Supporting Information

Straightforward synthesis of enantiomerically pure 1,2,3-triazoles derived from amino esters

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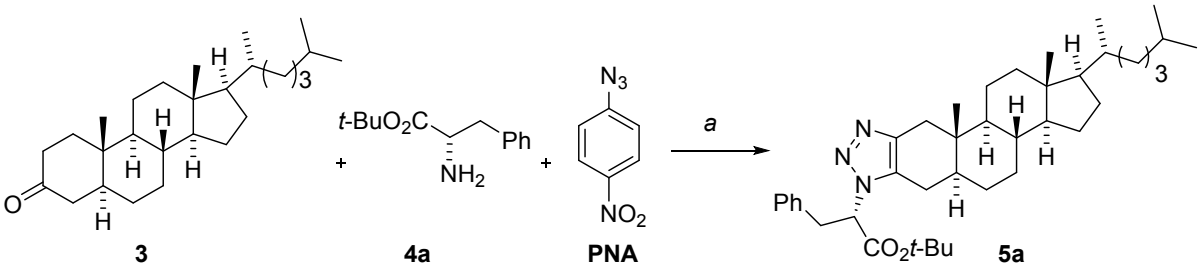
Supporting Information

1. General experimental methods

NMR spectra were acquired on commercial instruments (Bruker Avance 300 MHz, Bruker AMX 400 MHz or Bruker Avance II+ 600 MHz) and chemical shifts (δ) are reported in parts per million (ppm) referenced to tetramethylsilane (^{1}H), or the internal (NMR) solvent signal (^{13}C). Exact mass spectra were acquired on a quadrupole orthogonal acceleration time-of-flight mass spectrometer (Synapt G2 HDMS, Waters, Milford, MA). Samples were infused at 3uL/min and spectra were obtained in positive (or: negative) ionization mode with a resolution of 15000 (FWHM) using leucine enkephalin as lock mass. Melting points (not corrected) were determined using a Reichert Thermovar apparatus. For column chromatography 70-230 mesh silica 60 (E. M. Merck) was used as the stationary phase. Chemicals received from commercial sources were used without further purification. Dry- reaction solvents (toluene, DMF and DMSO) were used as received from commercial sources. Reactions were monitored using thin-layer chromatography (TLC) on aluminum packed percolated Silica Gel 60 F254 plates. Flash column chromatography was carried out with silica gel 60 (particle size less than 0.020 mm) by using appropriate mixtures of ethyl acetate and hexanes as eluent. Compounds were visualized on the TLC plates by use of UV light. Anhydrous magnesium sulfate was used for drying solutions. Chemical nomenclature was generated using Chem Bio Draw Ultra 13.0.

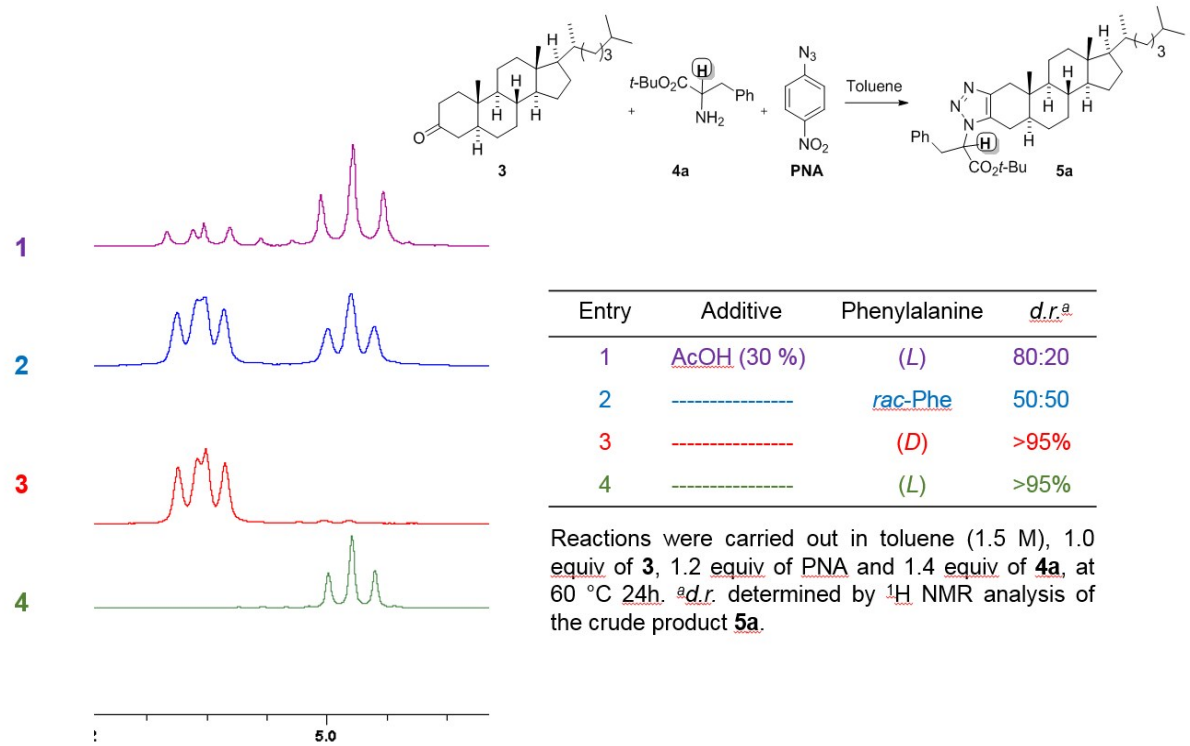
2. Methodological studies of 5a and studies on the influence of the ester

Table S1. Synthesis of derivative 5a applying the previously reported conditions.[12a]



Entry	T (°C)	Catalyst	Time (h)	*d.r.*[b]	Yield (%)
1[a]	100	AcOH	24	70/30	48
2[a]	60	AcOH	24	80/20	45
3	50	AcOH	24	80/20	40
3	100	-------	24	>95	50
4	60	------	24	>95	60
5	60	-------	48	>95	34
6	70	-------	24	>95	50
7	70	-------	48	>95	18

Reactions were carried out in toluene (1.5 M), 1.0 equiv of **3**, 1.2 equiv of PNA and 1.4 equiv of **4a.** [a]30% AcOH**.** [b]*d.r.* determined by ^{1}H-NMR analysis of the crude product **5a**.

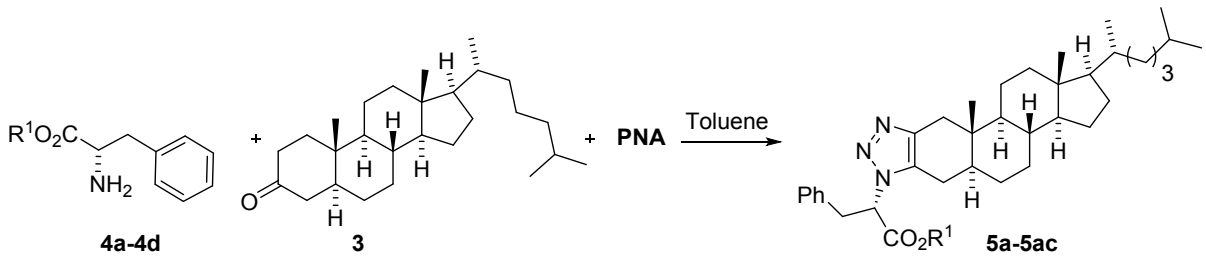


Entry	Additive	Phenylalanine	*d.r.*[a]
1	AcOH (30 %)	(*L*)	80:20
2	----------	*rac*-Phe	50:50
3	----------	(*D*)	>95%
4	----------	(*L*)	>95%

Reactions were carried out in toluene (1.5 M), 1.0 equiv of **3**, 1.2 equiv of PNA and 1.4 equiv of **4a**, at 60 °C 24h. [a]*d.r.* determined by ^{1}H NMR analysis of the crude product **5a**.

Figure S1. ^{1}H-NMR Comparison of both diastereoisomers of **5a**.

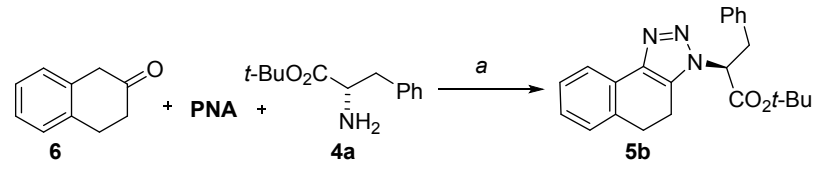
Table S2. Influence of the ester **5a-5ac**



Entry	Product	R^1	*d.r.*[a]	Yield (%)[b]
1	**5a**	*t*-Bu	>95	60
2	**5aa**	Me	>95	36
3	**5ab**	Et	>95	50
4	**5ac**	Bn	>95	20

Reactions conditions: toluene (1.5 M), 1.0 equiv of the ketone, 1.2 equiv of PNA and 1.4 equiv of the amino ester at 60 °C 24h. [a]*d.r.* as determined by ^{1}H-NMR analysis of the crude product **5a-5ac**, [b] pure product after column chromatography.

3. Chiral HPLC-spectrum of 5b and rac-5b



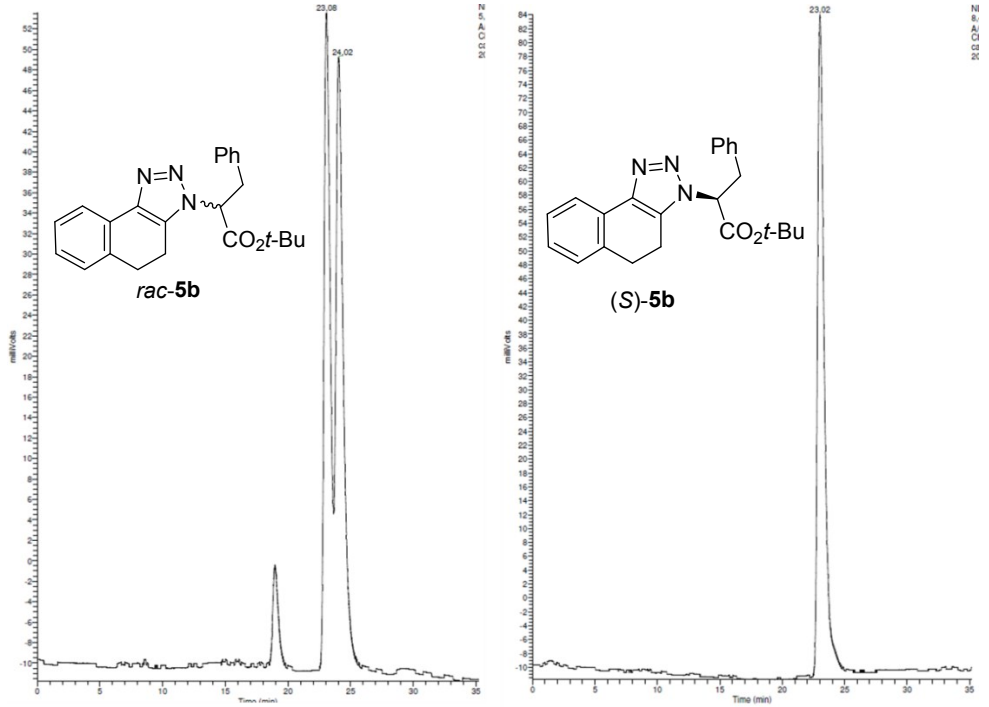
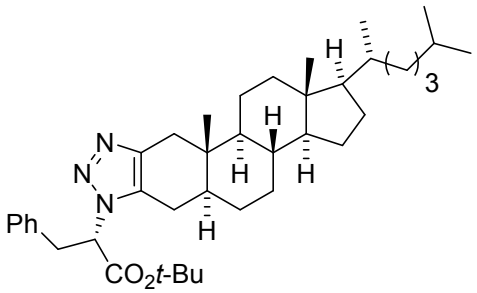


Figure S2. Representative chiral-HPLC analysis of *rac*-**5b** and (*S*) **5b**. The enantiomeric ratio was determined by HPLC analysis in comparison with racemic material (CHIRAL PAK IB column, 95.0/5.0 isocratic n-heptane/2-propanol, 0.5 mL/min, major isomer: tR = 23.02 min,

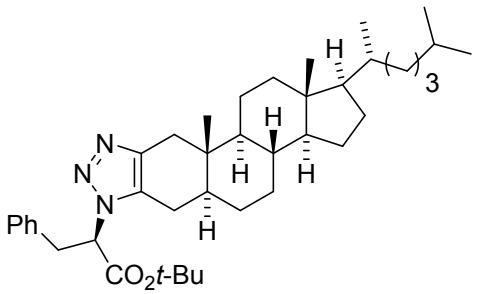
UV detection at 254.0 nm, 25 ºC). [a]Reactions conditions: toluene (1.5 M), 1.0 equiv of the ketone, 1.2 equiv of PNA and 1.4 equiv of the amino ester at 60 °C 24h.

4. Synthesis Procedures of 5a-p



5a (59%)

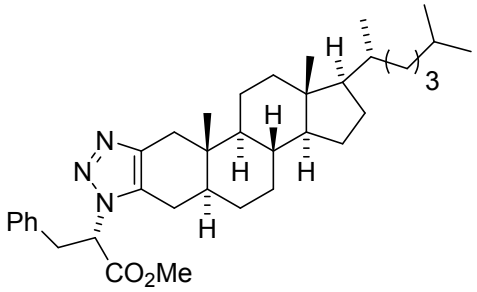
***Tert*-Butyl (*S*)-2-((1*R*,3a*S*,3b*R*,5a*S*,10a*S*,10b*S*,12a*R*)-10a,12a-dimethyl-1-((*R*)-6-methylheptan-2-yl)-2,3,3a,3b,4,5,5a,6,10,10a,10b,11,12,12a-tetradecahydrocyclopenta[7,8] phenanthro [2,3-d][1,2,3]triazol-9(1H)-yl)-3-phenylpropanoate:** 5α-Cholestan-3-one (46.5 mg, 0.12 mmol), *tert*-butyl $_L$-phenylalaninate (35.4 mg, 0.16 mmol), 4-nitrophenyl azide (21.3 mg, 0.13 mmol), 4 Å molecular sieves (50 mg) and toluene (0.2 mL) were mixed in a sealed reaction tube for 24 hours at 60 °C. After the solvent was removed under reduced pressure, the crude reaction mixture was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 9:1) affording **5a** (43 mg, 59% yield) as a yellow solid m.p. 165 – 167 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 - 7.15 (m, 3H), 6.98 - 6.96 (m, 2H), 4.98 (t, *J* = 8.0 Hz, 1H), 3.53 (d, *J* = 7.8 Hz, 2H), 2.78 (d, *J* = 15.7 Hz, 1H), 2.26 - 2.20 (m, 2H), 2.04 - 2.01 (m, 1H), 1.85 - 1.77 (m, 1H), 1.69 - 1.65 (m, 1H), 1.57 - 1.50 (m, 4H), 1.43 (s, 9H), 1.34 - 0.97 (m, 17 H), 0.92 (d, *J* = 6.4 Hz, 4H), 0.88 - 0.85 (m, 7H), 0.65 (s, 3H), 0.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 142.8, 136.4, 131.5, 1290, 128.6, 127.0, 83.2, 63.2, 56.2, 53.5, 42.4, 42.0, 39.8, 39.5, 37.4, 36.7, 36.1, 36.0, 35.8, 35.5, 31.5, 29.7, 28.2, 28.0, 27.9, 24.5, 24.3, 23.8, 22.8, 22.6, 21.1, 18.7, 11.9, 11.3. HRMS (ESI$^+$): m/z calcd for $C_{40}H_{61}N_3O_2$ $[M+H]^+$ 616.4797; found 616.4836.



5l (64%)

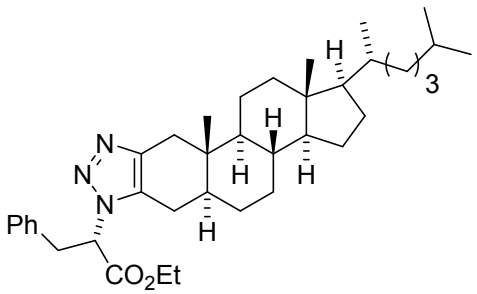
***Tert*-butyl (*R*)-2-((1*R*,3a*S*,3b*R*,5a*S*,10a*S*,10b*S*,12a*R*)-10a,12a-dimethyl-1-((*R*)-6-methylheptan-2-yl)-2,3,3a,3b,4,5,5a,6,10,10a,10b,11,12,12a-tetradecahydrocyclopenta[7,8] phenanthro- [2,3-d][1,2,3]triazol-9(1H)-yl)-3-phenylpropanoate:** The procedure described above was applied to 5α-cholestan-3-one (46.5 mg, 0.12 mmol), *tert*-butyl $_D$-phenylalaninate (35.4 mg, 0.16 mmol), 4-nitrophenyl azide (21.3 mg, 0.13 mmol), 4 Å molecular sieves (50 mg) and toluene (0.2 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 9:1) affording **5a** (44 mg, 64% yield) as a yellow solid m.p. 165 – 167 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 - 7.18 (m, 3H), 7.07 - 7.05 (m, 2H), 5.10

(dd, *J* = 6.2, 9.4 Hz, 1H), 3.58 - 3.54 (m, 2H), 2.80 (d, *J* = 15.7 Hz, 1H), 2.29 - 2.20 (m, 2H), 2.08 - 2.01 (m, 2H), 1.84 - 1.80 (m, 1H), 1.71 - 1.67 (m, 2H), 1.58 - 1.50 (m, 4H), 1.39 (s, 9H), 1.34 - 0.98 (m, 15H), 0.91 (d, *J* = 6.5 Hz, 4H), 0.86 (d, J = 5.9 Hz, 7H), 0.65 (d, *J* = 7.18 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.4, 11.9, 18.7, 21.1, 22.6, 22.8, 23.8, 24.3, 24.8, 27.8, 28.0, 28.2, 20.0, 31.6, 35.5, 35.8, 36.0, 36.1, 36.7, 39.5, 39.9, 39.9, 42.1, 42.4, 53.5, 56.2, 63.3, 83.1, 127.0, 128.6, 128.9, 131.4, 136.2, 143.2, 167.1. HRMS (ESI$^+$): m/z calcd for $C_{40}H_{61}N_3O_2$ $[M+H]^+$ 616.4797; found 616.4836.



5aa (36%)

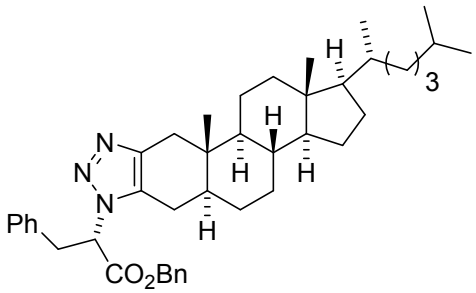
Methyl (*S*)-2-((1*R*,3a*S*,3b*R*,5a*S*,10a*S*,10b*S*,12a*R*)-10a,12a-dimethyl-1-((*R*)-6-methylheptan-2-yl)-2,3,3a,3b,4,5,5a,6,10,10a,10b,11,12,12a-tetradecahydrocyclopenta[7,8] phenanthro[2,3-d][1,2,3]triazol-9(1H)-yl)-3-phenylpropanoate: The procedure described above was applied to 5α-cholestan-3-one (108 mg, 0.28 mmol),), $_L$-phenylalanine methyl ester (70 mg, 0.39 mmol), 4-nitrophenyl azide (51 mg, 0.31 mmol), 4 Å molecular sieves (50 mg) and toluene (0.3 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **5aa** (66 mg, 36% yield) as a yellow solid m.p. 150 – 152 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 - 7.16 (m, 3H), 6.93 - 6.90 (m, 2H), 5.00 (dd, *J* = 5.8, 9.2 Hz, 1H), 3.77 (s, 3H), 3.59 - 3.27 (m, 2H), 2.77 (d, *J* = 15.4 Hz, 1H), 2.23 - 2.19 (m, 2H), 2.04 - 2.00 (m, 1H), 1.85 - 1.77 (m, 1H), 1.67 - 1.64 (m, 1H), 1.56 - 0.85 (m, 32H), 0.65 (s, 3H), 0.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 142.8, 136.0, 131.9, 128.9, 128.7, 127.1, 62.2, 56.2, 56.1, 53.5, 53.0, 42.4, 41.9, 39.8, 39.5, 37.8, 36.7, 36.1, 35.9, 35.8, 35.4, 31.5, 28.8, 28.2, 28.0, 24.2, 24.1, 23.8, 22.8, 22.6, 21.1, 18.7. HRMS (ESI$^+$): m/z calcd for $C_{37}H_{55}N_3O_2$ $[M+H]^+$: 574.4328, found 574.4381.



5ab (50 %)

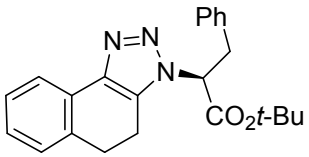
Ethyl (*S*)-2-((1*R*,3a*S*,3b*R*,5a*S*,10a*S*,10b*S*,12a*R*)-10a,12a-dimethyl-1-((*R*)-6-methylheptan-2-yl)-2,3,3a,3b,4,5,5a,6,10,10a,10b,11,12,12a-tetradecahydrocyclopenta[7,8]phenanthro [2,3-d][1,d2,3]triazol-9(1H)-yl)-3-phenylpropanoate: The procedure described above was applied to 5α-cholestan-3-one (100 mg, 0.26 mmol),), $_L$-phenylalanine methyl ester (72mg, 0.36 mmol), 4-nitrophenyl azide (47 mg, 0.28 mmol), 4 Å molecular sieves (50 mg) and toluene (0.3 mL). The product was purified

by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **5ab** (81 mg, 50% yield) as a yellow solid m.p. 155 – 156 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19-7.16 (m, 3H), 6.95 - 6.93 (m, 2H), 5.02 (dd, *J* = 5.8, 9.3 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 3.62 - 3.52 (m, 2H), 2.77 (d, *J* = 15.5 Hz, 1H), 2.23 - 2.19 (m, 1H), 2.04 - 2.00 (m, 1H), 1.85 - 1.77 (m, 1H), 1.68 - 1.64 (m, 1H), 1.57 - 0.81 (m, 36H), 0.65 (s, 3H), 0.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 142.8, 136.1, 131.7, 128.9, 128.7, 127.1, 62.4, 62.3, 56.22, 56.19, 53.5, 42.4, 41.9, 39.8, 39.5, 37.7, 36.7, 36.1, 35.9, 35.8, 35.4, 31.5, 28.9, 28.0, 24.3, 24.2, 23.8, 22.8, 22.6, 21.1, 18.7, 14.0, 11.9, 11.3. HRMS (ESI$^+$): m/z calcd for $C_{38}H_{57}N_3O_2$ [M+H]$^+$: 588.4484, found 588.4525.



5ac (20 %)

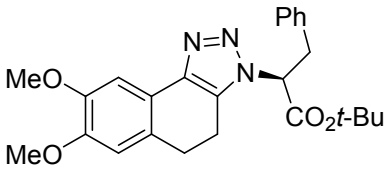
Benzyl (*S*)-2-((1*R*,3a*S*,3b*R*,5a*S*,10a*S*,10b*S*,12a*R*)-10a,12a-dimethyl-1-((*R*)-6-methyl heptan-2-yl)-2,3,3a,3b,4,5,5a,6,10,10a,10b,11,12,12a-tetradecahydrocyclopenta[7,8] phenanthro[2,3-d][1,2,3]triazol-9(1H)-yl)-3-phenylpropanoate: The procedure described above was applied to 5α-cholestan-3-one (70 mg, 0.18 mmol),), $_L$-phenylalanine benzyl ester (66mg, 0.25 mmol), 4-nitrophenyl azide (33 mg, 0.20 mmol), 4 Å molecular sieves (50 mg) and toluene (0.2 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **5ac** (23 mg, 20% yield) as a yellow solid 164 – 166 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 - 7.15 (m, 8H), 6.95 - 6.92 (m, 2H), 5.20 (s, 2H), 5.08 (dd, *J* = 6.2, 9.4 Hz, 1H), 3.60 - 3.58 (m, 2H), 2.76 (d, *J* = 15.8Hz, 1H), 2.22 - 2.14 (m, 2H), 2.03 - 2.00 (m, 1H), 1.84 - 1.77 (m, 1H), 1.66 - 1.63 (m, 1H), 1.56 - 1.50 (m, 3H), 1.42 - 0.85 (m, 29H), 0.65 (s, 3H), 0.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 142.9, 135.9, 134.9, 131.8, 128.9, 128.7, 128.6, 128.5, 128.4, 127.1, 67.8, 62.44, 56.2, 56.1, 53.5, 42.4, 41.9, 39.8, 39.5, 37.6, 36.7, 36.1, 35.9, 35.8, 35.4, 31.5, 28.8, 28.2, 28.0, 24.3, 24.2, 23.8, 22.8, 22.6, 21.1, 18.7, 11.9, 11.3. HRMS (ESI$^+$): m/z calcd for $C_{43}H_{59}N_3O_2$ [M+H]$^+$: 650.4641, found 650.4680.



5b (93%)

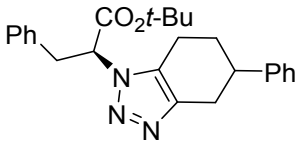
Tert-butyl (*S*)-2-(4,5-dihydro-1H-naphtho[1,2-d][1,2,3]triazol-1-yl)-3-phenylpropanoate. The procedure described above was applied to β-tetralone (33.6 mg, 0.23 mmol), *tert*-butyl $_L$-phenylalaninate (70 mg, 0.32 mmol), 4-nitrophenyl azide (42.7 mg, 0.26 mmol), 4 Å molecular sieves (50 mg) and toluene (0.2 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **5b** (80.2 mg, 93% yield) as a red brown solid m.p. 82 - 84 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.6

Hz, 1H), 7.31 - 7.27 (m, 1H), 7.20 - 7.17 (m, 5H), 7.06 - 7.04 (m, 2H), 5.22 (dd, *J* = 6.2, 9.3 Hz, 1H), 3.62 - 3.52 (m, 2H), 2.96 - 2.80 (m, 2H), 2.68 (ddd, *J* = 7.3, 9.0, 16.1 Hz, 1H), 2.58 - 2.50 (m, 1H), 1.43 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 143.2, 135.9, 133.4, 133.3, 129.0, 128.7, 128.0, 127.3, 127.2, 127.2, 122.1, 83.5, 63.6, 37.3, 28.5, 27.8, 19.5**.** HRMS (ESI$^+$): m/z calcd for $C_{23}H_{25}N_3O_2$ [M+H]$^+$: 376.2025 found 376.2034.



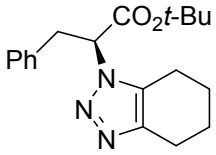
5c (56%)

Tert-butyl (*S*)-2-(7,8-dimethoxy-4,5-dihydro-1H-naphtho[1,2-d][1,2,3]triazol-1-yl)-3-phenylpropanoate: The procedure described above was applied to 6,7-dimethoxy-2-tetralone (30 mg, 0.15 mmol), *tert*-butyl $_L$-phenylalaninate (45.1 mg, 0.2 mmol), 4-nitrophenyl azide (26 mg, 0.16 mmol), 4 Å molecular sieves (50 mg) and toluene (0.2 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **5c** (35 mg, 56% yield) as a brown solid m.p. 91 – 93 . ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.23 - 7.16 (m, 3H), 7.06 - 7.04 (m, 2H), 6.71 (s, 1H), 5.22 (dd, *J* = 6.2, 9.2 Hz, 1H), 3.95 (s, 3H), 3.88 (s, 3H), 3.62 - 3.52 (m, 2H), 2.91 - 2.75 (m, 2H), 2.72 - 2.64 (m , 1H), 2.57 - 2.50 (m, 1H), 1.43 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 148.2, 148.1, 143.4, 135.9, 132.4, 129.0, 128.7, 127.2, 125.6, 121.4, 111.6, 105.6, 83.5, 63.7, 56.1, 56.0, 37.3, 28.2, 27.9, 12.97. HRMS (ESI$^+$): m/z calcd for $C_{25}H_{29}N_3O_4$ [M+H]$^+$: 436,2236; found 436.2226.



