Synthesis of 1,2,3-triazole containing compounds as potential antimicrobial agents

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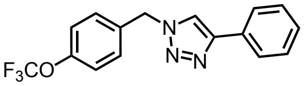
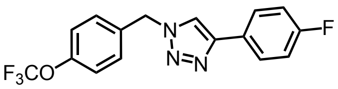
Supplemental Information

Synthetic Procedures and Spectroscopic Data:



1

4-phenyl-1-(4-(trifluoromethoxy)benzyl)-1*H*-1,2,3-triazole. Phenylacetylene (111 mg; 1.08 mmol) was added to a 25 mL pear-shaped flask along with 6 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (89 mg; 0.45 mmol), copper (II) sulfate pentahydrate (46 mg; 0.18 mmol) and THF-H_2O (2 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-(trifluoromethoxy)benzene (200 mg; 0.92 mmol) and an additional 2 mL of THF-H_20 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. 226 mg (77%) of a white solid was obtained upon purification by recrystallization from MeOH/H_2O; mp = 130-132°C. ^{1}H-NMR ($CDCl_3$): 7.81 (m, 2H), 7.69 (s, 1H), 7.41 (m, 2H), 7.34 (m, 3H), 7.23 (broad d, $J = 8.2$ Hz, 2H), 5.58 (s, 2H). ^{13}C-NMR ($CDCl_3$): 149.5, 148.5, 133.6, 130.5, 129.6, 128.9, 128.4, 125.8, 121.7, 119.6, 53.4. The NMR spectra obtained were consistent with the literature values[1].



2

4-(4-fluorophenyl)-1-(4-(trifluoromethoxy)benzyl)-1*H*-1,2,3-triazole.
4-Fluorophenylacetylene (95 mg; 0.79 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 2.0 mL). In a separate flask a mixture containing sodium ascorbate (84 mg; 0.42 mmol), copper (II) sulfate pentahydrate (33 mg; 0.13 mmol) and THF-H_2O (1:1; 1.0 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-(trifluoromethoxy)benzene (164 mg; 0.75 mmol) and THF-H_2O (1:1; 2.0 mL). This mixture was added all at once to the flask containing the alkyne using an additional 1.0 mL of THF-H_2O (1:1) to complete the transfer. The resulting mixture was stirred at room temperature

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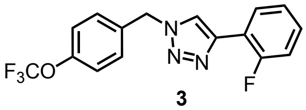
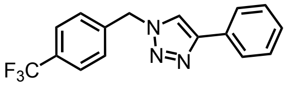
[1] Zhang, Z; Song, P; Zhou, J; Chen, Y; Lin, B; Li, Y *I. & E. Chem. Res.* **2016**, *55*, 12301-12308.

overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude off-white product was run through a 1 cm pad of silica gel using EtOAc-hexane (1:1) as the eluent and afforded, after trituration with warm hexane, 187 mg (73%) of a white solid; mp = 122-125°C. ^{1}H-NMR ($CDCl_3$): 7.77 (m, 2H), 7.65 (s, 1H), 7.34 (broad d, *J* = 8.7 Hz, 2H), 7.23 (broad d, *J* = 7.8 Hz 2H), 7.09 (m, 2H), 5.57 (s, 2H). ^{13}C-NMR ($CDCl_3$): 163.8, 161.9, 149.6, 147.7, 133.4, 129.6, 127.5 (d, *J* = 8.6 Hz), 126.7 (d, *J* = 3.8 Hz), 121.7, 119.3, 115.9 (d, *J* = 22.0 Hz), 53.5. HRMS (EI$^+$) calcd for $C_{16}H_{12}F_4N_3O$ (MH$^+$): 338.0917; found: 338.0923.



3

4-(2-fluorophenyl)-1-(4-(trifluoromethoxy)benzyl)-1*H*-1,2,3-triazole. 2-Fluorophenylacetylene (50 mg; 0.42 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 1.0 mL). In a separate flask a mixture containing sodium ascorbate (43 mg; 0.22 mmol), copper (II) sulfate pentahydrate (17 mg; 0.07 mmol) and THF-H_2O (1:1; 1.0 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-(trifluoromethoxy)benzene (84 mg; 0.39 mmol) and THF-H_2O (1:1; 1.0 mL). This mixture was added all at once to the flask containing the alkyne using an additional 1.0 mL of THF-H_2O (1:1) to complete the transfer. The resulting mixture was stirred at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. Purification of the crude product through a 1 cm pad of silica gel with CH_2Cl_2 afforded 78 mg (60%) of a white solid; mp = 104-106°C. ^{1}H-NMR ($CDCl_3$): 8.30 (dt, *J* = 7.6, 1.9 Hz, 1H), 7.89 (d, *J* = 3.6 Hz, 1H), 7.22-7.36 (m, 6H), 7.12 (m, 1H), 5.60 (s, 2H). ^{13}C-NMR ($CDCl_3$): 159.3 (d, *J* = 246.1 Hz), 149.5, 142.0, 133.5, 129.6, 129.5, 127.9 (d, *J* = 3.1 Hz), 124.7 (d, *J* = 3.3 Hz), 122.7 (d, *J* = 12.9 Hz), 121.7, 118.5 (d, *J* = 12.6 Hz), 115.7 (d, *J* = 21.6 Hz), 53.4. HRMS (EI$^+$) calcd for $C_{16}H_{12}F_4N_3O$ (MH+): 338.0916; found 338.0926.



4

4-phenyl-1-(4-(trifluoromethyl)benzyl)-1*H*-1,2,3-triazole. Phenylacetylene (80 mg; 0.78 mmol) was added to a 25 mL pear-shaped flask along with 6 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (72 mg; 0.36 mmol), copper (II) sulfate pentahydrate (35 mg; 0.14 mmol) and THF-H_2O (2 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-(trifluoromethyl)benzene (140 mg; 0.70 mmol) and an additional 2 mL of THF-H_20 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was passed through a 2 cm pad of silica gel using CH_2Cl_2 as the eluent affording 181 mg (86%) of a white solid; mp = 133-135°C. ^{1}H-NMR ($CDCl_3$): 7.81 (d, *J* = 7.5 Hz, 2H), 7.71 (s, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.41 (m, 4H), 7.33 (m, 1H), 5.64 (s, 2H). ^{13}C-NMR ($CDCl_3$): 148.7, 138.8, 131.21 (qr, J = 32.4 Hz), 130.4, 129.0, 128.5, 128.3, 126.2 (qr, J = 3.8 Hz), 125.9, 119.7, 53.6. The NMR spectra obtained were consistent with the literature values[2].

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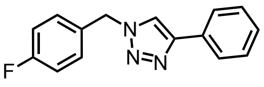
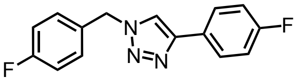
[2] Asano, K.; Matsubara, S. *Org. Lett.* **2010**, *12*, 4988-4991.



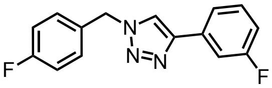
5

1-(4-fluorobenzyl)-4-phenyl-1*H*-1,2,3-triazole. Phenylacetylene (0.13 mL; 1.15 mmol) was added to a 100 mL round-bottom flask along with 10 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (0.12 g; 0.58 mmol), copper (II) sulfate pentahydrate (0.06 g; 0.23 mmol) and THF-H_2O (15 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-fluorobenzene (0.17 g; 1.15 mmol) and an additional 2 mL of THF-H_20 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.24 g (82%) of a white solid; mp = 138-140°C. ^{1}H-NMR ($CDCl_3$): δ 7.73 (d, J = 7 Hz, 2H), 7.66 (s, 1H), 7.40 (t, J = 7 Hz, 2H), 7.32 (m, 3H), 7.08 (t, J = 8.5 Hz, 2H), 5.55 (s, 2H). The NMR data obtained were consistent with the literature values.[3]



6

1-(4-fluorobenzyl)-4-(4-fluorophenyl)-1*H*-1,2,3-triazole. 4-Fluorophenylacetylene (0.13 mL; 1.14 mmol) was added to a 100 mL round-bottom flask along with 10 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (0.11 g; 0.57 mmol), copper (II) sulfate pentahydrate (0.06 mg; 0.22 mmol) and THF-H_2O (6 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-fluorobenzene (0.17 g; 1.14 mmol) and an additional 2 mL of THF-H_20 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.19 g (61%) of a white solid; mp = 144-146°C. ^{1}H-NMR: ($CDCl_3$): δ 7.77 (m, 2H), 7.61 (s, 1H), 7.31 (m, 2H), 7.09 (m, 4H), 5.55 (s, 2H). HRMS (EI$^+$) calcd for $C_{15}H_{12}N_3F_2$ (MH+): 272.0999; found 272.1005. The NMR data obtained were consistent with the literature values.[4]



7

1-(4-fluorobenzyl)-4-(3-fluorophenyl)-1*H*-1,2,3-triazole. 1-ethynyl-3-fluorobenzene (0.09 mL; 0.79 mmol) was added to a 50 mL round-bottom flask along with 6 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (0.078 g; 0.40 mmol), copper (II) sulfate pentahydrate (0.039 g; 0.16 mmol) and THF-H_2O (10 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-fluorobenzene (0.12 g; 0.79 mmol) and an additional 2 mL of THF-H_20 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.09 g (42%) of a white solid; mp = 136-139°C. ^{1}H-NMR ($CDCl_3$): δ 7.66 (s, 1H), 7.56 (m, 2H), 7.37 (m, 1H), 7.02 (dt, J = 8.5 Hz

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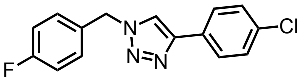
[3] Mohan, B.; Kang, H.; Park, K.H *Inorganic Chemistry Communications* **2013**, *35*, 239.

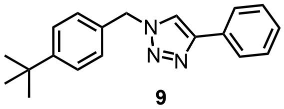
[4] Jia, X.; Xu, G.; Du, Z.; Fu, Y. *Polyhedron* **2018**, *151*, 515.

and J = 2.5 Hz, 1H), 6.80 (m, 2H), 5.55 (s, 2H). ^{13}C-NMR ($CDCl_3$): δ 164.0 (d, J = 26.5 Hz), 162.1 (d, J = 26.5 Hz), 147.2, 132.6 (d, J = 8.4 Hz), 130.5 (d, J = 8.1 Hz), 130.4, 130.0 (d, J = 8.3 Hz), 116.2 (d, J = 21.9 Hz), 115.0 (d, J = 21.2 Hz), 112.6 (d, J = 22.9 Hz), 53.5. HRMS (EI$^+$) calcd for $C_{15}H_{12}N_3F_2$ (MH+): 272.0999; found 272.1005.



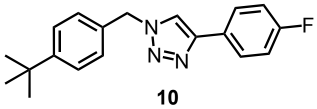
8

4-(4-chlorophenyl)-1-(4-fluorobenzyl)-1*H*-1,2,3-triazole. 1-chloro-4-ethynylbenzene (0.11 g; 0.79 mmol) was added to a 100 mL round-bottom flask along with 10 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (0.078 g; 0.40 mmol), copper (II) sulfate pentahydrate (0.039 g; 0.16 mmol) and THF-H_2O (15 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-fluorobenzene (0.12 g; 0.79 mmol) and an additional 2 mL of THF-H_20 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.16 g (70%) of a white solid; mp = 157-1359°C. ^{1}H-NMR ($CDCl_3$): δ 7.73 (m, 2H), 7.65 (s, 1H), 7.37 (m, 2H), 7.30 (m, 2H), 7.07 (m, 2H), 5.54 (s, 2H); ^{13}C-NMR ($CDCl_3$): δ 147.4, 134.1, 130.1, 130.0, 129.1, 127.0. 119.5, 116.4, 116.2, 53.6; HRMS (EI$^+$) calcd for $C_{15}H_{12}N_3FCl$ (MH+): 288.0704; found 288.0703.



9

1-(4-(*tert*-butyl)benzyl)-4-phenyl-1*H*-1,2,3-triazole. Phenylacetylene (0.11 mL; 0.95 mmol) was added to a 50 mL round-bottom flask along with 5 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (0.094 g; 0.48 mmol), copper (II) sulfate pentahydrate (0.05 g; 0.19 mmol) and THF-H_2O (10 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-(*tert*-butyl)benzene (0.18 g; 0.95 mmol) and an additional 2 mL of THF-H_20 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.18 g (65%) of a white solid; mp = 168-170°C. ^{1}H-NMR ($CDCl_3$): δ 7.80 (broad d, J = 7.5 Hz, 2H), 7.67 (s, 1H), 7.39 (m, 4H), 7.31 (broad t, J = 7.5 Hz, 1H), 7.25 (broad d, J = 8.0 Hz, 2H), 5.53 (s, 2H), 1.32 (s, 9H); HRMS (EI$^+$) calcd for $C_{19}H_{22}N_3$ (MH+): 292.1814; found 292.1824. The NMR and HRMS data obtained were consistent with the literature values.[5]



10

1-(4-(*tert*-butyl)benzyl)-4-(4-fluorophenyl)-1*H*-1,2,3-triazole. 4-Fluorophenylacetylene (0.11 mL; 0.95 mmol) was added to a 100 mL round-bottom flask along with 10 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (0.09 g; 0.48 mmol), copper (II) sulfate pentahydrate (0.05 mg; 0.19 mmol) and THF-H_2O (6 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-(*tert*-butyl)benzene (0.18 g; 0.95 mmol) and an

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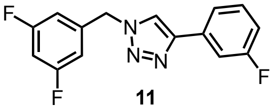
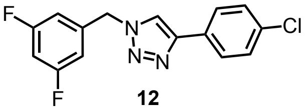
[5] Li, F.; Hor, T.S.A. *Chem. Eur. J.* **2009**, *15*, 10585.

additional 2 mL of THF-$H_2$0 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.17 g (58%) of a white solid; mp = 146-149°C. ^{1}H-NMR ($CDCl_3$): δ 7.76 (m, 2H), 7.63 (s, 1H), 7.40 (d, *J* = 8.5 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 7.07 (t, *J* = 8.5 Hz, 2H), 5.53 (s, 2H), 1.31 (s, 9H). HRMS (EI$^+$) calcd for $C_{19}H_{20}N_3F$ (MH+): 310.1720; found 310.1720. The NMR and HRMS data obtained were consistent with the literature values.[6]



11

1-(3,5-difluorobenzyl)-4-(3-fluorophenyl)-1*H*-1,2,3-triazole. 1-ethynyl-3-fluorobenzene (0.14 g; 1.24 mmol) was added to a 250 mL round-bottom flask along with 15 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (0.12 g; 0.62 mmol), copper (II) sulfate pentahydrate (0.06 g; 0.24 mmol) and THF-H_2O (8 mL) was prepared. To this mixture was added 1-(azidomethyl)-3,5-difluorobenzene (0.21 g; 1.24 mmol) and an additional 2 mL of THF-$H_2$0 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.24 g (67%) of a white solid; mp = 127-129°C. ^{1}H-NMR ($CDCl_3$): δ 7.76 (s, 1H), 7.54 (m, 2H), 7.34 (m, 3H), 7.00 (m, 2H), 7.01 (dt, *J* = 8.5 Hz and 2.5 Hz, 1H), 5.55 (s, 2H). ^{13}C-NMR ($CDCl_3$): δ 164.4 (t, *J* = 12.6 Hz), 162.4 (t, *J* = 12.5 Hz), 147.5, 138.4 (t, *J* = 9.2 Hz), 132.5 (d, *J* = 8.5 Hz), 130.6 (d, *J* = 8.1 Hz), 121.4, 120.3, 115.2 (d, *J* = 21 Hz), 112.7 (d, *J* = 23.1 Hz), 111.0 (d, *J* = 6 Hz), 110.8 (d, *J* = 6.6 Hz), 104.4 (t, *J* = 24.9 Hz). 100.0, 53.3; HRMS (EI$^+$) calcd for $C_{15}H_{11}N_3F_3$ (MH+): 290.0905; found 290.0913.



12

4-(4-chlorophenyl)-1-(3,5-difluorobenzyl)-1*H*-1,2,3-triazole. 1-chloro-4-ethynylbenzene (0.17 g; 1.24 mmol) was added to a 250 mL round-bottom flask along with 15 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (0.12 g; 0.62 mmol), copper (II) sulfate pentahydrate (0.06 g; 0.24 mmol) and THF-H_2O (8 mL) was prepared. To this mixture was added 1-(azidomethyl)-3,5-difluorobenzene (0.21 g; 1.24 mmol) and an additional 2 mL of THF-$H_2$0 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.18 g (48%) of a white solid; mp = 135-137°C. ^{1}H-NMR ($CDCl_3$): δ 7.75 (m, 2H), 7.72 (s, 1H), 7.39 (m, 2H), 6.81 (m, 3H), 5.55 (s, 2H); ^{13}C-NMR ($CDCl_3$): δ 164.4 (t, *J* = 12.6 Hz), 147.6 (t, *J* = 16 Hz), 138.3, 134.2, 129.2, 128.8, 127.1, 119.9, 111.0 (d, *J* = 6.1 Hz), 110.9 (d, *J* = 6.5 Hz), 104.5 (t, *J* = 24.9 Hz), 53.3. HRMS (EI$^+$) calcd for $C_{15}H_{11}N_3F_2Cl$ (MH+): 306.0610; found 306.0613.

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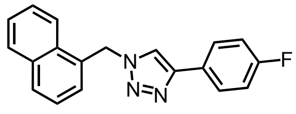
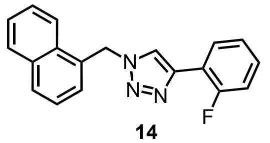
[6] Camberlein, V.; Kraupner, N.; Karroum, N.; Lipka, E.; Deprez-Poulain, R.; Deprez, B.; Bosc, D. *Tet. Lett.* **2021**, *73*, 153131.



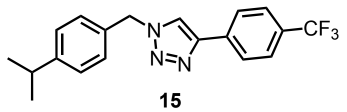
13

4-(4-fluorophenyl)-1-(naphthalen-1-ylmethyl)-1*H*-1,2,3-triazole. 4-Fluorophenylacetylene (65 mg; 0.54 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 1.0 mL). In a separate flask a mixture containing sodium ascorbate (31 mg; 0.15 mmol), copper (II) sulfate pentahydrate (15 mg; 0.06 mmol) and THF-H_2O (1:1; 0.5 mL) was prepared. To this mixture was added 1-(azidomethyl)naphthalene (91 mg; 0.50 mmol) and THF-H_2O (1:1; 1.0 mL). This mixture was added all at once to the flask containing the alkyne using an additional 0.5 mL of THF-H_2O (1:1) to complete the transfer. The resulting mixture was stirred at room temperature overnight. The resulting mixture was stirred at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation afforded an off-white solid. Further purification was achieved by recrystallization from CH_3OH-H_2O yielding 120 mg (80%) of a white solid; mp = 121-124°C. ^{1}H-NMR ($CDCl_3$): 8.00 (m, 1H), 7.91 (m, 2H), 7.69 (m, 2H), 7.54-7.47 (m, 5H), 7.03 (t, J = 8.5 Hz), 6.00 (s, 2H). ^{13}C-NMR ($CDCl_3$): 162.7 (d, J = 245.9 Hz), 147.3, 134.1, 131.3, 130.2, 129.9, 129.1, 128.0, 127.5 (d, J = 2.6 Hz), 127.4, 126.8 (d, J = 3.3 Hz), 125.5, 123.0, 119.3, 115.8 (d, J = 18 Hz), 52.5. HRMS (EI$^+$) calcd for $C_{19}H_{15}FN_3$ (MH+): 304.1250; found 304.1258.



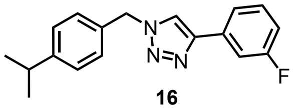
14

4-(2-fluorophenyl)-1-(naphthalen-1-ylmethyl)-1*H*-1,2,3-triazole. 2-Fluorophenylacetylene (78 mg; 0.66 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 1.0 mL). In a separate flask a mixture containing 1-(azidomethyl)naphthalene (110 mg; 0.60 mmol) and copper (II) sulfate pentahydrate (18 mg; 0.072 mmol) in THF-H_2O (1:1; 0.5 mL) was prepared. This mixture was added all at once to the flask containing the alkyne, followed by the addition of sodium ascorbate (36 mg; 0.18 mmol) using an additional 1.0 mL of THF-H_2O (1:1) to complete the transfer. The reaction was run overnight at room temperature. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation afforded a pale-yellow oil. The crude product was run through a 2 cm column of silica gel using CH_2Cl_2 as the eluent and afforded 145 mg (80%) of a white solid; mp = 119-122°C. ^{1}H-NMR ($CDCl_3$): 8.29 (dt, J = 8.0, 2.0 Hz, 1H), 8.04 (m, 1H), 7.90 (m, 2H), 7.75 (d, J = 3.5 Hz), 7.55-7.44 (m, 4H), 7.27-7.20 (m, 2H), 7.04 (m, 1H), 6.03 (s, 2H). ^{13}C-NMR ($CDCl_3$): 159.2 (d, J = 246.4 Hz), 141.6 (d, J = 2.8 Hz), 134.0, 131.2, 130.1, 130.0, 129.3 (d, J = 8.3 Hz), 129.0, 127.9 (d, J = 3.6 Hz), 127.8, 127.4, 126.5, 125.5, 124.6 (d, J = 3.1 Hz), 123.0, 122.8 (d, J = 12.6 Hz), 118.7 (d, J = 12.8 Hz), 115.6 (d, J = 21.5 Hz), 52.5. HRMS (EI$^+$) calcd for $C_{19}H_{15}FN_3$ (MH+): 304.1250; found 304.1260.



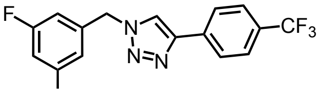
15

1-(4-isopropylbenzyl)-4-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole. 1-ethynyl-4-(trifluoromethyl)benzene (0.13 mL; 0.82 mmol) was added to a 100 mL round-bottom flask along with 10 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (0.08 g; 0.41 mmol), copper (II) sulfate pentahydrate (0.04 g; 0.16 mmol) and THF-H_2O (15 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-isopropylbenzene (0.14 g; 0.82 mmol) and an additional 2 mL of THF-$H_2$0 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.22 g (78%) of a white solid; mp = 150-152°C. ^{1}H-NMR (CDCl$_3$): δ 7.91 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.26 (m, 4H), 2.92 (sept, *J* = 7.0 Hz, 1H), 1.25 (d, *J* = 7.0 Hz, 6H); ^{13}C-NMR (CDCl$_3$): δ 149.9, 146.8, 134.2, 131.8, 128.3, 127.4, 125.9, 125.8, 120.4, 54.2, 34.0, 24.0; HRMS (EI$^+$) calcd for $C_{19}H_{19}N_3F$ (MH+): 346.1531; found 346.1531.



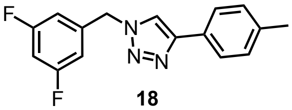
16

1-(4-(*sec*-butyl)benzyl)-4-(3-fluorophenyl)-1*H*-1,2,3-triazole. 1-ethynyl-3-fluorobenzene (0.095 mL; 0.82 mmol) was added to a 100 mL round-bottom flask along with 10 mL of THF-H$_2$O (1:1). In a separate flask a mixture containing sodium ascorbate (0.08 g; 0.41 mmol), copper (II) sulfate pentahydrate (0.04 g; 0.16 mmol) and THF-H$_2$O (15 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-isopropylbenzene (0.14 g; 0.82 mmol) and an additional 2 mL of THF-H$_2$0 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.21 g (87%) of a white solid; mp = 109-112°C. ^{1}H-NMR (CDCl$_3$): δ 7.69 (s, 1H), 7.53 (m, 2H), 7.33 (m, 1H), 7.24 (m, 4H), 6.98 (m, 1H), 5.52 (s,2H), 2.91 (sept, *J* = 6.5 Hz, 1H), 1.24 (d, *J* = 7.0 Hz, 6H); ^{13}C-NMR (CDCl$_3$): δ 163.2 (d, *J* = 244.0 Hz), 148.4 (d, *J* = 338.0 Hz), 133.0 (d, *J* = 8.4 Hz), 132.1, 130.5 (d, *J* = 8.2 Hz), 127.8 (d, *J* = 121.8 Hz), 120.8 (d, *J* = 144.4 Hz), 114.9 (d, *J* = 21.1 Hz), 112.6 (d, *J* = 22.9 Hz), 54.1, 33.9, 24.0; HRMS (EI$^+$) calcd for $C_{18}H_{19}N_3F$ (MH+): 296.1563; found 296.1558.



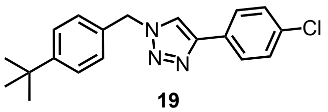
17

1-(3,5-difluorobenzyl)-4-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole.
1-ethynyl-4-(trifluoromethyl)benzene (0.18 mL; 1.09 mmol) was added to a 100 mL round-bottom flask along with 10 mL of THF-H$_2$O (1:1). In a separate flask a mixture containing sodium ascorbate (0.11 g; 0.55 mmol), copper (II) sulfate pentahydrate (0.05 g; 0.22 mmol) and THF-H$_2$O (15 mL) was prepared. To this mixture was added 1-(azidomethyl)-3,5-difluorobenzene (0.19 g; 1.09 mmol) and an additional 2 mL of THF-H$_2$0 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.21 g (87%) of a white solid; mp = 143-147°C. ^{1}H-NMR (CDCl$_3$): δ 7.94 (d, *J* = 8.5 Hz, 2H), 7.81 (s, 1H), 7.68 (d, *J* = 8.5 Hz, 2H), 6.83 (m, 3H), 5.58 (s, 2H); ^{13}C-NMR (CDCl$_3$): δ 164.5 (d, *J* = 12.6 Hz), 162.5 (d, *J* = 12.5 Hz), 147.3, 138.2 (t, *J* = 8.4 Hz), 133.7, 126.0, 125.9, 120.4, 111.1 (d, *J* = 6.6 Hz), 110.9 (d, *J* = 6.5 Hz), 104.6 (t, *J* = 25.0 Hz), 53.4; HRMS (EI$^+$) calcd for $C_{16}H_{11}N_3F_5$ (MH+): 340.0873; found 340.0875.



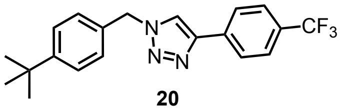
18

1-(3,5-difluorobenzyl)-4-(*p*-tolyl)-1*H*-1,2,3-triazole. 1-ethynyl-4-methylbenzene (0.14 mL; 1.09 mmol) was added to a 100 mL round-bottom flask along with 10 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (0.11 g; 0.55 mmol), copper (II) sulfate pentahydrate (0.05 g; 0.22 mmol) and THF-H_2O (15 mL) was prepared. To this mixture was added 1-(azidomethyl)-3,5-difluorobenzene (0.19 g; 1.09 mmol) and an additional 2 mL of THF-$H_2$0 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.08 g (25%) of a white solid; mp = 157-159°C. ^{1}H-NMR ($CDCl_3$): δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.69 (s, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.80 (m, 3H), 5.55 (s, 2H), 2.38 (s, 3H); ^{3}C-NMR ($CDCl_3$): δ 161.6 (d, *J* = 193.9 Hz), 149.1 (d, *J* = 78.5 Hz), 138.4, 129.7, 127.5, 125.7, 120.6., 119.4, 111.0 (d, *J* = 5.9 Hz), 110.8 (d, *J* = 6.6 Hz), 104.6 (d, *J* = 8.8 Hz), 104.4 (d, *J* = 24.9 Hz), 53.2, 21.4; HRMS (EI^+) calcd for $C_{16}H_{14}N_3F_2$ (MH+): 286.1156; found 286.1158.



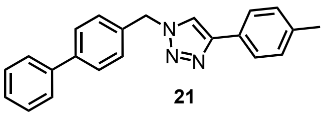
19

1-(4-(*tert*-butyl)benzyl)-4-(4-chlorophenyl)-1*H*-1,2,3-triazole. 1-ethynyl-4-chlorobenzene (0.13 g; 0.95 mmol) was added to a 100 mL round-bottom flask along with 10 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (0.09 g; 0.48 mmol), copper (II) sulfate pentahydrate (0.05 g; 0.19 mmol) and THF-H_2O (15 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-(*tert*-butyl)benzene (0.18 g; 0.95 mmol) and an additional 2 mL of THF-$H_2$0 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.22 g (71%) of a white solid; mp = 142-144°C. ^{1}H-NMR ($CDCl_3$): δ 7.73 (d, *J* = 9.0 Hz, 2H), 7.66 (s, 1H), 7.41(d, *J* = 8.5 Hz, 2H), 7.35 (d, *J* = 8.5 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 5.53 (s, 2H), 1.32 (s, 9H). ^{13}C-NMR ($CDCl_3$): δ 152.1, 147.1, 133.9, 131.7, 129.3, 129.1, 128.0, 127.0, 126.2, 119.9, 54.0, 34.7, 31.4; HRMS (EI^+) calcd for $C_{19}H_{21}N_3Cl$ (MH+): 326.1424; found 326.1428.



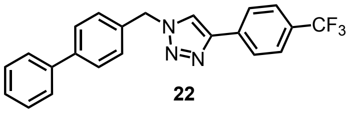
20

1-(4-(*tert*-butyl)benzyl)-4-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole. 1-ethynyl-4-(trifluoromethyl)benzene (0.16 mL; 0.95 mmol) was added to a 100 mL round-bottom flask along with 10 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (0.09 g; 0.48 mmol), copper (II) sulfate pentahydrate (0.05 g; 0.19 mmol) and THF-H_2O (15 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-(*tert*-butyl)benzene (0.18 g; 0.95 mmol) and an additional 2 mL of THF-$H_2$0 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.26 g (78%) of a white solid; mp = 159-161°C. ^{1}H-NMR (CDCl$_3$): δ 7.92 (d, *J* = 8.0 Hz, 2H), 7.74 (s, 1H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.42 (m, 2H), 7.27 (d, *J* = 7.5 Hz, 2H), 5.56 (s, 2H), 1.32 (s, 9H); ^{13}C-NMR (CDCl$_3$): δ 152.2, 146.8, 134.2, 131.5, 128.1, 126.2, 125.9, 125.9, 125.8 (q, *J* = 3.4 Hz), 120.5, 54.1, 34.7, 31.3; HRMS (EI$^+$) calcd for $C_{20}H_{21}N_3F_3$ (MH+): 360.1688; found 360.1694.



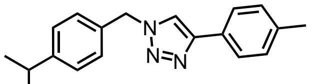
21

1-([1,1'-biphenyl]-4-ylmethyl)-4-(*p*-tolyl)-1*H*-1,2,3-triazole. 1-ethynyl-4-methylbenzene (0.03 mL; 0.24 mmol) was added to a 25 mL round-bottom flask along with 4 mL of THF-H$_2$O (1:1). In a separate flask a mixture containing sodium ascorbate (0.024 g; 0.12 mmol), copper (II) sulfate pentahydrate (0.012 g; 0.05 mmol) and THF-H$_2$O (5 mL) was prepared. To this mixture was added 4-(azidomethyl)-1,1'-biphenyl (0.05 g; 0.24 mmol) and an additional 1 mL of THF-H$_2$0 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.05 g (66%) of a white solid; mp = 215-217°C. ^{1}H-NMR (CDCl$_3$): δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.67 (s, 1H), 7.62-7.57 (m, 4H), 7.45 (t, *J* 7 = Hz, 2H), 7.39-7.36 (m, 3H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.61 (s, 2H), 2.37 (s, 3H); ^{13}C-NMR (CDCl$_3$): δ 148.5, 141.9, 140.3, 138,1, 133.8, 129.6, 129.0, 127.9, 127.8 (d, *J* = 5.3 Hz), 127.2, 125.7, 119.3, 54.0, 21.4; HRMS (EI$^+$) calcd for $C_{22}H_{20}N_3$ (MH+): 326.1657; found 326.1660.



22

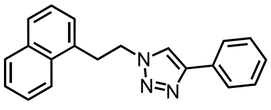
1-([1,1'-biphenyl]-4-ylmethyl)-4-(4-(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole. 1-ethynyl-4-(trifluoromethyl)benzene (0.04 mL; 0.24 mmol) was added to a 25 mL round-bottom flask along with 4 mL of THF-H$_2$O (1:1). In a separate flask a mixture containing sodium ascorbate (0.024 g; 0.12 mmol), copper (II) sulfate pentahydrate (0.012 g; 0.05 mmol) and THF-H$_2$O (5 mL) was prepared. To this mixture was added 4-(azidomethyl)-1,1'-biphenyl (0.05 g; 0.24 mmol) and an additional 1 mL of THF-H$_2$0 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.032 g (35%) of a white solid; mp = 205-208°C. ^{1}H-NMR (CDCl$_3$): δ 7.93 (d, *J* = 8.0 Hz, 2H), 7.79 (s, 1H), 7.67-7.62 (m, 4H), 7.58 (m, 2H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.41-7.36 (m, 3H), 5.64 (s, 2H); ^{13}C-NMR (CDCl$_3$): δ 142.1, 140.2, 134.1, 133.3, 129.0, 128.7, 128.00, 127.9, 127.2, 125.9, 120.3, 54.2; HRMS (EI$^+$) calcd for $C_{22}H_{17}F_3N_3$ (MH+): 380.1375; found 380.1370.



23

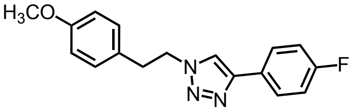
1-(4-isopropylbenzyl)-4-(*p*-tolyl)-1*H*-1,2,3-triazole. 1-ethynyl-4-methylbenzene (0.10 mL; 0.82 mmol) was added to a 100 mL round-bottom flask along with 10 mL of THF-H$_2$O (1:1).

In a separate flask a mixture containing sodium ascorbate (0.081 g; 0.41 mmol), copper (II) sulfate pentahydrate (0.040 g; 0.16 mmol) and THF-H_2O (5 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-isopropylbenzene (0.14 g; 0.82 mmol) and an additional 2 mL of THF-H_20 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.17 g (71%) of a white solid; mp = 128-130°C. ^{1}H-NMR ($CDCl_3$): δ 7.70 (d, *J* = 8 Hz, 2H), 7.64 (s, 1H), 7.24 (m, 4H), 7.20 (d, *J* = 8 Hz, 2H), 5.50 (s, 2H), 2.96 (sept, *J* = 7 Hz, 1H), 2.36 (s, 3H), 1.25 (d, *J* = 7 Hz, 6H); ^{13}C-NMR ($CDCl_3$): δ 149.5, 148.2, 137.9, 132.4, 129.6, 128.2, 128.0, 127.2, 125.7, 119.6, 54.0, 34.0, 24.0, 21.4; HRMS (EI$^+$) calcd for $C_{19}H_{22}N_3$ (MH+): 292.1814; found 292.1815.



24

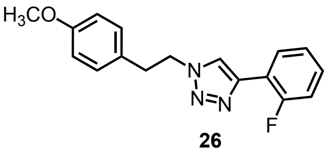
1-(2-(naphthalen-1-yl)ethyl)-4-phenyl-1*H*-1,2,3-triazole. Phenylacetylene (0.07 mL; 0.60 mmol) was added to a 25 mL round-bottom flask along with 2 mL of THF-H_2O (1:1). In a separate flask a mixture containing sodium ascorbate (0.06 g; 0.30 mmol), copper (II) sulfate pentahydrate (0.03 mg; 0.12 mmol) and THF-H_2O (6 mL) was prepared. To this mixture was added 1-(2-azidoethyl)naphthalene (0.118 g; 0.6 mmol) and an additional 2 mL of THF-H_20 (1:1). This mixture containing the azide was then added all at once to the flask containing the alkyne. The resulting mixture was allowed to stir at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. The crude product was purified via flash column chromatography (25:75 EtOAc:hexanes) to obtain 0.091 g (51%) of a white solid; mp = 124-126°C. ^{1}H-NMR ($CDCl_3$): δ 8.02 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 7.0 Hz, 1H), 7.59-7.51 (m, 2H), 7.41-7.35 (m, 4H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 7.0 Hz, 1H), 4.76 (t, *J* = 7.5 Hz, 2H), 3.72 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 134.0, 133.1, 131.6, 130.7, 129.2, 128.9, 128.2, 128.2, 127.4, 126.7, 126.0, 125.8, 125.7, 123.0, 51.0, 34.2. HRMS (EI$^+$) calcd for $C_{20}H_{18}N_3$ (MH+): 300.1501; found 300.1511.



25

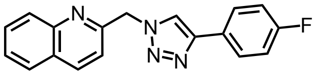
4-(4-fluorophenyl)-1-(4-methoxyphenethyl)-1*H*-1,2,3-triazole. 4-Fluorophenylacetylene (60 mg; 0.50 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 1.0 mL). In a separate flask a mixture containing sodium ascorbate (36 mg; 0.18 mmol), copper (II) sulfate pentahydrate (14 mg; 0.056 mmol) and THF-H_2O (1:1; 1.0 mL) was prepared. To this mixture was added 1-(azidomethyl)-4-methoxybenzene (85 mg; 0.48 mmol) and THF-H_2O (1:1; 1.0 mL). This mixture was added all at once to the flask containing the alkyne using an additional 0.5 mL of THF-H_2O (1:1) to complete the transfer. The resulting mixture was stirred at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. Recrystallization from CH_3OH-H_2O afforded 100 mg (70%) of a white solid; mp = 154-156°C. ^{1}H-NMR ($CDCl_3$): 7.73 (m, 2H), 7.44 (s, 1H), 7.09 (t, *J* = 8.5 Hz, 2H), 7.03 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 4.58 (t, *J* = 7.0 Hz, 2H), 3.78 (s, 3H), 3.18 (t, *J* =

7.5 Hz, 2H). ^{13}C-NMR ($CDCl_3$): 162.7 (d, J = 245.5 Hz), 158.8, 146.7, 129.8, 129.1, 127.5 (d, J = 8.0 Hz), 127.0 (d, J = 3.4 Hz), 119.8, 115.8 (d, J = 21.8 Hz), 114.3, 55.4, 52.1. HRMS (EI$^+$) calcd for $C_{17}H_{17}FN_3O$ (MH+): 298.1356; found 298.1360.



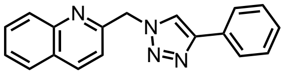
26

4-(2-fluorophenyl)-1-(4-methoxyphenethyl)-1*H*-1,2,3-triazole. 2-Fluorophenylacetylene (60 mg; 0.50 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 1.0 mL). In a separate vial a mixture containing sodium ascorbate (36 mg; 0.18 mmol), copper (II) sulfate pentahydrate (15 mg; 0.06 mmol) and THF-H_2O (1:1; 1.0 mL) was prepared. This mixture was added to another vial containing 1-(2-azidoethyl)-4-methoxybenzene (82 mg; 0.46 mmol). This combined mixture was added all at once to the flask containing the alkyne using two additional 0.25 mL portions of THF-H_2O (1:1) to complete the transfer. The reaction mixture was stirred at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation. Trituration with hexane followed by elution of the product through a 1 cm pad of silica gel using 2% CH_3OH in CH_2Cl_2 gave 117 mg (85%) of a white solid; mp = 109-111°C. ^{1}H-NMR ($CDCl_3$): 8.28 (dt, J = 8.0, 2.0 Hz, 1H), 7.70 (d, J = 3.5 Hz, 1H), 7.32-7.22 (m, 2H), 7.11 (m, 1H), 7.04 (m, 2H), 6.83 (m, 2H), 4.60 (t, J = 7.0 Hz, 2H), 3.78 (s, 3H), 3.20 (t, J = 7.0 Hz, 2H). ^{13}C-NMR ($CDCl_3$): 159.3 (d, J = 246.3 Hz), 158.8, 141.0 (d, J = 2.8 Hz), 129.8, 129.3 (d, J = 8.0 Hz), 129.0, 128.0 (d, J = 3.6 Hz), 124.7 (d, J = 2.9 Hz), 123.1 (d, J = 12.5 Hz), 118.8 (d, J = 12.5 Hz), 115.7 (d, J = 21.9 Hz), 114.3, 55.4, 52.0, 36.0. HRMS (EI$^+$) calcd for $C_{17}H_{17}FN_3O$ (MH+): 298.1356; found 298.1365.



