Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information for

First synthesis of novel 2,4-bis((*E*)-styryl)quinoline-3-carboxylate derivatives and their antitumor activity

Wentao Gao, Zhiyuan Li, Qiqi Xu and Yang Li*

Address:

Institute of Superfine Chemicals, Bohai University, Jinzhou 121000, P. R. China. E-mail: bhuzh@163.com

* Corresponding author

Content

Experimental

General methods

The chemicals used in this work were purchased from commercial suppliers and were used without further purification. Melting points (uncorrected) were determined by using a WRS-1B melting point apparatus. ^{1}H (400MHz) and ^{13}C (100MHz) NMR spectra were recorded on an Agilent 400-MR spectrometer using $CDCl_3$ or DMSO-d_6 as the solvent. The reported chemical shifts (δ values) are given in parts per million downfield from tetramethylsilane (TMS) as the internal standard (NMR abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet, J = coupling constant). Elemental analyses were carried out on an EA 2400II elemental analyzer (Perkin Elmer). HRMS (ESI) data were acquired on a Bruker Customer micrOTOF-Q 125 high resolution mass spectrometer using ESI ionization. The progress of reactions was monitored by thin-layer chromatography (TLC) on silica gel GF254 using ethyl acetate/petroleum ether as eluent.

Procedure for the preparation of ethyl 4-(bromomethyl)-2-(chloromethyl) quinoline-3-carboxylate (1).

o-Aminoacetophenone (**III**) (2.70 g, 20 mmol) and ethyl 4-chloro-3-oxobutanoate (3.30 g, 20 mmol) were added in a 100 ml reaction kettle and dissolved in DMF (40 ml). To this solution was added dropwise TMSCl (8.7 g, 80 mmol). The kettle was then sealed and heated at 100 °C for 10 h. After

cooling, the kettle was opened and the mixture separated into two layers; the upper one, the hexamethyldisiloxane, was decanted. And cold H_2O (20 mL) was added slowly to the residue with stirring. The resulting precipitate was filtered off and purified by recrystallization from *i*-PrOH to give pure ethyl 2-(chloromethyl)-4-methylquinoline-3-carboxylate (**IV**) in 76% yield. Subsequently, the newly-synthesized **IV** (3.96 g, 15 mmol) and a catalytic amount of benzoperoxide were dissolved in CCl_4 (70 mL) and heated with stirring until boiled gently. Then, a slightly excessive amount of NBS (1.85 g, 17 mmol) was added carefully in three batches to the stirred solution every 1.0 h. After addition of NBS was complete, the resulting reaction mixture was refluxed for 8 h. On completion as monitored by TLC, the reaction was cooled to room temperature, the precipitated succinimide was filtered, and the filtrate was evaporated under vacuum to dryness. The residue was subjected to column chromatography over silica gel (200–400 mesh) using hexane/ethyl acetate mixture as eluent (8:1, v/v) to give 3.91 g of **1**. White solid; yield 81%; mp 89-90 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.0 Hz, 1H, ArH), 8.01 (d, *J* = 8.0 Hz, 1H, ArH), 7.73 (t, *J* = 8.4 Hz, 1H, ArH), 7.58 (t, *J* = 8.0 Hz, 1H, ArH), 5.00 (s, 2H, $ArCH_2$), 4.93 (s, 2H, $ArCH_2$), 4.49 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 1.44 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.84, 153.52, 147.43, 142.10, 131.25, 130.31, 130.27, 128.58, 128.42, 123.87, 62.70, 46.23, 32.66, 14.10. Anal. Calcd for $C_{14}H_{13}BrClNO_2$: C, 49.08; H, 3.82; N, 4.09. Found: C, 48.84; H, 3.56; N, 4.37.

General procedure for the preparation of ethyl 2,4-di((*E*)-styryl) quinoline-3-carboxylate derivatives (3a-t).

Ethyl 4-(bromomethyl)-2-(chloromethyl)quinoline-3-carboxylate (**1**) (0.343 g, 1 mmol) was dissolved in triethyl phosphite (8 mL). The resulting reaction mixture was stirred at refluxing temperature for 3 h. The conversion was monitored by TLC. After TLC indicated the complete consumption of starting meterial, the excessive triethyl phosphite was removed in vacuo, and a solution of respective aldehyde (2.2 mmol) in DMF (8 mL) and NaH (0.053 g, 2.2 mmol) were added to the residue. The resulting reaction mixture was first stirred at room temperature for 1 h and then at 90 ^{o}C for 2 h. After the reaction was complete as inferred through TLC, the reaction was quenched with 10 mL cold H_2O followed by acidification with 1 M HCl to pH = 6~7. The resulting crude product was subjected to column chromatography over silica gel (200–400 mesh) using hexane/ethyl acetate mixture as eluent (10:1, v/v) to give the desired products **3a-t**.

Characterization data for products 3a-t.

Ethyl 2,4-bis((*E*)-styryl)quinoline-3-carboxylate (3a): Yellow solid; yield 83%; mp 105-106 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.23 (d, *J* = 8.4 Hz, 1H, ArH), 8.11 (d, *J* = 8.4 Hz, 1H, ArH), 8.04 (d, *J* = 15.6 Hz, 1H, CH=), 7.87 (t, *J* = 7.6 Hz, 1H, ArH), 7.81 (d, *J* = 16.4 Hz, 1H, CH=), 7.71-7.74 (m, 4H, ArH),

7.66 (t, *J* = 7.6 Hz, 1H, ArH), 7.44-7.48 (m, 4H, ArH), 7.37-7.41 (m, 2H, ArH), 7.30 (d, *J* = 15.6 Hz, 1H, CH=), 6.99 (d, *J* = 16.4 Hz, 1H, CH=), 4.43 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 1.26 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.43, 150.67, 147.58, 142.84, 137.78, 136.33, 136.17, 131.53, 129.70, 129.59, 129.45, 129.34, 129.30, 125.98, 125.85, 124.99, 124.14, 122.81, 62.24, 14.53. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{28}H_{24}NO_2$: 406.1802; found: 406.1804.

Ethyl 2,4-bis((*E*)-2-methylstyryl)quinoline-3-carboxylate (3b): Yellow solid; yield 79%;, mp 112-113 °C. ^1H NMR (400 MHz, DMSO-d_6): δ 8.27 (d, *J* = 8.4 Hz, 1H, ArH), 8.26 (d, *J* = 15.6 Hz, 1H, CH=), 8.11 (d, *J* = 8.4 Hz, 1H, ArH), 7.65-7.73 (m, 3H, ArH), 7.85-7.90 (m, 2H, ArH), 7.27-7.33 (m, 6H, ArH), 7.21 (d, *J* = 16.4 Hz, 1H, CH=), 7.18 (d, *J* = 15.6 Hz, 1H, CH=), 4.40 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 2.49 (s, 3H, Me), 2.36 (s, 3H, Me), 1.24 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.64, 150.81, 147.51, 143.08, 137.07, 136.37, 135.40, 135.14, 135.08, 133.68, 131.52, 131.18, 130.98, 129.79, 129.36, 129.20, 127.67, 126.95, 126.83, 126.21, 126.15, 125.95, 125.85, 125.38, 125.03, 123.83, 62.27, 20.07, 19.71, 14.43. Anal. Calcd for $C_{14}H_{13}BrClNO_2$: C, 49.08; H, 3.82; N, 4.09. Found: C, 48.84; H, 3.56; N, 4.37.

Ethyl 2,4-bis((*E*)-4-methylstyryl)quinoline-3-carboxylate (3c): Yellow solid; yield 85%; mp 115-116 °C. ^1H NMR (400 MHz, DMSO-d_6): δ 8.19 (d, *J* = 8.0 Hz, 1H, ArH), 8.08 (d, *J* = 8.4 Hz, 1H, ArH), 8.00 (d, *J* = 15.6 Hz, 1H, CH=), 7.84 (t, *J* = 7.6 Hz, 1H, ArH), 7.72 (d, *J* = 16.4 Hz, 1H, CH=), 7.58-7.65 (m, 5H,

ArH), 7.25 (d, *J* = 7.6 Hz, 4H, ArH), 7.22 (d, *J* = 15.6 Hz, 1H, CH=), 6.94 (d, *J* = 16.4 Hz, 1H, CH=), 4.41 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 2.34 (s, 6H, 2×Me), 1.25 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.55, 150.80, 147.60, 142.80, 139.27, 138.92, 137.67, 136.10, 133.64, 133.45, 131.39, 130.02, 129.86, 129.64, 127.85, 127.48, 127.40, 125.89, 125.74, 124.95, 123.10, 121.67, 62.15, 21.40, 14.53; Anal. Calcd for $C_{30}H_{27}NO_2$: C, 83.11; H, 6.28; N, 3.23. Found: C, 83.34; H, 6.53; N, 3.08.

Ethyl 2,4-bis((*E*)-2-methoxystyryl)quinoline-3-carboxylate (3d): Yellow solid; yield 76%; mp 136-137 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.26 (d, *J* = 15.6 Hz, 1H, CH=), 8.22 (d, *J* = 8.0 Hz, 1H, ArH), 8.10 (d, *J* = 8.4 Hz, 1H, ArH), 7.83-7.87 (m, 2H, ArH), 7.78 (d, *J* = 16.4 Hz, 1H, CH=), 7.62-7.68 (m, 2H, ArH), 7.40 (d, *J* = 15.6 Hz, 1H, CH=), 7.34-7.38 (m, 2H, ArH), 7.31 (d, *J* = 16.4 Hz, 1H, CH=), 7.02-7.13 (m, 4H, ArH), 4.42 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 3.92 (s, 3H, OMe), 3.86 (s, 3H, OMe), 1.29 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.70, 158.00, 157.27, 151.16, 147.59, 142.71, 132.39, 131.42, 131.37, 130.90, 130.78, 129.71, 128.51, 127.50, 127.45, 125.82, 125.75, 124.90, 124.80, 124.78, 124.61, 122.79, 121.28, 121.15, 112.11, 111.96, 62.10, 55.99, 14.34. Anal. Calcd for $C_{30}H_{27}NO_4$: C, 77.40; H, 5.85; N, 3.01. Found: C, 77.57; H, 5.71; N, 3.24.

