Supporting Information

Efficient copper-catalyzed domino synthesis of tetrazoloisoquinolines

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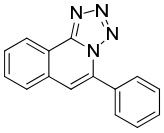
General experimental procedures

All reactions were carried out under nitrogen atmosphere. Proton and carbon magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded using tetramethylsilane (TMS) in the solvent of $CDCl_3$ as the internal standard (^{1}H NMR: TMS at 0.00 ppm, $CDCl_3$ at 7.26 ppm; ^{13}C NMR: $CDCl_3$ at 77.26 ppm).

General procedure for synthesis of compounds 3a-t

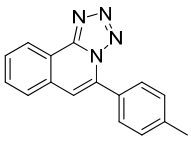
Substituted 5-(2-halophenyl)-1*H*-tetrazole (**1)** (0.25 mmol), alkynes (**2)** (0.5 mmol), CuI (0.025 mmol, 5 mg), NaOAc (0.5 mmol, 41 mg) or K_2CO_3 (0.5 mmol, 69 mg) (see Table 2) and DMSO (2.5 mL) were added to a round bottom flask with a magnetic stirrer. The mixture was allowed to stir under nitrogen atmosphere at 100 ^{o}C for 24 h. After completion of the reaction, the resulting solution was cooled to room temperature, and the solution was removed with the aid of a rotary evaporator. The residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (3:1) as eluent to provide the desired product (**3)**.

Characterization data of compounds 3a-t



3a

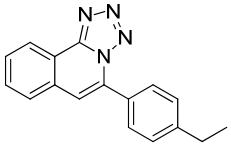
3a.[1] Eluent: petroleum ether/ethyl acetate (3:1). 5-Phenyltetrazolo[5,1-*a*]isoquinoline (54 mg, 88%) using 5-(2-bromophenyl)-1*H*-tetrazole (**1a**); (44 mg, 72%) using 5-(2-chorophenyl)-1*H*-tetrazole (**1g).** Light yellow solid, mp 216-219 ^{o}C (lit.[1] 210-211 ^{o}C). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.81 (d, 1H, *J* = 6.9 Hz), 8.02 – 7.94 (m, 3H), 7.89-7.81 (m, 2H), 7.60- 7.56 (m, 3H), 7.49 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.9, 135.4, 132.5, 131.9, 131.4, 130.7, 129.6, 129.4, 129.1, 127.7, 125.4, 119.3, 116.6. ESI-MS: $[M+H]^+$ m/z 247.2.



3b

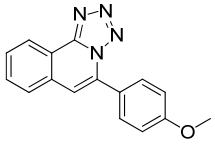
3b.[1] Eluent: petroleum ether/ethyl acetate (3:1). 5-(*p*-Tolyl)tetrazolo[5,1-a]isoquinoline (54 mg, 82%). Light yellow solid, mp 213-215

^{o}C (lit.[1] 210-211 ^{o}C). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.79 (d, 1H, *J* = 7.2 Hz), 7.94-7.78 (m, 5H), 7.44 (s, 1H), 7.40 (s, 1H), 7.37 (s, 1H), 2.47 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.9, 141.0, 135.4, 132.5, 131.9, 129.8, 129.3, 129.2, 128.5, 127.6, 125.3, 119.1, 116.1, 21.8. ESI-MS: $[M+H]^+$ m/z 261.1.



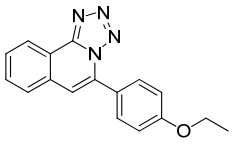
3c

3c. Eluent: petroleum ether/ethyl acetate (3:1). 5-(4-Ethylphenyl)tetrazolo[5,1-a]isoquinoline (60 mg, 87%) using 5-(2-bromophenyl)-1*H*-tetrazole (**1a**); (43 mg, 63%) using 5-(2-chorophenyl)-1*H*-tetrazole (**1g**). Light yellow solid, mp 134-136 ^{o}C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.77 (td, 1H, *J* = 8.1 Hz, *J* = 1.7 Hz), 8.92–7.90 (m, 3H), 7.84 – 7.74 (m, 2H), 7.44 (s, 1H), 7.42 (s, 1H), 7.39 (s, 1H), 2.76 (q, 2H, *J* = 7.6 Hz), 1.32 (t, 3H, *J* = 7.6 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.8, 147.3, 135.4, 132.5, 131.9, 129.3, 128.7，128.6, 127.6, 125.3, 119.1, 116.1, 29.0, 15.6. HR-MS (ESI): $[M+H]^+$ m/z calcd for ($C_{17}H_{14}N_4$+H^+) 275.1297, found 275.1293.



3d

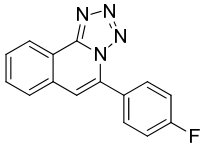
3d.[1] Eluent: petroleum ether/ethyl acetate (3:1). 5-(4-Methoxyphenyl)tetrazolo[5,1-*a*]isoquinoline (62 mg, 90%) Light yellow solid, mp 198-200 ^{o}C (lit.[1] 195-196 ^{o}C) . ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.78 (d, 1H, *J* = 7.2 Hz), 7.99 (s, 1H), 7.96 (s, 1H), 7.92 (d, 1H, *J* = 7.6 Hz), 7.83-7.77 (m, 2H), 7.42 (s, 1h), 7.11 (s, 1h), 7.08 (s, 1h), 3.91 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.5, 148.9, 135.2, 132.6, 131.9, 130.9, 129.2, 127.5, 125.4, 123.4, 119.0, 115.6, 114.5, 55.7. ESI-MS: $[M+H]^+$ m/z 277.1.



3e

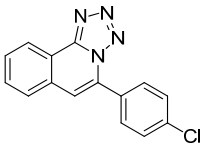
3e. Eluent: petroleum ether/ethyl acetate (3:1). 5-(4-Ethoxyphenyl)tetrazolo[5,1-a]isoquinoline (63 mg, 86%) using

5-(2-bromophenyl)-1*H*-tetrazole (**1a**); (51 mg, 68%) using 5-(2-chorophenyl)-1*H*-tetrazole (**1g**). Light yellow solid, mp 171-173 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.76 (dd, 1H, *J* = 8.1 Hz, *J* = 1.2 Hz), 7,96-7.89 (m, 3H), 7.83-7.73 (m, 2H), 7.41 (s, 1H), 7.08 (s, 1H), 7.05 (s, 1H), 4,13 (q, 2H, *J* = 6.9 Hz), 1.47 (t, 3H, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.9, 148.9, 135.2, 132.6, 131.9, 130.8, 129.2, 127.5, 125.3, 123.4, 118.9, 115.4, 114.9, 63.9, 15.0. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{17}H_{14}N_4O+Na^+$) 313.1065, found 313.1058.



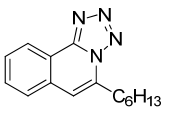
3f

3f. Eluent: petroleum ether/ethyl acetate (3:1). 5-(4-Fluorophenyl)tetrazolo[5,1-*a*]isoquinoline (62 mg ,94%). Light yellow solid, mp 243-245 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.81 (d, 1H, *J* = 6.9 Hz), 7.86-7.83 (m, 3H), 7.86-7.836 (m, 2H), 7.47 (s, 1H), 7.30-7.28 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.2 (*J* = 254.0 Hz), 148.9, 134.3, 132.4, 132.0, 131.6 (*J* = 8.6 Hz), 129.7, 127.7, 125.5, 119.3, 116.5, 116.4, 116.3. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{15}H_9FN_4+Na^+$) 287.0709, found 287.0698.



3g

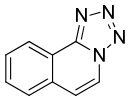
3g. Eluent: petroleum ether/ethyl acetate (3:1). 5-(4-Chlorophenyl)tetrazolo[5,1-*a*]isoquinoline (65 mg, 93%). Light yellow solid, mp 236-238 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.81 (d, 1H, *J* = 6.9 Hz), 7.98-7.94 (m, 3H), 7.89-7.81 (m, 2H), 7.89 (s, 1H), 7.56 (s, 1H), 7.48 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.9, 136.9, 134.2, 133.9, 132.3, 132.1, 130.7, 129.8, 129.4, 127.8, 125.5, 119.4, 116.7. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{15}H_9ClN_4+Na^+$) 303.0413, found 313.0404.



3h

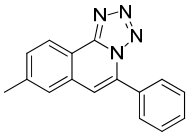
3h. Eluent: petroleum ether/ethyl acetate (3:1). 5-Hexyltetrazolo[5,1-a]isoquinoline

(53 mg, 83%) using 5-(2-bromophenyl)-1*H*-tetrazole (**1a**); (23 mg, 36%) using 5-(2-chorophenyl)-1*H*-tetrazole (**1g**). White solid, mp 101-103 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.66 (dd, 1H, *J* = 7.9 Hz, *J* = 0.7 Hz), 7.81-7.66 (m, 3H), 7.12 (s, 1H), 3.24 (t, 2H, *J* = 7.7 Hz), 1.94-1.84 (m, 2H), 1.47-1.21 (m, 6H), 0.86 (t, 3H, *J* = 7.1 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.2, 136.3, 132.3, 131.6, 128.7, 127.0, 125.0, 118.7, 111.5, 31.6, 31.0, 29.0, 26.9, 22.7, 14.2. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{15}H_{18}N_4+Na^+$) 277.1429, found 277.1422.



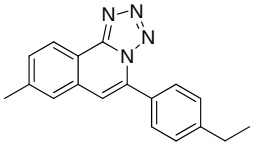
3i

3i.[2] Eluent: petroleum ether/ethyl acetate (3:1).Tetrazolo[5,1-*a*]isoquinoline (23 mg, 52%). White solid, mp 139-141 °C (lit.[2] 141-142 °C). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.78-8.74 (m, 1H), 8.56 (d, 1H, *J* = 7.2 Hz), 7.95-7.92 (m, 1H), 7.45 (d, 1H, *J* = 7.2 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.2, 131.9, 130.0, 127.9, 125.3, 121.3, 120.0, 117.9. ESI-MS: $[M+H]^+$ m/z 171.2.



3j

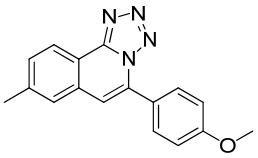
3j. Eluent: petroleum ether/ethyl acetate (3:1). 8-Methyl-5-phenyltetrazolo[5,1-*a*]isoquinoline (57mg, 88%) using 5-(2-bromo-4-methylphenyl)-1*H*-tetrazole (**1b**); (43mg, 66%) using 5-(2-chloro-4-methylphenyl)-1*H*-tetrazole (**1h**). Light yellow solid, mp 189-191 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.59 (d, 1H, *J* = 8.3 Hz), 7,97-7.94 (m, 2H), 7.65 (s, 1H), 7.57-7.52 (m, 4H), 7.35 (s, 1H), 2.56 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.7, 142.6, 135.1, 132.5, 131.4, 131.1, 130.5, 129.2, 128.9, 127.3, 124.9, 116.8, 116.3, 22.1. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{16}H_{12}N_4+Na^+$) 283.0960, found 283.0950.



3k

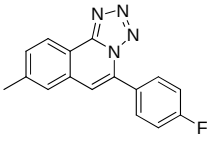
3k. Eluent: petroleum ether/ethyl acetate (3:1).

5-(4-Ethylphenyl)-8-methyltetrazolo[5,1-a]isoquinoline (61 mg, 85%) using 5-(2-bromo-4-methylphenyl)-1*H*-tetrazole (**1b**); (41 mg, 7%) using 5-(2-chloro-4-methylphenyl)-1*H*-tetrazole (**1h**). Light yellow solid, mp 158-160 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.59 (d, 1H, *J* = 8.3 Hz), 7.89 (s, 1H), 7.87 (s, 1H), 7.63 (s, 1H), 7.55 (d, 1H, *J* = 8.3 Hz), 7.39 (s, 1H), 7.36 (s, 1H), 7.33 (s, 1H), 2.75(q, 2H, *J* = 7.6 Hz), 2.56(s, 3H), 1.31(t, 3H, *J* = 7.6 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.7, 147.1, 142.5, 135.2, 132.6, 130.9, 129.2, 128.7, 128.5, 127.2, 124.9, 116.7, 115.8, 28.9,22.1, 15.5. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{18}H_{16}N_4$+Na^+) 311.1273, found 311.1264.



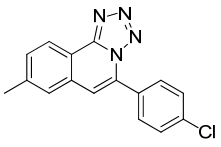
3l

3l. Eluent: petroleum ether/ethyl acetate (3:1). 5-(4-Methoxyphenyl)-8-methyltetrazolo[5,1-*a*]isoquinoline (63 mg, 86%). Light yellow solid, mp 208-210 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.62 (d, 1H, *J* = 8.6 Hz), 7.95 (s, 1H), 7.93 (s, 1H), 7.93 (s, 1H), 7.66 (s, 1H), 7.57 (d, 1H, *J* = 8.3 Hz), 7.32 (s, 1H), 7.08 (s, 1H), 7.06 (s, 1H), 3.90 (s, 3H), 2.58 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.4, 148.8, 142.5, 135.1, 132.8, 130.8, 127.2, 125.1, 123.8, 116.7, 115.3, 114.5, 55.7, 22.2. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{17}H_{14}N_4O$+Na^+) 313.1065, found 313.1054.



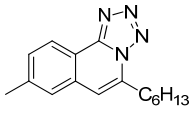
3m

3m. Eluent: petroleum ether/ethyl acetate (3:1). 5-(4-Fluorophenyl)-8-methyltetrazolo[5,1-*a*]isoquinoline (63 mg, 91%). Light yellow solid, mp 235-237 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.67 (d, 1H, *J* = 7.6 Hz), 8.01-7.99 (m, 2H), 7.72 (s, 1H), 7.63 (d, 1H, *J* = 8.3 Hz), 7.37 (s, 1H), 7.29-7.26 (m, 2H), 2.61 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.1 (*J* = 254.1 Hz), 148.9, 142.8, 134.2, 132.6, 131.5, 131.4, 131.3, 127.4, 125.3, 117.0, 116.3, 116.2, 22.2. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{16}H_{11}FN_4$+Na^+) 301.0865, found 301.0859.



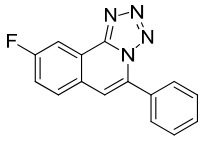
3n

3n. Eluent: petroleum ether/ethyl acetate (3:1). 5-(4-Chlorophenyl)-8-methyltetrazolo[5,1-*a*]isoquinoline (68 mg, 93%). Light yellow solid, mp 219-221 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.66 (d, 1H, *J* = 8.3 Hz), 7.96 (s, 1H), 7.95 (s, 1H), 7.72 (s, 1H), 7.63 (d, 1H, *J* = 8.3 Hz), 7.57 (s, 1H), 7.54 (s, 1H), 7.40 (s, 1H), 2.61 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.9, 142.8, 136.8, 134.1, 133.9, 132.5, 131.5, 130.6, 129.4, 127.5, 125.3, 117.1, 116.5, 22.3. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{16}H_{11}ClN_4$+Na^+) 317.0570, found 317.0560.



3o

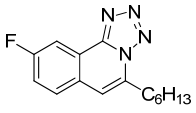
3o. Eluent: petroleum ether/ethyl acetate (3:1). 5-Hexyl-8-methyltetrazolo[5,1-*a*]isoquinoline **(**59 mg, 88%) using 5-(2-bromo-4-methylphenyl)-1H-tetrazole (**1b**); (22 mg, 32%) using 5-(2-chloro-4-methylphenyl)-1*H*-tetrazole (**1h**). White solid, mp 86-88 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.47 (d, 1H, *J* = 7.9 Hz), 7.51 (s, 1H), 7.44 (dd, 1H, *J* = 8.1 Hz, *J* = 1.2 Hz), 6.97 (s, 1H), 3.16 (t, 3H, *J* = 7.6 Hz), 1.88-1.77 (m, 2H), 1.39-1.31 (m, 6H), 0.81 (t, 3H, *J* = 7.1 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.2, 142.2, 136.2, 132.5, 130.3, 126.7, 124.9, 116.5, 114.3, 31.6, 30.9, 29.1, 26.9, 22.7, 22.1, 14.2. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{16}H_{20}N_4$+Na^+) 291.1586, found 291.1573.



3p

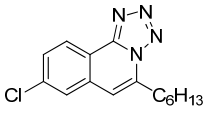
3p. Eluent: petroleum ether/ethyl acetate (3:1). 9-Fluoro-5-phenyltetrazolo[5,1-*a*]isoquinoline (48 mg, 72%). Light yellow solid, mp 229-231 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.45 (dd, 1H, *J* = 8.4 Hz, *J* = 2.6 Hz), 8.00-7.95 (m, 3H), 7.63-7.56 (m, 4H), 7.48 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 162.6 (*J* = 252.1 Hz), 148.5, 134.8, 131.1, 130.8, 130.3 (*J* = 9.4 Hz), 129.4, 129.2, 121.5 (*J* = 23.8 Hz), 120.8 (*J* = 10.1 Hz), 115.9, 111.2, 110.8. HR-MS (ESI): $[M+Na]^+$

m/z calcd for ($C_{15}H_9FN_4$+Na^+) 287.0709, found 287.0702.



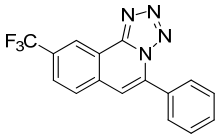
3q,

3q. Eluent: petroleum ether/ethyl acetate (3:1). 9-Fluoro-5-hexyltetrazolo[5,1-*a*]isoquinoline **(**60 mg, 88%).White solid, mp 113-115 ^oC. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.35 (dd, 1H, *J* = 8.3 Hz, *J* = 2.6 Hz), 7.87 (q, 1H, *J* = 3.4 Hz), 7.54 (td, 1H *J* = 8.6 Hz), 7.17 (s, 1H), 3.28 (t, 2H, *J* = 7.7 Hz), 1.99-1.88 (m, 2H,), 1.52-1.31 (m, 6H), 0.91 (t, 3H, *J* = 7.1 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz) δ162.1 (*J* = 252.4 Hz), 147.9, 135.8, 129.6 (*J* = 9.4 Hz), 120.7 (*J* = 23.8 Hz), 120.2 (*J* = 10.1 Hz), 113.9, 110.8, 110.5, 31.6, 30.9, 29.1, 26.9, 22.7, 14.2. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{15}H_{17}FN_4$+Na^+) 295.1335, found 295.1328.



3r

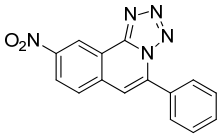
3r. Eluent: petroleum ether/ethyl acetate (3:1). 8-Chloro-5-hexyltetrazolo[5,1-*a*]isoquinoline (36 mg, 49%).White solid, mp 129-131 ^oC. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.67 (d, 1H, *J* = 8.3 Hz), 7.85 (d, 1H, *J* = 2.1 Hz), 7.71 (dd, 1H, *J* = 8.6 Hz, *J* = 2.1 Hz), 7.09 (s, 1H), 3.30 (t, 3H, *J* = 7.6 Hz), 1.96-1.91 (m, 2H), 1.51-1.47 (m, 2H), 1.39-1.32 (m, 4H), 0.91 (t, 3H, *J* = 7.2 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.0, 138.0, 137.9, 133.5, 129.5, 126.8, 126.4, 117.2, 113.4, 31.6, 31.1, 29.1, 26.9, 22.7, 14.3. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{15}H_{17}ClN_4$+Na^+) 311.1039, found 311.1034.



3s

3s. Eluent: petroleum ether/ethyl acetate (3:1). 5-Phenyl-9-(trifluoromethyl)tetrazolo[5,1-*a*]isoquinoline (62 mg, 79%). Light yellow solid, mp 239-241 ^oC. ^1H NMR ($CDCl_3$, 300 MHz) δ 9.13 (s, 1H), 8.09-8.01 (m, 4H), 7.64-7.62 (m, 3H), 7.55 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.6, 137.5, 134.5, 131.3, 130.7, 129.5, 129.3, 128.9 (d, *J* = 39.4 Hz), 128.6, 128.1, 123.7 (q, *J* = 273.1 Hz), 123.1, 119.1, 115.6. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{16}H_9F_3N_4$+Na^+)

337.0677, found 337.0668.



3t

3t. Eluent: petroleum ether/ethyl acetate (3:1). 9-Nitro-5-phenyltetrazolo[5,1-*a*]isoquinoline **(**46 mg, 63%) using 5-(2-bromo-5-nitrophenyl)-1*H*-tetrazole (**1f**); (42 mg, 56%) using 5-(2-chloro-5-nitrophenyl)-1*H*-tetrazole (**1i**). Yellow solid, mp 231-233 ^{o}C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.68 (d, 1H, *J* = 2.1 Hz), 8.64 (dd, 1H, *J* = 8.9 Hz, *J* = 2.1 Hz), 8.14 (d, 1H, *J* = 8.9 Hz), 8.05-8.04 (m, 2H), 7.65-7.63(m, 2H), 7.59(s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.7, 147.5, 138.8, 136.2, 131.7, 130.4, 129.5, 129.4, 129.3, 125.9, 121.6, 119.3, 115.2. HR-MS (ESI): $[M+Na]^+$ m/z calcd for ($C_{15}H_9N_5O_2$+Na^+) 314.0654, found 314.0642.

Crystal preparation and X-ray diffraction analysis of compound 3h

Crystal preparation of compound 3h. Compound **3h** (30 mg) was dissolved in 10 mL of $CHCl_3$, and it was crystallized to give crystal as colorless triclinic after the solvent was slowly volatilized in 2 days at room temperature (~ 25 °C). *The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number (CCDC 913654).*

X-Ray diffraction analysis of compound 3h. The low temperature (103.6°K) single-crystal X-ray experiments were performed on a X calibur, Eos, Gemini diffractometer equipped with graphite monochromatized Mo K_α radiation. Unit cell was obtained and refined by 4129 reflections with 3.4° < θ < 29.1°. No decay was observed except the statistic fluctuation in the data collection. Raw intensities were corrected for Lorentz and polarization effects. Direct phase determination yielded the positions of all non-hydrogen atoms. All non-hydrogen atoms were subjected to anisotropic refinement. All hydrogen atoms were generated geometrically with C-H bonds of 0.93-0.96 Å according to criteria described in the SHELXTL manual (Bruker, 1997). They were included in the refinement with $U_{iso}(H) = 1.2U_{eq}$ (for C) and 1.5 U_{eq} (for methyl). The final full-matric least-square refinement on F^2 converged with *R*1 =

0.0532 and *wR*2 = 0.1358 for 2588 observed reflections [I ≥ 2σ(I)]. The final difference electron density map shows no features. Details of crystal parameters, data collection and structure refinement are given in Table 1.

Data collection was controlled by CrysAlis^{Pro} (Oxford, 2011).[3] Computations were performed using the SHELXTL NT ver. 5.10 program package (Bruker, 1997)[4] on an IBM PC computer. Analytic expressions of atomic scattering factors were employed, and anomalous dispersion corrections were incorporated (*International Tables for X-ray Crystallography*, 1989).[5] Crystal drawings were produced with XP (Bruker, 1998).

