

Supporting Information

For

Copper-Catalyzed 1,1-Alkynylalkylation of Alkynes: Access toward Conjugated Enynes

Yunhe Lv,* Yanqin Wang, Weiya Pu, Xueli Zhu, Ning Wu and Yali Zhao

College of Chemistry and Chemical Engineering, Anyang Normal University, Anyang,
455000 China

luyh086@nenu.edu.cn; lyunhe0217@163.com

Table of Contents

I . General Considerations	S2
II . General Procedure for the Preparation of 2, 3 and 4	S2
III. Analytical Data of Compounds 3 and 4	S3
IV. Structure Analysis X-Ray Crystallography of 3b	S25
V . Mechanistic Study	S26
VI. References	S29
VII. ^1H and ^{13}C NMR Spectra of Compounds 3 and 4	S30

I . General Considerations

All reagents were purchased from commercial sources and used without further treatment, unless otherwise indicated. The following starting materials were prepared according to the procedures described previously in the literature: **5**,^[1] **6**,^[2] **7**,^[3] **8**.^[3] All reactions were run under air with no precautions taken to exclude moisture. ¹H NMR and ¹³C NMR spectra were recorded at 25 °C on a Varian (400 MHz and 100 MHz). Melting points were obtained with a micro melting point XT4A Beijing Keyi electrooptic apparatus and are uncorrected. High-resolution mass data were recorded on a Waters LCT PremierxeTM (USA). Single-crystal X-ray crystallography was carried out on a Bruker Smart Apex II diffractometer system. All reactions were monitored by TLC with Taizhou GF254 silica gel coated plates. Flash column chromatography was carried out using 200-300 mesh silica gel at increased pressure.

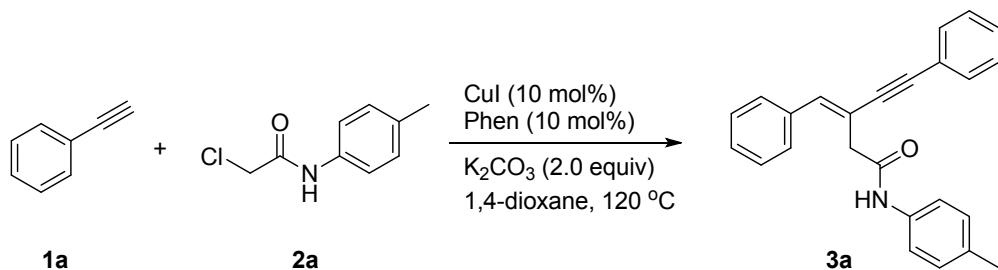
II . General Procedure for the Preparation of 2, 3 and 4

1. General Procedure for the Preparation of 2

Substrates **2** were prepared by the reaction of corresponding anilines (1 equiv) and acyl chlorides (1.2 equiv) in CH₂Cl₂ at room temperature according to procedures described in the literature reported before.^[4]

2. General Procedure for the Preparation of 3 and 4

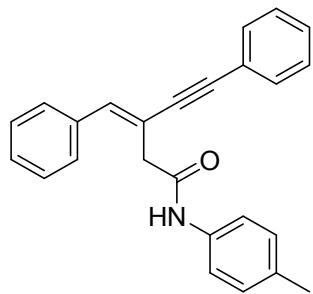
3a as an example



To a solution of the 2-chloro-*N*-(*p*-tolyl)acetamide **2a** (73.2 mg, 0.4 mmol) in 1,4-dioxane (0.8 ml) was added the ethynylbenzene **1a** (110 µL, 0.96 mmol), Phen (7.9 mg, 0.04 mmol), CuI (7.6 mg, 0.04 mmol), and K₂CO₃ (110.6 mg, 0.8 mmol) under air in a Schlenk tube. The reaction mixture was stirred at 120 °C for 1.0 h. After the reaction finished, the reaction mixture was

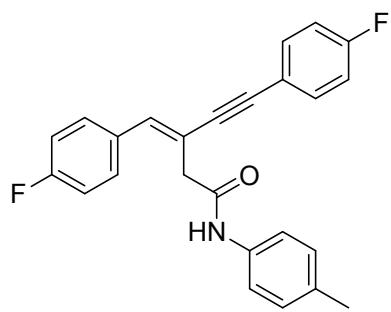
cooled to room temperature and quenched by water. The mixture was extracted with EtOAc (3.0 mL×3), the combined organic phases were dried over anhydrous Na₂SO₄ and the solvent was evaporated under vacuum. The residue was purified by column chromatography to give the corresponding products **3a** (112.0 mg, 80%).

III. Analytical Data of Compounds **3** and **4**



(*E*)-3-benzylidene-5-phenyl-N-(*p*-tolyl)pent-4-ynamide **3a**

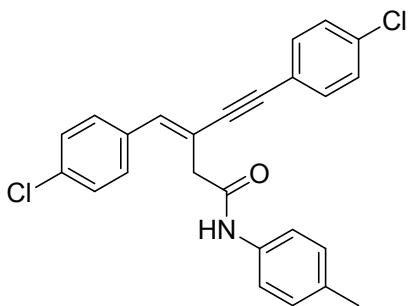
White solid. mp: 140 °C. ¹H NMR (400 MHz, CDCl₃): δ = 2.30 (s, 3H), 3.55 (s, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.23 (s, 1H), 7.29-7.34 (m, 4H), 7.37-7.40 (m, 6H), 7.47 (t, *J* = 3.6 Hz, 2H), 7.79 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 20.8, 41.3, 90.8, 91.1, 116.8, 120.1, 122.5, 128.3, 128.4, 128.6, 128.7, 128.9, 129.5, 131.6, 134.1, 135.2, 135.3, 140.1, 167.5. HRMS (ESI-TOF). Calcd for C₂₅H₂₂NO, [M+H]⁺ *m/z* 352.1701, Found 352.1710.



(*E*)-3-(4-fluorobenzylidene)-5-(4-fluorophenyl)-N-(*p*-tolyl)pent-4-ynamide **3b**

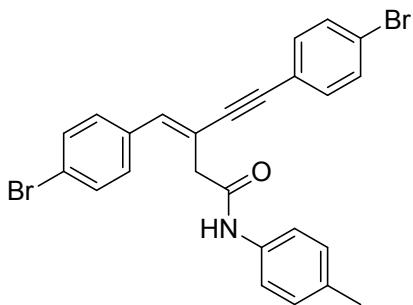
White solid. mp: 156 °C. ¹H NMR (400 MHz, CDCl₃): δ = 2.30 (s, 3H), 3.50 (s, 2H), 7.00-7.15 (m, 7H), 7.38-7.45 (m, 6H), 7.78 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 20.8, 41.2, 89.7, 90.6, 115.7 (d, *J*_{C-F} = 6.0 Hz), 115.9 (d, *J*_{C-F} = 6.0 Hz), 116.5, 118.6 (d, *J*_{C-F} = 4.0 Hz), 120.1, 129.5, 130.7 (d, *J*_{C-F} = 8.0 Hz), 131.3 (d, *J*_{C-F} = 3.0 Hz), 133.5 (d, *J*_{C-F} = 8.0 Hz), 134.3, 135.1, 138.9, 162.5 (d, *J*_{C-F} = 248.0 Hz), 162.7 (d, *J*_{C-F} = 249.0 Hz), 167.4. HRMS (ESI-TOF). Calcd for

$C_{25}H_{20}F_2NO$, $[M+H]^+$ m/z 388.1513, Found 388.1516.



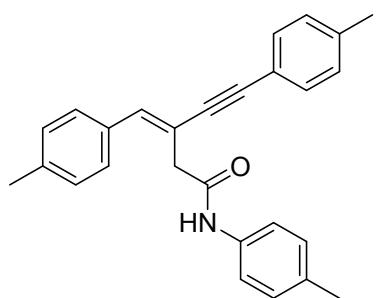
(E)-3-(4-chlorobenzylidene)-5-(4-chlorophenyl)-N-(p-tolyl)pent-4-ynamide 3c

White solid. mp: 180 °C. 1H NMR (400 MHz, $CDCl_3$): δ = 2.31 (s, 3H), 3.50 (s, 2H), 7.11 (d, J = 8.4 Hz, 2H), 7.15 (s, 1H), 7.30 (d, J = 8.8 Hz, 2H), 7.35-7.39 (m, 8H), 7.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.8, 41.2, 90.0, 91.7, 117.2, 120.1, 120.9, 128.8, 128.9, 129.5, 130.2, 132.8, 133.6, 134.3, 134.4, 134.8, 135.0, 139.0, 167.2. HRMS (ESI-TOF). Calcd for $C_{25}H_{20}Cl_2NO$, $[M+H]^+$ m/z 420.0922, Found 420.0918.



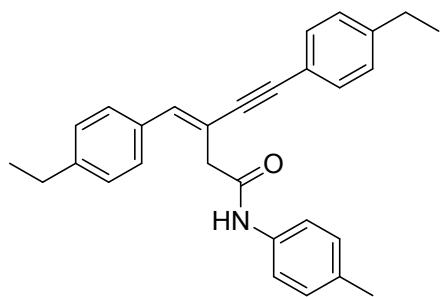
(E)-3-(4-bromobenzylidene)-5-(4-bromophenyl)-N-(p-tolyl)pent-4-ynamide 3d

White solid. mp: 174 °C. 1H NMR (400 MHz, $CDCl_3$): δ = 2.31 (s, 3H), 3.49 (s, 2H), 7.12 (d, J = 9.2 Hz, 3H), 7.29-7.32 (m, 4H), 7.38 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 7.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9, 41.2, 90.1, 91.9, 117.3, 120.1, 121.4, 122.7, 123.1, 129.5, 130.4, 131.8, 131.9, 133.0, 134.0, 134.4, 135.0, 139.1, 167.1. HRMS (ESI-TOF). Calcd for $C_{25}H_{20}Br_2NO$, $[M+H]^+$ m/z 509.9891, Found 509.9896.



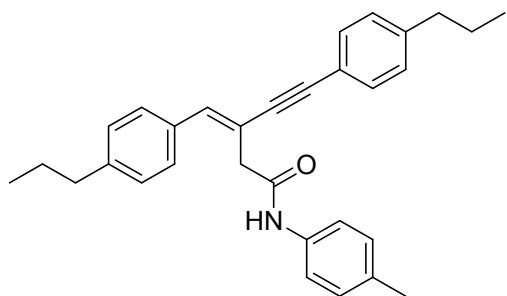
(E)-3-(4-methylbenzylidene)-N,5-di-p-tolylpent-4-ynamide 3e

White solid. mp: 169-170 °C. ^1H NMR (400 MHz, CDCl_3): δ = 2.30 (s, 3H), 2.36 (s, 3H), 2.36 (s, 3H), 3.56 (s, 2H), 7.11 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 7.6 Hz, 2H), 7.19 (d, J = 9.2 Hz, 3H), 7.30 (d, J = 8.0 Hz, 2H), 7.38 (t, J = 8.4 Hz, 4H), 7.81 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 20.8, 21.3, 21.5, 41.5, 41.5, 90.8, 90.9, 115.9, 119.5, 120.1, 128.9, 129.2, 129.4, 129.5, 131.5, 132.5, 134.1, 135.2, 138.4, 138.8, 139.9, 167.6. HRMS (ESI-TOF). Calcd for $\text{C}_{27}\text{H}_{26}\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 380.2014, Found 380.2014.



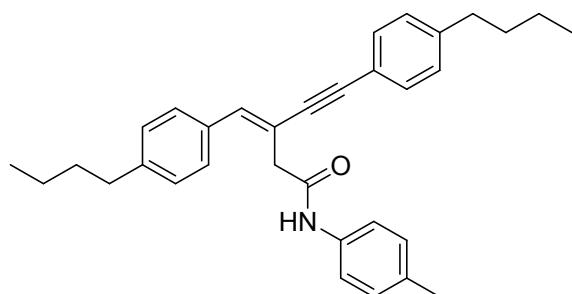
(E)-3-(4-ethylbenzylidene)-5-(4-ethylphenyl)-N-(p-tolyl)pent-4-ynamide 3f

White solid. mp: 138-139 °C. ^1H NMR (400 MHz, CDCl_3): δ = 1.24 (t, J = 7.6 Hz, 6H), 2.30 (s, 3H), 2.65 (q, J = 7.6 Hz, 4H), 3.56 (s, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 7.19 (s, 1H), 7.22 (d, J = 8.0 Hz, 2H), 7.32 (d, J = 7.6 Hz, 2H), 7.39 (d, J = 8.0 Hz, 4H), 7.83 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 15.3, 15.4, 20.8, 28.6, 28.8, 41.5, 90.8, 90.9, 116.0, 119.8, 120.1, 128.0, 128.2, 128.9, 129.4, 131.6, 132.8, 134.0, 135.2, 139.9, 144.7, 145.1, 167.7. HRMS (ESI-TOF). Calcd for $\text{C}_{29}\text{H}_{30}\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 408.2327, Found 408.2327.



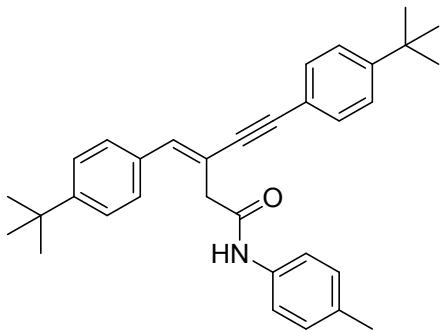
(E)-3-(4-propylbenzylidene)-5-(4-propylphenyl)-N-(p-tolyl)pent-4-ynamide 3g

White solid. mp: 126-128 °C. ^1H NMR (400 MHz, CDCl_3): δ = 0.94 (t, J = 7.2 Hz, 6H), 1.59-1.68 (m, 4H), 2.30 (s, 3H), 2.58 (t, J = 7.6 Hz, 4H), 3.56 (s, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 3H), 7.31 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 4.4 Hz, 2H), 7.40 (d, J = 4.4 Hz, 2H), 7.85 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 13.7, 13.8, 20.8, 24.3, 24.3, 37.8, 37.9, 41.5, 90.8, 90.9, 115.9, 119.8, 120.1, 128.6, 128.8, 128.8, 129.4, 131.5, 132.8, 134.0, 135.2, 139.9, 143.1, 143.6, 167.7. HRMS (ESI-TOF). Calcd for $\text{C}_{31}\text{H}_{34}\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 436.2640, Found 436.2647.



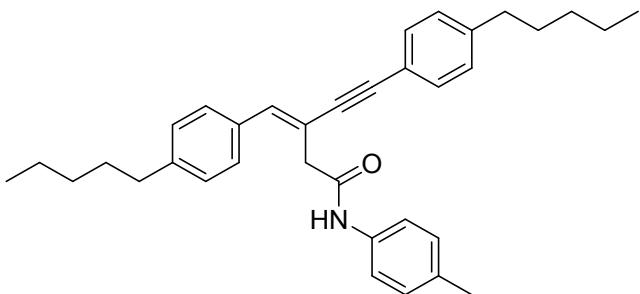
(E)-3-(4-butylbenzylidene)-5-(4-butylphenyl)-N-(p-tolyl)pent-4-ynamide 3h

White solid. mp: 128-129 °C. ^1H NMR (400 MHz, CDCl_3): δ = 0.92 (t, J = 7.6 Hz, 6H), 1.30-1.39 (m, 4H), 1.55-1.63 (m, 4H), 2.29 (s, 3H), 2.60 (t, J = 7.6 Hz, 4H), 3.56 (s, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 7.6 Hz, 2H), 7.19 (d, J = 8.4 Hz, 3H), 7.31 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 6.0 Hz, 2H), 7.40 (d, J = 6.4 Hz, 2H), 7.86 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 13.9, 20.8, 22.3, 22.3, 33.3, 33.4, 35.4, 35.6, 41.5, 90.8, 90.9, 115.9, 119.7, 120.1, 128.5, 128.7, 128.8, 129.4, 131.5, 132.7, 134.0, 135.2, 139.8, 143.3, 143.8, 167.7. HRMS (ESI-TOF). Calcd for $\text{C}_{33}\text{H}_{38}\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 464.2953, Found 464.2948.



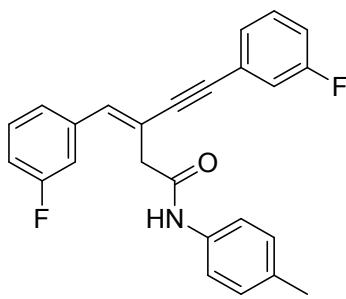
(E)-3-(4-(tert-butyl)benzylidene)-5-(4-(tert-butyl)phenyl)-N-(p-tolyl)pent-4-ynamide 3i

White solid. mp: 172-174 °C. ^1H NMR (400 MHz, CDCl_3): δ = 1.31 (s, 18H), 2.29 (s, 3H), 3.57 (s, 2H), 7.09 (d, J = 8.0 Hz, 2H), 7.19 (s, 1H), 7.34 (d, J = 8.4 Hz, 4H), 7.40 (d, J = 8.0 Hz, 6H), 7.91 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 20.8, 31.1, 31.2, 34.6, 34.8, 41.5, 90.8, 90.8, 116.1, 119.6, 120.1, 125.4, 125.6, 128.7, 129.4, 131.3, 132.5, 134.0, 135.2, 139.7, 151.4, 151.9, 167.7. HRMS (ESI-TOF). Calcd for $\text{C}_{33}\text{H}_{38}\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 464.2953, Found 464.2963.



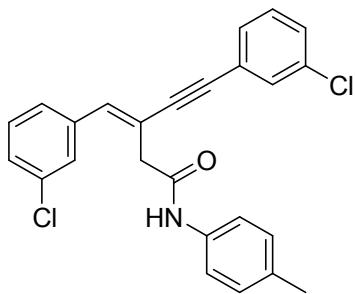
(E)-3-(4-pentylbenzylidene)-5-(4-pentylphenyl)-N-(p-tolyl)pent-4-ynamide 3j

White solid. mp: 129-130 °C. ^1H NMR (400 MHz, CDCl_3): δ = 0.89 (t, J = 6.8 Hz, 6H), 1.31-1.32 (m, 8H), 1.57-1.64 (m, 4H), 2.30 (s, 3H), 2.60 (t, J = 7.6 Hz, 4H), 3.56 (s, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.4 Hz, 3H), 7.31 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 5.2 Hz, 2H), 7.40 (d, J = 5.6 Hz, 2H), 7.84 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 14.0, 20.8, 22.5, 30.9, 30.9, 31.4, 31.4, 35.7, 35.9, 41.5, 90.8, 90.9, 115.9, 119.7, 120.1, 128.6, 128.7, 128.9, 129.4, 131.5, 132.7, 134.0, 135.2, 139.9, 143.4, 143.8, 167.7. HRMS (ESI-TOF). Calcd for $\text{C}_{35}\text{H}_{42}\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 492.3266, Found 492.3268.



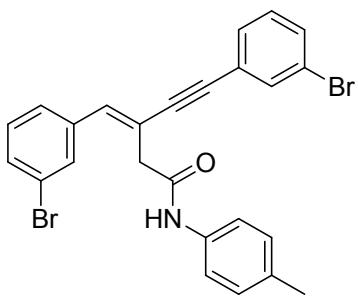
(E)-3-(3-fluorobenzylidene)-5-(3-fluorophenyl)-N-(p-tolyl)pent-4-ynamide 3k

White solid. mp: 141-142 °C. ^1H NMR (400 MHz, CDCl_3): δ = 2.30 (s, 3H), 3.52 (s, 2H), 7.00-7.07 (m, 2H), 7.10-7.36 (m, 9H), 7.40 (d, J = 8.4 Hz, 2H), 7.68 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 20.8, 41.1, 89.9 (d, $J_{\text{C}-\text{F}}$ = 4.0 Hz), 91.4, 115.3 (d, $J_{\text{C}-\text{F}}$ = 21.0 Hz), 115.7 (d, $J_{\text{C}-\text{F}}$ = 22.0 Hz), 116.1 (d, $J_{\text{C}-\text{F}}$ = 21.0 Hz), 117.8, 118.4 (d, $J_{\text{C}-\text{F}}$ = 22.0 Hz), 120.1, 124.2 (d, $J_{\text{C}-\text{F}}$ = 9.0 Hz), 124.6 (d, $J_{\text{C}-\text{F}}$ = 3.0 Hz), 127.5 (d, $J_{\text{C}-\text{F}}$ = 3.0 Hz), 129.5, 130.1 (d, $J_{\text{C}-\text{F}}$ = 8.0 Hz), 130.3 (d, $J_{\text{C}-\text{F}}$ = 8.0 Hz), 134.3, 135.0, 137.2 (d, $J_{\text{C}-\text{F}}$ = 8.0 Hz), 139.2 (d, $J_{\text{C}-\text{F}}$ = 2.0 Hz), 162.4 (d, $J_{\text{C}-\text{F}}$ = 246.0 Hz), 162.8 (d, $J_{\text{C}-\text{F}}$ = 245.0 Hz), 167.1. HRMS (ESI-TOF). Calcd for $\text{C}_{25}\text{H}_{20}\text{F}_2\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 388.1513, Found 388.1517.



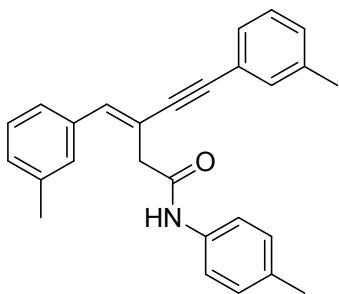
(E)-3-(3-chlorobenzylidene)-5-(3-chlorophenyl)-N-(p-tolyl)pent-4-ynamide 3l

White solid. mp: 130 °C. ^1H NMR (400 MHz, CDCl_3): δ = 2.30 (s, 3H), 3.50 (s, 2H), 7.09 (s, 1H), 7.12 (d, J = 6.0 Hz, 2H), 7.22-7.34 (m, 6H), 7.38 (d, J = 4.4 Hz, 2H), 7.41 (d, J = 4.4 Hz, 2H), 7.76 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 20.8, 41.0, 89.7, 91.6, 118.1, 120.2, 124.1, 126.8, 128.4, 128.8, 128.9, 129.5, 129.6, 129.7, 129.9, 131.4, 134.3, 134.3, 134.6, 135.0, 136.9, 138.9, 167.1. HRMS (ESI-TOF). Calcd for $\text{C}_{25}\text{H}_{20}\text{Cl}_2\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 420.0922, Found 420.0918.



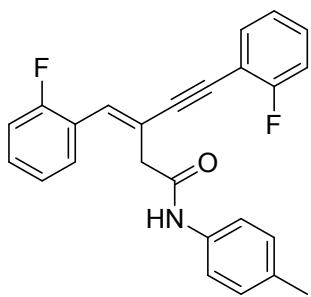
(E)-3-(3-bromobenzylidene)-5-(3-bromophenyl)-N-(p-tolyl)pent-4-ynamide 3m

White solid. mp: 112 °C. ^1H NMR (400 MHz, CDCl_3): δ = 2.29 (s, 3H), 3.49 (s, 2H), 7.09-7.23 (m, 5H), 7.34-7.46 (m, 6H), 7.52 (m, 1H), 7.57 (m, 1H), 7.76 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 20.8, 41.0, 89.6, 91.7, 118.1, 120.2, 122.2, 122.7, 124.4, 127.3, 129.5, 129.8, 130.1, 131.3, 131.7, 131.8, 134.3, 135.0, 137.2, 138.8, 167.1. HRMS (ESI-TOF). Calcd for $\text{C}_{25}\text{H}_{20}\text{Br}_2\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 509.9891, Found 509.9896.



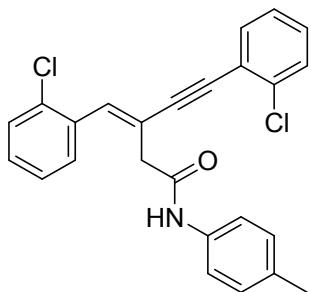
(E)-3-(3-methylbenzylidene)-5-(m-tolyl)-N-(p-tolyl)pent-4-ynamide 3n

White solid. mp: 128-129 °C. ^1H NMR (400 MHz, CDCl_3): δ = 2.30 (s, 3H), 2.32 (s, 3H), 2.36 (s, 3H), 3.56 (s, 2H), 7.09-7.15 (m, 4H), 7.19-7.24 (m, 4H), 7.26-7.29 (m, 3H), 7.40 (d, J = 8.4 Hz, 2H), 7.80 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 20.8, 21.2, 21.4, 41.4, 90.8, 91.0, 116.6, 120.1, 122.4, 125.9, 128.3, 128.6, 128.7, 129.1, 129.4, 129.5, 129.6, 132.2, 134.1, 135.2, 135.3, 138.1, 138.3, 140.1, 167.6. HRMS (ESI-TOF). Calcd for $\text{C}_{27}\text{H}_{26}\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 380.2014, Found 380.2022.



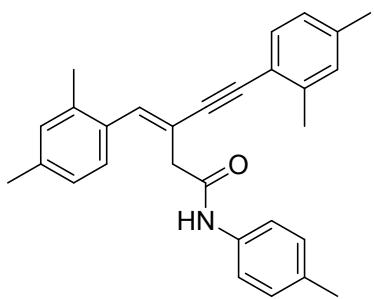
(E)-3-(2-fluorobenzylidene)-5-(2-fluorophenyl)-N-(p-tolyl)pent-4-ynamide 3o

White solid. mp: 120-122 °C. ^1H NMR (400 MHz, CDCl_3): δ = 2.30 (s, 3H), 3.49 (s, 2H), 7.07-7.14 (m, 5H), 7.19 (t, J = 7.6 Hz, 1H), 7.27 (s, 1H), 7.29-7.35 (m, 2H), 7.42-7.48 (m, 3H), 7.63 (t, J = 7.6 Hz, 1H), 7.84 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 20.8, 41.5, 84.5, 95.6 (d, $J_{\text{C}-\text{F}}$ = 3.0 Hz), 111.1 (d, $J_{\text{C}-\text{F}}$ = 16.0 Hz), 115.5 (d, $J_{\text{C}-\text{F}}$ = 22.0 Hz), 118.6, 120.2, 123.0 (d, $J_{\text{C}-\text{F}}$ = 14.0 Hz), 124.2 (d, $J_{\text{C}-\text{F}}$ = 4.0 Hz), 124.3 (d, $J_{\text{C}-\text{F}}$ = 3.0 Hz), 129.4, 130.3 (d, $J_{\text{C}-\text{F}}$ = 9.0 Hz), 130.5 (d, $J_{\text{C}-\text{F}}$ = 3.0 Hz), 130.5 (d, $J_{\text{C}-\text{F}}$ = 2.0 Hz), 133.0 (d, $J_{\text{C}-\text{F}}$ = 3.0 Hz), 133.3, 134.1, 135.2, 160.1 (d, $J_{\text{C}-\text{F}}$ = 247.0 Hz), 162.7 (d, $J_{\text{C}-\text{F}}$ = 250.0 Hz), 167.2. HRMS (ESI-TOF). Calcd for $\text{C}_{25}\text{H}_{20}\text{F}_2\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 388.1513, Found 388.1515.



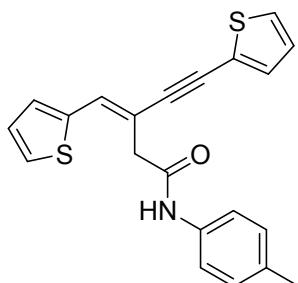
(E)-3-(2-chlorobenzylidene)-5-(2-chlorophenyl)-N-(p-tolyl)pent-4-ynamide 3p

White solid. mp: 122 °C. ^1H NMR (400 MHz, CDCl_3): δ = 2.30 (s, 3H), 3.46 (s, 2H), 7.11 (d, J = 8.0 Hz, 2H), 7.22-7.32 (m, 4H), 7.35 (s, 1H), 7.42 (d, J = 8.0 Hz, 4H), 7.53 (d, J = 6.4 Hz, 1H), 7.64 (d, J = 6.8 Hz, 1H), 7.85 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 20.8, 41.2, 88.2, 95.4, 118.4, 120.3, 122.4, 126.7, 127.0, 129.3, 129.4, 129.6, 129.7, 129.8, 130.8, 133.3, 133.4, 133.8, 134.2, 135.1, 135.9, 137.6, 167.1. HRMS (ESI-TOF). Calcd for $\text{C}_{25}\text{H}_{20}\text{Cl}_2\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 420.0922, Found 420.0922.



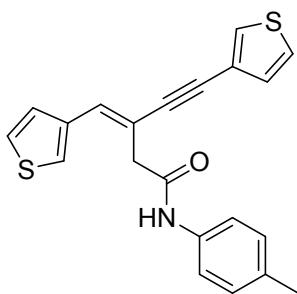
(E)-3-(2,4-dimethylbenzylidene)-5-(2,4-dimethylphenyl)-N-(p-tolyl)pent-4-ynamide 3q

White solid. mp: 142-144 °C. ^1H NMR (400 MHz, CDCl_3): δ = 2.30 (s, 6H), 2.32 (s, 6H), 2.40 (s, 3H), 3.45 (s, 2H), 6.97 (d, J = 7.6 Hz, 1H), 7.03 (d, J = 6.0 Hz, 3H), 7.10 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 8.4 Hz, 2H), 7.72 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 20.0, 20.7, 20.8, 21.2, 21.4, 41.3, 89.9, 93.9, 117.1, 119.3, 120.0, 126.5, 126.7, 128.7, 129.5, 130.4, 131.1, 131.6, 131.8, 134.0, 135.3, 136.5, 138.3, 138.6, 138.8, 140.1, 167.7. HRMS (ESI-TOF). Calcd for $\text{C}_{29}\text{H}_{30}\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 408.2327, Found 408.2326.



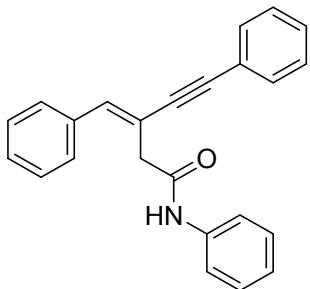
(E)-5-(thiophen-2-yl)-3-(thiophen-2-ylmethylene)-N-(p-tolyl)pent-4-ynamide 3r

White solid. mp: 139-140 °C. ^1H NMR (400 MHz, CDCl_3): δ = 2.28 (s, 3H), 3.70 (s, 2H), 6.98 (dd, J_1 = 4.0 Hz, J_2 = 4.8 Hz, 1H), 7.05-7.09 (m, 3H), 7.22 (d, J = 3.2 Hz, 2H), 7.28 (d, J = 4.4 Hz, 2H), 7.37 (d, J = 7.6 Hz, 3H), 7.69 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 20.8, 41.8, 84.6, 95.2, 113.7, 120.3, 122.7, 127.2, 127.7, 127.8, 128.0, 129.4, 130.0, 132.3, 134.1, 135.1, 138.4, 166.6. HRMS (ESI-TOF). Calcd for $\text{C}_{21}\text{H}_{18}\text{NOS}_2$, $[\text{M}+\text{H}]^+$ m/z 364.0830, Found 364.0839.



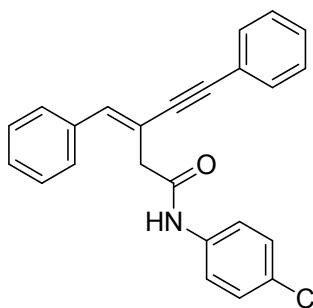
(*E*)-5-(thiophen-3-yl)-3-(thiophen-3-ylmethylene)-*N*-(*p*-tolyl)pent-4-ynamide 3s

White solid. mp: 146-148 °C. ^1H NMR (400 MHz, CDCl_3): δ = 2.29 (s, 3H), 3.58 (s, 2H), 7.05-7.13 (m, 4H), 7.18 (d, J = 4.4 Hz, 1H), 7.28 (dd, J_1 = 3.2 Hz, J_2 = 4.8 Hz, 1H), 7.32 (dd, J_1 = 3.2 Hz, J_2 = 4.8 Hz, 1H), 7.38 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 2.4 Hz, 1H), 7.50 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 20.8, 41.8, 85.9, 90.9, 115.2, 120.1, 121.6, 125.6, 125.7, 126.1, 128.3, 129.0, 129.4, 129.7, 133.8, 134.1, 135.1, 136.5, 167.4. HRMS (ESI-TOF). Calcd for $\text{C}_{21}\text{H}_{18}\text{NOS}_2$, $[\text{M}+\text{H}]^+$ m/z 364.0830, Found 364.0837.