Ethyl 2,4-bis((*E*)-4-methoxystyryl)quinoline-3-carboxylate (3e): Yellow solid; yield 80%; mp 140-141 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.20 (d, *J* = 8.4 Hz, 1H, ArH), 8.06 (d, *J* = 8.4 Hz, 1H, ArH), 7.99 (d, *J* = 15.6 Hz, 1H, CH=),

7.83 (t, *J* = 7.6 Hz, 1H, ArH), 7.60-7.67 (m, 6H, ArH), 7.12 (d, *J* = 15.6 Hz, 1H, CH=), 7.01 (d, *J* = 8.4 Hz, 2H, ArH), 6.99 (d, *J* = 8.8 Hz, 2H, ArH), 6.93 (d, *J* = 16.4 Hz, 1H, CH=), 4.42 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 3.81 (s, 6H, 2×OMe), 1.26 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.68, 160.53, 160.29, 150.96, 147.63, 142.81, 137.39, 135.81, 131.31, 129.56, 129.44, 129.06, 129.02, 128.84, 127.20, 125.90, 125.61, 124.89, 121.70, 120.19, 114.88, 114.68, 62.12, 55.67, 55.66, 14.56. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{30}H_{28}NO_4$: 466.2013; found: 466.2018.

Ethyl 2,4-bis((*E*)-4-ethoxystyryl)quinoline-3-carboxylate (3f): Yellow solid; yield 71%; mp 145-146 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.20 (d, *J* = 8.4 Hz, 1H, ArH), 8.06 (d, *J* = 8.4 Hz, 1H, ArH), 7.98 (d, *J* = 15.6 Hz, 1H, CH=), 7.83 (t, *J* = 7.6 Hz, 1H, ArH), 7.59-7.64 (m, 6H, ArH), 7.11 (d, *J* = 15.6 Hz, 1H, CH=), 6.98 (d, *J* = 7.6 Hz, 4H, ArH), 6.93 (d, *J* = 16.4 Hz, 1H, CH=), 4.42 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 4.06 (q, *J* = 7.2 Hz, 4H, 2×OCH_2CH_3), 1.34 (t, *J* = 7.2 Hz, 6H, 2×OCH_2CH_3), 1.26 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.68, 159.84, 159.59,150.97, 147.61, 142.83, 137.43, 135.85, 131.34, 129.55, 129.46, 129.04, 128.92, 128.68, 127.21,125.92, 125.59, 124.89, 121.59, 120.10, 115.29, 115.10, 63.62, 63.59, 62.12, 19.00, 15.05, 14.56. Anal. Calcd for $C_{32}H_{31}NO_4$: C, 77.87; H, 6.33; N, 2.84. Found: C, 78.16; H, 6.13; N, 2.73.

Ethyl 2,4-bis((*E*)-2,4-dimethylstyryl)quinoline-3-carboxylate (3g): Yellow solid; yield 84%; mp 132-133 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.24 (d, *J* =

8.4 Hz, 1H, ArH), 8.21 (d, *J* = 15.6 Hz, 1H, CH=),8.09 (d, *J* = 8.4 Hz, 1H, ArH), 7.85 (t, *J* = 7.6 Hz, 1H, ArH), 7.79 (d, *J* = 8.0 Hz, 1H, ArH), 7.67 (d, *J* = 15.6 Hz, 1H, CH=),7.65 (s, 1H, ArH), 7.57 (d, *J* = 7.6 Hz, 1H, ArH), 7.07-7.18 (m, 6H, ArH), 4.38 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 2.44 (s, 3H, Me), 2.32 (s, 3H, Me), 2.30 (s, 6H, 2×Me), 1.22 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.75, 150.95, 147.52, 143.06, 138.93, 138.67, 136.95, 136.23, 135.24, 133.56, 132.33, 132.25, 131.83, 131.60, 131.41, 129.74, 127.63, 127.50, 126.11, 125.87, 125.75, 124.98, 124.31, 122.68, 62.20, 21.27, 21.24, 19.99, 19.61, 14.42. Anal. Calcd for $C_{32}H_{31}NO_2$: C, 83.26; H, 6.77; N, 3.03. Found: C, 82.98; H, 6.88; N, 3.32.

Ethyl 2,4-bis((*E*)-3,4-dimethoxystyryl)quinoline-3-carboxylate (3h): Yellow solid; yield 79%; mp 116-117 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.24 (d, *J* = 8.4 Hz, 1H, ArH), 8.06 (d, *J* = 8.4 Hz, 1H, ArH), 7.98 (d, *J* = 15.6 Hz, 1H, CH=), 7.84 (t, *J* = 7.6 Hz, 1H, ArH), 7.70 (d, *J* = 16.4 Hz, 1H, CH=), 7.64 (t, *J* = 7.6 Hz, 1H, ArH), 7.42 (d, *J* = 1.2 Hz, 1H, ArH), 7.25-7.28 (m, 2H, ArH), 7.14 (d, *J* = 15.6 Hz, 1H, CH=), 7.13 (d, *J* = 1.2 Hz, 1H, ArH), 7.02 (d, *J* = 8.4 Hz, 1H, ArH), 6.99 (d, *J* = 8.4 Hz, 1H, ArH), 6.93 (d, *J* = 16.4 Hz, 1H, CH=), 4.44 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 3.87 (s, 3H, OMe), 3.85 (s, 3H, OMe), 3.81 (s, 3H, OMe), 3.80 (s, 3H, OMe), 1.31 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.68, 151.02, 150.32, 150.13, 149.46, 149.37, 147.66, 142.84, 137.83, 136.22, 131.34, 129.54, 129.32, 129.07, 127.18, 125.99, 125.61, 124.91, 121.96, 121.59, 121.39, 120.37, 112.27, 111.99, 110.61,

109.76, 62.13, 56.06, 55.96, 55.94, 55.86, 14.58. Anal. Calcd for $C_{32}H_{31}NO_6$: C, 73.13; H, 5.94; N, 2.66. Found: C, 72.98; H, 5.87; N, 2.74.

Ethyl 2,4-bis((*E*)-2,5-dimethoxystyryl)quinoline-3-carboxylate (3i): Yellow solid; yield 80%; mp 125-126 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.25 (d, *J* = 8.4 Hz, 1H, ArH), 8.20 (d, *J* = 15.6 Hz, 1H, CH=), 8.09 (d, *J* = 8.4 Hz, 1H, ArH), 7.86 (t, *J* = 7.6 Hz, 1H, ArH), 7.84 (d, *J* = 16.4 Hz, 1H, CH=), 7.65 (t, *J* = 7.6 Hz, 1H, ArH), 7.46 (d, *J* = 2.8 Hz, 1H, ArH), 7.38 (d, *J* = 15.6 Hz, 1H, CH=), 7.29 (d, *J* = 16.4 Hz, 1H, CH=), 7.20 (d, *J* = 2.8 Hz, 1H, ArH), 7.05 (d, *J* = 8.8 Hz, 1H, ArH), 7.02 (d, *J* = 8.8 Hz, 1H, ArH), 6.96 (d, *J* = 8.8 Hz, 1H, ArH), 6.94 (d, *J* = 8.4 Hz, 1H, ArH), 4.42 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 3.87 (s, 3H, OMe), 3.81 (s, 3H, OMe), 3.80 (s, 3H, OMe), 3.78 (s, 3H, OMe), 1.31 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.65, 153.78, 153.64, 152.41, 151.66, 151.15, 147.59, 142.75, 132.10, 131.40, 131.36, 129.69, 127.45, 125.86, 125.82, 125.41, 125.32, 125.25, 124.94, 123.10, 116.12, 113.28, 113.22, 112.14, 62.09, 56.47, 56.38, 56.02, 55.83, 14.34. Anal. Calcd for $C_{32}H_{31}NO_6$: C, 73.13; H, 5.94; N, 2.66. Found: C, 73.34; H, 6.08; N, 2.51.

Ethyl 2,4-bis((*E*)-2-(benzo[d][1,3]dioxol-5-yl)vinyl)quinoline-3-carboxylate (3j): Yellow solid; yield 75%; mp 163-164 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.21 (d, *J* = 8.4 Hz, 1H, ArH), 8.06 (d, *J* = 8.4 Hz, 1H, ArH), 7.94 (d, *J* = 15.6 Hz, 1H, CH=), 7.84 (t, *J* = 7.2 Hz, 1H, ArH), 7.67 (d, *J* = 16.4 Hz, 1H, CH=), 7.62 (d, *J* = 8.4 Hz, 1H, ArH), 7.35 (s, 1H, ArH), 7.51 (s, 1H, ArH), 7.21 (d, *J* = 8.4 Hz, 1H, ArH), 7.11 (d, *J* = 15.6 Hz, 1H, CH=), 7.08 (d, *J* = 8.0 Hz, 1H, ArH),

6.96-7.00 (m, 2H, ArH), 6.89 (d, *J* = 16.4 Hz, 1H, CH=), 6.10 (s, 4H, 2×OCH_2O), 4.42 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 1.26 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.51, 150.92, 148.67, 148.47, 148.39, 147.58, 142.77, 137.44, 135.99, 131.38, 130.92, 130.70, 129.56, 127.28, 125.95, 125.63, 124.92, 123.67, 123.34, 122.34, 120.81, 109.10, 108.86, 106.67, 106.22, 101.85, 101.79, 62.17, 14.53. Anal. Calcd for $C_{30}H_{23}NO_6$: C, 73.01; H, 4.70; N, 2.84. Found: C, 73.22; H, 4.77; N, 2.70.

Ethyl 2,4-bis((*E*)-3,4,5-trimethoxystyryl)quinoline-3-carboxylate (3k): Yellow solid; yield 77%; mp 125-126 °C. ^1H NMR (400 MHz, DMSO-d_6): δ 8.25 (d, *J* = 8.4 Hz, 1H, ArH), 8.08 (d, *J* = 8.4 Hz, 1H, ArH), 7.98 (d, *J* = 15.6 Hz, 1H, CH=), 7.87 (t, *J* = 8.0 Hz, 1H, ArH), 7.79 (d, *J* = 16.4 Hz, 1H, CH=), 7.67 (t, *J* = 7.6 Hz, 1H, ArH), 7.21 (d, *J* = 15.6 Hz, 1H, CH=), 7.04 (s, 2H, ArH), 7.02 (s, 2H, ArH), 6.93 (d, *J* = 16.4 Hz, 1H, CH=), 4.48 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 3.87 (s, 12H, 4×OMe), 3.71 (s, 6H, 2×OMe), 1.36 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.44, 153.58, 153.56, 150.82, 147.64, 142.80, 138.87, 138.63, 137.99, 136.35, 132.08, 131.85, 131.50, 129.59, 127.45, 126.06, 125.78, 124.95, 123.62, 122.15, 105.21, 104.99, 62.23, 60.55, 56.44, 56.31, 14.60. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{34}H_{36}NO_8$: 586.2435; found: 586.2439.

Ethyl 2,4-bis((*E*)-2,4,5-trimethoxystyryl)quinoline-3-carboxylate (3l): Yellow solid; yield 70%; mp 113-114 °C. ^1H NMR (400 MHz, DMSO-d_6): δ 8.26 (d, *J* = 8.4 Hz, 1H, ArH), 8.18 (d, *J* = 15.6 Hz, 1H, CH=), 8.05 (d, *J* = 8.0

Hz, 1H, ArH), 7.82 (t, *J* = 7.6 Hz, 1H, ArH), 7.70 (d, *J* = 16.4 Hz, 1H, CH=), 7.62 (t, *J* = 7.6 Hz, 1H, ArH), 7.47 (s, 1H, ArH), 7.30 (d, *J* = 15.6 Hz, 1H, CH=), 7.22 (d, *J* = 15.6 Hz, 1H, CH=), 7.19 (s, 1H, ArH), 6.78 (s, 1H, ArH), 6.75 (s, 1H, ArH), 4.43 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 3.92 (s, 3H, OMe), 3.87 (s, 3H, OMe), 3.86 (s, 3H, OMe), 3.85 (s, 3H, OMe), 3.84 (s, 3H, OMe), 3.80 (s, 3H, OMe), 1.34 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.98, 153.35, 152.47, 151.64, 151.32, 151.29, 147.66, 143.52, 143.30, 142.83, 131.86, 131.25, 131.17, 129.51, 126.91, 125.83, 125.47, 124.83, 122.36, 119.78, 116.26, 115.99, 111.67, 110.48, 98.31, 98.27, 61.93, 56.80, 56.77, 56.65, 56.44, 56.22, 56.19, 14.38. Anal. Calcd for $C_{34}H_{35}NO_8$: C, 69.73; H, 6.02; N, 2.39. Found: C, 69.44; H, 5.91; N, 2.45.

Ethyl 2,4-bis((*E*)-2,6-dichlorostyryl)quinoline-3-carboxylate (3m): Yellow solid; yield 78%; mp 161-162 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.28 (d, *J* = 8.0 Hz, 1H, ArH), 8.15 (d, *J* = 8.4 Hz, 1H, ArH), 8.09 (d, *J* = 16.0 Hz, 1H, CH=), 7.90 (t, *J* = 7.6 Hz, 1H, ArH), 7.73 (t, *J* = 7.6 Hz, 1H, ArH), 7.66 (d, *J* = 16.4 Hz, 1H, CH=), 7.58-7.63 (m, 4H, ArH), 7.37-7.43 (m, 3H, ArH), 6.94 (d, *J* = 16.4 Hz, 1H, CH=), 4.39 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 1.27 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 167.85, 149.63, 147.52, 142.06, 134.30, 134.03, 133.45, 133.17, 132.33, 131.86, 131.75, 131.60, 130.80, 130.69, 130.07, 129.70, 129.60, 129.47, 128.49, 126.09, 125.95, 124.99, 62.68, 14.31. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{28}H_{20}{}^{35}Cl_4NO_2$: 544.0214; found: 544.0290.

Ethyl 2,4-bis((*E*)-4-bromostyryl)quinoline-3-carboxylate (3n): Yellow solid; yield 84%; mp 121-122 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.20 (d, *J* = 8.0 Hz, 1H, ArH), 8.09 (d, *J* = 8.4 Hz, 1H, ArH), 7.98 (d, *J* = 15.6 Hz, 1H, CH=), 7.87 (t, *J* = 7.6 Hz, 1H, ArH), 7.83 (d, *J* = 16.4 Hz, 1H, CH=), 7.63-7.67 (m, 9H, ArH), 7.31 (d, *J* = 15.6 Hz, 1H, CH=), 6.94 (d, *J* = 16.4 Hz, 1H, CH=), 4.41 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 1.23 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.25, 150.50, 147.56, 142.77, 136.47, 135.60, 135.44, 134.91, 132.32, 132.20, 131.61, 129.87, 129.70, 129.53, 127.74, 126.01, 125.80, 125.00, 124.95, 123.85, 122.68, 122.46, 62.28, 14.52. Anal. Calcd for $C_{28}H_{21}Br_2NO_2$: C, 59.70; H, 3.76; N, 2.49. Found: C, 59.88; H, 3.58; N, 2.42.

Ethyl 2,4-bis((*E*)-2-(naphthalen-1-yl)vinyl)quinoline-3-carboxylate (3o): Yellow solid; yield 75%; mp 170-172 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.86 (d, *J* = 15.6 Hz, 1H, CH=), 8.34 (t, *J* = 7.6 Hz, 2H, ArH), 8.22 (d, *J* = 8.4 Hz, 1H, ArH), 8.18 (d, *J* = 8.0 Hz, 1H, ArH), 8.12 (d, *J* = 7.6 Hz, 1H, ArH), 8.00-8.04 (m, 4H, ArH), 7.89-7.96 (m, 3H, ArH), 7.81 (d, *J* = 16.0 Hz, 1H, CH=), 7.55-7.73 (m, 7H, ArH), 7.41 (d, *J* = 15.6 Hz, 1H, CH=), 4.40 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 1.19 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.77, 150.77, 147.63, 143.22, 134.70, 133.87, 133.76, 133.46, 133.36, 132.75, 131.63, 131.35, 131.05, 129.90, 129.80, 129.59, 129.20, 129.12, 127.84, 127.37, 127.21, 127.07, 126.71, 126.61, 126.38, 126.29, 126.07, 125.70, 125.20, 124.80, 124.71, 123.68, 123.55, 62.39, 14.42. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{36}H_{28}NO_2$: 506.2115; found: 506.2111.

Ethyl 2,4-bis((*E*)-2-(naphthalen-2-yl)vinyl)quinoline-3-carboxylate (3p): Yellow solid; yield 78%; mp 173-175 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.29 (d, *J* = 8.4 Hz, 1H, ArH), 8.23 (d, *J* = 8.8 Hz, 1H, ArH), 8.20 (s, 1H, ArH), 8.15 (d, *J* = 8.8 Hz, 1H, ArH), 8.12 (s, 1H, ArH), 8.06 (d, *J* = 8.4 Hz, 1H, ArH), 7.88-8.01 (m, 9H, ArH), 7.69 (t, *J* = 7.6 Hz, 1H, ArH), 7.55-7.58 (m, 4H, ArH), 7.45 (d, *J* = 15.6 Hz, 1H, CH=), 7.17 (d, *J* = 16.4 Hz, 1H, CH=), 4.47 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 1.27 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.53, 150.77, 147.67, 142.89, 137.79, 136.27, 133.96, 133.75, 133.63, 133.54, 131.59, 129.76, 129.09, 129.02, 128.88, 128.75, 128.63, 128.21, 128.11, 127.66, 127.23, 127.11, 126.03, 125.87, 125.04,124.52, 124.01, 123.32, 62.33, 14.53. Anal. Calcd for $C_{36}H_{27}NO_2$: C, 85.52; H, 5.38; N, 2.77. Found: C, 85.21; H, 5.54; N, 3.07.

Ethyl 2,4-bis((*E*)-2-(furan-2-yl)vinyl)quinoline-3-carboxylate (3q): Yellow solid; yield 76%; mp 160-161 ^{o}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.15 (d, *J* = 8.4 Hz, 1H, ArH), 8.04 (d, *J* = 8.4 Hz, 1H, ArH), 7.88 (d, *J* = 15.6 Hz, 1H, CH=), 7.83-7.86 (m, 3H, ArH), 7.63 (t, *J* = 7.6 Hz, 1H, ArH), 7.45 (d, *J* = 16.4 Hz, 1H, CH=), 7.04 (d, *J* = 15.6 Hz, 1H, CH=), 6.90 (d, *J* = 15.6 Hz, 1H, CH=), 6.88 (d, *J* = 3.6 Hz, 1H, ArH), 6.79 (d, *J* = 3.2 Hz, 1H, ArH), 6.62-6.65 (m, 2H, ArH), 4.43 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 1.29 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.47, 152.22, 151.83, 150.20, 147.68, 145.13, 144.75, 141.81, 131.52, 129.64, 127.61, 125.79, 125.65, 125.46, 124.60, 123.44, 121.23, 119.74, 114.01, 113.02, 112.75, 112.33, 62.27, 14.34. HRMS

(ESI): *m/z* $[M+H]^+$ calcd for $C_{24}H_{20}NO_4$: 386.1387; found: 386.1369.

Ethyl 2,4-bis((*E*)-2-(thiophen-2-yl)vinyl)quinoline-3-carboxylate (3r): Yellow solid; yield 72%; mp 164-166 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.19 (d, *J* = 15.6 Hz, 1H, CH=), 8.16 (d, *J* = 8.4 Hz, 1H, ArH), 8.06 (d, *J* = 8.4 Hz, 1H, ArH), 7.85 (t, *J* = 7.6 Hz, 1H, ArH), 7.63-7.66 (m, 3H, ArH), 7.50 (d, *J* = 3.2 Hz, 1H, ArH), 7.43 (d, *J* = 16.4 Hz, 1H, CH=), 7.40 (d, *J* = 3.6 Hz, 1H, ArH), 7.19 (d, *J* = 16.4 Hz, 1H, CH=), 7.12-7.16 (m, 2H, ArH), 6.98 (d, *J* = 15.6 Hz, 1H, CH=), 4.44 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 1.33 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.38, 150.20, 147.71, 141.99, 141.41, 141.18, 131.57, 131.21, 130.60, 129.61, 129.30, 129.25, 128.96, 128.65, 128.05, 127.81, 127.61, 125.83, 125.41, 124.67, 122.86, 121.13, 62.29, 14.59. Anal. Calcd for $C_{24}H_{19}NO_2S_2$: C, 69.04; H, 4.59; N, 3.35. Found: C, 68.70; H, 4.89; N, 3.72.

Ethyl 2,4-bis((*E*)-2-(pyridin-2-yl)vinyl)quinoline-3-carboxylate (3s): Yellow solid; yield 73%; mp 170-172 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.66-8.68 (m, 2H, ArH), 8.13-8.20 (m, 3H, ArH), 8.06 (d, *J* = 15.6 Hz, 1H, CH=), 7.83-7.91 (m, 4H, ArH), 7.67-7.73 (m, 3H, ArH), 7.39 (d, *J* = 8.0 Hz, 1H, ArH), 7.35 (d, *J* = 8.0 Hz, 1H, ArH), 7.10 (d, *J* = 16.0 Hz, 1H, CH=), 4.42 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 1.25 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.24, 153.99, 153.93, 150.38, 150.24, 150.20, 147.66, 142.34, 137.60, 137.59, 137.53, 135.41, 131.70, 129.89, 128.11, 127.50, 126.27, 126.06, 125.81, 124.97, 124.83, 124.10, 124.05, 123.55, 62.31, 14.41. Anal.

Calcd for $C_{26}H_{21}N_3O_2$: C, 76.64; H, 5.19; N, 10.31. Found: C, 76.99; H, 4.94; N, 9.99.

Ethyl 2,4-bis((*E*)-ferrocenylvinyl)quinoline-3-carboxylate (3t): Purple solid; yield 71%; mp 185-186 ^oC. ^1H NMR (400 MHz, DMSO-d_6): δ 8.18 (d, *J* = 8.4 Hz, 1H, ArH), 8.04 (d, *J* = 8.4 Hz, 1H, ArH), 7.84 (t, *J* = 7.6 Hz, 1H, ArH), 7.82 (d, *J* = 16.4 Hz, 1H, CH=), 7.63 (t, *J* = 7.6 Hz, 1H, ArH), 7.30 (d, *J* = 16.4 Hz, 1H, CH=), 6.84 (d, *J* = 15.6 Hz, 1H, CH=), 6.78 (d, *J* = 15.6 Hz, 1H, CH=), 4.73 (s, 2H, Fc-H), 4.69 (s, 2H, Fc-H), 4.56 (q, *J* = 7.2 Hz, 2H, CH_2CH_3), 4.46 (s, 2H, Fc-H), 4.42 (s, 2H, Fc-H), 4.24 (s, 5H, Fc-H), 4.19 (s, 5H, Fc-H), 1.47 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.90, 150.97, 147.86, 142.06, 137.70, 136.30, 131.18, 129.47, 126.88, 125.65, 124.59, 124.34, 121.37, 119.10, 70.51, 70.13, 69.74, 69.56, 68.27, 67.96, 62.10, 14.67. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{36}H_{32}Fe_2NO_2$: 622.1126; found: 622.1119.

Experimental procedure for cancer cell growth inhibition assay (MTT assay)

Cell culture: A549, HT29, and T24 cells were cultured on Cell culture flask using 2 mM L-glutamine adjusted to contain 1.5 g/L sodium bicarbonate, 4.5 g/L glucose, 10 mM 4-(2-hydroxyethyl)piperazine-1-ethanesulfonic acid (HEPES) and 1.0 mM sodium pyruvate in the Roswell Park Memorial Institute (RPMI) 1640 nutrient medium supplemented with 0.5 mg/ml G418 and 10%

heat-inactivated fetal calf serum (FCS) (pH 7.2).

MTT assay: Cytotoxicity of the newly-synthesized compounds was investigated by MTT assay, in comparison to cisplatin (CDDP). Briefly, A549, HT29 and T24 cells were cultured in culture medium containing 10% fetal calf serum, and been in the logarithmic growth phase. The three cell types were seeded in 96-well culture platet at the cell density of 5×10^4 cells per well in 100 μL of culture medium at 37 ^oC in 5% CO_2 incubator for 24 h seeding. The stock solutions of test compounds **3** were prepared in DMSO. After incubation, the cells were treated with different concentrations of the tested compounds, made by serial dilution in culture medium, and incubated for 72 h with each concentration located three wells. Then the drug containing medium was removed and replaced by 100 μL fresh medium with 0.5 mg/mL MTT solution. After 4 h incubation, the medium with MTT was removed and 100 μL DMSO was added to each well. The plates were gently agitated until the color reaction was uniform. The OD values were measured using SPECTRA max 190Cell microplate reader under 490 nm (for absorbance of MTT formazan) and 630 nm (for the reference wavelength). Cell growth inhibition rate formula is (AC－AT)/AC×100%. AC, absorbance value of the blank control group; AT, absorbance value of the experimental group. The IC_{50} was calculated using GraphPad Prism version 6.00 software from the non-linear curve.

Spectra for all the synthesised compounds 1 and 3a-t

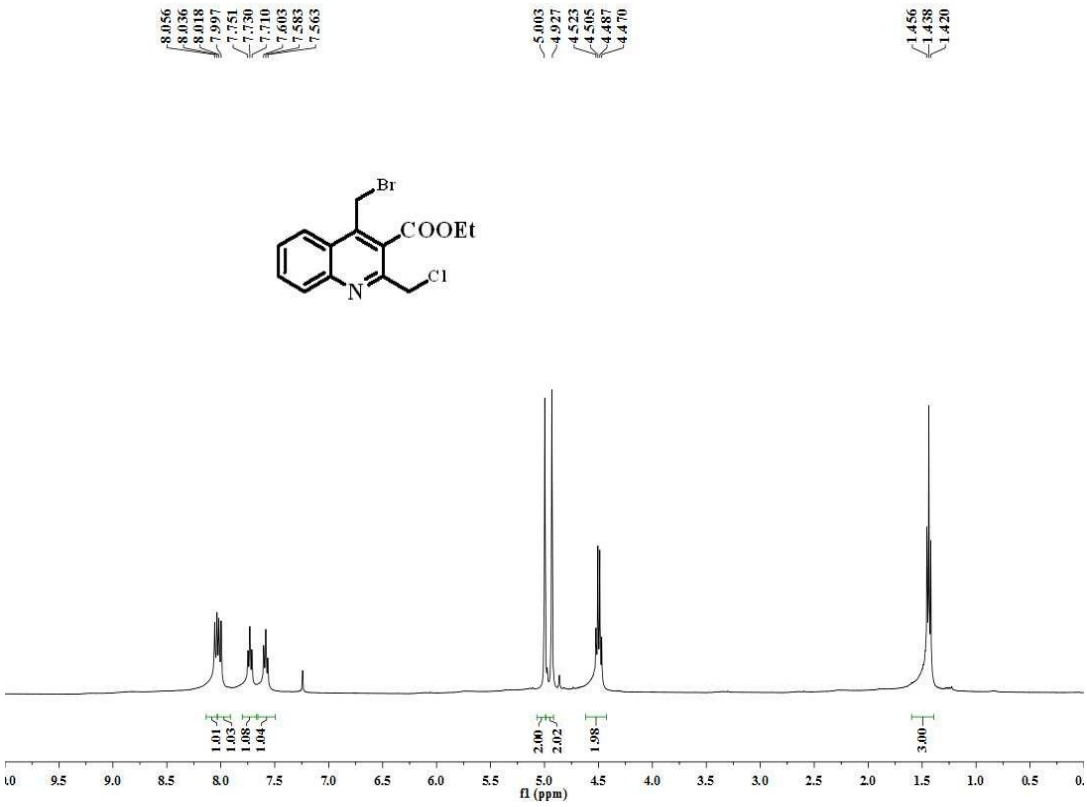

Fig. S1 ^{1}H NMR spectrum of **1**

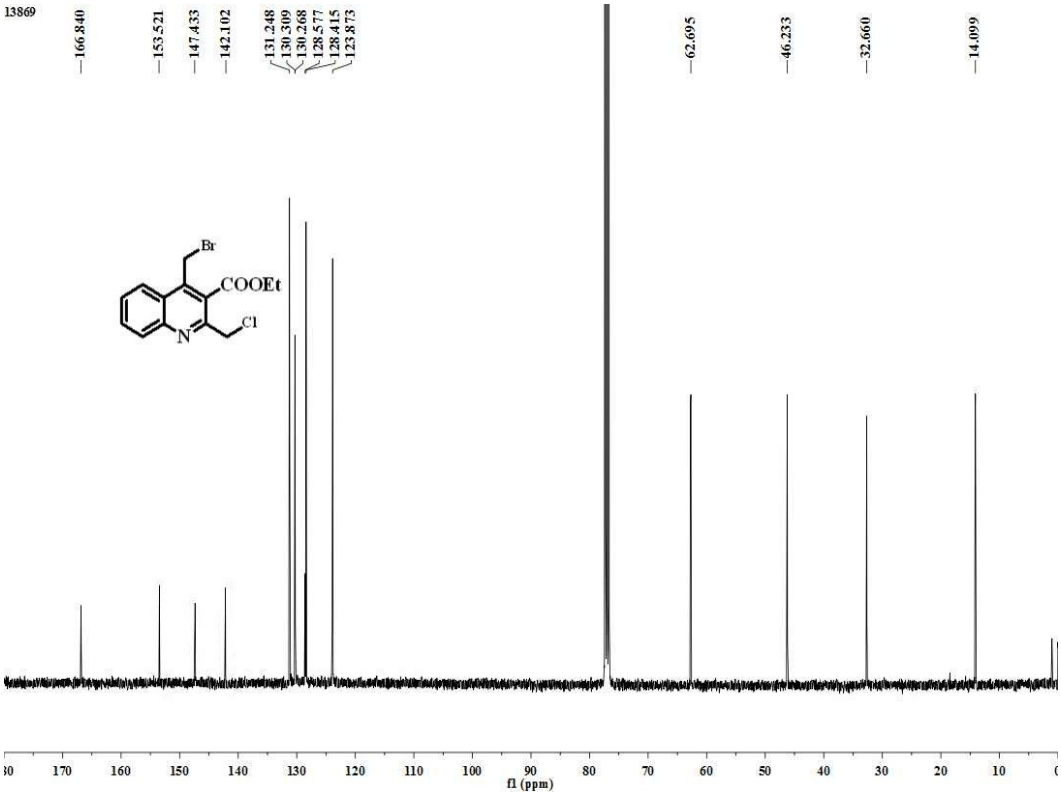

Fig. S2 ^{13}C NMR spectrum of **1**

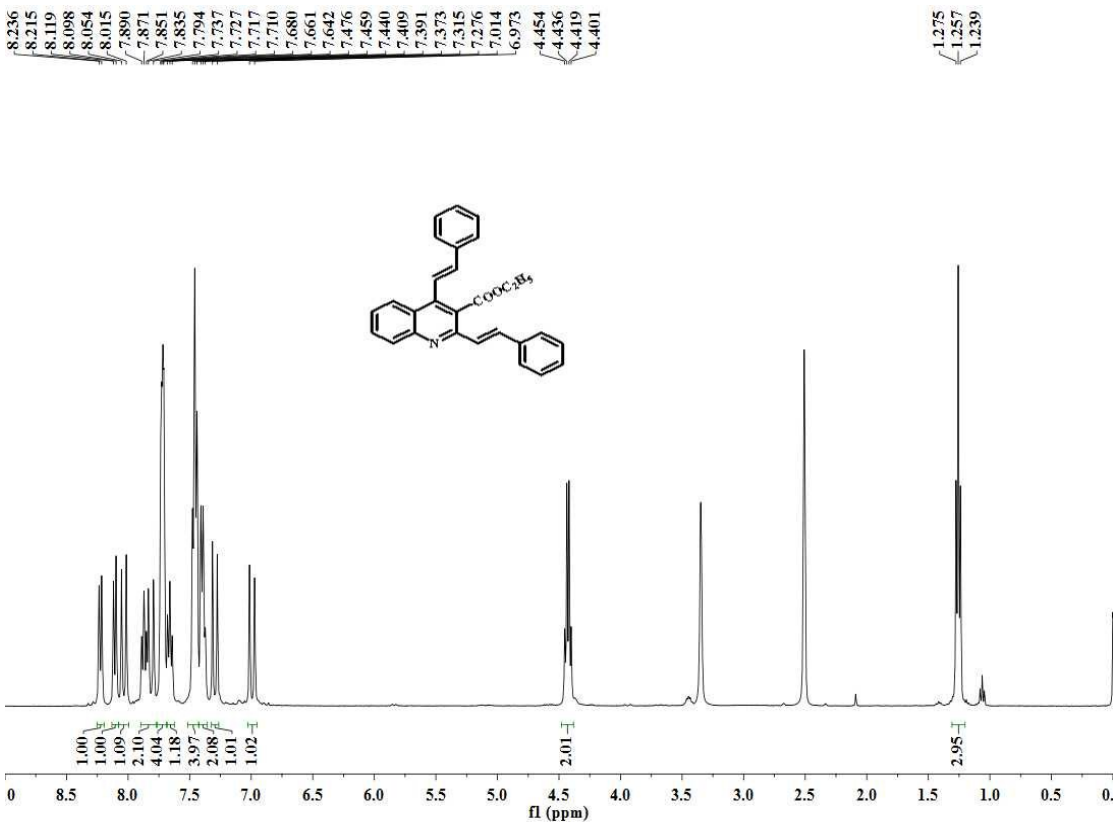

Fig. S3 ^{1}H NMR spectrum of **3a**

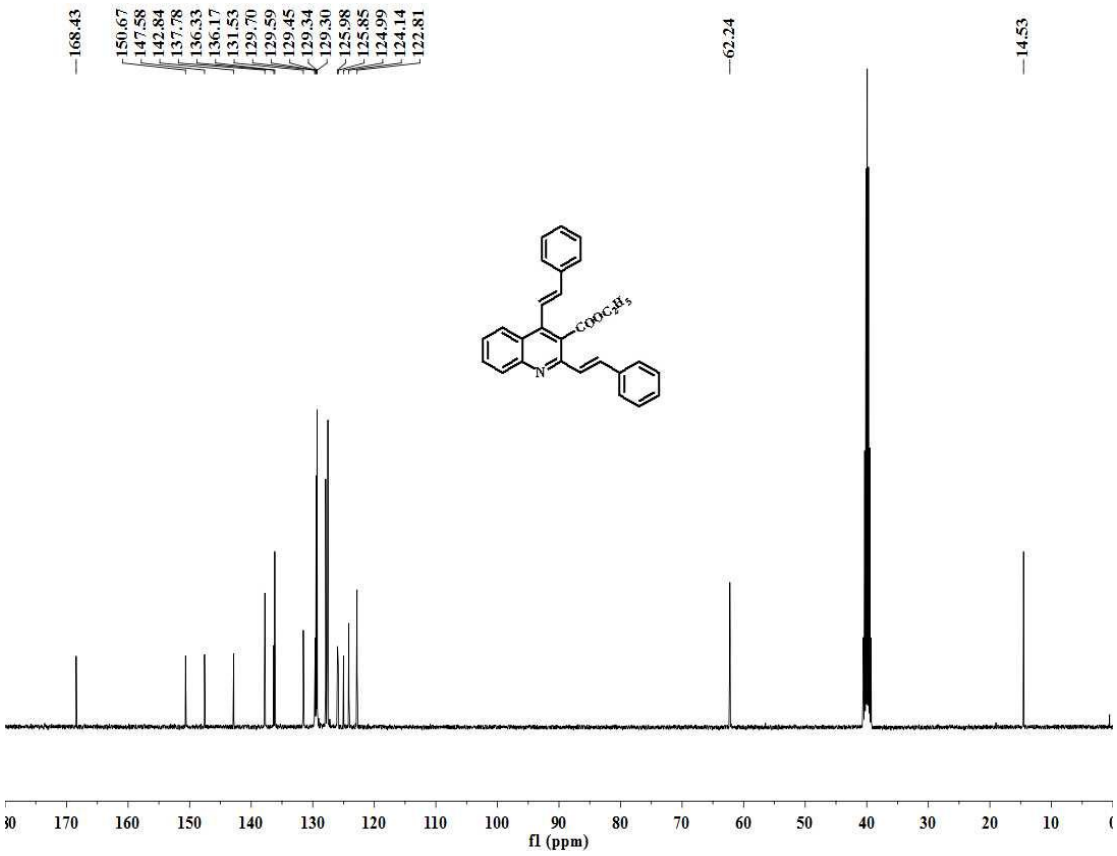

Fig. S4 ^{13}C NMR spectrum of **3a**

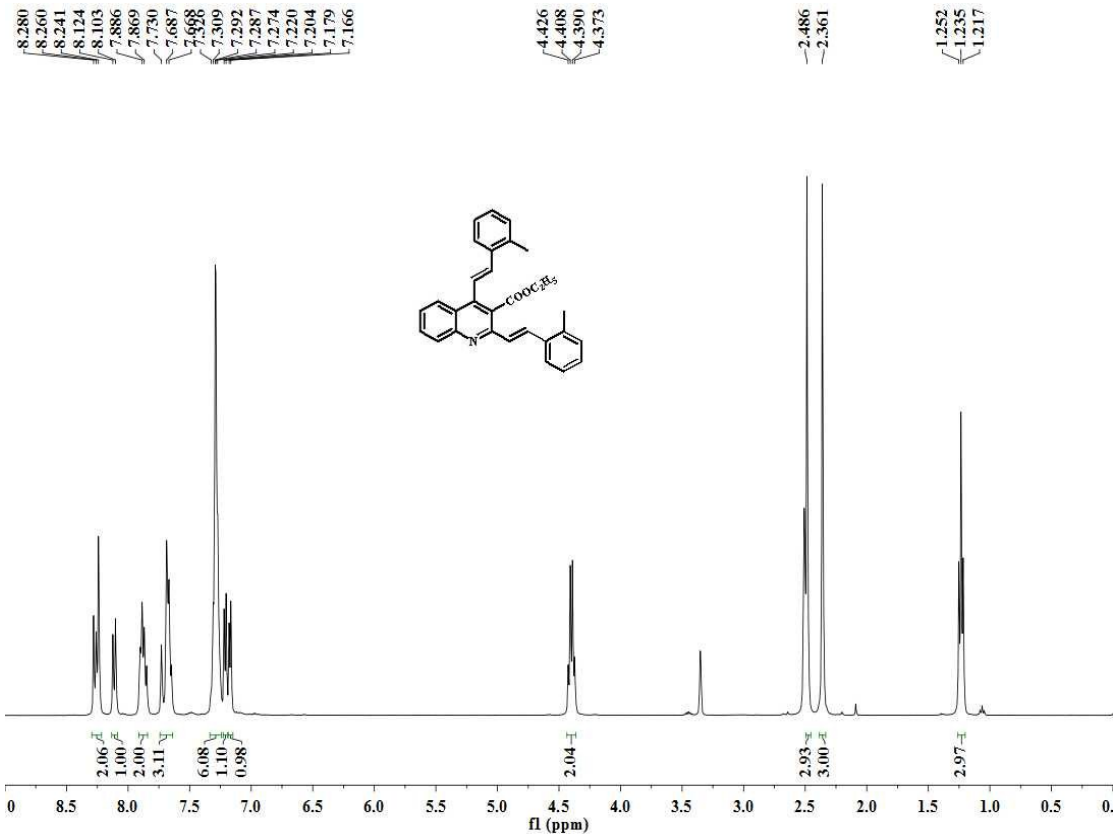

Fig. S5 ^{1}H NMR spectrum of **3b**

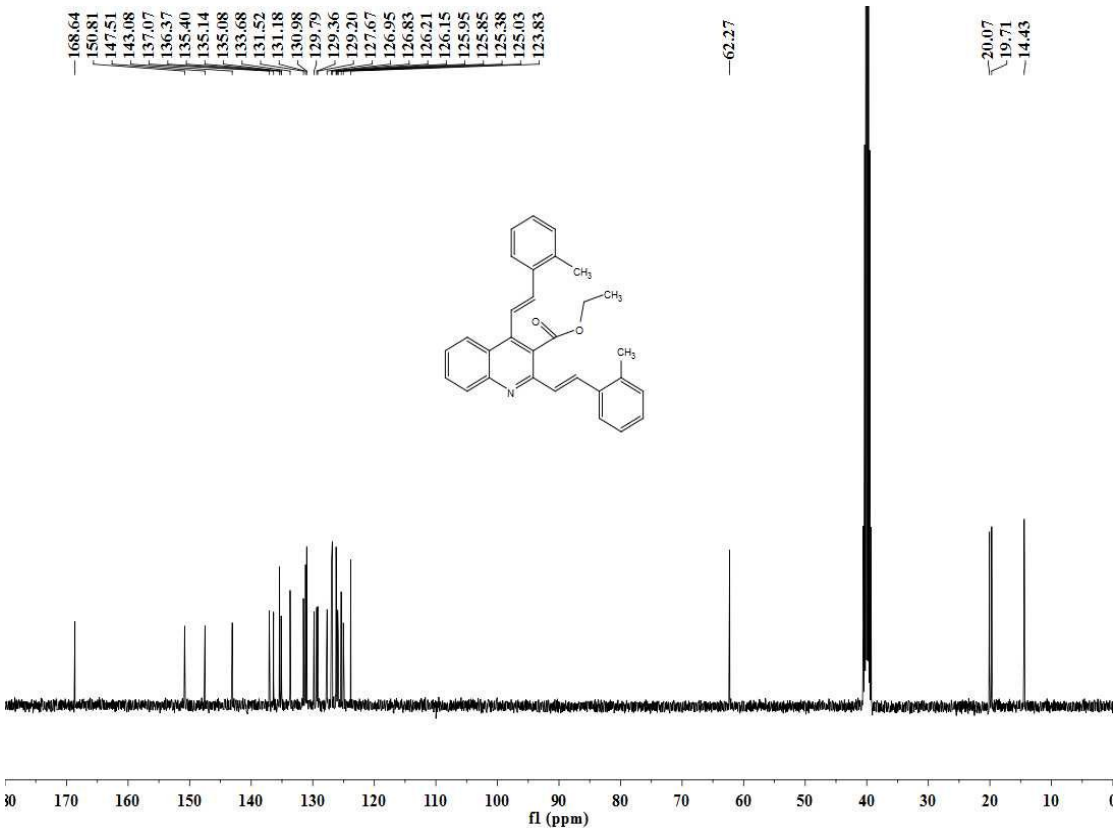

Fig. S6 ^{1}H NMR spectrum of **3b**

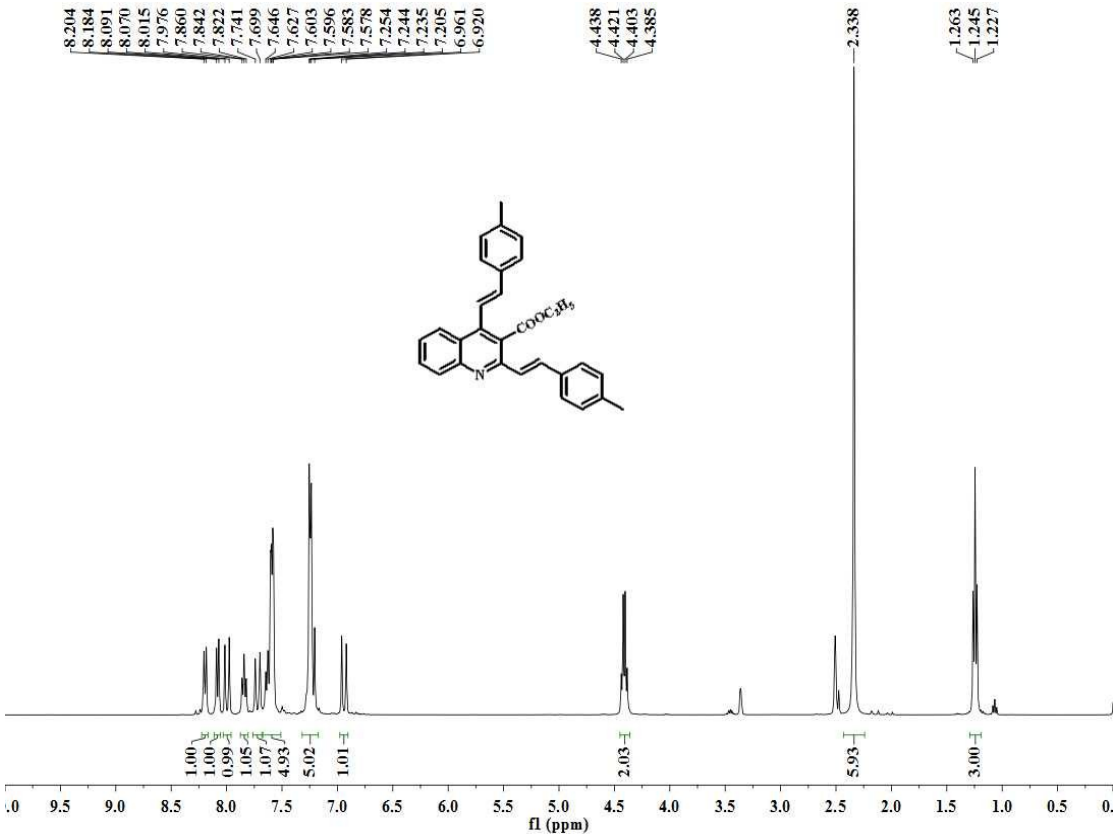

Fig. S7 ^{1}H NMR spectrum of **3c**

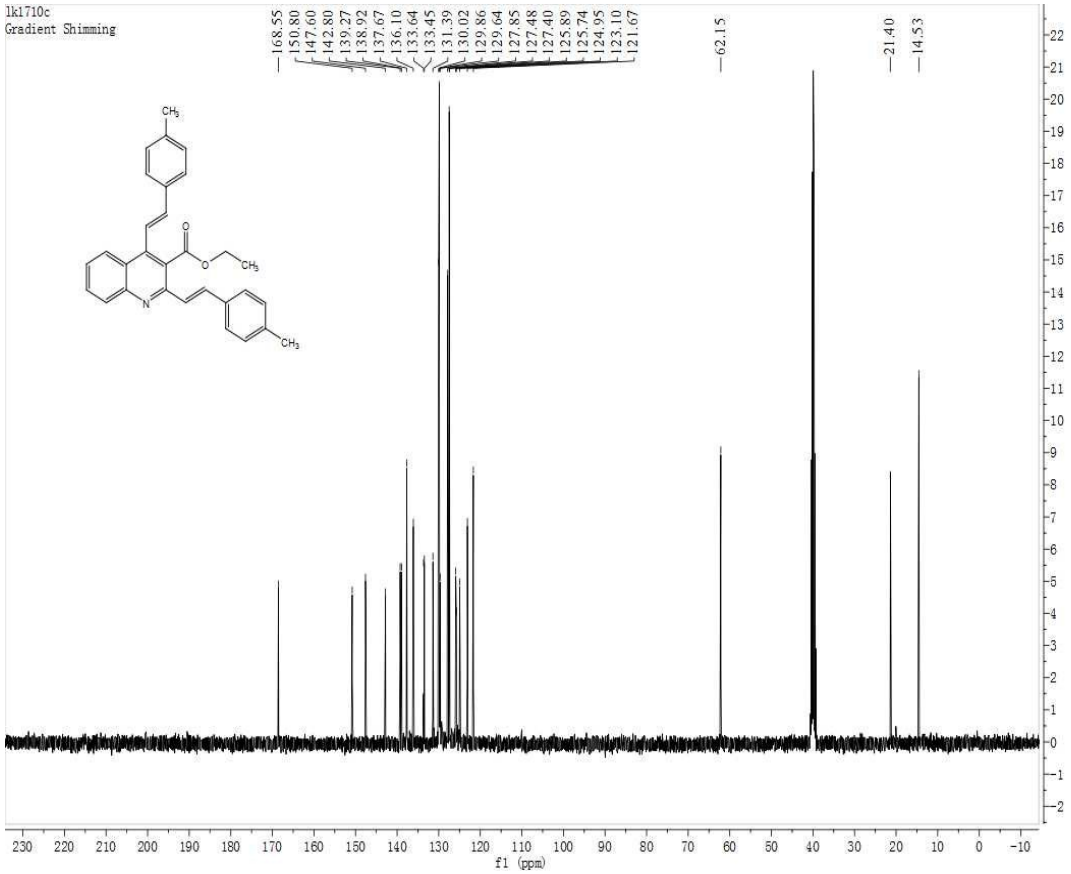

Fig. S8 ^{13}C NMR spectrum of **3c**

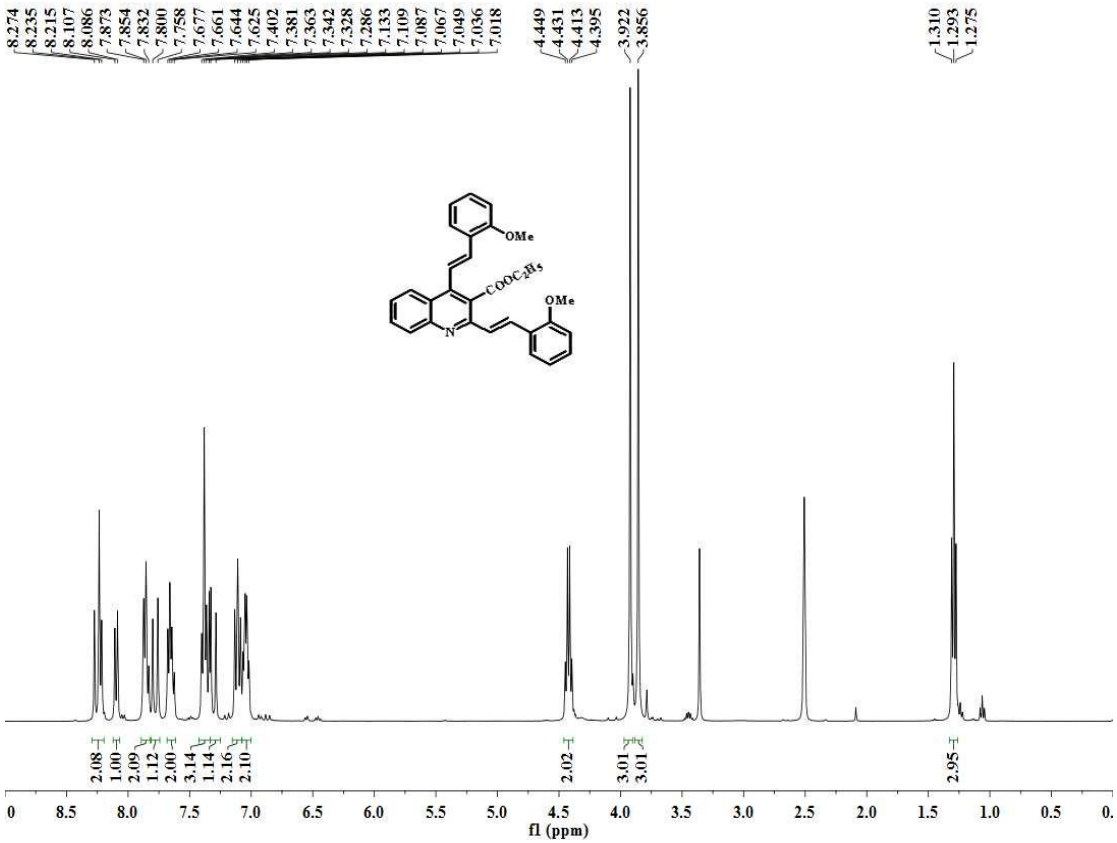

Fig. S9 ^{1}H NMR spectrum of **3d**

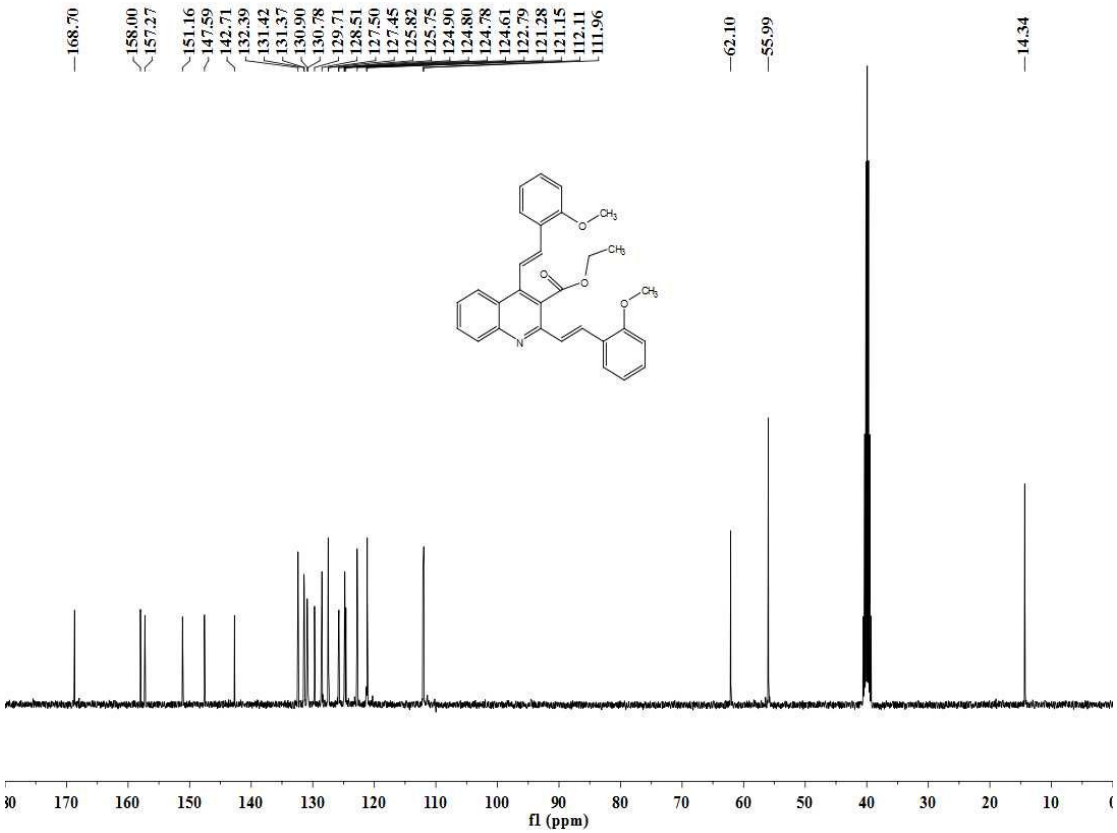

Fig. S10 ^{13}C NMR spectrum of **3d**

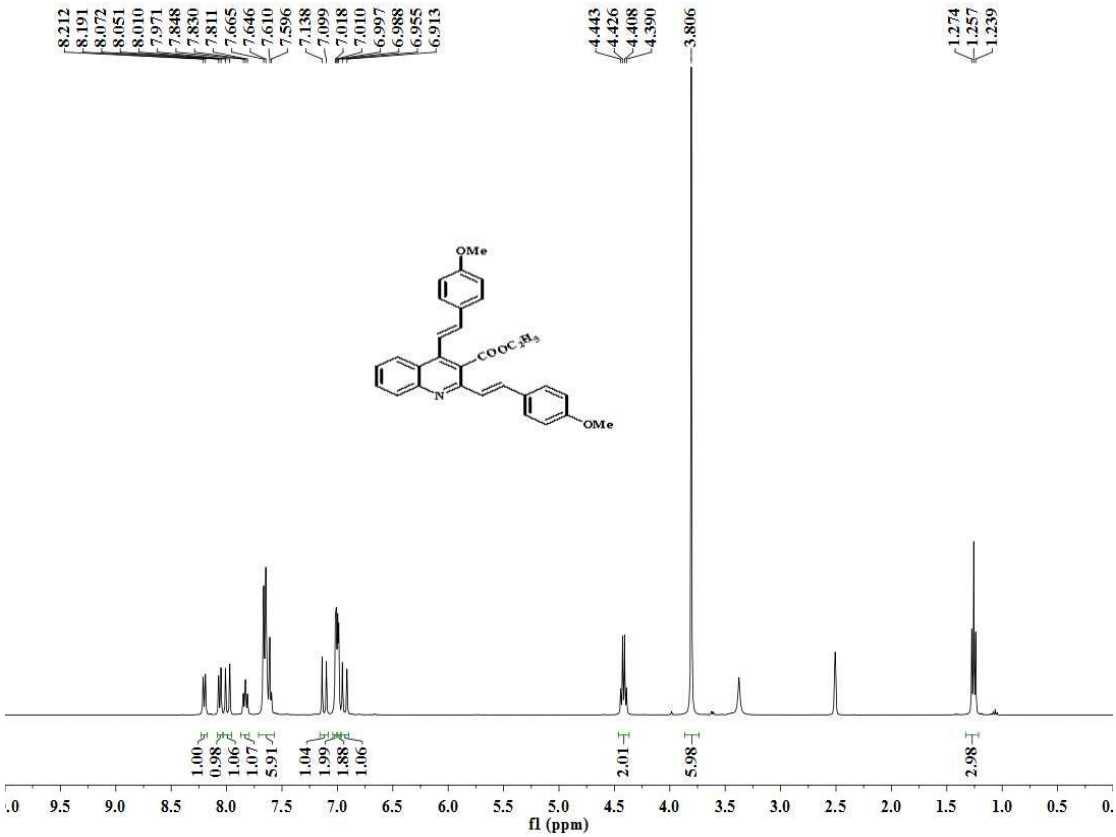

Fig. S11 ^{1}H NMR spectrum of **3e**

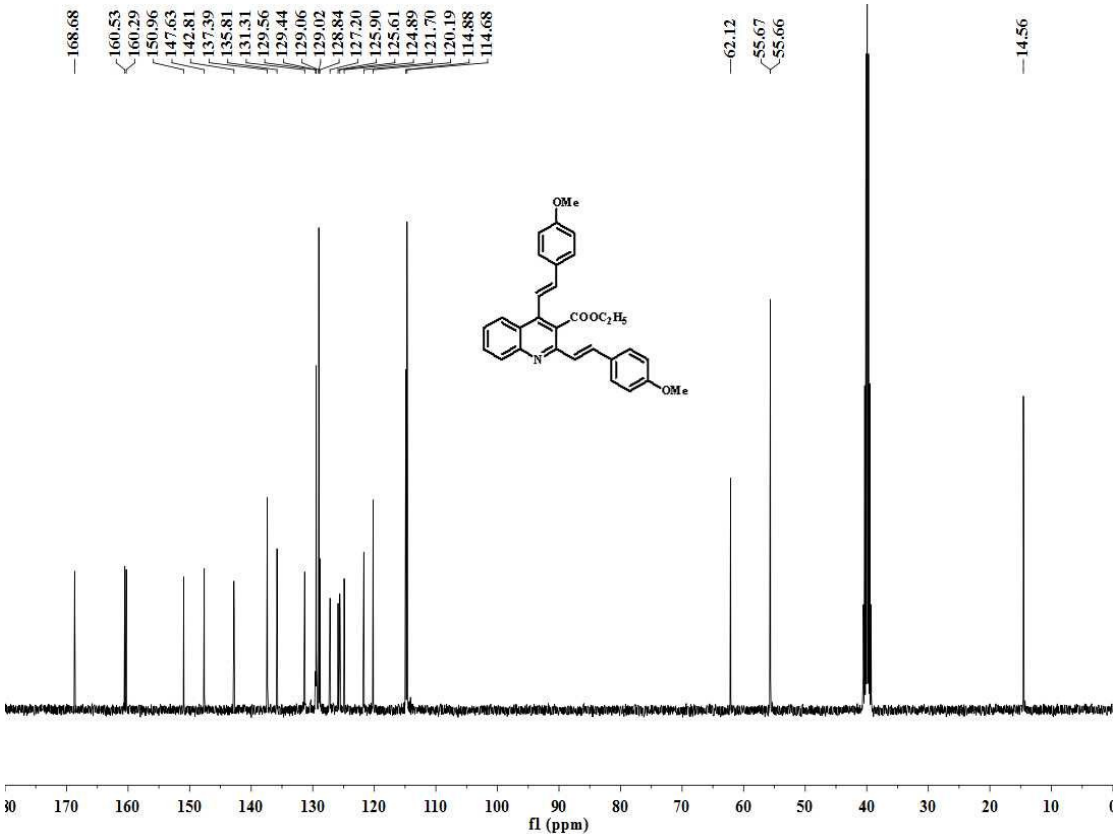

Fig. S12 ^{13}C NMR spectrum of **3e**