Table 1 Crystal data and structure refinement for compound **3h**

Sample code	**EXP-1015**
Molecular formula	$C_{15}H_{18}N_4$
Molecular weight	254.33
Temperature	103.6 K
Crystal system	triclinic
Space group	*P*-1
Unit cell parameters	*a* = 8.2705(16) Å α = 82.682°(14) *b* = 9.4515(14) Å β = 64.188°(19) *c* = 9.4618(19) Å γ = 85.910°(14)
Density (calcd)	1.279 g/cm^3
Volume/A^3	660.3(2)
Z	2
μ / mm^{-1}	0.079 mm^{-1}
F(000)	272
Crystal size	0.80 × 0.30 × 0.10 mm
2Θ range for data collection	6.82 to 52°
Index range	-10 ≤ *h* ≤ 9, -11≤ *k* ≤ 11, -11 ≤ *l* ≤ 11;
Reflections collected	4129
Independent reflections	2588[R(int) = 0.0328 (inf-0.9Å)]
Data/restraints/parameters	2588/0/173
Goodness-of-fit on F^2	1.055
Final R indexes [I>2 σ (I) i.e. Fo>4 σ (Fo)]	R1 = 0.0532, wR2 = 0.1358
Final R indexes [all data]	R1 = 0.0674, wR2 = 0.1483
Largest diff. peak/hole / e Å^{-3}	0.286/-0.341
Flack Parameters	N
Completeness	0.997

Table 2 Fractional atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for compound **3h**

Atoms	*x*	*y*	*z*	$U_{eq.}$
N(1)	2815.1(17)	5848.5(13)	1978.9(14)	20.7(13)
C(9)	2311(2)	4765.3(16)	1382.6(18)	21.0(4)
C(1)	3549(2)	7108.9(16)	1143.4(18)	20.8(4)
C(7)	3354(2)	6341.3(16)	-1114.8(18)	21.6(4)
C(2)	3808(2)	7423.6(16)	-461.8(18)	20.5(4)
C(13)	-136(2)	-179.9(16)	2176.8(17)	22.7(4)
N(4)	3909.9(18)	7842.1(14)	2076.3(15)	25.8(4)
C(10)	1506(2)	3466.1(16)	2512.7(18)	23.9(4)
C(3)	4495(2)	8724.3(16)	-1378.3(18)	22.8(4)
C(5)	4313(2)	7870.1(17)	-3588.5(18)	24.5(4)
N(2)	2719.7(19)	5803.5(14)	3461.8(15)	25.3(4)
C(11)	1099(2)	2289.9(16)	1755.3(18)	23.5(4)
C(6)	3630(2)	6595.4(16)	-2705.5(18)	23.1(4)
N(3)	3377.2(19)	7002.2(14)	3483.1(15)	28.5(4)
C(14)	-926(2)	-1502.5(16)	3337.9(18)	25.6(4)
C(8)	2601(2)	5024.8(15)	-146.1(17)	21.2(4)
C(15)	-1518(2)	-2623.6(17)	2650(2)	31.3(4)
C(12)	345(2)	967.5(16)	2911.9(18)	23.7(4)
C(4)	4735(2)	8940.6(17)	-2919.3(18)	23.8(4)

*$U_{eq.}$ defined as one third of the trace of the orthogonalized UIJ tensor.

Table 3 Bond lengths (Å) and bond angles (°) for compound **3h**

N(1)-C(9)	1.398(2)	C(13)-C(14)	1.529(2)
N(1)-C(1)	1.363(19)	C(13)-C(12)	1.520(2)
N(1)-N(2)	1.366(18)	N(3)-N(4)	1.366(19)
C(9)-C(10)	1.502(2)	C(10)-C(11)	1.526(2)
C(9)-C(8)	1.351(2)	C(3)-C(4)	1.373(2)
C(1)-C(2)	1.432(2)	C(5)-C(6)	1.378(2)
C(1)-N(4)	1.328(2)	C(5)-C(4)	1.397(2)
C(7)-C(2)	1.410(2)	N(2)-N(3)	1.297(19)
C(7)-C(6)	1.411(2)	C(11)-C(12)	1.522(2)
C(7)-C(8)	1.449(2)	C(14)-C(15)	1.521(2)
C(2)-C(3)	1.409(2)		
C(1)-N(1)-C(9)	125.07(14)	C(3)-C(2)-C(7)	120.37(15)
C(1)-N(1)-N(2)	108.84(13)	C(12)-C(13)-C(14)	112.89(13)
N(2)-N(1)-C(9)	126.05(13)	C(1)-N(4)-N(3)	105.57(12)
N(1)-C(9)-C(10)	116.43(14)	C(9)-C(10)-C(11)	113.56(13)
C(8)-C(9)-N(1)	115.55(13)	C(4)-C(3)-C(2)	120.01(15)
C(8)-C(9)-C(10)	128.02(15)	C(6)-C(5)-C(4)	120.46(15)

N(1)-C(1)-C(2)	120.16(14)	N(3)-N(2)-N(1)	105.15(12)
N(4)-C(1)-N(1)	107.99(14)	C(12)-C(11)-C(10)	112.47(14)
N(4)-C(1)-C(2)	131.86(14)	C(5)-C(6)-C(7)	120.80(15)
C(2)-C(7)-C(6)	118.11(14)	N(2)-N(3)-N(4)	122.46(13)
C(2)-C(7)-C(8)	119.80(14)	C(15)-C(14)-C(13)	113.55(14)
C(6)-C(7)-C(8)	122.09(14)	C(9)-C(8)-C(7)	123.04(15)
C(7)-C(2)-C(1)	116.31(14)	C(13)-C(12)-C(11)	112.48(13)
C(3)-C(2)-C(1)	123.31(15)	C(3)-C(4)-C(5)	120.24(14)

Table 4 Anisotropic displacement parameters ($Å^2 \times 10^3$) for compound **3h**

Atoms	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N(1)	24.3(7)	18.9(7)	19.8(7)	-0.9(5)	-10.1(6)	-4.1(5)
C(9)	22.3(8)	15.9(8)	25.6(8)	-2.0(6)	-10.8(7)	-3.0(6)
C(1)	21.0(8)	17.9(8)	25.3(8)	-3.8(6)	-10.7(7)	-3.3(6)
C(7)	20.7(8)	20.4(8)	25.2(8)	-3.2(6)	-10.9(7)	-2.3(6)
C(2)	20.4(8)	19.5(8)	22.6(8)	-3.1(6)	-9.6(7)	-2.6(6)
C(13)	25.2(8)	21.9(9)	21.9(8)	-2.3(6)	-10.5(7)	-4.1(6)
N(4)	32.3(8)	24.2(7)	24.9(7)	-4.7(6)	-14.7(6)	-5.5(6)
C(10)	27.8(9)	21.3(9)	23.1(8)	-0.4(6)	-11.3(7)	-5.1(7)
C(3)	23.3(8)	20.1(8)	27.6(9)	-4.4(6)	-12.1(7)	-5.2(6)
C(5)	26.1(8)	27.4(9)	21.3(8)	-0.9(6)	-11.5(7)	-2.6(7)
N(2)	31.3(8)	25.6(8)	23.4(8)	-2.6(5)	-15.2(6)	-4.7(6)
C(11)	25.6(8)	21.6(9)	24.1(8)	0.0(6)	-11.3(7)	-5.4(6)
C(6)	25.4(8)	23.6(9)	22.7(8)	-4.2(6)	-11.4(7)	-4.3(7)
N(3)	35.3(8)	26.9(8)	27.9(8)	-3.5(6)	-16.8(6)	-6.7(6)
C(14)	27.3(9)	25.0(9)	24.6(8)	-2.9(7)	-10.2(7)	-7.8(7)
C(8)	24.5(8)	17.3(8)	23.6(8)	-3.1(6)	-11.2(7)	-4.4(6)
C(15)	33.7(10)	24.7(9)	38.1(10)	-6.7(7)	-15.5(8)	-8.9(7)
C(12)	26.9(8)	21.2(8)	24.6(8)	-0.8(6)	-12.1(7)	-5.8(6)
C(4)	24,4(8)	18.8(8)	26.1(8)	2.0(6)	-9.4(7)	-5.2(6)

*The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+...+2hka\times b\times U_{12}]$

Table 5 Hydrogen atom coordinates ($Å \times 10^4$) and isotropic displacement parameters ($Å^2 \times 10^3$) for compound **3h**

Atoms	*x*	*y*	*z*	$U_{eq.}$
H(13A)	957	-465	1264	27
H(13B)	-1016	221	1778	27
H(3C)	379	3751	3393	29
H(4A)	2347	3081	2963	29

H(3)	4792	9452	-930	27
H(5)	4498	8022	-4660	29
H(11A)	222	2660	1339	28
H(11B)	2216	2023	854	28
H(6)	3342	5879	-3173	28
H(14A)	-17	-1935	3687	31
H(14B)	-1973	-1206	4281	31
H(8)	2299	4311	-607	25
H(15A)	-493	-2917	1709	47
H(15B)	-2472	-2223	2360	47
H(15C)	-1970	-3454	3437	47
H(12A)	1243	573	3292	28
H(12B)	-743	1242	3836	28
H(4)	5189	9821	-3533	29

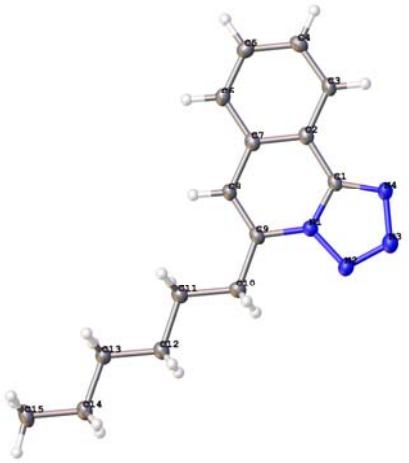


Figure 1. ORTEP drawing of $C_{15}H_{18}N_4$ with 50% probability ellipsoids, showing the atomic numbering scheme.

References

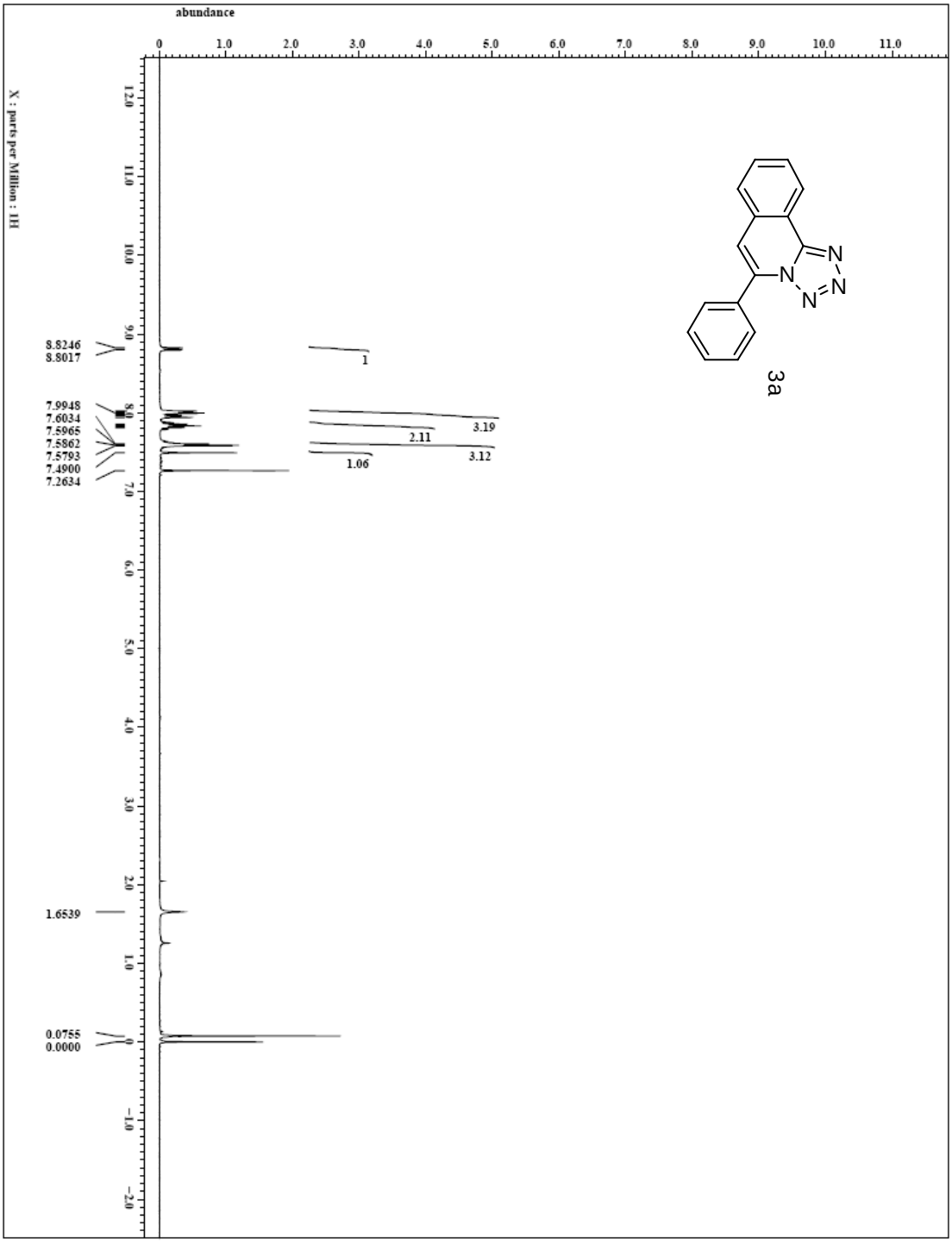
1 C.-W. Tsai, S.-C. Yang, Y.-M. Liu, M.-J. Wu. *Tetrahedron* 2009, **65**, 8367.

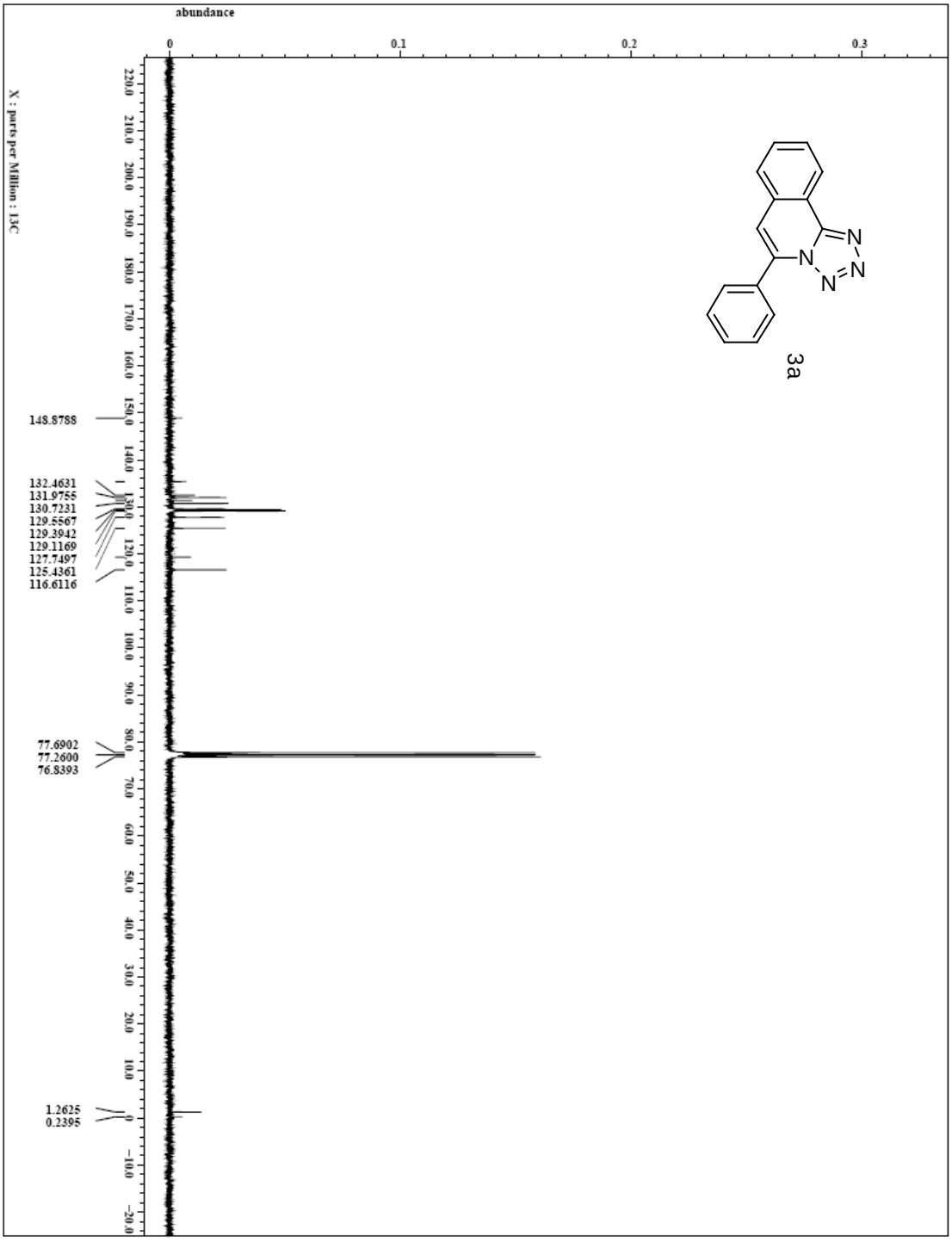
2 J. M. Keith. *J. Org. Chem.* 2006, **71**, 9540.

3 Oxford (2011) CrysAlis^{Pro}, Version 1.171.35.11, Oxford Diffraction Ltd.

4 Bruker. (1997) SHELXTL. Structure Determination Programs, Version 5.10, Bruker AXS Inc.,6300 Enterprise Lane, Madison, WI 53719-1173, USA.

5 *International Tables for X-ray Crystallography*: (1989) Vol. C (Kluwer Academic Publishers, Dordrecht) Tables 4.2.6.8 and 6.1.1.4.

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0.3
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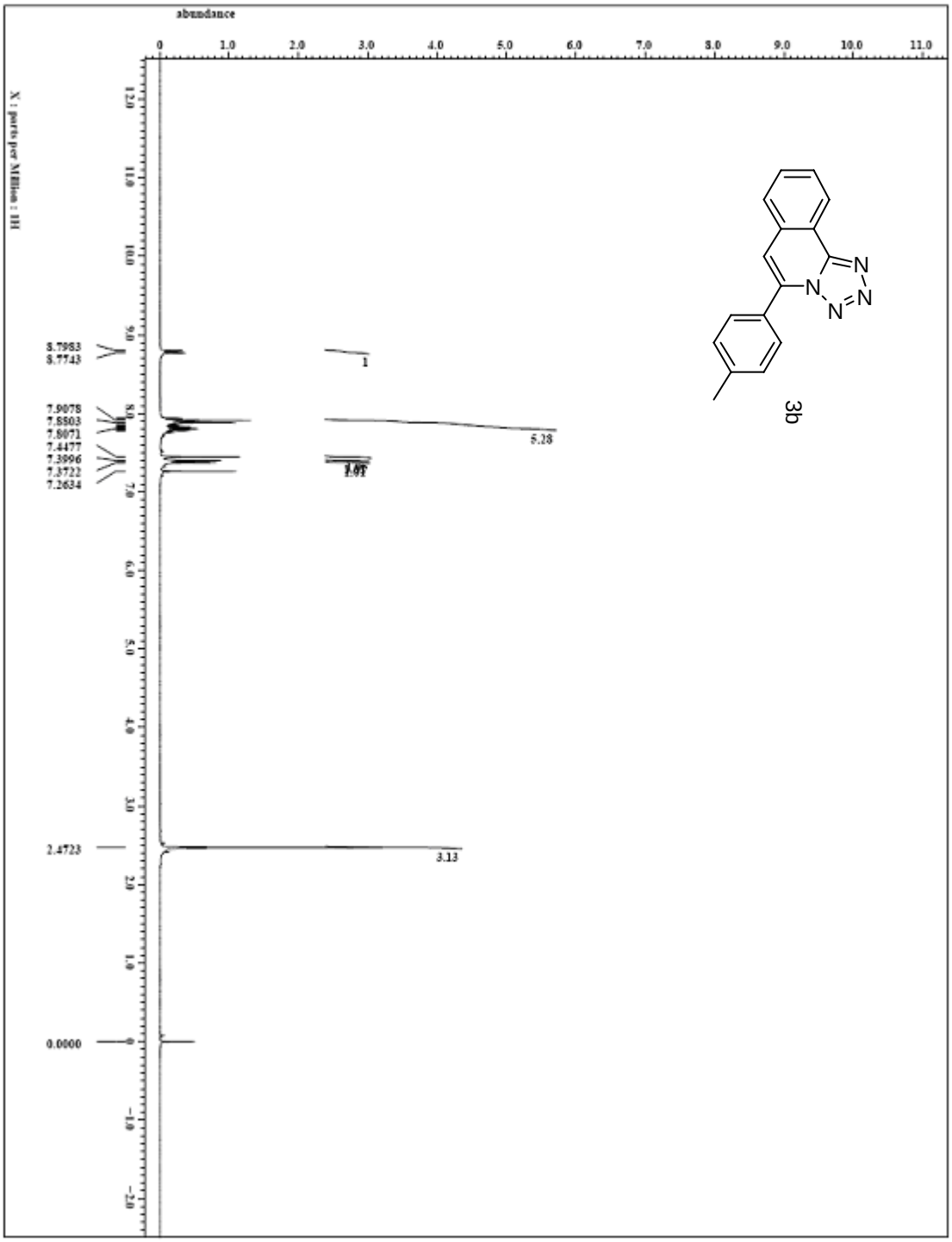