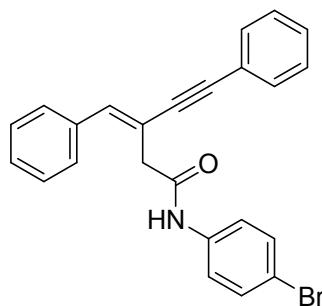
(*E*)-3-benzylidene-*N*,5-diphenylpent-4-ynamide 4b

White solid. mp: 146-148 °C. ^1H NMR (400 MHz, CDCl_3): δ = 3.57 (s, 2H), 7.11 (t, J = 7.2 Hz, 1H), 7.24 (s, 1H), 7.29-7.35 (m, 6H), 7.38-7.41 (m, 4H), 7.48 (t, J = 3.2 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.86 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 41.4, 90.9, 91.0, 116.6, 120.0, 122.5, 124.5, 128.3, 128.5, 128.7, 128.9, 129.0, 131.6, 135.2, 137.7, 140.2, 167.6. HRMS (ESI-TOF). Calcd for $\text{C}_{24}\text{H}_{20}\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 338.1545, Found 338.1541.



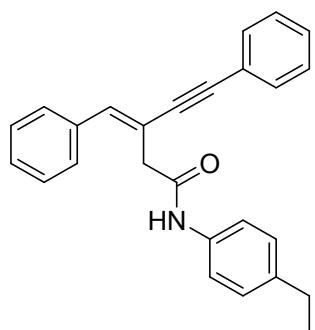
(E)-3-benzylidene-N-(4-chlorophenyl)-5-phenylpent-4-ynamide 4c

White solid. mp: 170 °C. ¹H NMR (400 MHz, CDCl₃): δ = 3.56 (s, 2H), 7.24 (d, J = 8.8 Hz, 3H), 7.33-7.39 (m, 8H), 7.45-7.47 (m, 4H), 7.93 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 41.3, 90.9, 91.0, 116.4, 121.2, 122.4, 128.4, 128.5, 128.7, 128.7, 128.8, 129.0, 129.4, 131.6, 135.2, 136.3, 140.3, 167.7. HRMS (ESI-TOF). Calcd for C₂₄H₁₉ClNO, [M+H]⁺ m/z 372.1155, Found 372.1157.



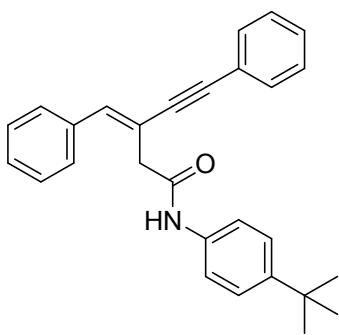
(E)-3-benzylidene-N-(4-bromophenyl)-5-phenylpent-4-ynamide 4d

White solid. mp: 1704-175 °C. ¹H NMR (400 MHz, CDCl₃): δ = 3.57 (s, 2H), 7.24 (s, 1H), 7.32-7.36 (m, 4H), 7.39-7.42 (m, 8H), 7.46-7.48 (m, 2H), 7.84 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 41.4, 90.9, 91.0, 116.3, 117.1, 121.5, 122.4, 128.4, 128.5, 128.8, 128.8, 128.9, 131.6, 132.0, 135.2, 136.8, 140.4, 167.7. HRMS (ESI-TOF). Calcd for C₂₄H₁₉BrNO, [M+H]⁺ m/z 416.0650, Found 416.0647.



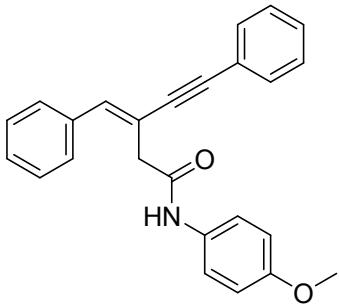
(E)-3-benzylidene-N-(4-ethylphenyl)-5-phenylpent-4-ynamide 4e

White solid. mp: 132-133 °C. ^1H NMR (400 MHz, CDCl_3): δ = 1.20 (t, J = 7.6 Hz, 3H), 2.60 (q, J = 7.6 Hz, 1H), 3.56 (s, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.23 (s, 1H), 7.29-7.34 (m, 4H), 7.36-7.44 (m, 6H), 7.46-7.48 (m, 2H), 7.83 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 15.6, 28.3, 41.3, 90.8, 91.1, 116.7, 120.2, 122.5, 128.3, 128.4, 128.6, 128.7, 128.9, 131.6, 135.3, 135.3, 140.1, 140.6, 167.5. HRMS (ESI-TOF). Calcd for $\text{C}_{26}\text{H}_{24}\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 366.1858, Found 366.1861.



(E)-3-benzylidene-N-(4-(*tert*-butyl)phenyl)-5-phenylpent-4-ynamide 4f

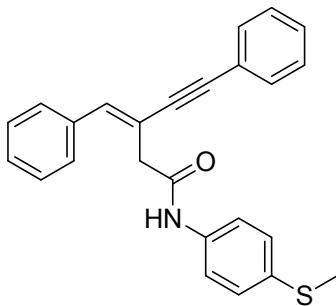
White solid. mp: 140 °C. ^1H NMR (400 MHz, CDCl_3): δ = 1.29 (s, 9H), 3.56 (s, 2H), 7.23 (s, 1H), 7.29-7.34 (m, 6H), 7.36-7.49 (m, 8H), 7.83 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 31.3, 34.3, 41.4, 90.8, 91.1, 116.8, 119.9, 122.5, 125.8, 128.3, 128.4, 128.6, 128.7, 128.9, 131.6, 135.1, 135.3, 140.1, 147.5, 167.5. HRMS (ESI-TOF). Calcd for $\text{C}_{28}\text{H}_{28}\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 394.2171, Found 394.2176.



(E)-3-benzylidene-N-(4-methoxyphenyl)-5-phenylpent-4-ynamide 4g

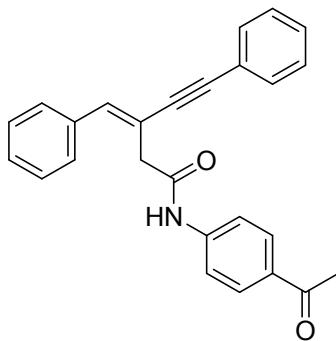
White solid. mp: 160-161 °C. ^1H NMR (400 MHz, CDCl_3): δ = 3.57 (s, 2H), 3.78 (s, 3H), 6.85 (d, J = 8.4 Hz, 2H), 7.24 (s, 1H), 7.34-7.49 (m, 12H), 7.71 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 41.3, 55.5, 90.9, 91.1, 114.2, 116.8, 122.0, 122.6, 128.4, 128.5, 128.7, 128.7, 128.9, 130.8, 131.6,

135.3, 140.2, 156.6, 167.5. HRMS (ESI-TOF). Calcd for C₂₅H₂₂NO₂, [M+H]⁺ *m/z* 368.1651, Found 368.1653.



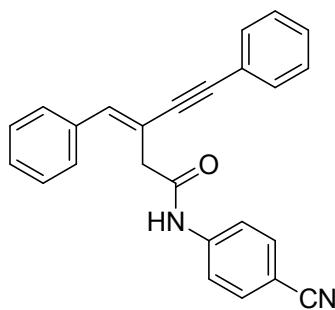
(E)-3-benzylidene-N-(4-(methylthio)phenyl)-5-phenylpent-4-ynamide 4h

White solid. mp: 162-163 °C. ¹H NMR (400 MHz, CDCl₃): δ = 2.45 (s, 3H), 3.56 (s, 2H), 7.21-7.25 (m, 3H), 7.32-7.48 (m, 12H), 7.80 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 16.7, 41.4, 91.0, 91.0, 116.5, 120.6, 122.5, 128.0, 128.4, 128.5, 128.7, 128.9, 131.6, 133.9, 135.2, 135.4, 140.3, 167.6. HRMS (ESI-TOF). Calcd for C₂₅H₂₂NOS, [M+H]⁺ *m/z* 384.1422, Found 384.1425.



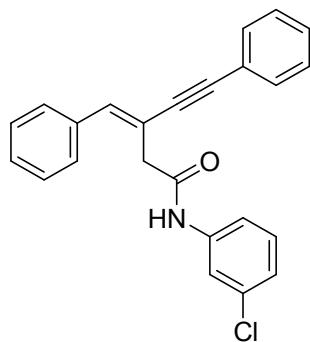
(E)-N-(4-acetylphenyl)-3-benzylidene-5-phenylpent-4-ynamide 4i

White solid. mp: 182-183 °C. ¹H NMR (400 MHz, CDCl₃): δ = 2.57 (s, 3H), 3.60 (s, 2H), 7.26 (s, 1H), 7.34-7.49 (m, 10H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.93 (d, *J* = 7.6 Hz, 2H), 8.02 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 26.4, 41.5, 90.9, 91.2, 116.2, 119.0, 122.3, 128.5, 128.6, 128.8, 128.9, 129.8, 131.6, 133.1, 135.1, 140.5, 142.0, 167.9, 196.8. HRMS (ESI-TOF). Calcd for C₂₆H₂₂NO₂, [M+H]⁺ *m/z* 380.1651, Found 380.1655.



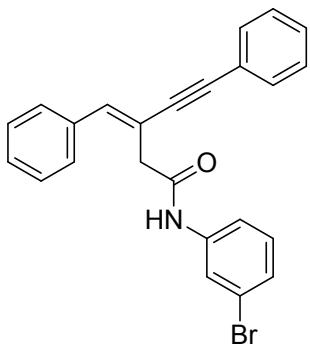
(E)-3-benzylidene-N-(4-cyanophenyl)-5-phenylpent-4-ynamide 4j

White solid. mp: 177-178 °C. ^1H NMR (400 MHz, CDCl_3): δ = 3.60 (s, 2H), 7.25 (s, 1H), 7.31-7.47 (m, 10H), 7.58 (d, J = 8.4 Hz, 2H), 7.65 (d, J = 8.0 Hz, 2H), 8.08 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 41.4, 90.7, 91.2, 107.3, 115.9, 118.7, 119.6, 122.2, 128.5, 128.6, 128.8, 128.8, 128.9, 131.6, 133.3, 135.1, 140.6, 141.7, 168.1. HRMS (ESI-TOF). Calcd for $\text{C}_{25}\text{H}_{19}\text{N}_2\text{O}$, $[\text{M}+\text{H}]^+$ m/z 363.1497, Found 363.1504.



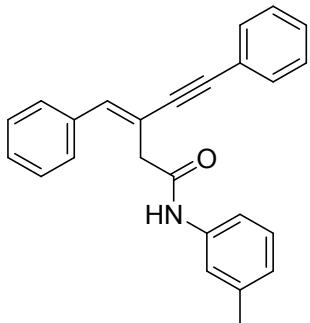
(E)-3-benzylidene-N-(3-chlorophenyl)-5-phenylpent-4-ynamide 4k

White solid. mp: 140 °C. ^1H NMR (400 MHz, CDCl_3): δ = 3.57 (s, 2H), 7.08 (d, J = 7.6 Hz, 1H), 7.19-7.24 (m, 2H), 7.32-7.39 (m, 9H), 7.47 (t, J = 3.6 Hz, 2H), 7.66 (s, 1H), 7.85 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 41.4, 90.9, 91.1, 116.4, 117.9, 120.1, 122.4, 124.5, 128.4, 128.5, 128.8, 128.8, 128.8, 130.0, 131.6, 134.7, 135.2, 138.9, 140.4, 167.7. HRMS (ESI-TOF). Calcd for $\text{C}_{24}\text{H}_{19}\text{ClNO}$, $[\text{M}+\text{H}]^+$ m/z 372.1155, Found 372.1145.



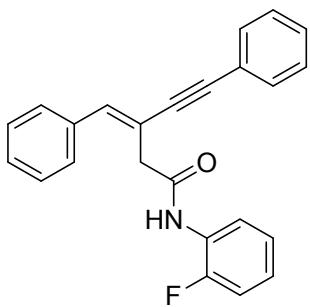
(E)-3-benzylidene-N-(3-bromophenyl)pent-4-ynamide 4l

White solid. mp: 110-112 °C. ¹H NMR (400 MHz, CDCl₃): δ = 3.55 (s, 2H), 7.11 (t, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 9.6 Hz, 2H), 7.29-7.40 (m, 9H), 7.44-7.46 (m, 2H), 7.80 (s, 1H), 7.98 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 41.1, 90.8, 90.9, 116.5, 118.4, 122.4, 122.5, 122.9, 127.3, 128.3, 128.4, 128.6, 128.7, 130.1, 131.5, 135.2, 139.0, 140.1, 168.0. HRMS (ESI-TOF). Calcd for C₂₄H₁₉BrNO, [M+H]⁺ *m/z* 416.0650, Found 416.0646.



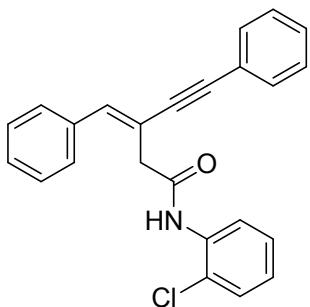
(E)-3-benzylidene-5-phenyl-N-(*m*-tolyl)pent-4-ynamide 4m

White solid. mp: 106-108 °C. ¹H NMR (400 MHz, CDCl₃): δ = 2.30 (s, 3H), 3.55 (s, 2H), 6.91 (d, *J* = 7.2 Hz, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.23 (s, 1H), 7.28-7.33 (m, 5H), 7.36-7.40 (m, 5H), 7.47 (d, *J* = 3.2 Hz, 2H), 7.83 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 21.4, 41.4, 90.9, 91.1, 116.7, 117.1, 120.7, 122.5, 125.3, 128.3, 128.4, 128.6, 128.7, 128.8, 128.9, 131.6, 135.3, 137.7, 138.9, 140.1, 167.6. HRMS (ESI-TOF). Calcd for C₂₅H₂₂NO, [M+H]⁺ *m/z* 352.1701, Found 352.1710.



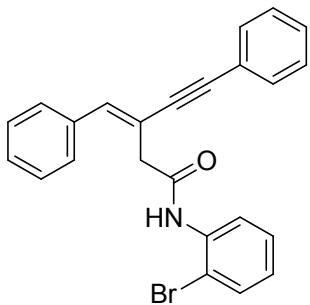
(E)-3-benzylidene-N-(2-fluorophenyl)-5-phenylpent-4-ynamide 4n

White solid. mp: 132-133 °C. ^1H NMR (400 MHz, CDCl_3): δ = 3.60 (s, 2H), 7.04-7.09 (m, 2H), 7.12-7.16 (m, 1H), 7.31-7.35 (m, 4H), 7.39-7.44 (m, 4H), 7.49-7.51 (m, 2H), 8.14 (s, 1H), 8.38 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 41.6, 90.7, 91.0, 114.8 (d, $J_{\text{C}-\text{F}} = 19.0$ Hz), 116.4, 121.8, 122.5, 124.4 (d, $J_{\text{C}-\text{F}} = 8.0$ Hz), 124.6 (d, $J_{\text{C}-\text{F}} = 4.0$ Hz), 126.4 (d, $J_{\text{C}-\text{F}} = 10.0$ Hz), 128.4, 128.5 (d, $J_{\text{C}-\text{F}} = 31.0$ Hz), 128.7, 128.9, 131.7, 135.3, 140.3, 152.5 (d, $J_{\text{C}-\text{F}} = 242.0$ Hz), 167.7. HRMS (ESI-TOF). Calcd for $\text{C}_{24}\text{H}_{19}\text{FNO}$, $[\text{M}+\text{H}]^+$ m/z 356.1451, Found 356.1461.



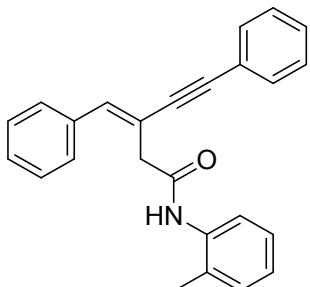
(E)-3-benzylidene-N-(2-chlorophenyl)-5-phenylpent-4-ynamide 4o

White solid. mp: 140-141 °C. ^1H NMR (400 MHz, CDCl_3): δ = 3.63 (s, 2H), 7.01-7.05 (m, 1H), 7.25-7.34 (m, 7H), 7.38-7.42 (m, 4H), 7.48-7.50 (m, 2H), 8.41 (s, 1H), 8.45 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 41.8, 91.0, 91.0, 116.4, 121.7, 122.7, 123.0, 124.8, 127.7, 128.4, 128.6, 128.7, 128.9, 129.0, 131.7, 134.7, 135.3, 140.4, 167.8. HRMS (ESI-TOF). Calcd for $\text{C}_{24}\text{H}_{19}\text{ClNO}$, $[\text{M}+\text{H}]^+$ m/z 372.1155, Found 372.1157.



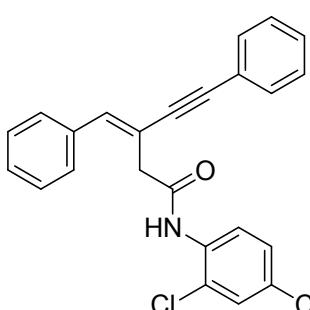
(E)-3-benzylidene-N-(2-bromophenyl)-5-phenylpent-4-ynamide 4p

White solid. mp: 140-141 °C. ^1H NMR (400 MHz, CDCl_3): δ = 3.63 (s, 2H), 6.95-6.99 (m, 1H), 7.29-7.34 (m, 6H), 7.38-7.42 (m, 4H), 7.48-7.51 (m, 3H), 8.36 (s, 1H), 8.43 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 41.9, 91.0, 91.1, 113.6, 116.4, 122.0, 122.7, 125.3, 128.3, 128.4, 128.6, 128.7, 128.9, 131.7, 132.3, 135.3, 135.8, 140.5, 167.8. HRMS (ESI-TOF). Calcd for $\text{C}_{24}\text{H}_{19}\text{BrNO}$, $[\text{M}+\text{H}]^+$ m/z 416.0650, Found 416.0644.



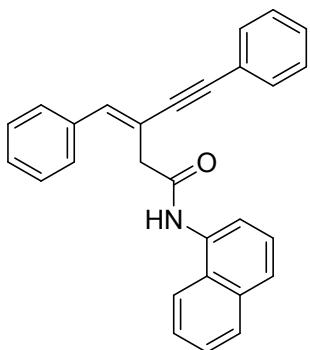
(E)-3-benzylidene-5-phenyl-N-(o-tolyl)pent-4-ynamide 4q

White solid. mp: 170-171 °C. ^1H NMR (400 MHz, CDCl_3): δ = 2.21 (s, 3H), 3.63 (s, 2H), 7.06 (t, J = 7.6 Hz, 1H), 7.14 (d, J = 7.2 Hz, 1H), 7.20-7.25 (m, 2H), 7.34-7.35 (m, 4H), 7.38-7.48 (m, 6H), 7.77 (s, 1H), 7.93 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 17.6, 41.5, 90.8, 91.3, 116.7, 122.5, 122.8, 125.2, 126.8, 128.4, 128.5, 128.7, 128.9, 128.9, 130.4, 131.6, 135.2, 135.7, 140.3, 167.6. HRMS (ESI-TOF). Calcd for $\text{C}_{25}\text{H}_{22}\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 352.1701, Found 352.1698.



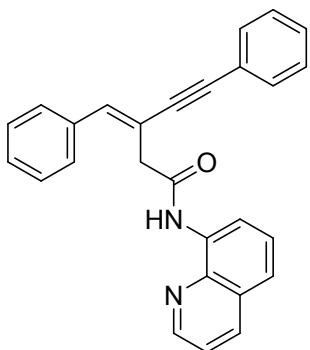
(E)-3-benzylidene-N-(2,4-dichlorophenyl)-5-phenylpent-4-ynamide 4r

White solid. mp: 130-131 °C. ^1H NMR (400 MHz, CDCl_3): δ = 3.62 (s, 2H), 7.25-7.41 (m, 11H), 7.48 (d, J = 3.6 Hz, 2H), 8.37 (s, 1H), 8.43 (d, J = 9.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 41.8, 90.9, 91.1, 116.2, 122.4, 122.6, 123.5, 127.8, 128.4, 128.4, 128.7, 128.8, 128.9, 129.2, 131.7, 132.5, 133.5, 135.2, 140.5, 167.8. HRMS (ESI-TOF). Calcd for $\text{C}_{24}\text{H}_{18}\text{Cl}_2\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 406.0765, Found 406.0771.



(E)-3-benzylidene-N-(naphthalen-1-yl)-5-phenylpent-4-ynamide 4s

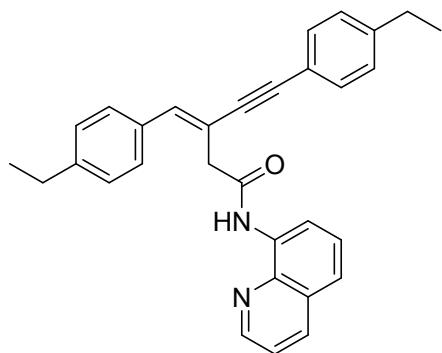
White solid. mp: 160 °C. ^1H NMR (400 MHz, CDCl_3): δ = 3.73 (s, 2H), 7.19 (t, J = 7.6 Hz, 1H), 7.33-7.49 (m, 11H), 7.50 (d, J = 3.6 Hz, 2H), 7.68 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 7.2 Hz, 1H), 8.36 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 41.6, 91.2, 91.5, 116.6, 120.6, 122.5, 125.7, 125.9, 126.3, 127.0, 128.5, 128.5, 128.7, 128.8, 128.8, 129.0, 131.8, 132.2, 134.1, 135.2, 140.6, 168.1. HRMS (ESI-TOF). Calcd for $\text{C}_{28}\text{H}_{22}\text{NO}$, $[\text{M}+\text{H}]^+$ m/z 388.1701, Found 388.1693.



(E)-3-benzylidene-5-phenyl-N-(quinolin-8-yl)pent-4-ynamide 4t

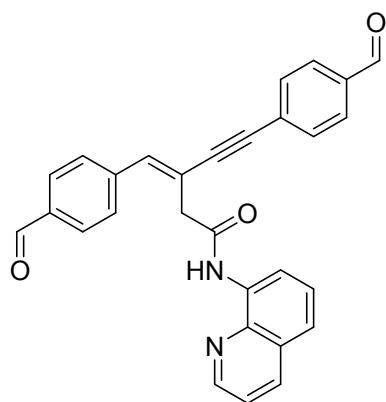
White solid. mp: 88-90 °C. ^1H NMR (400 MHz, CDCl_3): δ = 3.72 (s, 2H), 7.29-7.37 (m, 6H), 7.41 (t, J = 7.6 Hz, 2H), 7.49-7.56 (m, 6H), 8.10-8.12 (m, 1H), 8.46-8.47 (m, 1H), 8.86 (d, J = 7.2 Hz,

1H), 10.48 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 42.1, 90.7, 91.3, 116.6, 117.0, 121.4, 121.6, 123.0, 127.2, 127.8, 128.0, 128.2, 128.3, 128.5, 128.9, 131.7, 134.6, 135.5, 136.0, 138.5, 139.7, 148.1, 168.2. HRMS (ESI-TOF). Calcd for $\text{C}_{27}\text{H}_{21}\text{N}_2\text{O}$, $[\text{M}+\text{H}]^+$ m/z 389.1654, Found 389.1646.



(E)-3-(4-ethylbenzylidene)-5-(4-ethylphenyl)-N-(quinolin-8-yl)pent-4-ynamide 4u

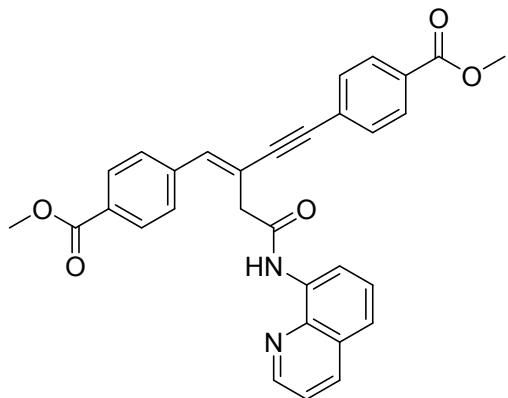
White solid. mp: 170-171 °C. ^1H NMR (400 MHz, CDCl_3): δ = 1.21-1.26 (m, 6H), 2.61-2.68 (m, 4H), 3.72 (s, 2H), 7.12 (d, J = 8.0 Hz, 2H), 7.22-7.25 (m, 3H), 7.34-7.37 (m, 1H), 7.41-7.45 (m, 4H), 7.48-7.56 (m, 2H), 8.10-8.12 (m, 1H), 8.47 (dd, J_1 = 1.2 Hz, J_2 = 4.4 Hz, 1H), 8.85 (d, J = 7.6 Hz, 1H), 10.49 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 15.4, 15.4, 28.7, 28.8, 42.2, 90.7, 90.9, 116.4, 116.7, 120.4, 121.5, 121.6, 127.3, 127.8, 127.9, 128.1, 129.0, 131.8, 133.2, 134.7, 136.1, 138.7, 139.5, 144.3, 144.7, 148.2, 168.5. HRMS (ESI-TOF). Calcd for $\text{C}_{31}\text{H}_{29}\text{N}_2\text{O}$, $[\text{M}+\text{H}]^+$ m/z 445.2280, Found 445.2283.



(E)-3-(4-formylbenzylidene)-5-(4-formylphenyl)-N-(quinolin-8-yl)pent-4-ynamide 4v

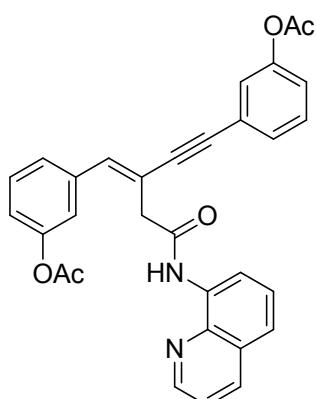
White solid. mp: 173-174 °C. ^1H NMR (400 MHz, CDCl_3): δ = 3.73 (s, 2H), 7.06 (s, 1H), 7.42 (dd, J_1 = 4.0 Hz, J_2 = 8.0 Hz, 1H), 7.52-7.61 (m, 4H), 7.82 (d, J = 7.2 Hz, 2H), 7.93 (d, J = 7.6 Hz, 2H), 8.06 (d, J = 8.0 Hz, 2H), 8.17 (d, J = 8.0 Hz, 1H), 8.58 (d, J = 4.0 Hz, 1H), 8.81 (d, J = 7.2 Hz,

1H), 10.01 (s, 1H), 10.03 (s, 1H), 10.36 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 48.4, 91.9, 96.8, 116.9, 117.9, 121.6, 121.9, 127.5, 128.0, 128.6, 129.2, 129.5, 129.7, 132.3, 134.2, 135.8, 135.9, 136.6, 138.2, 138.3, 141.7, 148.0, 167.4, 191.2, 191.6. HRMS (ESI-TOF). Calcd for $\text{C}_{29}\text{H}_{21}\text{N}_2\text{O}_3$, $[\text{M}+\text{H}]^+$ m/z 445.1552, Found 445.1561.



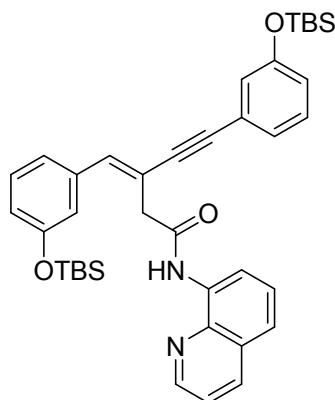
**(E)-dimethyl 4,4'-(2-(2-oxo-2-(quinolin-8-ylamino)ethyl)but-1-en-3-yne-1,4-diyl)dibenzoate
4w**

White solid. mp: 165-166 °C. ^1H NMR (400 MHz, CDCl_3): δ = 3.69 (s, 2H), 3.92 (s, 3H), 3.93 (s, 3H), 7.01 (s, 1H), 7.39 (dd, J_1 = 4.0 Hz, J_2 = 8.0 Hz, 1H), 7.49-7.56 (m, 4H), 7.97 (d, J = 8.4 Hz, 4H), 8.07 (d, J = 8.0 Hz, 2H), 8.13 (d, J = 8.4 Hz, 1H), 8.54 (d, J = 4.0 Hz, 1H), 8.81 (d, J = 7.2 Hz, 1H), 10.37 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 48.4, 52.1, 52.2, 91.1, 96.7, 116.7, 117.1, 121.6, 121.8, 127.2, 127.4, 127.9, 128.6, 129.5, 129.5, 129.7, 130.0, 131.6, 134.3, 136.4, 138.1, 138.4, 140.3, 148.0, 166.3, 166.7, 167.6. HRMS (ESI-TOF). Calcd for $\text{C}_{31}\text{H}_{25}\text{N}_2\text{O}_5$, $[\text{M}+\text{H}]^+$ m/z 505.1763, Found 505.1764.



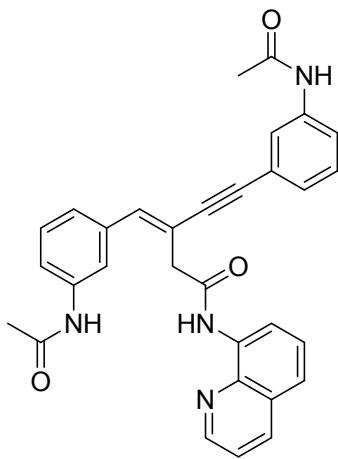
(E)-3-(3-acetoxybenzylidene)-5-(3-acetoxyphenyl)-N-(quinolin-8-yl)pent-4-ynamide 4x

Colorless oil. ^1H NMR (400 MHz, CDCl_3): $\delta = 2.26$ (s, 3H), 2.29 (s, 3H), 3.70 (s, 2H), 7.04 (d, $J = 5.2$ Hz, 2H), 7.22-7.55 (m, 10H), 8.11 (d, $J = 8.4$ Hz, 1H), 8.52 (d, $J = 4.4$ Hz, 1H), 8.83 (d, $J = 7.2$ Hz, 1H), 10.40 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = 21.0, 21.1, 41.9, 90.0, 91.7, 116.7, 117.9, 121.4, 121.5, 121.7, 122.0, 122.0, 124.3, 124.8, 126.4, 127.3, 127.9, 129.2, 129.2, 129.5, 134.5, 136.2, 136.9, 138.4, 138.9, 148.2, 150.4, 150.7, 167.8, 169.0, 169.3$. HRMS (ESI-TOF). Calcd for $\text{C}_{31}\text{H}_{25}\text{N}_2\text{O}_5$, $[\text{M}+\text{H}]^+$ m/z 505.1763, Found 505.1752.