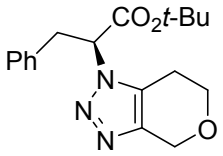
5d (71%)

Tert-butyl (2*S*)-3-phenyl-2-(5-phenyl-4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazol-1-yl)propanoate: The procedure described above was applied to 4-Phenylcyclohexanone (50 mg, 0.3 mmol),), *tert*-butyl $_L$-phenylalaninate (88.5 mg, 0.4 mmol), 4-nitrophenyl azide (54.1 mg, 0.33 mmol), 4 Å molecular sieves (50 mg) and toluene (0.3 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **5d** (85 mg, 71% yield) as a yellow semi-solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 - 7.18 (m, 8H), 7.08 - 7.01 (m, 2H), 5.13 – 5.05 (m, 1H), 3.60 - 3.56 (m, 2H), 3.12 - 3.03 (m, 1H), 2.89 - 2.75 (m, 2H), 2.58 - 2.37 (m, 1H), 2.19 - 1.74 (m, 3H), 1.43 + 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 166.9, 144.9, 144.8, 143.3, 143.1, 136.2, 132.6, 132.4, 129.0, 128.9, 128.6, 128.5, 127.1, 126.9, 126.8, 126.5, 83.3, 63.4, 63.3, 40.5, 40.2, 37.1, 37.0, 30.0, 29.8, 29.6, 29.3, 27.8, 20.1, 19.7. HRMS (ESI+): m/z calcd for $C_{25}H_{29}N_3O_{24}$ [M+H]+: 404.2293; found 404.2336.



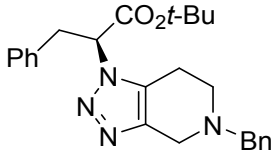
5e (65%)

Tert-butyl (*S*)-3-phenyl-2-(4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazol-1-yl)propanoate: The procedure described above was applied to cyclohexanone (50 mg, 0.51 mmol),), *tert*-butyl L-phenylalaninate (157 mg, 0.7 mmol), 4-nitrophenyl azide (90.2 mg, 0.56 mmol), 4 Å molecular sieves (50 mg) and toluene (0.5 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **5e** (97 mg, 65% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22-7.19 (m, 3H), 7.04 - 7.02 (m, 2H), 5.03 (dd, *J* = 7.3, 8.8 Hz, 1H), 3.57 - 3.56 (m, 2H), 2.74 - 2.65 (m, 2H), 2.41 - 2.36 (m, 1H), 2.14 - 2.09 (m, 1H), 1.76 - 1.62 (m, 4H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2, 21.9, 22.4, 22.6, 27.8, 37.1, 63.1, 83.1, 127.0, 128.5, 129.0, 132.8, 136.3, 143.0, 167.0. HRMS (ESI$^+$): m/z calcd for $C_{19}H_{25}N_3O_2$ $[M+H]^+$: 328.1980; found 328.2019.



5f (60%)

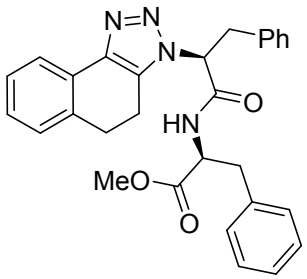
Tert-butyl (S)-2-(6,7-dihydropyrano[2,3-d][1,2,3]triazol-1(5H)-yl)-3-phenylpropanoate: The procedure described above was applied to tetrahydro-4H-pyran-4-one (50 mg, 0.5 mmol), *tert*-butyl L-phenylalaninate (155 mg, 0.7 mmol), 4-nitrophenyl azide (90 mg, 0.55 mmol), 4 Å molecular sieves (50 mg) and toluene (0.5 mL). The product was purified by flash column chromatography (CH_2Cl_2) followed by petroleum ether/EtOAc = 7:3) affording **5f** (99 mg, 60% yield) as a brown solid m.p. 80 - 81 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.18 (m, 3H), 7.04-7.01 (m, 2H), 5.15 (dd, *J* = 6.3, 9.6 Hz, 1H), 4.77 (*AB*syst, *J* = 13.8 Hz, 2H), 3.89-3.84 (m, 1H), 3.71-3.66 (m, 1H), 349-3.60 (m, 2H), 2.57 (dt, *J* = 5.7, 15.8 Hz. 1H), 2.33 (dt, *J* = 4.9, 15.8 Hz, 1H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0, 27.8, 37.2, 63.6, 63.8, 63.9, 83.5, 127.3, 128.7, 128.9, 130.4, 135.9, 141.3, 166.8. HRMS (ESI+): m/z calcd for $C_{18}H_{23}N_3O_3$ $[M+H]$+: 330.1773; found 330.1808**.**



5g (65%)

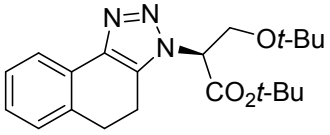
Tert-butyl (*S*)-2-(6,7-dihydropyrano[2,3-d][1,2,3]triazol-1(5H)-yl)-3-phenylpropanoate: The procedure described above was applied to 1-benzyl-4-piperidone (50 mg, 0.26 mmol), *tert*-butyl L-phenylalaninate (82 mg, 0.37 mmol), 4-nitrophenyl azide (44 mg, 0.28 mmol), 4 Å molecular sieves (50 mg) and toluene (0.3 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **5g** (70.6 mg, 65% yield) as a yellow solid 98 – 100 ˚C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 - 7.20 (m, 8H), 7.05 - 7.03 (m, 2H), 5.10 (dd, *J* = 6.3, 9.3 Hz, 1H), 3.74 - 3.59 (m, 4H), 3.57 - 3.50 (m, 2H),

2.77 - 2.72 (m, 1H), 2.61 - 2.47 (m, 2H), 2.32 - 2.26 (m, 1H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 142.0, 138.0, 136.1, 131.4, 129.0, 128.9, 128.4, 127.3, 127.1, 83.4, 63.5, 61.2, 49.6, 49.0, 37.2, 27.8, 20.8. HRMS (ESI$^+$): m/z calcd for $C_{25}H_{30}N_4O_2$ $[M+H]^+$: 419,2402 found 419,2439



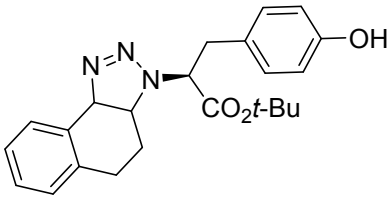
5h (60%)

Methyl ((*S*)-2-(4,5-dihydro-1H-naphtho[1,2-d][1,2,3]triazol-1-yl)-3-phenylpropanoyl)-L-phenylalaninate: The procedure described above was applied to β-tetralone (20 mg, 0.14 mmol), methyl $_L$-phenylalanyl-$_L$-phenylalaninate (62.5 mg, 0.19 mmol), 4-nitrophenyl azide (24.7 mg, 0.15 mmol), 4 Å molecular sieves (50 mg) and toluene (0.15 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **5h** (39.2 mg, 60% yield) as a yellow semisolid solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 0.7, 7.6 Hz, 1H), 7.48 (d, *J* = 7.9 Hz, 1H), 7.32-7.12 (m, 10H), 6.91 - 6.89 (m, 2H), 4.93 (dd, *J* = 4.0, 11.3 Hz, 1H), 4.87 (td, *J* = 5.3, 15.8, 1H), 3.69 (s, 3H), 4.70 (dd, *J* = 4.0, 13.8 Hz, 1H), 3.26 (m, 2H), 3.03 (dd, *J* = 8.0, 13.8 Hz, 1H), 2.82 - 2.74 (m, 1H), 2.61 - 2.51 (m, 2H), 2.04 - 1.96 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 167.2, 143.3, 135.9, 135.5, 134.5, 133.6, 129.2, 128.8, 128.76, 128.73, 128.06, 127.7, 127.3, 127.27, 122.1, 65.1, 53.7, 52.5, 39.7, 37.8, 29.7, 28.1, 18.6. HRMS (ESI$^+$): m/z calcd for $C_{29}H_{28}N_4O_3$ $[M+H]^+$: 481.2195; found 481.2226.



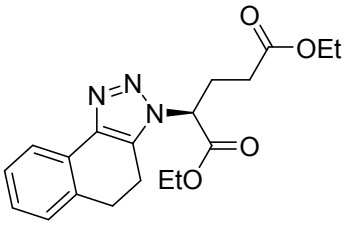
5i (50%)

Tert-butyl (*S*)-3-(tert-butoxy)-2-(4,5-dihydro-1H-naphtho[1,2-d][1,2,3]triazol-1-yl)propanoate. The procedure described above was applied to β-tetralone (30 mg, 0.20 mmol), *O*-tert-butyl-$_L$-serine tert-butyl ester (65.2 mg, 0.3 mmol), 4-nitrophenyl azide (36 mg, 0.22 mmol), 4 Å molecular sieves (50 mg) and toluene (0.2 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **5i** (37 mg, 50% yield) as a brown semi- solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.4 Hz, 1H), 7.30 (td, J = 1.7, 7.5 Hz, 1H), 7.24 - 7.18 (m, 2H), 5.44 (dd, *J* = 3.5, 5.7 Hz, 1H), 4.16 (dd, *J* = 5.6, 9.5 Hz, 1H), 3.88 (dd, *J* = 3.5, 9.5 Hz, 1H), 3.09 - 3.00 (m, 4H), 1.48 (s, 9H), 1.13 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 143.6, 134.6, 133.9, 128.9, 127.9, 127.2, 127.1, 122.0, 83.3, 77.3, 77.0, 76.7, 73.9, 63.4, 62.2, 28.8, 27.9, 27.3, 20.9. HRMS (ESI$^+$): m/z calcd for $C_{21}H_{29}N_3O_3$ $[M+H]^+$: 372,2287; found 372,2275.



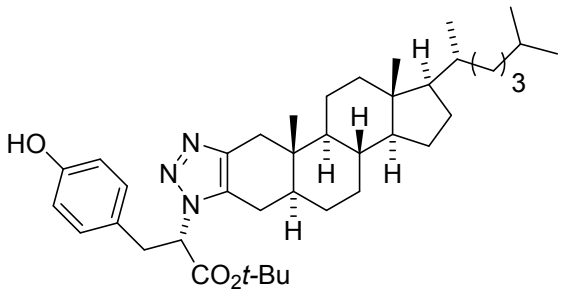
5j (58%)

Tert-butyl (*S*)-2-(4,5-dihydro-1H-naphtho[1,2-d][1,2,3]triazol-1-yl)-3-(4-hydroxyphenyl) propanoate. The procedure described above was applied to β-tetralone (30.7 mg, 0.21 mmol), L-tyrosine *tert*-butyl ester (71.1 mg, 0.3 mmol), 4-nitrophenyl azide (37 mg, 0.23 mmol), 4 Å molecular sieves (50 mg) and toluene (0.2 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **5j** (59 mg, 68% yield) as a brown solid m.p. 100 – 102 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.5 Hz, 1H), 7.27 - 7.23 (m, 1H), 7.17 – 7.15 (m, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.66 (d, *J* = 8.6Hz, 2H), 5.21 (dd, *J* = 6.8, 8.8Hz, 1H), 3.51 - 3.49 (m, 2H), 2.98 - 2.86 (m, 2H), 2.78 - 2.61 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 155.5, 143.2, 133.6, 133.4, 130.0, 128.2, 128.0, 127.5, 127.3, 126.9, 122.2, 115.7, 83.6, 63.9, 36.2, 28.5, 27.9, 19.5. HRMS (ESI$^+$): m/z calcd for $C_{23}H_{25}N_3O_3$ $[M+H]^+$: 392,1974; found 392.1966.



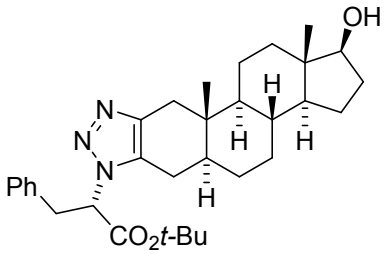
5k (40%)

Diethyl (*S*)-2-(4,5-dihydro-1H-naphtho[1,2-d][1,2,3]triazol-1-yl)pentanedioate: The procedure described above was applied to β-tetralone (30 mg, 0.21 mmol), L-glutamic acid diethyl ester (58.4 mg, 0.29 mmol), 4-nitrophenyl azide (37 mg, 0.23 mmol), 4 Å molecular sieves (50 mg) and toluene (0.2 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **5k** (29.3 mg, 40% yield) as a brown semi-solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.4 Hz, 1H), 7.32 (td, *J* = 2.4, 6.5 Hz, 1H), 7.25 - 7.19 (m, 2H), 5.41 (dd, *J* = 5.3, 10.6 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.11 - 3.07 (m, 2H), 3.02 - 2.87 (m, 2H), 2.74 - 2.66 (m, 1H), 2.63 - 2.54 (m, 1H), 2.40 - 2.25 (m, 2H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 168.1, 143.9, 133.4, 133.3, 128.5, 128.1, 127.5, 127.3, 122.1, 62.4, 60.8, 60.2, 29.9, 28.5, 26.0, 19.6, 14.1, 14.0. HRMS (ESI$^+$): m/z calcd for $C_{19}H_{23}N_3O_4$ $[M+H]^+$: 358.1722; found 358.1762**.**



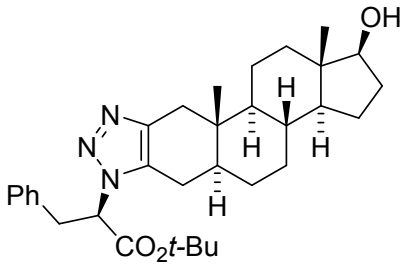
5m (60%)

Tert-butyl (*S*)-2-((1*R*,3a*S*,3b*R*,5a*S*,10a*S*,10b*S*,12a*R*)-10a,12a-dimethyl-1-((*R*)-6-methyl heptan-2-yl)-2,3,3a,3b,4,5,5a,6,10,10a,10b,11,12,12a-tetradecahydrocyclopenta[7,8] phenanthro[2,3-d][1,2,3]triazol-9(1H)-yl)-3-(4-hydroxyphenyl)propanoate: The procedure described above was applied to 5α-cholestan-3-one (45 mg, 0.12 mmol),), L-tyrosine *tert*-butyl ester (21 mg, 0.13 mmol), 4-nitrophenyl azide (28 mg, 0.16 mmol), 4 Å molecular sieves (50 mg) and toluene (0.1 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **5m** (34 mg, 60% yield) as a brown solid m.p. 150 – 152 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (br, 1H), 6.79 (d, *J* = 8.1 Hz, 2H), 6.63 (d, *J* = 8.1 Hz, 2H), 5.05 (t, *J* = 7.8 Hz, 1H), 3.46 (d, *J* = 8.0 Hz, 2H), 2.73 (d, *J* = 15.6 Hz, 1H), 2.33 (dd, *J* = 4.4 Hz, 16.6 Hz, 1H), 2.20 (d, *J* = 15.9 Hz, 1H), 2.01 - 1.98 (m, 1H), 1.84 - 1.66 (m, 4H), 1.55 - 0.85 (m, 39H), 0.64 (s, 3H), 0.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 155.9, 142.9, 131.9, 129.8, 126.9, 115.6, 83.3, 63.5, 56.2, 53.5, 42.4, 42.0, 39.8, 39.5, 36.7, 36.2, 35.8, 35.7, 35.5, 31.5, 28.9, 28.2, 28.0, 27.9, 24.7, 24.2, 23.8, 22.8, 22.6, 21.1, 18.7, 12.0, 11.2. HRMS (ESI$^+$): m/z calcd for $C_{40}H_{61}N_3O_3$ $[M+H]^+$: 632,4791, found 632,4797.



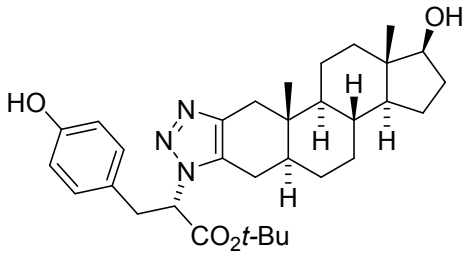
5n (65%)

Tert-butyl (*S*)-2-((1*S*,3a*S*,3b*R*,5a*S*,10a*S*,10b*S*,12a*S*)-1-hydroxy-3a,10a,12a-trimethyl-2,3,3a,3b,4,5,5a,6,10,10a,10b,11,12,12a-tetradecahydrocyclopenta[7,8]phenanthro[2,3-d][1,2,3]triazol-9(1H)-yl)-3-phenylpropanoate. The procedure described above was applied to stanolone (50 mg, 0.17 mmol),), *tert*-butyl L-phenylalaninate (52.6 mg, 0.24 mmol), 4-nitrophenyl azide (31 mg, 0.16 mmol), 4 Å molecular sieves (50 mg) and toluene (0.2 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **5n** (54.4 mg, 65% yield) as a yellow solid m.p. 160 – 162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.17 (m, 3H), 6.98 - 6.96 (m, 2H), 4.98 (t, *J* = 8.0 Hz, 1H), 3.64 (t, *J* = 8.6 Hz, 1H), 3.53 (d, *J* = 7.7 Hz, 2H), 2.79 (d, *J* = 15.8 Hz, 1H), 2.27 - 2.21 (m, 2H), 2.07 - 2.03 (m, 1H), 1.86 - 1.83 (m, 1H), 1.69 - 1.48 (m, 6H), 1.43 (s, 9H), 1.39 – 0.79 (m, 10H), 0.74 (s, 3H), 0.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 142.7, 136.3, 131.5, 128.9, 128.6, 127.0, 83.2, 81.8, 63.2, 53.6, 50.8, 42.8, 42.1, 37.5, 36.8, 36.6, 36.0, 35.5, 31.1, 30.4, 28.8, 27.9, 24.5, 23.4, 20.7, 11.3, 11.0. HRMS (ESI$^+$): m/z calcd for $C_{32}H_{45}N_3O_3$ $[M+H]^+$: 520.3494, found 520.3531.



5o (65%)

Tert-butyl (*R*)-2-((1*S*,3a*S*,3b*R*,5a*S*,10a*S*,10b*S*,12a*S*)-1-hydroxy-3a,10a,12a-trimethyl-2,3,3a,3b,4,5,5a,6,10,10a,10b,11,12,12a-tetradecahydrocyclopenta[7,8]phenanthro[2,3-d][1,2,3]triazol-9(1H)-yl)-3-phenylpropanoate: The procedure described above was applied to stanolone (50 mg, 0.17 mmol),), *tert*-butyl $_D$-phenylalaninate (52.6 mg, 0.24 mmol), 4-nitrophenyl azide (31 mg, 0.16 mmol), 4 Å molecular sieves (50 mg) and toluene (0.2 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **5o** (54.4 mg, 65% yield) as a yellow solid m.p. 160 – 162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 - 7.18 (m, 3H), 7.07 - 7.05 (m, 2H), 5.11 (dd, *J* = 6.2, 9.3 Hz, 1H), 3.65 (t, *J* = 8.51 Hz, 1H), 3.58 – 3.55 (m, 2H), 2.82 (d, *J* = 15.4 Hz, 1H), 2.30 - 2.22 (m, 2H), 2.09 - 2.02 (m ,2H), 1.87 - 1.84 (m , 1H), 1.68 - 1.52 (m, 4H), 1.43 - 1.35 (m, 11H), 1.28 – 1.10 (m, 4H), 0.96 - 0.85 (m, 4H), 0.75 (s, 3H), 0.66 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 143.1, 136.2, 131.3, 128.9, 128.6, 127.0, 83.2, 81.8, 63.4, 53.6, 50.8, 42.8, 42.1, 36.8, 36.7, 36.1, 36.0, 35.5, 31.1, 30.4, 28.8, 27.8, 24.8, 23.4, 20.7, 11.4, 11.0. HRMS (ESI$^+$): m/z calcd for $C_{32}H_{45}N_3O_3$ $[M+H]^+$: 520.3494, found 520.3531.

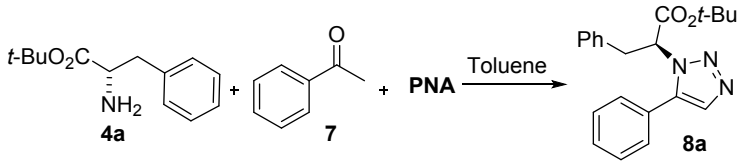


5p (71%)

Tert-butyl (*S*)-2-((1*S*,3a*S*,3b*R*,5a*S*,10a*S*,10b*S*,12a*S*)-1-hydroxy-10a,12a-dimethyl-2,3,3a,3b,4,5,5a,6,10,10a,10b,11,12,12a-tetradecahydrocyclopenta[7,8]phenanthro[2,3-d][1,2,3]triazol-9(1H)-yl)-3-(4-hydroxyphenyl)propanoate: The procedure described above was applied to stanolone (45 mg, 0.15 mmol),), $_L$-tyrosine *tert*-butyl ester (50 mg, 0.21 mmol), 4-nitrophenyl azide (28 mg, 0.17 mmol), 4 Å molecular sieves (50 mg) and toluene (0.2 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **5p** (67 mg, 71% yield) as a yellow solid m.p. 155 - 156 ˚C**.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (br, 1H), 6.75 (d, *J* = 8.0 Hz, 2H), 6.64 (d, *J* = 8.0 Hz, 2H), 4.98 (t, *J* = 8.0 Hz, 1H), 3.66 (t, *J* = 8.5 Hz, 1H), 3.45 (d, *J* = 7.8 Hz, 2H), 2.72 (d, *J* = 15.6 Hz, 1H), 2.32 (dd, *J* = 4.7, 15.7 Hz, 1H), 2.19 (d, *J* = 15Hz, 1H), 2.08 – 2.00 (m, 1H), 1.83 (d, *J* = 11.4Hz, 1H), 1.70 - 1.18 (m, 20H), 1.07 (td, J = 4.0, 13.0 Hz, 1H), 0.97-0.77 (m, 3H), 0.73 (s, 3H), 0.47 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 142.6, 131.9, 129.8, 16.8, 115.6, 83.3, 81.8, 63.5, 53.6, 50.8, 42.8, 42.0, 36.8, 36.6, 36.3, 35.8, 35.5, 31.1, 30.3, 28.8, 27.9, 24.6, 23.4, 20.7, 11.3, 11.1. HRMS (ESI$^+$): m/z calcd for $C_{32}H_{45}N_3O_4$ $[M+H]^+$: 536,3488; found 536,3483

5. Methodological studies of 8a and ester influence

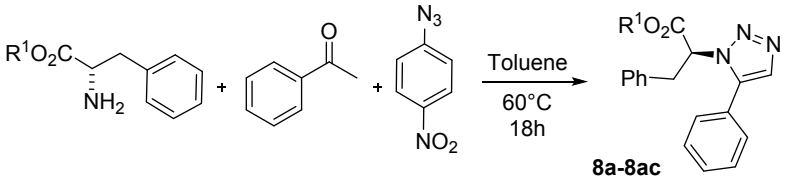
Table S3. Influence of the temperature and time on the yield of the reaction



Entry	T (°C)	Time (h)	Yield (%)
1	60	24	10
2	80	24	56
3	100	24	69
4	100	48	60

Reactions were carried out in toluene (1.5 M), 1.0 equiv of **7**, 1.2 equiv of PNA and 1.4 equiv of **4a**.

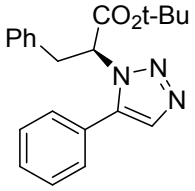
Table S4. Influence of the ester on the yield of the reaction



Entry	Product	R^1	Yiled (%)
1	**8a**	*t*-Bu	71
2	**8aa**	Me	20
3	**8ab**	Et	41
4	**8ac**	Bn	32

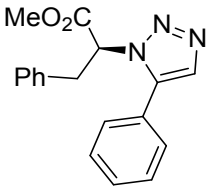
Reaction conditions: toluene (1.5 M), 1.0 equiv of the ketone, 1.2 equiv of PNA and 1.4 equiv of the amino ester at 100 °C 24h.

6. Synthesis procedure of 8a-8o



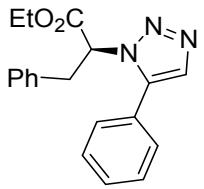
8a (71%)

***Tert*-butyl (*S*)-3-phenyl-2-(5-phenyl-1H-1,2,3-triazol-1-yl)propanoate:** The procedure described above was applied to acetophenone (50 mg, 0.42 mmol), *tert*-butyl $_L$-phenylalaninate (132 mg, 0.58), 4-nitrophenyl azide (75 mg, 0.46 mmol) 4 Å molecular sieves (50 mg) and toluene (0.4 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **8a** (95 mg, 71% yield) as a yellow solid m.p. 94 - 96 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.45 – 7.35 (m, *J* = 7.4 Hz, 1H), 7.35 – 7.28 (m, *J* = 7.4 Hz, 2H), 7.23 – 7.10 (m, *J* = 7.0 Hz, 3H), 6.88 (d, *J* = 7.2 Hz, 2H), 6.77 (d, *J* = 7.2 Hz, 2H), 4.91 (dd, *J* = 11.4, 4.2 Hz, 1H), 3.79 – 3.67 (m, 1H), 3.55 (dd, *J* = 14.0, 4.2 Hz, 1H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 139.4, 136.3, 132.3, 129.4, 129.1, 129.0, 128.7, 128.5, 127.0, 126.6, 83.3, 62.4, 37.3, 27.8. (M^+); HRMS (ESI^+): m/z calcd for $C_{21}H_{23}N_3O_2$ $[M+H]^+$: 350.1824; found 350.1859.



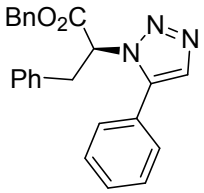
8aa (**20%**)

Methyl (*S*)-3-phenyl-2- (5-phenyl-1H-1,2,3-triazol-1-yl)propanoate: The procedure described above was applied to acetophenone (34 mg, 0.28 mmol), methyl $_L$-phenylalaninate (71 mg, 0.40 mmol), 4-nitrophenyl azide (50 mg, 0.31 mmol), 4 Å molecular sieves (50 mg) and toluene (0.3 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether /EtOAc = 8:2) affording **8aa** (15.1 mg, 20% yield) as a yellow solid m.p. 89 - 91 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.41 - 7.37 (m, 1H), 7.33 - 7.29 (m, 2H), 7.19 - 7.12 (m, 3H), 6.85 - 6.82 (m, 2H), 6.75 - 6.73 (m, 2H), 5.03 (dd, *J* = 4.1, 11.6 Hz, 1H), 3.78 (s, 3H), 3.74 - 3.70 (m, 1H), 3.63 - 3.58 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 139.6, 135.9, 132.4, 129.6, 129.1, 129.0, 128.8, 128.6, 127.1, 126.3, 61.6, 53.2, 37.7; HRMS (ESI^+): m/z calcd for $C_{18}H_{18}N_3O_2$ $[M+H]^+$: 308.1393, found 308.1395.



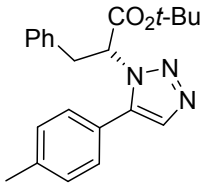
8ab (44%)

Ethyl (*S*)-3-phenyl-2-(5-phenyl-1H-1,2,3-triazol-1-yl)propanoate: The procedure described above was applied to acetophenone (32 mg, 0.26 mmol), ethyl $_L$-phenylalaninate (70 mg, 0.36 mmol), 4-nitrophenyl azide (46 mg, 0.28 mmol), 4 Å molecular sieves (50 mg) and toluene (0.3 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether /EtOAc = 8:2) affording **8ab** (37 mg, 44% yield) as a yellow solid m.p. 92 - 93 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.41 - 7.37 (m, 1H), 7.33 - 7.29 (m, 2H), 7.19 - 7.13 (m, 3H), 6.87 - 6.84 (m, 2H), 6.77 - 6.75 (m, 2H), 5.01 (dd, *J* = 4.2, 11.4 Hz, 1H), 4.27 - 4.19 (m, 2H), 3.74 (dd, *J* = 11.4, 13.0 Hz, 1H), 3.60 (dd, *J* = 4.2, 14.0 Hz, 1H), 1.23 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 139.6, 136.0, 132.4, 129.5, 129.1, 129.0, 128.7, 128.6, 127.1, 16.4, 62.4, 61.8, 37.6, 14.0. HRMS (ESI$^+$): m/z calcd for $C_{19}H_{19}N_3O_2$ $[M+H]^+$: 322.1511, found 322.1547.



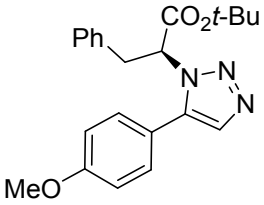
8ac (32%)

Benzyl (*S*)-3-phenyl-2-(5-phenyl-1H-1,2,3-triazol-1-yl)propanoate: The procedure described above was applied to acetophenone (50 mg, 0.42 mmol), benzyl $_L$-phenylalaninate (149 mg, 0.58 mmol), 4-nitrophenyl azide (76 mg, 0.46 mmol), 4 Å molecular sieves (50 mg) and toluene (0.4 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether /EtOAc = 8:2) affording **8ac** (51.5 mg, 32% yield) as a yellow solid m.p. 96 - 98 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.38 - 7.31 (m,4H), 7.27 - 7.22 (m, 4H), 7.18 - 7.12 (m, 3H), 6.87 - 6.84 (m, 2H), 6.69 - 6.67 (m , 2H), 5.20 (dd, *J* = 12.4, 29.2 Hz, 2H), 5.05 (dd, *J* = 4.1, 12.4, Hz, 1H), 3.77 (dd, *J* = 11.5, 14.1 Hz, 1H), 3.61 (dd, *J* = 4.2, 13.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 139.6, 135.9, 134.8, 132.4, 129.5, 129.1, 129.0, 128.8, 128.7, 128.61, 128.59, 128.5, 128.1, 127.1, 126.2, 67.8, 61.8, 37.4. HRMS (ESI$^+$): m/z calcd for $C_{24}H_{21}N_3O_2$ $[M+H]^+$: 384.1667, found 384.1704.