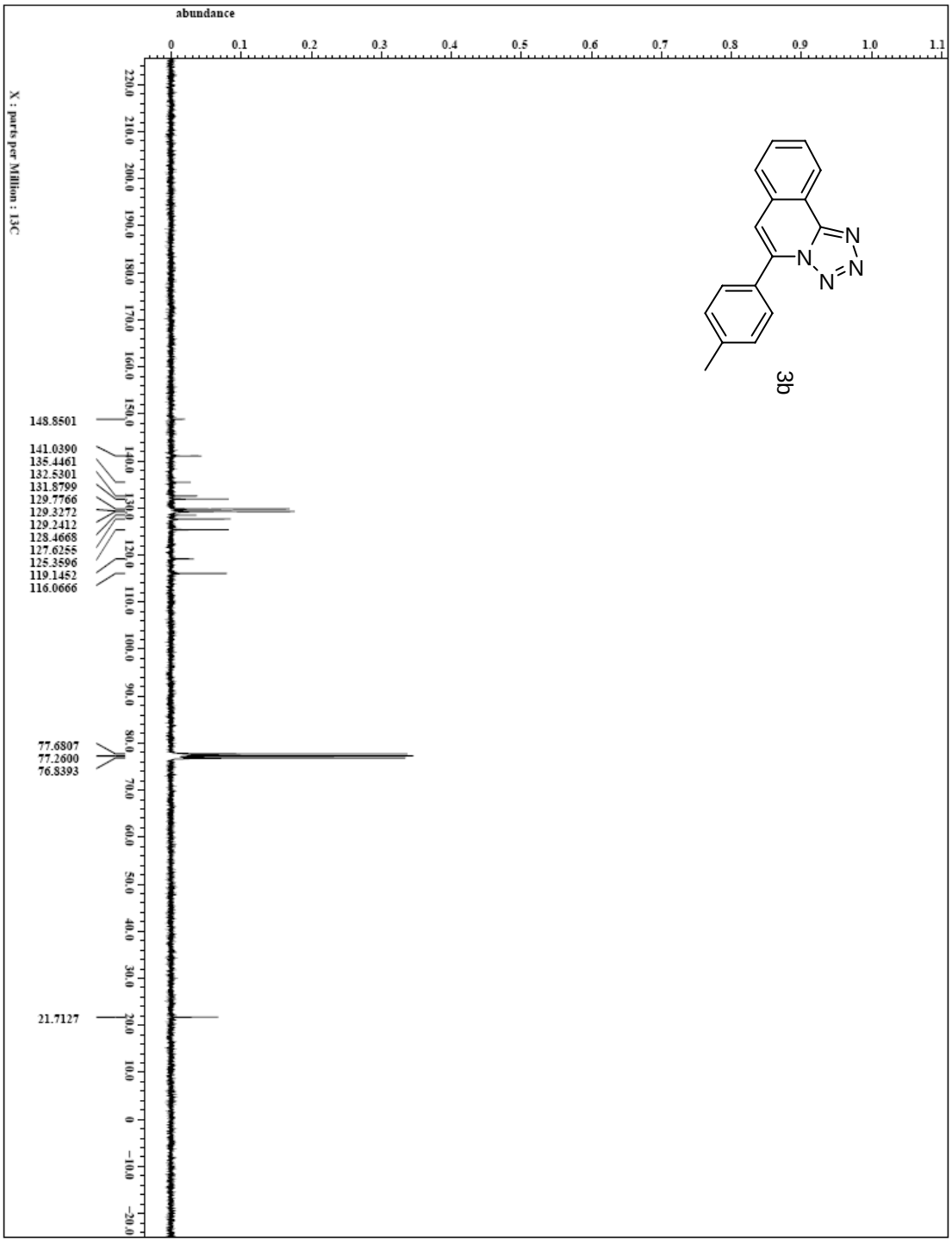

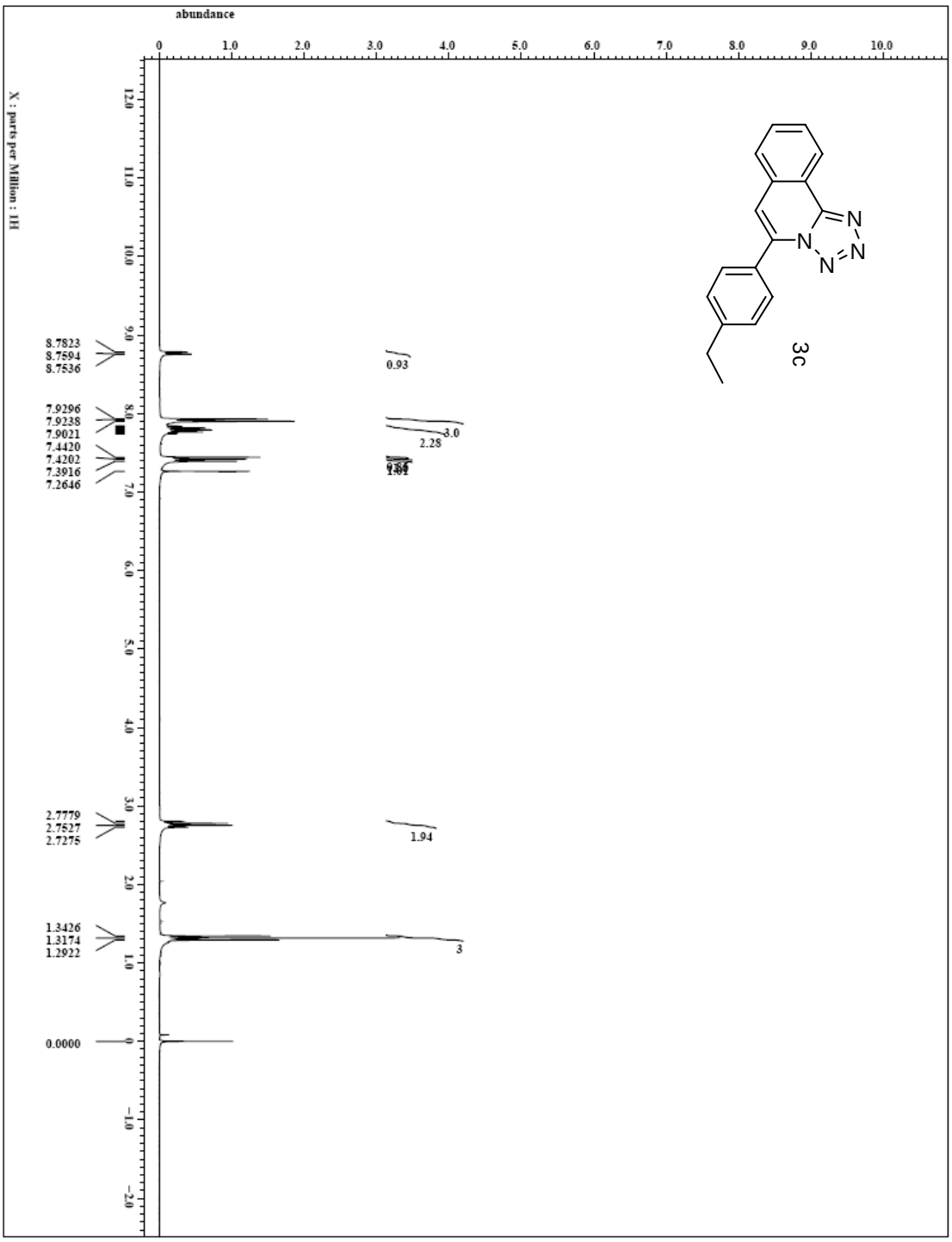

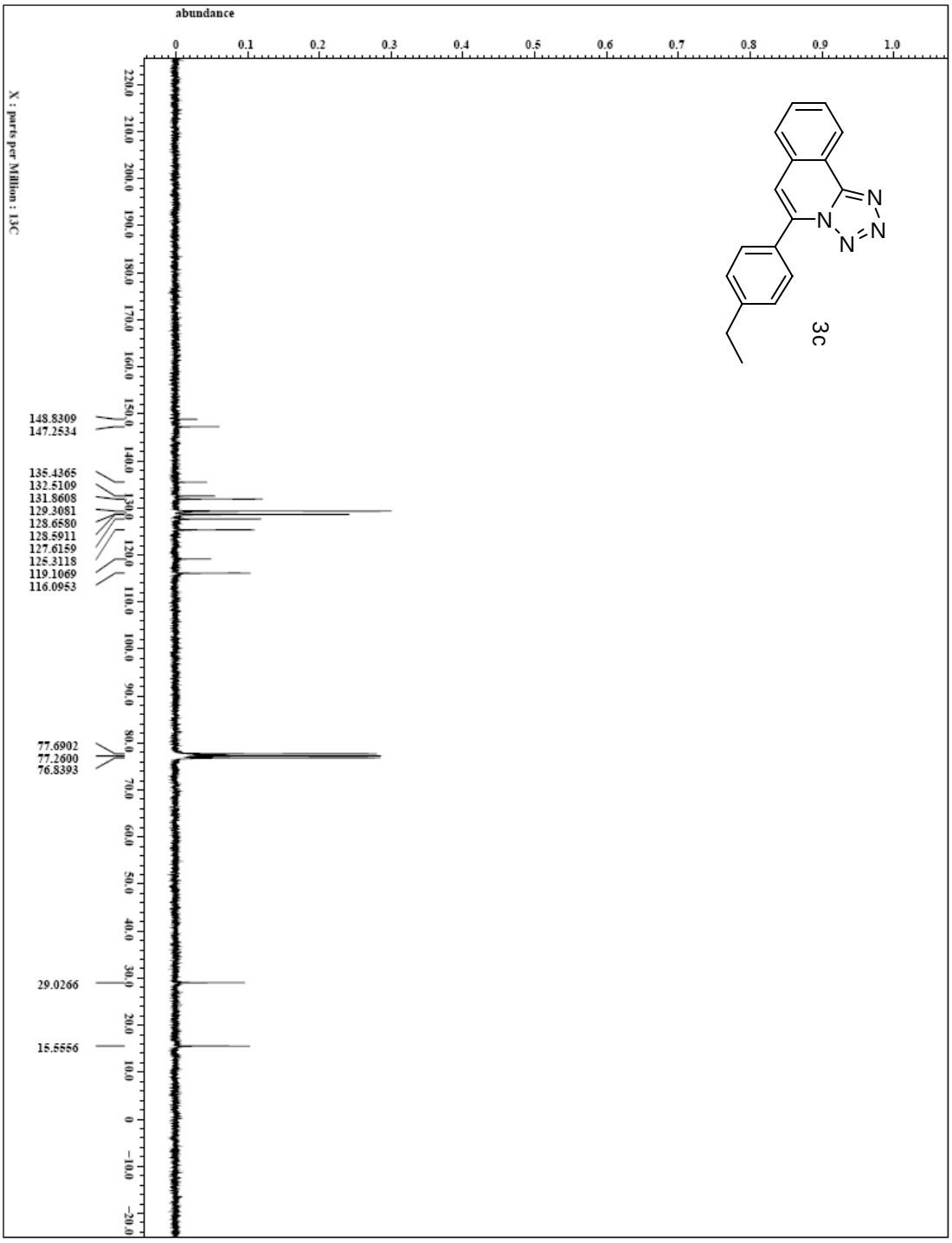
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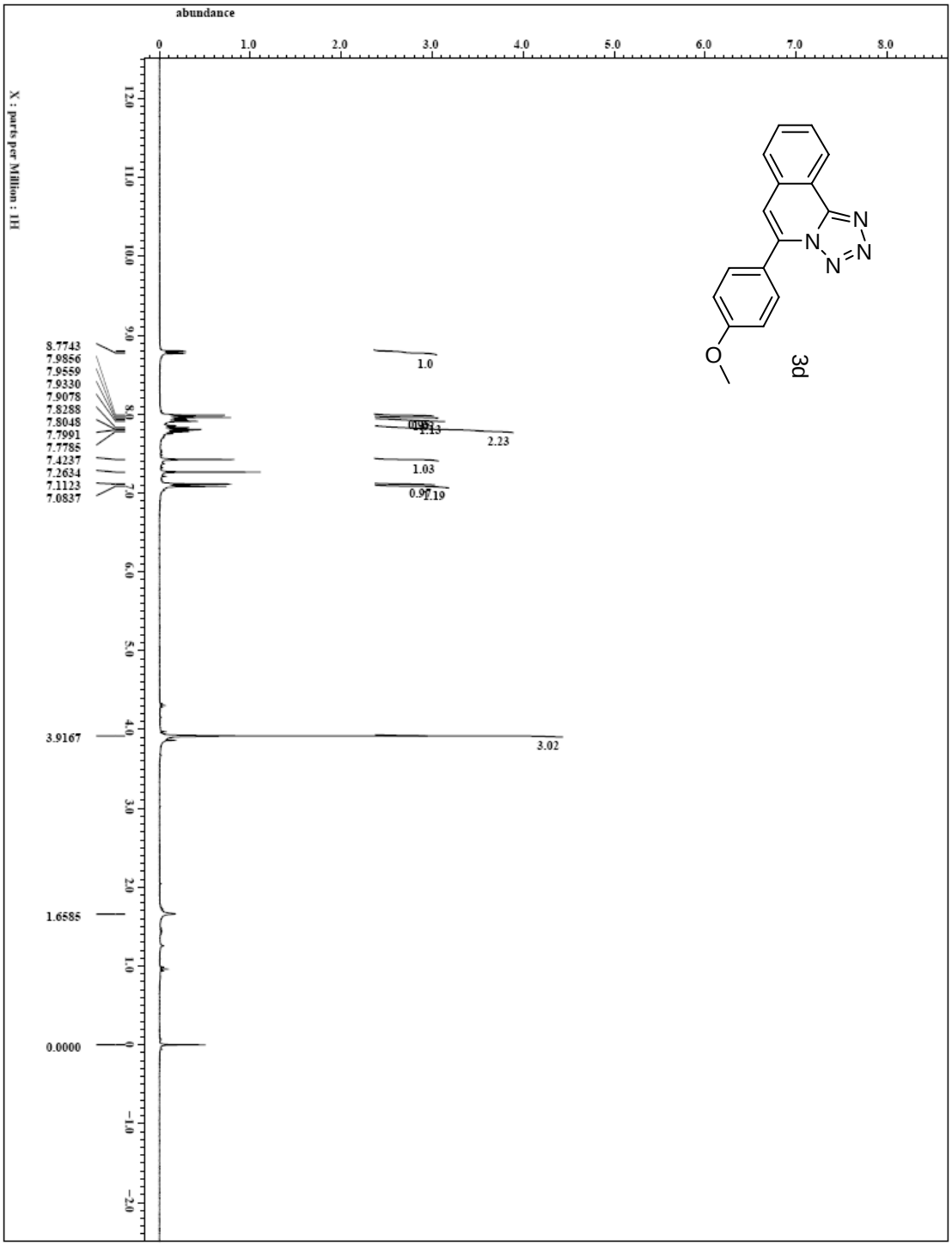
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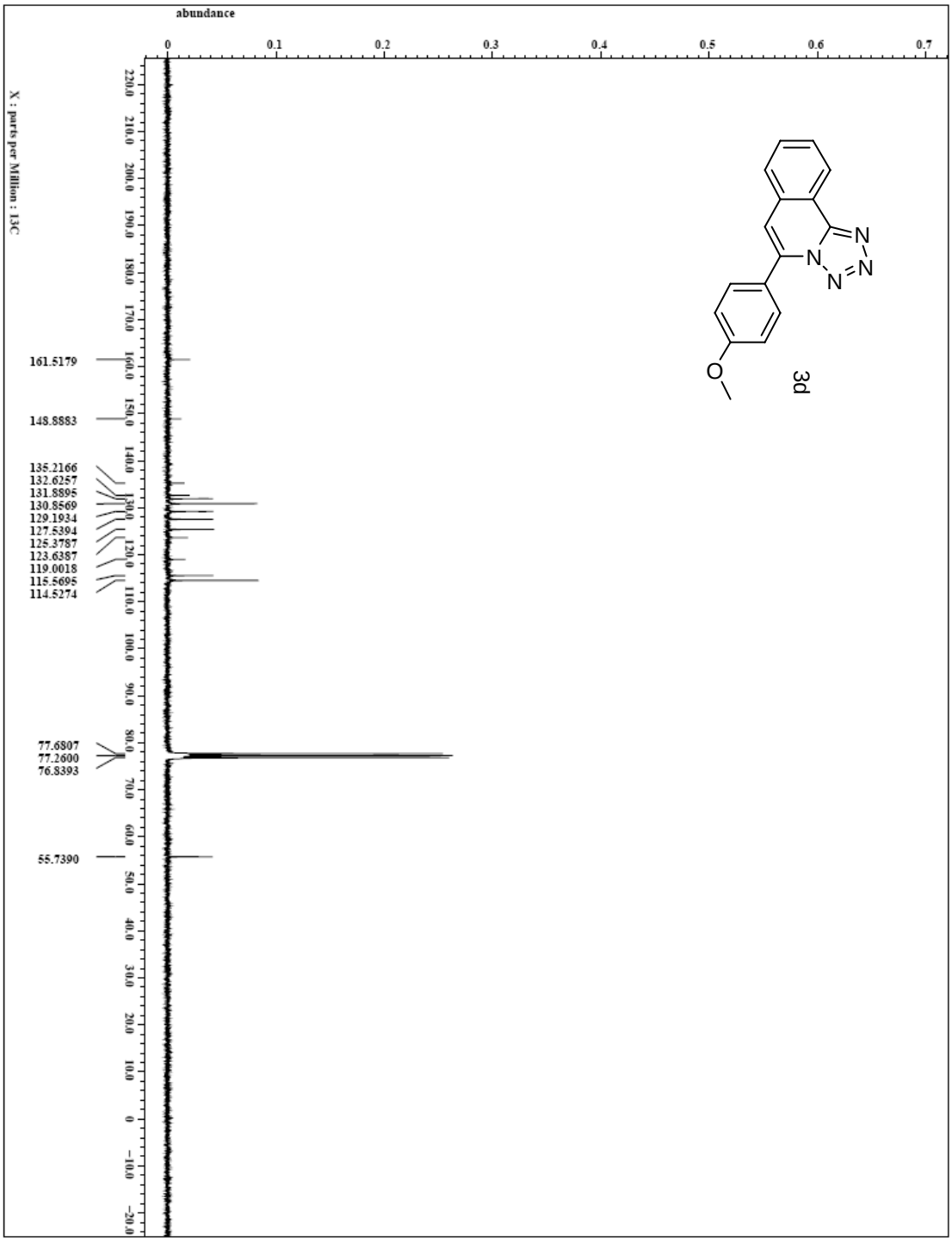

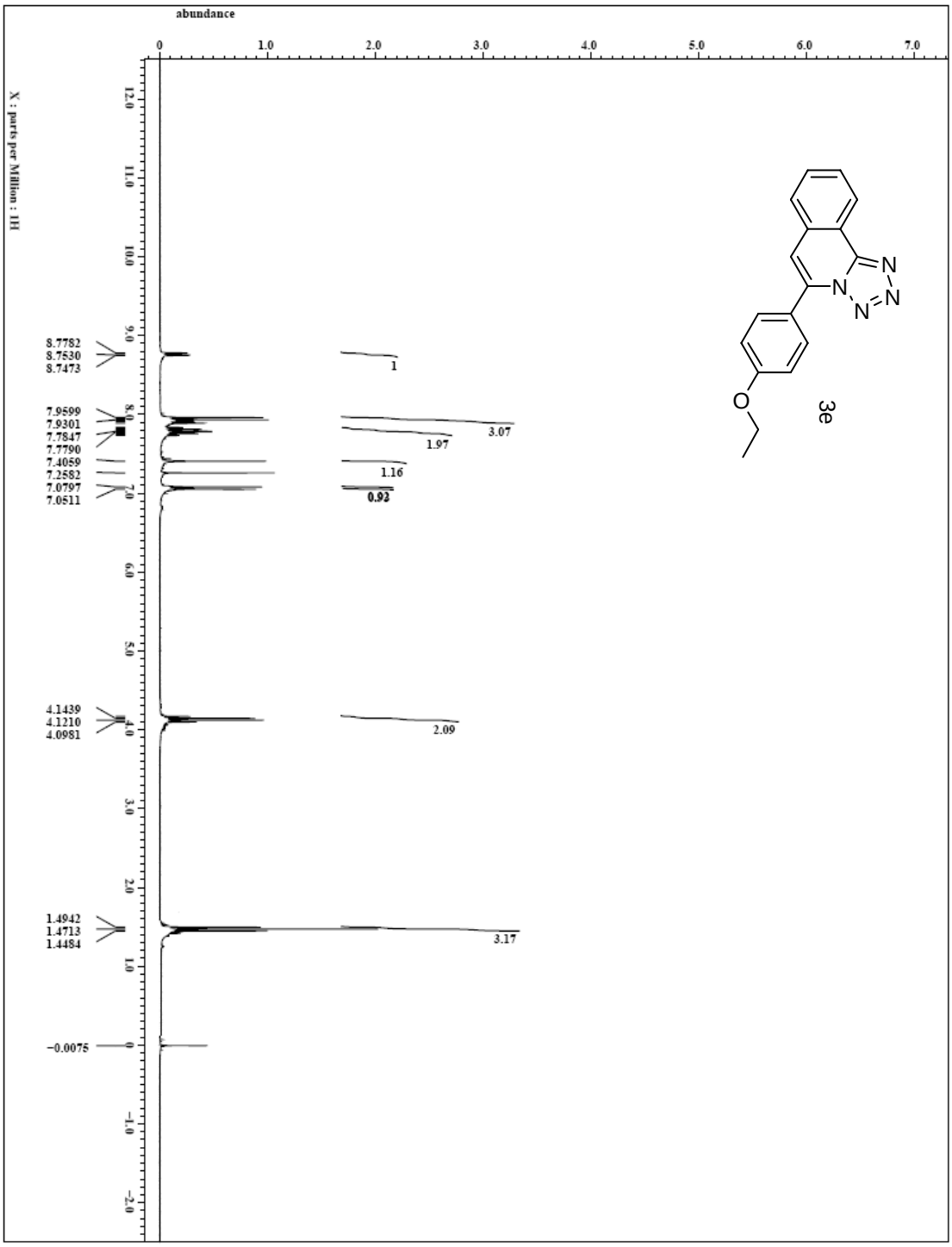
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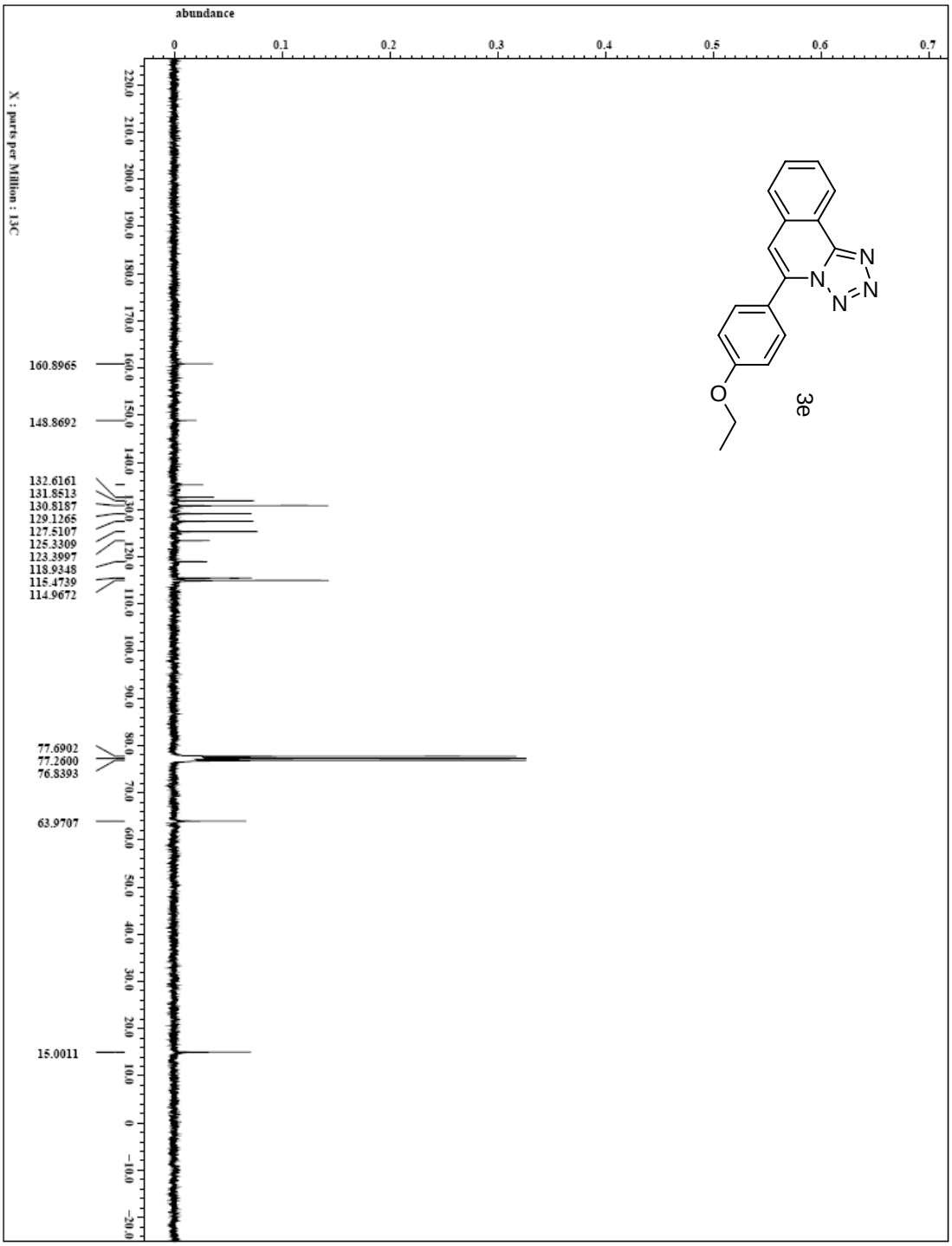

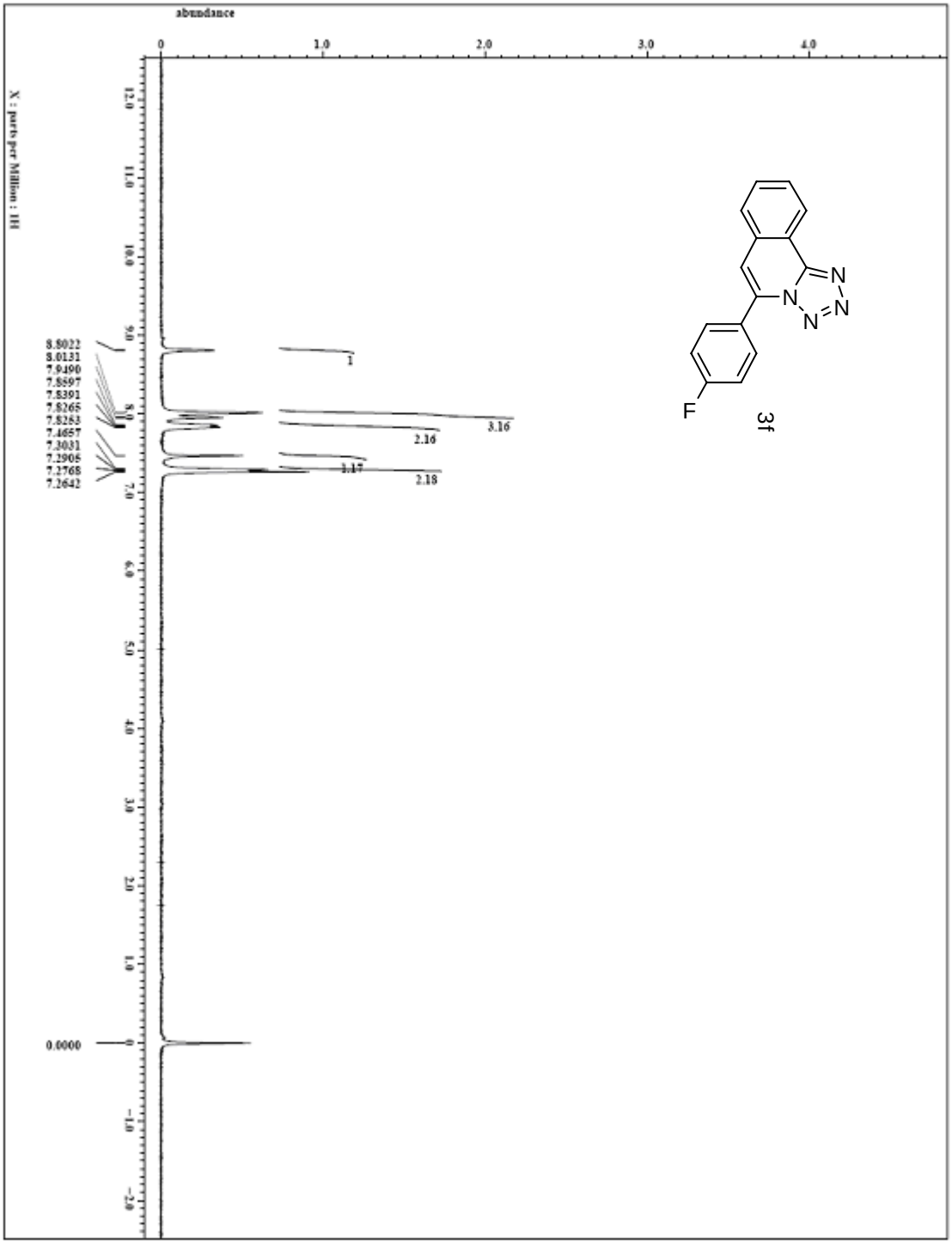
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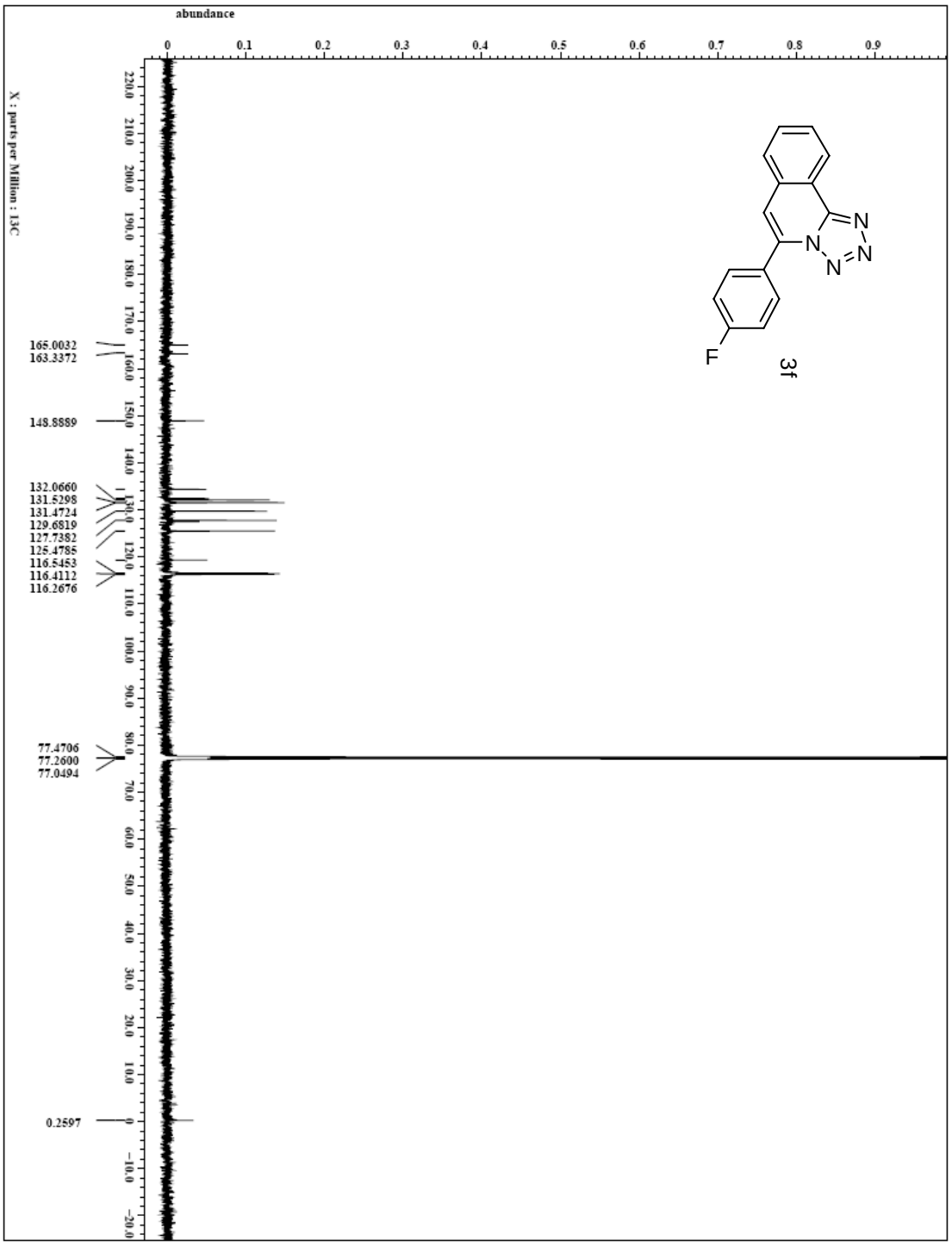
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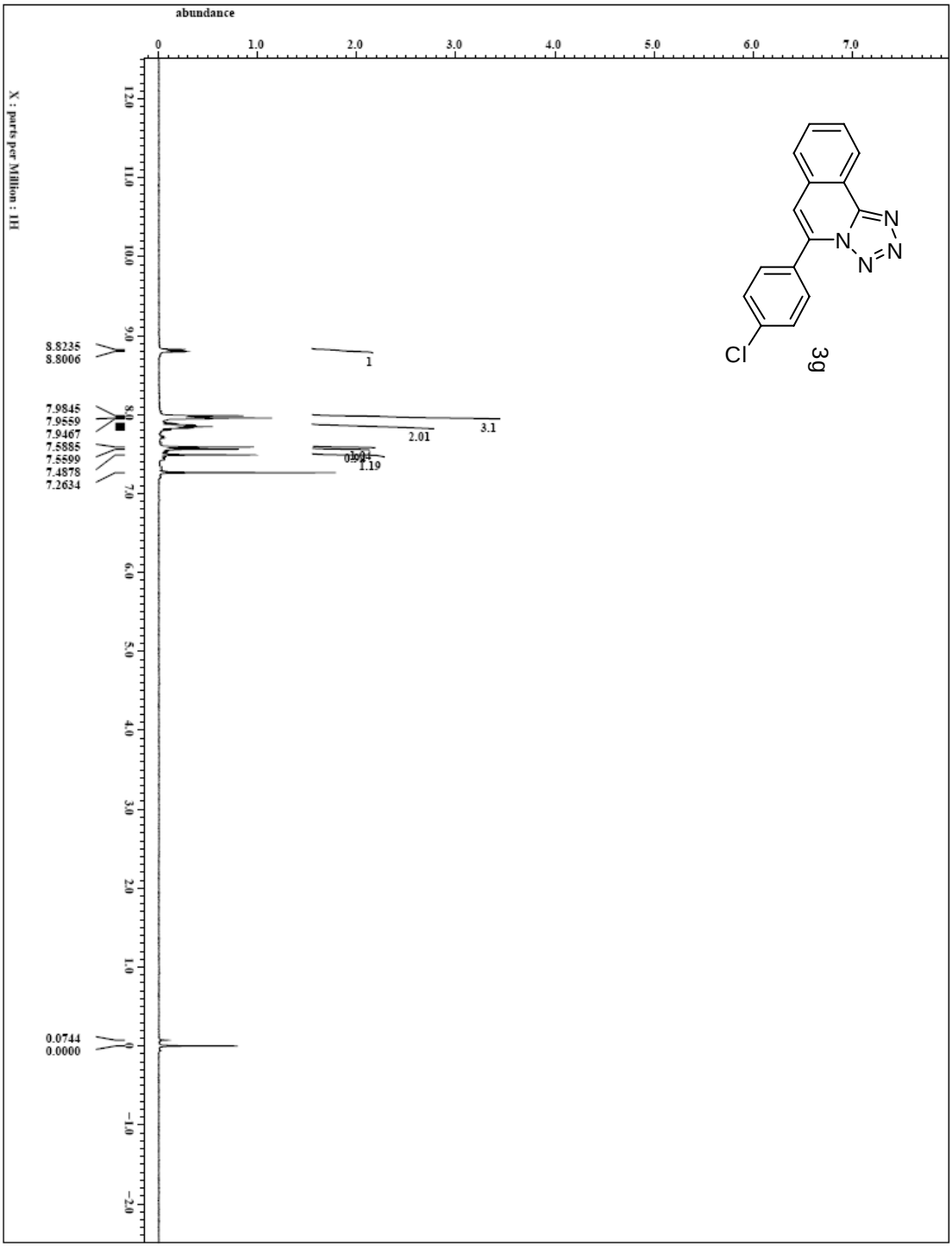
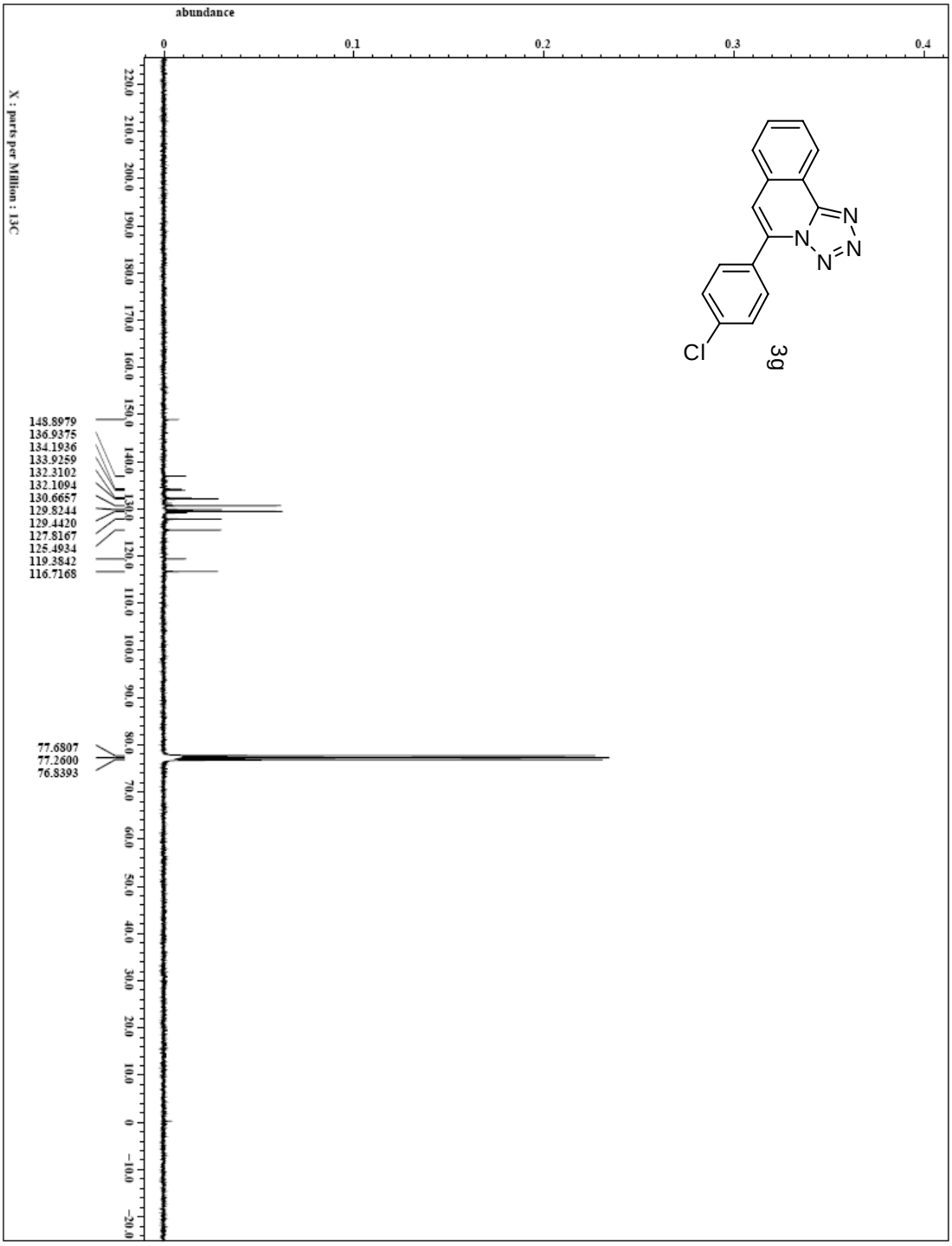
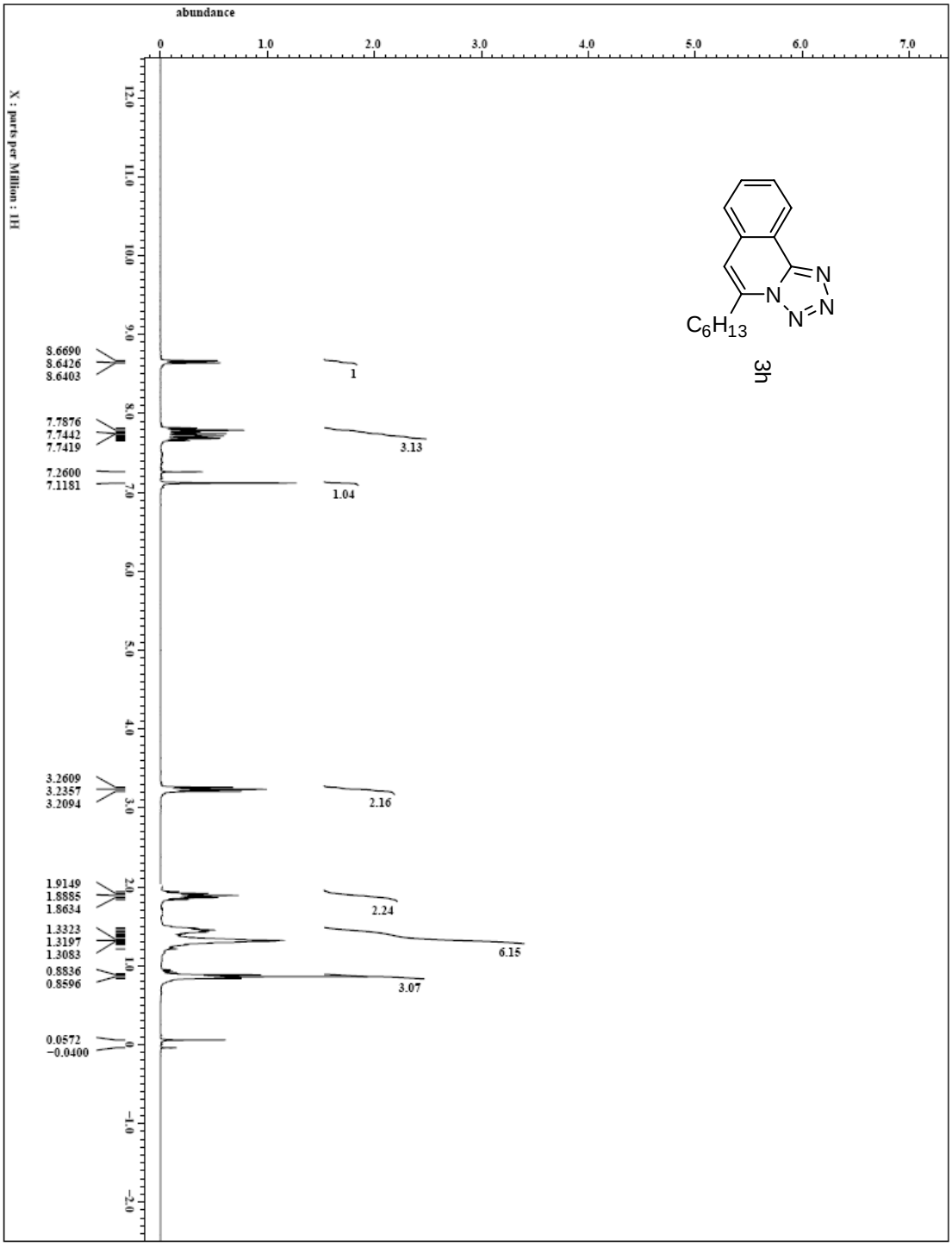
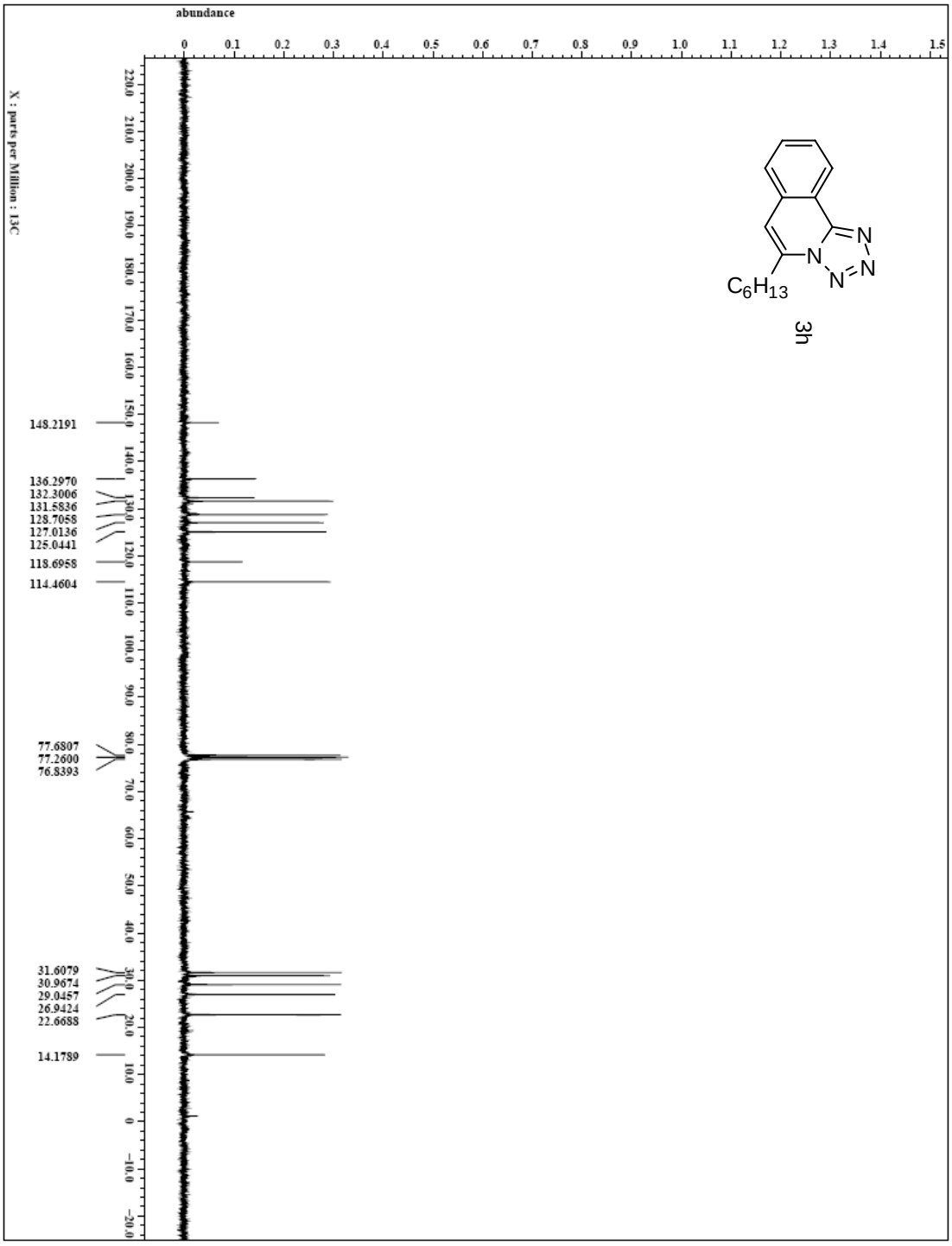
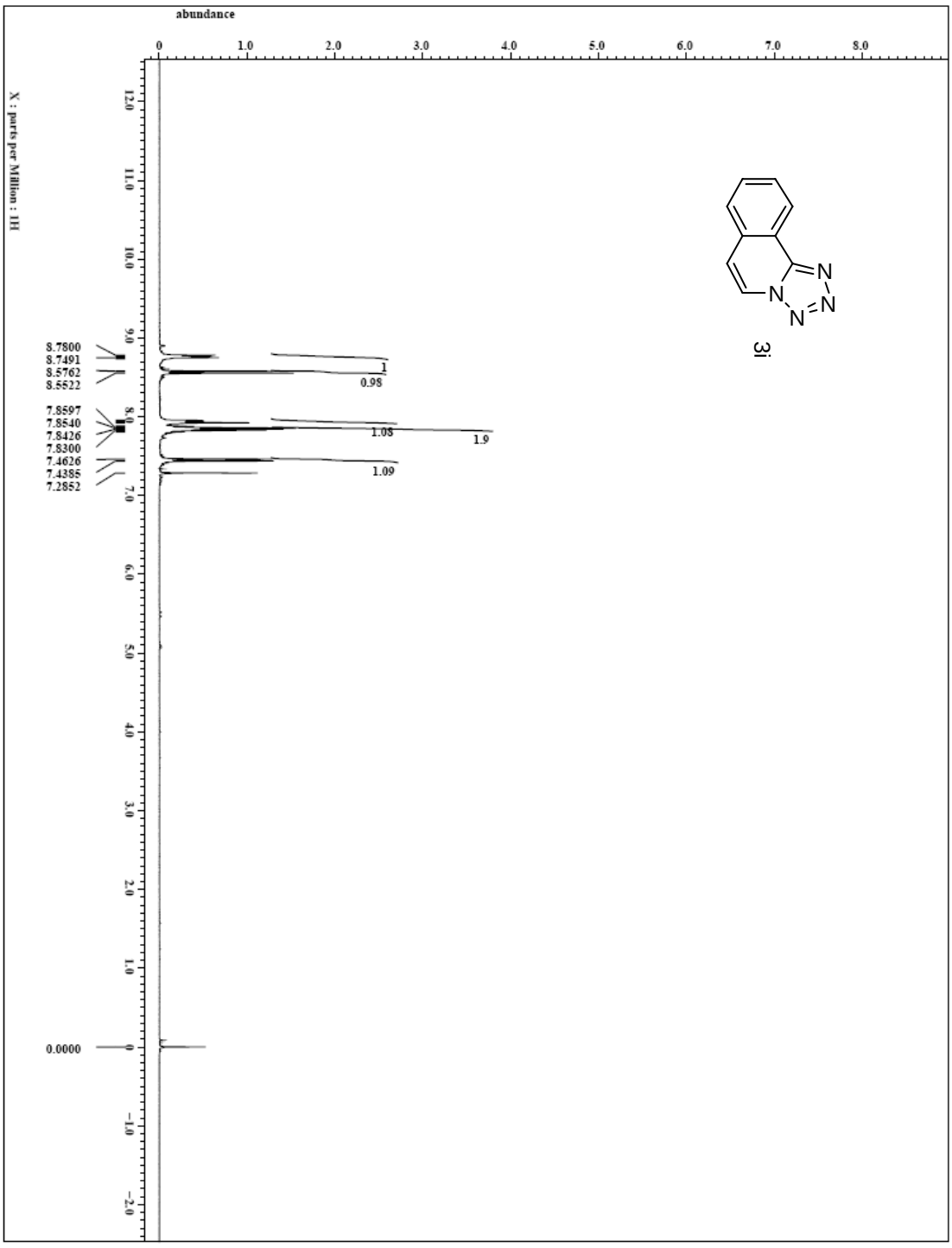
77.2600
77.0494
0.2597
F
3f

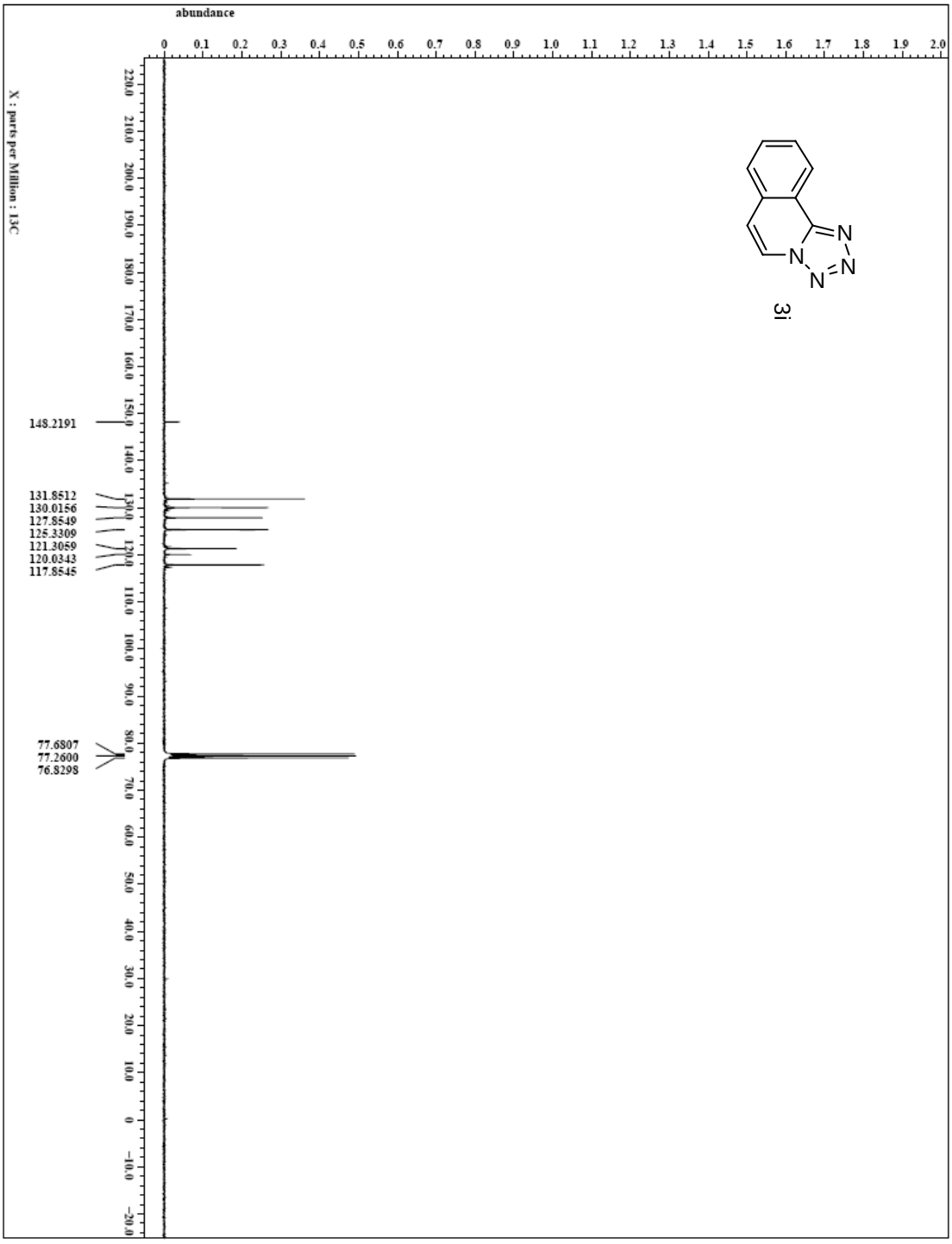

abundance
X : parts per Million : 1H
8.8235
8.8006
7.9845
7.9559
7.9467
7.5885
7.5599
7.4878
7.2634
0.0744
0.0000
1
3.1
2.01
1.19
Cl
3g

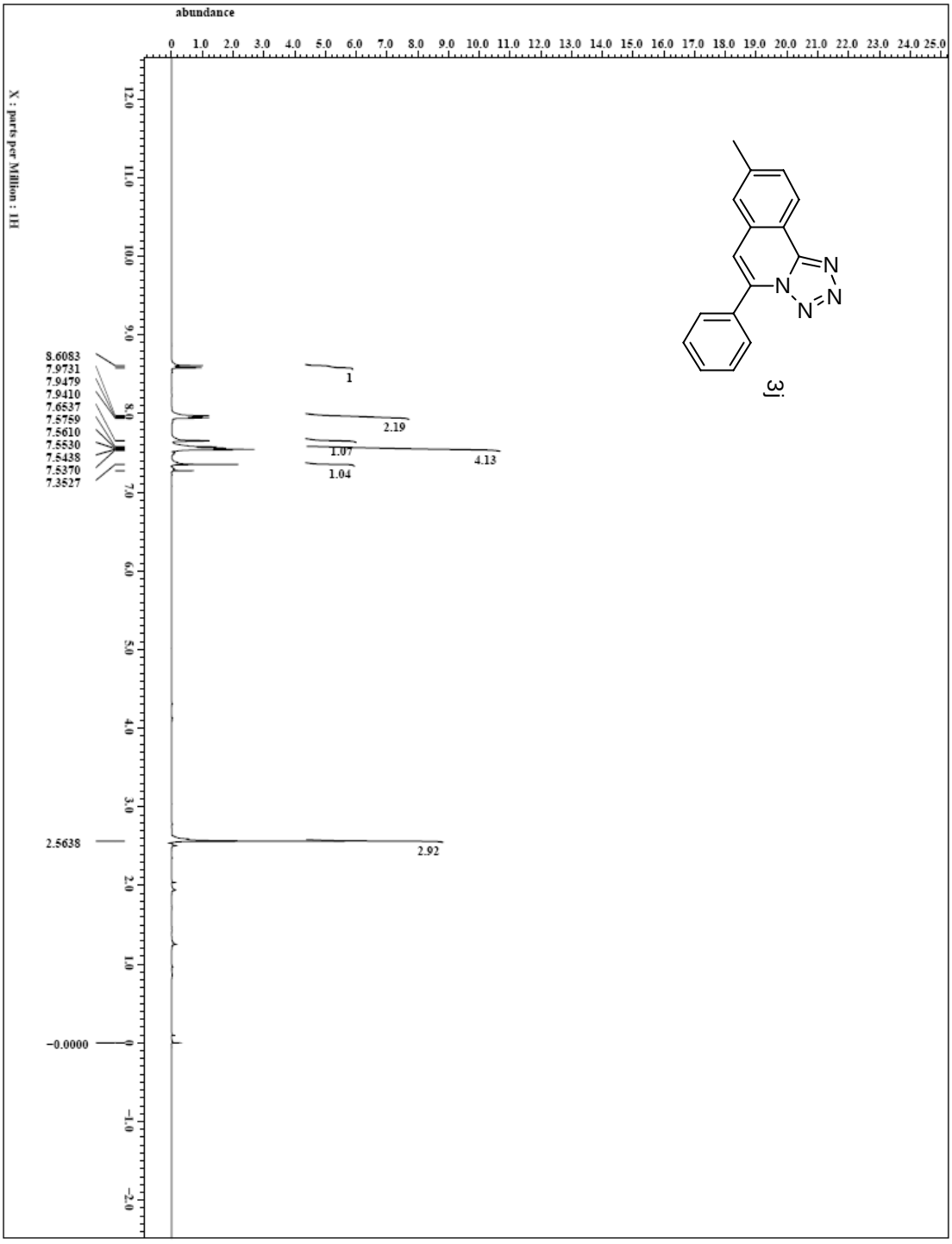


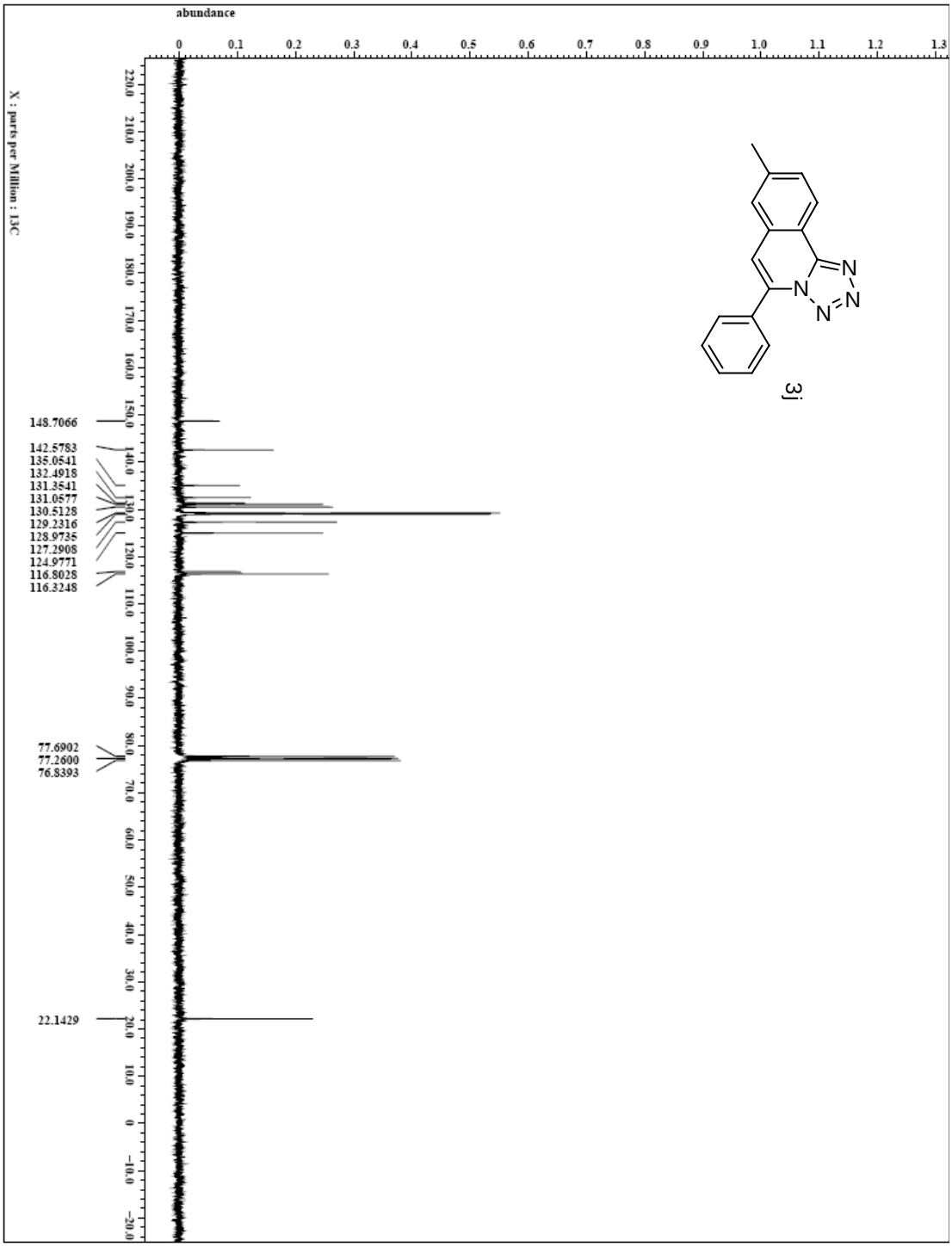

abundance
X : parts per Million : 1H
8.6690
8.6426
8.6403
7.7876
7.7442
7.7419
7.2600
7.1181
3.2609
3.2357
3.2094
1.9149
1.8885
1.8634
1.3323
1.3197
1.3083
0.8836
0.8596
0.0572
−0.0400
1
3.13
1.04
2.16
2.24
6.15
3.07
N
N
N
C6H13
3h

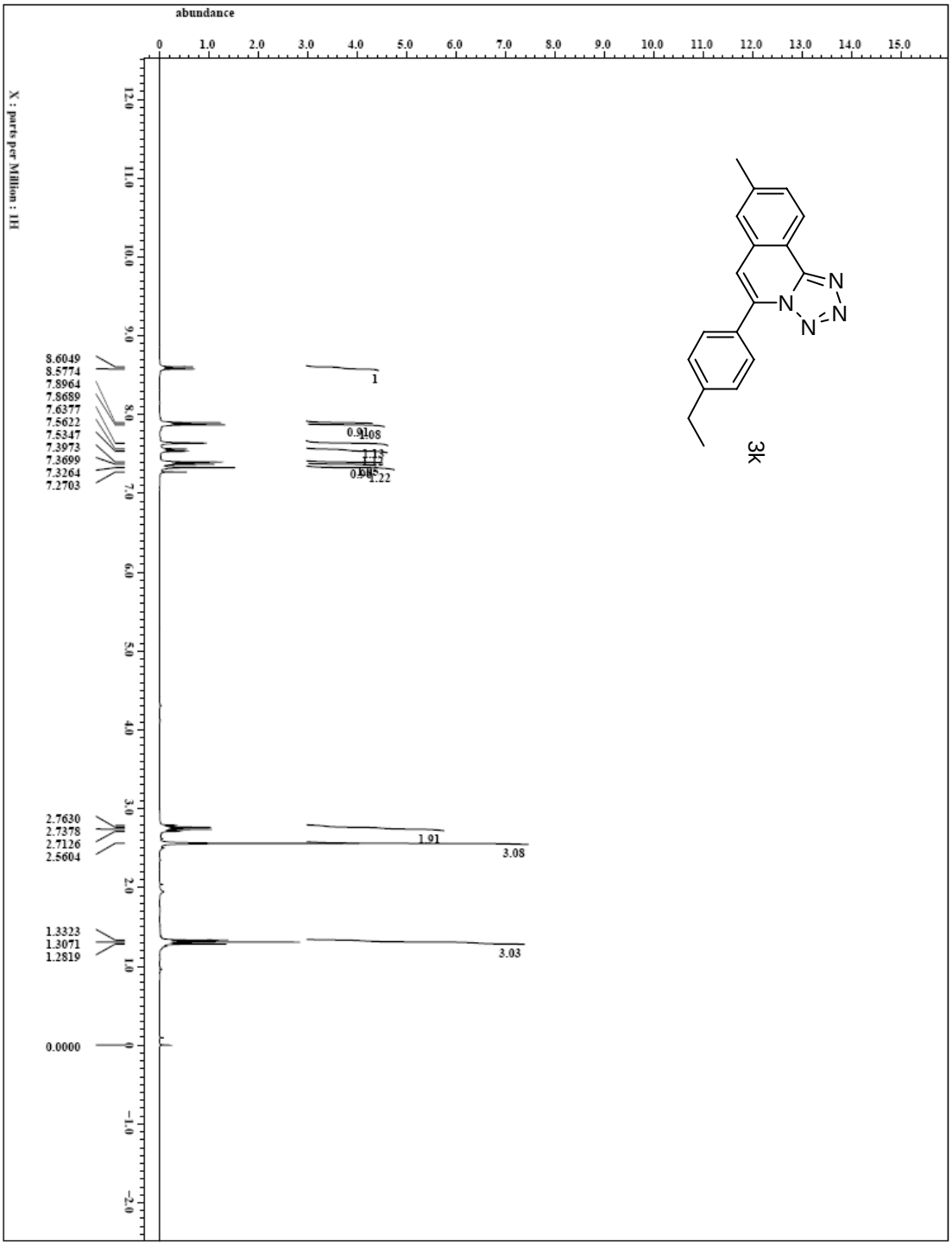

abundance
X : parts per Million : 13C
148.2191
136.2970
132.3006
131.5836
128.7058
127.0136
125.0441
118.6958
114.4604
77.6807
77.2600
76.8393
31.6079
30.9674
29.0457
26.9424
22.6688
14.1789
C6H13
3h

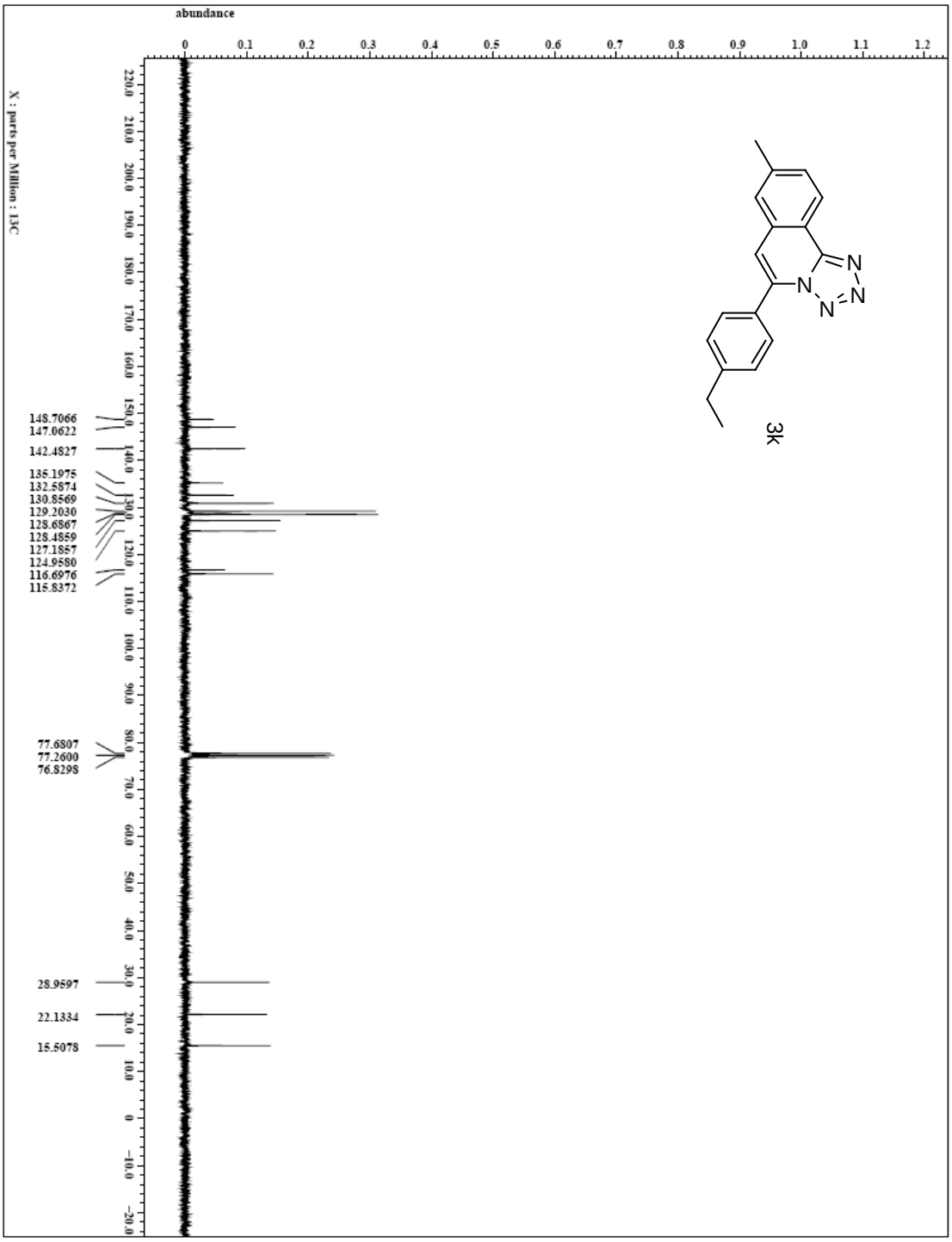

abundance
X : parts per Million : 1H
8.7800
8.7491
8.5762
8.5522
7.8597
7.8540
7.8426
7.8300
7.4626
7.4385
7.2852
0.0000
1
0.98
1.08
1.9
1.09
3i

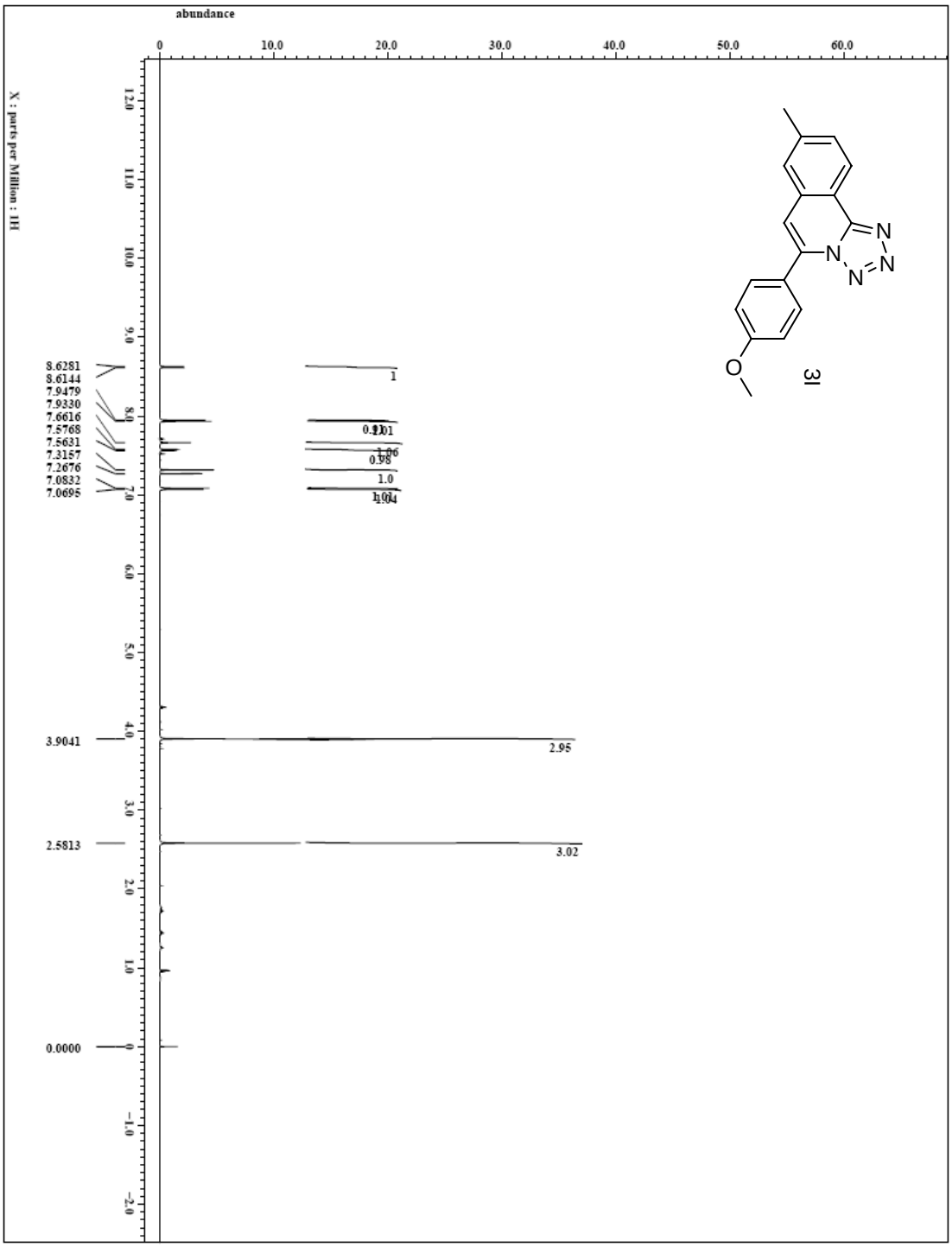

abundance
X : parts per Million : 13C
148.2191
131.8512
130.0156
127.8549
125.3309
121.3059
120.0343
117.8545
77.6807
77.2600
76.8298
3i

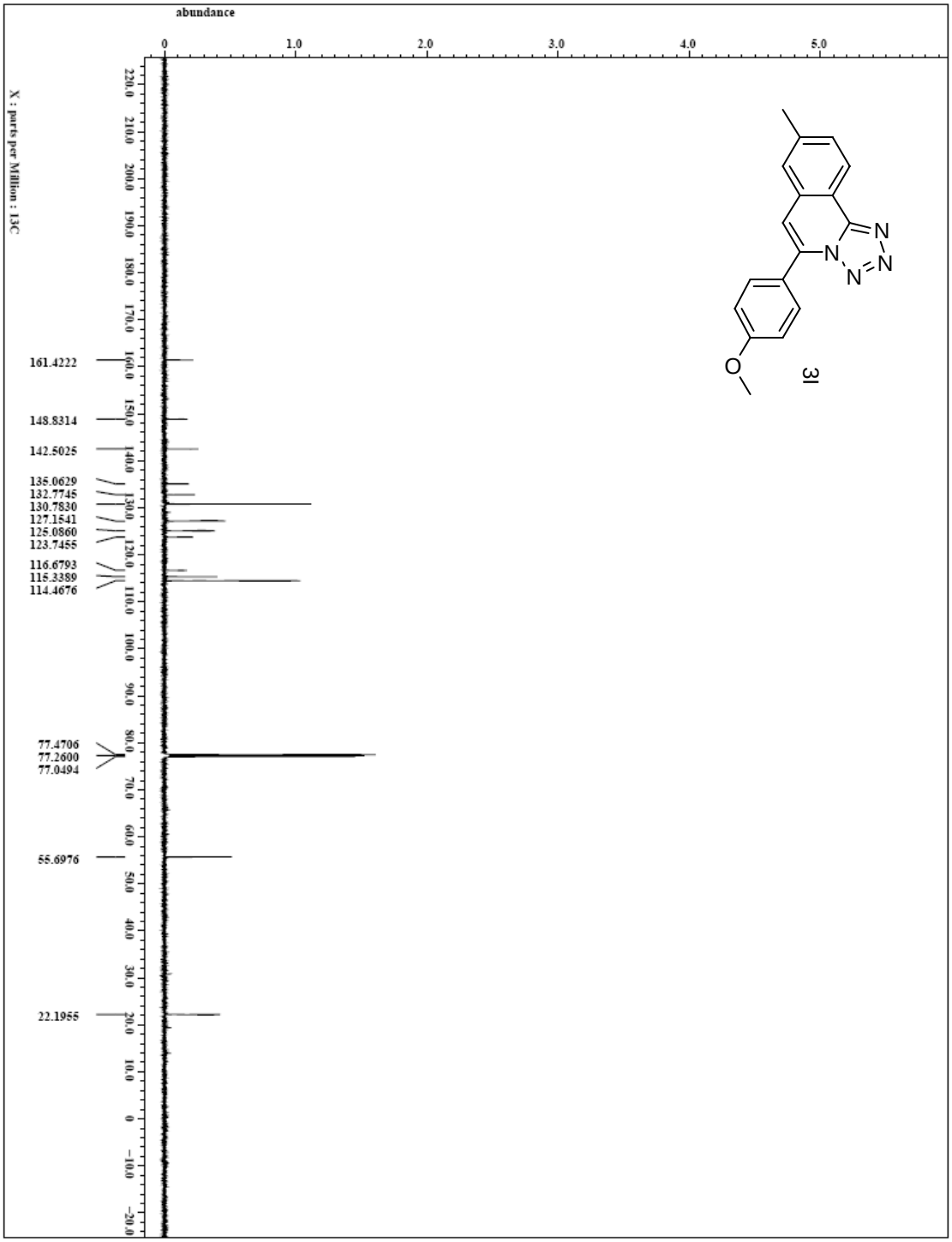

abundance
X : parts per Million : 1H
8.6083
7.9731
7.9479
7.9410
7.6537
7.5759
7.5610
7.5530
7.5438
7.5370
7.3527
2.5638
−0.0000
1
2.19
1.07
4.13
1.04
2.92
N
N
N
N
3j

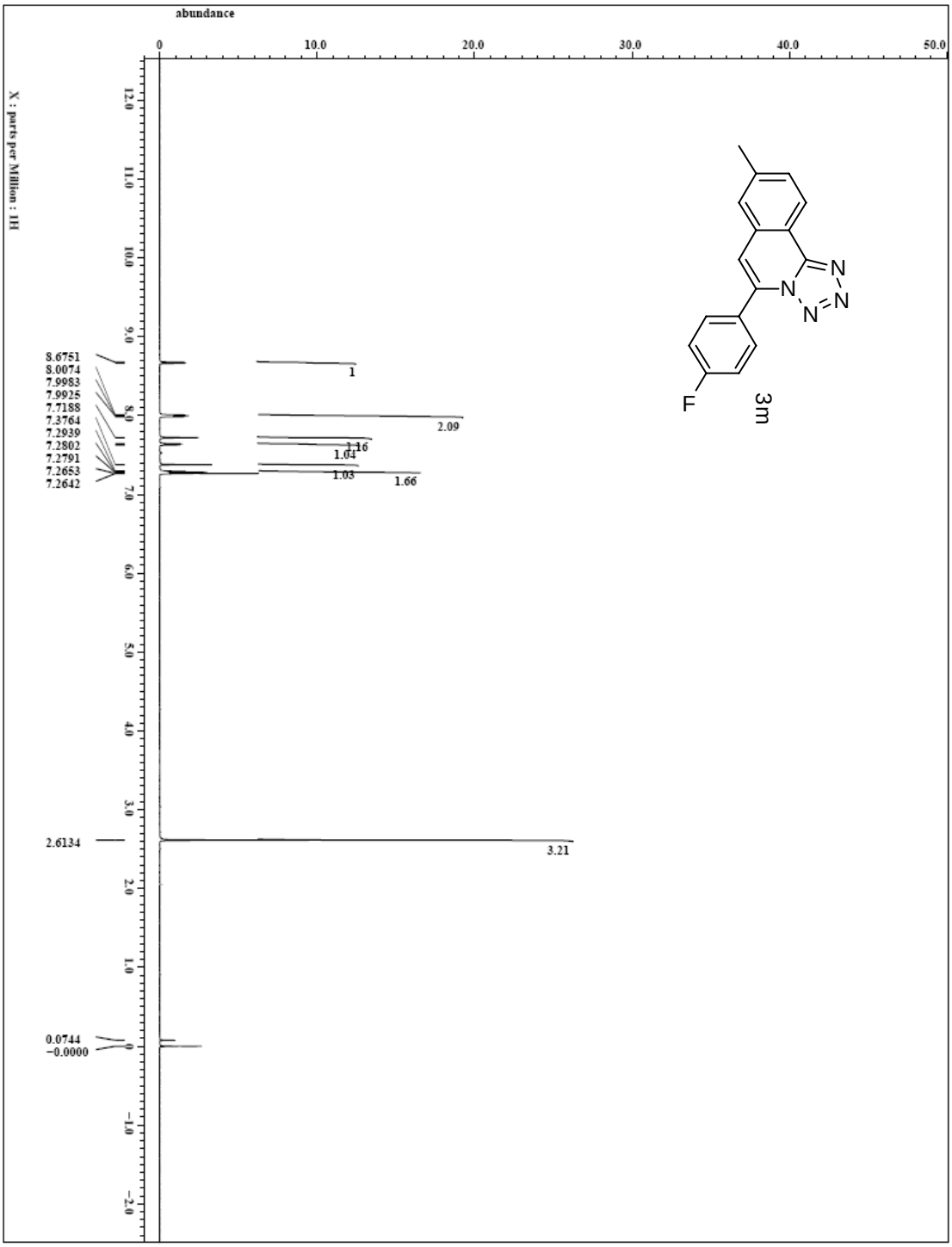

abundance
X : parts per Million : 13C
148.7066
142.5783
135.0541
132.4918
131.3541
131.0577
130.5128
129.2316
128.9735
127.2908
124.9771
116.8028
116.3248
77.6902
77.2600
76.8393
22.1429
3j

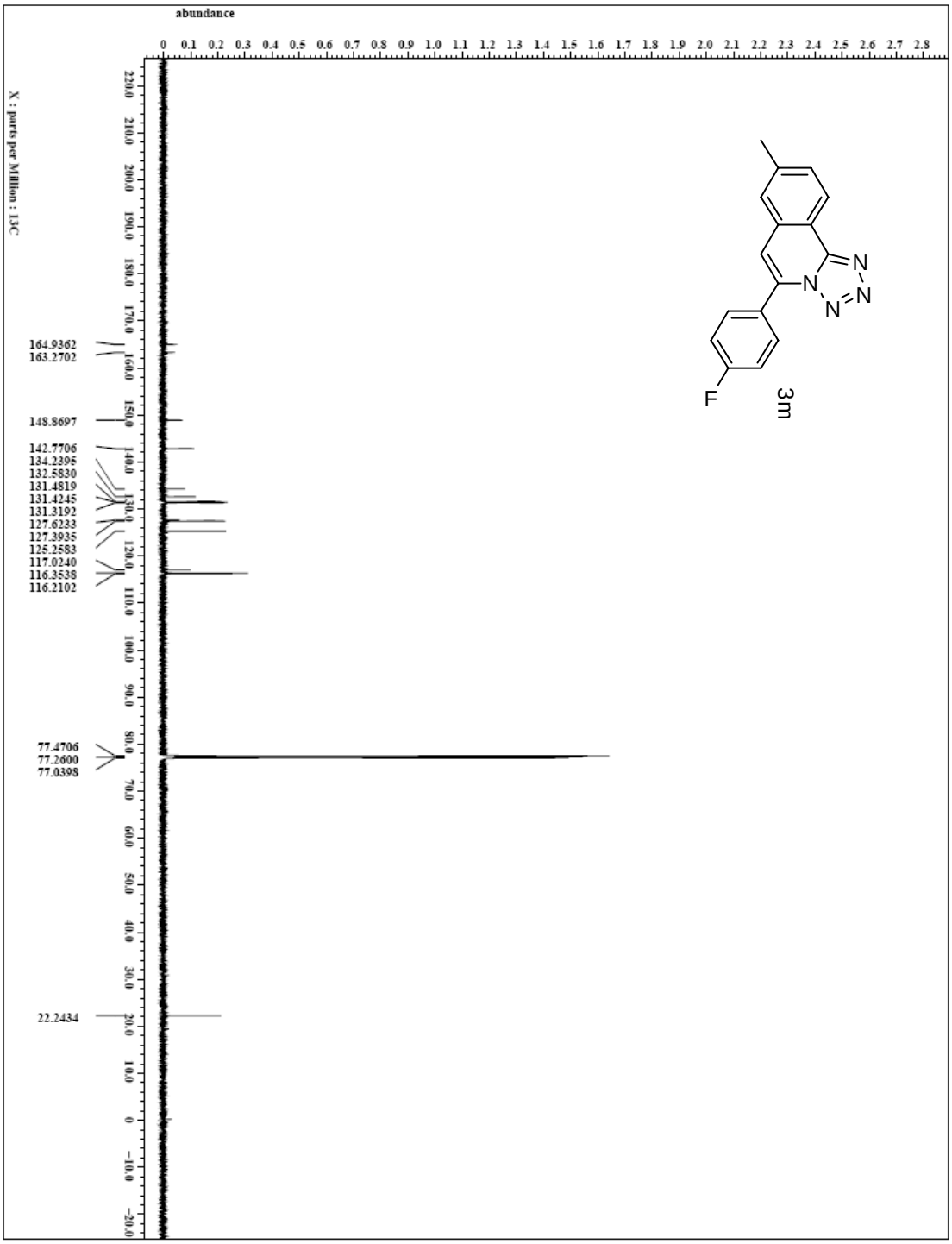


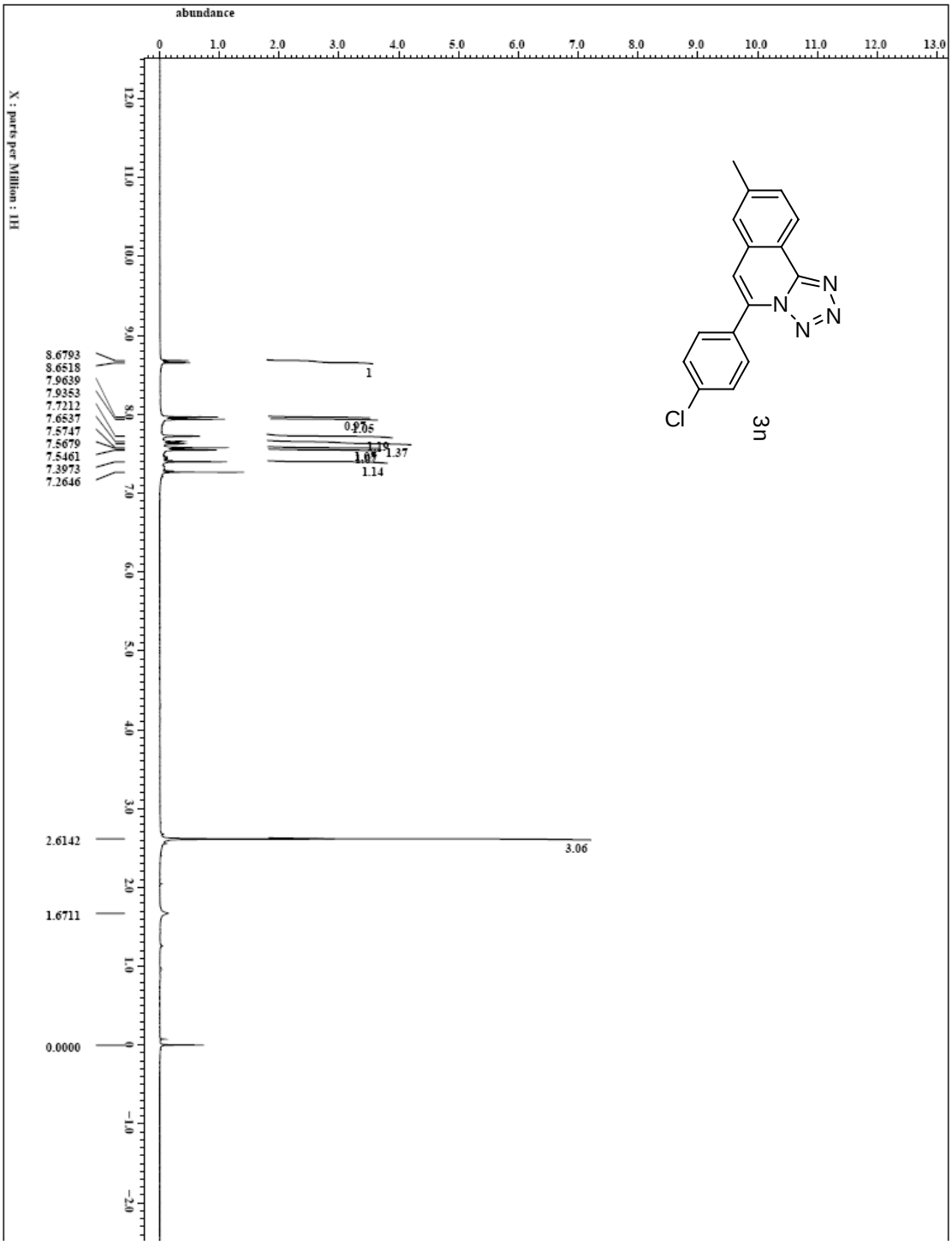


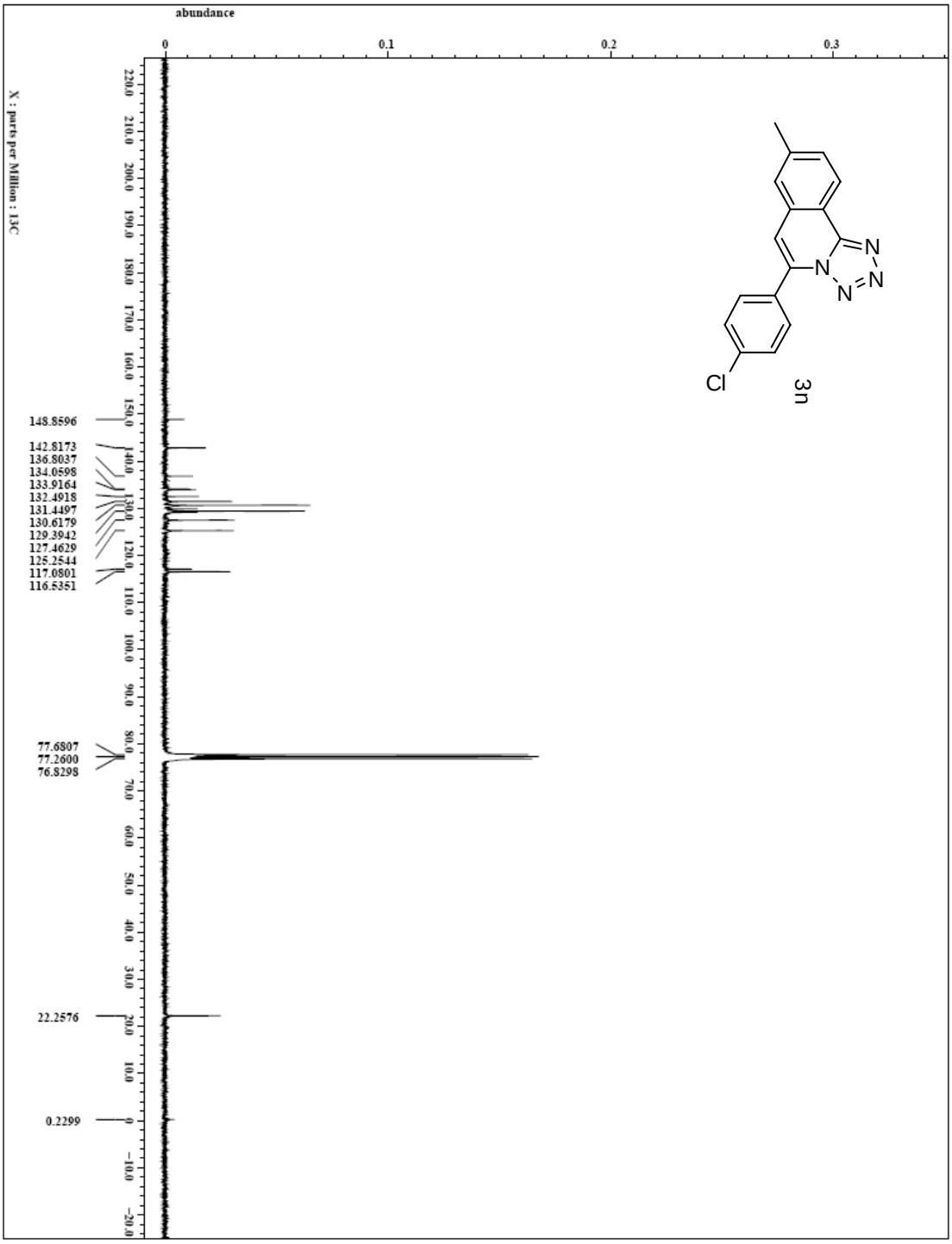

abundance
X : parts per Million : 1H
8.6281
8.6144
7.9479
7.9330
7.6616
7.5768
7.5631
7.3157
7.2676
7.0832
7.0695
3.9041
2.5813
0.0000
1
2.95
3.02
1.0
31