27

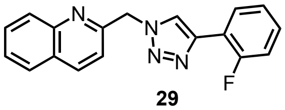
2-((4-(4-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)methyl)quinoline. 4-Fluorophenylacetylene (86 mg; 0.72 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 1.0 mL) and copper (II) sulfate pentahydrate (21 mg; 0.084 mmol) To this flask was added a solution of 2-(azidomethyl)quinoline (125 mg; 0.68 mmol) in THF-H_2O (1:1; 1.0 mL), followed by sodium ascorbate (36 mg; 0.18 mmol), and additional THF-H_2O (1:1; 1.0 mL). The resulting mixture was stirred at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation afforded a light orange solid. Purification by recrystallization from EtOAc-hexanes afforded 164 mg (79%) of off-white needles; mp = 138-140°C. ^{1}H-NMR ($CDCl_3$): 8.16 (d, J = 8.5 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.90 (s, 1H), 7.83-7.75 (m, 4H), 7.58 (t, J = 8.0 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.09 (m, 2H), 5.88 (s, 2H). ^{13}C-NMR ($CDCl_3$): 162.78 (d, J = 245.9 Hz), 154.6, 147.7 (d, J = 19.5 Hz), 137.9, 130.3, 129.3, 127.8, 127.7, 127.6 (d, J = 8.4 Hz), 127.3, 126.8 (d, J = 3.4 Hz), 120.1, 119.8, 115.9 (d, J = 21.9 Hz), 56.6. HRMS (EI$^+$) calcd for $C_{18}H_{14}FN_4$ (MH$^+$): 305.1202; found: 305.1204.



28

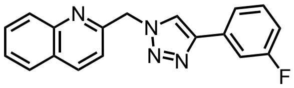
2-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)quinoline. Phenylacetylene (74 mg; 0.73 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 1.0 mL) and copper (II) sulfate pentahydrate (25 mg; 0.10 mmol) To this flask was added a solution of 2-

(azidomethyl)quinoline (123 mg; 0.67 mmol) in THF-H_2O (1:1; 1.0 mL), followed by sodium ascorbate (37 mg; 0.19 mmol), and additional THF-H_2O (1:1; 1.0 mL). The resulting mixture was stirred at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation afforded a light orange solid afforded a tan solid. Purification by CombiFlash Rf flash chromatography system (Teledyne Isco) (silica gel, 100% hexane for 4 minutes, then 0-30% ethyl acetate in hexane over 20 minutes) gave 94 mg (49%) of white needles; mp = 171-173°C. ^{1}H-NMR ($CDCl_3$): 8.15 (d, J = 8.5 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.93 (s, 1H), 7.82 (d, J = 7.0 Hz, 3H), 7.76 (dt, J = 8.5, 1.5 Hz, 1H), 7.57 (dt, J = 8.0, 1.0 Hz, 1H), 7.40 (t, J = 7.5 Hz, 2H), 7.31 (m, 2H), 5.88 (s, 2H). ^{13}C-NMR ($CDCl_3$): 154.7, 148.5, 147.8, 137.9, 130.6, 130.3, 129.3, 128.9, 128.3, 127.8, 127.7, 127.3, 125.8, 120.3, 119.7, 56.6. HRMS (EI^+) calcd for $C_{18}H_{15}N_4$ (MH^+): 287.1297; found 287.1295.



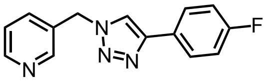
29

2-((4-(2-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)methyl)quinoline. 2-Fluorophenylacetylene (79 mg; 0.66 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 1.0 mL). In a separate vial a mixture of 2-(azidomethyl)quinoline (117 mg; 0.63 mmol), copper (II) sulfate pentahydrate (24 mg; 0.096 mmol), sodium ascorbate (60 mg; 0.30 mmol) and THF-H_2O (1:1; 1.5 mL). This mixture was added all at once to the flask containing the alkyne and washed in with an additional THF-H_2O (1:1; 1.0 mL). The resulting mixture was stirred at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation afforded a light orange solid afforded a dark orange solid. Purification by CombiFlash Rf flash chromatography system (Teledyne Isco) (silica gel; 100% hexanes, 3 min; then 0-26% EtOAc in hexanes over 25 min) afforded 102 mg (53%) of yellow needles; mp = 155-158°C. ^{1}H-NMR ($CDCl_3$): 8.31 (dt, J = 7.5, 1.5 Hz, 1H), 8.14 (d, J = 8.5 Hz, 1H), 8.12 (d, J = 4.0 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.80 (broad d, J = 8.0 Hz, 1H), 7.75 (dt, J = 8.0, 1.0 Hz, 1H), 7.57 (dt, J = 8.0, 1.0 Hz, 1H), 7.31-7.22 (m, 3H), 7.10 (m, 1H), 5.91 (s, 2H). ^{13}C-NMR ($CDCl_3$): 159.33 (d, J = 246.9 Hz), 154.7, 147.8, 141.9 (d, J = 2.1 Hz), 137.8, 130.3, 129.4 (d, J = 8.1 Hz), 129.3, 127.9 (d, J = 3.5 Hz), 127.8, 127.7, 127.2, 124.7 (d, J = 3.0 Hz), 123.5 (d, J = 12.6 Hz), 119.6, 118.6 (d, J = 12.6 Hz), 115.7 (d, J = 21.3 Hz), 56.5. HRMS (EI^+) calcd for $C_{18}H_{14}FN_4$ (MH^+): 305.1202; found: 305.1199.



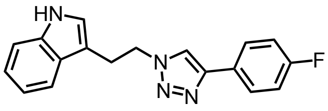
30

2-((4-(3-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)methyl)quinoline. 3-Fluorophenylacetylene (93 mg; 0.77 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 1.0 mL). In a separate vial a mixture of 2-(azidomethyl)quinoline (135 mg; 0.73 mmol), copper (II) sulfate pentahydrate (28 mg; 0.11 mmol), sodium ascorbate (69 mg; 0.35 mmol) and THF-H_2O (1:1; 1.5 mL). This mixture was added all at once to the flask containing the alkyne and washed in with an additional THF-H_2O (1:1; 1.0 mL). The resulting mixture was stirred at room temperature overnight. The resulting mixture was stirred at room temperature overnight. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation afforded a light orange solid afforded a yellow solid. Purification by recrystallization from MeOH-H_2O gave 180 mg (81%) of light-yellow needles; mp = 131-133°C. ^{1}H-NMR ($CDCl_3$): 8.16 (d, J = 8.5 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.95 (s, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.76 (dt, J = 8.5, 1.5 Hz, 1H), 7.59-7.53 (m, 3H), 7.37-7.33 (m, 2H), 6.99 (dt, J = 8.5, 2.5 Hz, 1H), 5.88 (s, 2H). ^{13}C-NMR ($CDCl_3$): 163.3 (d, J = 244.2 Hz), 154.5, 147.8, 147.4, 137.9, 132.8 (d, J = 8.6 Hz), 130.5 (d, J = 8.6 Hz), 130.4, 129.3, 127.8, 127.7, 127.3, 121.4, 120.7, 119.8, 115.1 (d, *J* = 21.0 Hz), 112.76 (d, *J* = 22.9 Hz), 56.6. HRMS (EI^+) calcd for $C_{18}H_{14}FN_4$ (MH^+): 305.1202; found: 305.1197.



31

3-((4-(4-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)methyl)pyridine. 4-Fluorophenylacetylene (88 mg; 0.74 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 1.0 mL). In a separate flask a mixture containing sodium ascorbate (68 mg; 0.34 mmol), copper (II) sulfate pentahydrate (27 mg; 0.11 mmol) and THF-H_2O (1:1; 0.5 mL) was prepared. To this mixture was added 3-(azidomethyl)pyridine (90 mg; 0.70 mmol). This mixture was added all at once to the flask containing the alkyne and washed in with an additional THF-H_2O (1:1; 1.0 mL). The resulting reaction was stirred overnight at room temperature. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation afforded a light orange solid afforded an off-white solid. After trituration with hexanes and recrystallization from MeOH-H_2O, 132 mg (78%) of a white solid was obtained; mp = 123-125°C. ^{1}H-NMR ($CDCl_3$): 8.63 (m, 2H), 7.75 (m, 2H), 7.68 (s, 1H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.31 (m, 1H), 7.31 (t, *J* = 8.5 Hz, 1H), 5.58 (s, 2H). ^{13}C-NMR ($CDCl_3$): 162.8 (d, *J* = 246.1 Hz), 150.4, 149.2, 147.8, 135.8, 127.6 (d, *J* = 8.1 Hz), 126.6 (d, *J* = 3.0 Hz), 124.2, 119.3, 116.0 (d, *J* = 21.8 Hz), 51.7. HRMS (EI^+) calcd for $C_{14}H_{12}FN_4$ (MH^+): 255.1046; found: 255.1042.



32

3-(2-(4-(4-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-1*H*-indole. 4-Fluorophenylacetylene (72 mg; 0.60 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 1.5 mL). In a separate flask a mixture containing sodium ascorbate (52 mg; 0.26 mmol), copper (II) sulfate pentahydrate (22 mg; 0.09 mmol) and THF-H_2O (1:1; 1.5 mL) was prepared. To this mixture was added 3-(2-azidoethyl)-1*H*-indole[7] (98 mg; 0.52 mmol). This mixture was added all at once to the flask containing the alkyne and washed in with additional THF-H_2O (1:1; 2 X 0.5 mL). The yellow reaction was stirred overnight at room temperature. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation to afford an off-white solid. Purification was accomplished via flash column chromatography (2 cm column of silica with EtOAc:Hexane (1:2)) and afforded 111 mg (69%) of a white solid; mp = 174-176°C. ^{1}H-NMR ($CDCl_3$): 8.11 (bs, 1H), 7.72 (m, 2H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.42 (m, 2H), 7.26 (t, *J* = 7.5 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.10 (t, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 1.9 Hz, 1H), 4.73 (t, *J* = 7.0 Hz, 2H), 3.44 (t, *J* = 7.0 Hz, 2H). ^{13}C-NMR ($CDCl_3$): 162.6 (d, *J* = 245.3 Hz), 146.5, 136.3, 127.4 (d, *J* = 7.9 Hz), 126.9 (d, *J* = 3.5 Hz), 126.8, 122.5 (d, *J* = 26.7 Hz), 119.9, 119.8, 118.3, 115.7 (d, *J* = 21.8 Hz), 111.5, 111.2, 50.8, 26.6. HRMS (EI^+) calcd for $C_{18}H_{15}FN_4$ (MH^+): 307.1359; found: 307.1370.

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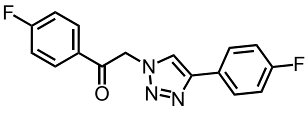
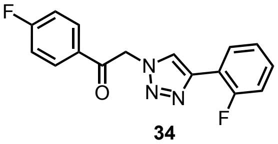
[7] Iannazzo, L., Soroka, D., Triboulet, S., Fonvielle, M., Compain, F., Dubee, V., Mainardi, J-L., Hugonnet, J-E., Braud, E., Arthur, M., Etheve-Quelquejeu, M. *J. Med. Chem.* **2016**, *59*, 3427-3438.



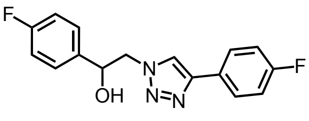
33

1-(4-fluorophenyl)-2-(4-(4-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)ethan-1-one.
4-Fluorophenylacetylene (100 mg; 0.83 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 4.5 mL). In a separate flask a mixture containing sodium ascorbate (79 mg; 0.40 mmol), copper (II) sulfate pentahydrate (30 mg; 0.12 mmol) and THF-H_2O (1:1; 2.0 mL) was prepared. To this mixture was added 2-azido-1-(4-fluorophenyl)ethan-1-one[8] (140 mg; 0.78 mmol). This mixture was added all at once to the flask containing the alkyne and washed in with additional THF-H_2O (1:1; 2 X 0.5 mL). The reaction was stirred overnight at room temperature. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation to afford an off-white solid. Purification was accomplished by preparative thin layer chromatography (silica gel; EtOAc-hexanes, 1:1) yielding 103 mg (44%) of a white solid; mp = 177-181°C. ^{1}H-NMR (acetone-d$_6$): 8.39 (s, 1H), 8.26 (m, 2H), 7.98 (m, 2H), 7.40 (t, J = 7.8 Hz, 2H), 7.24 (t, J = 7.9 Hz, 2H), 6.24 (s, 2H). ^{13}C-NMR (acetone-d$_6$): 190.0, 166.2 (d, J = 252.1 Hz), 162.4 (d, J = 243.0 Hz), 146.2, 131.2 (d, J = 9.8 Hz), 127.9 (d, J = 2.9 Hz), 127.3 (d, J = 8.0 Hz), 127.3 (d, J = 8.0 Hz), 122.2, 115.6 (d, J = 22.3 Hz), 115.6 (d, J = 21.6 Hz), 55.67. HRMS (EI$^+$) calcd for $C_{16}H_{12}F_2N_3O$ (MH$^+$): 300.0948; found: 300.0957.



34

1-(4-fluorophenyl)-2-(4-(2-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)ethan-1-one.
2-Fluorophenylacetylene (212 mg; 1.77 mmol) was added to a 25 mL pear-shaped flask along with THF-H_2O (1:1; 6.0 mL). In a separate flask a mixture containing sodium ascorbate (166 mg; 0.84 mmol), copper (II) sulfate pentahydrate (68 mg; 0.27 mmol) and THF-H_2O (1:1; 4.0 mL) was prepared. To this mixture was added 2-azido-1-(4-fluorophenyl)ethan-1-one[8] (283 mg; 1.58 mmol). This mixture was added all at once to the flask containing the alkyne and washed in with additional THF-H_2O (1:1; 2 X 1.0 mL). The reaction was stirred overnight at room temperature. Work up consisted of partitioning the reaction between ethyl acetate and water, washing the organic layer with water, then brine, drying over anhydrous sodium sulfate and concentration by rotary evaporation to afford an off-white solid. Purification by CombiFlash Rf flash chromatography system (Teledyne Isco) (silica gel; 100% hexanes for 2 min., then 0-40% EtOAc in hexanes over 26 min. gave 163 mg (37%) of a white solid; mp = 168-171°C. ^{1}H-NMR (CDCl$_3$): 8.34 (dt, J = 7.6, 1.7 Hz, 1H), 8.12 (d, J = 3.6 Hz, 1H), 8.08 (m, 2H), 7.33 (m, 1H), 7.26 (m, 3H), 7.16 (m, 1H), 5.91 (s, 2H). ^{13}C-NMR (CDCl$_3$): 188.7, 166.6 (d, J = 255.9 Hz), 159.3 (d, J = 246.5 Hz), 141.7 (d, J = 2.3 Hz), 131.0 (d, J = 9.7 Hz), 130.4 (d, J = 2.9 Hz), 129.4 (d, J = 8.3 Hz), 127.8 (d, J = 3.4 Hz), 124.6 (d, J = 3.5 Hz), 124.5, 118.5 (d, J = 12.7 Hz), 116.5 (d, J = 22.0 Hz), 115.7 (d, J = 21.7 Hz), 55.4. HRMS (EI+) calcd for $C_{16}H_{12}F_2N_3O$ (MH$^+$): 300.0948; found: 300.0962.



35

1-(4-fluorophenyl)-2-(4-(4-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)ethan-1-ol. 1-(4-fluorophenyl)-2-(4-(4-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)ethan-1-one (119 mg; 0.39

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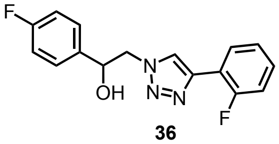
[8] Yu, P., Wang, Y., Zeng, Z., Chen, Y. *J. Org. Chem.* **2019**, *84*, 14883-14891.

mmol) was dissolved in dry methanol (25 mL) under argon. Sodium borohydride (100 mg; 2.8 mmol) was added to the solution and the reaction was stirred for 1 h at room temperature. Nearly all of the methanol was removed under reduced pressure and the residue was partitioned between EtOAc and water. The organic layer was washed with water, brine and dried over Na_2SO_4. The crude product obtained was purified by preparative thin layer chromatography (silica gel; EtOAc-hexanes, 1:1) and afforded 55 mg (45%) of a white solid; mp = 177-181°C. ^{1}H-NMR ($CDCl_3$): 7.78 (s, 1H), 7.75 (m, 2H), 7.43 (m, 2H), 7.12 (m, 4H), 5.26 (m, 1H), 4.65 (dd, *J* = 14.0, 3.2 Hz, 1H), 3.36 (bs, 1H). ^{13}C-NMR (DMSO-d$_6$): 158.9 (d, *J* = 245.5 Hz), 158.5, 139.9 (d, *J* = 2.0 Hz), 130.2, 130.0 (d, *J* = 8.4 Hz), 129.9, 127.8 (d, *J* = 3.5 Hz), 125.4 (d, *J* = 3.3 Hz), 124.2 (d, *J* = 11.2 Hz), 119.0 (d, *J* = 12.9 Hz), 116.5 (d, *J* = 21.1 Hz), 114.3, 55.5, 51.3, 35.3. HRMS (EI$^+$) calcd. for $C_{16}H_{13}F_2N_3O$ (MH$^+$): 302.1105; found 302.1113.



36

1-(4-fluorophenyl)-2-(4-(2-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)ethan-1-ol. 1-(4-fluorophenyl)-2-(4-(2-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)ethan-1-one (110 mg; 0.35 mmol) was dissolved in dry methanol (20 mL) under argon. Sodium borohydride (98 mg; 2.6 mmol) was added to the solution and the reaction was stirred for 1 h at room temperature. Nearly all of the methanol was removed under reduced pressure and the residue was partitioned between EtOAc and water. The organic layer was washed with water, brine and dried over Na_2SO_4. The crude product obtained was purified by CombiFlash Rf flash chromatography system (Teledyne Isco) (silica gel; 100% hexanes for 3 min., then 0-35% EtOAc in hexanes over 30 min.) and gave 54 mg (49%) of a white solid; mp = 134-136°C. ^{1}H-NMR ($CDCl_3$): 8.19 (t, *J* = 7.5 Hz, 1H), 7.97 (d, *J* = 3.4 Hz, 1H), 7.44 (t, *J*= 7.5 Hz, 2H), 7.33-7.23 (m, 2H), 7.12-7.06 (m, 3H), 5.30 (d, *J* = 8.2 Hz, 1H), 4.65 (dd, *J* = 14.0, 3.3 Hz, 1H), 4.48 (dd, *J* = 14.0, 8.8 Hz, 1H), 3.88 (bs, 1H). ^{13}C-NMR ($CDCl_3$): 162.7 (d, *J* = 245.7 Hz), 159.2 (d, *J* = 246.8 Hz), 140.9, 135.9 (d, *J* = 3.1 Hz), 129.3 (d, *J* = 8.4 Hz), 127.7 (d, *J* = 8.2 Hz), 124.6 (d, *J* = 2.9 Hz), 124.2 (d, *J* = 13.1 Hz), 118.2, 115.8 (d, *J* = 21.4 Hz), 115.6 (d, *J* = 21.6 Hz), 72.3, 57.5. HRMS (EI+) calcd for $C_{16}H_{14}F_2N_3O$ (MH$^+$): 302.1105; found 302.1112.

Biological Assay Data:

MIC (μg/mL)											
Compound	A (9)	B (10)	C (28)	D (29)	E (30)	F (31)	G (47)	H (51)	I (52)	J (53)	K (56)	L (92)
1	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
2	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
3	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
4	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
5	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
6	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
7	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
8	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
9	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
10	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
11	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
12	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
13	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
14	16	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
15	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
16	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
17	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
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26	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
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28	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
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31	> 128	> 128	> 32	> 32	> 32	> 128	> 32	> 128	> 128	> 32	> 64	> 64
AMP	> 128	128	≤ 32	> 32	> 32	4	> 32	> 128	≤ 0.5	≤ 32	--	--
KanA	≤ 4	> 128	≤ 32	≤ 32	≤ 32	≤ 0.5	≤ 32	≤ 0.5	≤ 0.5	≤ 32	--	--
AmB	--	--	--	--	--	--	--	--	--	--	16	> 64
Flu	--	--	--	--	--	--	--	--	--	--	64	> 64

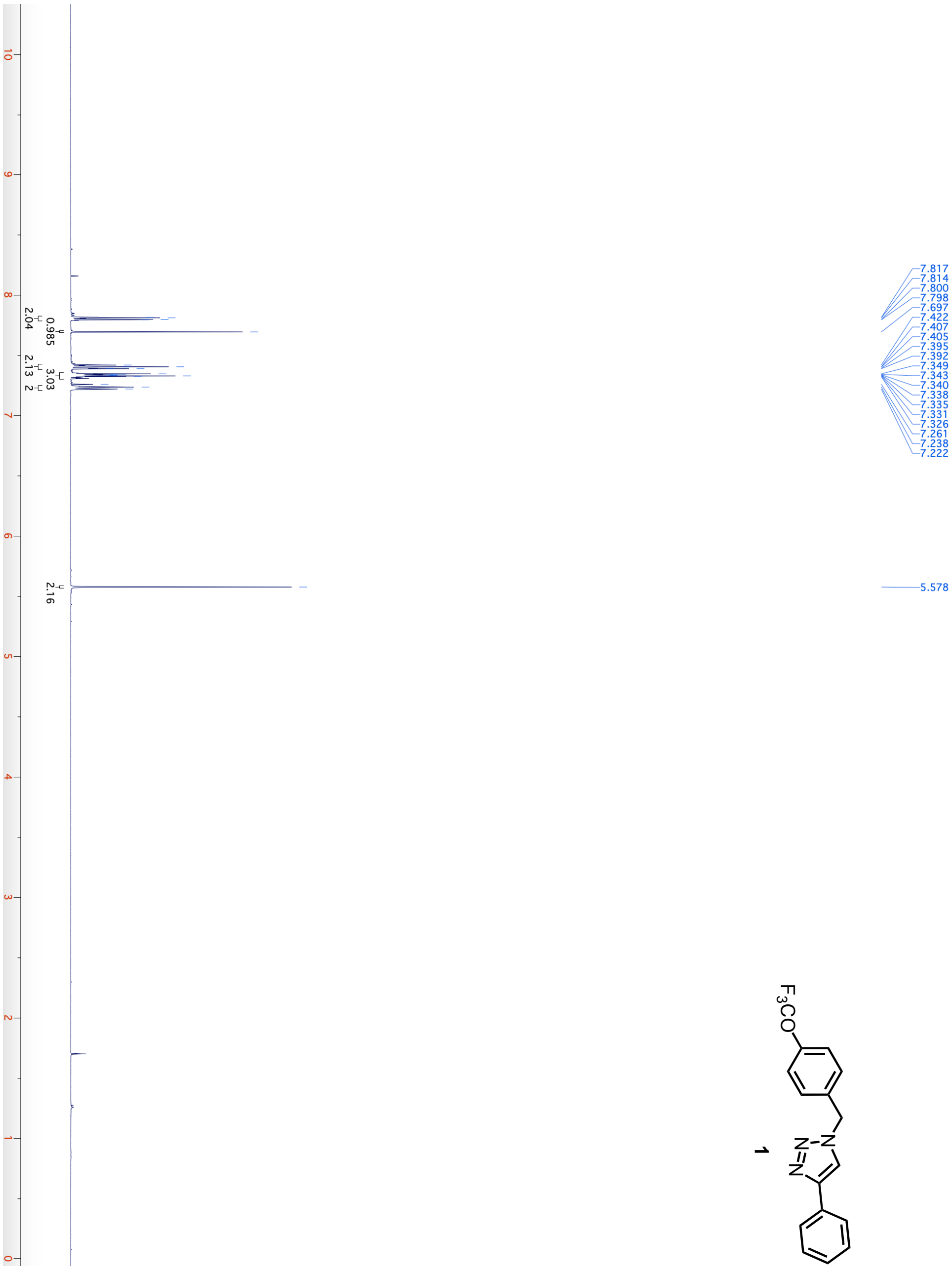
A. *M. smegmatis* mc^{2}155, B. *B. anthracis* Sterne F32, C. *S. enterica* ATCC 14028, D. *K. pneumoniae* ATCC 27736, E. *A. baumannii* ATCC 19606, F. *E. coli* MC1061, G. *P. aeruginosa* ATCC 27853, H. *E. cloacae* ATCC 13047, I. *S. epidermidis* ATCC 12228, J. *S. aureus* ATCC 25923. K. *C. albicans* ATCC 10231, L. *A. terreus* ATCC MYA-3633; AMP = ampicillin, KanA = Kanamycin A, AmB = amphotericin B, Flu = fluconazole

	MIC (μg/mL)					
Compound	*A. baumannii* ATCC 19606	*E. coli* MC1061	*S. aureus* ATCC	*S. epidermidis ATCC*	*M. smegmatis* mc^{2}155	*C. albicans* ATCC 10231
32	>64	>64	>64	>64	>64	>64
33	>64	>64	>64	>64	>64	>64
34	>64	>64	>64	>64	>64	>64
35	>64	>64	>64	>64	>64	>64
36	>64	>64	>64	>64	>64	>64
KanA	≤2	≤2	32	≤2	≤2	2 (AmB)

KanA = Kanamycin A, AmB = amphotericin B, Flu = fluconazole

Supplemental Information – NMR Data

NMR spectra were obtained using a JEOL 500 MHz spectrometer or a Bruker 500 MHz spectrometer. NMR spectra were processed using iNMR for Mac version 7.0.4 (https://www.inmr.net/index.html) or TopSpin version 3.6.3.



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7.407
7.405
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7.392
7.349
7.343
7.340
7.338
7.335
7.331
7.326
7.261
7.238
7.222
5.578
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2.13
3.03
2
2.16
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9
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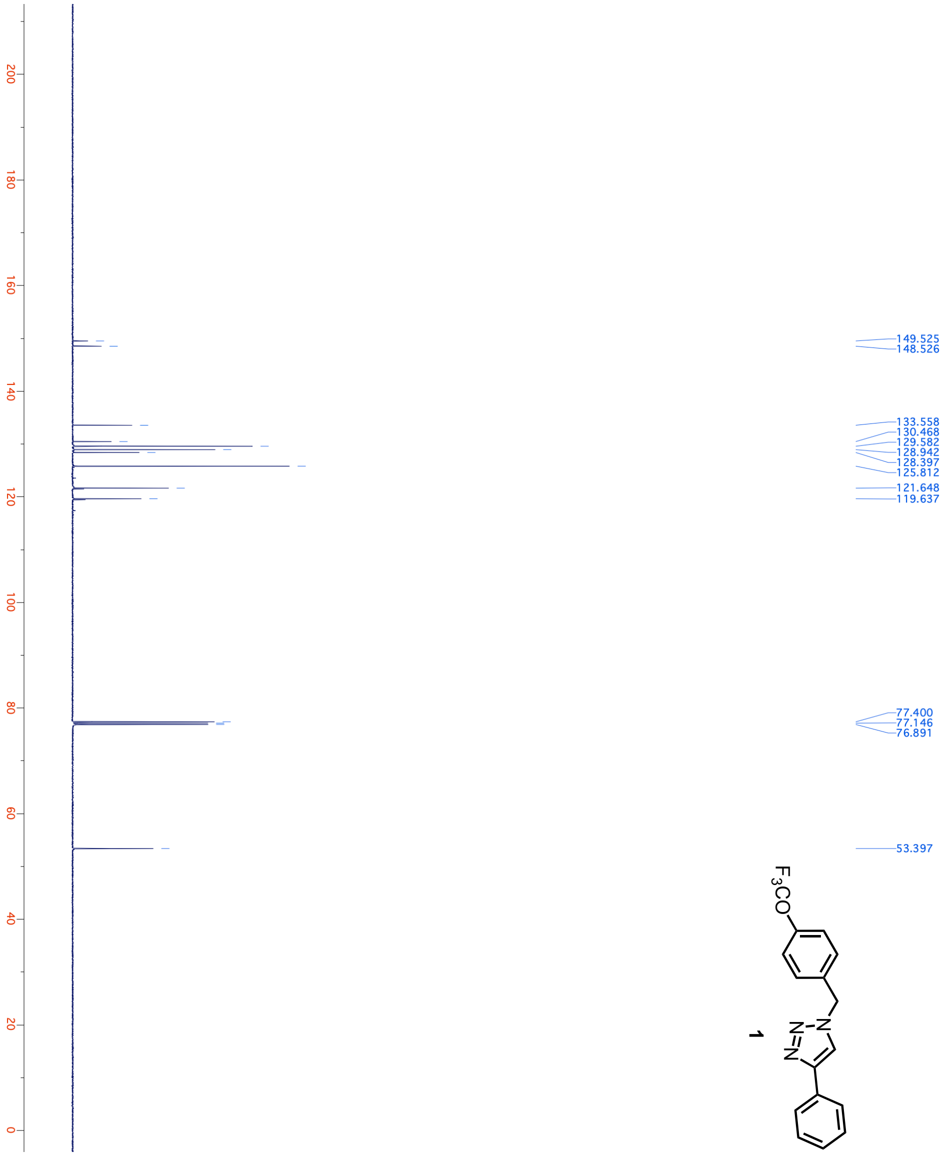
7
6
5
4
3
2
1
0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20
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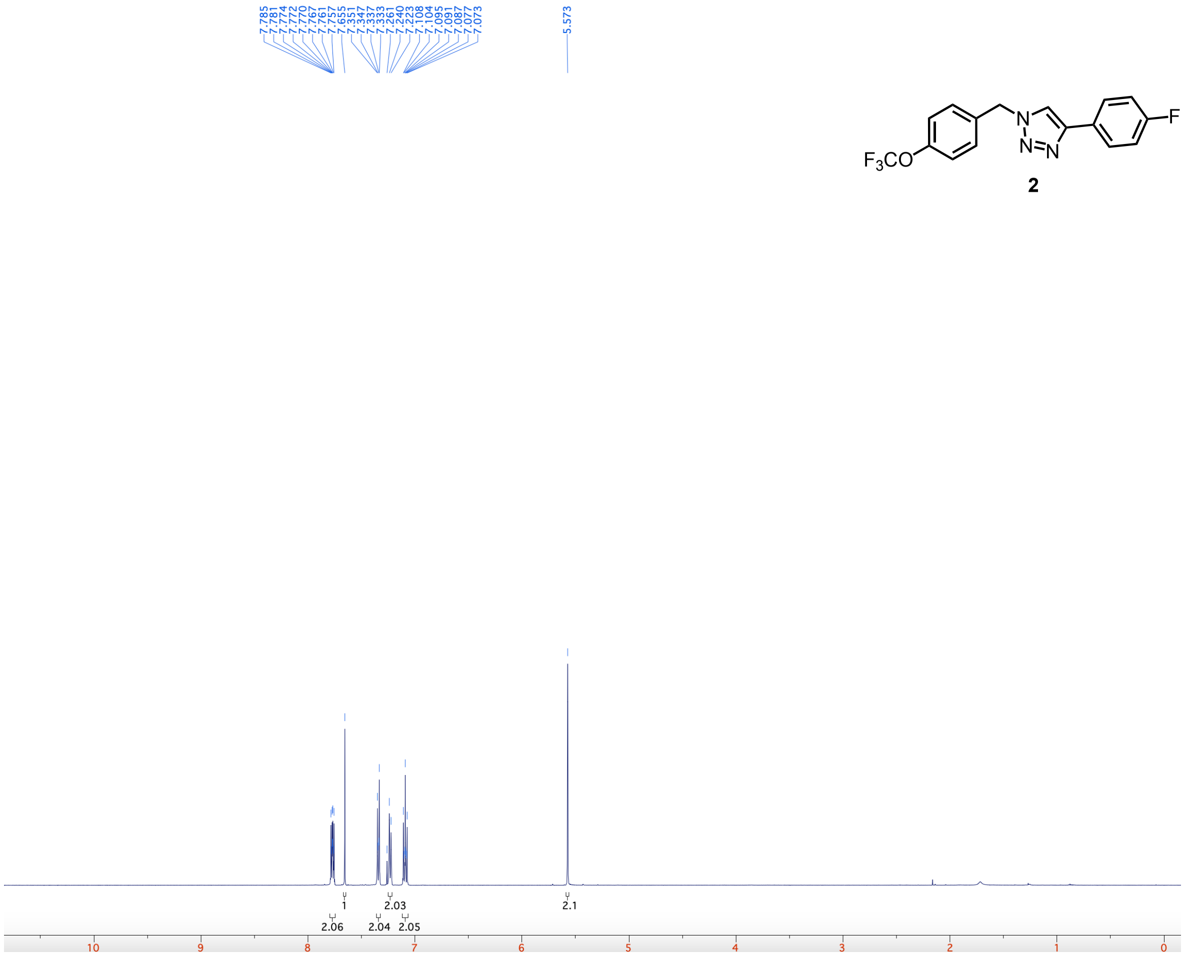
N
N

1



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7.223
7.108
7.104
7.095
7.091
7.087
7.077
7.073
5.573
F3CO
N
N
N
F
1
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2.05
2.1
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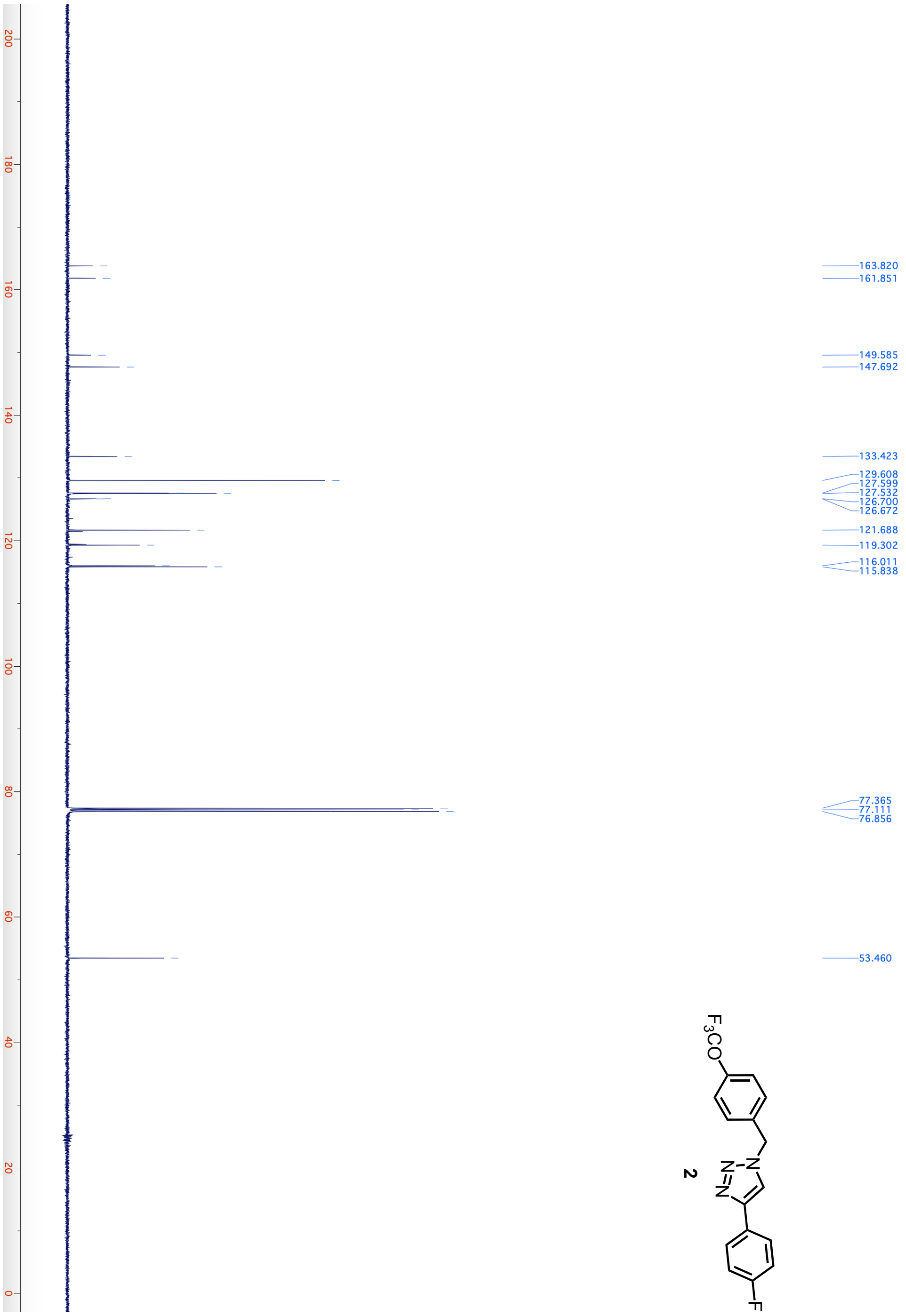
0

2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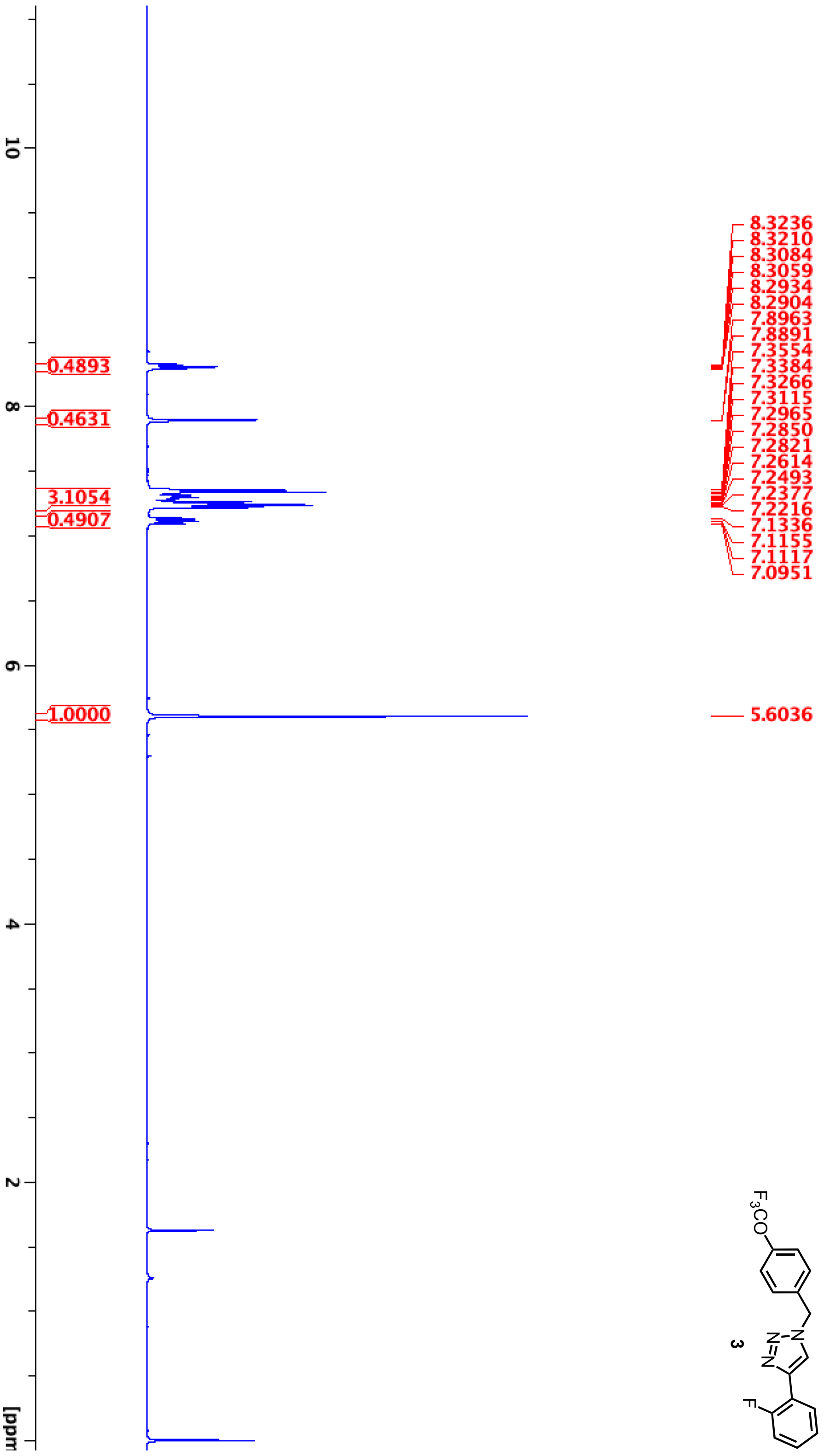
53.460
F3CO
N
N
N
F

2



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7.2377
7.2216
7.1336
7.1155
7.1117
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0.4893
0.4631
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1.0000
10
8
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4
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[ppm]
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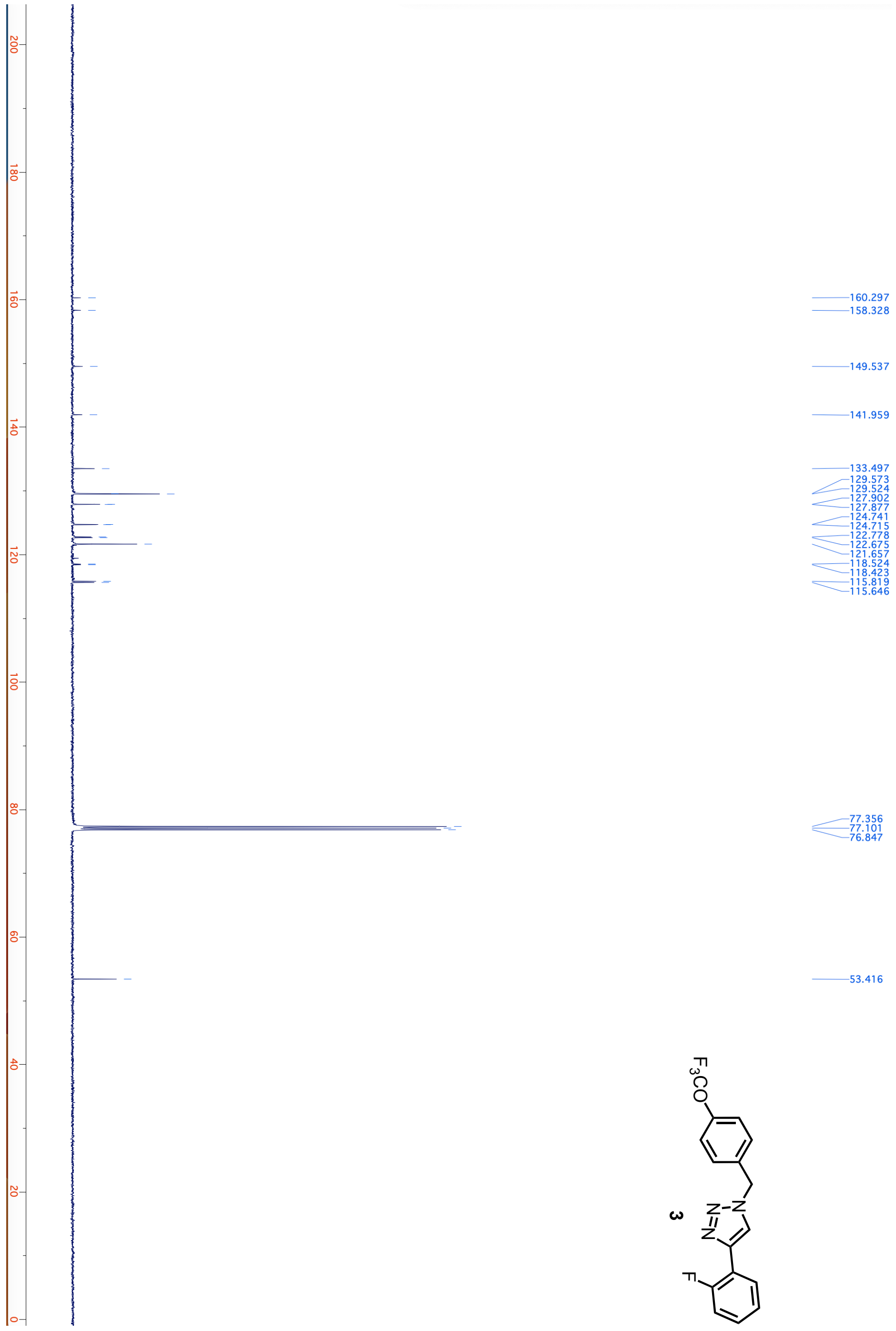
N
N=N
F

3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76.847
53.416
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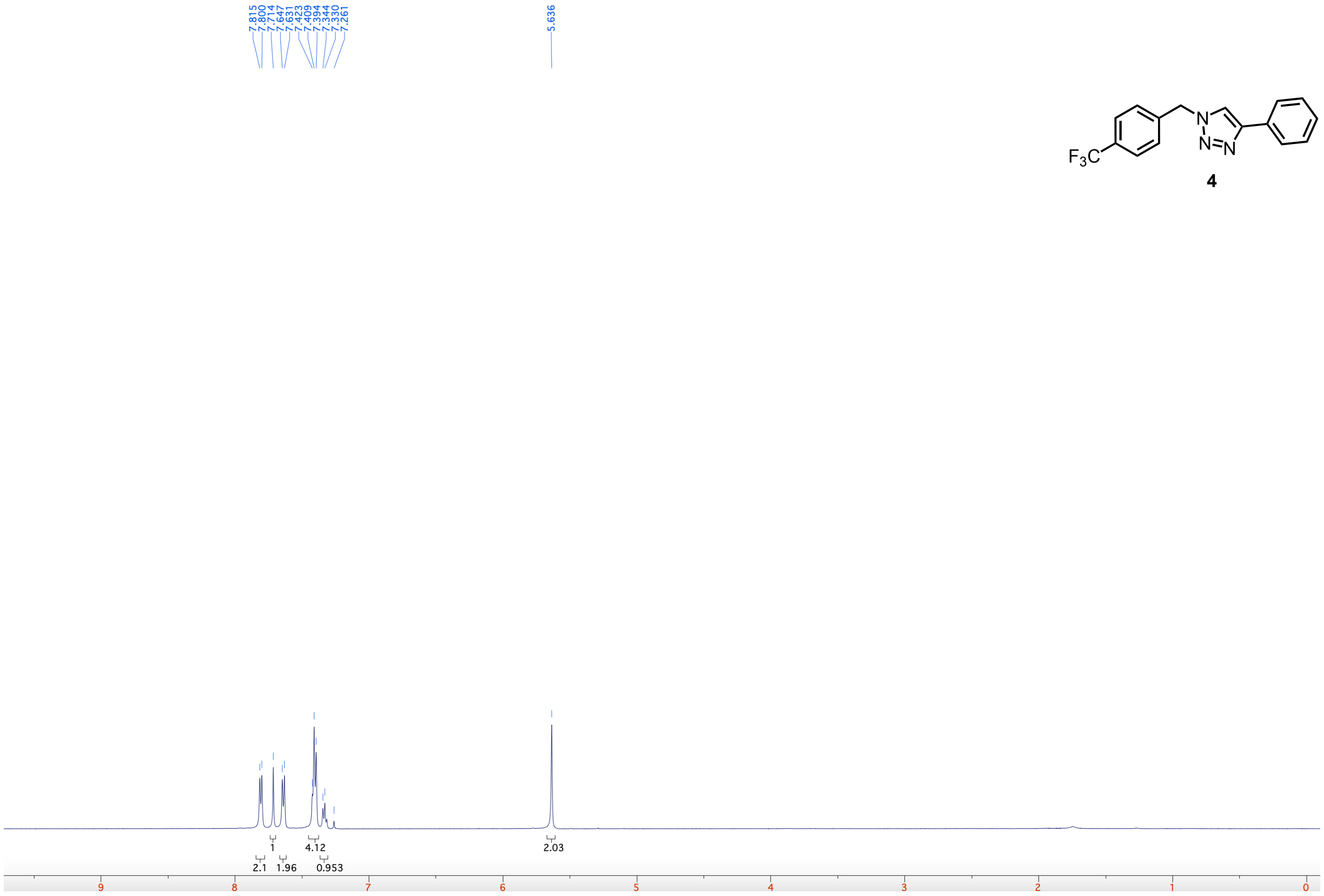
N
N
F

3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4
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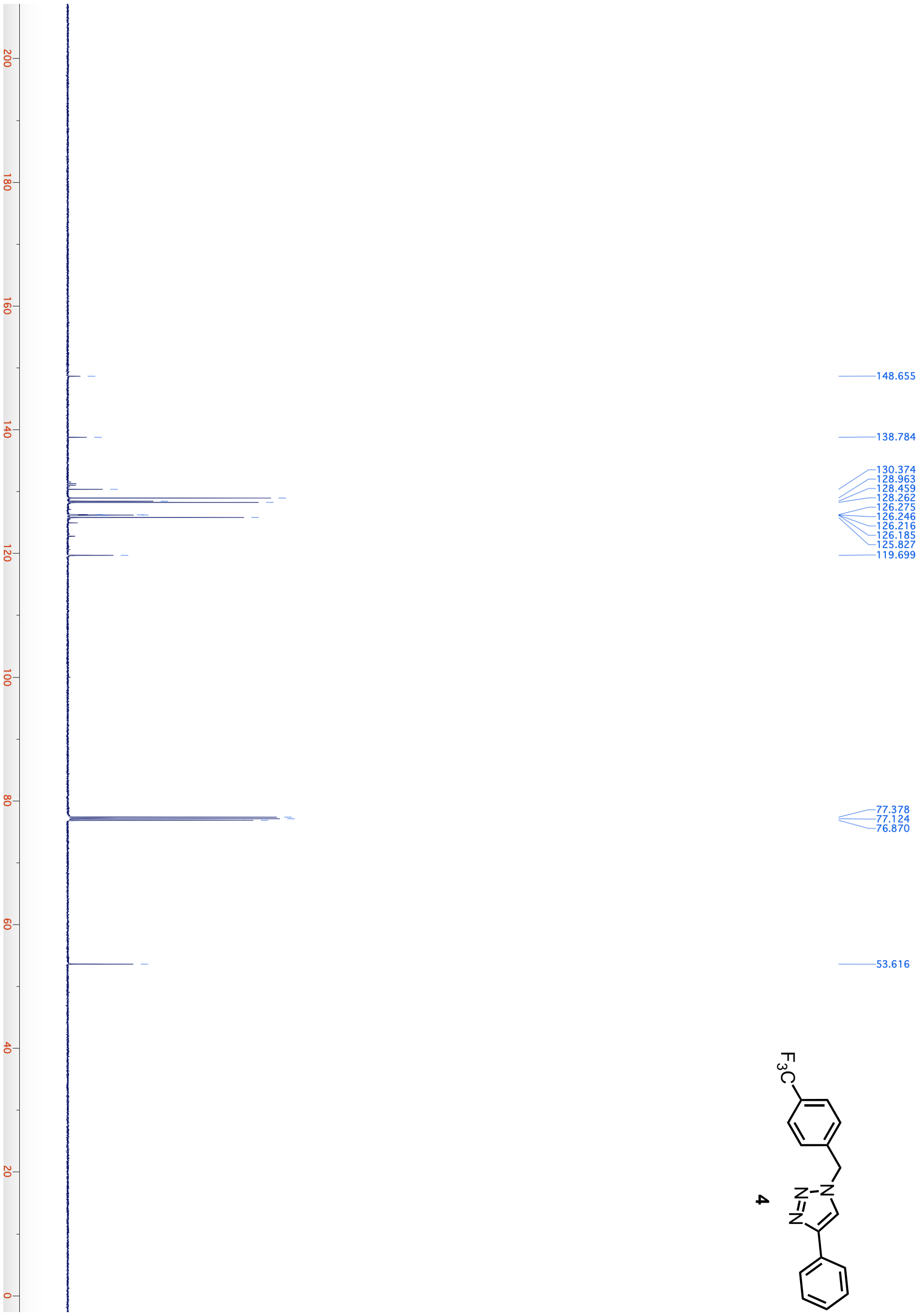
4



4

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F3C
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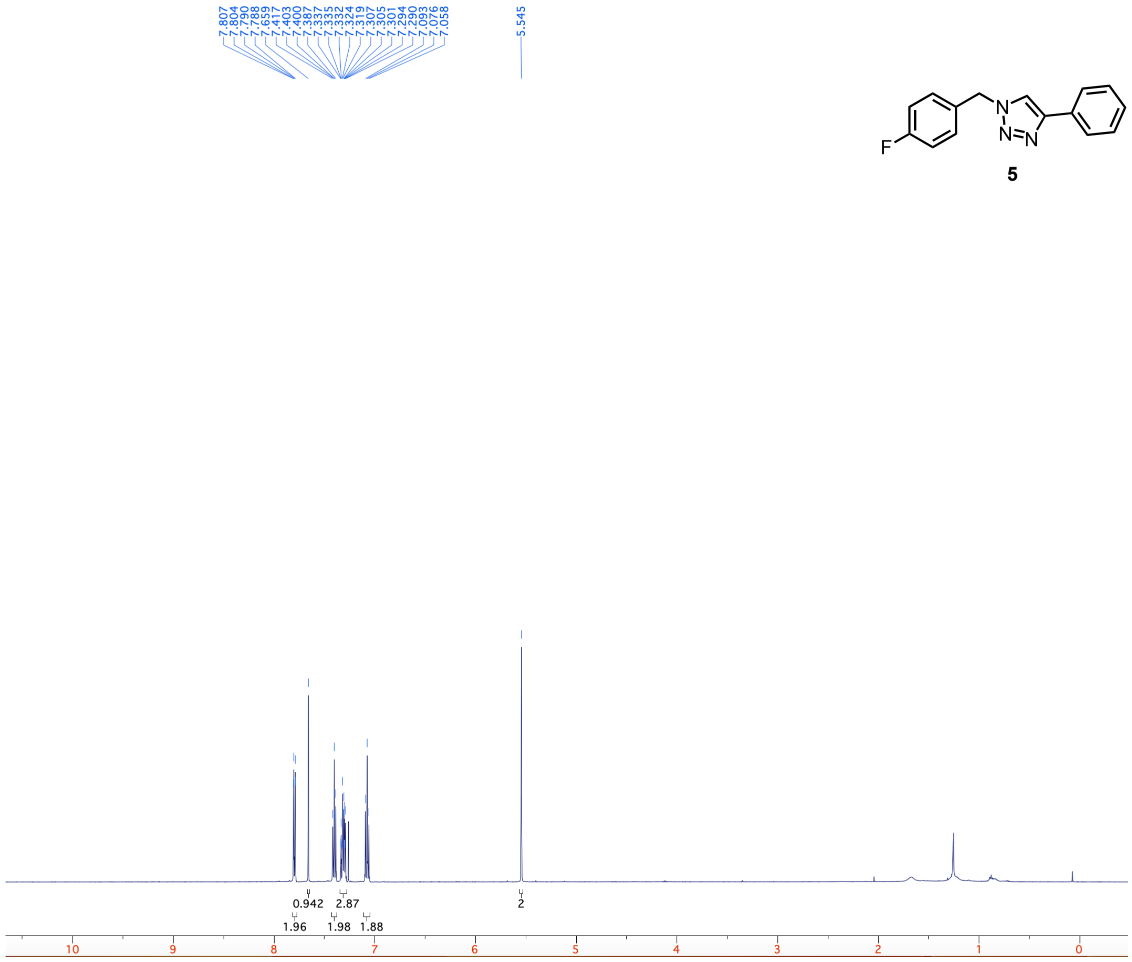
N
N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7.058
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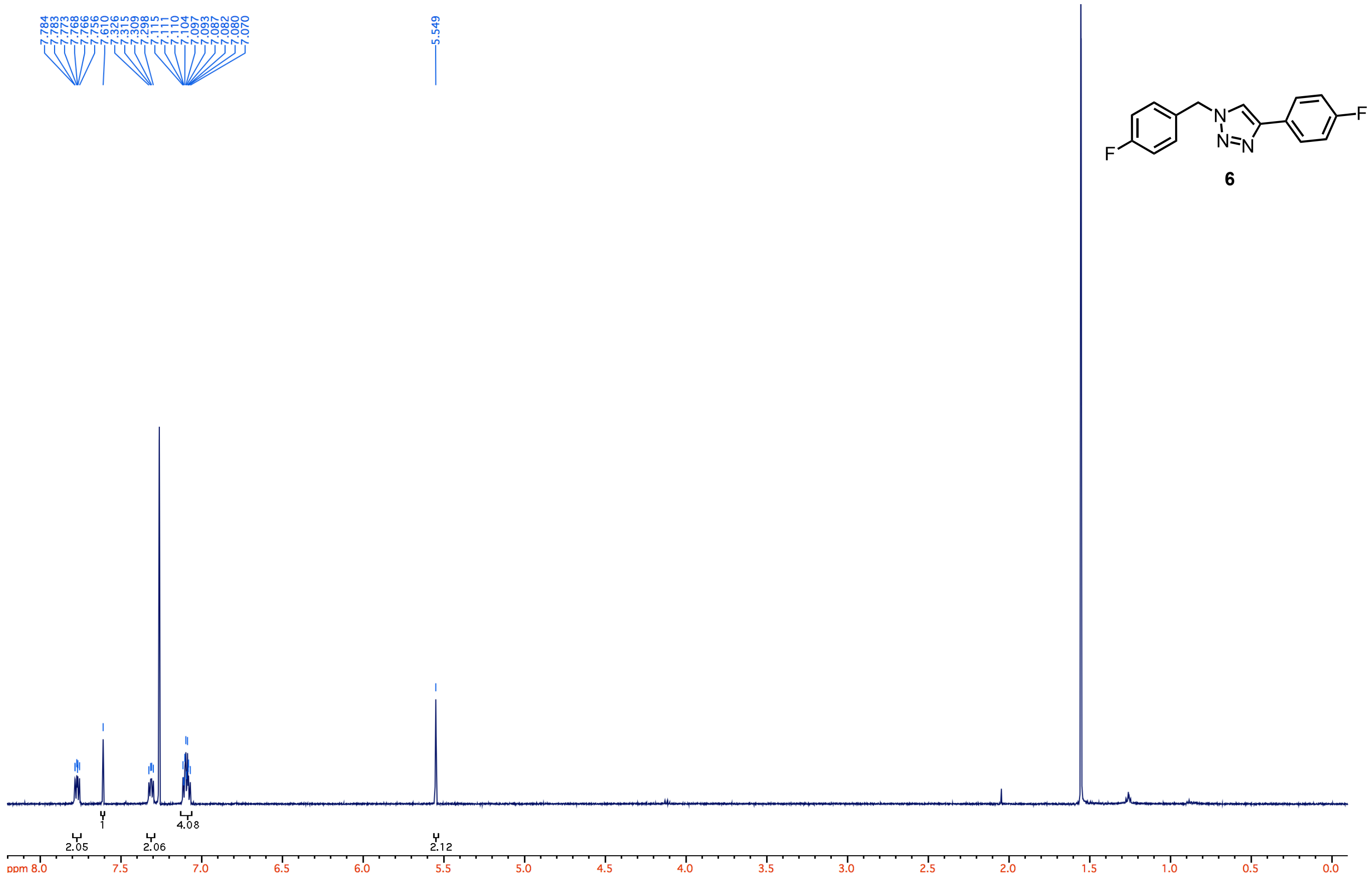
5



6

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7.093
7.087
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7.080
7.070
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2.06
4.08
2.12
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6.5
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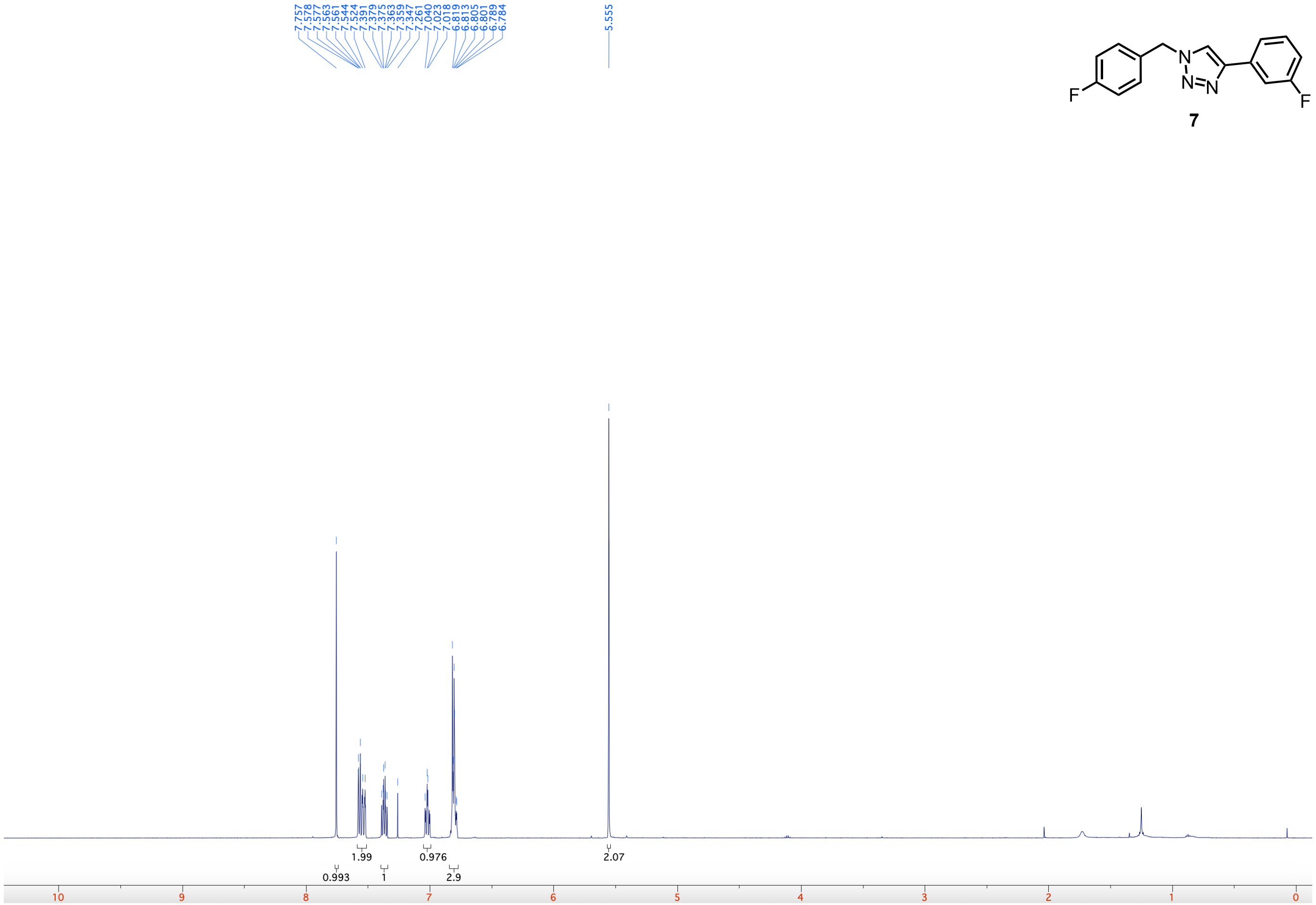
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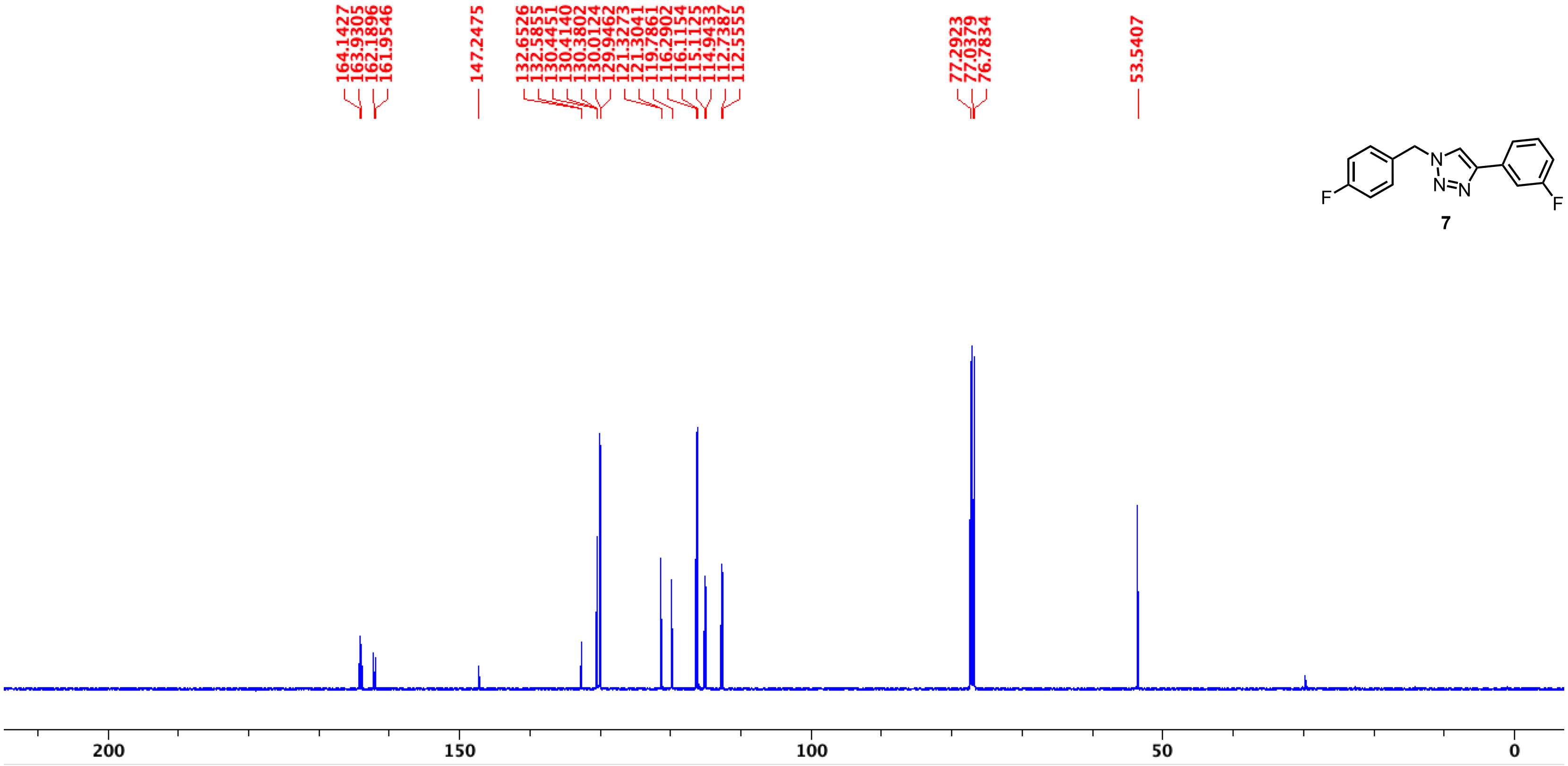
F

7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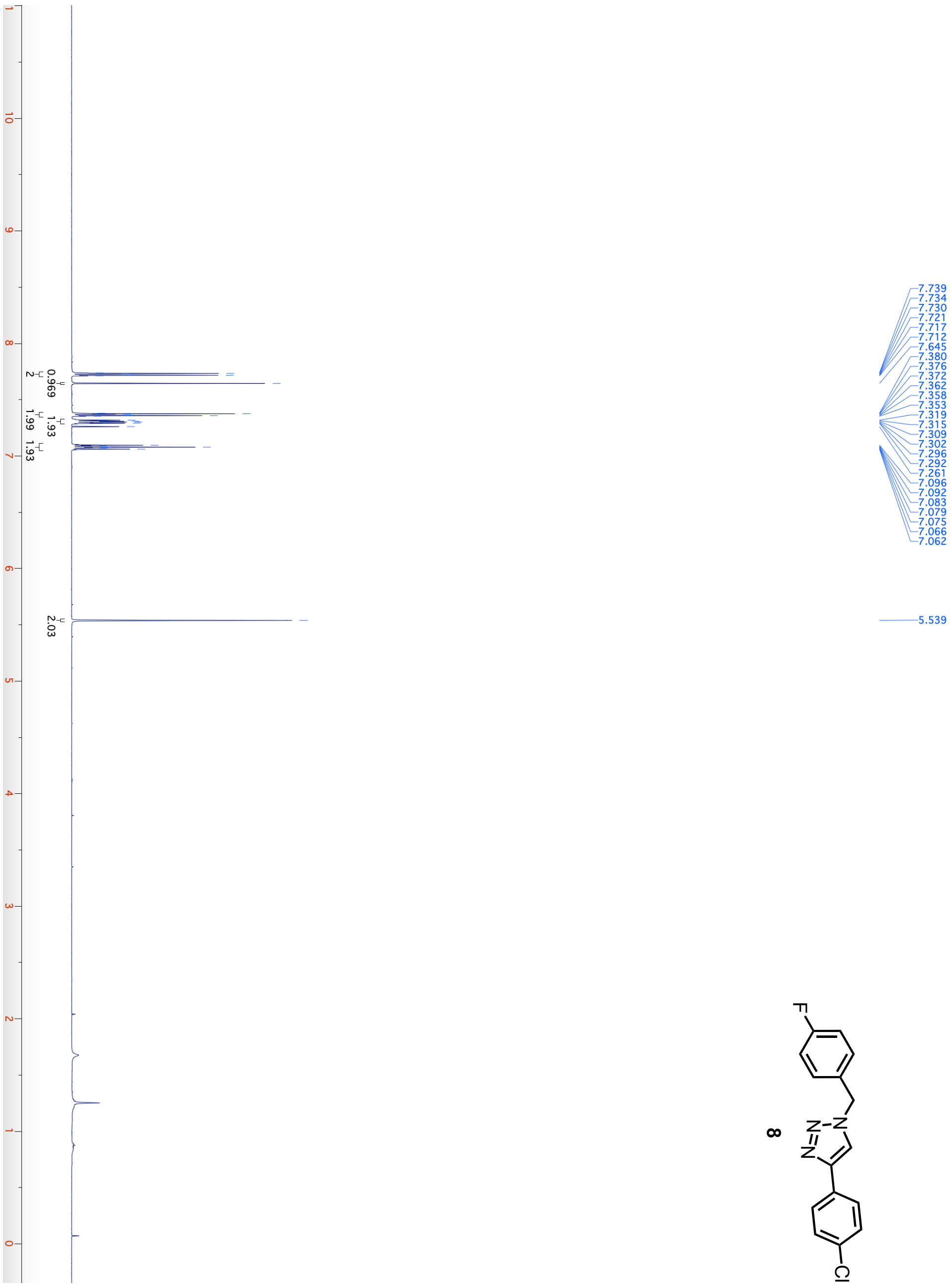
7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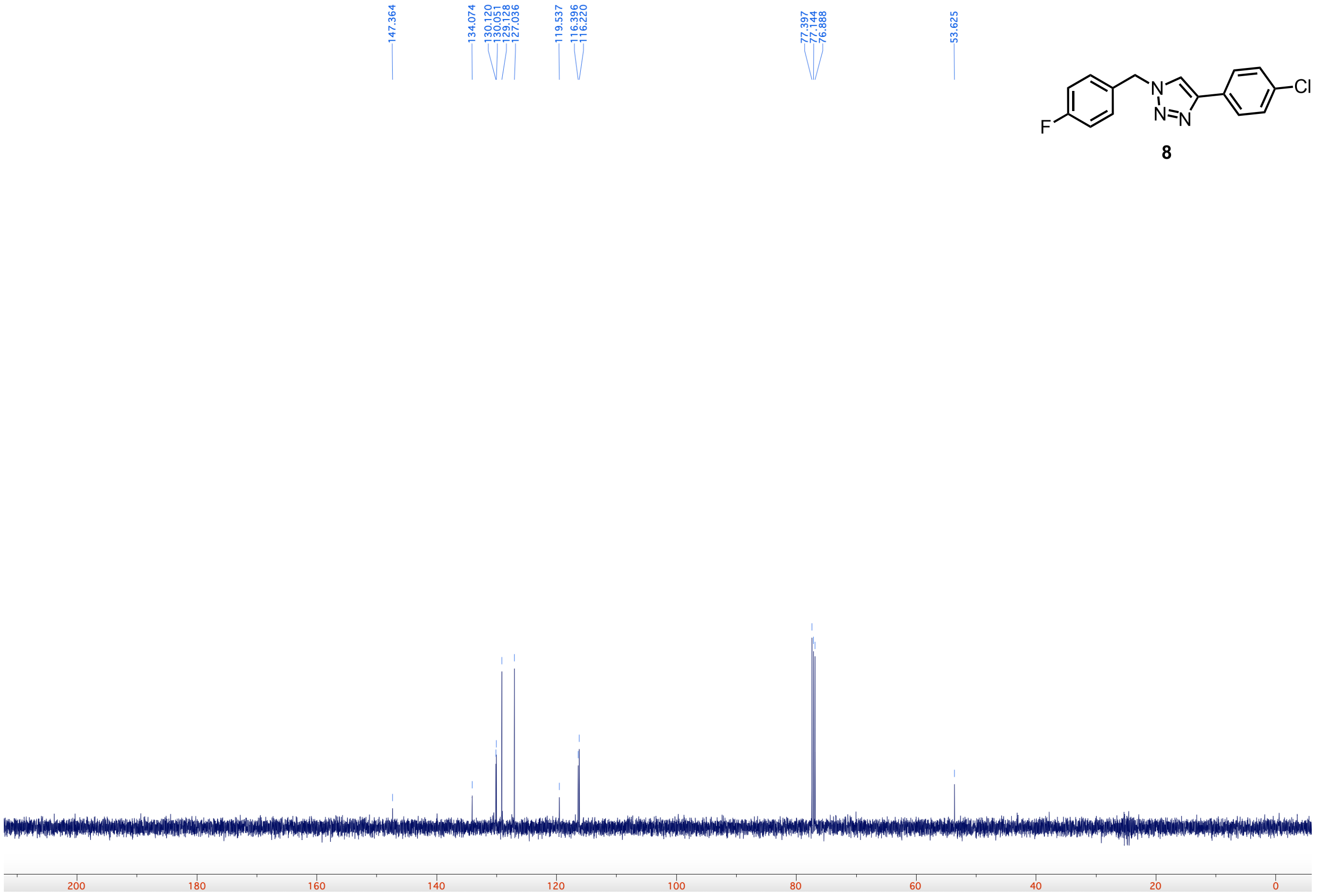

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Cl

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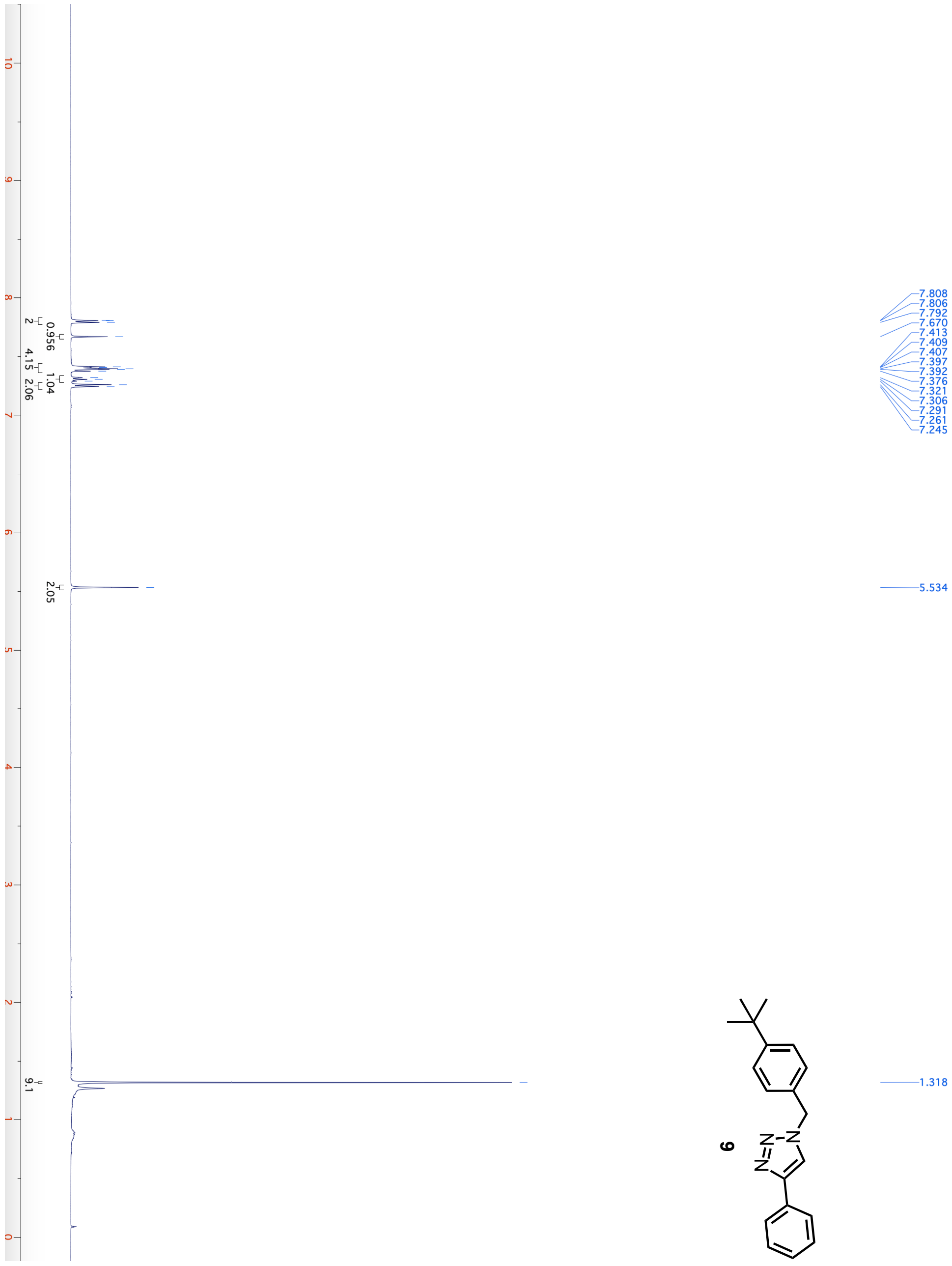

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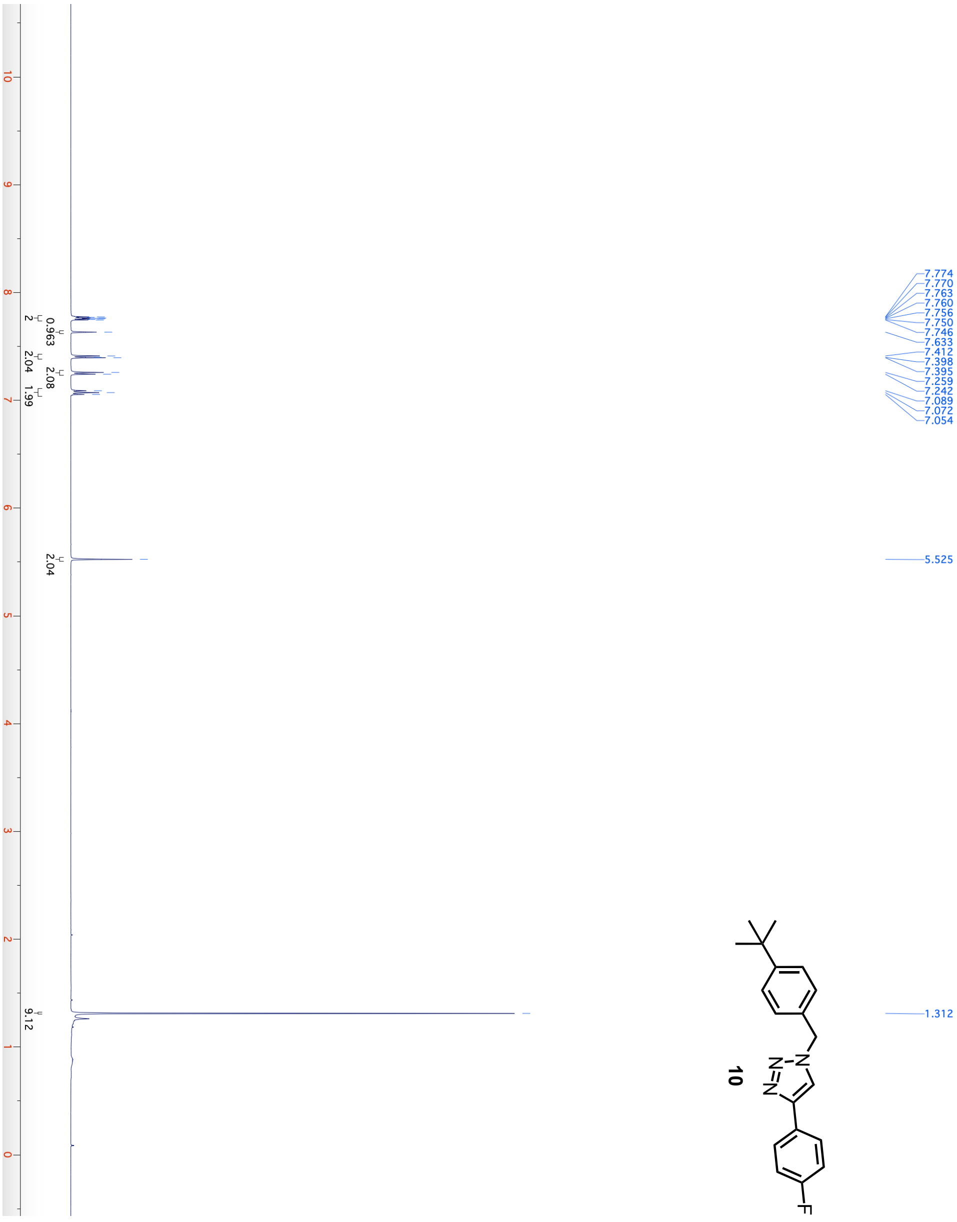
9



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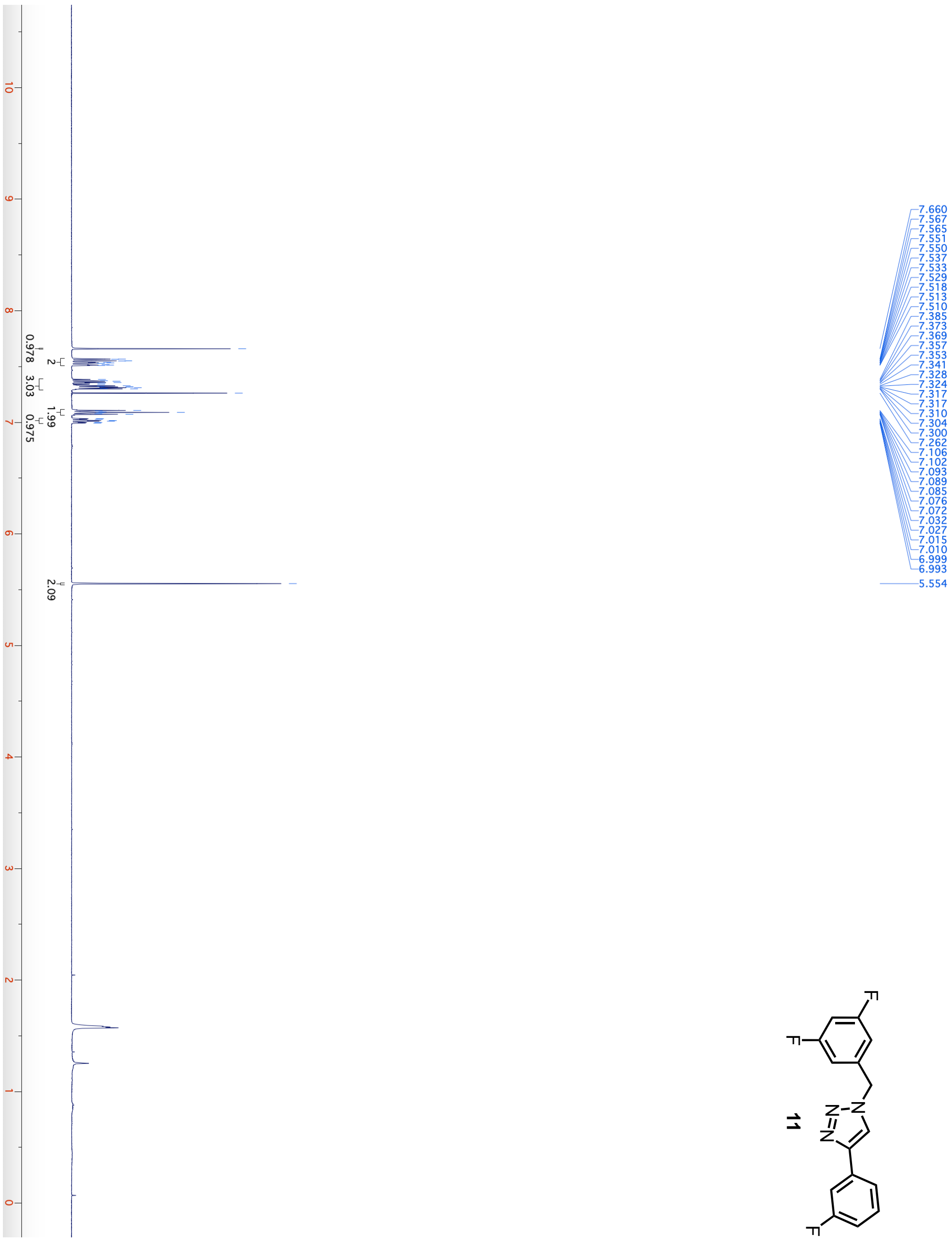
10



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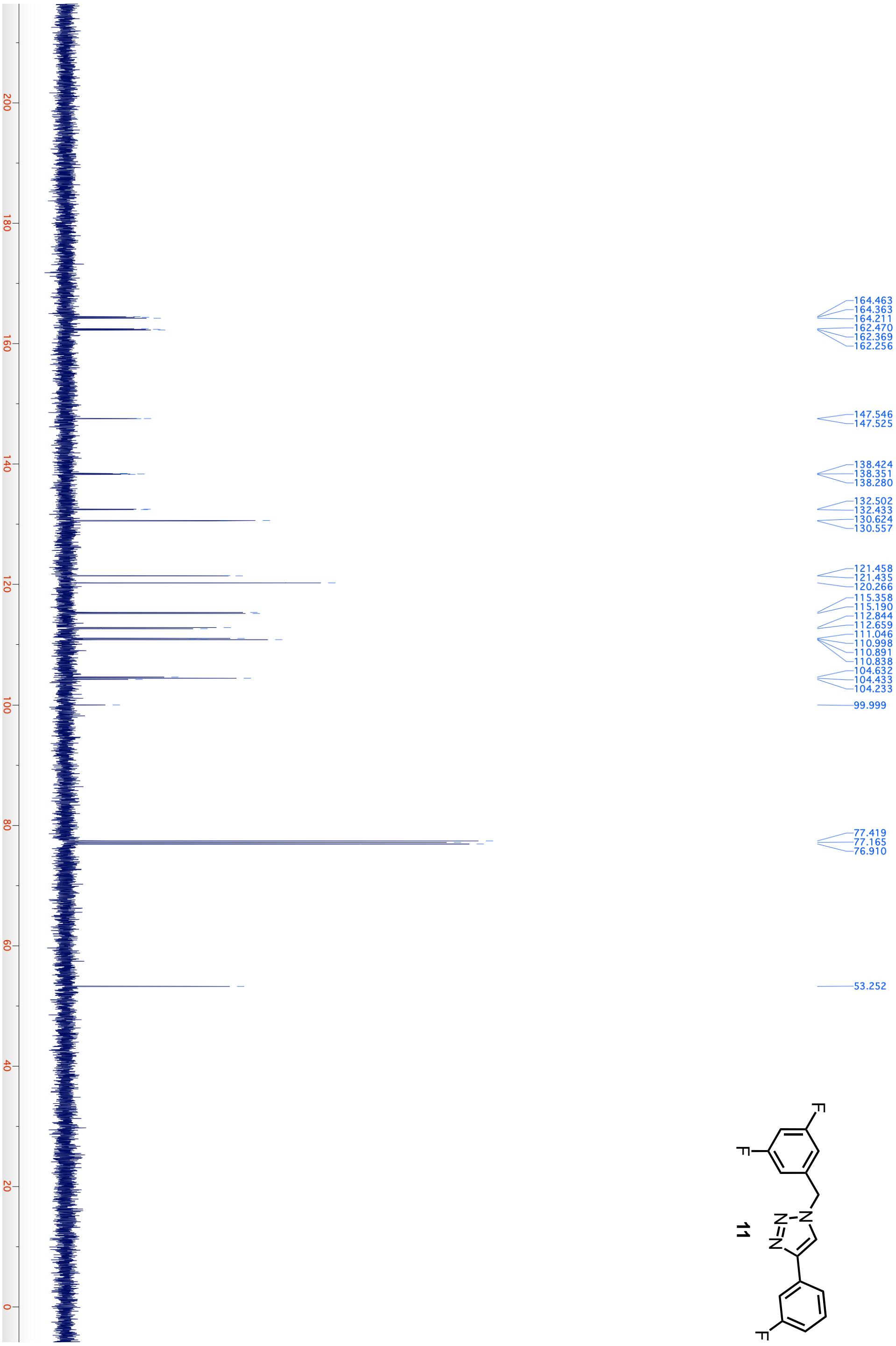
11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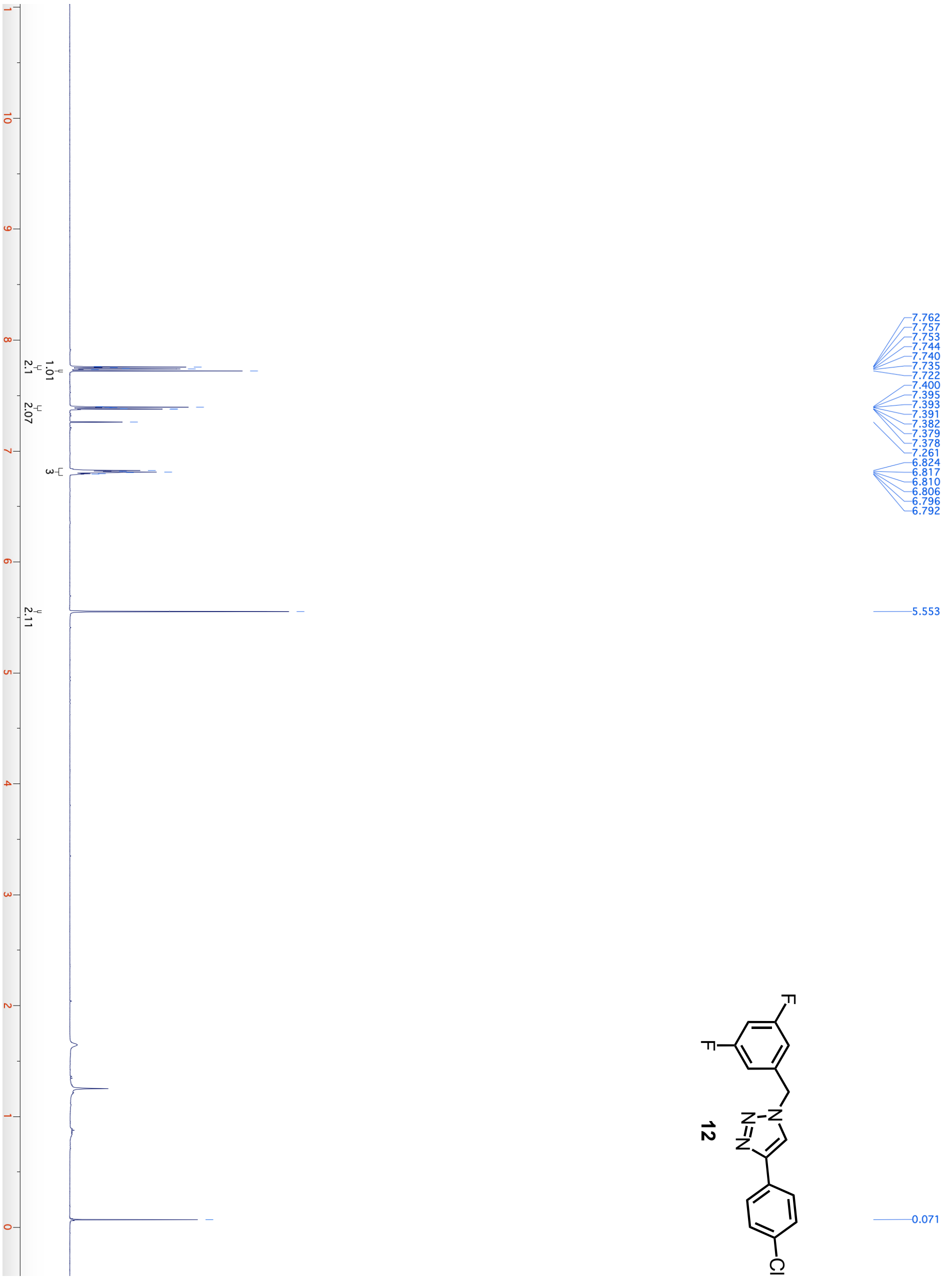
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7.261
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2.1
2.07
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2.11
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8
7
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N
N
N
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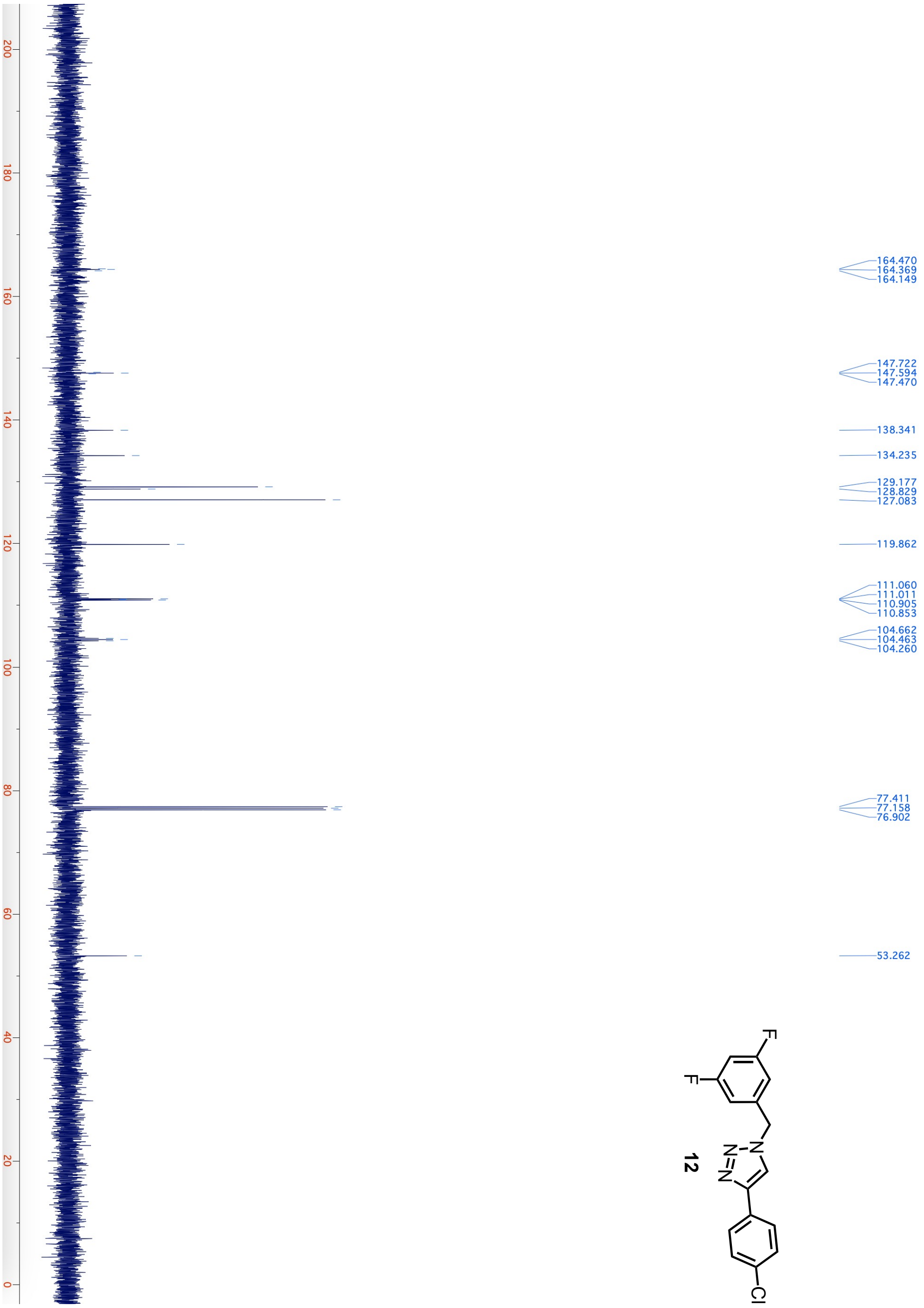
12



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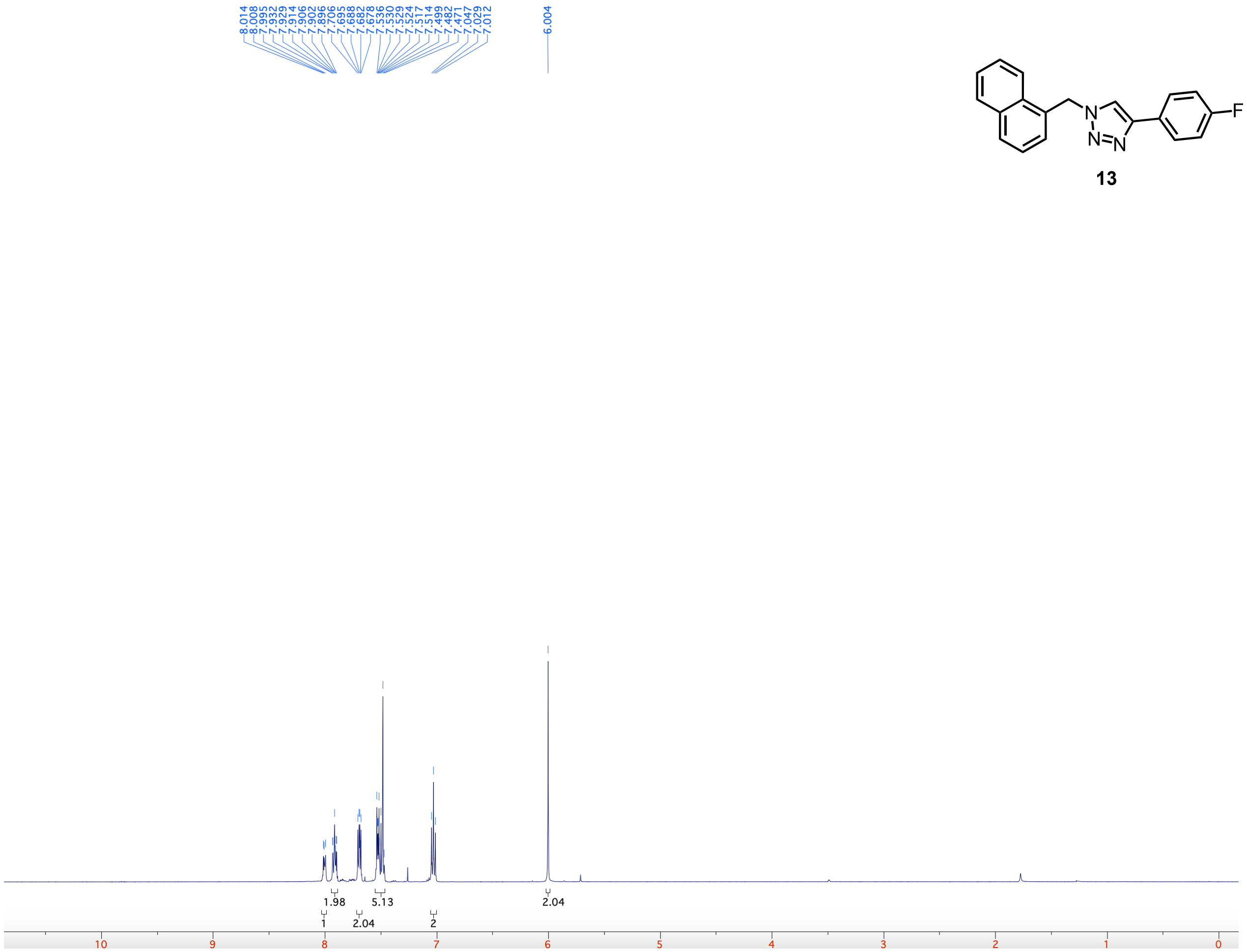
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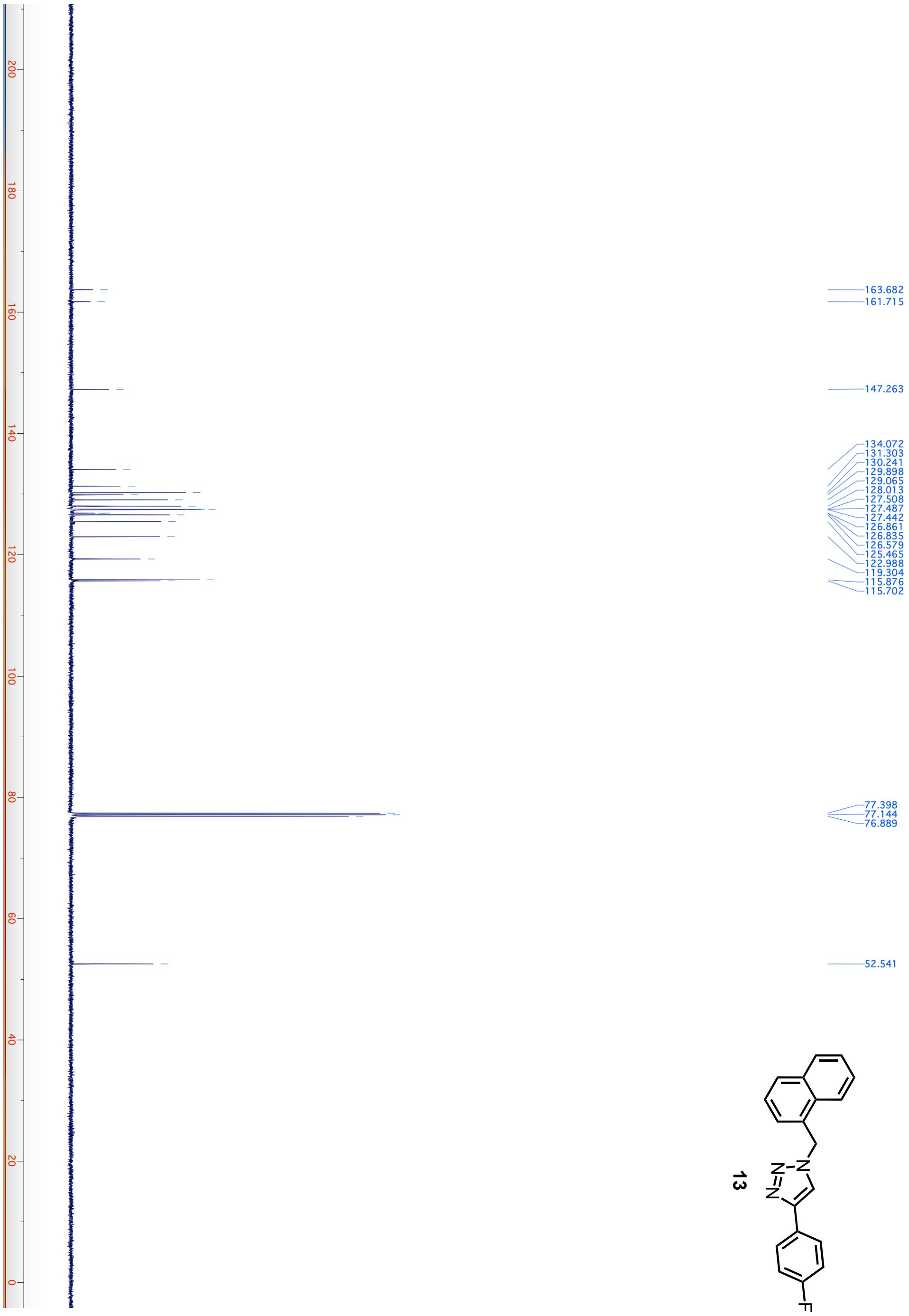
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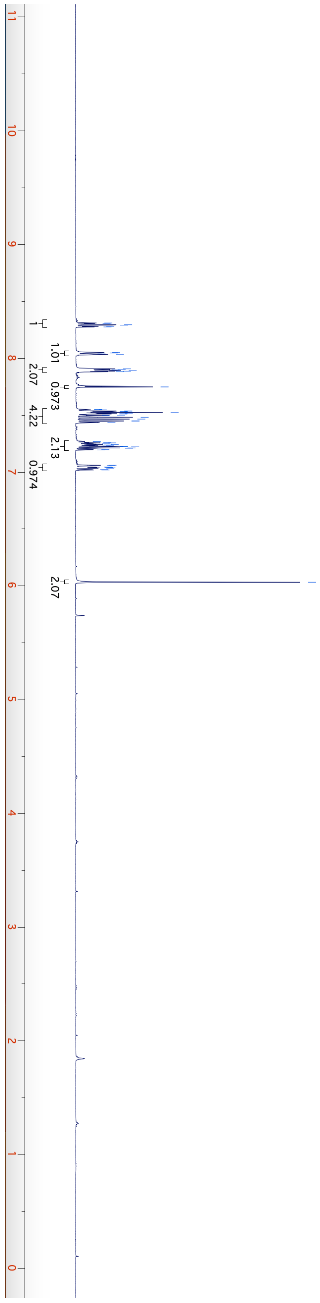
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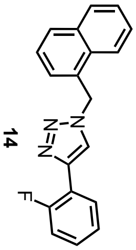
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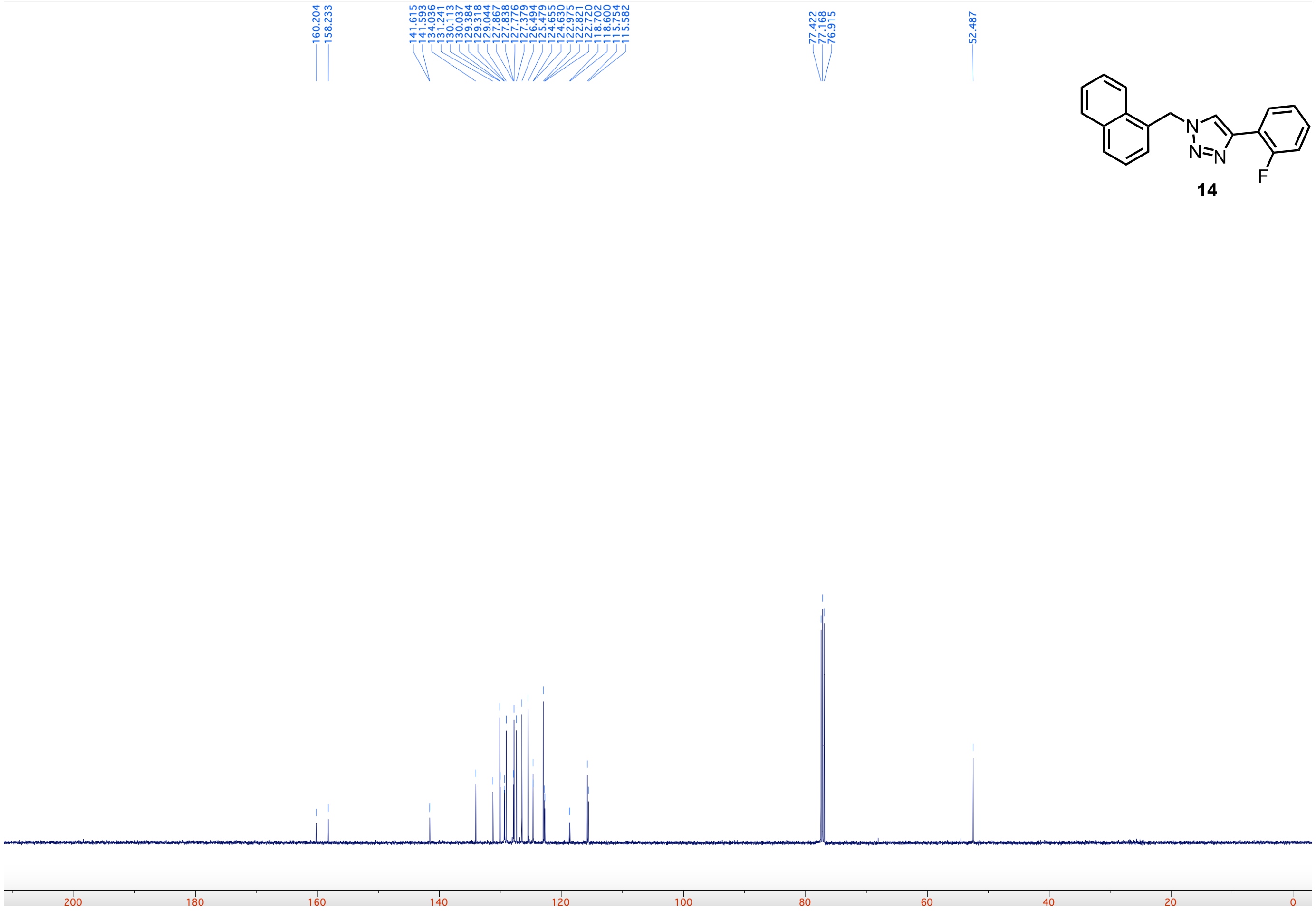
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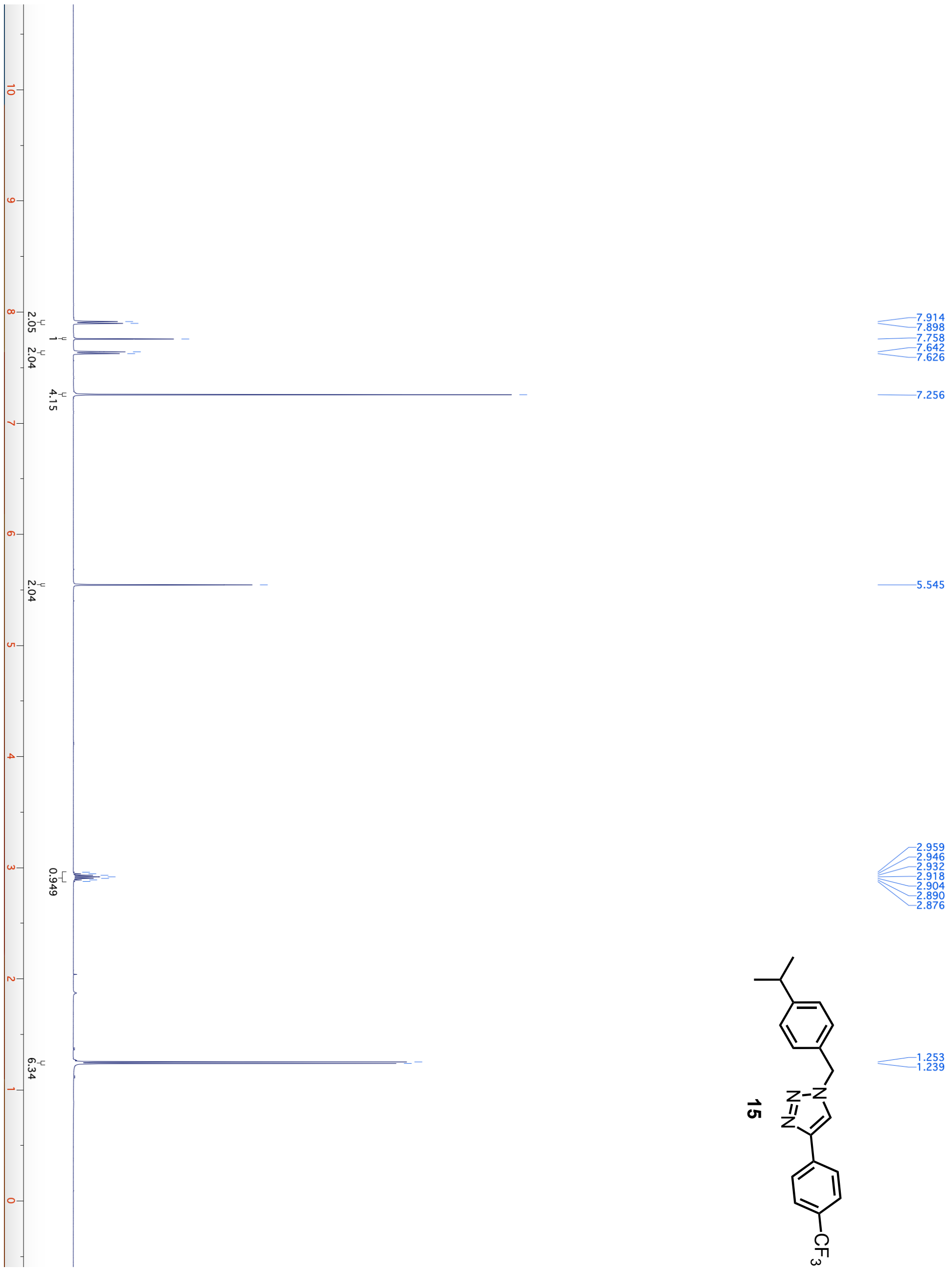

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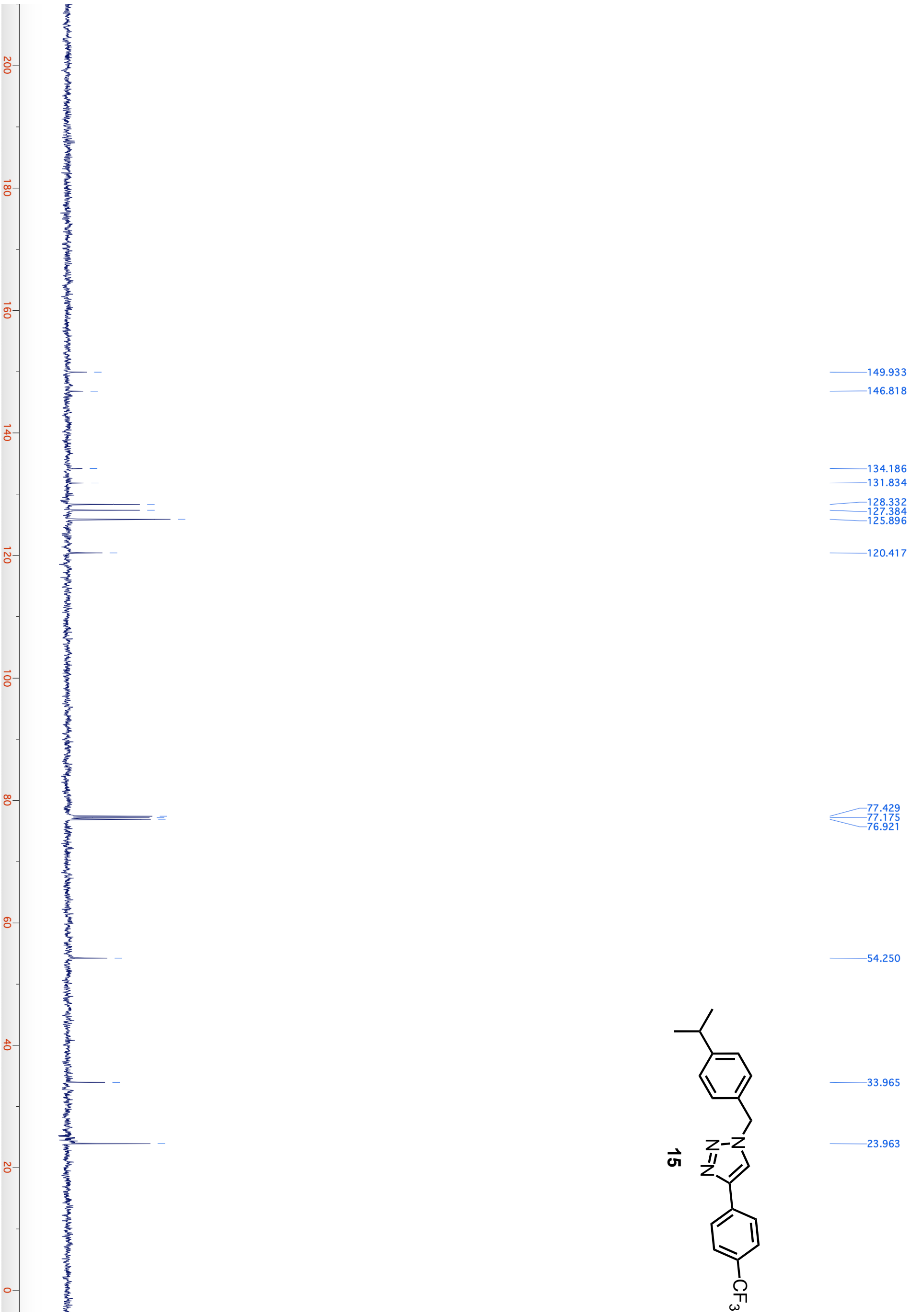
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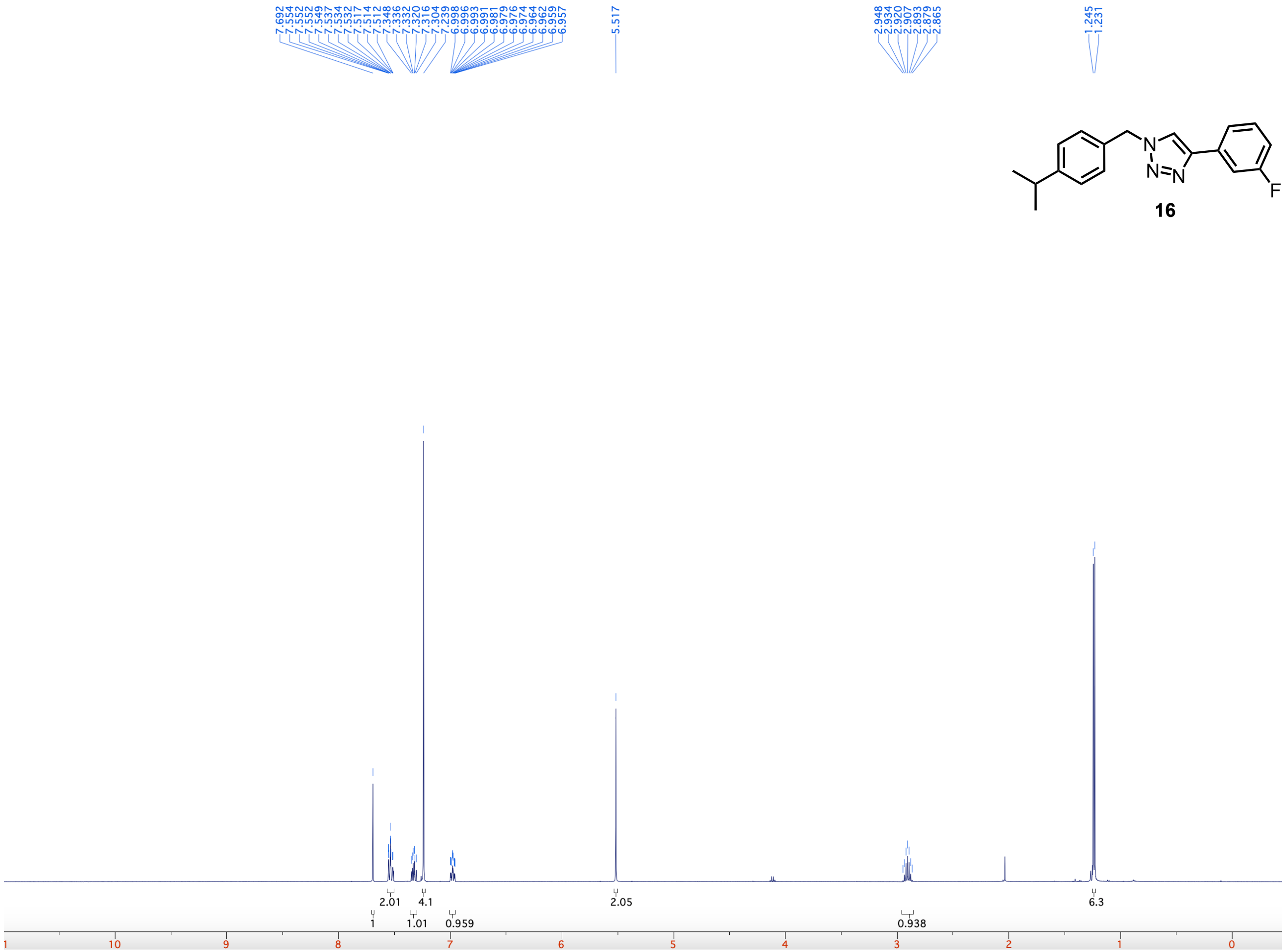

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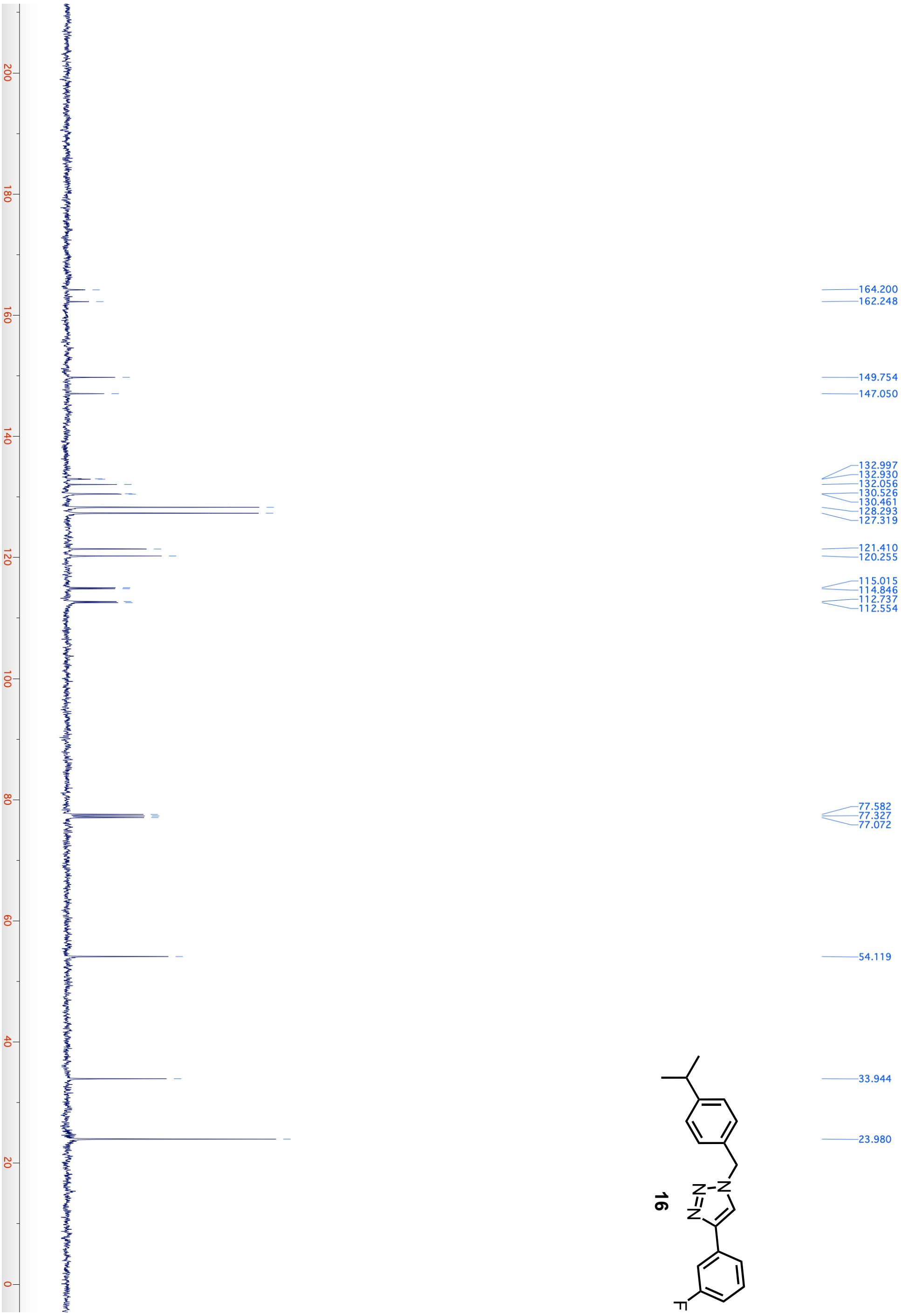
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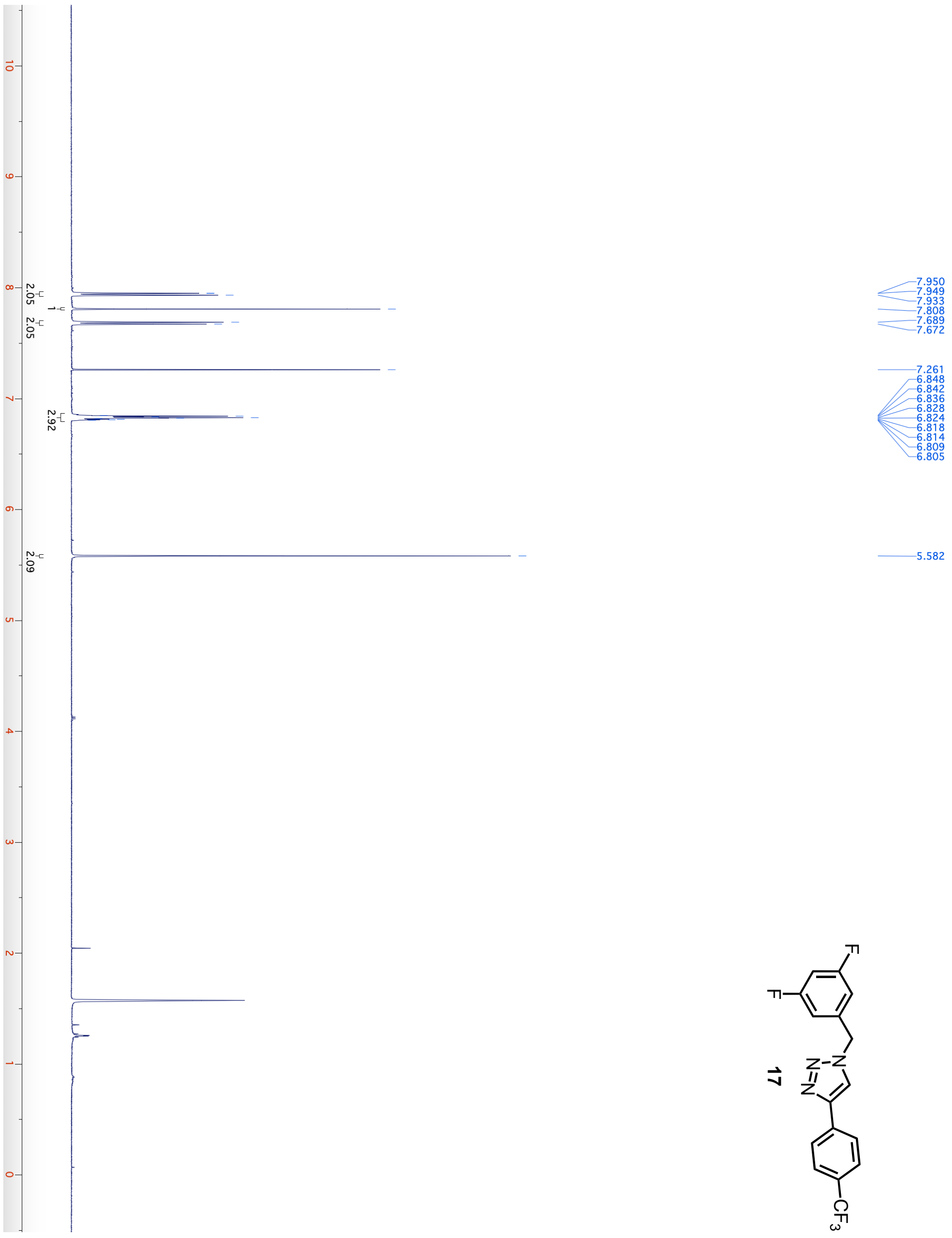
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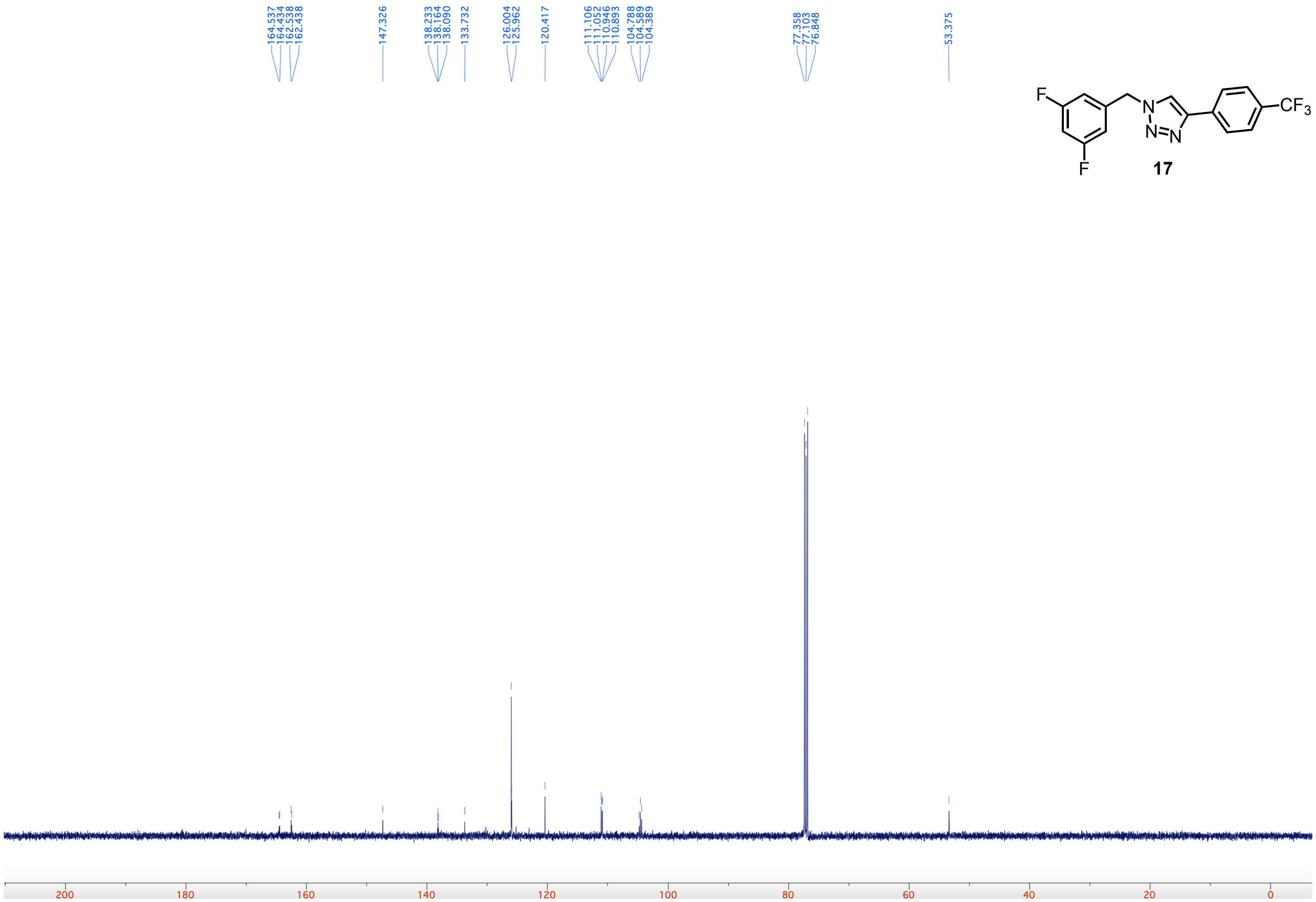
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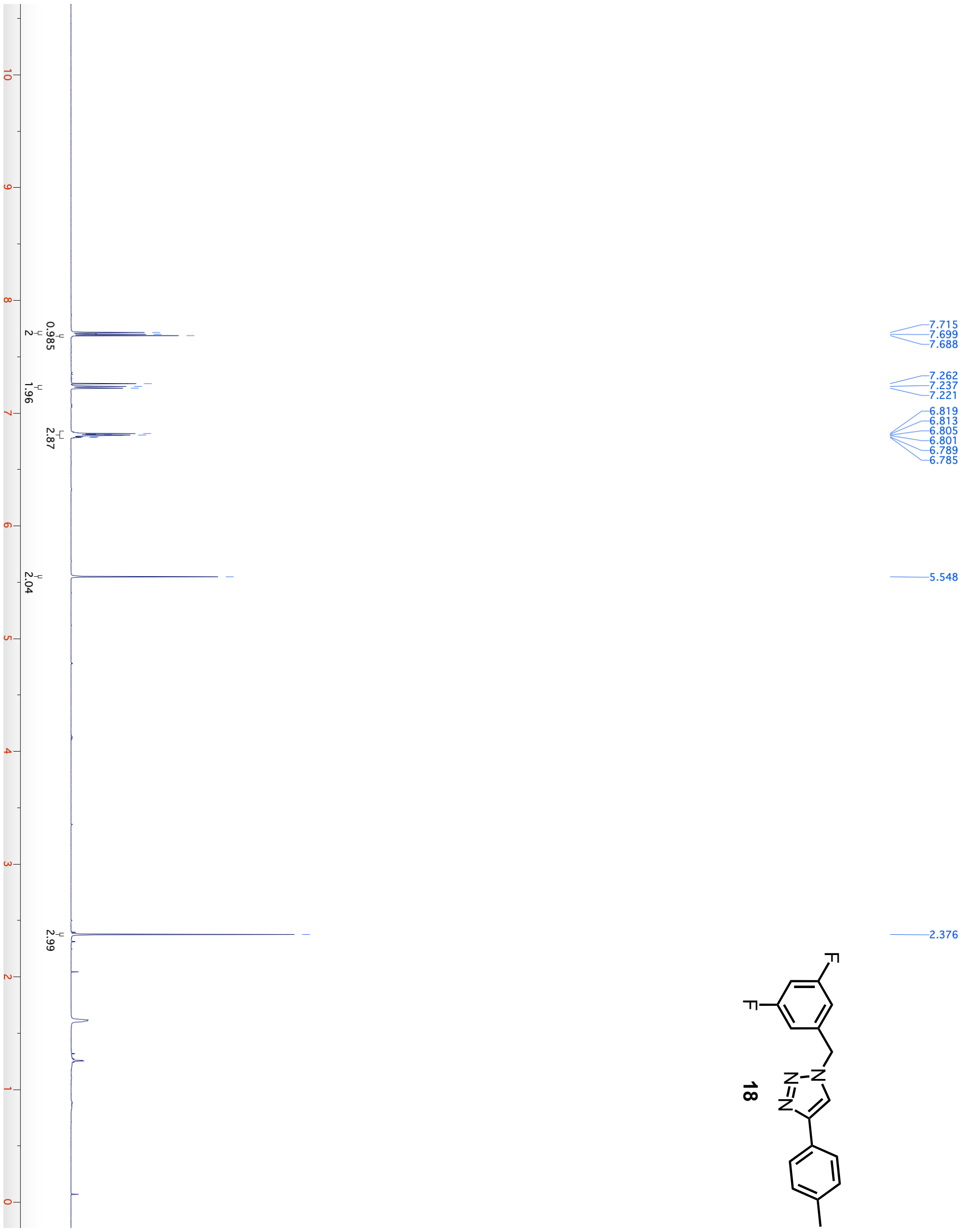

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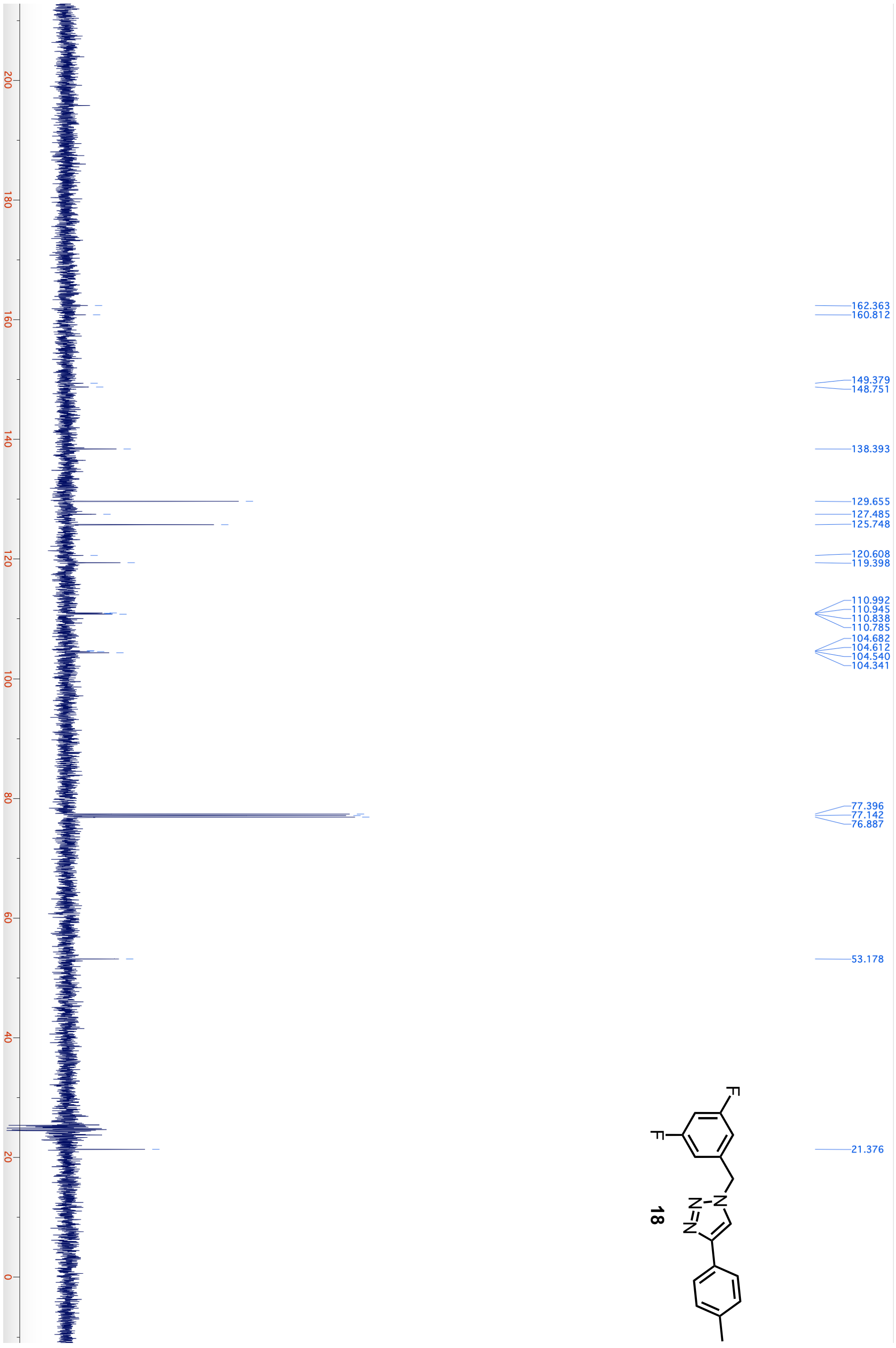
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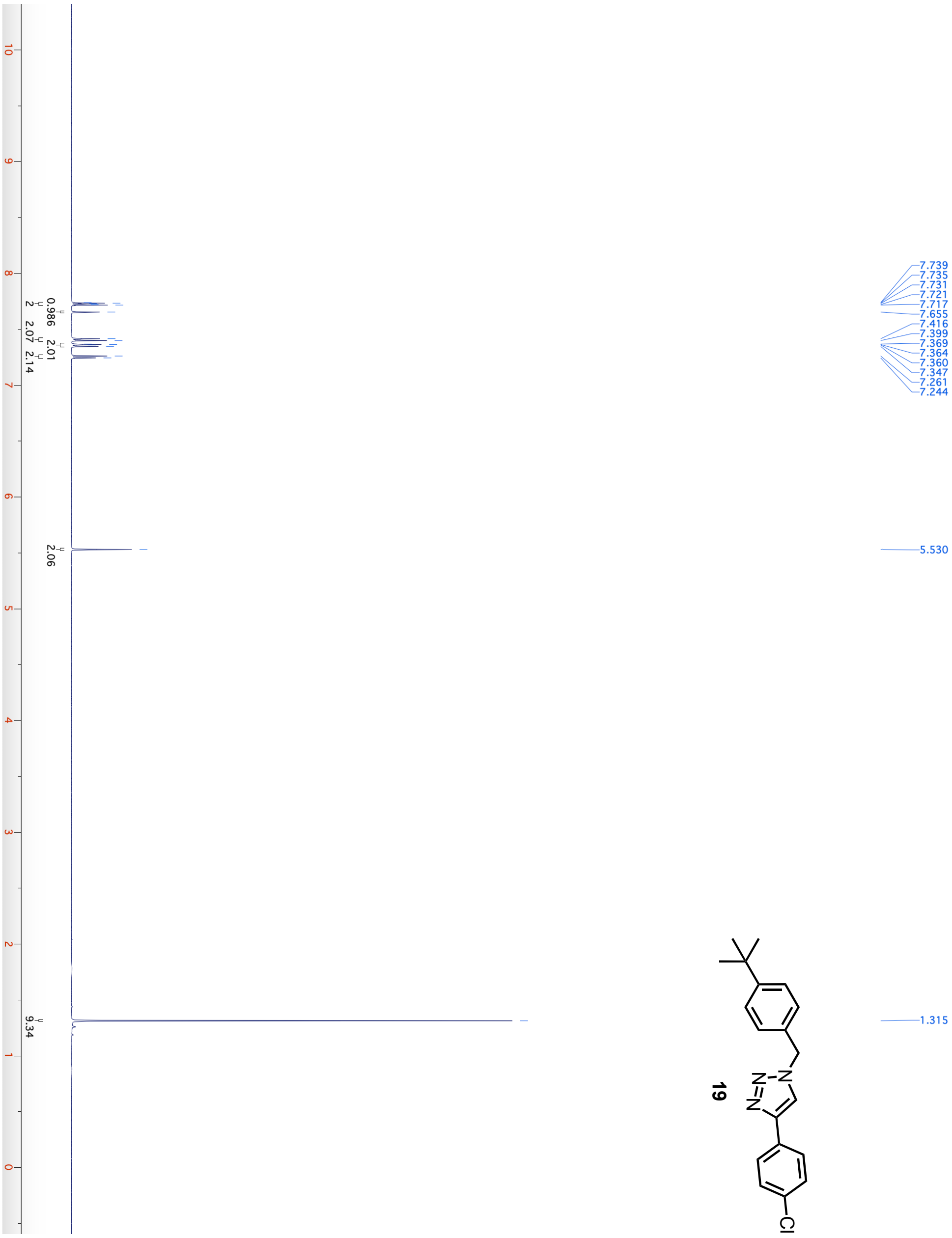7.739
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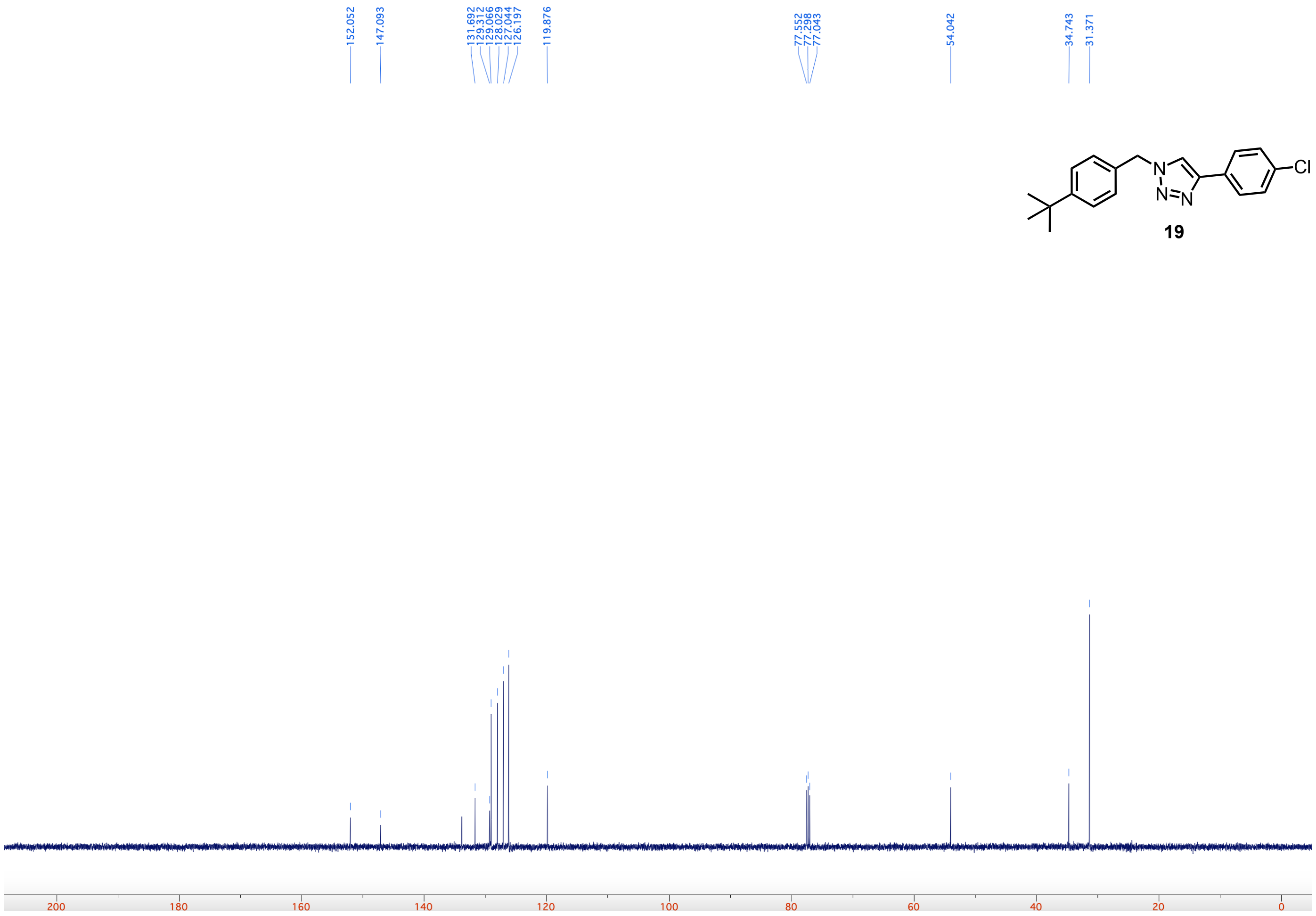
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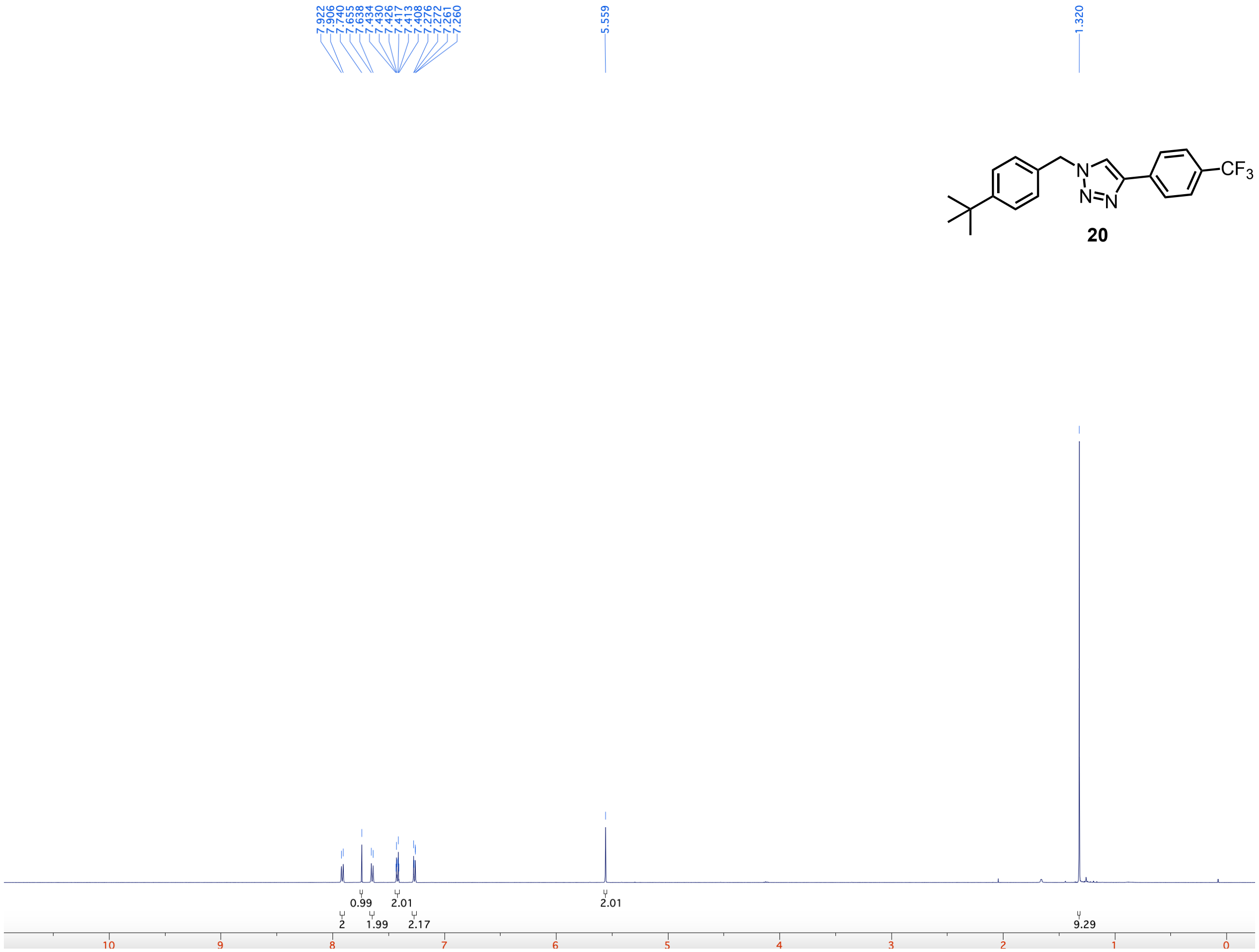
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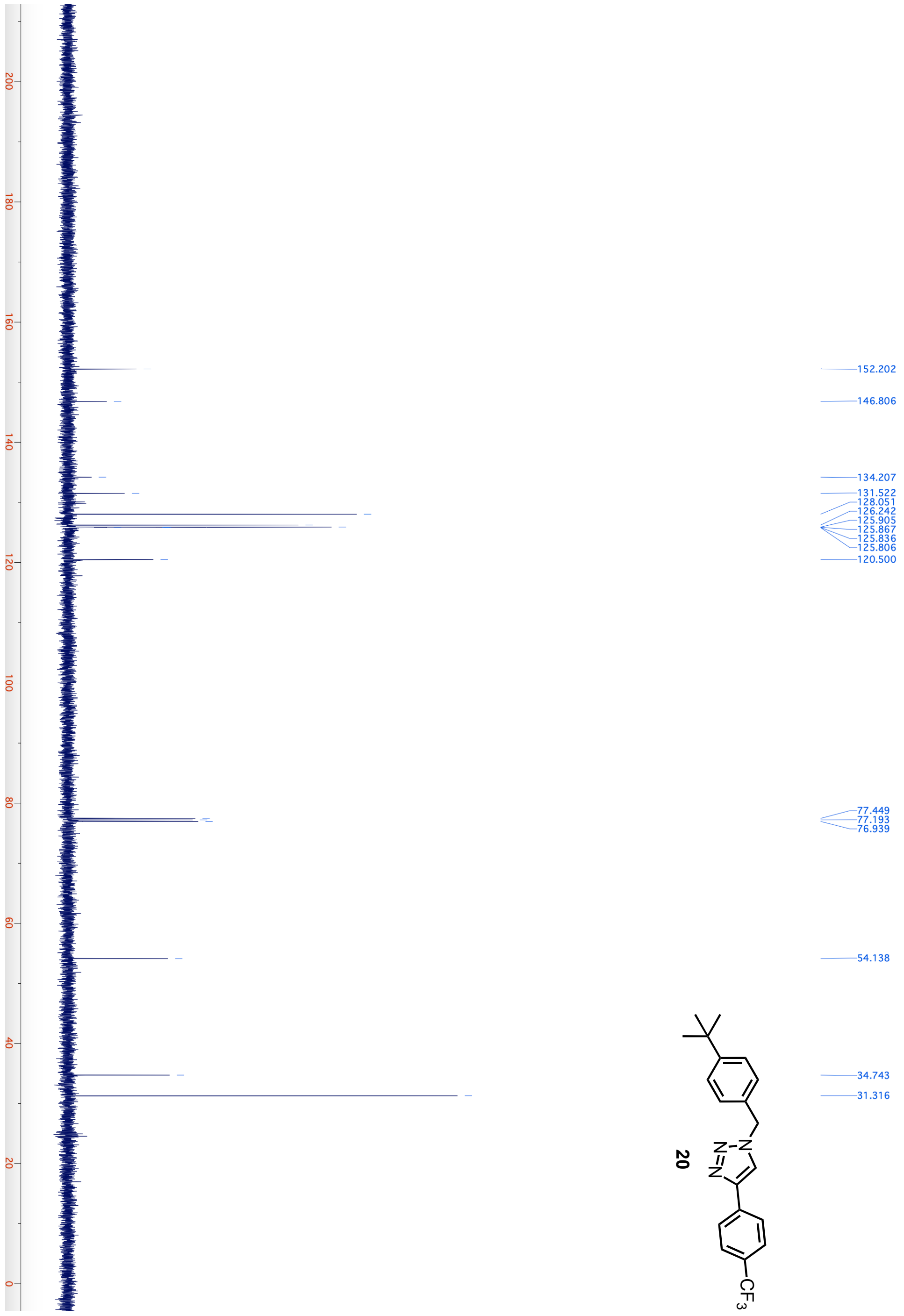
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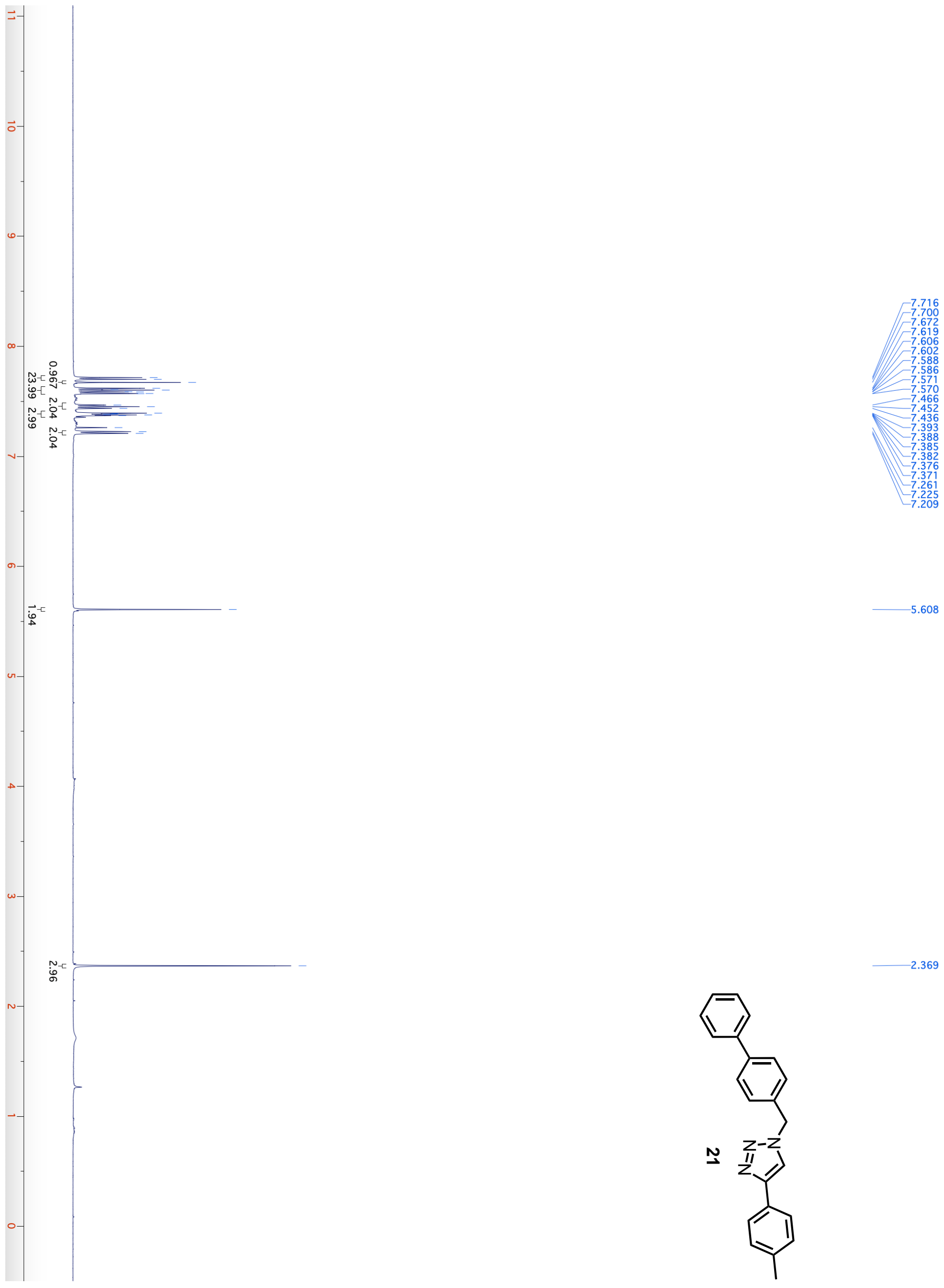
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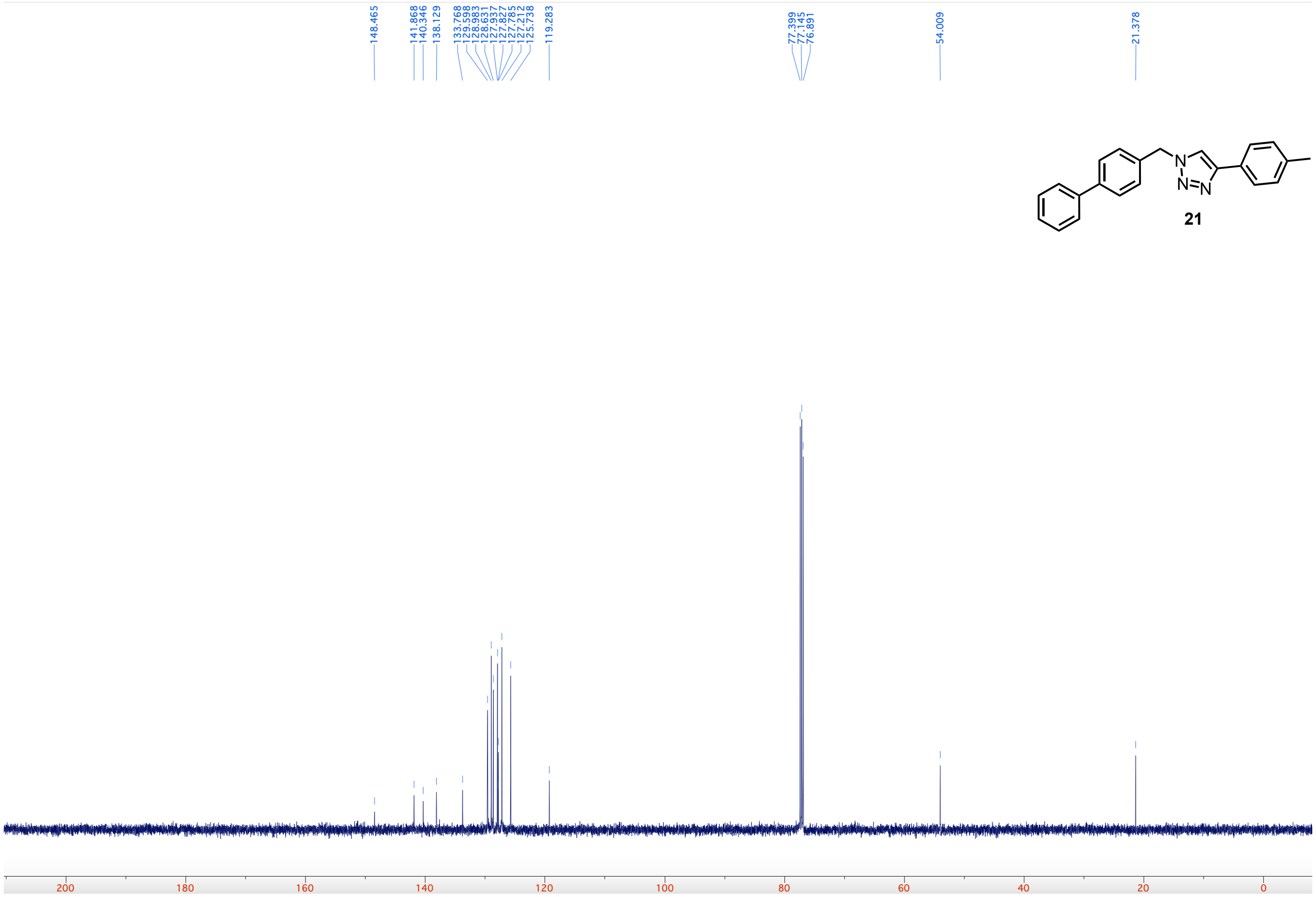

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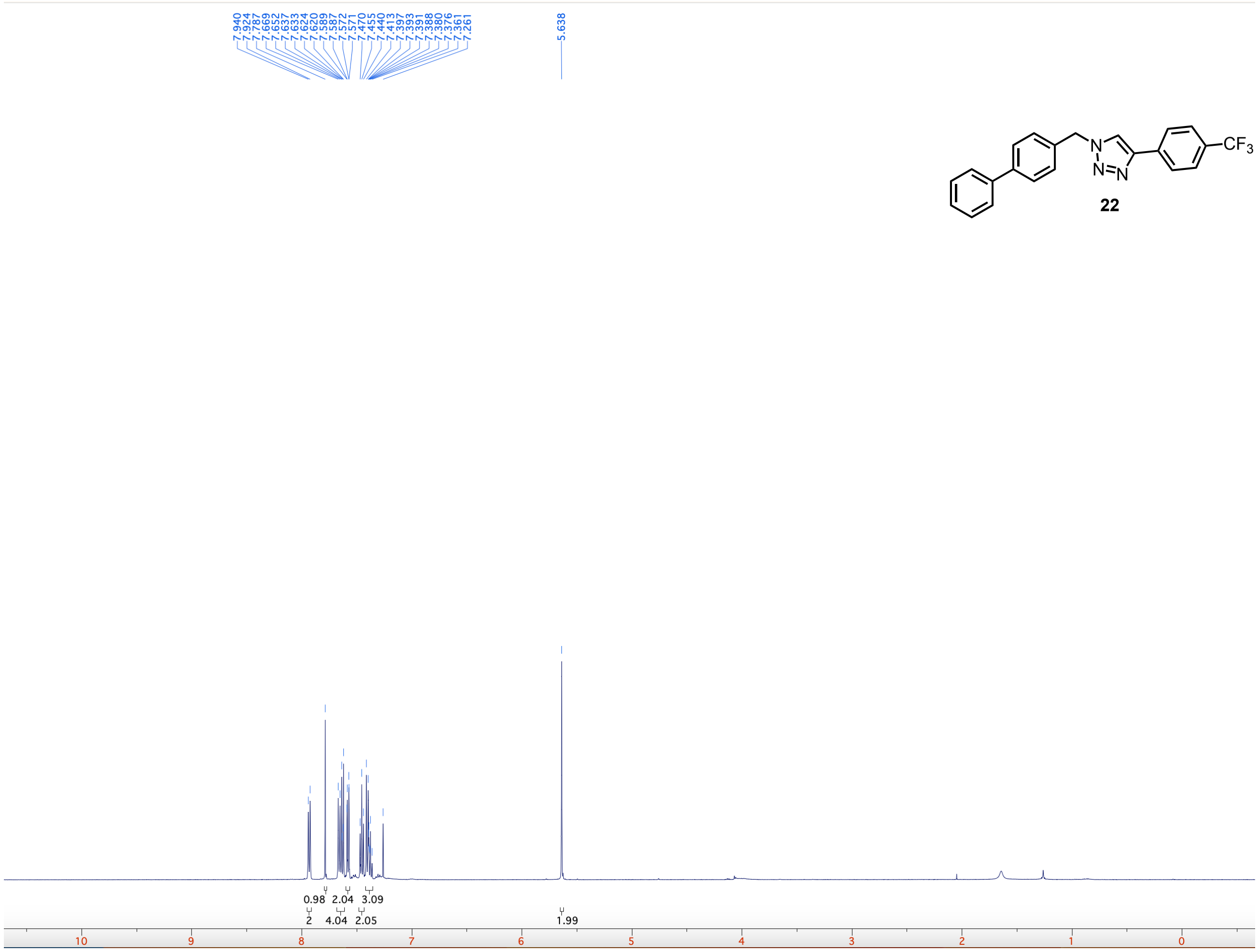

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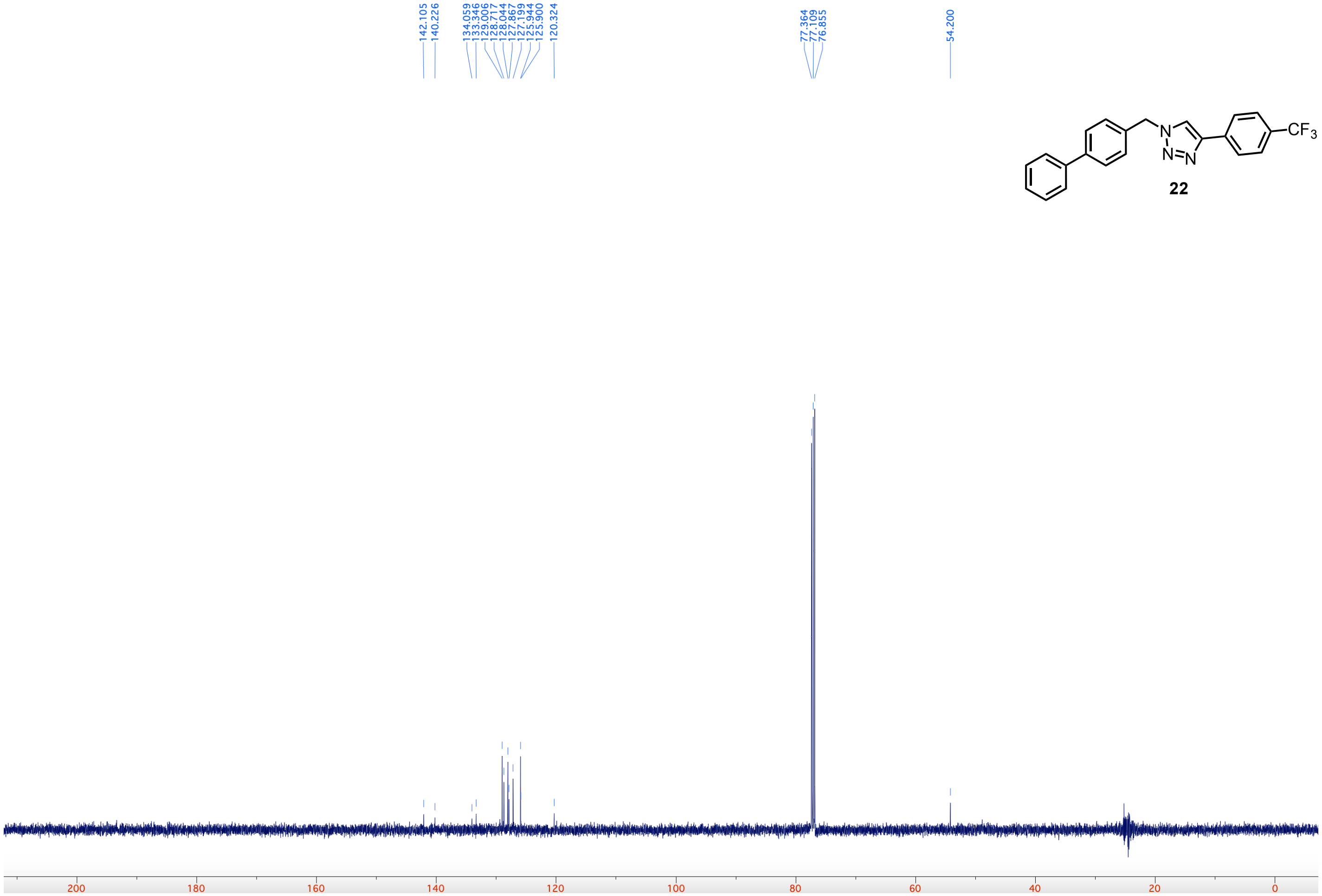
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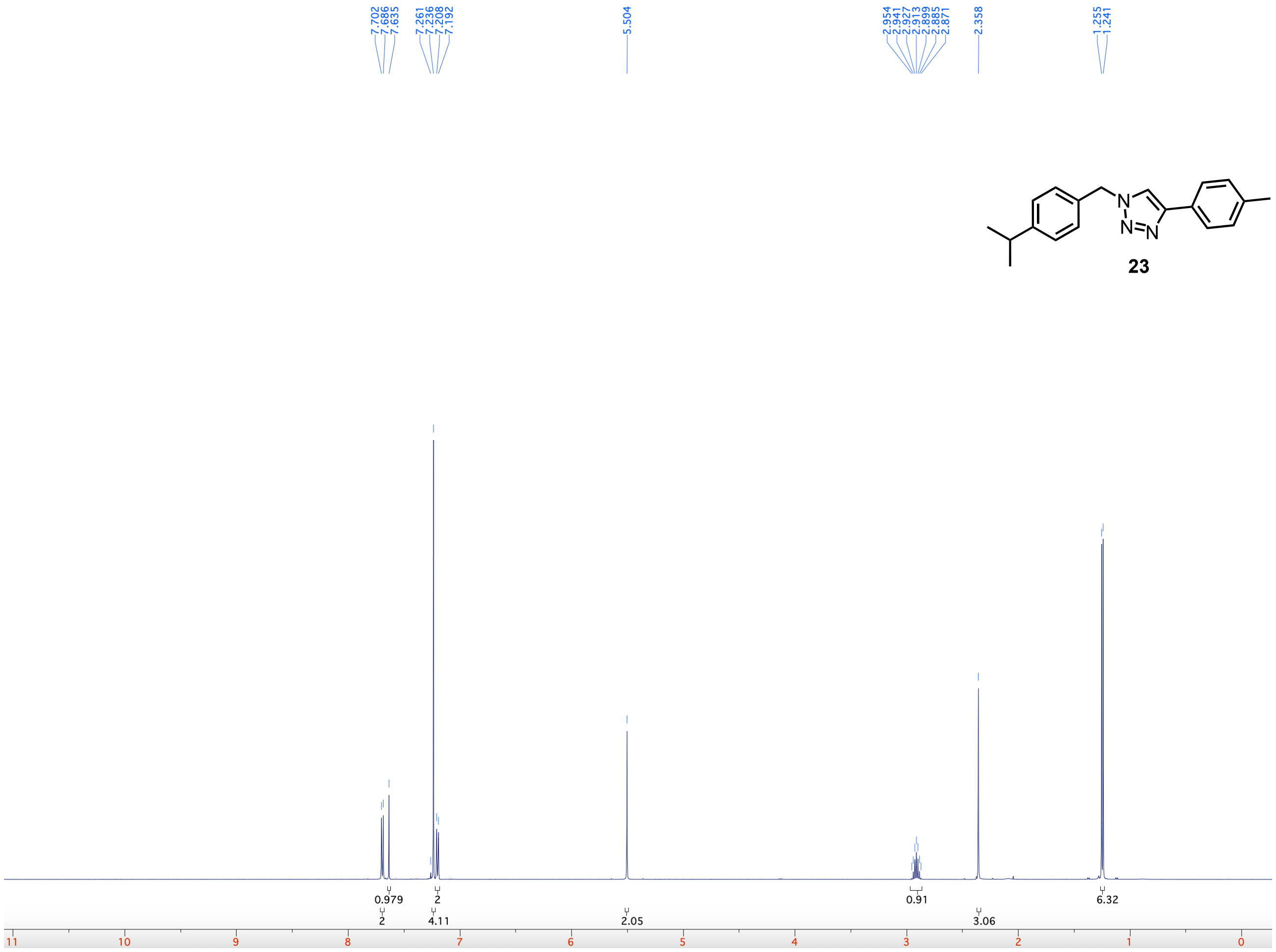
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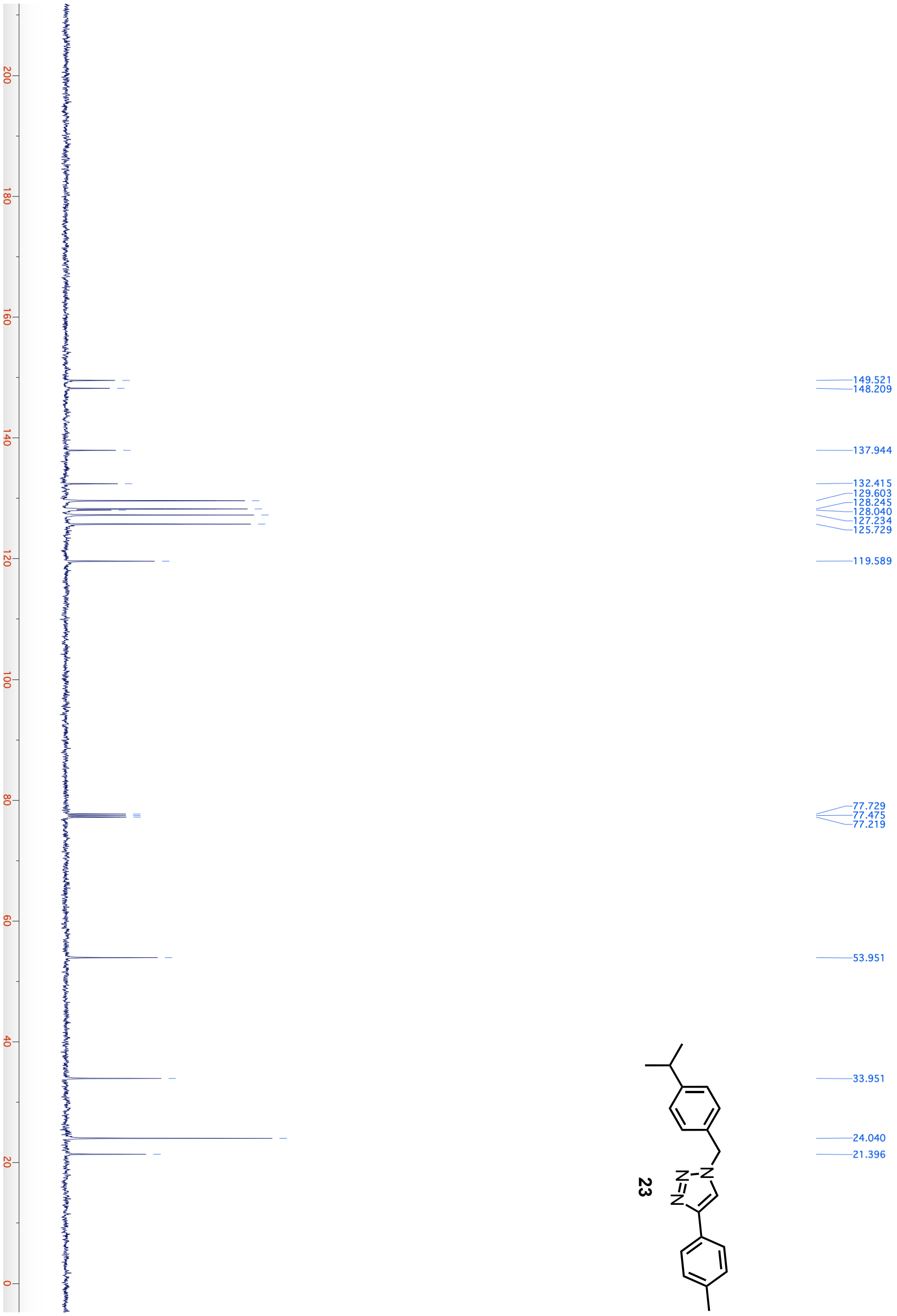
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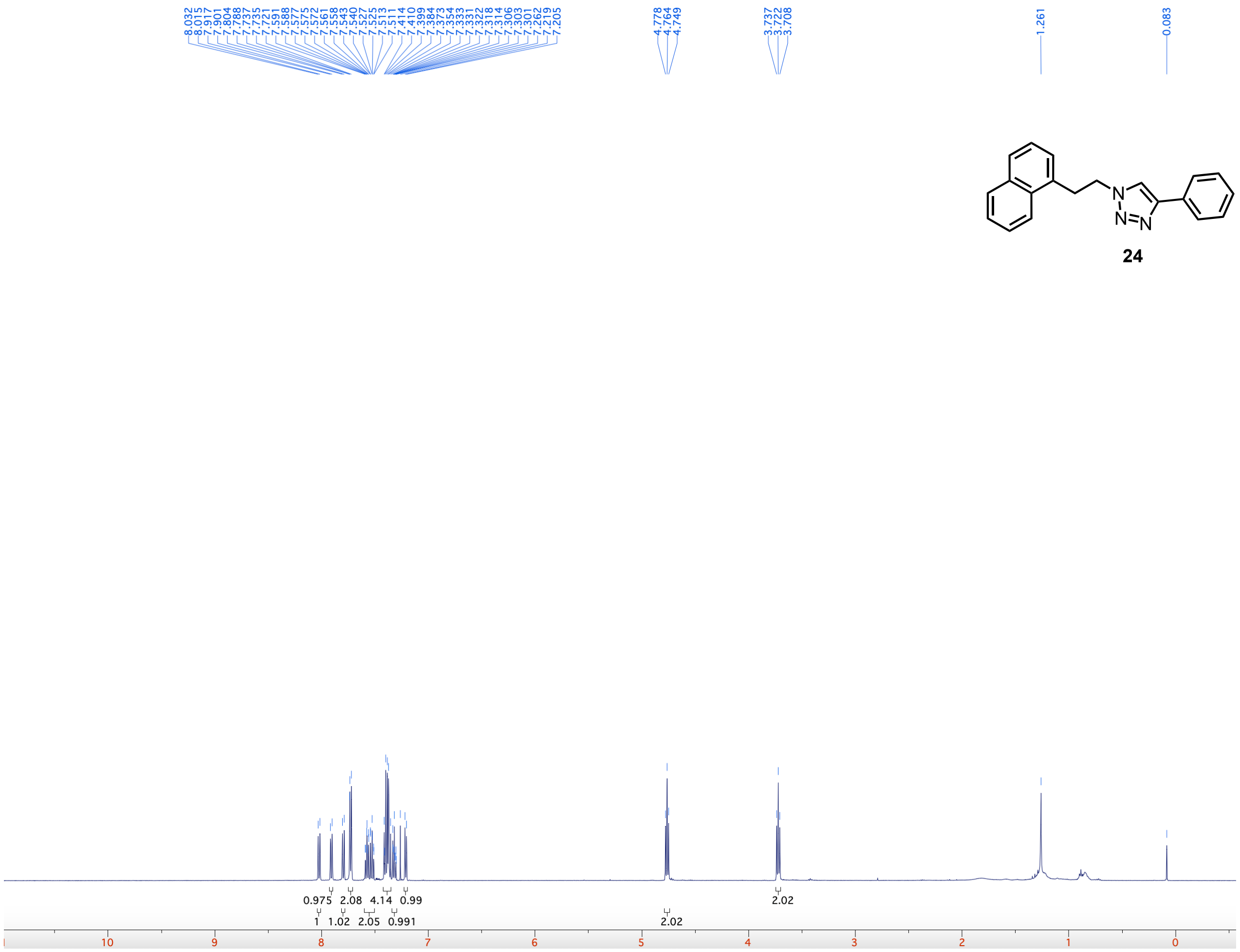

24

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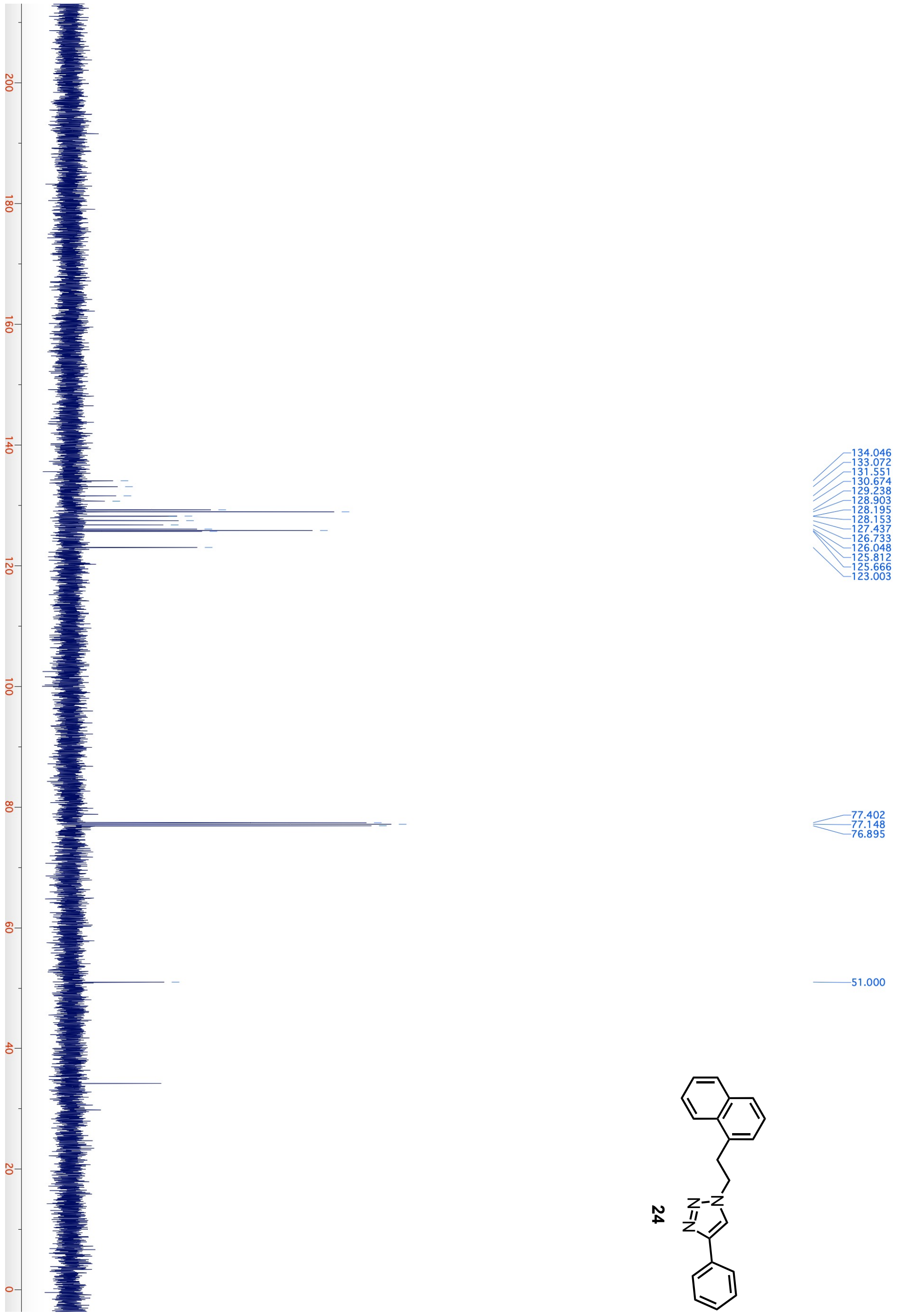

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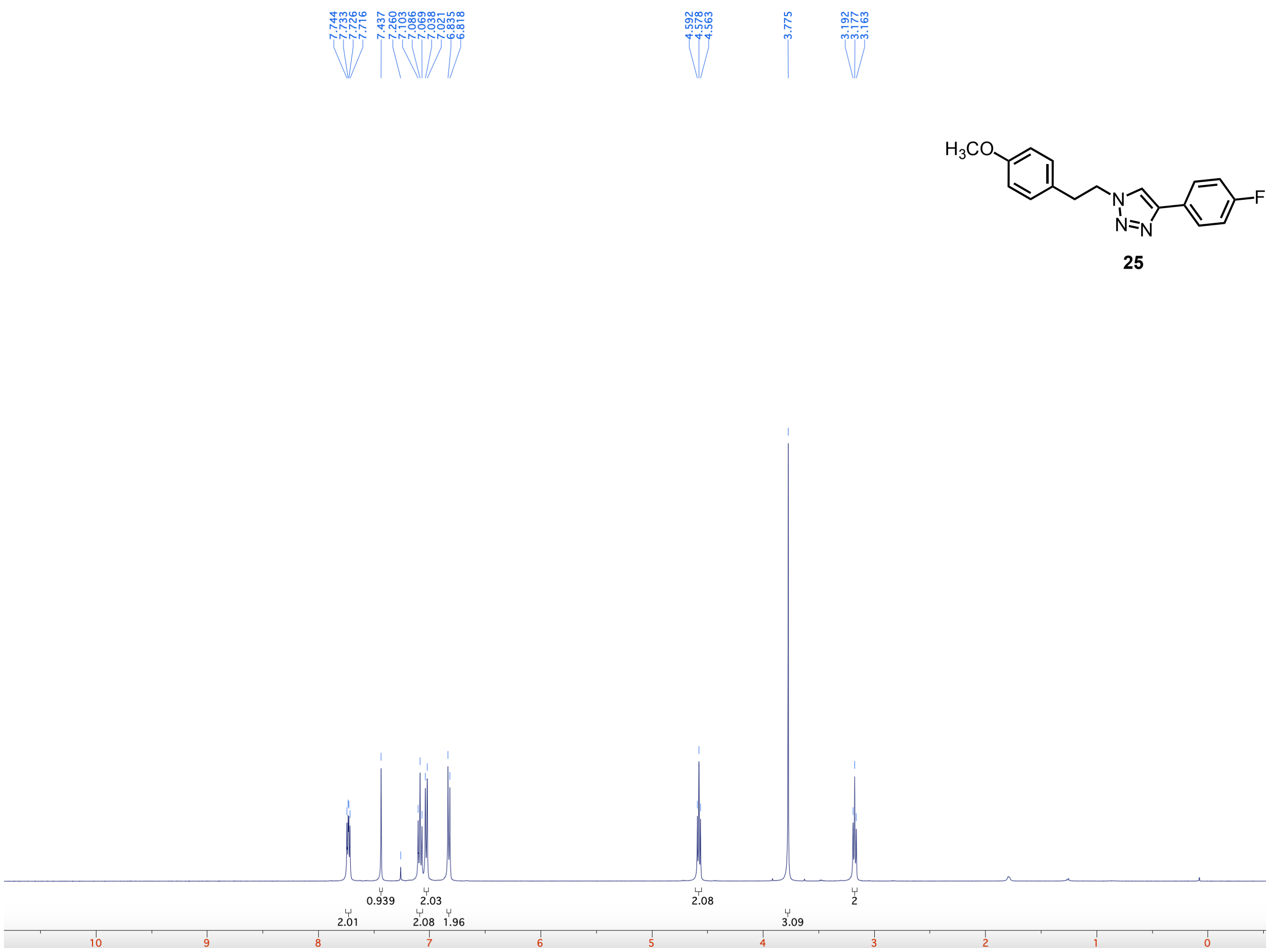
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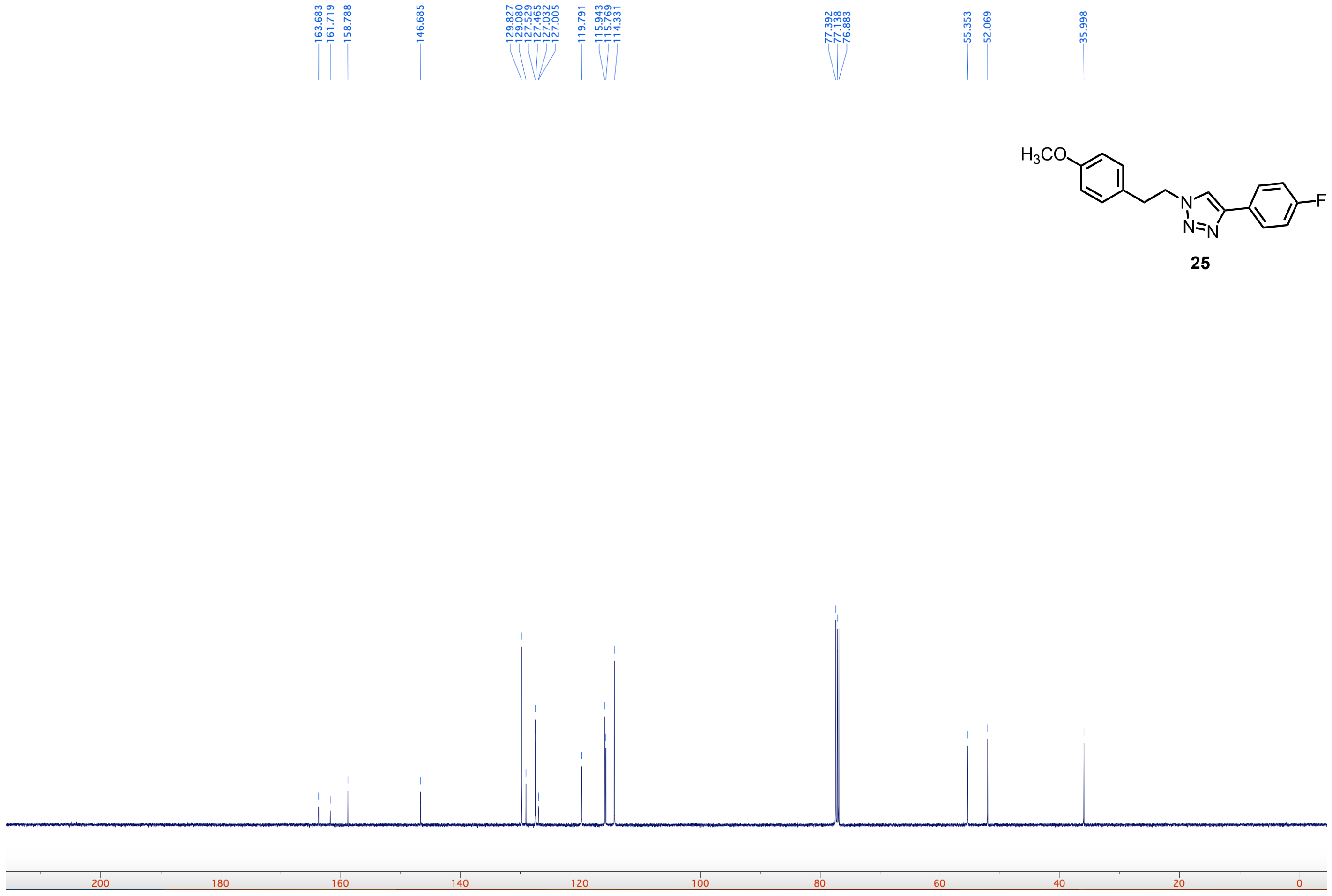163.683
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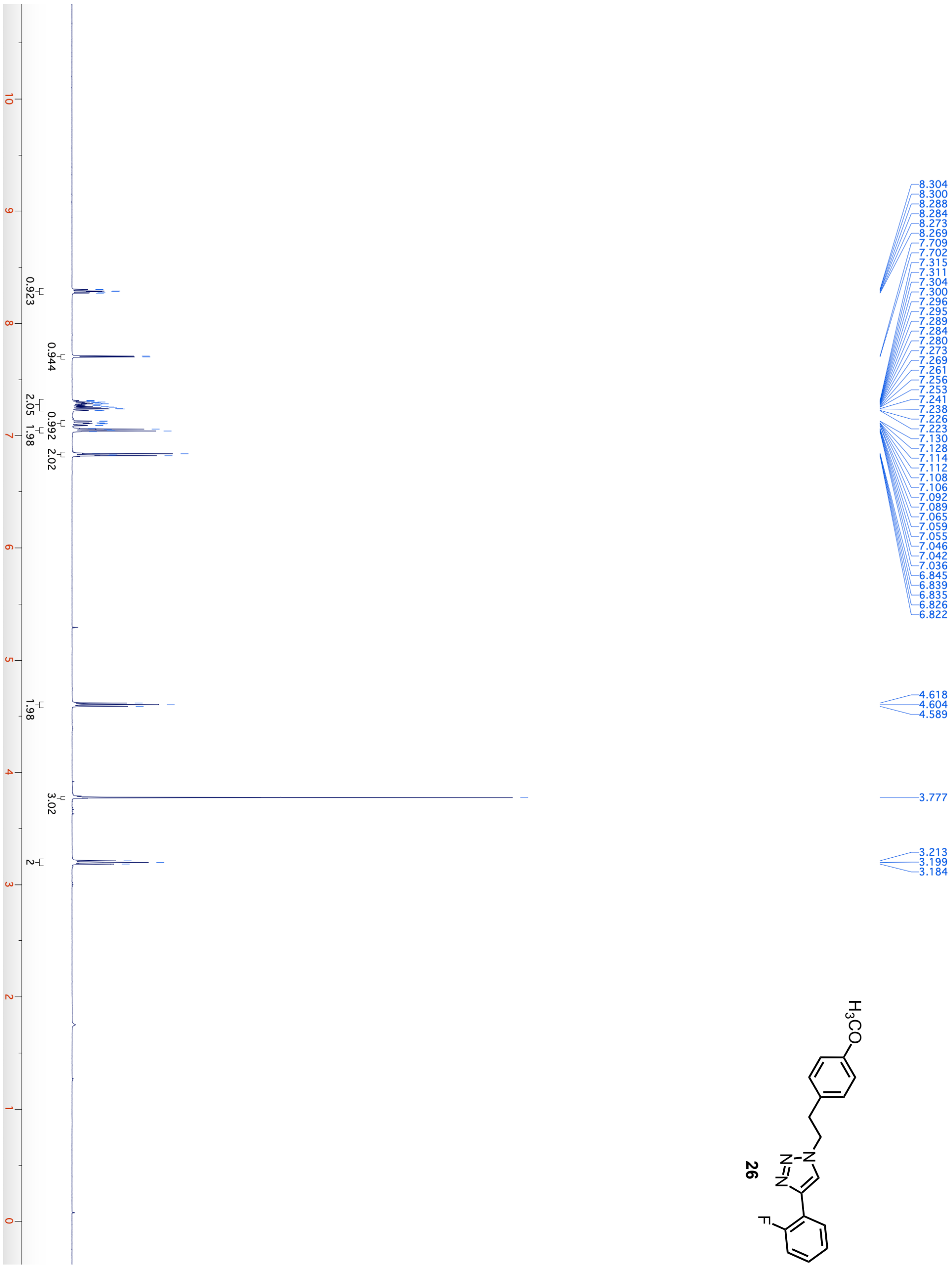
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7.108
7.106
7.092
7.089
7.065
7.059
7.055
7.046
7.042
7.036
6.845
6.839
6.835
6.826
6.822
4.618
4.604
4.589
3.777
3.213
3.199
3.184
0.923
0.944
2.05
0.992
1.98
2.02
1.98
3.02
2
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8
7
6
5
4
3
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0
H3CO
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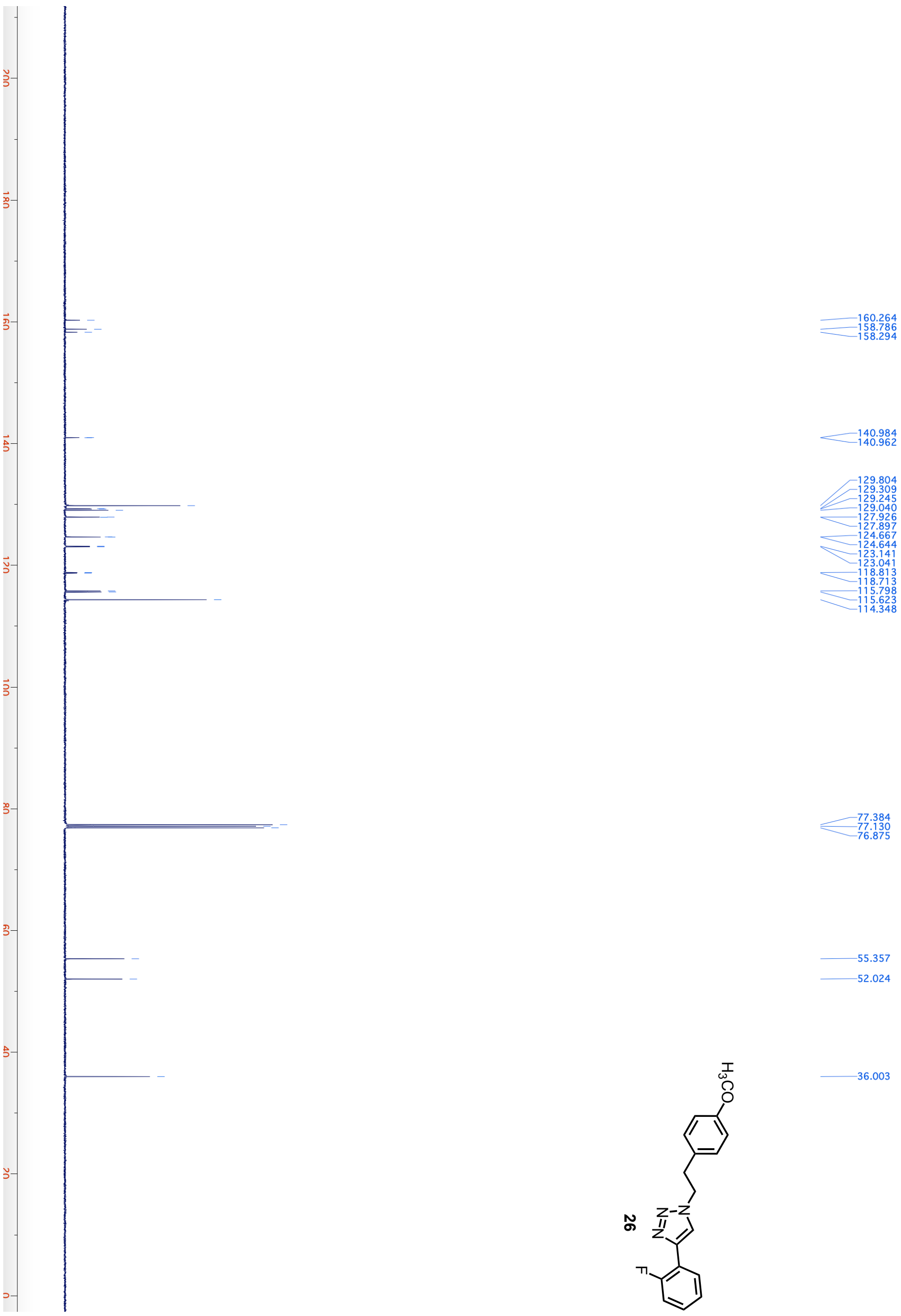
N
N
F
26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129.309
129.245
129.040
127.926
127.897
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124.644
123.141
123.041
118.813
118.713
115.798
115.623
114.348
77.384
77.130
76.875
55.357
52.024
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140
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100
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60
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20
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H3CO
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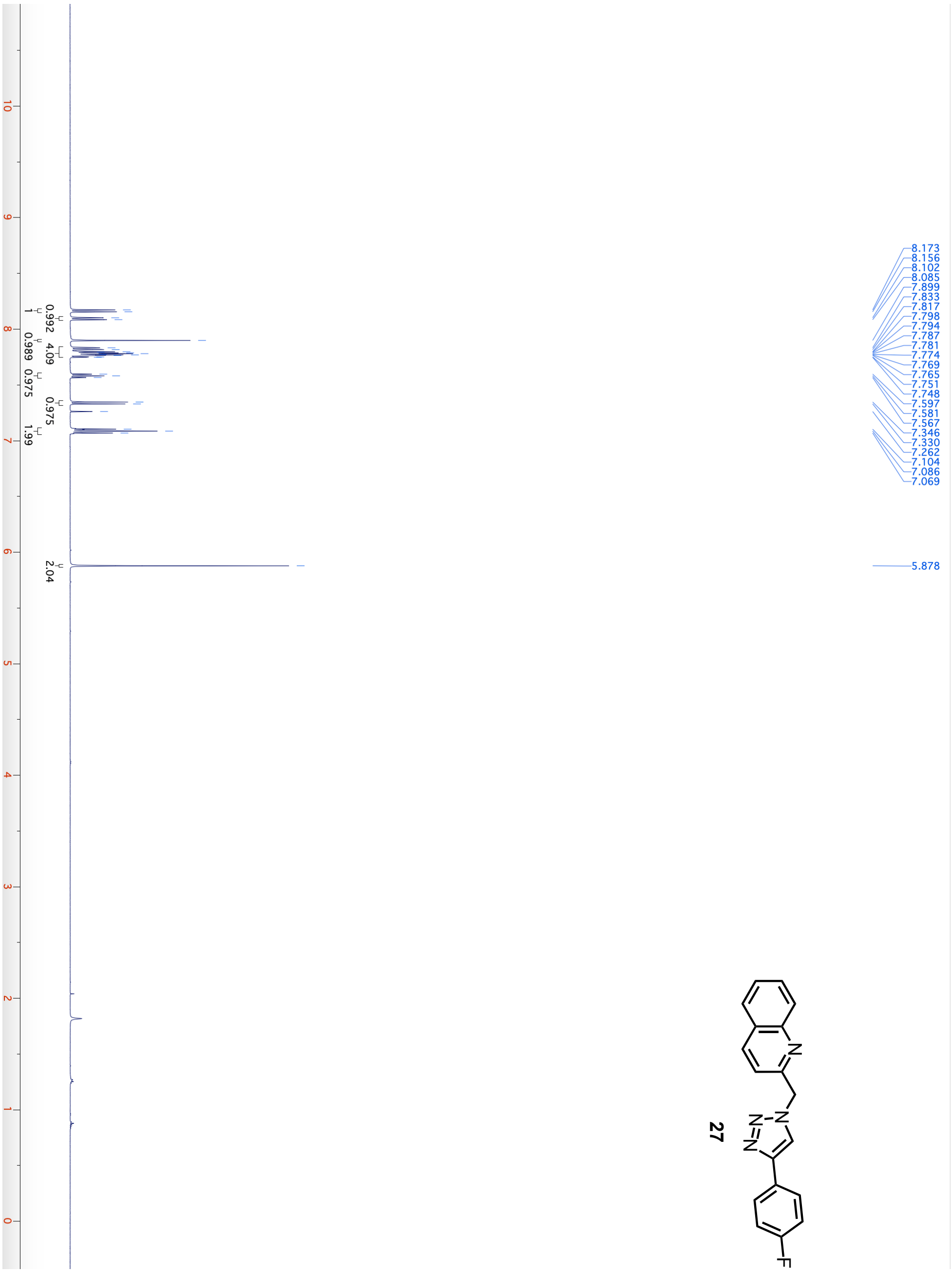
F

26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7.798
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7.787
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7.774
7.769
7.765
7.751
7.748
7.597
7.581
7.567
7.346
7.330
7.262
7.104
7.086
7.069
5.878
0.992
1
4.09
0.989
0.975
0.975
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9
8
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5
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3
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1
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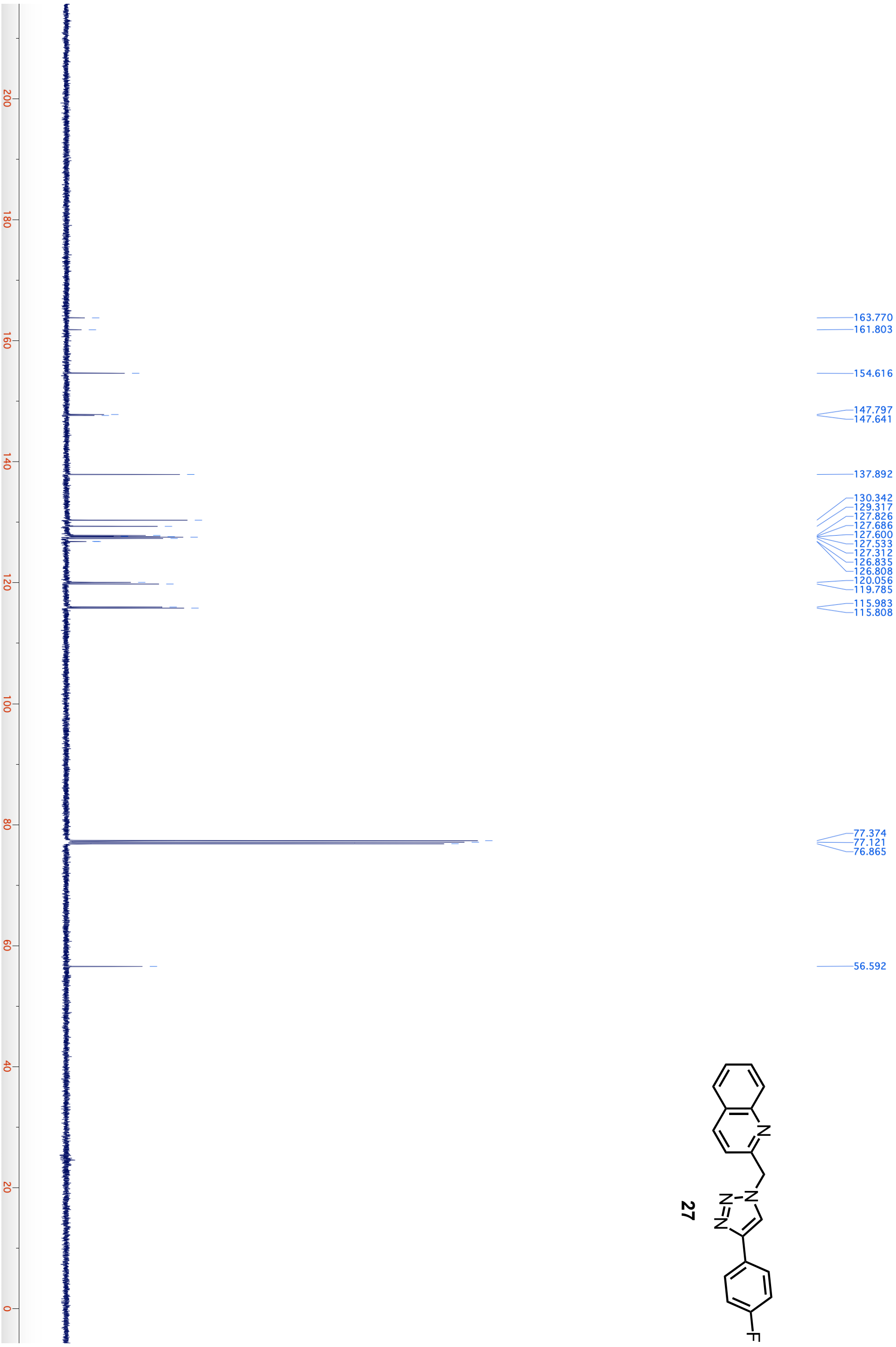
N
N
N
F

27



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137.892
130.342
129.317
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127.600
127.533
127.312
126.835
126.808
120.056
119.785
115.983
115.808
77.374
77.121
76.865
56.592
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180
160
140
120
100
80
60
40
20
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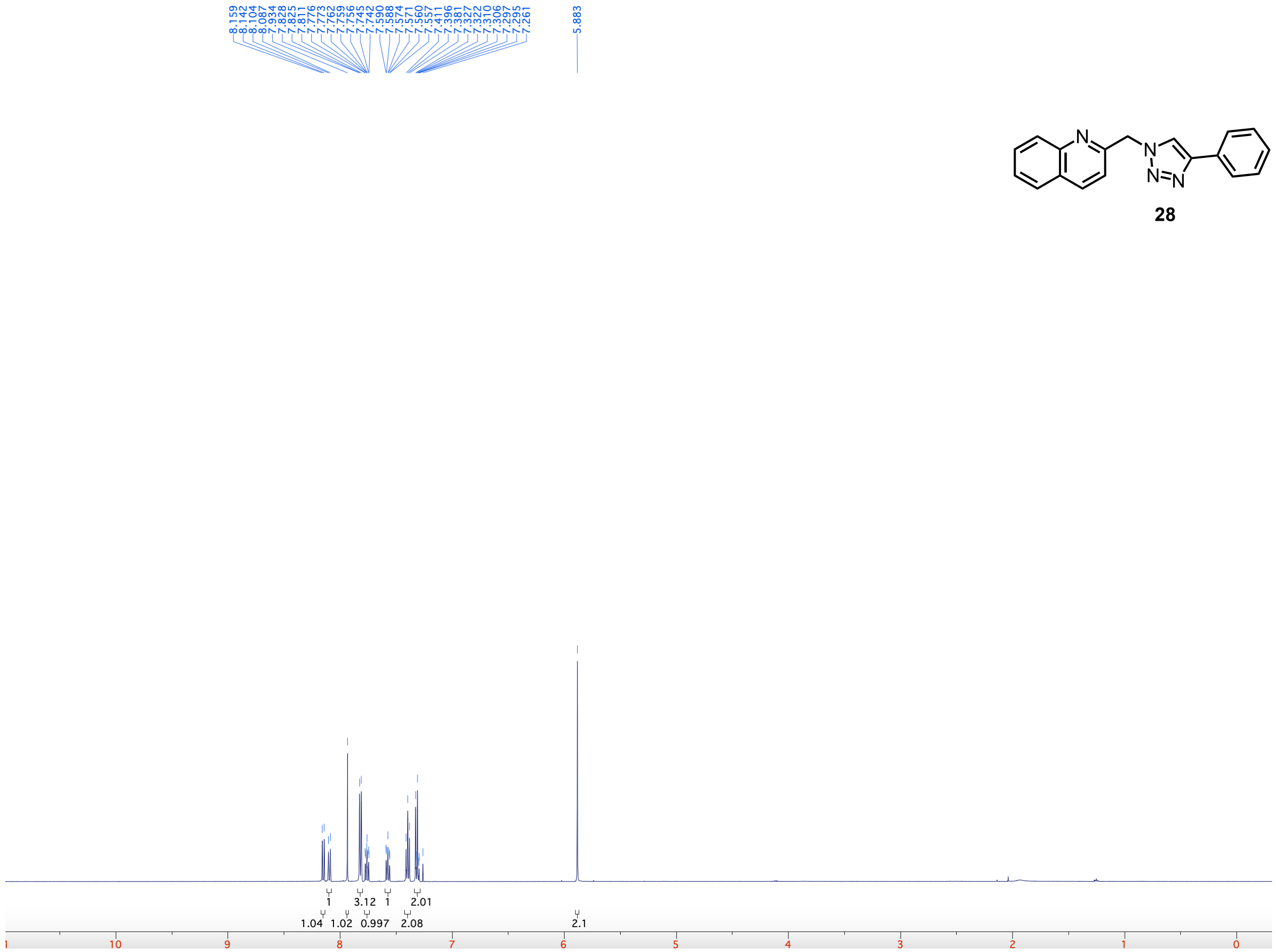
N
N
N
N
F

27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8.142
8.104
8.087
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7.825
7.811
7.776
7.773
7.762
7.759
7.756
7.745
7.742
7.590
7.588
7.574
7.571
7.560
7.557
7.411
7.396
7.381
7.327
7.322
7.310
7.306
7.297
7.295
7.261
5.883
1
3.12
1
2.01
1.04
1.02
0.997
2.08
2.1
10
9
8
7
6
5
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2
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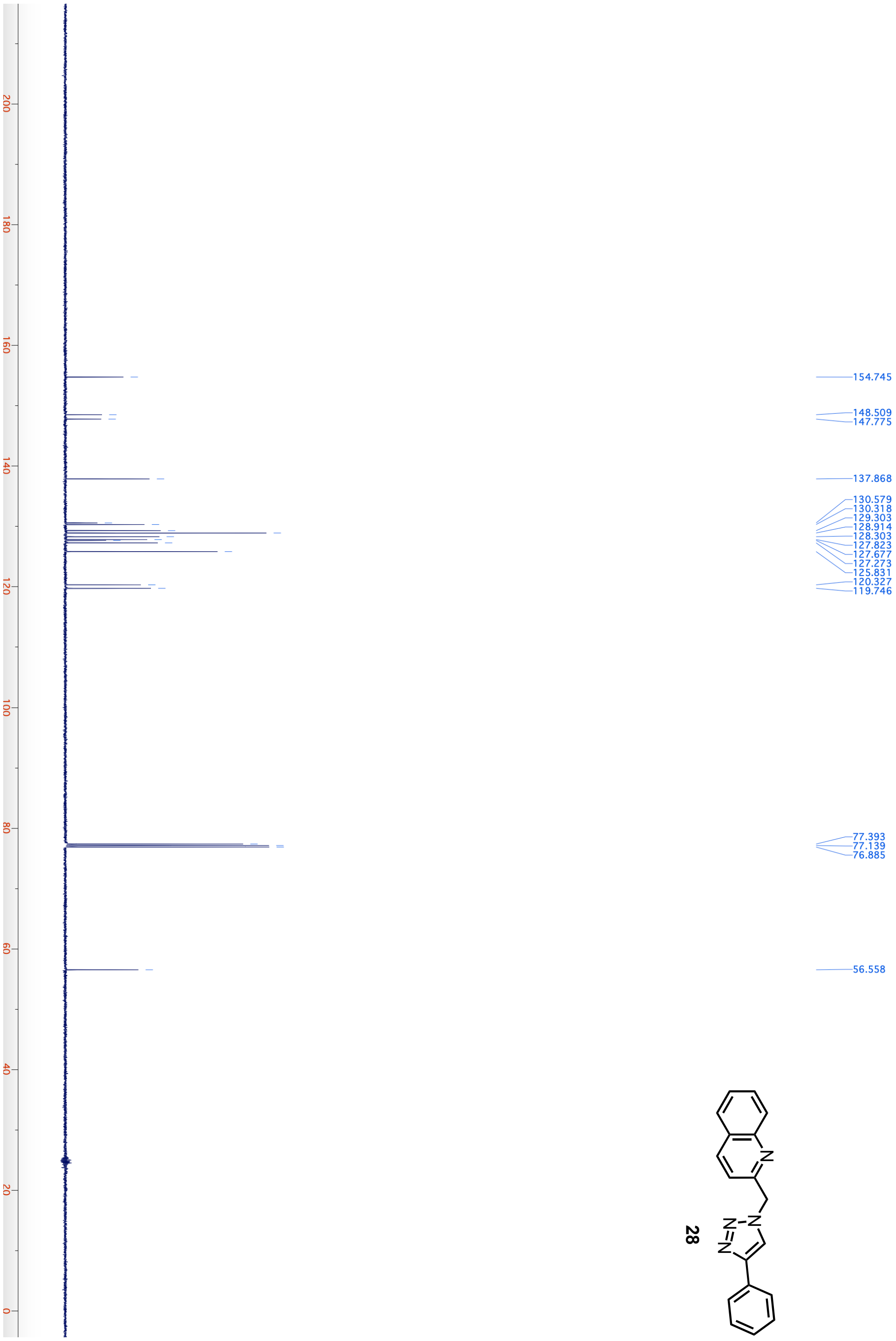
N
N
N

28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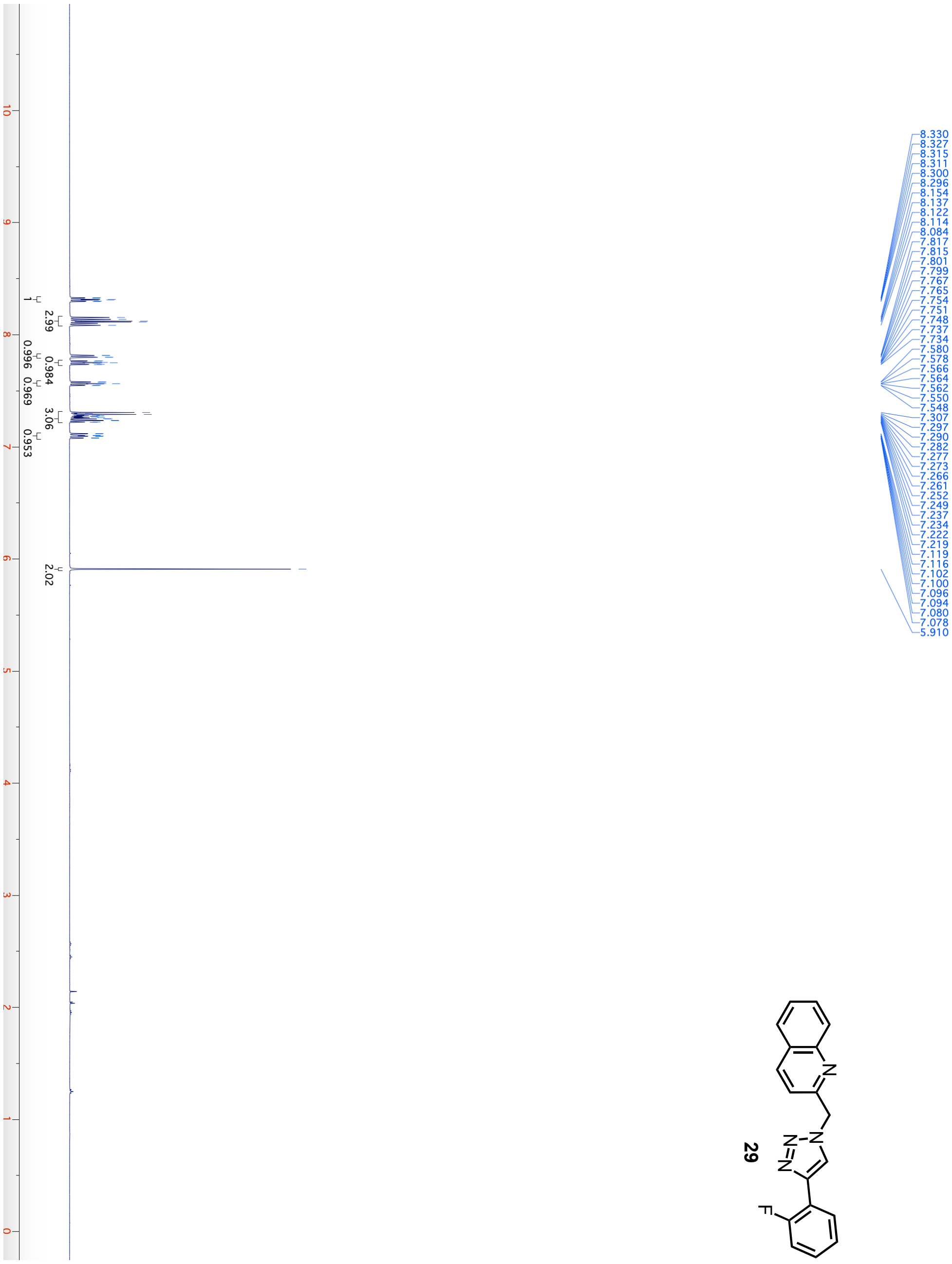
128.914
128.303
127.823
127.677
127.273
125.831
120.327
119.746
77.393
77.139
76.885
56.558
200
180
160
140
120
100
80
60
40
20
0
N
N
N
N
28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8.137
8.122
8.114
8.084
7.817
7.815
7.801
7.799
7.767
7.765
7.754
7.751
7.748
7.737
7.734
7.580
7.578
7.566
7.564
7.562
7.550
7.548
7.307
7.297
7.290
7.282
7.277
7.273
7.266
7.261
7.252
7.249
7.237
7.234
7.222
7.219
7.119
7.116
7.102
7.100
7.096
7.094
7.080
7.078
5.910
1
2.99
0.984
0.996
0.969
3.06
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2.02
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9
8
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5
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3
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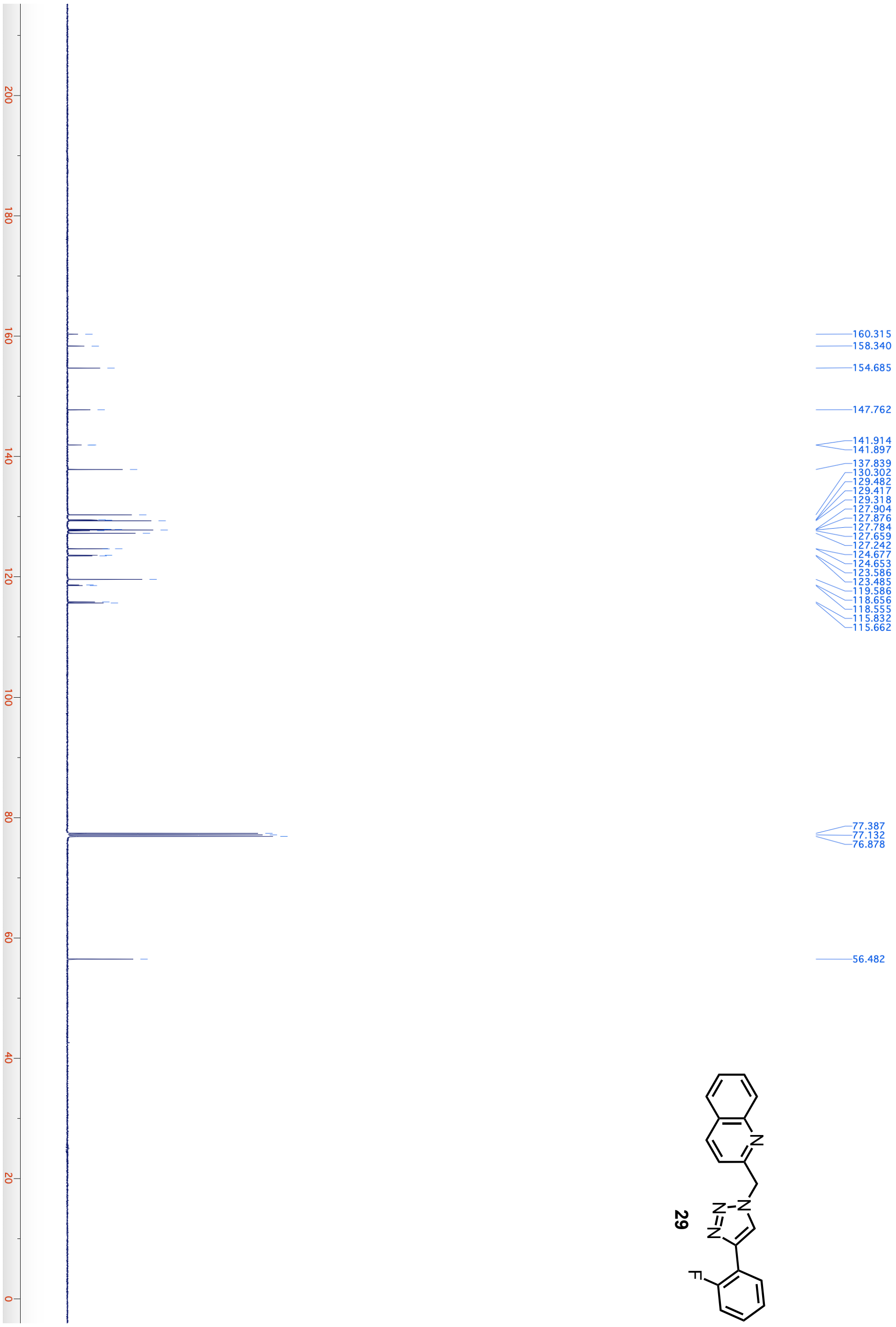
N
N
F

29



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141.897
137.839
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129.417
129.318
127.904
127.876
127.784
127.659
127.242
124.677
124.653
123.586
123.485
119.586
118.656
118.555
115.832
115.662
77.387
77.132
76.878
56.482
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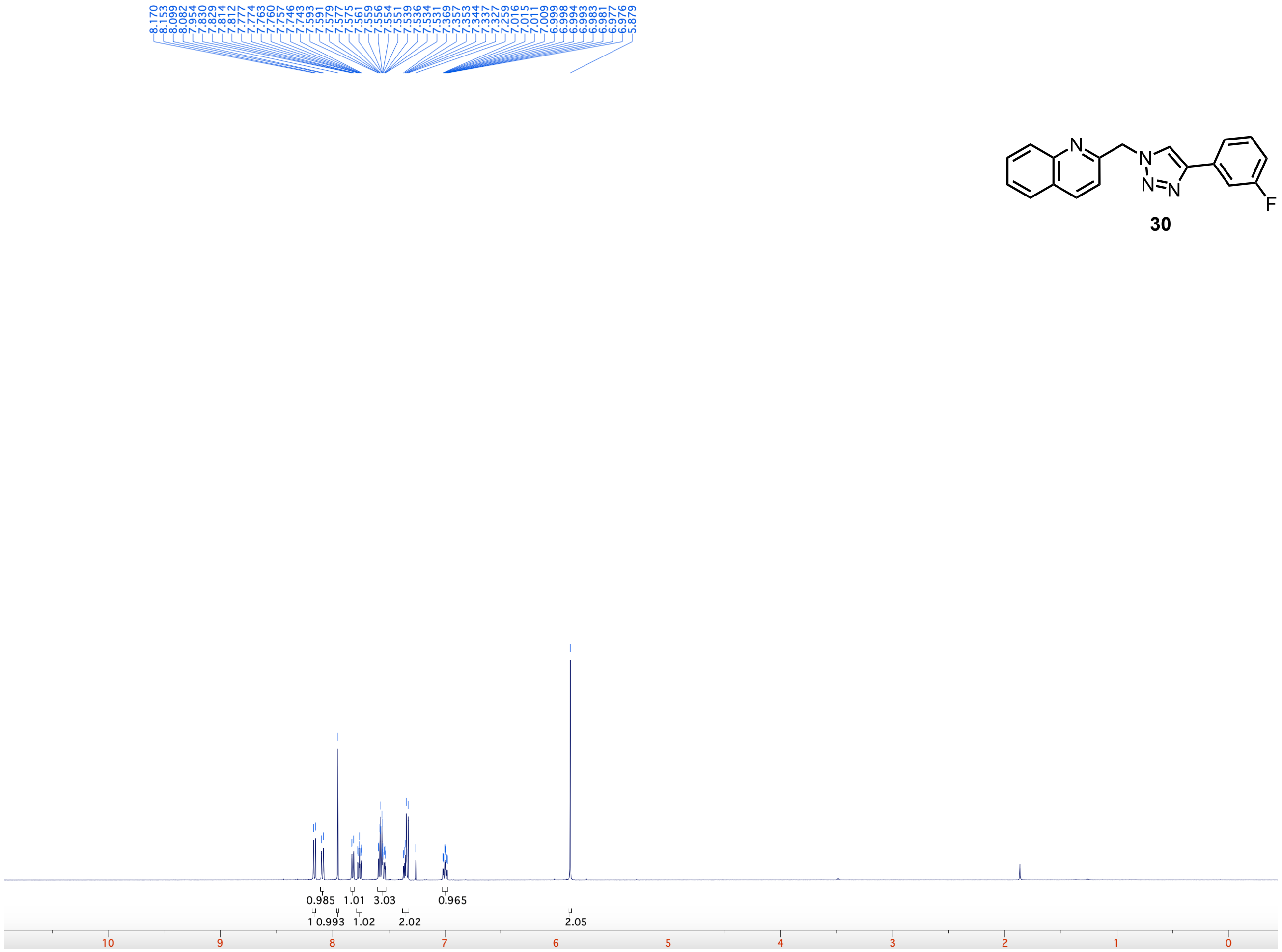
180
160
140
120
100
80
60
40
20
0
N
N
N
N
F
29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7.830
7.829
7.814
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7.777
7.774
7.763
7.760
7.757
7.746
7.743
7.593
7.591
7.579
7.577
7.575
7.561
7.559
7.556
7.554
7.551
7.539
7.536
7.534
7.531
7.369
7.357
7.353
7.344
7.337
7.327
7.259
7.016
7.015
7.011
7.009
6.999
6.998
6.994
6.993
6.983
6.981
6.977
6.976
5.879
N
N
N
N
F
0.985
1.01
3.03
0.965
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0.993
1.02
2.02
2.05
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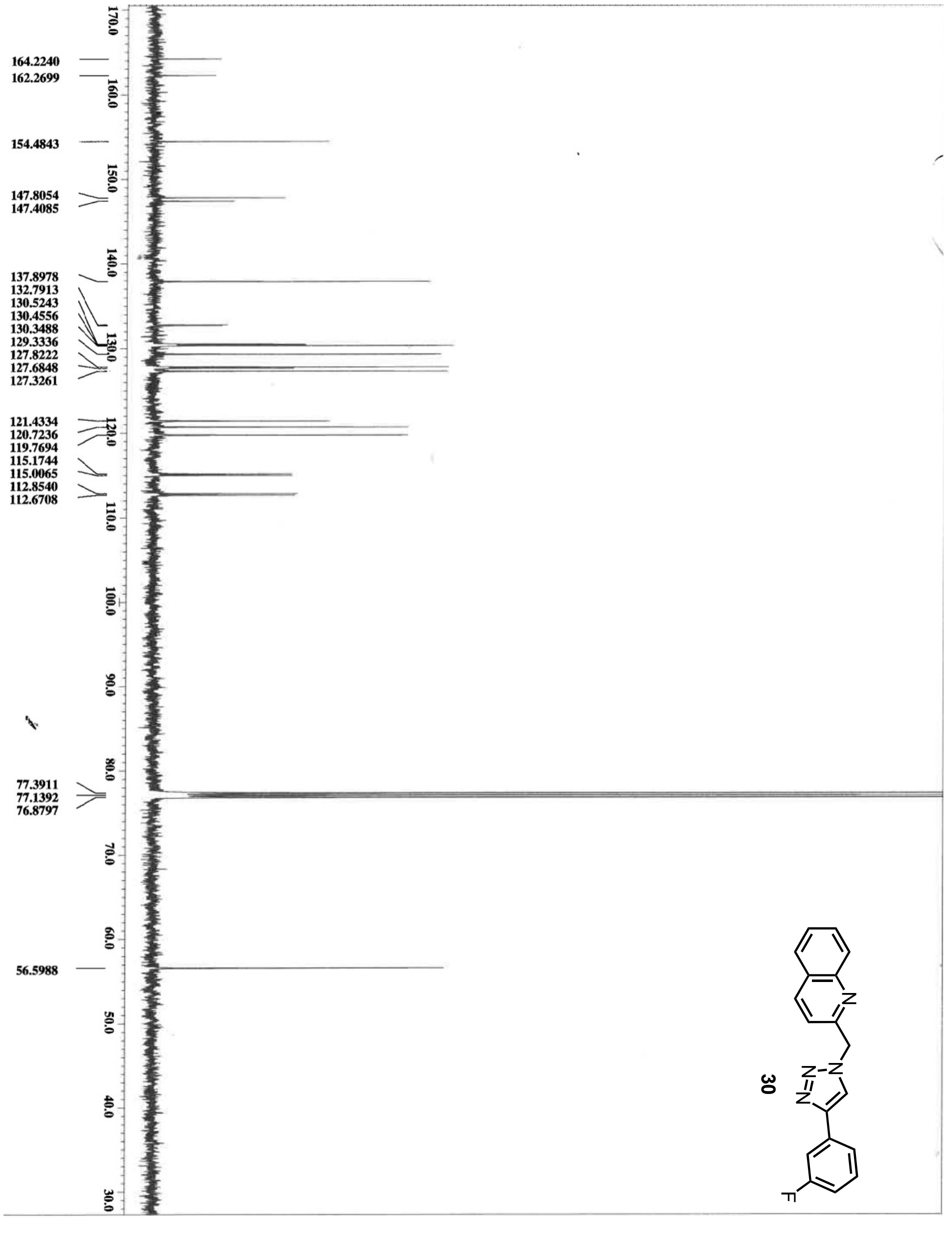
7
6
5
4
3
2
1
0

30

164.2240
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147.4085
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130.4556
130.3488
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127.8222
127.6848
127.3261
121.4334
120.7236
119.7694
115.1744
115.0065
112.8540
112.6708
77.3911
77.1392
76.8797
56.5988
170.0
160.0
150.0
140.0
130.0
120.0
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80.0
70.0
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30.0
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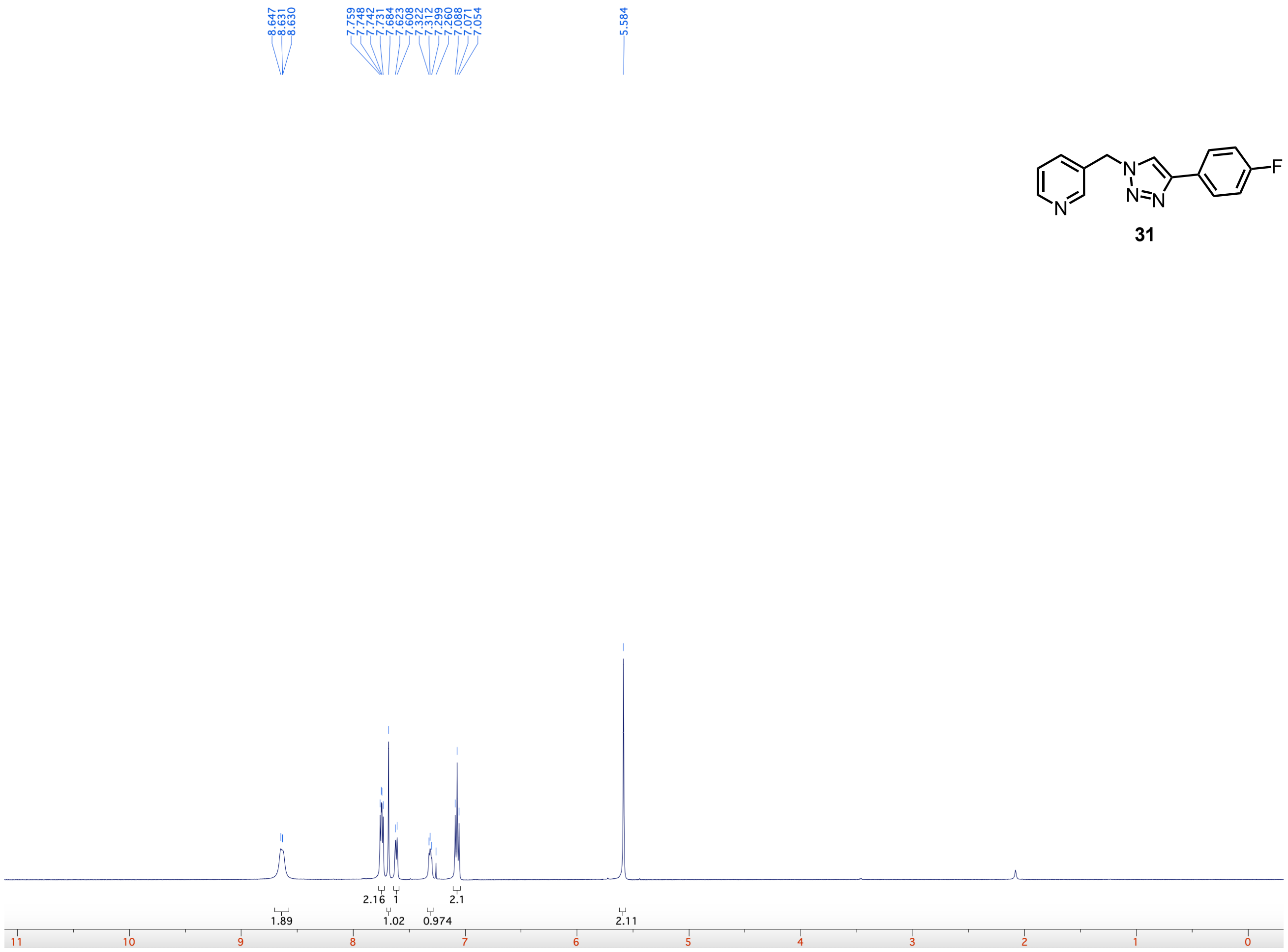
N
N
F

30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7.312
7.299
7.260
7.088
7.071
7.054
5.584
2.16
1
2.1
1.89
1.02
0.974
2.11
11
10
9
8
7
6
5
4
3
2
1
0

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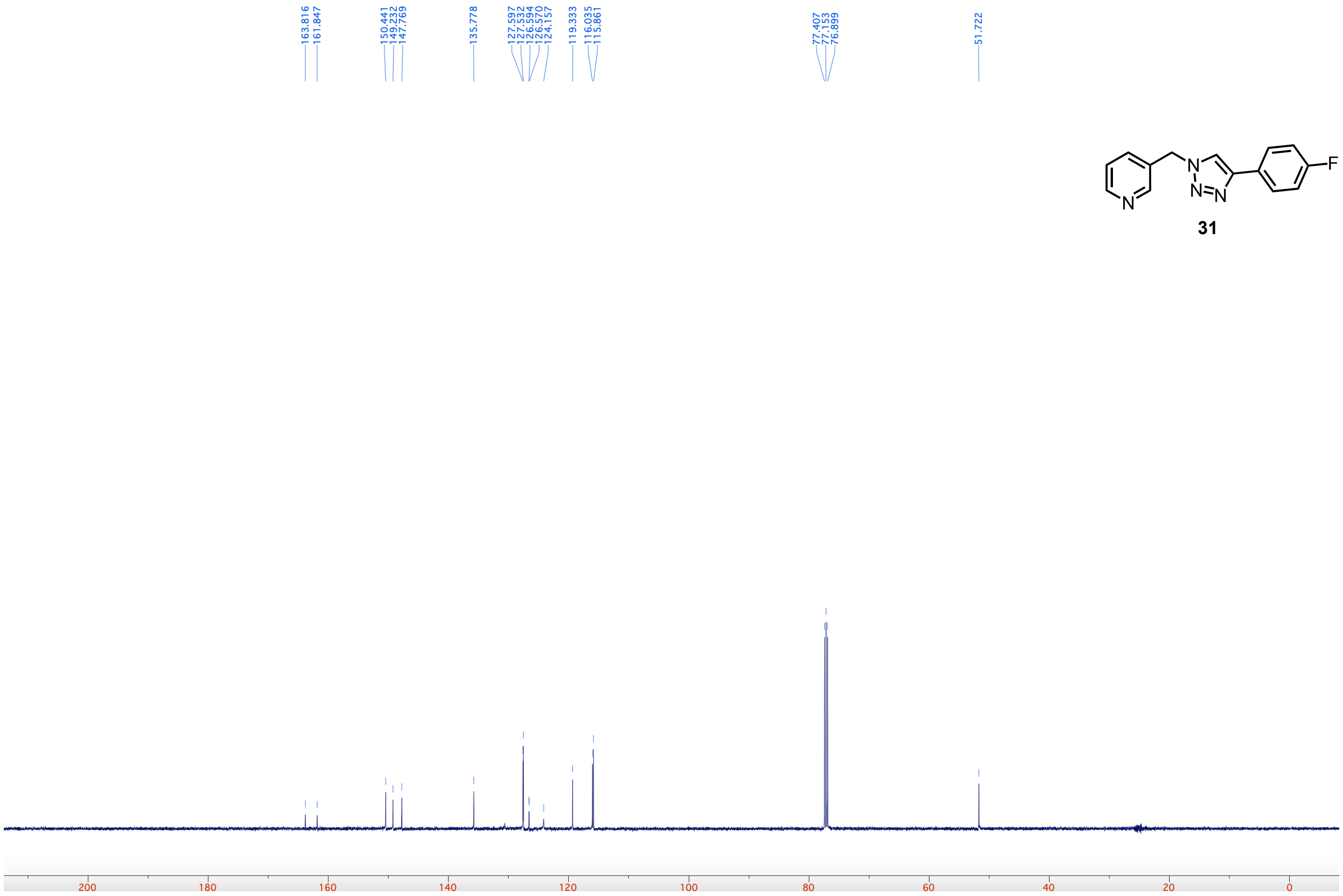
N
N
N
F

31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127.532
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126.570
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119.333
116.035
115.861
77.407
77.153
76.899
51.722
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N
N
N
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120
100
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60
40
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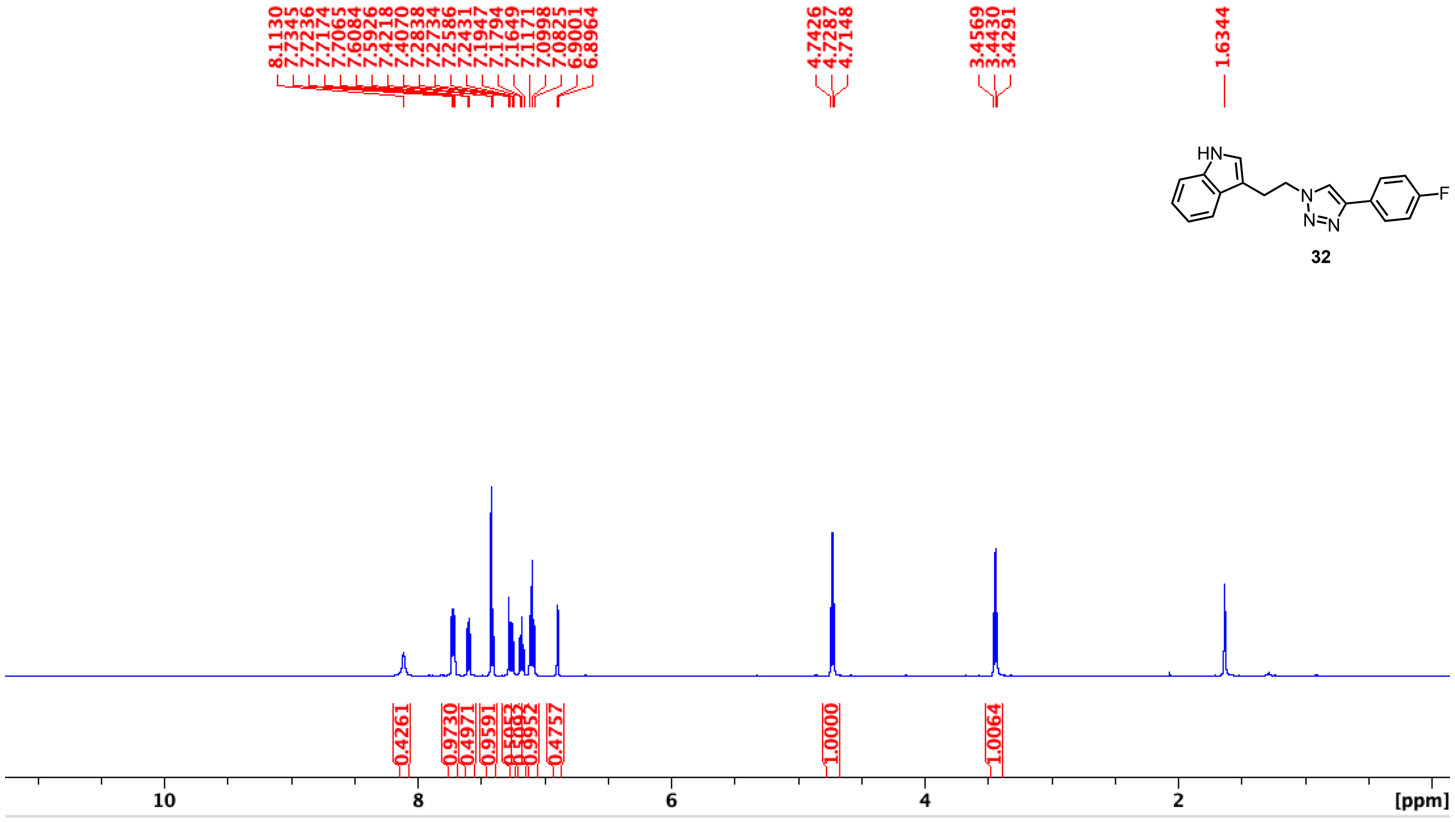
0

31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7.4070
7.2838
7.2734
7.2586
7.2431
7.1947
7.1794
7.1649
7.1171
7.0998
7.0825
6.9001
6.8964
4.7426
4.7287
4.7148
3.4569
3.4430
3.4291
1.6344
HN
N
N
N
F
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0.9730
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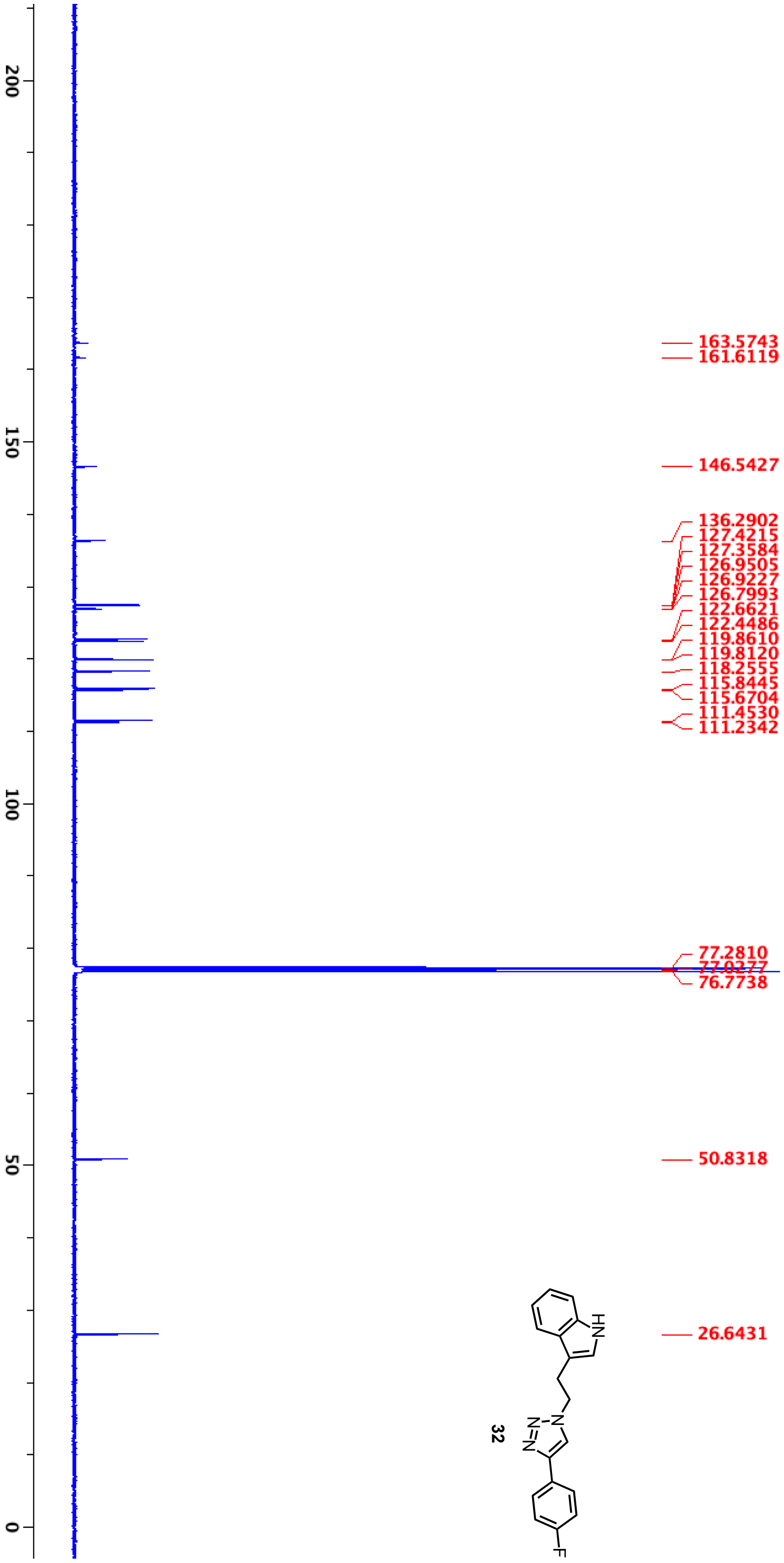
2
[ppm]

32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126.7993
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122.4486
119.8610
119.8120
118.2555
115.8445
115.6704
111.4530
111.2342
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76.7738
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100
50
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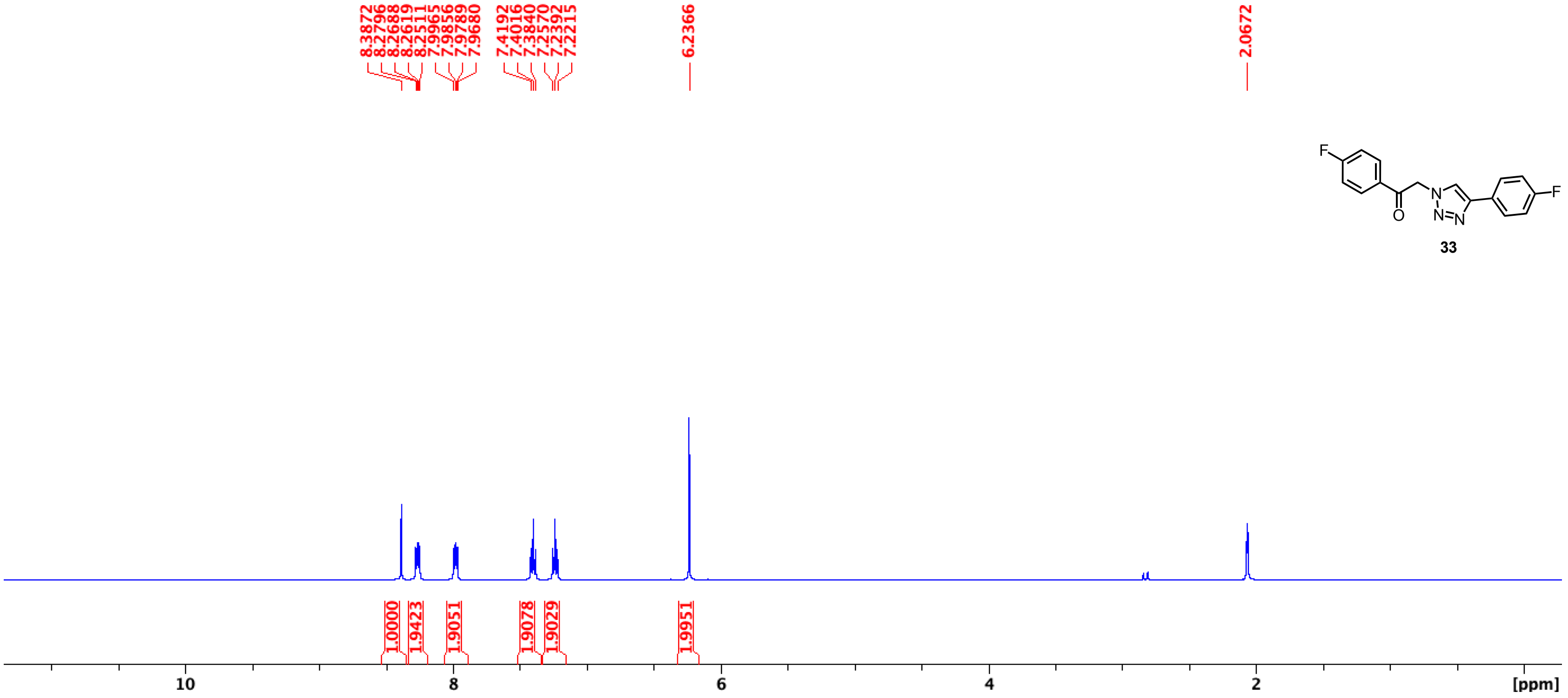
N
N=N
F

32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8.2619
8.2511
7.9965
7.9856
7.9789
7.9680
7.4192
7.4016
7.3840
7.2570
7.2392
7.2215
6.2366
2.0672
1.0000
1.9423
1.9051
1.9078
1.9029
1.9951
10
8
6
4
2
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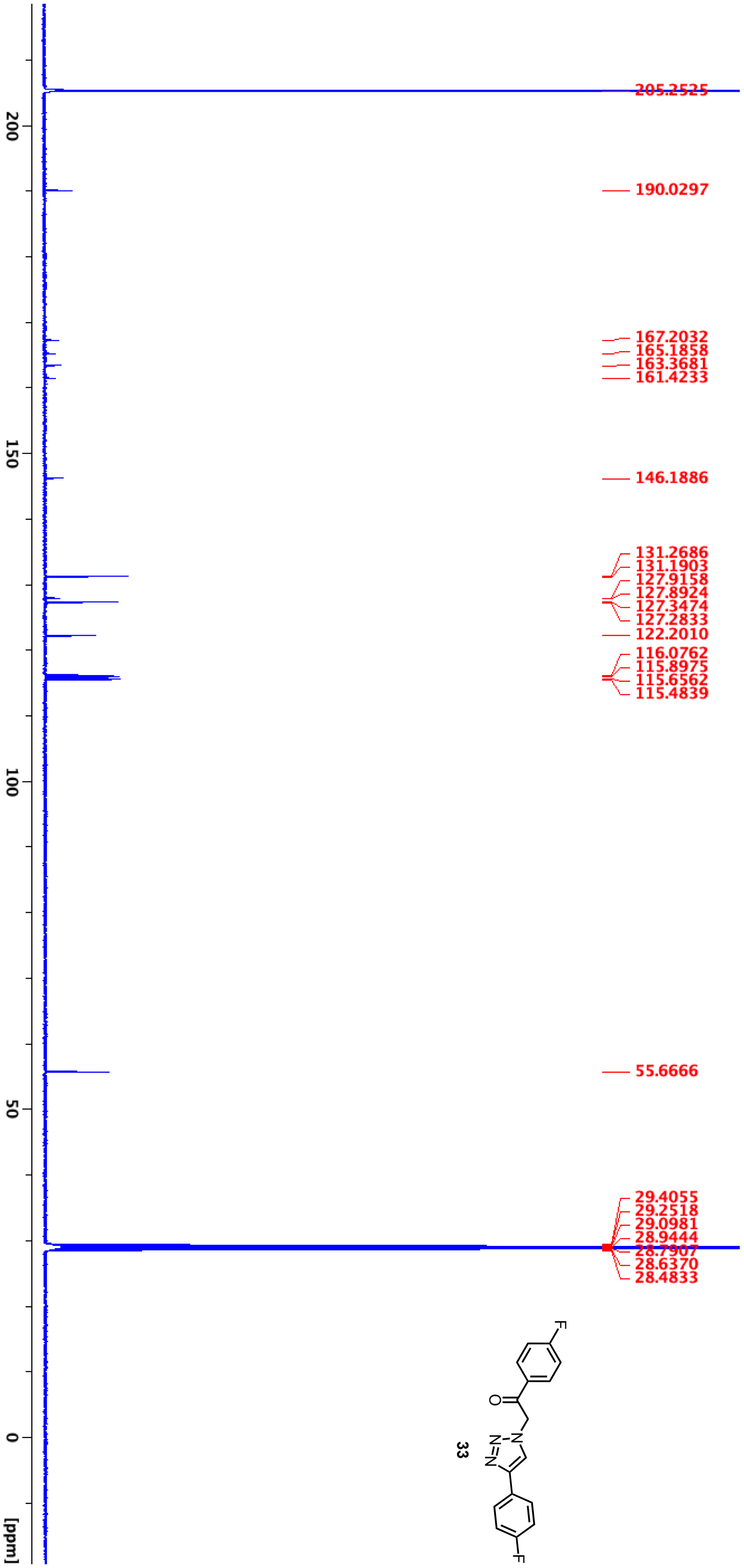
N
N
F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127.3474
127.2833
122.2010
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115.8975
115.6562
115.4839
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29.4055
29.2518
29.0981
28.9444
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200
150
100
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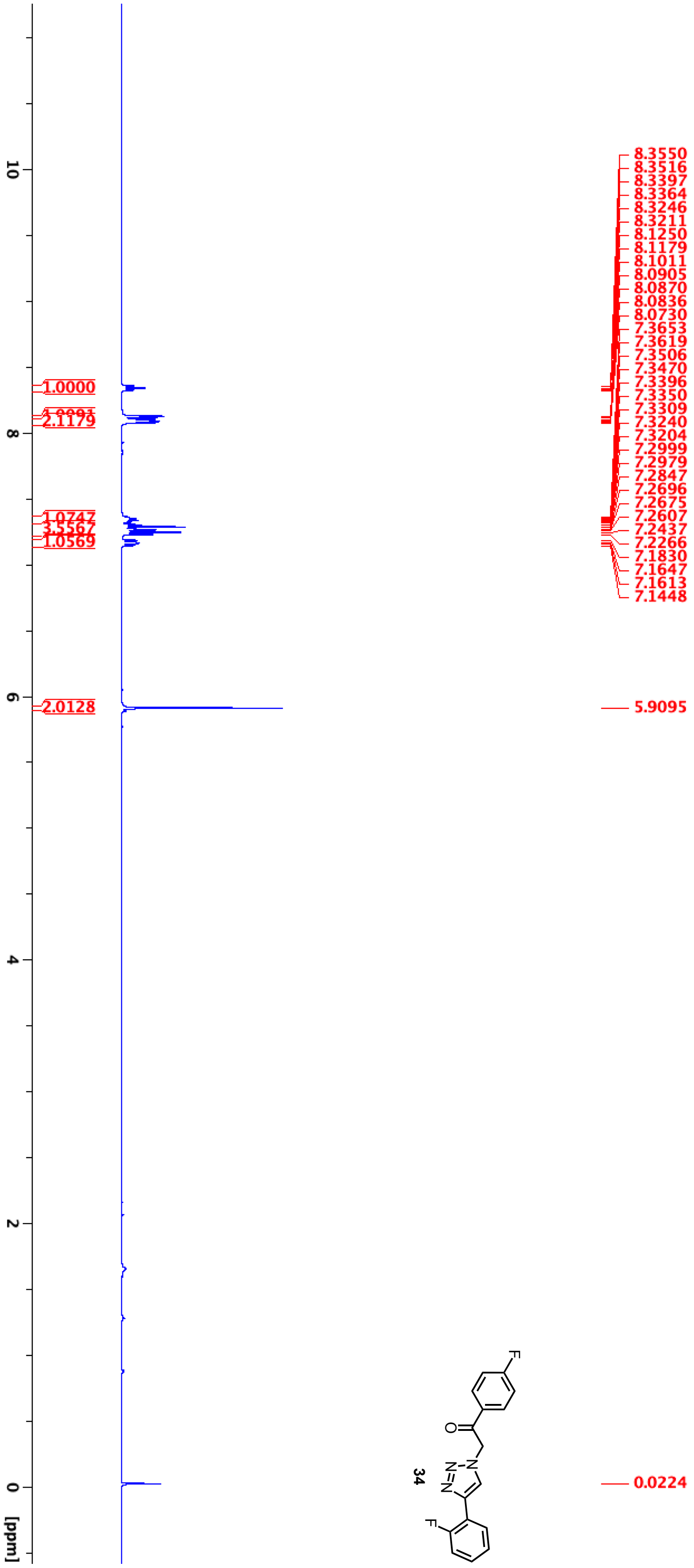
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8.3397
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8.3211
8.1250
8.1179
8.1011
8.0905
8.0870
8.0836
8.0730
7.3653
7.3619
7.3506
7.3470
7.3396
7.3350
7.3309
7.3240
7.3204
7.2999
7.2979
7.2847
7.2696
7.2675
7.2607
7.2437
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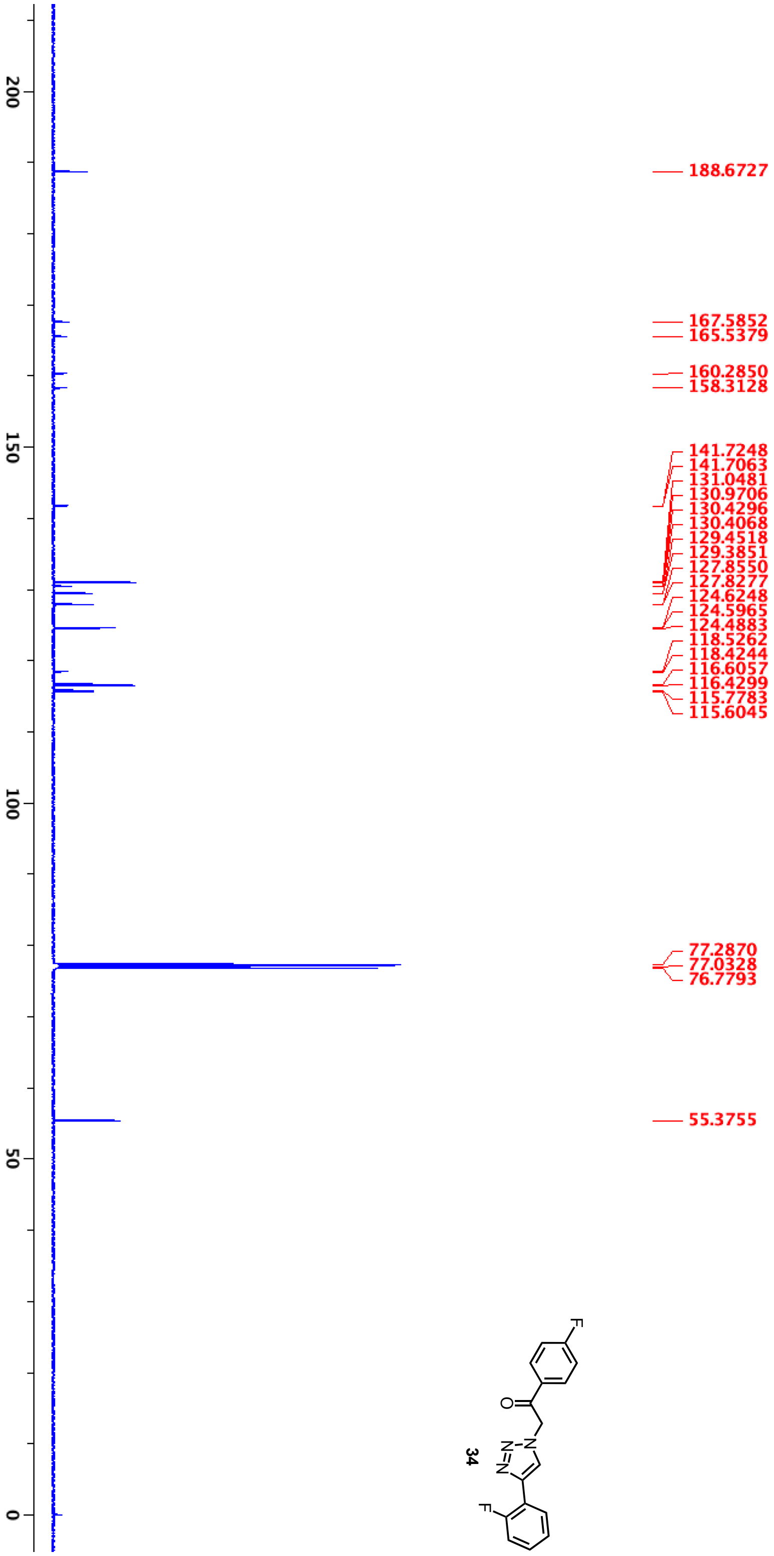
34



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0
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130.4068
129.4518
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127.8277
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124.5965
124.4883
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76.7793
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O
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N
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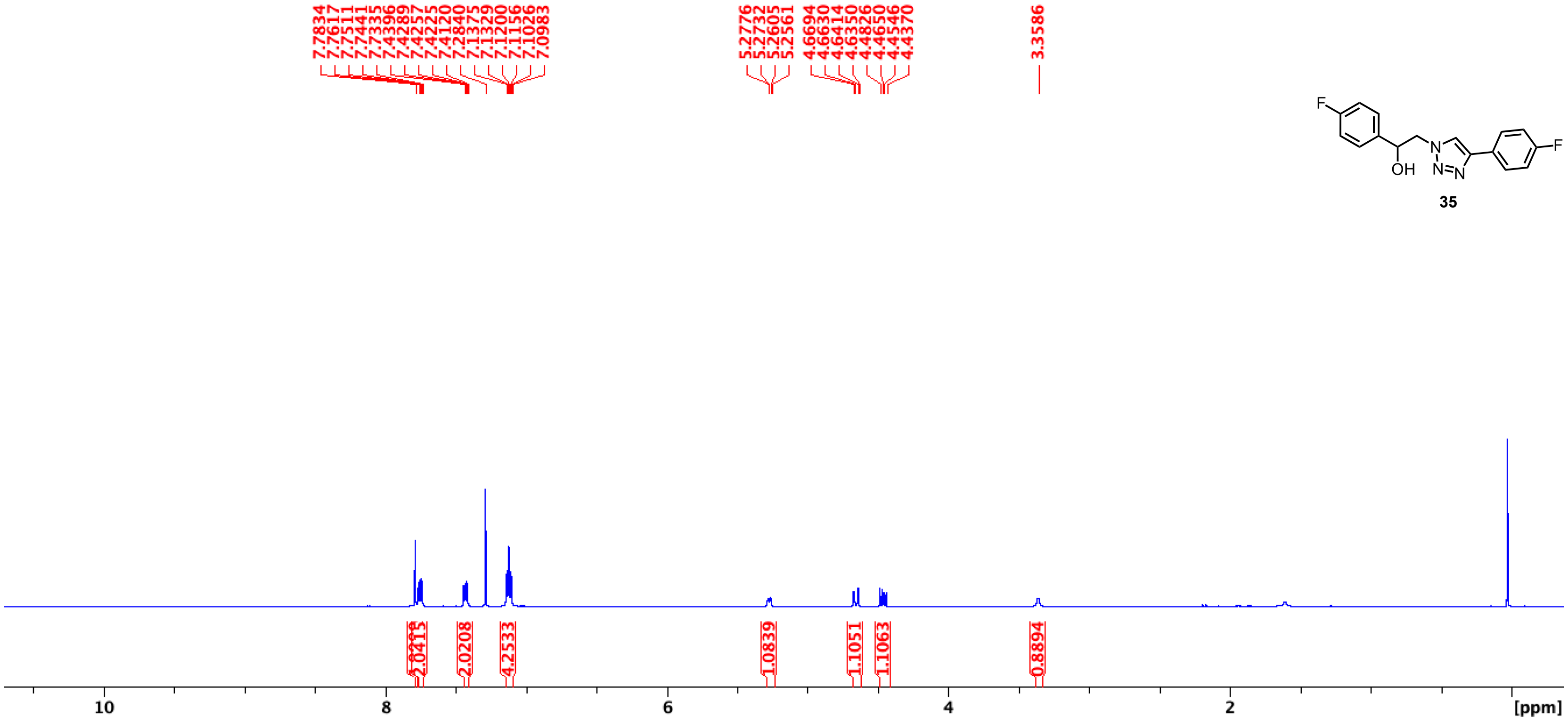
F

34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7.1375
7.1329
7.1200
7.1156
7.1026
7.0983
5.2776
5.2732
5.2605
5.2561
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4.6630
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4.6350
4.4826
4.4650
4.4546
4.4370
3.3586
F
OH
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N
N
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2
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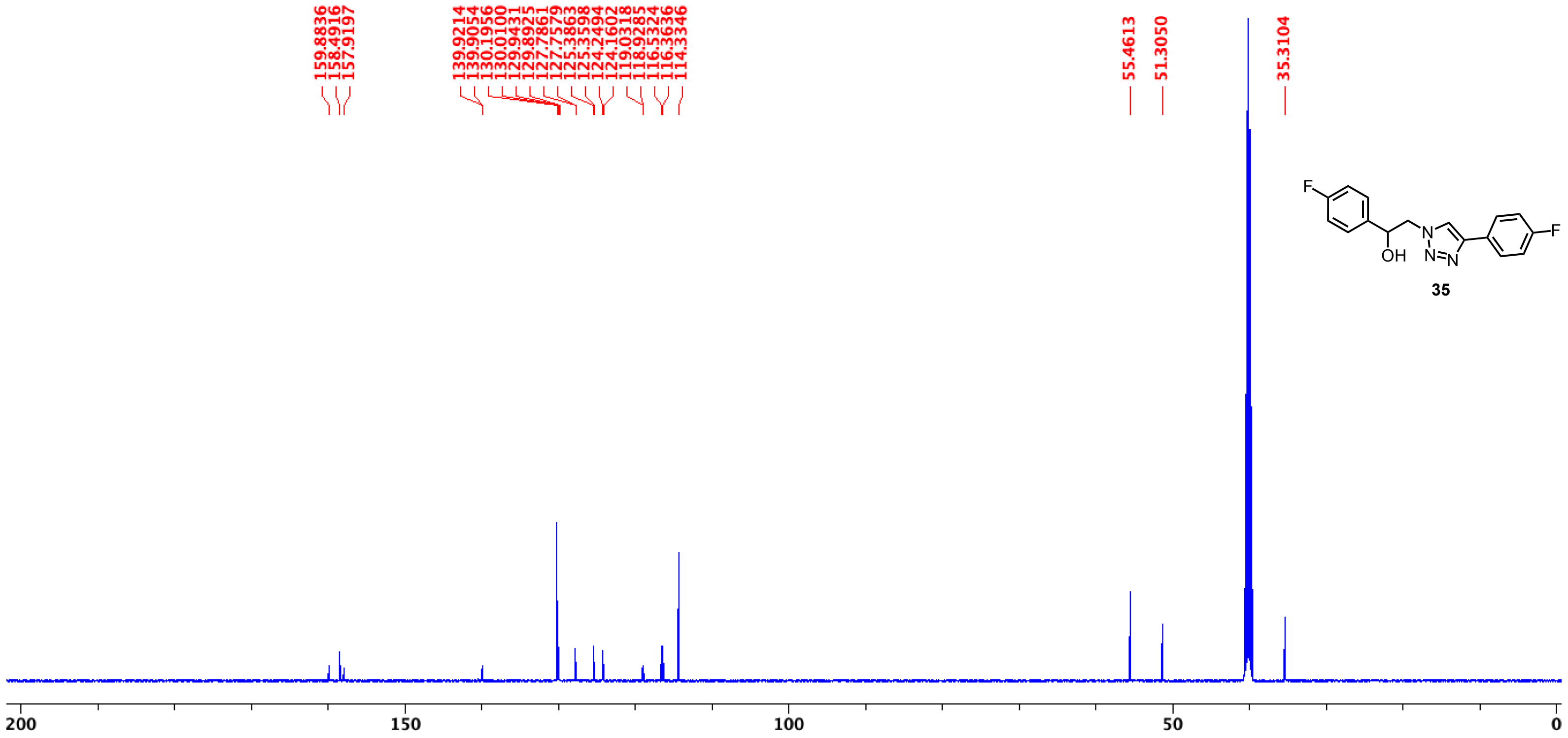
35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124.2494
124.1602
119.0318
118.9285
116.5324
116.3636
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51.3050
35.3104
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N
F
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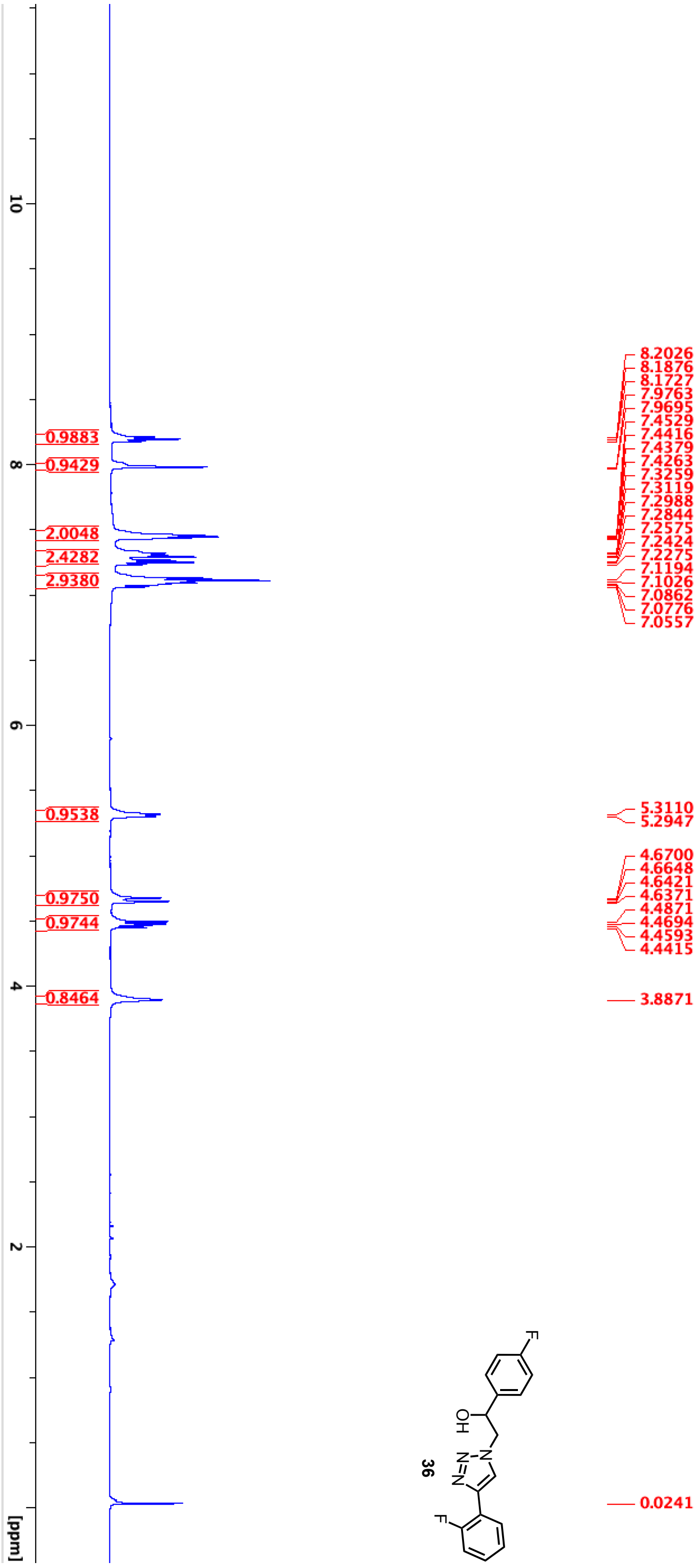
0

35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0.9744
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8.1727
7.9763
7.9695
7.4529
7.4416
7.4379
7.4263
7.3259
7.3119
7.2988
7.2844
7.2575
7.2424
7.2275
7.1194
7.1026
7.0862
7.0776
7.0557
5.3110
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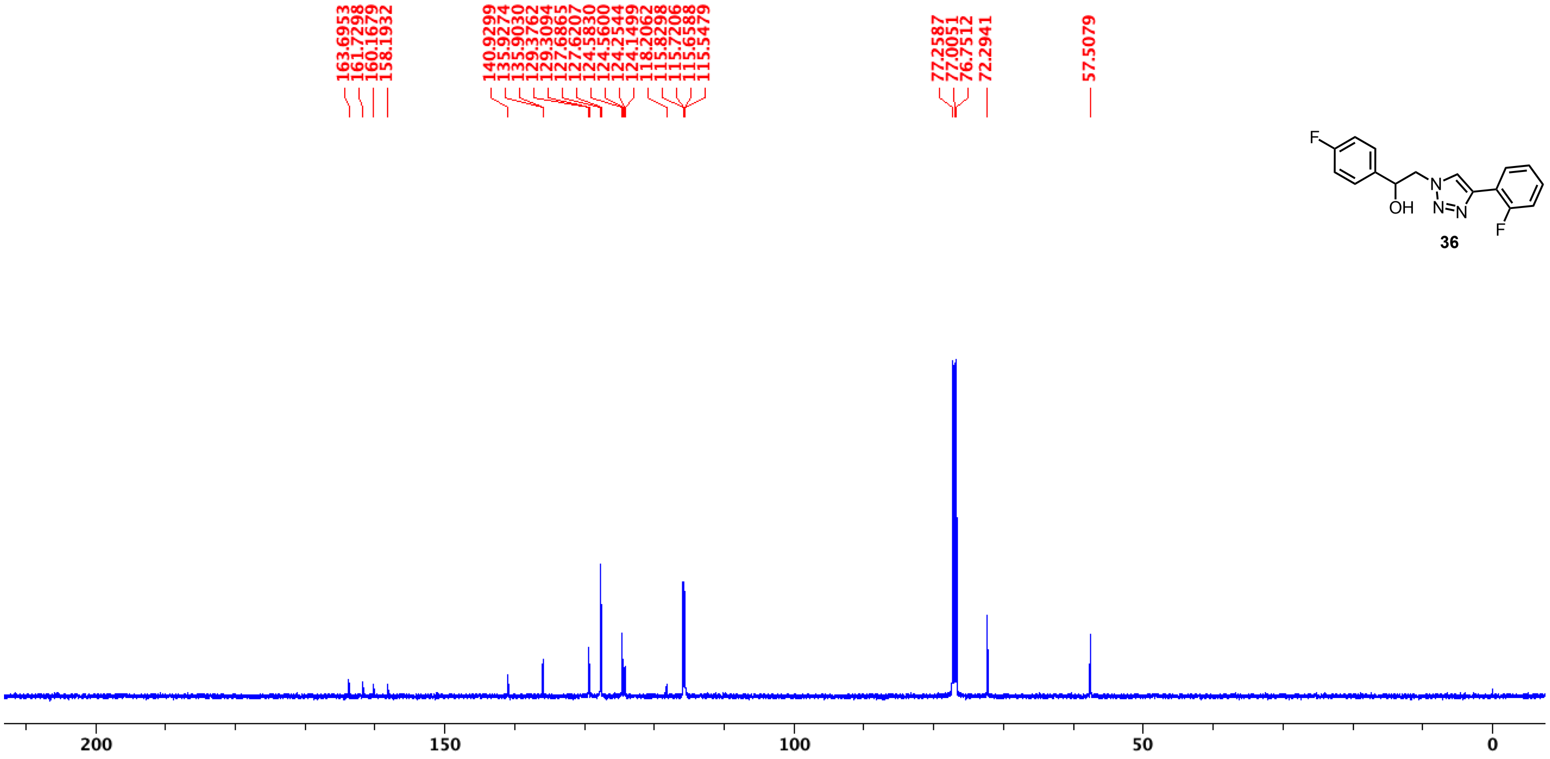
F

36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124.5600
124.2544
124.1499
118.2062
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115.7206
115.6588
115.5479
77.2587
77.0051
76.7512
72.2941
57.5079
200
150
100
50
0

F
OH
N
N
N
F

36