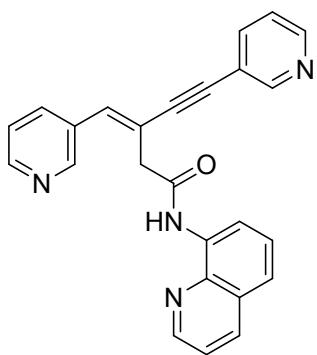
(E)-3-((tert-butyldimethylsilyl)oxy)benzylidene)-5-((tert-butyldimethylsilyl)oxy)phenyl)-*N*-(quinolin-8-yl)pent-4-ynamide 4

Colorless oil. ^1H NMR (400 MHz, CDCl_3): $\delta = 0.15$ (s, 6H), 0.18 (s, 6H), 0.95 (s, 18H), 3.73 (s, 2H), 6.79 (d, $J = 8.0$ Hz, 2H), 6.97 (s, 2H), 7.08-7.15 (m, 3H), 7.24-7.28 (m, 2H), 7.35 (dd, $J_1 = 4.0$ Hz, $J_2 = 8.0$ Hz, 1H), 7.47-7.55 (m, 2H), 8.10 (d, $J = 8.0$ Hz, 1H), 8.54 (d, $J = 4.0$ Hz, 1H), 8.85 (d, $J = 7.6$ Hz, 1H), 10.43 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): $\delta = -4.5, -4.5, 18.1, 18.1, 25.6, 42.0, 90.5, 91.0, 116.7, 117.2, 120.0, 120.5, 120.6, 121.5, 121.6, 122.1, 123.2, 124.1, 125.1, 127.3, 127.9, 129.2, 129.6, 134.6, 136.1, 136.9, 138.5, 139.7, 148.2, 155.4, 155.7, 168.1$. HRMS (ESI-TOF). Calcd for $\text{C}_{39}\text{H}_{49}\text{N}_2\text{O}_3\text{Si}_2$, $[\text{M}+\text{H}]^+$ m/z 649.3282, Found 649.3276.



(E)-3-(3-acetamidobenzylidene)-5-(3-acetamidophenyl)-N-(quinolin-8-yl)pent-4-ynamide 4z

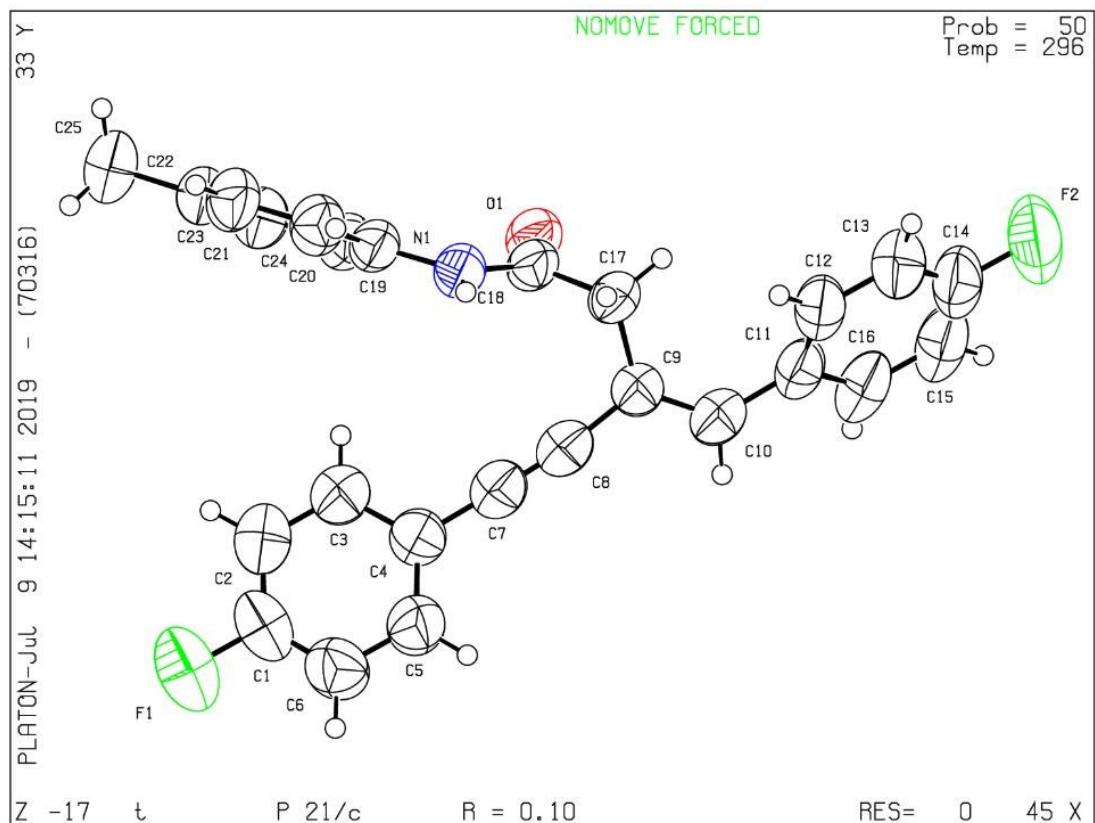
White solid. mp: 142-143 °C. ^1H NMR (400 MHz, CDCl_3): δ = 2.09 (s, 6H), 3.63 (s, 2H), 7.02 (s, 1H), 7.11-7.14 (m, 3H), 7.23-7.30 (m, 2H), 7.41-7.49 (m, 4H), 7.58 (d, J = 6.4 Hz, 1H), 7.65 (d, J = 7.6 Hz, 1H), 8.02 (d, J = 8.4 Hz, 1H), 8.25 (s, 1H), 8.42 (s, 1H), 8.46 (s, 1H), 8.72 (s, 1H), 10.34 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 24.4, 24.4, 41.8, 90.5, 91.2, 116.7, 117.2, 119.9, 120.0, 120.2, 121.6, 122.0, 122.8, 123.4, 124.6, 127.1, 127.4, 127.8, 128.8, 129.2, 134.2, 136.0, 136.2, 138.2, 138.3, 138.4, 139.4, 148.3, 168.5, 169.0, 169.1. HRMS (ESI-TOF). Calcd for $\text{C}_{31}\text{H}_{27}\text{N}_4\text{O}_3$, $[\text{M}+\text{H}]^+$ m/z 503.2083, Found 503.2094.



(E)-5-(pyridin-3-yl)-3-(pyridin-3-ylmethylene)-N-(quinolin-8-yl)pent-4-ynamide 4aa

White solid. mp: 172-173 °C. ^1H NMR (400 MHz, CDCl_3): δ = 3.70 (s, 2H), 7.22-7.27 (m, 2H), 7.39-7.42 (m, 2H), 7.51-7.57 (m, 2H), 7.76 (d, J = 7.2 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 8.14 (d, J = 8.4 Hz, 1H), 8.55-8.84 (m, 6H), 10.36 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ = 41.8, 88.0, 93.8, 116.7, 119.1, 119.9, 121.7, 121.9, 122.9, 123.6, 127.3, 127.9, 131.3, 134.3, 135.9, 136.3, 136.6, 138.4, 138.6, 148.2, 148.8, 149.0, 150.0, 152.4, 167.3. HRMS (ESI-TOF). Calcd for $\text{C}_{25}\text{H}_{19}\text{N}_4\text{O}$, $[\text{M}+\text{H}]^+$ m/z 391.1559, Found 391.1546.

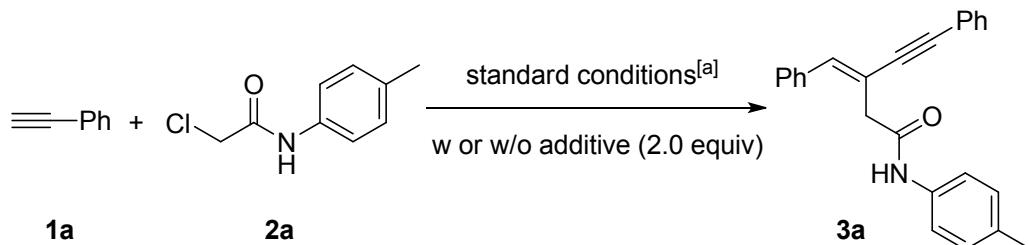
IV. Structure Analysis X-Ray Crystallography of 3b



Compound	3b
Empirical formula	C ₂₅ H ₁₉ F ₂ NO
Formula weight	387.41
Crystal system	Monoclinic
Space group	P 21/c
a (Å)	12.515(3)
b (Å)	8.4989(17)
c (Å)	19.132(4)
α (°)	90
β (°)	95.95(3)
γ (°)	90
V (Å ³)	2024.1(7)
Z	4
D/g cm ⁻³	1.271
μ/mm ⁻¹	0.090
F(000)	808.0
Parameters	263
R _{int}	0.0844
GOF	1.075
wR ₂ ^b (all data)	0.3009

V. Mechanistic Study

1. Radical Inhibition Experiments

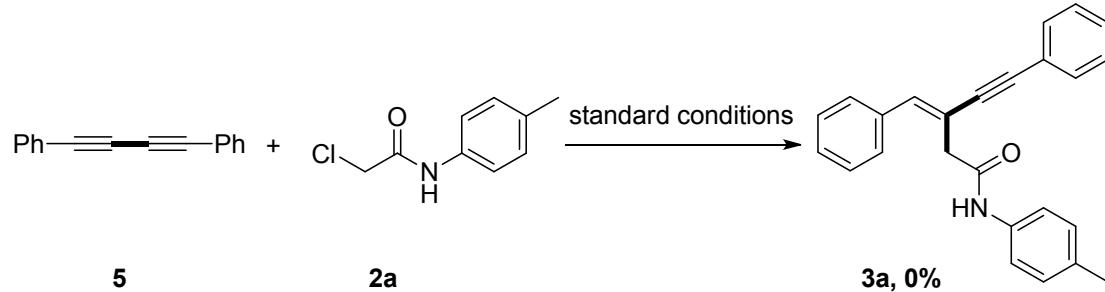


Additive	Yield ^[b] (%)
none	80
TEMPO (2 equiv)	70
BHT (2 equiv)	68

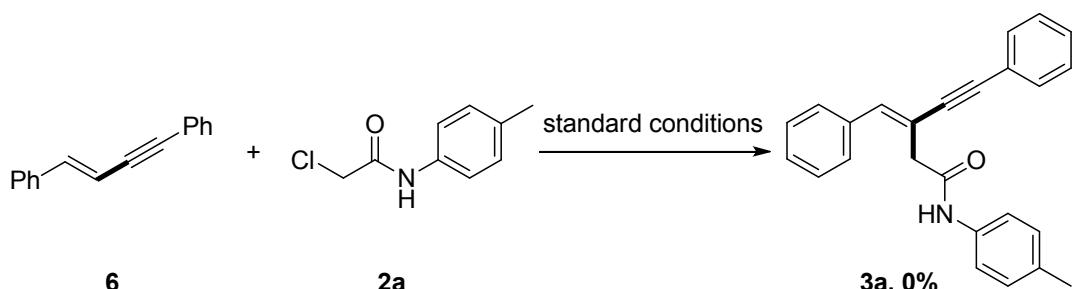
[a] Standard conditions: **1a** (0.96 mmol), **2a** (0.4 mmol), CuI (10 mol %), Phen (10 mol %) and K₂CO₃ (2.0 equiv) in dioxane (0.8 mL) under air atmosphere at 120 °C for 1 h. [b] Yield of the isolated product.

2. Control Experiment

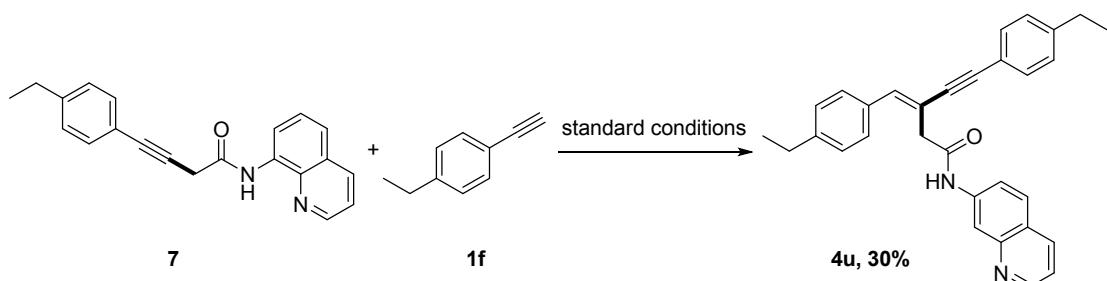
To probe the reaction mechanism, compounds **5–8** were prepared as possible reaction intermediate that may be constructed from any two coupling partners, and reacted with another coupling partner under the standard reaction conditions. We conducted the following experiments.



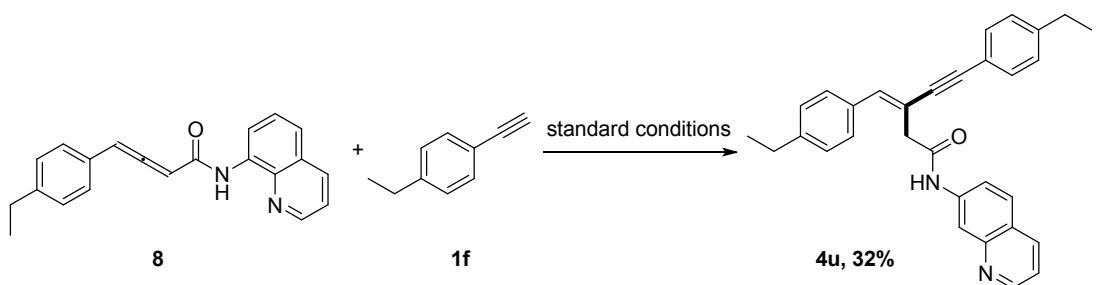
Following the general procedure II.2, to a solution of **5** (80.8 mg, 0.4 mmol) in 1,4-dioxane (0.8 mL) was added 2-chloro-*N*-(*p*-tolyl)acetamide **2a** (73.2 mg, 0.4 mmol), Phen (7.9 mg, 0.04 mmol), CuI (7.6 mg, 0.04 mmol), and K₂CO₃ (110.6 mg, 0.8 mmol) under air in screw-cap test tube. The reaction mixture was stirred at 120 °C for 1.0 h. After the reaction finished, **3a** was not detected in the reaction. This result suggested that **5** might not be the active intermediate.



Following the general procedure II.2, to a solution of **6** (81.6 mg, 0.4 mmol) in 1,4-dioxane (0.8 mL) was added 2-chloro-*N*-(*p*-tolyl)acetamide **2a** (73.2 mg, 0.4 mmol), Phen (7.9 mg, 0.04 mmol), CuI (7.6 mg, 0.04 mmol), and K₂CO₃ (110.6 mg, 0.8 mmol) under air in screw-cap test tube. The reaction mixture was stirred at 120 °C for 1.0 h. After the reaction finished, **3a** was not detected in the reaction. This result suggested that **6** might not be the active intermediate.



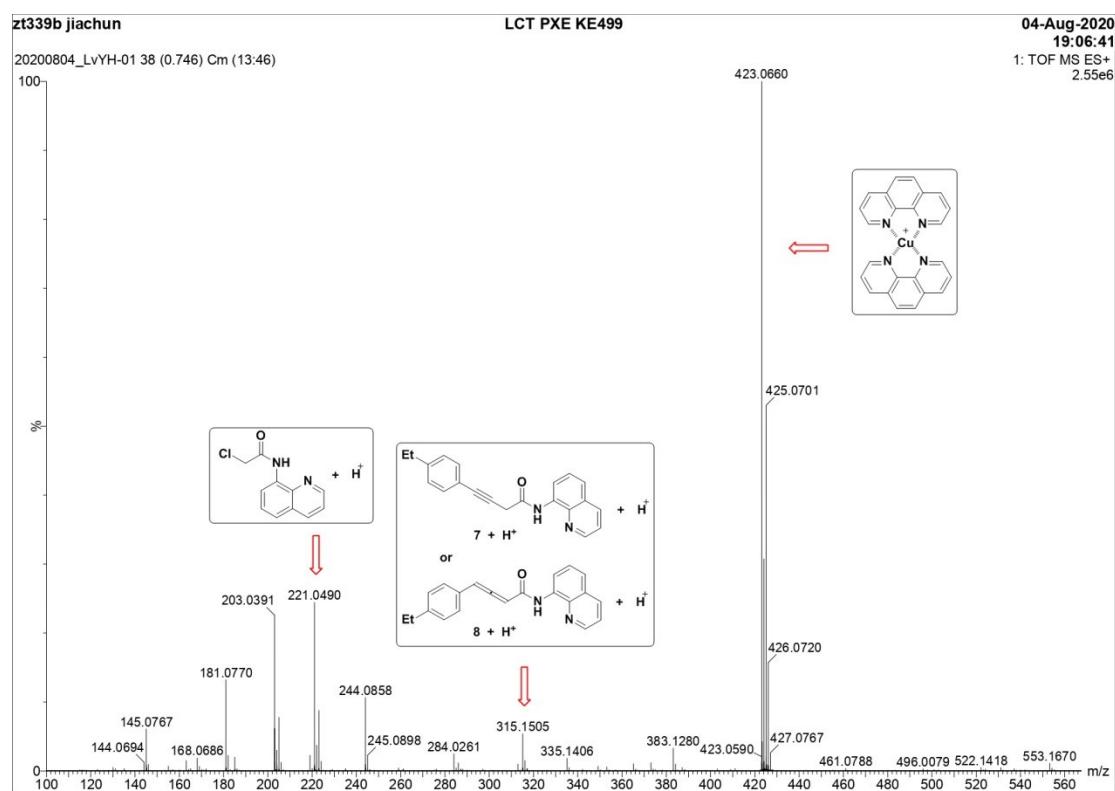
Following the general procedure II.2, to a solution of **7** (94.2 mg, 0.3 mmol) in 1,4-dioxane (0.6 mL) was added the 1-ethyl-4-ethynylbenzene **1f** (51 µL, 0.36 mmol), Phen (5.4 mg, 0.03 mmol), CuI (5.7 mg, 0.03 mmol), and K₂CO₃ (82.8 mg, 0.6 mmol) under air in screw-cap test tube. The reaction mixture was stirred at 120 °C for 1.0 h. After the reaction finished, the reaction mixture was cooled to room temperature and quenched by water. The mixture was extracted with EtOAc (3.0 mL×3), the combined organic phases were dried over anhydrous Na₂SO₄ and the solvent was evaporated under vacuum. The residue was purified by column chromatography to give the corresponding products **4u** (40.0 mg, 30%). This result also suggested that **7** might be the active intermediate.



Following the general procedure II.2, to a solution of **8** (94.2 mg, 0.3 mmol) in 1,4-dioxane (0.6 mL) was added the 1-ethyl-4-ethynylbenzene **1f** (51 μ L, 0.36 mmol), Phen (5.4 mg, 0.03 mmol), CuI (5.7 mg, 0.03 mmol), and K_2CO_3 (82.8 mg, 0.6 mmol) under air in screw-cap test tube. The reaction mixture was stirred at 120 °C for 1.0 h. After the reaction finished, the reaction mixture was cooled to room temperature and quenched by water. The mixture was extracted with EtOAc (3.0 mL \times 3), the combined organic phases were dried over anhydrous Na_2SO_4 and the solvent was evaporated under vacuum. The residue was purified by column chromatography to give the corresponding products **4u** (42.5 mg, 32%). This result also suggested that **8** might be the active intermediate.

Conclusions:

When **5** and **6** were used as starting material under the standard reaction conditions, **3a** was not detected in the reaction. By the treatment 1-ethyl-4-ethynylbenzene **1f** with **7** or **8** under the standard reaction conditions, the desired product **4u** was observed. These results suggested that **7** and **8** is a highly probable reaction intermediate that can be generated in situ from 1-ethyl-4-ethynylbenzene **1f** and 2-chloro-*N*-(quinolin-8-yl)acetamide **2t** via Sonogashira reactions. Furthermore, ESI/MS experiments were performed to gain evidence for the possible intermediates **7** and **8** in the proposed mechanism. A mixture of **1f** (0.96 mmol), **2t** (0.4 mmol), CuI (10 mol %), Phen (10 mol %) and K_2CO_3 (2.0 equiv) in dioxane (0.8 mL) was reacted at 90 °C for 10 minutes and 50 μ L of the mixture was used for the ESI analysis in CH₃OH. The ESI/MS analyses showed a peak at m/z 315.1505, which was identified as intermediates **7** and **8**.

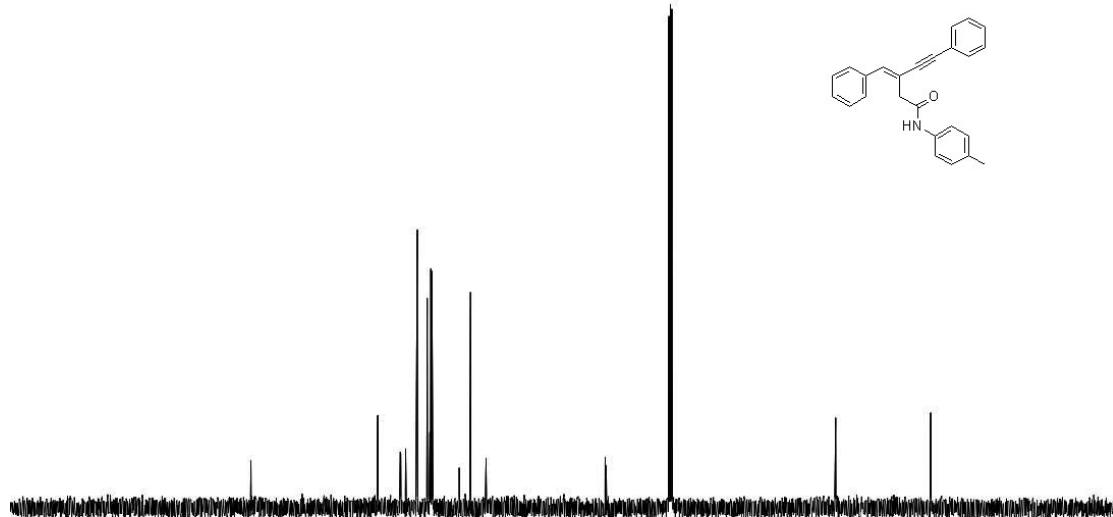
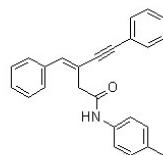
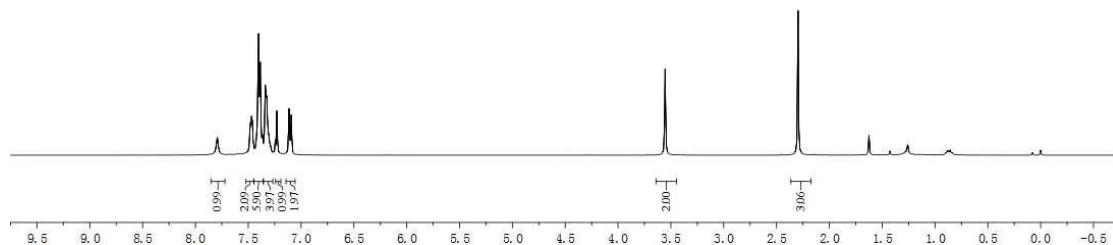
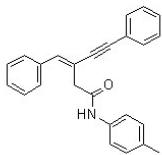


VI. References

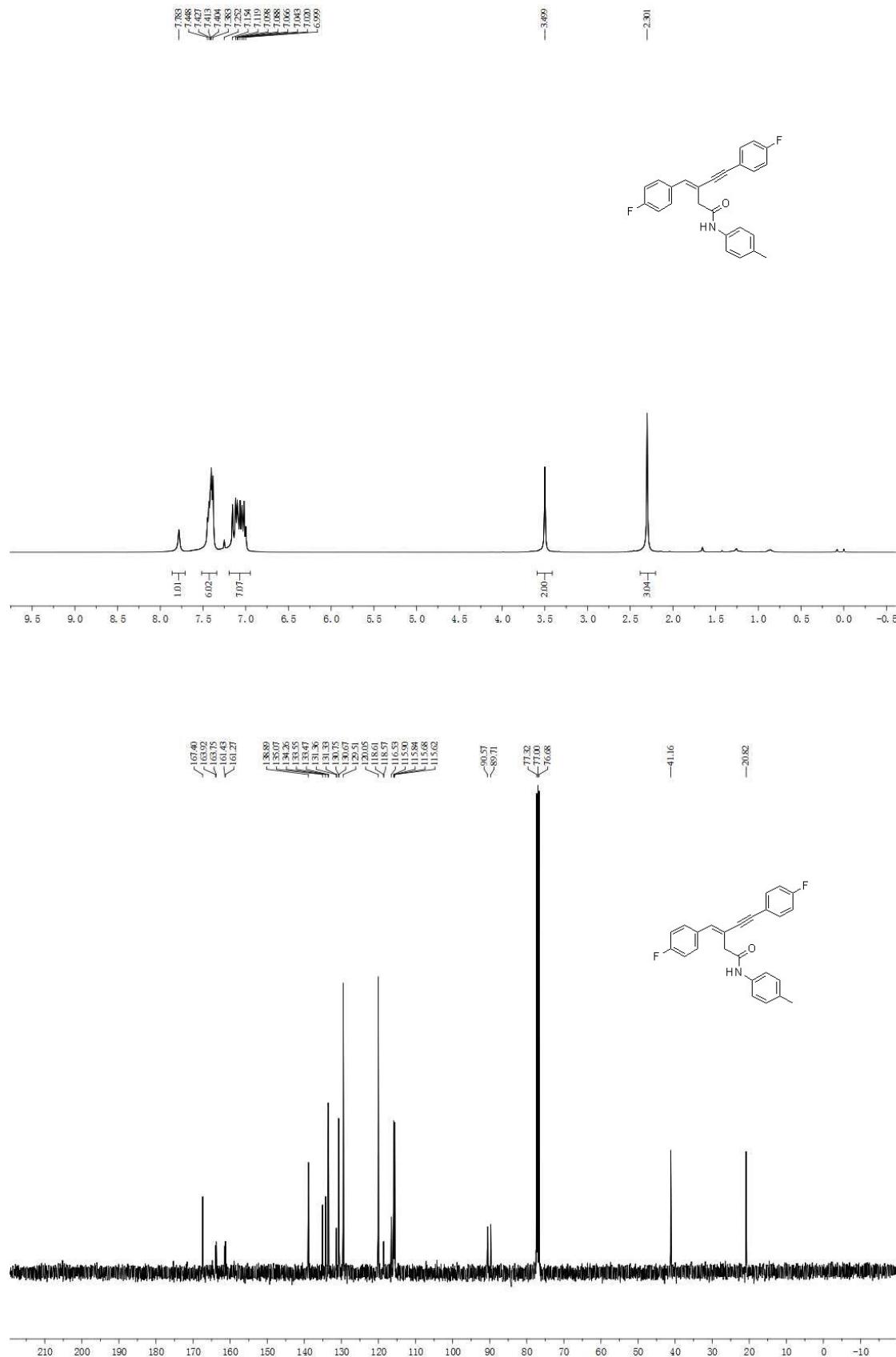
- [1] J.-H. Li, Y. Liang, Y.-X. Xie, *J. Org. Chem.* **2005**, *70*, 4393.
- [2] Y. Liu, J. Yang, W. Bao, *Eur. J. Org. Chem.* **2009**, 5317.
- [3] J. Li, D. Ding, L. Liu, J. Sun, *RSC Adv.* **2013**, *3*, 21260.
- [4] Y. Lv, W. Pu, X. Zhu, T. Zhao, F. Lin, *Adv. Synth. Catal.* **2018**, *360*, 1397.