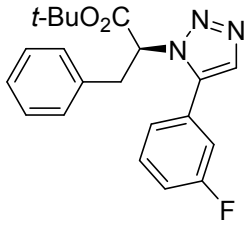
8b (52%)

***Tert*-butyl (*R*)-3-phenyl-2-(5-(p-tolyl)-1H-1,2,3-triazol-1-yl)propanoate:** The procedure described above was applied to 4-methylacetophenone (50 mg, 0.37 mmol), *tert*-butyl $_D$-phenylalaninate (115.5 mg, 0.52), 4-nitrophenyl azide (67 mg, 0.41 mmol) 4Å molecular sieves (50 mg) and toluene (0.4 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **8b** (71 mg, 52% yield) as a yellow-red solid m.p. 82 - 84 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 2H), 7.21 – 7.14 (m, 3H), 7.12 (d, *J* = 7.8 Hz, 2H), 6.89 (d, *J* = 6.1 Hz, 2H), 6.65 (d, *J* = 7.8 Hz, 2H), 4.91 (dd, *J* = 11.3, 4.2 Hz, 1H), 3.78 – 3.68 (m, 1H), 3.55 (dd, *J* = 14.1, 4.1 Hz, 1H), 2.37 (s, 3H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 139.6, 139.5, 136.4, 132.3, 129.4, 129.0, 129.0, 128.5, 126.9, 123.5, 83.2, 62.3, 37.3, 27.8, 21.3. HRMS (ESI$^+$): m/z calcd for $C_{22}H_{25}N_3O_2$ [M+H]$^+$: 364.1980; found 364.2016.



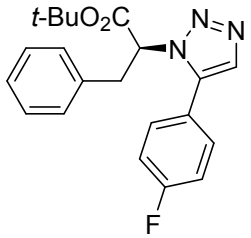
8c (58%)

***Tert*-butyl (*S*)-2-(5-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)-3-phenylpropanoate:** The procedure described above was applied to 4-methoxyacetophenone (50 mg, 0.33 mmol), *tert*-butyl $_L$-phenylalaninate (103 mg, 0.47), 4-nitrophenyl azide (60 mg, 0.37 mmol) 4 Å molecular sieves (50 mg) and toluene (0.3 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **8c** (85 mg, 71% yield) as a yellow-brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.23 – 7.11 (m, 3H), 6.89 (d, *J* = 6.4 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 6.68 (d, *J* = 8.4 Hz, 2H), 4.89 (dd, *J* = 11.4, 4.1 Hz, 1H), 3.82 (s, 3H), 3.77 – 3.67 (m, 1H), 3.54 (dd, *J* = 14.0, 4.1 Hz, 1H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 160.5, 139.3, 136.4, 132.3, 130.5, 129.1, 128.5, 127.0, 118.5, 114.2, 83.2, 62.3, 55.3, 37.3, 27.8. HRMS (ESI$^+$): m/z calcd for $C_{22}H_{25}N_3O_3$ [M+H]$^+$: 380.1929; found 380.1967.



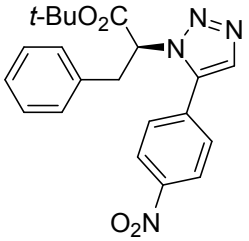
8d (50%)

***Tert*-butyl (*S*)-2-(5-(3-fluorophenyl)-1H-1,2,3-triazol-1-yl)-3-phenylpropanoate:** The procedure described above was applied to 3-fluoroacetophenone (50 mg, 0.36 mmol), *tert*-butyl L-phenylalaninate (112 mg, 0.51), 4-nitrophenyl azide (65 mg, 0.40 mmol) 4 Å molecular sieves (50 mg) and toluene (0.4 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **8d** (66 mg, 50% yield) as a yellow solid m.p. 62 - 64 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.30 (dd, *J* = 14.0, 7.6 Hz, 1H), 7.23 – 7.13 (m, 3H), 7.13 – 7.06 (m, 1H), 6.87 (d, *J* = 6.9 Hz, 2H), 6.58 (d, *J* = 7.6 Hz, 1H), 6.41 (d, *J* = 9.1 Hz, 1H), 4.88 (dd, *J* = 11.5, 4.0 Hz, 1H), 3.77 – 3.67 (m, 1H), 3.55 (dd, *J* = 14.1, 4.0 Hz, 1H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 163.7, 161.2, 138.3, 138.3, 136.2, 132.4, 130.5, 130.4, 129.0, 128.6, 128.5, 128.5, 127.1, 124.9, 124.9, 83.5, 62.6, 37.3, 27.8. HRMS (ESI$^+$): m/z calcd for $C_{21}H_{22}FN_3O_2$ $[M+H]^+$ 368.1730; found 368.1764.



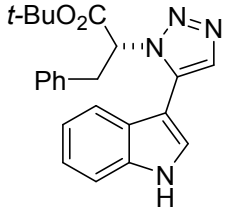
8e (45%)

Tert-butyl (*S*)-2-(5-(4-fluorophenyl)-1H-1,2,3-triazol-1-yl)-3-phenylpropanoate: The procedure described above was applied to 4-fluoroacetophenone (50 mg, 0.36 mmol), *tert*-butyl L-phenylalaninate (112 mg, 0.51), 4-nitrophenyl azide (65 mg, 0.40 mmol) 4 Å molecular sieves (50 mg) and toluene (0.4 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **8e** (60 mg, 45% yield) as a yellow solid m.p. 87 - 89 ˚C ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (s, 1H), 7.23 – 7.12 (m, 3H), 7.00 (t, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 6.9 Hz, 2H), 6.73 – 6.67 (m, 2H), 4.82 (dd, *J* = 11.5, 4.0 Hz, 1H), 3.77 – 3.67 (m, 1H), 3.53 (dd, *J* = 14.0, 3.9 Hz, 1H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 164.6, 162.1, 138.5, 136.4, 132.4, 131.2, 131.1, 129.0, 128.6, 127.0, 122.5, 122.5, 116.0, 115.8, 83.4, 62.5, 37.3, 27.8. HRMS (ESI$^+$): m/z calcd for $C_{21}H_{22}FN_3O_2$ $[M+H]^+$ 368.1730; found 368.1762.



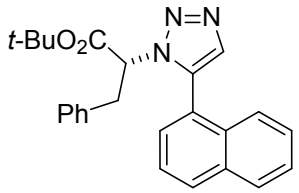
8f (71%)

Tert-butyl (*S*)-2-(5-(4-nitrophenyl)-1H-1,2,3-triazol-1-yl)-3-phenylpropanoate: The procedure described above was applied to 4-fluoroacetophenone (50 mg, 0.30 mmol), *tert*-butyl L-phenylalaninate (94 mg, 0.42), 4-nitrophenyl azide (55 mg, 0.33 mmol) 4 Å molecular sieves (50 mg) and toluene (0.3 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **8f** (85 mg, 71% yield) as a yellow-brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.5 Hz, 2H), 7.64 (s, 1H), 7.25 – 7.13 (m, 3H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 7.1 Hz, 2H), 4.81 (dd, *J* = 11.6, 3.8 Hz, 1H), 3.79 – 3.67 (m, 1H), 3.55 (dd, *J* = 14.1, 3.7 Hz, 1H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 148.4, 137.5, 136.2, 133.1, 132.8, 130.1, 129.0, 128.8, 127.3, 123.9, 83.8, 63.0, 37.4, 27.8. HRMS (ESI$^+$): m/z calcd for $C_{21}H_{22}N_4O_4$ $[M+H]^+$: 395.1675; found 395.1711.



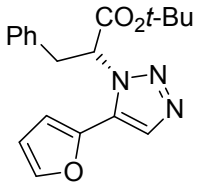
8g (41%)

Tert-butyl (*S*)-2-(5-(1H-indol-3-yl)-1H-1,2,3-triazol-1-yl)-3-phenylpropanoate: The procedure described above was applied to 3-acetylindole (50 mg, 0.31 mmol), *tert*-butyl L-phenylalaninate (97 mg, 0.43), 4-nitrophenyl azide (57 mg, 0.34 mmol) 4 Å molecular sieves (50 mg) and toluene (0.3 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **8g** (50 mg, 41% yield) as an off white solid. m.p. 155 - 156 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (s, 1H), 7.68 (s, 1H), 7.44 (d, *J* = 8.2 Hz, 1H), 7.28 – 7.22 (m, 1H), 7.21 – 7.05 (m, 5H), 6.88 (d, *J* = 6.9 Hz, 2H), 6.57 – 6.52 (m, 1H), 5.04 (dd, *J* = 11.2, 4.2 Hz, 1H), 3.79 – 3.69 (m, 1H), 3.56 (dd, *J* = 14.0, 4.2 Hz, 1H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 136.6, 135.8, 133.4, 133.2, 129.2, 128.5, 126.9, 126.6, 124.7, 123.0, 120.8, 119.0, 111.5, 101.3, 83.2, 62.4, 37.6, 27.8. HRMS (ESI$^+$): m/z calcd for $C_{23}H_{24}N_4O_2$ $[M+H]^+$ 389.1933; found 389.1965.



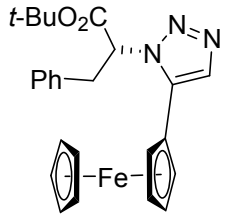
8h (**45%**)

Tert-butyl (R)-2-(5-(naphthalen-1-yl)-1H-1,2,3-triazol-1-yl)-3-phenylpropanoate: The procedure described above was applied to 1-acetonaphthone (50 mg, 0.29 mmol) *tert*-butyl $_D$-phenylalaninate (91 mg, 0.41), 4-nitrophenyl azide (53 mg, 0.32 mmol) 4 Å molecular sieves (50 mg) and toluene (0.3 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **8h** (53 mg, 45% yield) as a yellow-brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.83 (m, 2H), 7.65 (s, 1H), 7.60 – 7.33 (m, 3H), 7.26 – 7.04 (m, 4H), 6.93 – 6.73 (m, 2H), 5.84 (bs, 1H), 4.61 (bs, 1H), 3.90 – 3.60 (m, 1H), 3.49 (dd, *J* = 13.9, 3.7 Hz, 1H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 137.4, 136.4, 133.7, 133.2, 132.0, 130.2, 129.3, 128.8, 128.7, 128.6, 128.4, 128.2, 127.0, 126.4, 126.1, 125.9, 124.8, 113.4, 83.4, 62.6, 27.8. HRMS (ESI$^+$): m/z calcd for $C_{25}H_{25}N_3O_2$ $[M+H]^+$: 400.2010; found 400.2012.



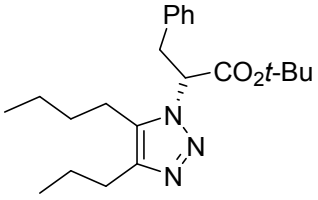
8i (69%)

***Tert*-butyl (*R*)-2-(5-(furan-2-yl)-1H-1,2,3-triazol-1-yl)-3-phenylpropanoate:** The procedure described above was applied to 2-acetylfuran (50 mg, 0.45 mmol), *tert*-butyl D-phenylalaninate (111 mg, 0.64), 4-nitrophenyl azide (82 mg, 0.50 mmol) 4 Å molecular sieves (50 mg) and toluene (0.4 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **8i** (106 mg, 69% yield) brown solid m.p. 63 - 65 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.51 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.20 – 7.14 (m, 3H), 7.11 – 7.06 (m, 2H), 6.49 (dd, *J* = 3.4, 1.8 Hz, 1H), 6.47 (dd, *J* = 3.5, 0.7 Hz, 1H), 5.53 (dd, *J* = 9.3, 6.1 Hz, 1H), 3.74 (d, *J* = 5.7 Hz, 1H), 3.71 (d, *J* = 2.4 Hz, 1H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 143.7, 141.2, 136.4, 132.0, 129.7, 129.0, 128.5, 127.0, 111.7, 110.5, 83.3, 64.1, 36.9, 27.7. HRMS (ESI$^+$): m/z calcd for $C_{19}H_{21}N_3O_3$ $[M+H]^+$ 340.1616; found 340.1647



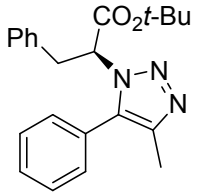
8j (12%)

Tert-butyl (*R*)-2-(5-(ferrocenyl)-1H-1,2,3-triazol-1-yl)-3-phenylpropanoate. The procedure described above was applied to acetylferrocene (100 mg, 0.44 mmol) *tert*-butyl $_D$-phenylalaninate (136 mg, 0.61), 4-nitrophenyl azide (80 mg, 0.48 mmol) 4 Å molecular sieves (50 mg) and toluene (0.4 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **8j** (24 mg, 12% yield) as a dark yellow solid m.p. 123 - 125 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.23 – 7.16 (m, 3H), 7.05 – 6.97 (m, 2H), 5.17 (dd, *J* = 10.8, 4.4 Hz, 1H), 4.30 – 4.22 (m, 3H), 4.03 (s, 5H), 3.88 (d, *J* = 22.1 Hz, 1H), 3.79 (dd, *J* = 13.8, 11.1 Hz, 1H), 3.61 (dd, *J* = 14.1, 4.4 Hz, 1H), 1.41 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 137.3, 136.6, 132.9, 129.2, 128.6, 127.0, 83.3, 70.8, 69.6, 69.4, 69.4, 68.9, 68.5, 62.6, 37.2, 27.8. HRMS (ESI$^+$): m/z calcd for $C_{25}H_{27}FeN_3O_2$ $[M+H]^+$: 458.1486; found 458.1516.



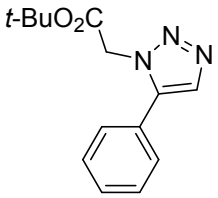
8k (20%)

***Tert*-butyl (*R*)-2-(5-butyl-4-propyl-1H-1,2,3-triazol-1-yl)-3-phenylpropanoate.** The procedure described above was applied to nonan-5-one (50 mg, 0.35 mmol), *tert*-butyl $_L$-phenylalaninate (108 mg, 0.49), 4-nitrophenyl azide (63.5 mg, 0.39 mmol) 4 Å molecular sieves (50 mg) and toluene (0.3 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **8k** (26 mg, 20% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 - 1.16 (m, 3H), 7.00 - 6.97 (m, 2H), 4.78 (dd, *J* = 4.3, 10.7 Hz, 1H), 3.75 - 3.70 (m, 1H), 3.58 (dd, *J* = 4.3, 13.9 Hz, 1H), 2.56 - 2.48 (m, 2H), 2.30 - 2.23 (m, 1H), 2.16 - 2.08 (m, 1H), 1.72 - 1.63 (m, 3H), 1.39 (s, 9H), 1.13 - 1.03 (m, 4H), 0.89 (t, *J* = 7.3 Hz, 3H), 0.78 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 144.0, 136.8, 134.2, 129.1, 128.5, 126.9, 83.0, 62.6, 37.3, 30.8, 27.8, 26.9, 22.8, 22.2, 21.7, 13.7, 13.6. HRMS (ESI$^+$): m/z calcd for $C_{22}H_{33}N_3O_2$ $[M+H]^+$: 372.2606; found 372.2642.



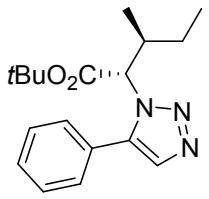
8l (**52%)**

***Tert*-butyl (*R*)-3-phenyl-2-(5-(p-tolyl)-1H-1,2,3-triazol-1-yl)propanoate:** The procedure described above was applied to propiophenone (50 mg, 0.37 mmol)*, tert*-butyl $_D$-phenylalaninate (115.5 mg, 0.52), 4-nitrophenyl azide (67 mg, 0.41 mmol) 4 Å molecular sieves (50 mg) and toluene (0.4 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 7:3) affording **8l** (71 mg, 52% yield) as a yellow solid m.p. 58 - 60 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 2H), 7.21 – 7.14 (m, 3H), 7.12 (d, *J* = 7.8 Hz, 2H), 6.89 (d, *J* = 6.1 Hz, 2H), 6.65 (d, *J* = 7.8 Hz, 2H), 4.91 (dd, *J* = 11.3, 4.2 Hz, 1H), 3.78 – 3.68 (m, 1H), 3.55 (dd, *J* = 14.1, 4.1 Hz, 1H), 2.37 (s, 3H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 139.6, 139.5, 136.4, 132.3, 129.4, 129.1, 129.0, 128.5, 127.0, 123.5, 83.2, 62.3, 37.3, 27.8, 21.3. HRMS (ESI$^+$): m/z calcd for $C_{22}H_{25}N_3O_2$ $[M+H]^+$: 364.1980; found 364.2016.



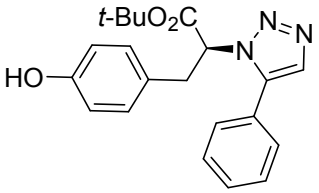
8m (95%)

***Tert*-butyl 2- (5-phenyl-1H-1,2,3-triazol-1-yl)acetate**: Acetophenone (52 mg, 0.42 mmol), *tert*-butyl glycinate (77 mg, 0.58 mmol), 4-nitrophenyl azide (75 mg, 0.46 mmol), 4Å molecular sieves (50 mg) and toluene (0.4 mL) were mixed in a sealed reaction tube 24 hours at 100 °C. After the solvent was removed under reduced pressure and the crude reaction mixture was purified by flash column chromatography (CH_2Cl_2 followed by heptane/EtOAc = 6:4) affording **8m** (106 mg, 95% yield) as an off white semi solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.49 - 7.47 (m, 3H), 7.41 - 7.37 (m, 2H), 5.04 (s, 1H), 1.39 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 138.7, 133.0, 129.8, 129.2, 128.7, 126.9, 83.6, 50.3, 27.9; HRMS (ESI$^+$): m/z calcd for $C_{14}H_{18}N_3O_2$ $[M+H]^+$: 260.1393, found 260.1392.



8n (71%)

***Tert*-butyl (2*S*,3*S*)-3-methyl-2-(5-phenyl-1H-1,2,3-triazol-1-yl)pentanoate:** The procedure described above was applied to acetophenone (50 mg, 0.42 mmol), *tert*-butyl L-isoleucinate (109 mg, 0.58 mmol), 4-nitrophenyl azide (75 mg, 0.46 mmol), 4Å molecular sieves (50 mg) and toluene (0.4 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **8n** (93 mg, 71% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.53 – 7.47 (m, 3H), 7.42 – 7.36 (m, 2H), 4.59 (d, *J* = 9.0 Hz, 1H), 2.77 – 2.68 (m, 1H), 1.44 (s, 9H), 1.28 – 1.17 (m, 1H), 1.09 – 0.96 (m, 4H), 0.77 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.15, 139.20, 132.49, 129.64, 129.31, 129.07, 126.98, 82.92, 66.07, 36.62, 27.85, 25.45, 15.85, 10.81. HRMS (ESI$^+$): m/z calcd for $C_{18}H_{25}N_3O_2$ [M+H]$^+$: 316.1980; found 316.2021.



8o (64%)

***Tert*-butyl (*S*)-3-(4-hydroxyphenyl)-2-(5-phenyl-1H-1,2,3-triazol-1-yl)propanoate:** The procedure described above was applied to acetophenone (50 mg, 0.42 mmol), L-tyrosine *tert*-butyl ester (138 mg, 0.58), 4-nitrophenyl azide (75 mg, 0.46 mmol) 4Å molecular sieves (50 mg) and toluene (0.4 mL). The product was purified by flash column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 8:2) affording **8o** (96 mg, 63% yield as a yellow solid m.p. 140 - 142 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.47 – 7.31 (m, 3H), 6.87 (d, *J* = 7.4 Hz, 2H), 6.80 – 6.73 (m, 2H), 6.71 – 6.63 (m, 2H), 4.98 – 4.90 (m, 1H), 3.74 – 3.63 (m, 1H), 3.51 – 3.43 (m, 1H), 1.41 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 155.7, 139.8, 132.1, 130.1, 130.1, 129.7, 129.2, 128.8, 127.2, 126.3, 115.6, 83.4, 62.8, 36.3, 27.8. HRMS (ESI$^+$): m/z calcd for $C_{21}H_{23}N_3O_3$ [M+H]$^+$: 366.1773; found 366.1808

7. ^{1}H and ^{13}C NMR spectra for compound of 5a-p

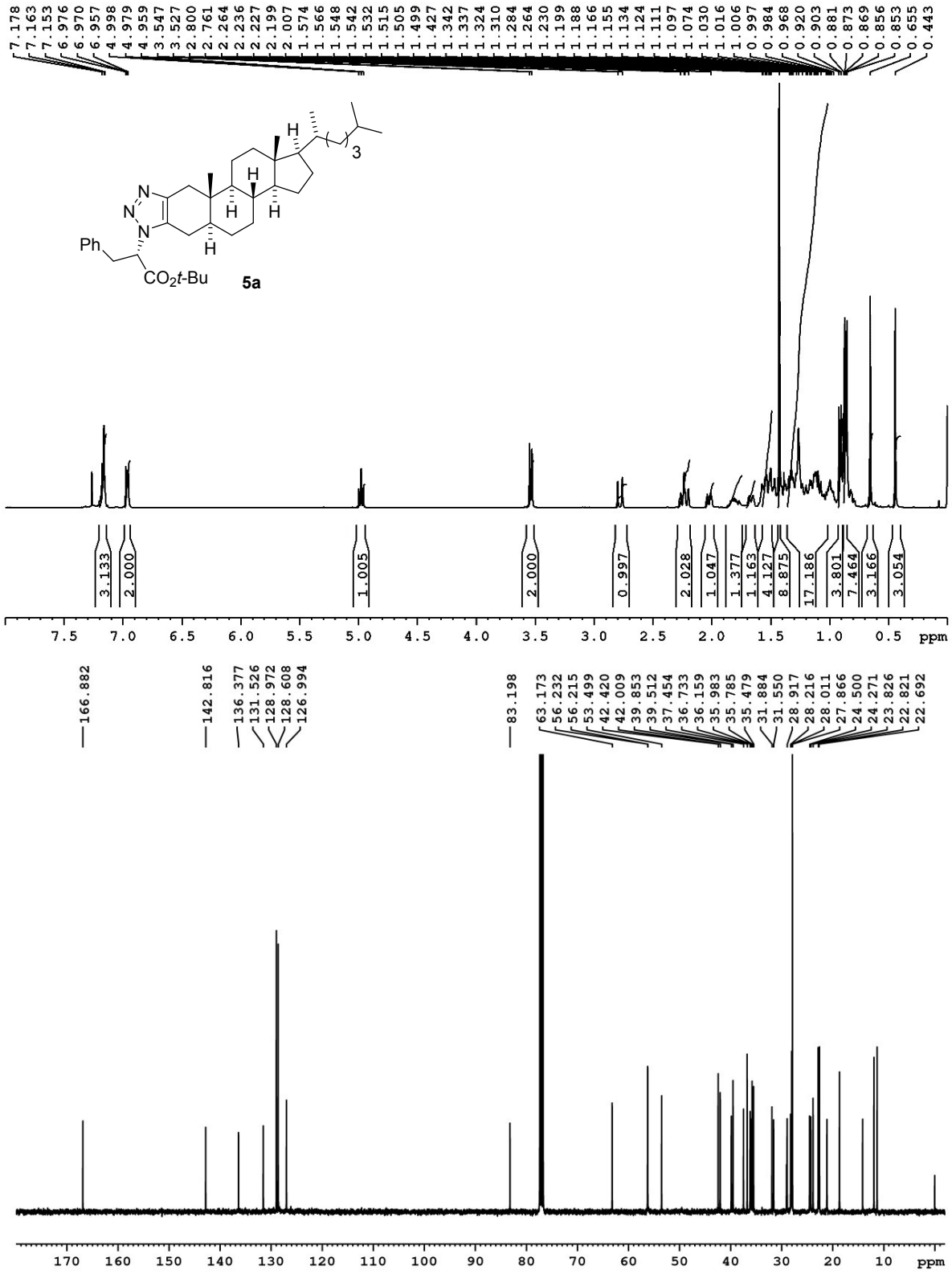


Figure S3. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5a**.

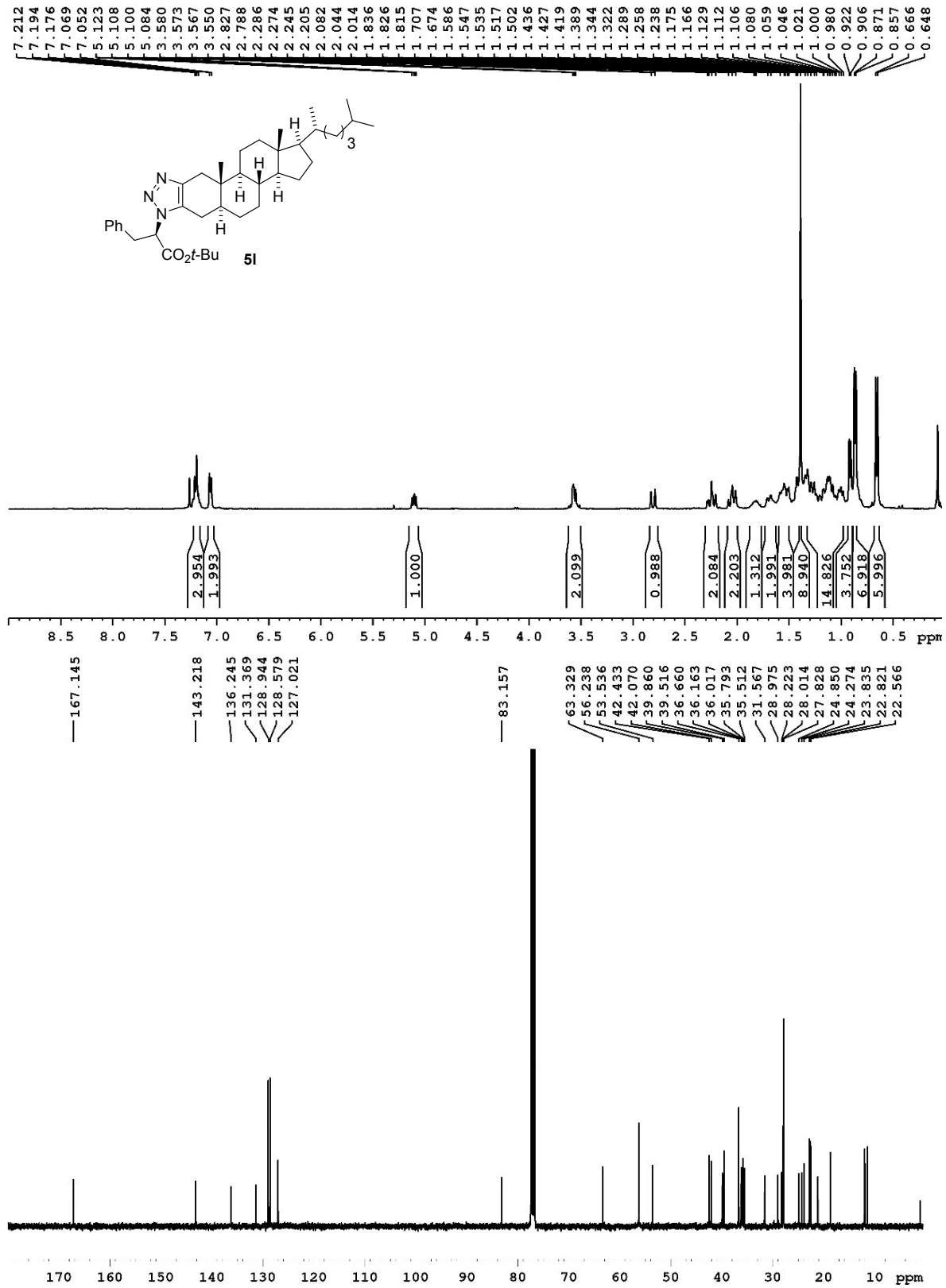


Figure S4. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5l**.

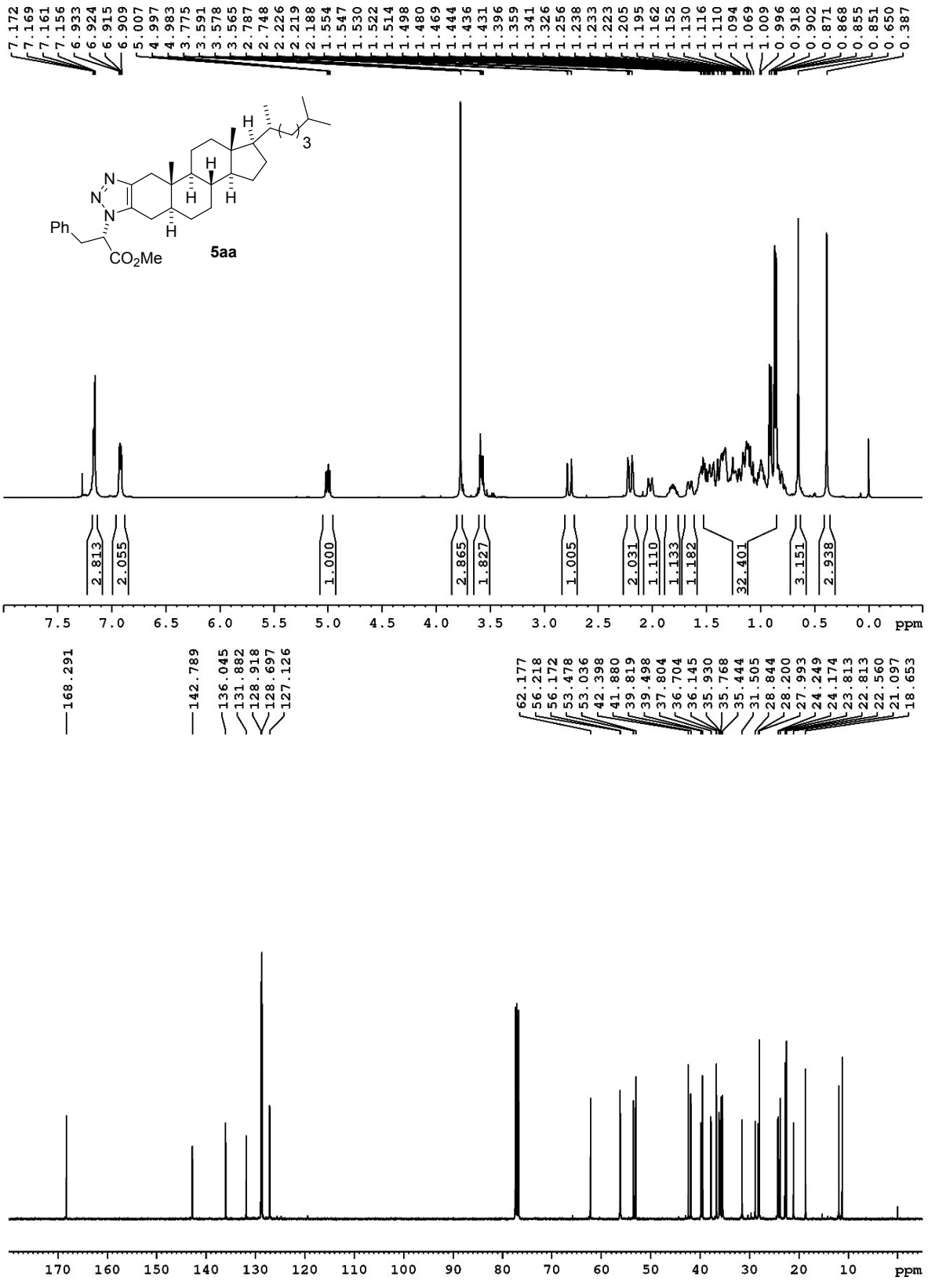


Figure S5. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5ab**

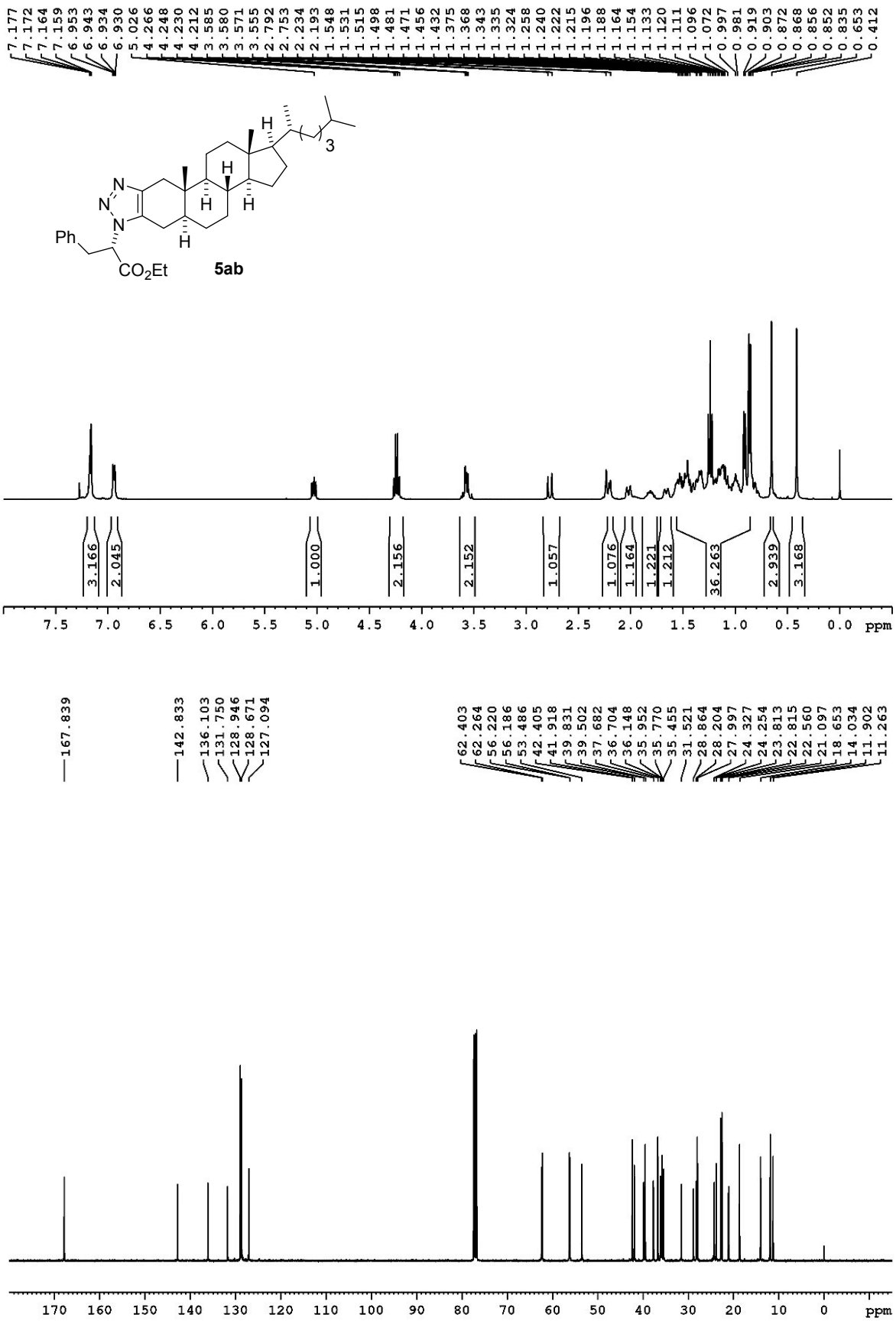


Figure S5. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5ac**

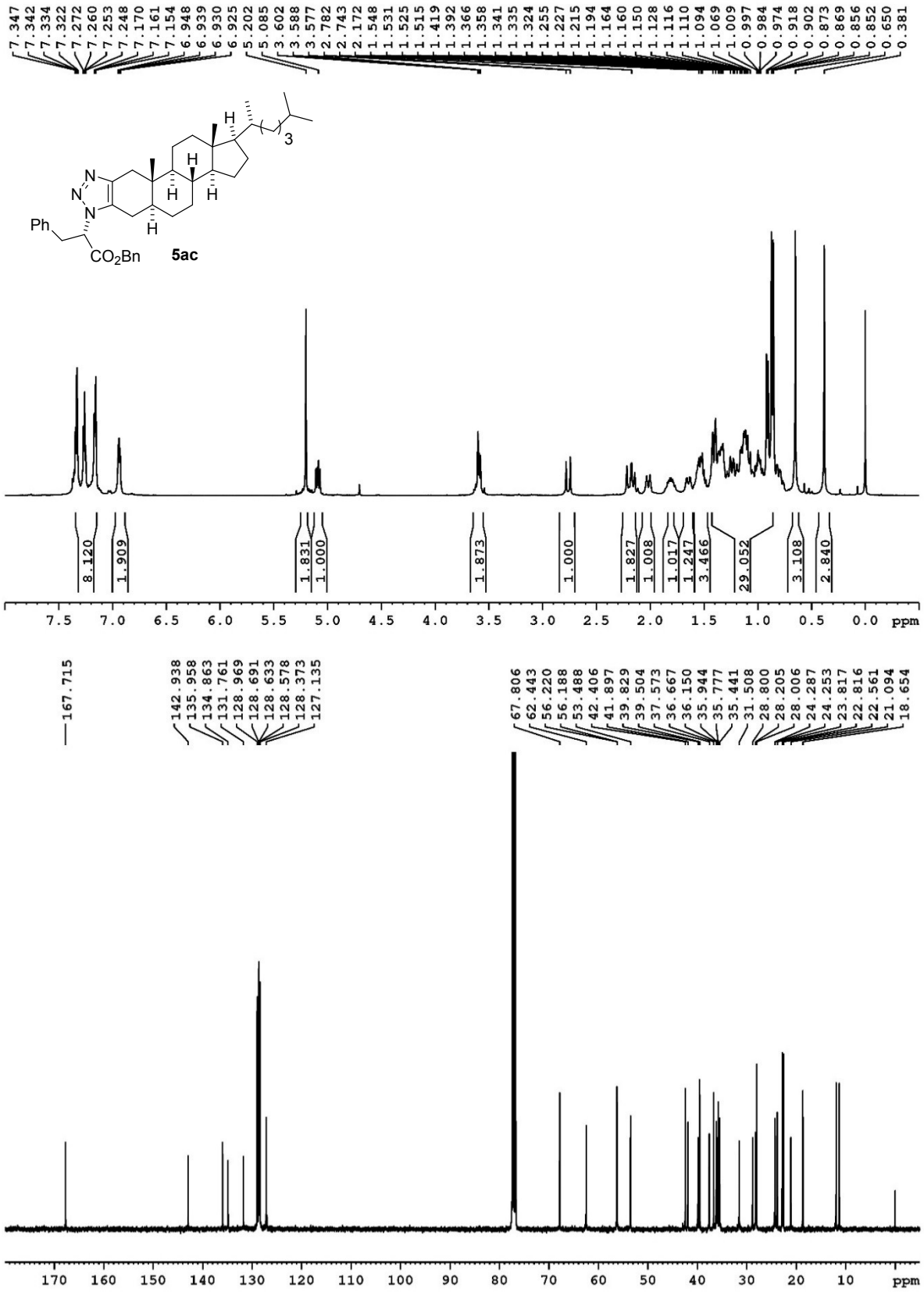


Figure S6. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5ad**

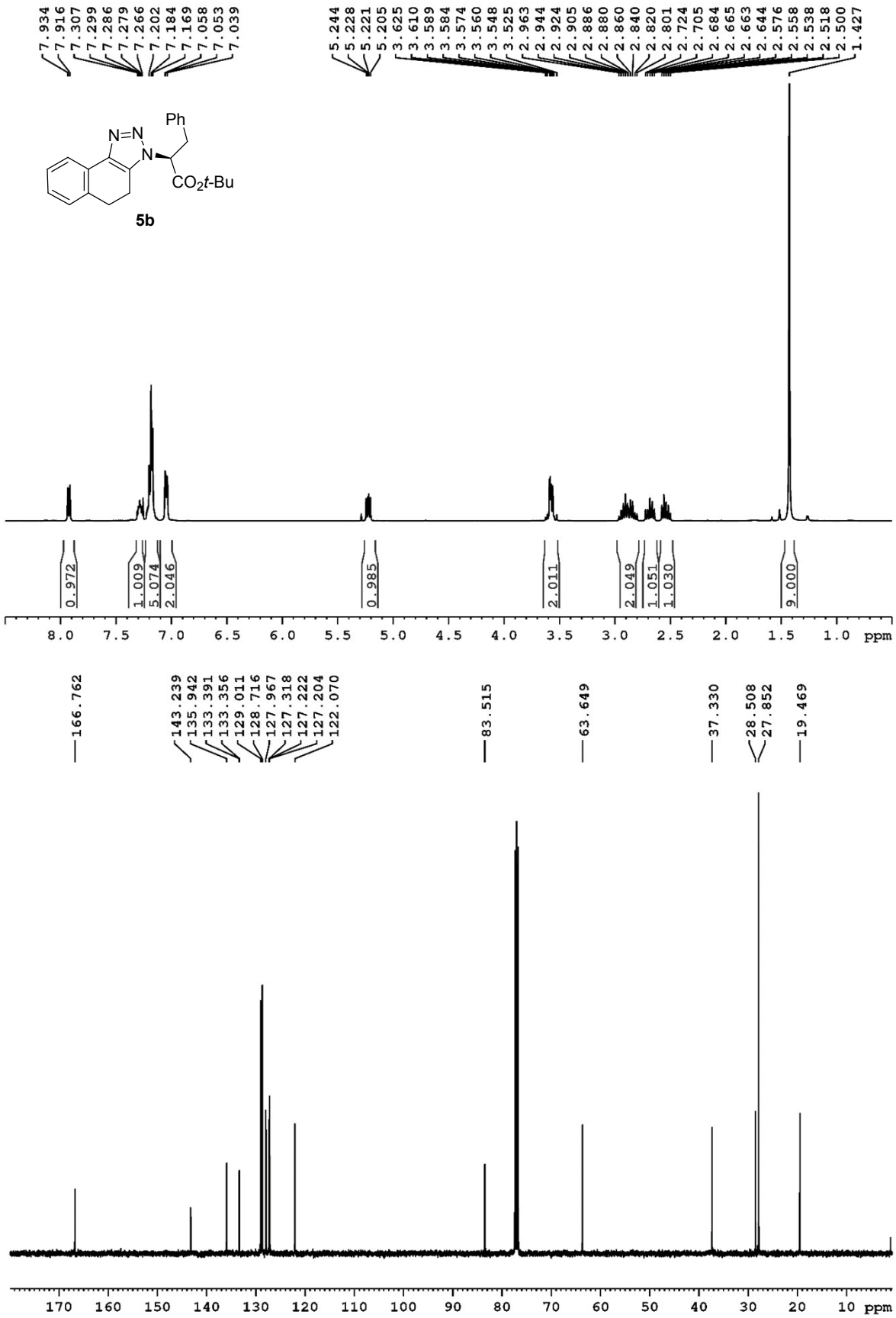


Figure S7. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5b**.

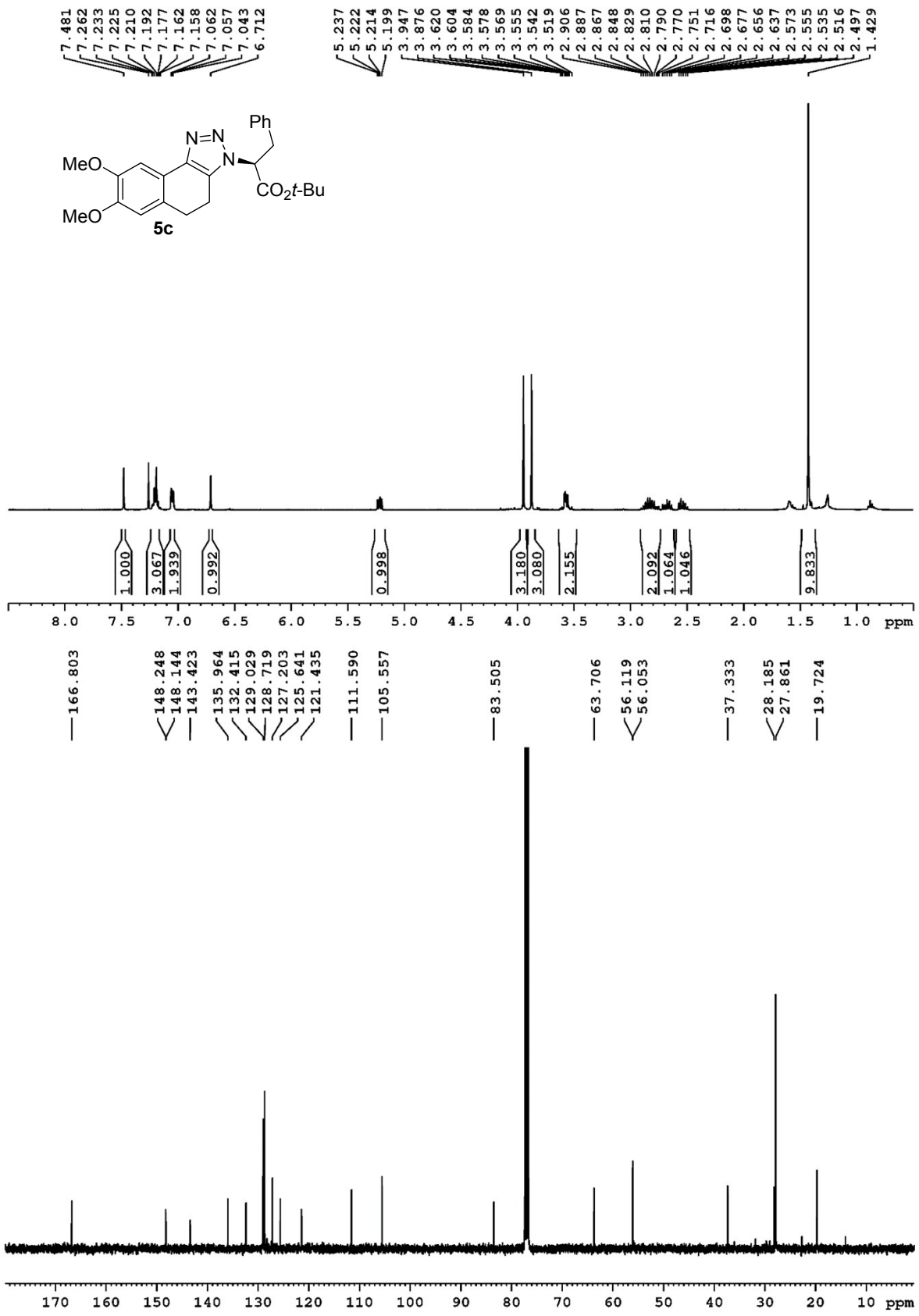


Figure S8. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5c**.

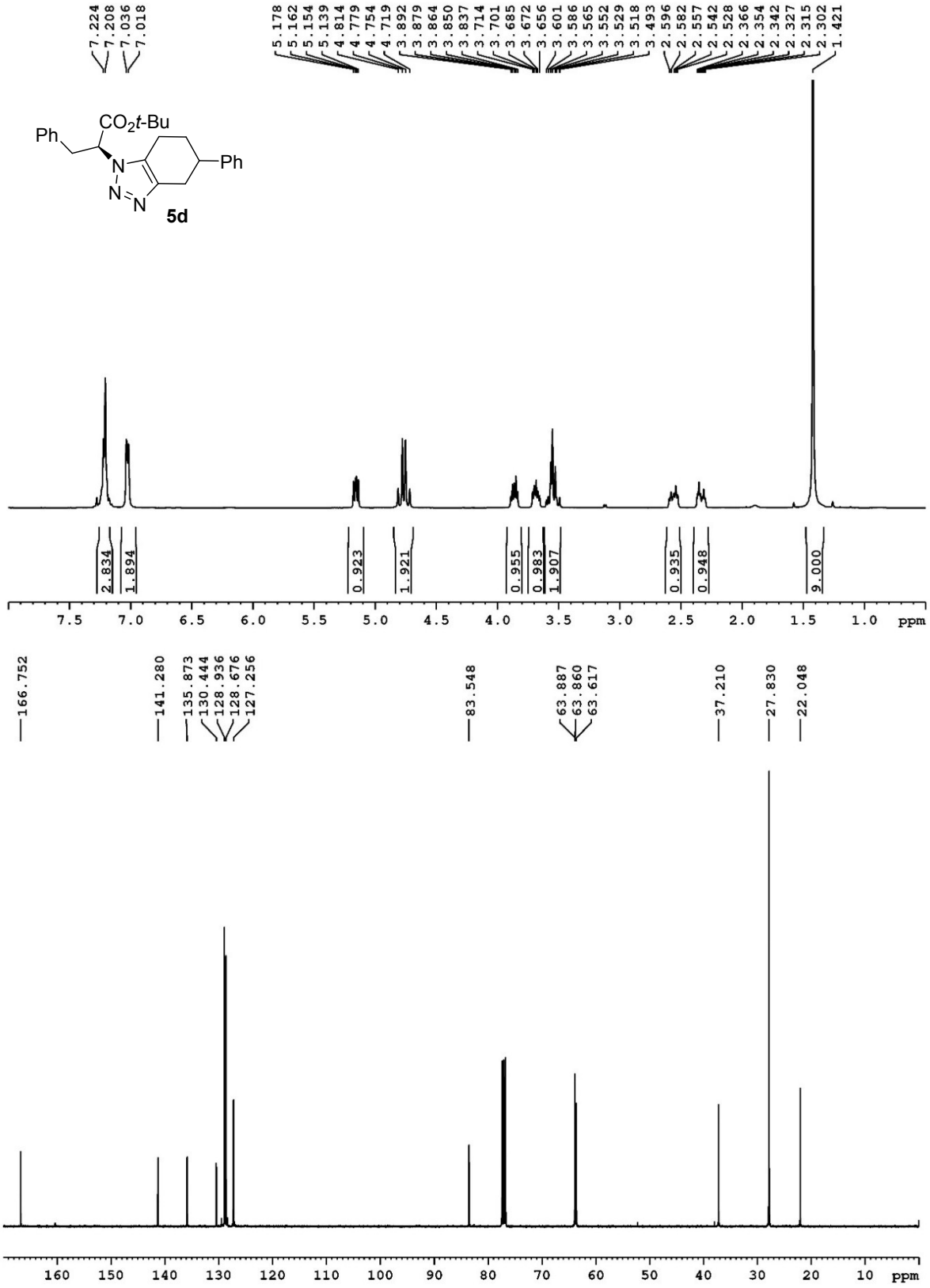


Figure S9. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5d**.

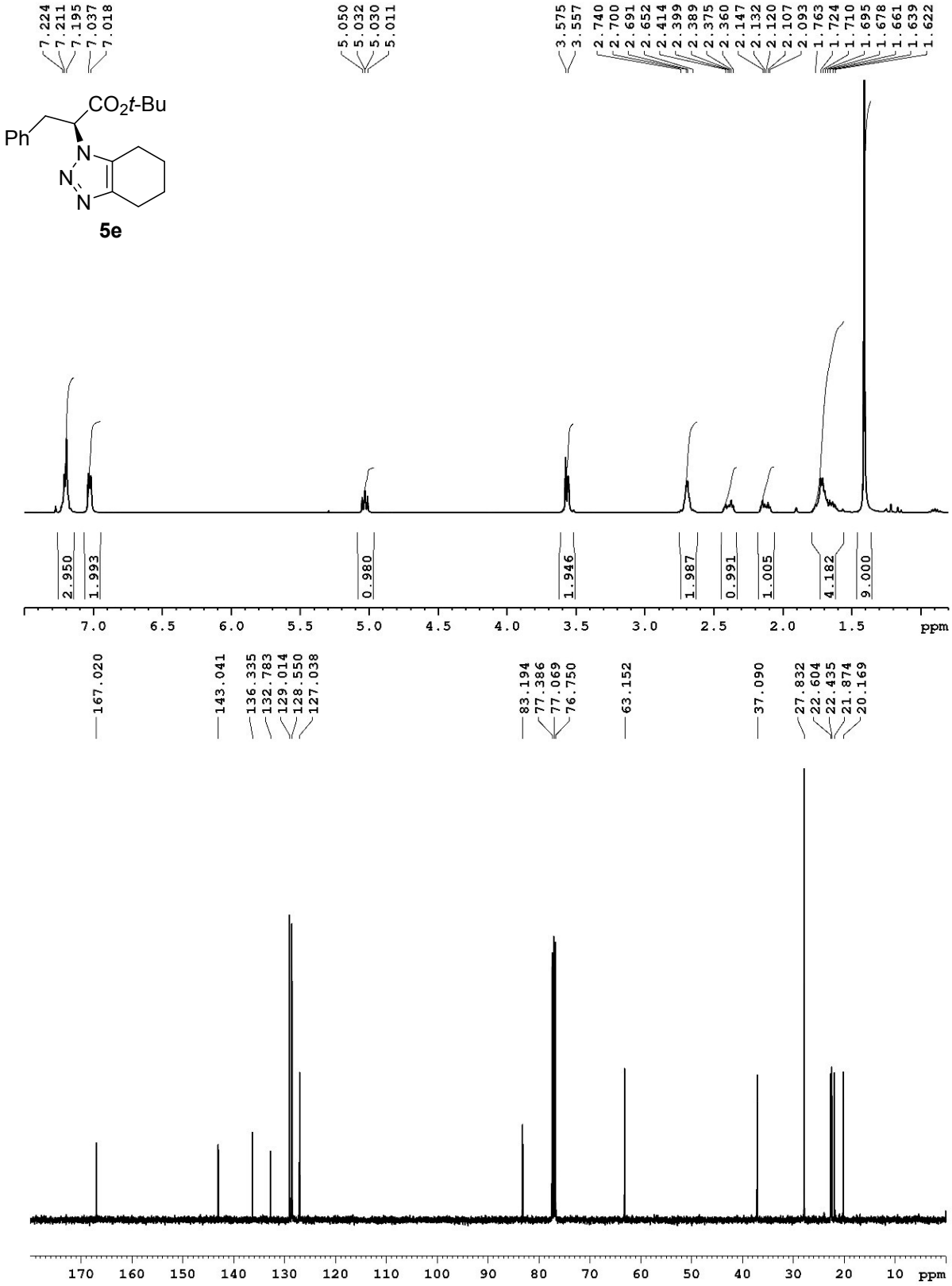


Figure S10. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5e**

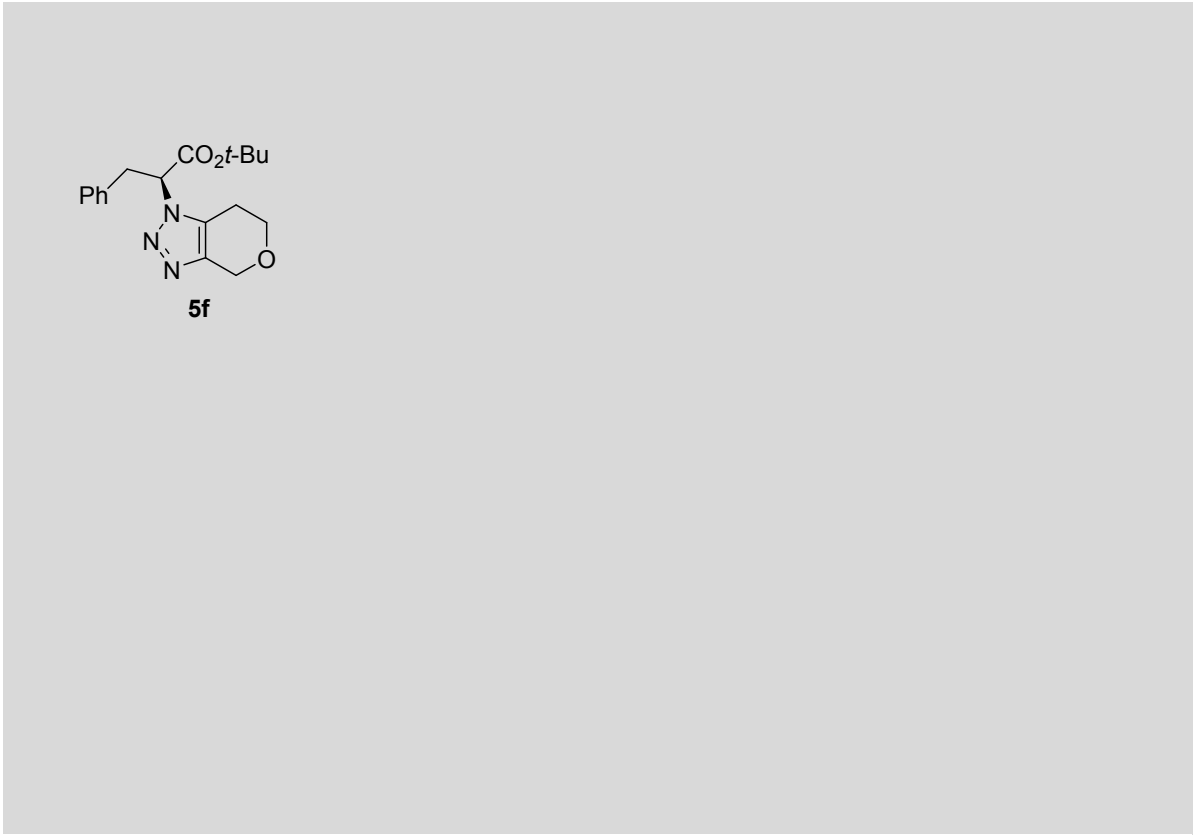


Figure S11. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5f**.

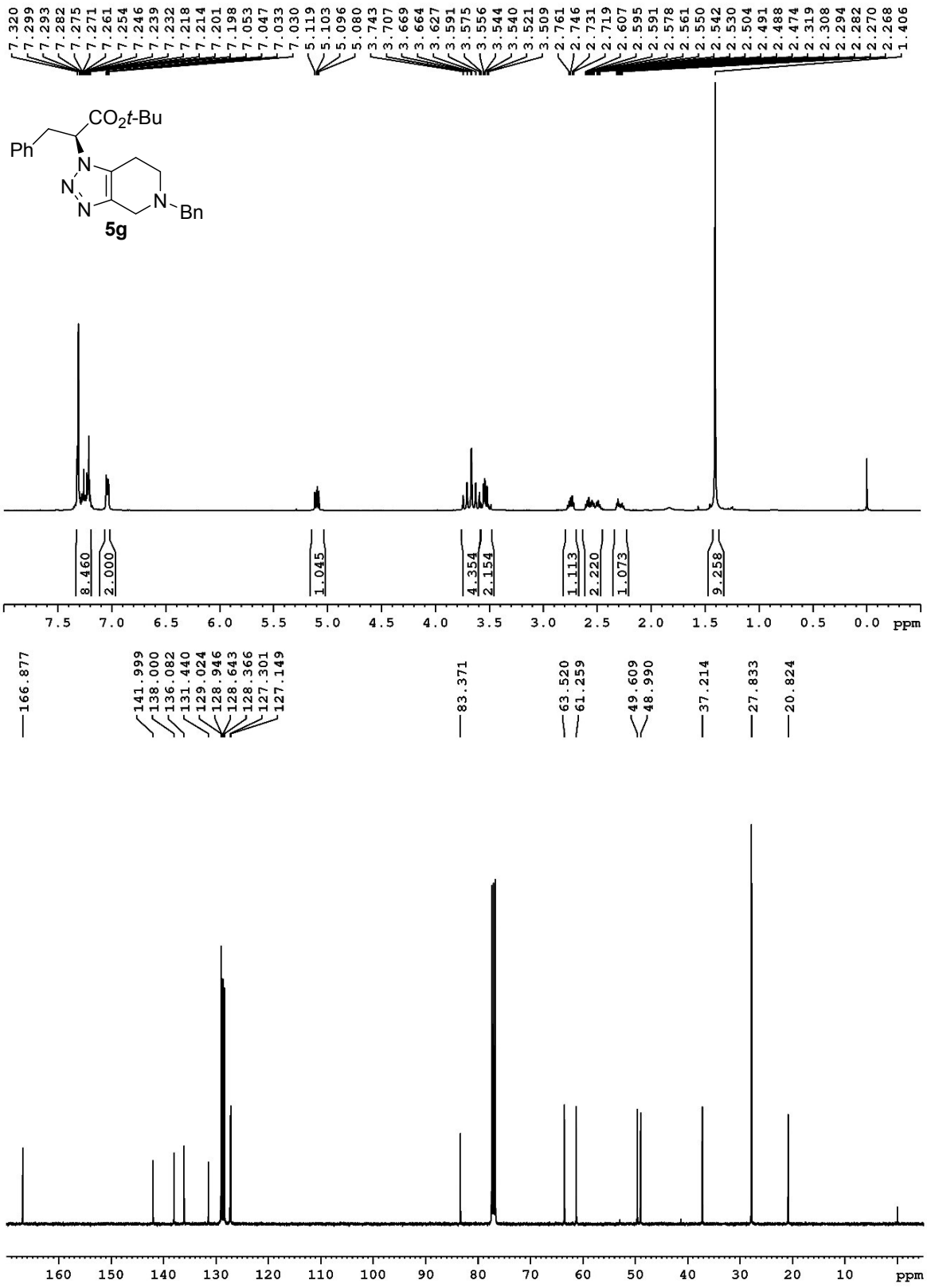


Figure S12. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5g**.

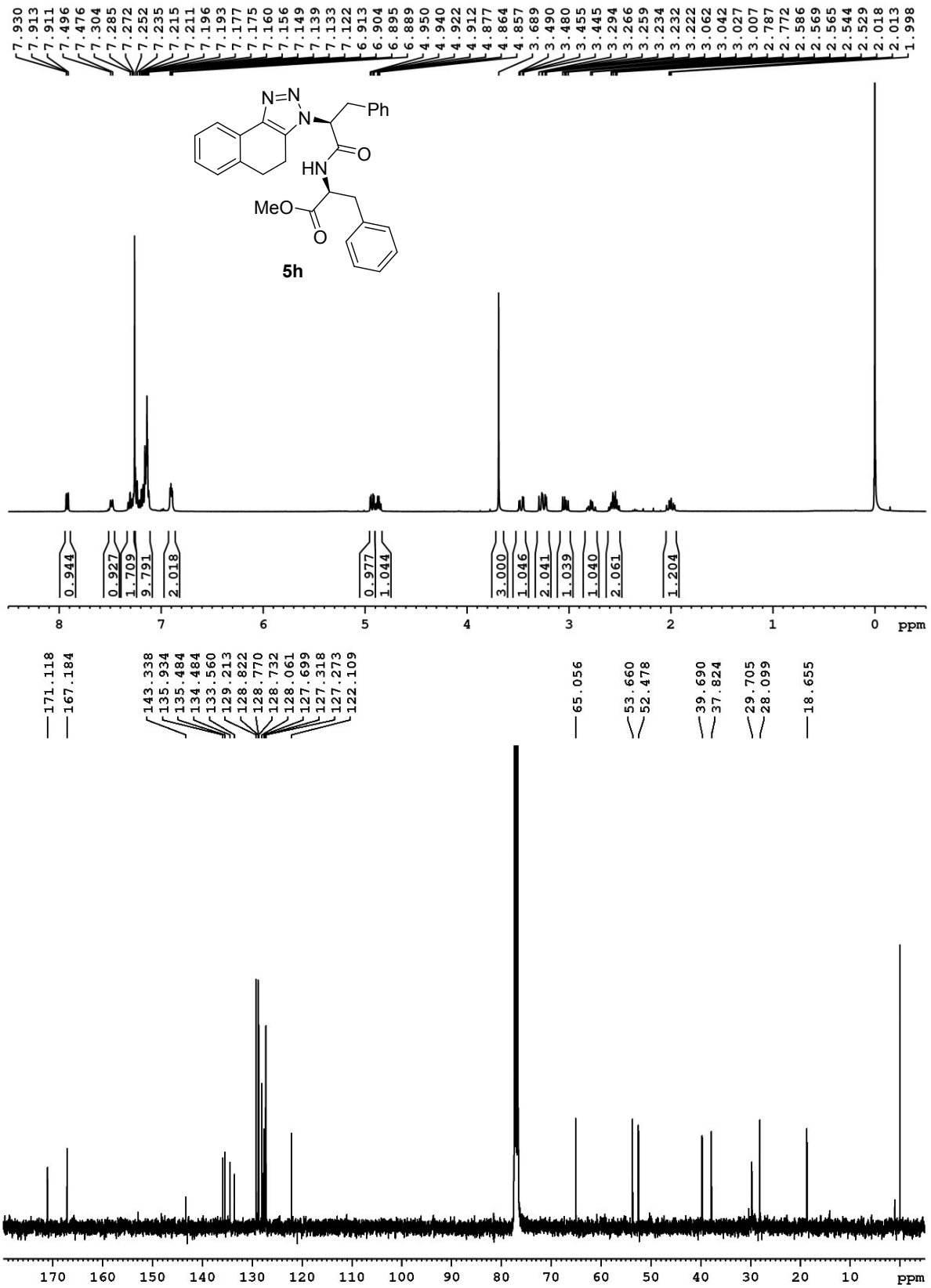


Figure S13. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5h**.

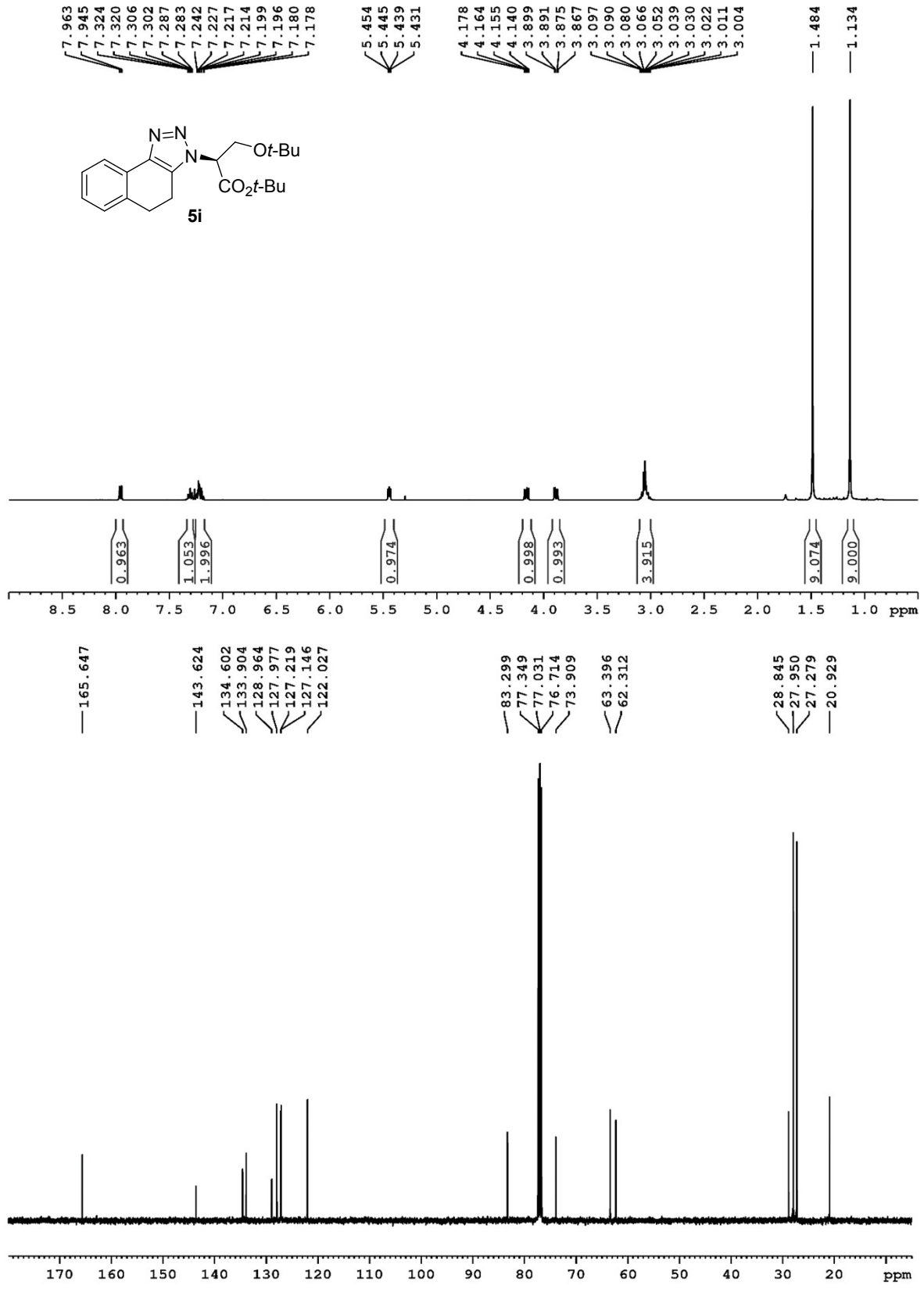


Figure S14. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5i**.

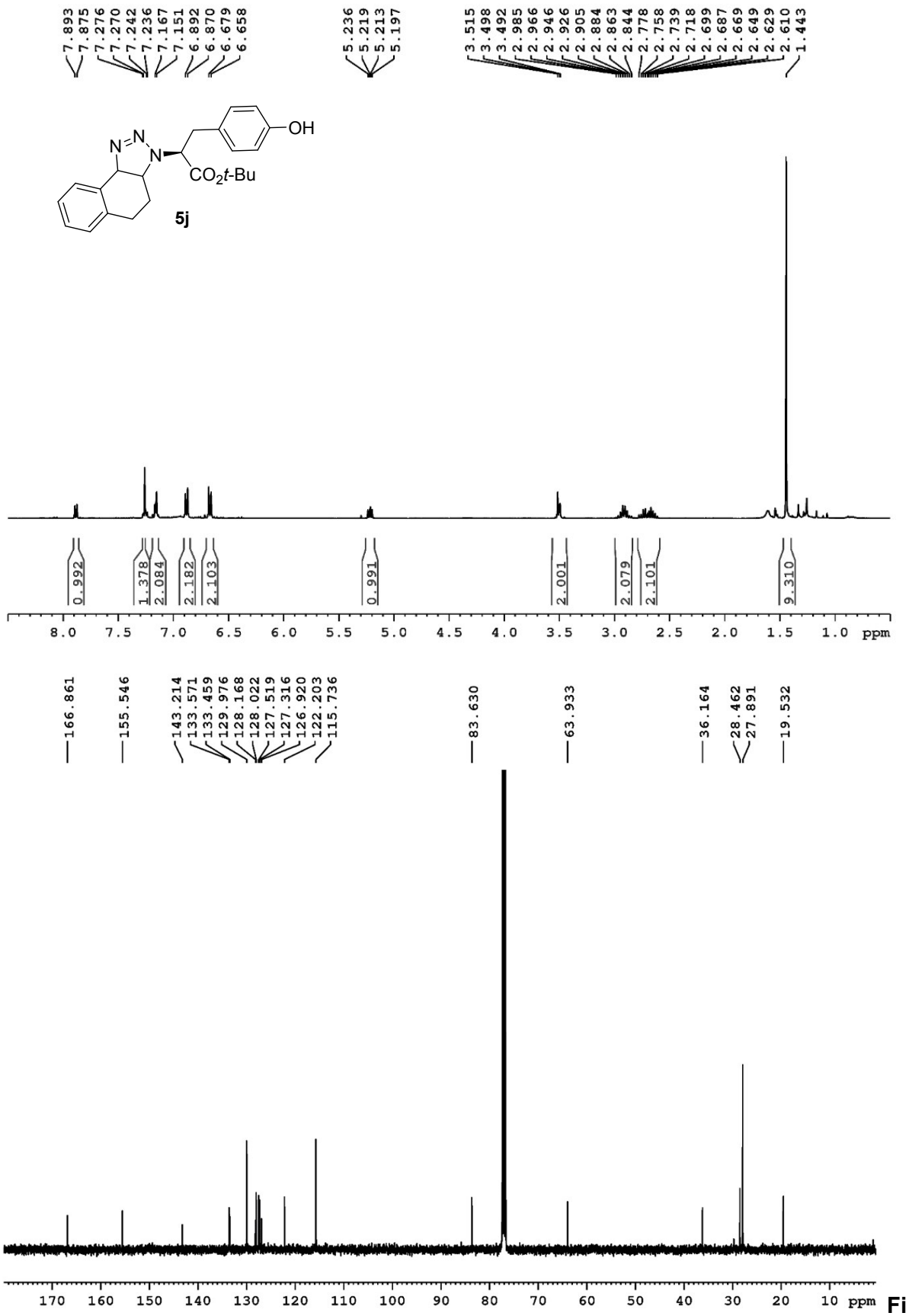


Figure S15. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5j**.

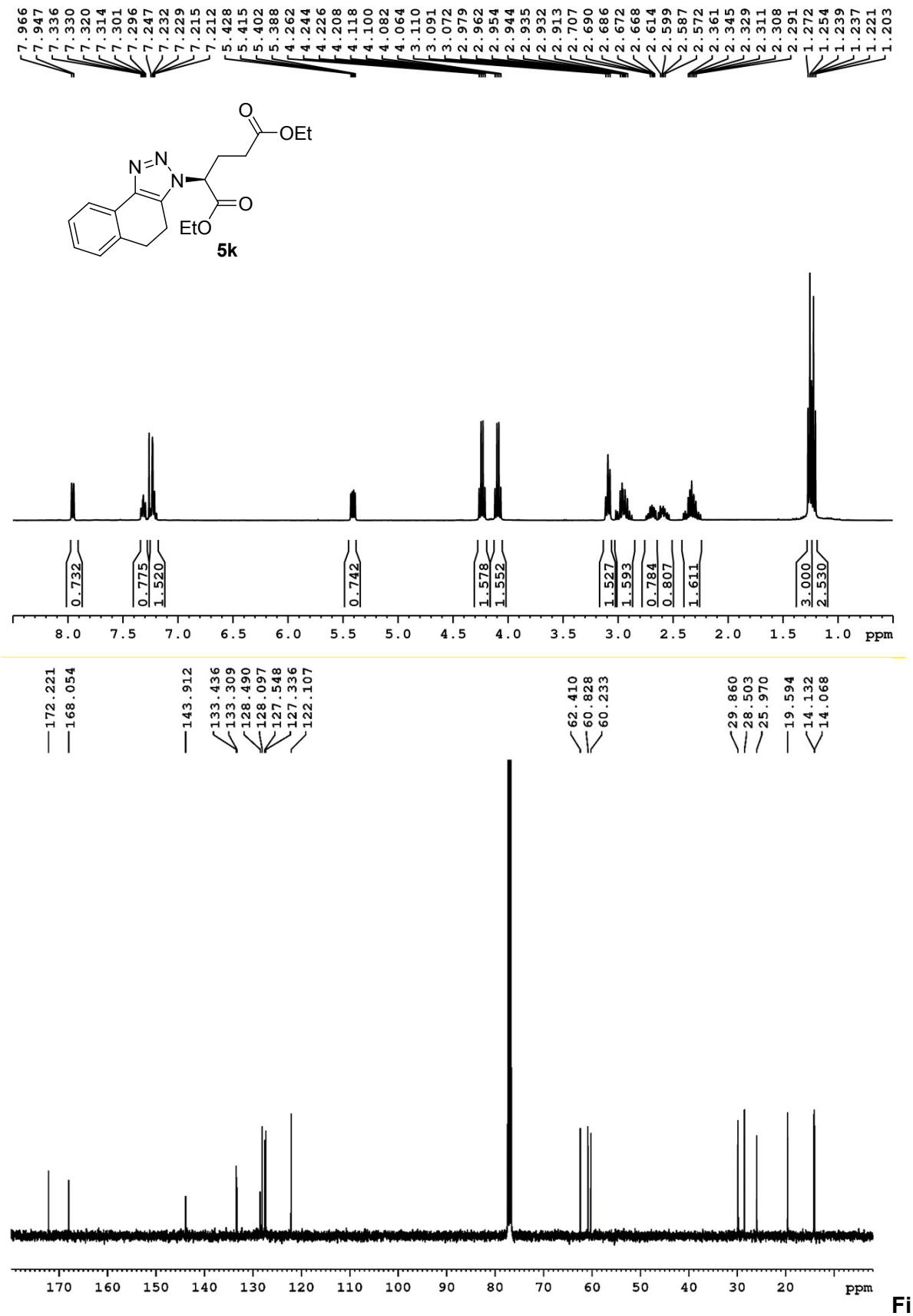


Figure S16. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5k**.

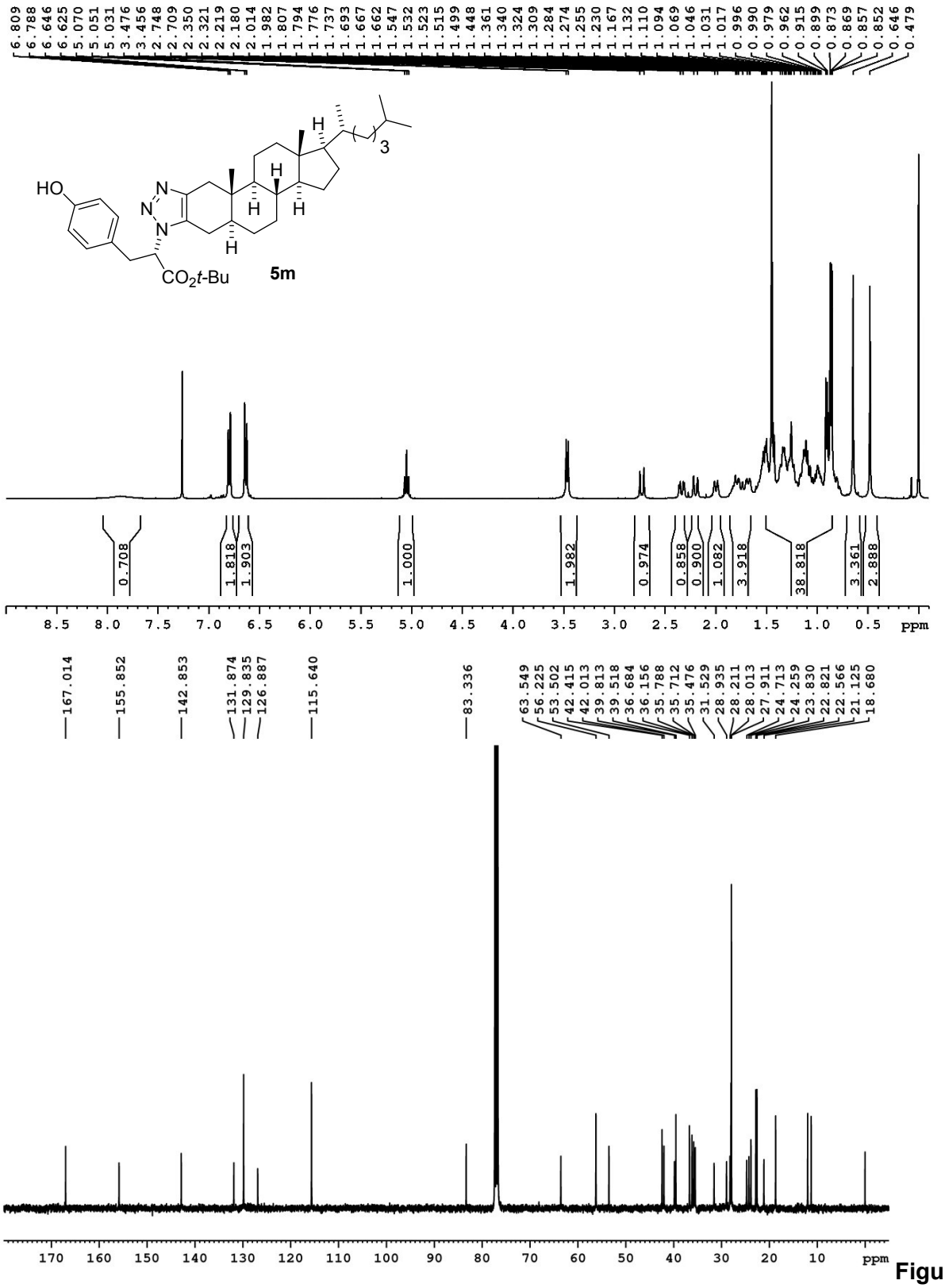


Figure S17. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5m**.

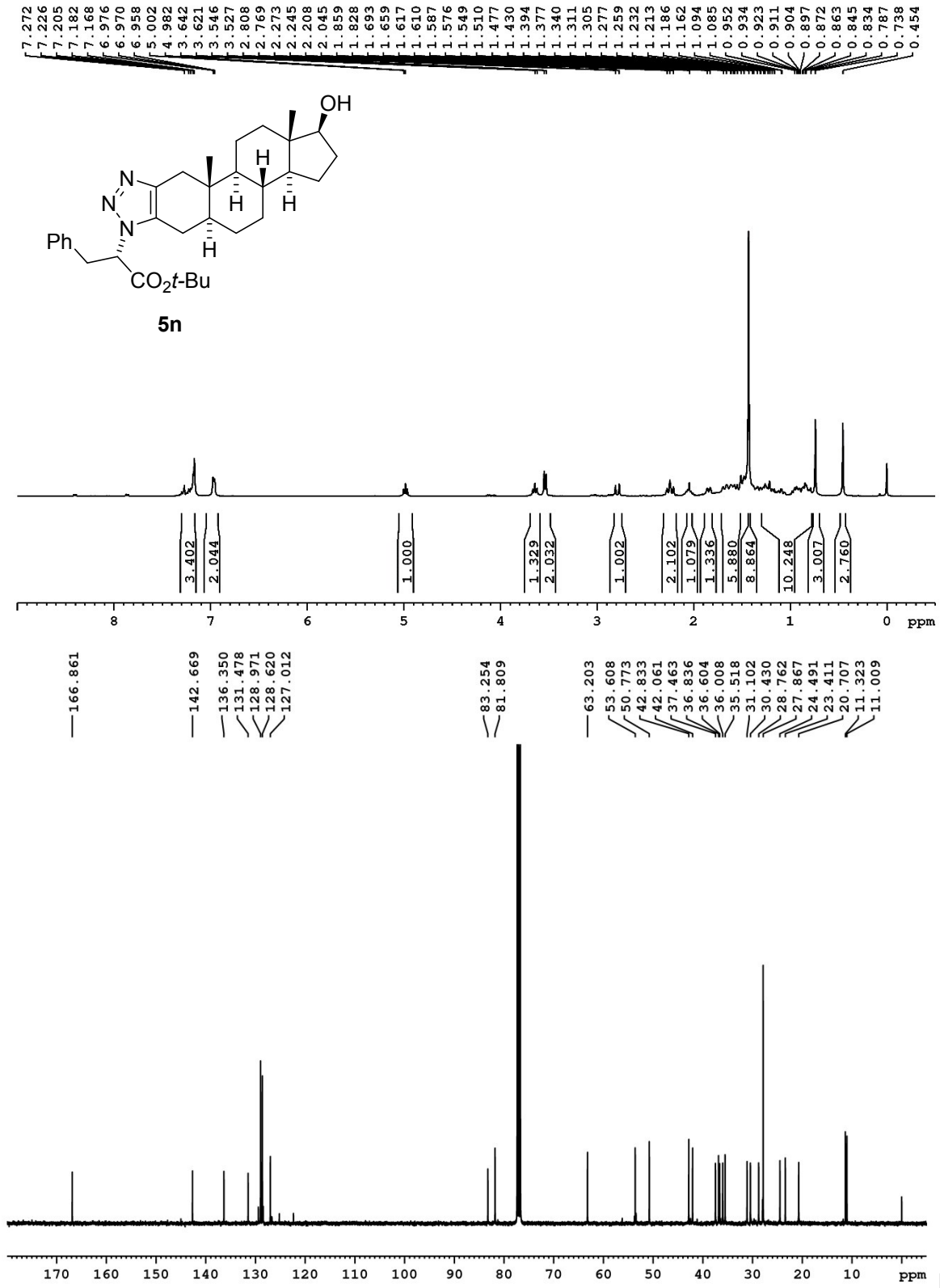


Figure S18. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5n**.

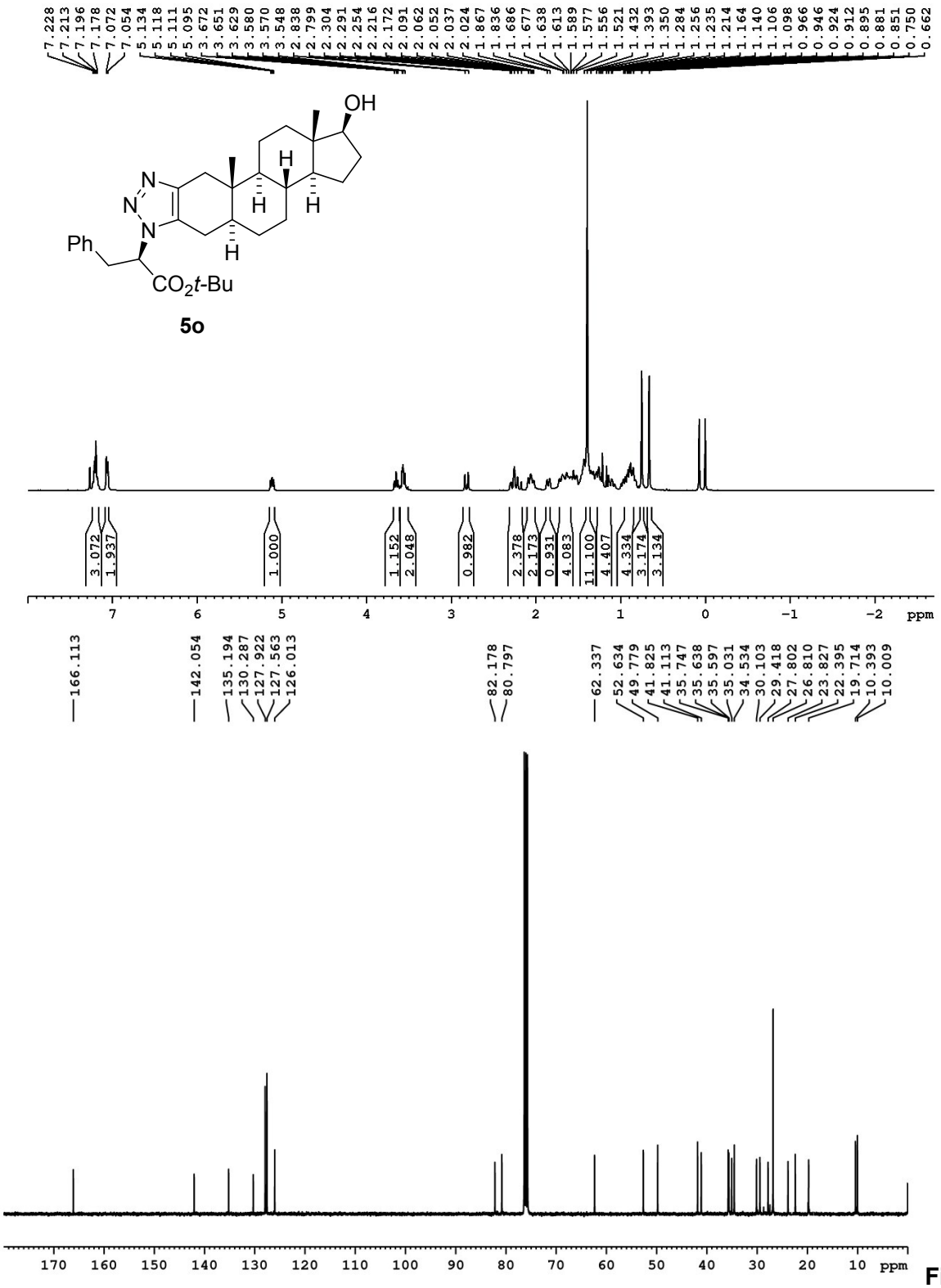


Figure S19. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5o**.

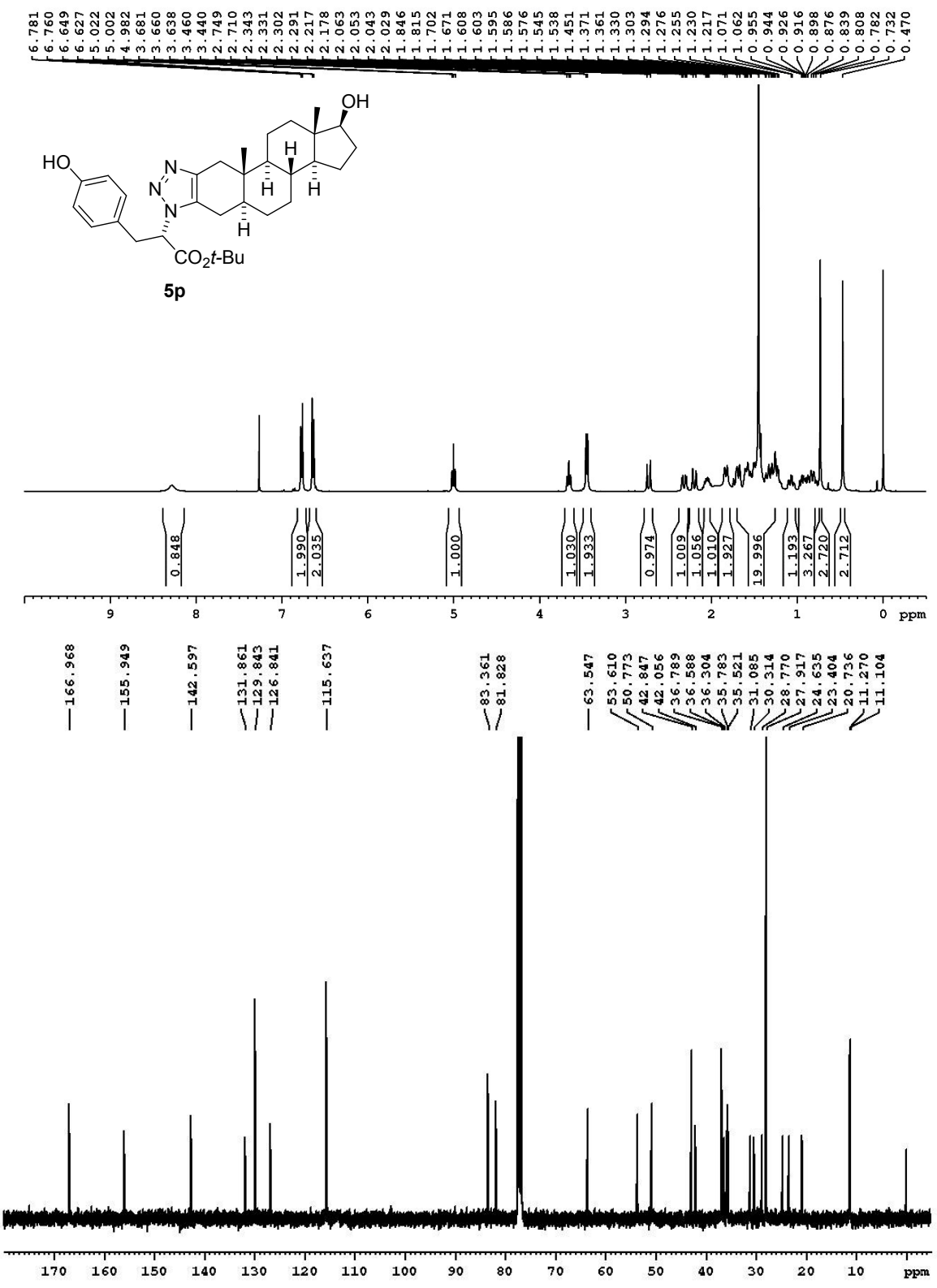


Figure S20. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **5p**.

8. ^{1}H and ^{13}C NMR spectra for compound 8a-o

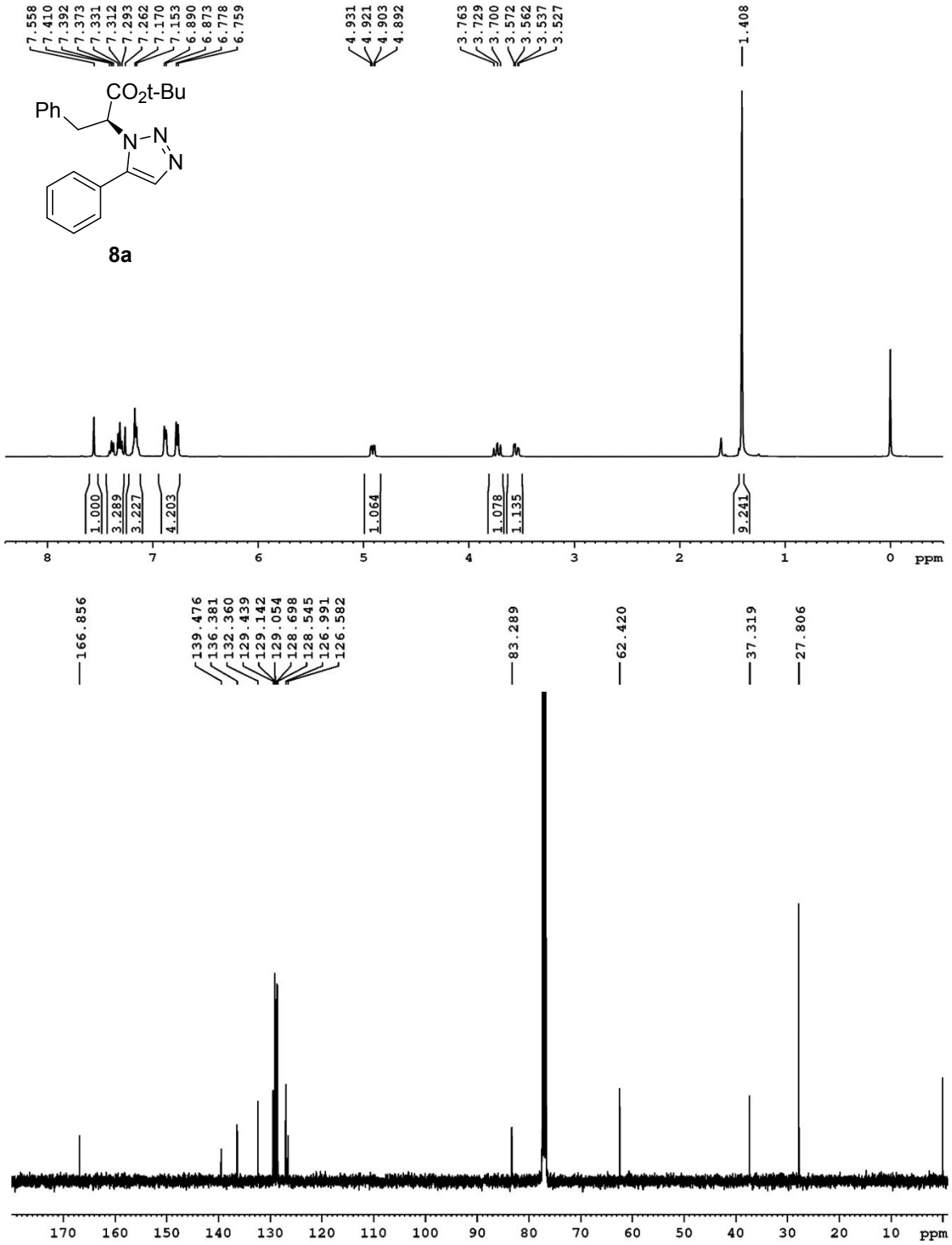


Figure S21. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8a.**

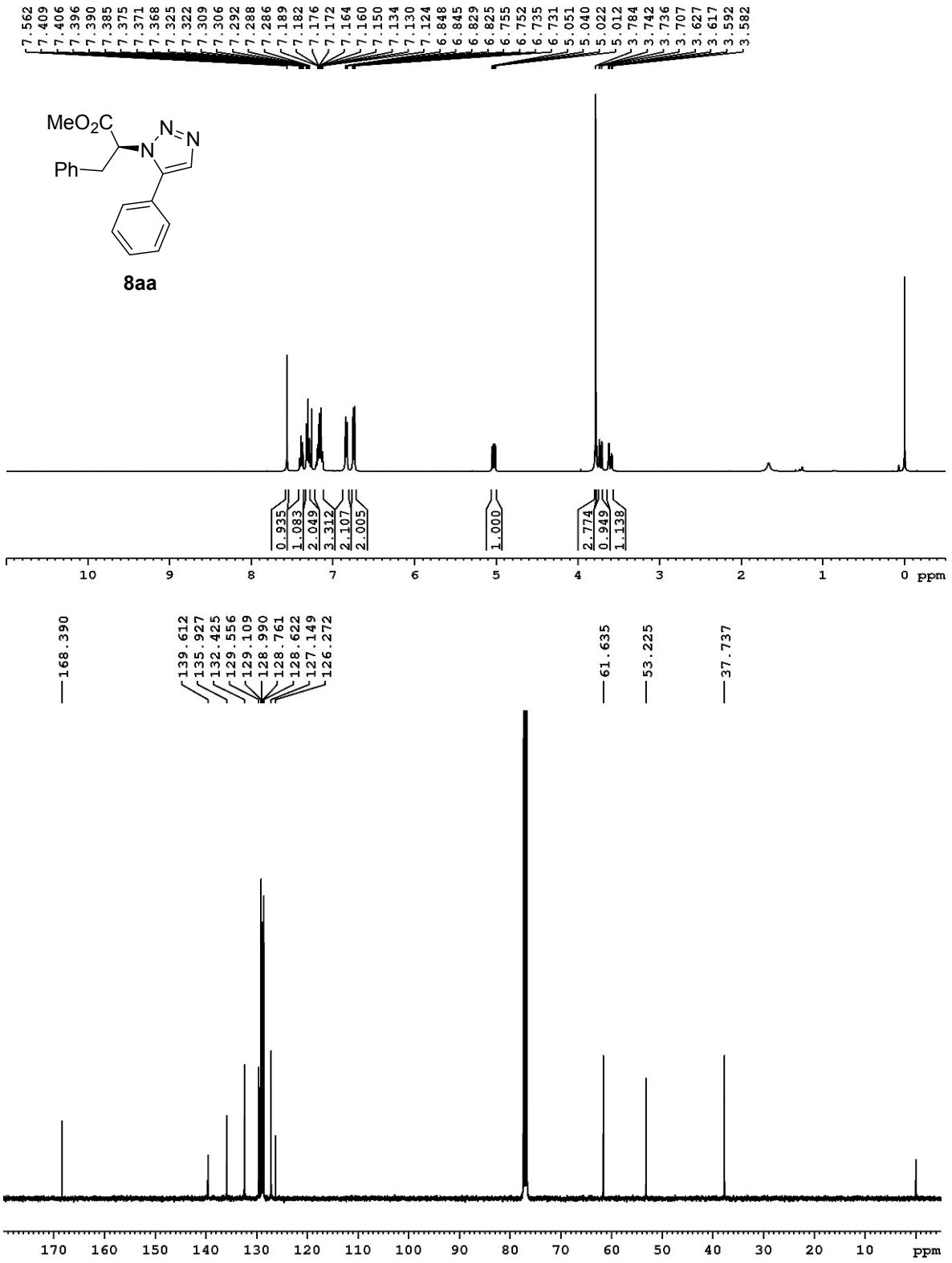


Figure S22. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8aa.**

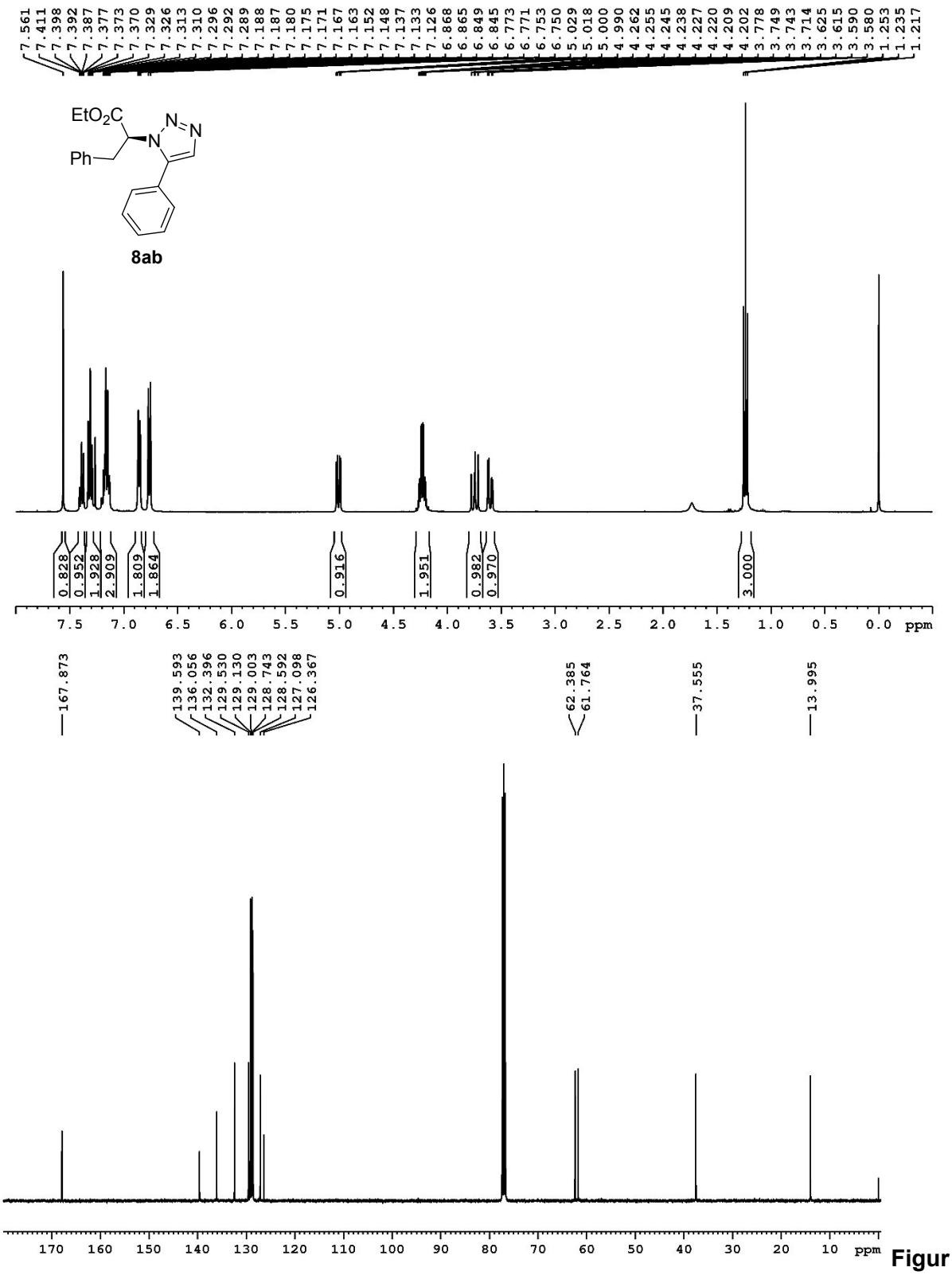


Figure S23. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8ab.**

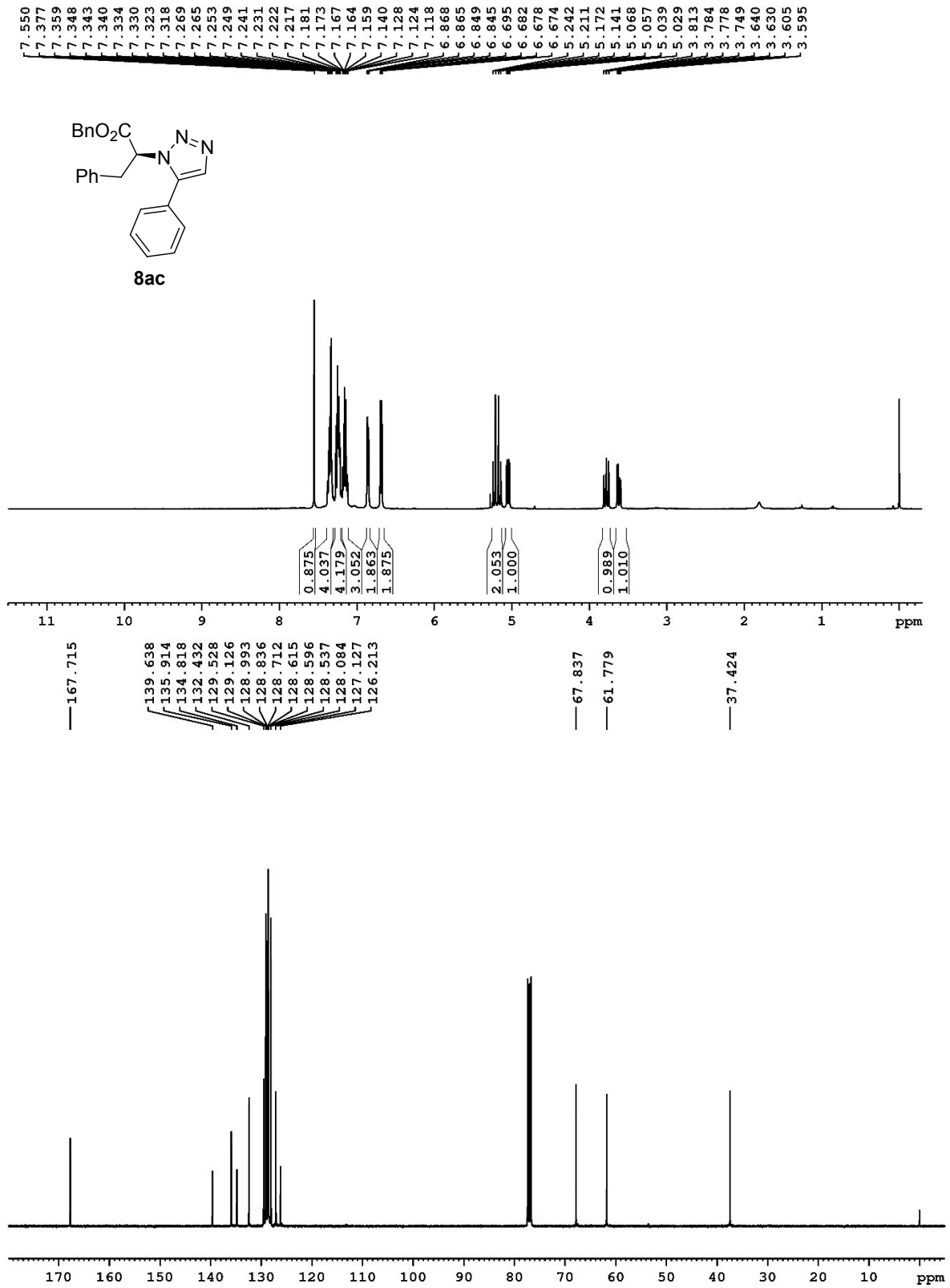
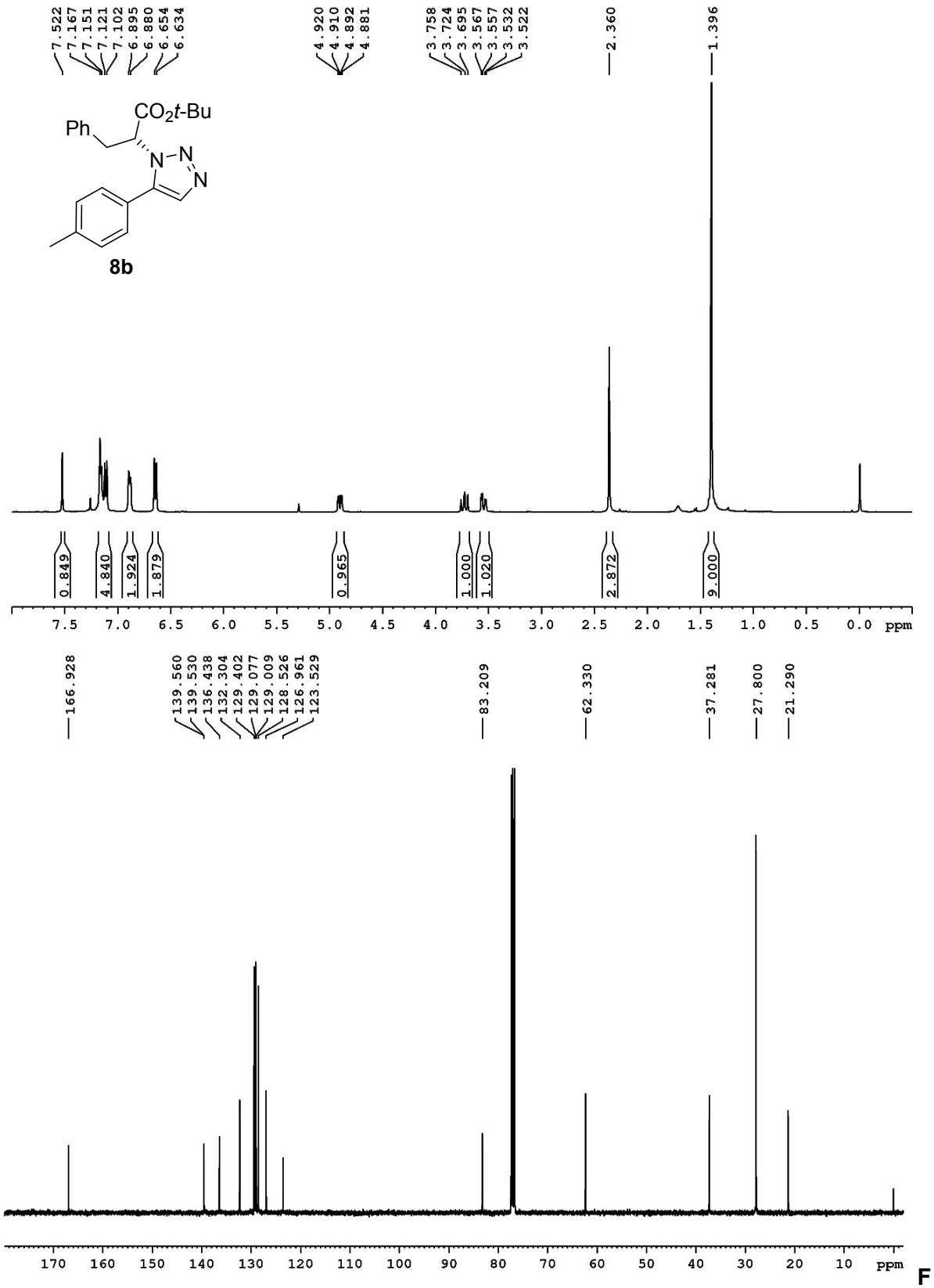


Figure S24. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8ac.**



F igure S25. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8b.**

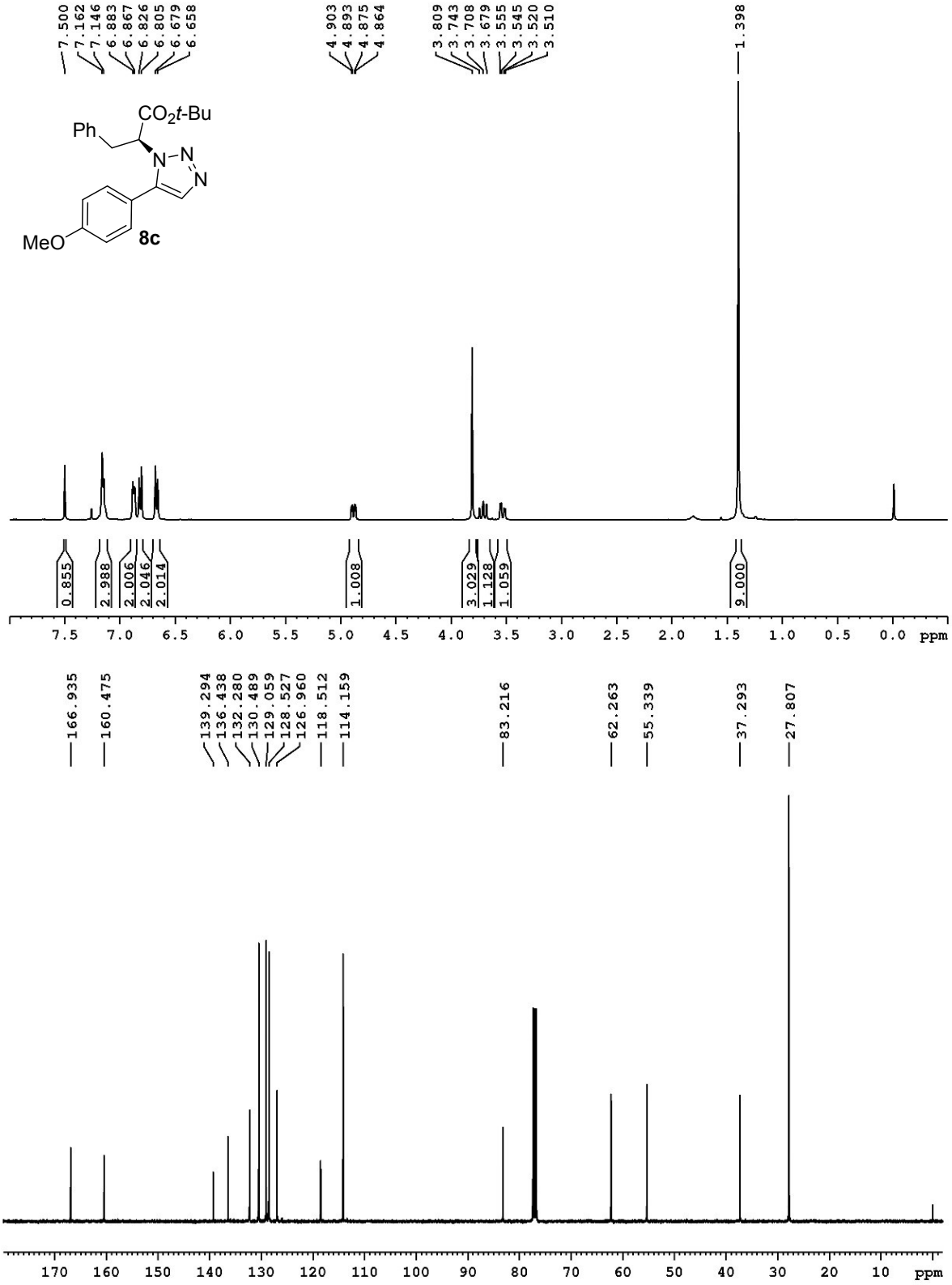


Figure S26. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8c.**

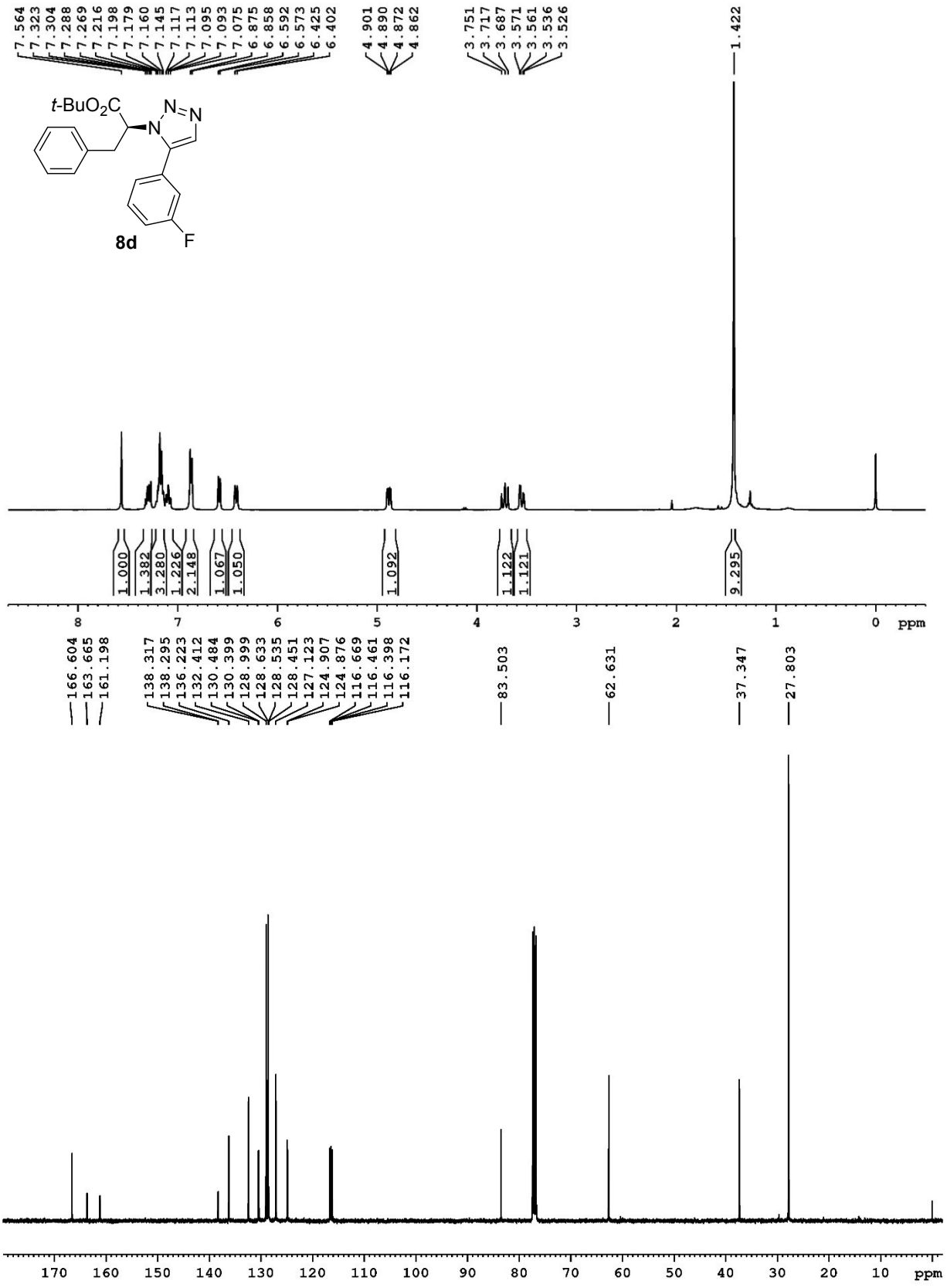


Figure S27. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8d.**

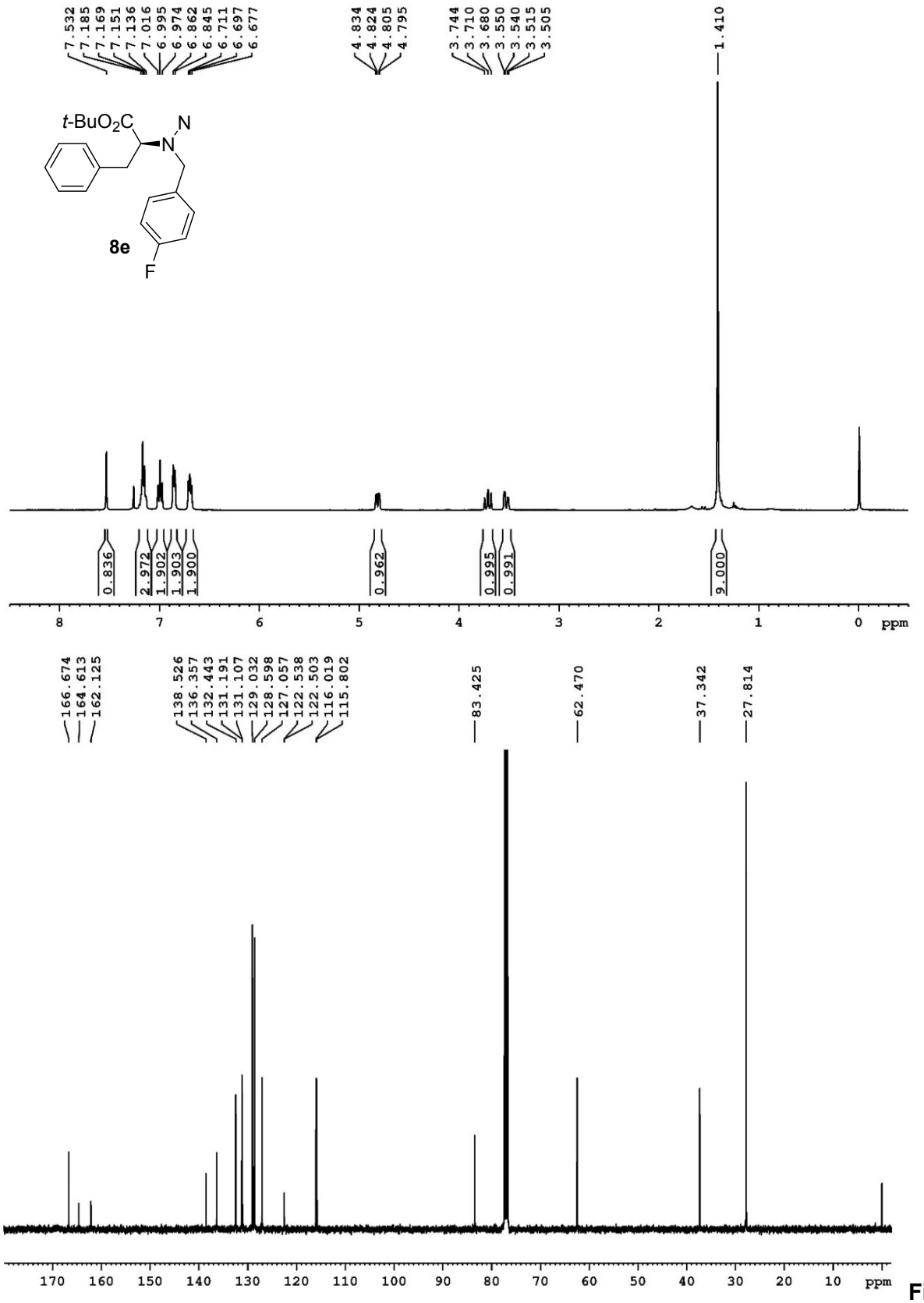


Figure S28. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8e.**

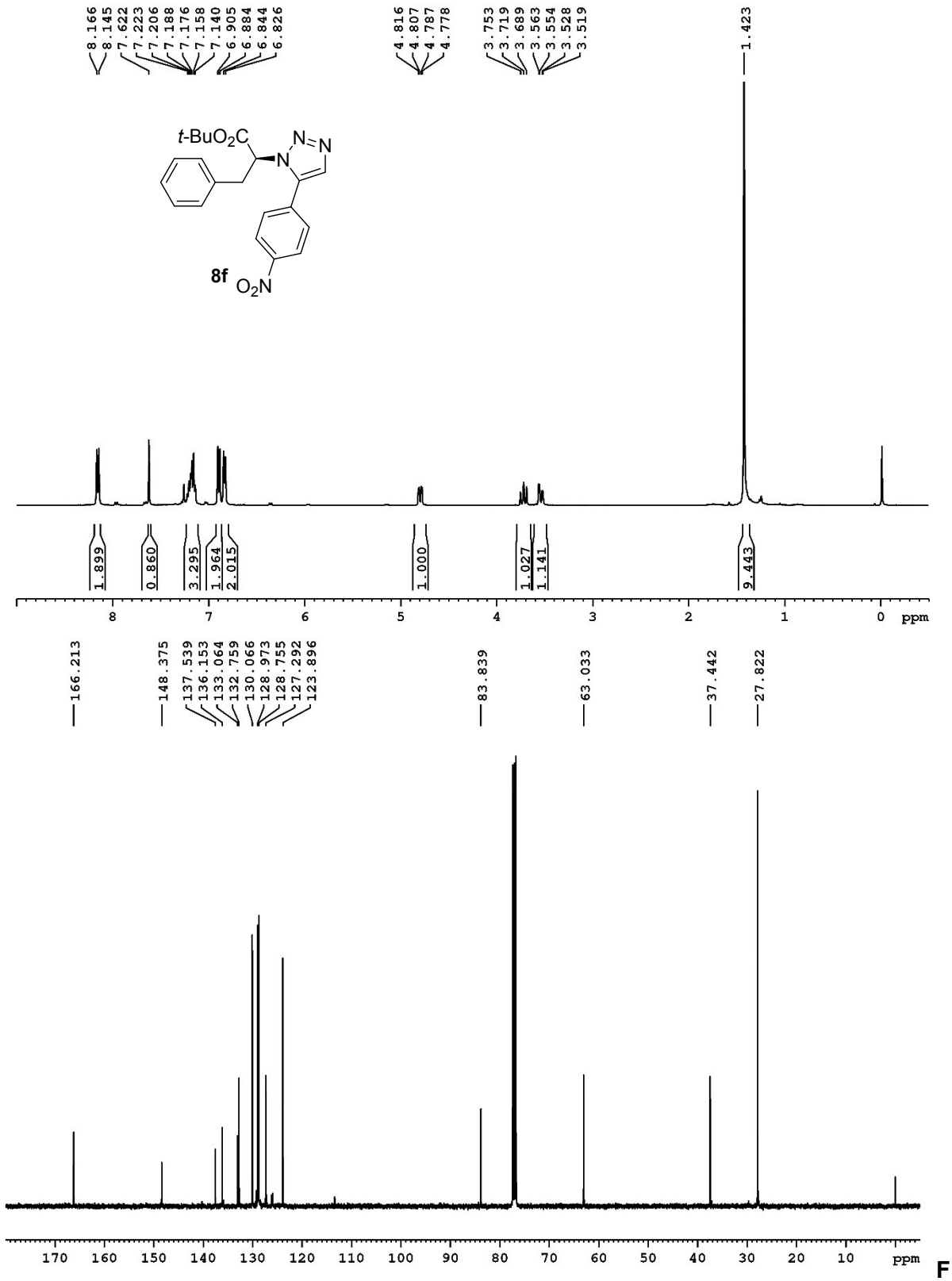


Figure S29. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8f.**

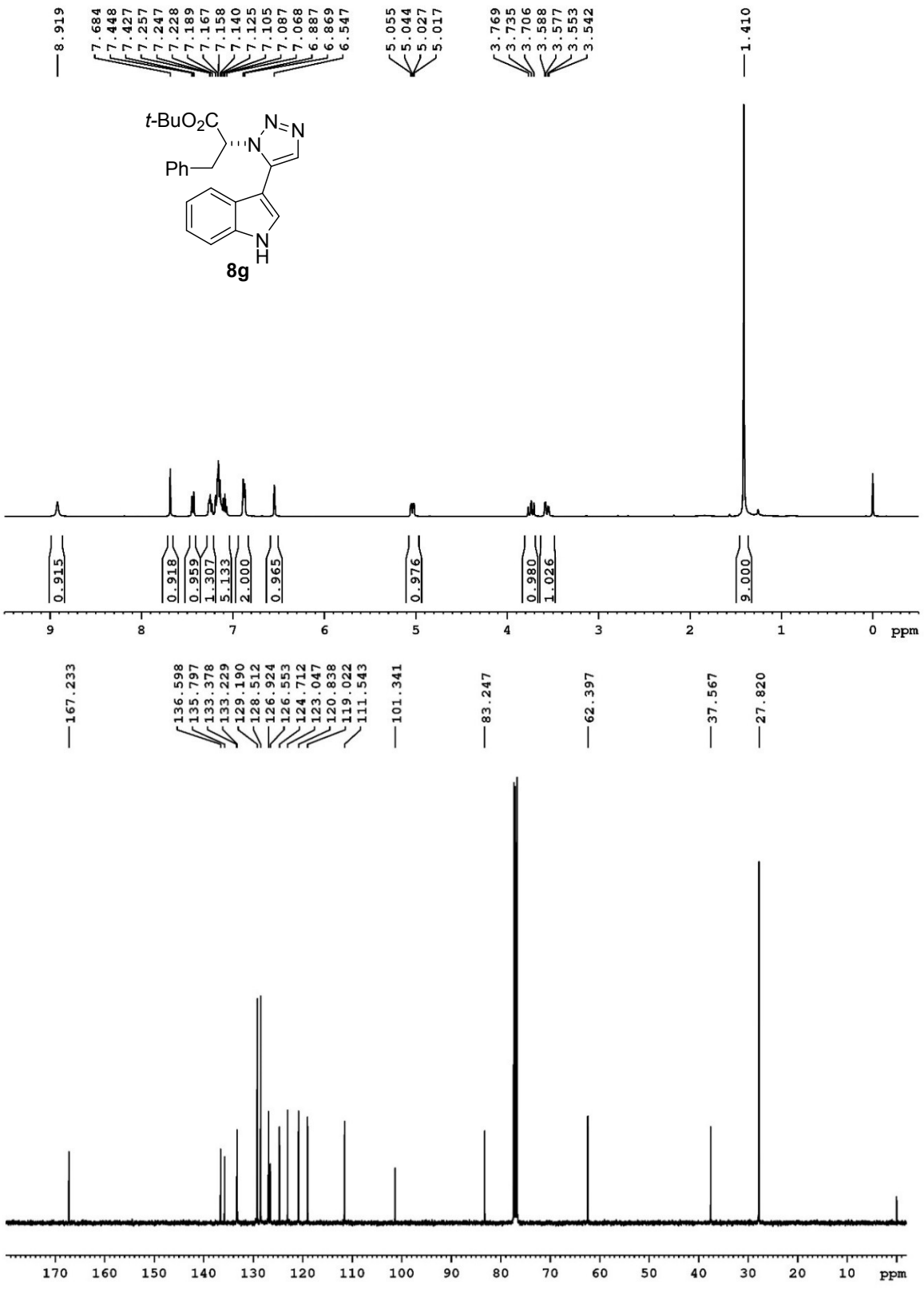


Figure S30. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8g**.

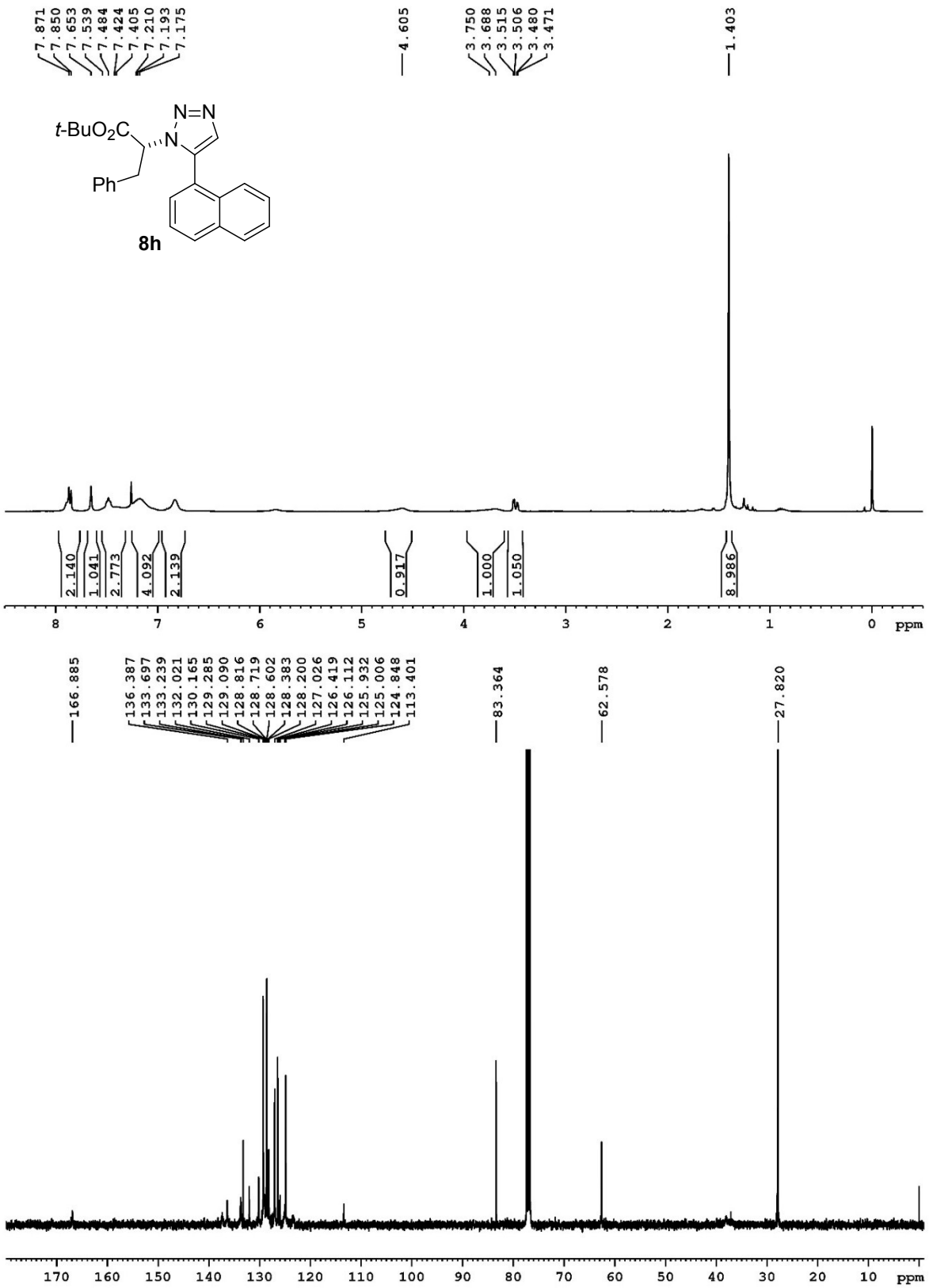


Figure S31. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8h**.

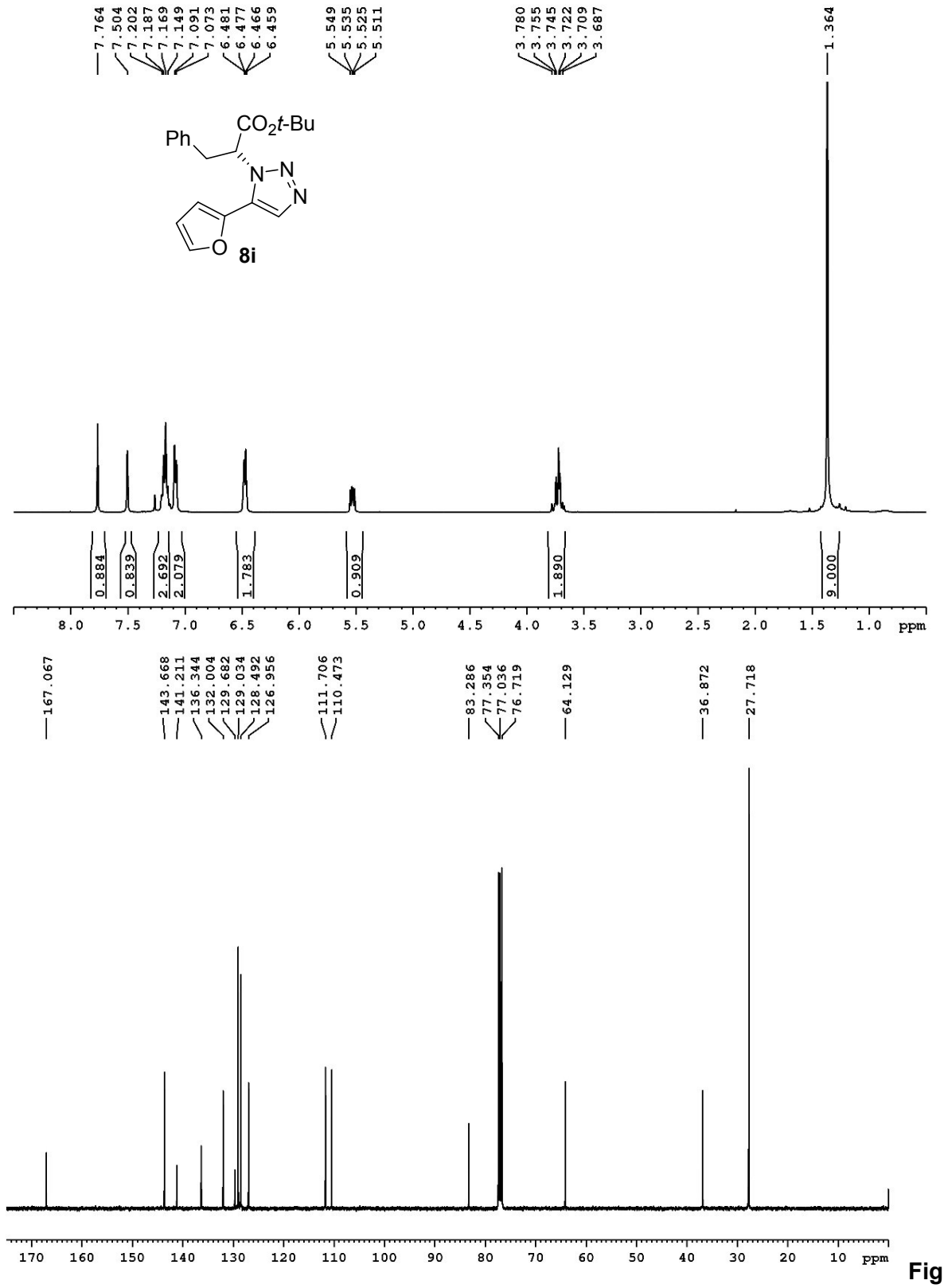


Figure S32. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8i**.

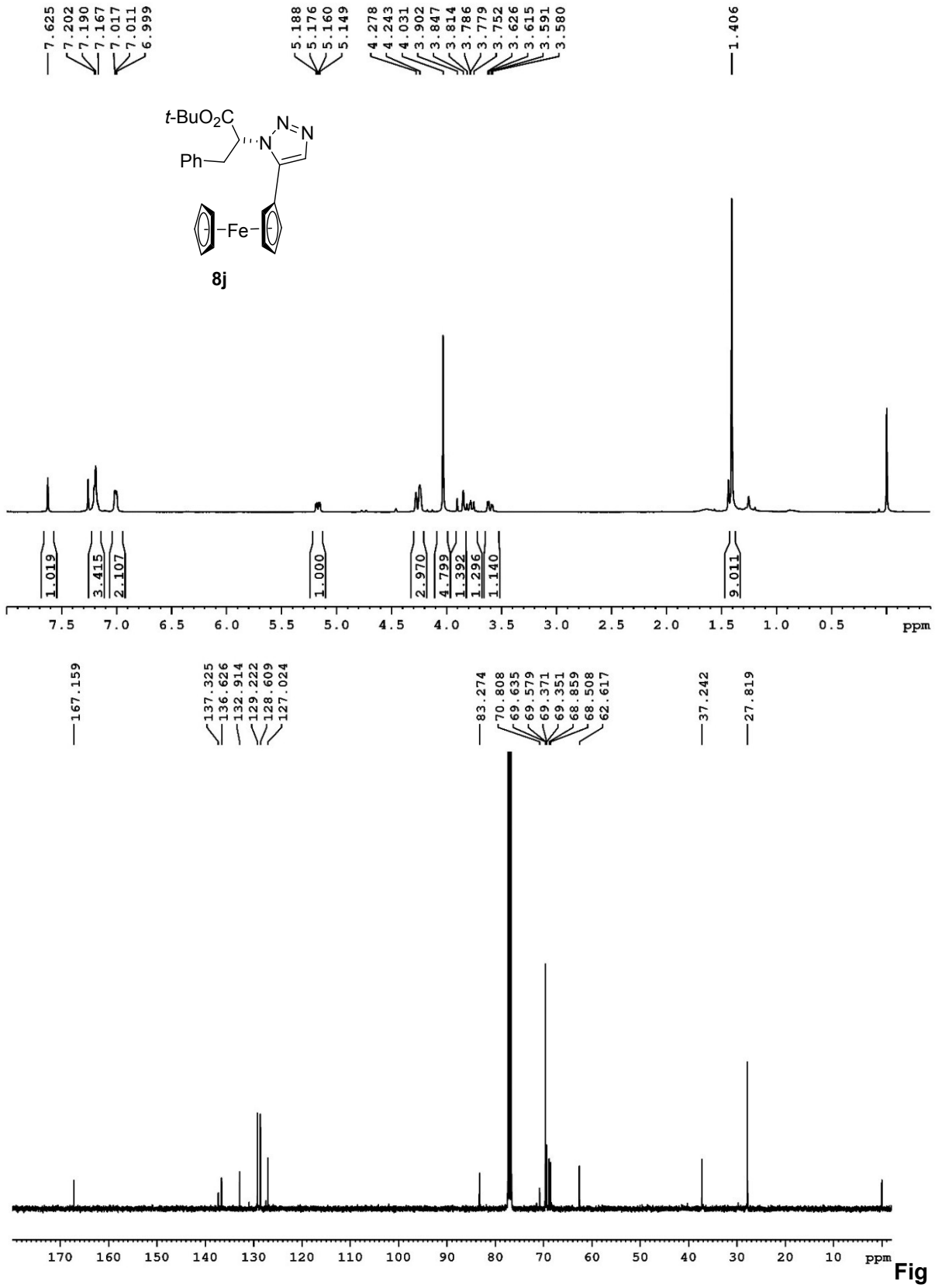


Figure S33. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8j.**

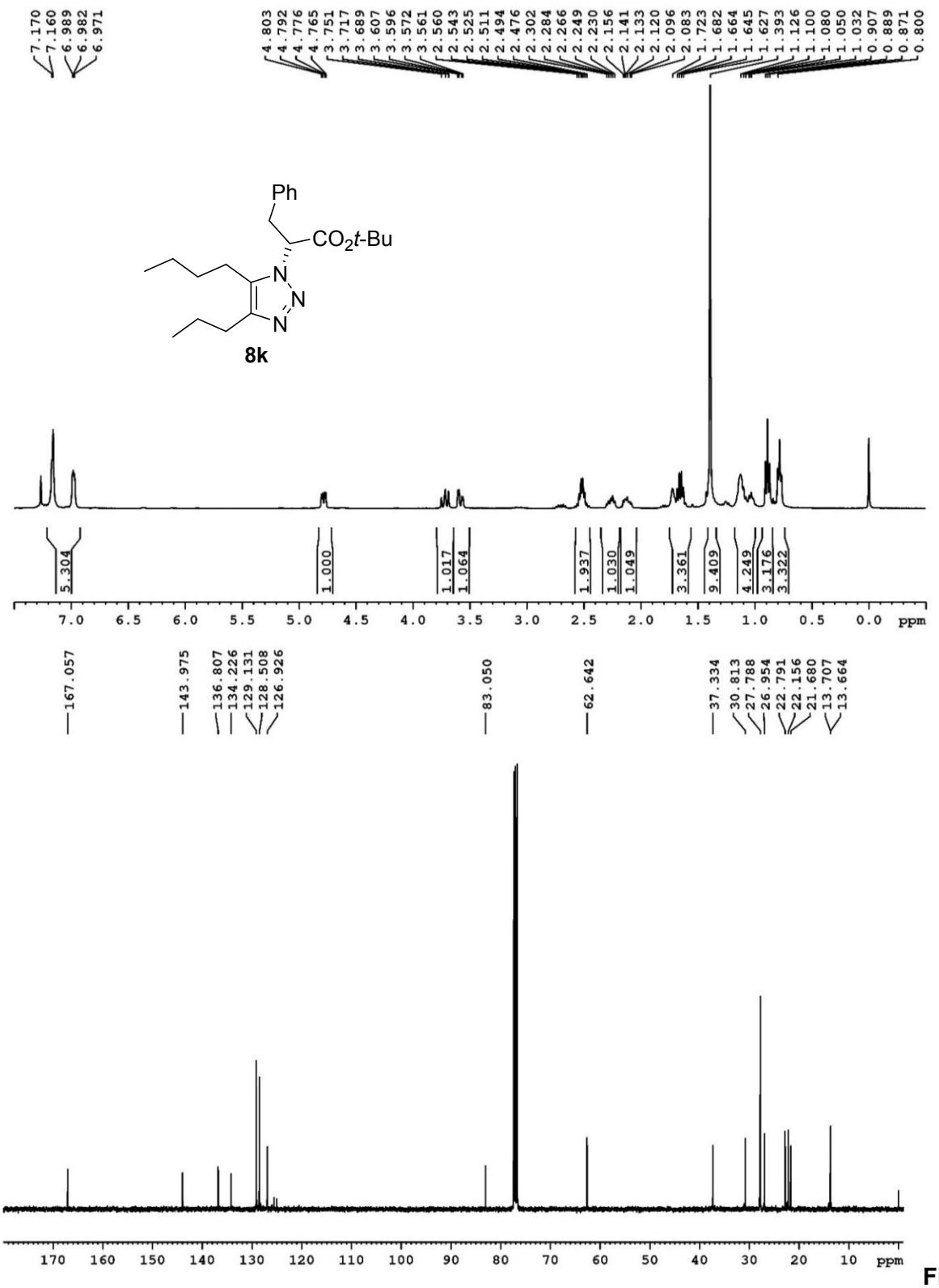


Figure S34. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8k.**

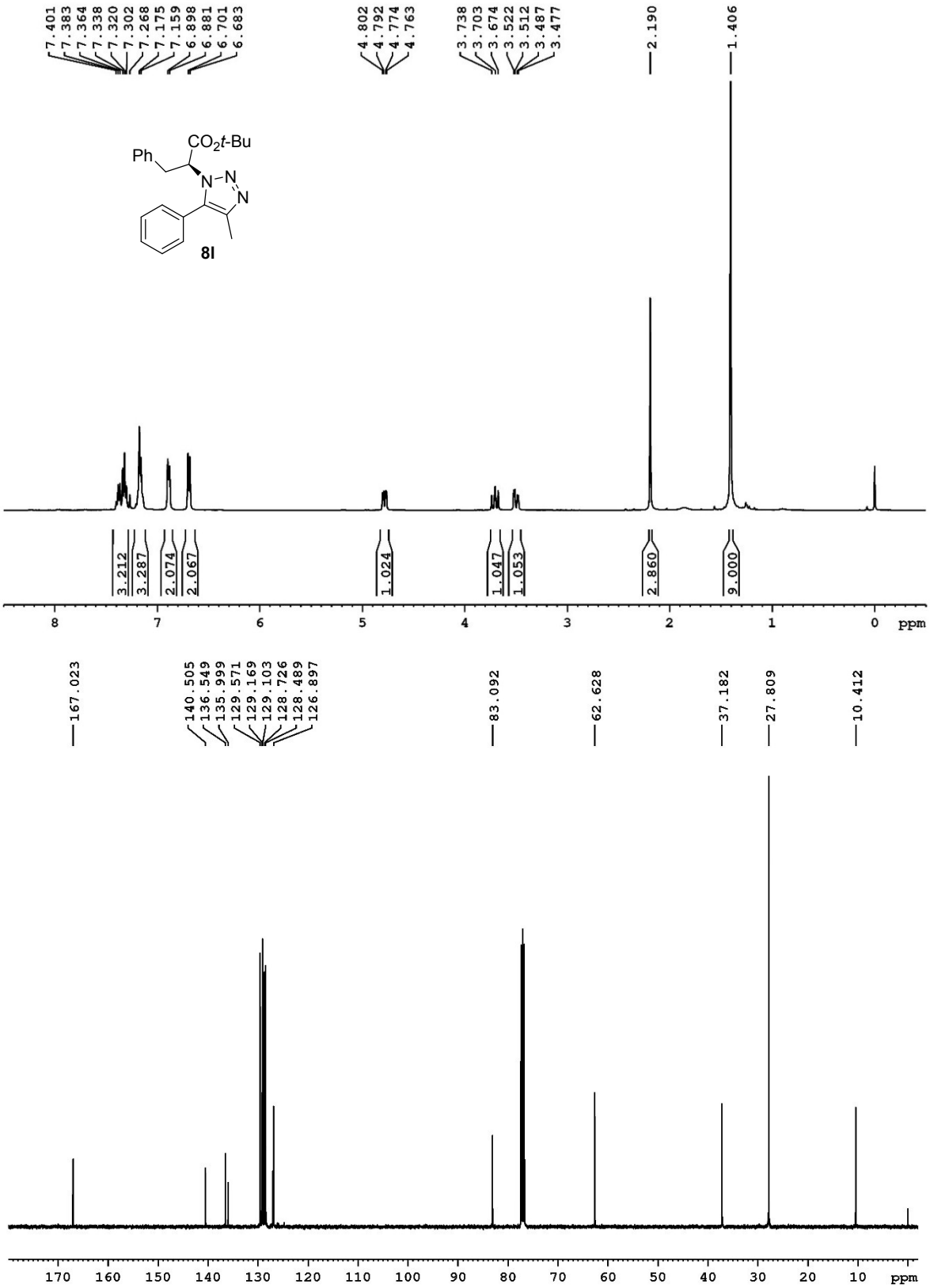
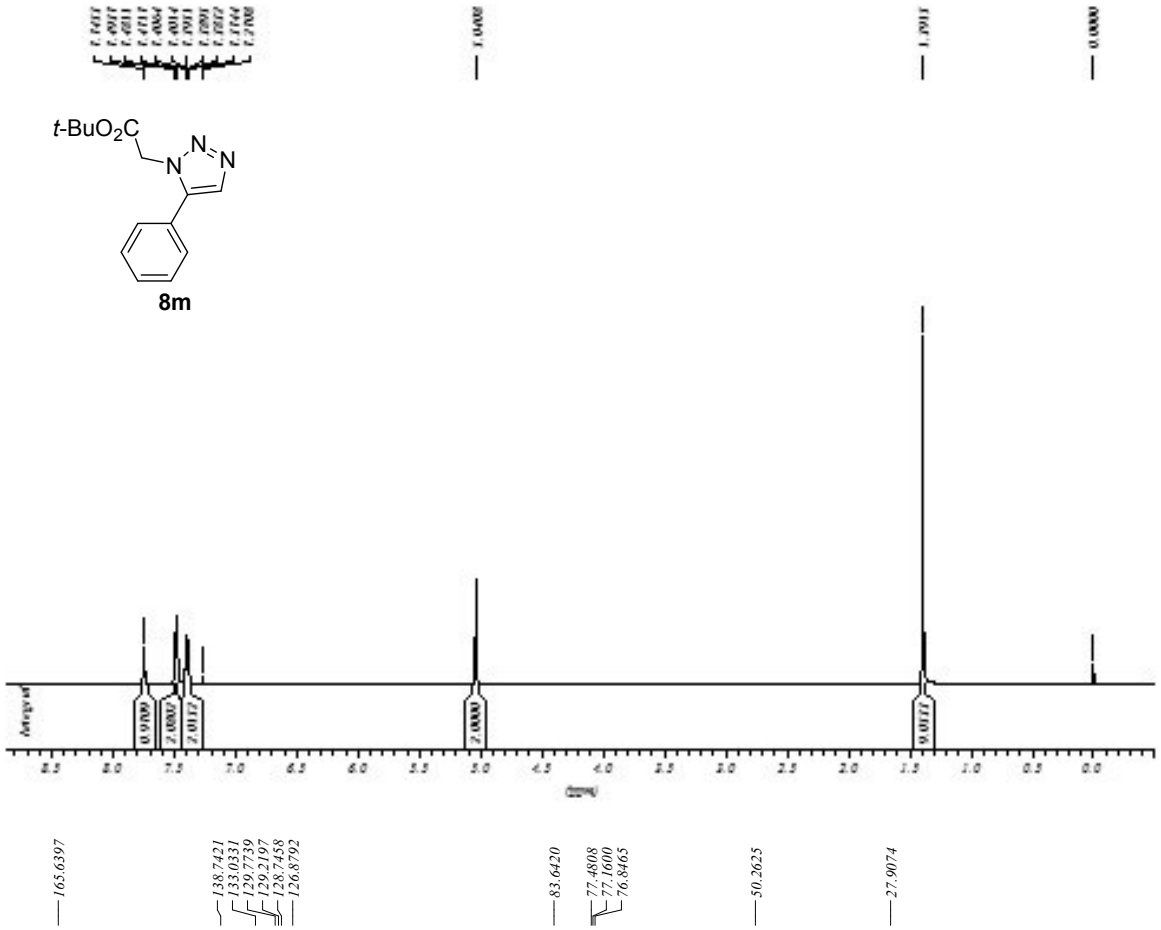


Figure S35. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **8l.**



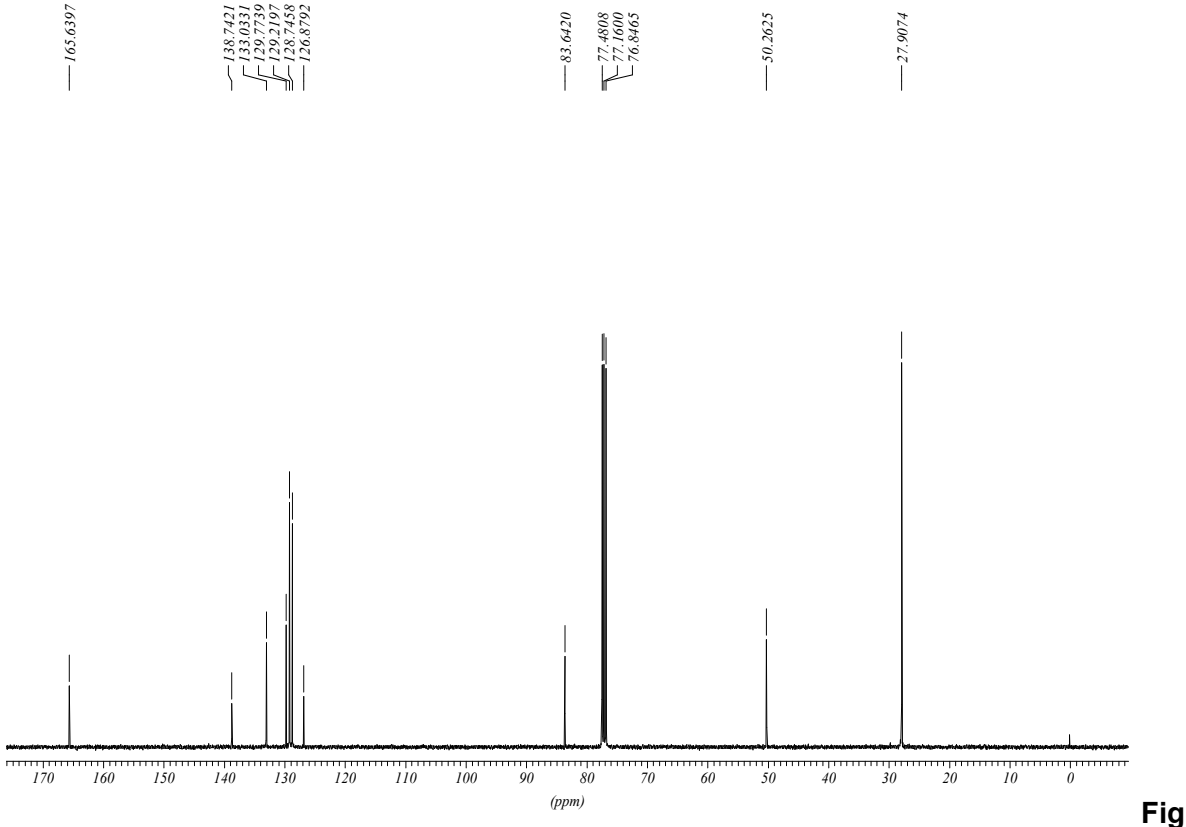


Figure S36. ^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, $CDCl_3$) Spectra of **8m.**

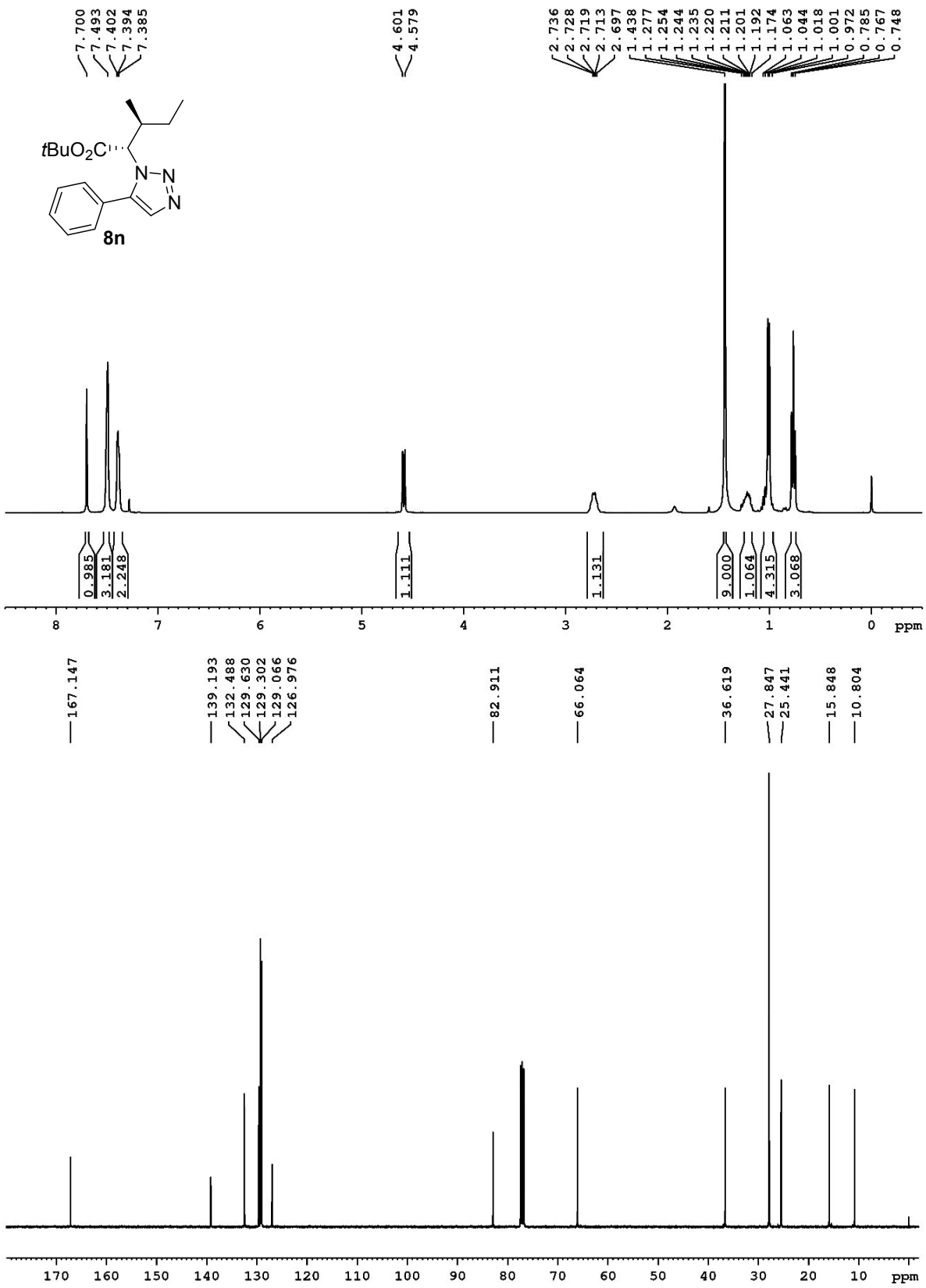


Figure S37. ^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, $CDCl_3$) Spectra of **8n.**

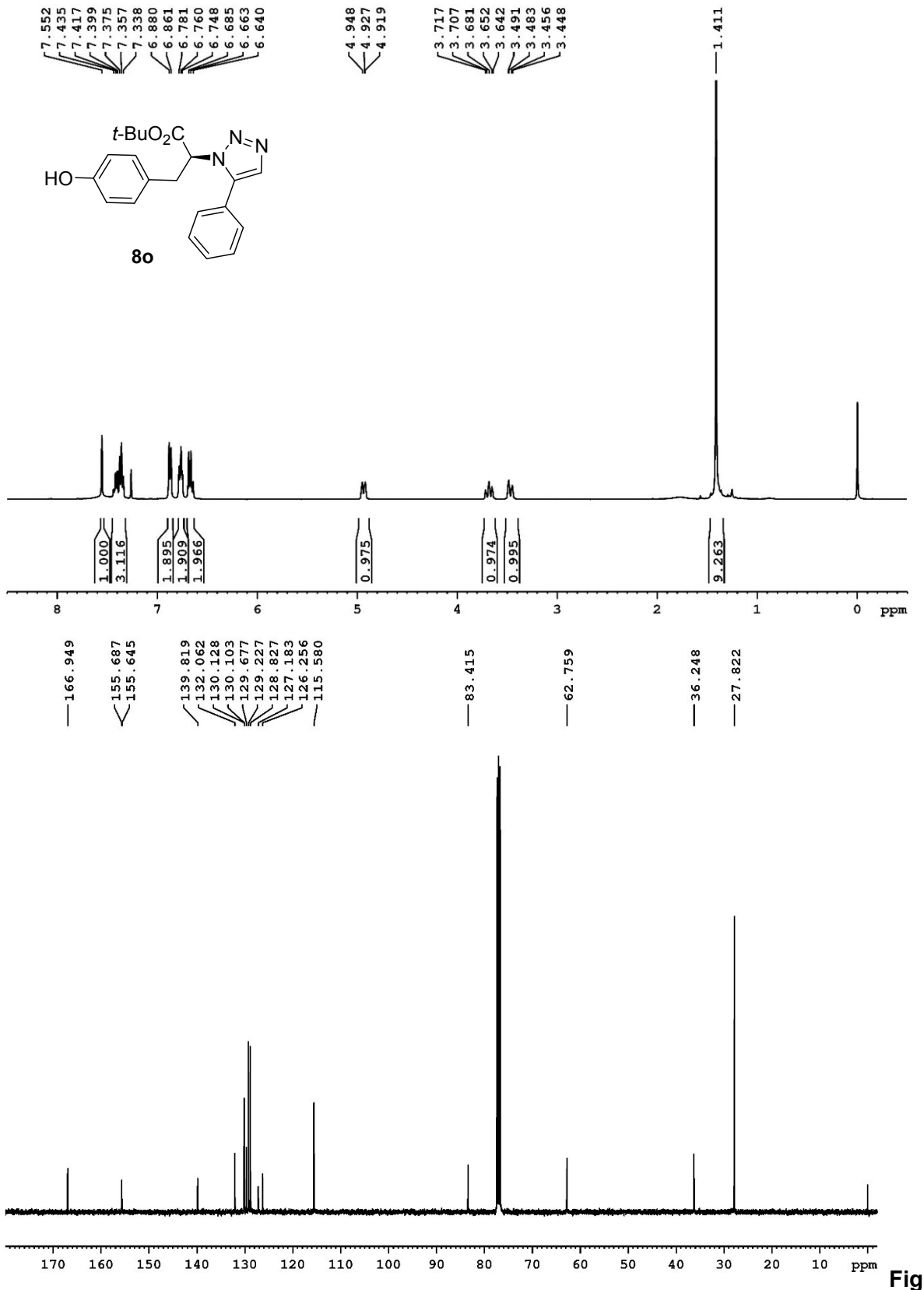


Figure S38. ^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, $CDCl_3$) Spectra of **8o**.

9. Synthesis procedure of 9a

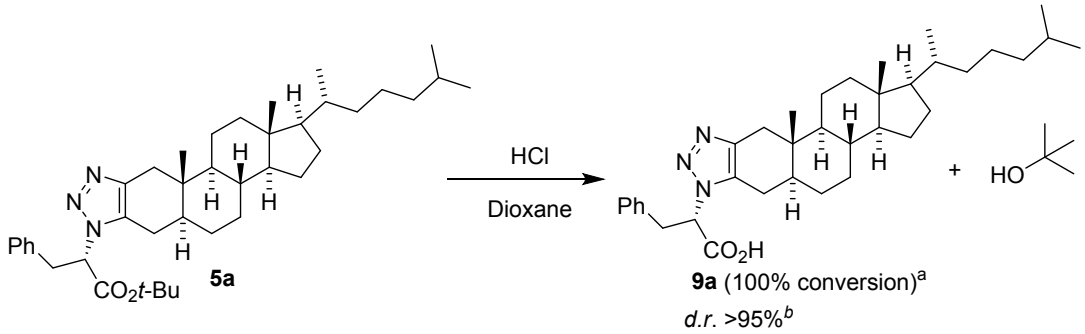


Figure S39. Carboxylic acid derivative obtained from acid hydrolysis. [a]Determined by ^{1}H-NMR spectroscopy, no side products were observed. [b]*d.r.* determined by ^{1}H-NMR analysis of the crude product 9a.

(*S*)-2-((1*R*,3a*S*,3b*R*,5a*S*,10a*S*,10b*S*,12a*R*)-10a,12a-dimethyl-1-((*R*)-4-methylpentan-2-yl)-2,3,3a,3b,4,5,5a,6,10,10a,10b,11,12,12a-tetradecahydrocyclopenta[7,8]phenanthro[2,3-d][1,2,3]triazol-7(1H)-yl)-3-phenylpropanoic acid : 5a (20 mg, 0.03 mmol) was dissolved in 1,4-dioxane (1.0 mL), then 0.5 mL of 6M HCl (aq) was added at R.T. and the reaction was stirred 5h at 85 °C. After, the mixture was cooled to R.T. and water and ether were added. The mixture was then separated and the aqueous layer was extracted with ether 3 times. The combined organic fractions were recollected and dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure affording a mixture of **9a** and *tert*-butanol (100% conversion). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 – 7.19 (m, 3H), 6.93 (m, 2H), 5.03 (dd, *J* = 3.4, 11.5 Hz, 1H), 3.65 (dd, *J* = 3.7, 13.7 Hz, 1H), 3.56 – 3.51 (m, 1H), 2.78 (d, *J* = 15.6 Hz, 1H), 2.22 – 2.17 (m, 2H), 2.05 – 2.03 (m, 2H), 1.87 – 1.84 (m, 2H), 1.67 – 1.66 (m, 2H), 1.56 – 1.51 (m, 4H), 1.41 – 1.32 (m, 7H), 1.20 – 1.09 (m, 5H), 1.06 – 0.98 (m, 4H), 0.94 – 0.88 (m, 11H), 0.67 (s, 3H), 0.38 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 143.0, 135.8, 133.0, 128.9, 128.8, 127.3, 62.8, 56.2, 56.1, 53.4, 42.4, 41.7, 39.8, 39.5, 39.07, 36.7, 36.2, 35.8, 35.6, 35.4, 31.4, 29.7, 28.8, 28.2, 28.0, 24.2, 23.8, 22.8, 22.6, 21.1, 18.7, 14.1, 11.9, 11.3. HRMS (ESI$^+$): m/z calcd for $C_{36}H_{53}N_3O_2$ $[M+H]^+$ 560.4171; found 560.4192.

10. ^{1}H and ^{13}C NMR spectra for compound 9a and *rac*-9a

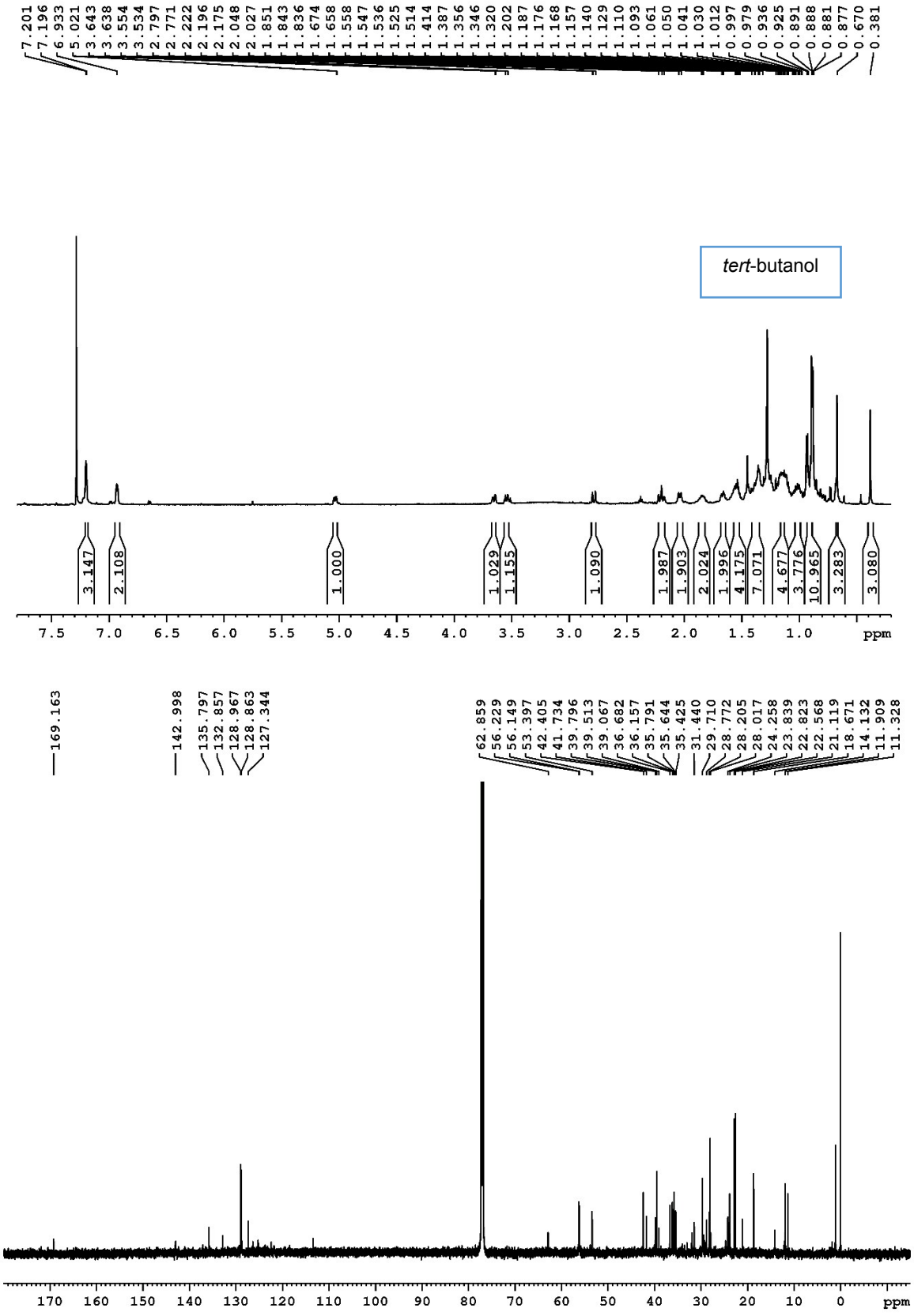
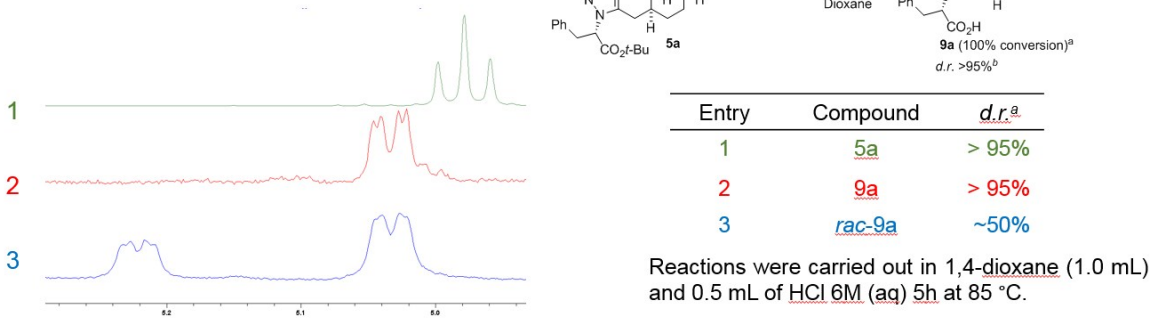


Figure S39. ^{1}H-NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) Spectra of **9a** (mixture *tert*-butanol **9a**).



Entry	Compound	*d.r.*[a]
1	5a	> 95%
2	9a	> 95%
3	*rac*-9a	~50%

Reactions were carried out in 1,4-dioxane (1.0 mL) and 0.5 mL of HCl 6M (aq) 5h at 85 °C.

Figure S40. ^{1}H-NMR comparison between **9a**, ***rac*-9a** and **5a**.