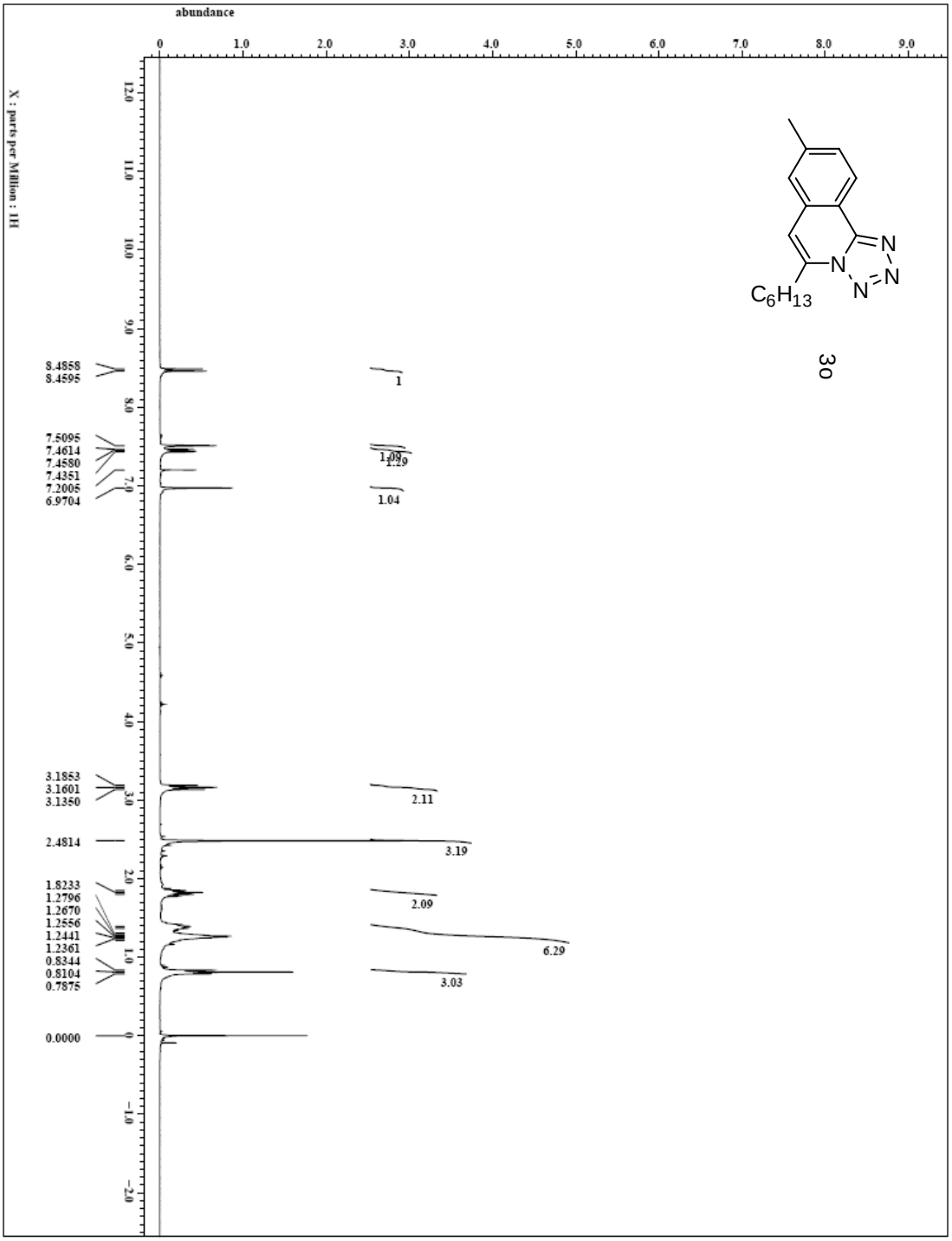

abundance
X : parts per Million : 13C
161.4222
148.8314
142.5025
135.0629
132.7745
130.7830
127.1541
125.0860
123.7455
116.6793
115.3389
114.4676
77.4706
77.2600
77.0494
55.6976
22.1955
N
N
N
O
31

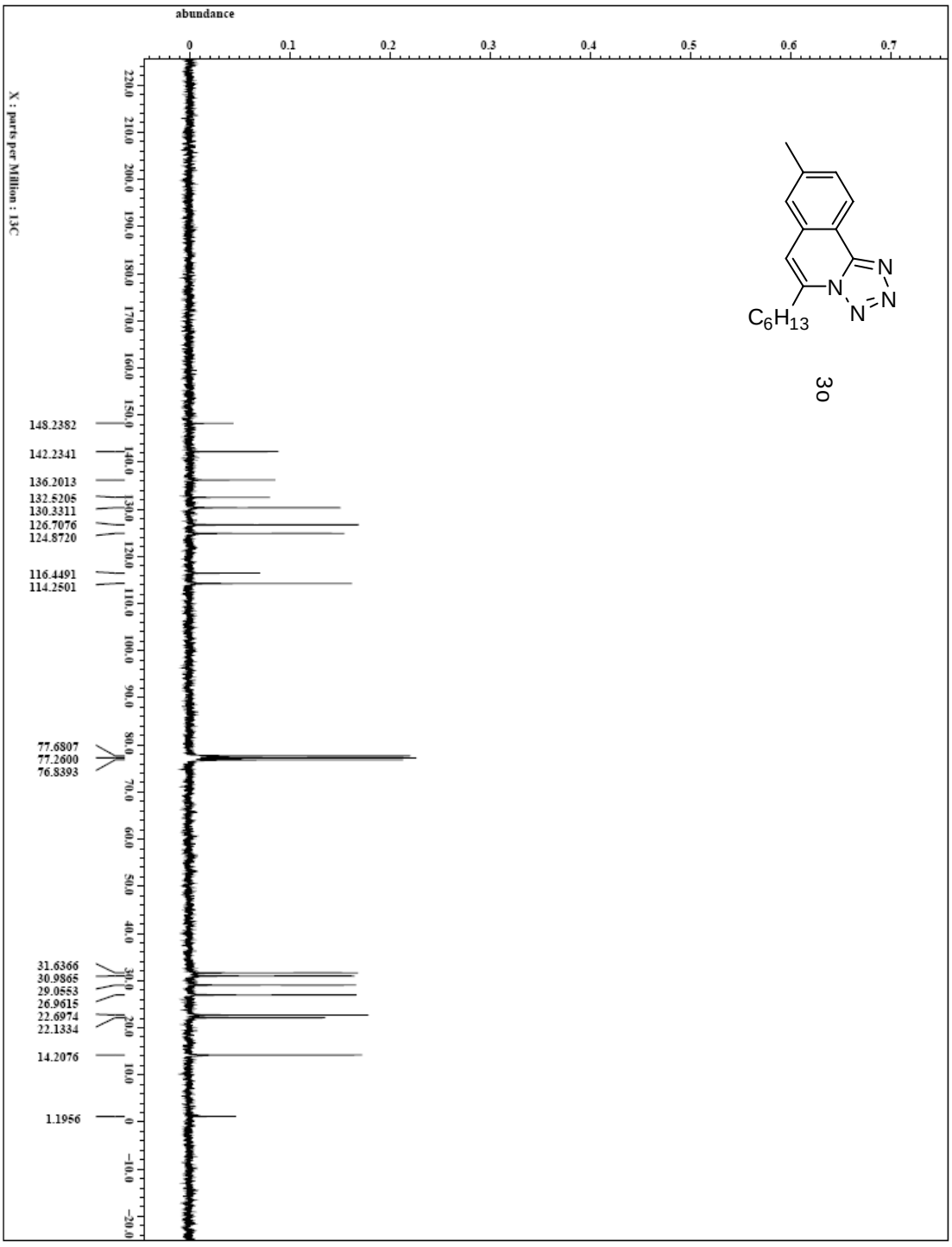

abundance
X : parts per Million : 1H
8.6751
8.0074
7.9983
7.9925
7.7188
7.3764
7.2939
7.2802
7.2791
7.2653
7.2642
2.6134
0.0744
−0.0000
1
2.09
1.16
1.04
1.03
1.66
3.21
F
3m

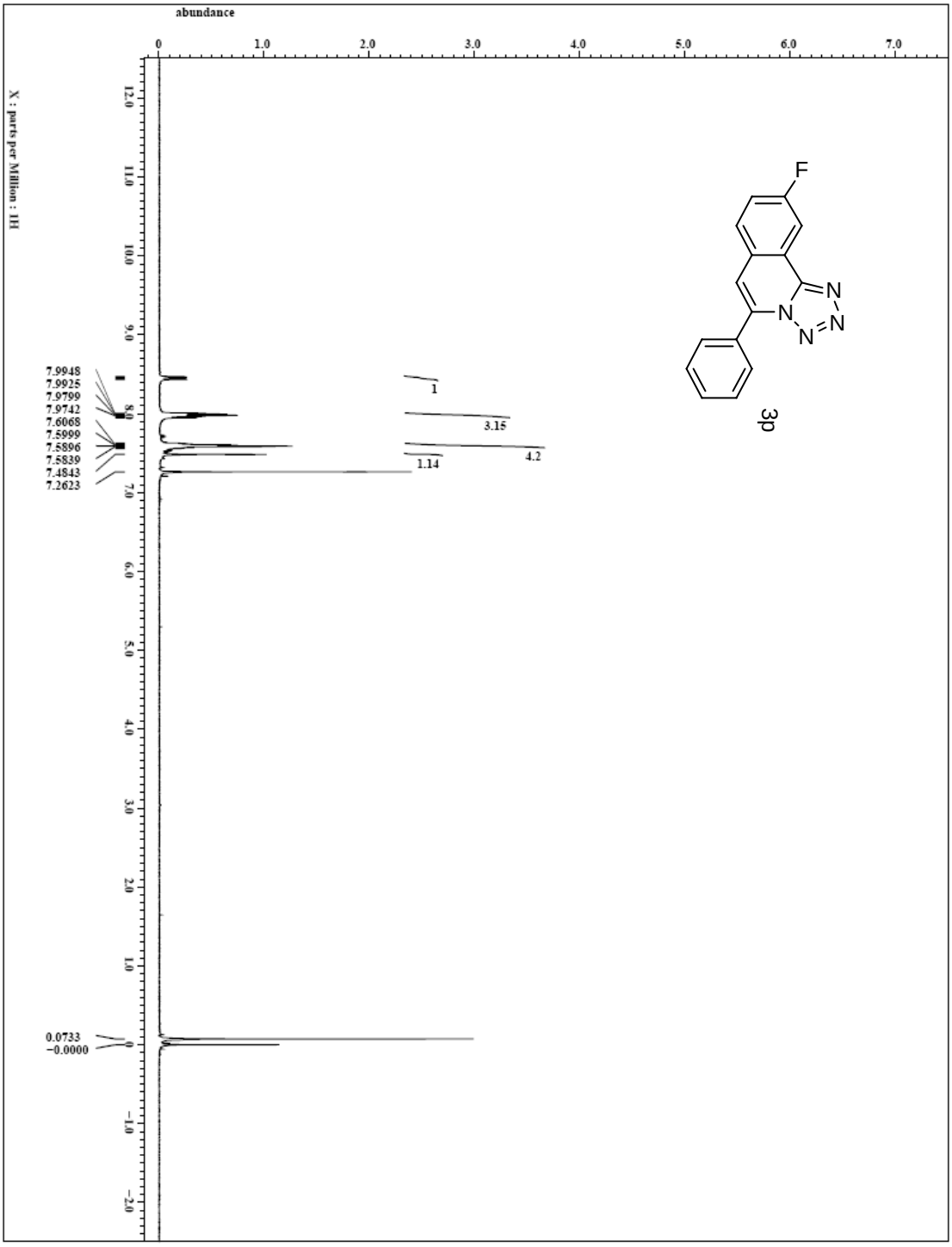


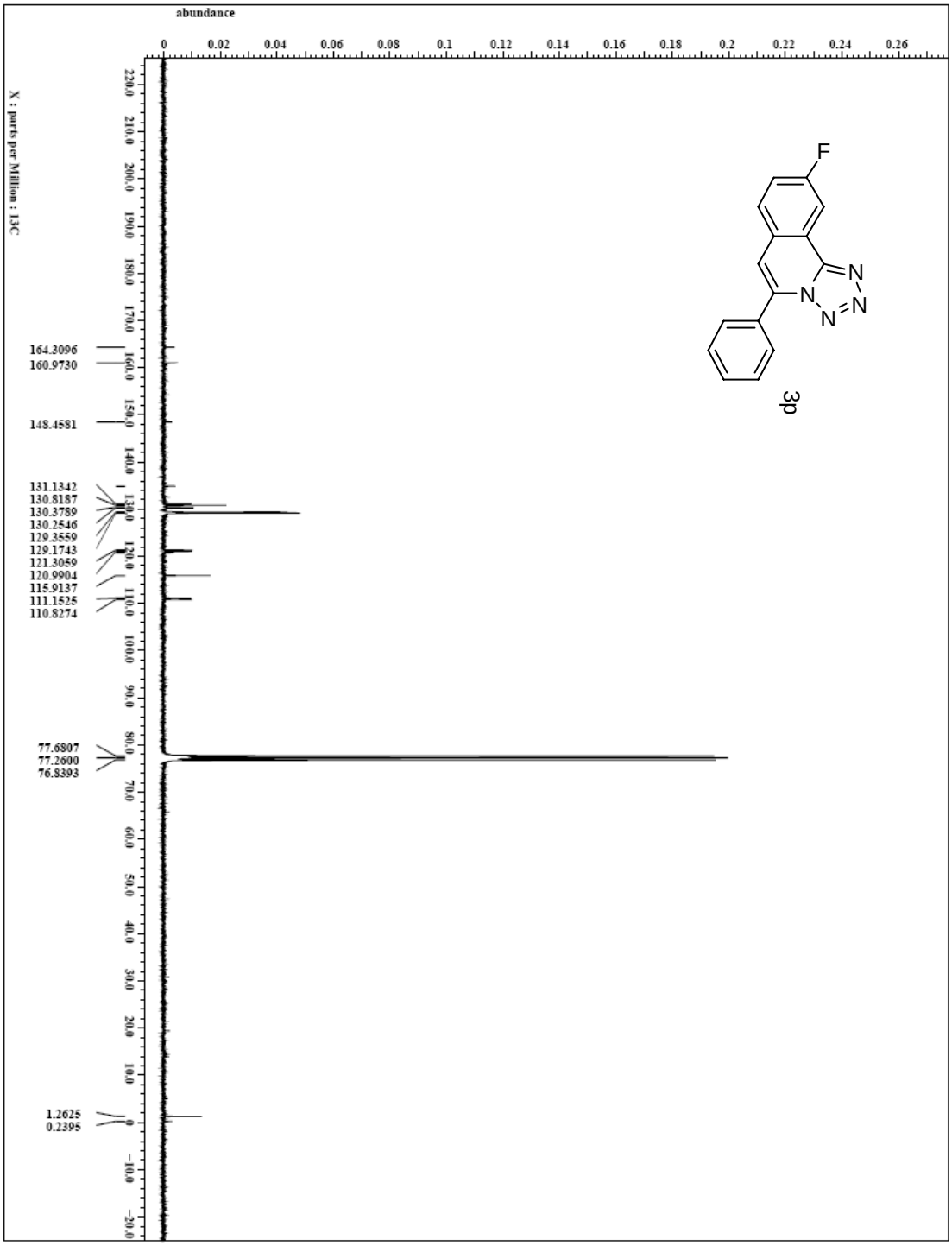

abundance
X : parts per Million : 1H
8.6793
8.6518
7.9639
7.9353
7.7212
7.6537
7.5747
7.5679
7.5461
7.3973
7.2646
2.6142
1.6711
0.0000
1
0.95
1.05
1.19
1.37
1.07
1.14
3.06
Cl
3n

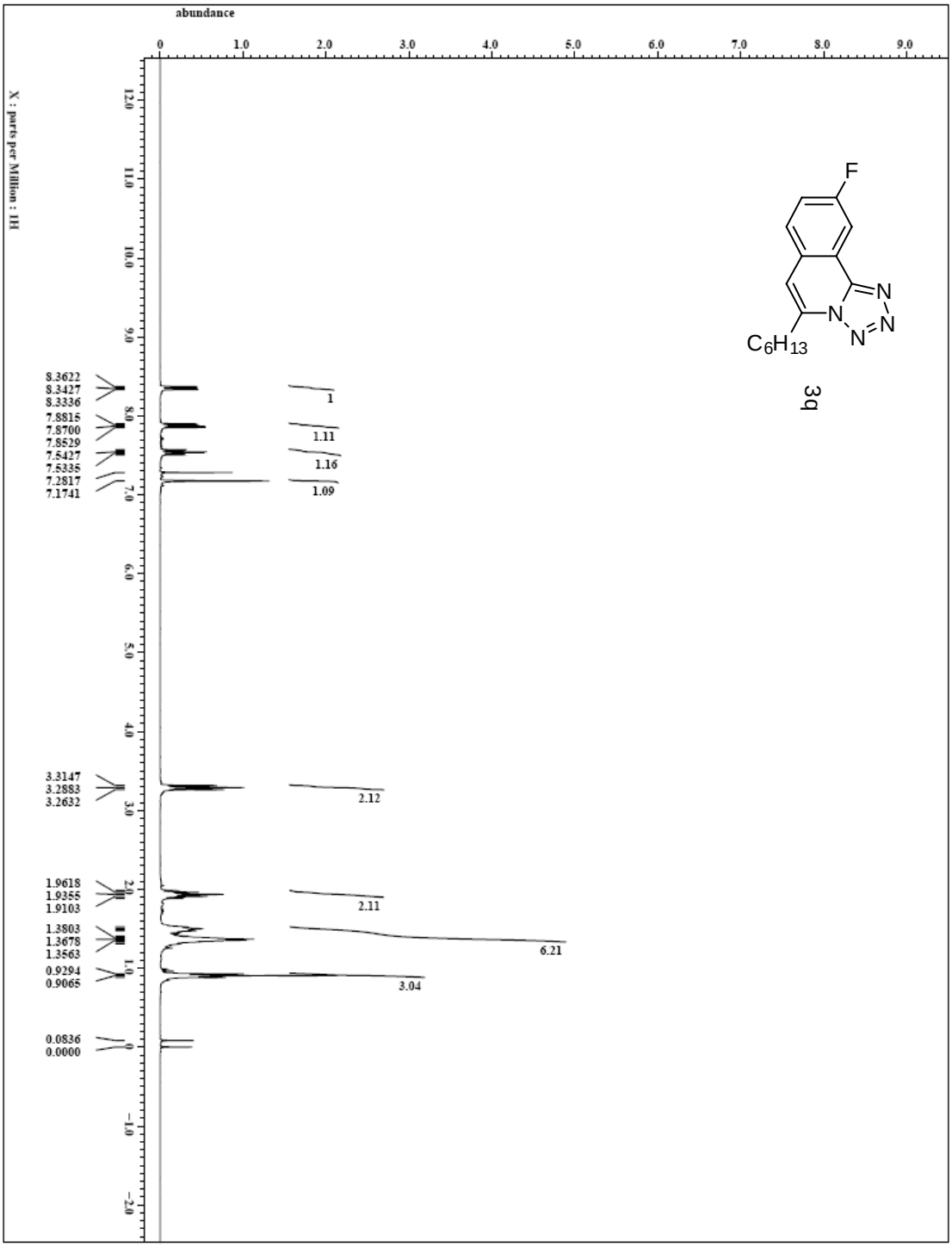

abundance
0
0.1
0.2
0.3
X : parts per Million : 13C
148.8596
142.8173
136.8037
134.0598
133.9164
132.4918
131.4497
130.6179
129.3942
127.4629
125.2544
117.0801
116.5351
77.6807
77.2600
76.8298
22.2576
0.2299
N
N
N
Cl
3n

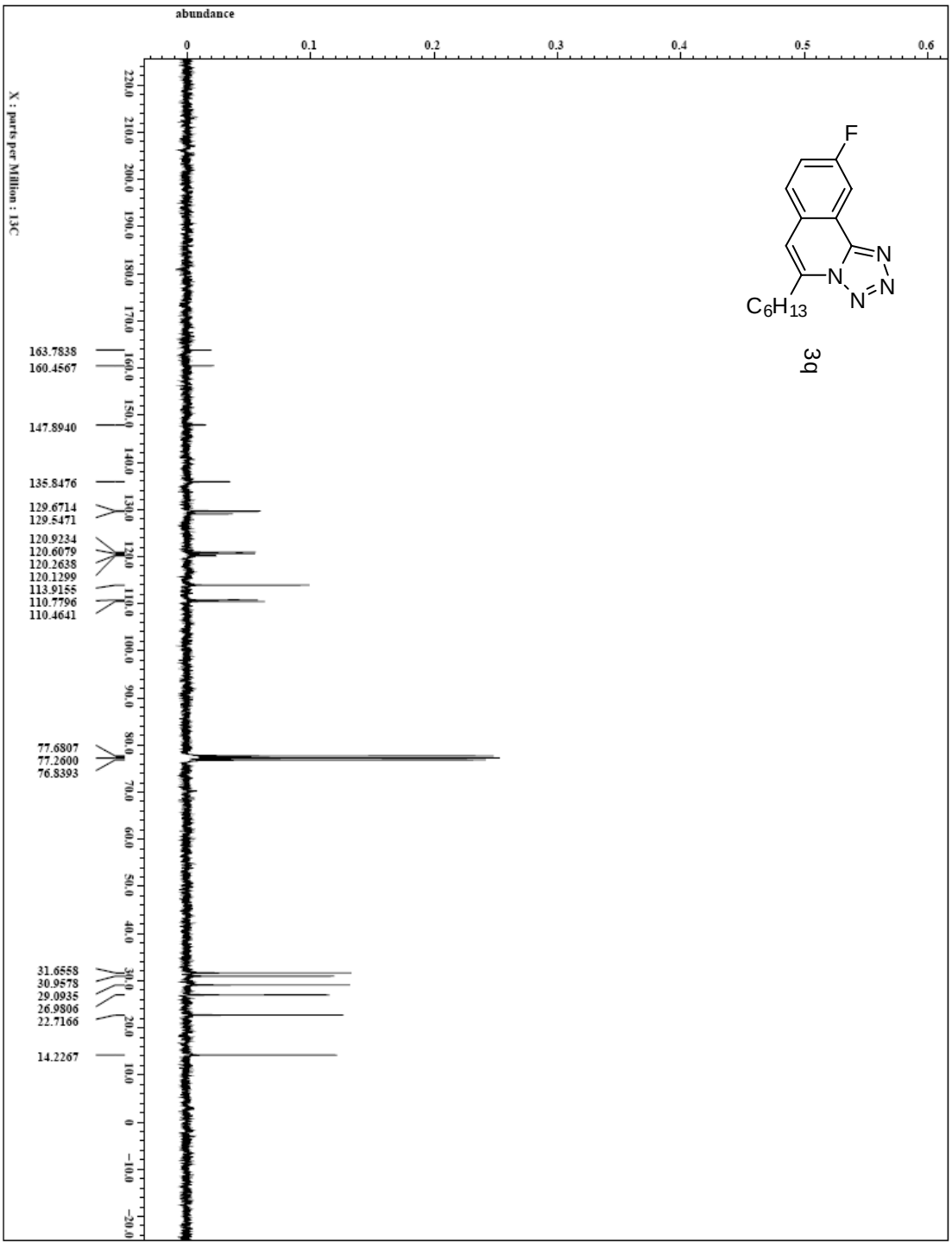

abundance
X : parts per Million : 1H
8.4858
8.4595
7.5095
7.4614
7.4580
7.4351
7.2005
6.9704
3.1853
3.1601
3.1350
2.4814
1.8233
1.2796
1.2670
1.2556
1.2441
1.2361
0.8344
0.8104
0.7875
0.0000
1
1.09
1.29
1.04
2.11
3.19
2.09
6.29
3.03
N
N
N
C_6H_{13}
3o

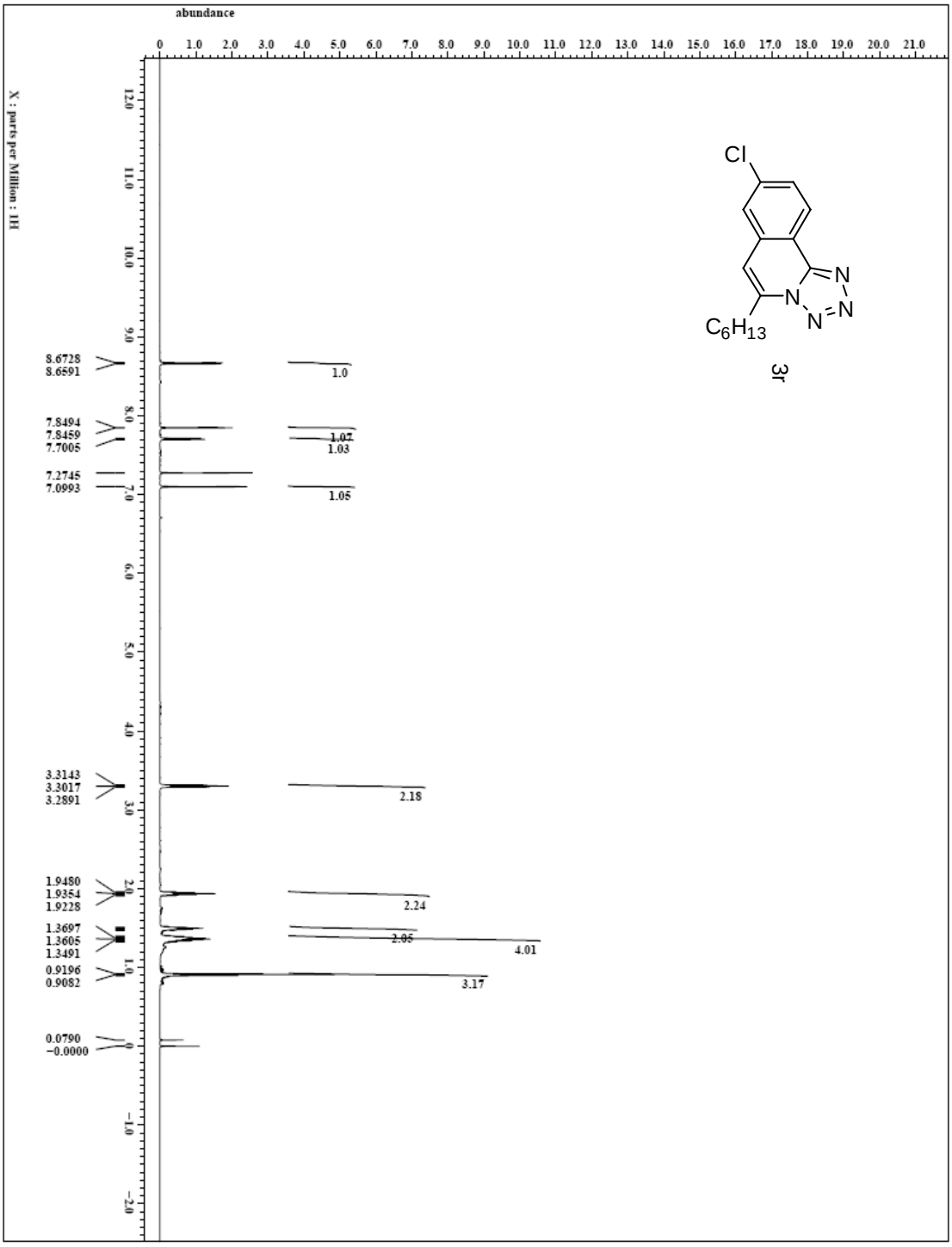

abundance
X : parts per Million : 13C
148.2382
142.2341
136.2013
132.5205
130.3311
126.7076
124.8720
116.4491
114.2501
77.6807
77.2600
76.8393
31.6366
30.9865
29.0553
26.9615
22.6974
22.1334
14.2076
1.1956
N
N
N
N
C6H13
30

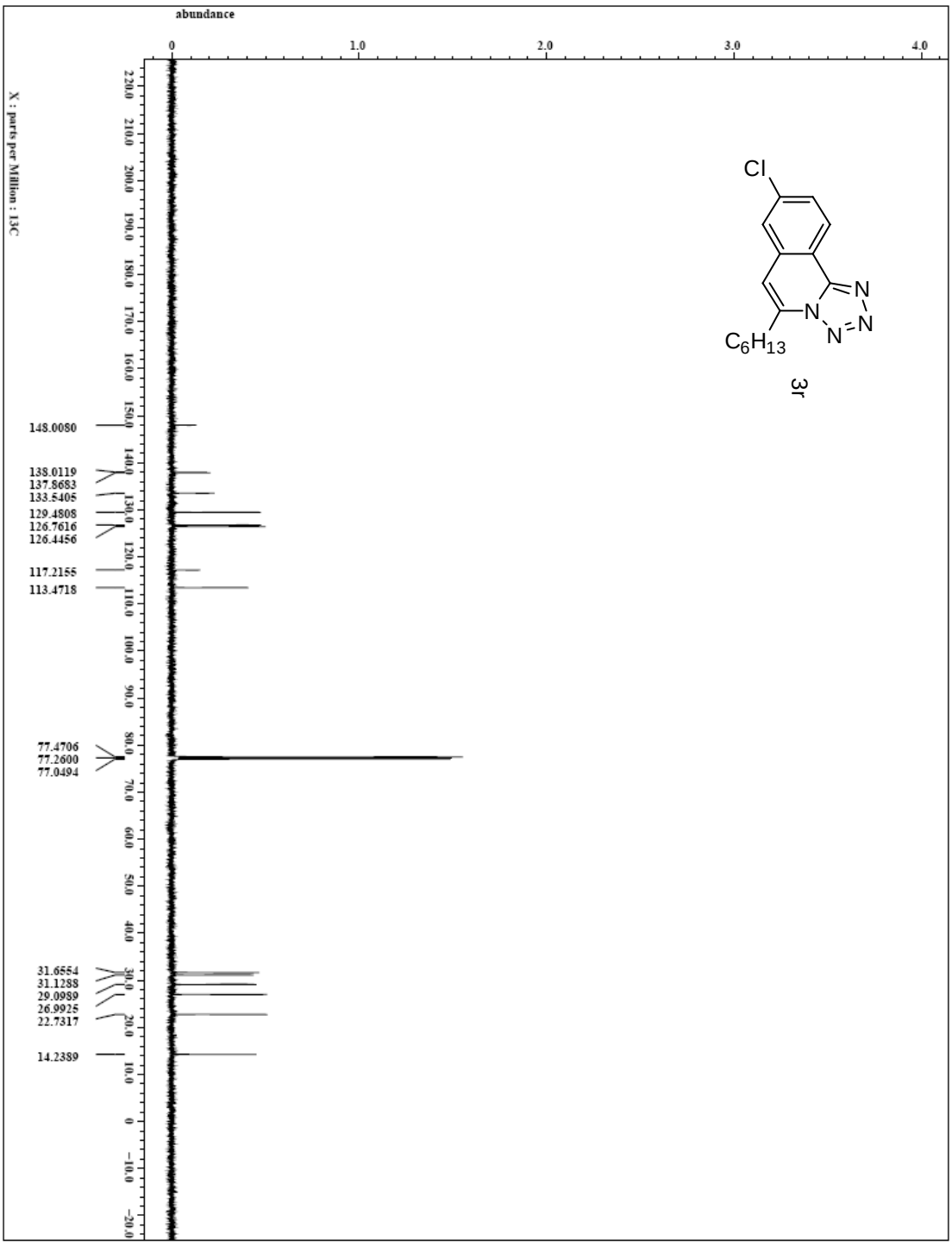


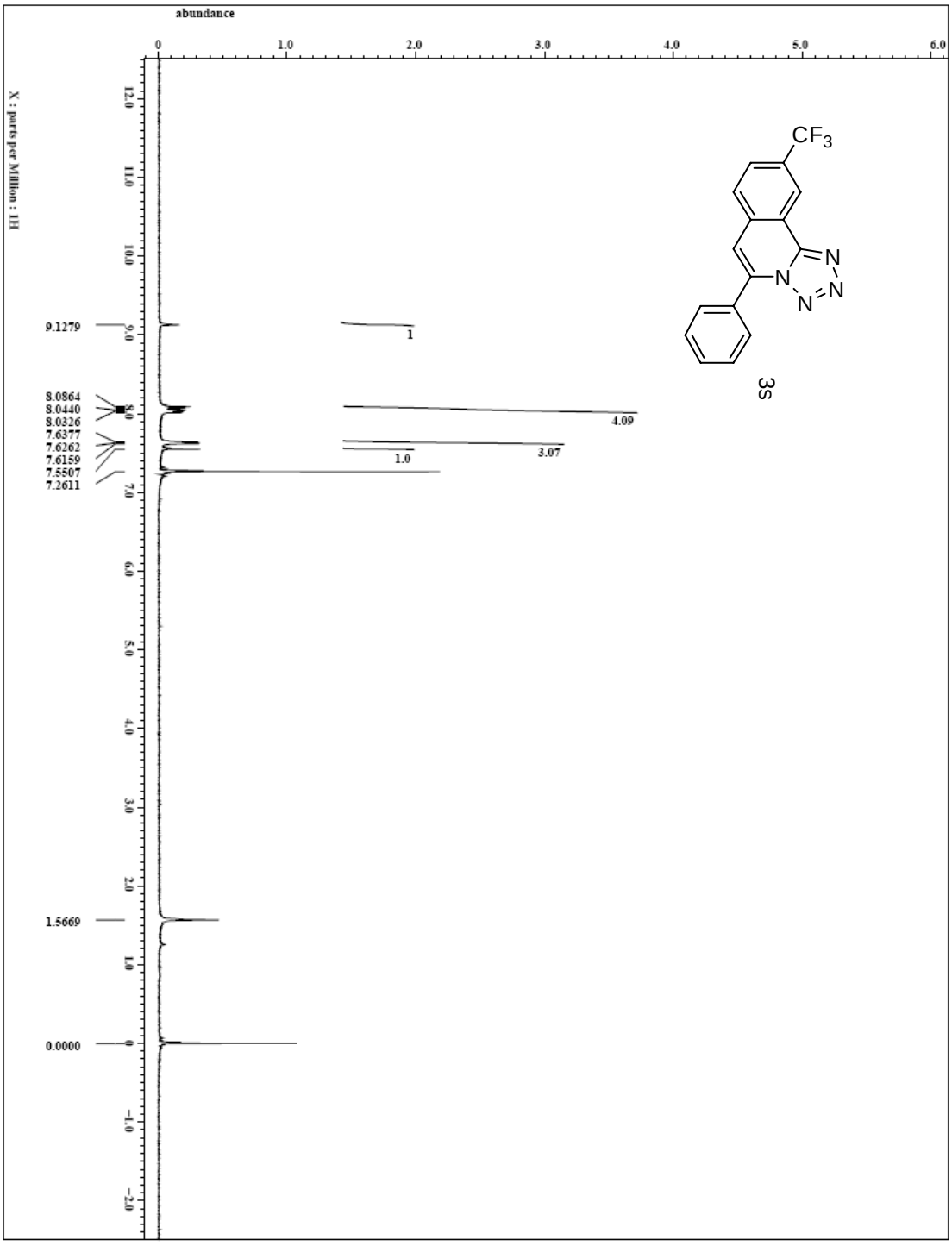


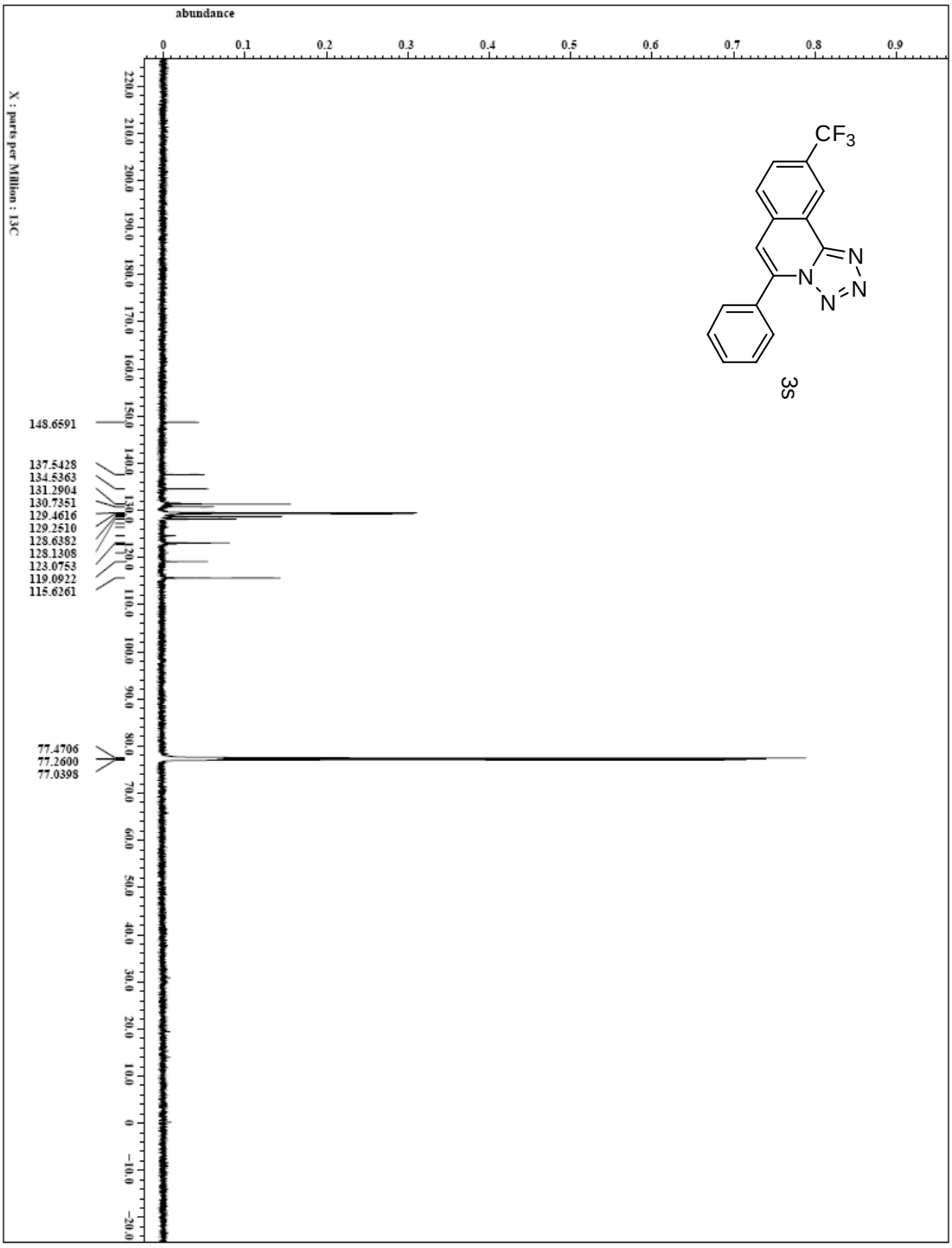

abundance
X : parts per Million : 1H
8.3622
8.3427
8.3336
7.8815
7.8700
7.8529
7.5427
7.5335
7.2817
7.1741
3.3147
3.2883
3.2632
1.9618
1.9355
1.9103
1.3803
1.3678
1.3563
0.9294
0.9065
0.0836
0.0000
1
1.11
1.16
1.09
2.12
2.11
6.21
3.04
F
N
N
N
C6H13
3q

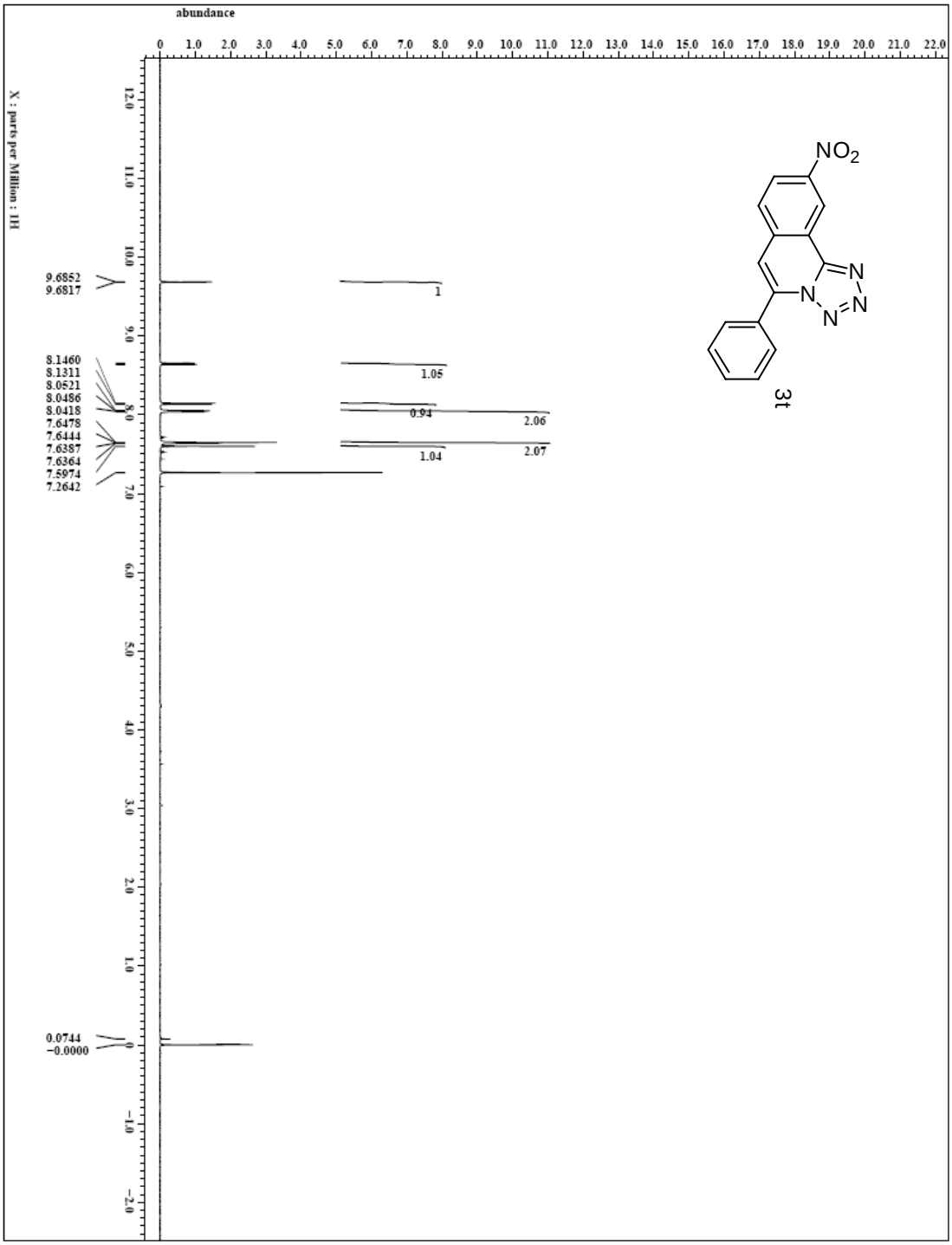


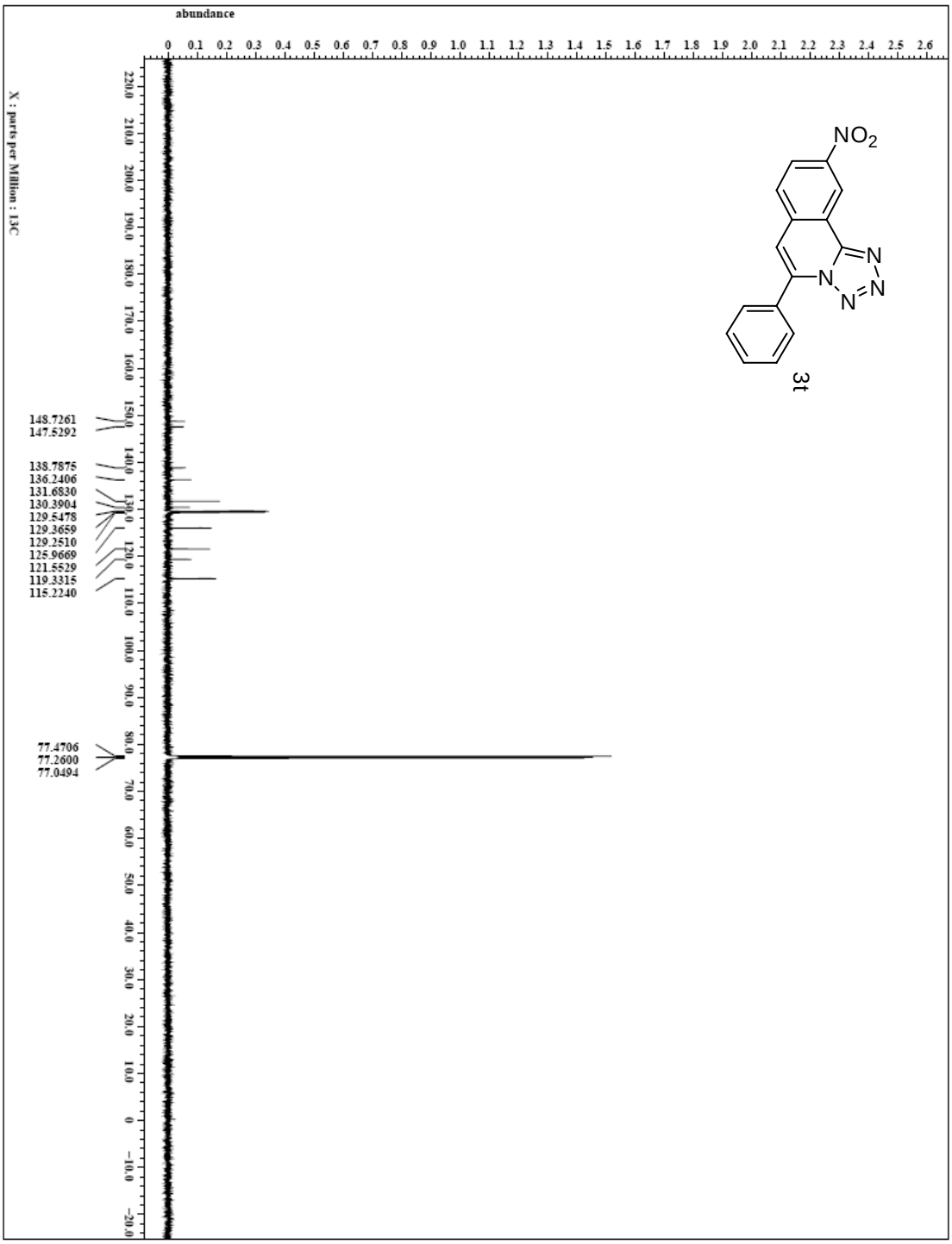

abundance
X : parts per Million : 1H
8.6728
8.6591
7.8494
7.8459
7.7005
7.2745
7.0993
3.3143
3.3017
3.2891
1.9480
1.9354
1.9228
1.3697
1.3605
1.3491
0.9196
0.9082
0.0790
−0.0000
1.0
1.07
1.03
1.05
2.18
2.24
2.05
4.01
3.17
Cl
N
N
N
C6H13
3r


abundance
X : parts per Million : 13C
148.0080
138.0119
137.8683
133.5405
129.4808
126.7616
126.4456
117.2155
113.4718
77.4706
77.2600
77.0494
31.6554
31.1288
29.0989
26.9925
22.7317
14.2389
Cl
N
N
N
C6H13
3r


abundance
X : parts per Million : 1H
9.1279
8.0864
8.0440
8.0326
7.6377
7.6262
7.6159
7.5507
7.2611
1.5669
0.0000
1
4.09
1.0
3.07
CF3
N
N
N
3s






abundance
X : parts per Million : 13C
148.7261
147.5292
138.7875
136.2406
131.6830
130.3904
129.5478
129.3659
129.2510
125.9669
121.5529
119.3315
115.2240
77.4706
77.2600
77.0494
NO2
N
N
N
N
3t