VII. ^1H and ^{13}C NMR Spectra of Compounds 3 and 4

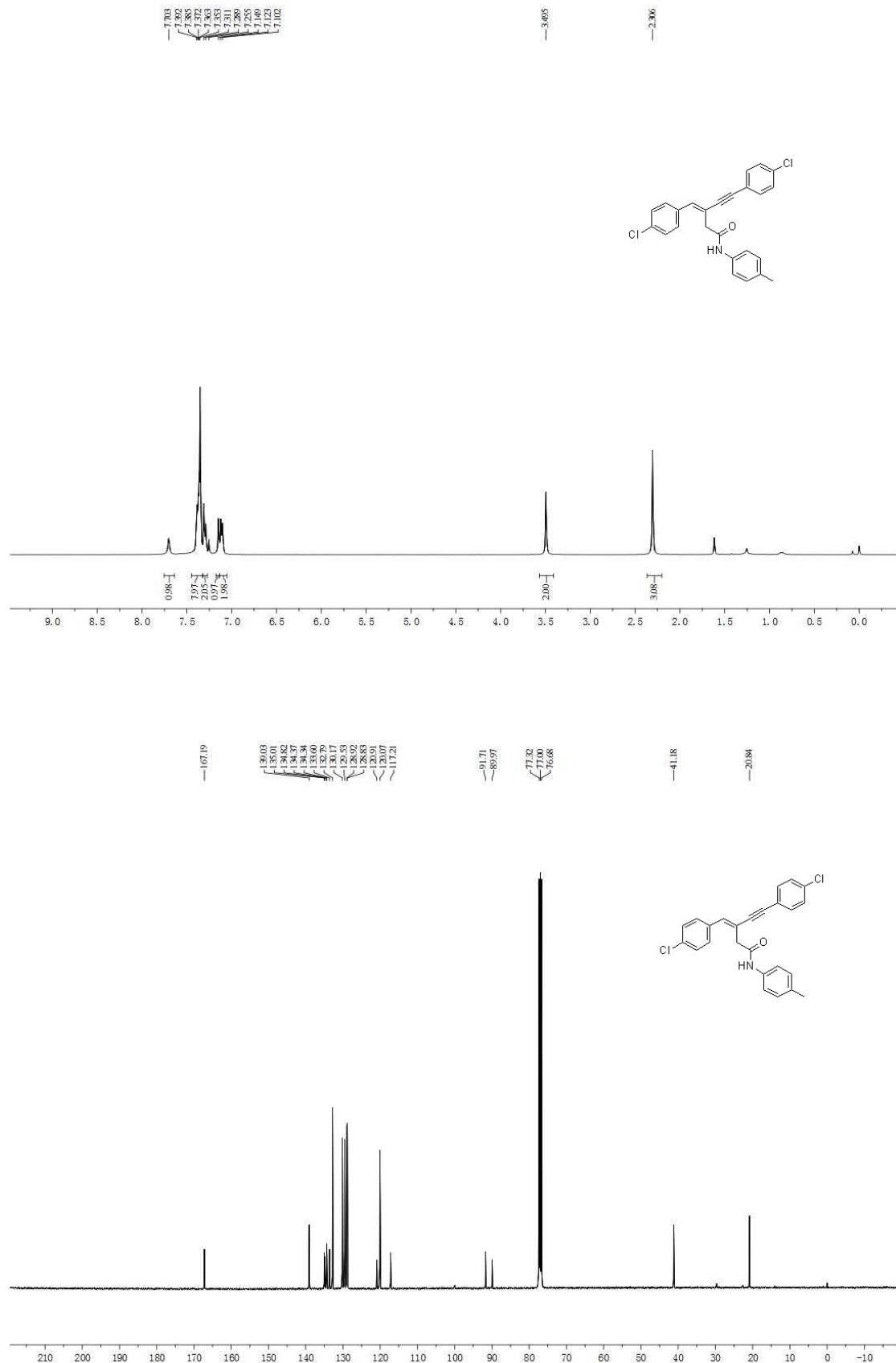
Product 3a



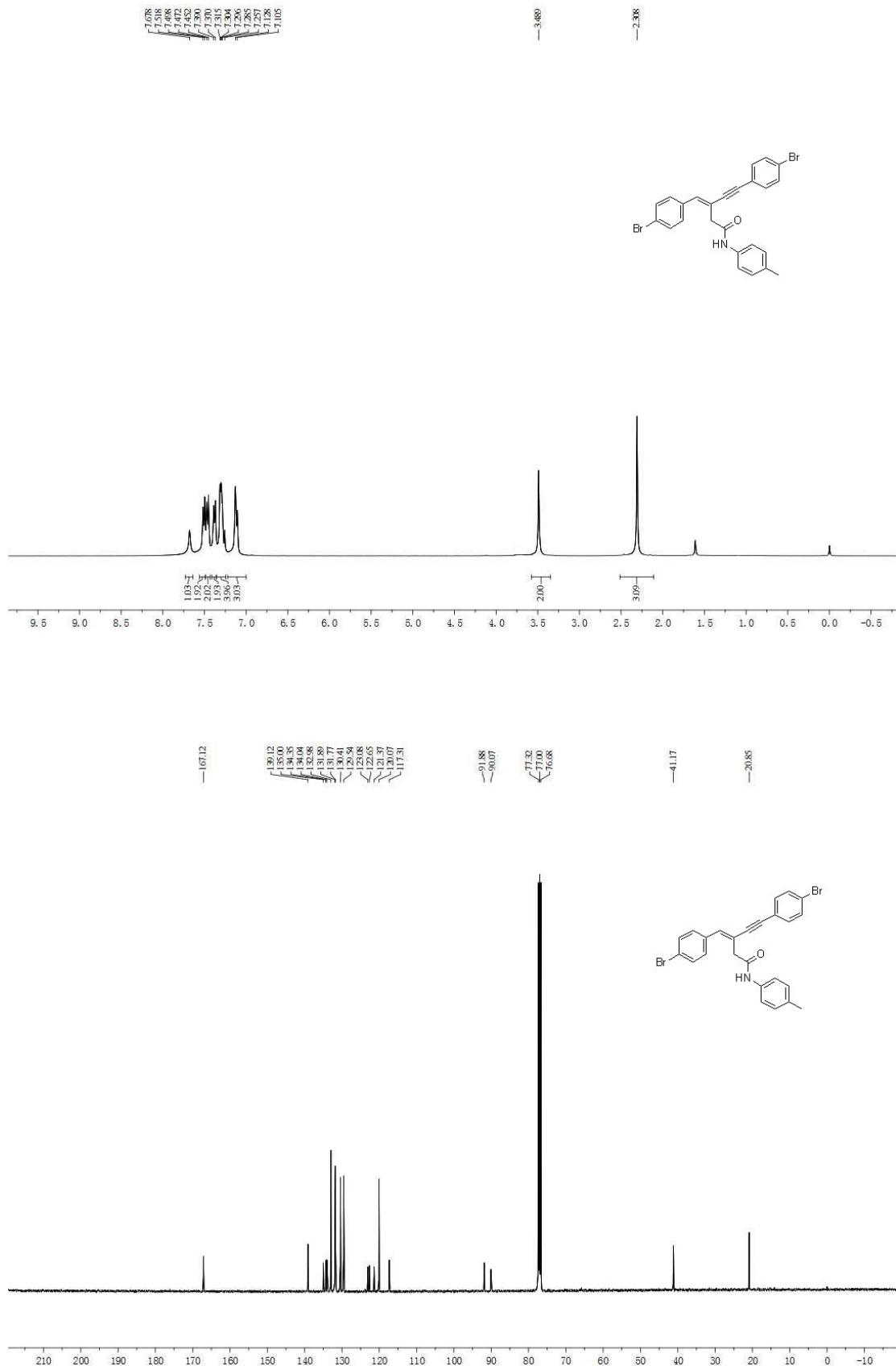
Product 3b



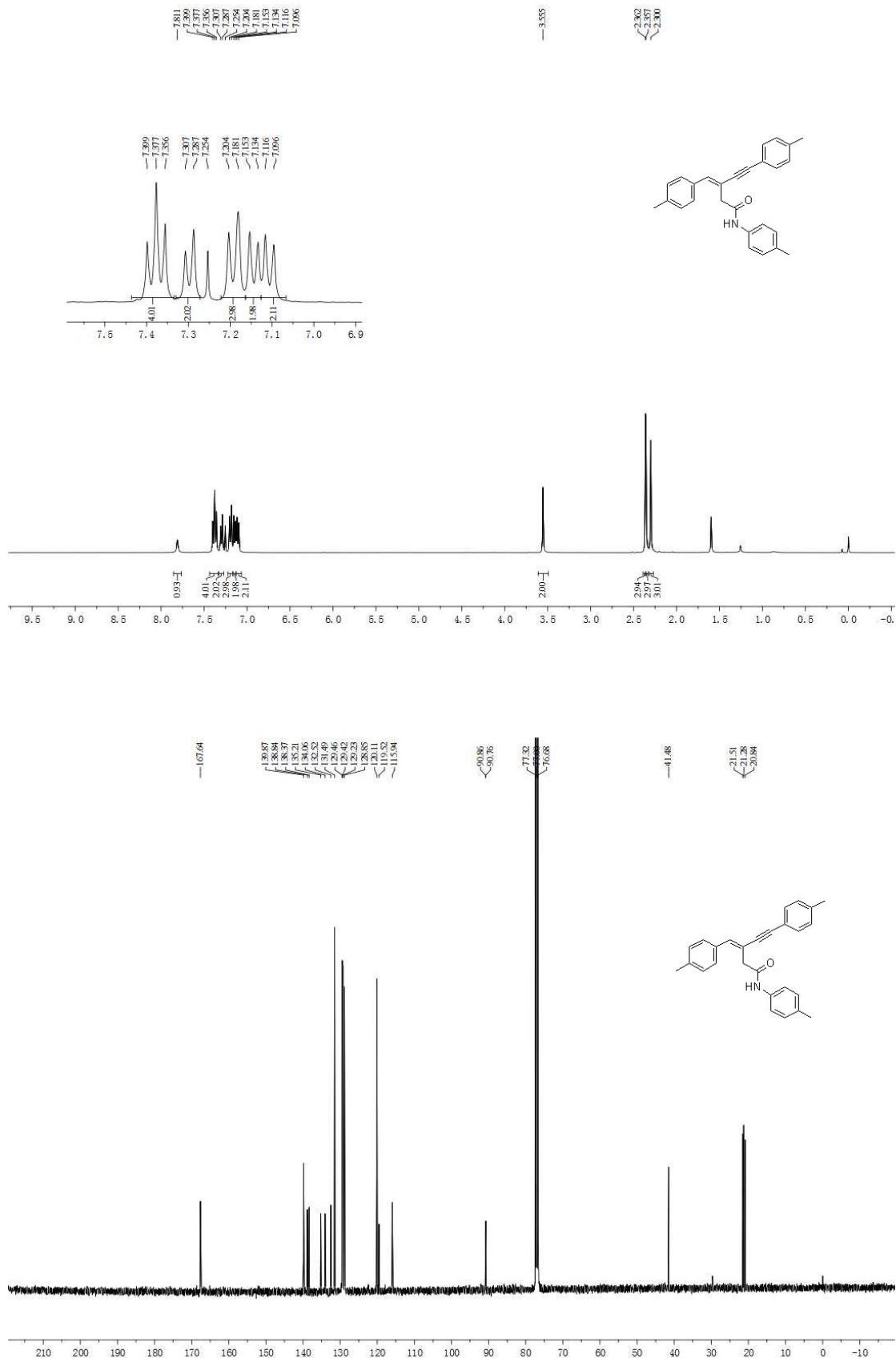
Product 3c



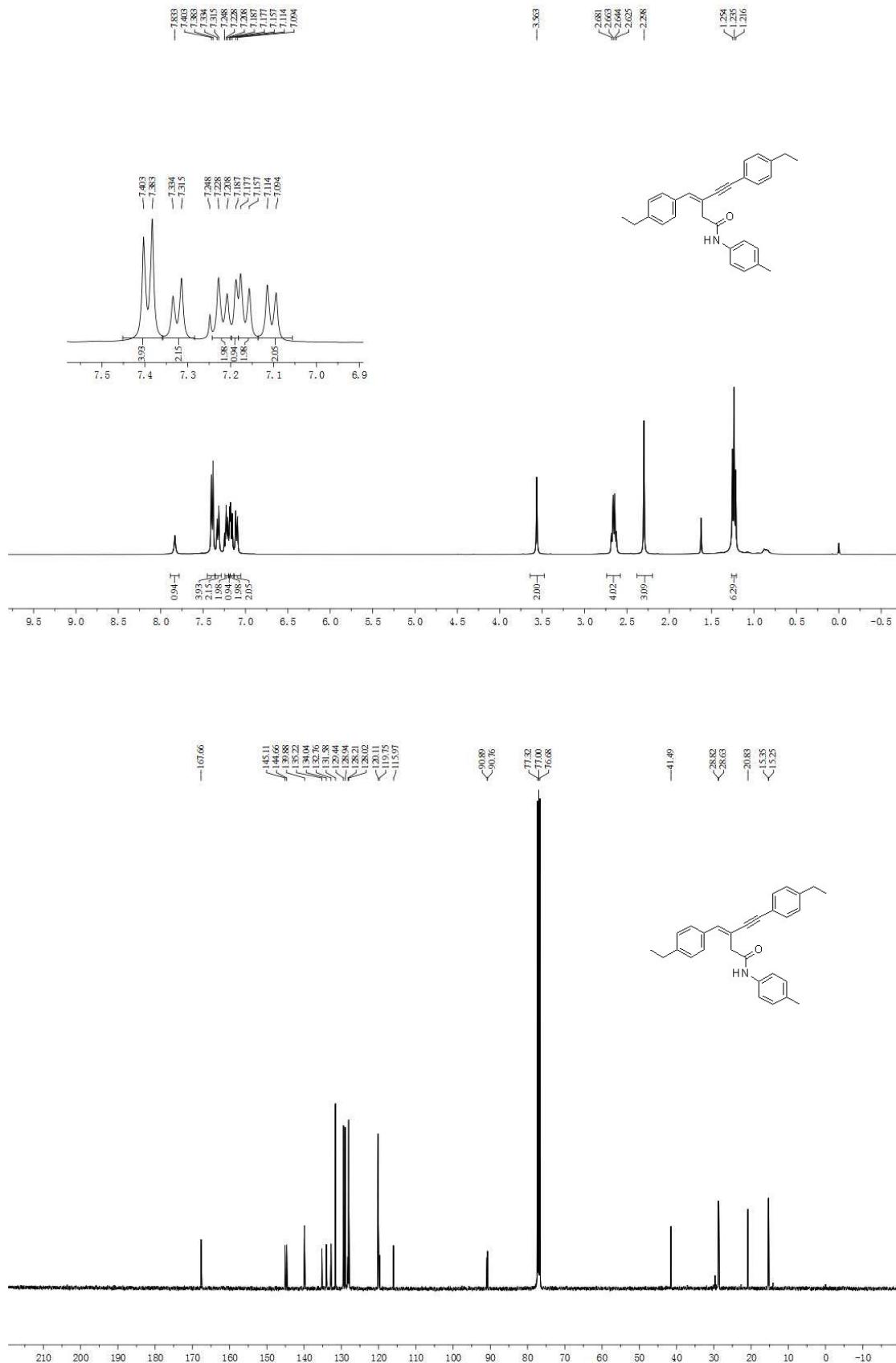
Product 3d



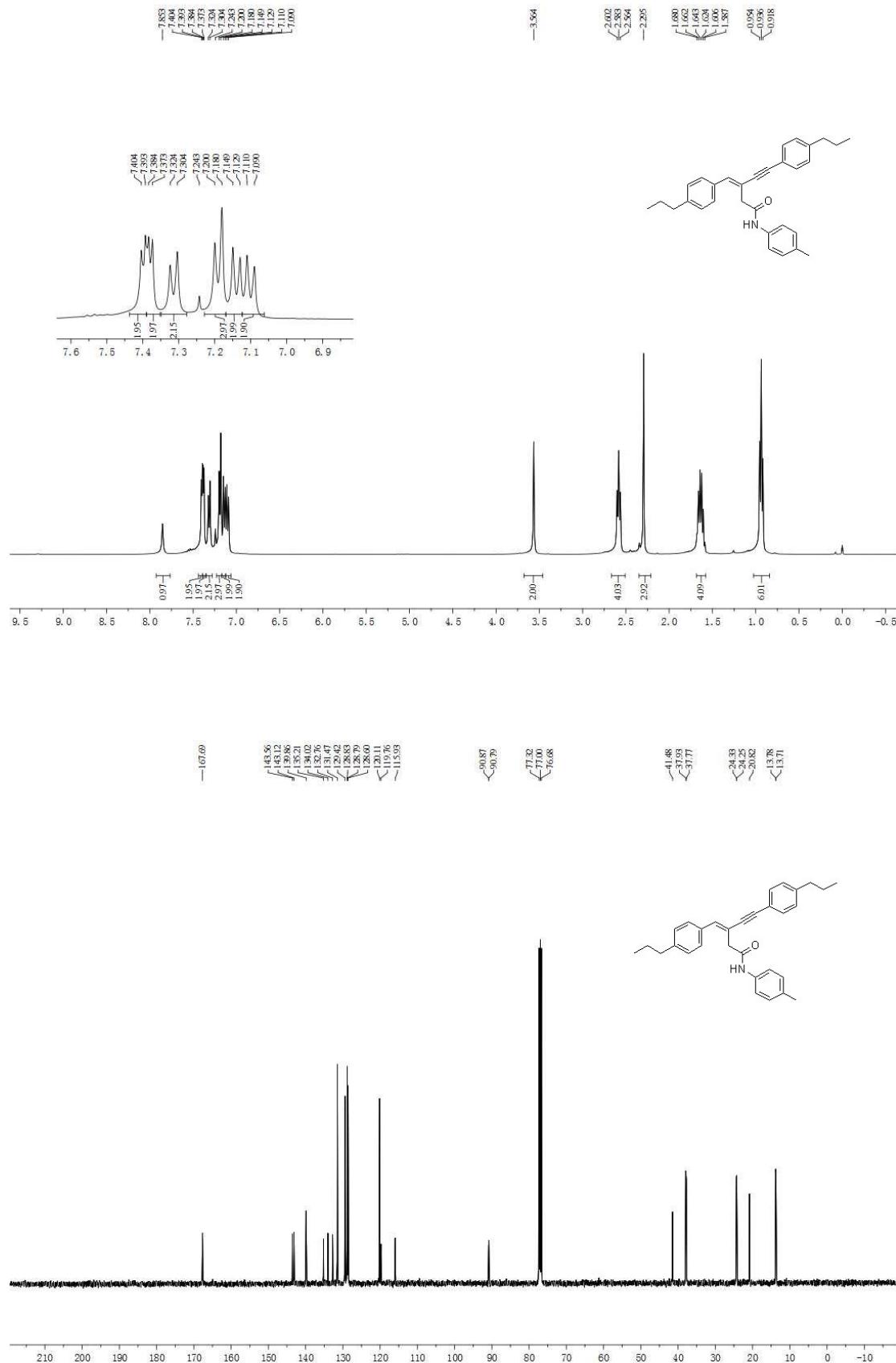
Product 3e



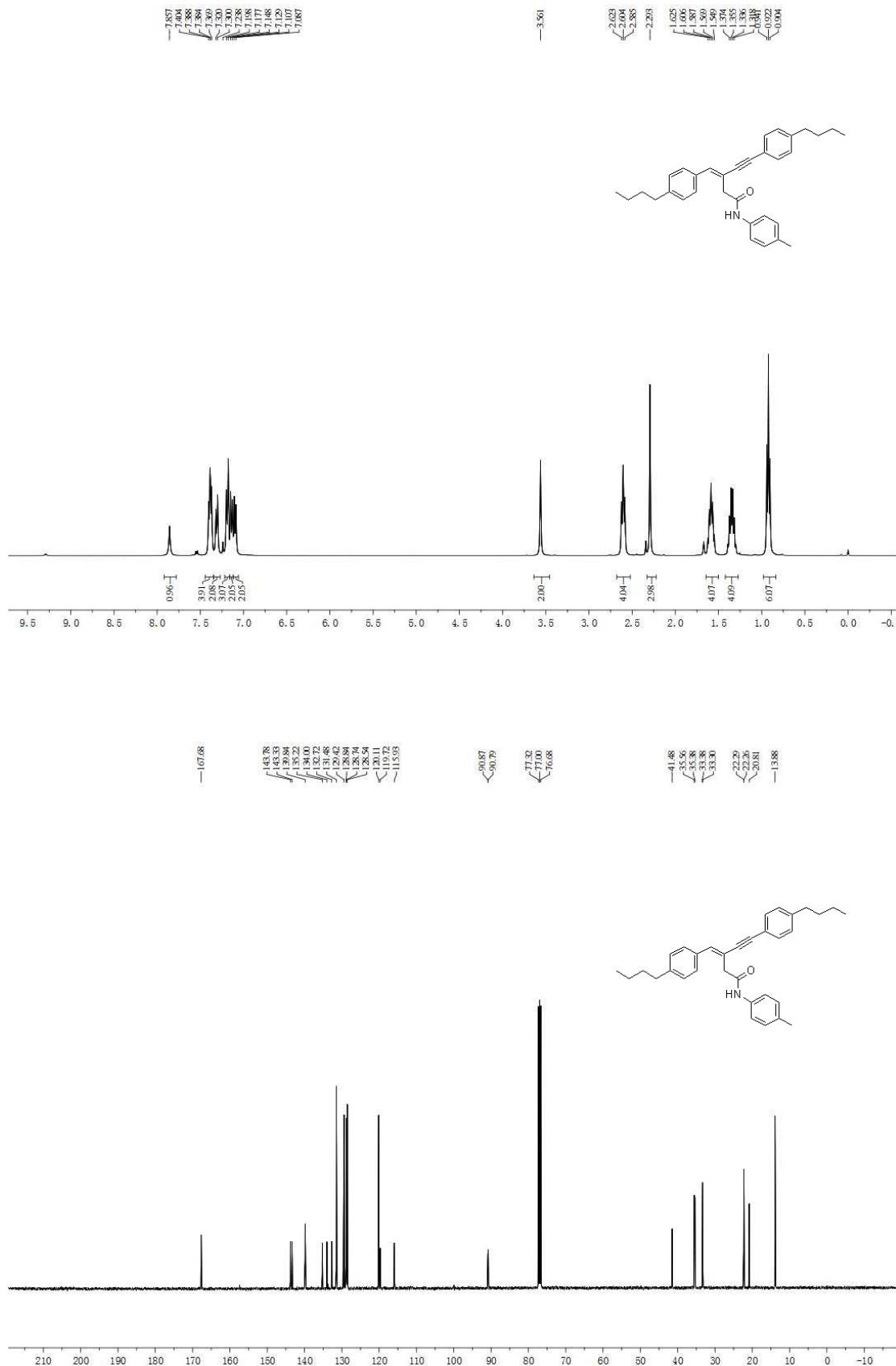
Product 3f



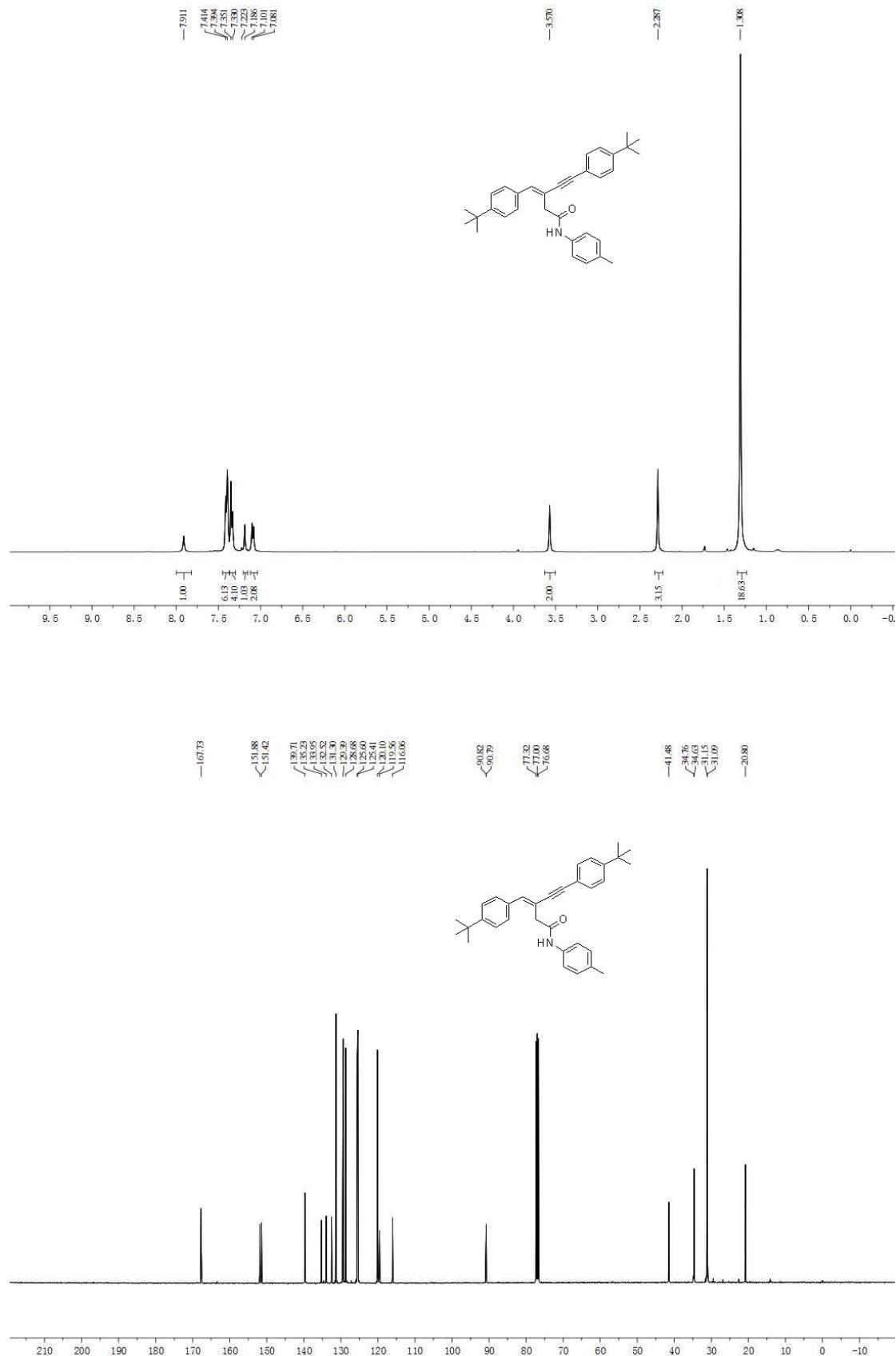
Product 3g



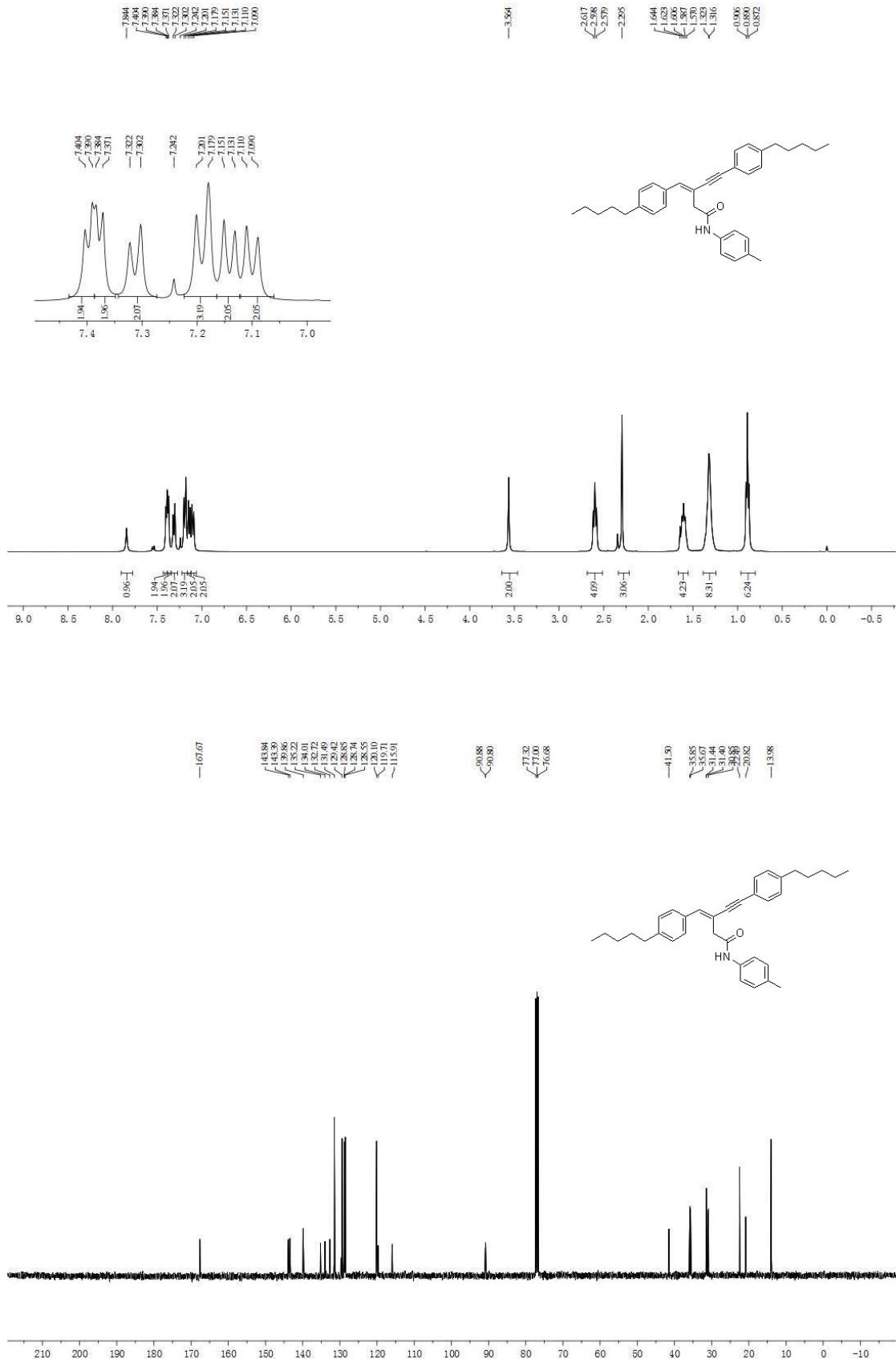
