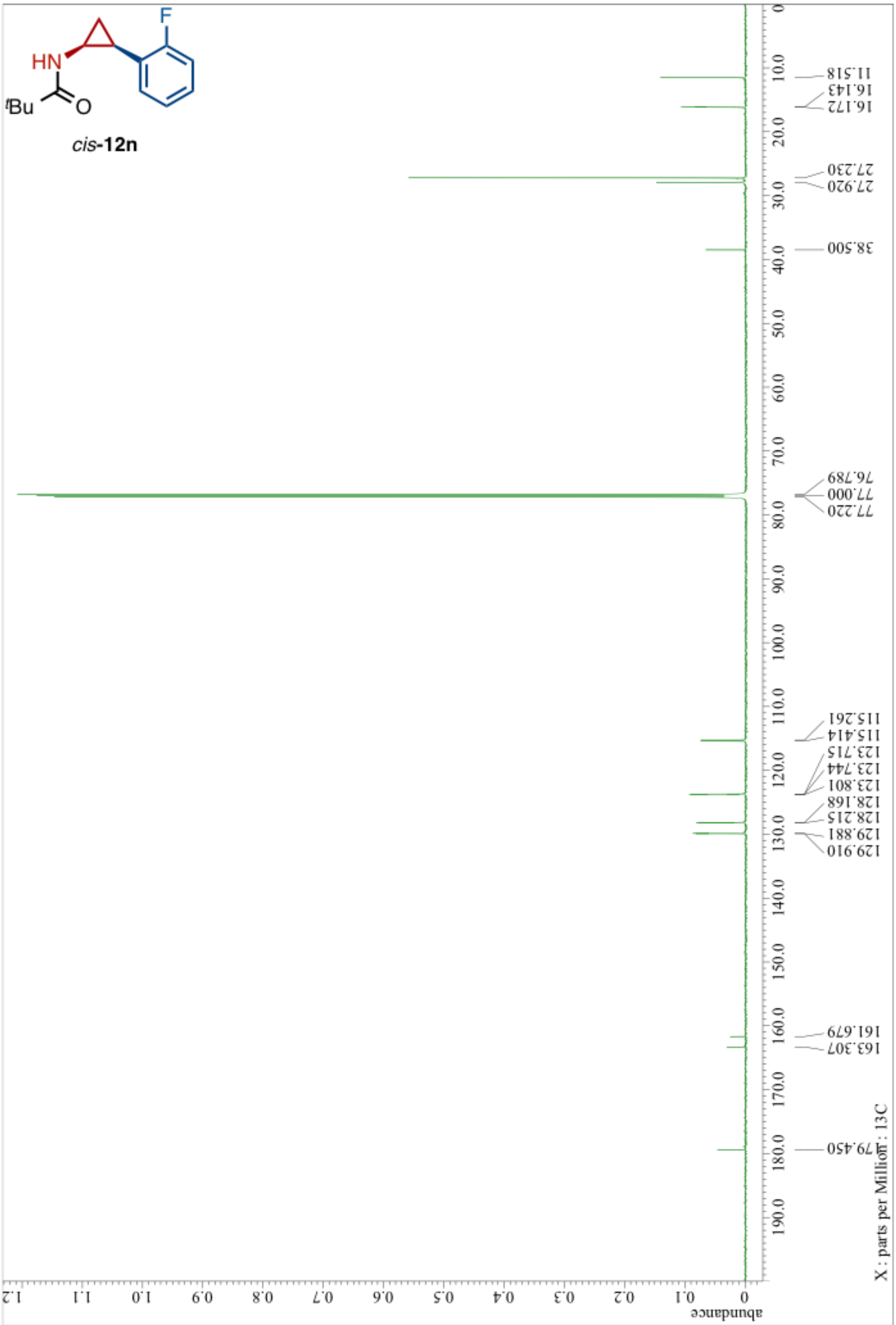
^{13}C NMR (150 MHz, CDCl$_3$) of *trans*-12n:



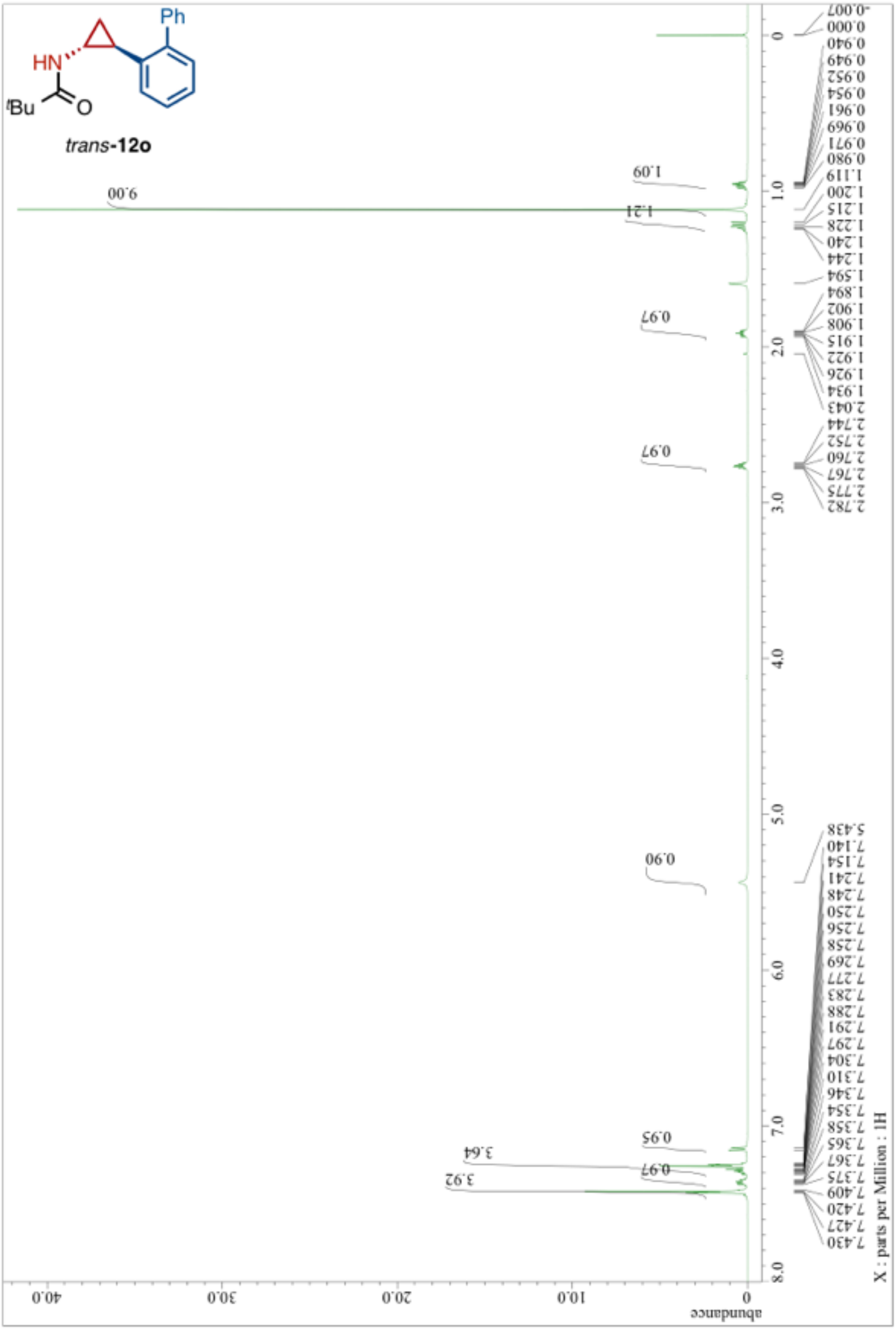
[1]H NMR (600 MHz, $CDCl_3$) of *cis*-12n:



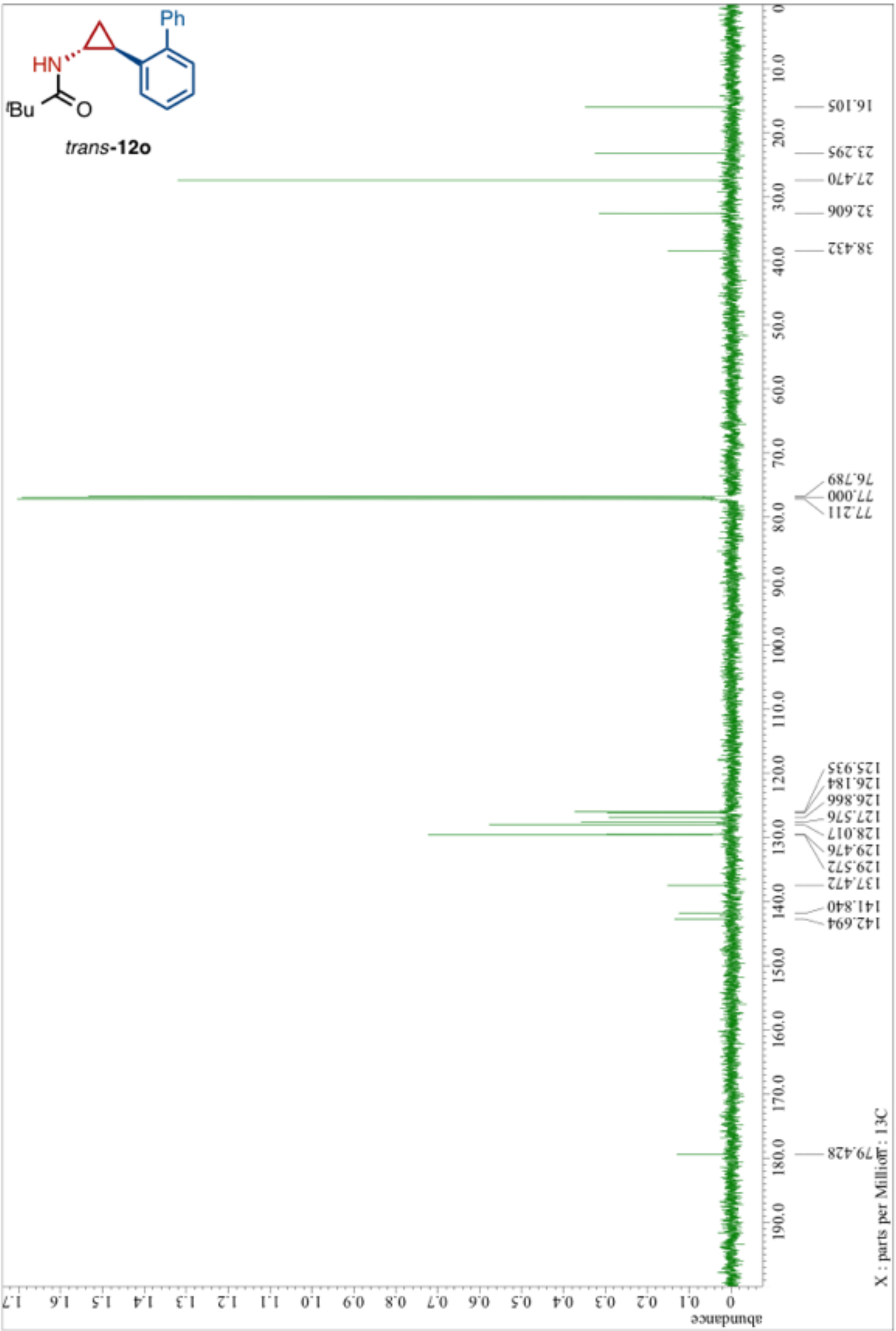
^{13}C NMR (150 MHz, CDCl$_3$) of *cis*-12n:



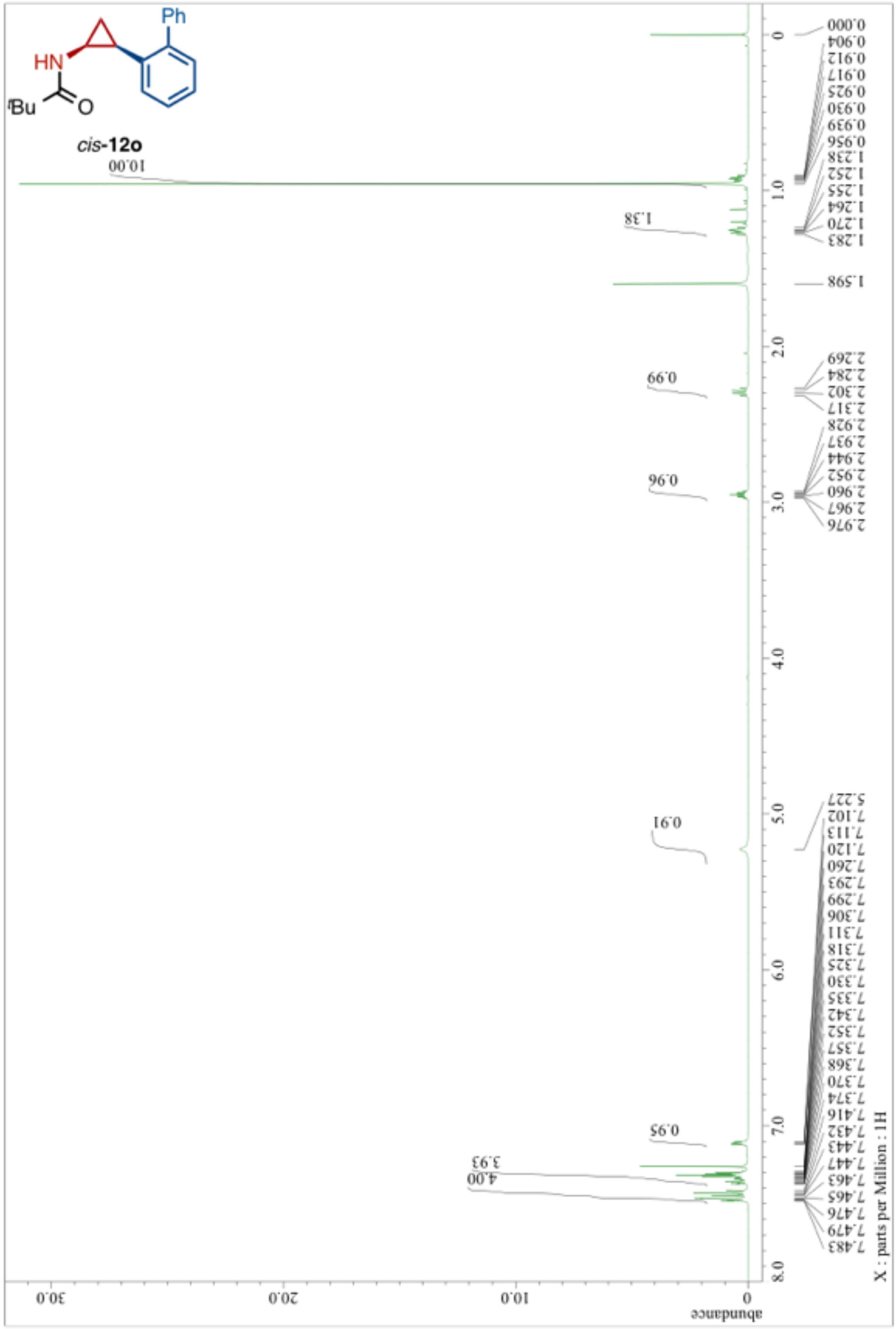
^{1}H NMR (600 MHz, CDCl$_3$) of *trans*-12o:



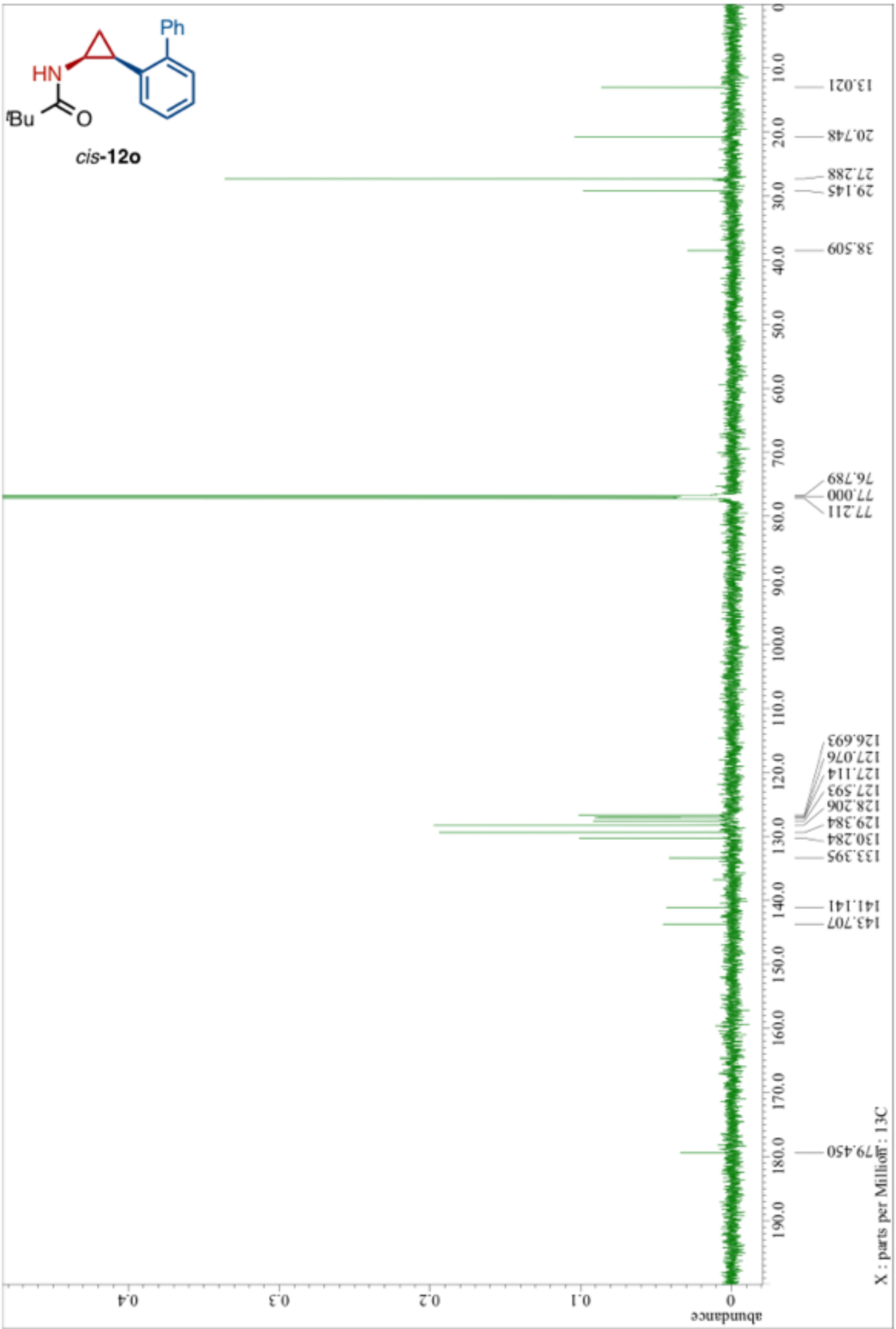
[13]C NMR (150 MHz, $CDCl_3$) of *trans*-12o:



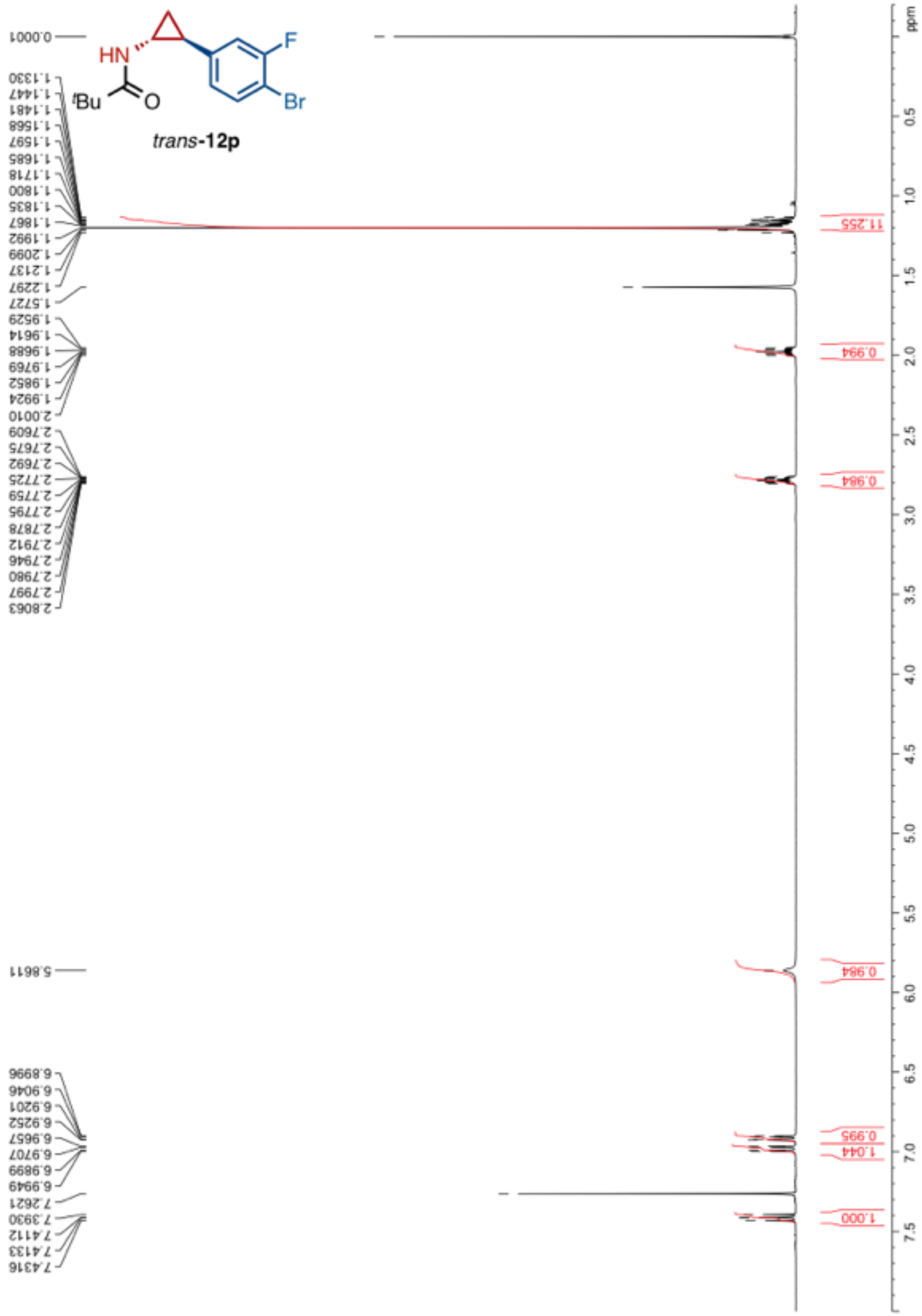
^{1}H NMR (600 MHz, CDCl$_3$) of *cis*-12o:



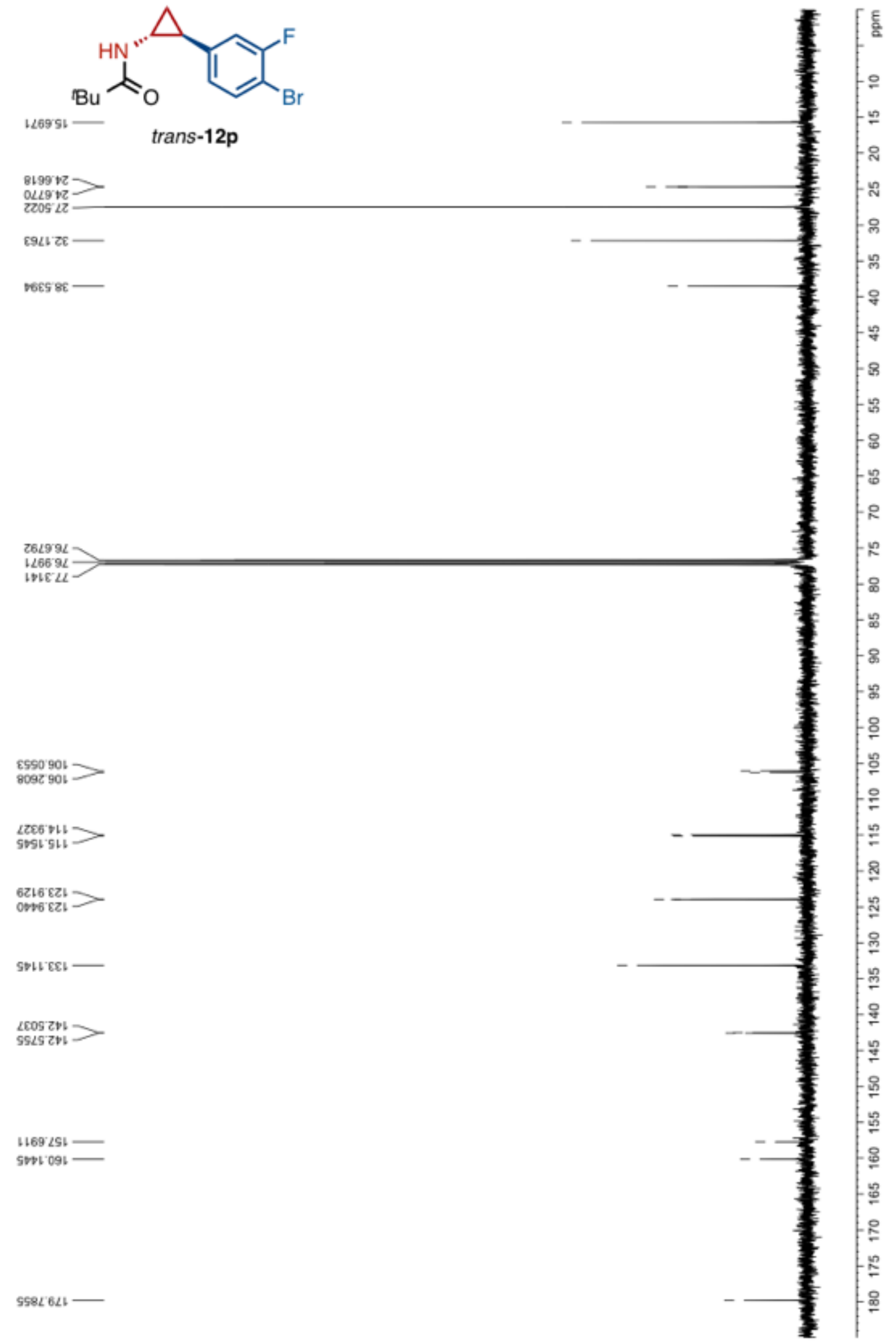
^{13}C NMR (150 MHz, CDCl$_3$) of *cis*-12o:



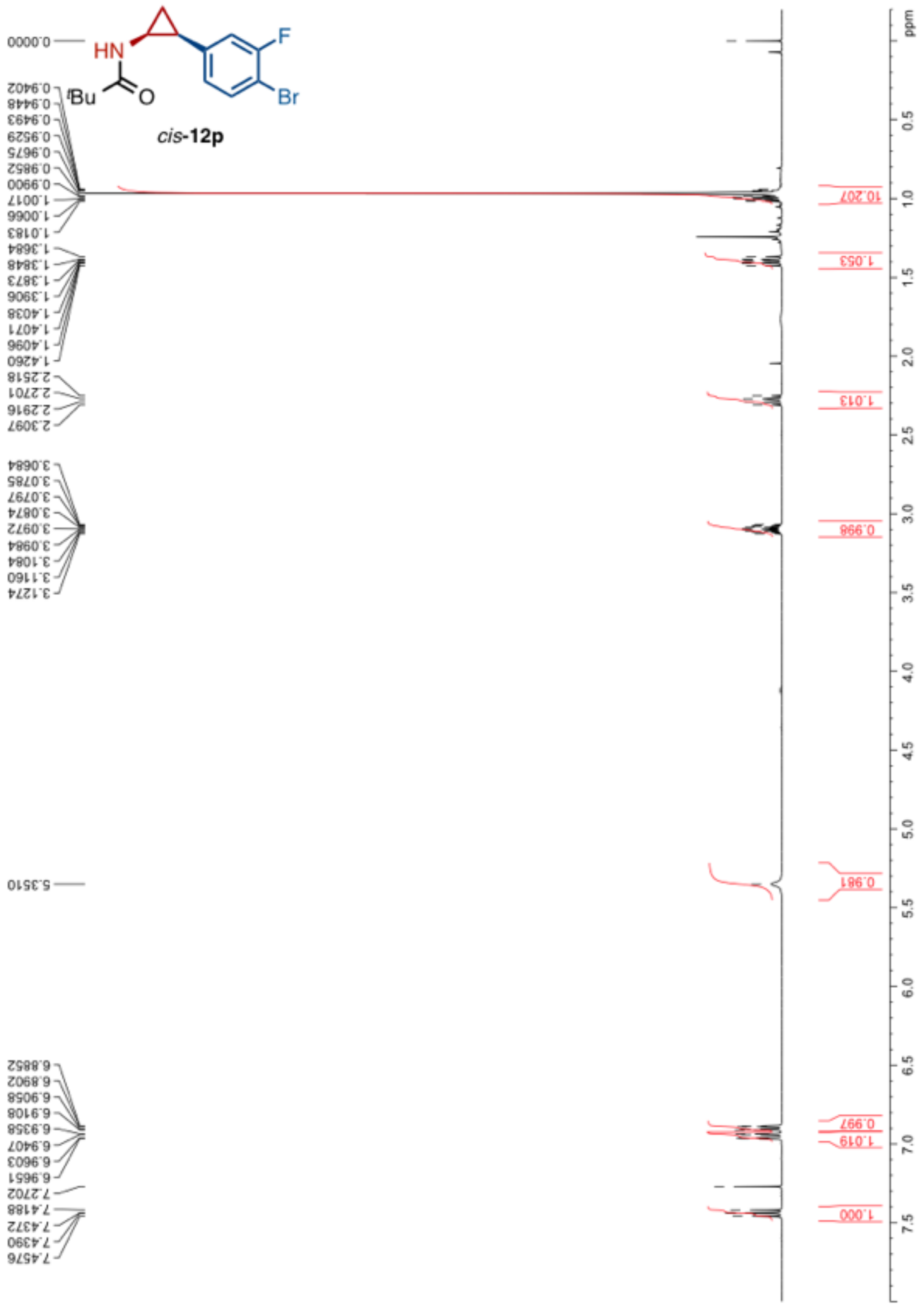
[1]H NMR (400 MHz, $CDCl_3$) of *trans*-12p:



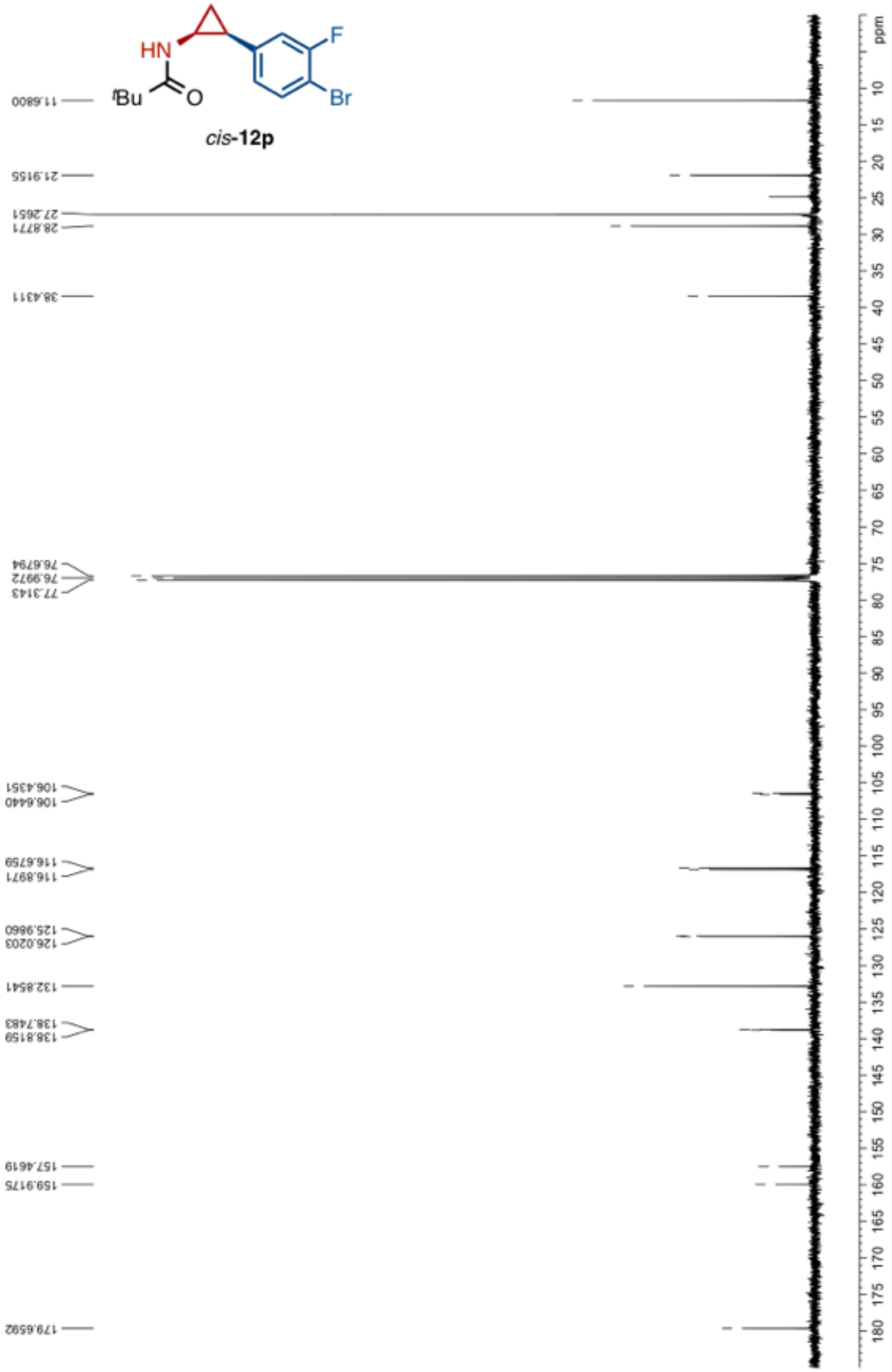
[13]C NMR (150 MHz, CDCl$_3$) of *trans*-12p:



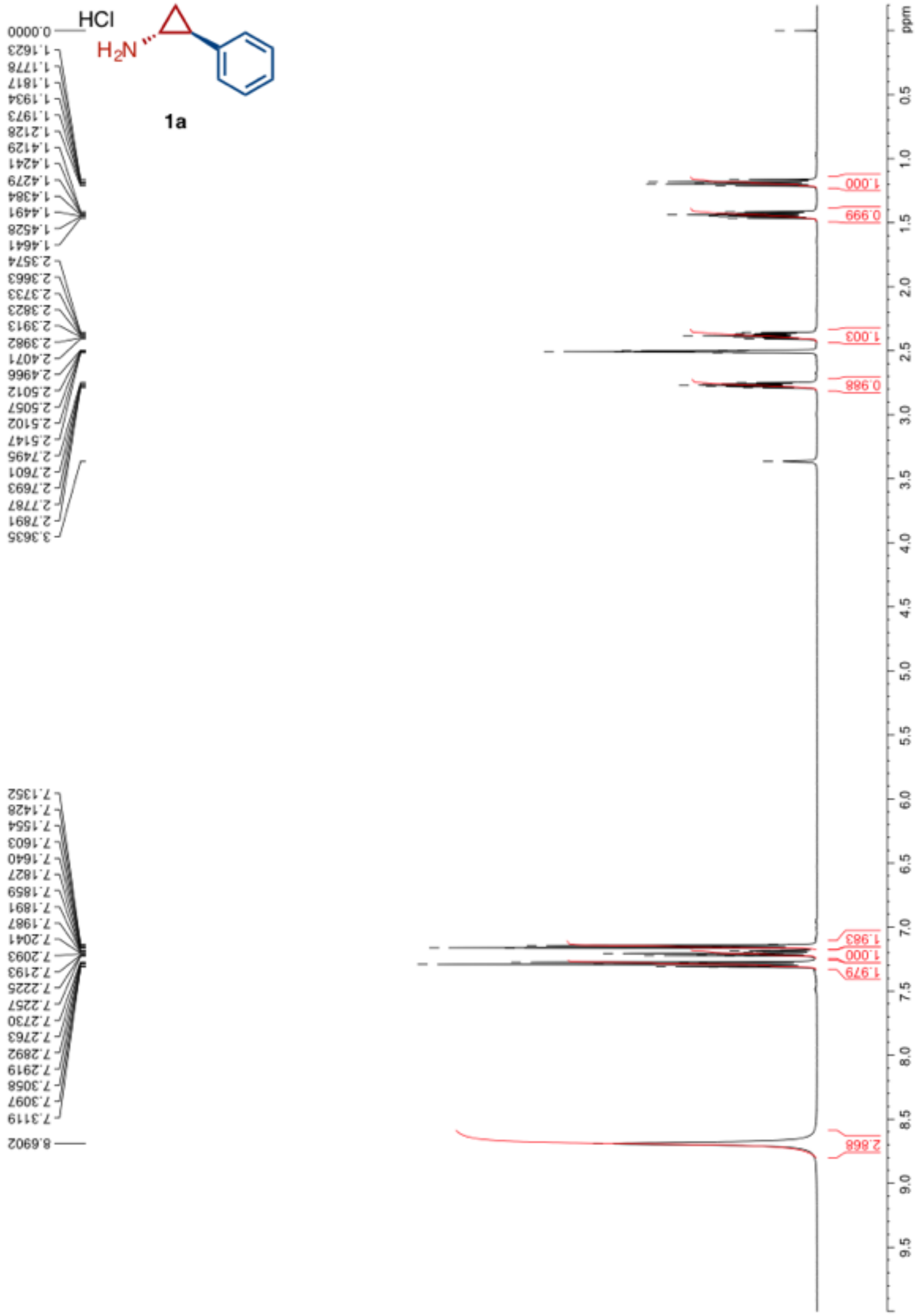
[1]H NMR (400 MHz, $CDCl_3$) of *cis*-12p:



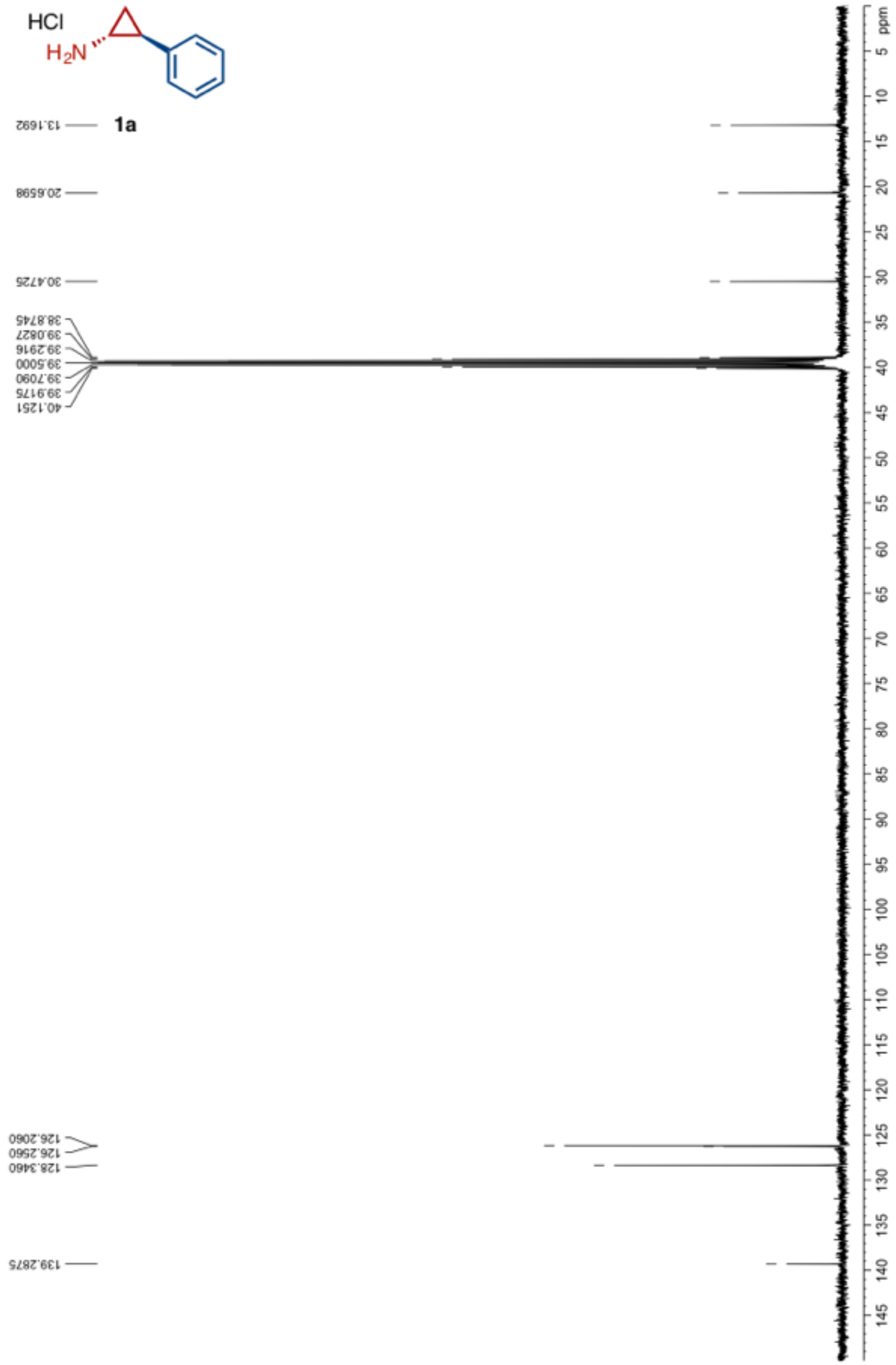
^{13}C NMR (100 MHz, CDCl$_3$) of *cis*-12p:



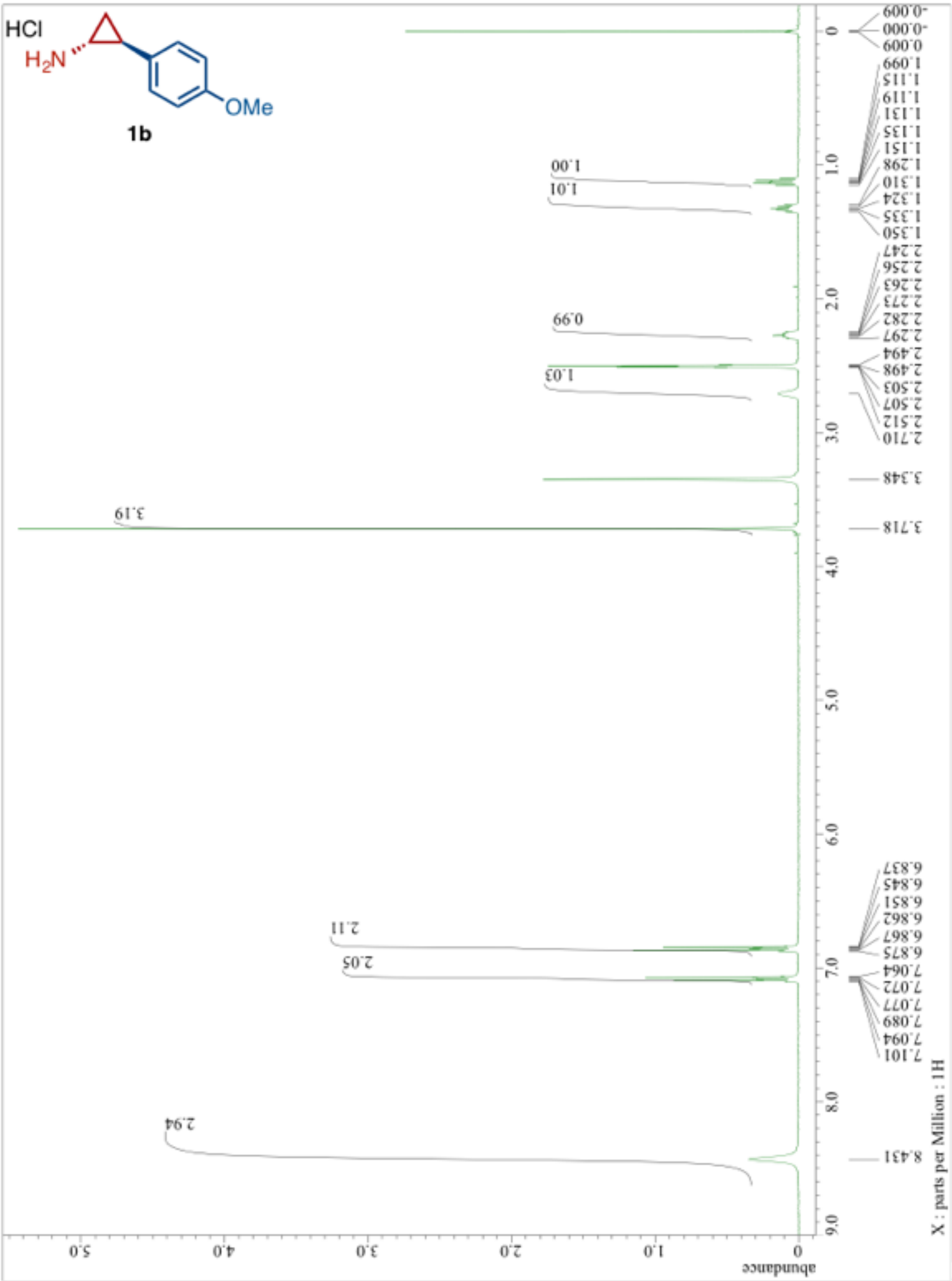
[1]H NMR (400 MHz, DMSO-d_6) of 1a:



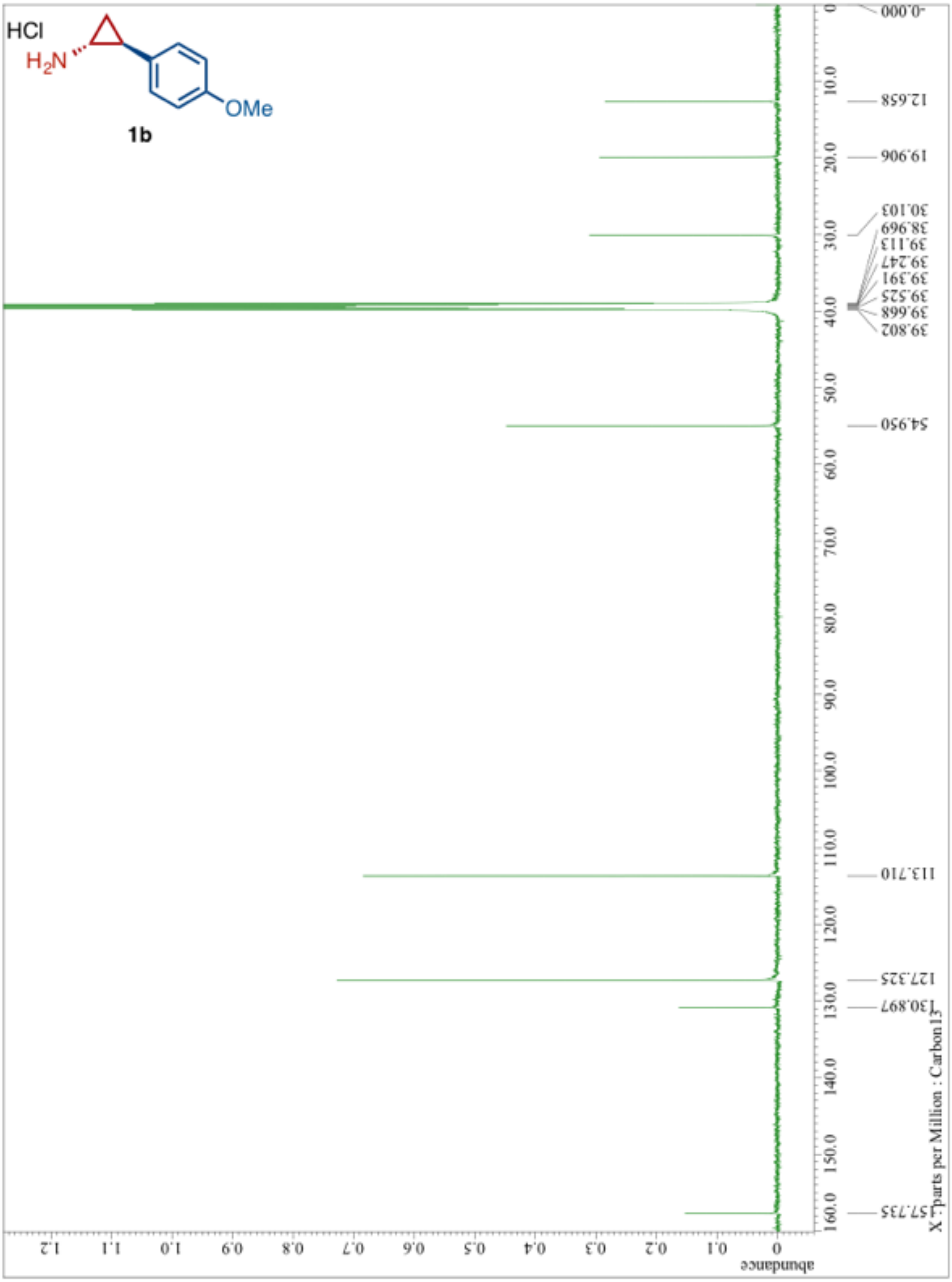
^{13}C NMR (100 MHz, DMSO-d_6) of 1a:



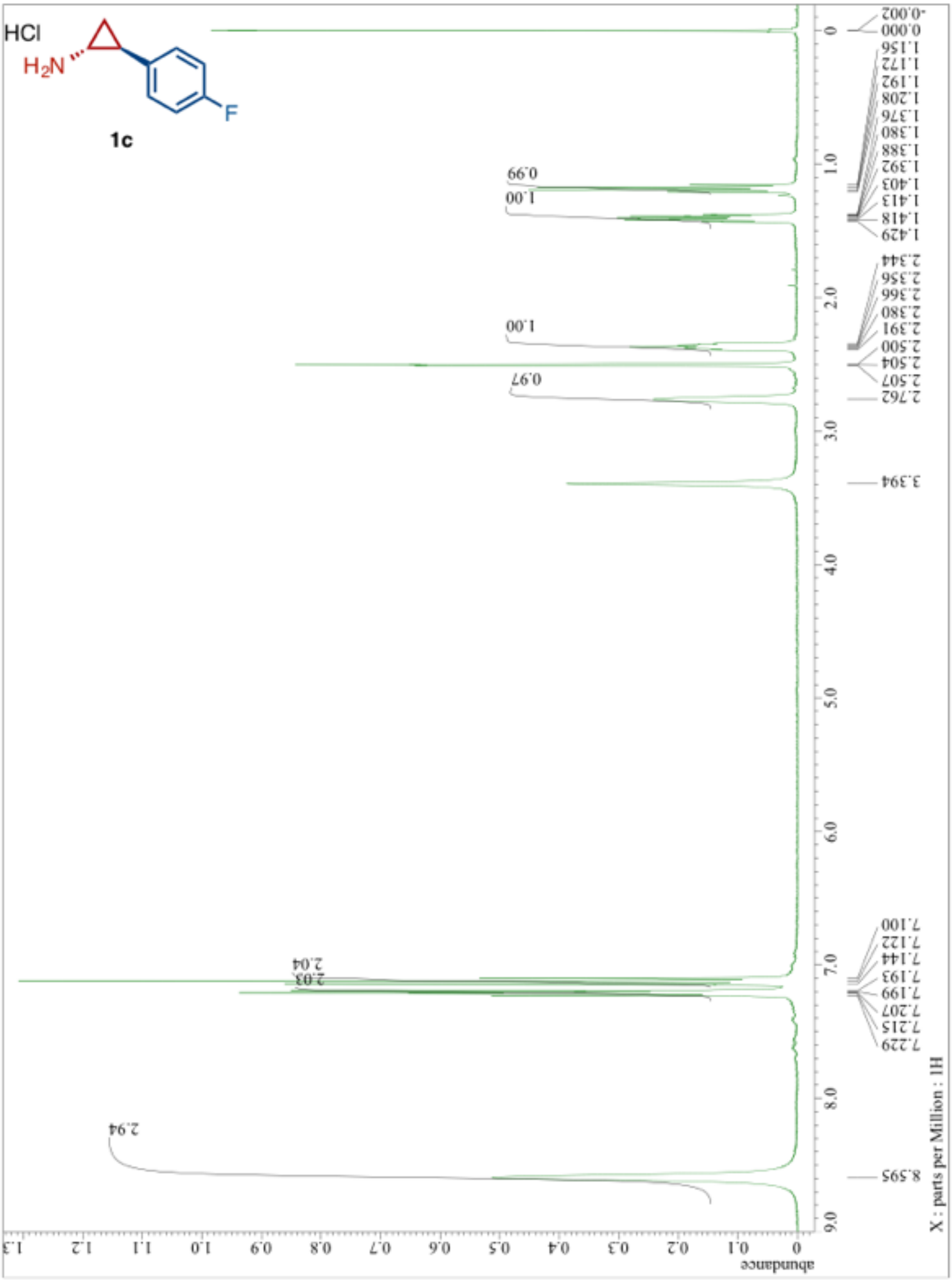
[1]H NMR (400 MHz, DMSO-d_6) of 1b:



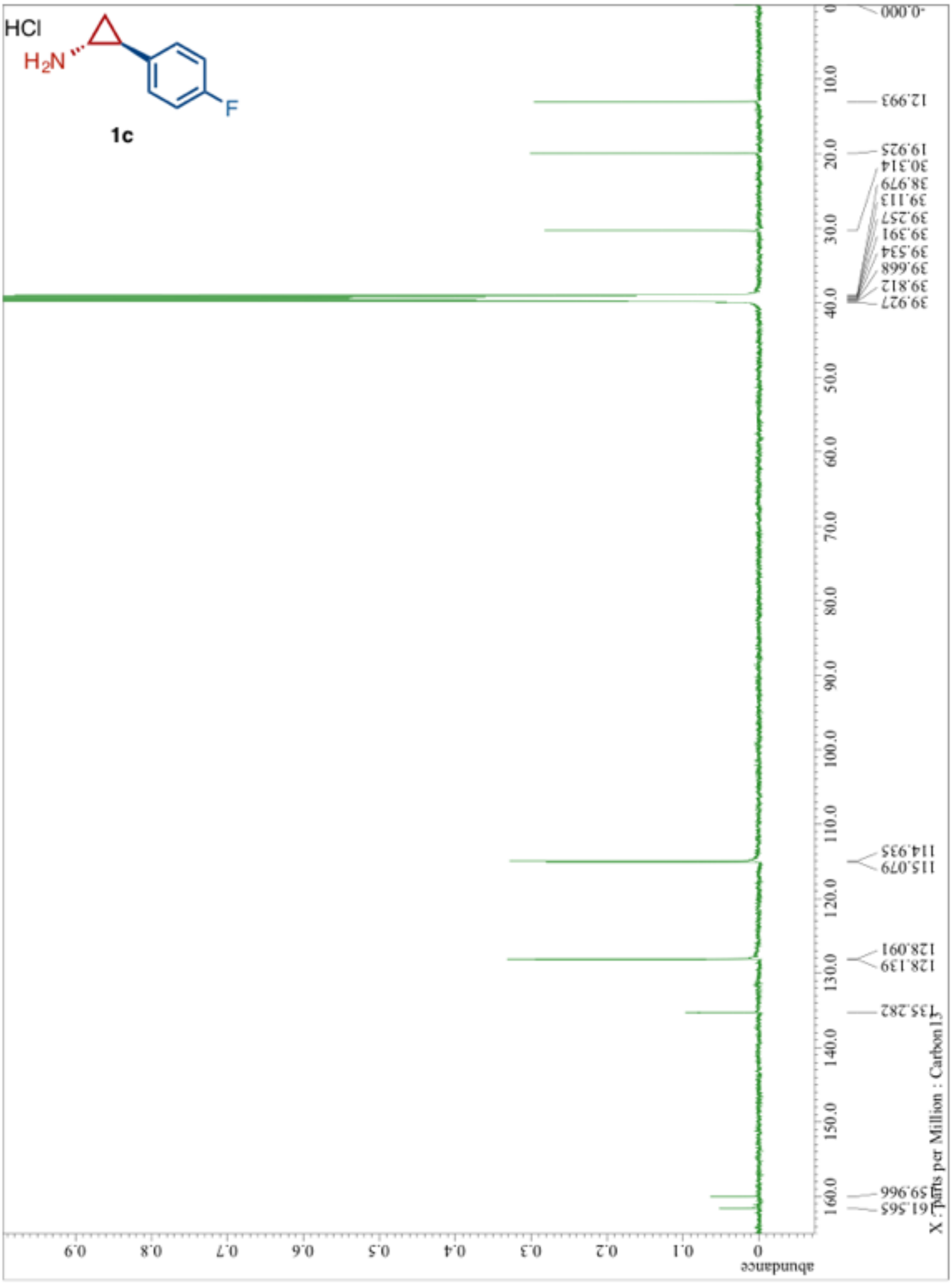
^{13}C NMR (150 MHz, DMSO-d_6) of 1b:



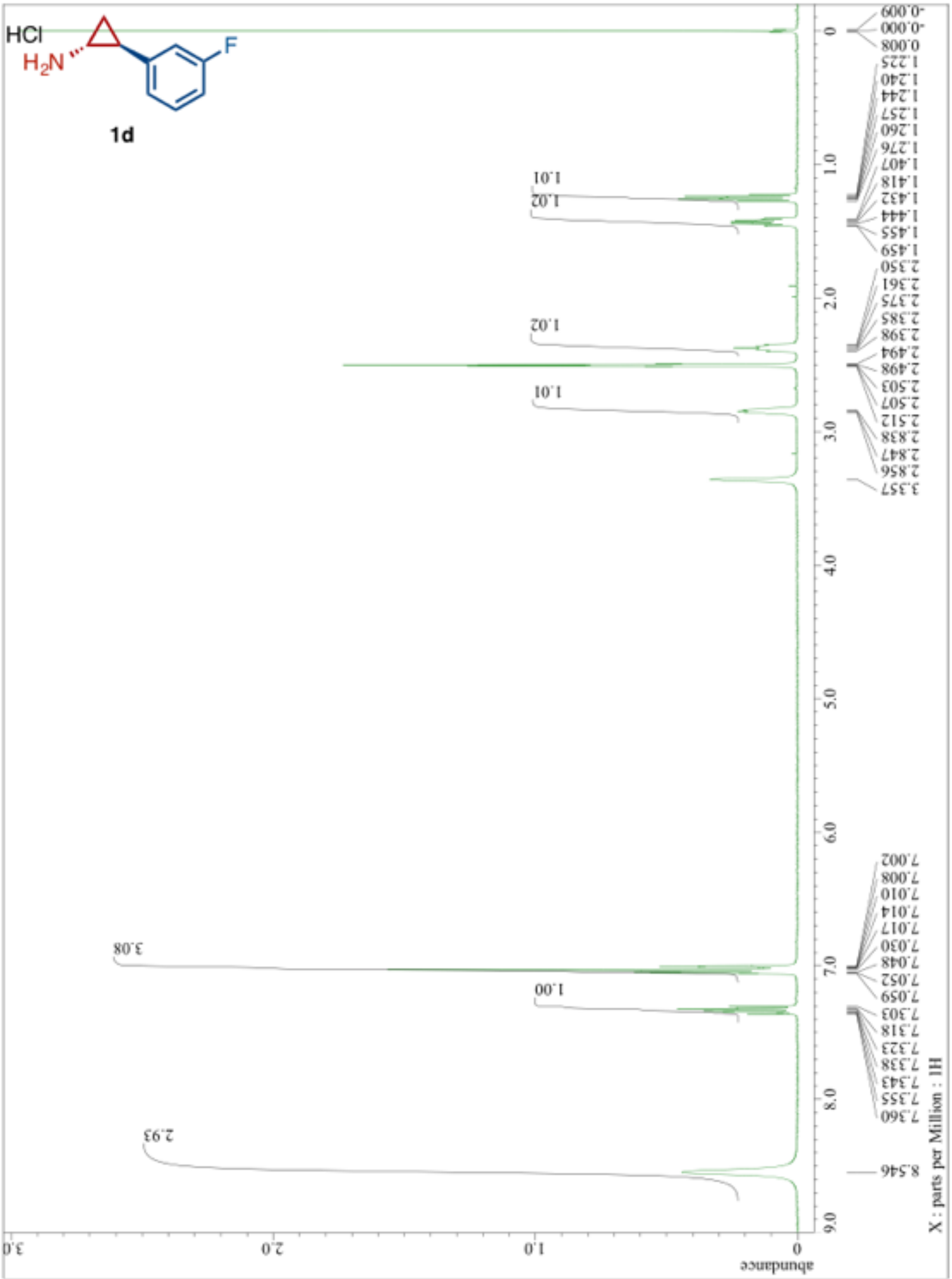
^{1}H NMR (400 MHz, DMSO-d_6) of 1c:



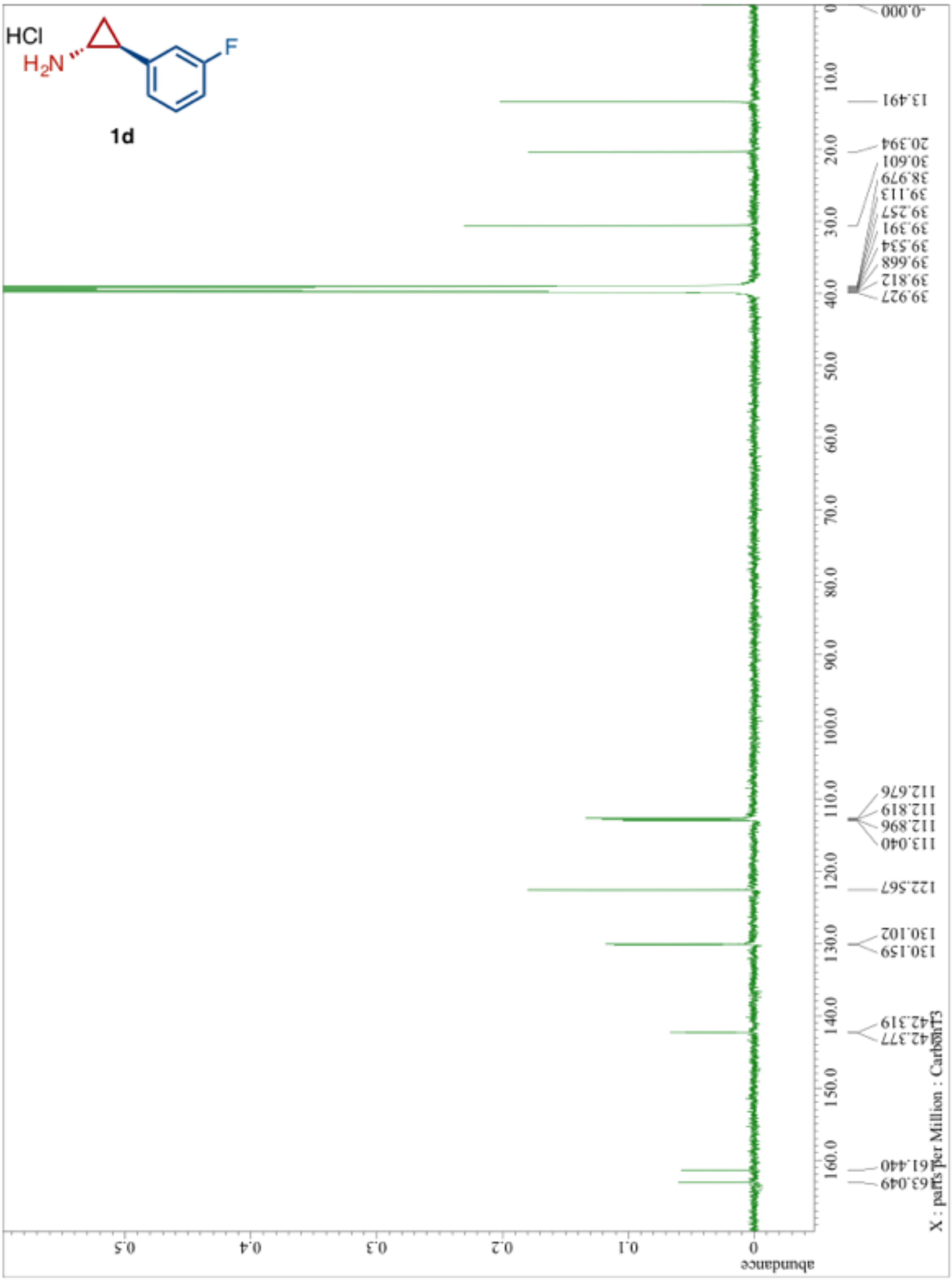
^{13}C NMR (150 MHz, DMSO-d_6) of 1c:



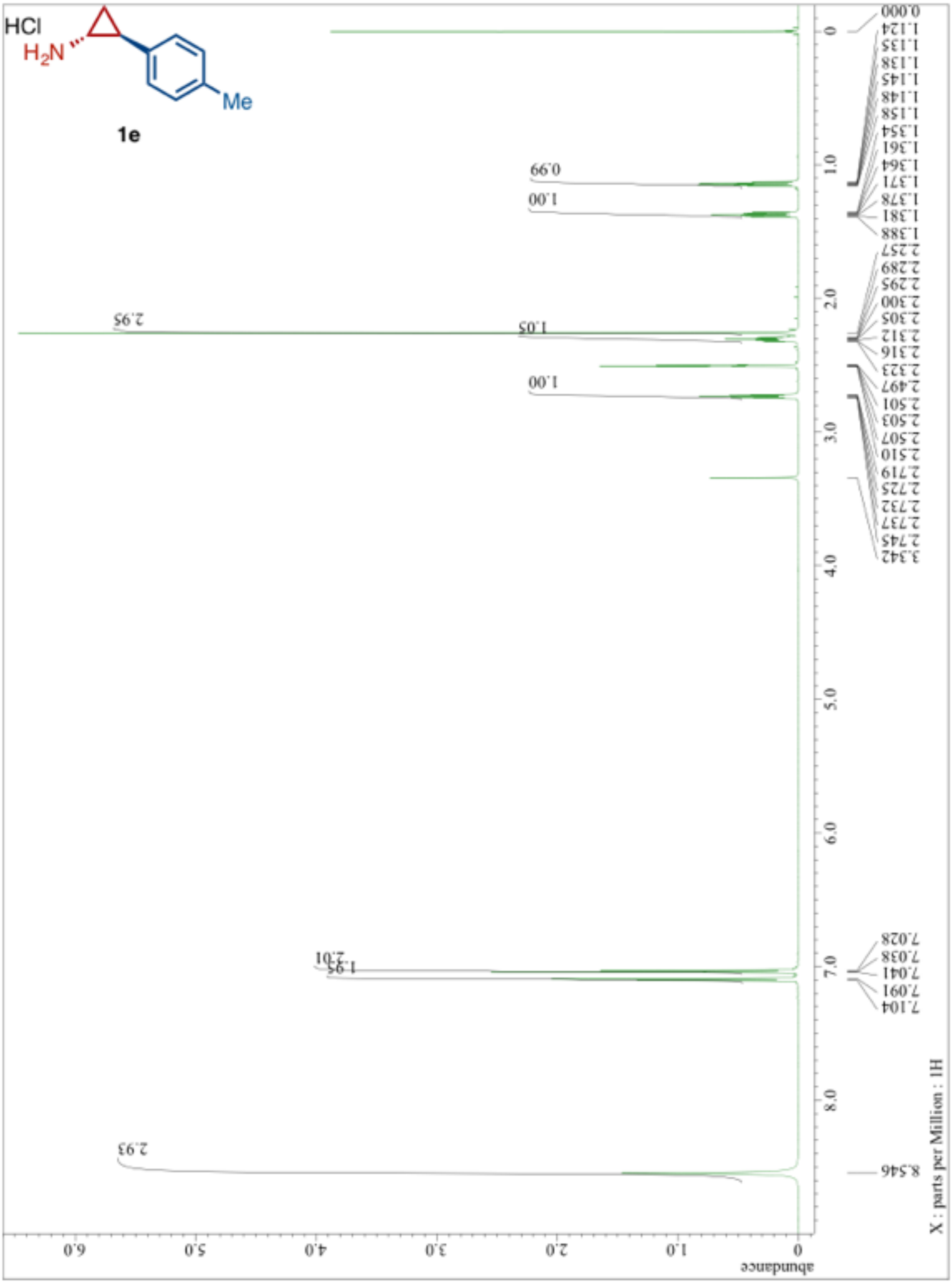
[1]H NMR (400 MHz, DMSO-d_6) of 1d:



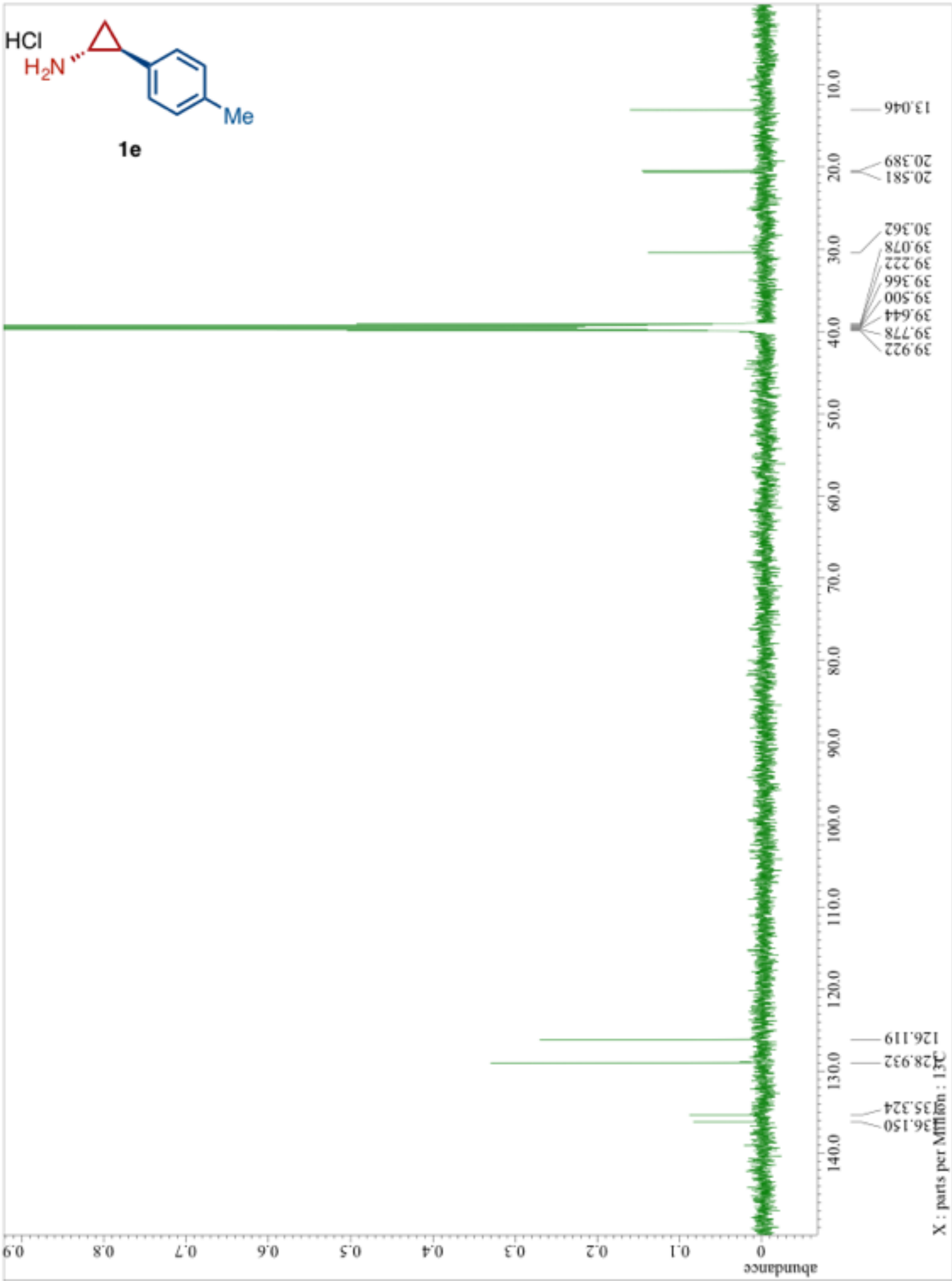
^{13}C NMR (150 MHz, DMSO-d_6) of 1d:



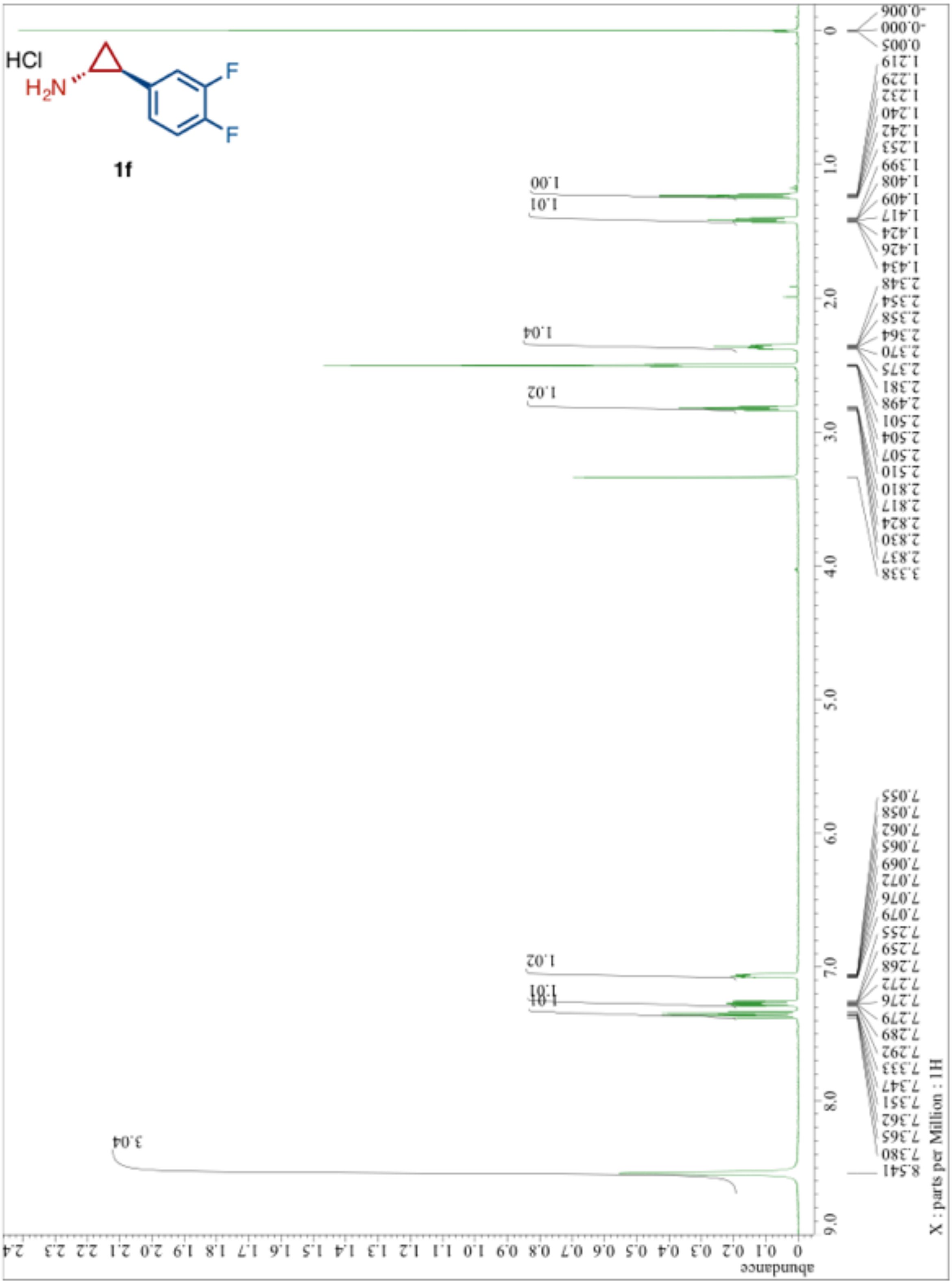
[1]H NMR (600 MHz, DMSO-d_6) of 1e:



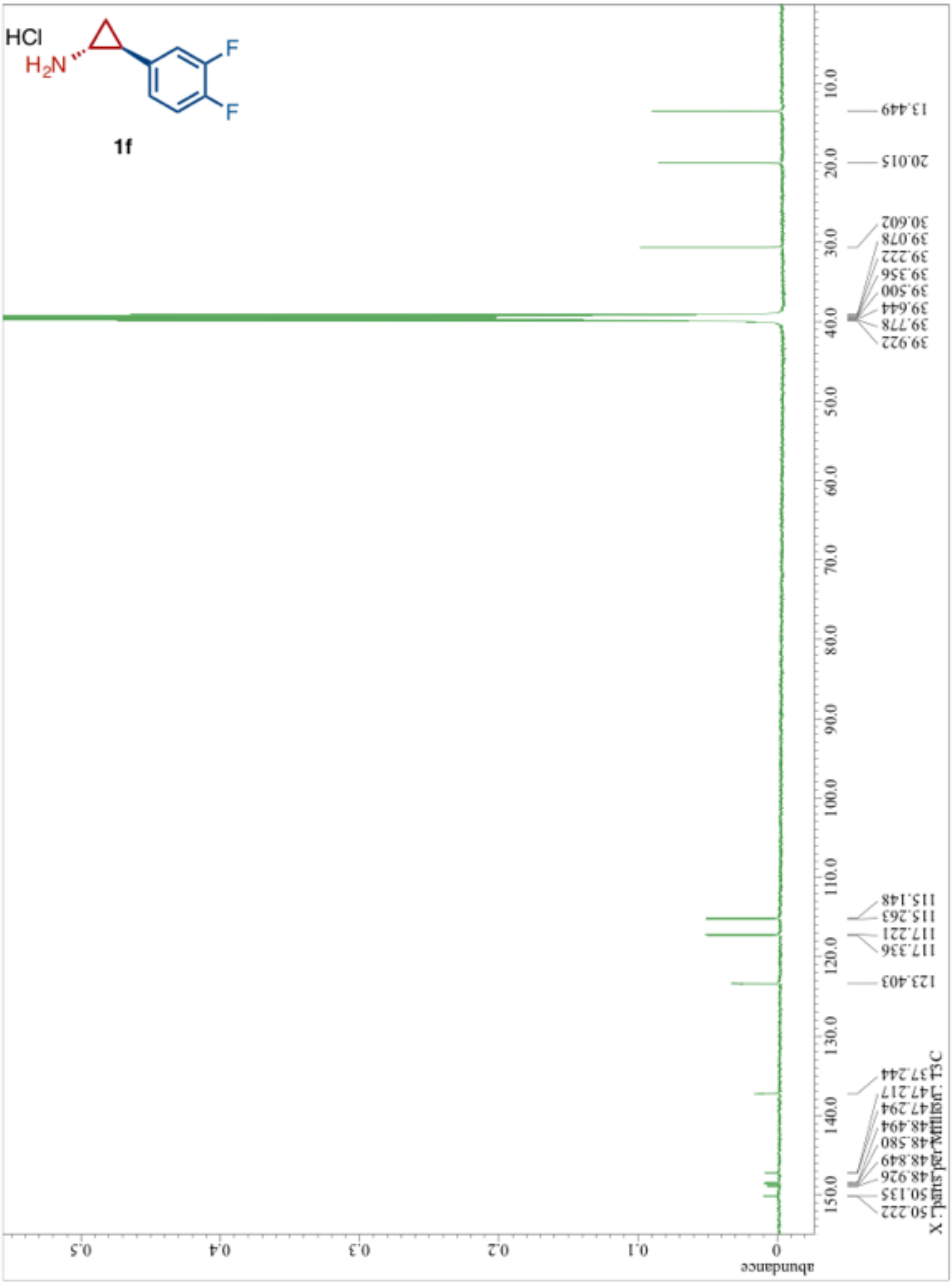
^{13}C NMR (150 MHz, DMSO-d_6) of 1e:



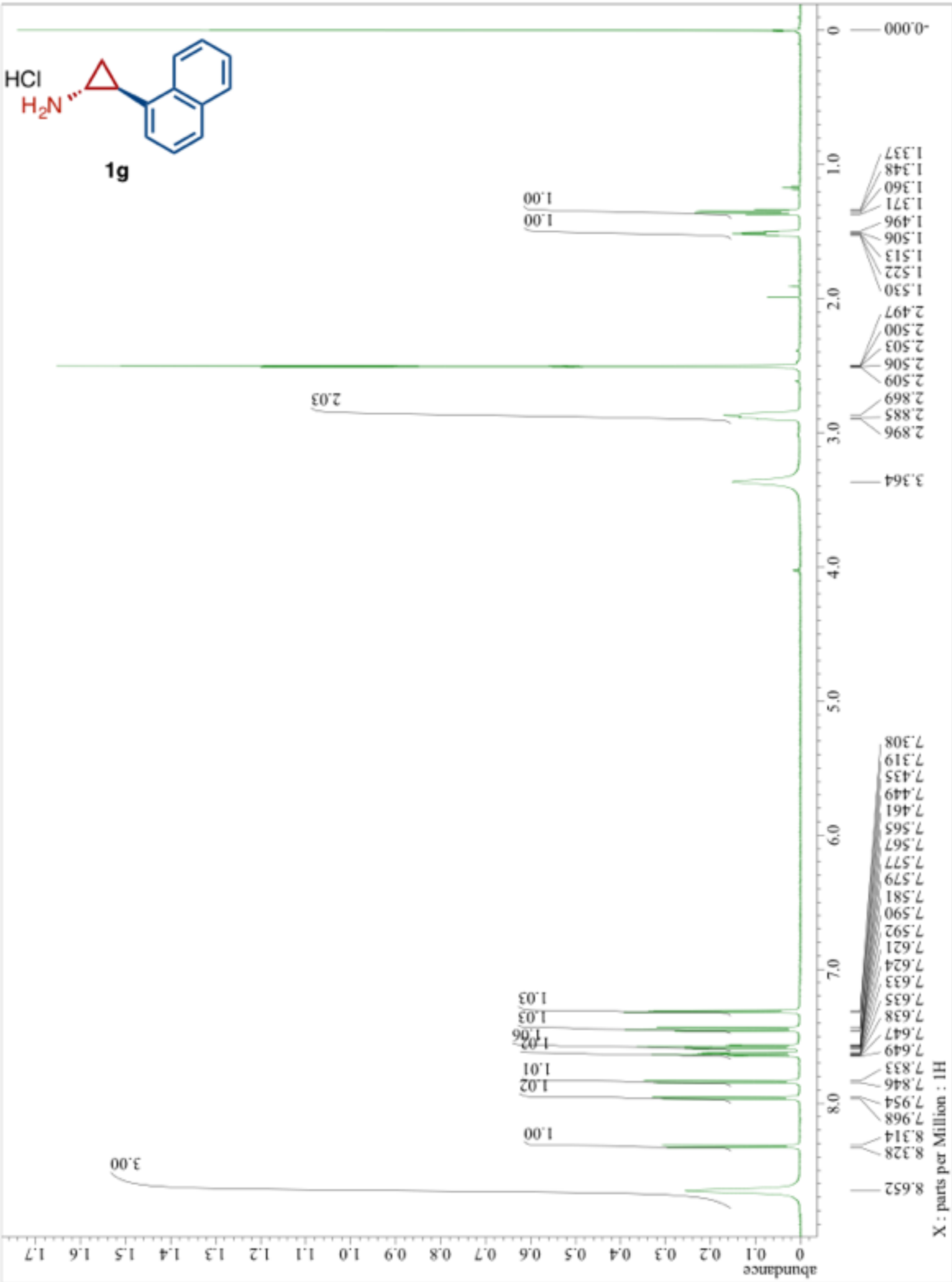
[1]H NMR (600 MHz, DMSO-d_6) of 1f:



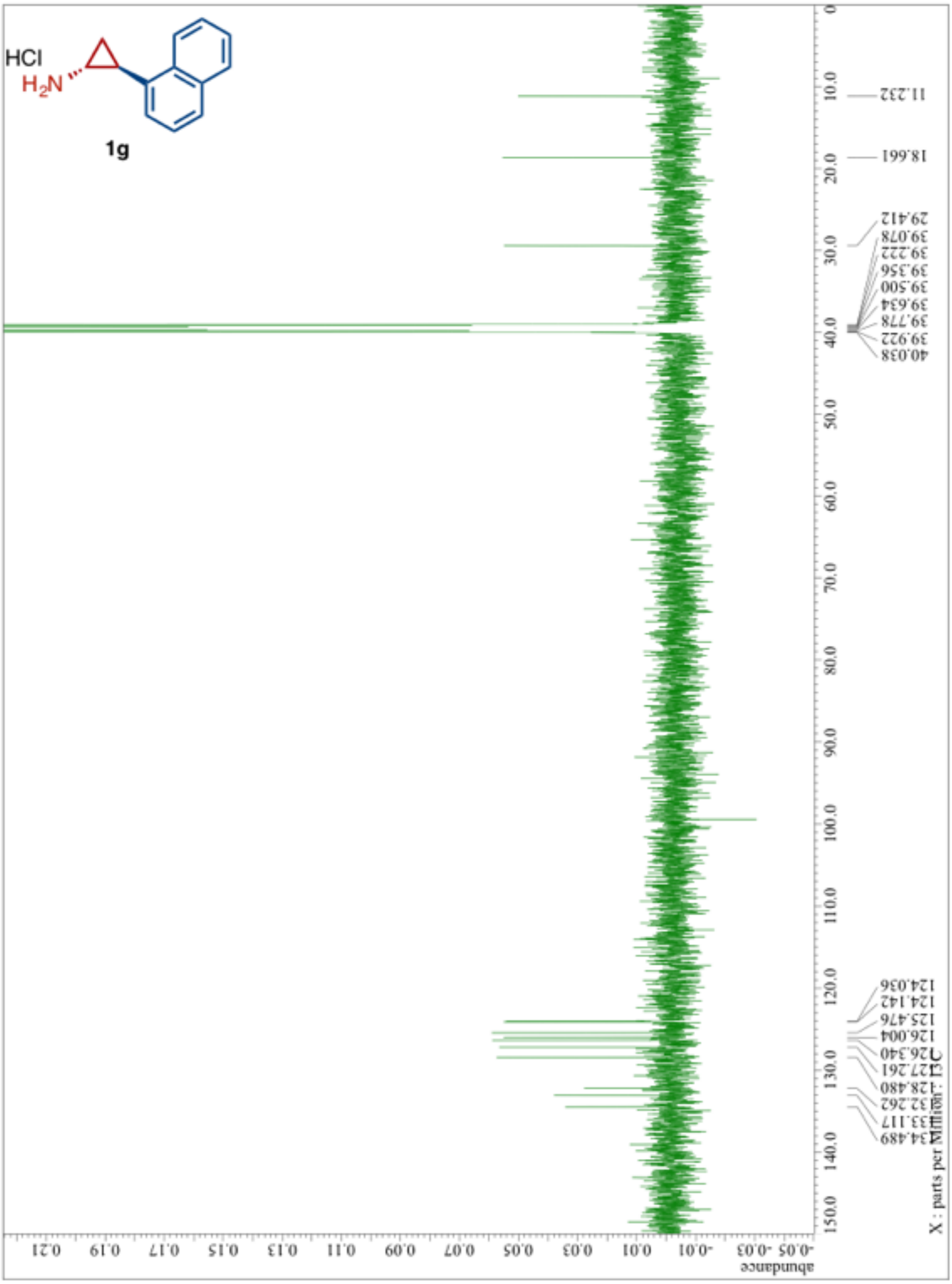
^{13}C NMR (150 MHz, DMSO-d_6) of 1f:



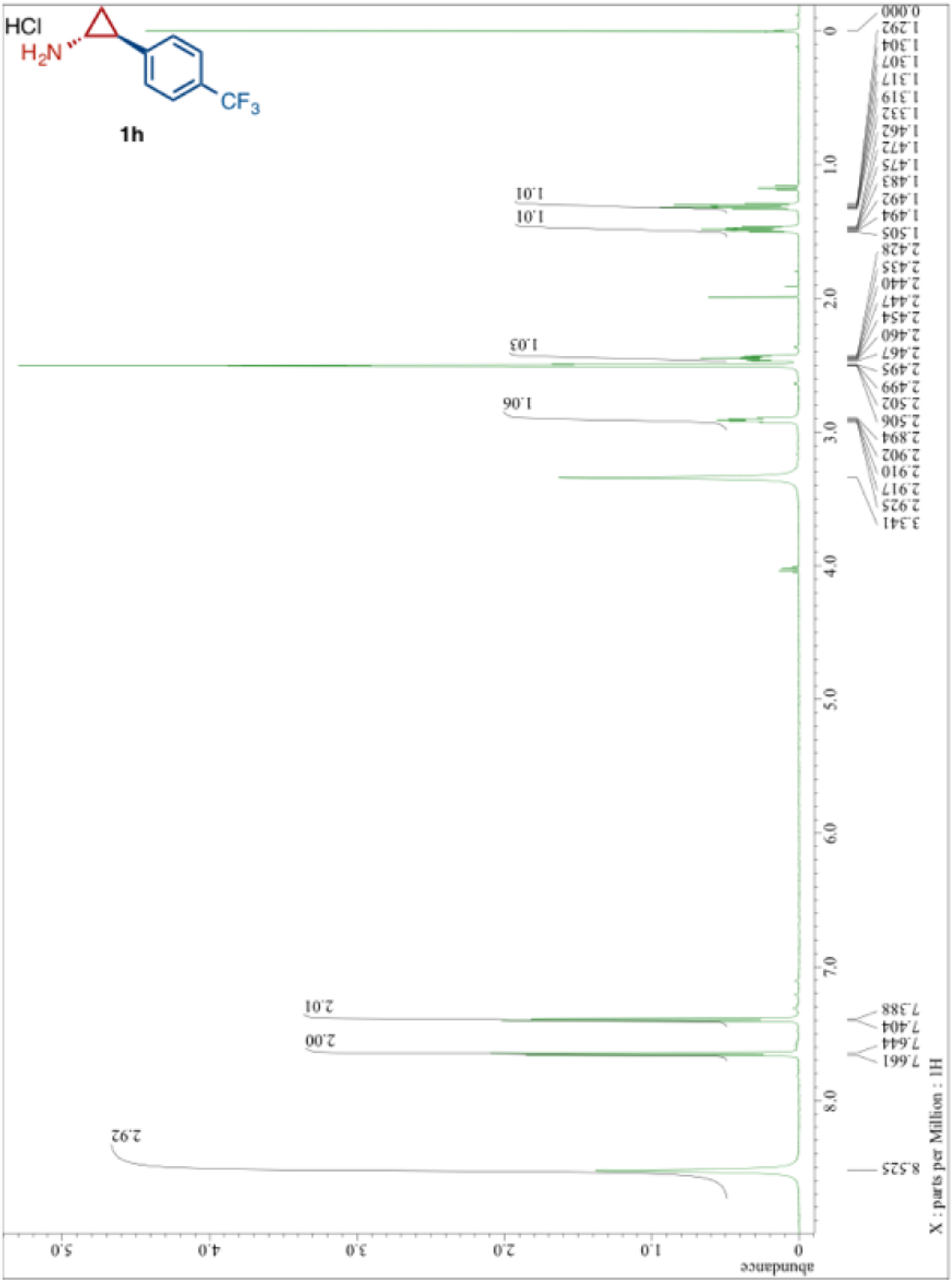
[1]H NMR (600 MHz, DMSO-d_6) of 1g:



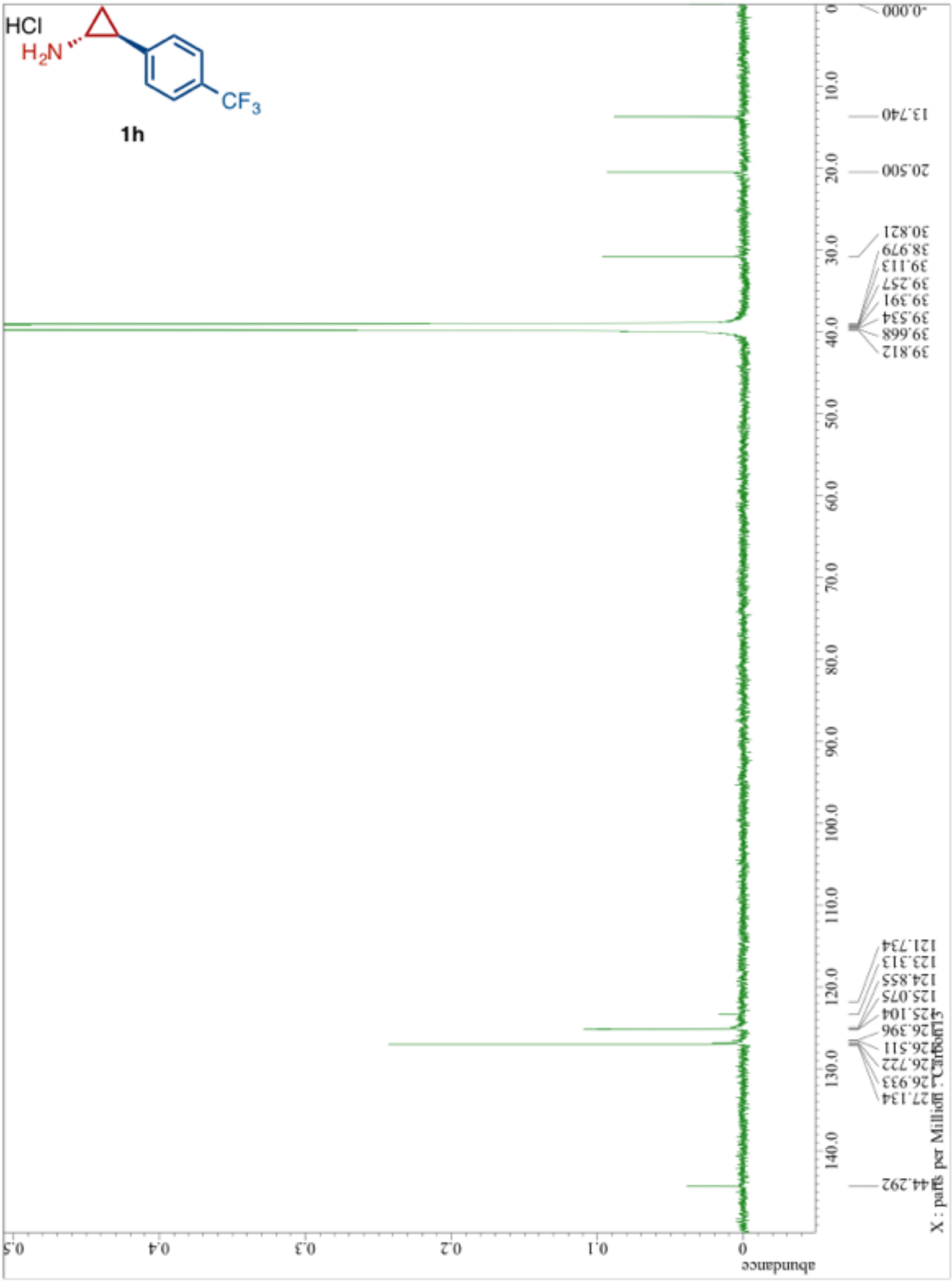
^{13}C NMR (150 MHz, DMSO-d_6) of 1g:



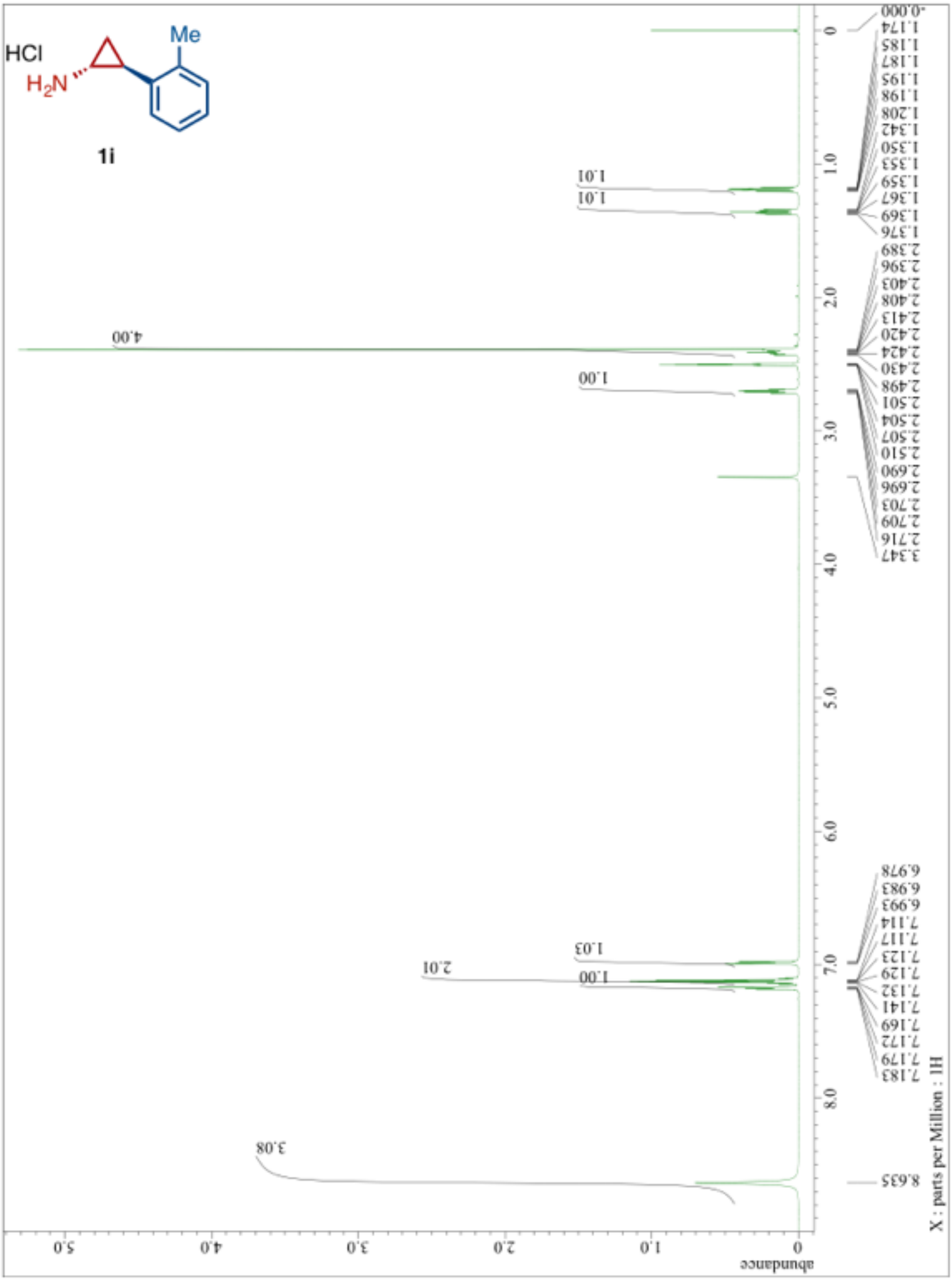
^{1}H NMR (500 MHz, DMSO-d_6) of 1h:



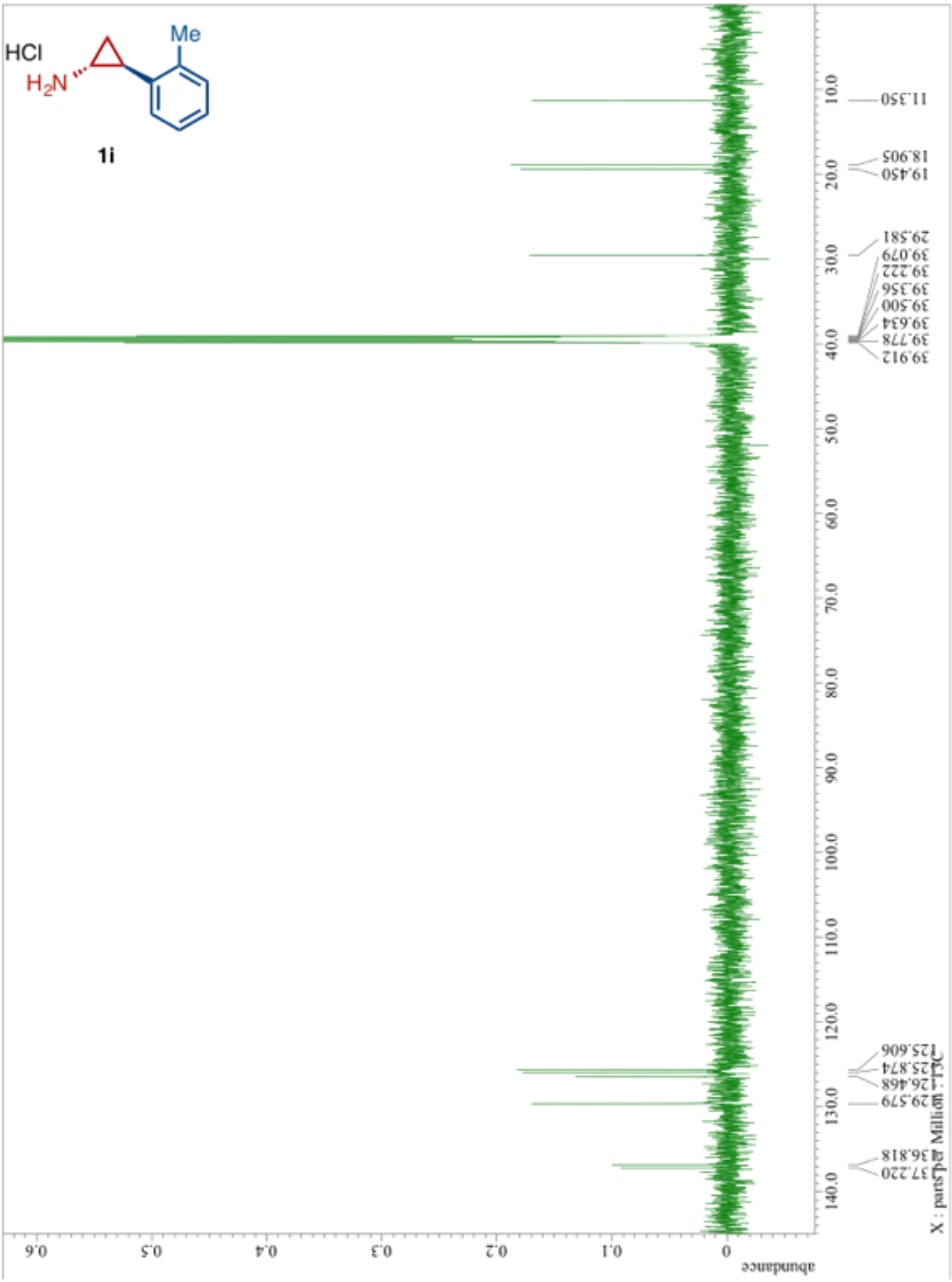
^{13}C NMR (150 MHz, DMSO-d_6) of 1h:



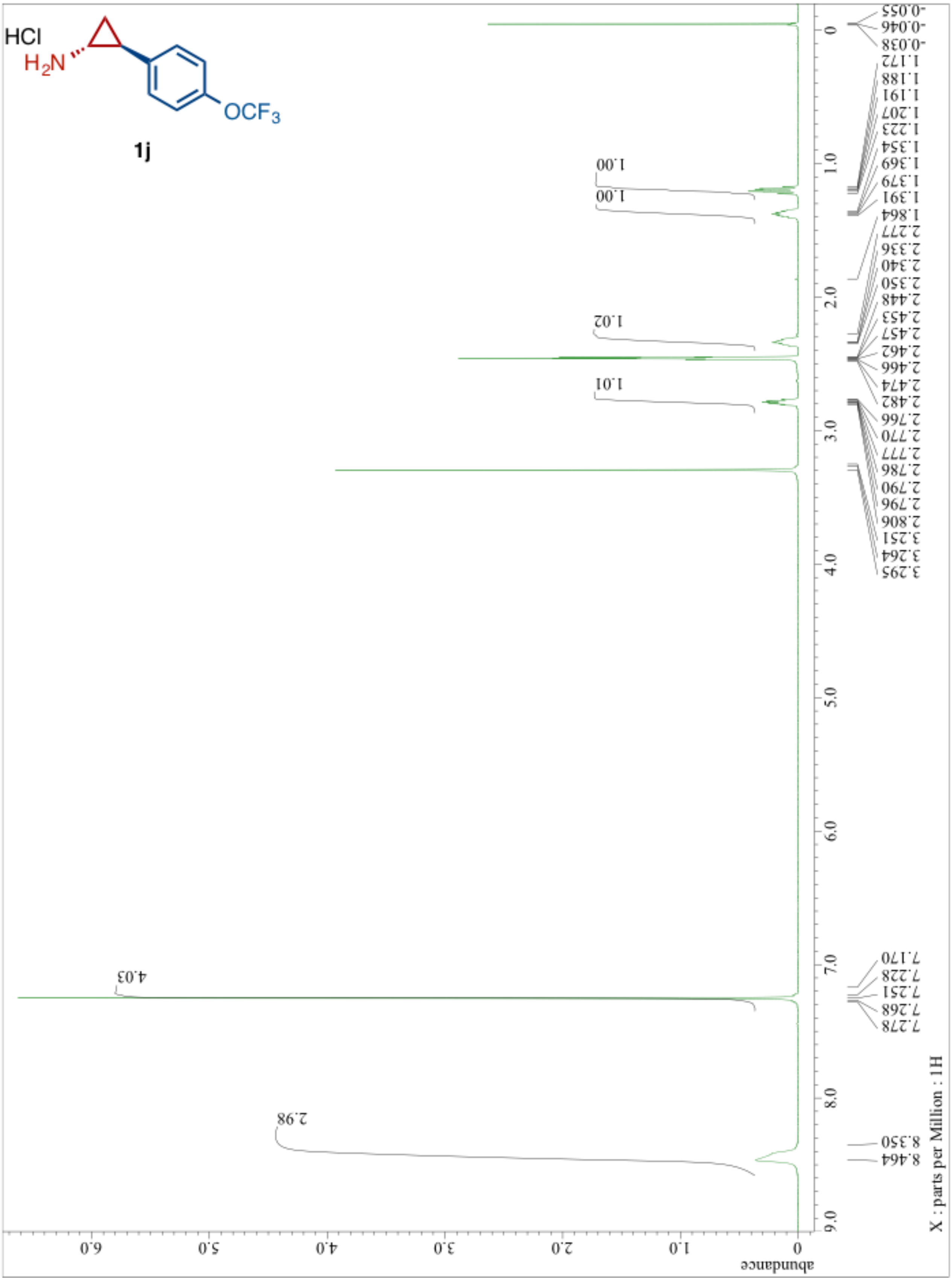
[1]H NMR (600 MHz, DMSO-d_6) of 1i:



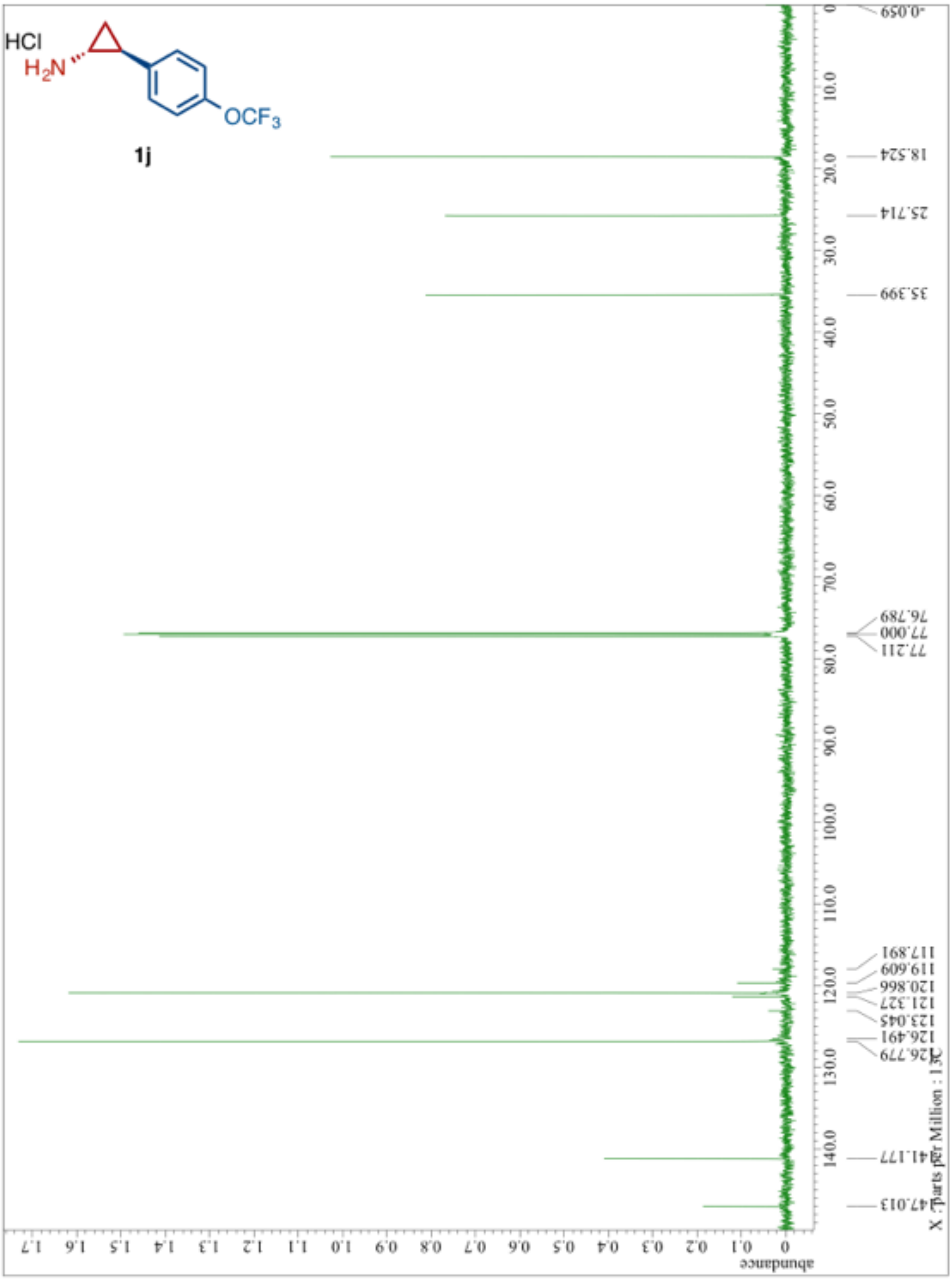
^{13}C NMR (150 MHz, DMSO-d_6) of 1i:



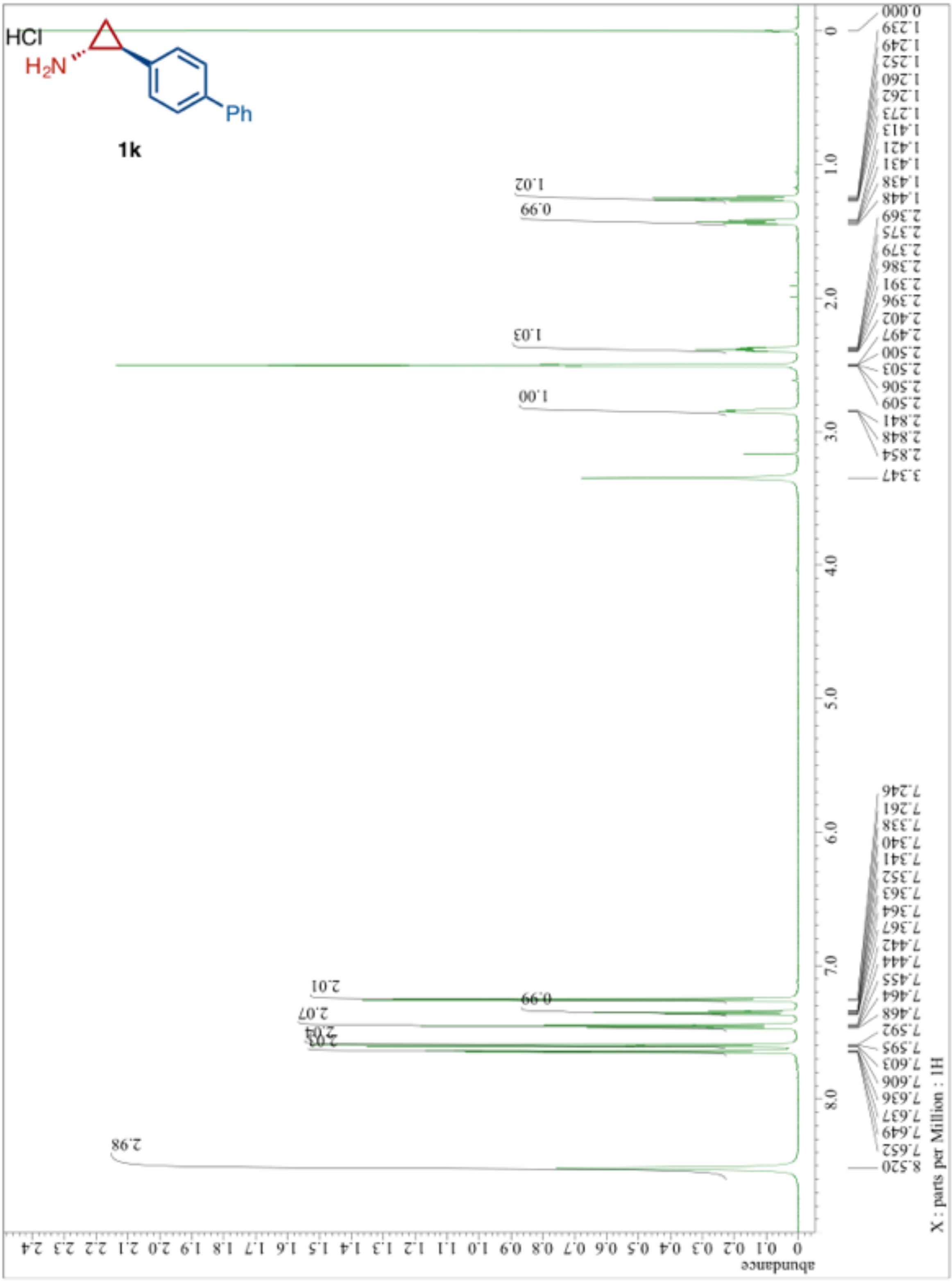
[1]H NMR (400 MHz, DMSO-d_6) of 1j:



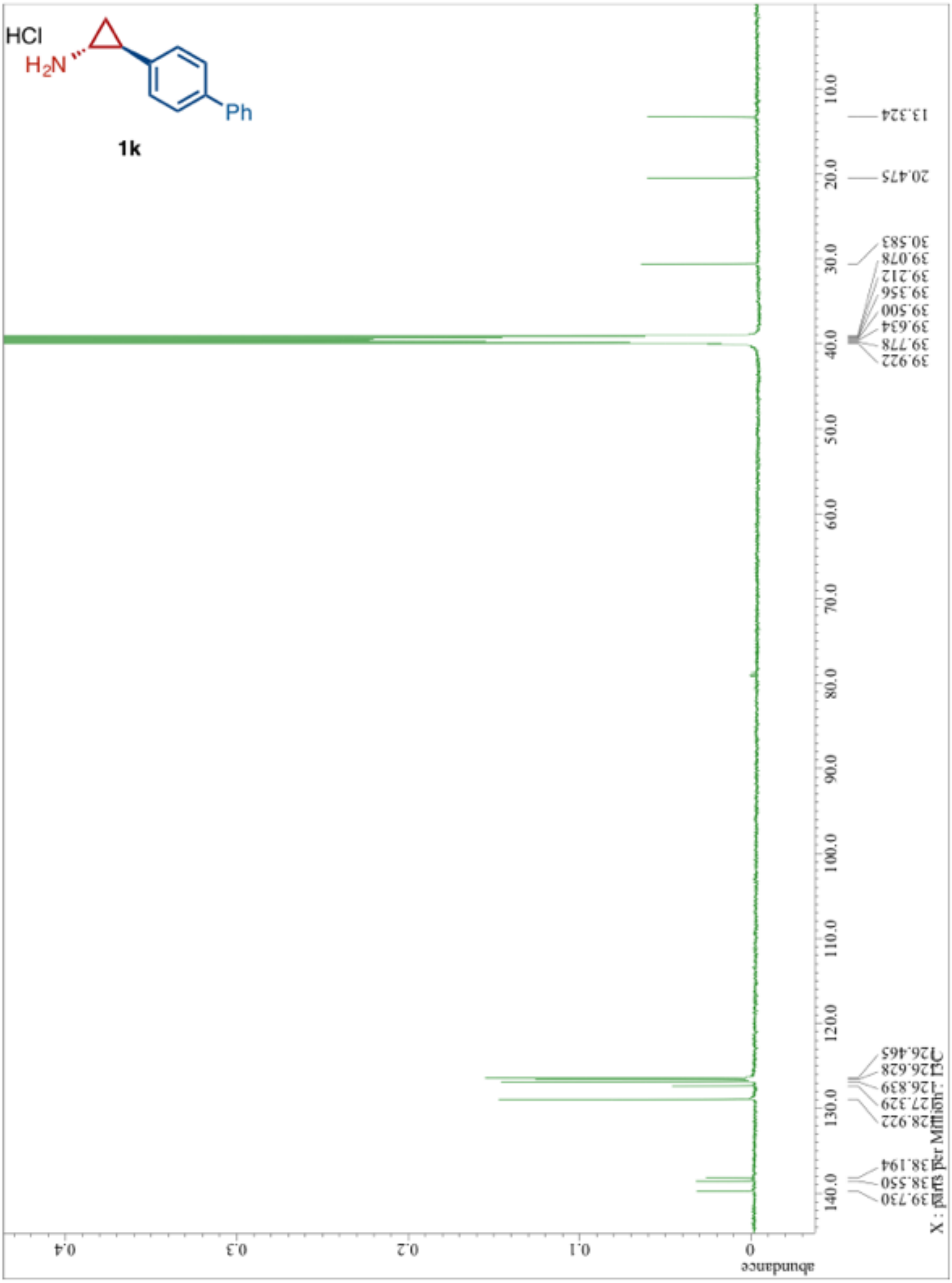
^{13}C NMR (150 MHz, DMSO-d_6) of 1j:



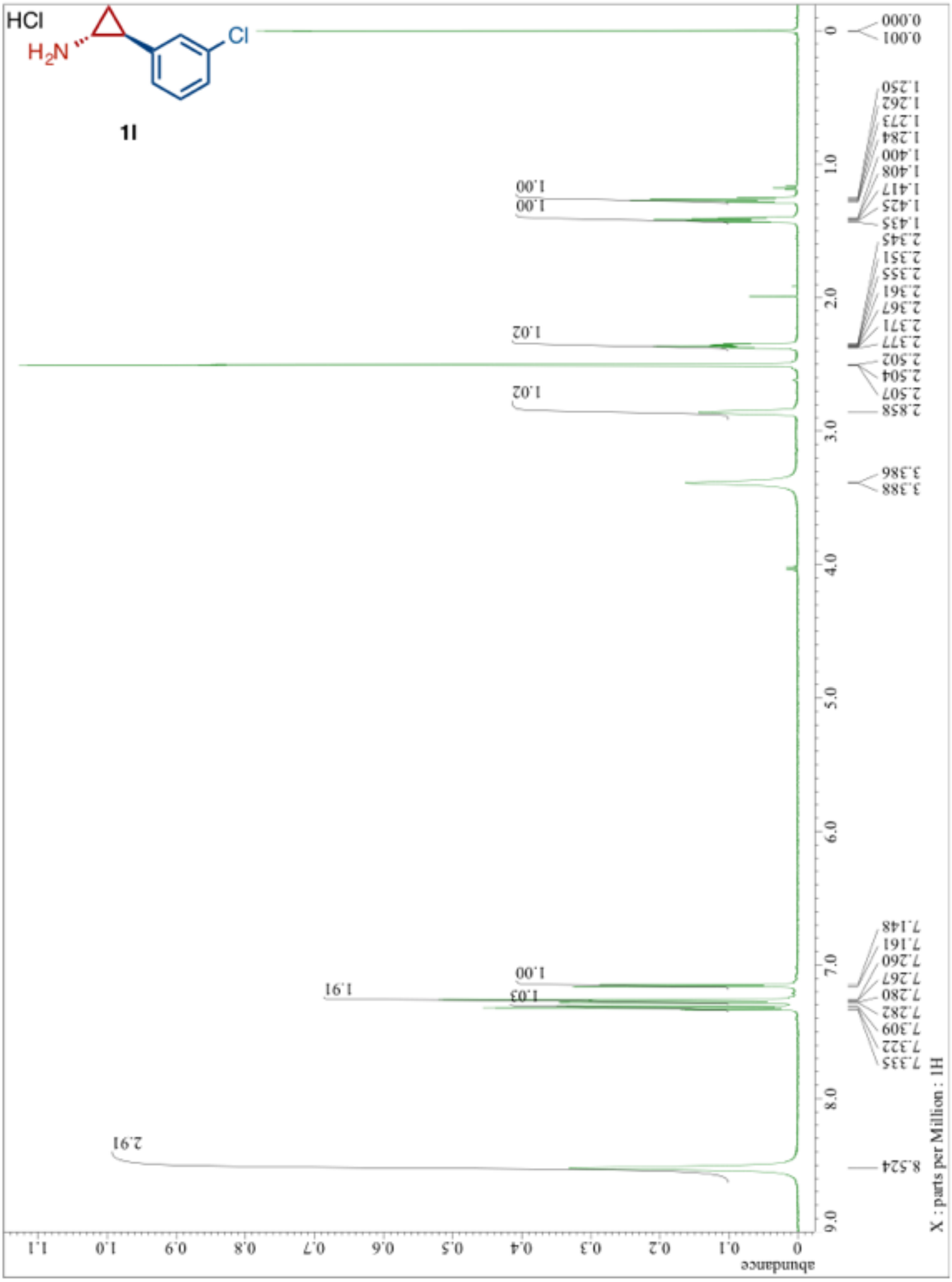
[1]H NMR (600 MHz, DMSO-d_6) of 1k:



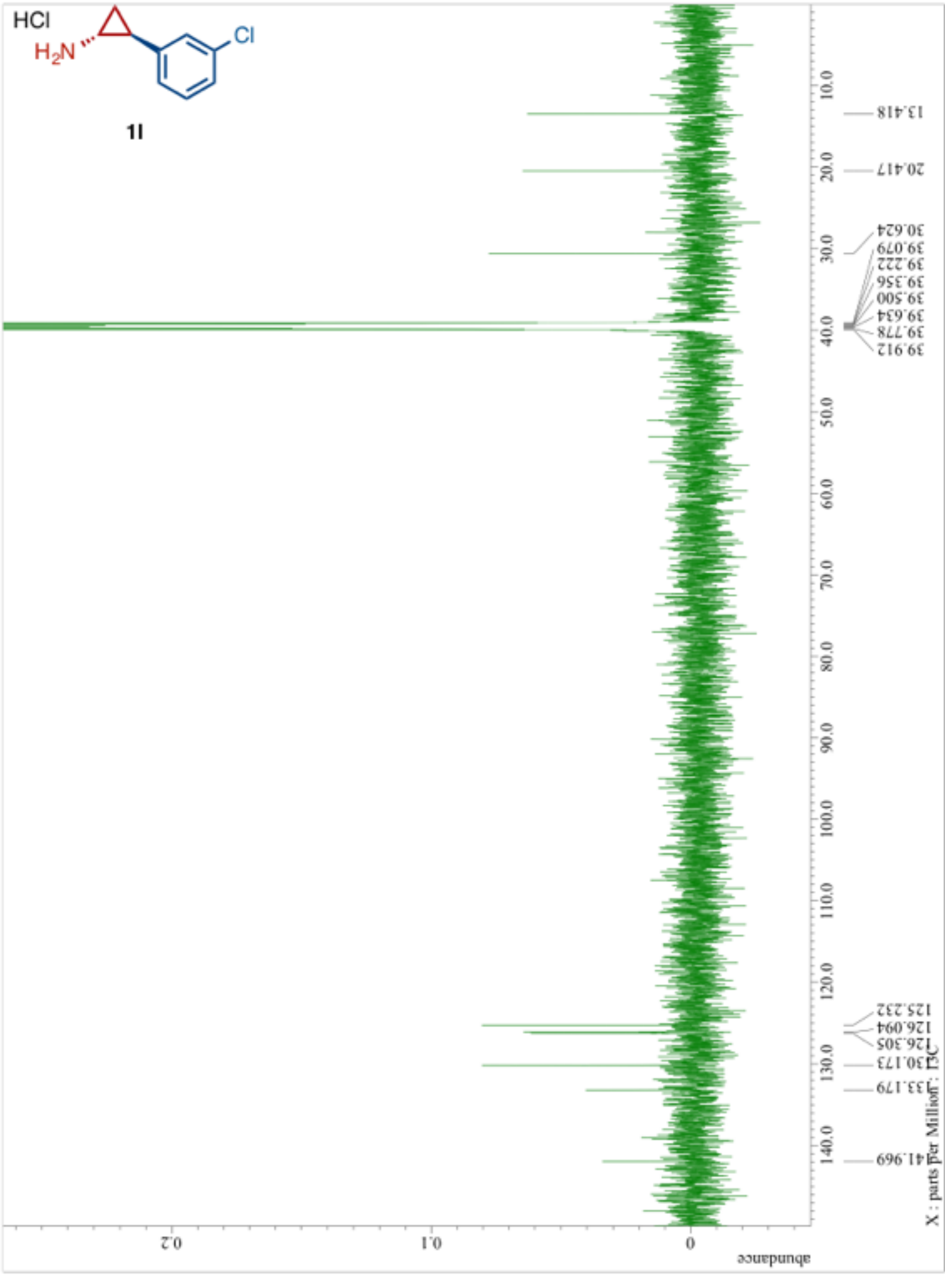
^{13}C NMR (150 MHz, DMSO-d_6) of 1k:



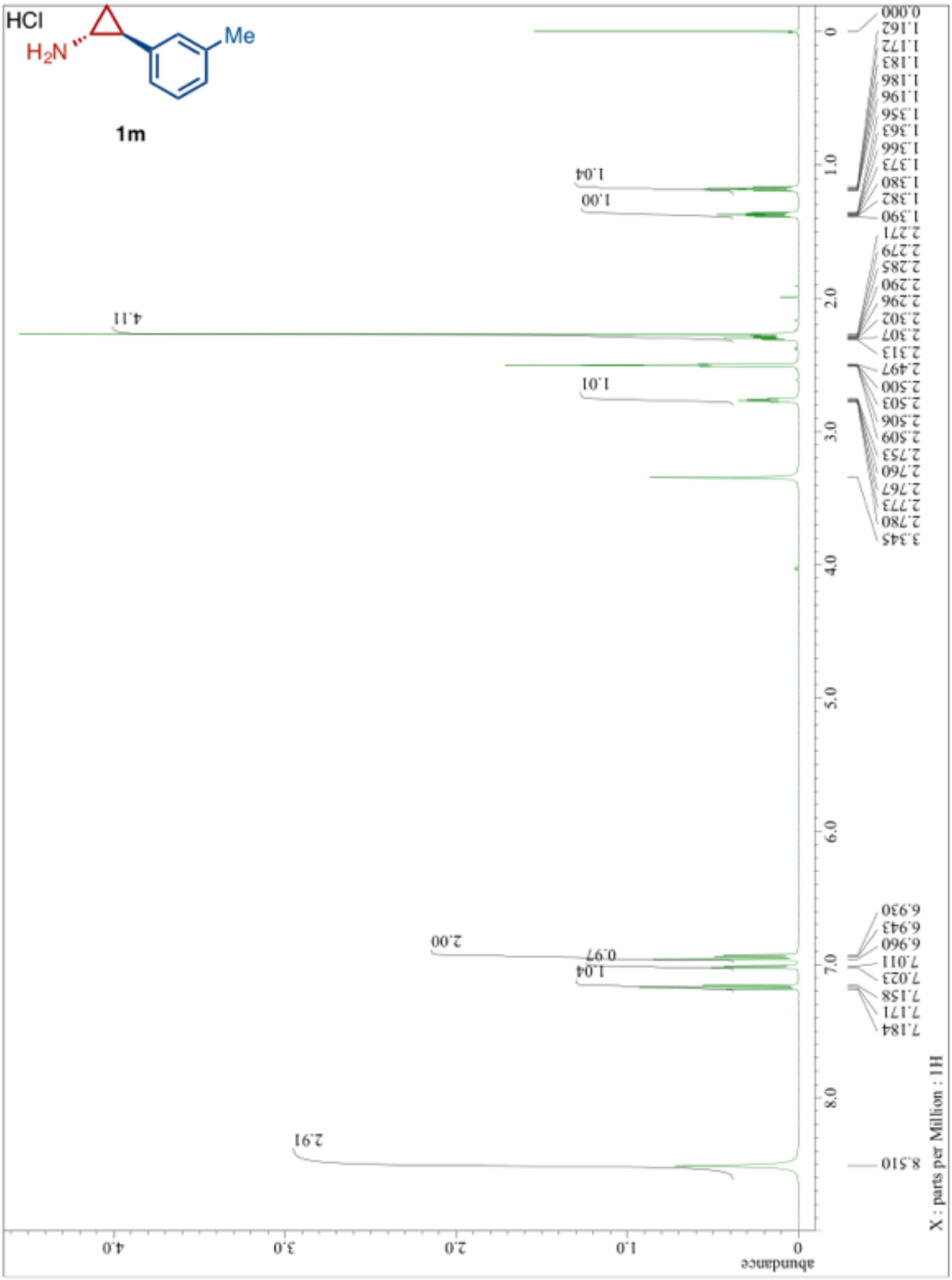
^{1}H NMR (600 MHz, DMSO-d_6) of 1l:



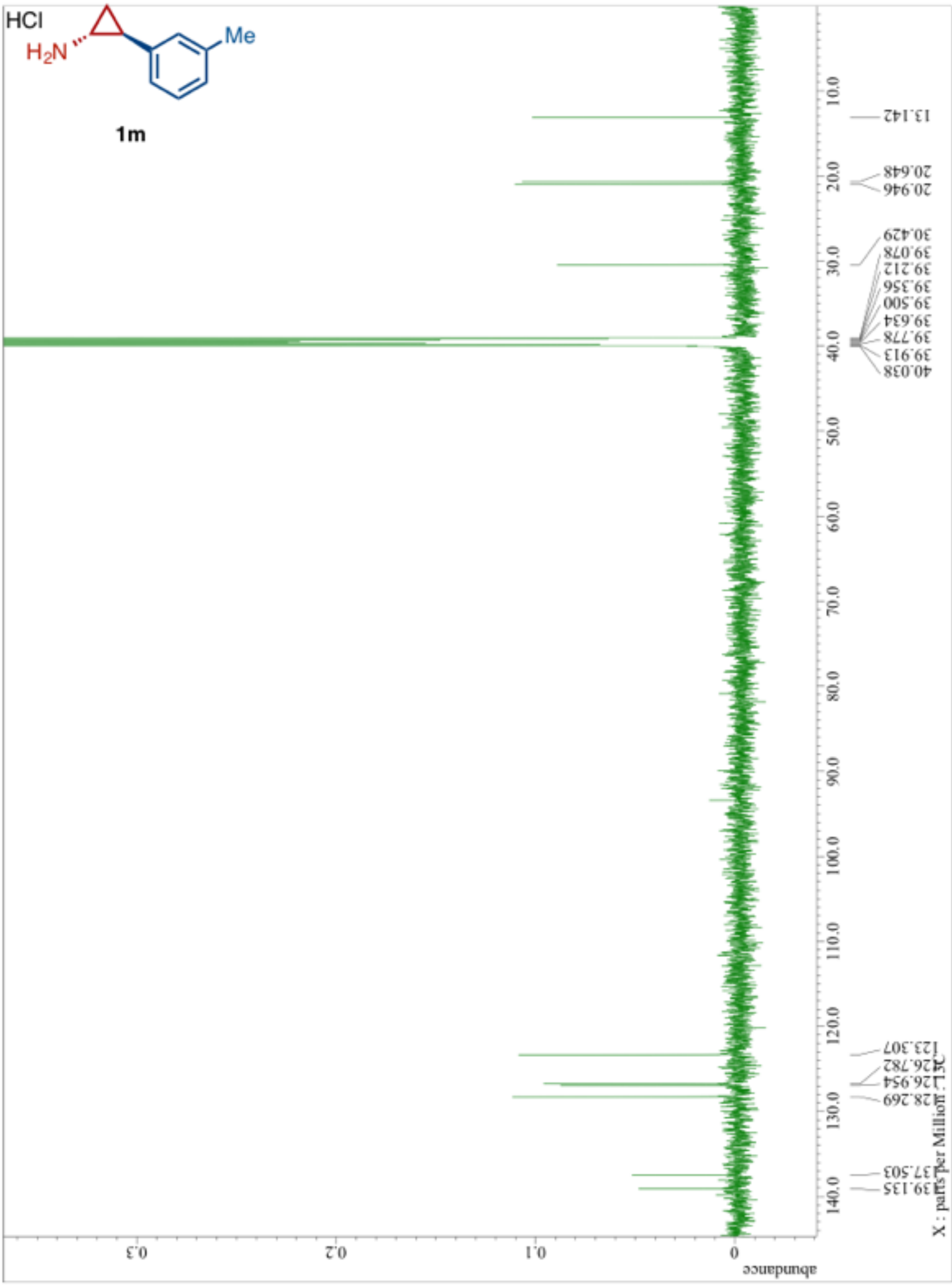
^{13}C NMR (150 MHz, DMSO-d_6) of 1l:



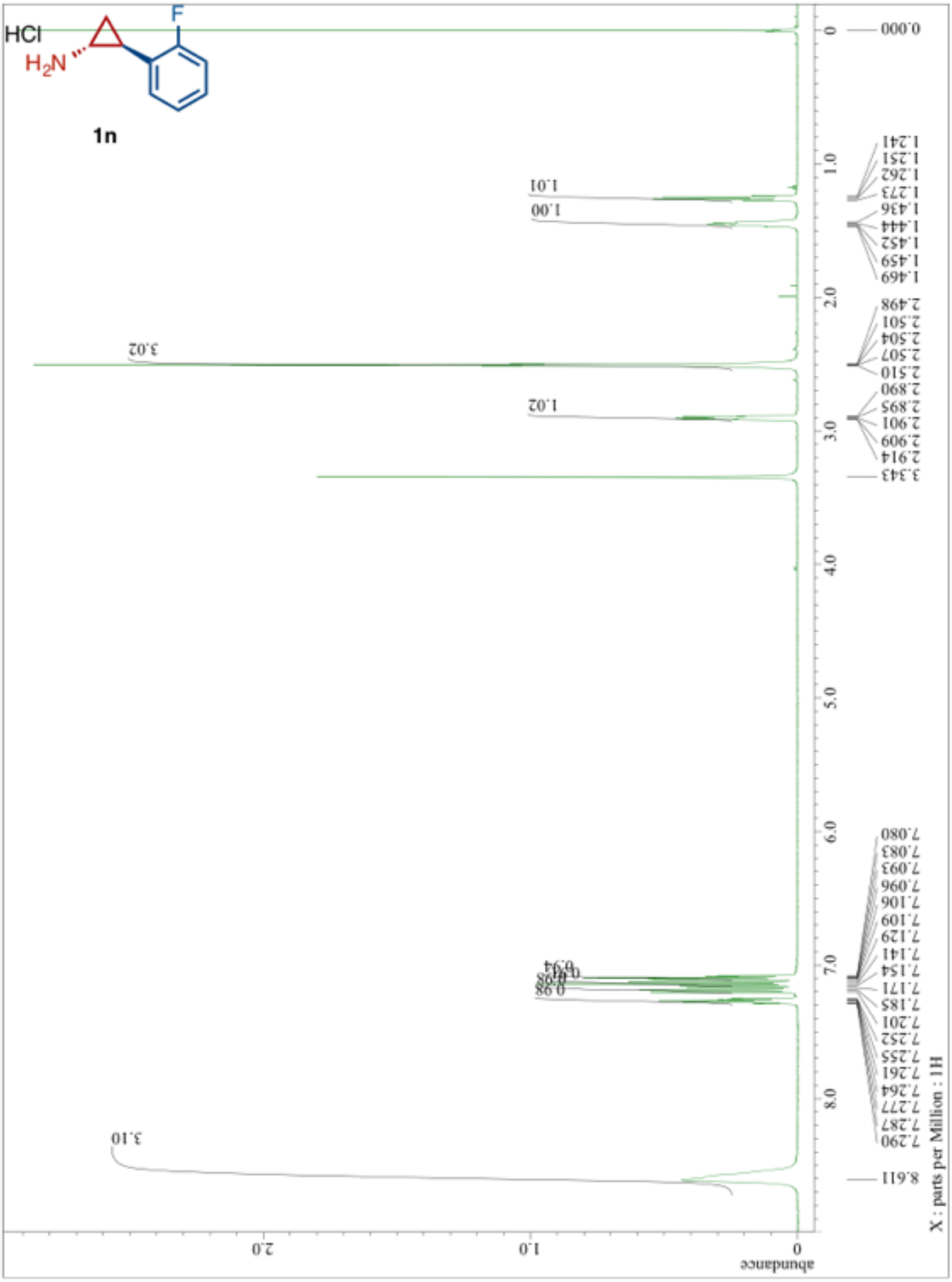
^{1}H NMR (600 MHz, DMSO-d_6) of 1m:



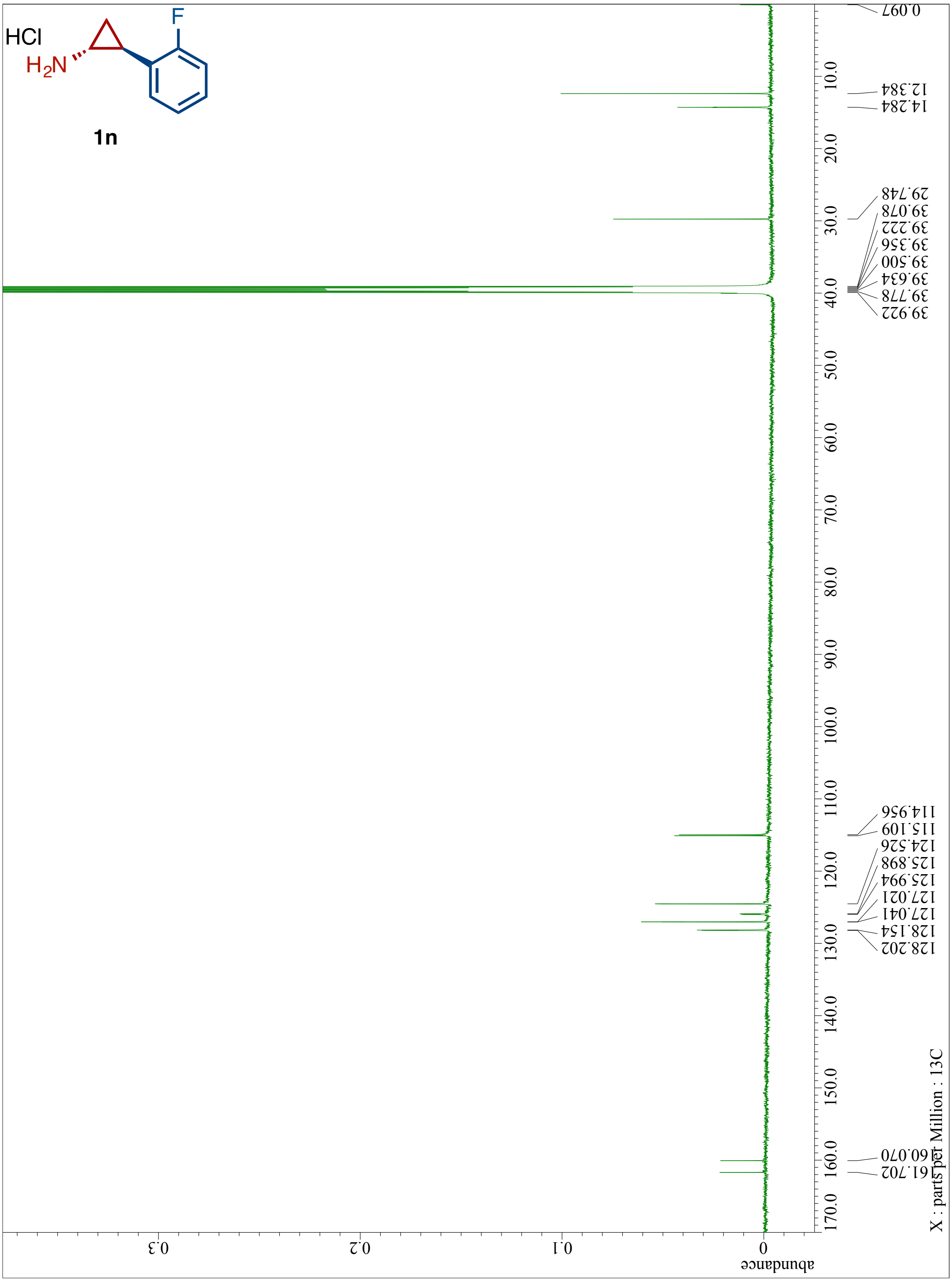
^{13}C NMR (150 MHz, DMSO-d_6) of 1m:



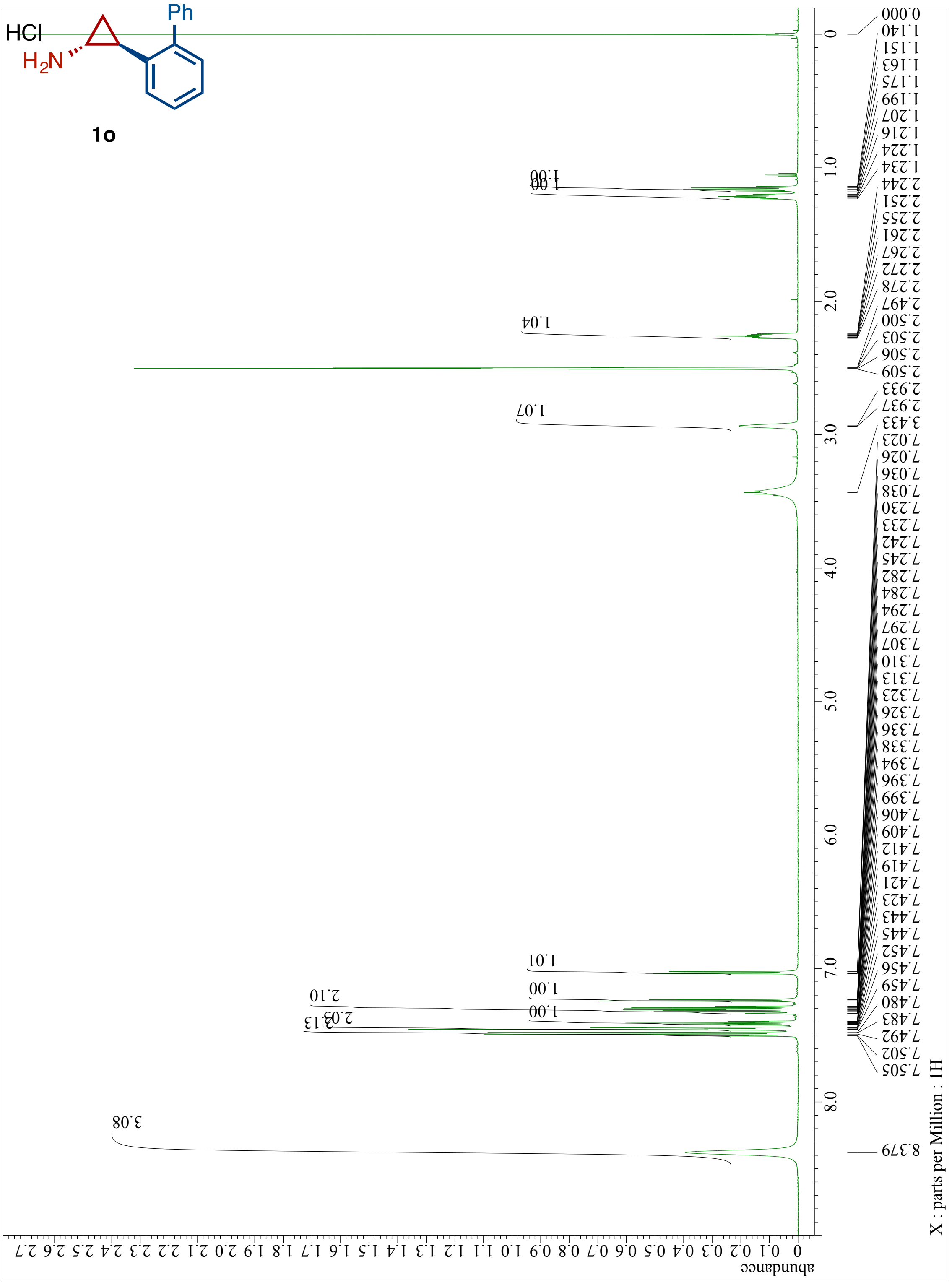
^{1}H NMR (600 MHz, DMSO-d_6) of 1n:



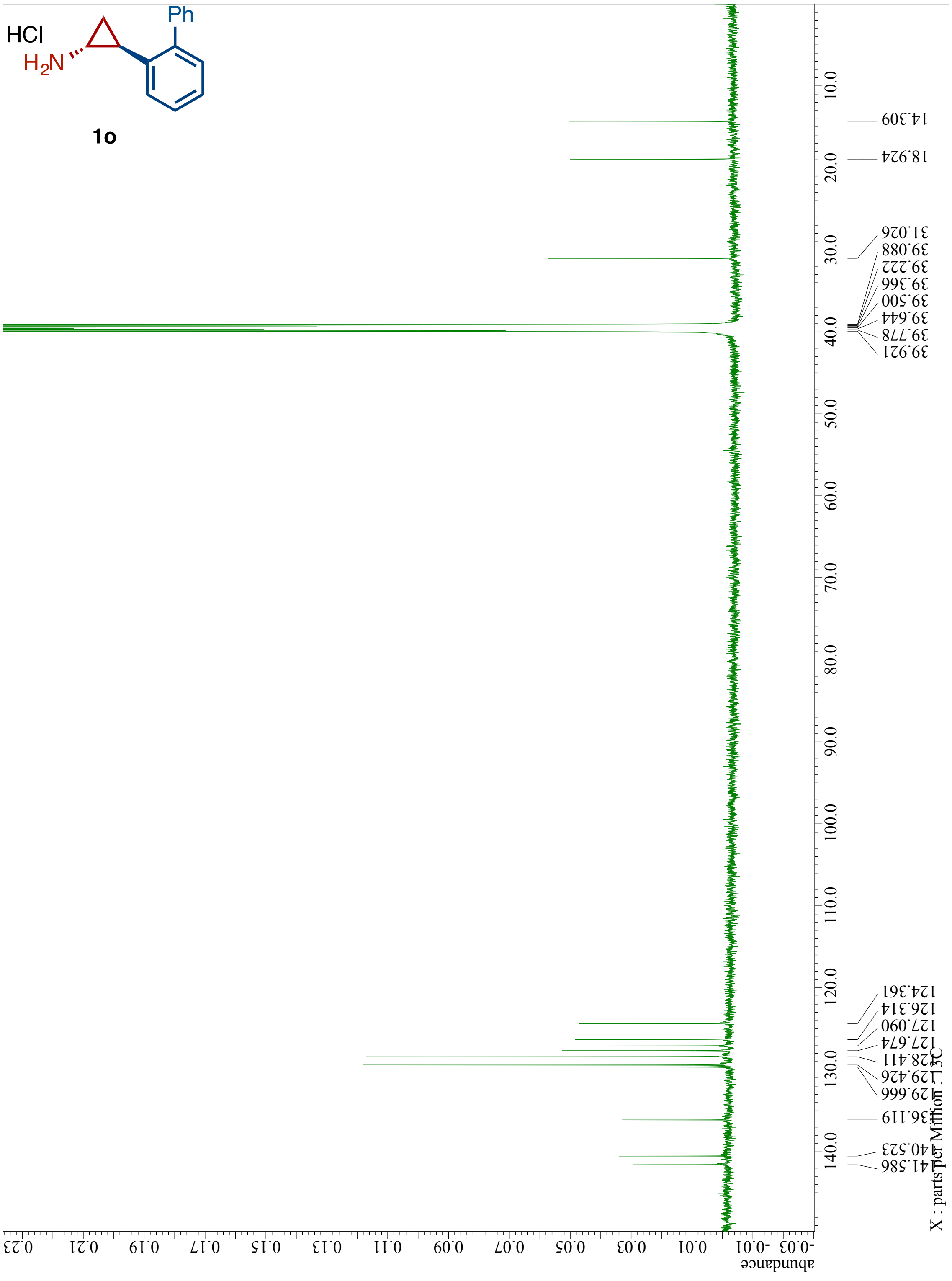
^{13}C NMR (150 MHz, DMSO-d_6) of 1n



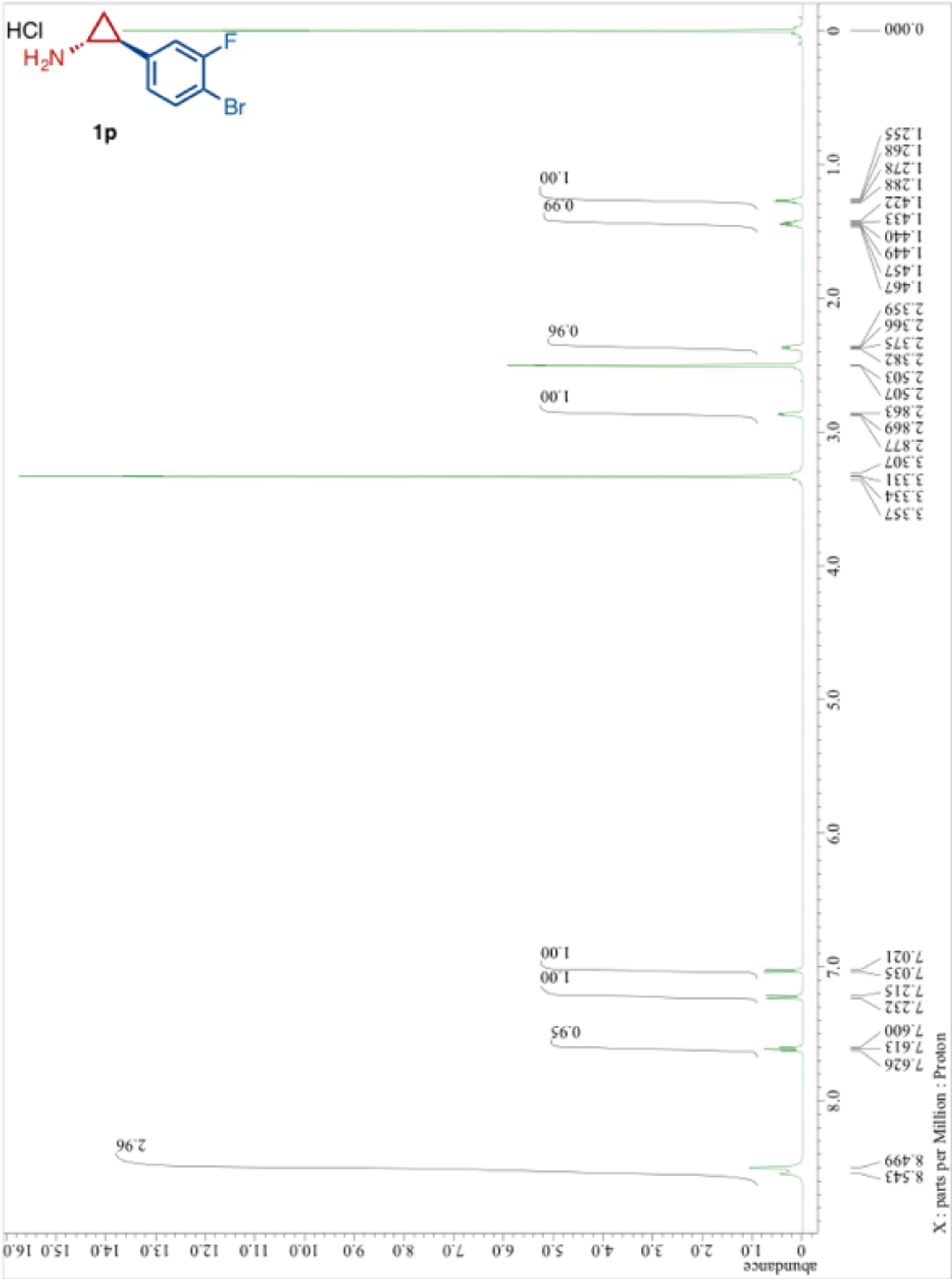
^{1}H NMR (600 MHz, DMSO-d_6) of 1o:



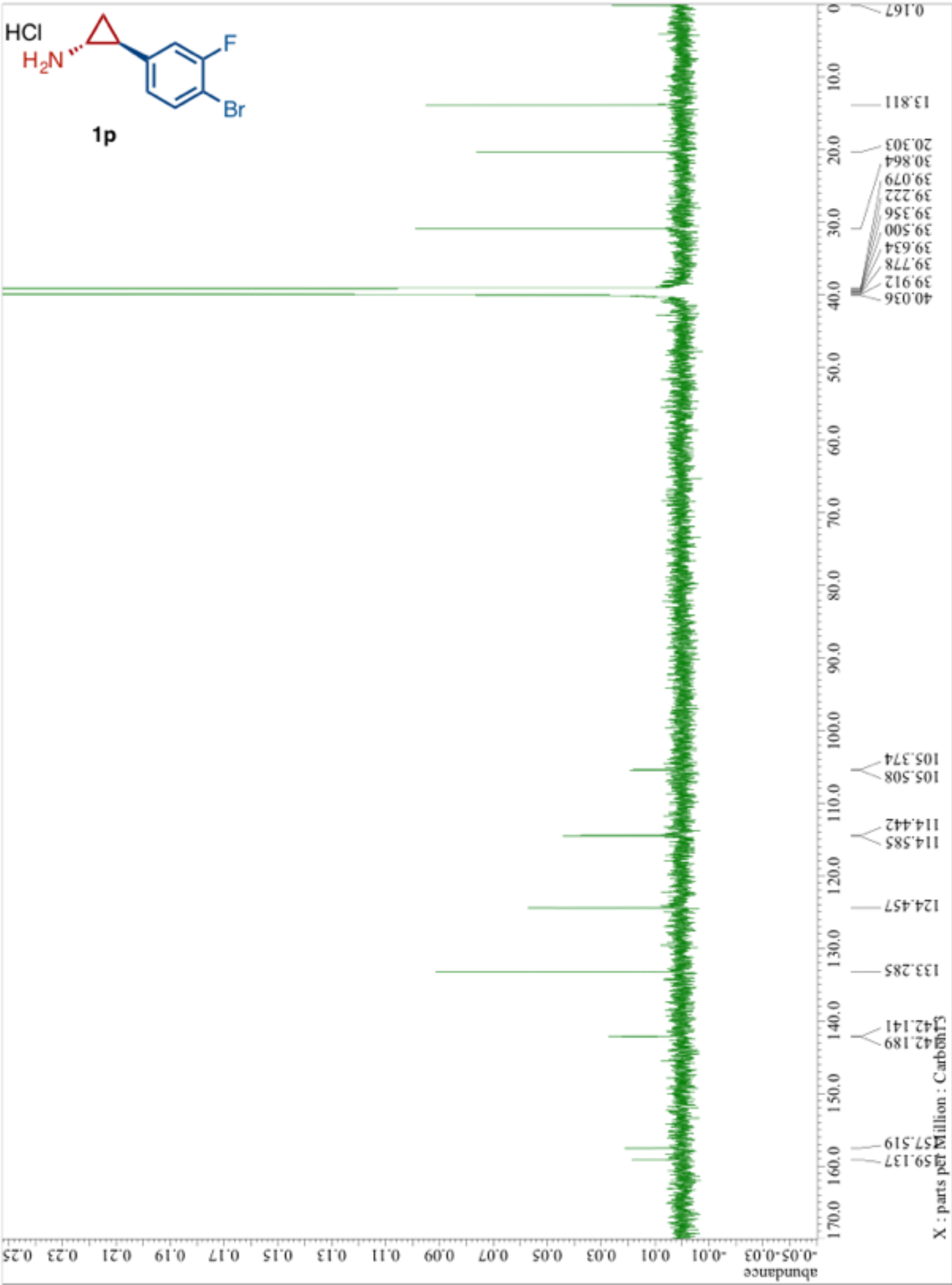
[13]C NMR (150 MHz, DMSO-d_6) of 1o:



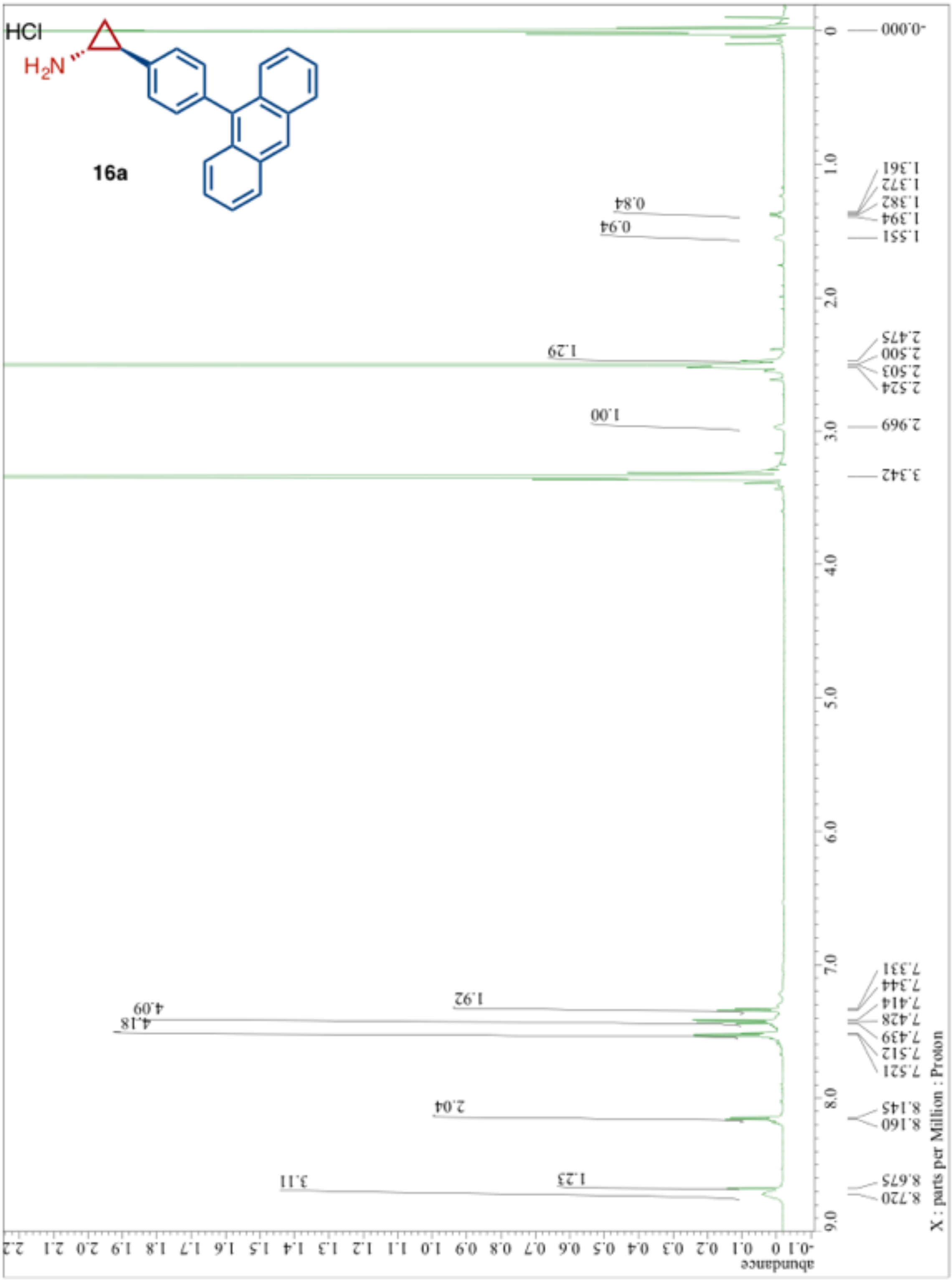
^{1}H NMR (600 MHz, DMSO-d_6) of 1p:



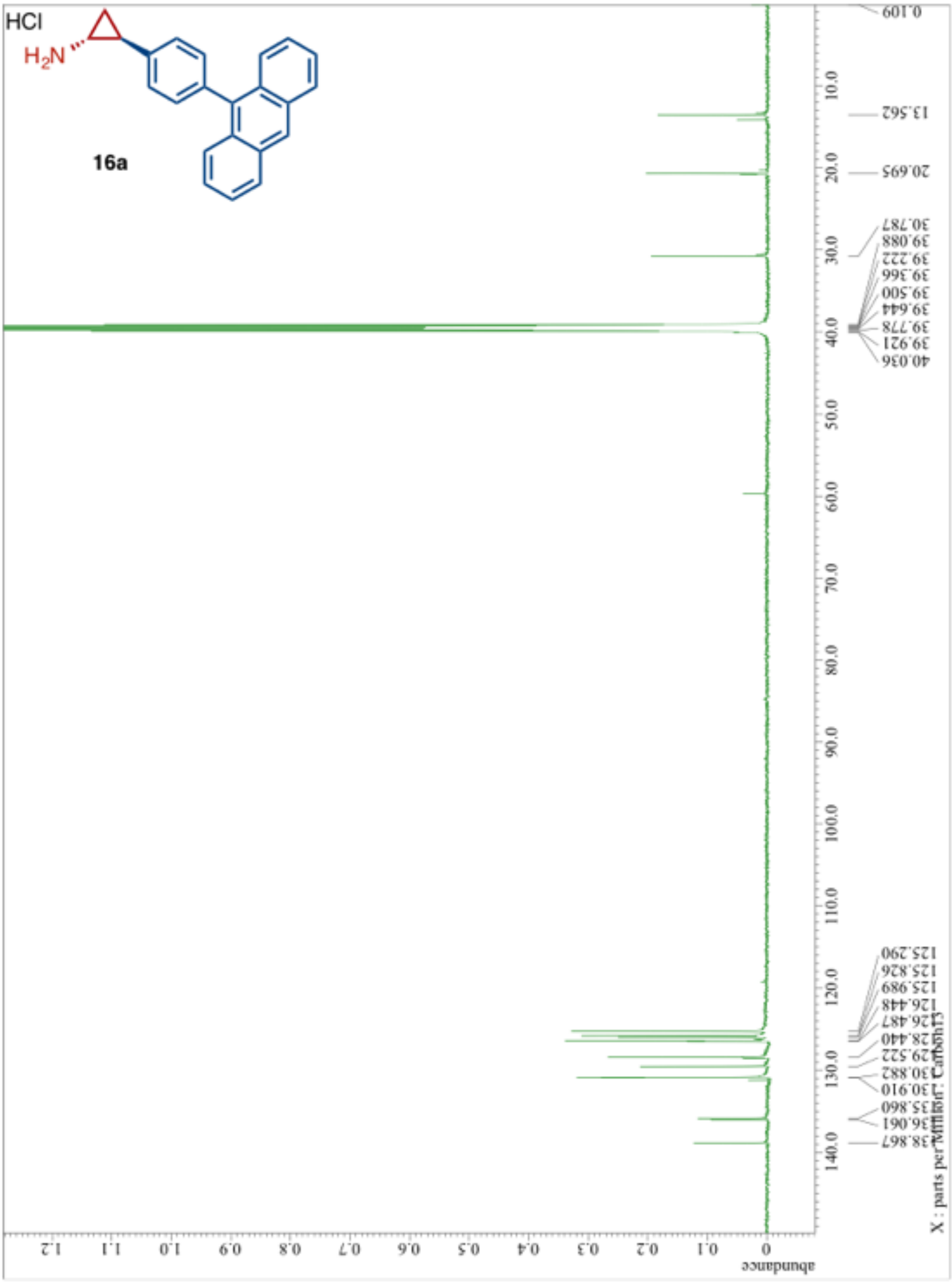
^{13}C NMR (150 MHz, CDCl$_3$) of 1p:



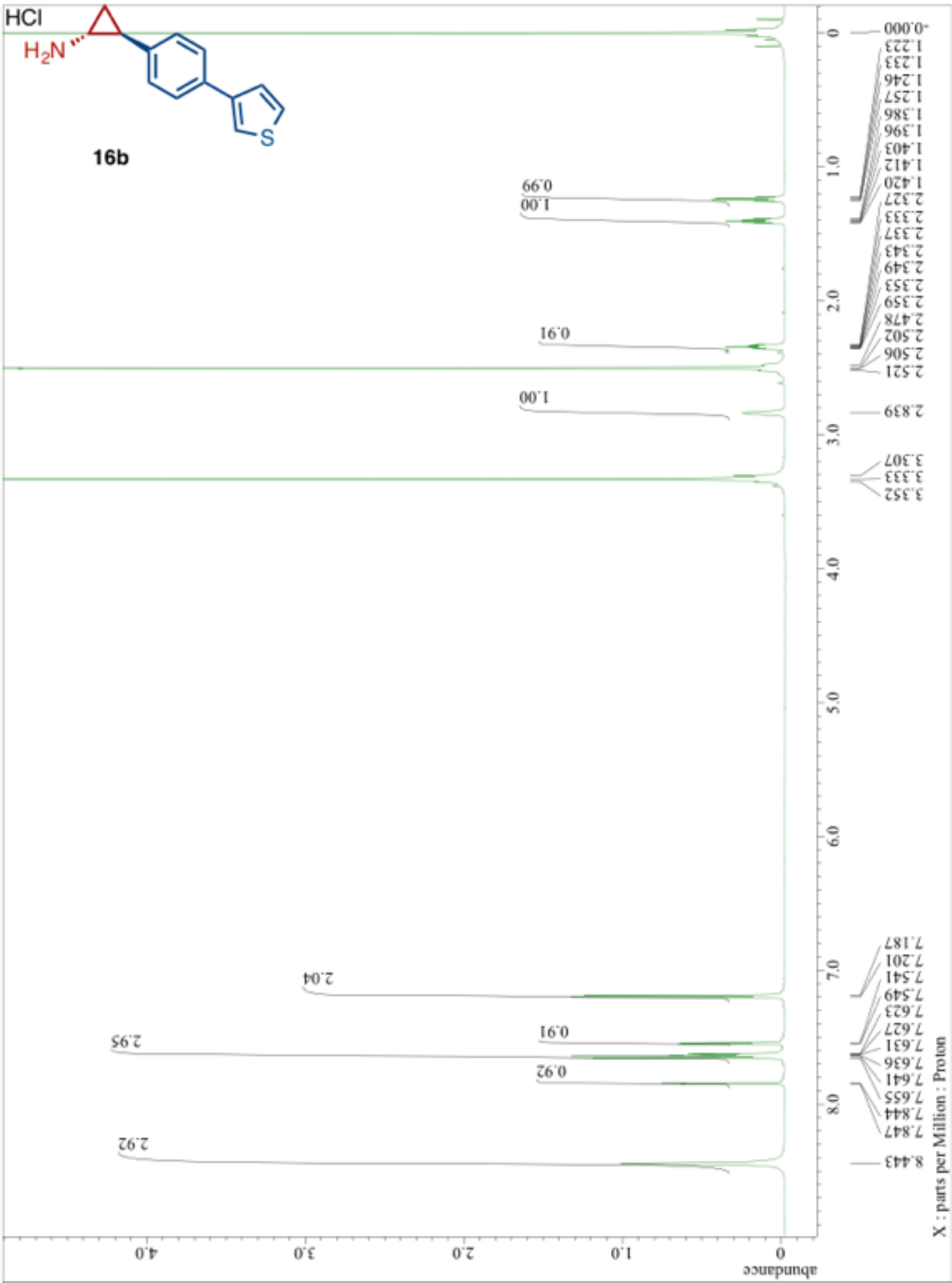
^{1}H NMR (600 MHz, DMSO-d_6) of 16a:



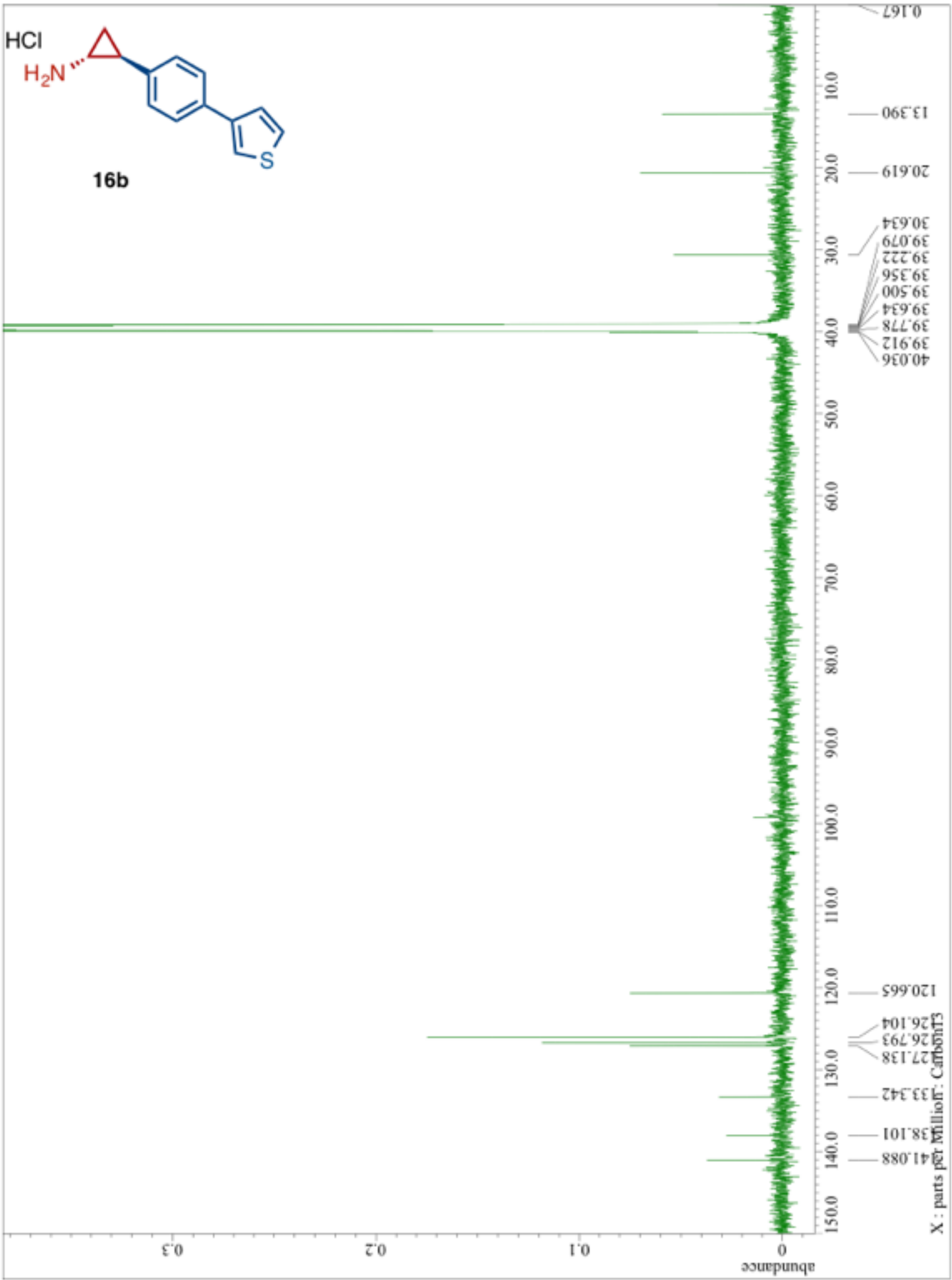
^{13}C NMR (150 MHz, DMSO-d_6) of 16a:



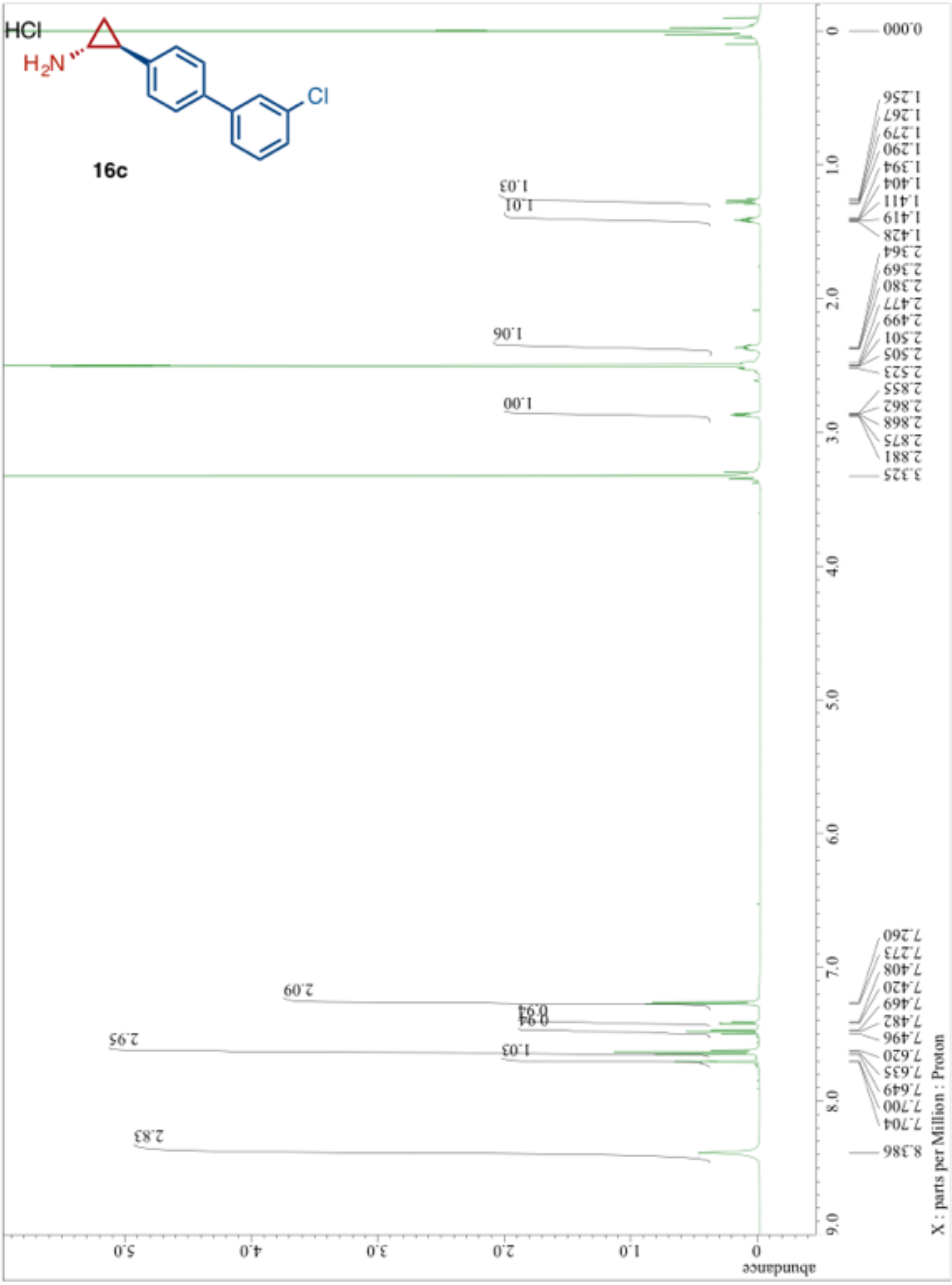
[1]H NMR (600 MHz, DMSO-d_6) of 16b:



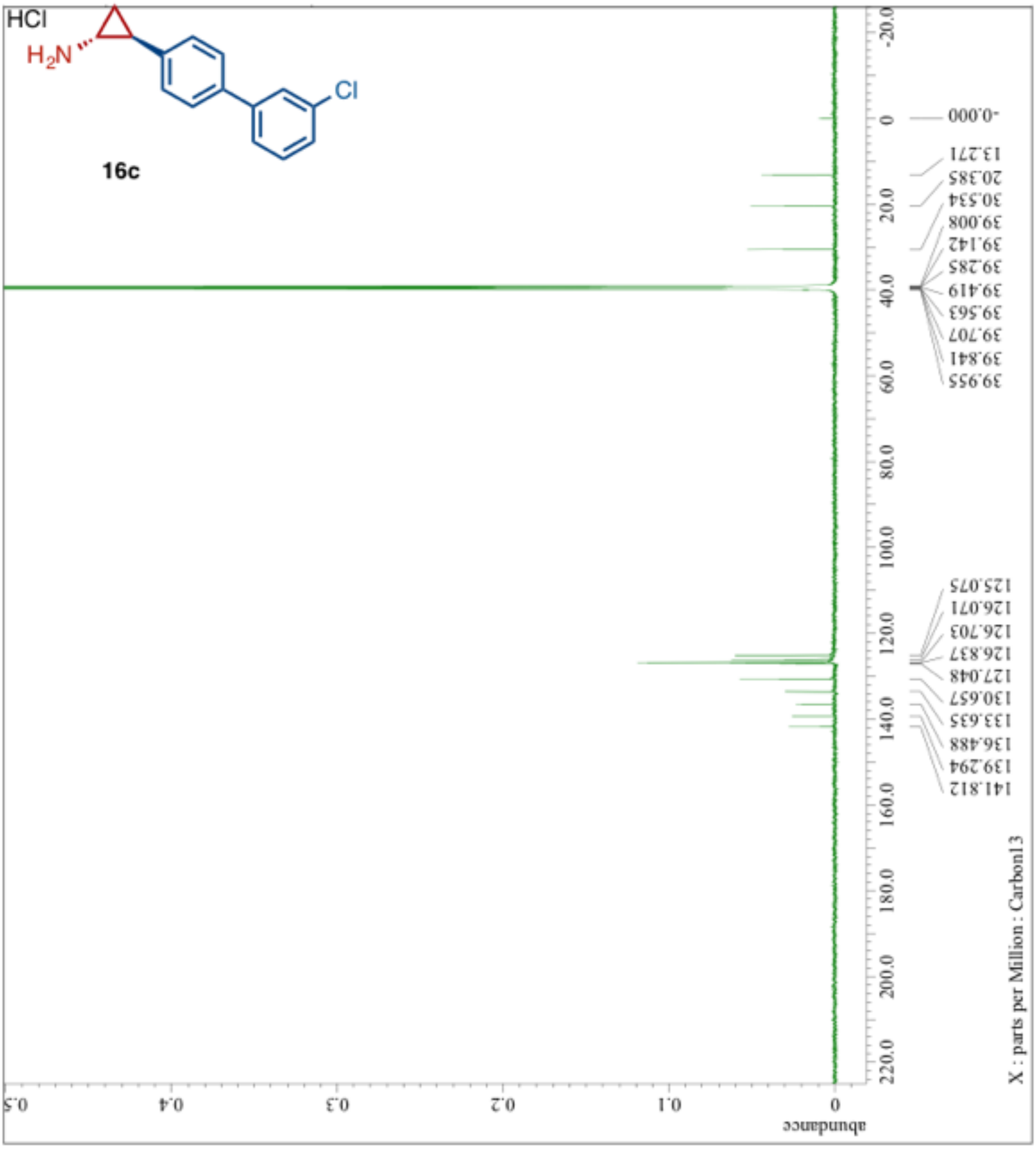
[13]C NMR (150 MHz, DMSO-d_6) of 16b:



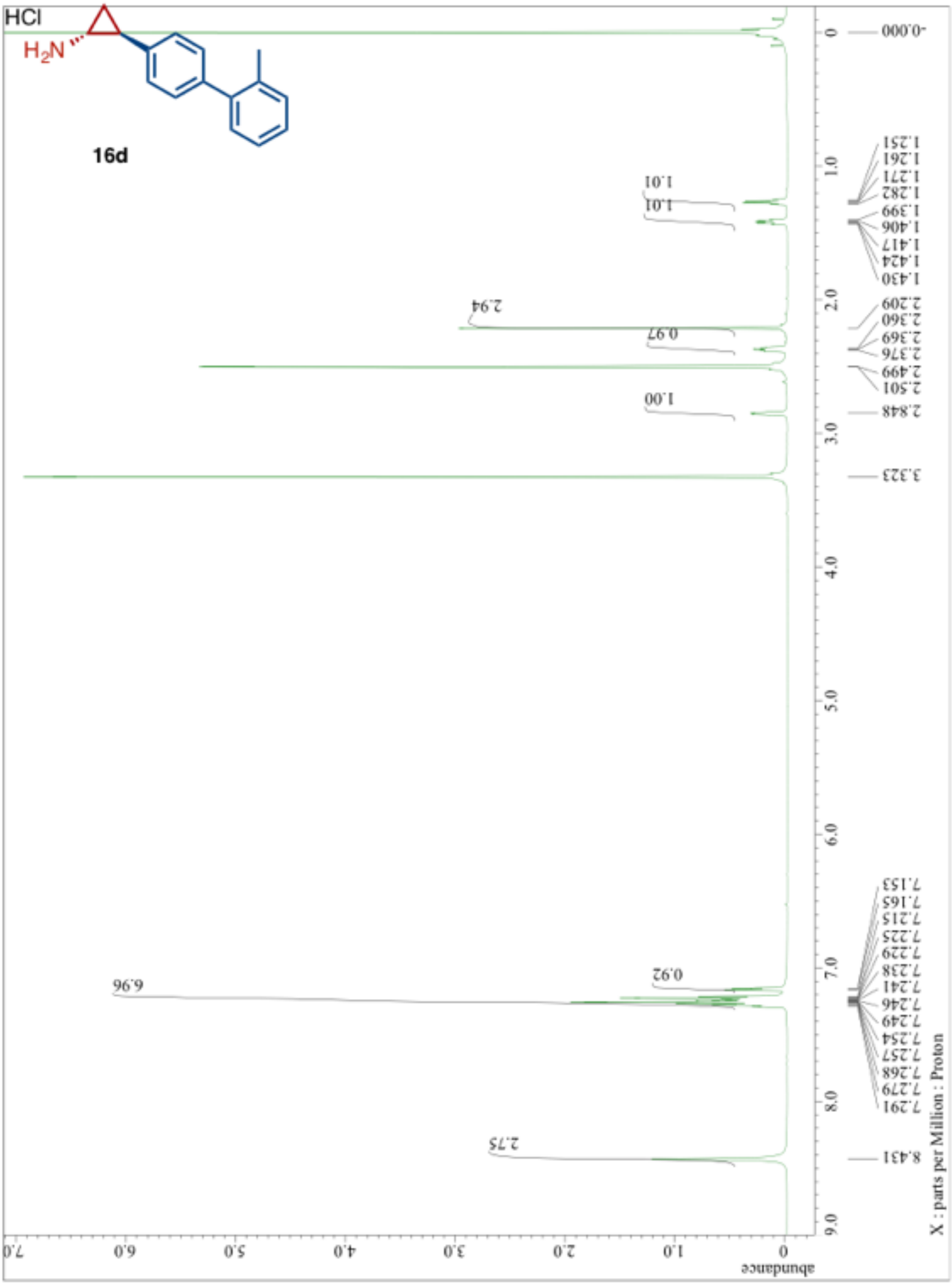
^{1}H NMR (600 MHz, DMSO-d_6) of 16c:



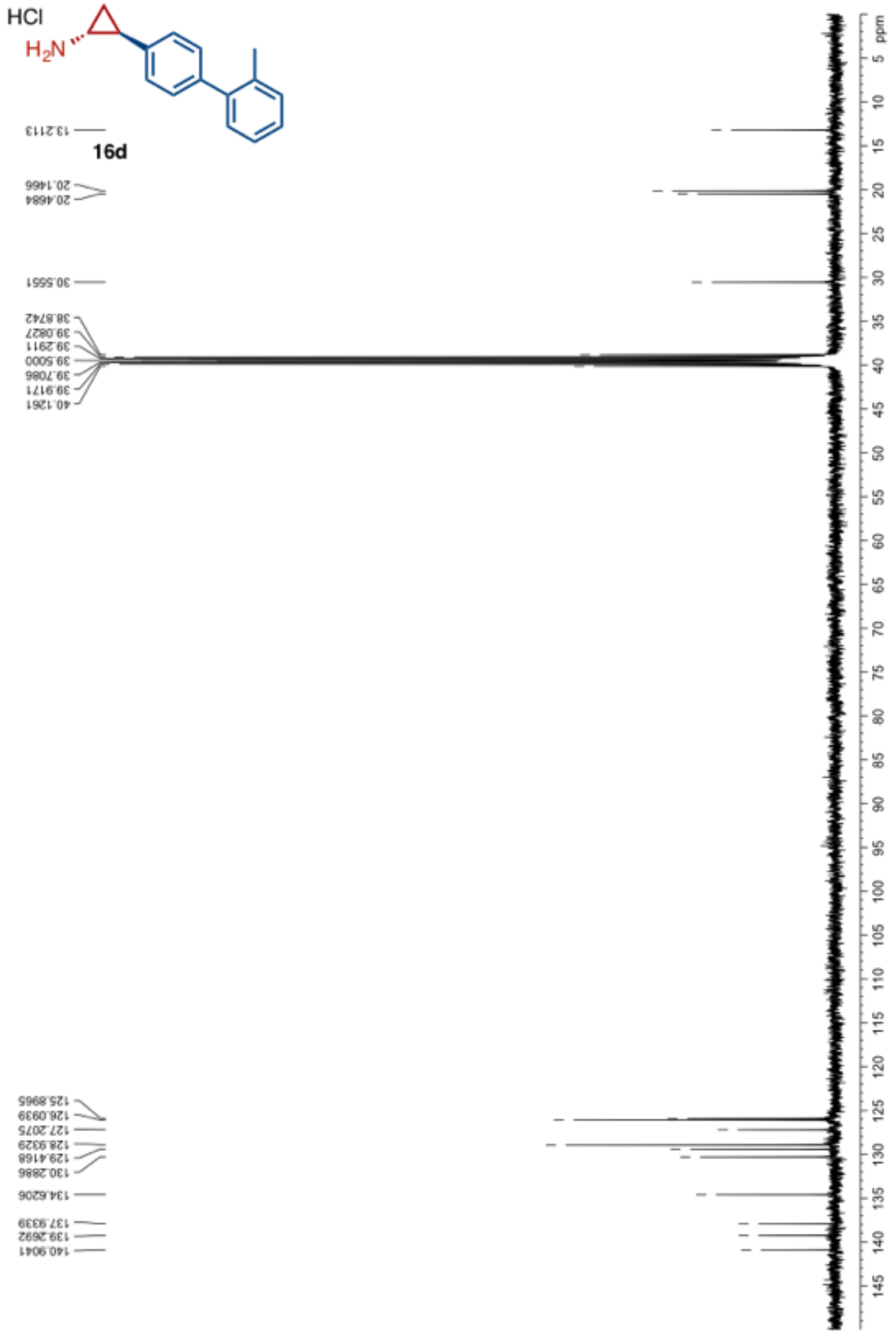
^{13}C NMR (150 MHz, DMSO-d_6) of 16c:



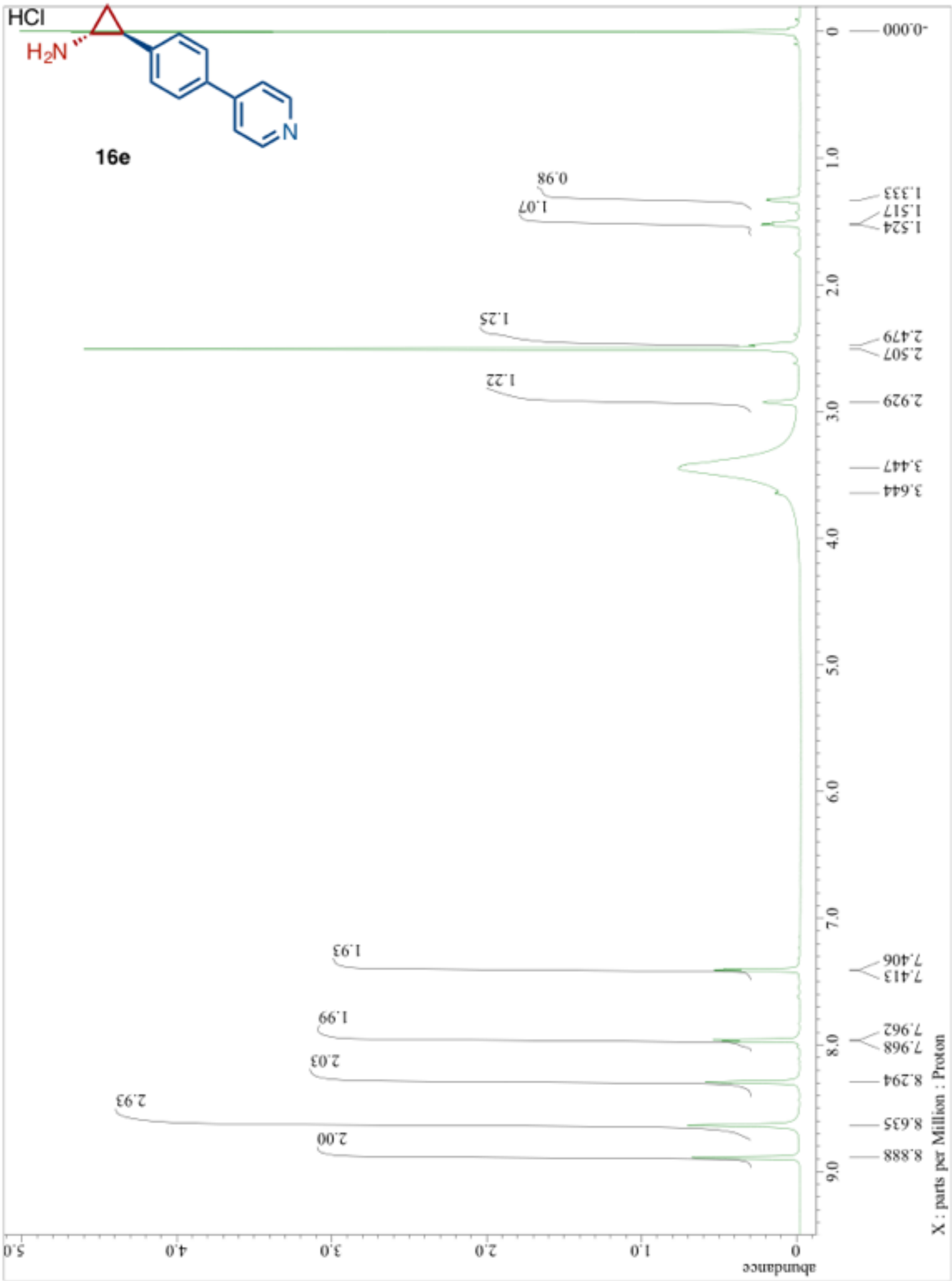
^{1}H NMR (600 MHz, DMSO-d_6) of 16d:



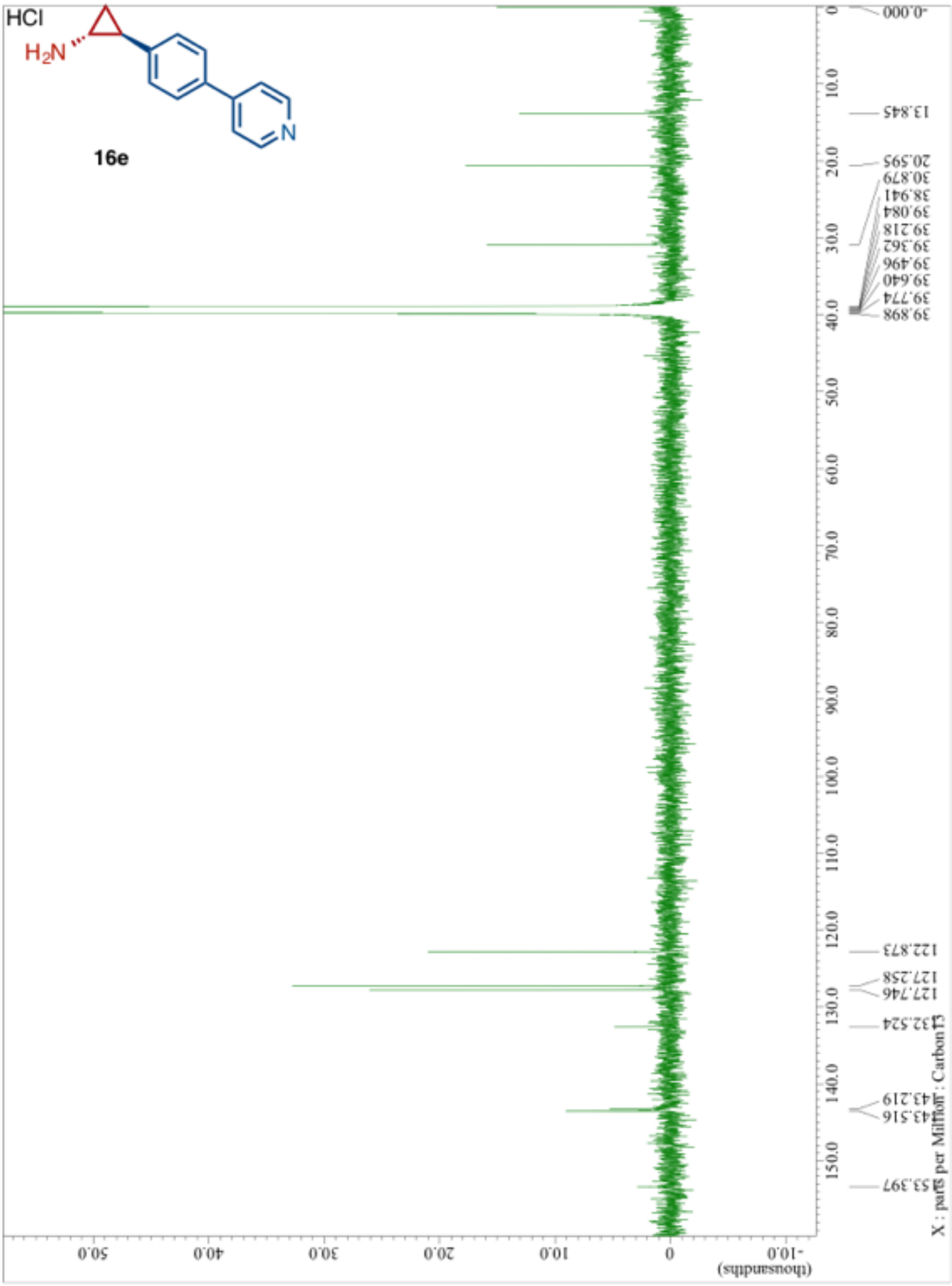
[13]C NMR (100 MHz, DMSO-d_6) of 16d:



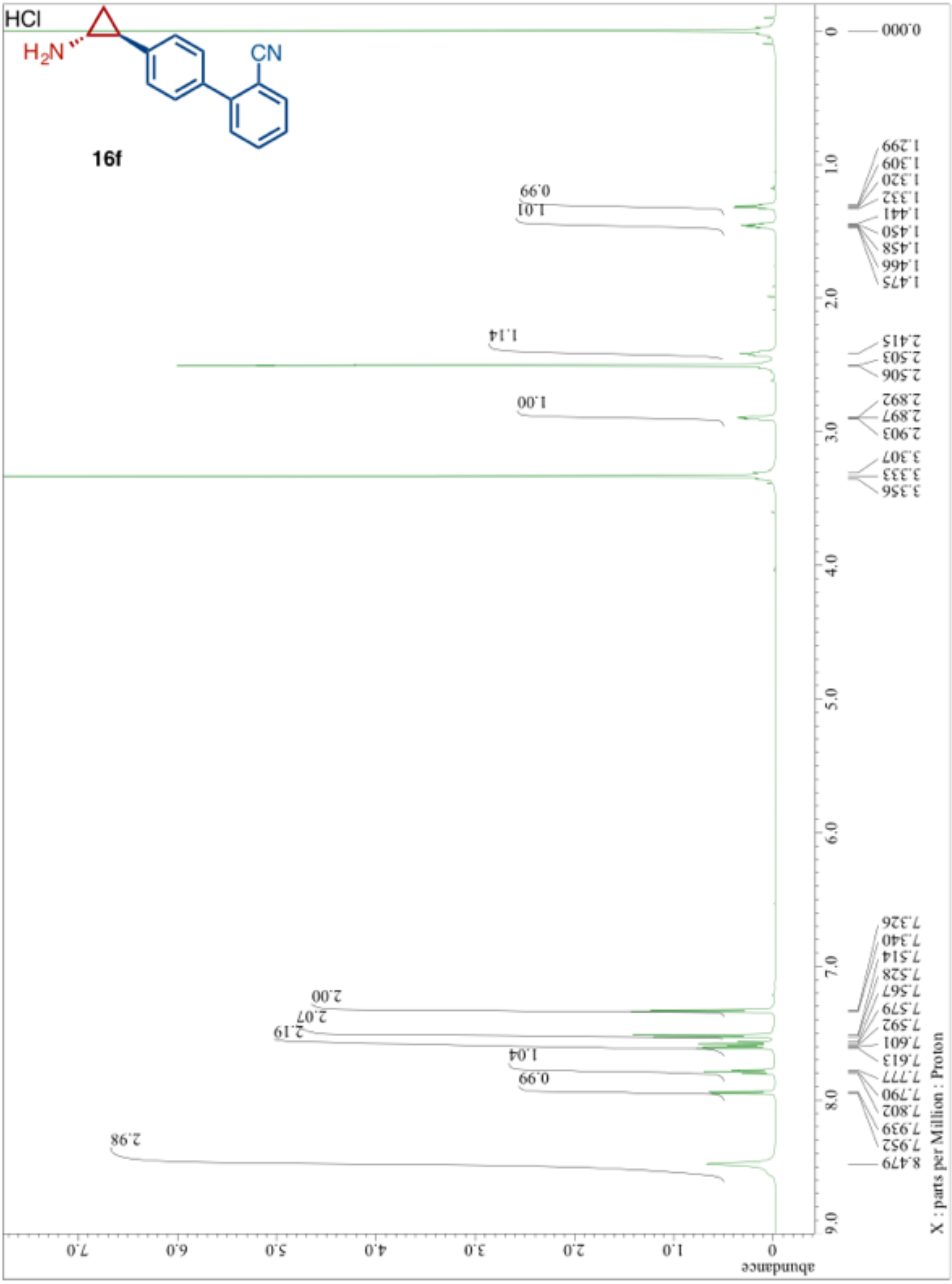
^1H NMR (600 MHz, DMSO-d_6) of 16e:



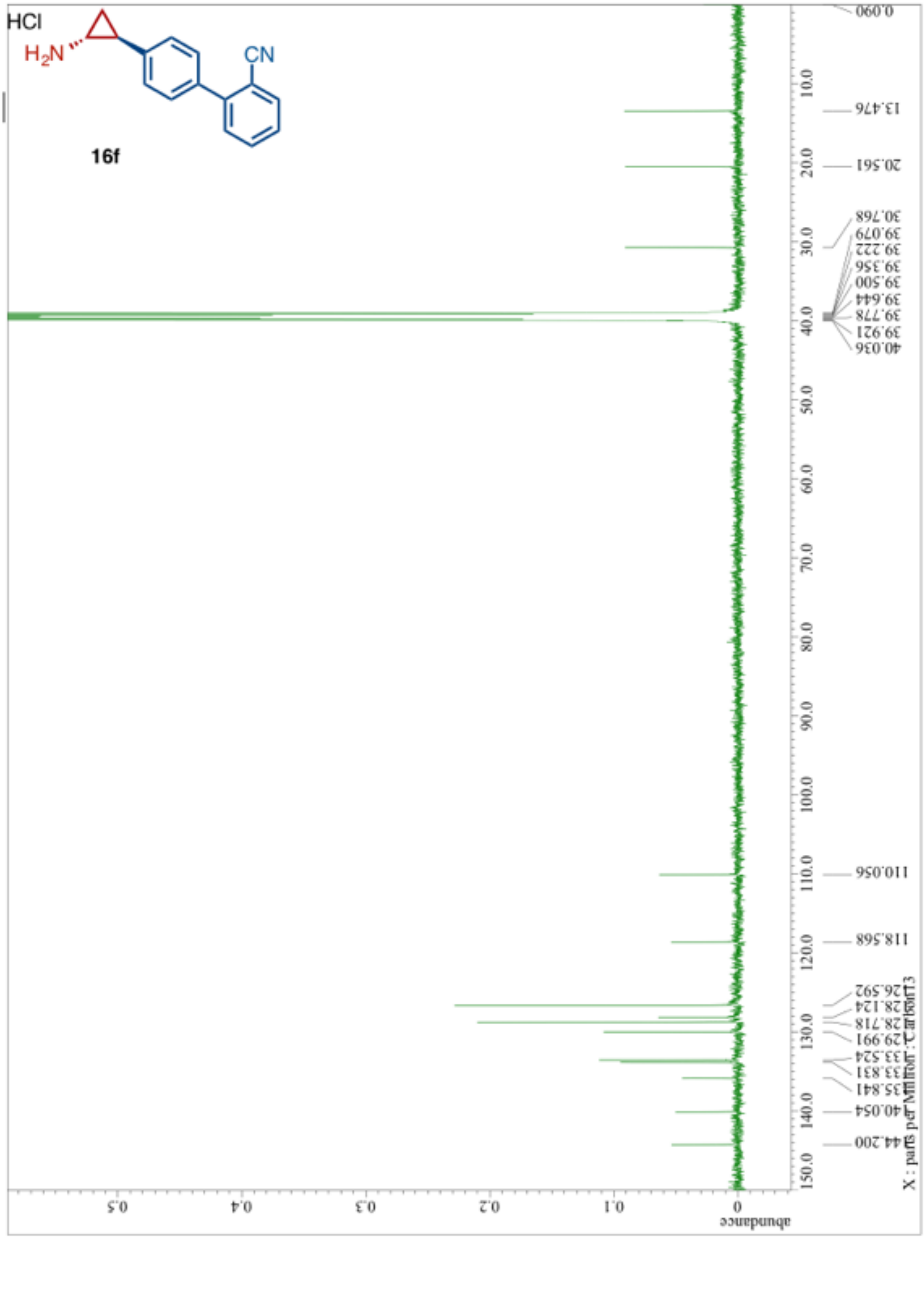
^{13}C NMR (150 MHz, DMSO-d_6) of 16e:



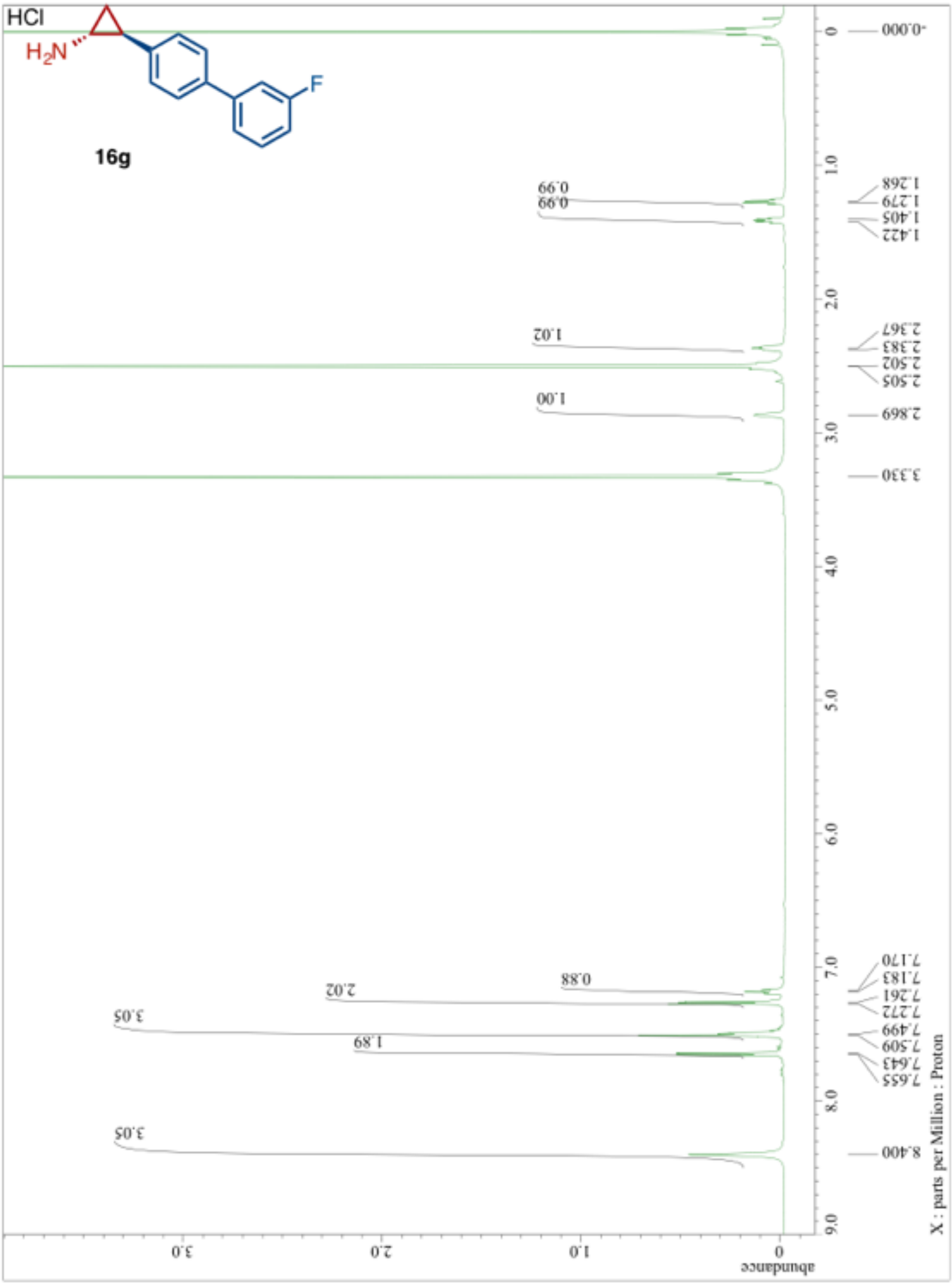
[1]H NMR (600 MHz, DMSO-d_6) of 16f:



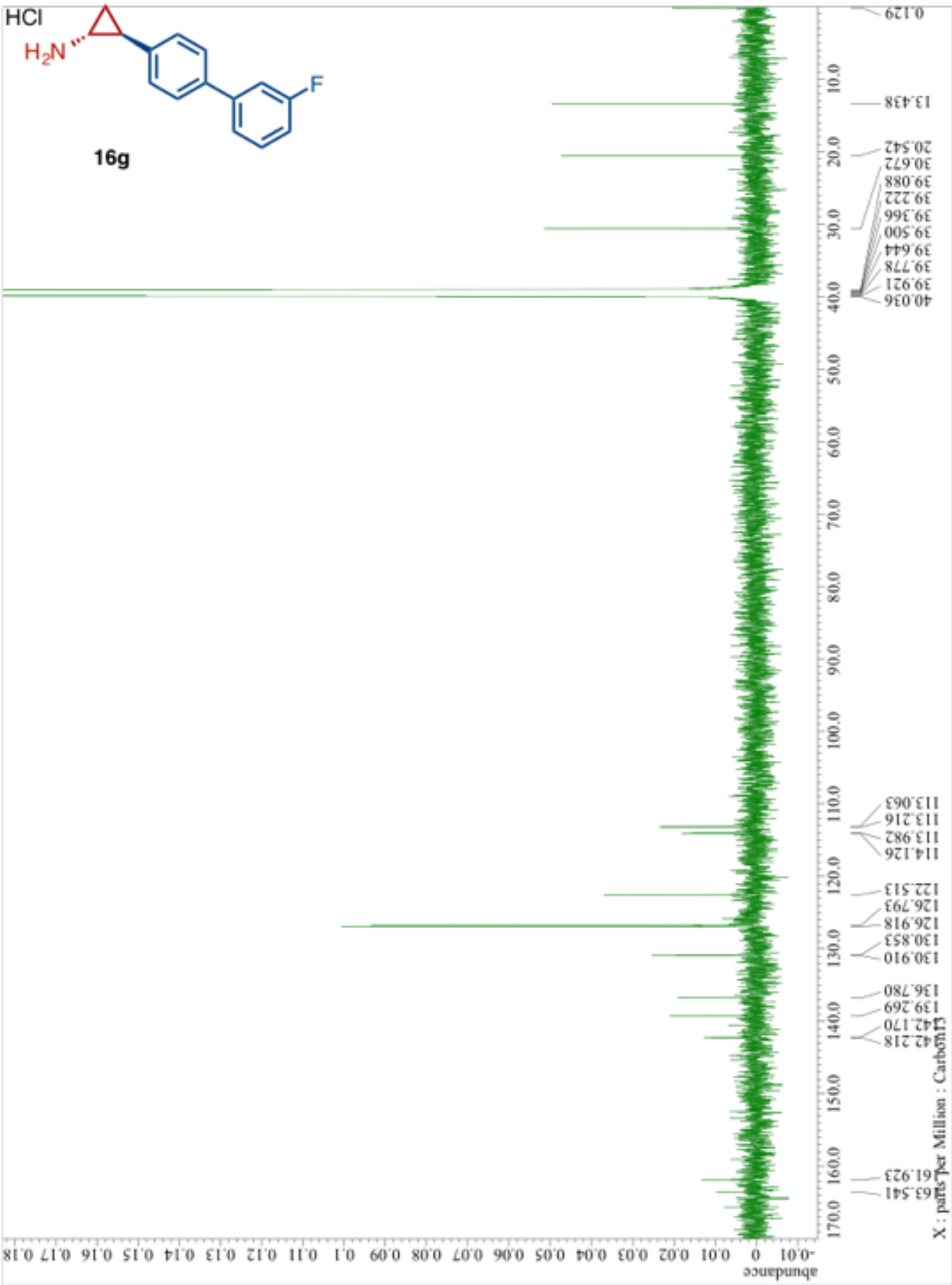
^{13}C NMR (150 MHz, DMSO-d_6) of 16f:



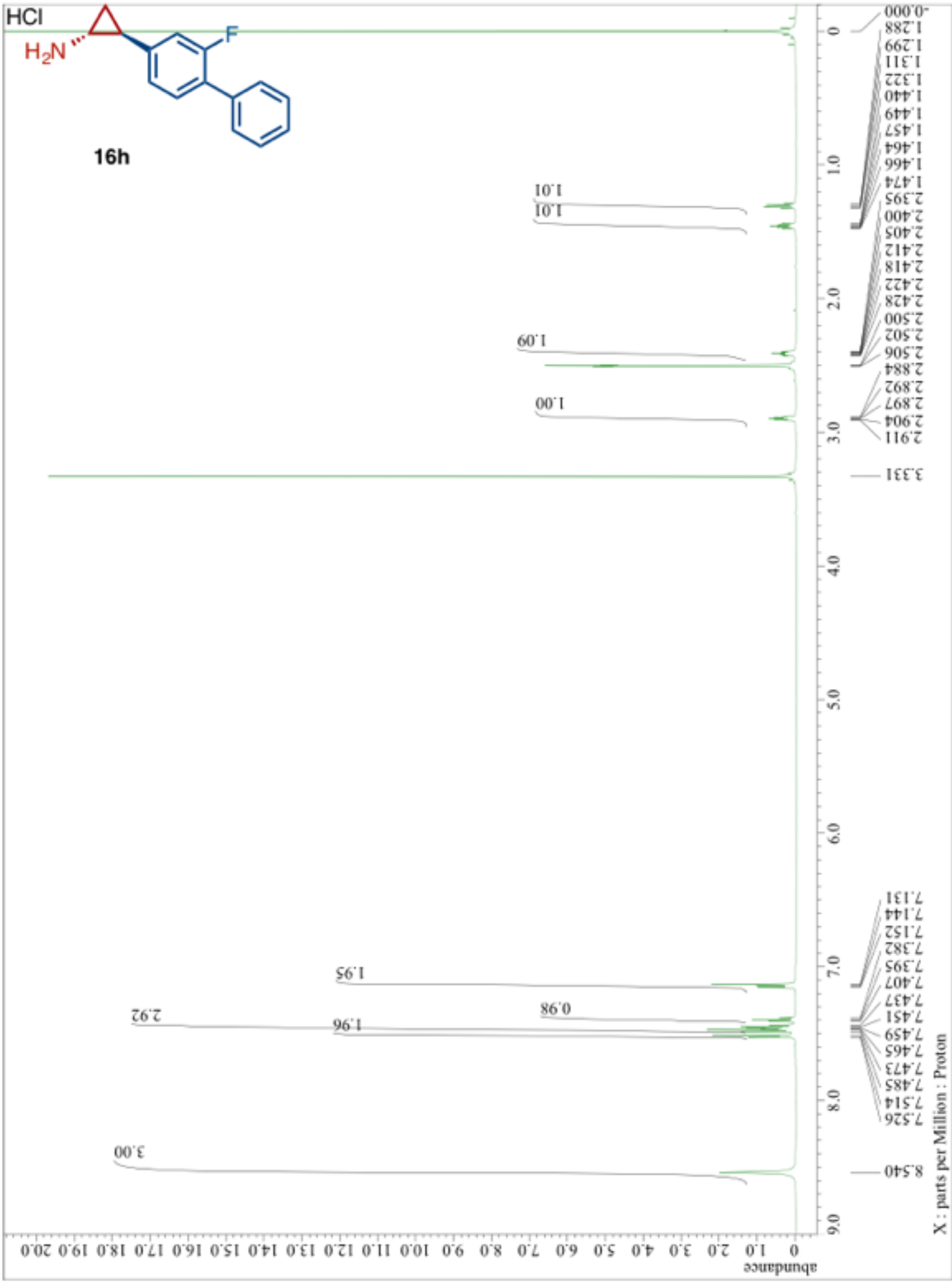
^{1}H NMR (600 MHz, DMSO-d_6) of 16g:



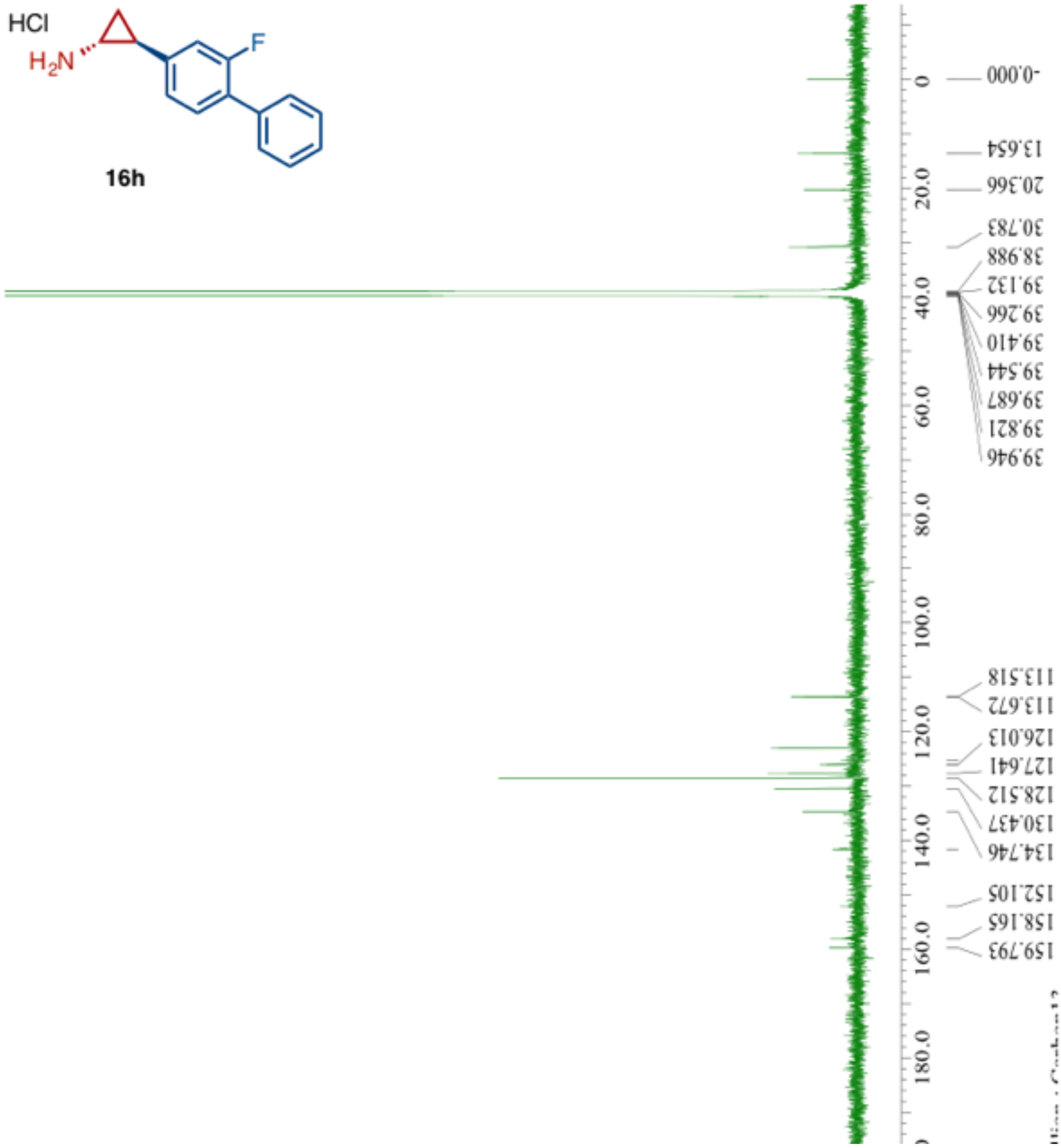
^{13}C NMR (150 MHz, DMSO-d_6) of 16g:



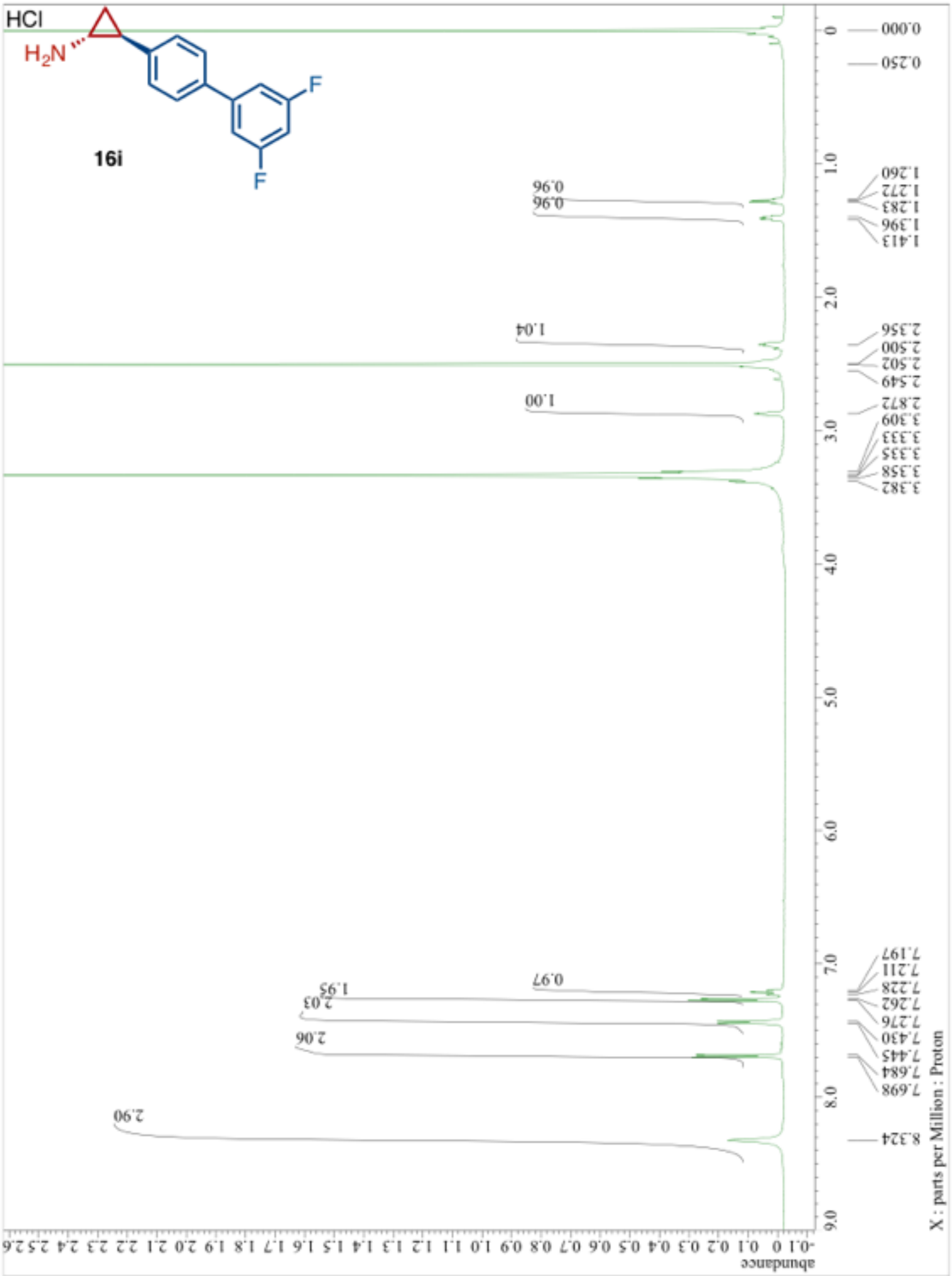
^{1}H NMR (600 MHz, DMSO-d_6) of 16h:



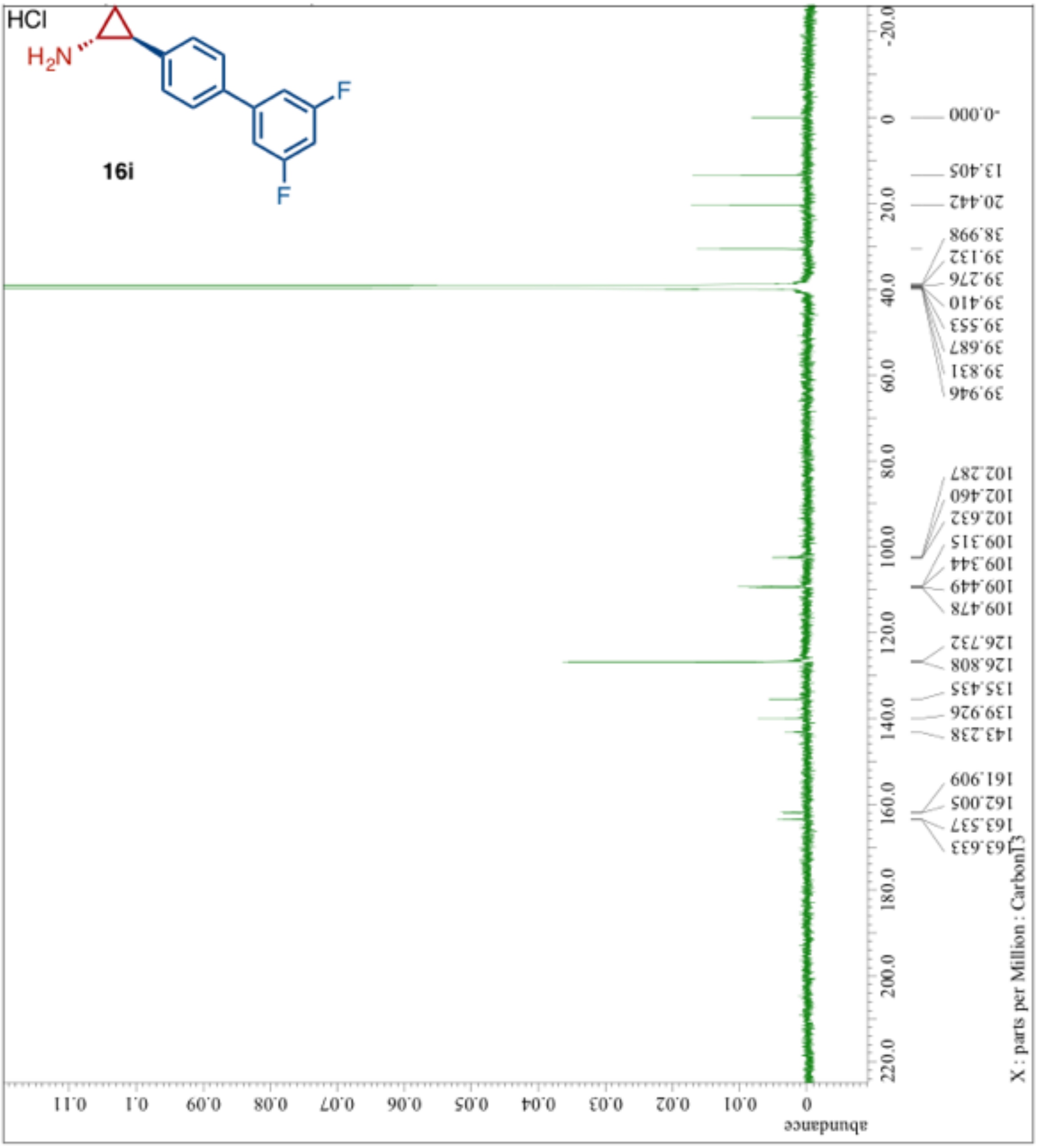
[13]C NMR (150 MHz, DMSO-d_6) of 16h:



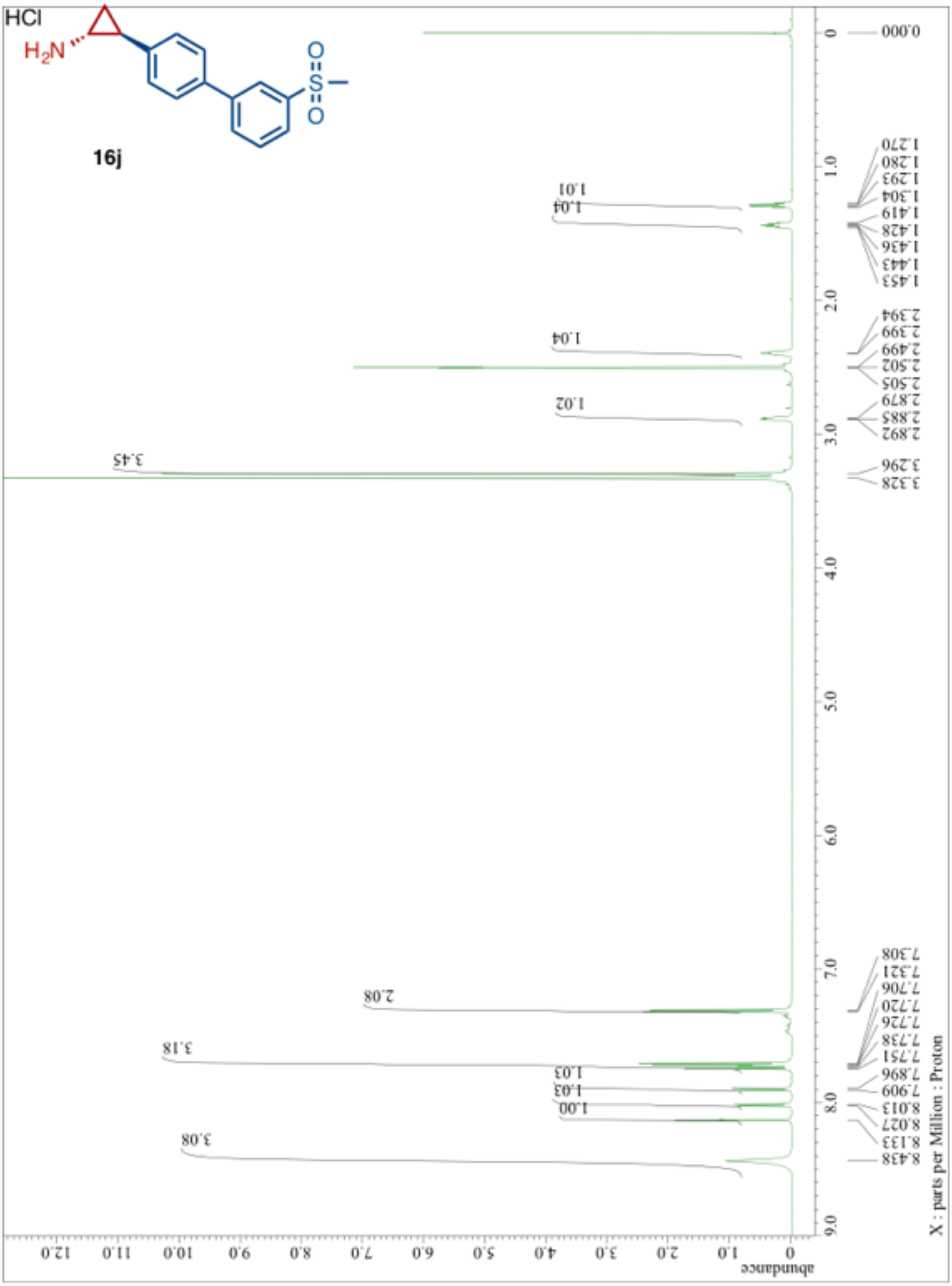
^{1}H NMR (600 MHz, DMSO-d_6) of 16i:



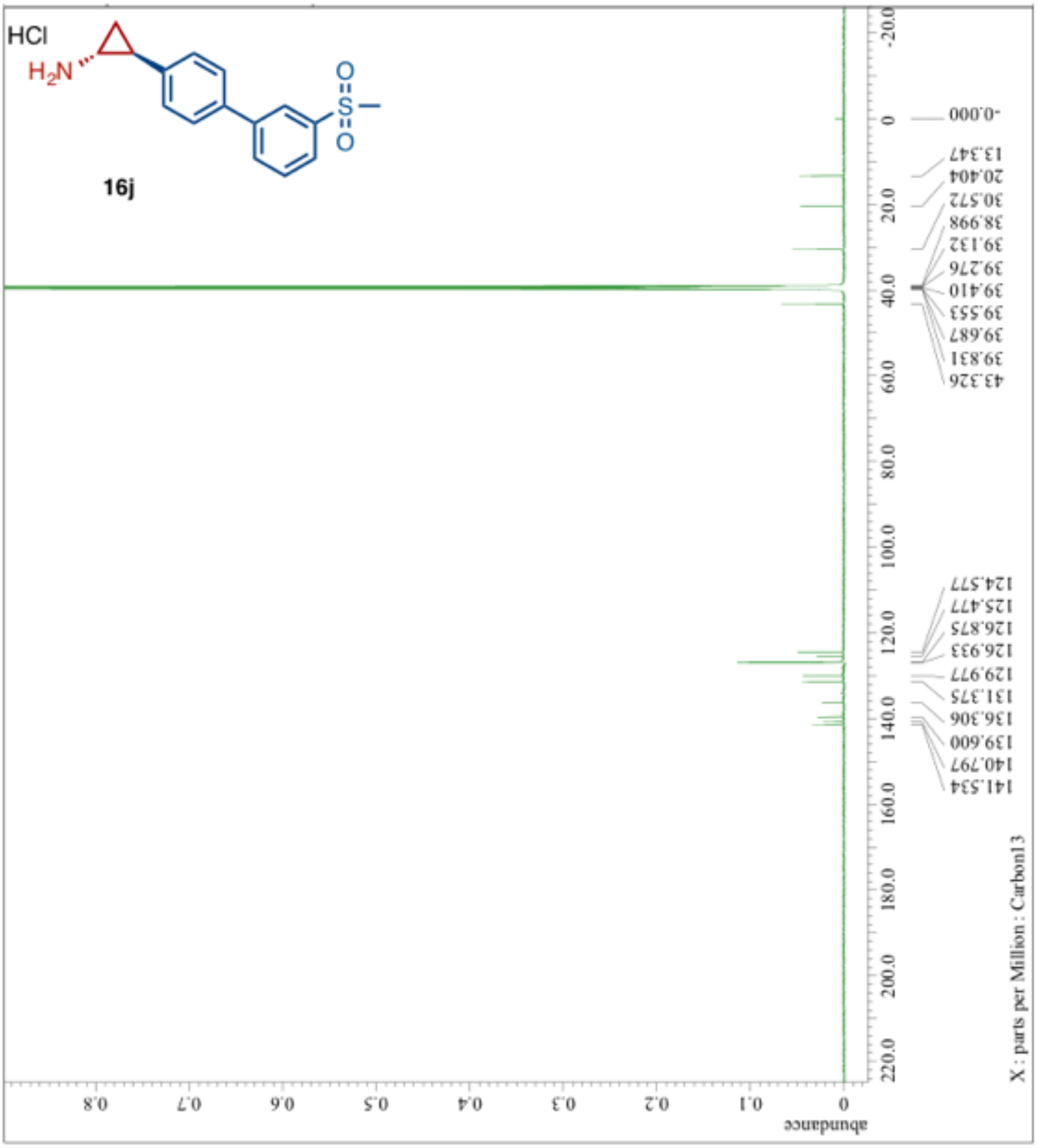
^{13}C NMR (150 MHz, DMSO-d_6) of 16i:



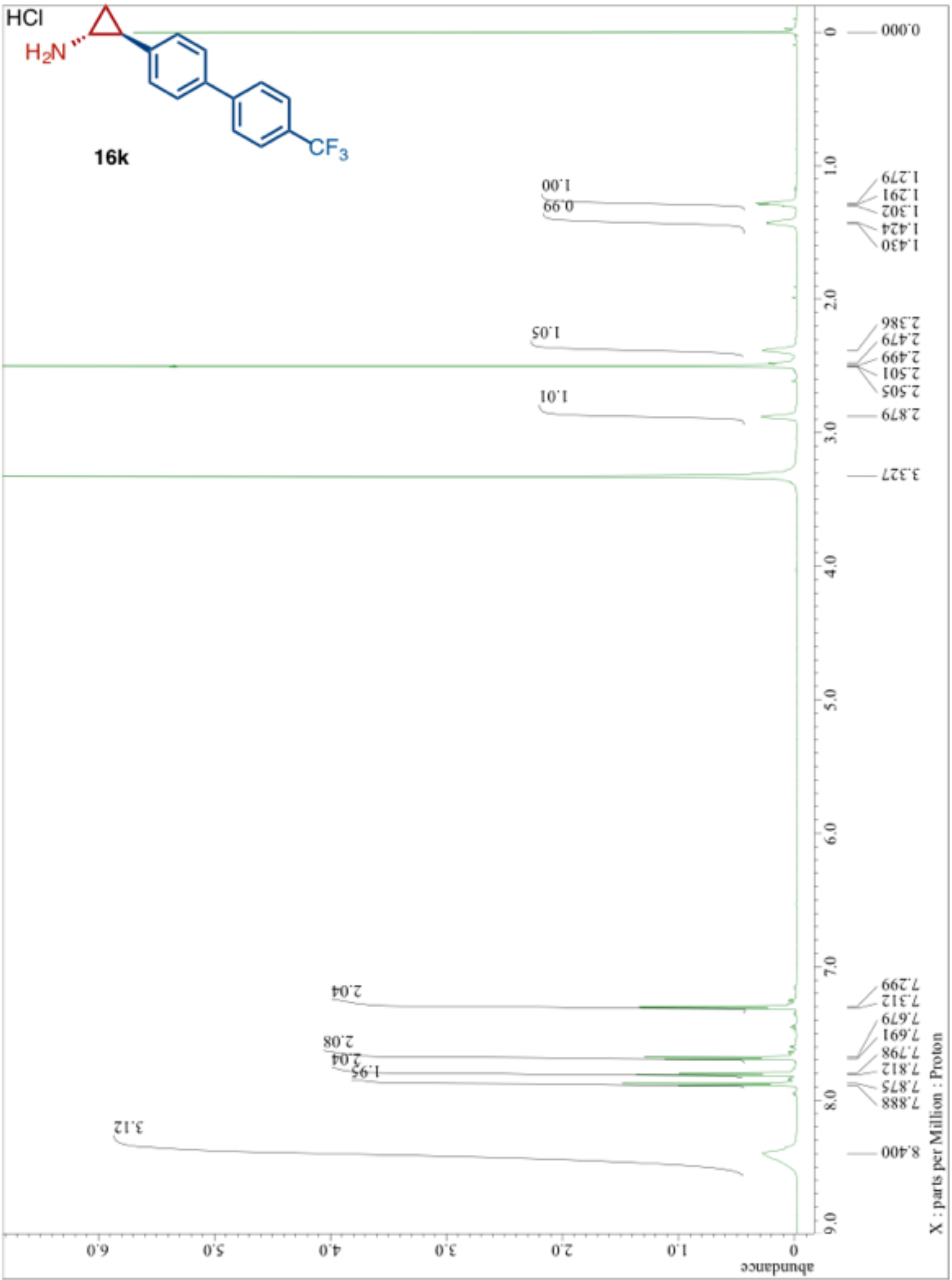
[1]H NMR (600 MHz, DMSO-d_6) of 16j:



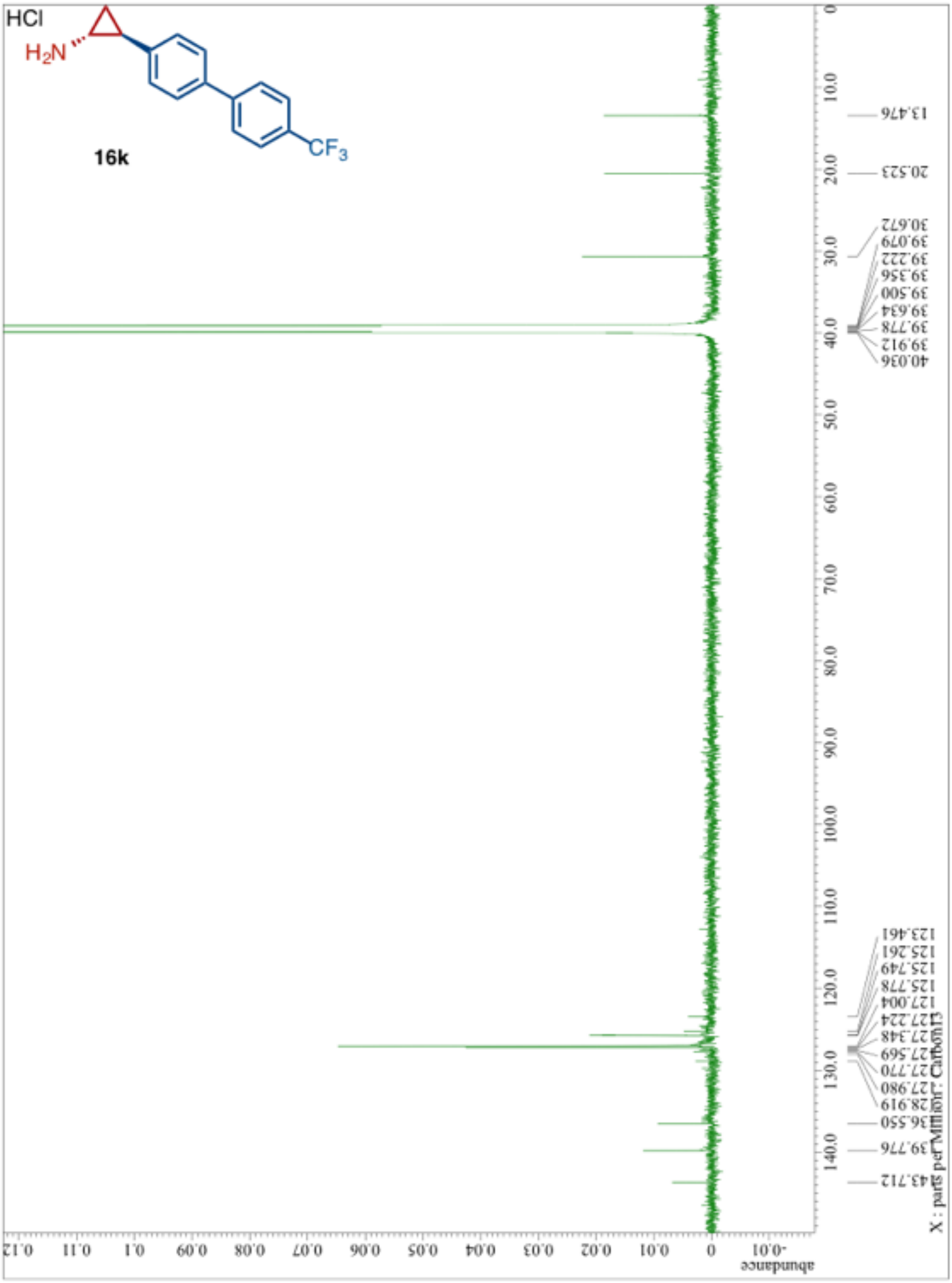
^{13}C NMR (150 MHz, DMSO-d_6) of 16j:



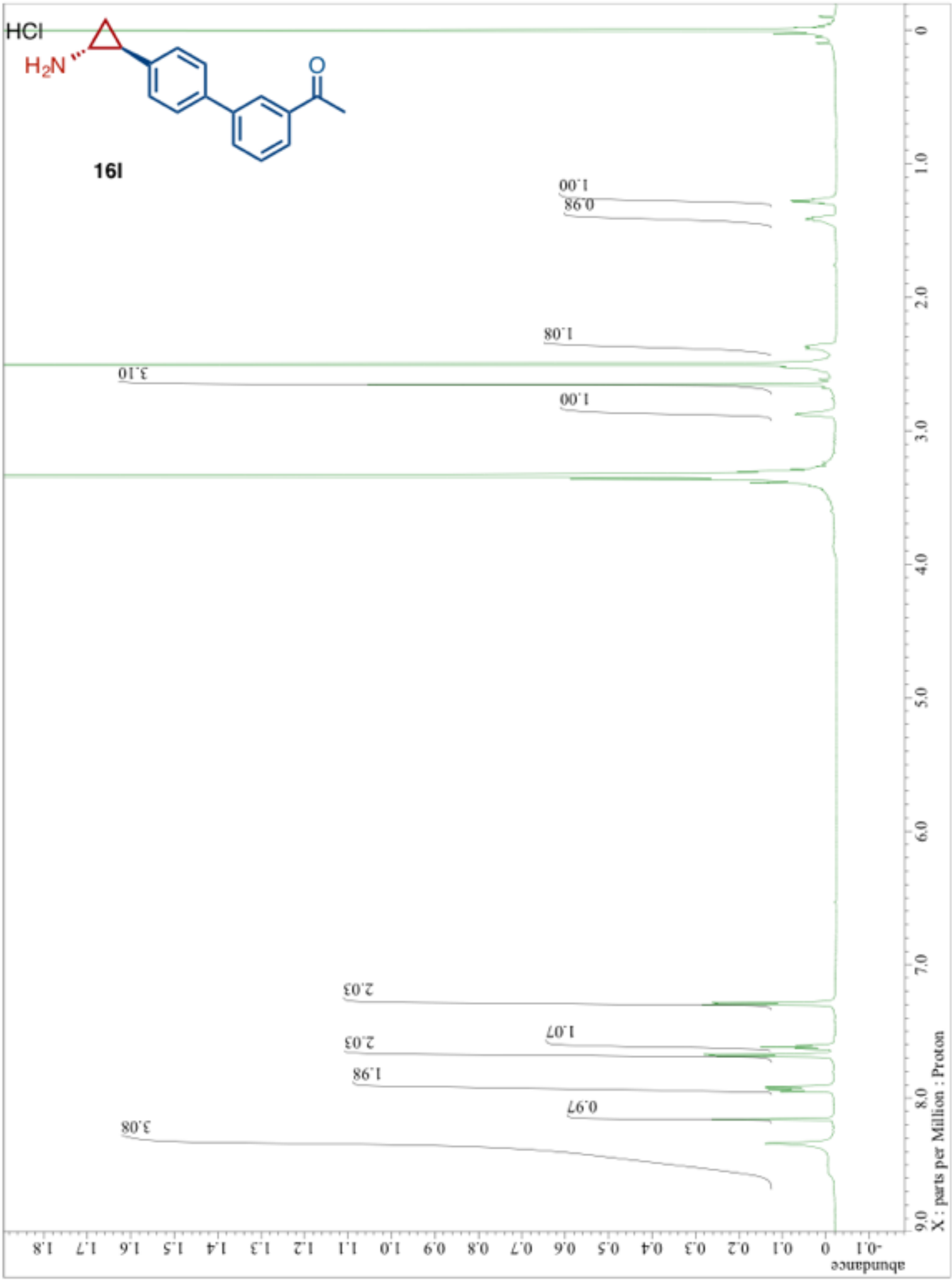
[1]H NMR (600 MHz, DMSO-d_6) of 16k:



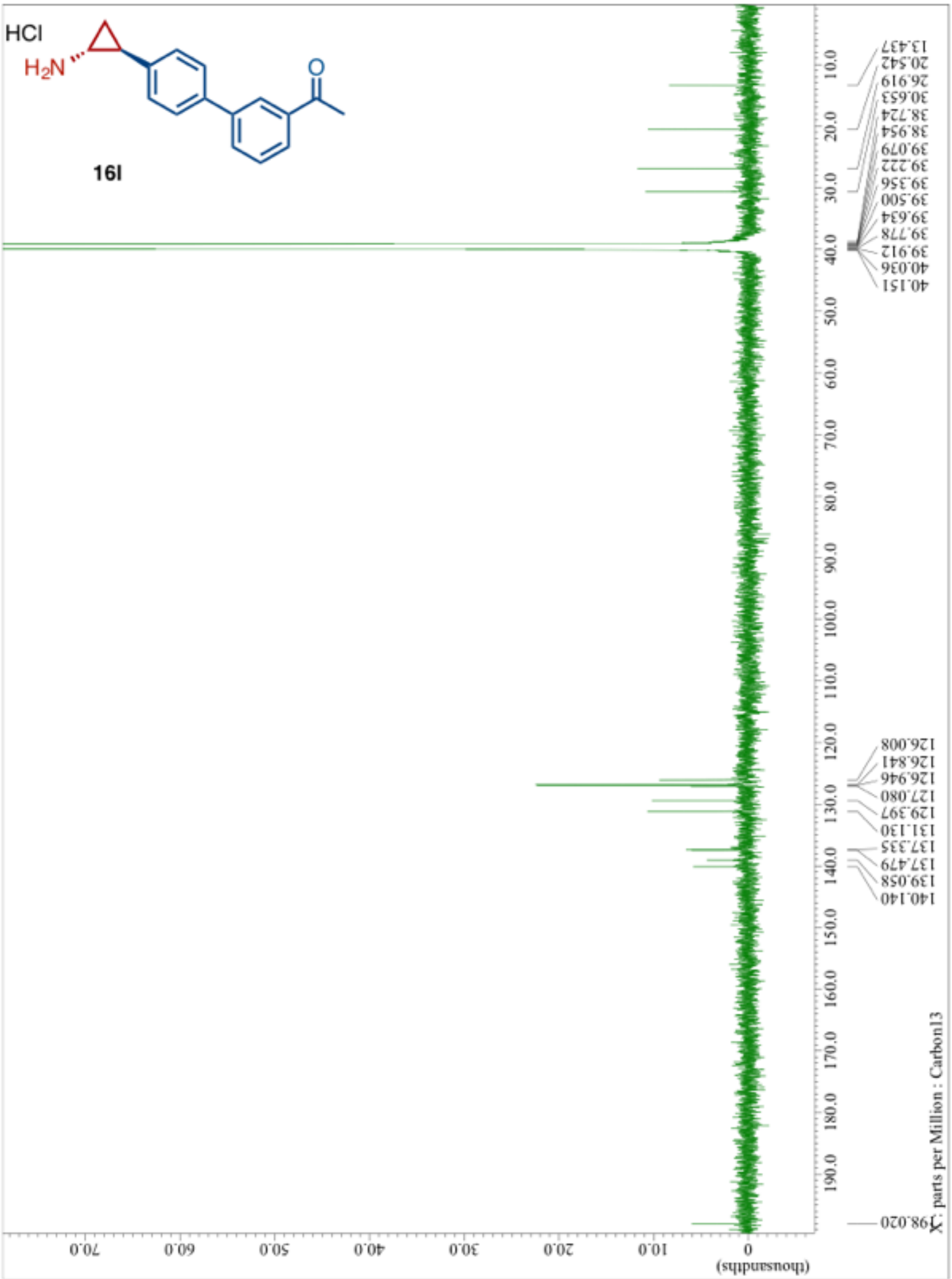
^{13}C NMR (150 MHz, DMSO-d_6) of 16k:



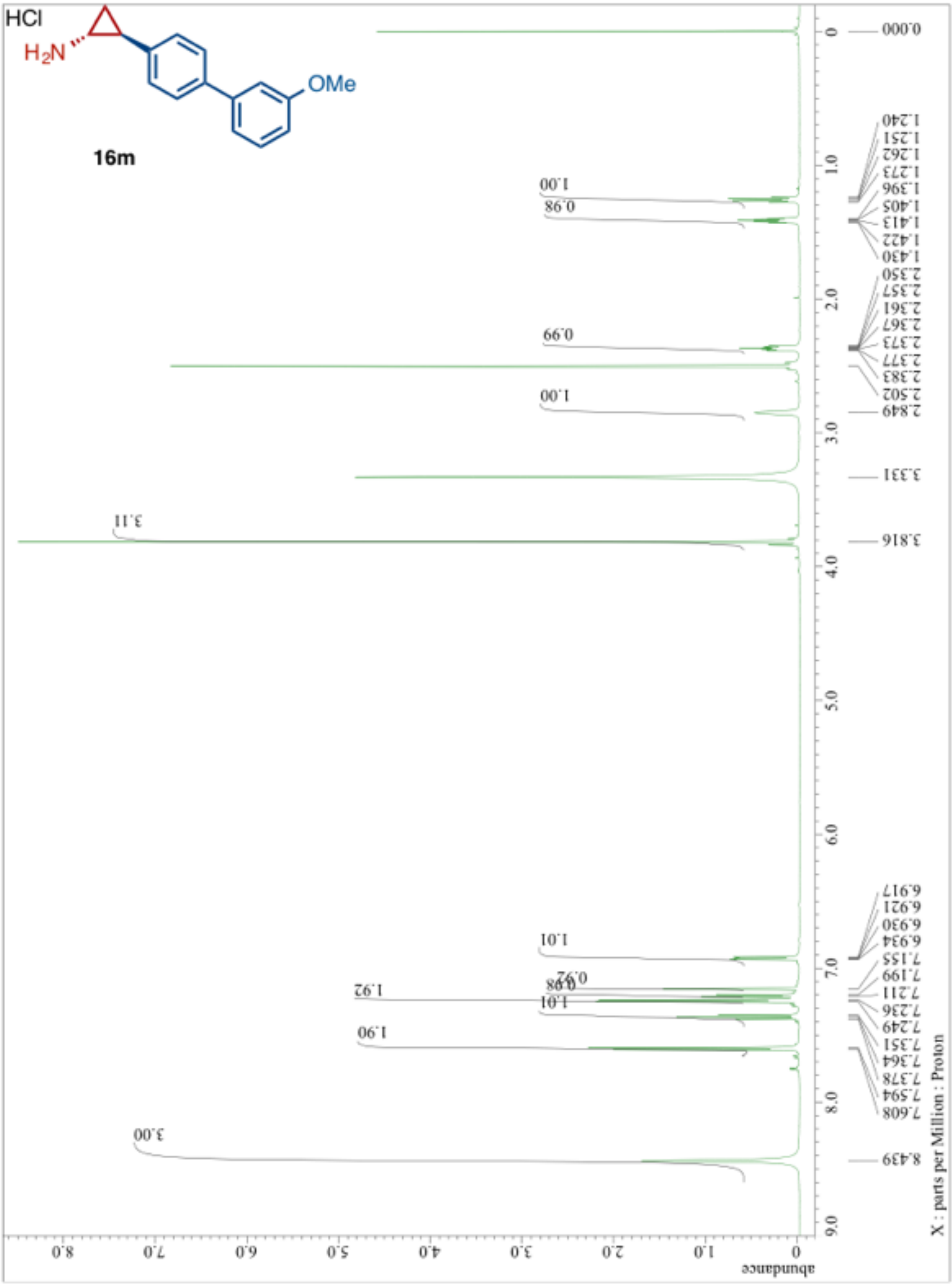
[1]H NMR (600 MHz, DMSO-d_6) of 16l:



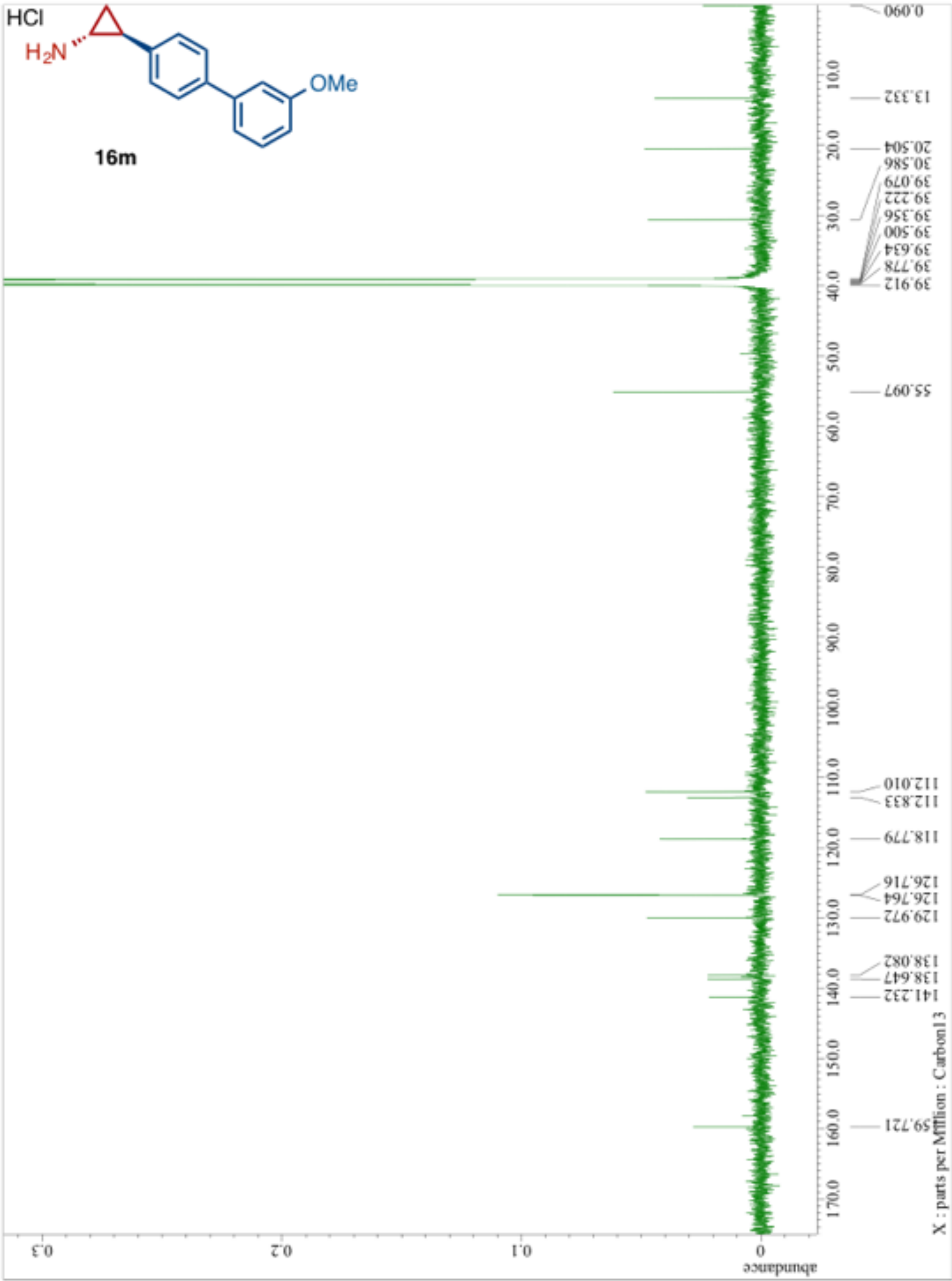
^{13}C NMR (150 MHz, DMSO-d_6) of 16l:



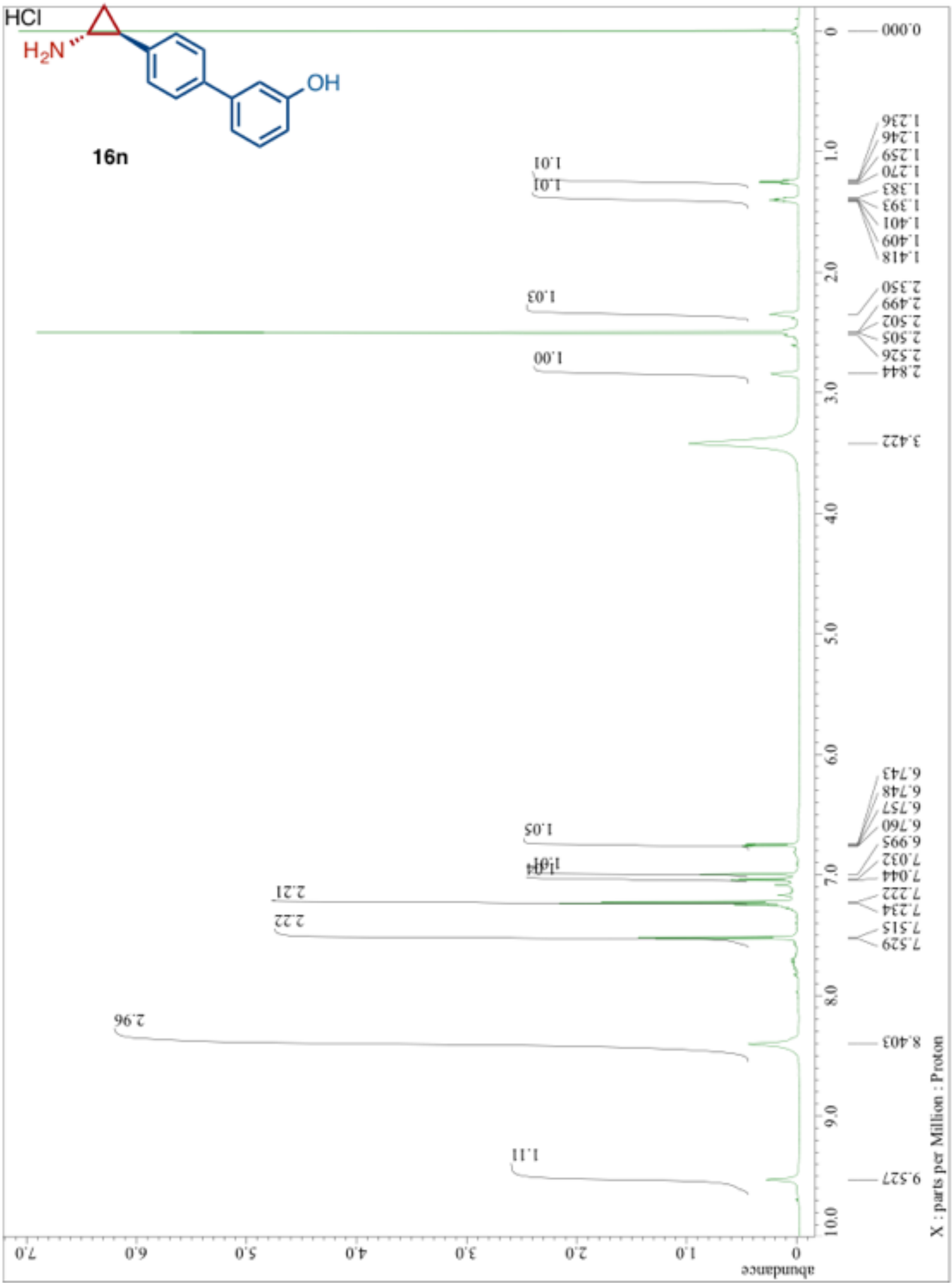
[1]H NMR (600 MHz, DMSO-d_6) of 16m:



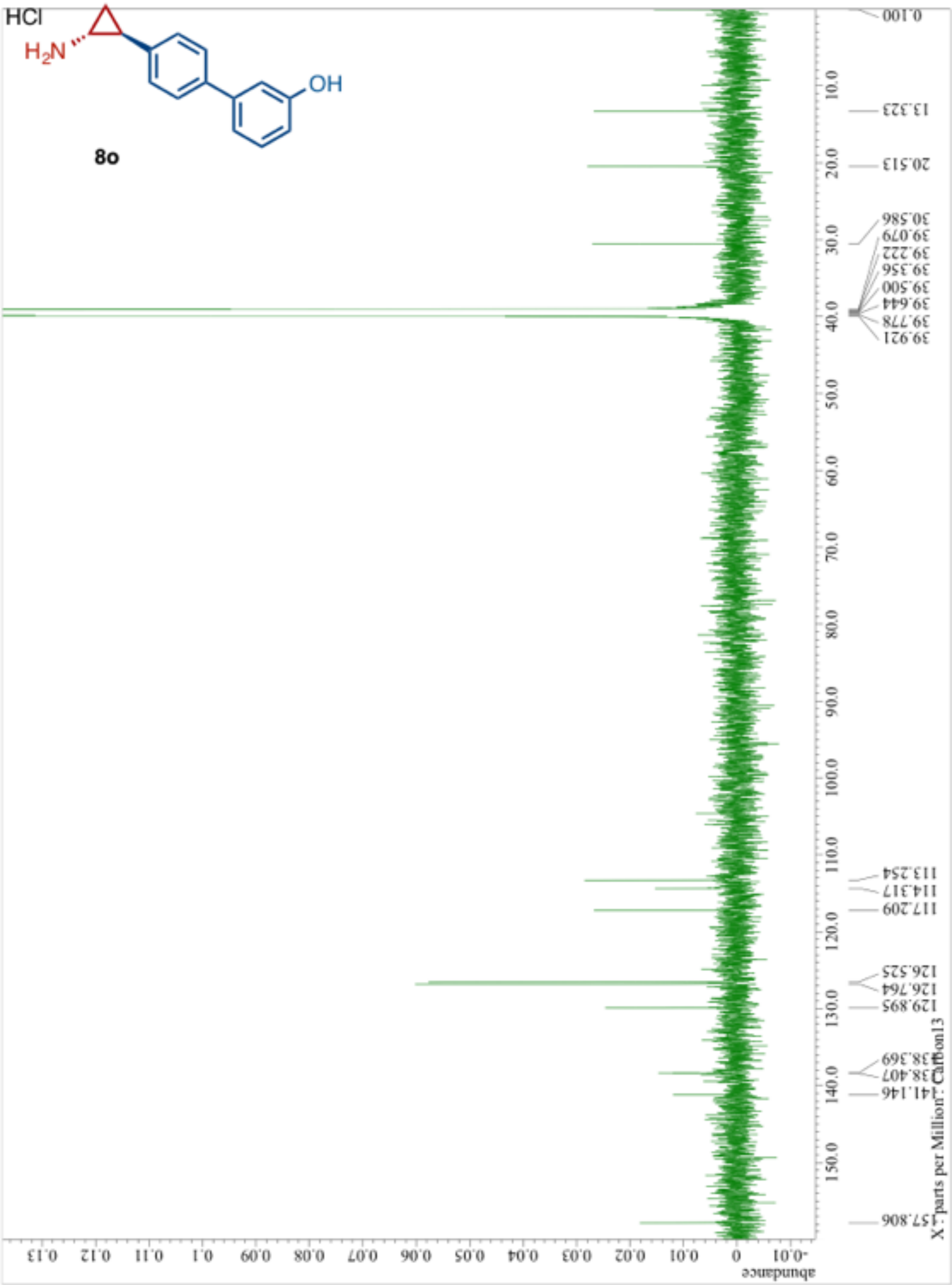
^{13}C NMR (150 MHz, DMSO-d_6) of 16m:



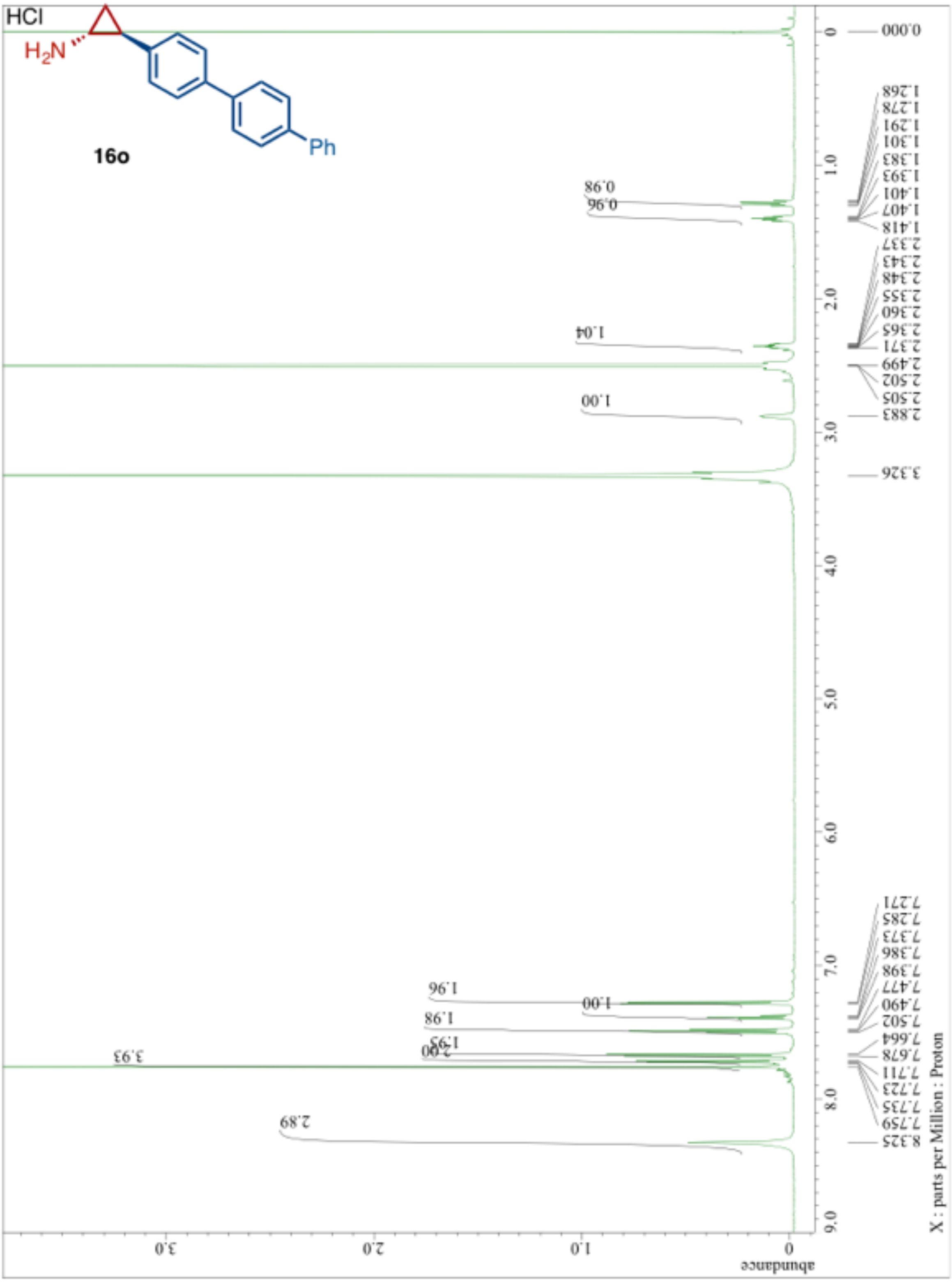
[1]H NMR (600 MHz, DMSO-d_6) of 16n:



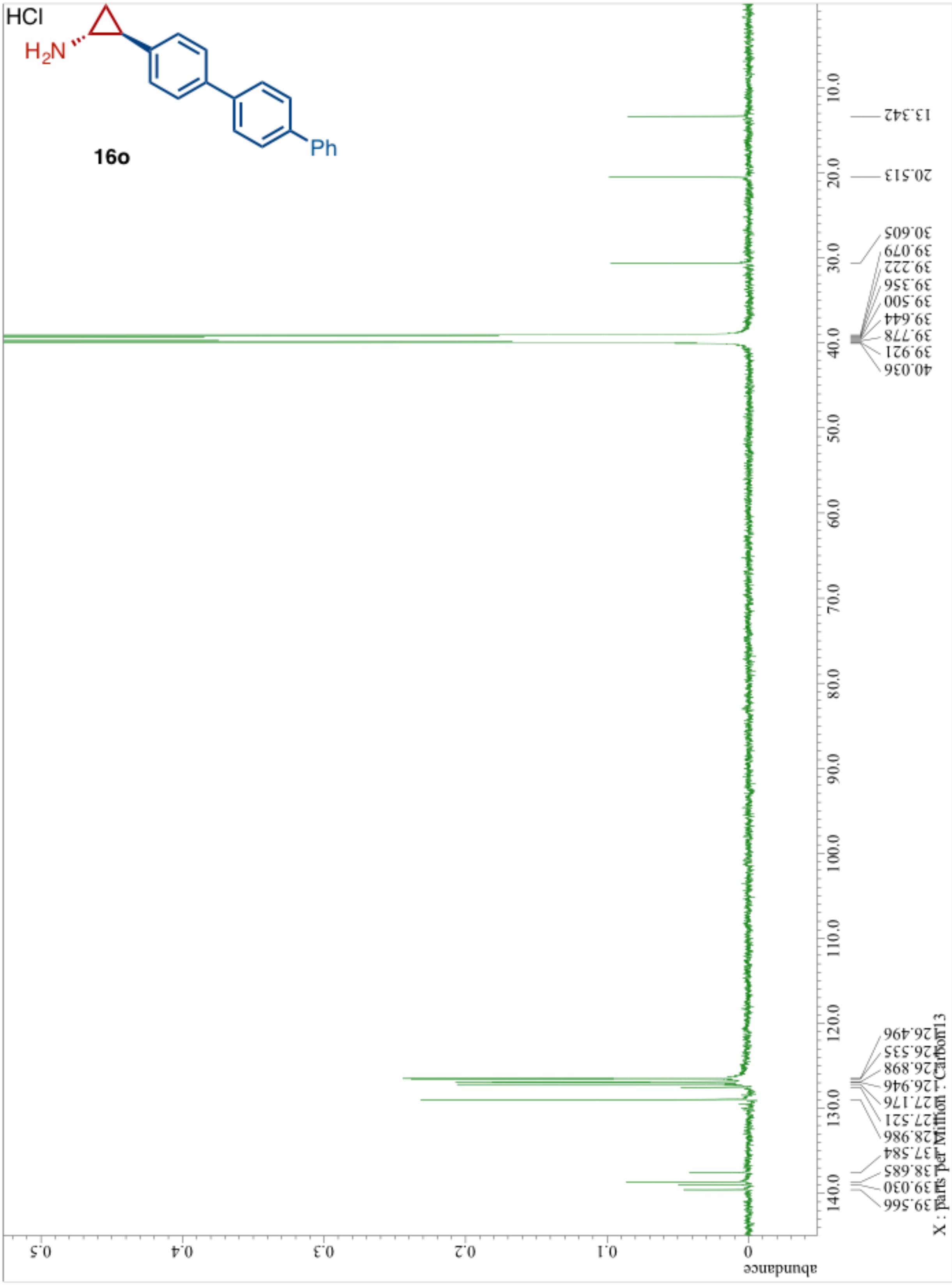
^{13}C NMR (150 MHz, DMSO-d_6) of 16n:



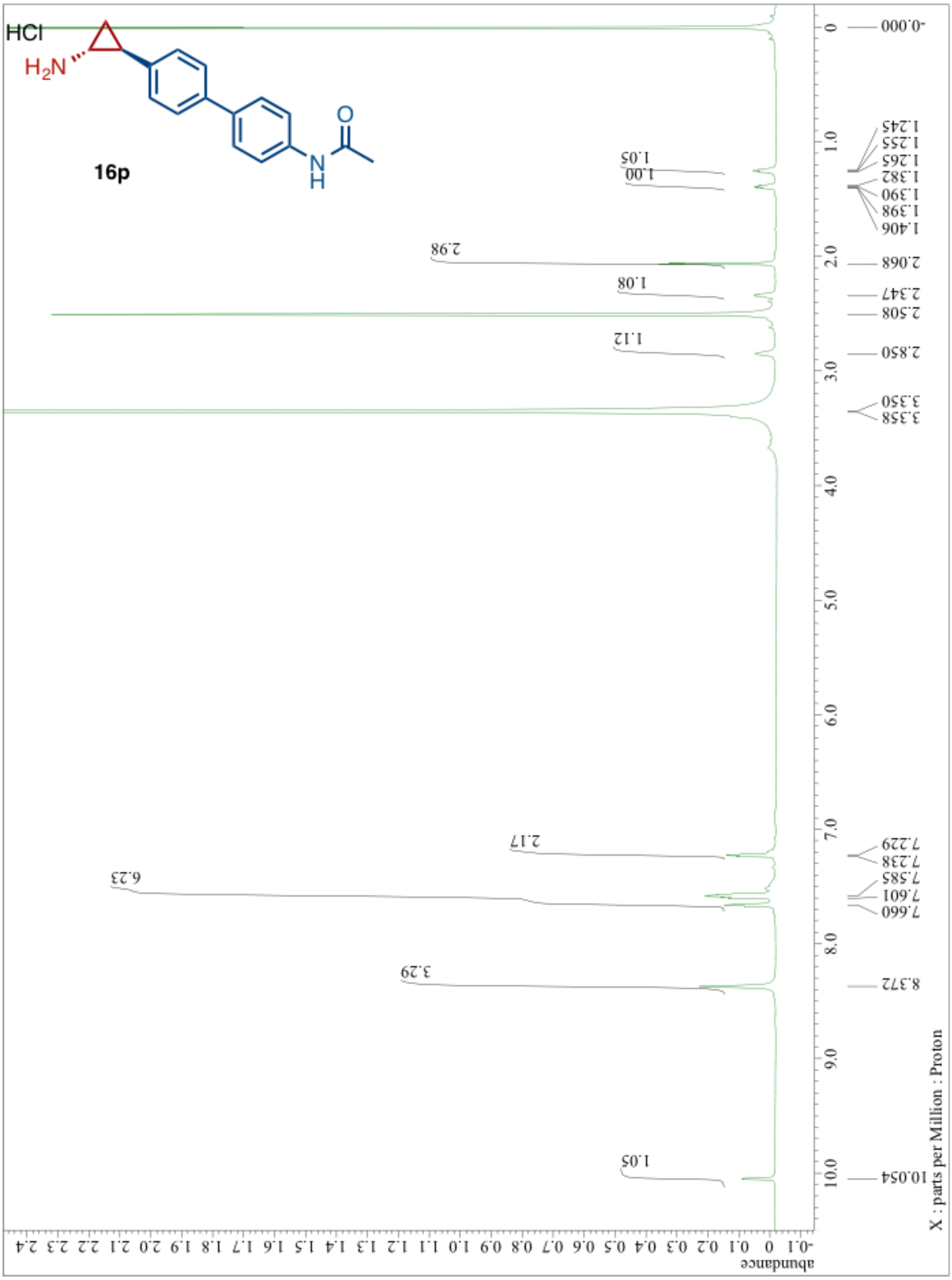
^{1}H NMR (600 MHz, DMSO-d_6) of 16o:



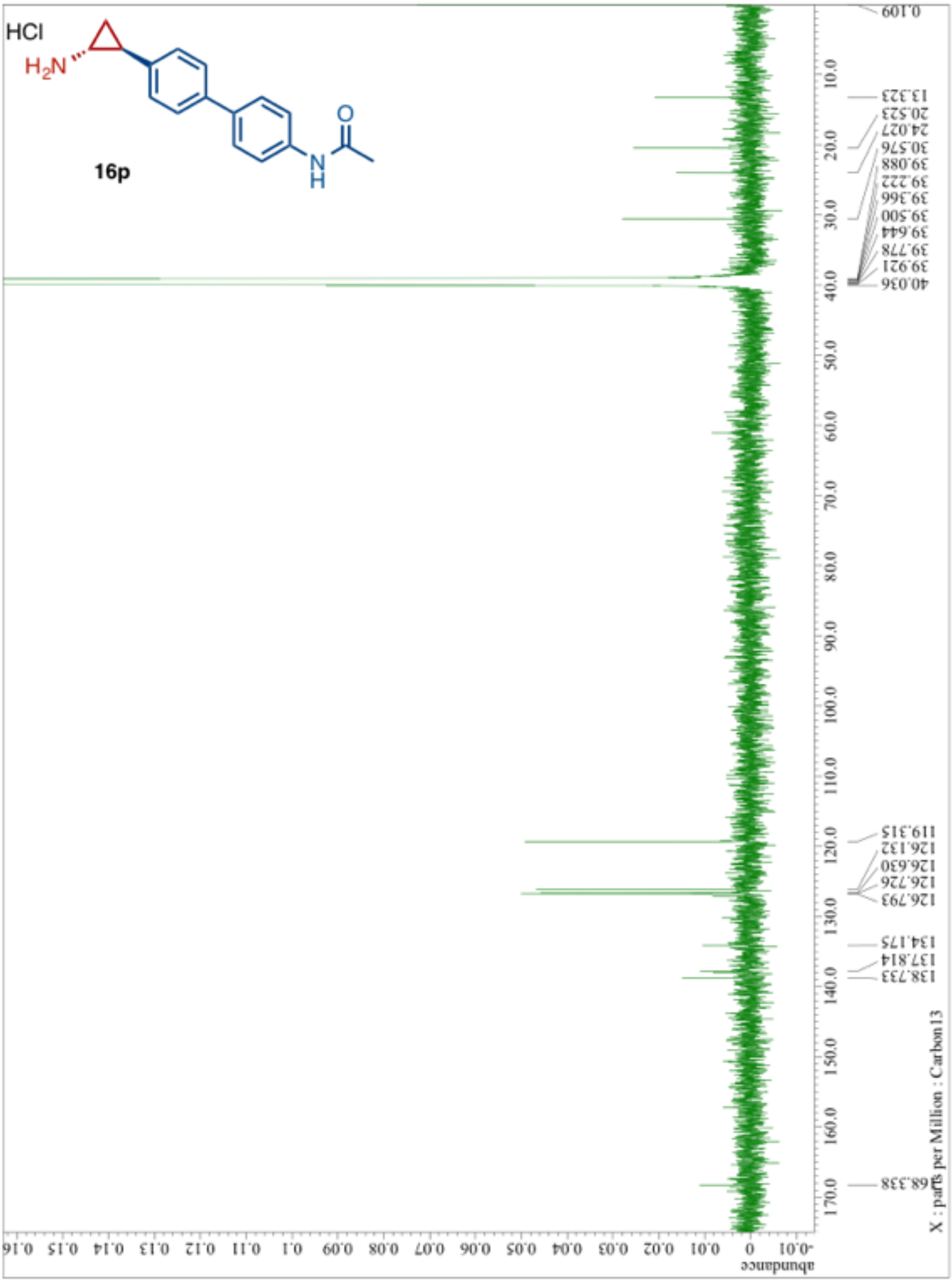
^{13}C NMR (150 MHz, DMSO-d_6) of 16o:



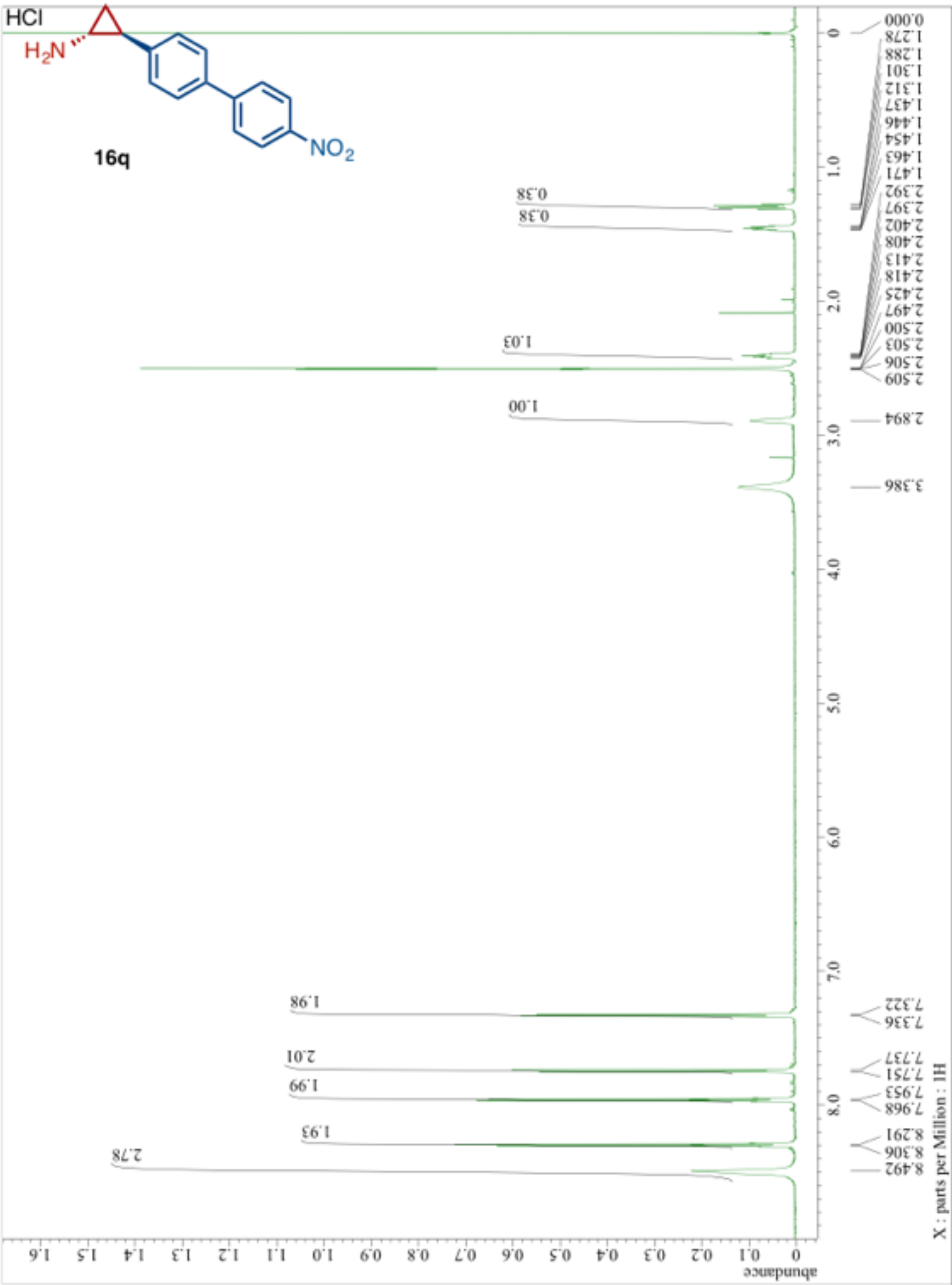
[1]H NMR (600 MHz, DMSO-d_6) of 16p:



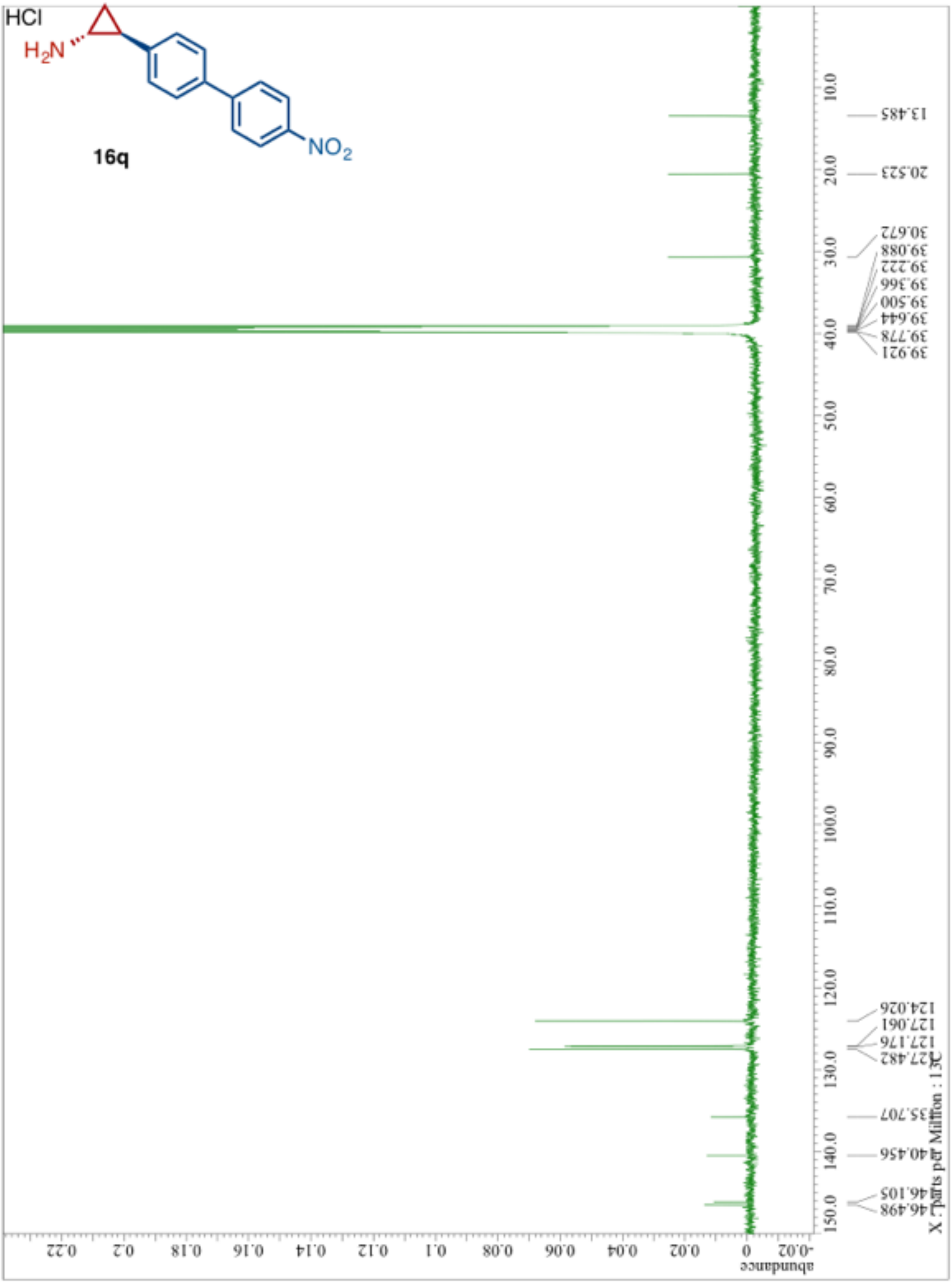
[13]C NMR (150 MHz, DMSO-d_6) of 16p:



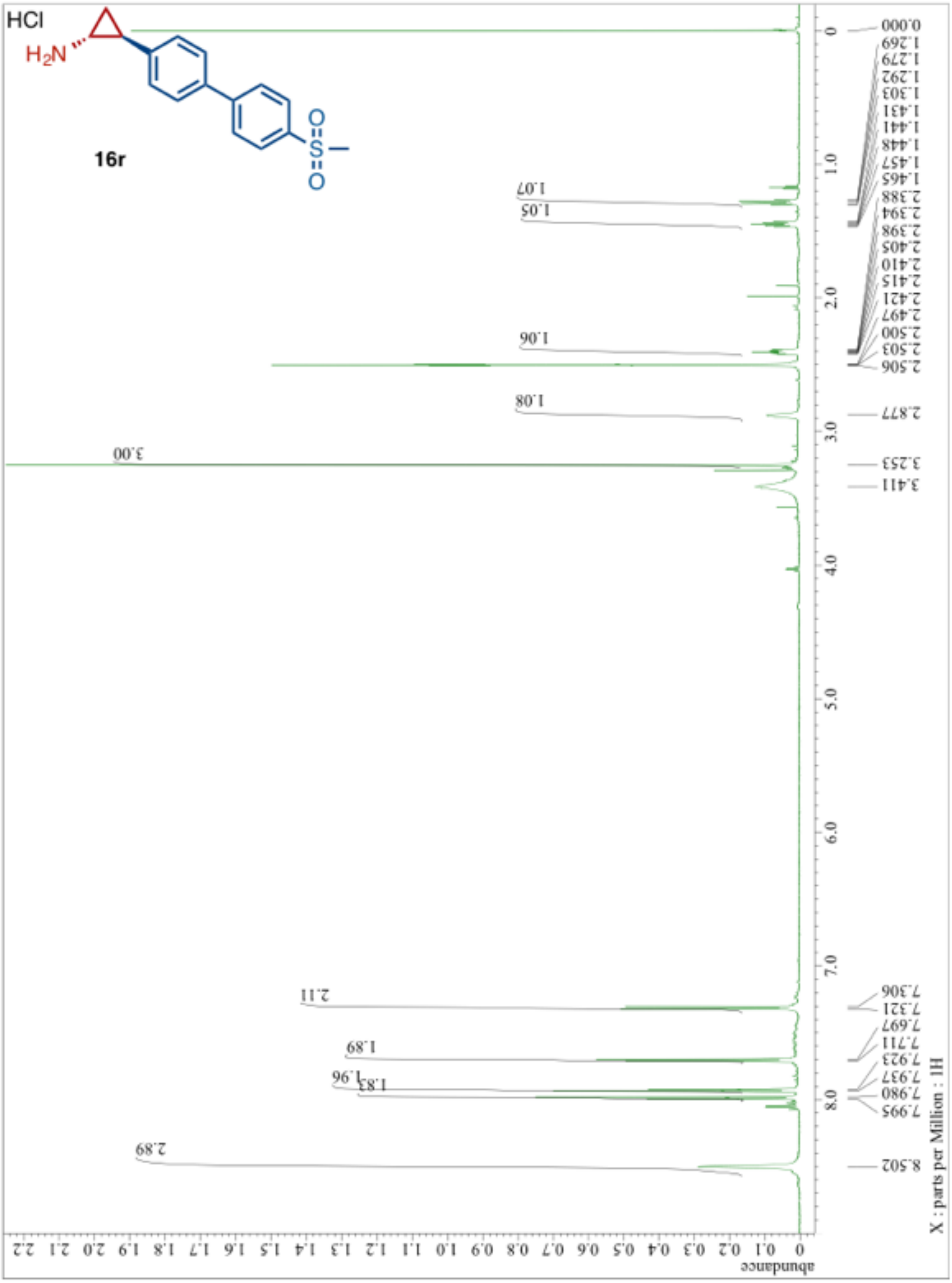
[1]H NMR (600 MHz, DMSO-d_6) of 16q:



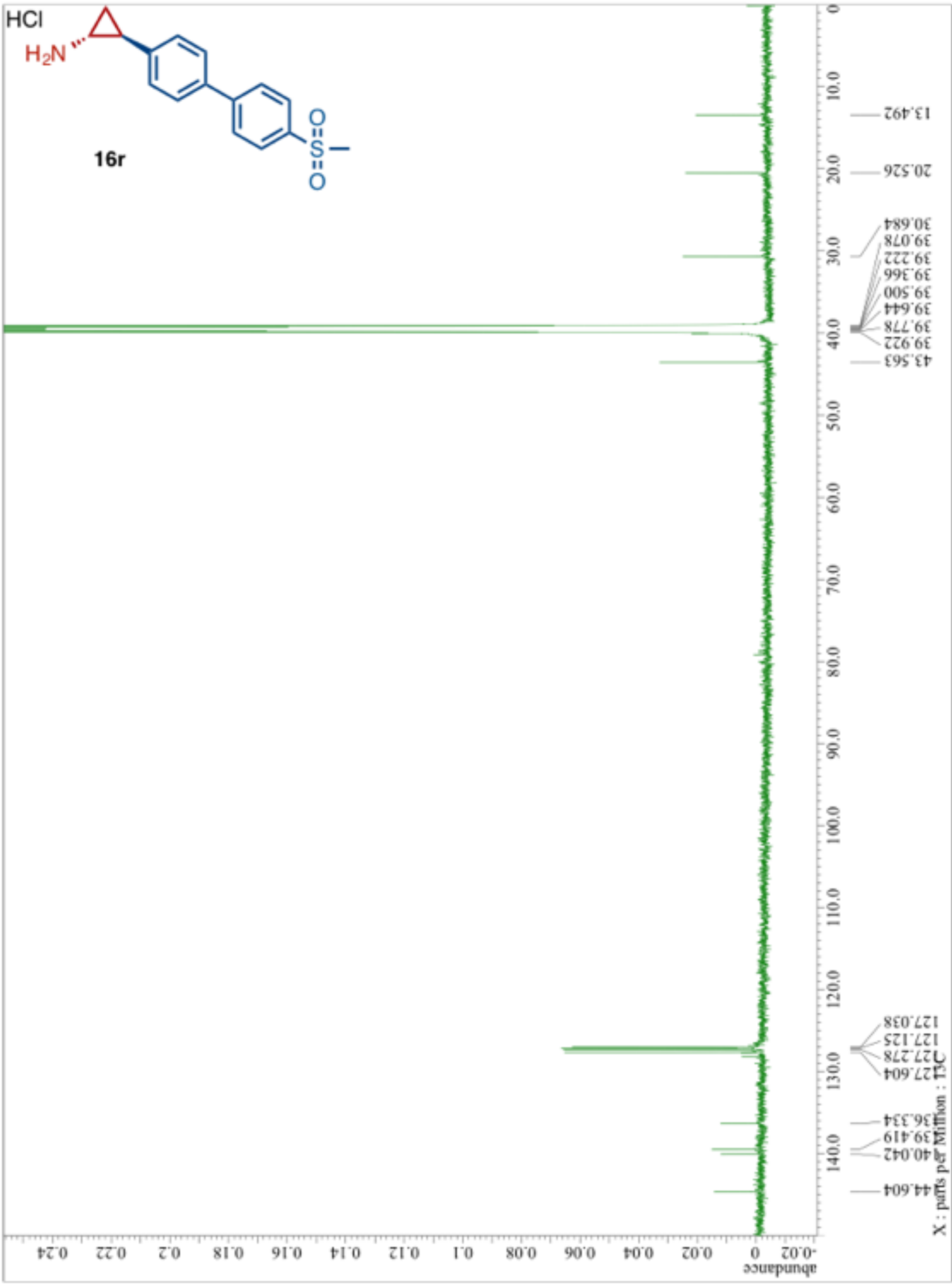
^{13}C NMR (150 MHz, DMSO-d_6) of 16q:



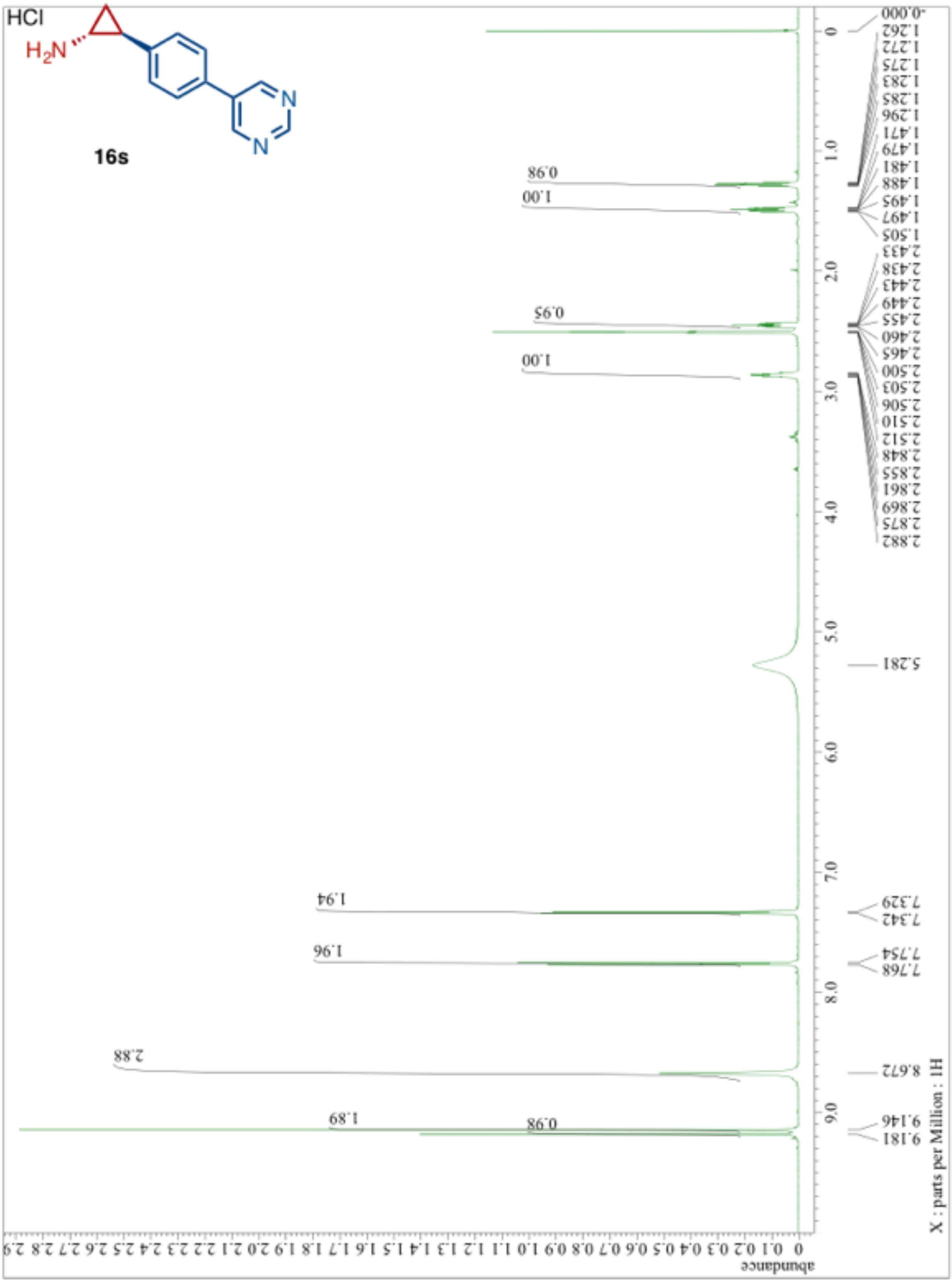
^{1}H NMR (600 MHz, DMSO-d_6) of 16r:



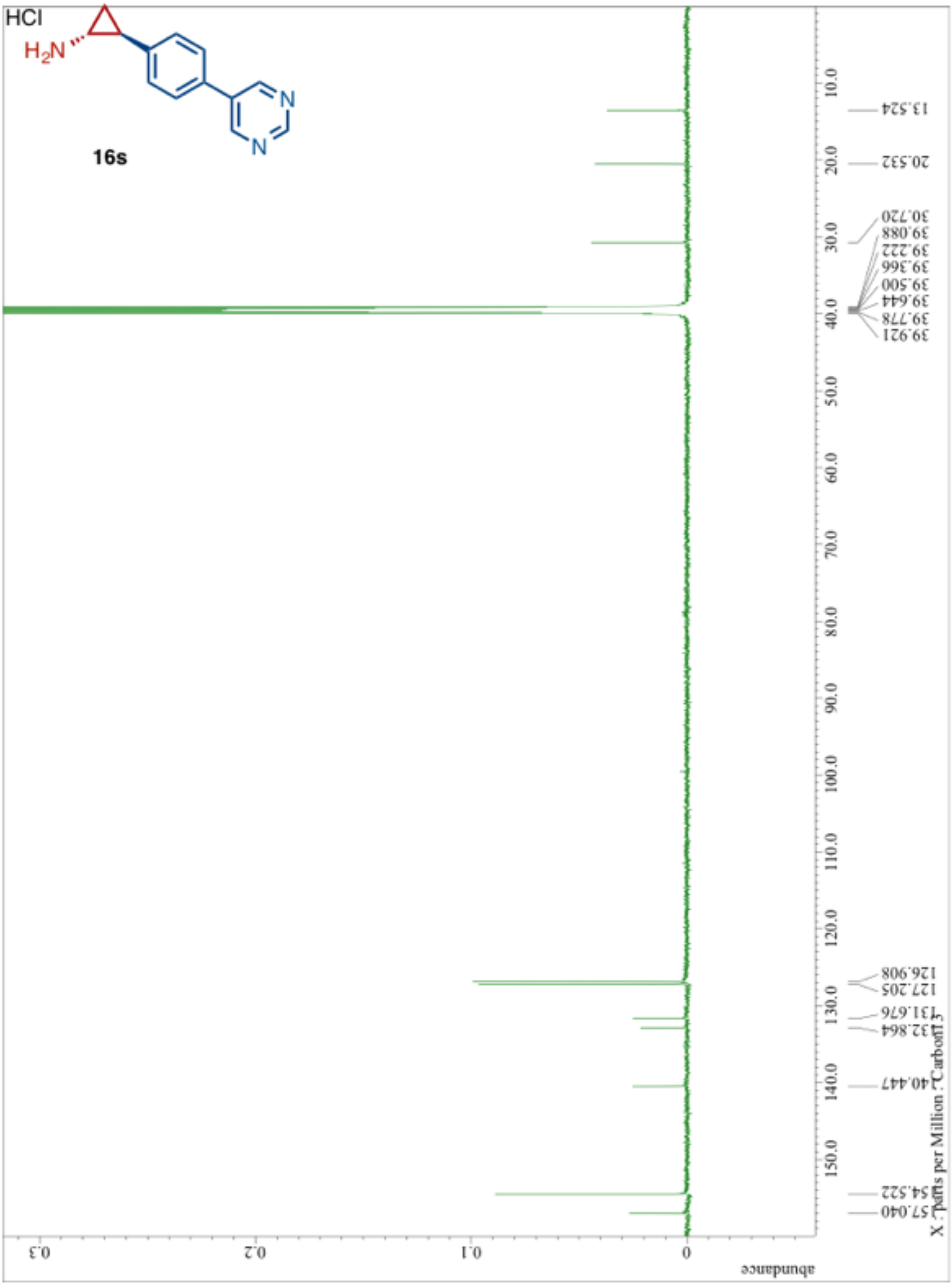
^{13}C NMR (150 MHz, DMSO-d_6) of 16r:



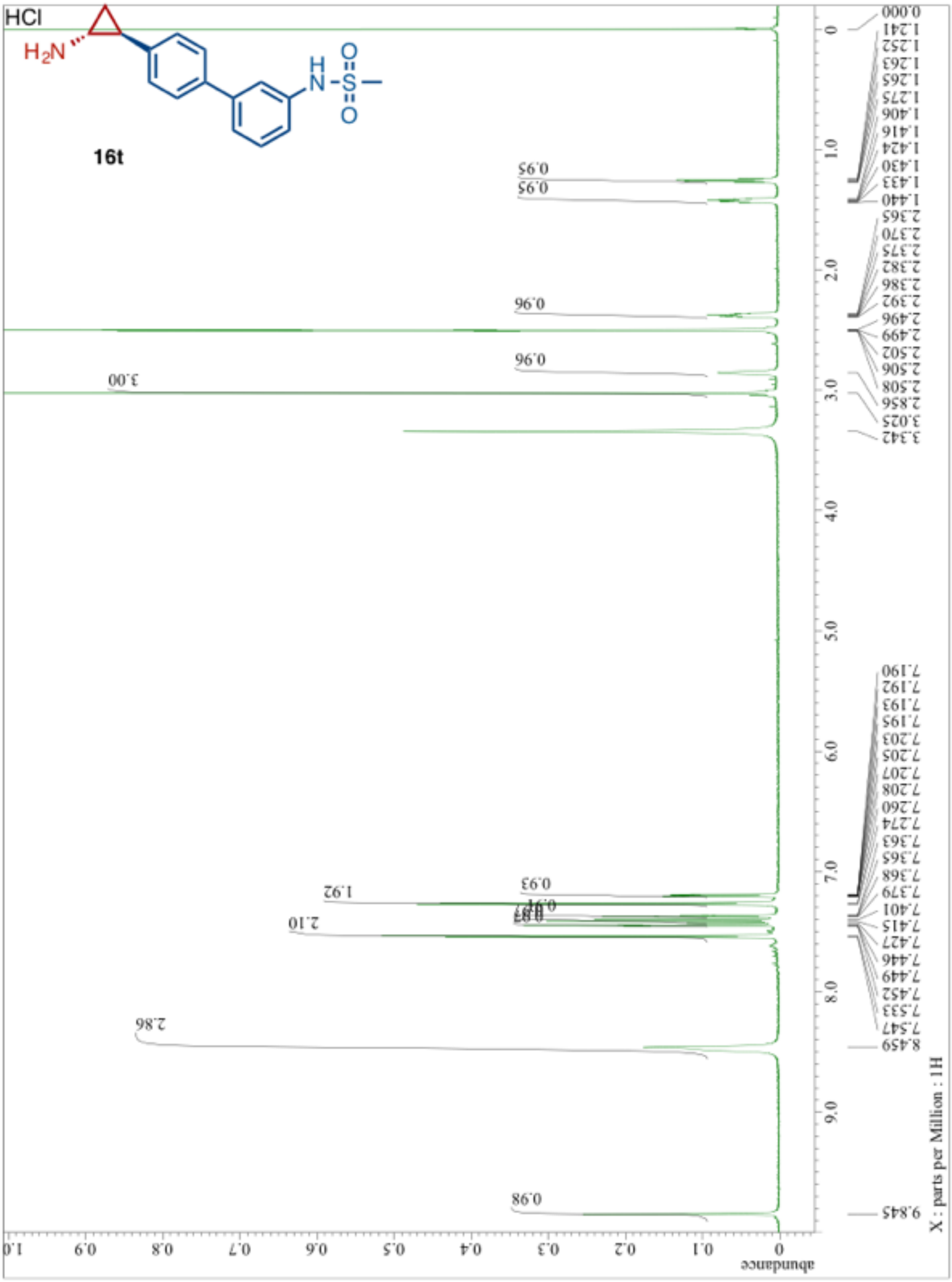
[1]H NMR (600 MHz, DMSO-d_6) of 16s:



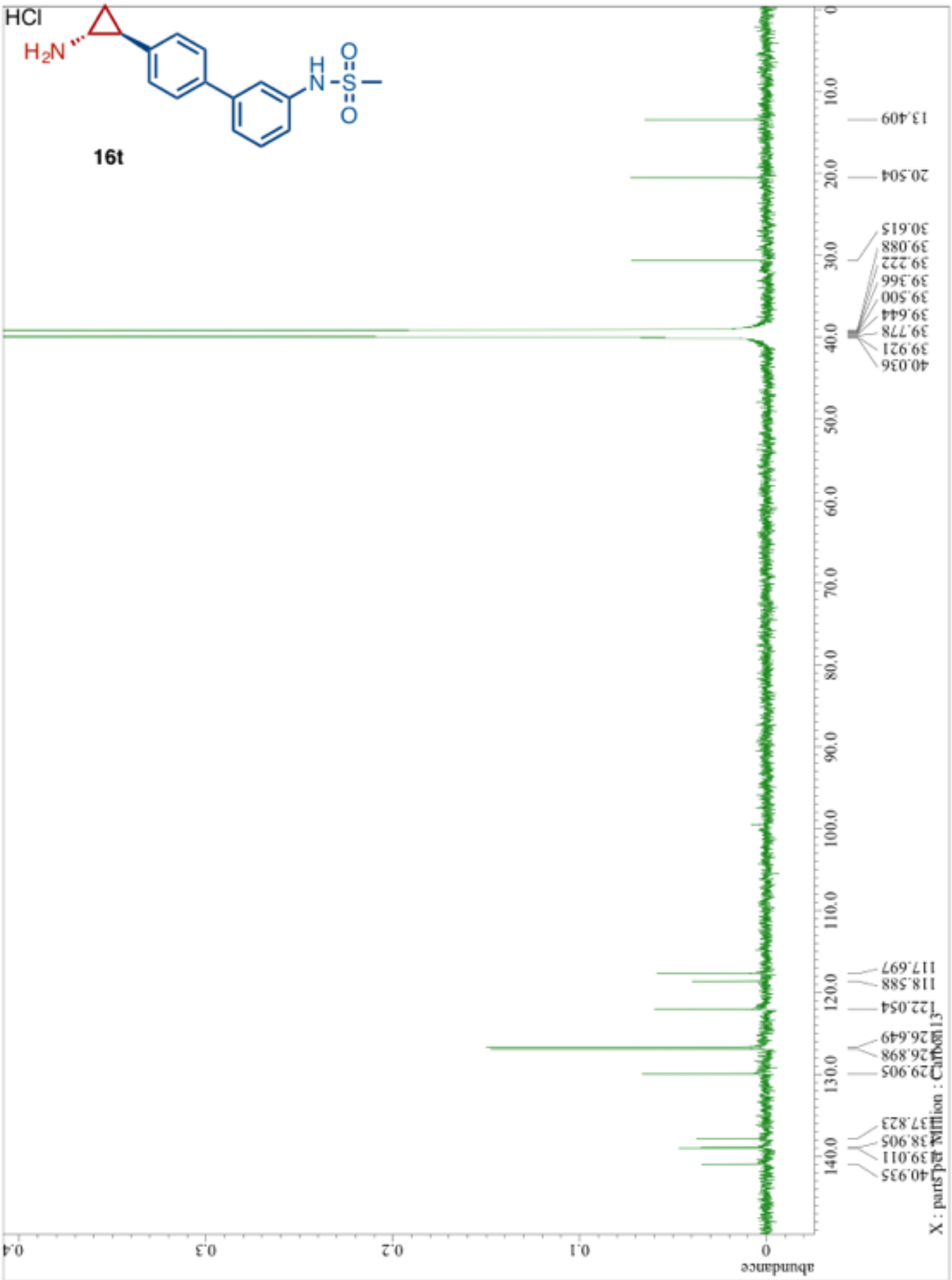
^{13}C NMR (150 MHz, DMSO-d_6) of 16s:



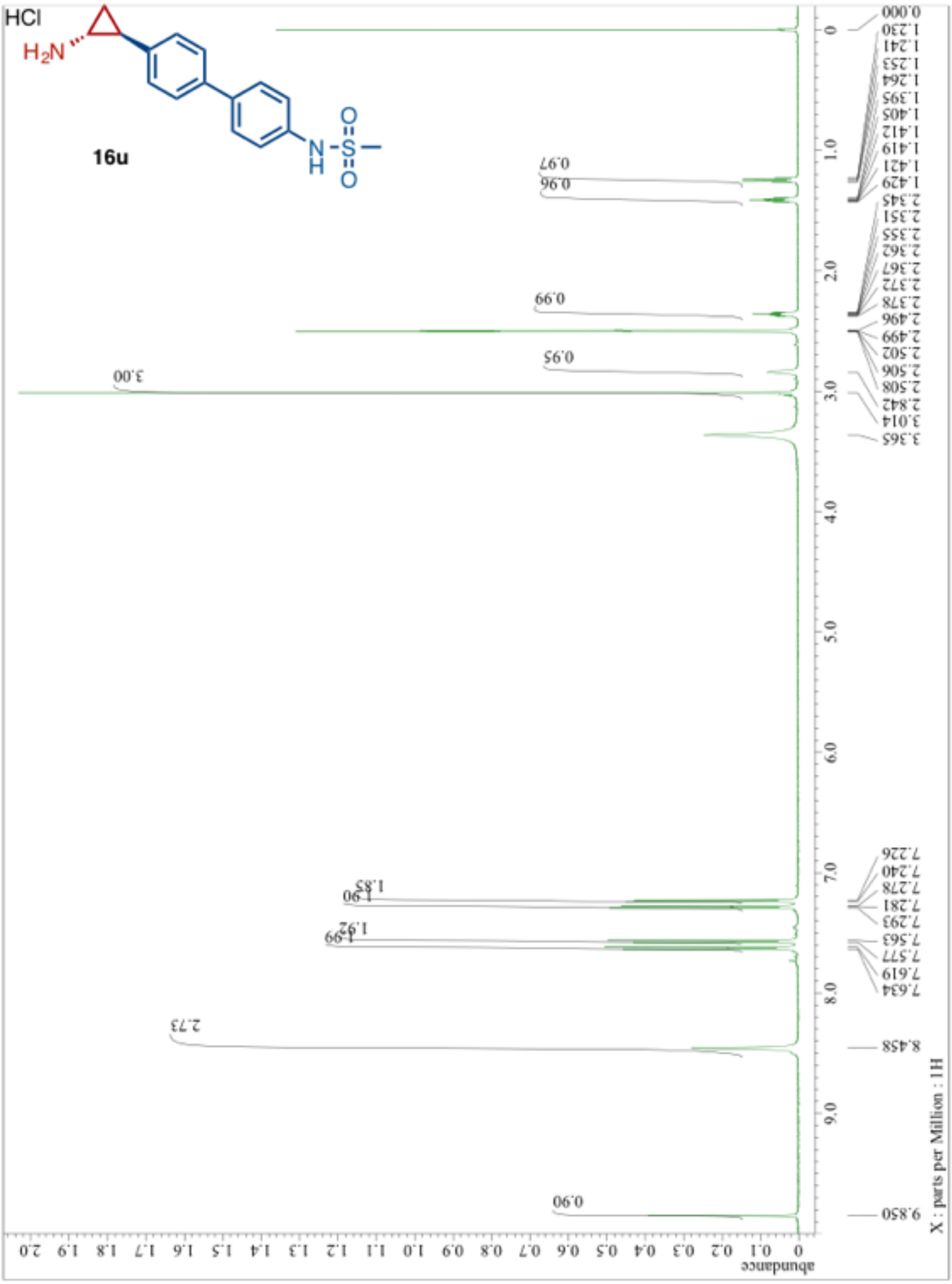
[1]H NMR (600 MHz, DMSO-d_6) of 16t:



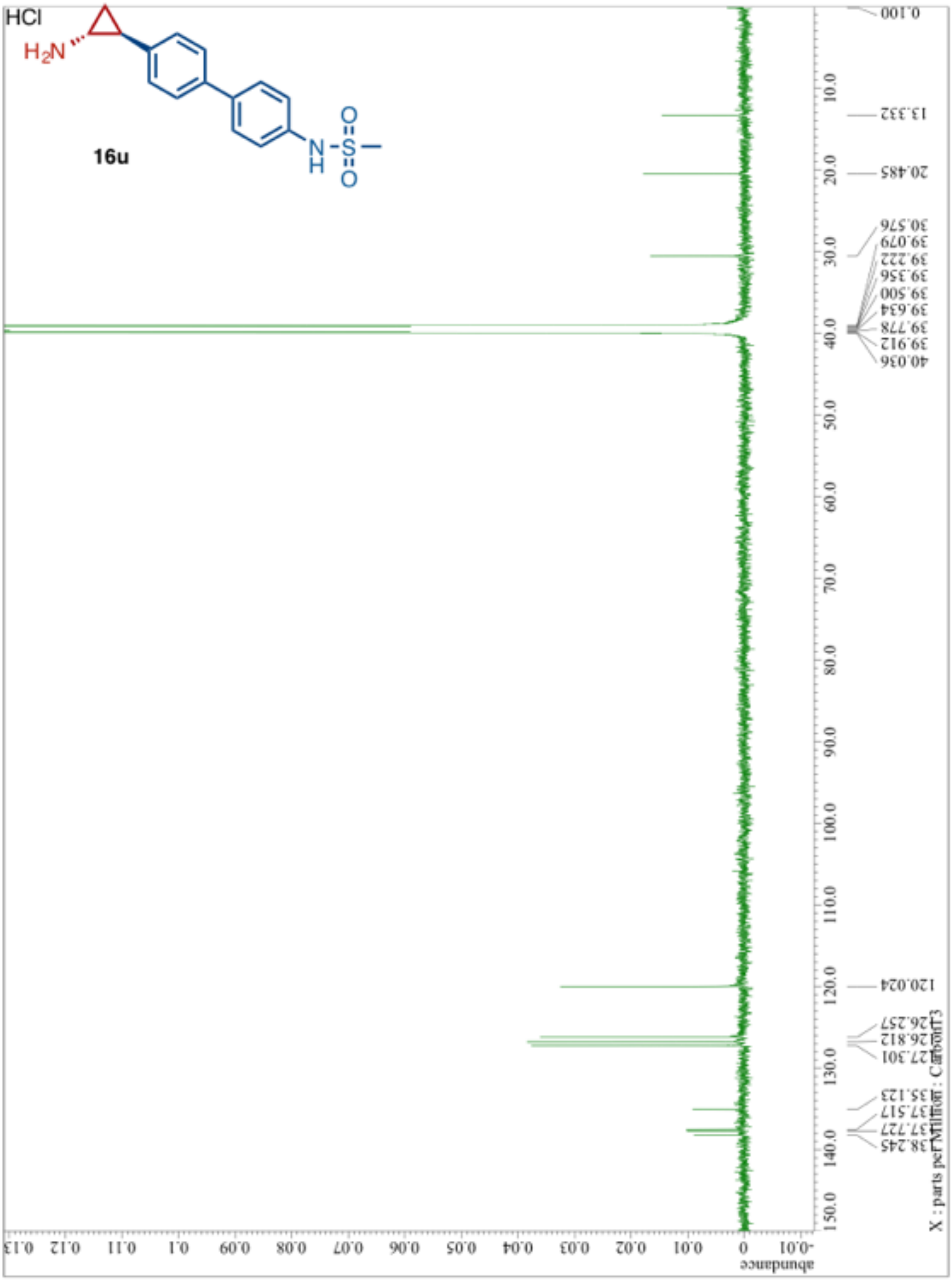
[13]C NMR (150 MHz, DMSO-d_6) of 16t:



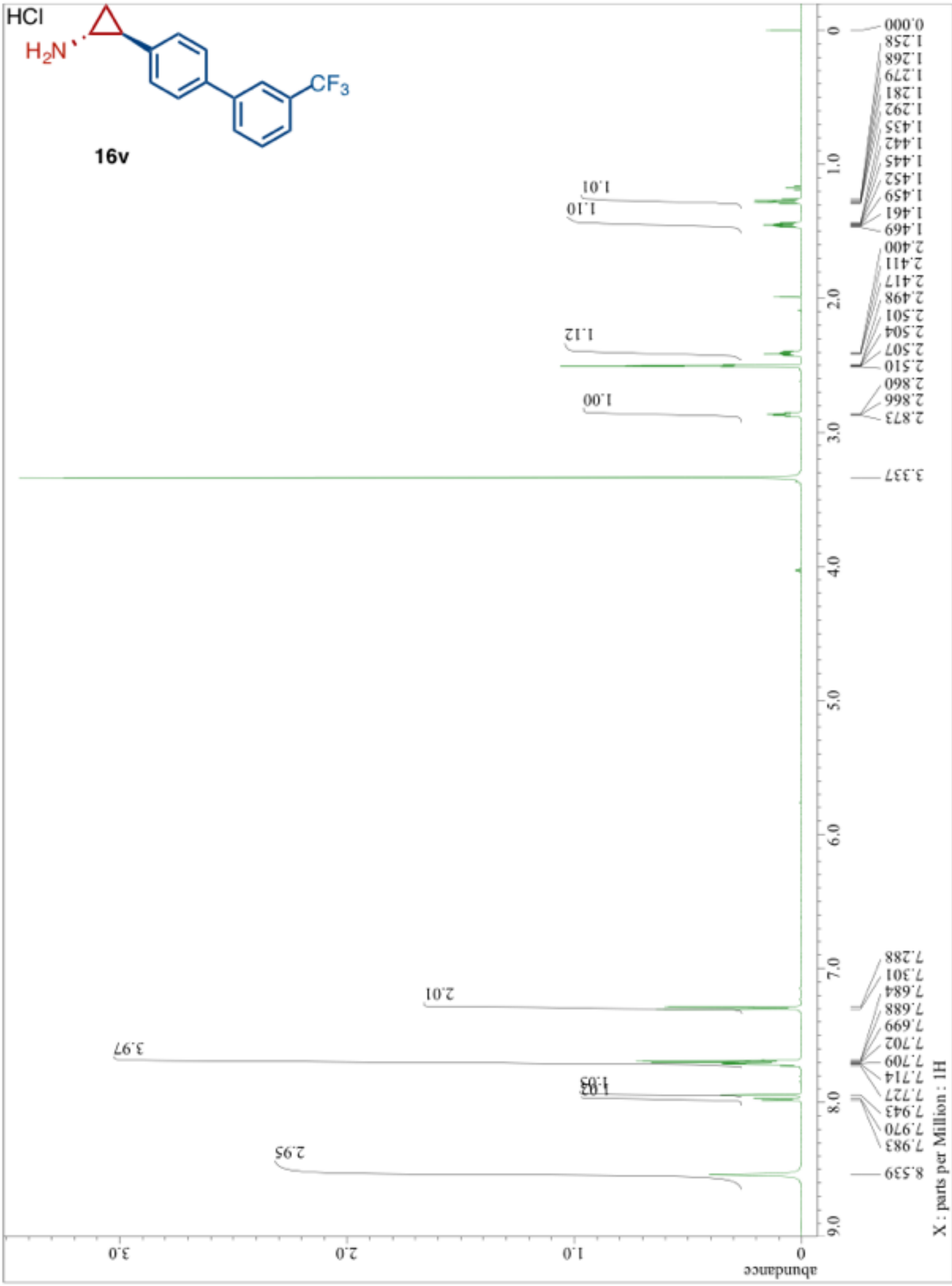
^{1}H NMR (600 MHz, DMSO-d_6) of 16u:



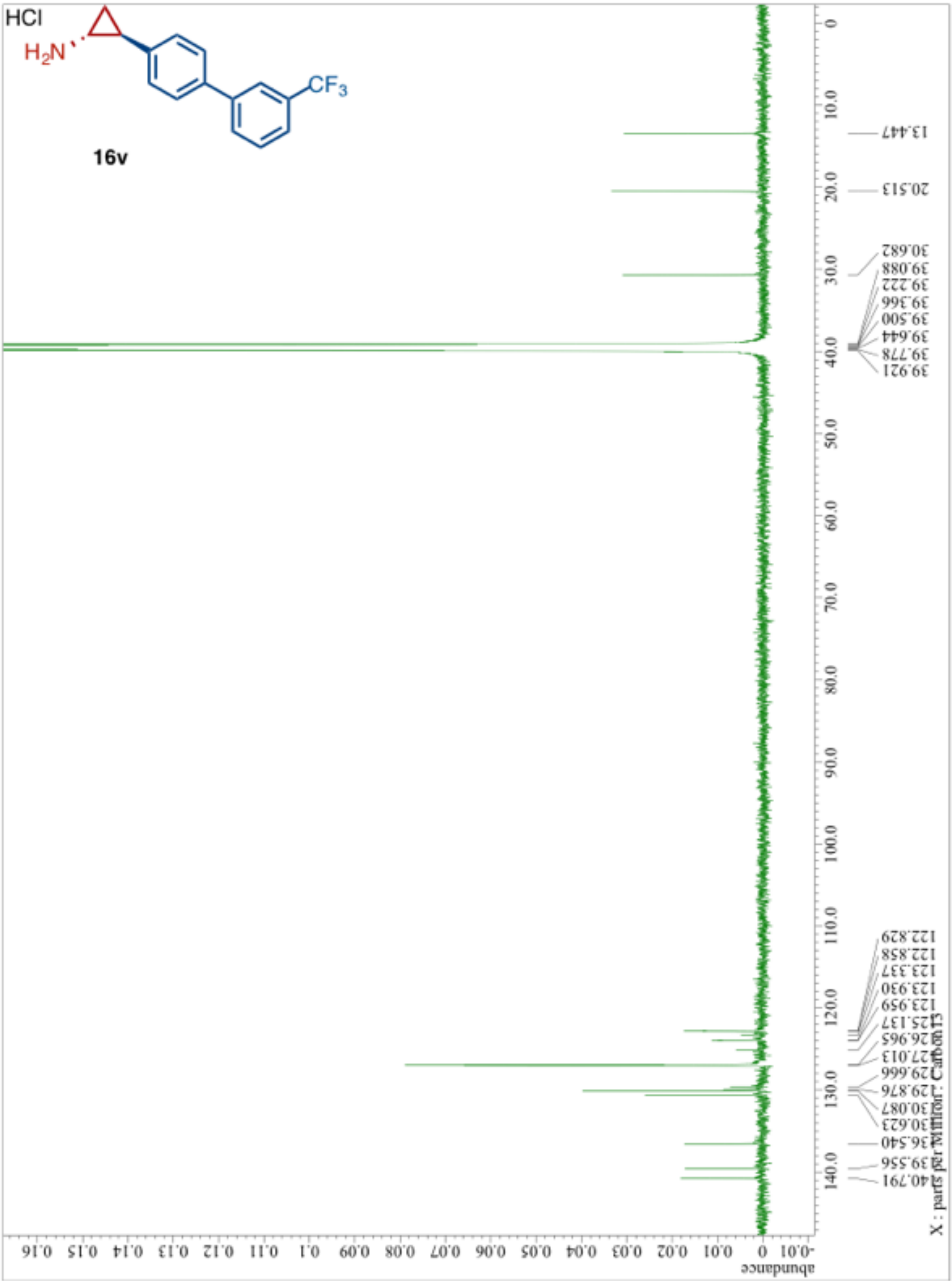
^{13}C NMR (150 MHz, DMSO-d_6) of 16u:



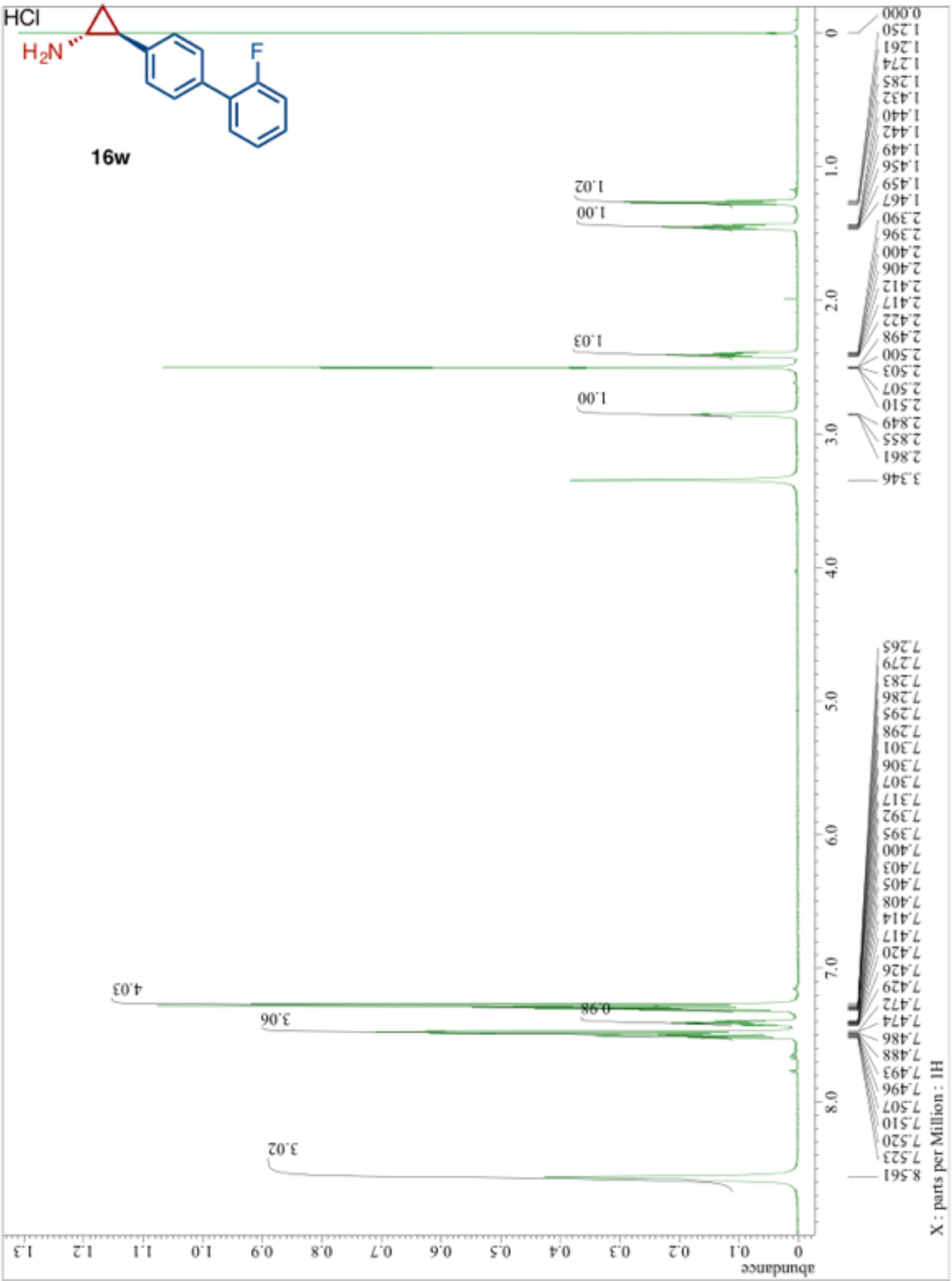
[1]H NMR (600 MHz, DMSO-d_6) of 16v:



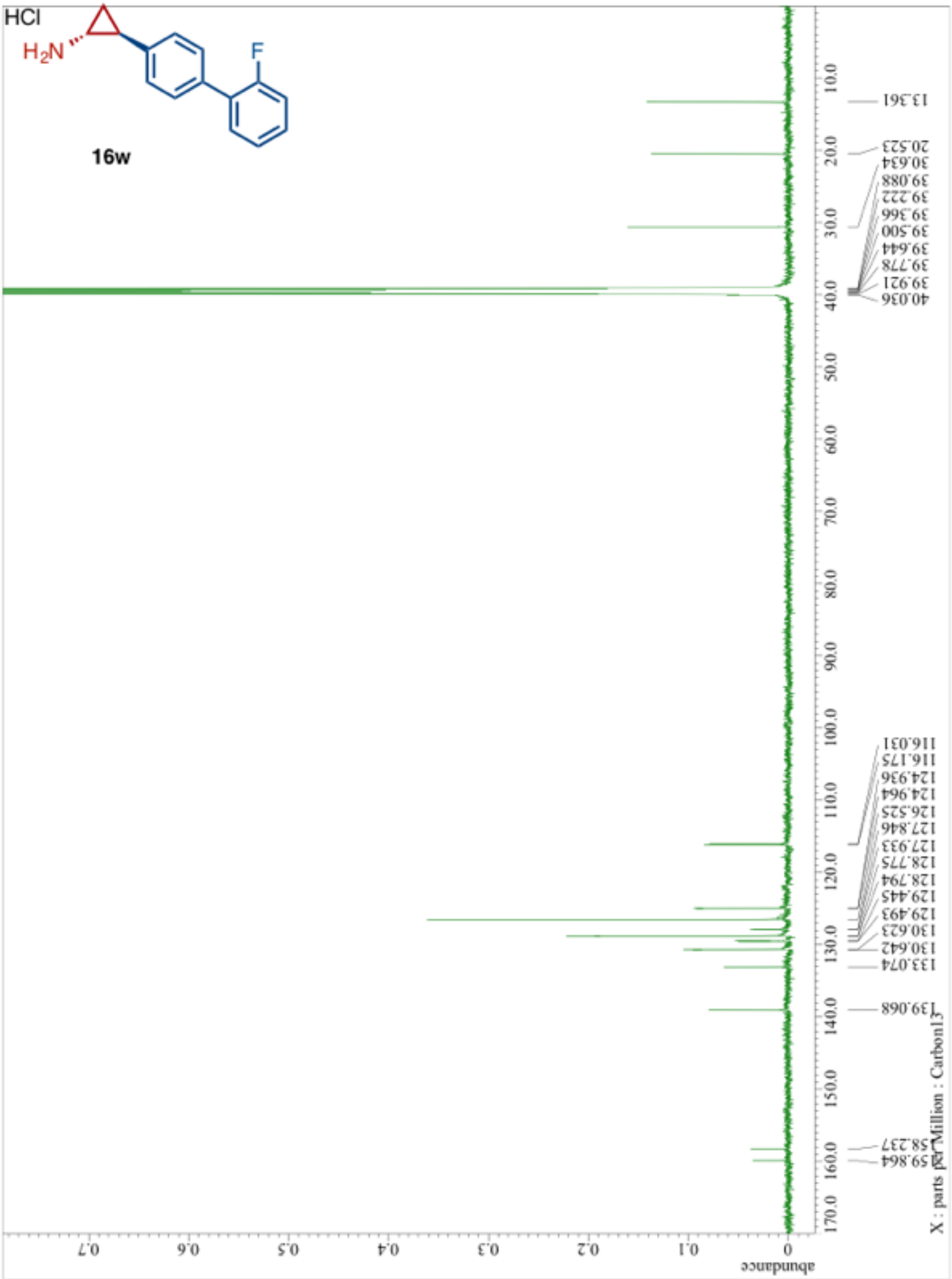
^{13}C NMR (150 MHz, DMSO-d_6) of 16v:



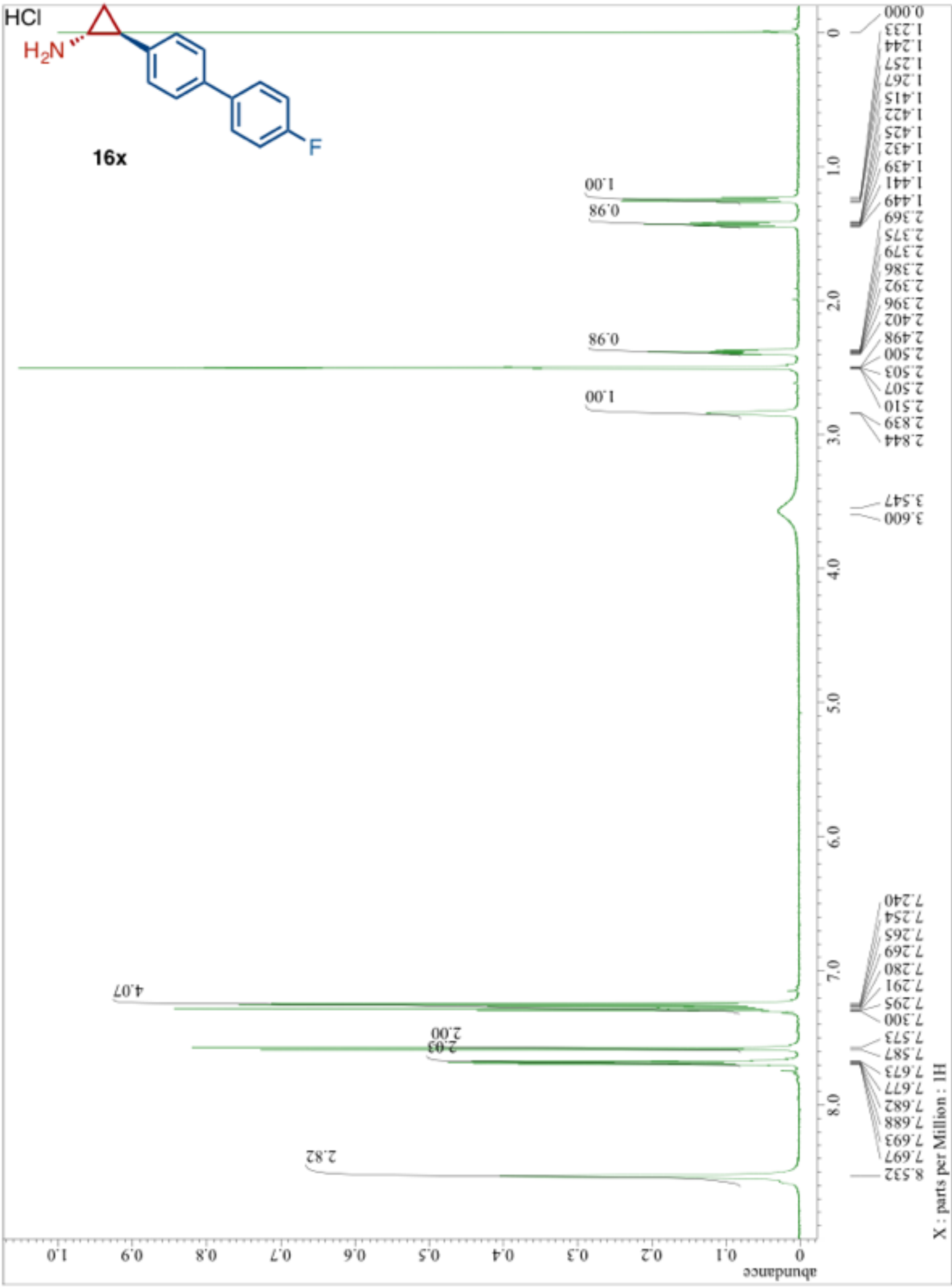
^{1}H NMR (600 MHz, DMSO-d_6) of 16w:



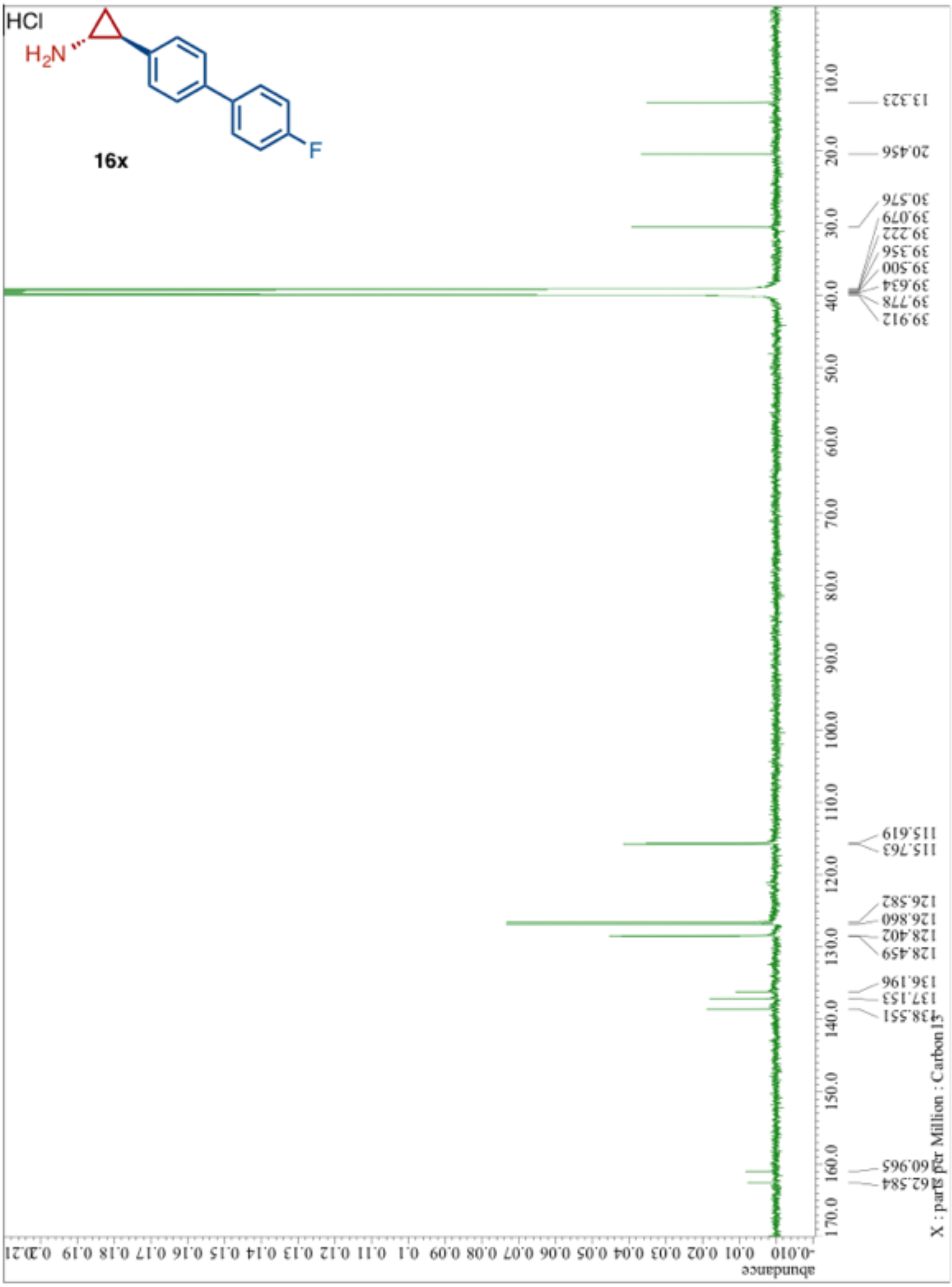
^{13}C NMR (150 MHz, DMSO-d_6) of 16w:



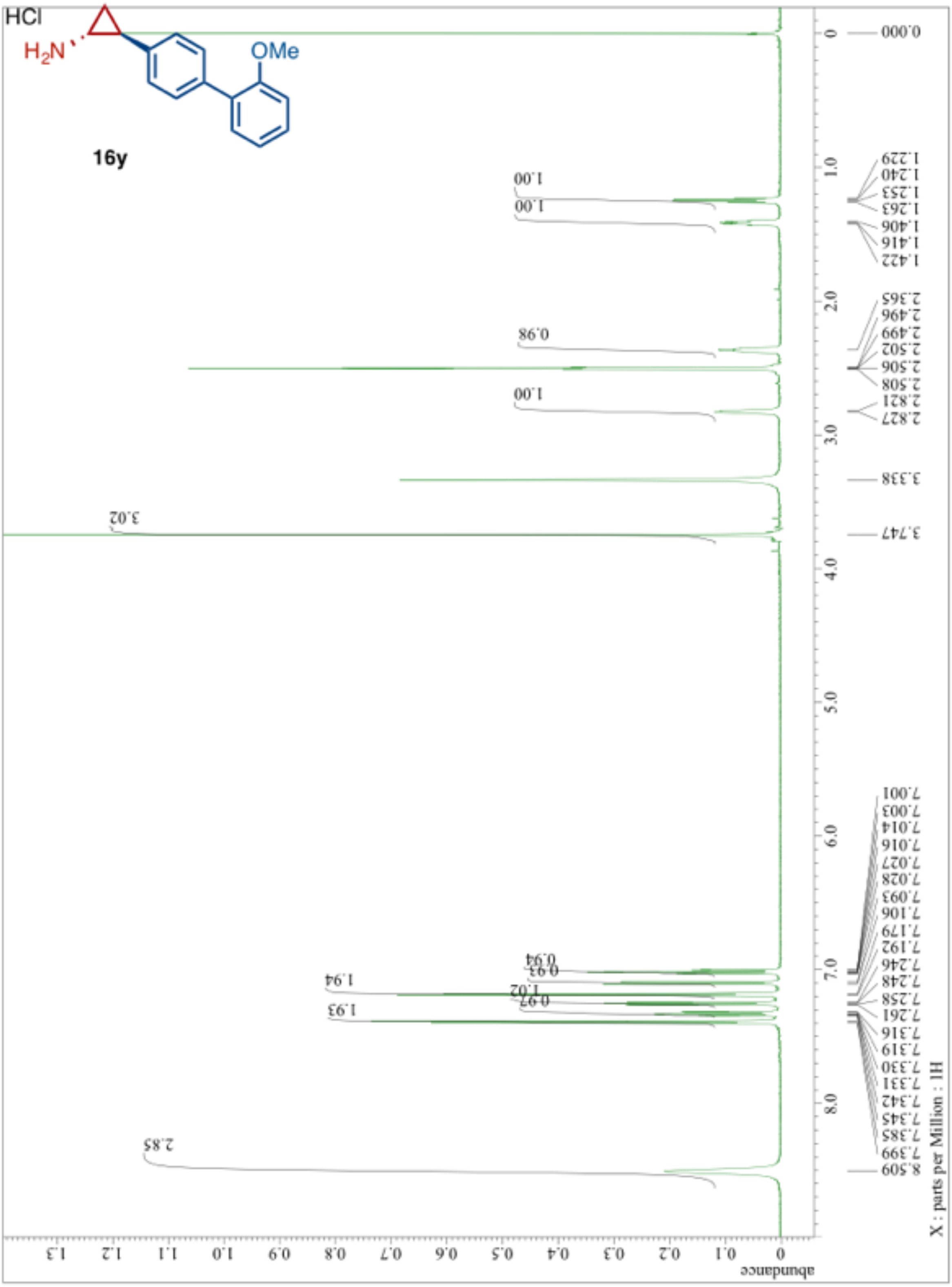
[1]H NMR (600 MHz, DMSO-d_6) of 16x:



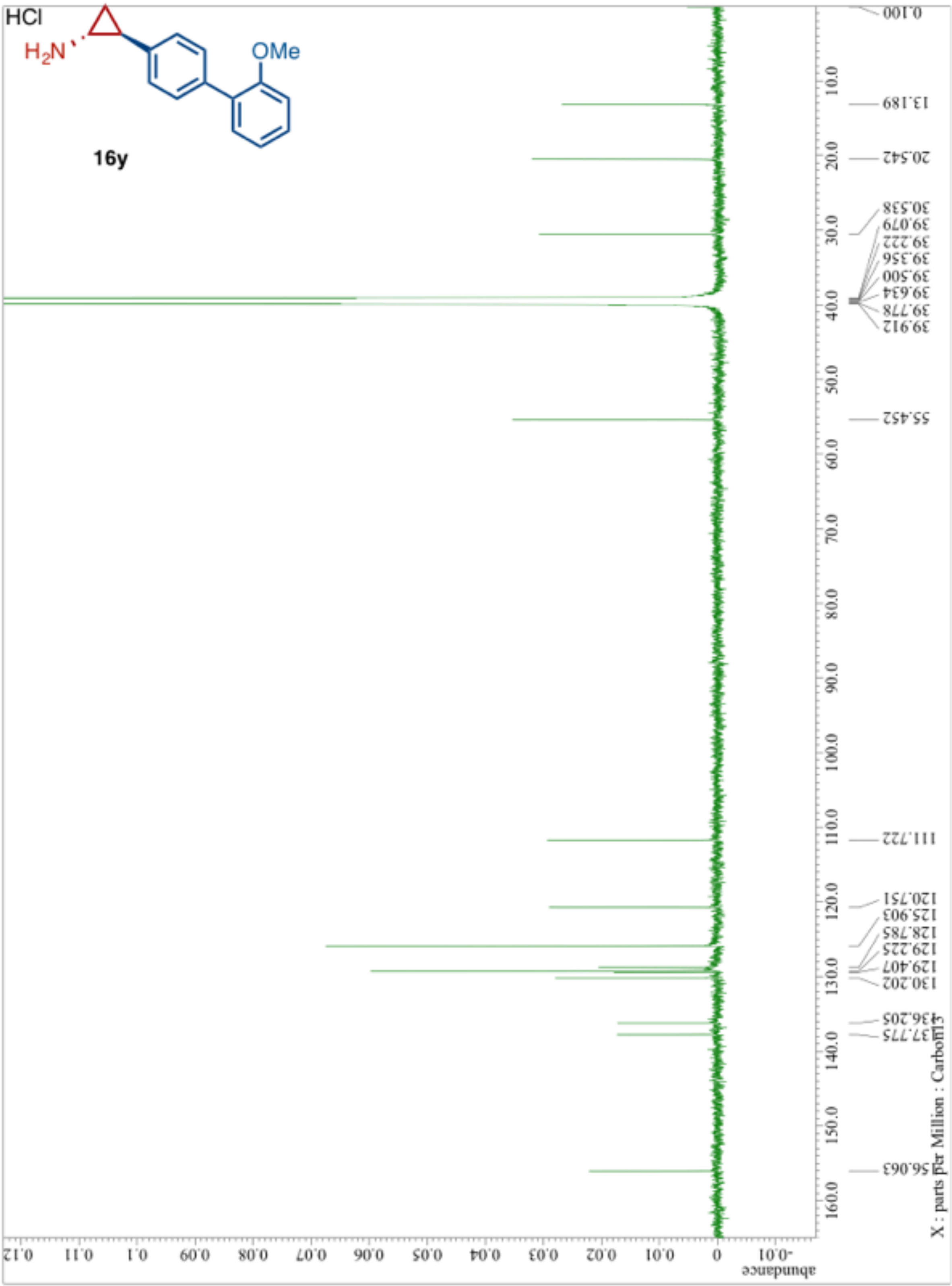
^{13}C NMR (150 MHz, DMSO-d_6) of 16x:



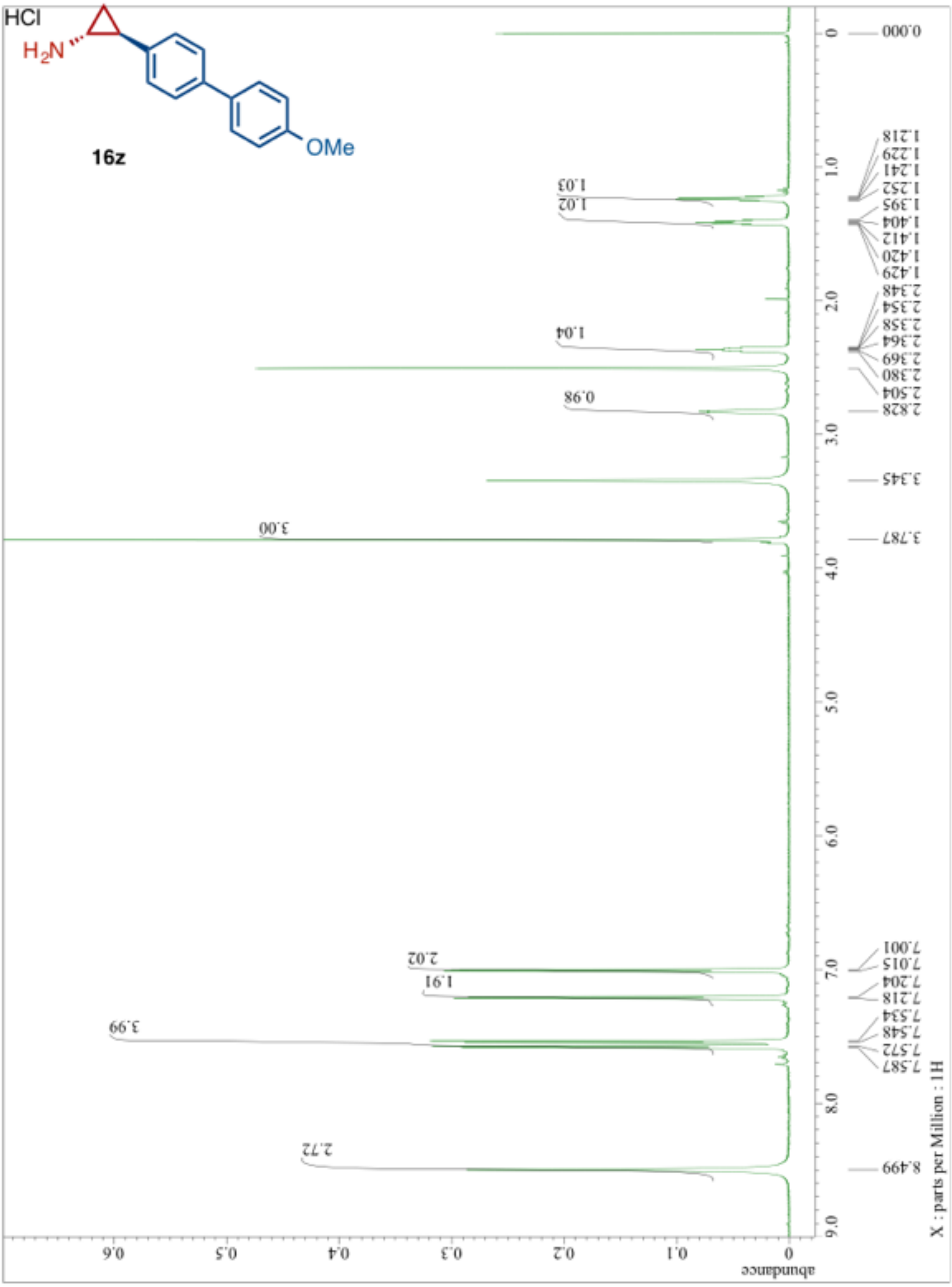
^{1}H NMR (600 MHz, DMSO-d_6) of 16y:



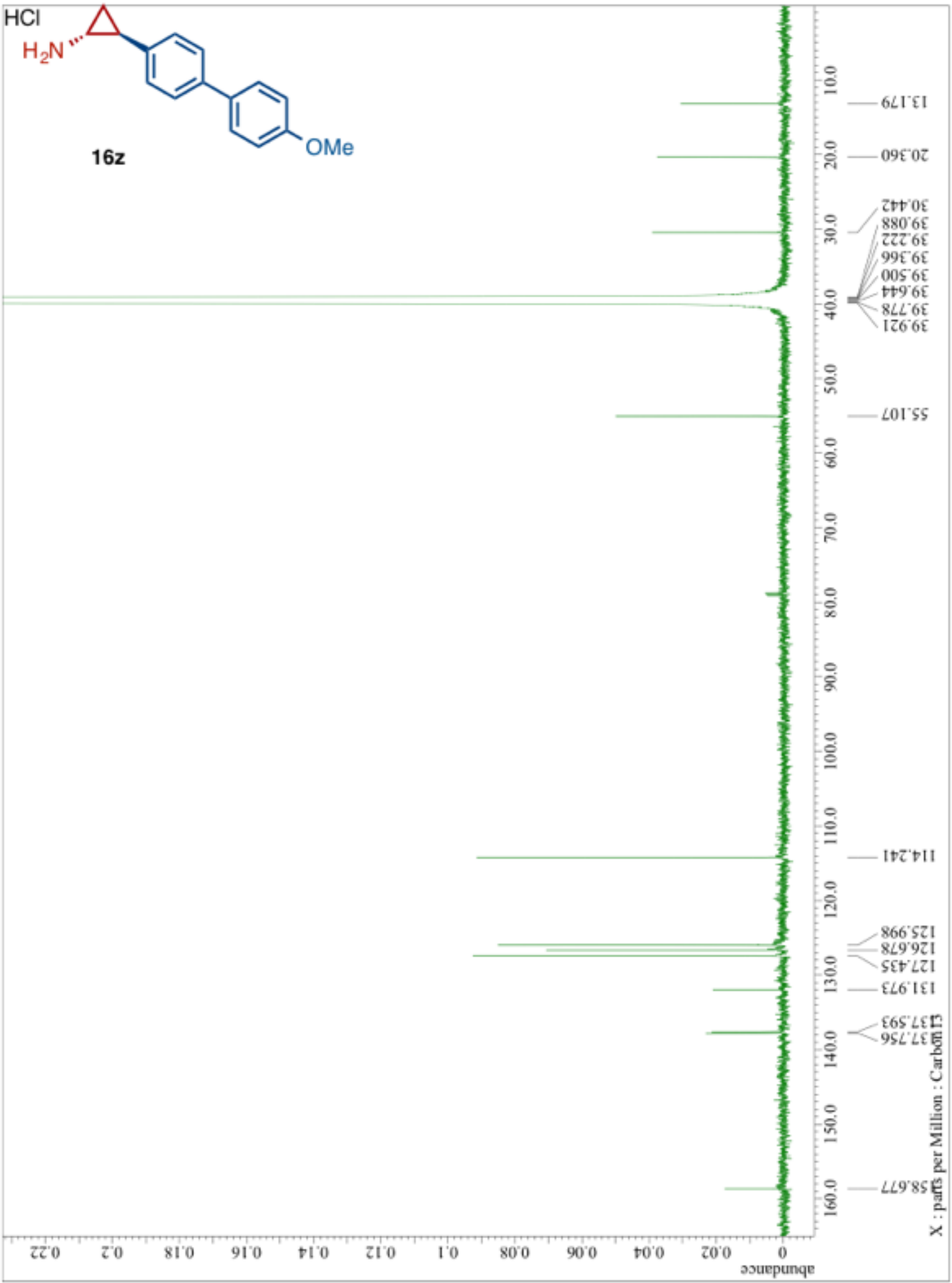
^{13}C NMR (150 MHz, DMSO-d_6) of 16y:



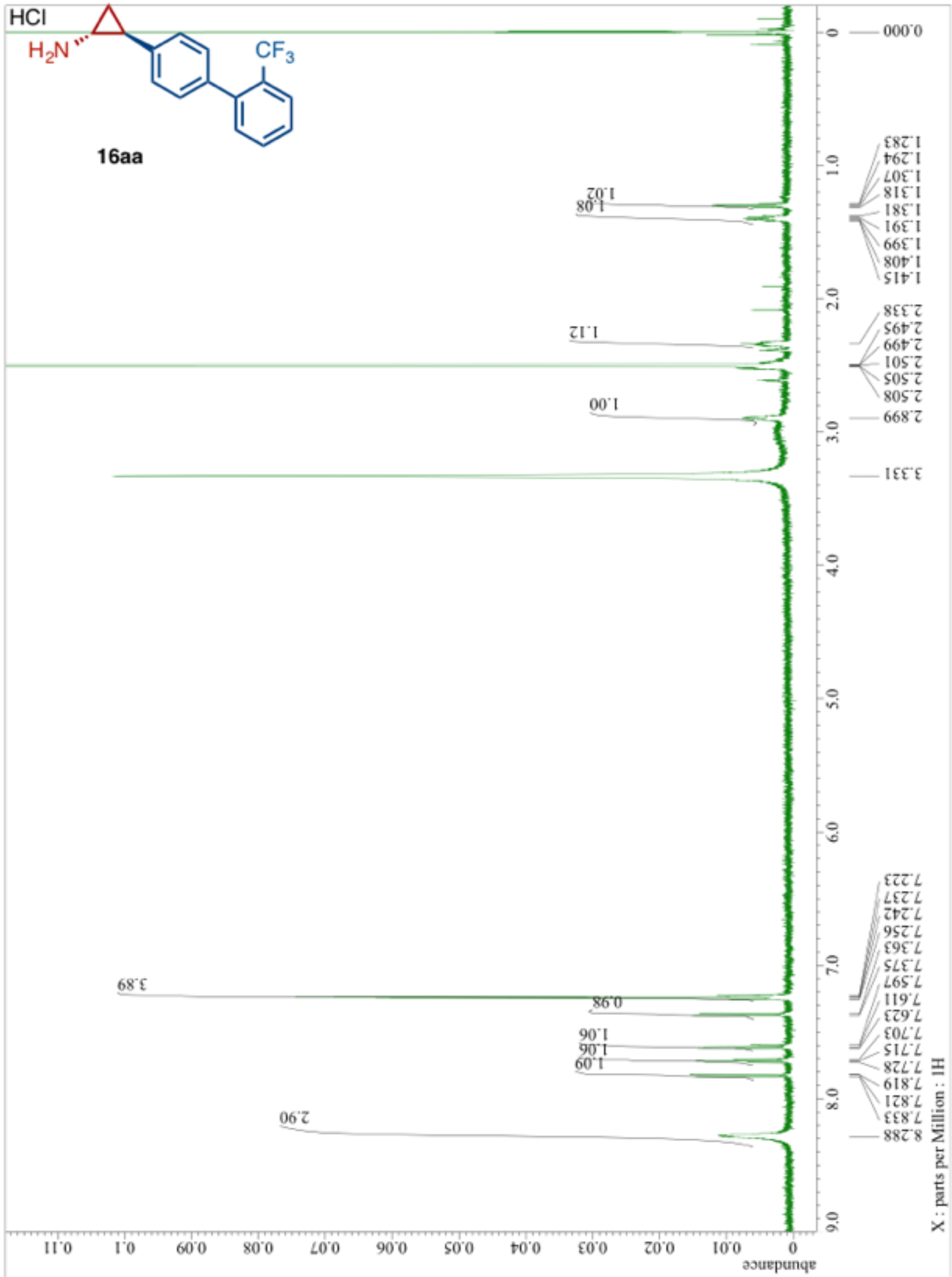
[1]H NMR (600 MHz, DMSO-d_6) of 16z:



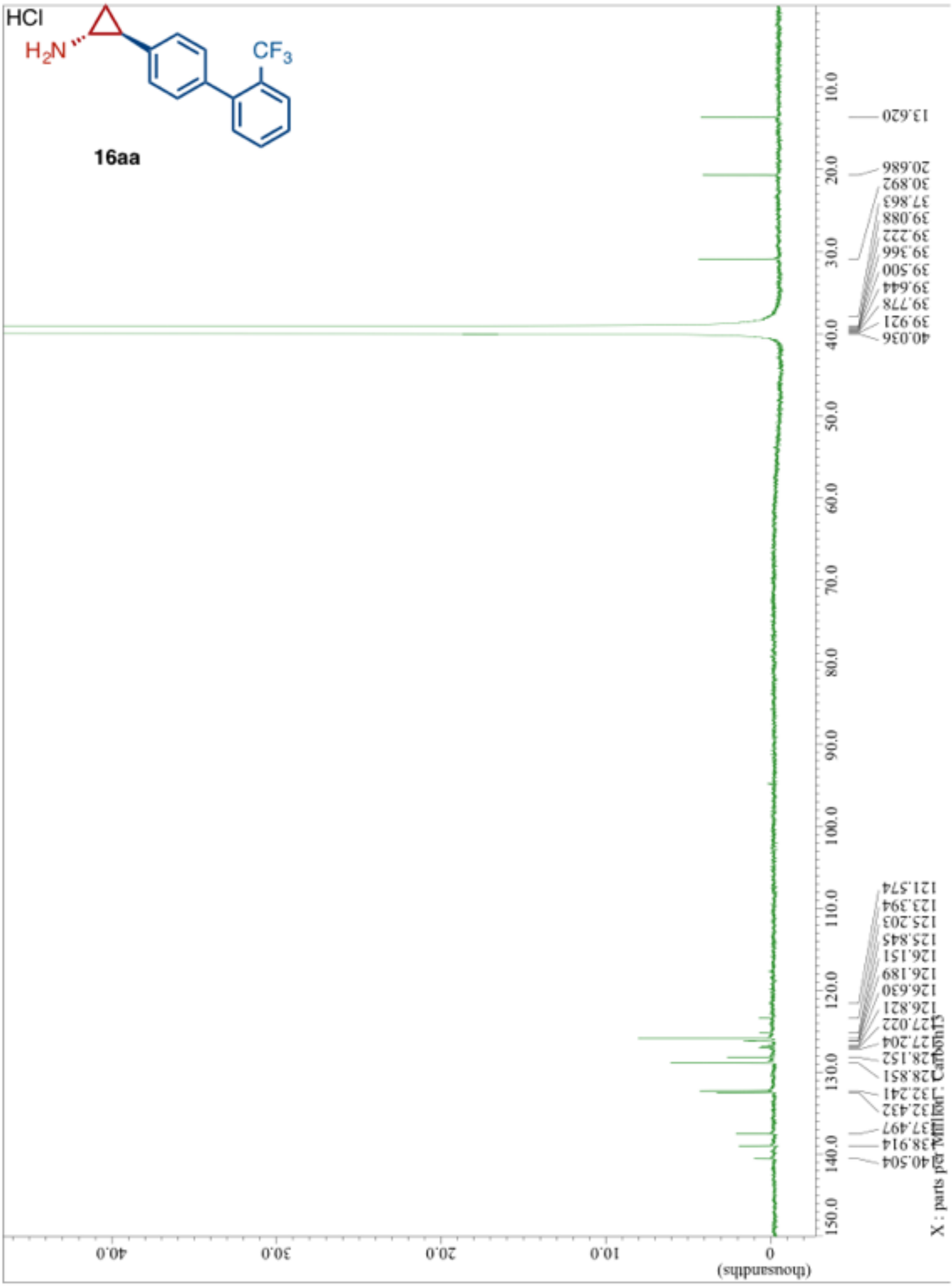
[13]C NMR (150 MHz, DMSO-d_6) of 16z:



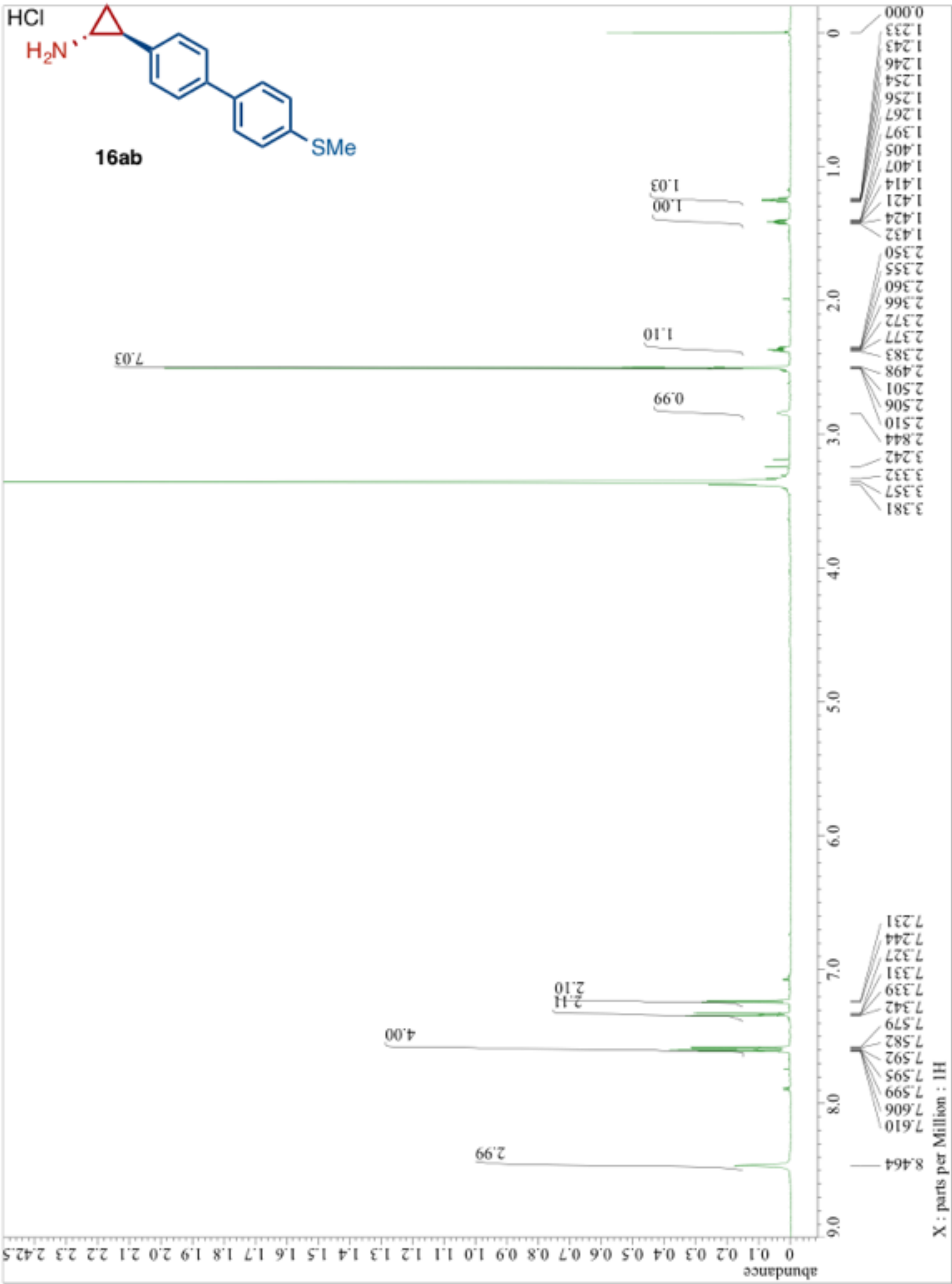
[1]H NMR (600 MHz, DMSO-d_6) of 16aa:



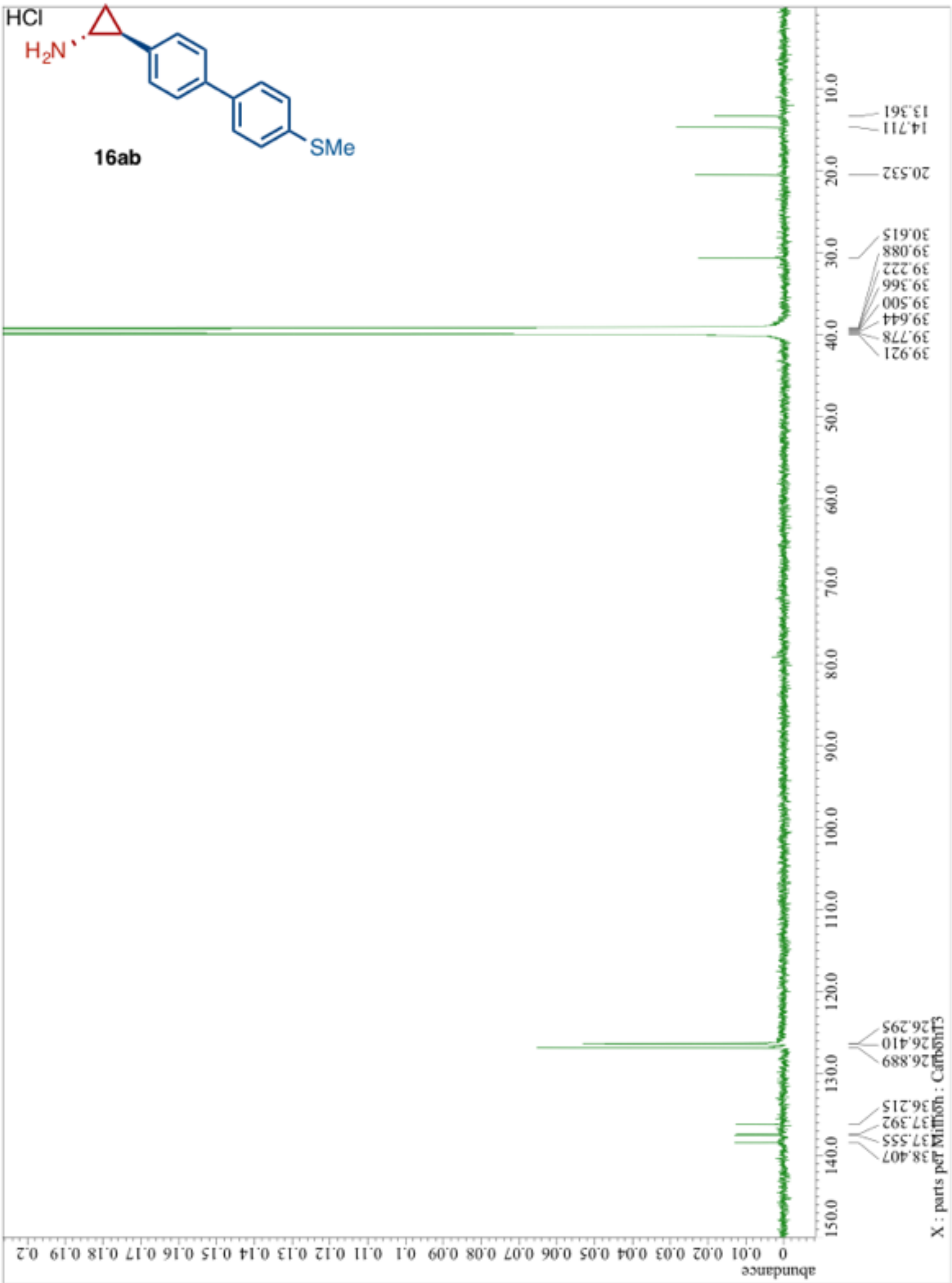
^{13}C NMR (150 MHz, DMSO-d_6) of 16aa:



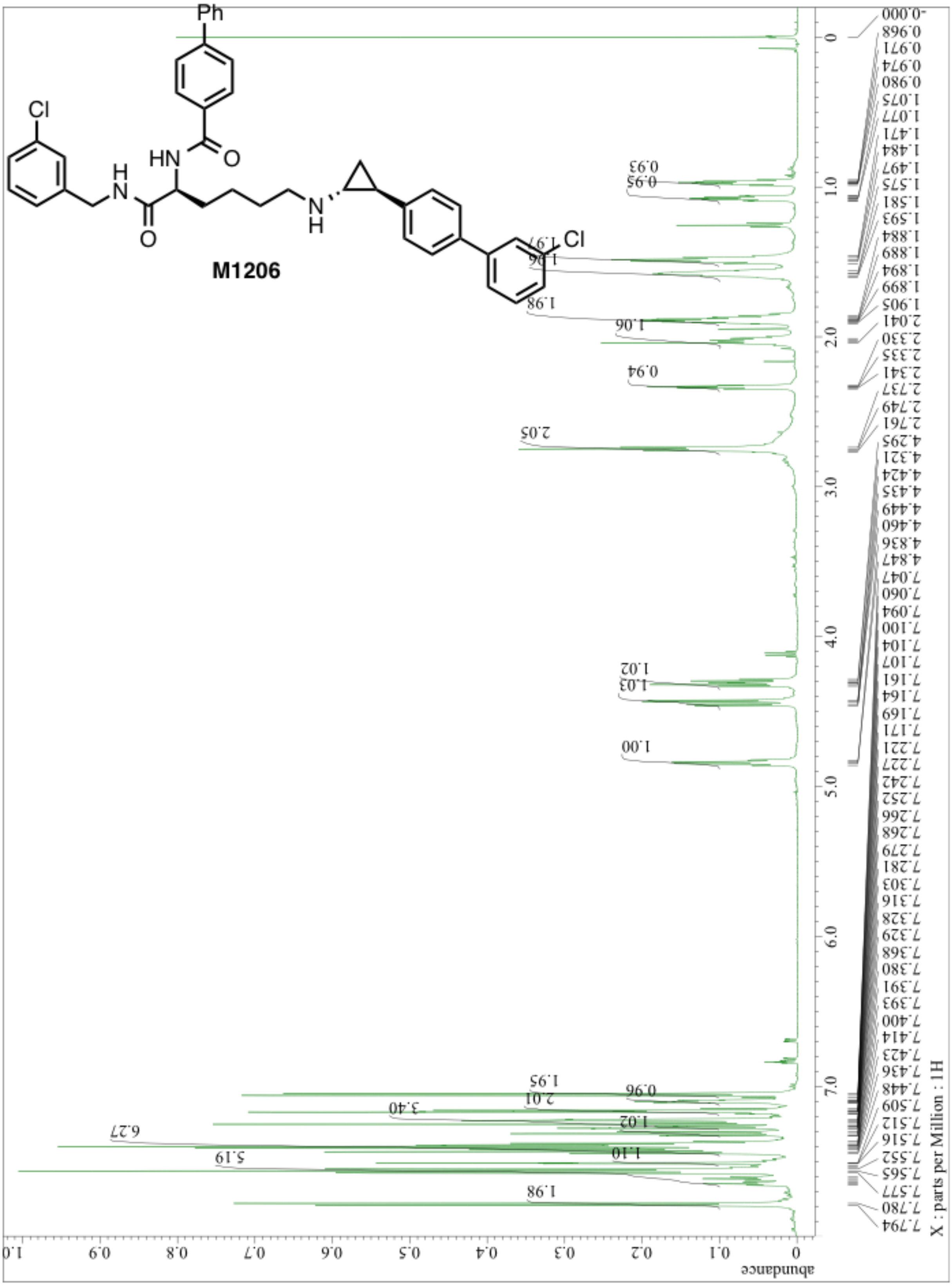
^{1}H NMR (600 MHz, DMSO-d_6) of 16ab:



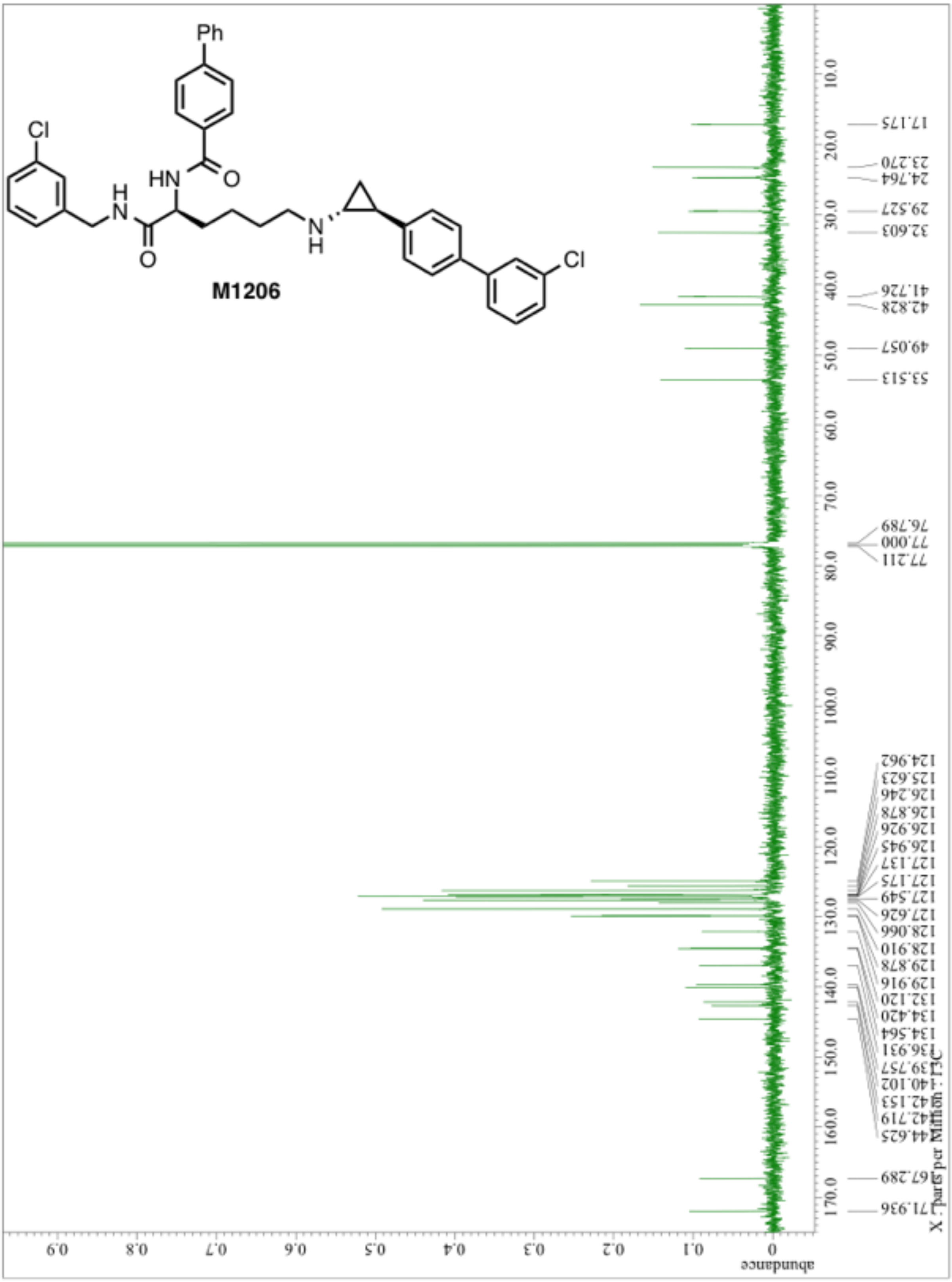
^{13}C NMR (150 MHz, DMSO-d_6) of 16ab:



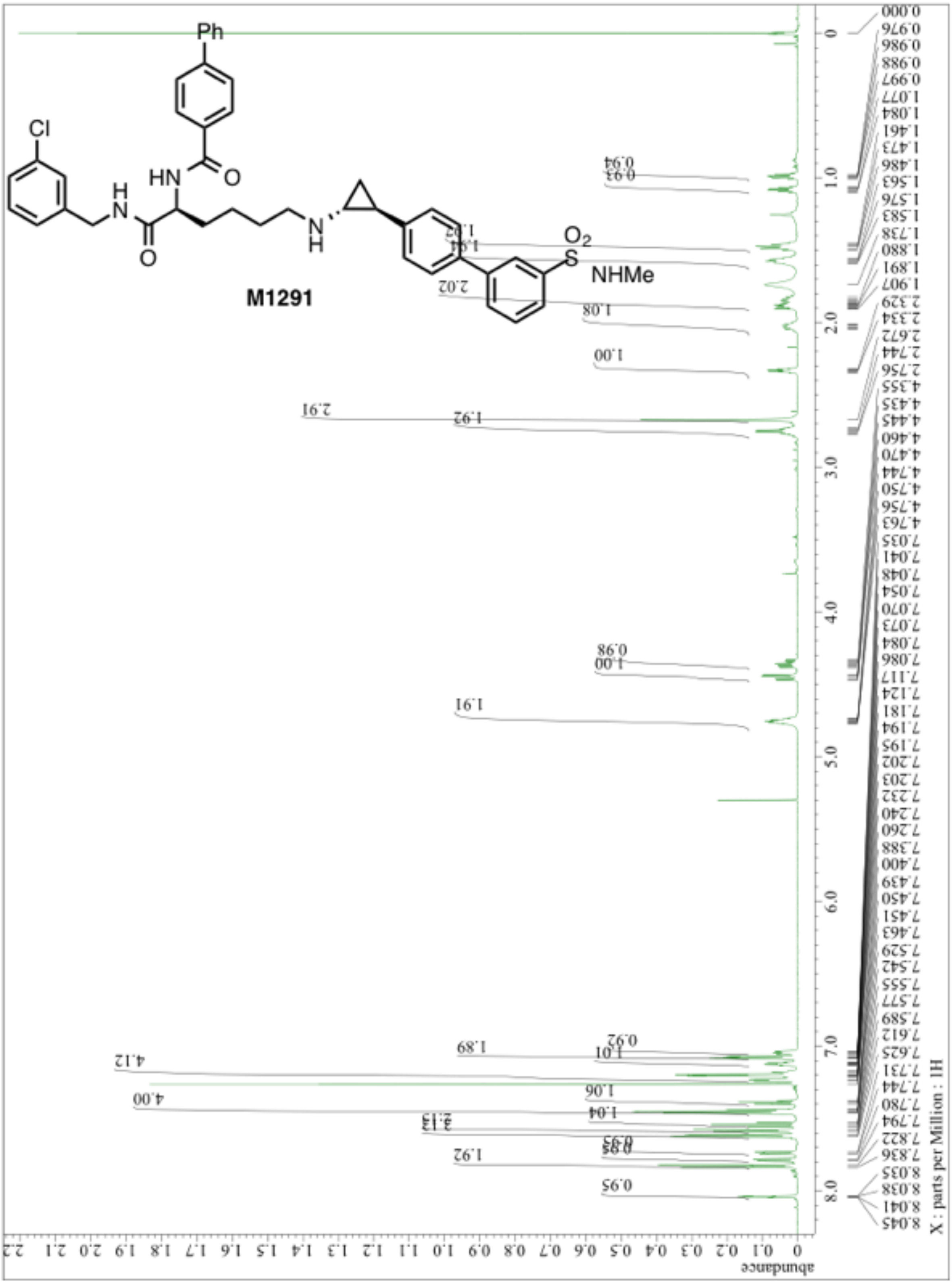
[1]H NMR (600 MHz, $CDCl_3$) of M1206:



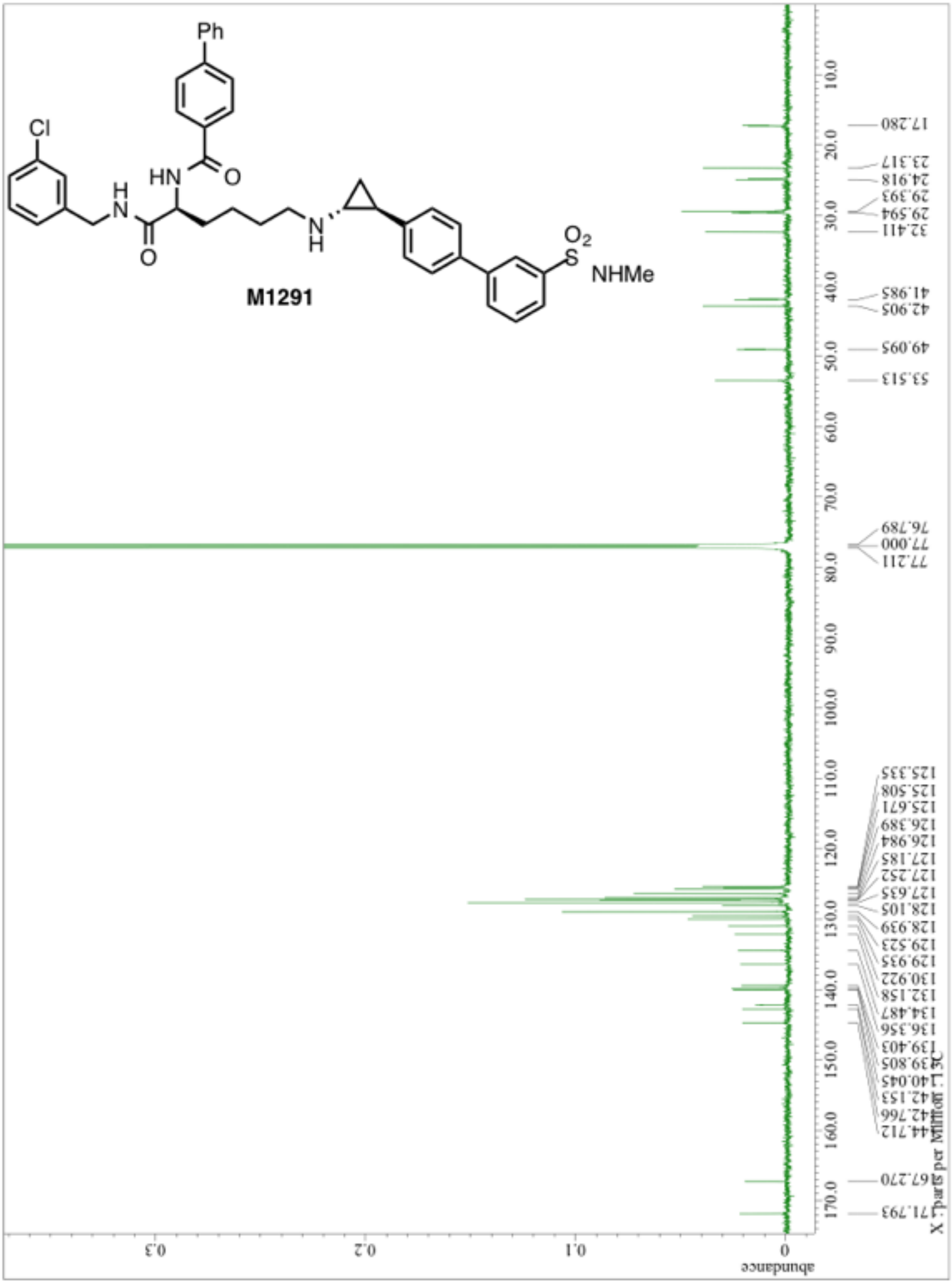
^{13}C NMR (150 MHz, CDCl$_3$) of M1206:



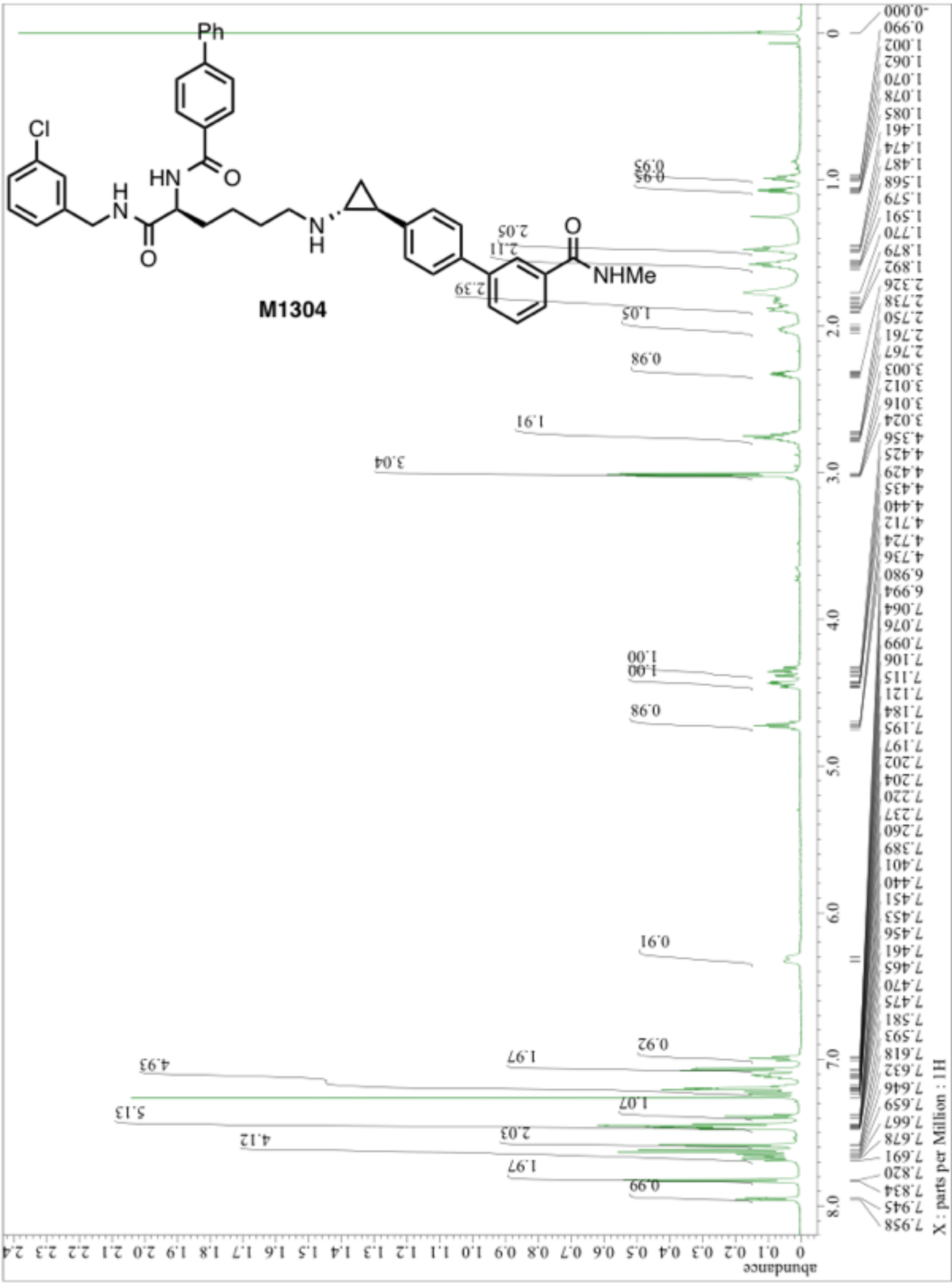
^{1}H NMR (600 MHz, CDCl$_3$) of M1291:



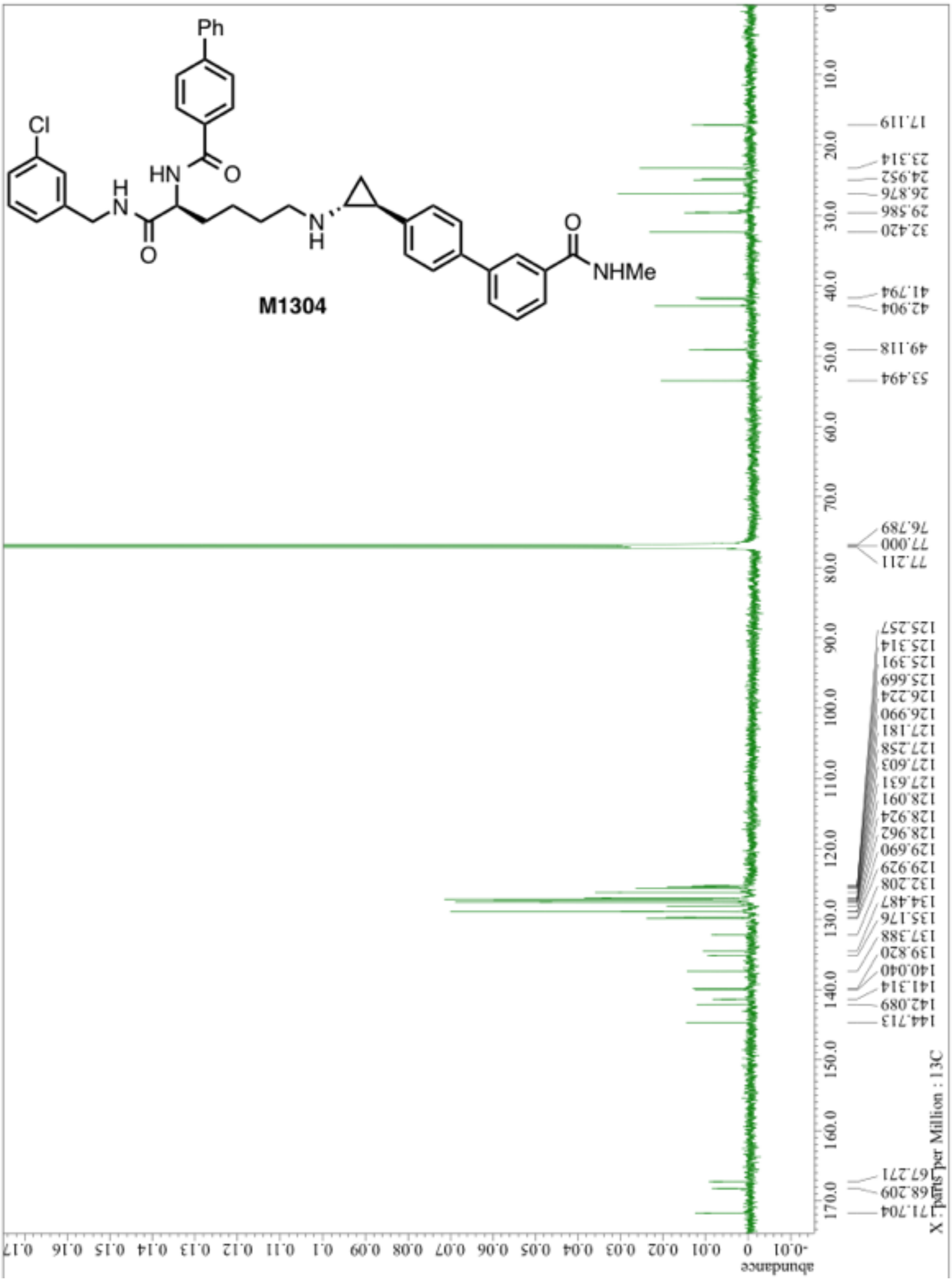
^{13}C NMR (150 MHz, CDCl$_3$) of M1291:



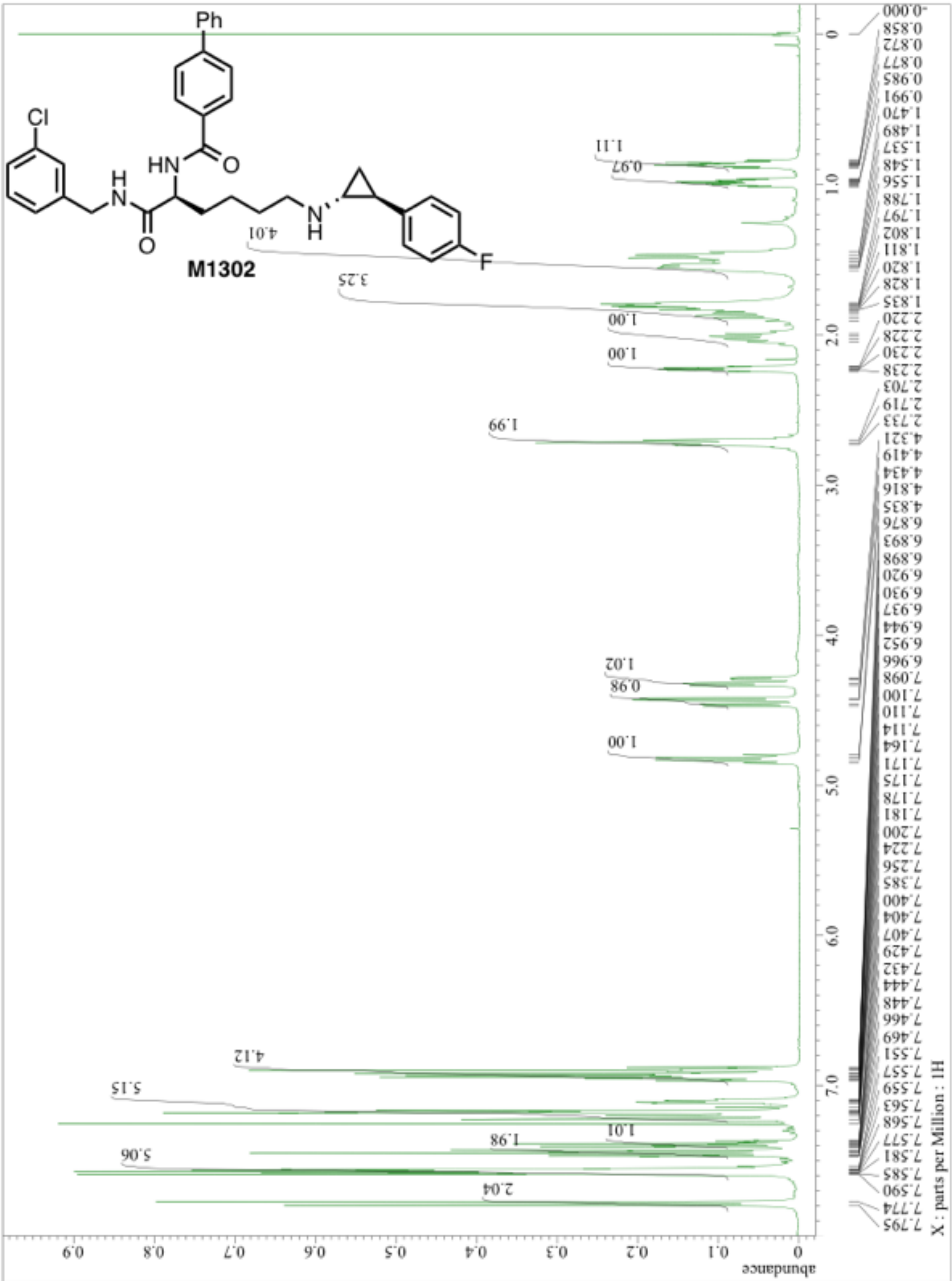
^{1}H NMR (600 MHz, $CDCl_3$) of M1304:



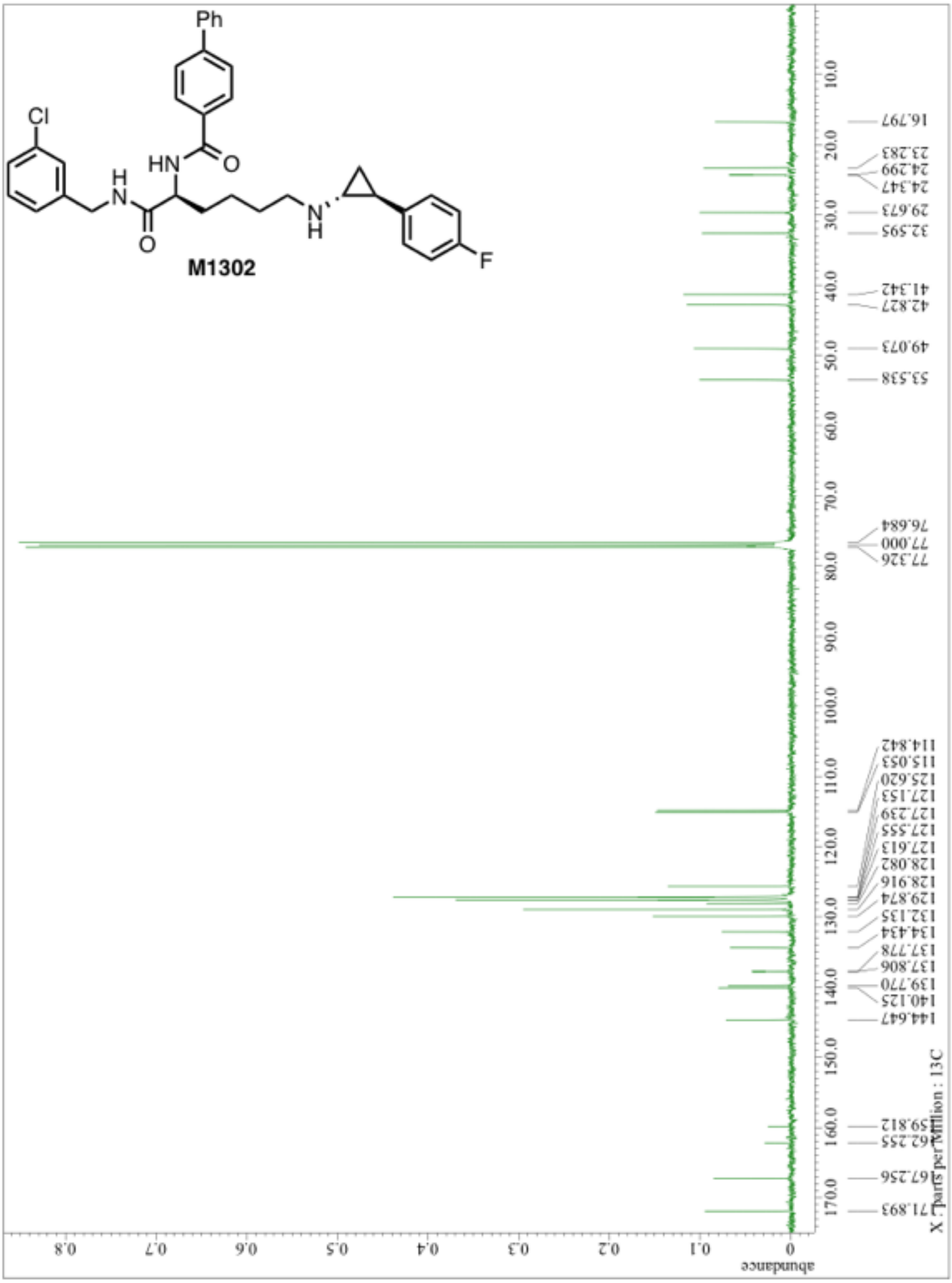
^{13}C NMR (150 MHz, CDCl$_3$) of M1304:



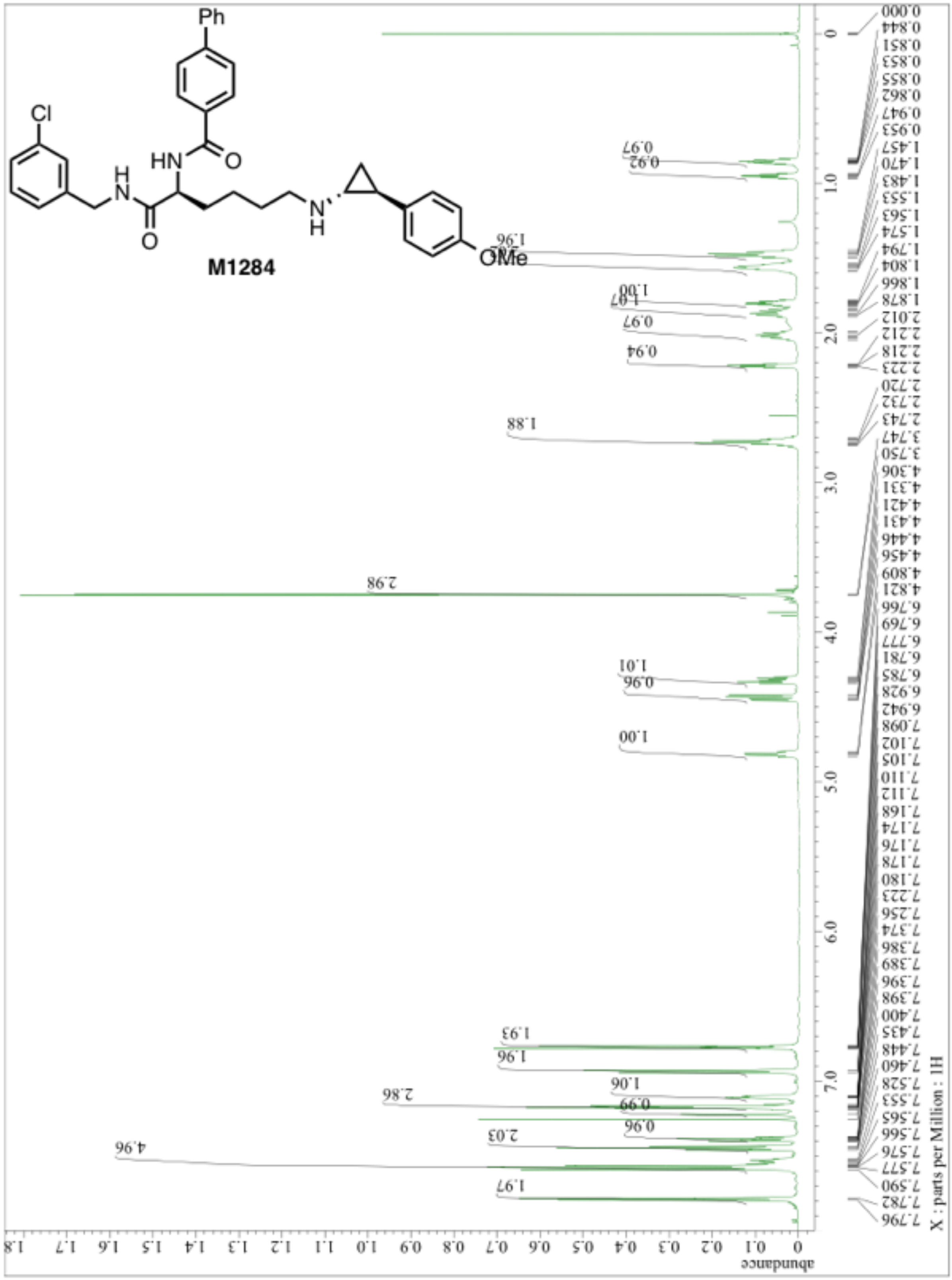
[1]H NMR (400 MHz, $CDCl_3$) of M1302:



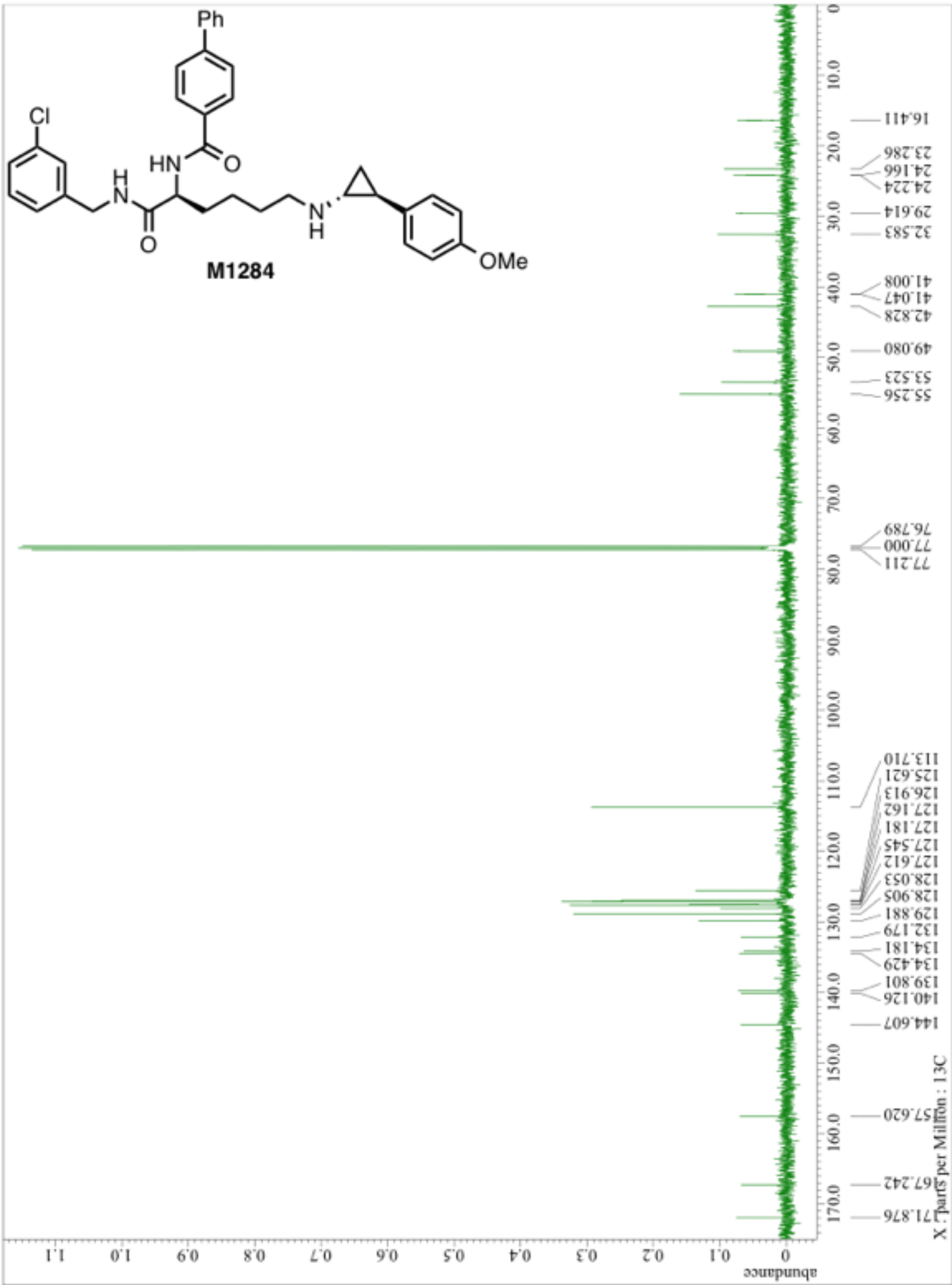
^{13}C NMR (100 MHz, $CDCl_3$) of M1302:



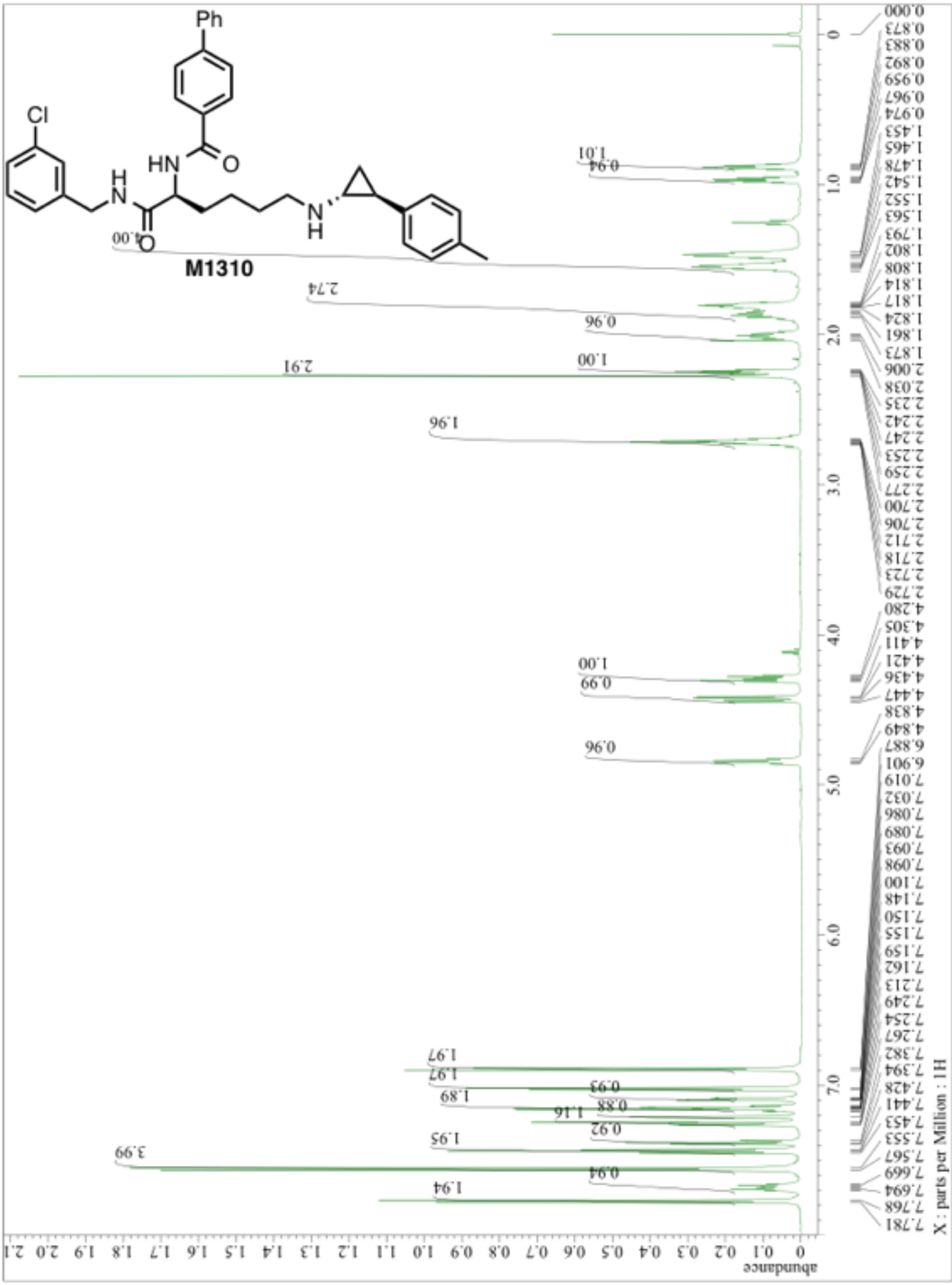
^{1}H NMR (600 MHz, $CDCl_3$) of M1284:



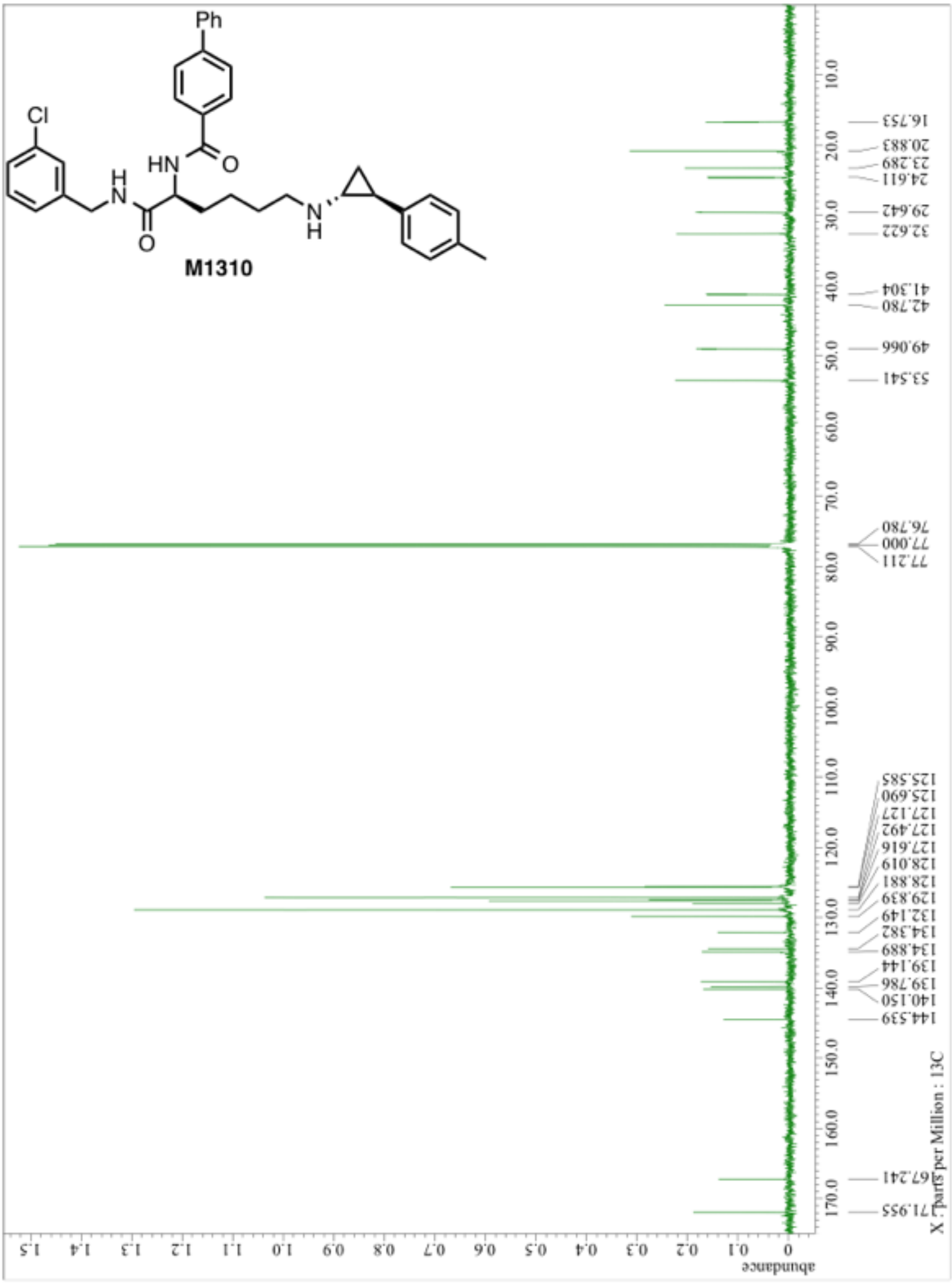
[13]C NMR (150 MHz, $CDCl_3$) of M1284:



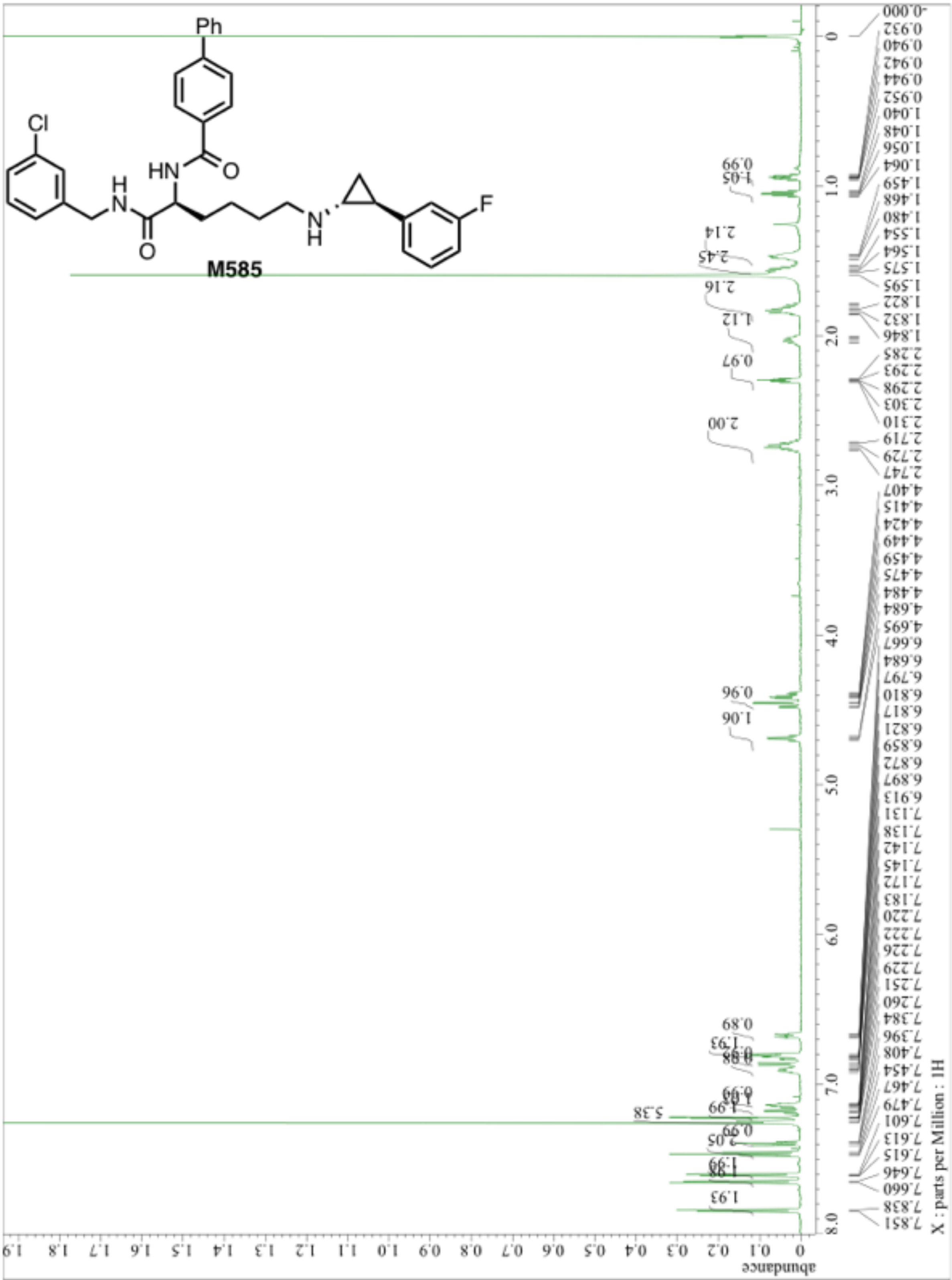
[1]H NMR (600 MHz, $CDCl_3$) of M1310:



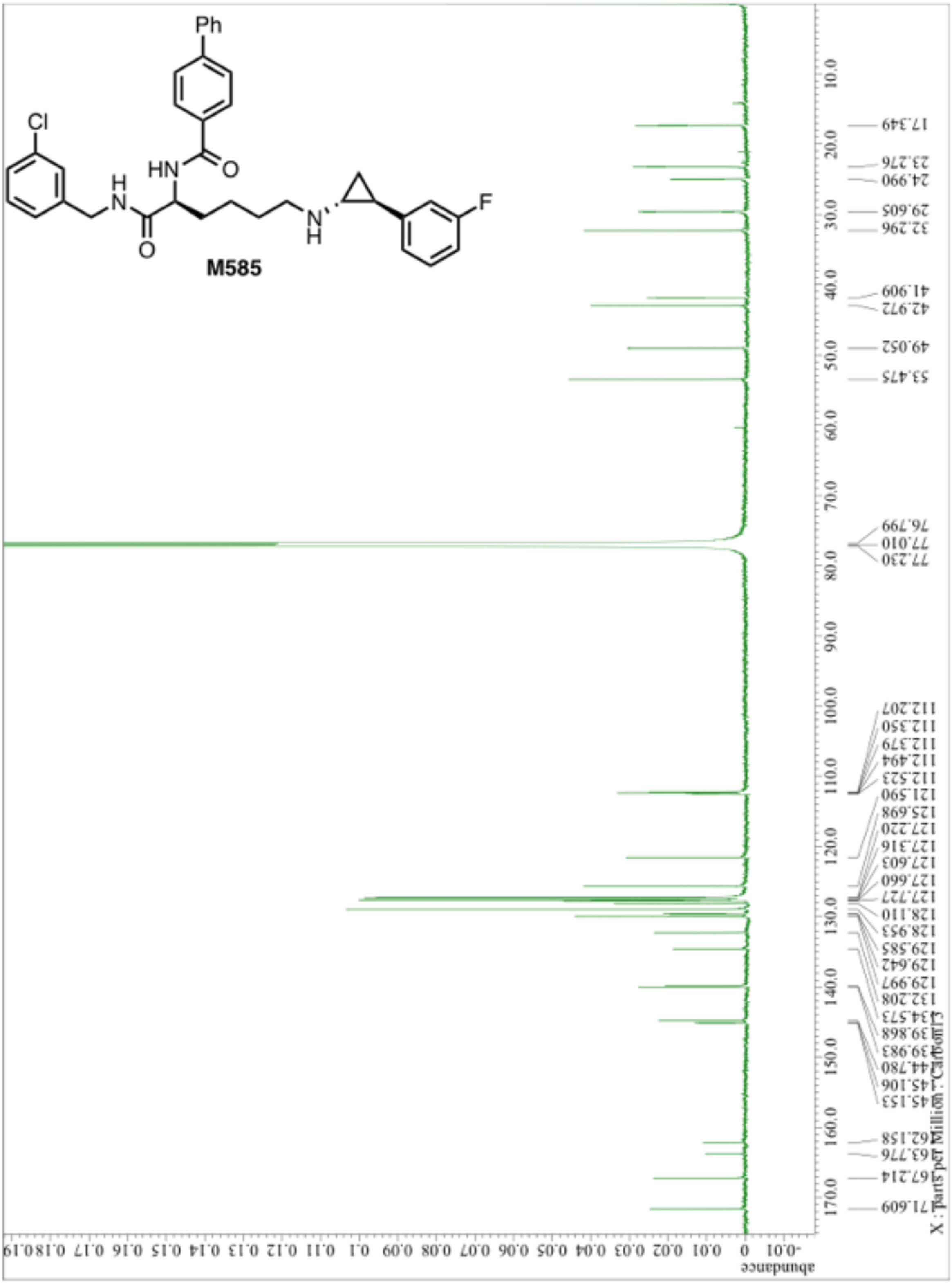
^{13}C NMR (150 MHz, $CDCl_3$) of M1310:



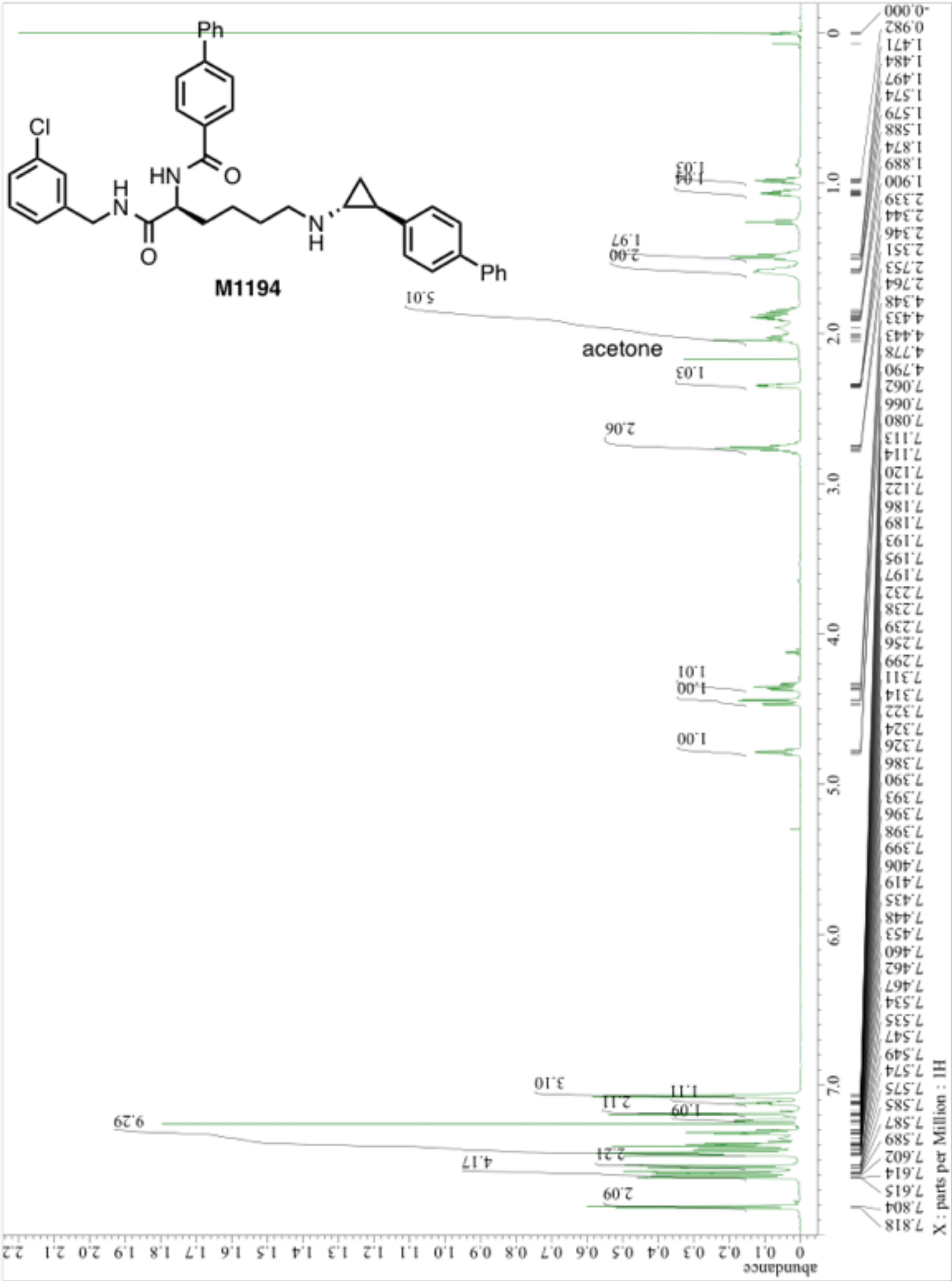
^{1}H NMR (600 MHz, CDCl$_3$) of M585:



^{13}C NMR (150 MHz, CDCl$_3$) of M585:

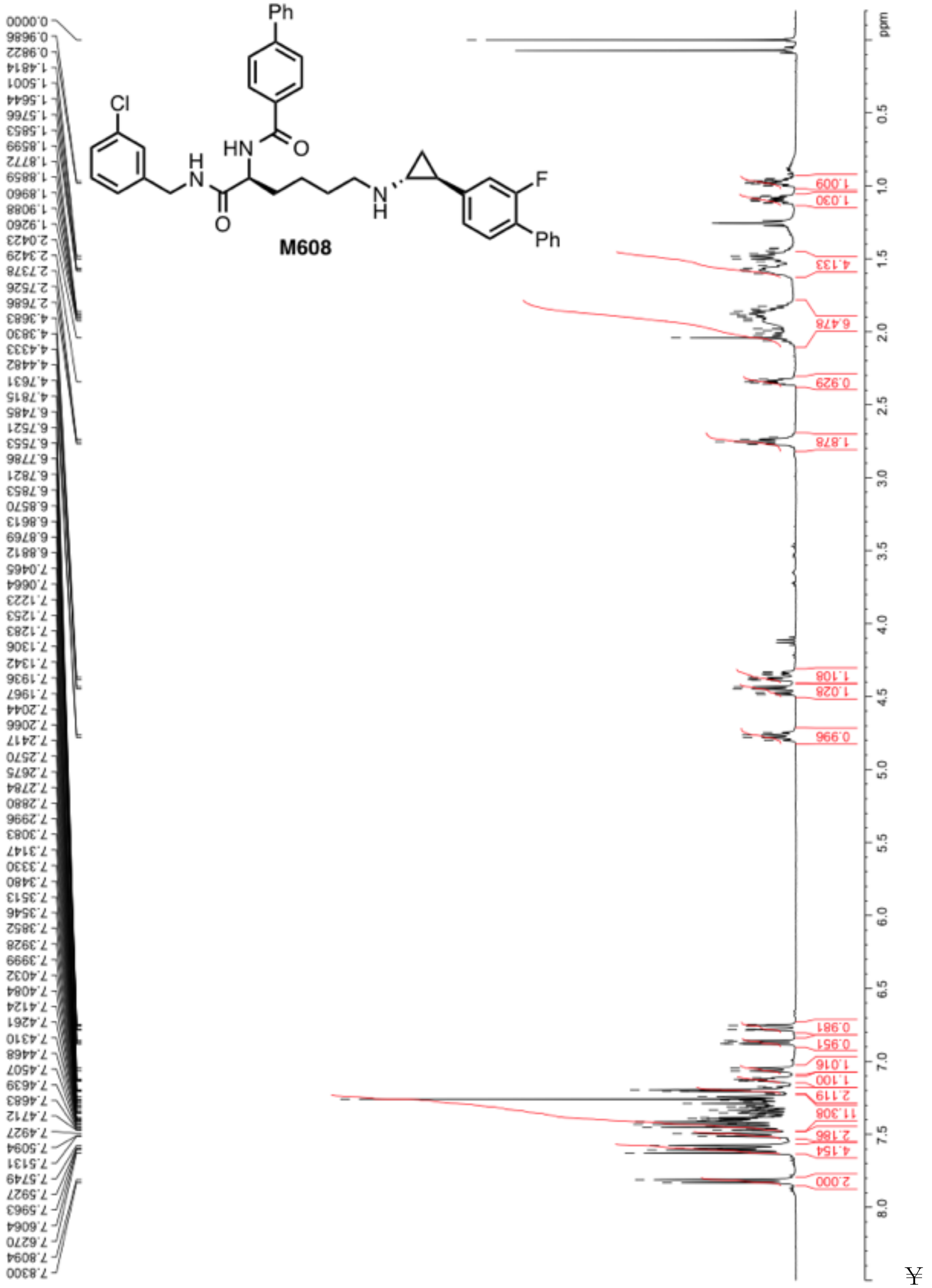


^{1}H NMR (600 MHz, $CDCl_3$) of M1194:

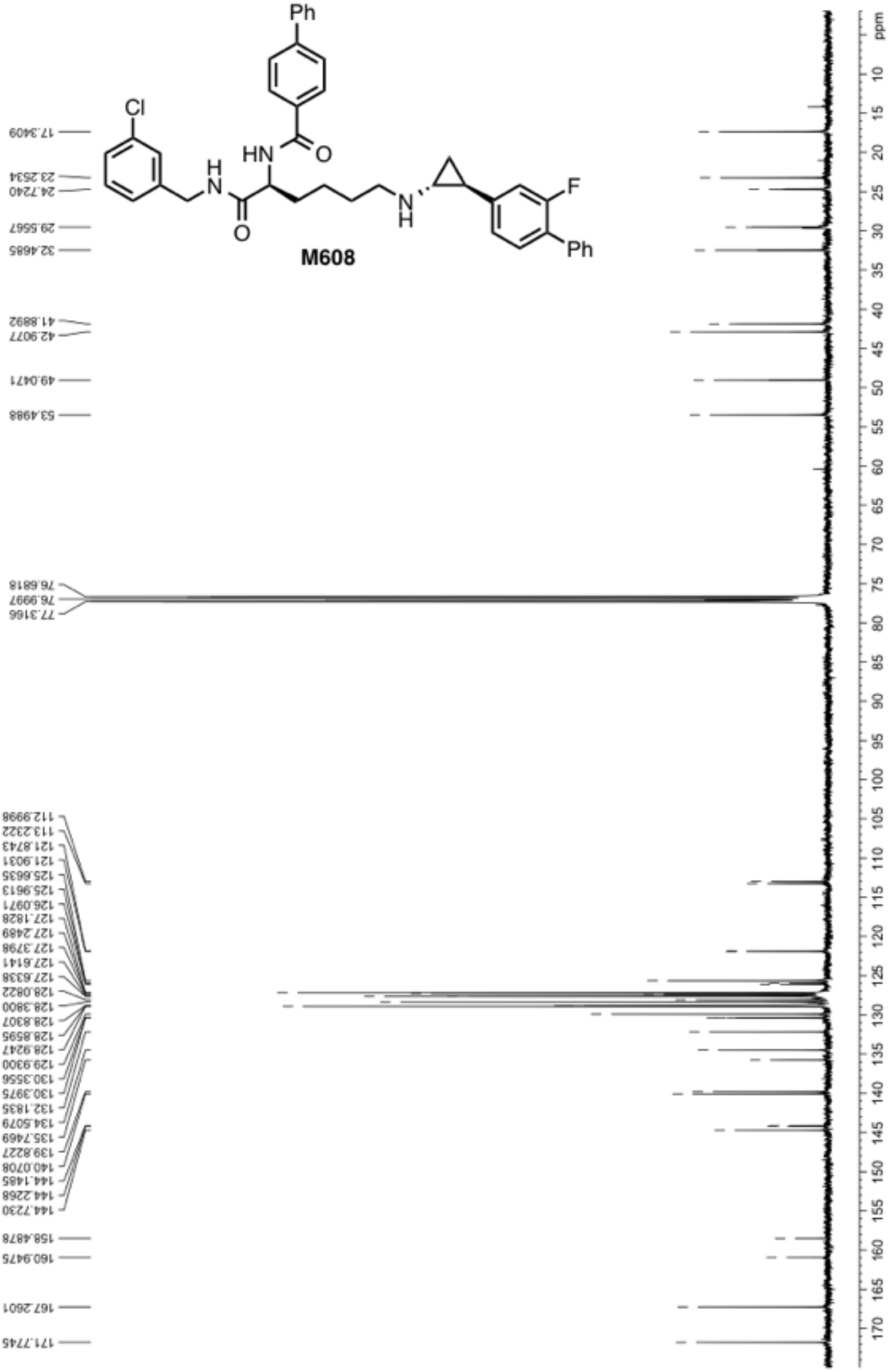


[13]C NMR (150 MHz, $CDCl_3$) of M1194

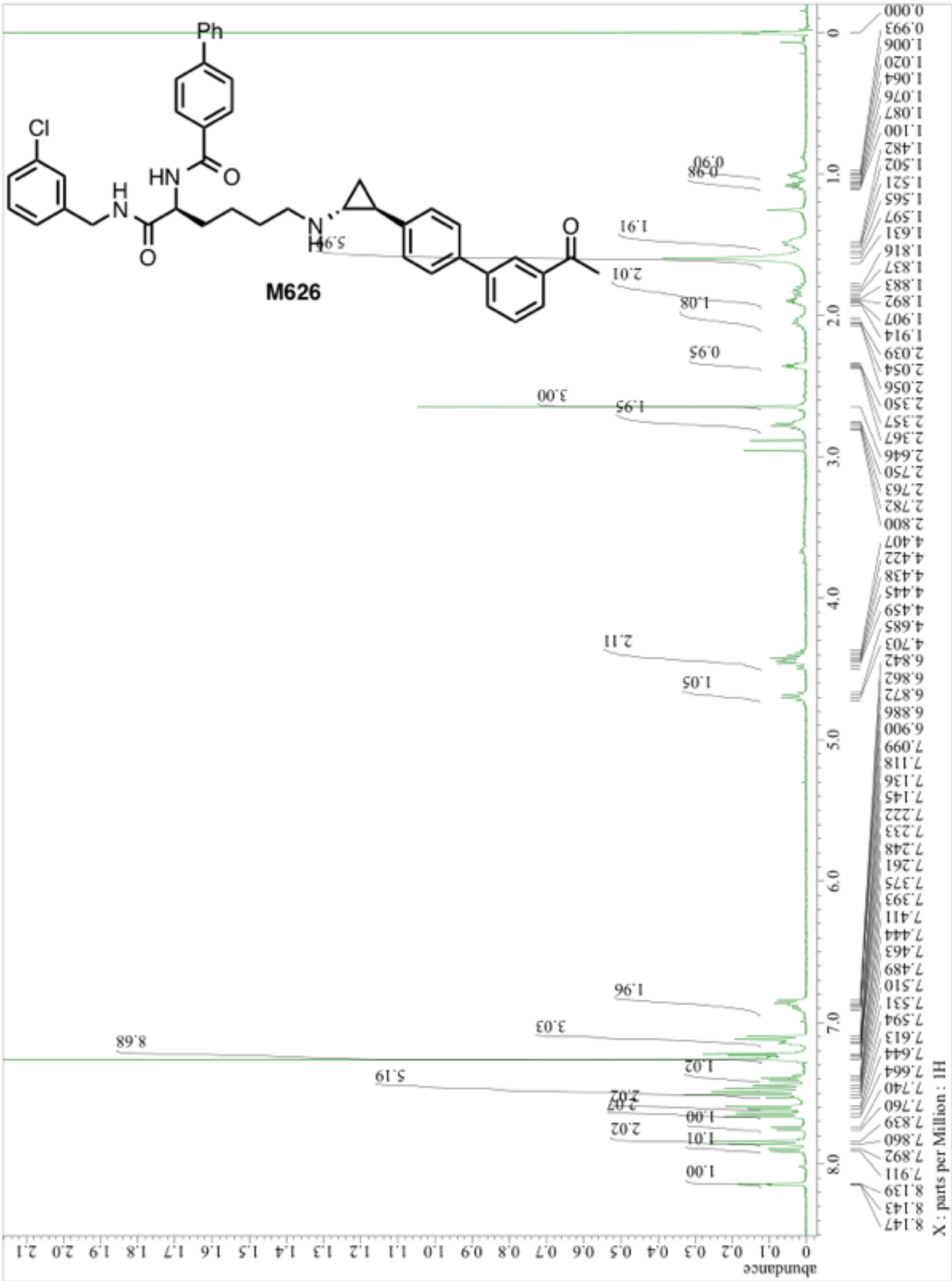
[1]H NMR (400 MHz, $CDCl_3$) of M608:



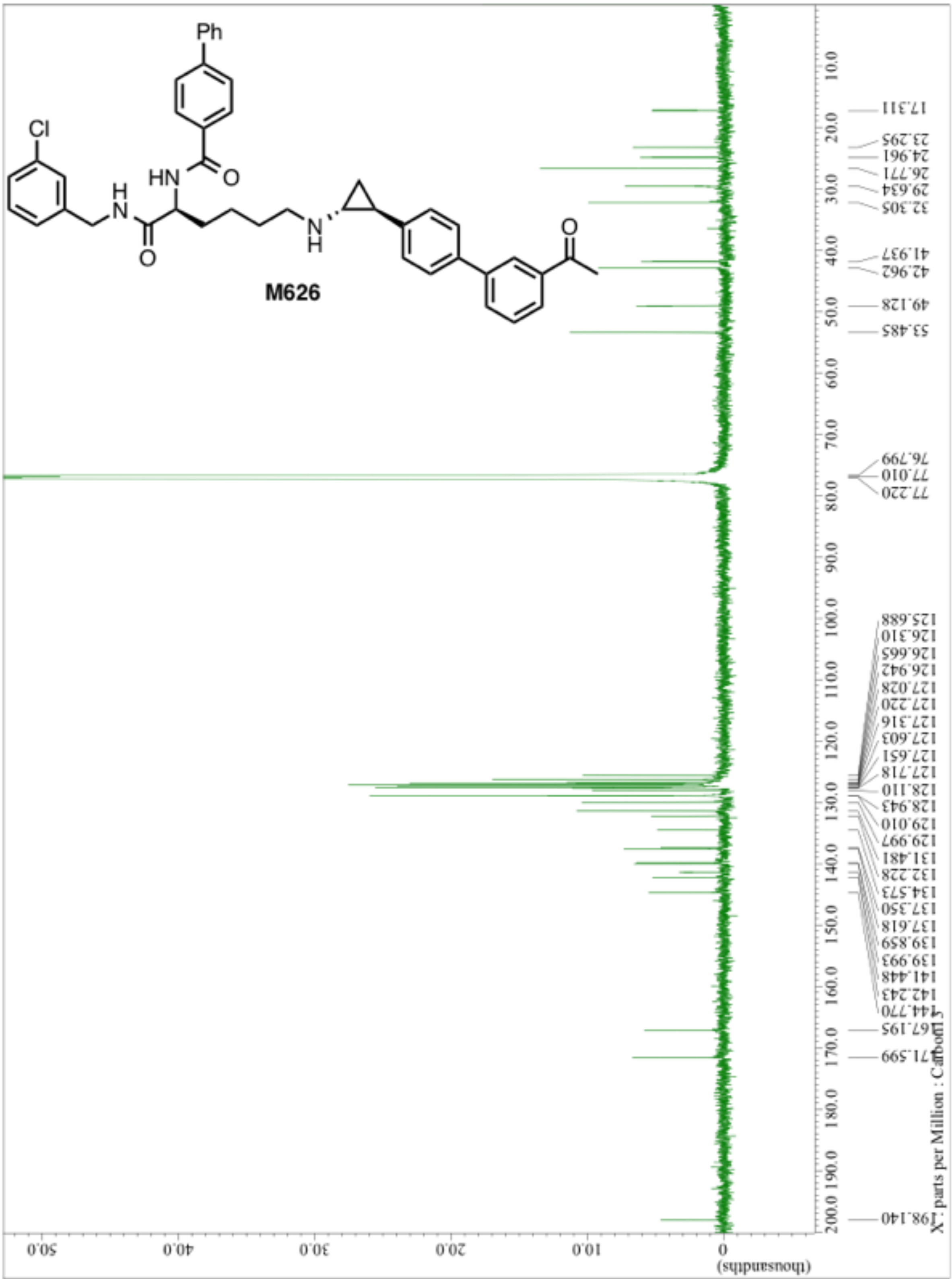
^{13}C NMR (100 MHz, $CDCl_3$) of M608:



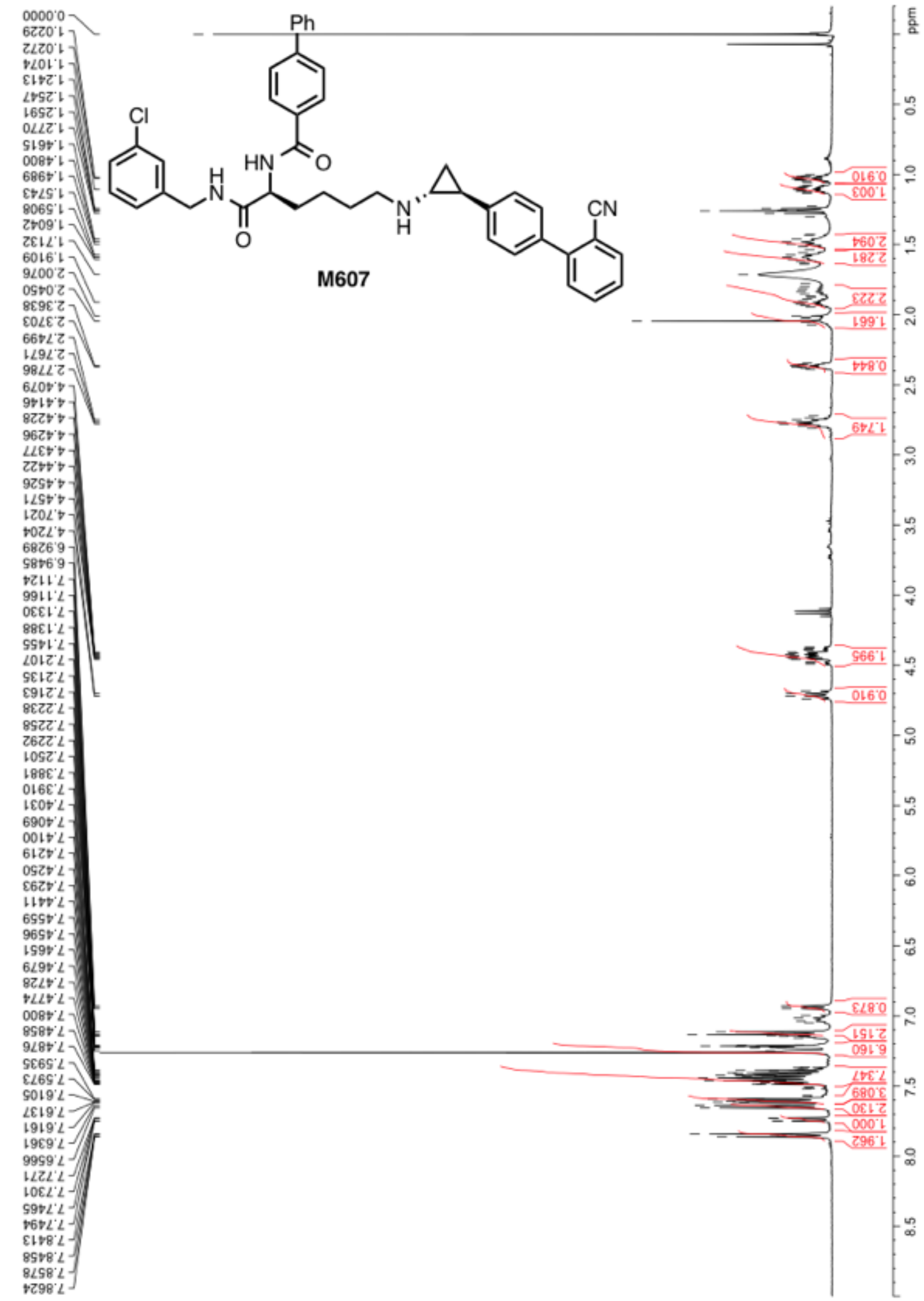
^{1}H NMR (400 MHz, $CDCl_3$) of M626:



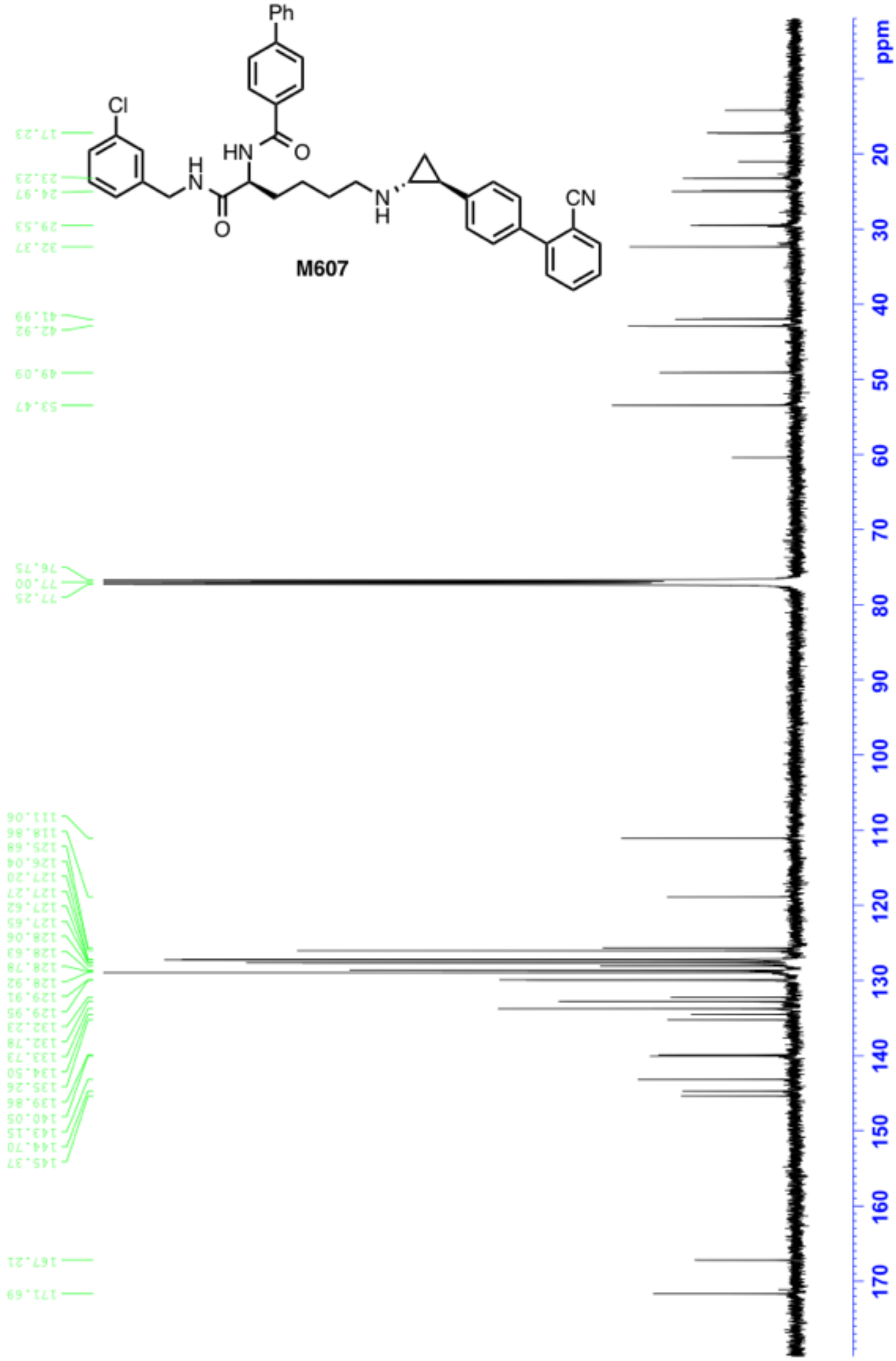
^{13}C NMR (150 MHz, CDCl$_3$) of M626:



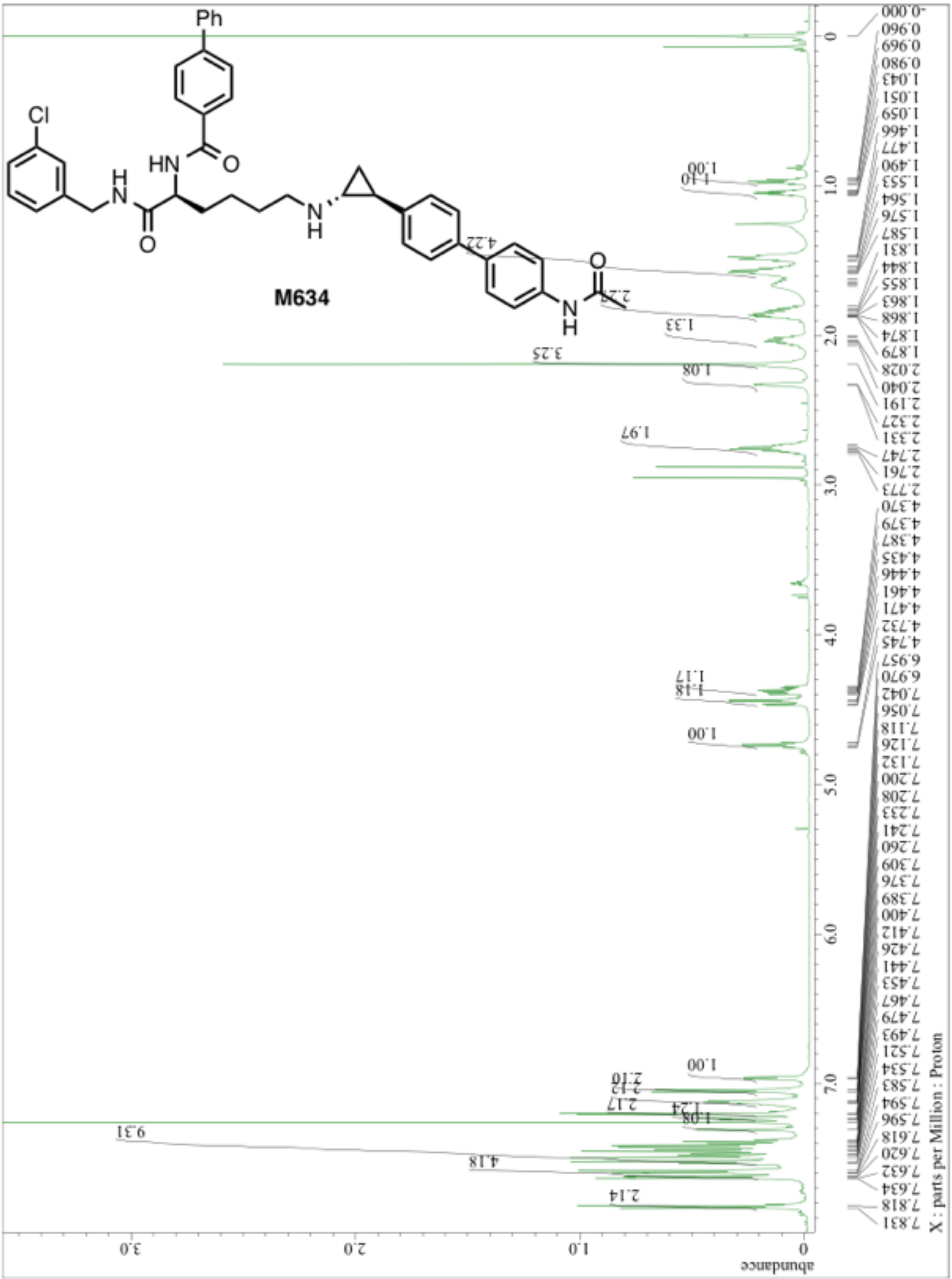
^{1}H NMR (400 MHz, CDCl$_3$) of M607:



^{13}C NMR (125 MHz, $CDCl_3$) of M607:



^{1}H NMR (400 MHz, $CDCl_3$) of M634:



^{13}C NMR (150 MHz, $CDCl_3$) of M634: