Supporting Information

Copper-Catalyzed Ring-Expansion Cascade of Azirines with Alkynes: Synthesis of Multisubstituted Pyridines at Room Temperature

Chandragiri Sujatha,[1] Chandra S. Bhatt,[2] Mahesh Kumar Ravva,[2] Anil K. Suresh[2] and Kayambu Namitharan*[1,2]

[1]Organic Synthesis and Catalysis Laboratory, SRM Research Institute, SRM Institute of Science and Technology, Chennai-603203, India.

[2]SRM University-AP, Amaravati-522502, India.

E-mail: namitharan25@gmail.com, namitharan.k@res.srmuniv.ac.in

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1. General Information

a) Synthesis:

Commercially available materials purchased from Alfa Aesar, Merck, Loba chemie, Aldrich and Combi blocks was used as received. Azirines **1** were prepared according to the published methods.[1] Except product **3a**,[2] all the other products **3b-s**, **4a-c** and **5a-b** are new. Proton nuclear magnetic resonance (1H NMR) spectra were recorded on a Bruker BBFO (500 MHz) spectrometer. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00) or chloroform (δ = 7.26, singlet). 1H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets), m (multiplets), and etc. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker BBFO (125 MHz) spectrometer. High resolution mass spectral analysis (HRMS) was performed on Bruker Impact HD mass spectrometer. X-ray crystallography analysis was performed on Bruker X8 APEX X-ray diffraction meter. Analytical thin-layer chromatography (TLC) was carried out on Merck 60 F254 pre-coated silica gel plate (0.2 mm thickness). Visualization was performed using a UV lamp.

b) Computational:

All of the reactants, transition states, and intermediate geometries were optimized in the gas phase using M062X and B3LYP functionals. The standard 6-31G (d, p) basis set for all nonmetals and LANL2DZ basis set for Cu were used. After geometry optimization, harmonic vibrational frequency analyses were performed at the same level for all structures to confirm that each local minimum has no imaginary frequency and that each transition state has only one imaginary frequency. To ensure each transition state correctly links to reactant and intermediate, intrinsic reaction coordinate (IRC) method was used. All calculations were carried out using Gaussian 16 software.[3]

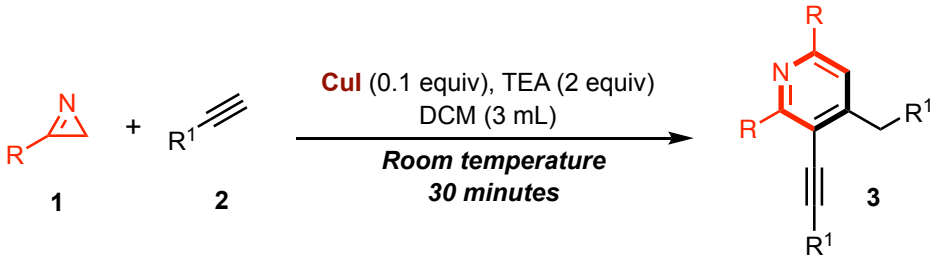
c) Biological Studies:

Anti-cancerous potential assessment of random pyridine derivatives (3a, 3b and 3h) were performed using the MTT assay as described earlier with slight modifications.[4] Briefly, the oral

cancer cells were seeded at 5 × 103 per well in a 96-well tissue culture plate and grown to 80% confluence in 200 µL of Roswell Park Memorial Institute medium (RPMI) (Invitrogen) supplemented with 0.2 mM L-glutamine, 100 U mL−1 penicillin, 100 µg mL−1 streptomycin and 10% FBS in a 5% CO2 humidified atmosphere. For each treatment the cells were washed twice with PBS and then incubated with a range of concentrations of different silver nanoparticles for 4 and 12 h. As the cytotoxicity trends for both these time points were similar, data for only 4 h is shown. Cells treated with the different capping agents alone and cells treated with silver nitrate (AgNO3), served as controls. For statistical data analysis and to ensure reproducibility, each treatment was performed in octuplet and each assay was repeated at least three times. After exposure to the nanoparticles, the cells were rinsed once with PBS, 200 µL of supplemented RPMI was added and the plate was incubated at 37 °C for 18−24 h. The MTT reagent (3-(4,5-dimethylthiazol-2-yl)-2,5- diphenyl tetrazolium bromide) was then added to each well (250 µg/ mL) and the cells were reincubated at 37 °C for additional 4 h. After a final wash with PBS, the PBS was aspirated and 200 µL of DMSO was added to each well and the absorbance at 560 nm was measured using a spectrophotometer.

2. Experiment procedures

a) General Procedure for the Synthesis of 3.



A solution of alkyne **2** (0.93 mmol, 0.1 g) in one mL of DCM was added slowly to a mixture of CuI (0.085 mmol, 0.016 g), azirine **1** (0.85 mmol, 0.1 g), and Et_3N (1.7 mmol, 0.237 g) taken in 2 mL of DCM. After stirring at room temperature for 30 minutes, the reaction mixture was concentrated under reduced pressure. The crude residue was directly applied to the silica gel chromatography (hexane/ethyl acetate, 99:1 ml) to give desired product **3.**

The crystal structure of compound **3a** has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 1570536 (Figure S1).

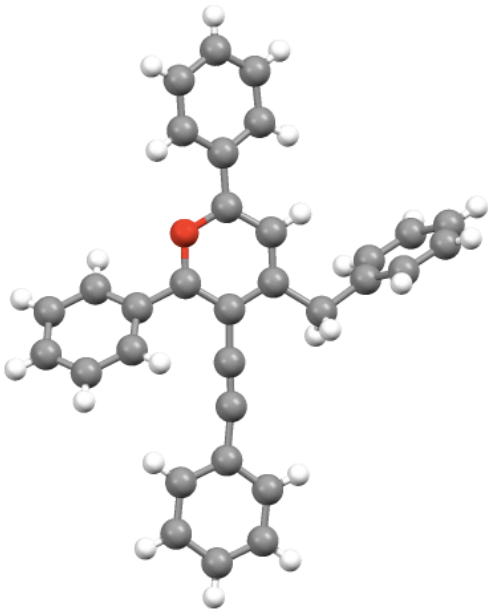
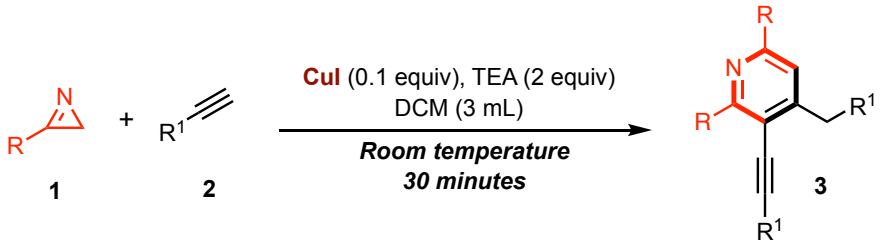


Figure S1 single crystal X-ray structure of compound **3a**.

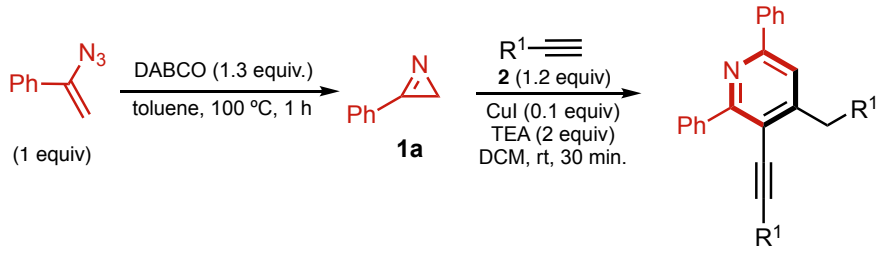
b) Gram scale synthesis of 3a



A solution of alkyne **2** (9.38 mmol, 1 g) in one mL of DCM was added slowly to a mixture of CuI (0.85 mmol, 0.162 g), azirine **1** (8.53 mmol, 1 g), and Et_3N (1.7 mmol, 2.37 g) taken in 15 mL of DCM. After stirring at room temperature for 30 minutes, the reaction mixture was concentrated under reduced pressure. The crude residue was directly applied to the silica gel chromatography (hexane/ethyl acetate, 99:1) to give desired product **3** (88%).

c) General procedure for the one pot synthesis of 3 from vinyl azides

Vinyl azide and DABCO were heated in toluene for 60 min. After the consumption of all the vinyl azide (from TLC), the reaction was allowed to drop to room temperature and the solvent was removed under reduced pressure. To the residue, DCM, CuI, TEA, and different alkynes were added and stirred for additional 30 minutes. The reaction mixture was concentrated under reduced pressure and the crude residue was directly applied to the silica gel chromatography (hexane/ethyl acetate) to give desired product **3.**



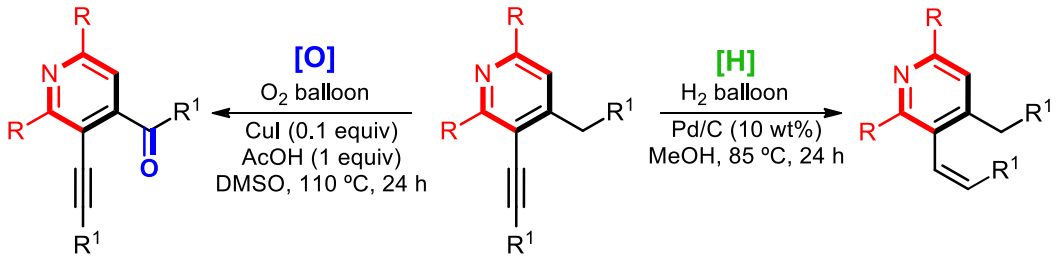
3a: R^1 = Ph, 87%

3b: R^1 = 4-MePh, 89%

3n: R^1 = cyclohexenyl, 75%

3s: R^1 = 5-chloropentyl, 71%

Synthetic Elaboration of 3



d) Synthesis of 4

A dry schlenk reaction tube was charged with 3 (0.5 mmol, 0.1 g), CuI (0.05 mmol, 0.004 g), DMSO (1 mL) and acetic acid (0.5 mmol, 0.013 g). The mixture was flushed with oxygen and stirred at 110 ºC for 24 h under oxygen atmosphere using an oxygen balloon. The reaction mixture was then cooled to room temperature, quenched with saturated aqueous $NaHCO_3$ and extracted with DCM (2 x 100 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure and the residue was applied to silica gel column chromatography (hexanes/ethyl acetate, 98:2) to give desired product **4**.

e) Synthesis of 5

A dry schlenk reaction tube was charged with 3 (0.5 mmol, 0.1 g), Pd/C (10 wt %, 0.01 g) and methanol (3 mL). The mixture was flushed with hydrogen and stirred at 85 ºC for 24 h under hydrogen atmosphere using a hydrogen balloon. The reaction mixture was then cooled to room temperature, diluted with DCM (10 mL) and filtered through a pad of silica. The solvent was evaporated under reduced pressure and the residue was applied to silica gel column chromatography (hexanes/ethyl acetate, 97:3) to give desired product **5**.

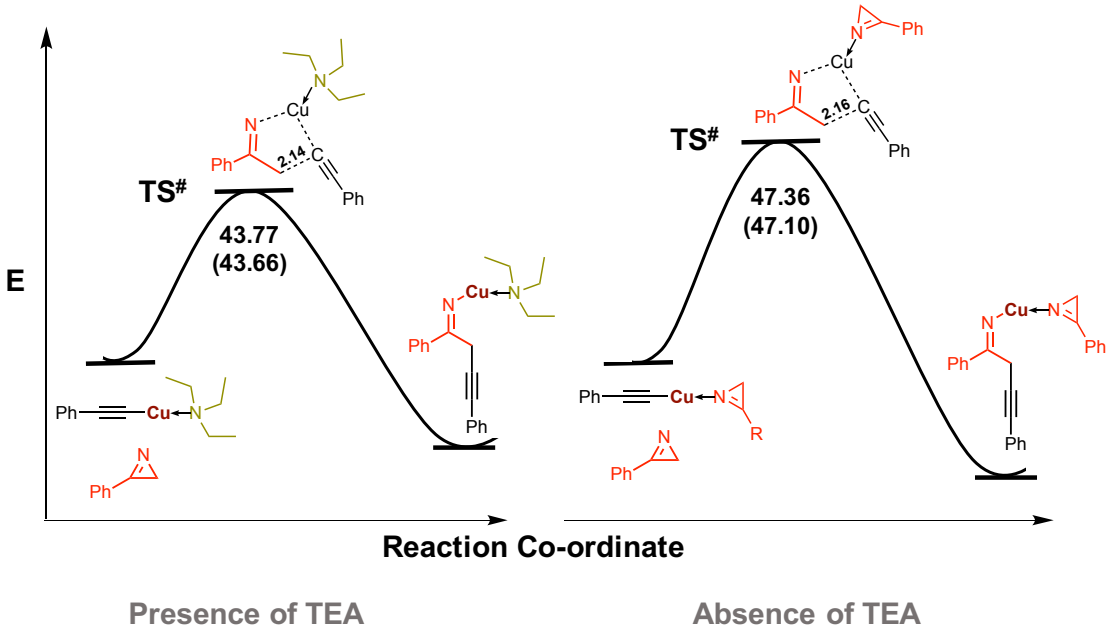
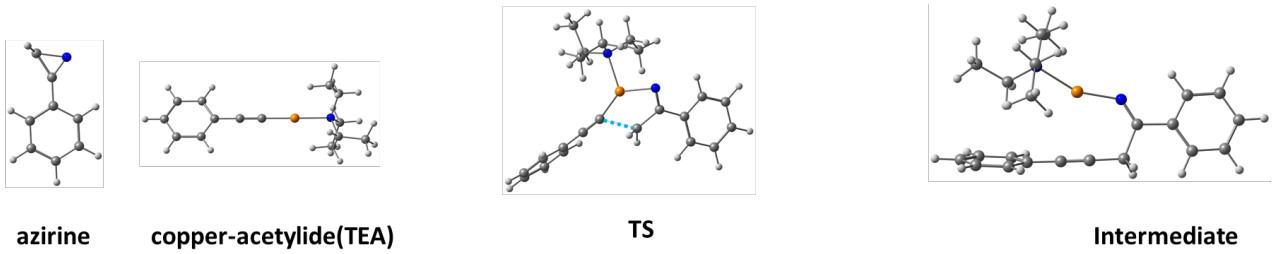
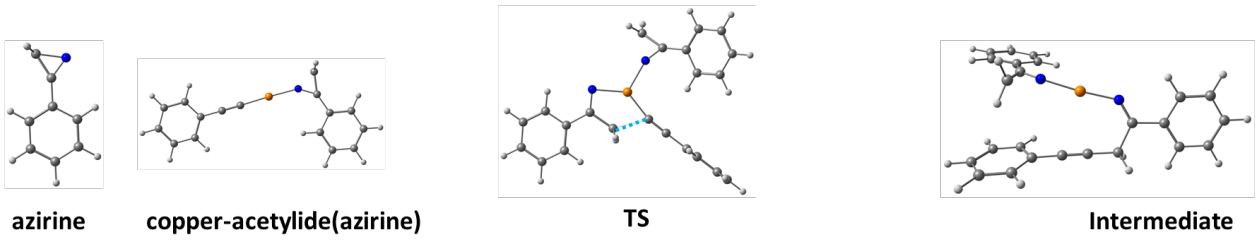


Figure S2. Relative free energy (kcal/mol) profiles of azirine reaction with copper-acetylide in the presence (left) and absence (right) of triethylamine. Bond distances are given in Å.



In the presence of TEA



In the absence of TEA

Figure S3. Optimized Geometries of Reactants, Transition States, and Intermediates.

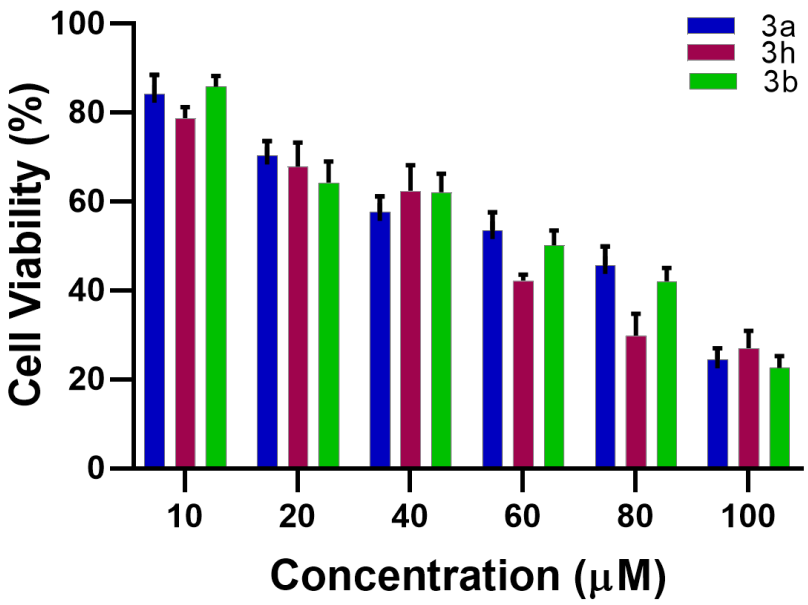
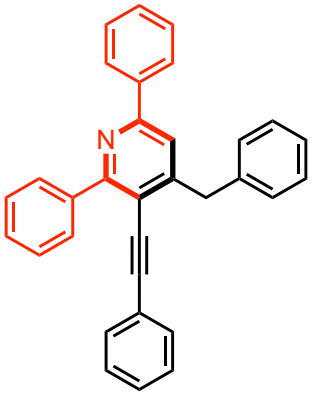


Figure S4. Anti-cancerous activity of the various (**3a**, **3b** and **3h**) pyridine derivatives as determined by MTT assay against human oral cancerous KB cells. Percent live cells were normalized to the cells only control. Error bars indicate the standard deviation of three different experiments with triplicates per experiment.

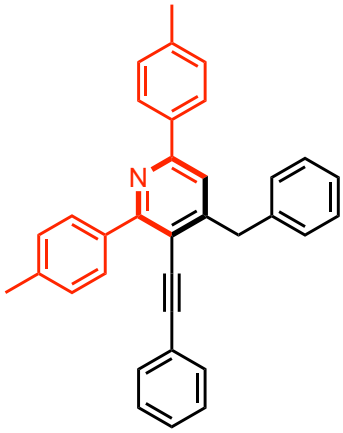
References:

1. a) Timen, A.; Risberg, E.; Somfai, P. *Tetrahedron Lett.* **2003***, 44,* 5339*; b)* Wang, R.; Yu, F.; Liu, P.; Chen, L. *Chem. Commun.* **2012***, 48,* 5310*; c)* Wang, Y.; Kah, T.; Lee, J.; Chiba, S. *Angew. Chem. Int. Ed.* **2011***, 50,* 5927.
2. He, Y.; Guo, S.; Zhang, X.; Fan, X.; *J. Org. Chem.* **2014**, *79*, 10611.
3. Gaussian 16, Revision A.03, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, **2016**.
4. a) Suresh, A. K.; Pelletier D. A.; and Doktycz, M. J. *Nanoscale*. **2013**, *5*, 463; b) Suresh, A. K.; Weng, Y.; Li, Z.; Zerda, R.; Haute, D. V.; Williams, J. C.; Berlin, J. M. *J. Mater. Chem. B* **2013**, *1*, 2341.

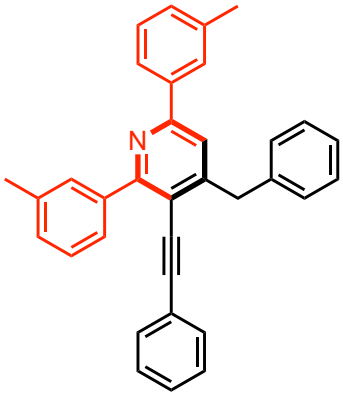
3. Characterization data



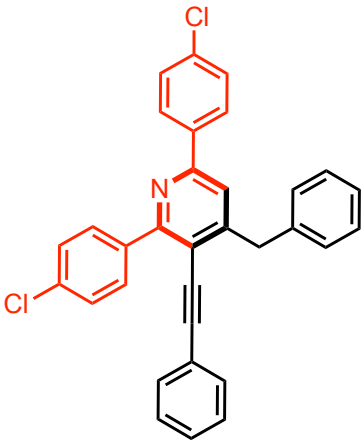
4-benzyl-2,6-diphenyl-3-(phenylethynyl) pyridine (3a): Light yellow solid (175 mg, 90% yield). Mp: 128-129 ^{o}C. **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.05 (d, *J* = 6.9 Hz, 2H), 7.98 (d, *J* = 8.1 Hz, 2H), 7.44-7.35 (m, 7H), 7.32-7.31(m, 1H), 7.27-7.23 (m, 8H), 7.19- 7.17 (m, 1H), 4.30 (s, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 158.95, 154.18, 152.26, 139.05, 137.82 , 137.77, 130.21, 128.72, 128.16, 128.12, 127.69, 127.63, 127.49, 127.37, 126.68, 126.06, 125.61, 122.15, 117.80, 115.14, 98.23, 85.68, 39.52; **HRMS** for **$C_{32}H_{24}N$** $[M+H]^+$ Calculated: **422.1909**, Found: **422.1907**.



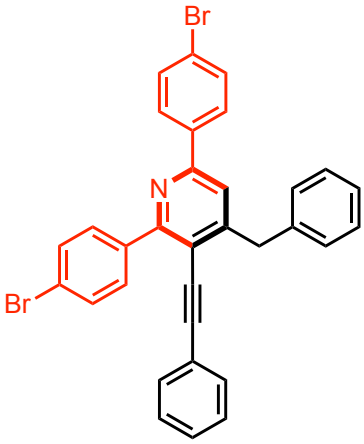
4-benzyl-3-(phenylethynyl)-2,6-di-p-tolylpyridine (3b): Light yellow solid (174 mg, 90% yield). Mp: 146.8-147.6 ^{o}C. **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.05-8.04 (m, 2H), 7.96-7.94 (m, 2H), 7.47 (s, 1H), 7.38 -7.35 (m, 2H), 7.34-7.29 (m, 9H), 7.27-7.23 (m, 3H), 4.35 (s, 2H), 2.44 (s, 3H), 2.39 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 159.75, 155.17, 153.19, 139.23, 138.99,138.61, 137.35, 136.11, 131.25, 129.67, 129.38, 129.17, 128.69, 126.98, 126.59, 123.36, 118.30, 115.56, 99.00, 87.00, 40.56, 21.45, 21.34; **HRMS** for **$C_{34}H_{27}N$** $[M+H]^+$Calculated: **450.2222**, Found: **450.2237**.



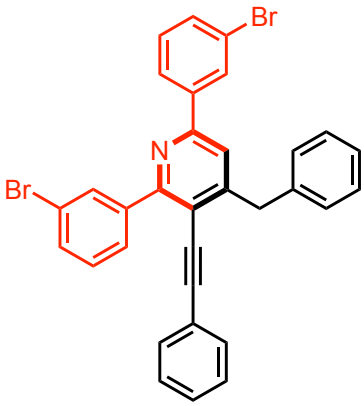
4-benzyl-3-(phenylethynyl)-2,6-di-m-tolyl pyridine (3c): Light yellow solid (164 mg, 85% yield). Mp: 125.5-126.7 ^{o}C. **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 7.91-7.89 (m, 3H), 7.80 (d, *J* = 12.4 Hz, 1H), 7.50 (s, 1H), 7.40-7.19 (m, 14H), 4.36 (s, 2H), 2.45 (s, 3H), 2.41 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 160.25, 155.50, 153.14, 140.08, 138.99, 138.90, 138.36, 137.27, 131.28, 130.43, 130.02, 129.51, 129.16, 128.74, 128.59, 128.50, 128.43, 127.86, 127.63, 126.97, 126.64, 124.30, 123.31, 119.03, 116.16, 99.23, 86.91, 40.60, 21.68, 21.60; **HRMS** for **$C_{34}H_{27}N$** $[M+H]^+$ Calculated: **450.2222**, Found: **450.2218**.



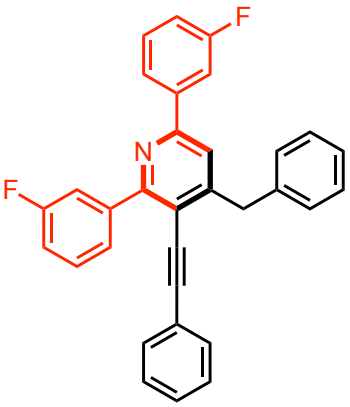
4-benzyl-2,6-bis(4-chlorophenyl)-3-(phenyl ethynyl) pyridine (3d): White solid (166 mg, 86% yield). Mp: 181.6-182.7°C. **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.07 (d, *J* = 7.6 Hz, 2H), 7.97 (d, *J* = 15.2 Hz, 2H), 7.48-7.46 (m, 3H), 7.41-7.40 (m, 2H), 7.35-7.27 (m, 10H), 4.36 (s, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 158.67, 154.03, 153.75, 138.59, 138.34, 137.02, 135.48, 134.94, 131.28, 131.10, 129.13, 128.91, 128.81, 128.53, 128.31, 127.98, 126.79, 122.85, 118.79, 116.37, 99.92, 86.17, 40.54 ; **HRMS** for **$C_{32}H_{22}Cl_2N$** $[M+H]^+$ Calculated: **490.1130**, Found: **490.1127**.



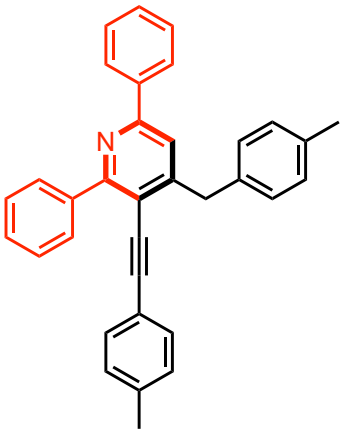
4-benzyl-2,6-bis(4-bromophenyl)-3-(phenyl ethynyl)pyridine (3e): Light yellow solid (169 mg, 87% yield). Mp: 190-190.5 °C. **^{1}H NMR**(500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.00 (d, *J* = 16.2 Hz, 2H),7.90 (d, *J* = 15.7 Hz, 2H), 7.63 (d, *J* = 13.8 Hz, 2H), 7.57 (d, *J* = 13.8 Hz, 2H), 7.48 (s, 1H), 7.35-7.34 (m, 9H), 7.28-7.27 (m, 1H), 4.36 (s, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 158.70, 154.09, 153.80, 138.78, 138.57, 137.45, 131.87, 131.39, 131.29, 130.94, 129.13, 128.82, 128.59, 128.55, 126.80, 123.87, 123.35, 122.82, 118.80, 116.41, 99.99, 86.14, 40.53; **HRMS** for **$C_{32}H_{22}Br_2N$** $[M+H]^+$ Calculated: **580.0120**, Found: **580.0101**.



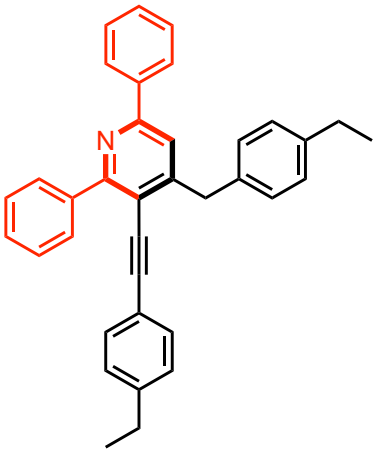
4-benzyl-2,6-bis(3-bromophenyl)-3-(phenylethynl)pyridine (3f): Light yellow solid (161 mg, 83% yield). Mp: 152.5-153.5 °C.**^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.31 (t, *J* = 1.9 Hz, 1H), 8.2 (t, *J* = 1.9 Hz, 1H), 8.02 (dt, *J* = 7.8 Hz, 1.6 Hz, 1H), 7.93 (dt, *J* = 7.8 Hz, 1.6 Hz, 1H), 7.61-7.59 (m, 1H), 7.54-7.52 (m, 1H), 7.51 (s, 1H), 7.42-7.40 (m, 2H), 7.38-7.37 (m, 1H), 7.35-7.33 (m, 8H), 7.32-7.30 (m,1H), 4.37 (s, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 158.38, 153.73, 141.73, 140.62, 138.53, 132.65, 132.25, 131.83, 131.44, 130.24, 130.08, 129.45, 129.08, 128.87, 128.50, 128.45, 126.82, 125.63, 123.07, 122.73, 121.76, 119.41, 116.99, 100.33, 85.90, 40.54; **HRMS** for **$C_{32}H_{22}Br_2N$** $[M+H]^+$ Calculated: **580.0120**, Found: **580.0101**.



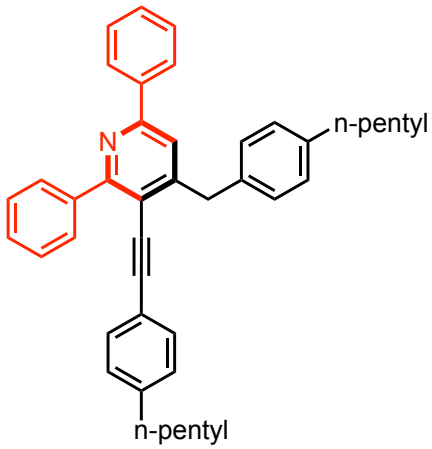
4-benzyl-2,6-bis(3-fluorophenyl)-3-(phenylethyny l)pyridine (3g): Light yellow solid (155 mg, 80% yield). Mp: 116-117 ^{o}C. **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 7.93-7.86 (m, 2H), 7.79-7.78 (m, 2H), 7.51 (s, 1H), 7.49-7.29 (m, 12H), 7.19-7.15 (m, 1H), 7.11-7.08 (m, 1H), 4.38 (s, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 162.36 (d, J = 116.9 Hz, 1C), 160.41 (d, J = 111.2 Hz, 1C), 157.40, 152.73, 137.49, 130.25, 129.18, 129.11, 128.22, 128.16, 128.08, 127.78, 127.46, 125.76, 124.45, 121.77, 121.51, 118.20, 115.80, 115.77, 115.59, 115.21, 115.04, 114.76, 114.59 , 113.04, 112.85, 99.14, 84.99, 39.48; **HRMS** for **$C_{32}H_{22}F_2N$** $[M+H]^+$ Calculated: **458.1721**, found: **458.1717**.



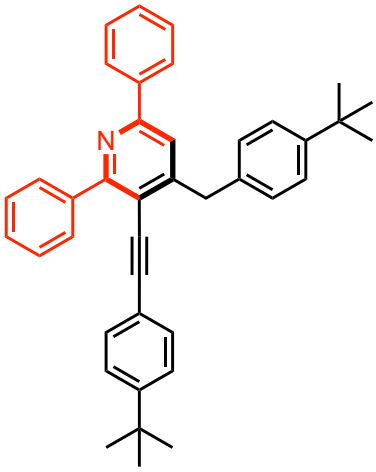
4-(4-methylbenzyl)-2,6-diphenyl-3-(p-tolylethynyl) pyridine (3h): White solid (174 mg, 90% yield). Mp: 98-99 ^{o}C. **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.12-8.10 (m, 2H), 8.05-8.04 (m, 2H), 7.51-7.43 (m, 6H), 7.40-7.39 (m, 1H), 7.27-7.24 (m, 4H), 7.15-7.12 (m, 4H), 4.32 (s, 2H), 2.36 (s, 3H), 2.34 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 158.80, 154.01, 152.49, 139.16, 137.91, 137.71, 135.13, 134.84, 130.14, 128.75, 128.37, 128.15, 128.08, 128.03, 127.61, 126.65, 126.07, 119.18, 117.76, 115.33, 98.49, 85.13, 39.11, 20.51, 20.04; **HRMS** for **$C_{34}H_{28}N$** $[M+H]^+$ Calculated: **450.2222**, Found: **450.2224**.



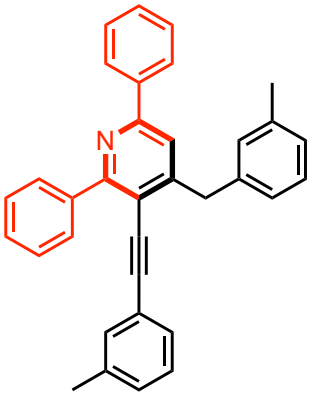
4-(4-ethylbenzyl)-3-((4-ethylphenyl)ethynyl)-2,6-diphenylpyridine (3i): Brown semi solid (161 mg, 83% yield) **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.13-8.11 (m, 2H), 8.06-8.04 (m, 2H), 7.52-7.43 (m, 7H), 7.29-7.27 (m, 4H), 7.17-7.14 (m, 4H), 4.33 (s, 2H), 2.67-2.63 (m, 4H), 1.24-1.21 (m, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 158.76, 153.96, 152.43, 143.99, 141.49, 139.12, 137.88, 135.09, 130.47, 130.22, 128.73, 128.06, 128.03, 127.59, 127.56, 127.15, 126.94, 126.63, 126.05, 119.38, 117.78, 115.31, 98.46, 85.13, 39.11, 27.83, 27.44, 14.57, 14.34; **HRMS** for **$C_{36}H_{32}N$** $[M+H]^+$ Calculated: **478.2536**, Found: **478.2537**.



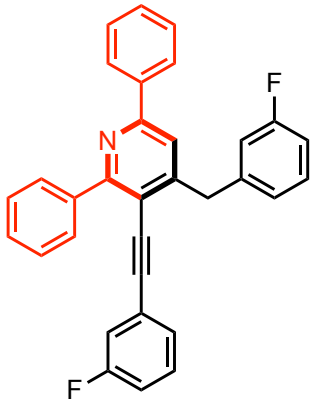
4-(4-pentylbenzyl)-3-((4-pentylphenyl)ethynyl)-2,6-diphenylpyridine (3j): Brown semi solid (144 mg, 74% yield) **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.13-8.12 (m, 2H), 8.05-8.04 (m, 2H), 7.51-7.47 (m, 3H), 7.45-7.42 (m, 3H), 7.39-7.36 (m, 1H), 7.28-7.23 (m, 4H), 7.15-7.12 (m, 4H), 4.33 (s, 2H), 2.61-2.57 (m, 4H), 1.61-1.58 (m, 4H), 1.34-1.30 (m, 8H), 0.90-0.87 (m, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 159.80, 155.00, 153.53, 143.80, 141.27, 140.21, 138.96, 136.10, 131.21, 129.80, 129.13, 129.04, 128.77, 128.67, 128.55, 127.71, 127.11, 120.41, 118.85, 116.40, 99.59, 86.21, 40.19, 35.94, 35.59, 31.55, 31.45, 31.23, 30.98, 22.59, 22.56, 14.09, 14.06; **HRMS** for **$C_{42}H_{44}N$** $[M+H]^+$ Calculated: **562.3475**, Found: **562.3488**.



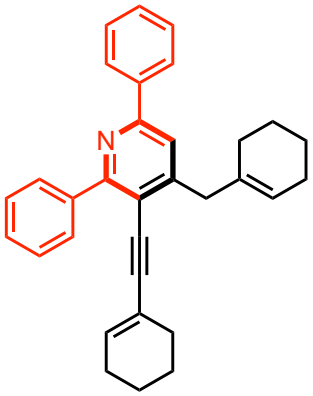
4-(4-(tert-butyl)benzyl)-3-((4-(tert-butyl) phenyl) ethynyl)-2,6-diphenylpyridine (3k): Brown solid (155 mg, 80% yield). Mp: 160-161.2 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.13-8.10 (m, 2H), 8.05 (d, J = 6.9 Hz, 2H), 7.55 (s, 1H), 7.49-7.39 (m, 6H), 7.36-7.34 (m, 4H), 7.31-7.29 (m, 4H), 4.33 (s, 2H), 1.31 (s, 18H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 158.82, 153.96, 152.38, 150.81, 148.35, 139.14, 137.90, 134.93, 131.22, 129.98, 128.73, 128.06, 127.70, 127.60, 126.63, 126.06, 124.57, 124.43, 124.37, 119.20, 117.86, 115.33, 98.38, 85.20, 39.00, 33.79, 33.40, 30.34, 30.12, 30.07, 28.67; **HRMS** for **$C_{40}H_{40}N$** $[M+H]^+$ Calculated: **534.3162**, Found: **534.3159**.



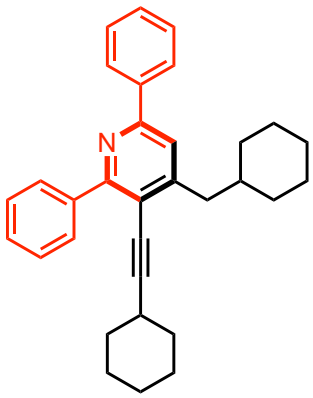
4-(3-methylbenzyl)-2,6-diphenyl-3-(m-tolyl ethynyl) pyridine (3l): White solid (172 mg, 89% yield). Mp: 125.5-126.7 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.13-8.05 (m, 4H),7.52-7.48 (m, 3H), 7.46-7.43 (m, 3H), 7.40-7.37 (m, 1H), 7.23-7.12 (m, 7H), 7.08-7.06 (m, 1H), 4.33 (s, 2H), 2.33 (s, 3H), 2.32 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 159.87, 155.12, 153.43, 140.14, 138.90, 138.82, 138.32, 138.09, 131.82, 130.03, 129.79, 129.44, 129.18, 128.71, 128.08, 128.60, 128.37, 128.31, 127.72, 127.40, 127.12, 126.23, 123.05, 118.89, 116.29, 99.55, 86.42, 40.53, 21.47, 21.28; **HRMS** for **$C_{34}H_{28}N$** $[M+H]^+$ Calculated: **450.2222**, Found: **450.2237**.



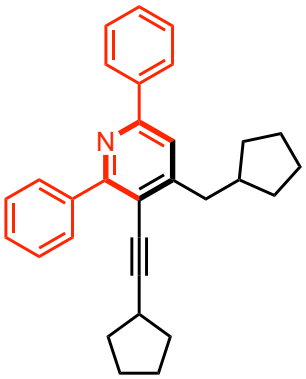
4-(3-fluorobenzyl)-3-((3-fluorophenyl)ethynyl)-2,6-diphenylpyridine (3m): Light yellow solid (153 mg, 79% yield). Mp: 131.4-132.3°C. **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.09-8.06 (m, 4H), 7.53-7.41 (m, 7H), 7.33-7.27 (m, 2H), 7.11 (d, *J* = 12.1 Hz, 2H), 7.04-6.95 (m, 4H), 4.34 (s, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 163.37 (d, *J* = 94.5 Hz, 1C), 162.07 (d, *J* = 93.2 Hz, 1C), 160.42, 155.69, 152.53, 138.87, 138.58, 130.24, 130.17, 130.10, 130.03, 129.71, 129.45, 128.97, 128.76, 127.82, 127.15, 124.76, 124.74, 118.86, 118.05, 117.87, 116.10, 116.06, 115.93, 115.89, 115.73, 113.78, 113.61, 97.97, 87.41, 40.29; **HRMS** for **$C_{32}H_{22}F_2N$** $[M+H]^+$ Calculated: **458.1721**, Found: **458.1734**.



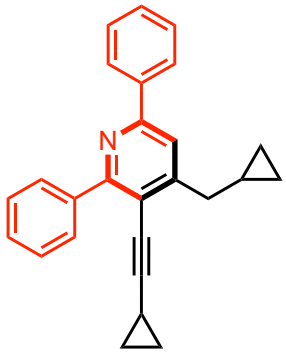
3-(cyclohex-1-en-1-ylethynyl)-4-(cyclohex-1-en-1-ylmethyl)-2,6-diphenylpyridine (3n): yellow semi solid (153 mg, 79% yield) **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.11-8.09 (m, 2H), 8.07-8.05 (m, 2H), 7.56 (s, 1H), 7.48-7.43 (m, 4H), 7.42-7.39 (m, 2H), 6.06 (t, *J* = 3.7 Hz, 1H), 5.56 (t, *J* = 2.4 Hz, 1H), 3.55 (s, 2H), 2.15-2.12 (m, 4H), 2.06-1.99(m, 4H), 1.66-1.63 (m, 4H), 1.61-1.58 (m, 4H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 159.35, 154.32, 152.49, 140.30, 139.15, 135.35, 135.27, 129.74, 128.96, 128.65, 128.43, 127.54, 127.00, 124.40, 121.12, 118.49, 117.09, 100.95, 84.08, 42.73, 28.66, 28.35, 25.81, 25.44, 23.00, 22.37, 22.26, 21.52; **HRMS** for **$C_{32}H_{32}N$** $[M+H]^+$ Calculated: **430.2536**, Found: **430.2532**.



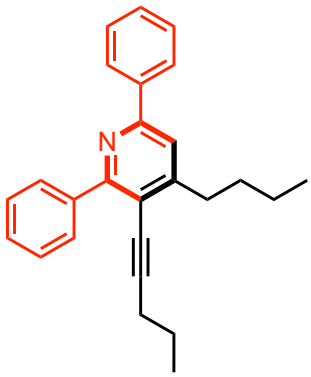
3-(cyclohexylethynyl)-4-(cyclohexylmethyl)-2,6-diphenylpyridine (3o): yellow liquid (135 mg, 70% yield) **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.10-8.05 (m, 4H), 7.48-7.39 (m, 7H), 2.76 (d, *J* = 9.9 Hz, 2H), 2.63-2.59 (m, 1H), 1.81-1.71 (m, 11H), 1.52-1.49 (m, 2H), 1.36-1.29 (m, 4H), 1.19-1.10 (m, 2H), 1.08-1.05 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 159.56, 153.83, 153.79, 140.37, 139.21, 129.75, 128.88, 128.64, 128.32, 127.49, 127.04, 119.41, 117.15, 104.13, 42.94, 38.30, 33.40, 32.23, 26.54, 26.31, 25.95, 24.75; **HRMS** for **$C_{32}H_{36}N$** $[M+H]^+$ Calculated: **434.2849**, Found: **434.2855**.



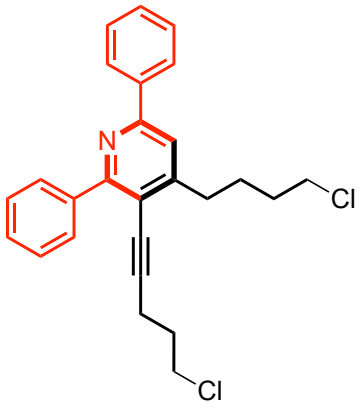
3-(cyclopentylethynyl)-4-(cyclopentylmethyl)-2,6-diphenylpyridine (3p): Brown viscous liquid (142 mg, 74% yield) **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.10-8.04 (m, 4H), 7.53 (s, 1H), 7.47-7.38 (m, 6H), 2.88 (d, *J* = 7.2 Hz, 2H), 2.84-2.81 (m, 1H), 2.33-2.30 (m, 1H), 1.92-1.90 (m, 2H), 1.76-1.66 (m, 10H), 1.33-1.31 (m, 4H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 167.79, 159.45, 154.58, 154.06, 140.43, 139.24, 130.91, 129.69, 128.87, 128.83, 128.64, 128.32, 127.50, 127.02, 118.79, 116.97, 104.45, 68.17, 40.74, 40.38, 33.48, 32.59, 31.24, 25.00, 24.95; **HRMS** for **$C_{30}H_{32}N$** $[M+H]^+$Calculated: **406.2536**, Found: **406.2541**.



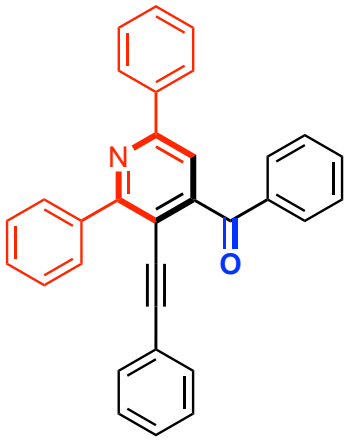
3-(cyclopropylethynyl)-4-(cyclopropylmethyl)-2,6-diphenylpyridine (3q): Brown semi solid (152 mg, 80% yield) **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS)δ; 8.09 (d, *J* = 11.3 Hz, 2H), 8.0 (d, *J* = 11.3 Hz, 2H), 7.71 (s, 1H), 7.45-7.40 (m, 6H), 2.78 (d, *J* = 11.3 Hz, 2H), 1.42-1.41 (m, 1H), 1.18-1.14 (m, 1H), 0.83-0.82 (m, 2H), 0.70-0.60 (m, 4H), 0.31-0.30 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 158.80, 153.74, 153.56, 139.71, 138.57, 128.87, 128.17, 127.92, 127.64, 126.80, 117.18, 115.95, 102.87, 71.76, 38.14, 9.52, 7.86, 4.12; **HRMS** for **$C_{26}H_{24}N$** $[M+H]^+$ Calculated: **350.1909**, Found: **350.1906**.



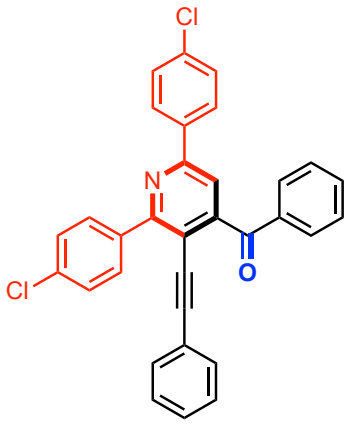
4-butyl-3-(pent-1-yn-1-yl)-2,6-diphenyl pyridine (3r): yellow liquid (131 mg, 69% yield) **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.09 (d, *J* = 7.6 Hz, 2H), 8.03(d, *J* = 7.6 Hz, 2H), 7.55 (s, 1H), 7.46-7.40 (m, 6H), 2.89 (t, J= 8.8 Hz, 2H), 2.37 (t, J= 7.9 Hz, 2H),1.73-1.71 (m, 2 H), 1.48-1.44 (m, 2H), 0.98 (t, *J* = 7 Hz, 6H), 0.88-0.87 (m, 2 H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 159.67, 155.28, 154.29, 140.47, 139.22, 129.66, 128.89, 128.63, 128.31, 127.57, 127.03, 118.31, 116.7, 100.09, 34.64, 31.95, 22.72, 21.94, 21.88, 13.97, 13.61; **HRMS** for **$C_{26}H_{28}N$** $[M+H]^+$ Calculated: **354.2222**, Found: **354.2221**.



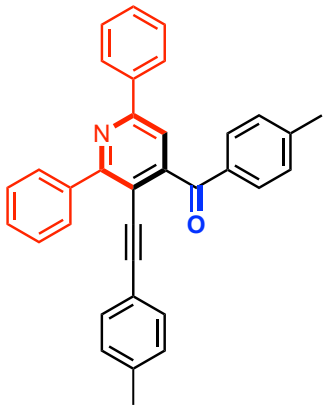
4-(4-chlorobutyl)-3-(5-chloropent-1-yn-1-yl)-2,6-diphenylpyridine (3s): Brown semi solid (142 mg, 74% yield) **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.10-8.08 (m, 2H), 7.98-7.96 (m, 2H), 7.56 (s, 1H), 7.48-7.46 (m, 3H), 7.45-7.44 (m, 1H), 7.43-7.40 (m, 2H), 3.62 (t, *J* = 5.9 Hz, 2H), 3.53 (t, *J* = 6.3 Hz, 2H), 2.93-2.89 (m, 2H), 2.62 (t, J= 6.7 Hz, 2H), 1.97 (t, J= 6.5 Hz, 2H), 1.93-1.90 (m, 4H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 160.22, 154.77, 154.23, 140.31, 138.92, 129.53, 129.11, 128.69, 128.52, 127.70, 127.06, 118.22, 116.32, 97.97, 44.72, 43.57, 34.03, 32.30, 31.04, 26.95, 17.22; **HRMS** for **$C_{26}H_{26}Cl_2N$** $[M+H]^+$ Calculated: **422.1443**, Found: **422.1446**.



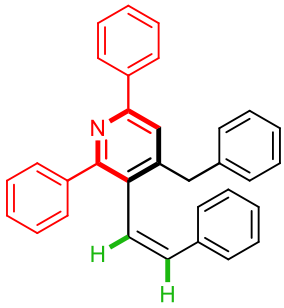
(2,6-diphenyl-3-(phenylethynyl)pyridin-4-yl) (phenyl)methanone (4a): yellow solid (93 mg, 90% yield). Mp: 119.5-120.6 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.19-8.16 (m, 4H), 8.0-7.98 (m, 2H), 7.78 (s, 1H), 7.65-7.61 (m, 1H), 7.54-7.48 (m, 7H), 7.46-7.43 (m, 1H), 7.24-7.21 (m, 1H), 7.18-7.15 (m, 2H), 6.91-6.89 (m, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 195.84, 159.84, 155.62, 151.47, 139.17, 138.04, 135.98, 134.06, 131.15, 130.23, 129.82, 129.77, 129.26, 128.89, 128.82, 128.71, 128.16, 127.90, 127.15, 122.42, 116.01, 112.96, 100.35, 85.78; **HRMS** for **$C_{32}H_{22}NO$** $[M+H]^+$ Calculated: **436.1702**, Found: **436.1719**.



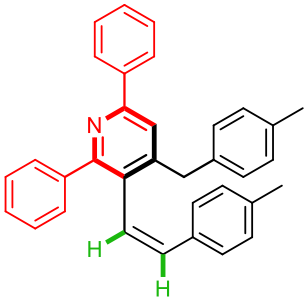
4-benzyl-2,6-bis(4-chlorophenyl)-3-(phenyl ethynyl)pyridine (4b): yellow solid (94 mg, 91% yield). Mp: 161.5-162.2 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.14-8.09 (m, 4H), 7.98 (d, *J* = 8.1 Hz, 2H), 7.75 (s, 1H), 7.65 (t, *J* = 7.7 Hz, 1H), 7.54-7.46 (m, 6H), 7.27-7.24 (m, 1H), 7.21-7.18 (m, 2H), 6.91 (d, *J* = 8.5 Hz, 2H) ; **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 195.43, 158.53, 154.45, 151.81, 137.42, 136.26, 136.15, 135.51, 134.16, 131.15, 131.07, 130.18, 129.13, 128.96, 128.86, 128.36, 128.25, 128.15, 122.08, 116.01, 113.14, 101.01, 85.28 ; **HRMS** for **$C_{32}H_{20}Cl_2NO$** $[M+H]^+$ Calculated: **504.0923**, Found: **504.0910**.



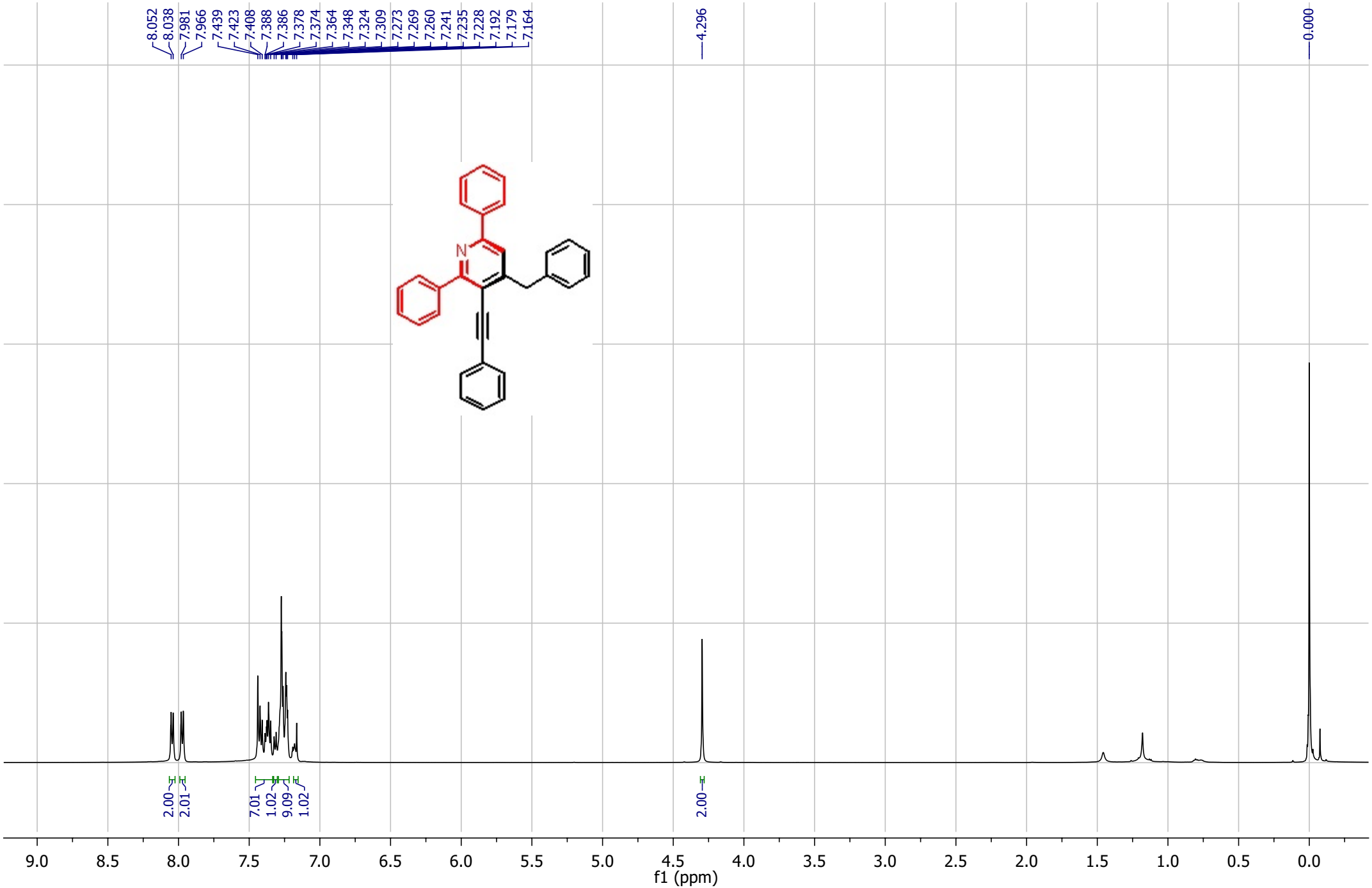
(2,6-diphenyl-3-(p-tolylethynyl)pyridin-4-yl)(p-tolyl)methanone (4c): yellow solid (91 mg, 88% yield). Mp: 171.9-172.8 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 8.19-8.15 (m, 4H), 7.88 (d, *J* = 10.7 Hz, 2H), 7.75 (s, 1H), 7.53-7.44 (m, 6H), 7.3 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 9.7 Hz, 2H), 6.83 (d, *J* = 10.2 Hz, 2H), 2.43 (s, 3H), 2.28 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 195.51, 159.62, 155.31, 151.63, 145.10, 139.27, 138.94, 138.13, 133.56, 131.19, 131.00, 130.51, 130.29, 129.86, 129.68, 129.53, 129.43, 128.96, 128.89, 128.76, 127.96, 127.75, 127.21, 127.02, 119.48, 116.05, 115.82, 113.18, 100.47, 85.25, 21.92, 21.77; **HRMS** for **$C_{34}H_{26}NO$** $[M+H]^+$ Calculated: **464.2015**, Found: **464.2022**.



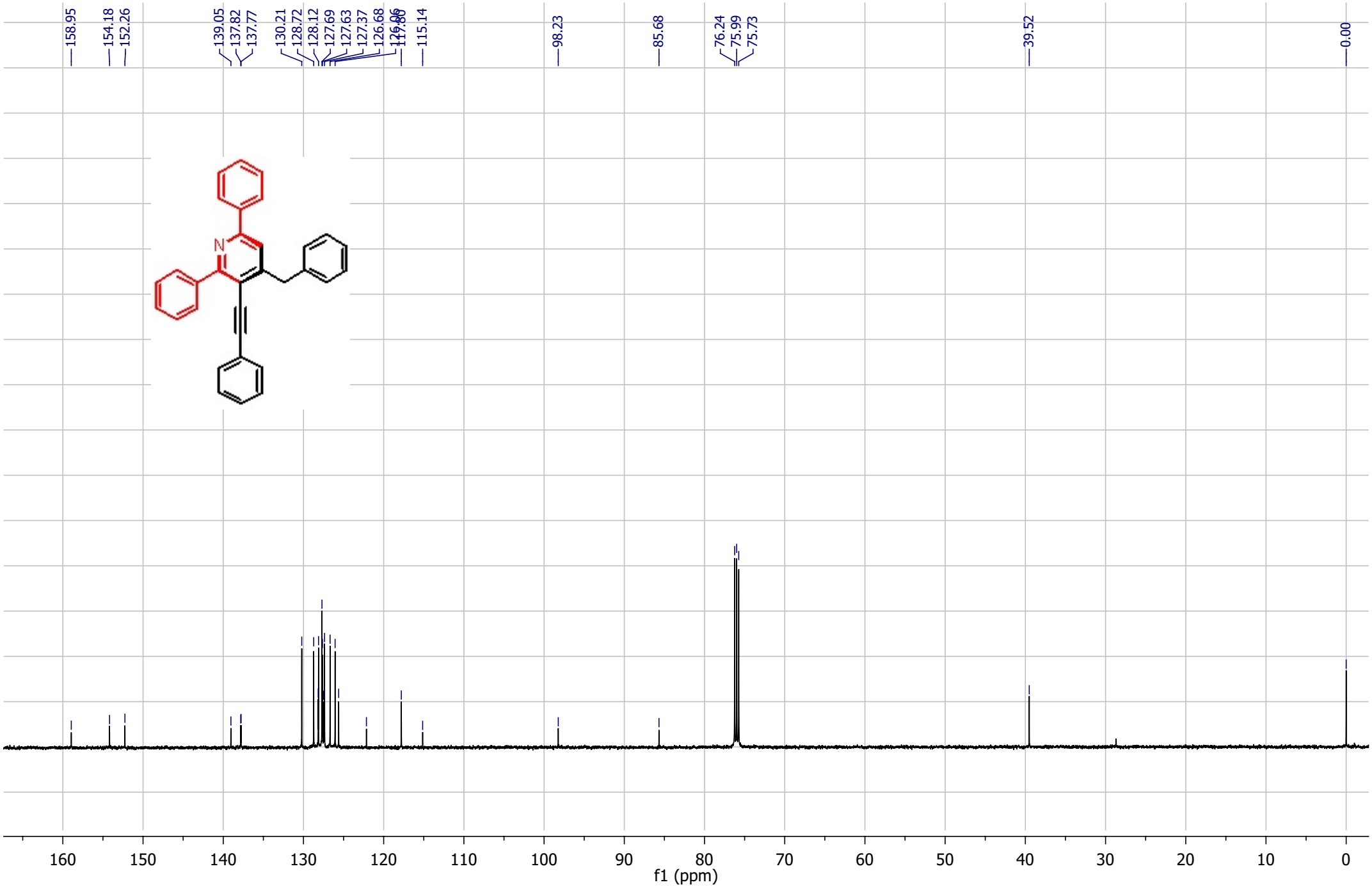
(Z)-4-benzyl-2,6-diphenyl-3-styrylpyridine (5a): Light yellow viscous liquid (89 mg, 88% yield) **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 7.95 (d, *J* = 16.4 Hz, 2H), 7.54 (d, *J* = 17.2 Hz, 2H), 7.44-7.16 (m, 13H), 7.06-7.02 (m, 4H), 6.51 (d, *J* = 15.1 Hz, 1H), 6.42 (d, *J* = 15.0 Hz, 1H), 3.96 (s, 1H), 3.77 (s, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 157.44, 155.47, 149.43, 140.97, 139.16, 139.09, 137.03, 133.20, 130.06, 129.55, 129.25, 128.91, 128.65, 128.59 ,128.48, 128.27, 127.94, 127.64, 127.60, 126.95, 126.69, 126.44, 119.91, 39.28; **HRMS** for **$C_{32}H_{26}N$** $[M+H]^+$ Calculated: **424.5588**, Found: **424.5586**.



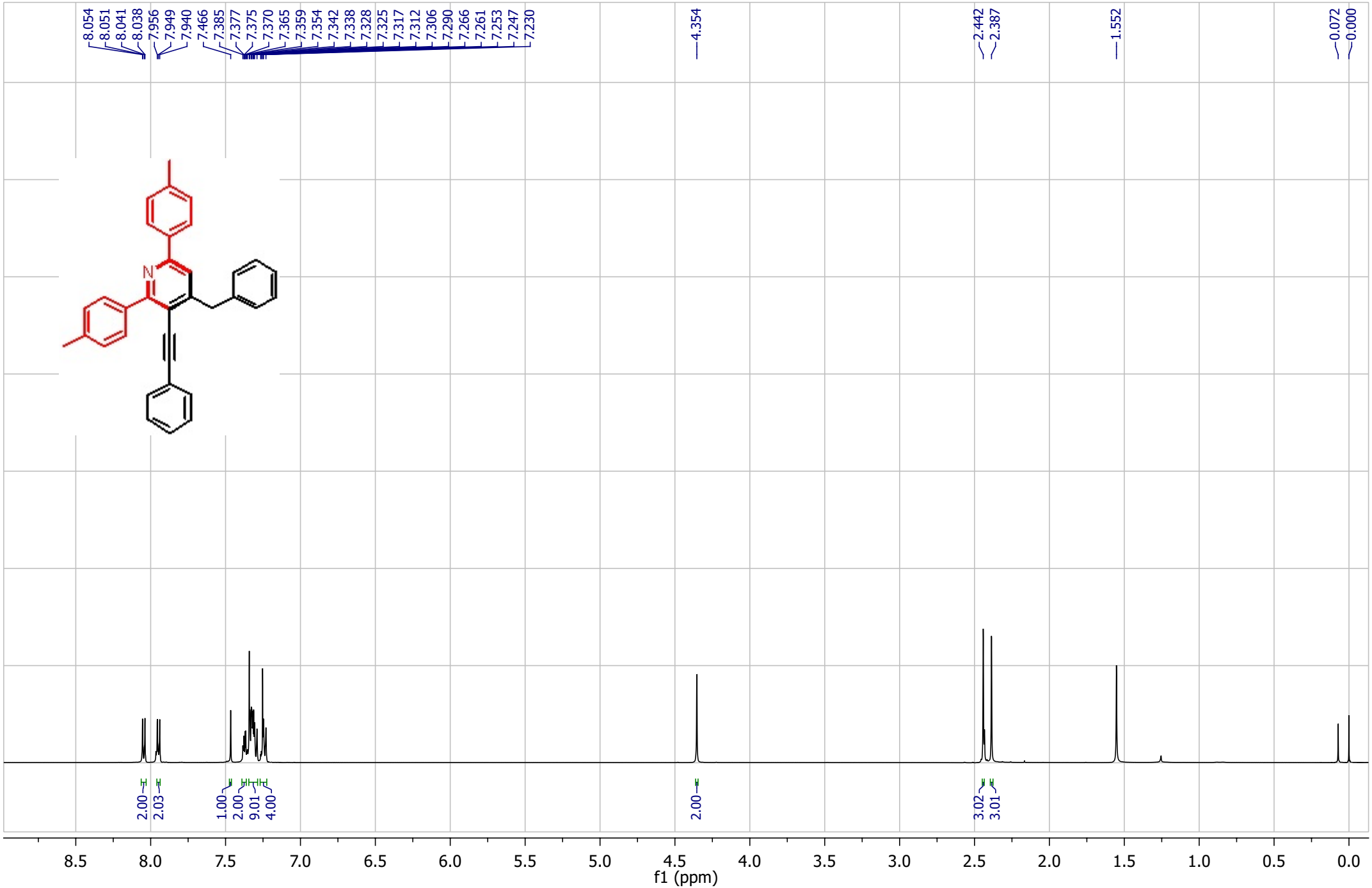
(Z)-4-(4-methylbenzyl)-3-(4-methylstyryl)-2,6-diphenylpyridine (5b): Light yellow viscous liquid (92 mg, 91% yield) **^{1}H NMR** (500 MHz, $CDCl_3$, 25°C, TMS) δ; 7.92 (d, *J* = 16.8 Hz, 2H), 7.57 (d, *J* = 17.7 Hz, 2H), 7.38 (s, 1H), 7.24-7.07 (m, 12H), 7.04-7.02 (m, 2H), 6.6 (d, *J* = 15.0 Hz, 1H), 6.48 (d, *J* = 15.0 Hz, 1H), 3.97 (s, 1H), 3.70 (s, 1H), 2.37 (s, 3H), 2.35 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$, 25°C, TMS) δ; 157.26, 155.39, 149.07, 139.23, 138.80, 138.22, 137.74, 137.13, 136.40, 132.69, 129.61, 129.46, 129.32, 129.23, 128.51, 128.49, 128.38, 128.27, 127.57, 127.02, 126.79, 126.32, 119.44, 39.18, 21.32; **HRMS** for **$C_{34}H_{30}N$** $[M+H]^+$ Calculated: **452.2379**, Found: **452.2368**.



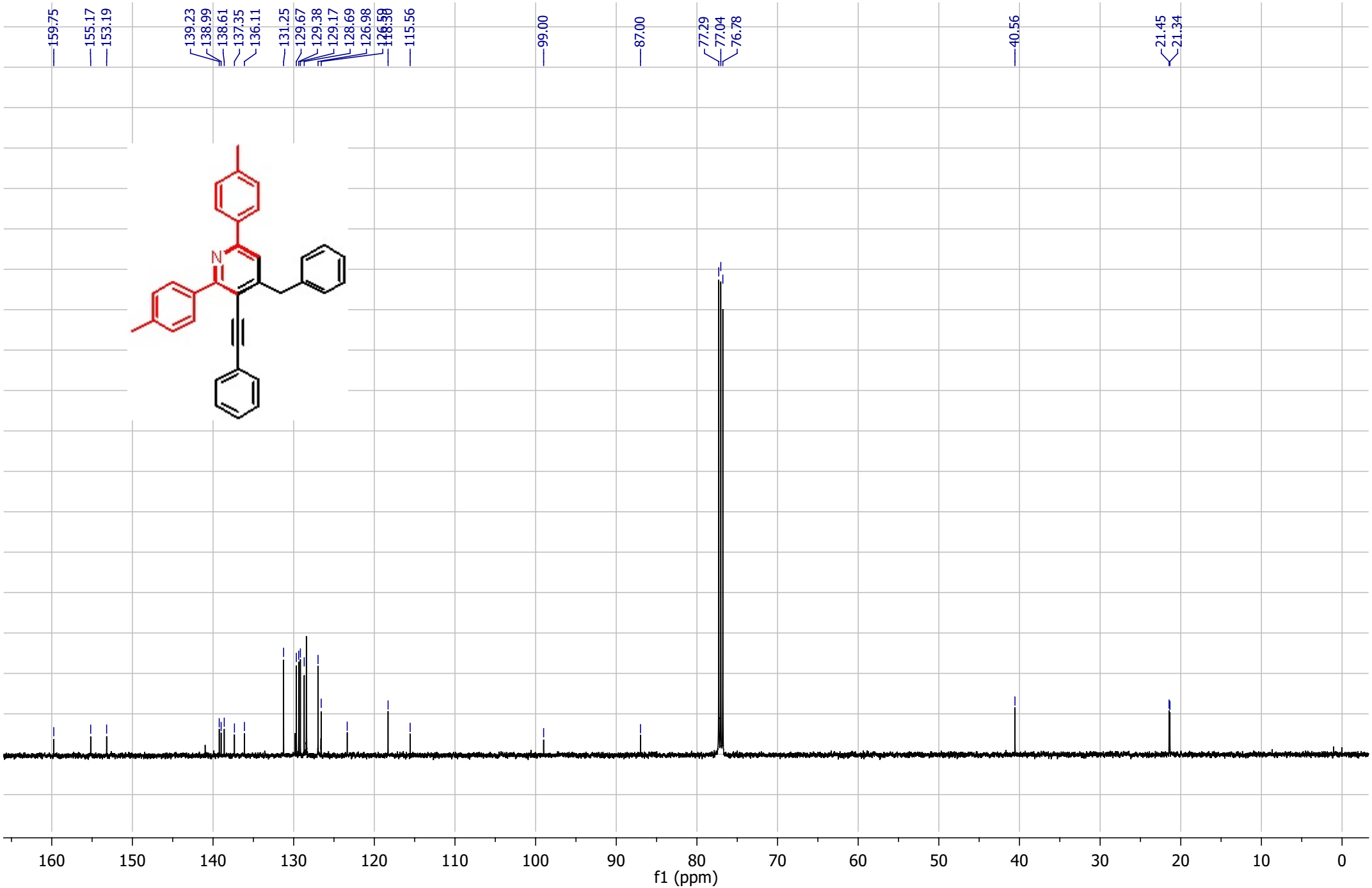
4-benzyl-2,6-diphenyl-3-(phenylethynyl)pyridine (3a)



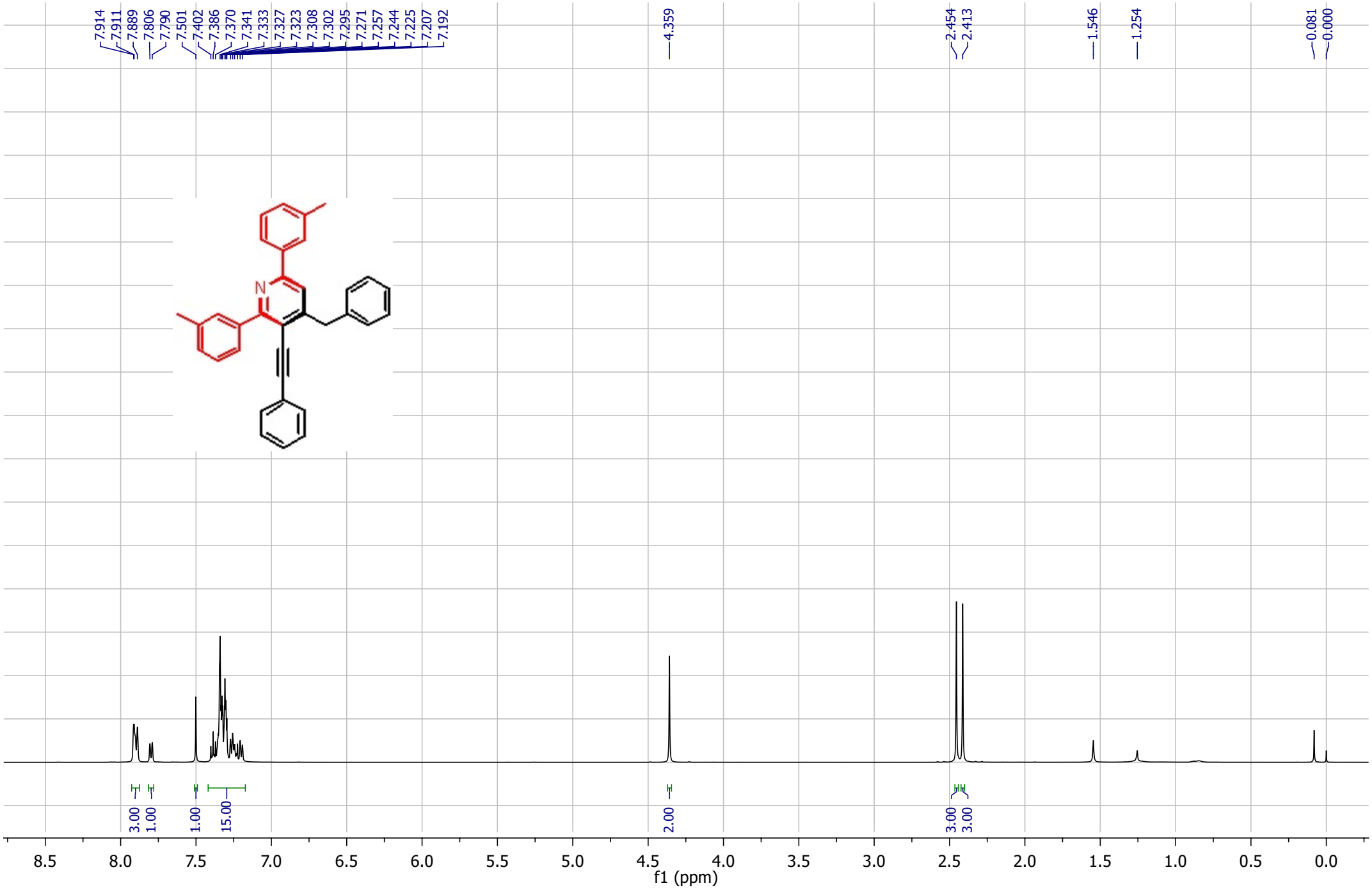
4-benzyl-2,6-diphenyl-3-(phenylethynyl)pyridine (3a)



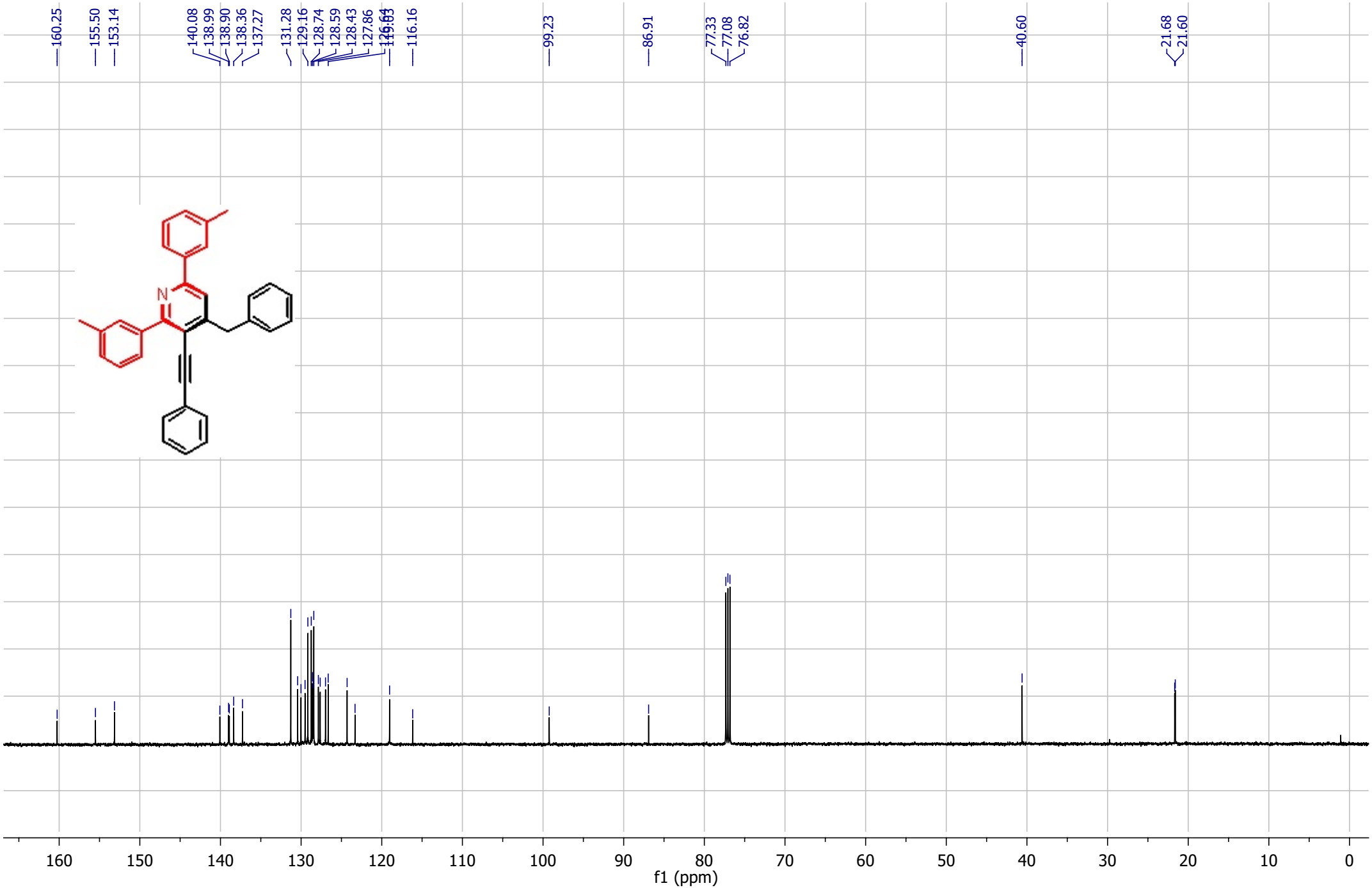
4-benzyl-3-(phenylethynyl)-2,6-di-p-tolylpyridine (3b)



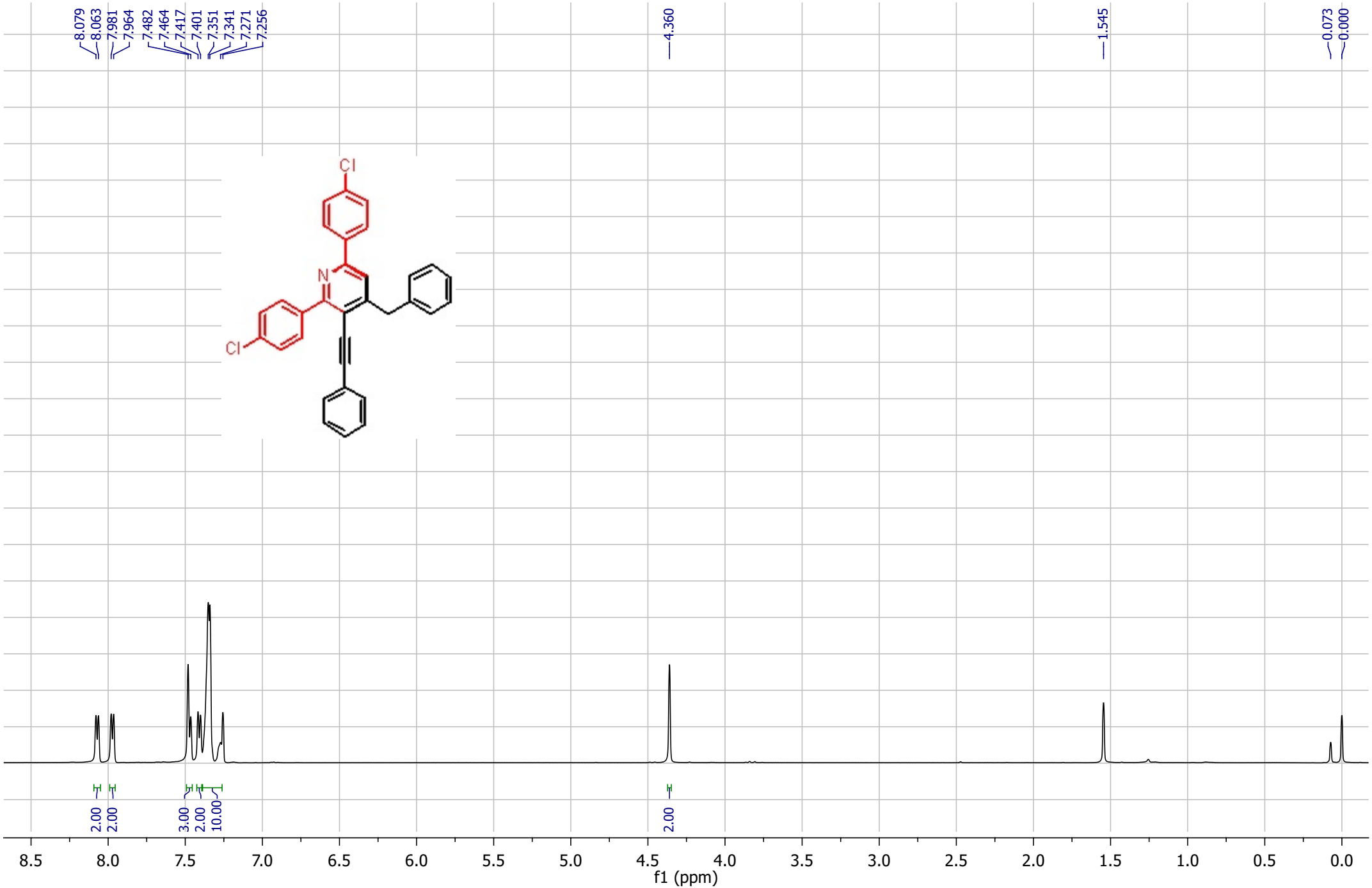
4-benzyl-3-(phenylethynyl)-2,6-di-p-tolylpyridine (3b)



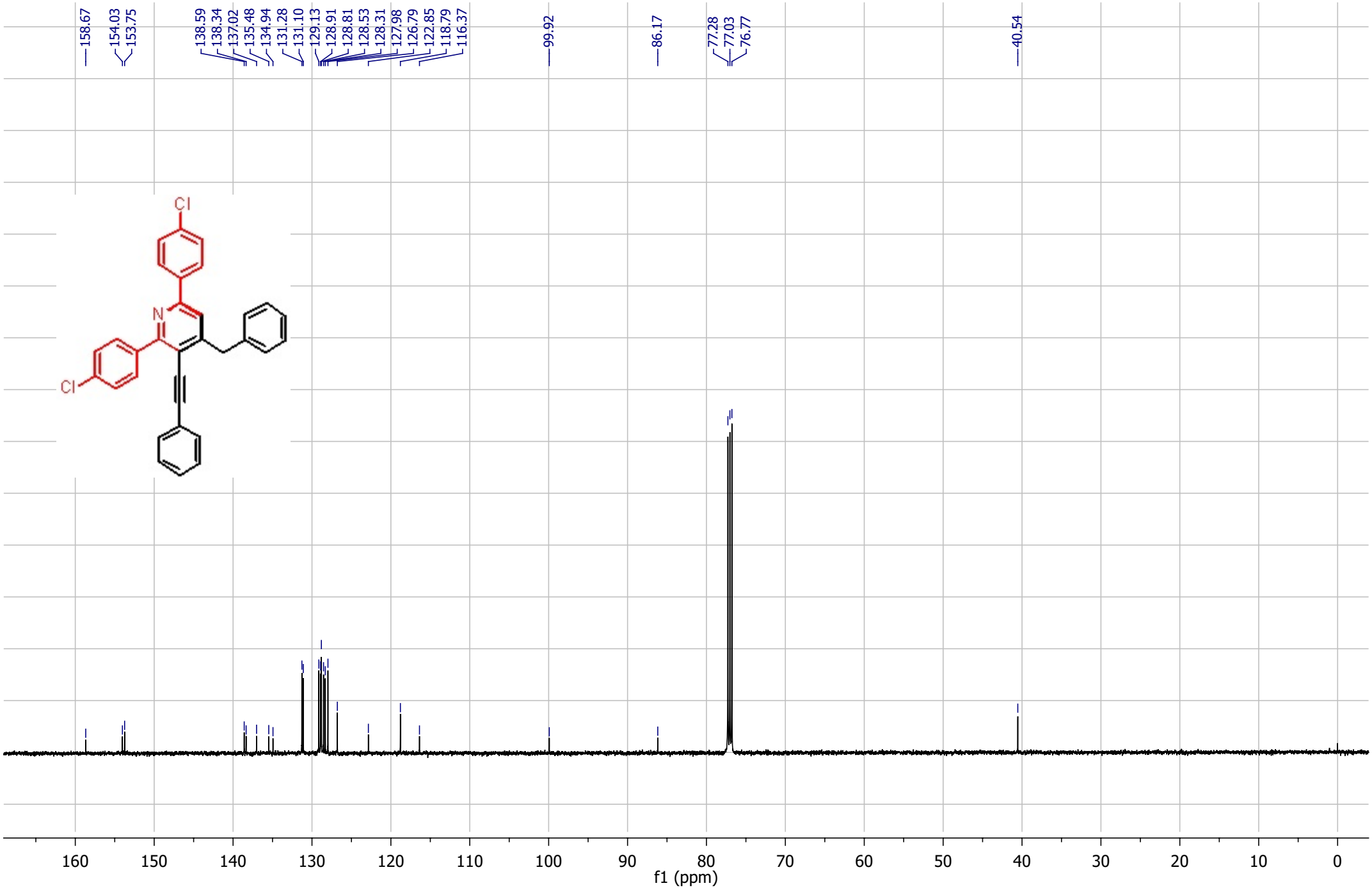
4-benzyl-3-(phenylethynyl)-2,6-di-m-tolylpyridine (3c)



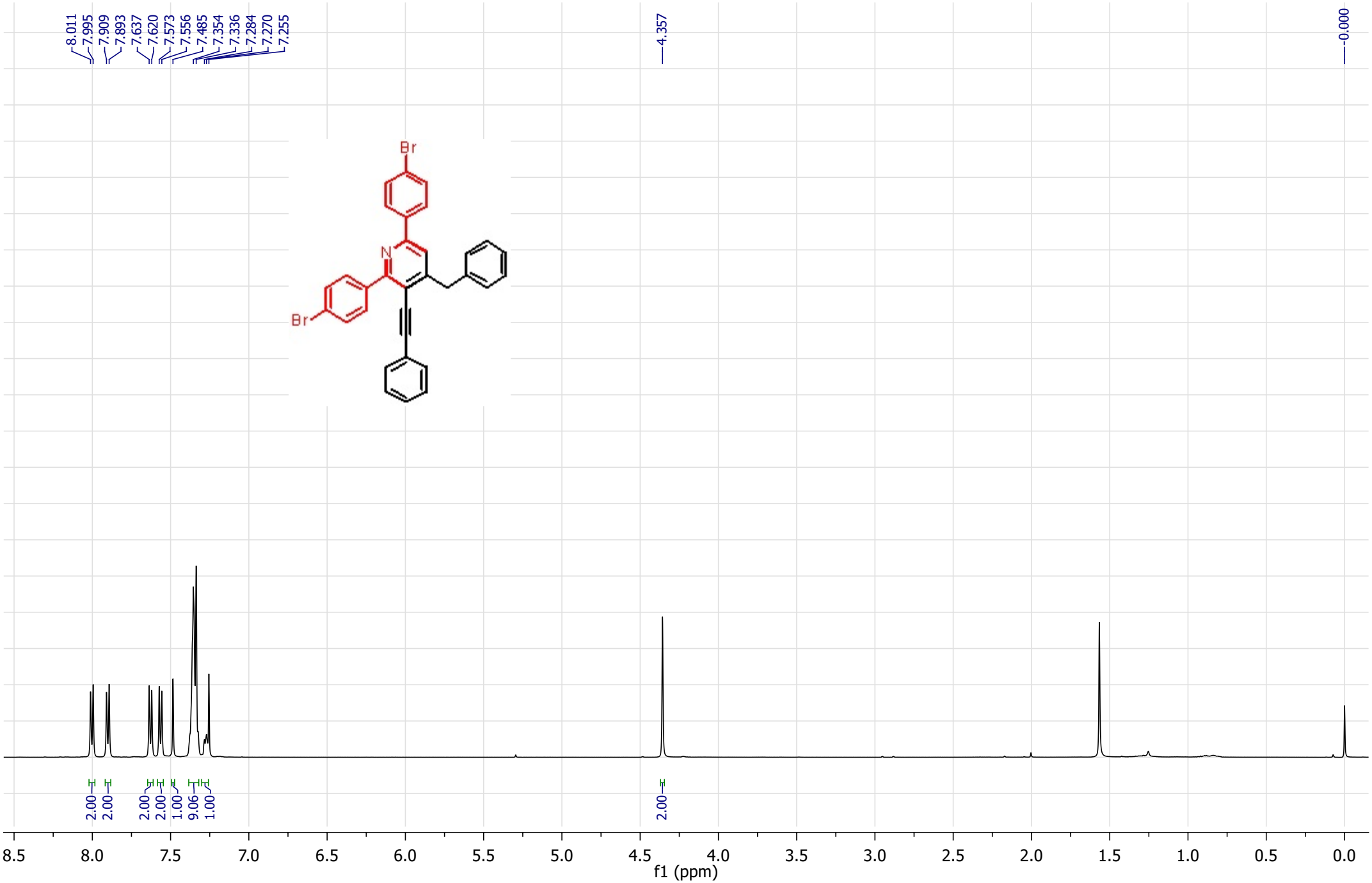
4-benzyl-3-(phenylethynyl)-2,6-di-m-tolylpyridine(3c)



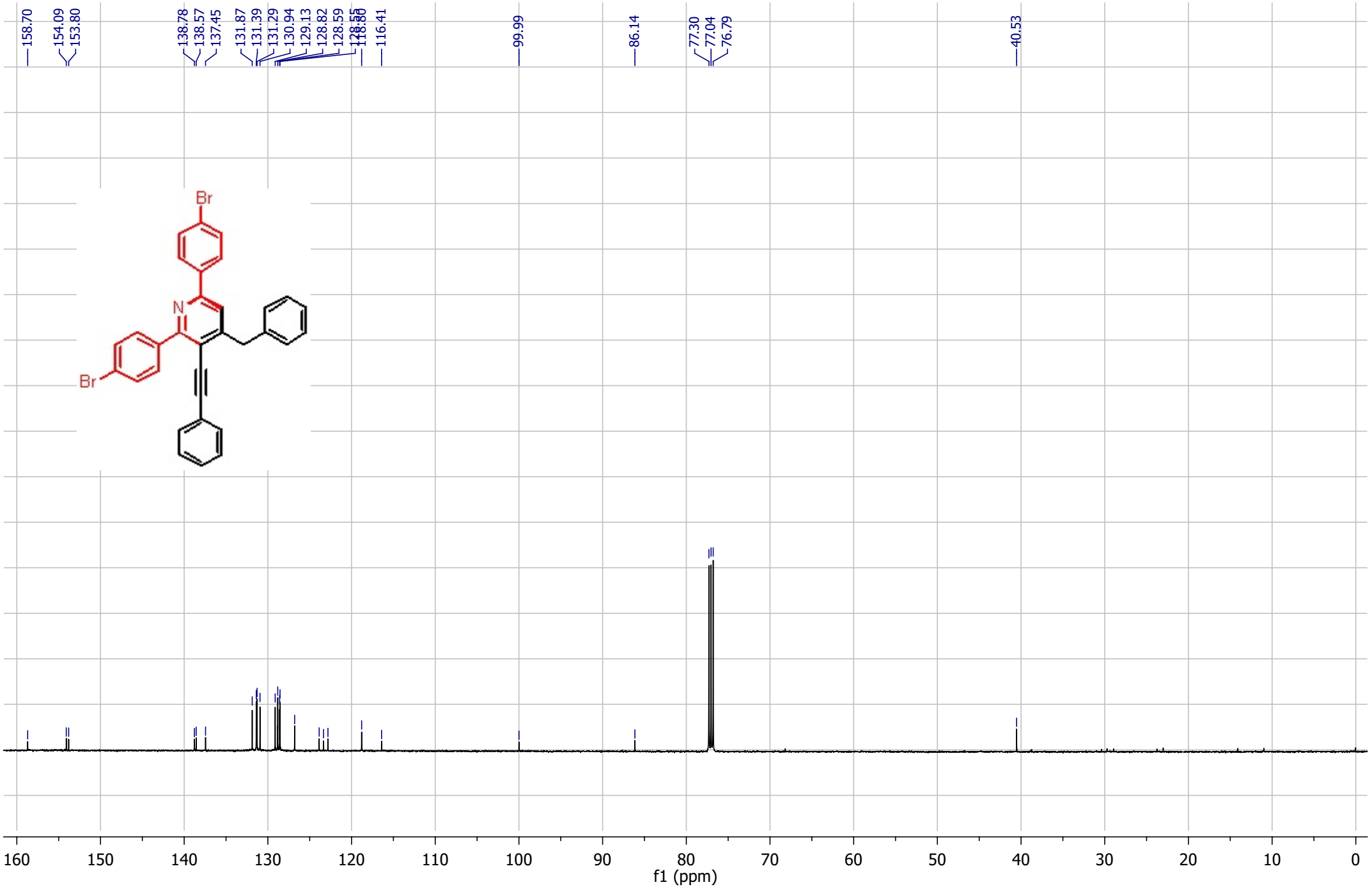
4-benzyl-2,6-bis(4-chlorophenyl)-3-(phenylethynyl)pyridine(3d)



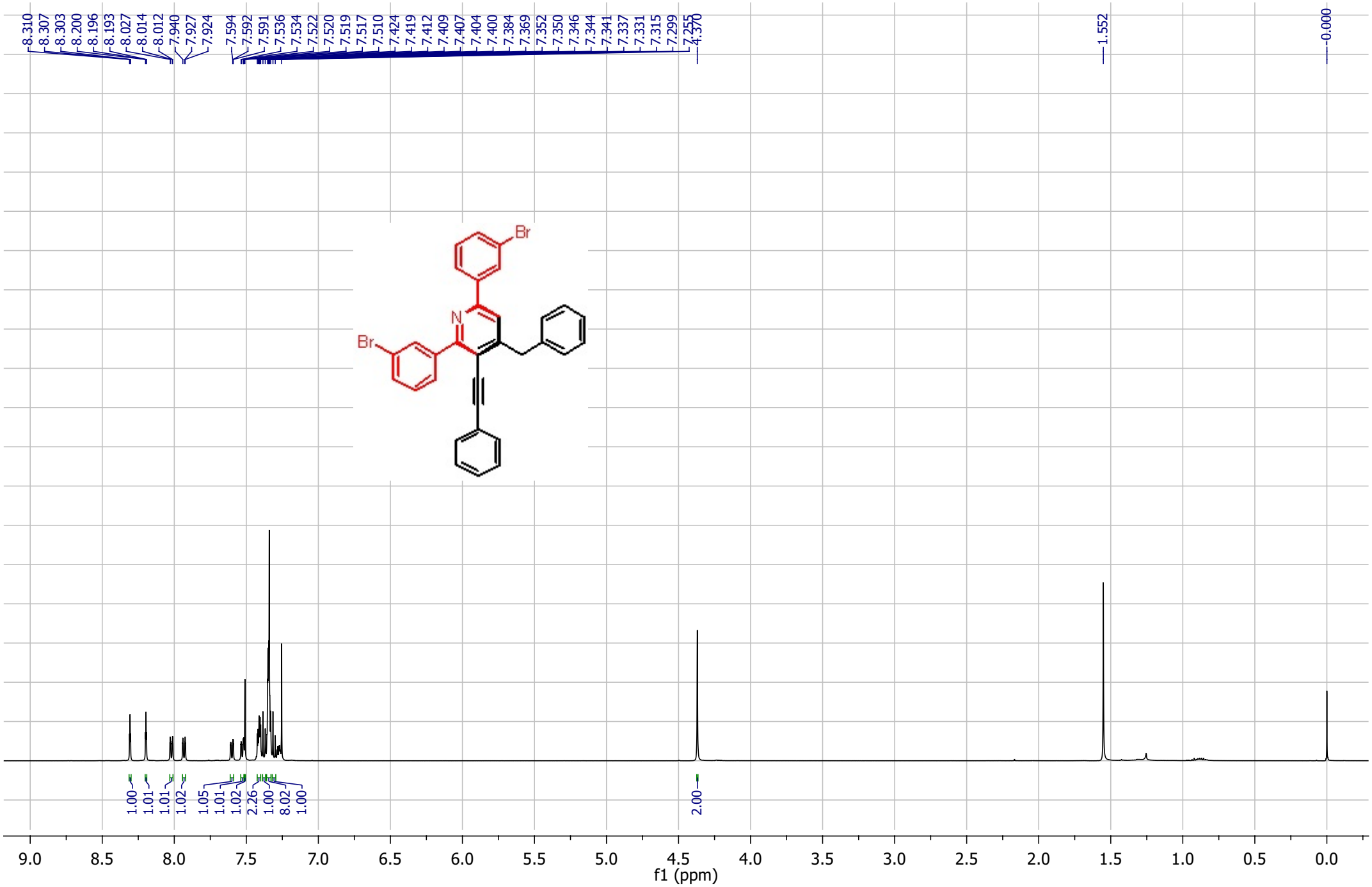
4-benzyl-2,6-bis(4-chlorophenyl)-3-(phenylethynyl)pyridine(3d)



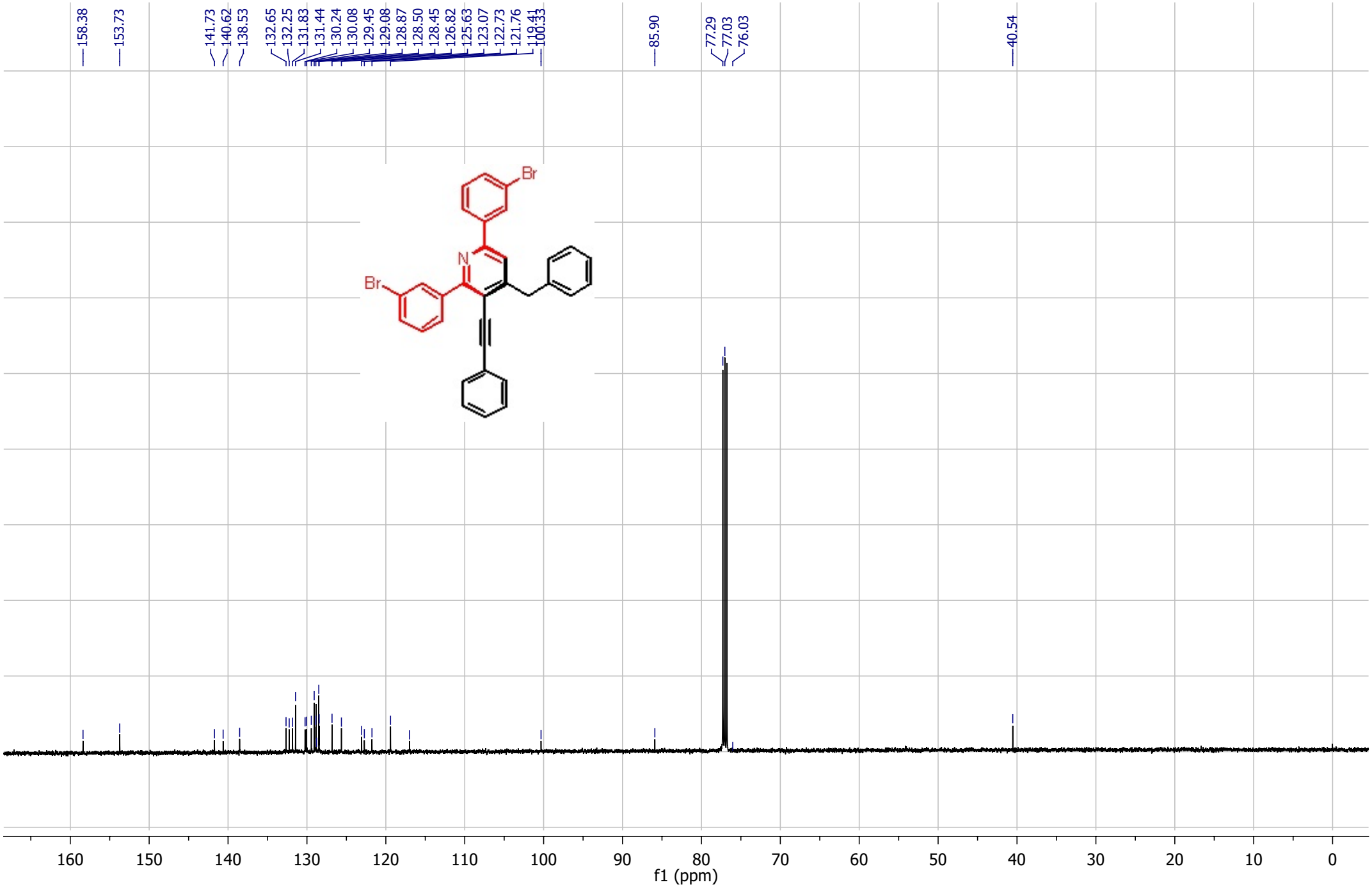
4-benzyl-2,6-bis(4-bromophenyl)-3-(phenyl ethynyl)pyridine (3e)



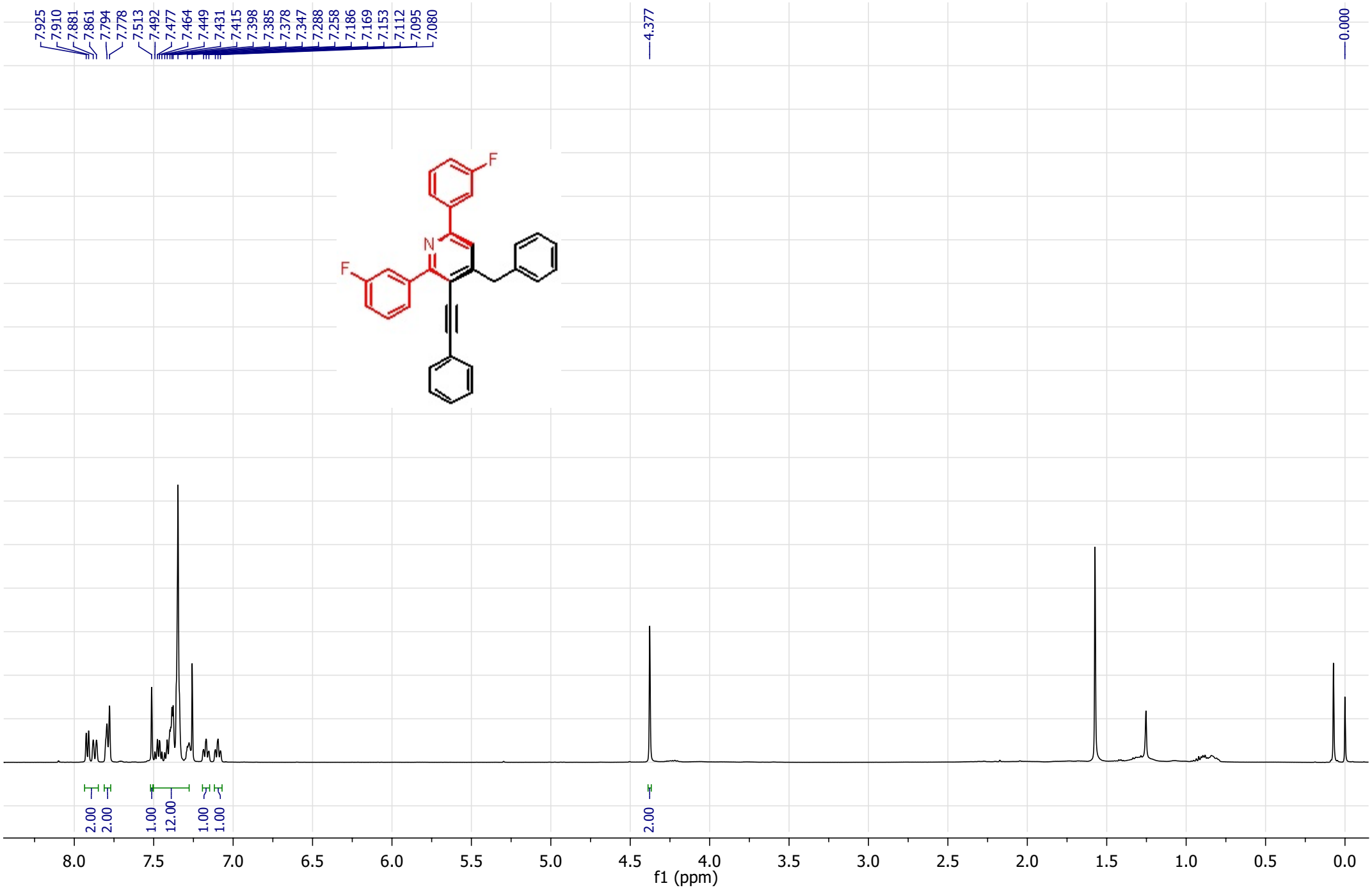
4-benzyl-2,6-bis(4-bromophenyl)-3-(phenylethynyl)pyridine(3e)



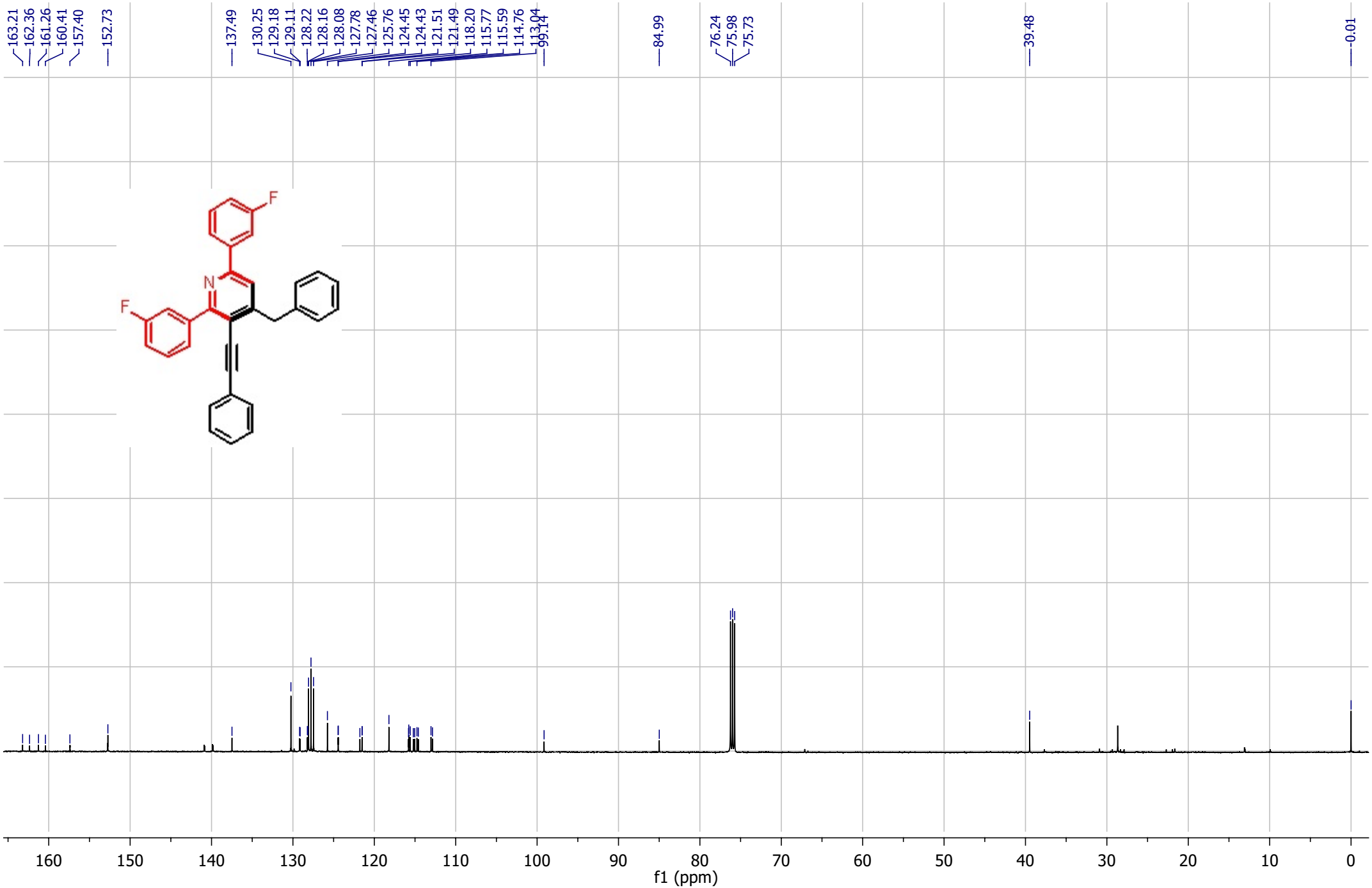
4-(4-bromobenzyl)-3-((4-bromophenyl)ethynyl)-2,6-diphenylpyridine (3f)



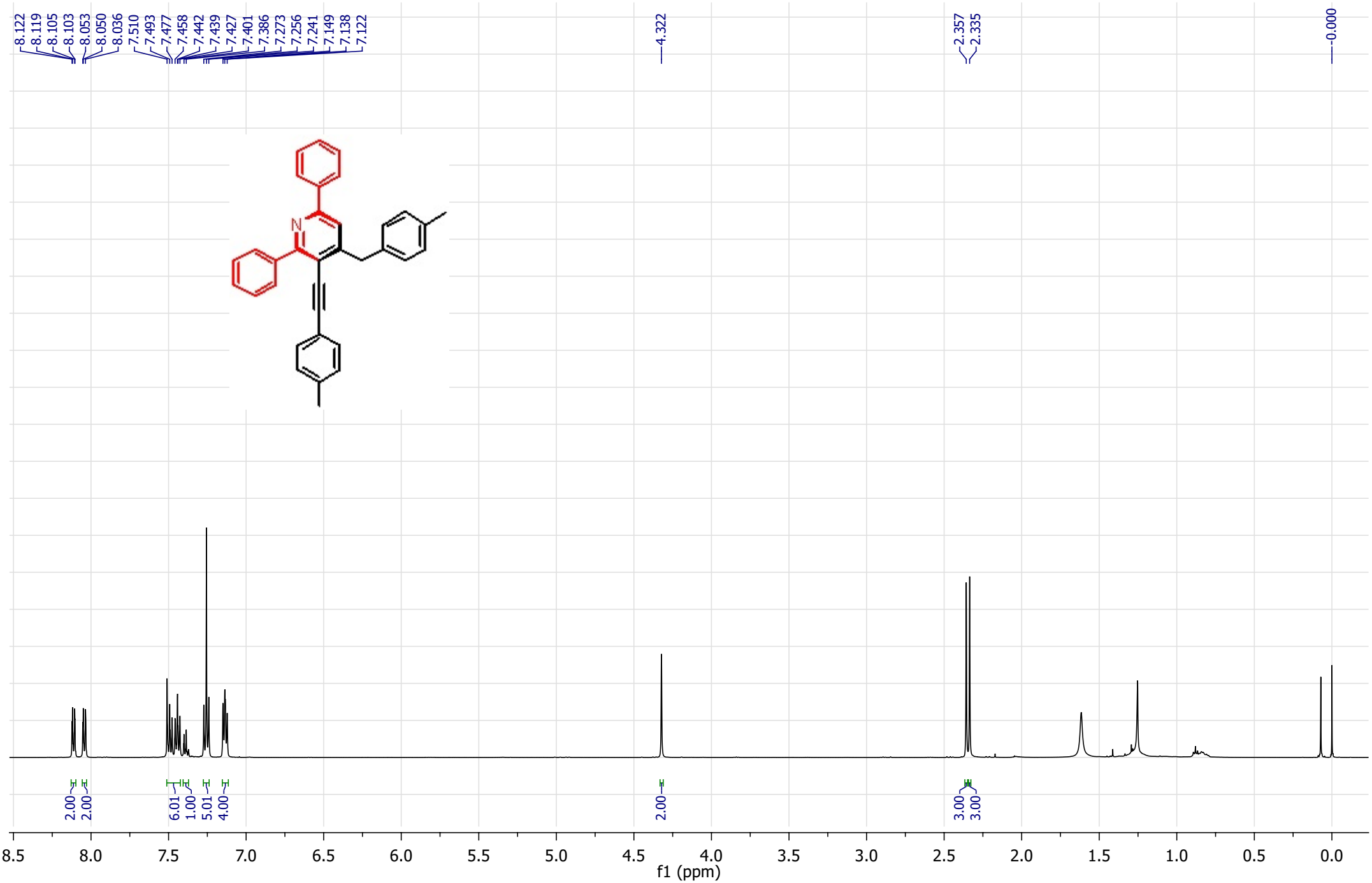
4-benzyl-2,6-bis(3-bromophenyl)-3-(phenylethynyl)pyridine (3f)



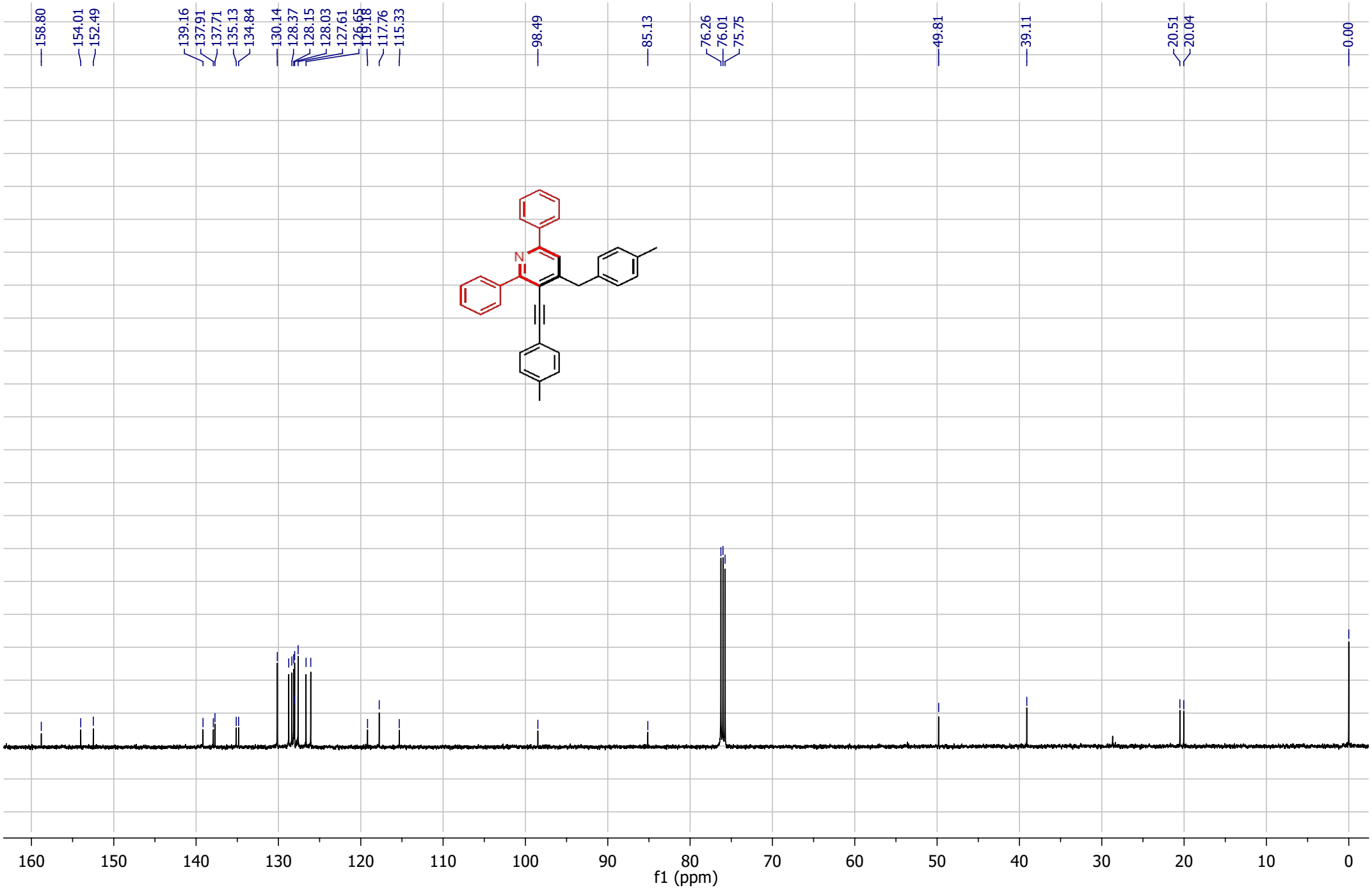
4-benzyl-2,6-bis(3-fluorophenyl)-3-(phenylethyny l)pyridine (3g)



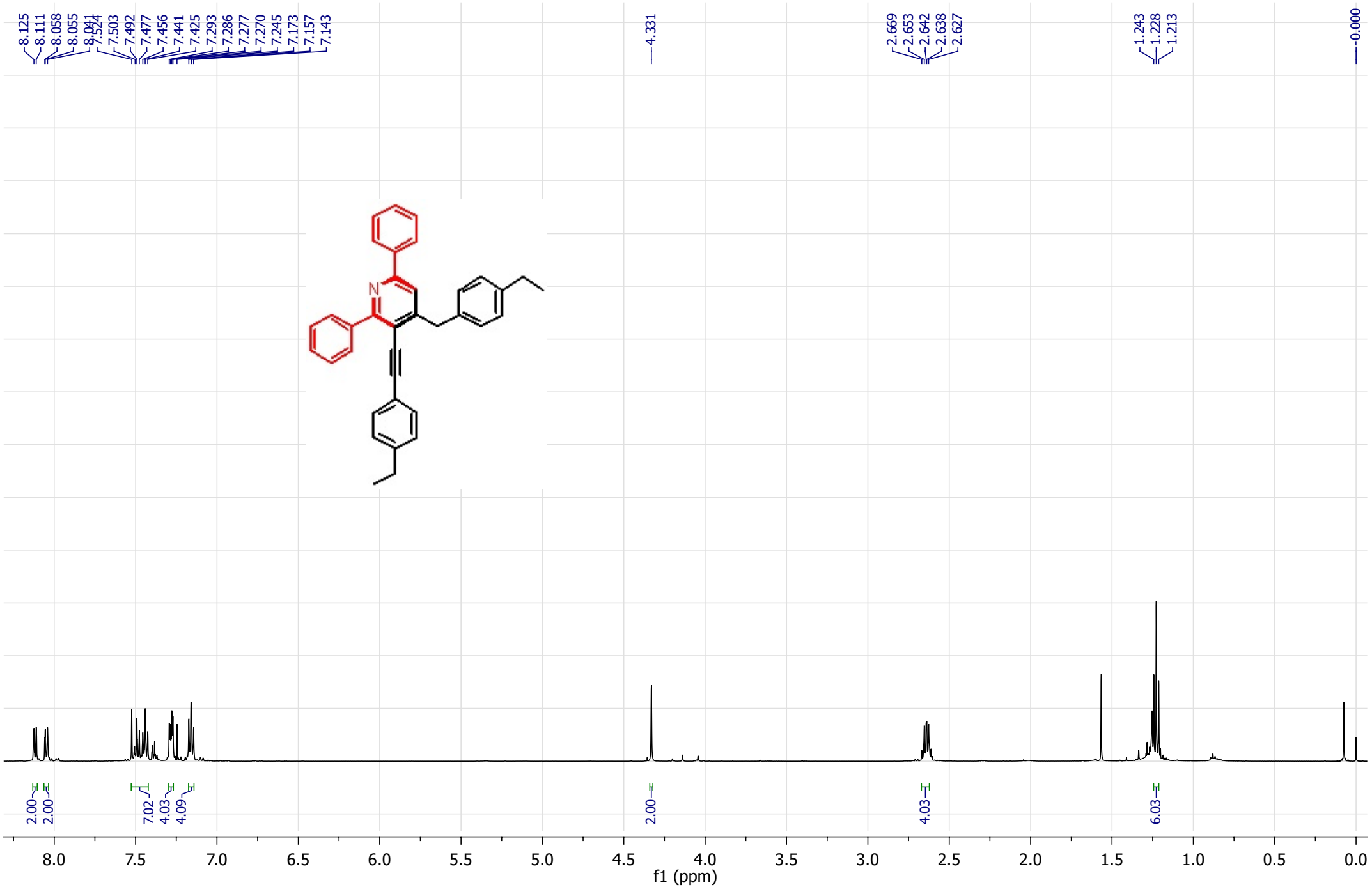
4-benzyl-2,6-bis(3-fluorophenyl)-3-(phenylethynyl)pyridine (3g)



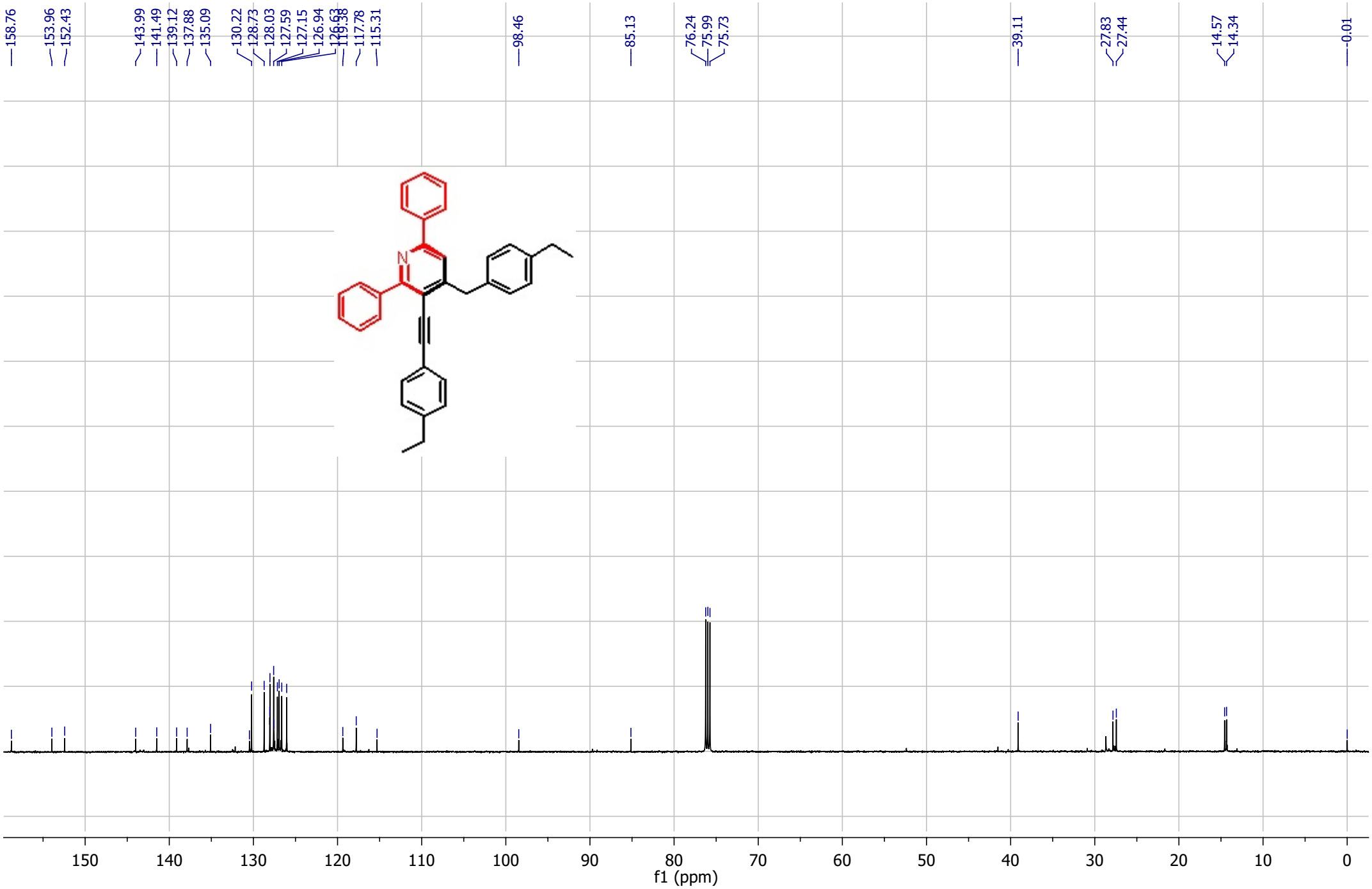
4-(4-methylbenzyl)-2,6-diphenyl-3-(p-tolylethynyl) pyridine (3h)



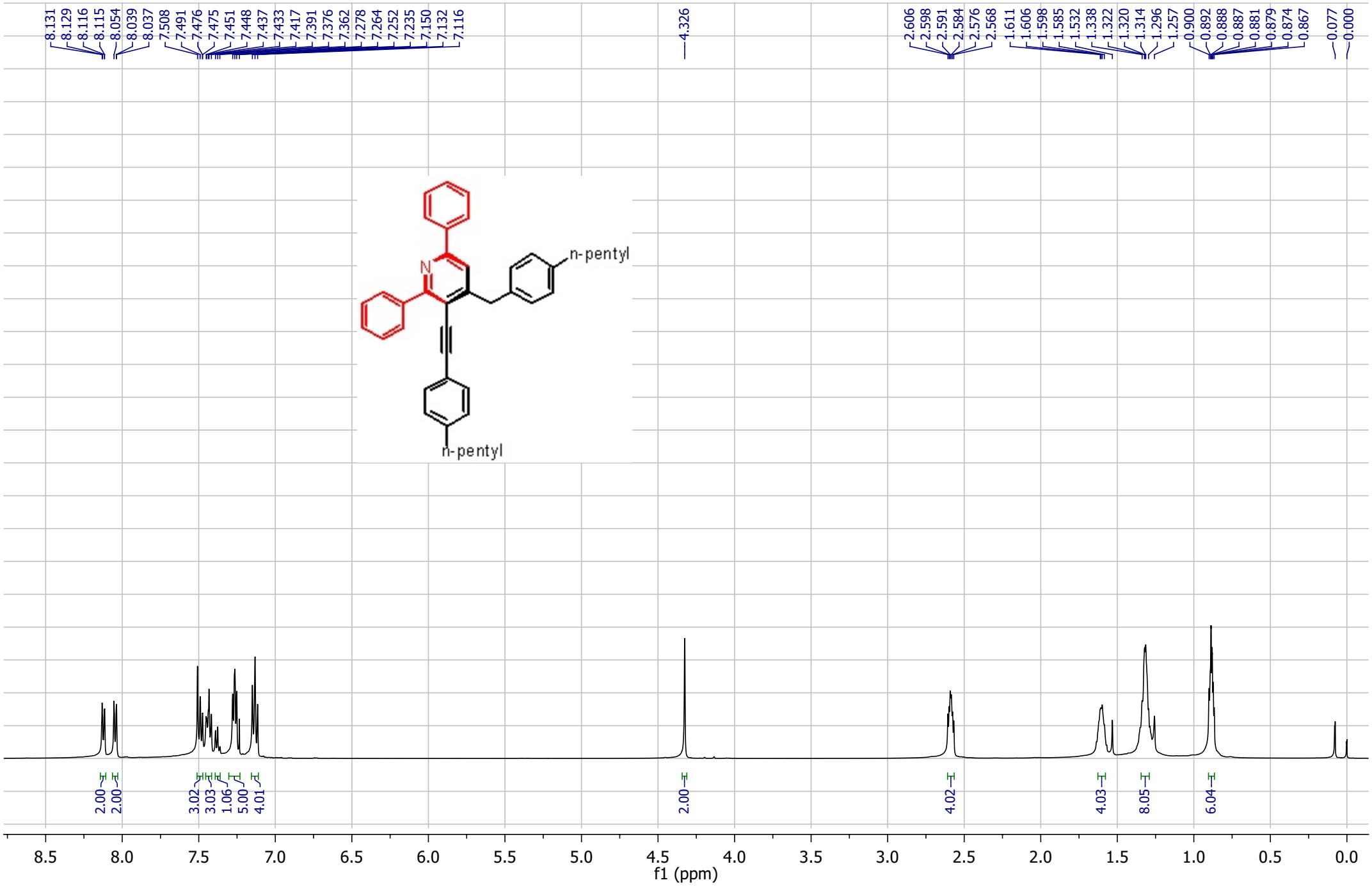
4-(4-methylbenzyl)-2,6-diphenyl-3-(p-tolylethynyl)pyridine (3h)



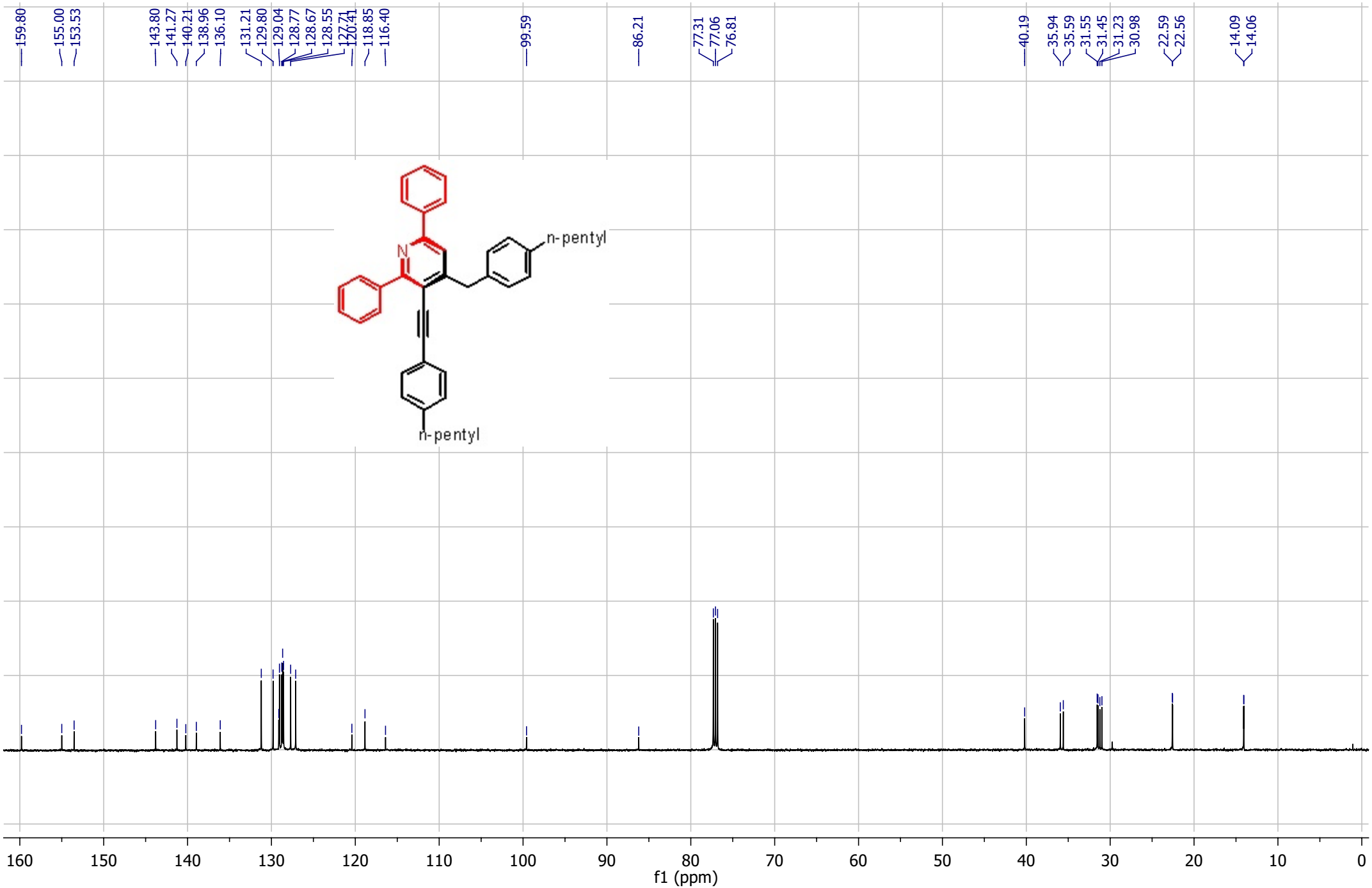
4-(4-ethylbenzyl)-3-((4-ethylphenyl)ethynyl)-2,6-diphenylpyridine (3i)



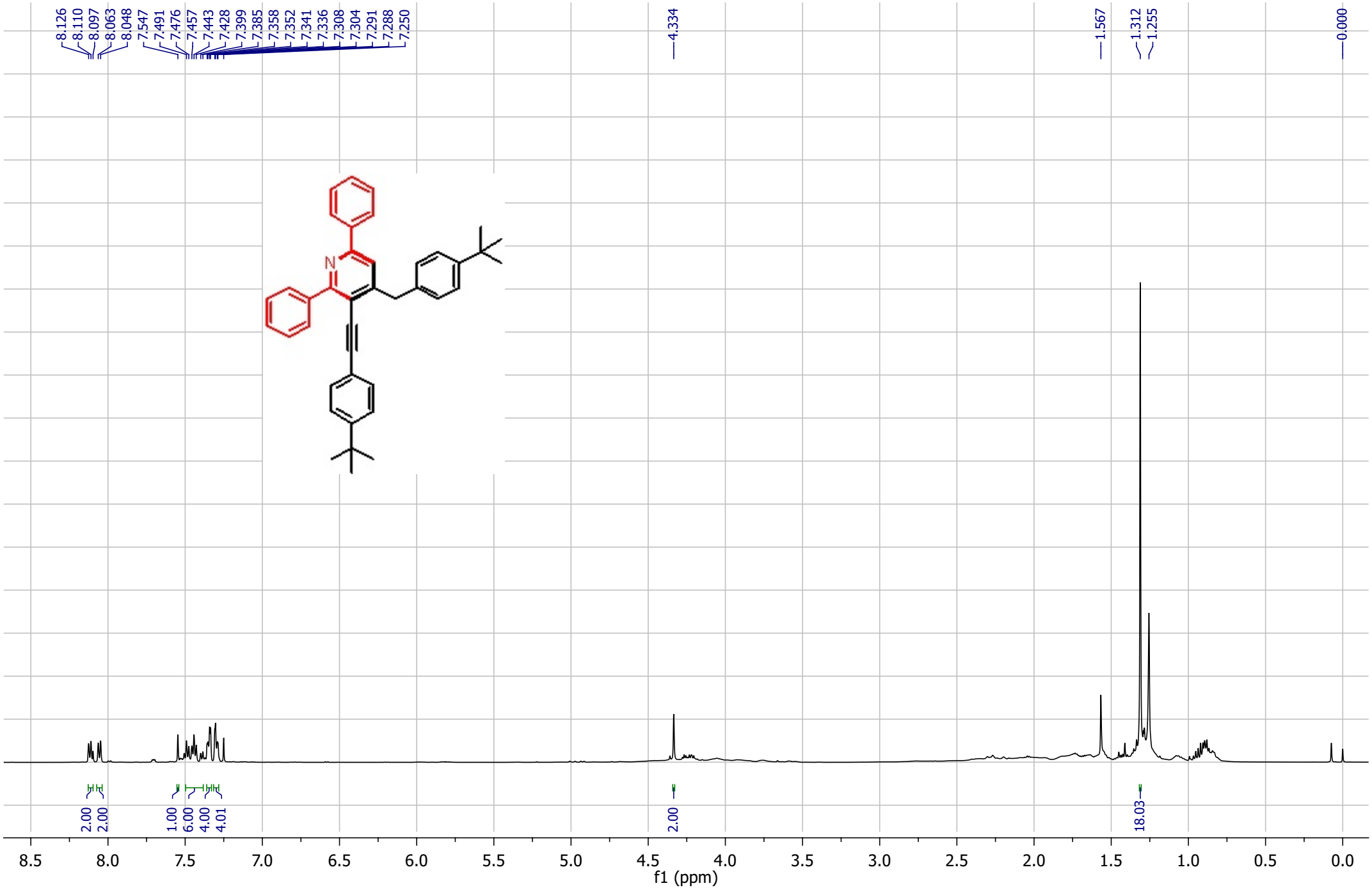
4-(4-ethylbenzyl)-3-((4-ethylphenyl)ethynyl)-2,6-diphenylpyridine (3i)



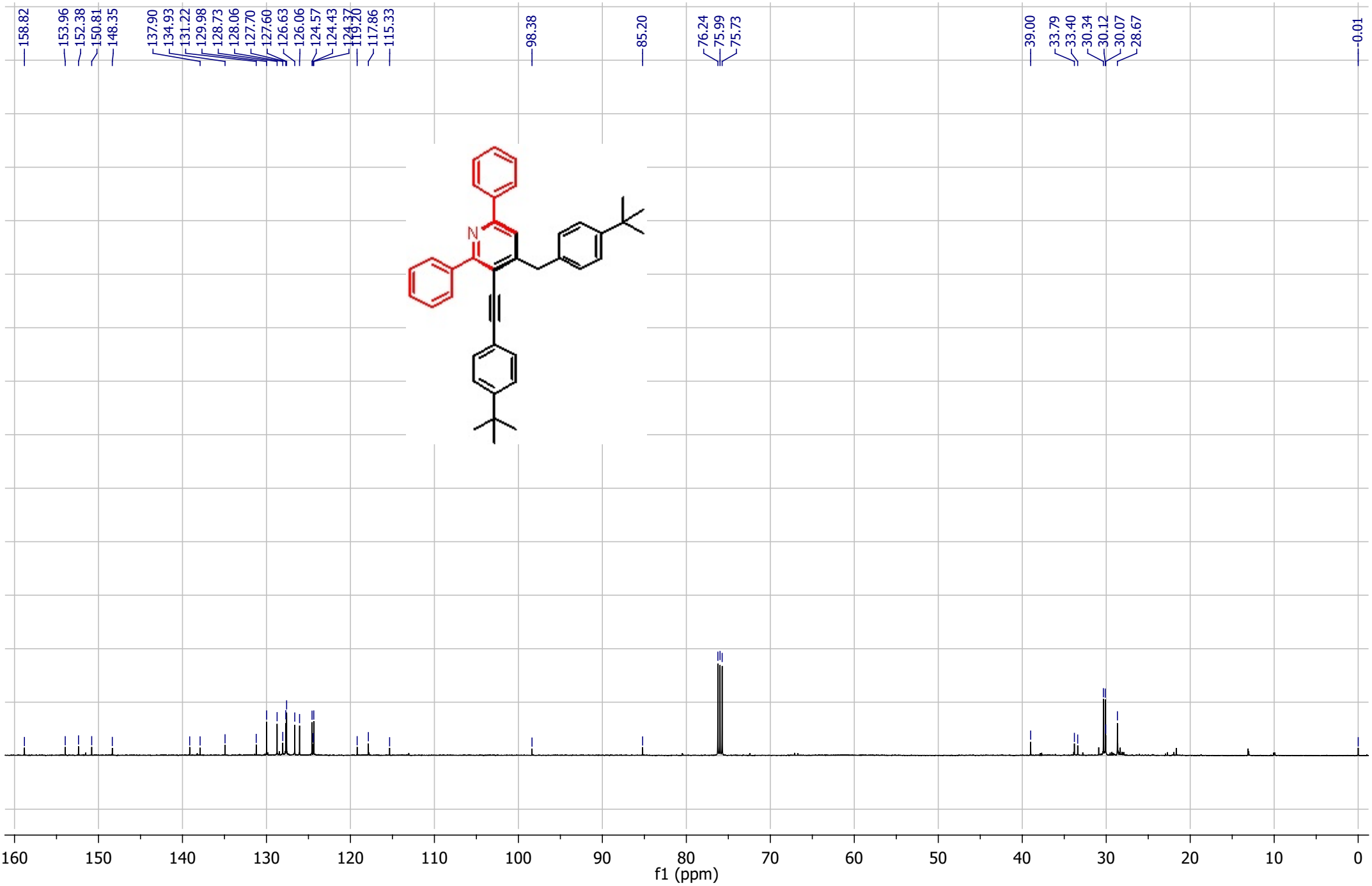
4-(4-pentylbenzyl)-3-((4-pentylphenyl)ethynyl)-2,6-diphenylpyridine (3j)



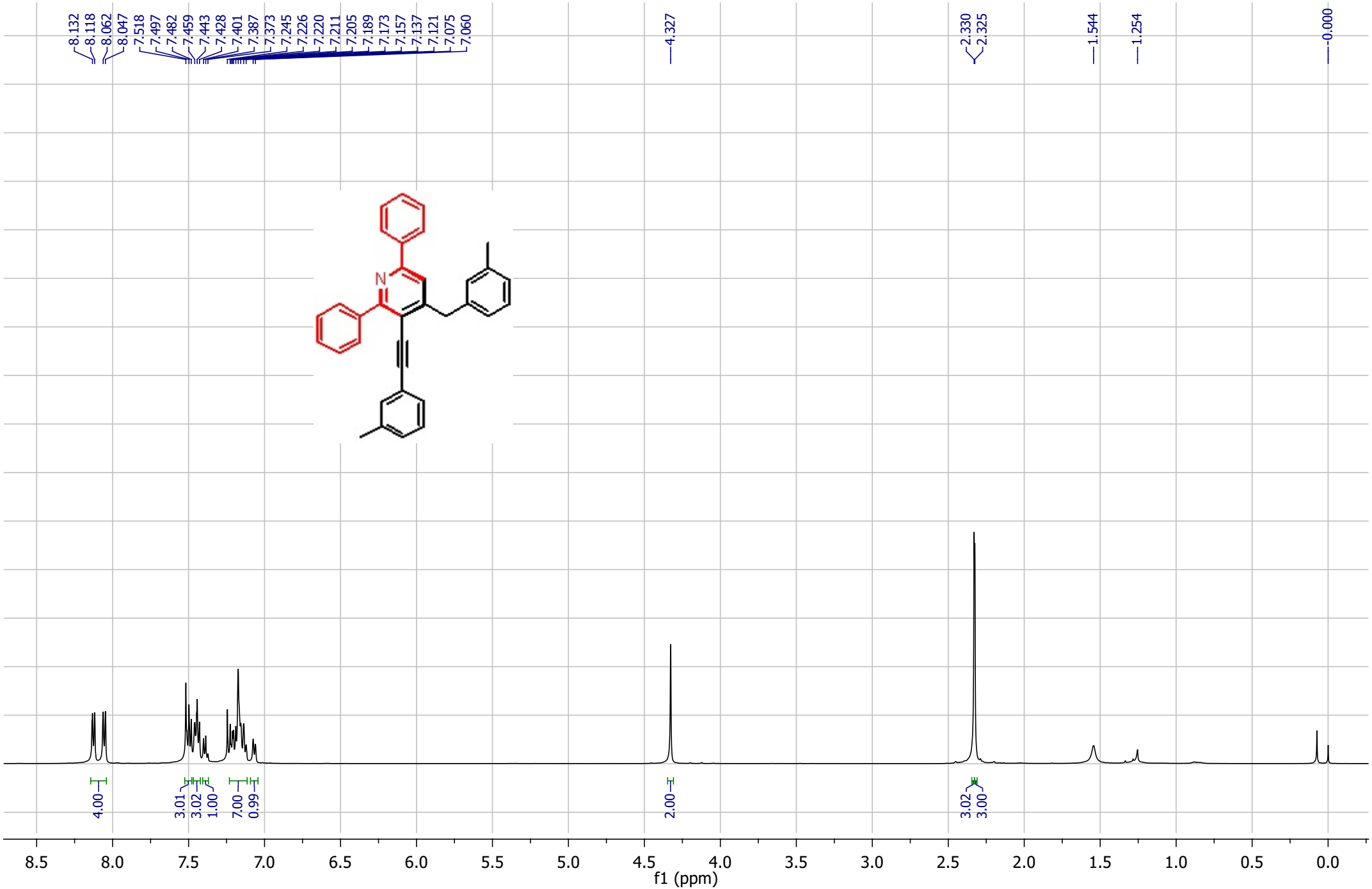
4-(4-pentylbenzyl)-3-((4-pentylphenyl)ethynyl)-2,6-diphenylpyridine (3j)



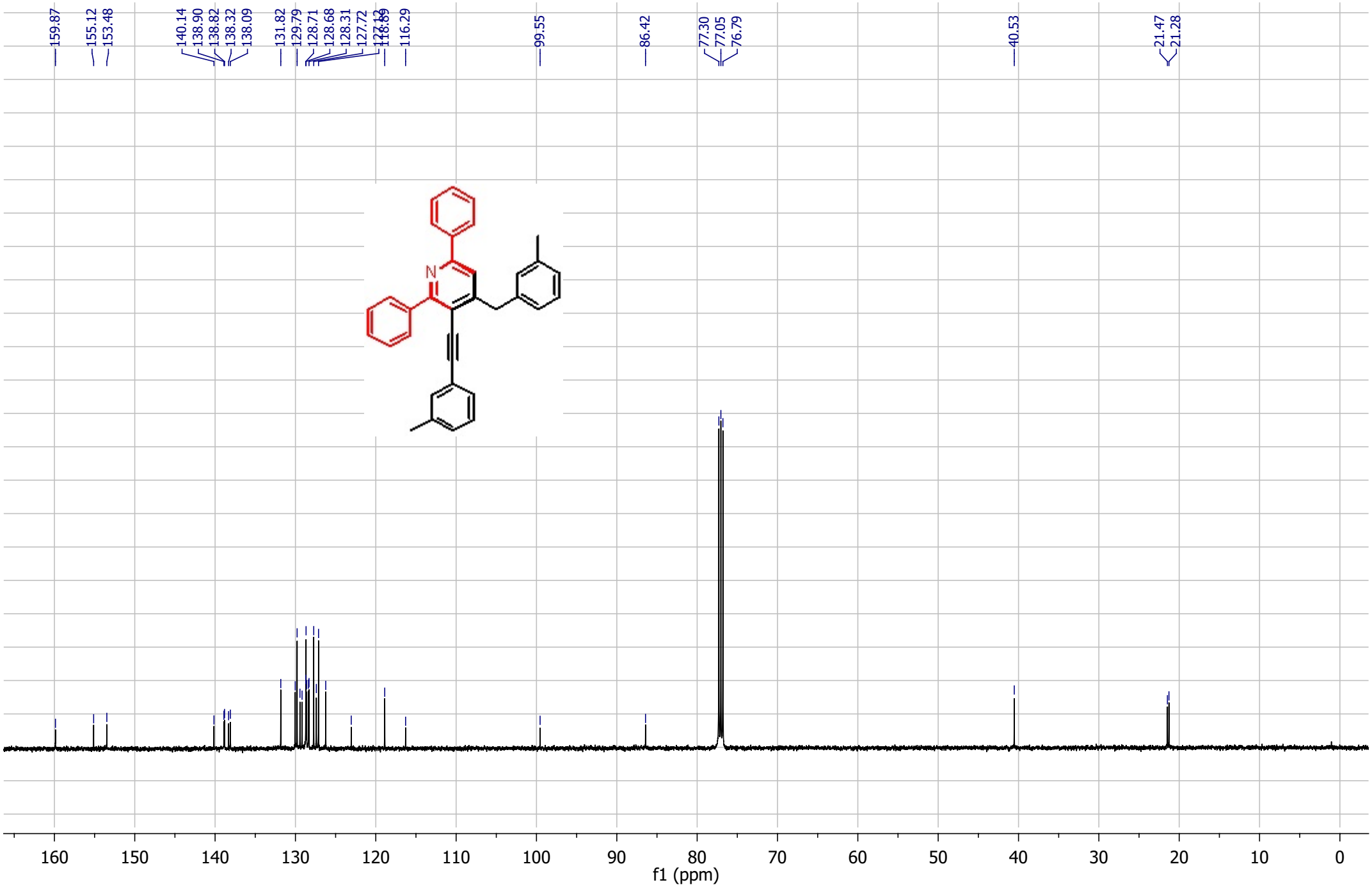
4-(4-(tert-butyl)benzyl)-3-((4-(tert-butyl)phenyl)ethynyl)-2,6-diphenylpyridine (3k)



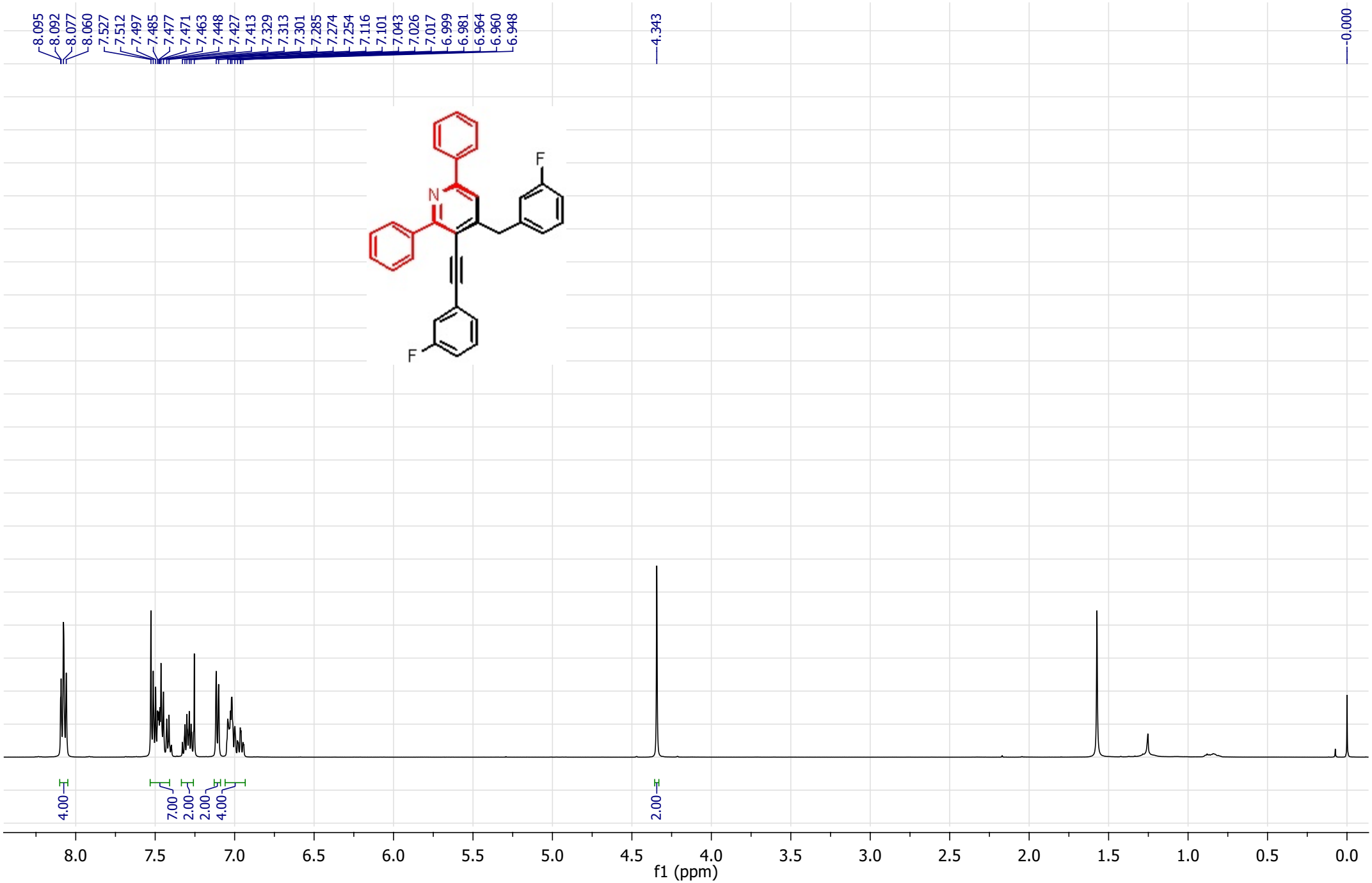
4-(4-(tert-butyl)benzyl)-3-((4-(tert-butyl)phenyl)ethynyl)-2,6-diphenylpyridine (3k)



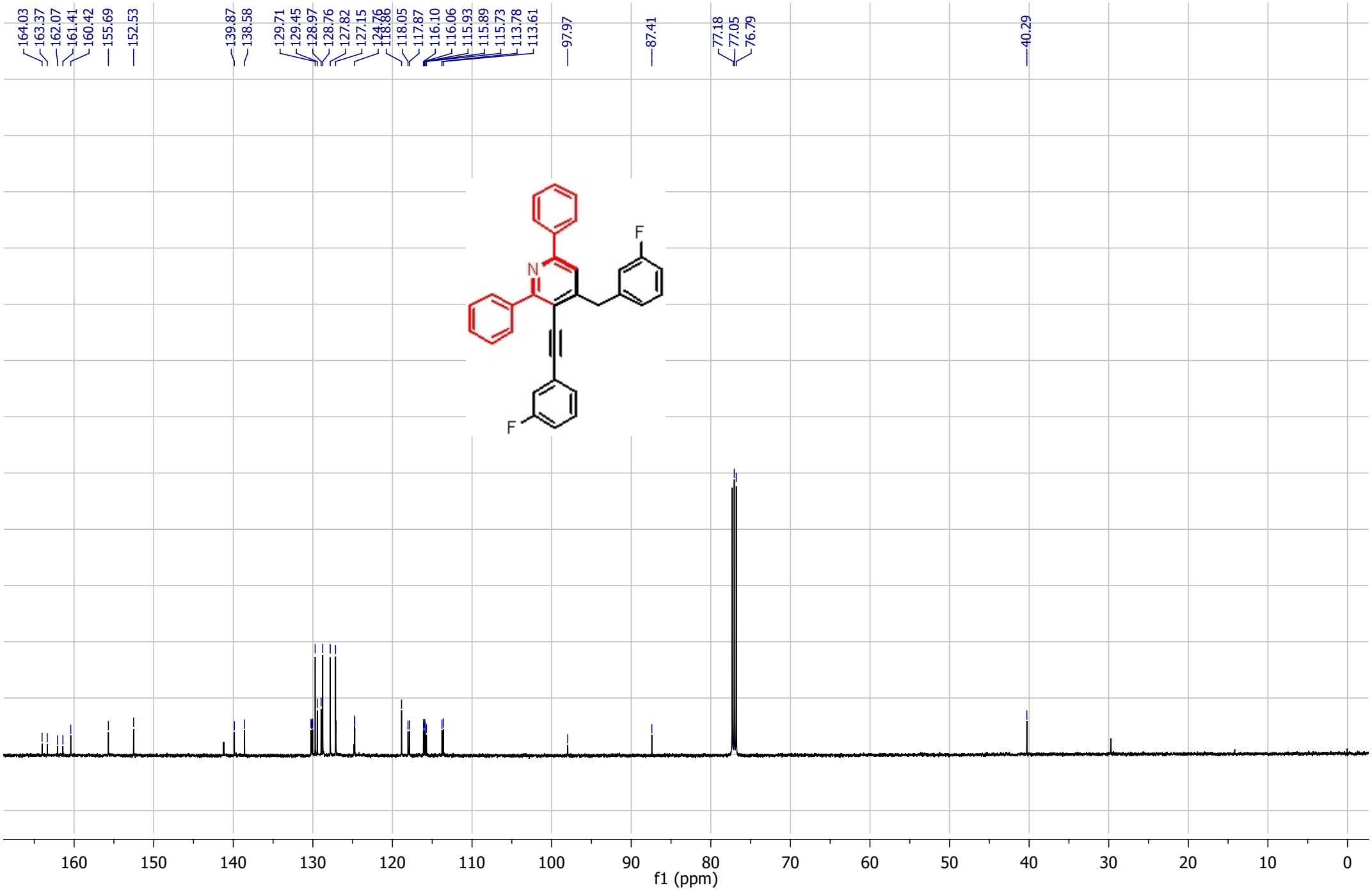
4-(3-methylbenzyl)-2,6-diphenyl-3-(m-tolylethynyl)pyridine (3l)



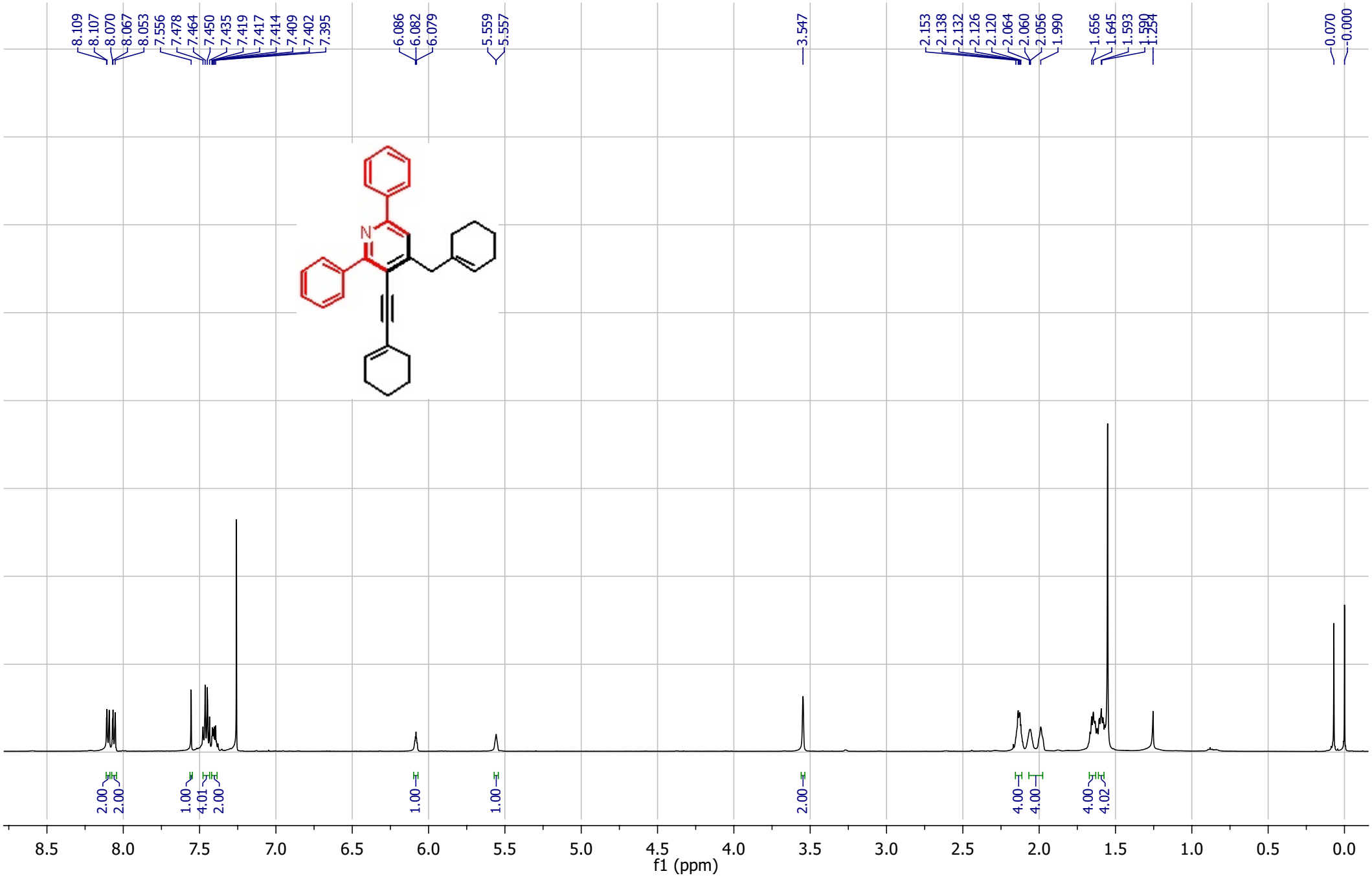
4-(3-methylbenzyl)-2,6-diphenyl-3-(m-tolylethynyl)pyridine (3l)



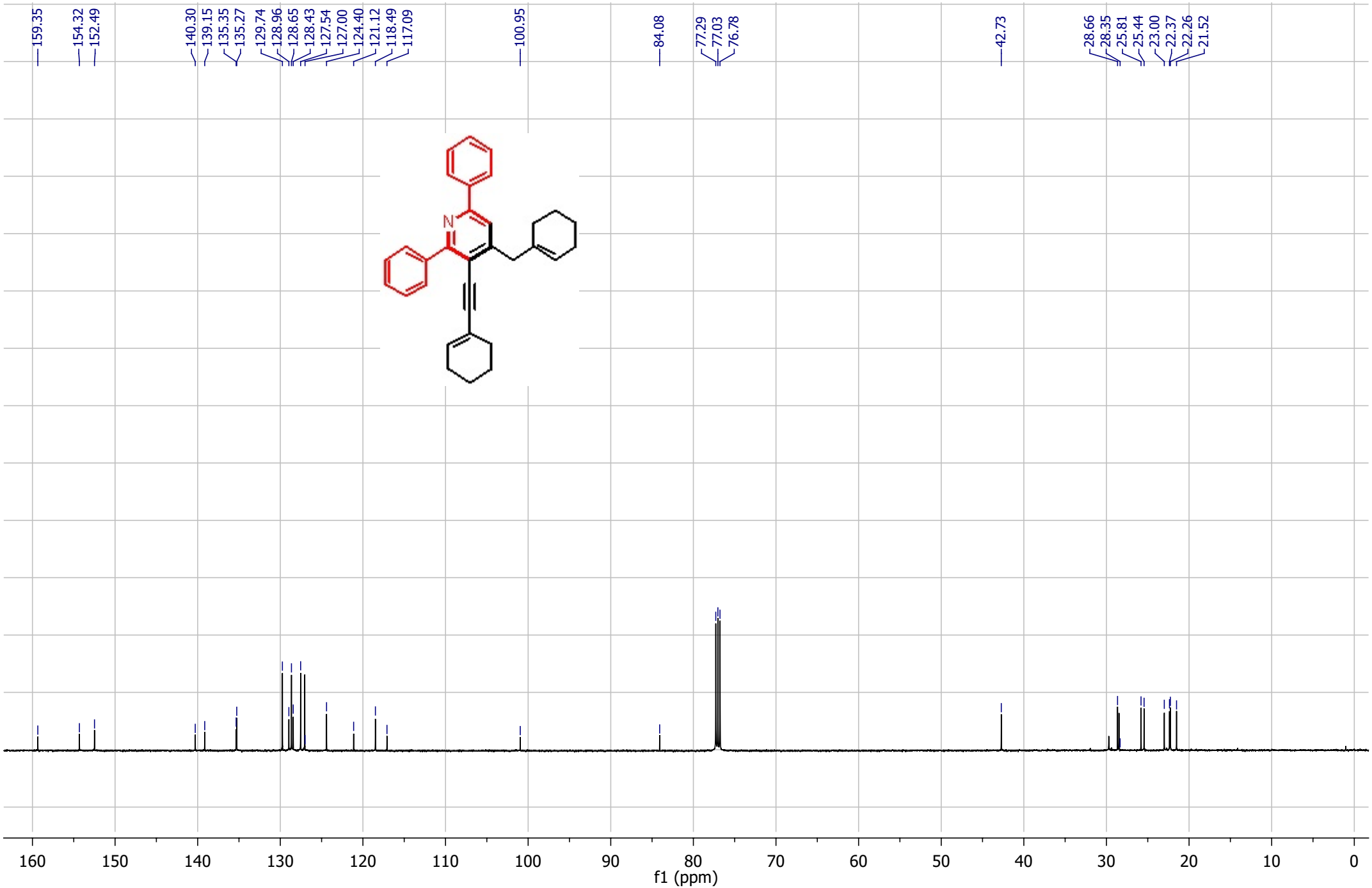
4-(3-fluorobenzyl)-3-((3-fluorophenyl)ethynyl)-2,6-diphenylpyridine (3m)



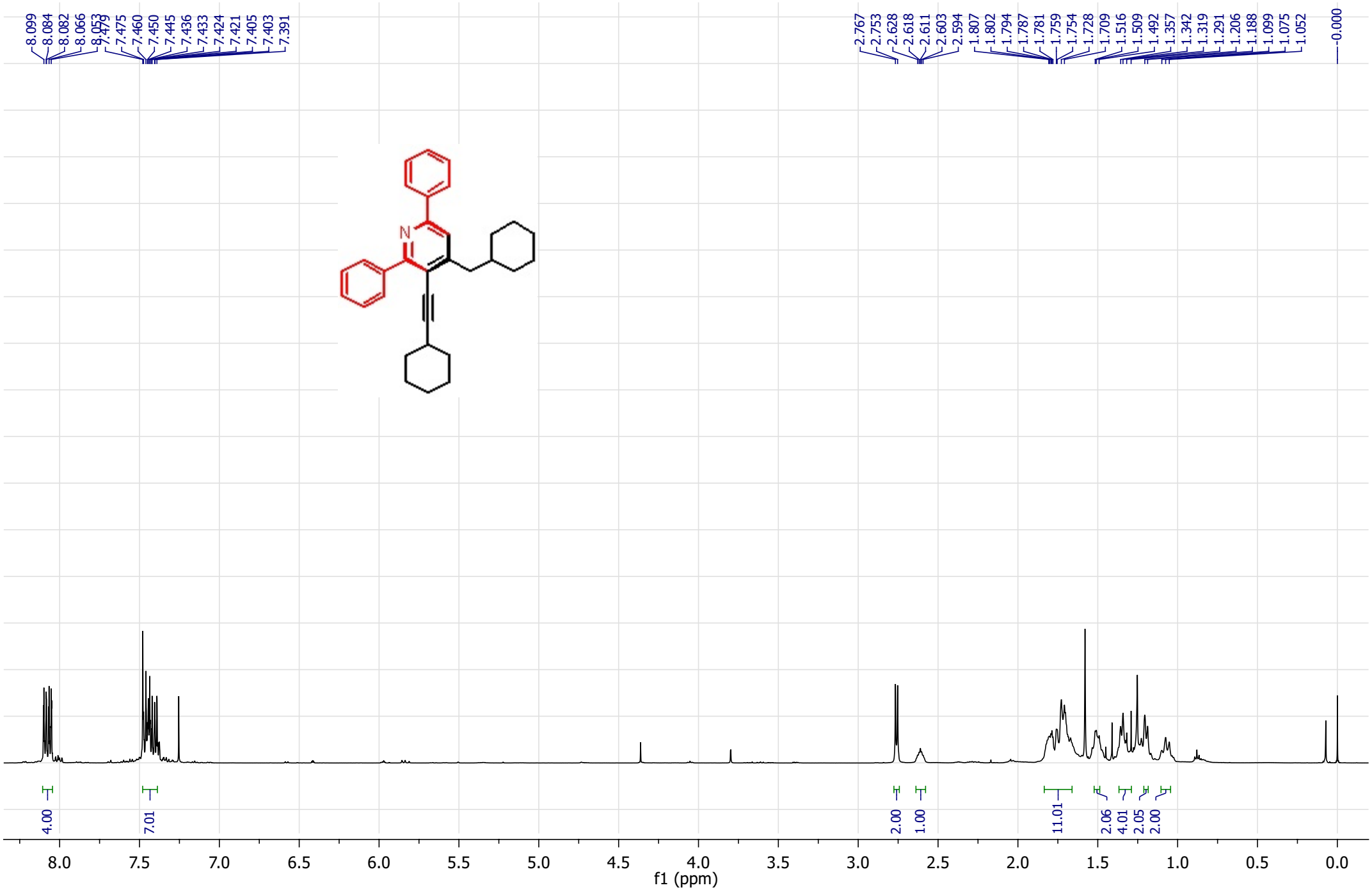
4-(3-fluorobenzyl)-3-((3-fluorophenyl)ethynyl)-2,6-diphenylpyridine (3m)



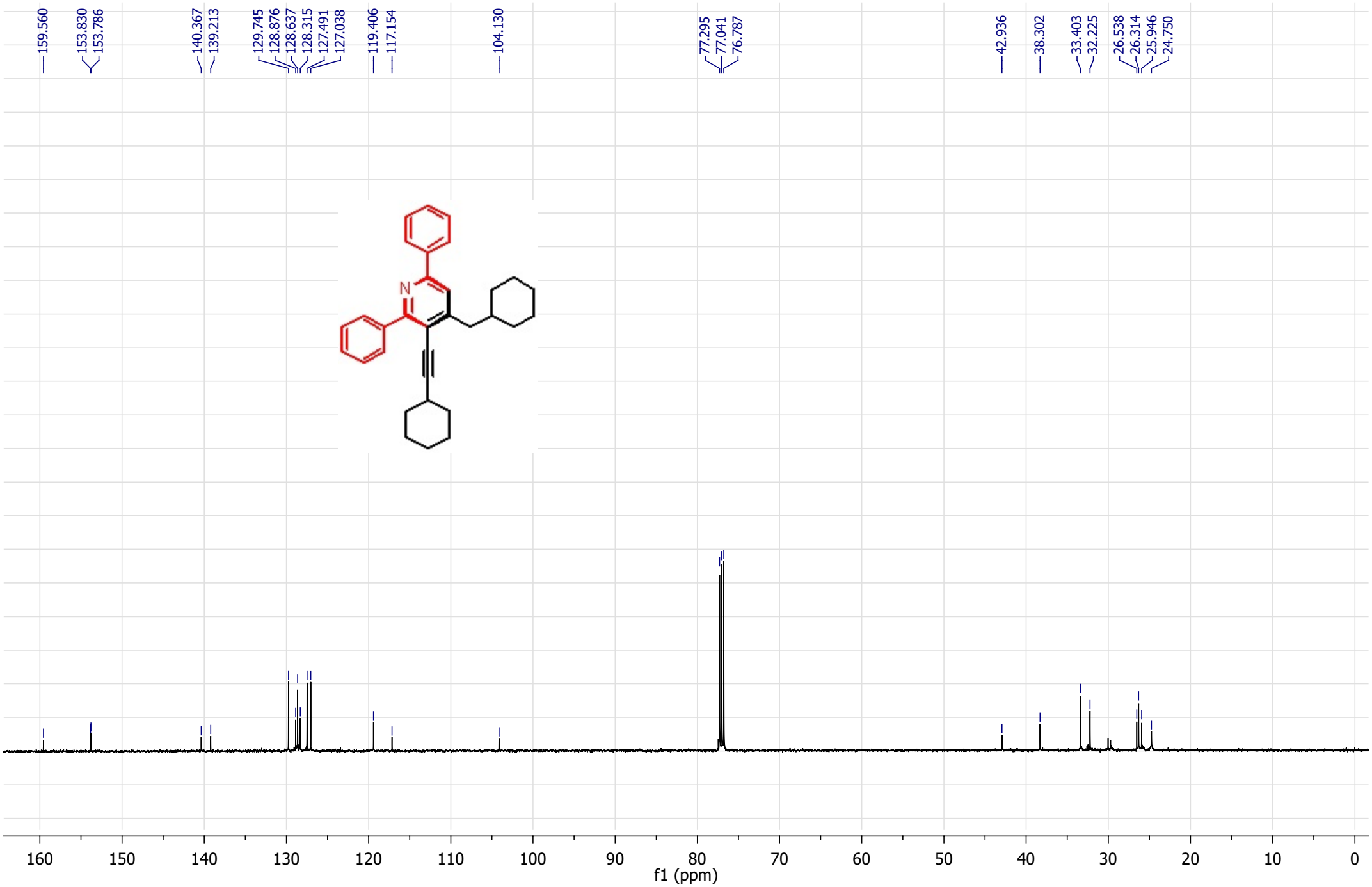
3-(cyclohex-1-en-1-ylethynyl)-4-(cyclohex-1-en-1-ylmethyl)-2,6-diphenylpyridine (3n)



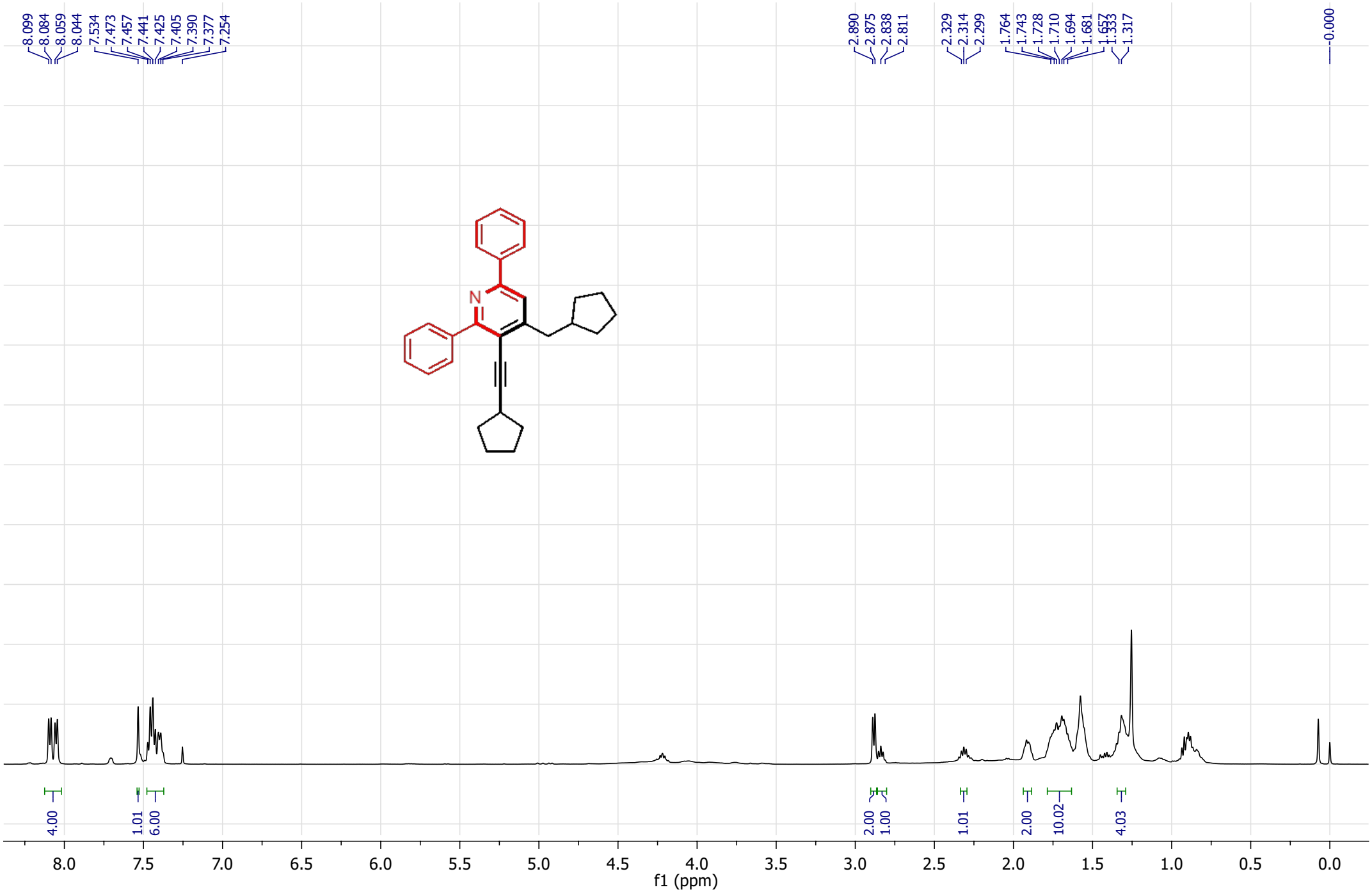
3-(cyclohex-1-en-1-ylethynyl)-4-(cyclohex-1-en-1-ylmethyl)-2,6-diphenylpyridine (3n)



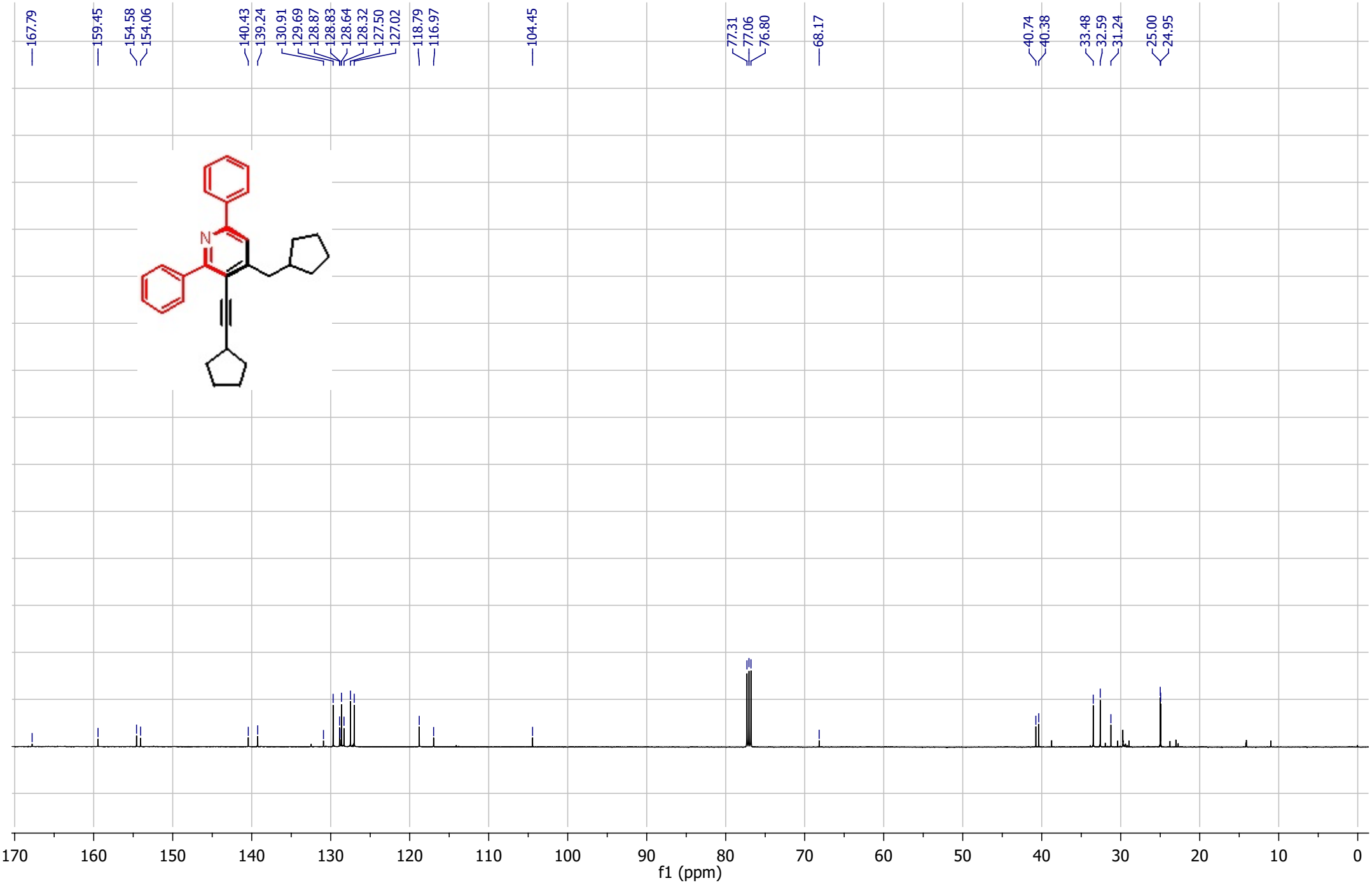
3-(cyclohexylethynyl)-4-(cyclohexylmethyl)-2,6-diphenylpyridine (3o)



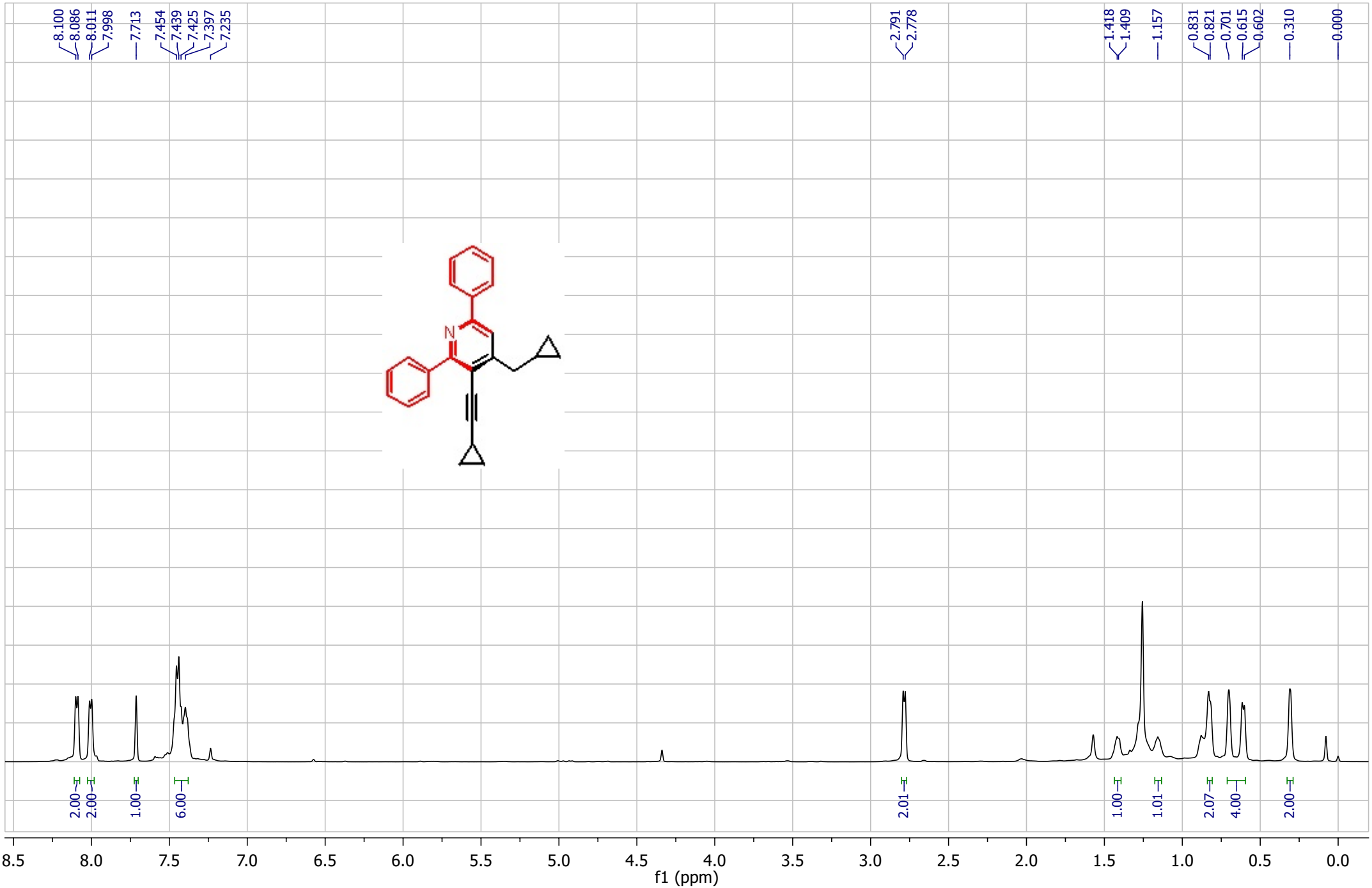
3-(cyclohexylethynyl)-4-(cyclohexylmethyl)-2,6-diphenylpyridine (3o)



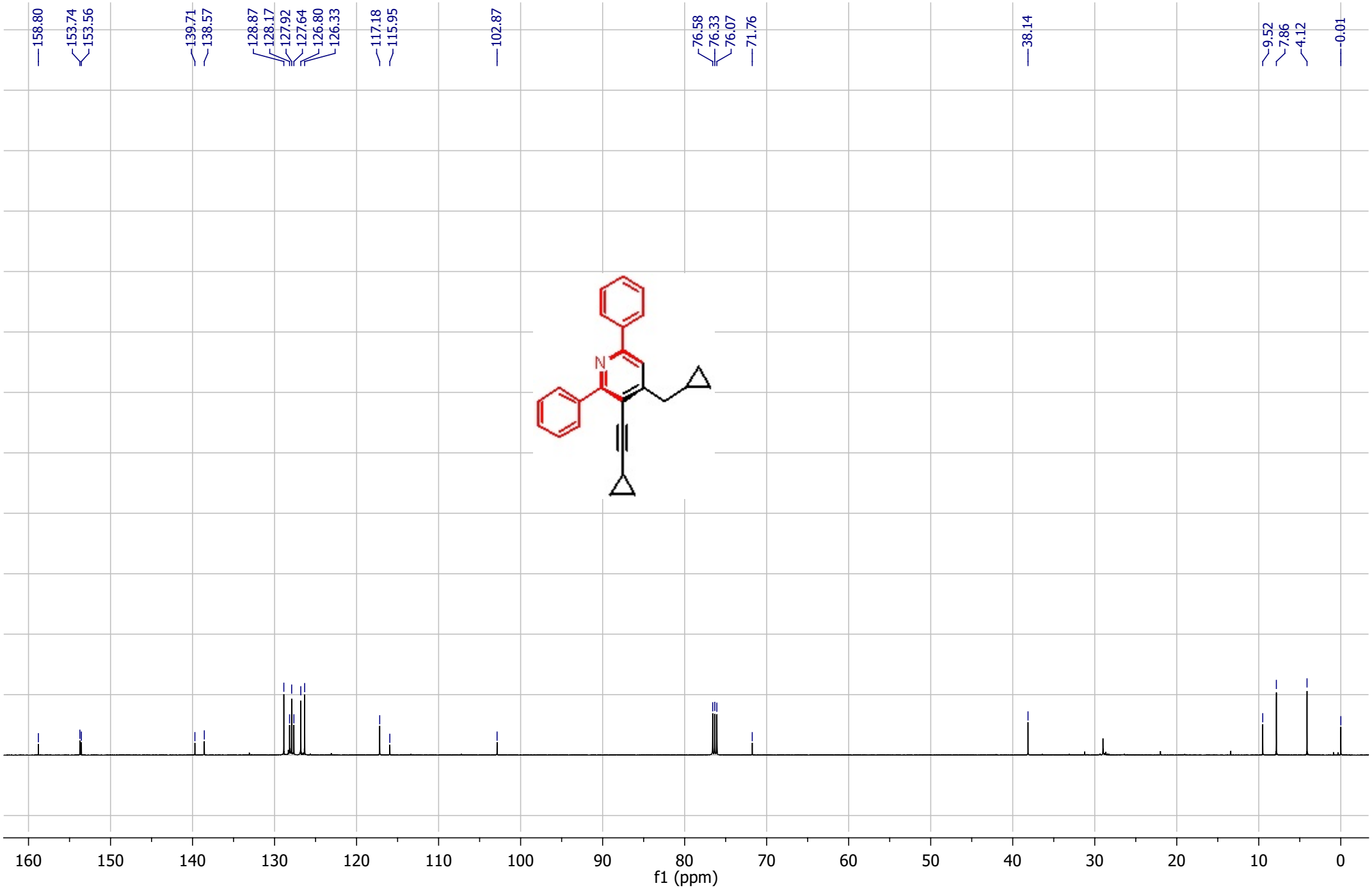
3-(cyclopentylethynyl)-4-(cyclopentylmethyl)-2,6-diphenylpyridine (3p)



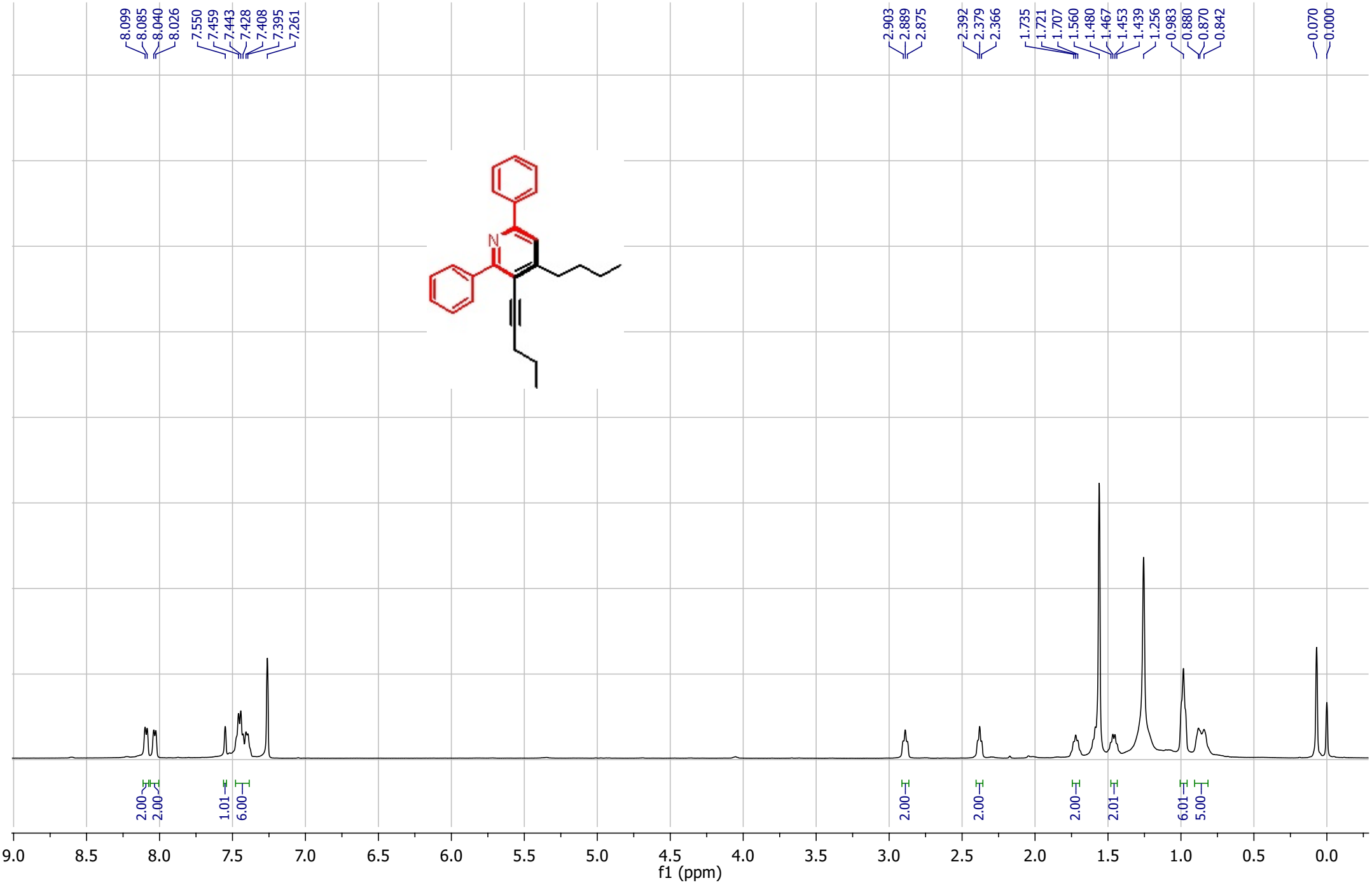
3-(cyclopentylethynyl)-4-(cyclopentylmethyl)-2,6-diphenylpyridine (3p)



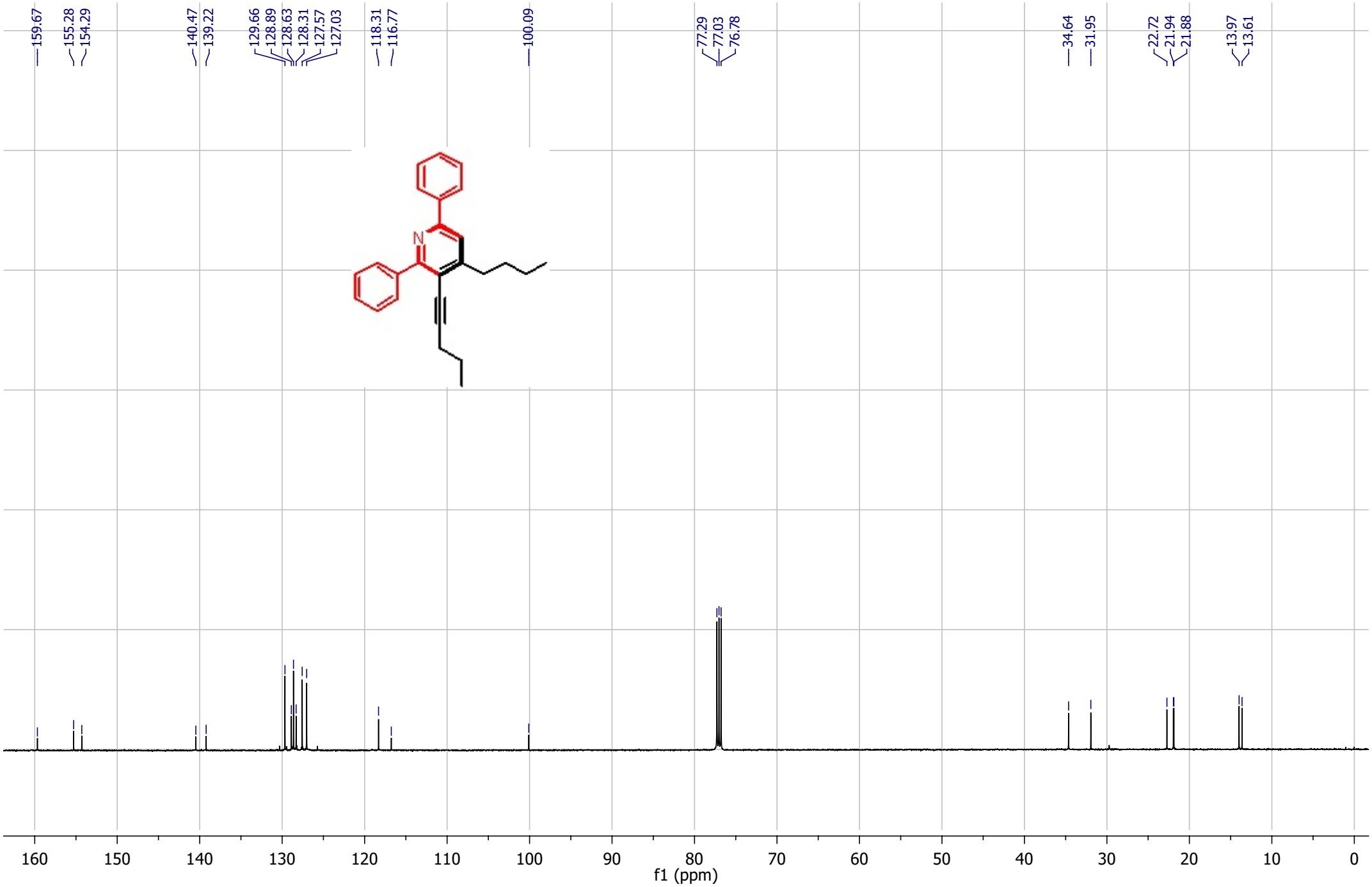
3-(cyclopropylethynyl)-4-(cyclopropylmethyl)-2,6-diphenylpyridine (3q)



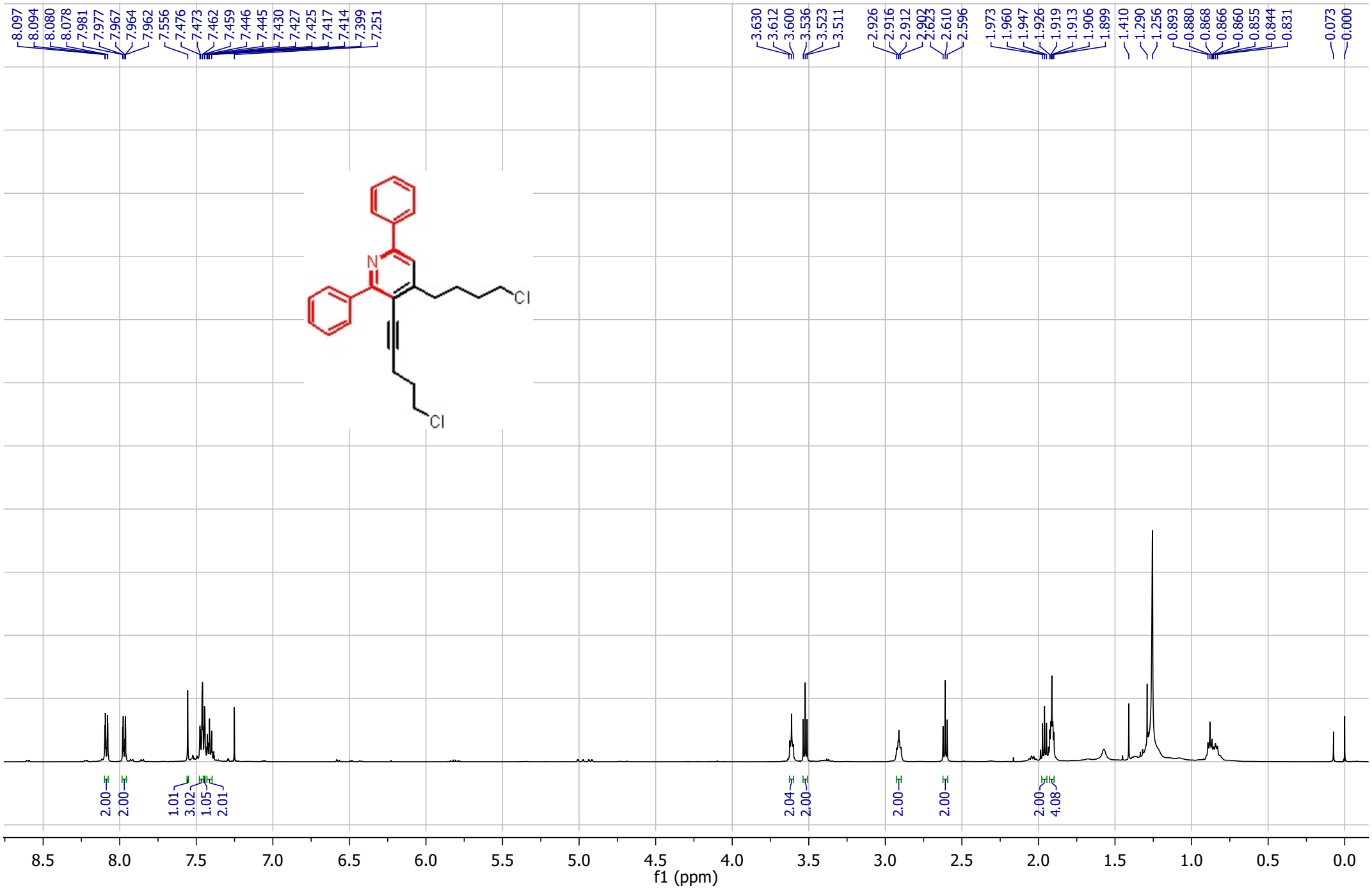
3-(cyclopropylethynyl)-4-(cyclopropylmethyl)-2,6-diphenylpyridine (3q)



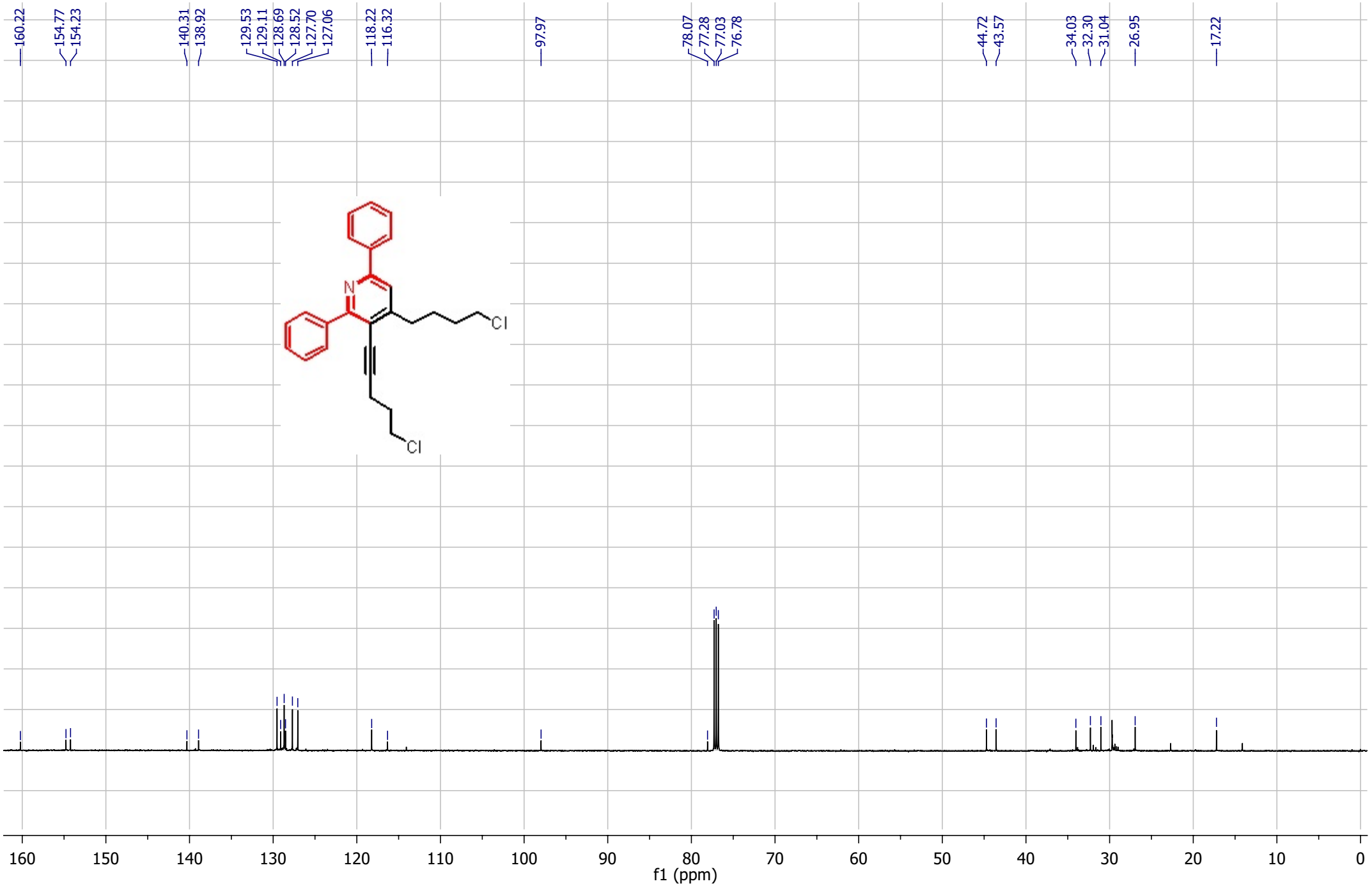
4-butyl-3-(pent-1-yn-1-yl)-2,6-diphenylpyridine (3r)



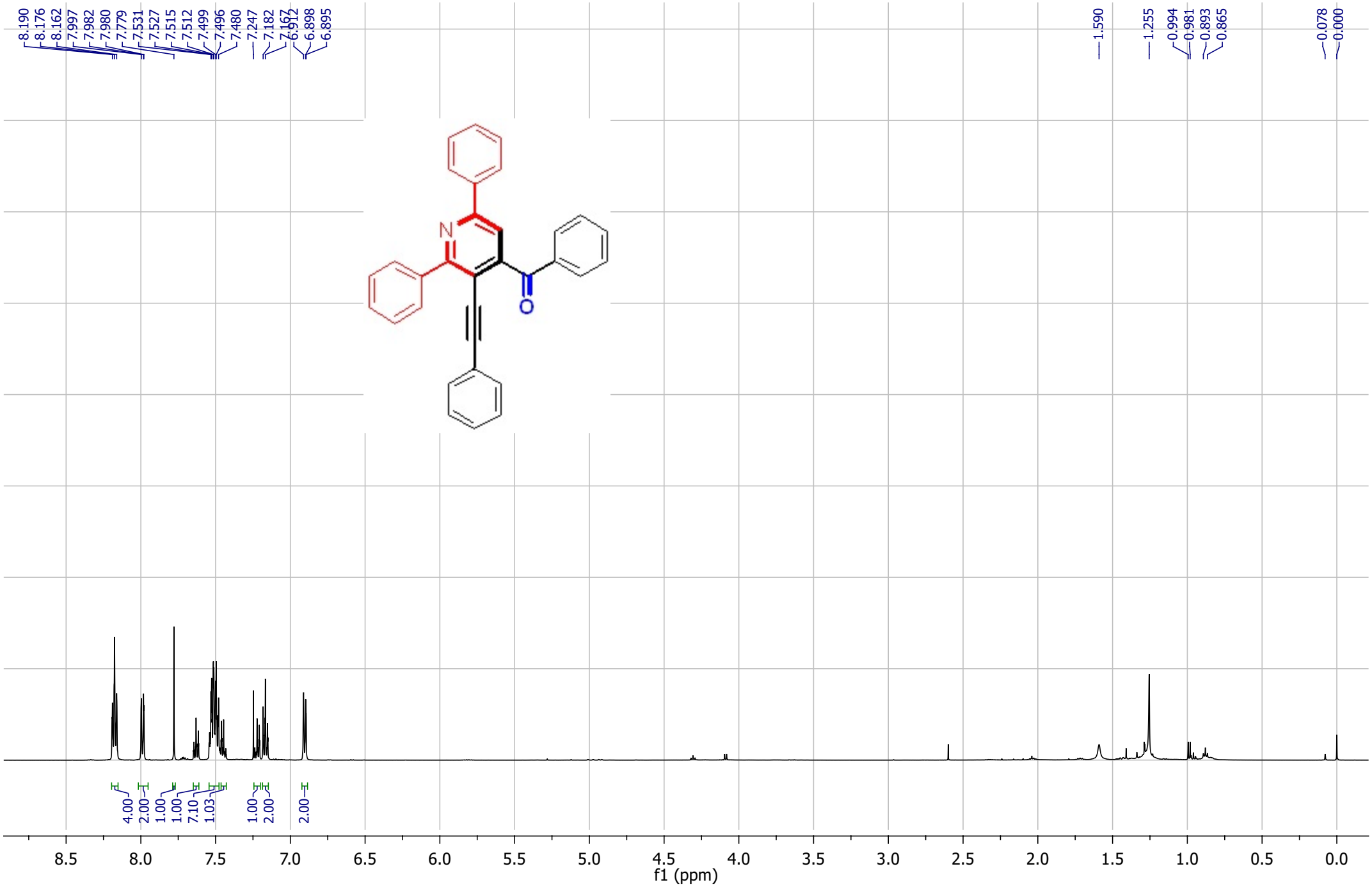
4-butyl-3-(pent-1-yn-1-yl)-2,6-diphenylpyridine (3r)



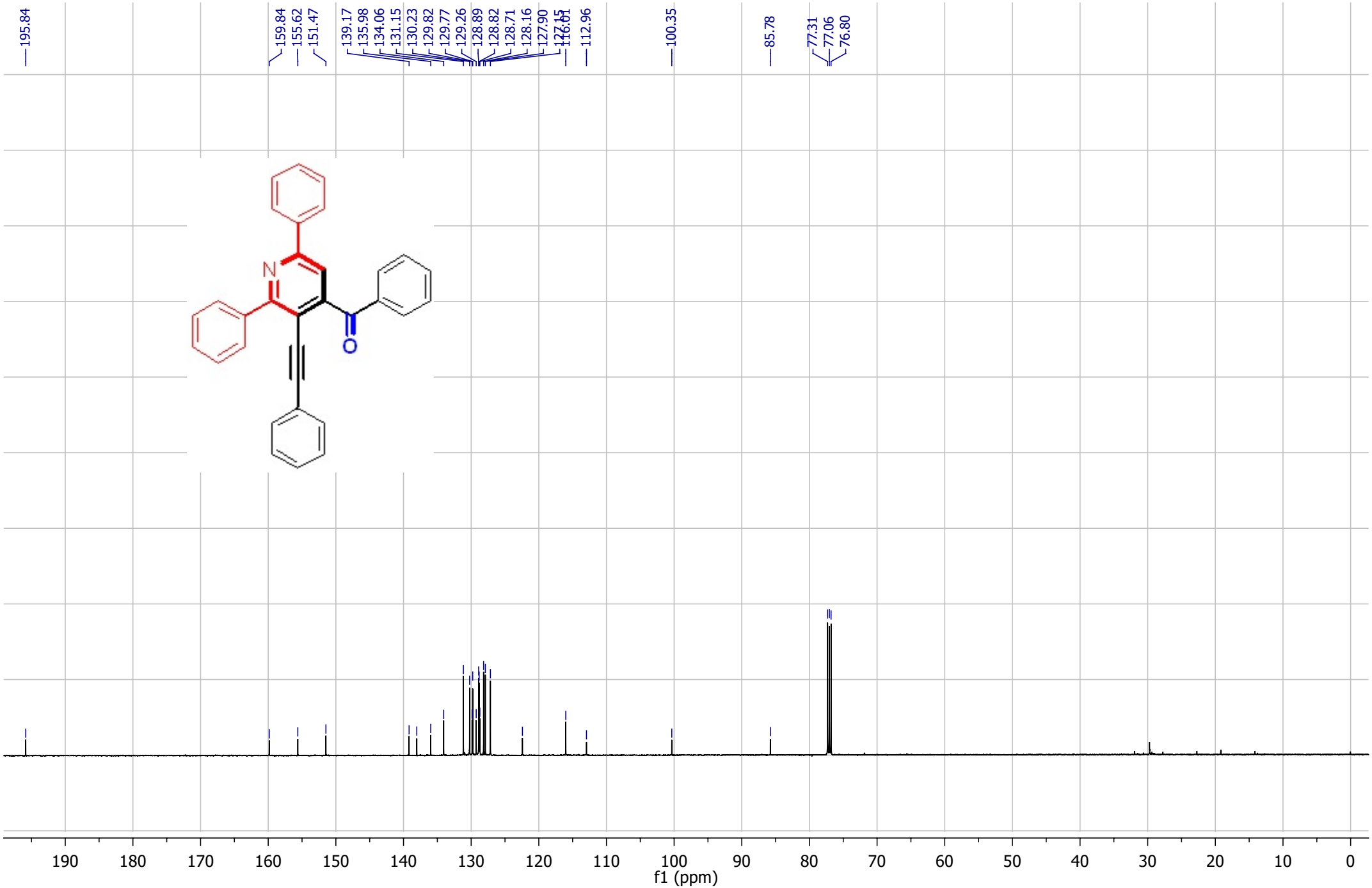
3-(4-chlorobut-1-yn-1-yl)-4-(3-chloropropyl)-2,6-diphenylpyridine (3s)



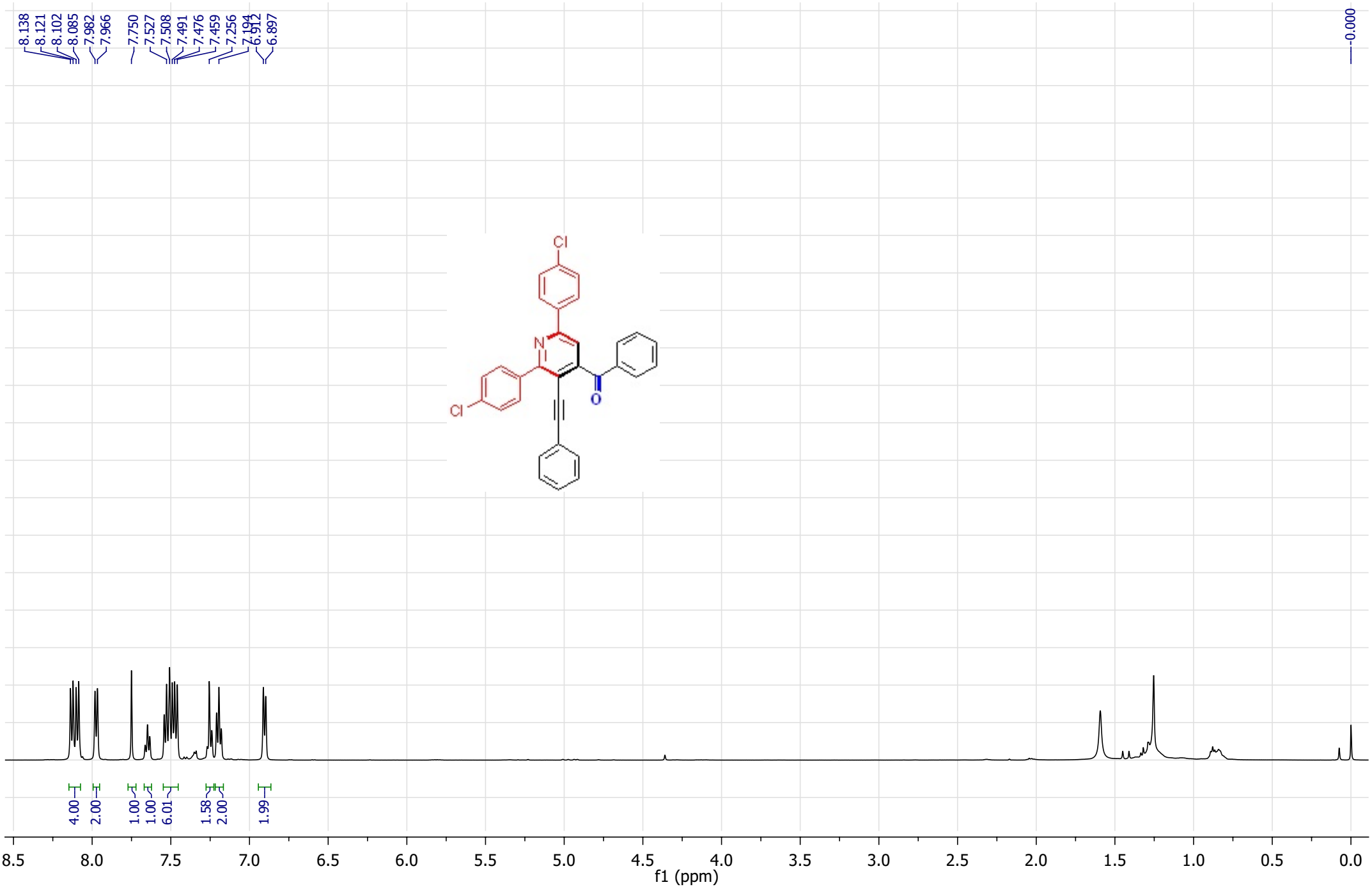
4-(4-chlorobutyl)-3-(5-chloropent-1-yn-1-yl)-2,6-diphenylpyridine (3s)



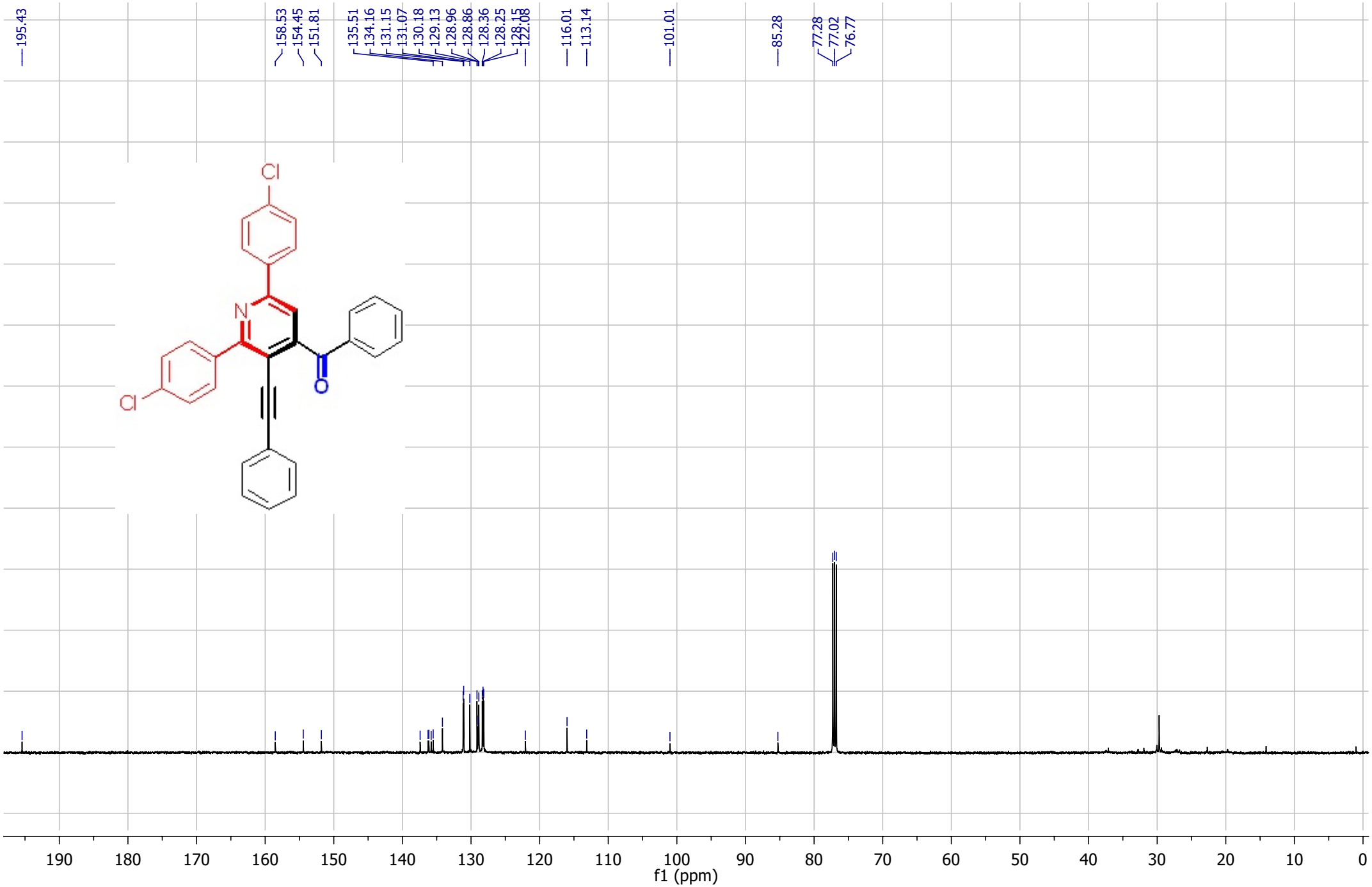
(2,6-diphenyl-3-(phenylethynyl)pyridin-4-yl)(phenyl)methanone (4a)



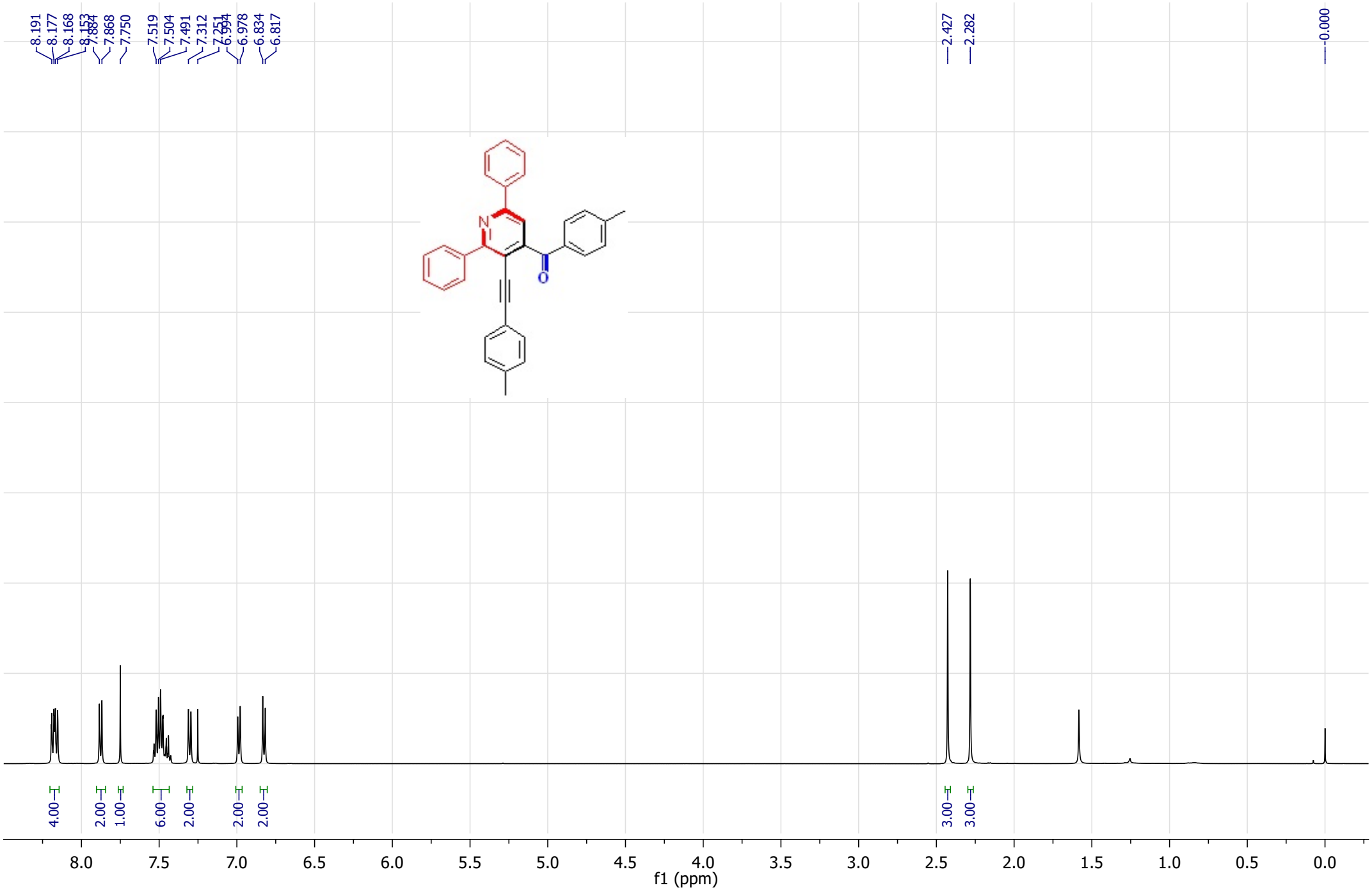
(2,6-diphenyl-3-(phenylethynyl)pyridin-4-yl)(phenyl)methanone (4a)



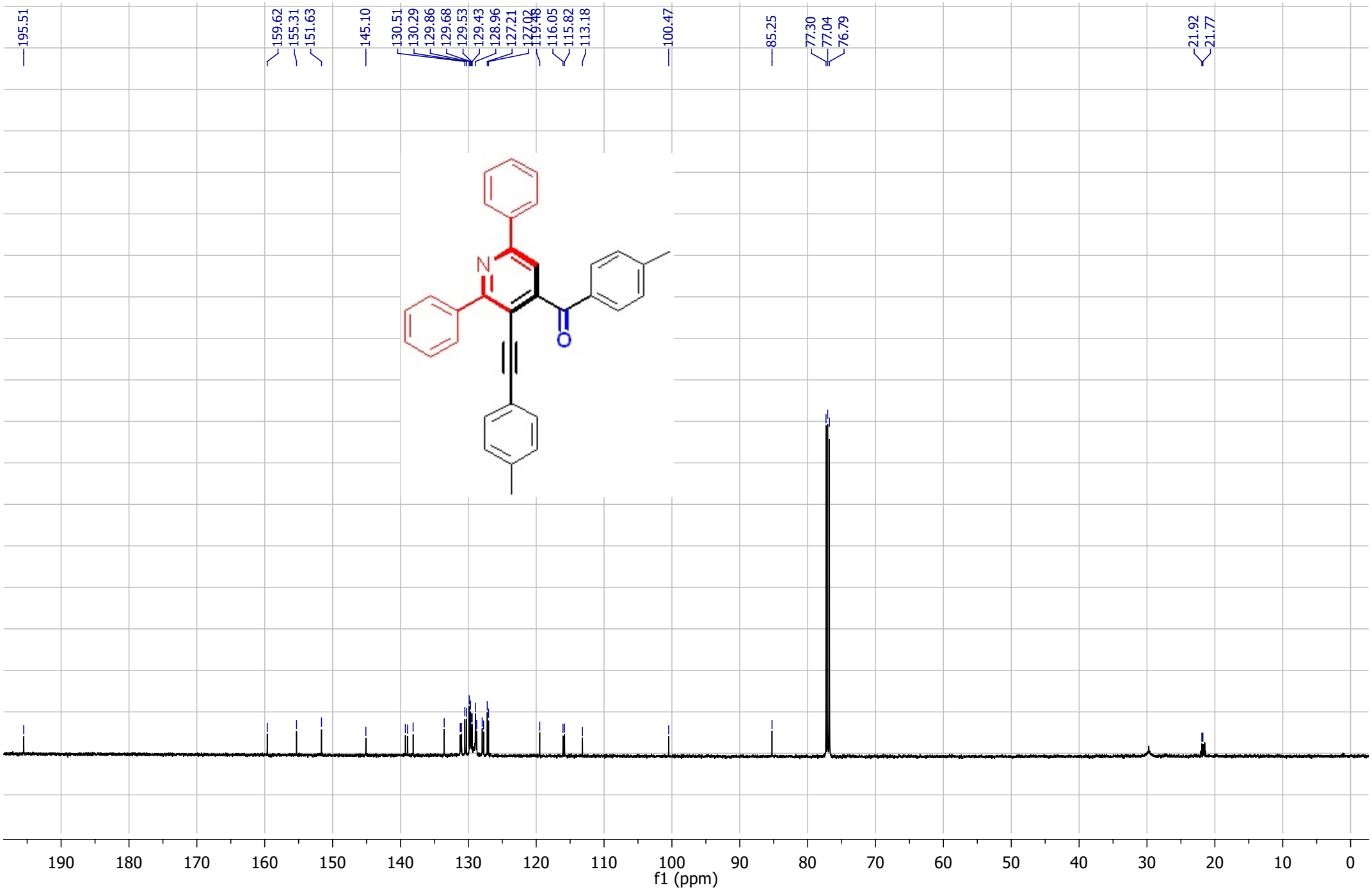
4-benzyl-2,6-bis(4-chlorophenyl)-3-(phenyl ethynyl)pyridine (4b)



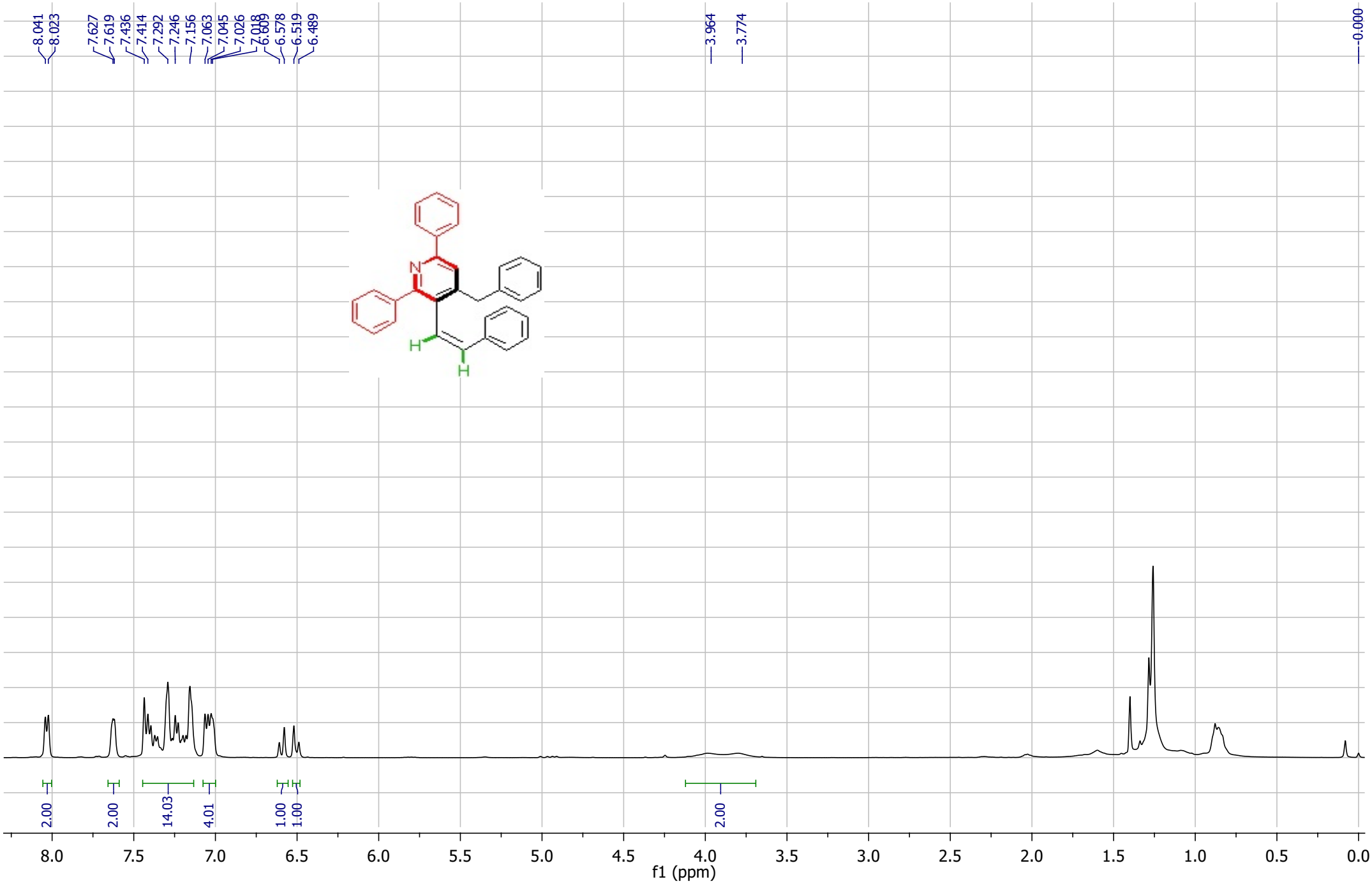
(2,6-bis(4-chlorophenyl)-3-(phenylethynyl)pyridin-4-yl)(phenyl)methanone (4b)



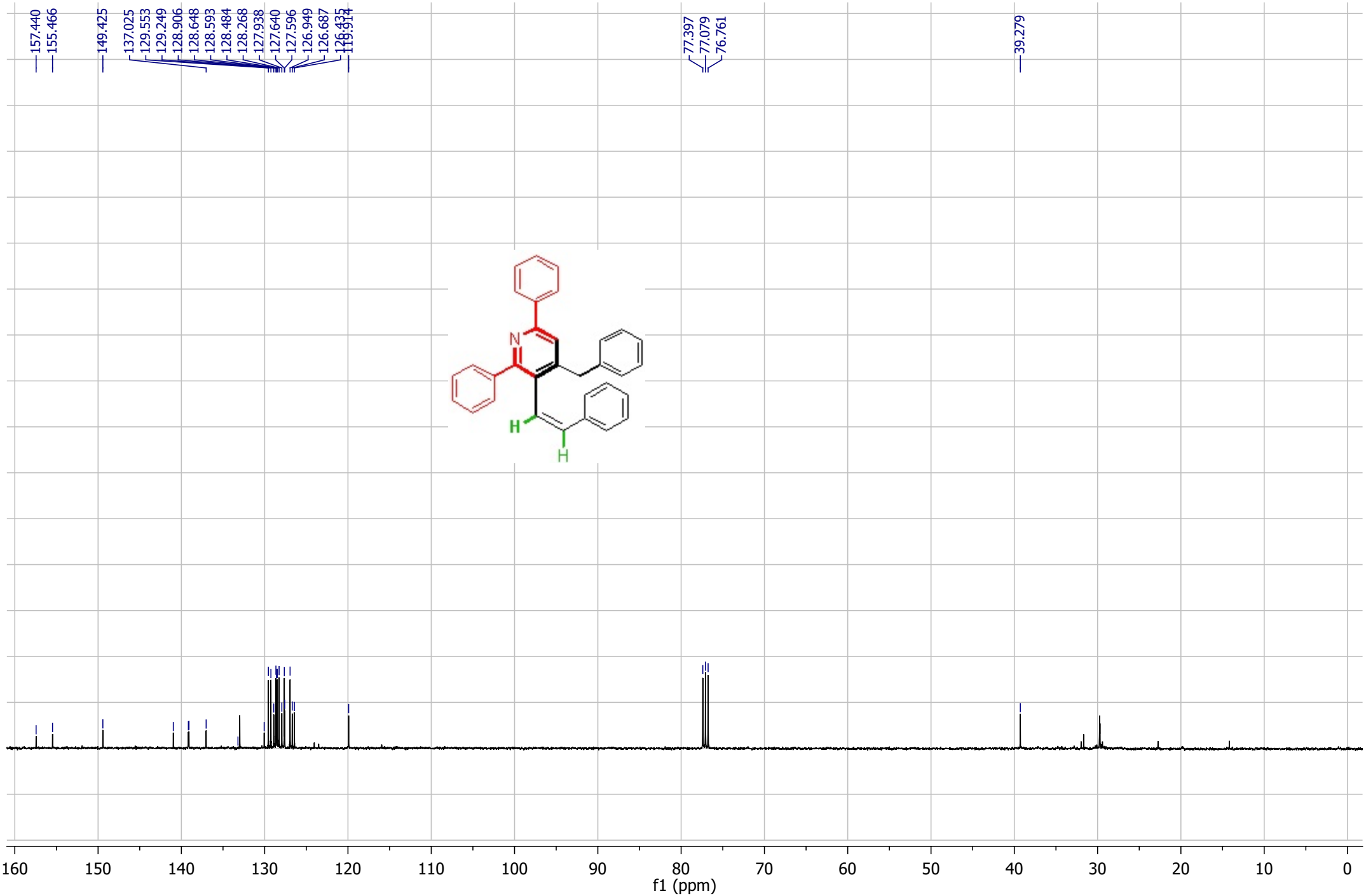
2,6-diphenyl-3-(p-tolylethynyl)pyridin-4-yl)(p-tolyl)methanone (4c)



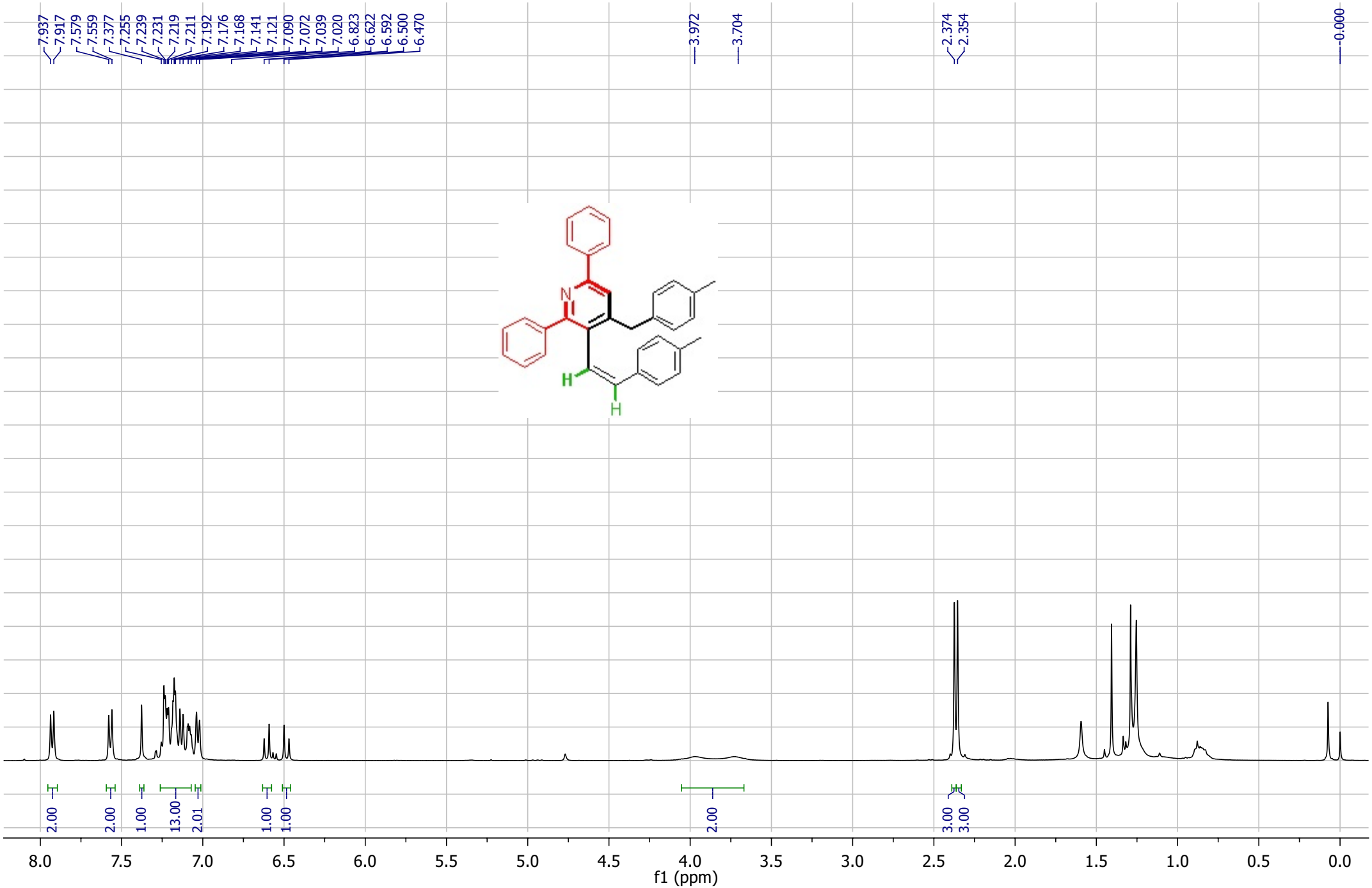
(2,6-diphenyl-3-(p-tolylethynyl)pyridin-4-yl)(p-tolyl)methanone (4c)



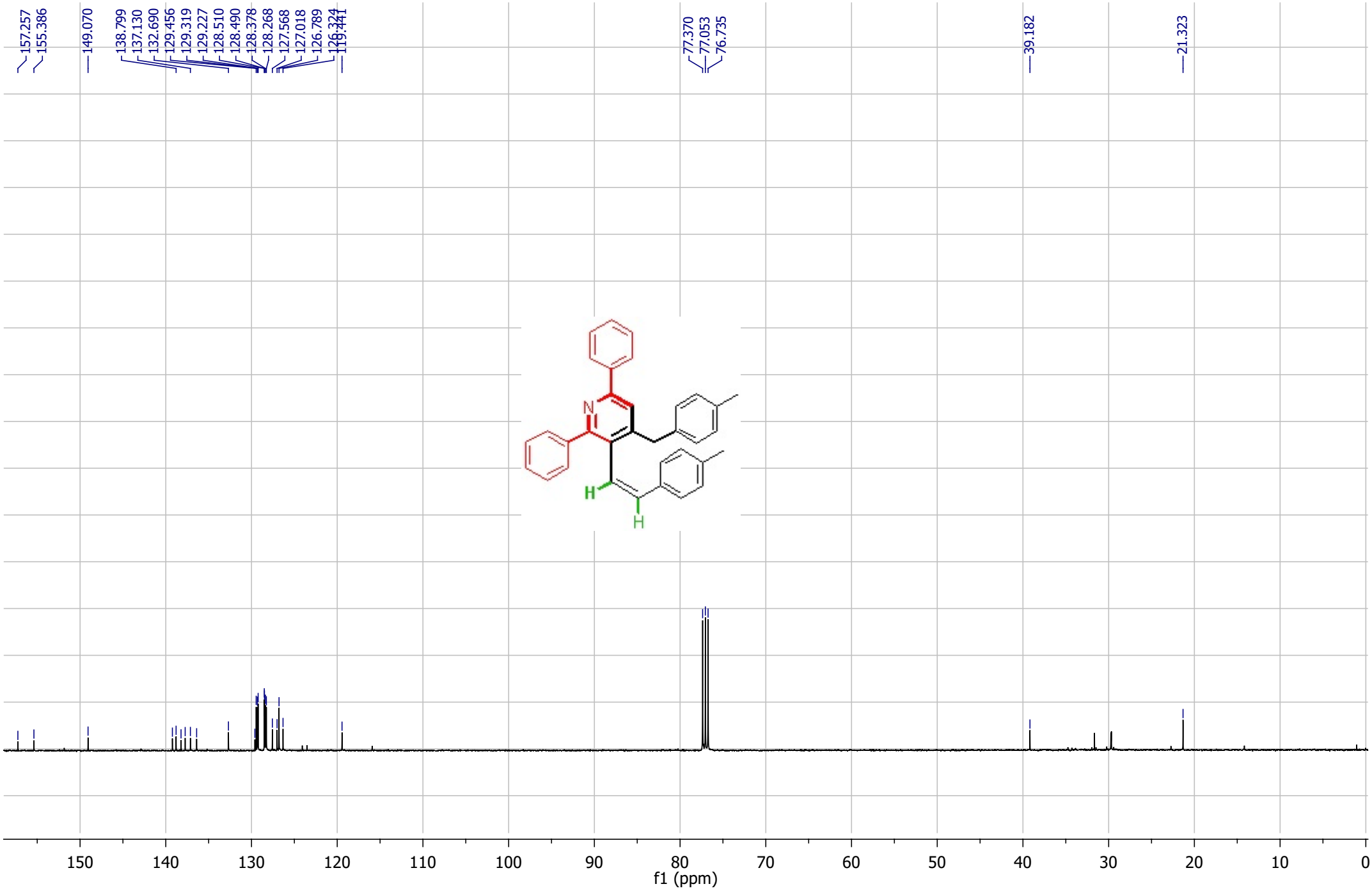
(Z)-4-benzyl-2,6-diphenyl-3-styrylpyridine (5a)



(Z)-4-benzyl-2,6-diphenyl-3-styrylpyridine (5a)



(Z)-4-(4-methylbenzyl)-3-(4-methylstyryl)-2,6-diphenylpyridine (5b)



(Z)-4-(4-methylbenzyl)-3-(4-methylstyryl)-2,6-diphenylpyridine (5b)