Product 3h



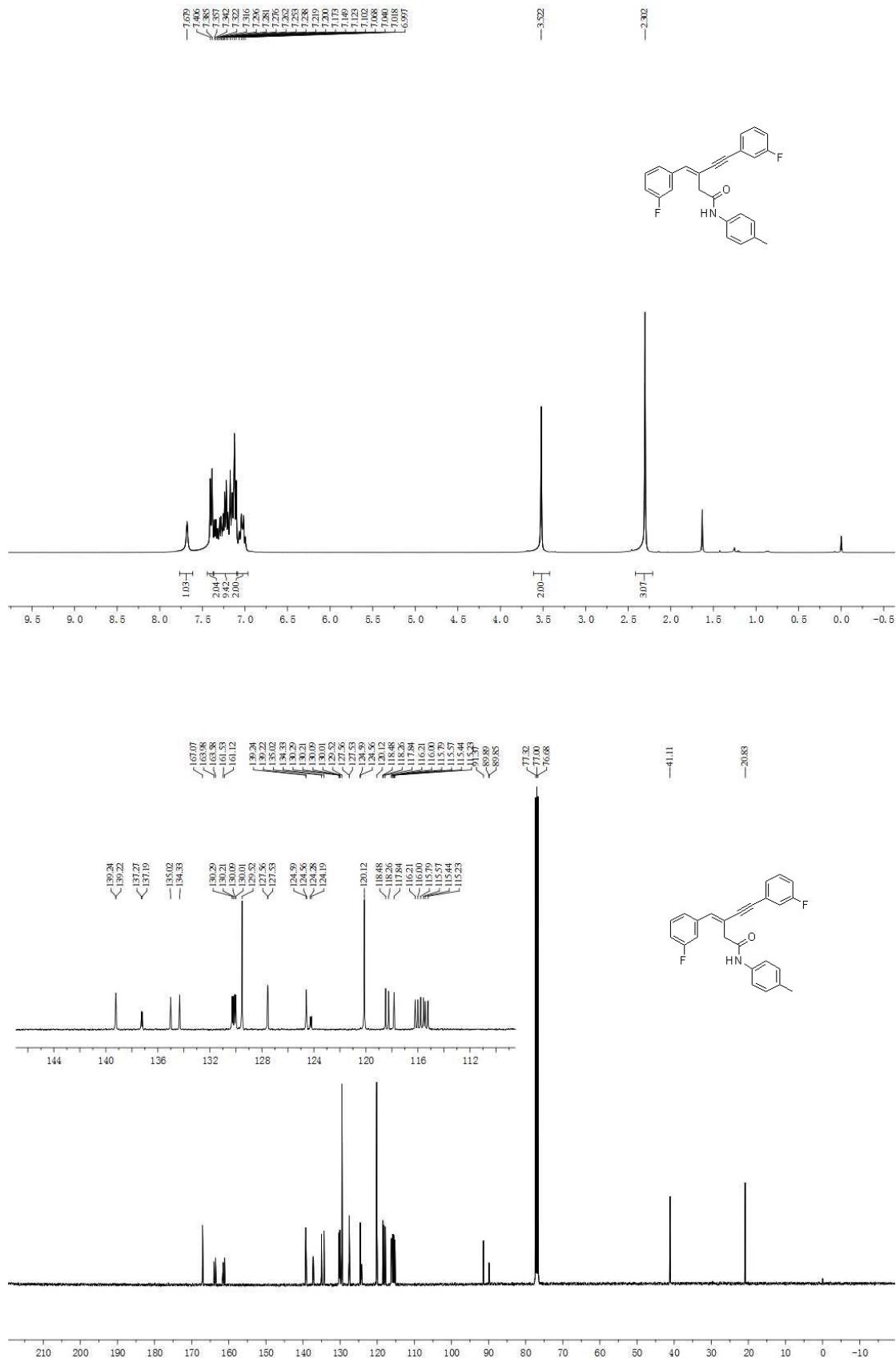
Product 3i



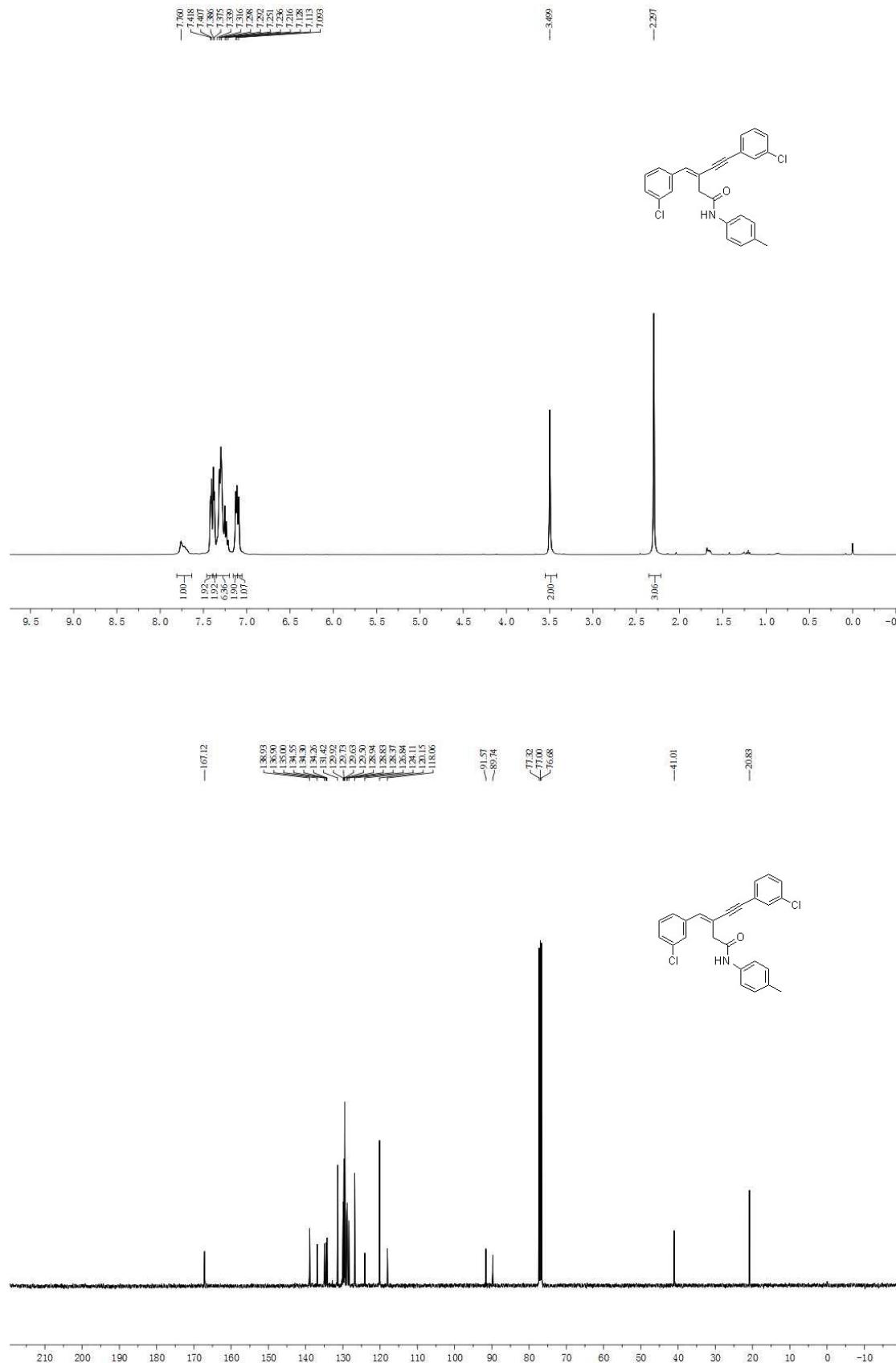
Product 3j



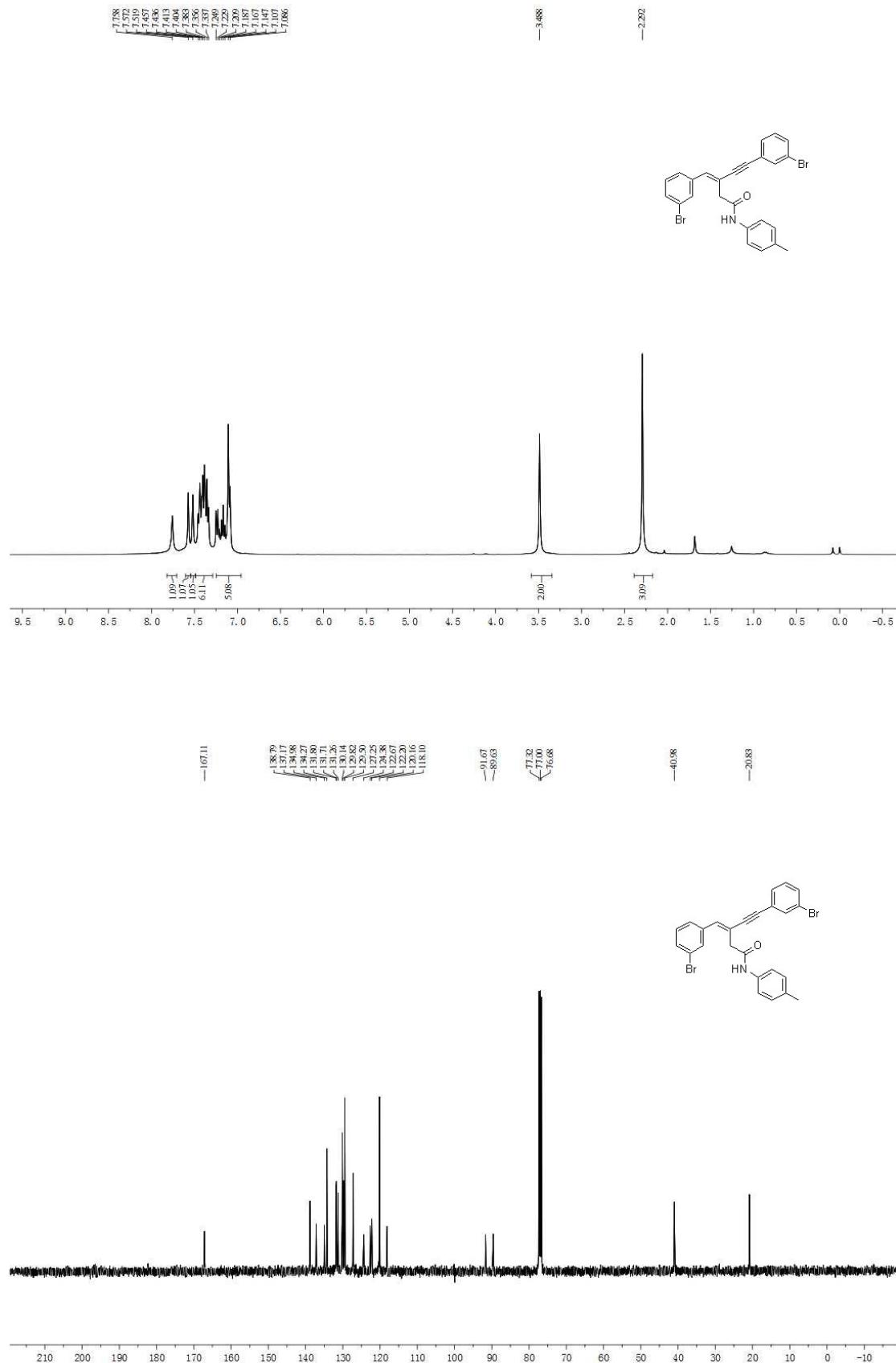
Product 3k



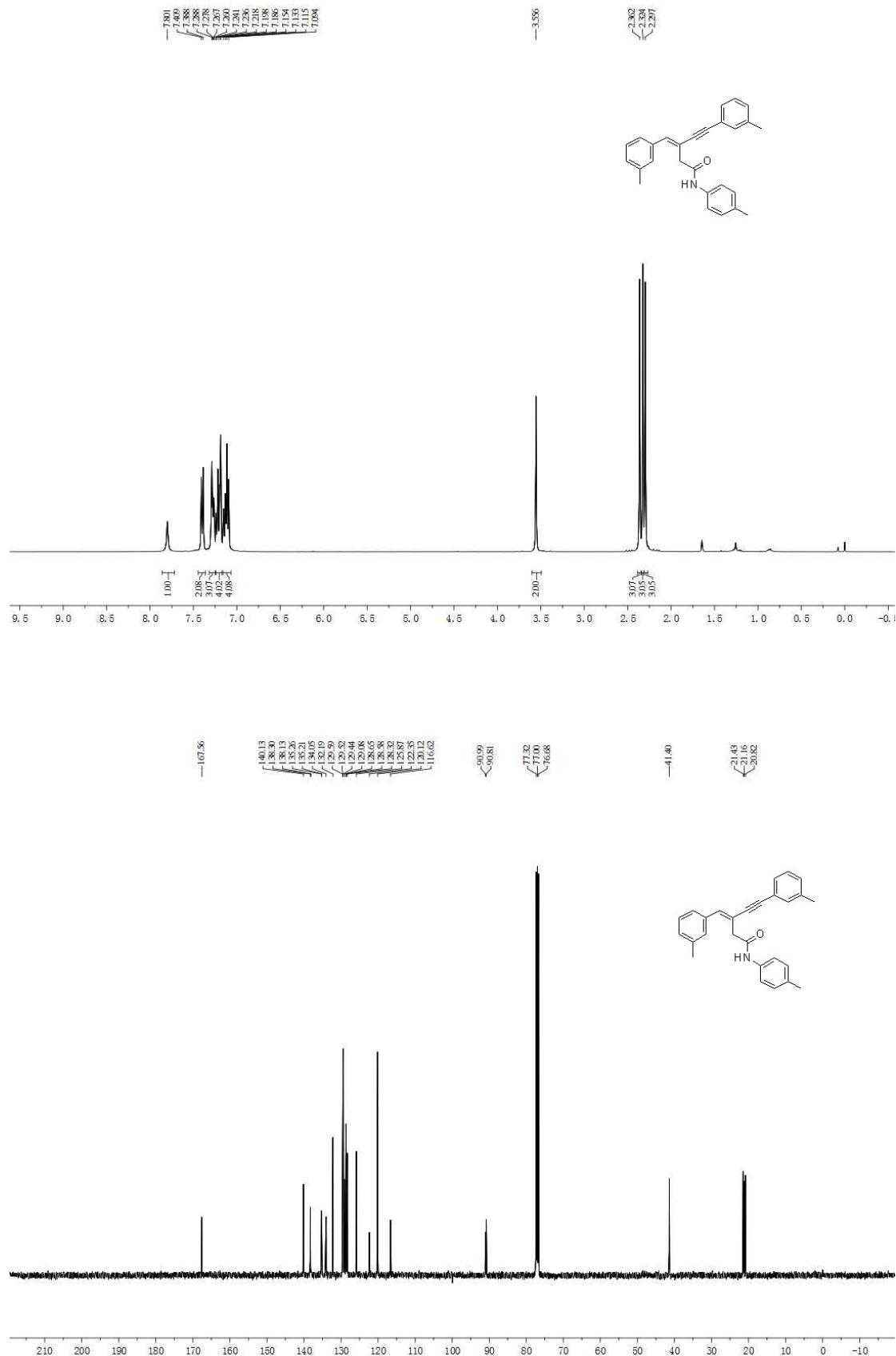
Product 3l



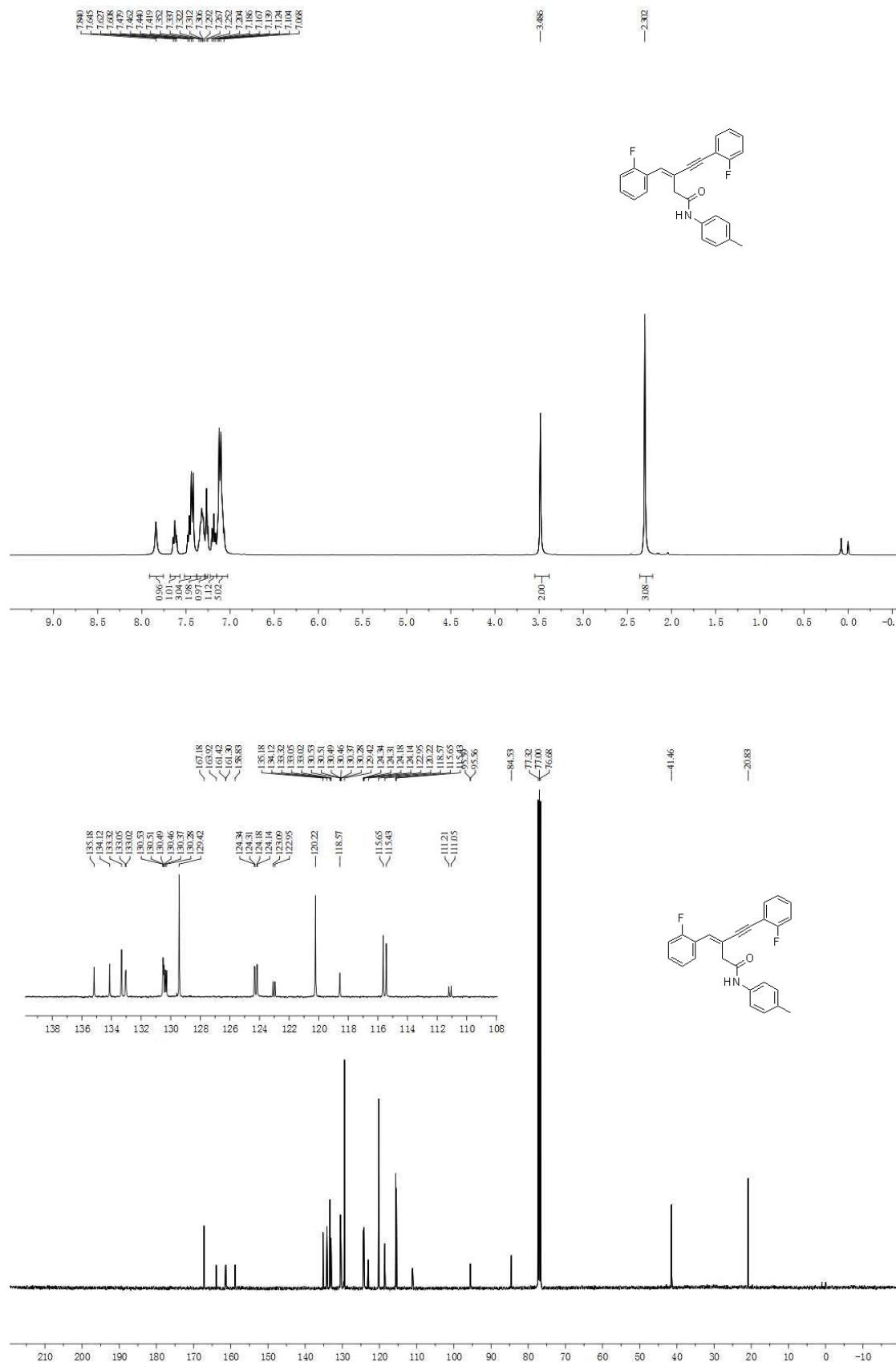
Product 3m



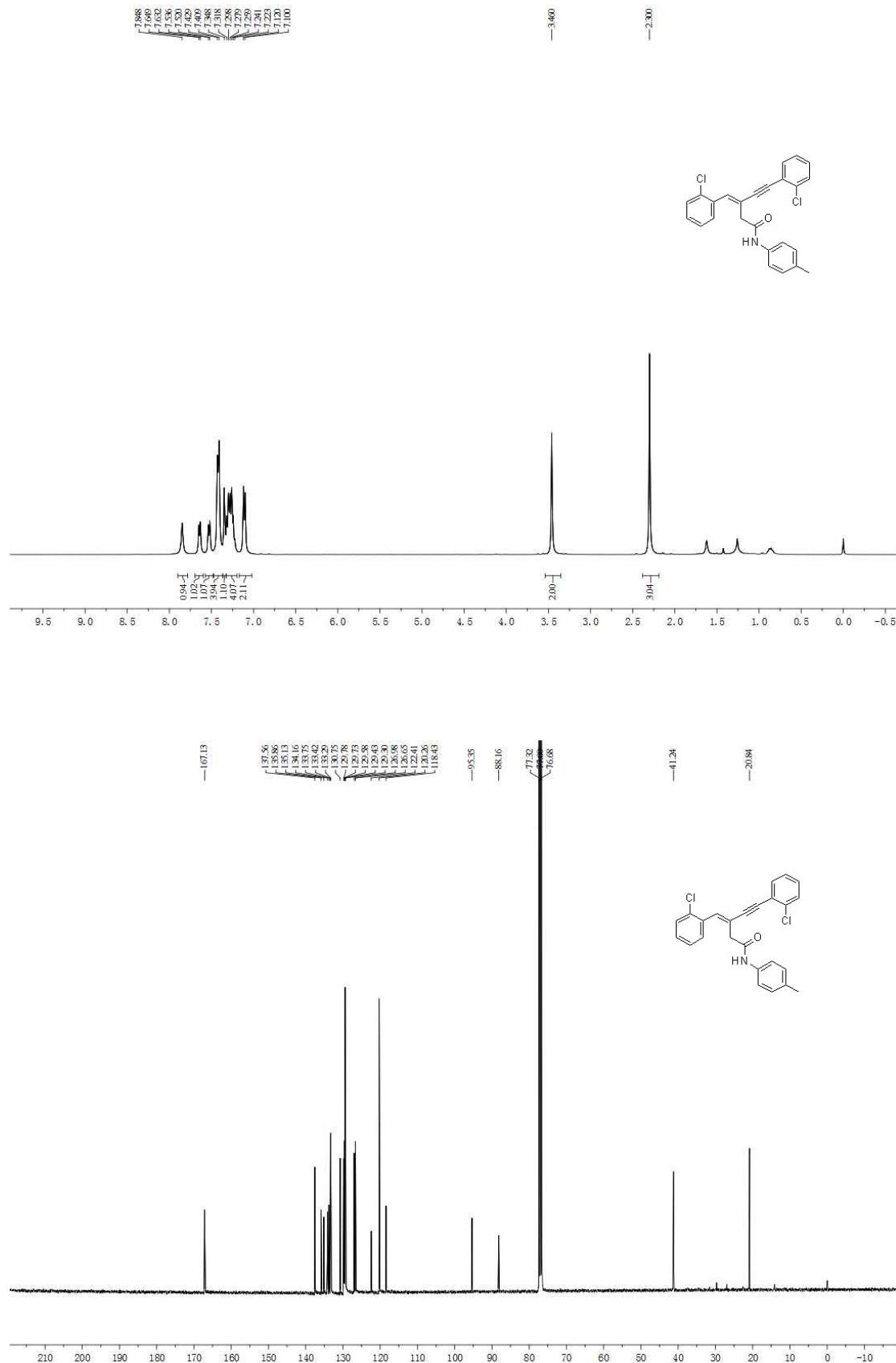
Product 3n



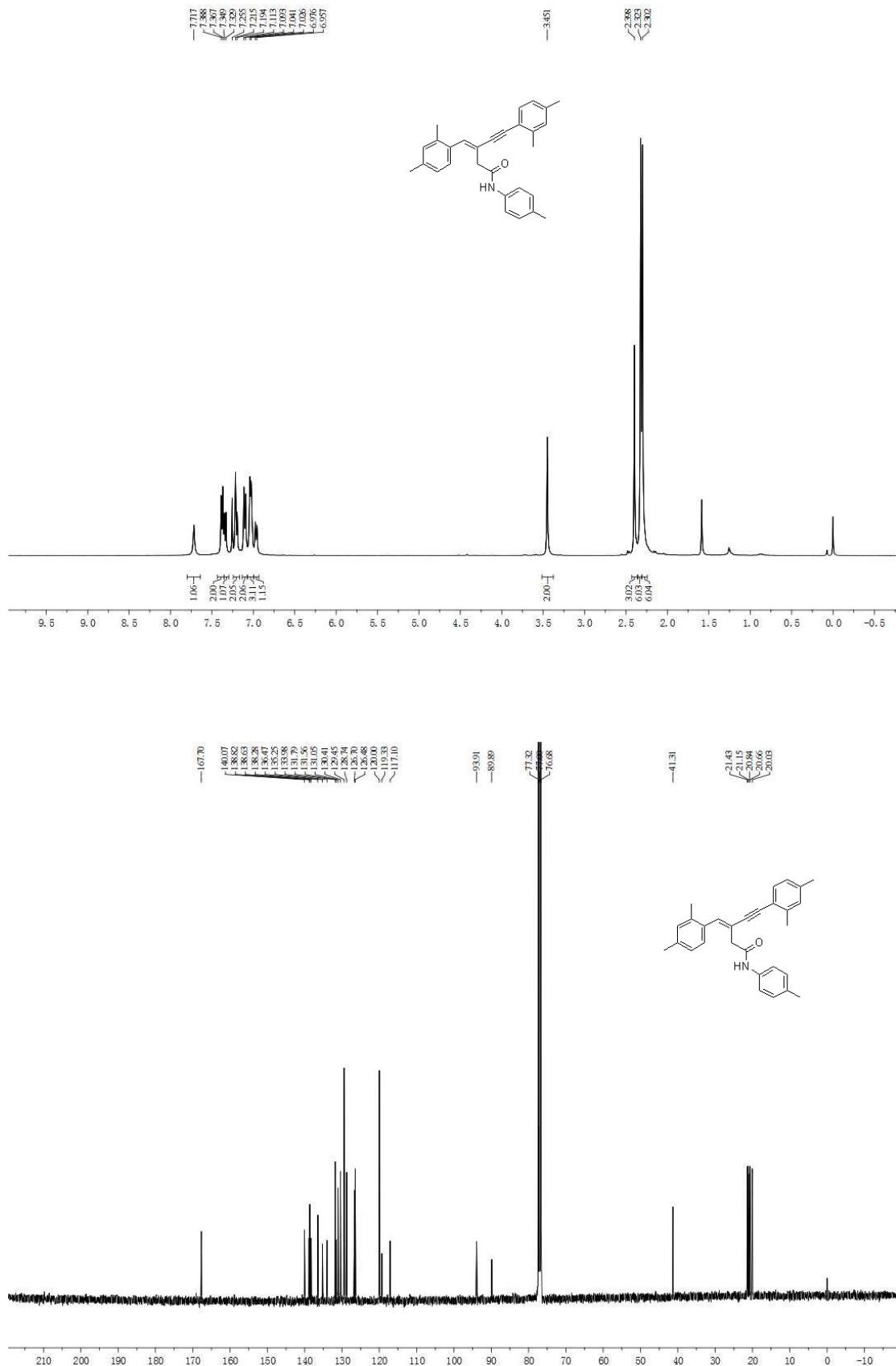
Product 3o



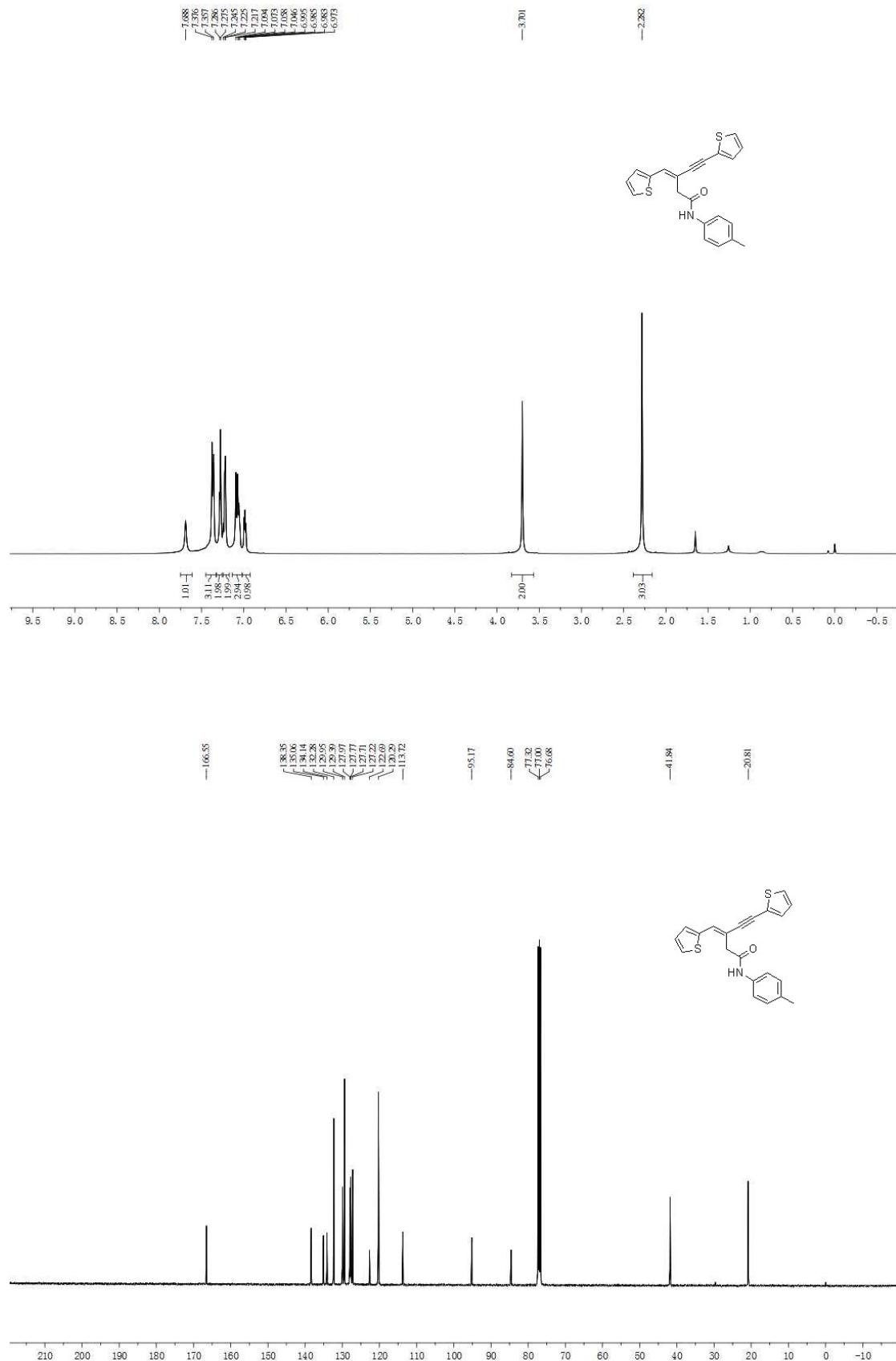
Product 3p



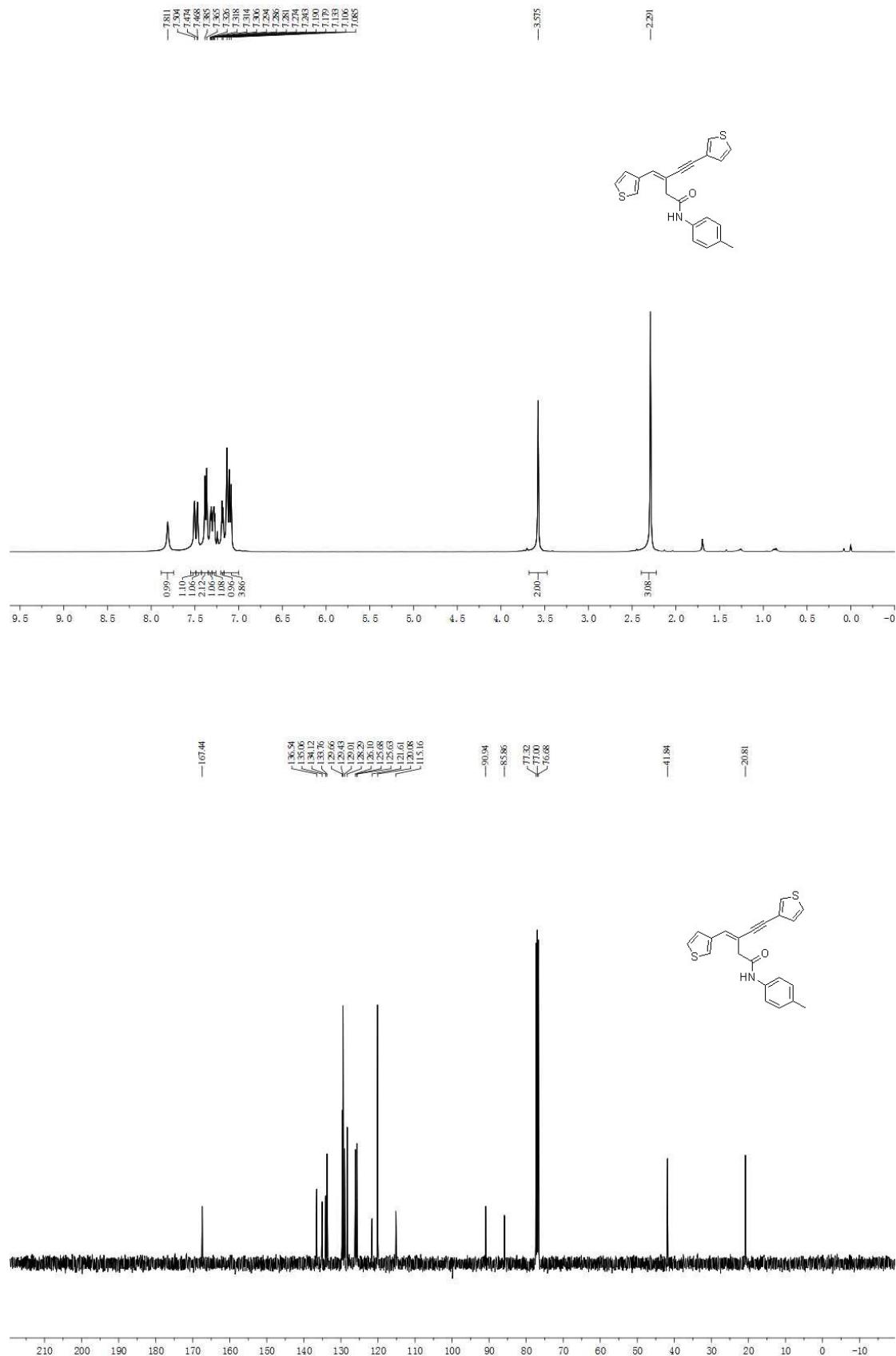
Product 3q



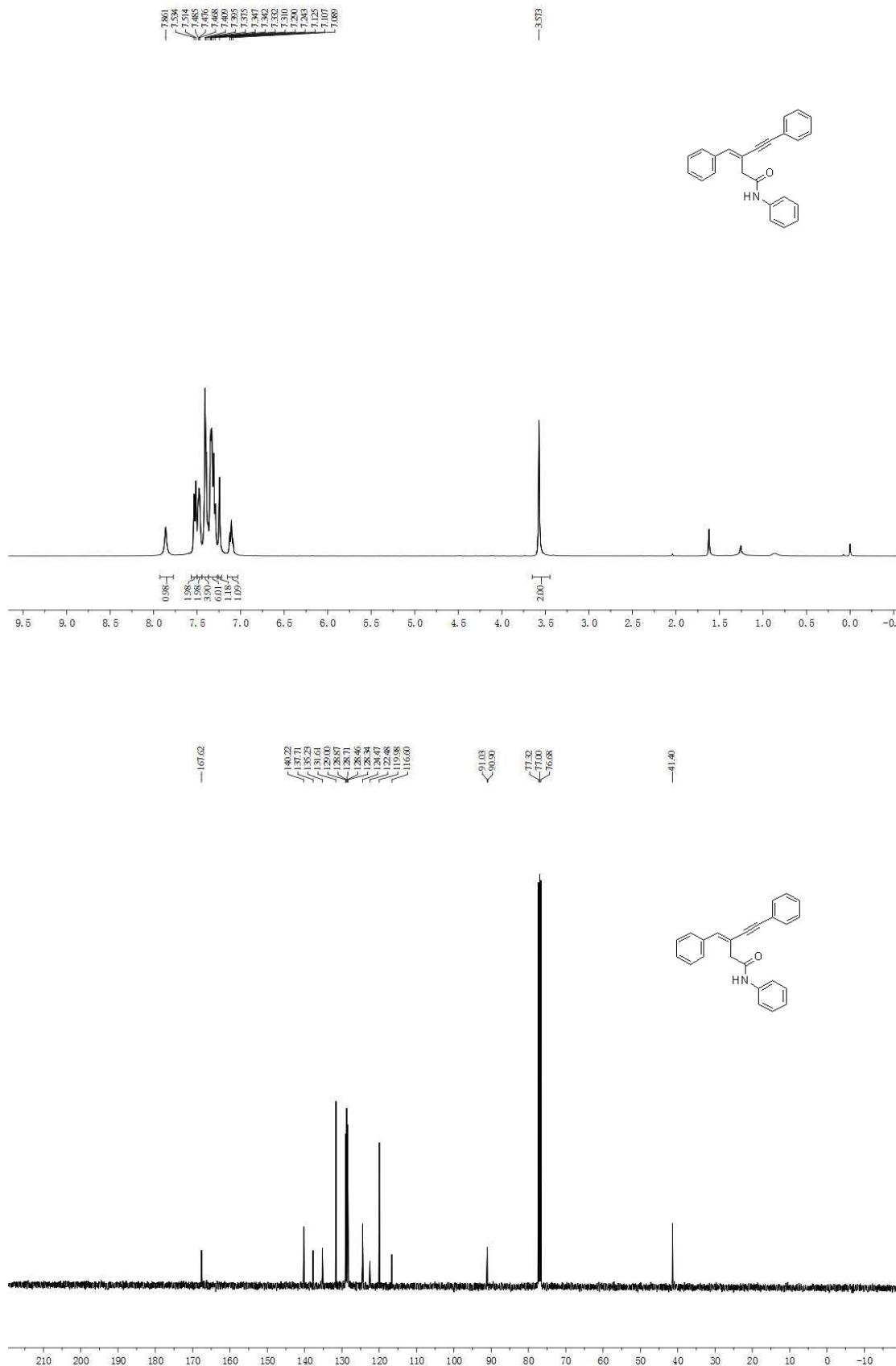
Product 3r



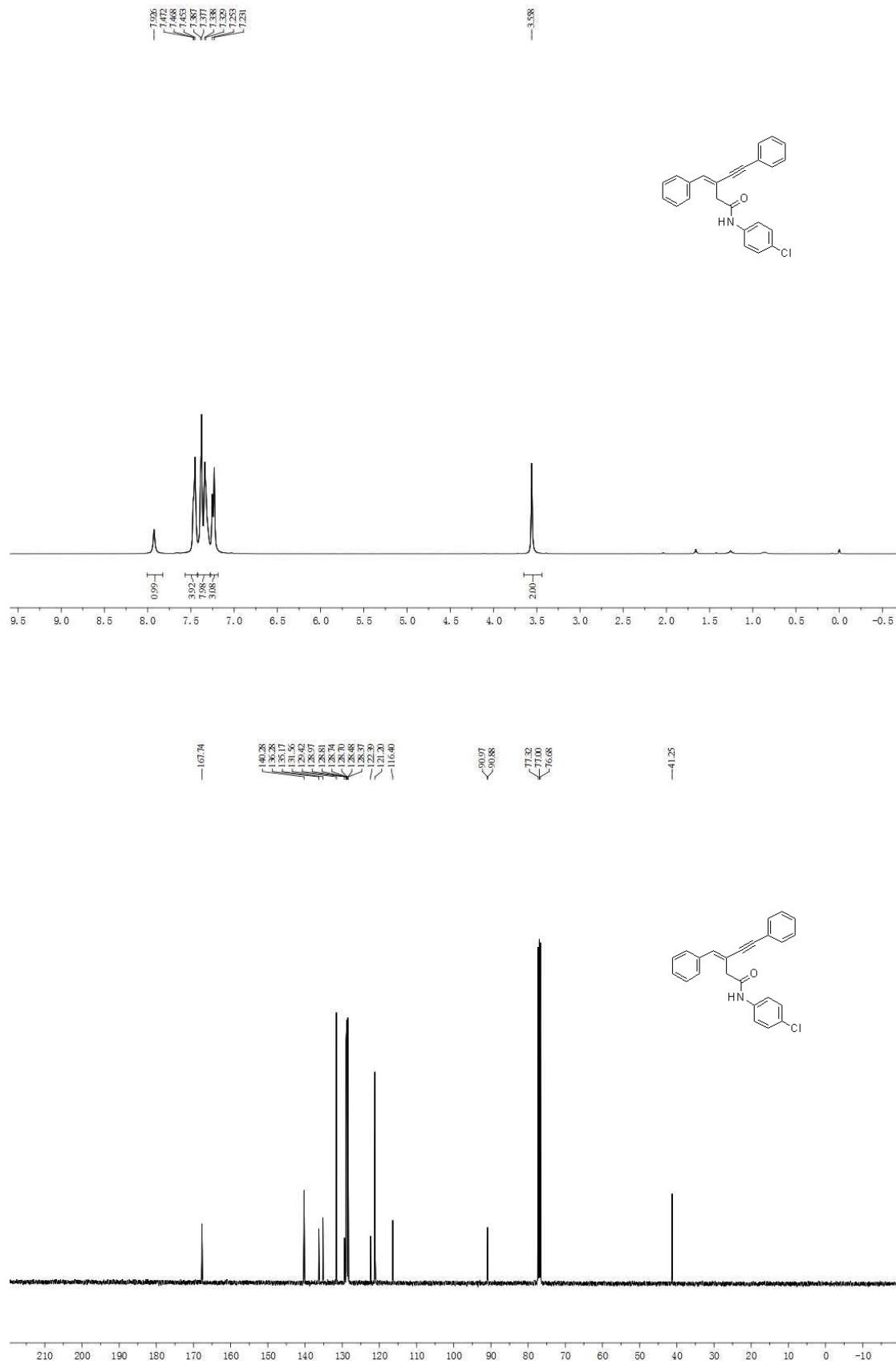
Product 3s



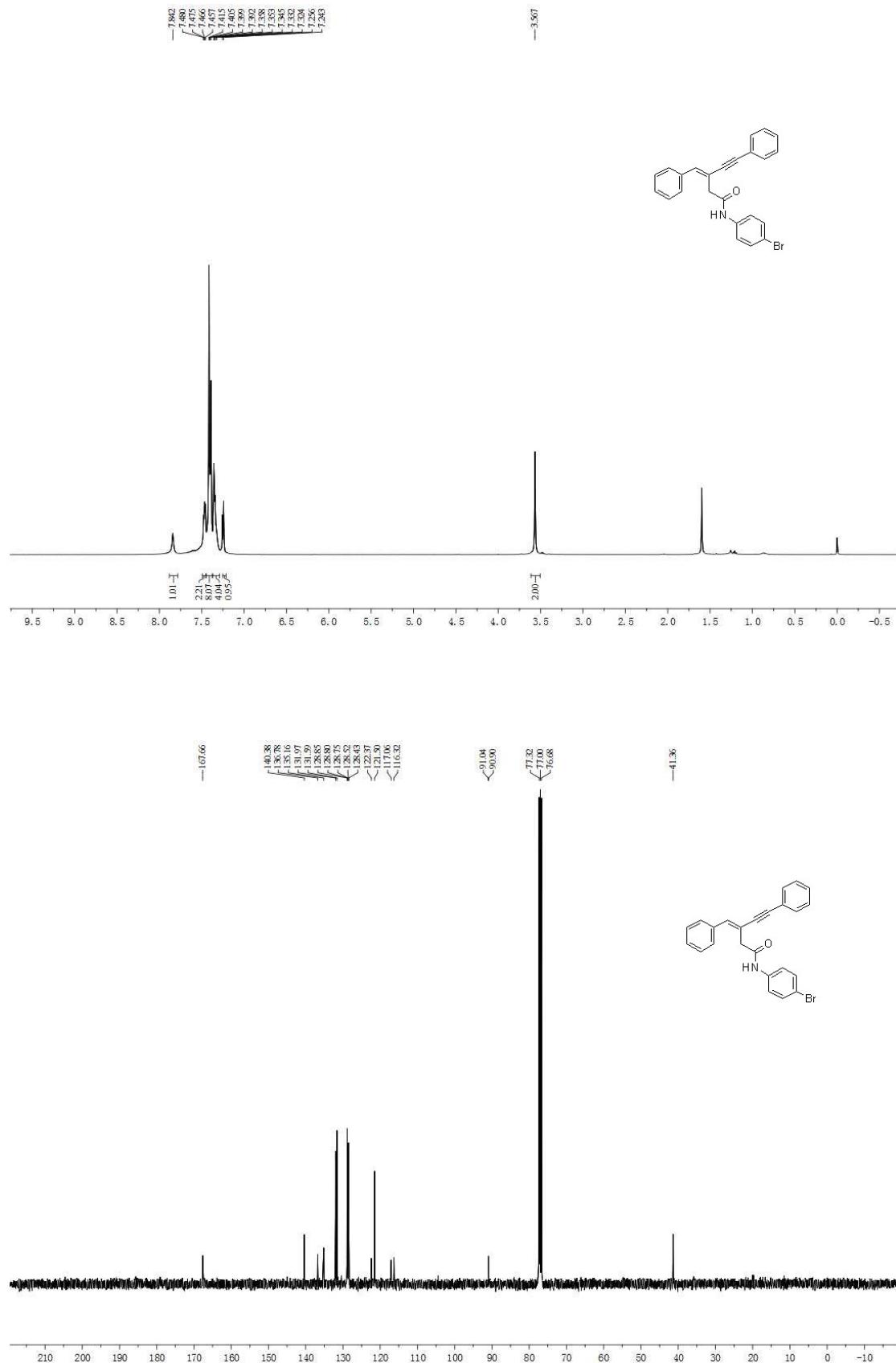
Product 4b



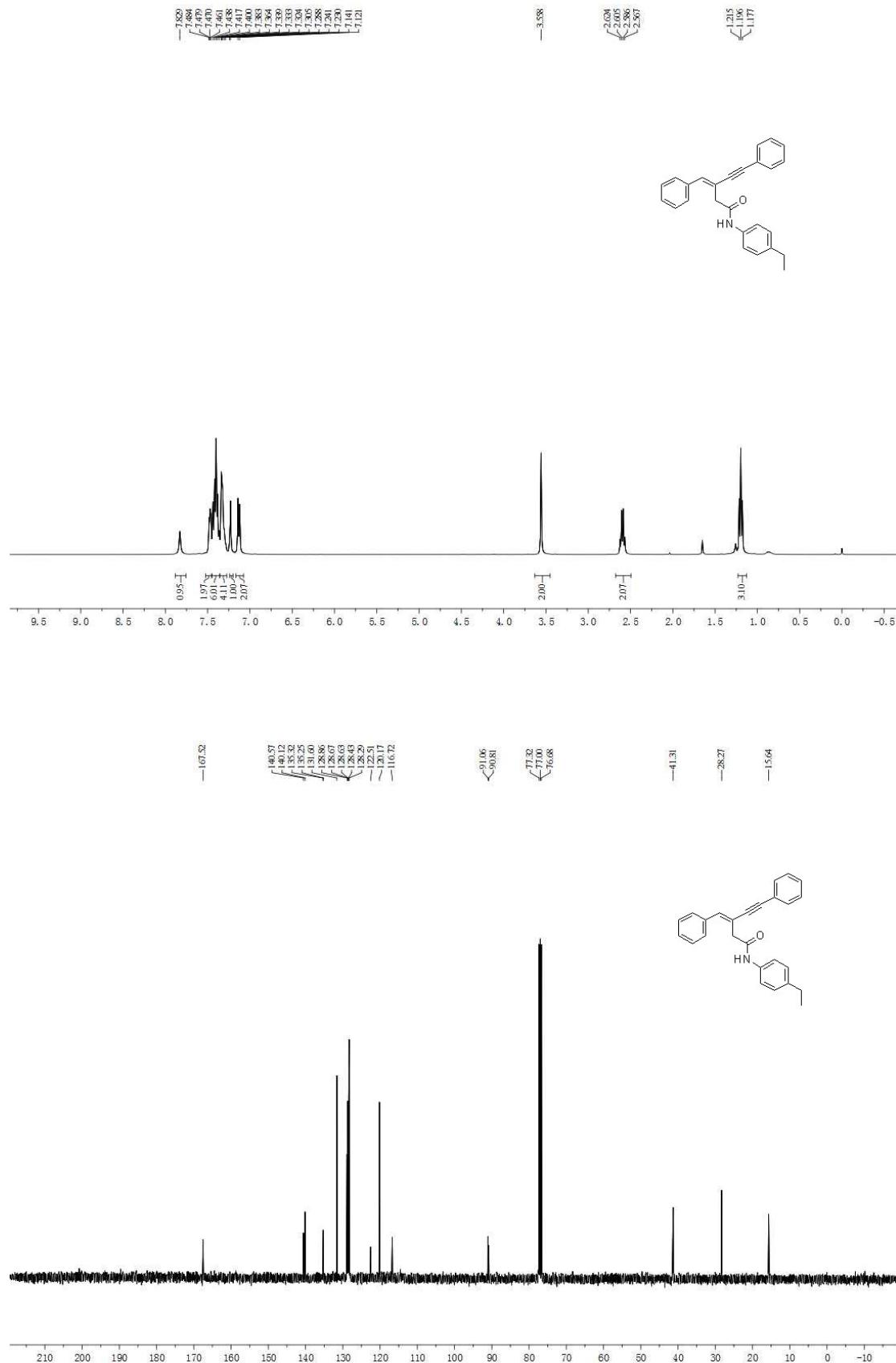
Product 4c



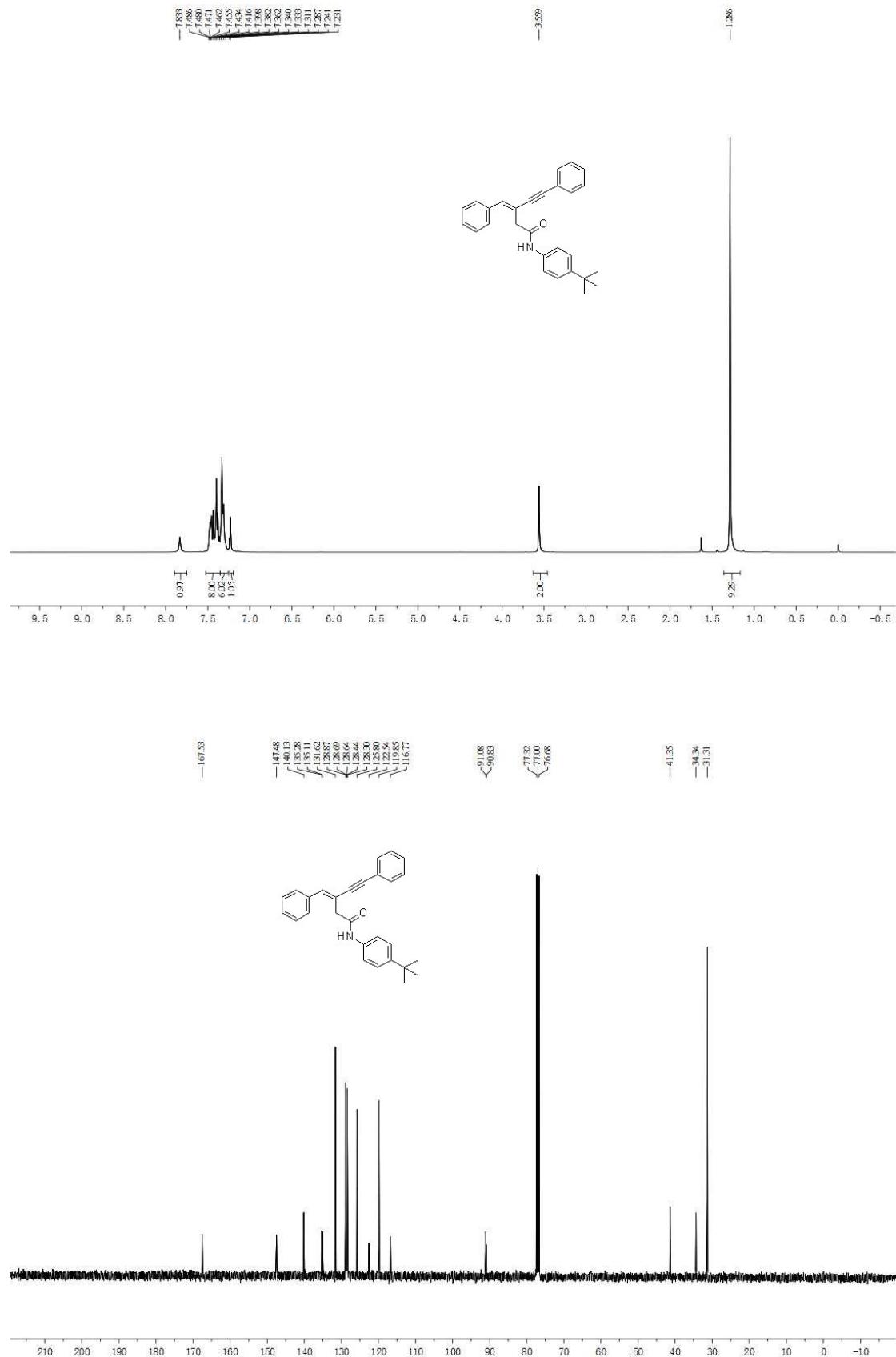
Product 4d



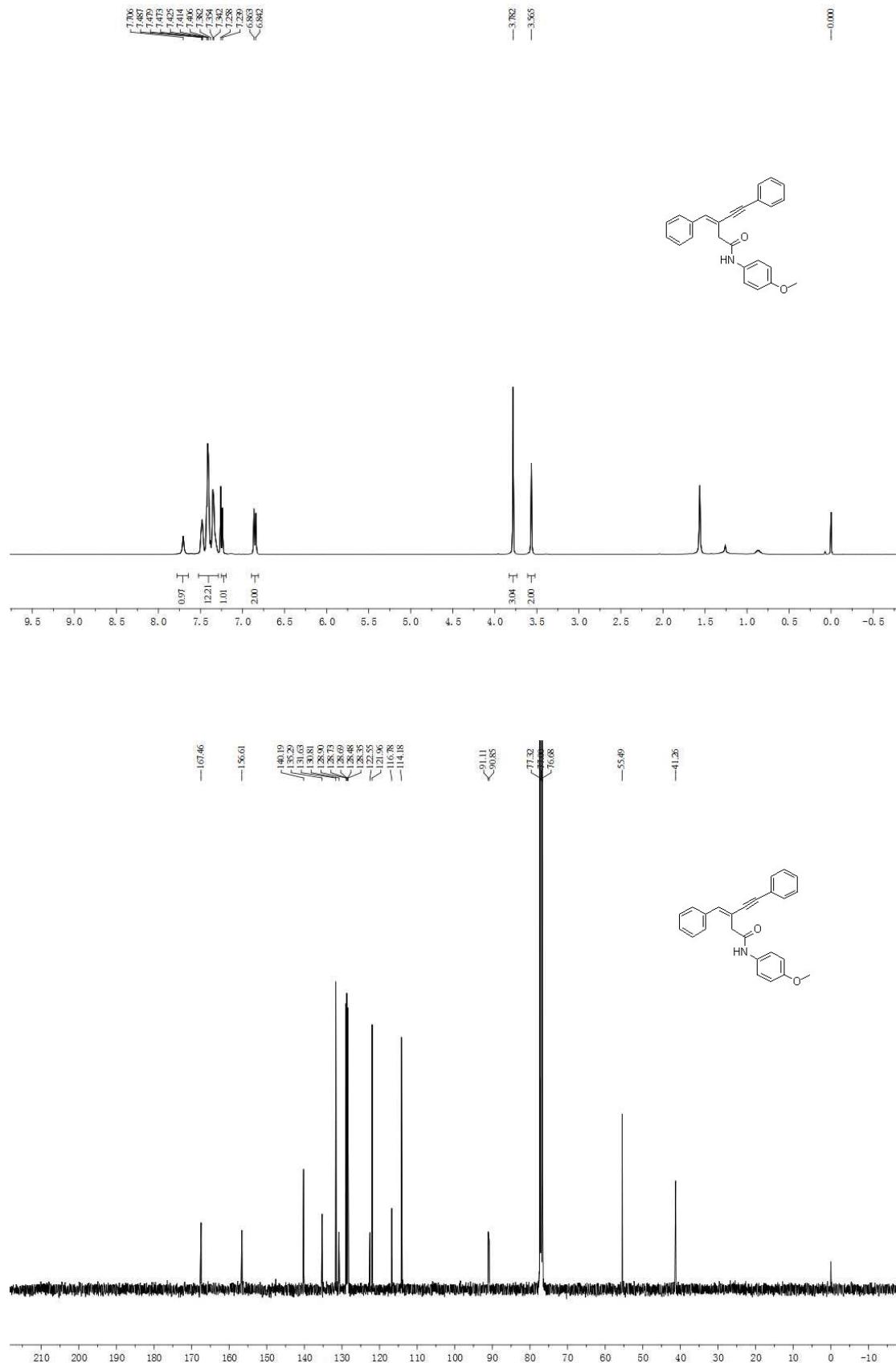
Product 4e



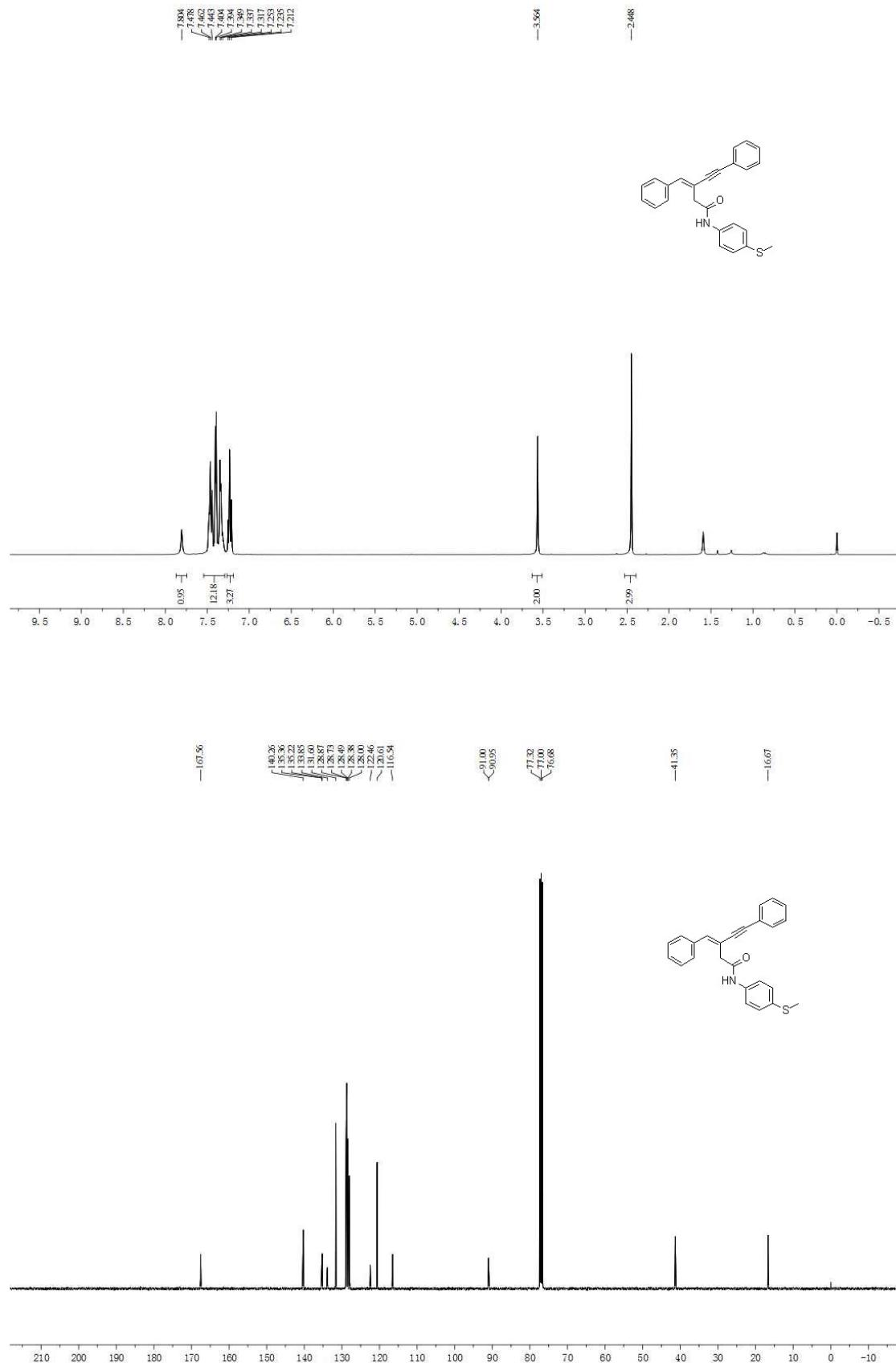
Product 4f



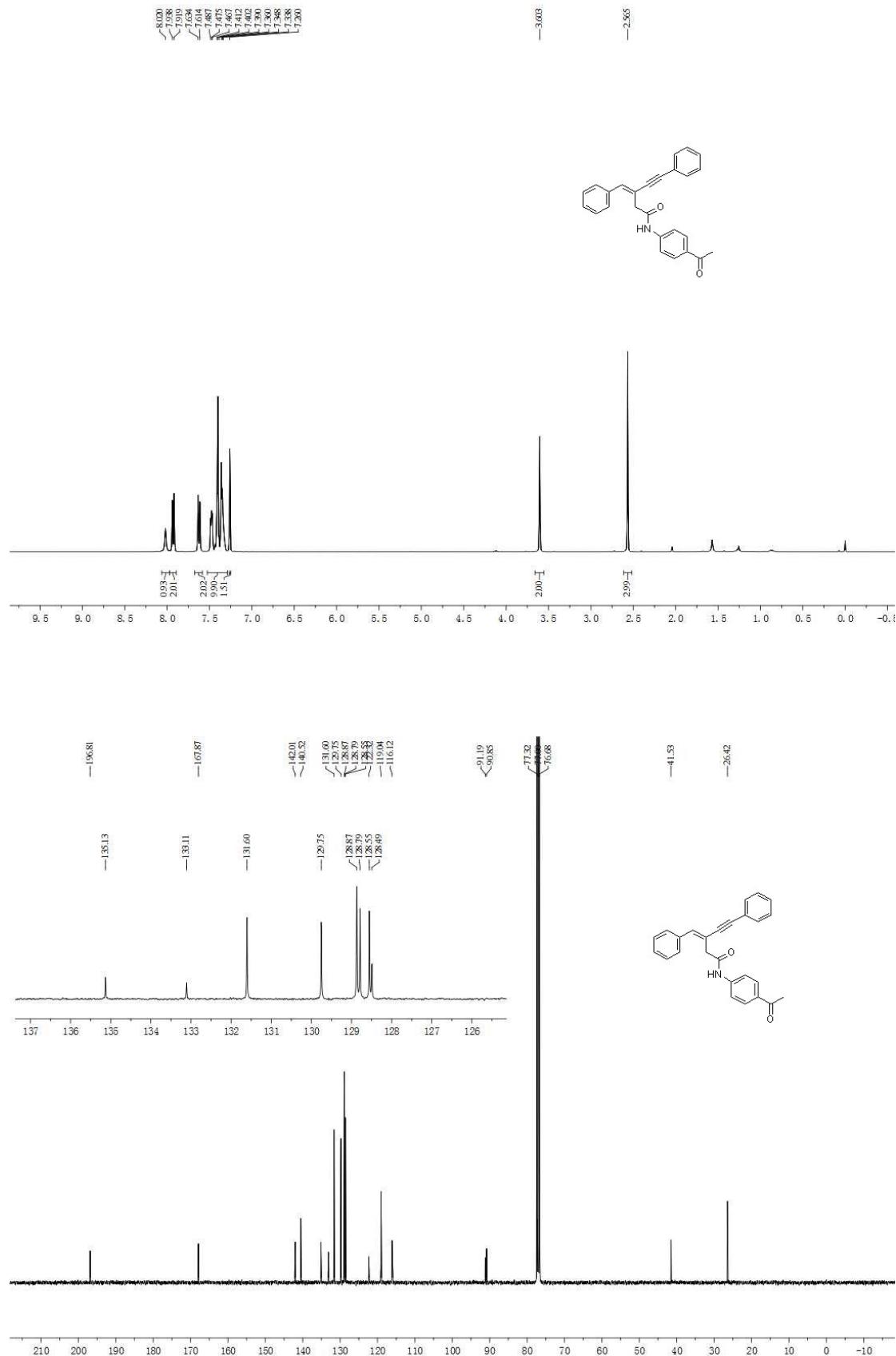
Product 4g



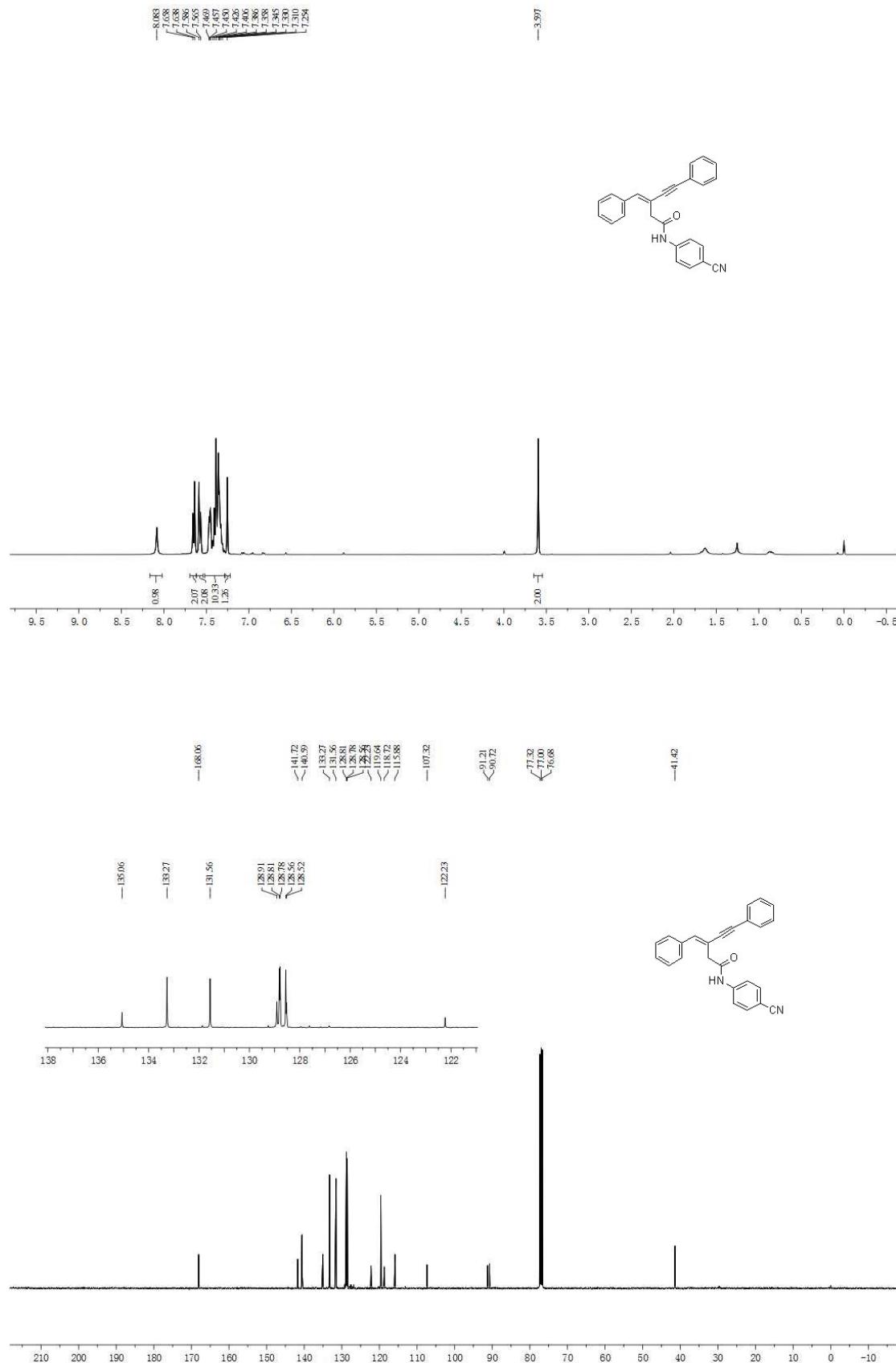
Product 4h



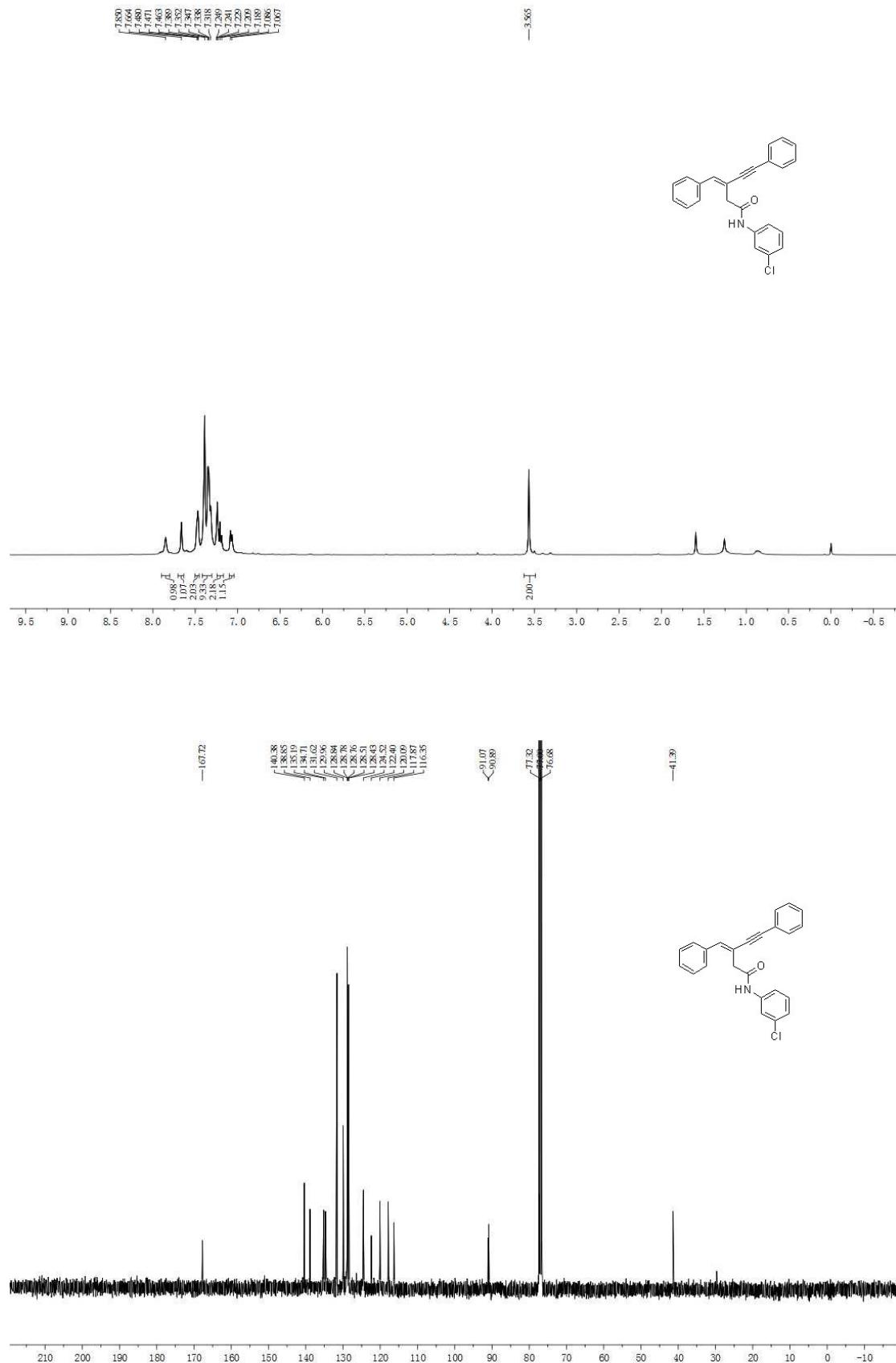
Product 4i



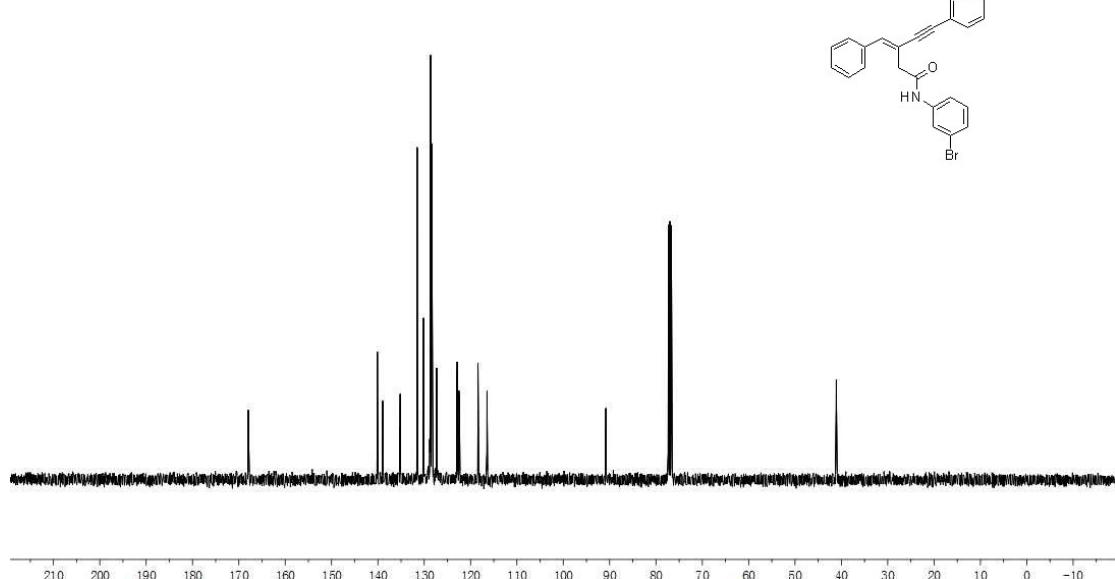
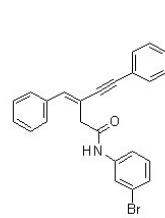
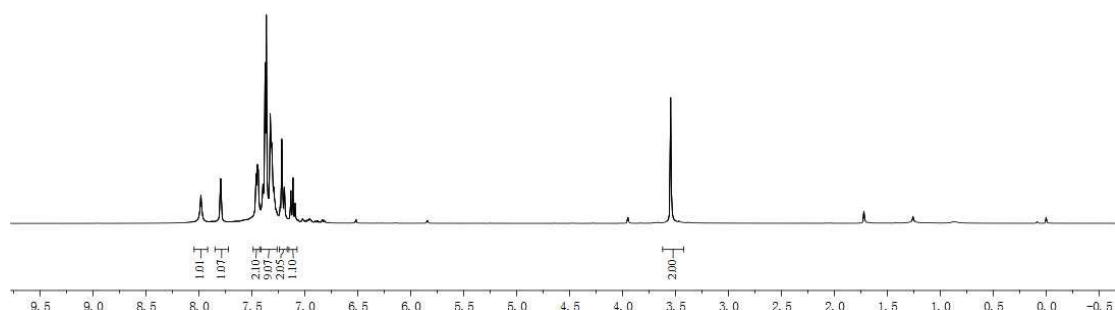
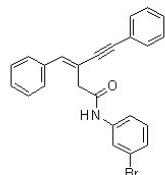
Product 4j



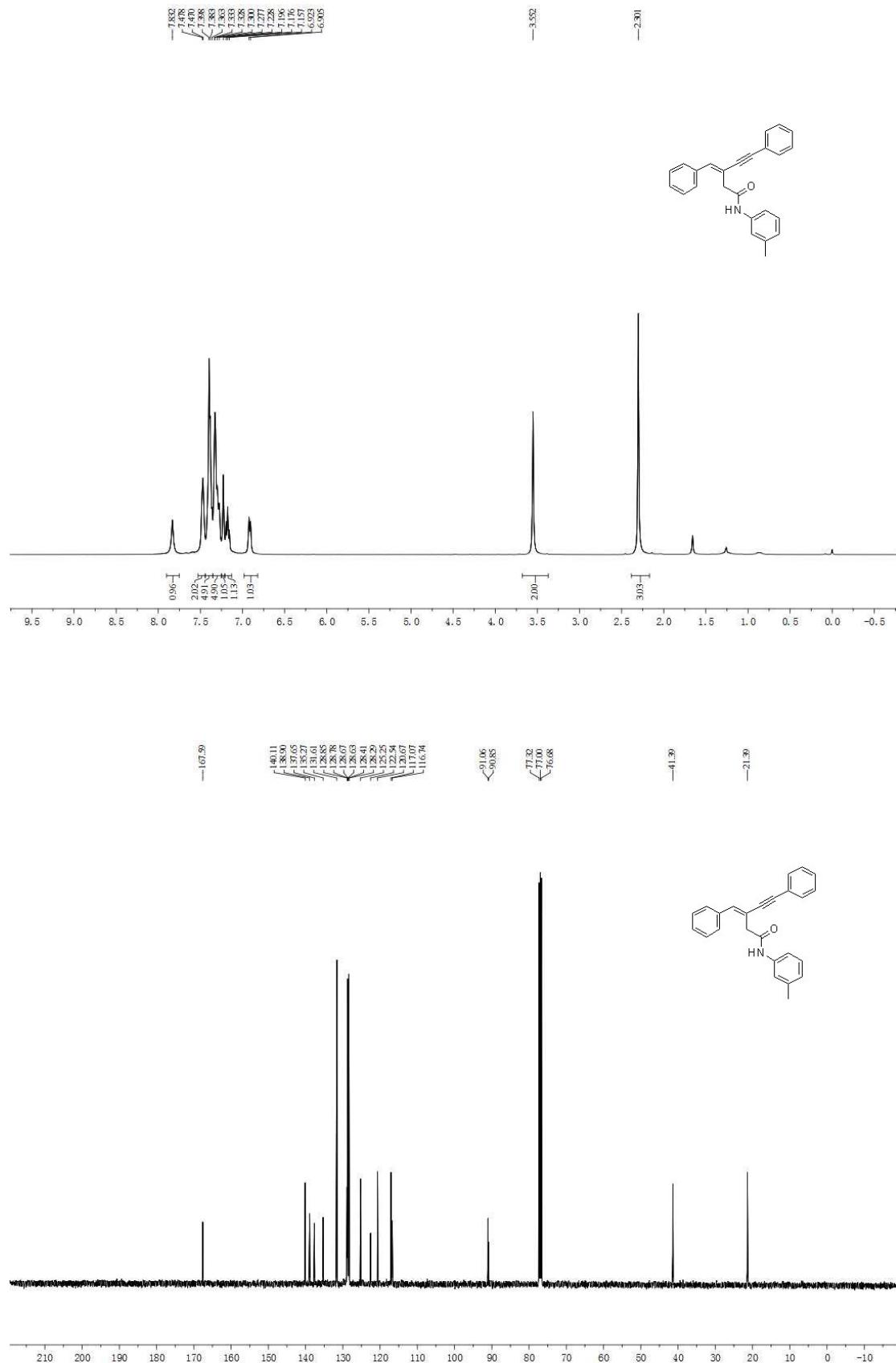
Product 4k



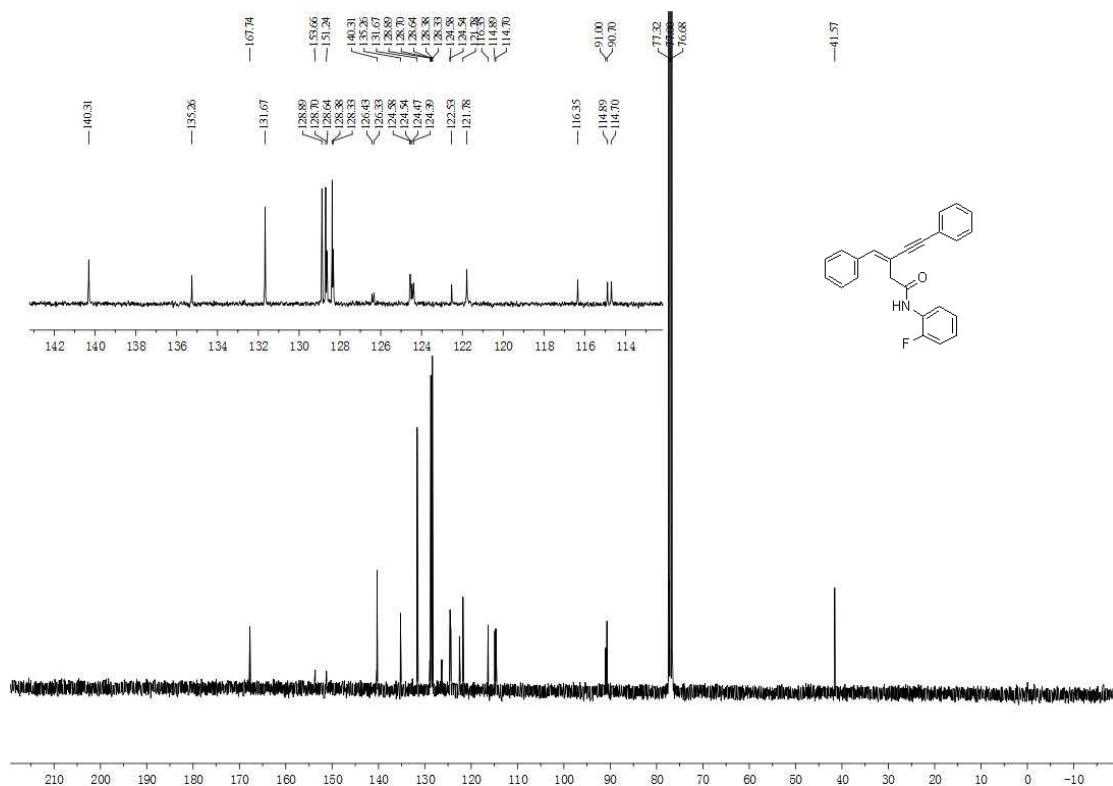
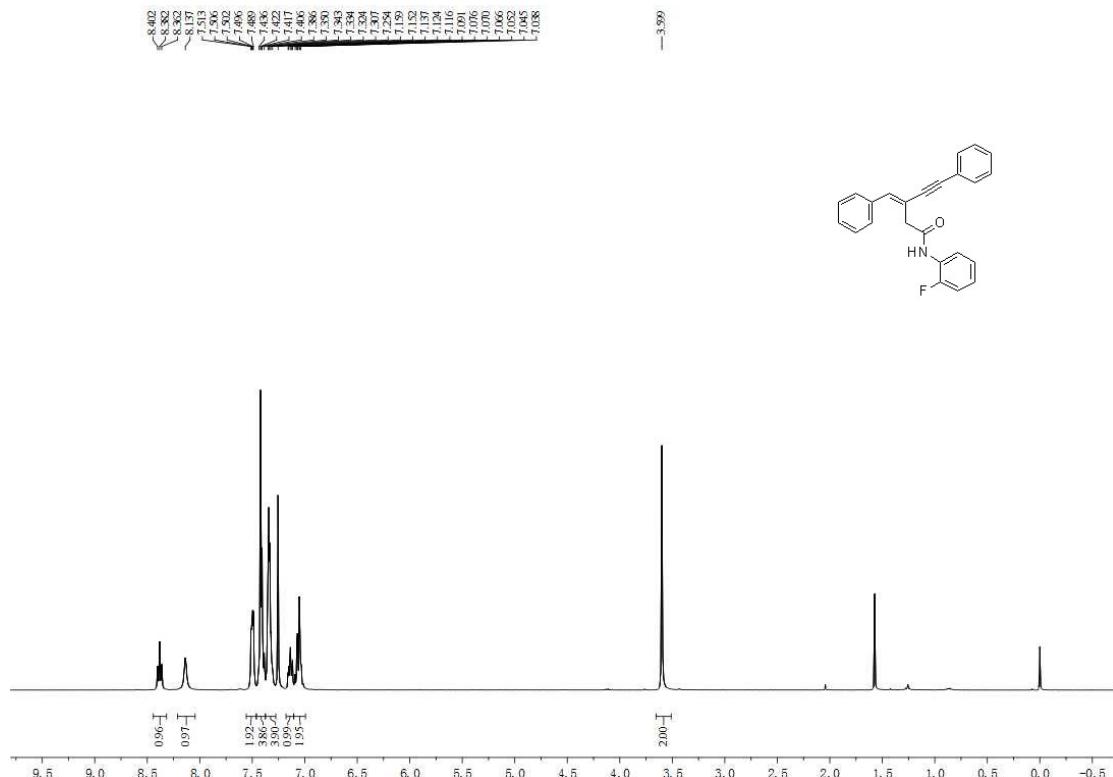
Product 4I



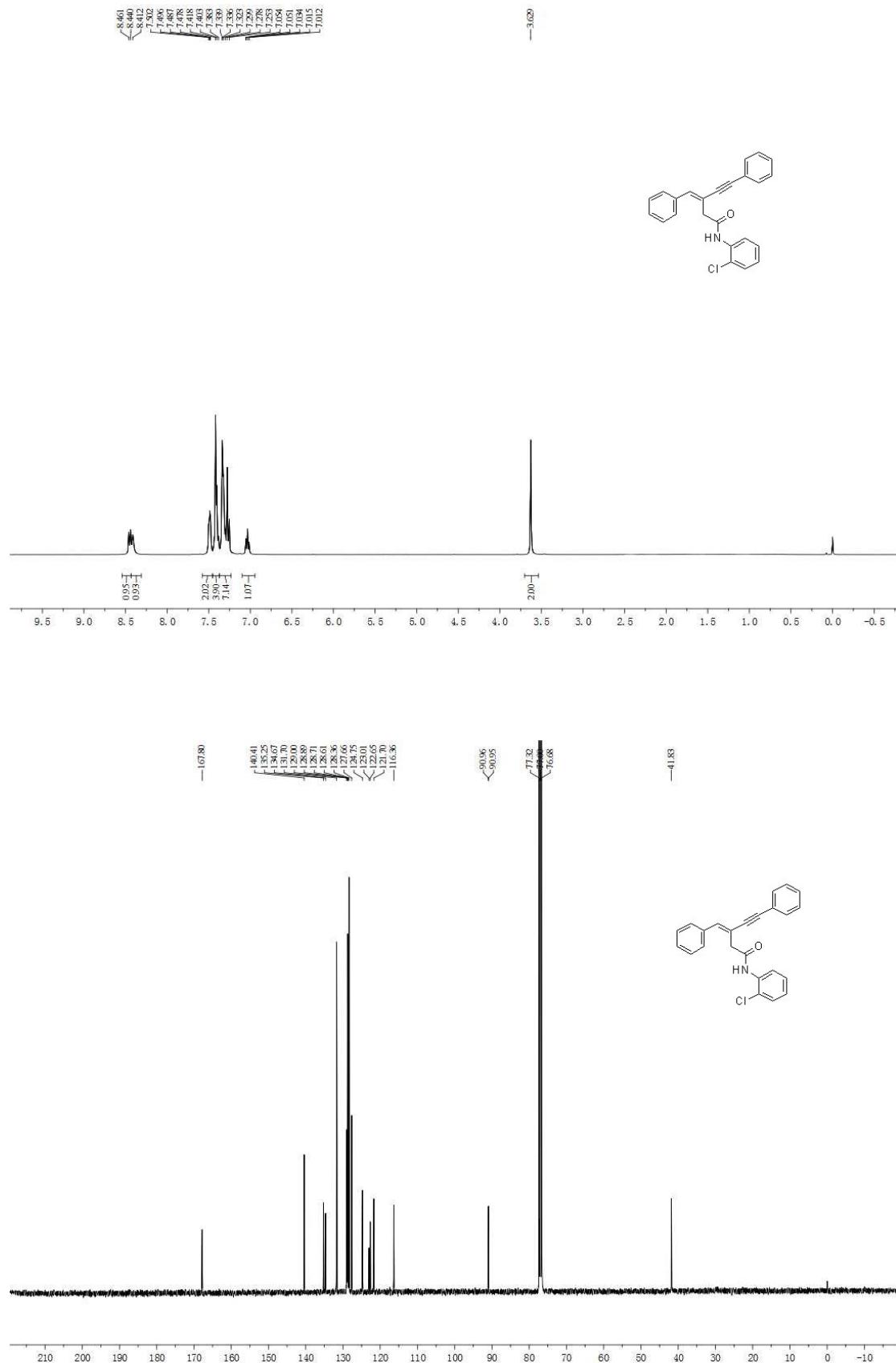
Product 4m



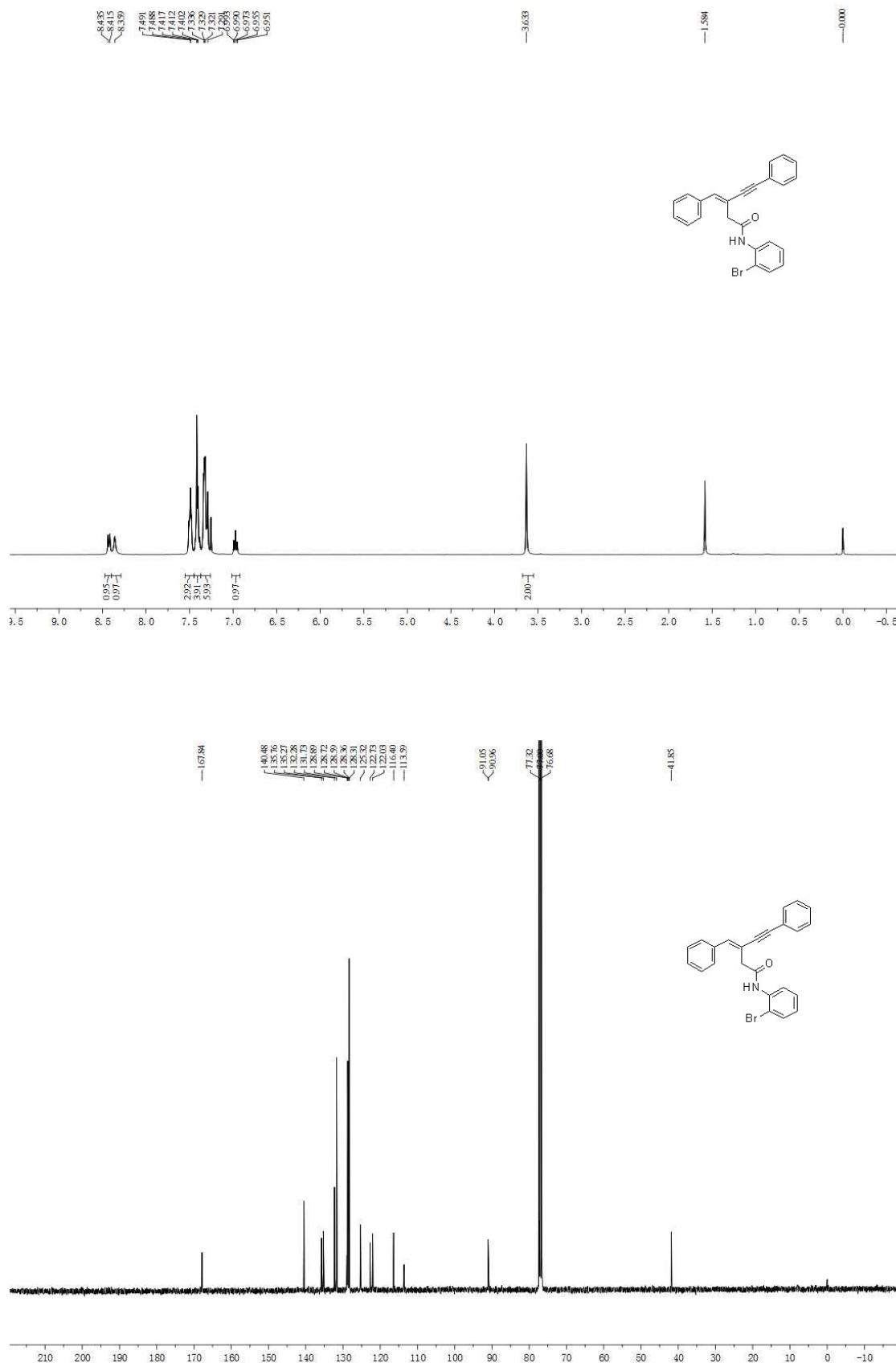
Product 4n



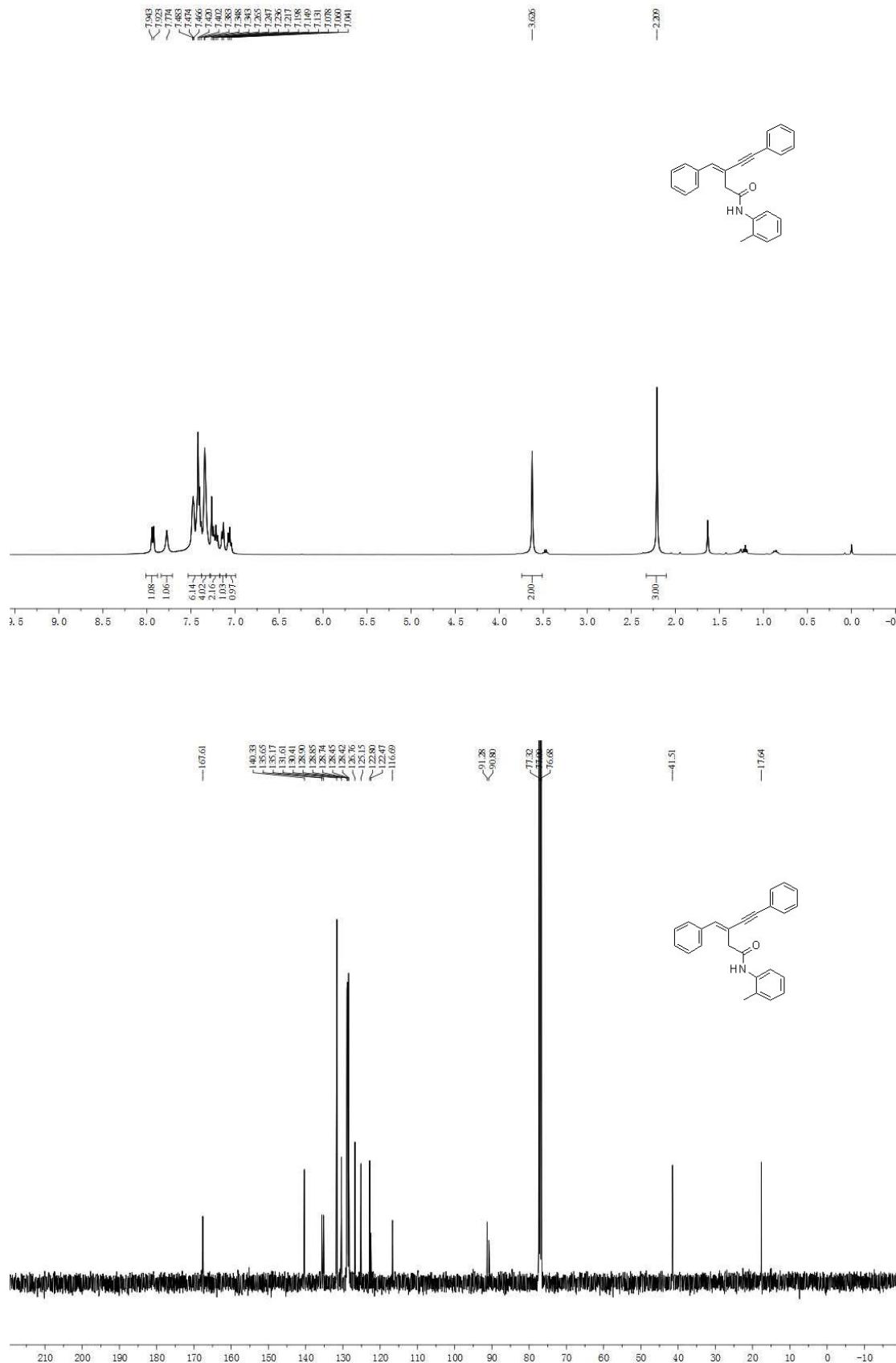
Product 4o



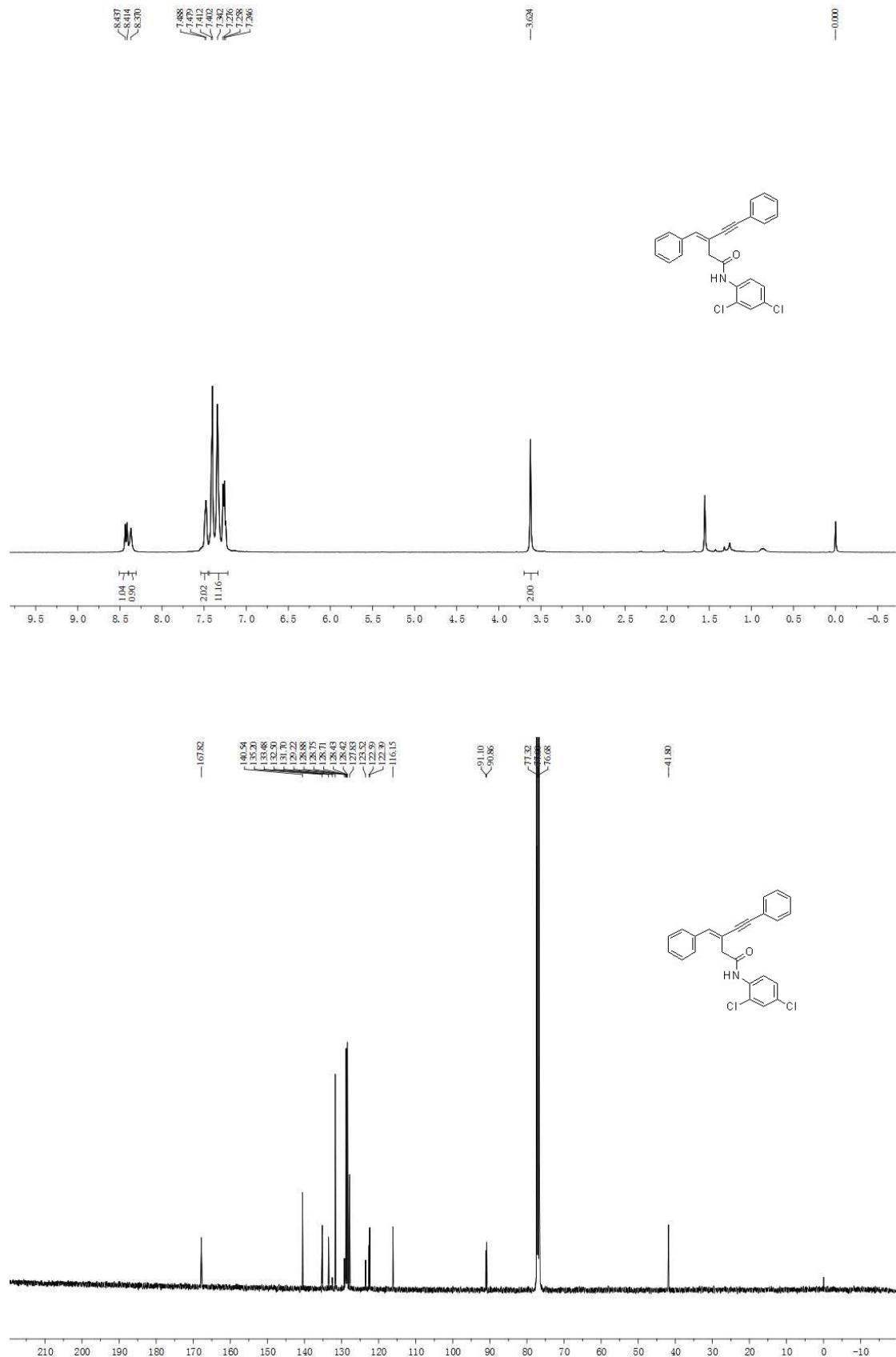
Product 4p



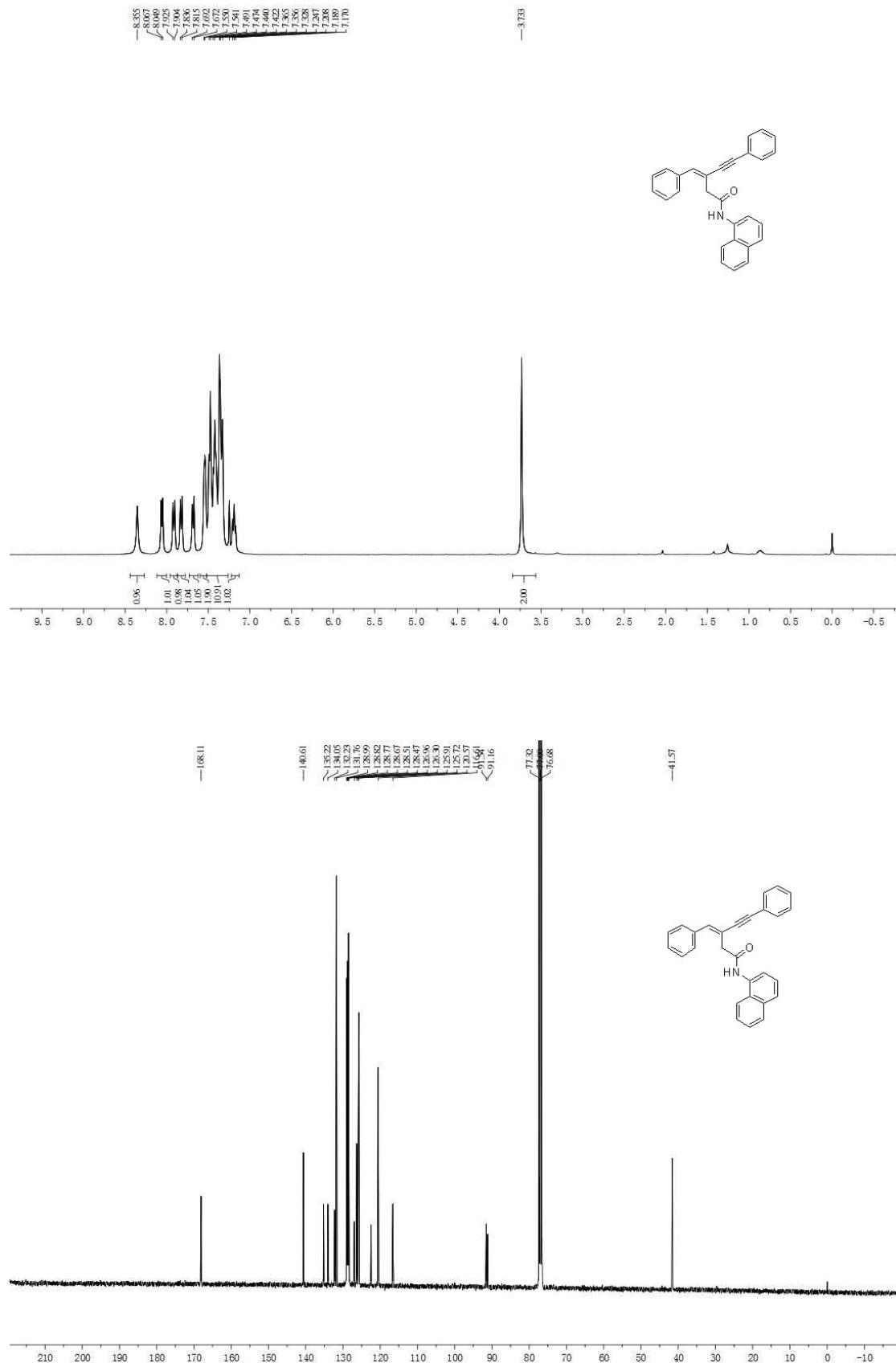
Product 4q



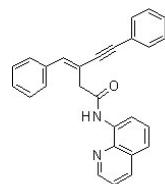
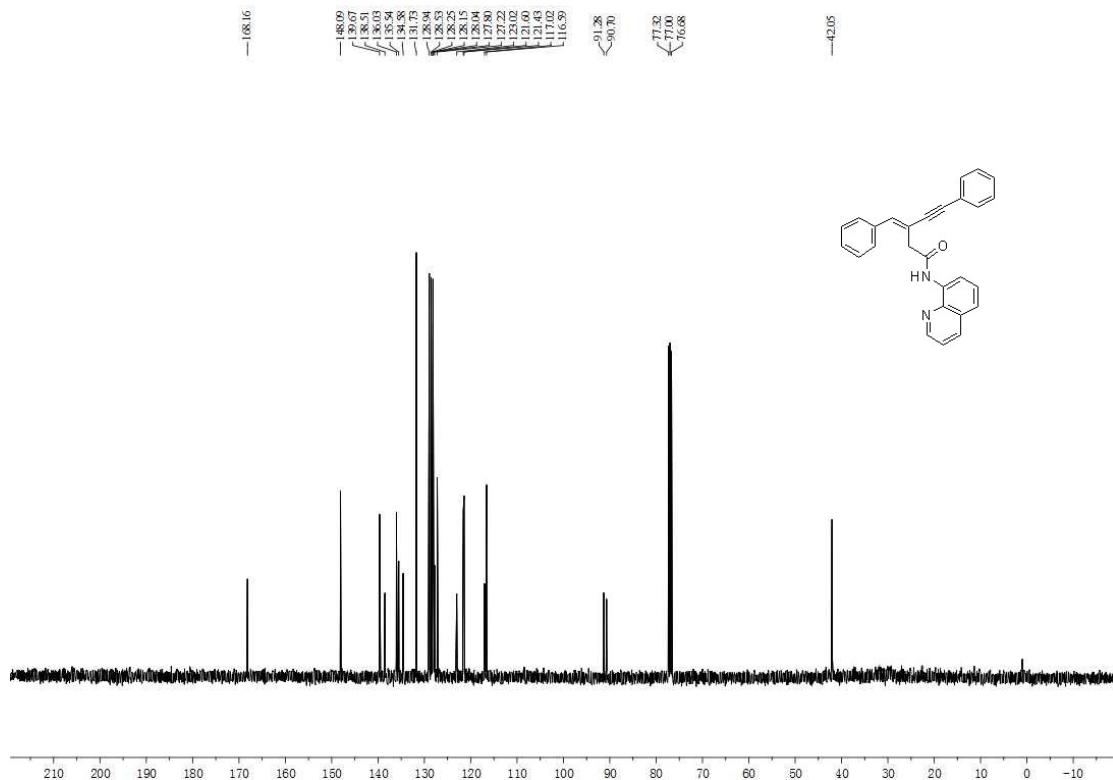
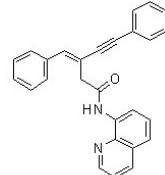
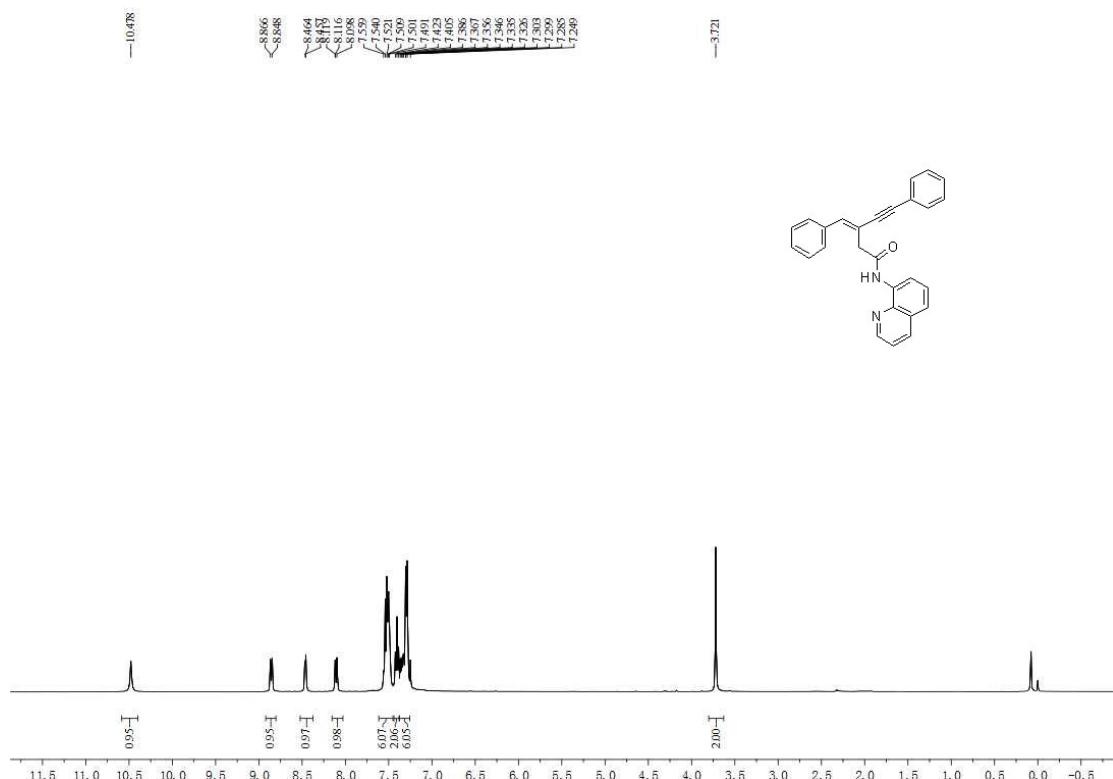
Product 4r



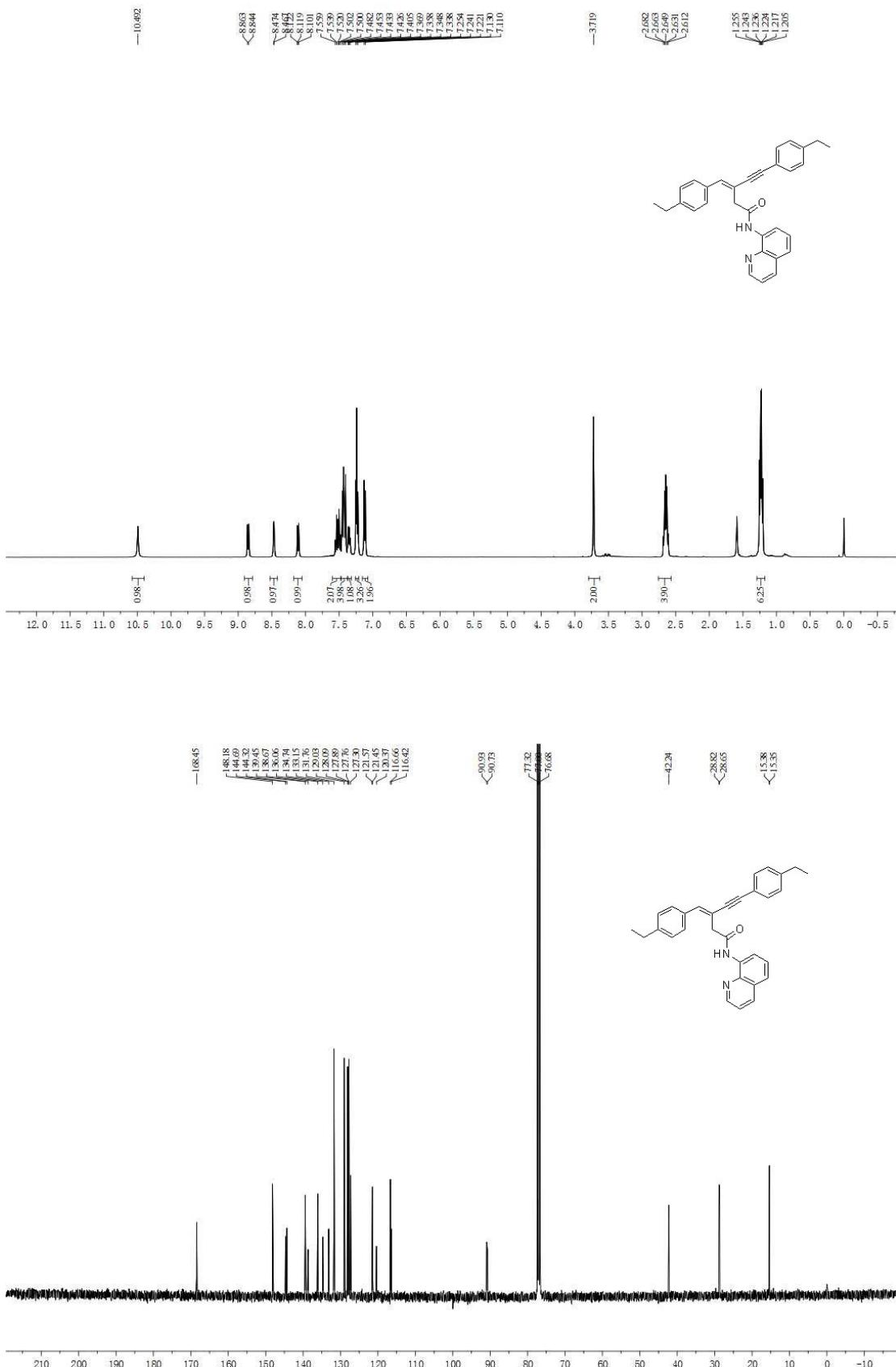
Product 4s



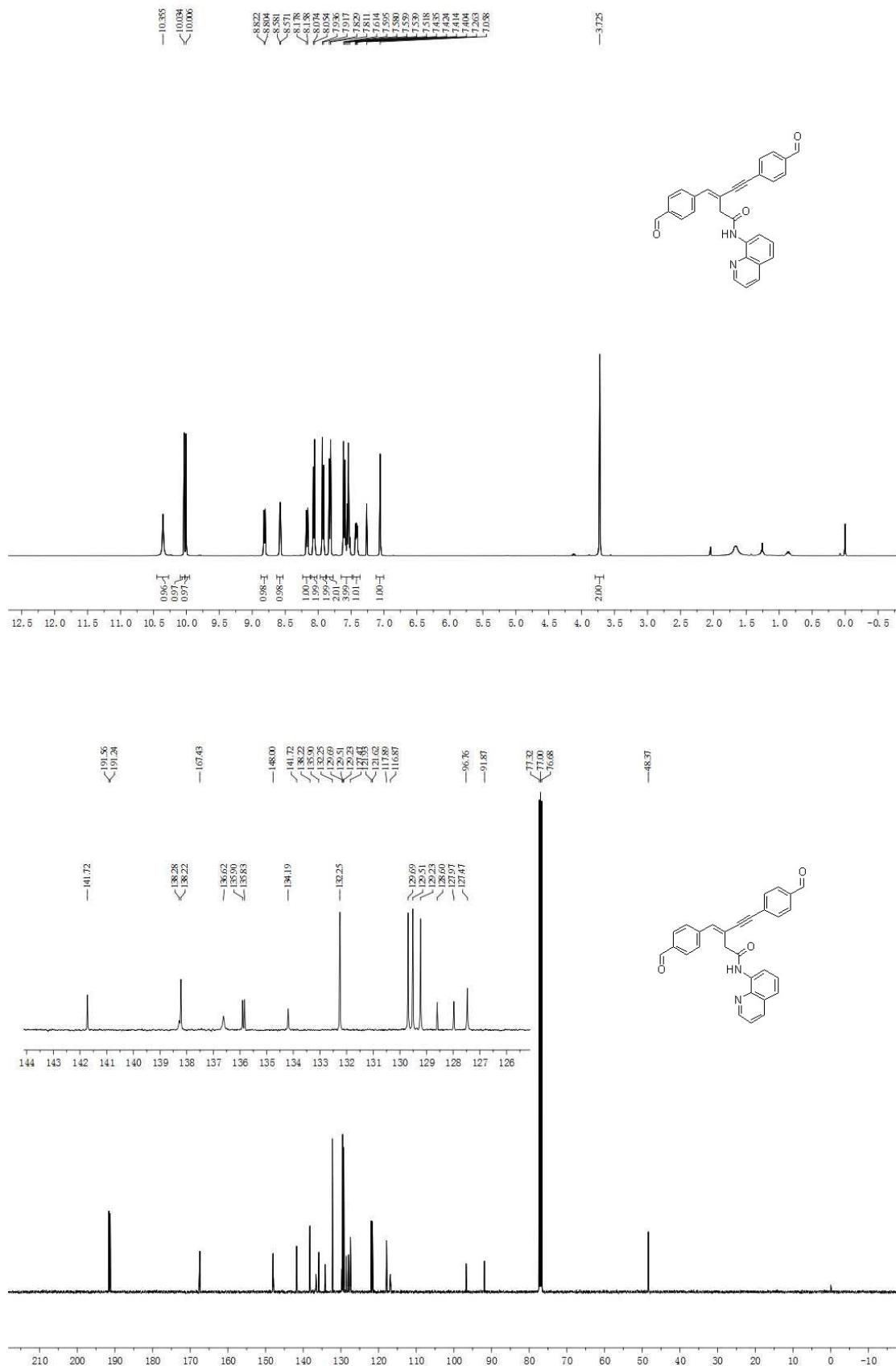
Product 4t



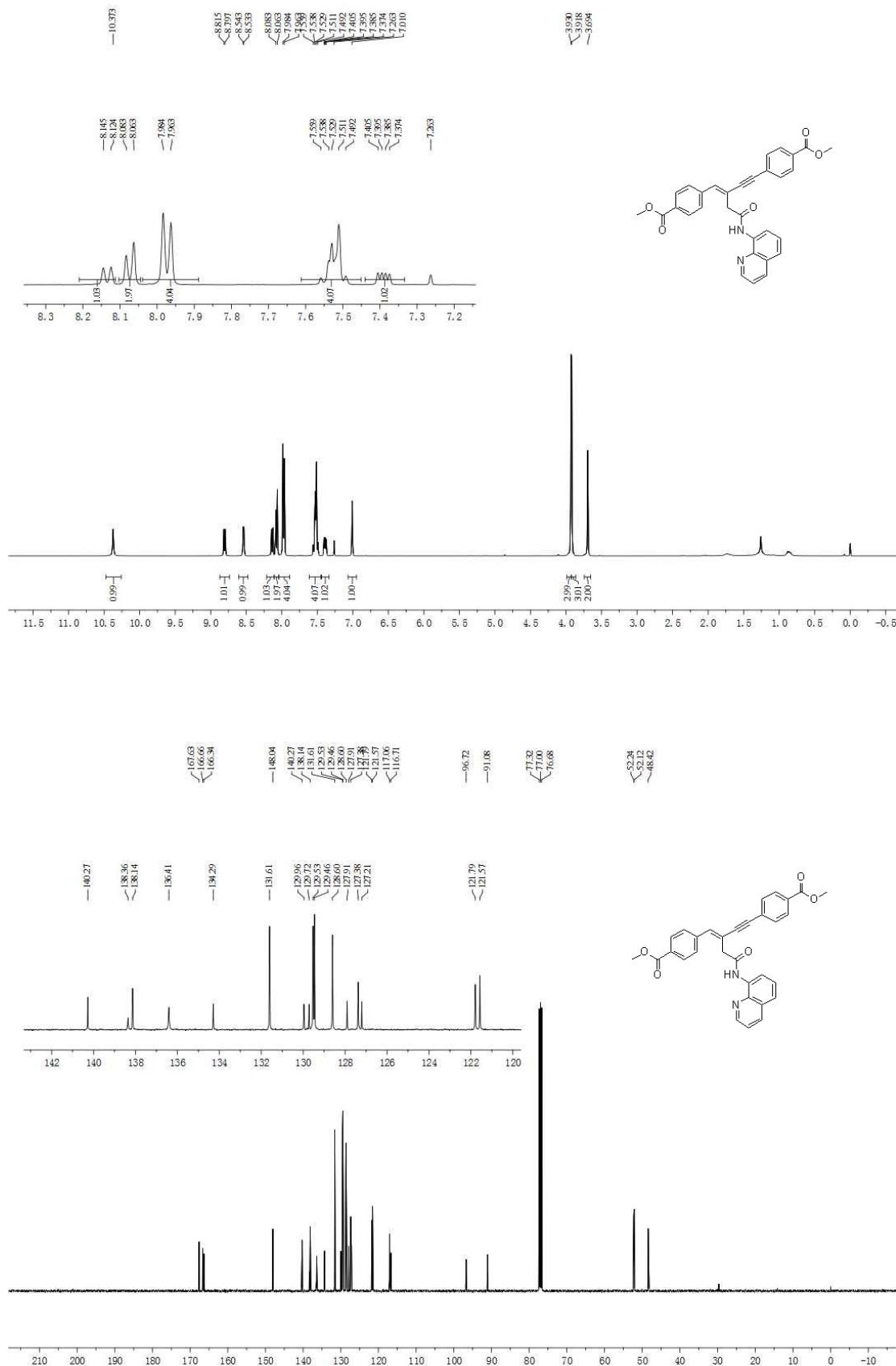
Product 4u



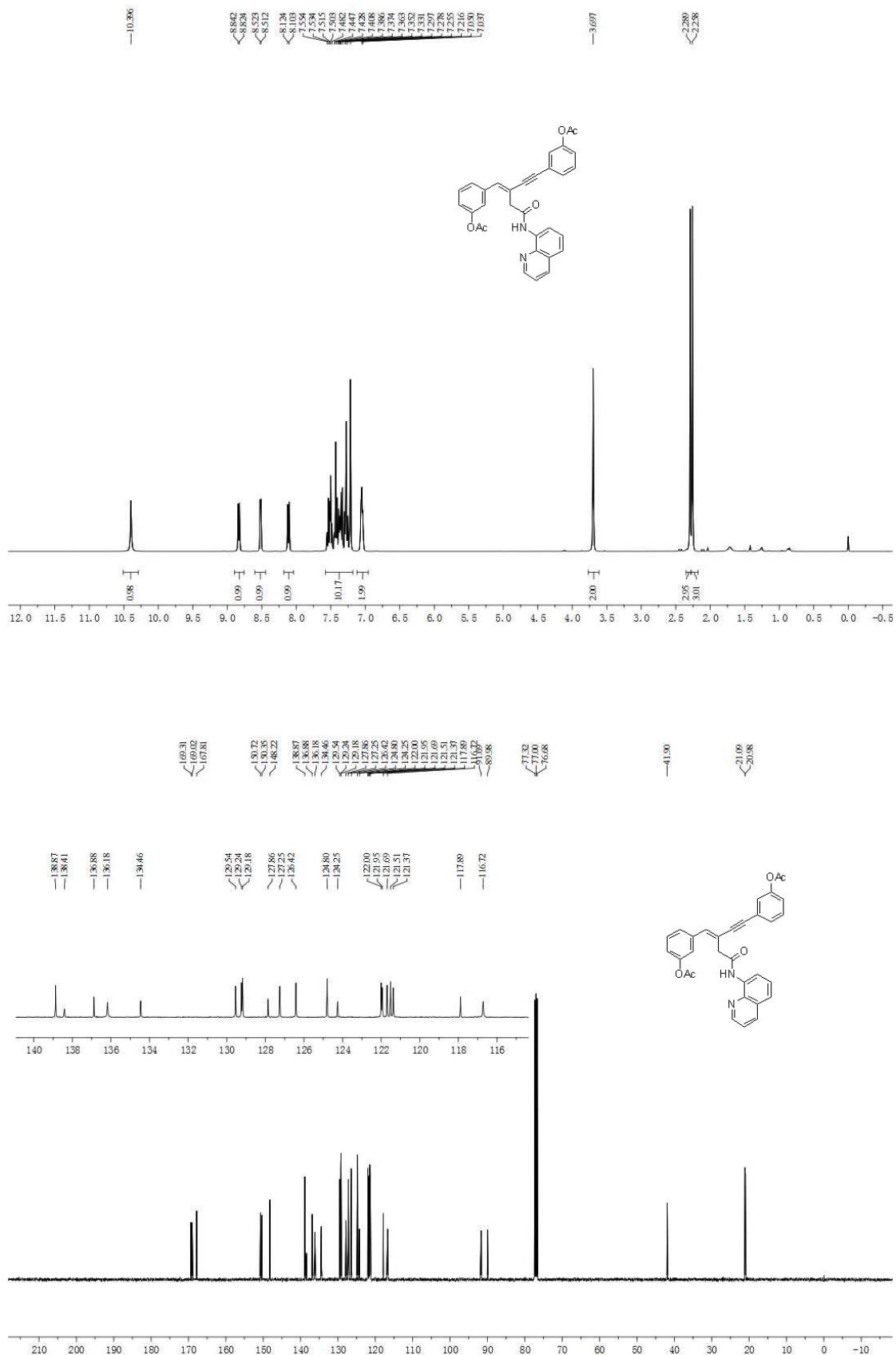
Product 4v



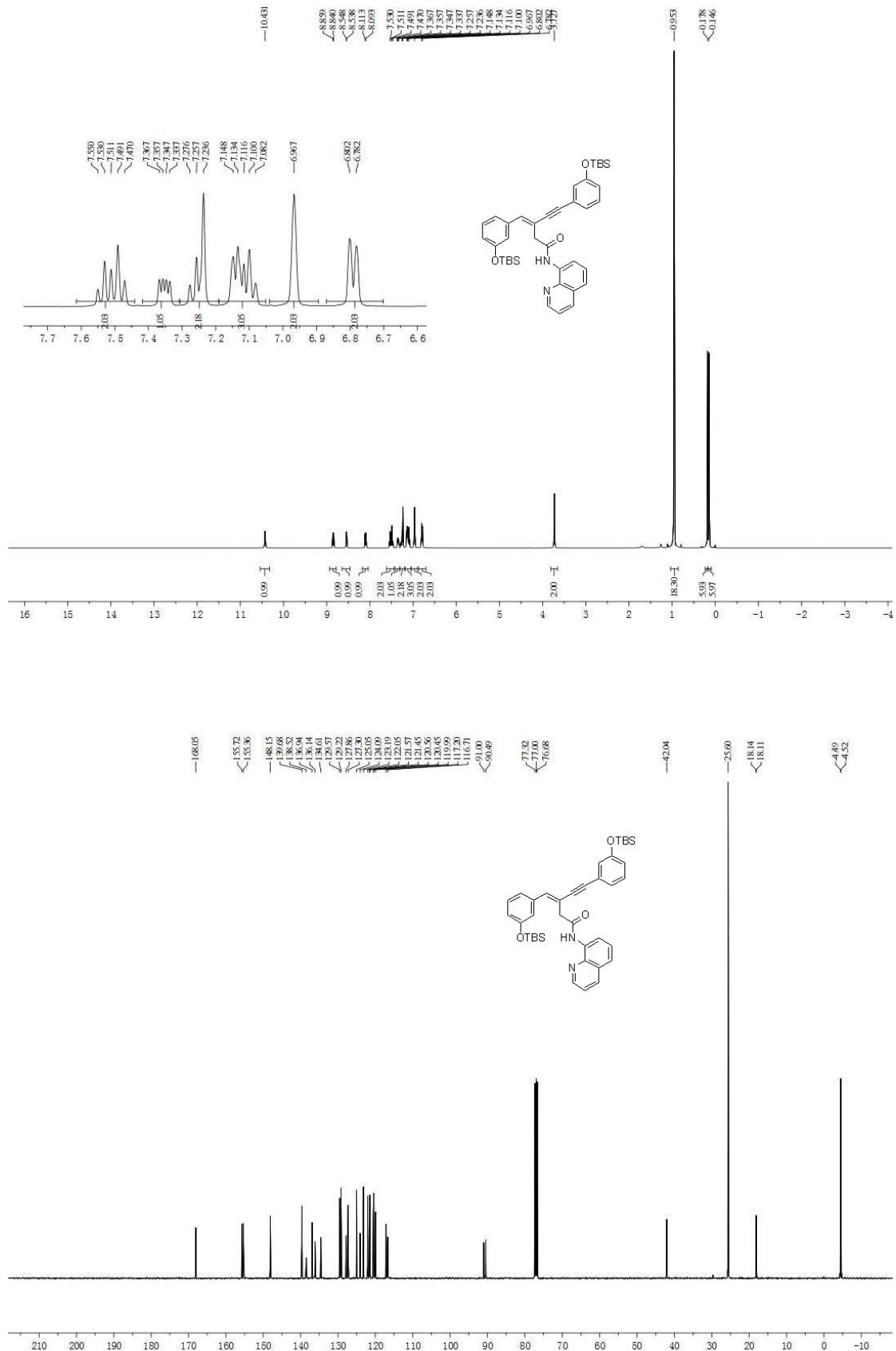
Product 4w



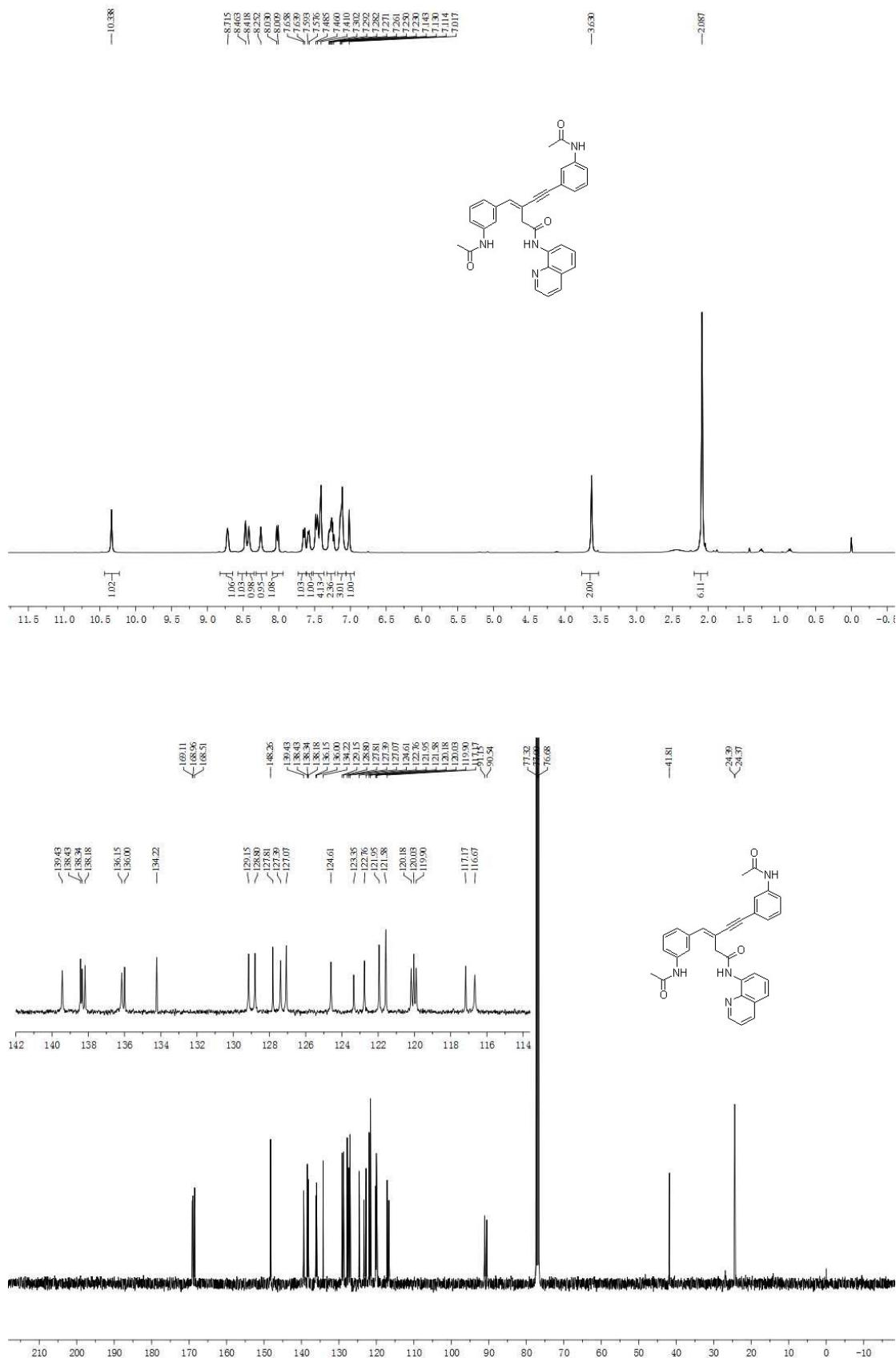
Product 4x



Product 4y



Product 4z



Product 4aa