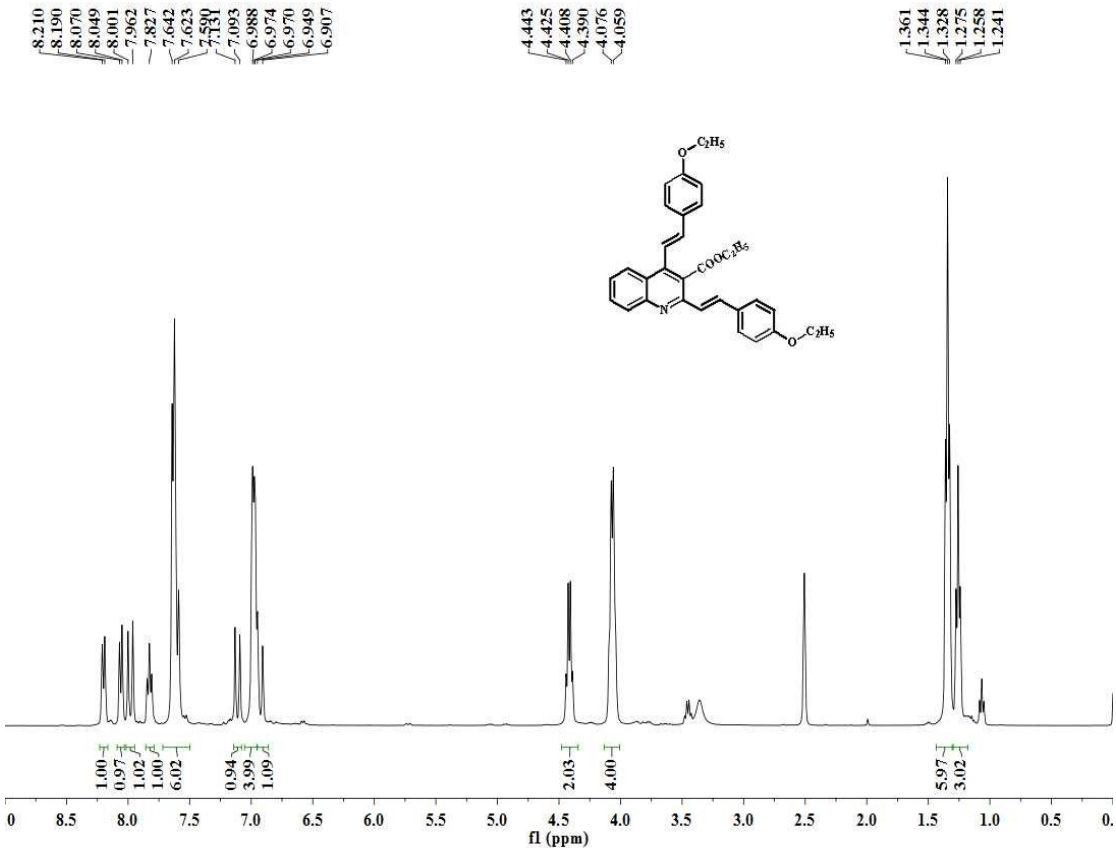

Fig. S13 ^{1}H NMR spectrum of **3f**

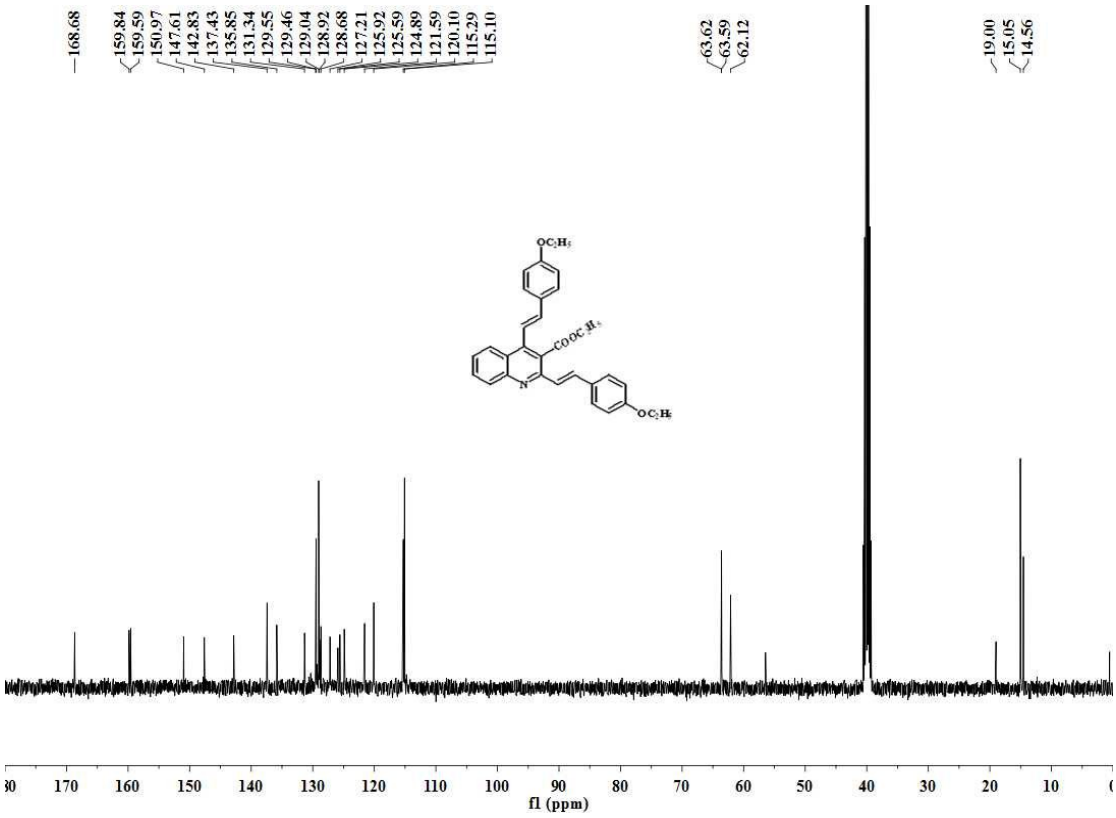

Fig. S14 ^{13}C NMR spectrum of **3f**

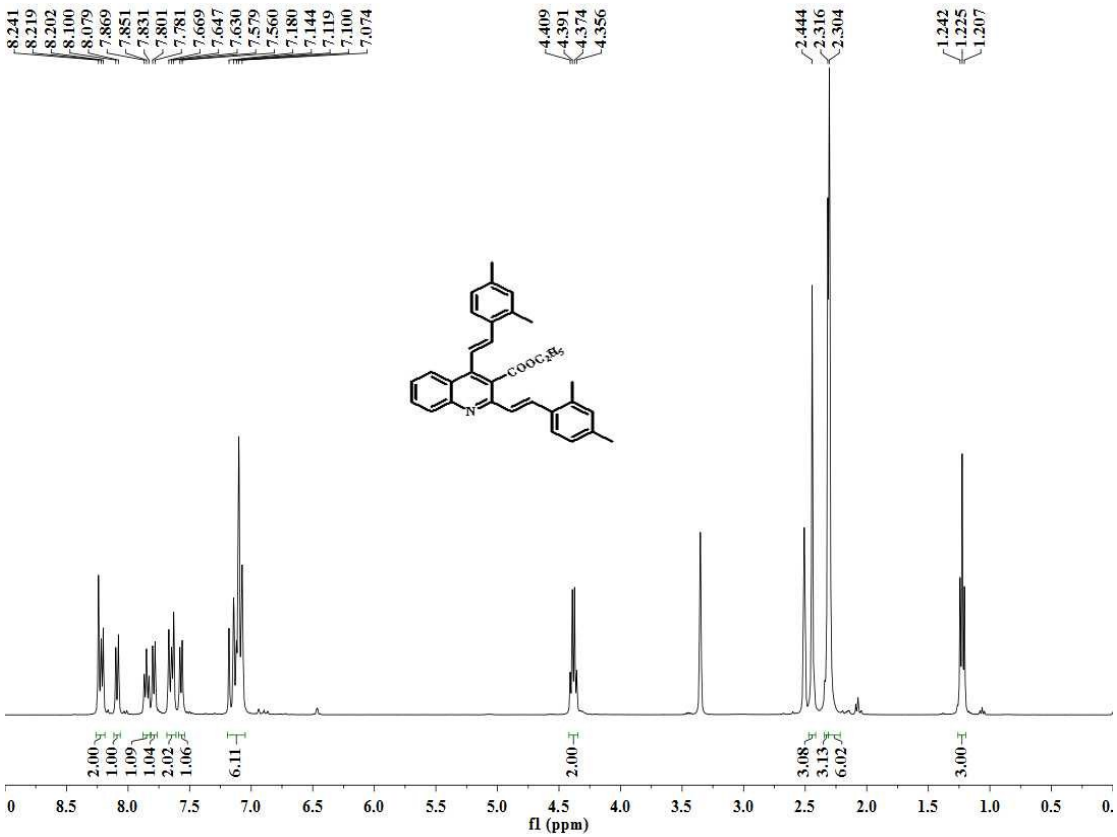

Fig. S15 ^{1}H NMR spectrum of **3g**

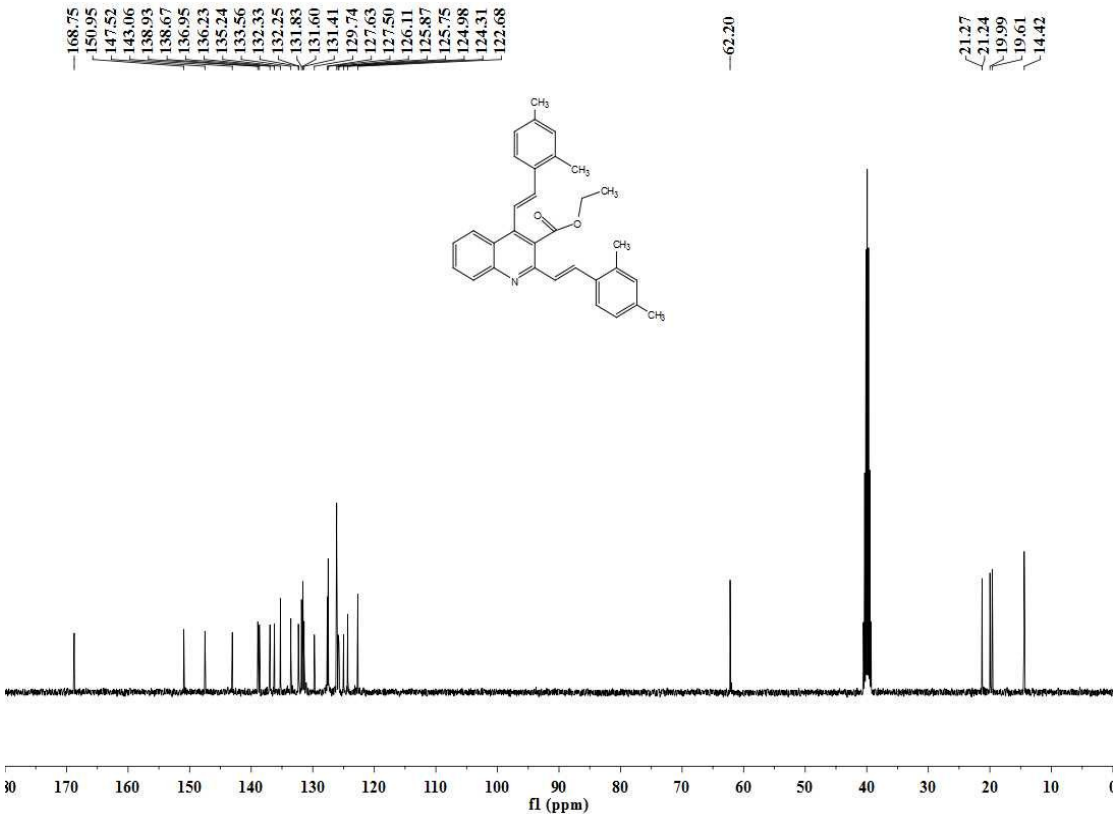

Fig. S16 ^{1}H NMR spectrum of **3g**

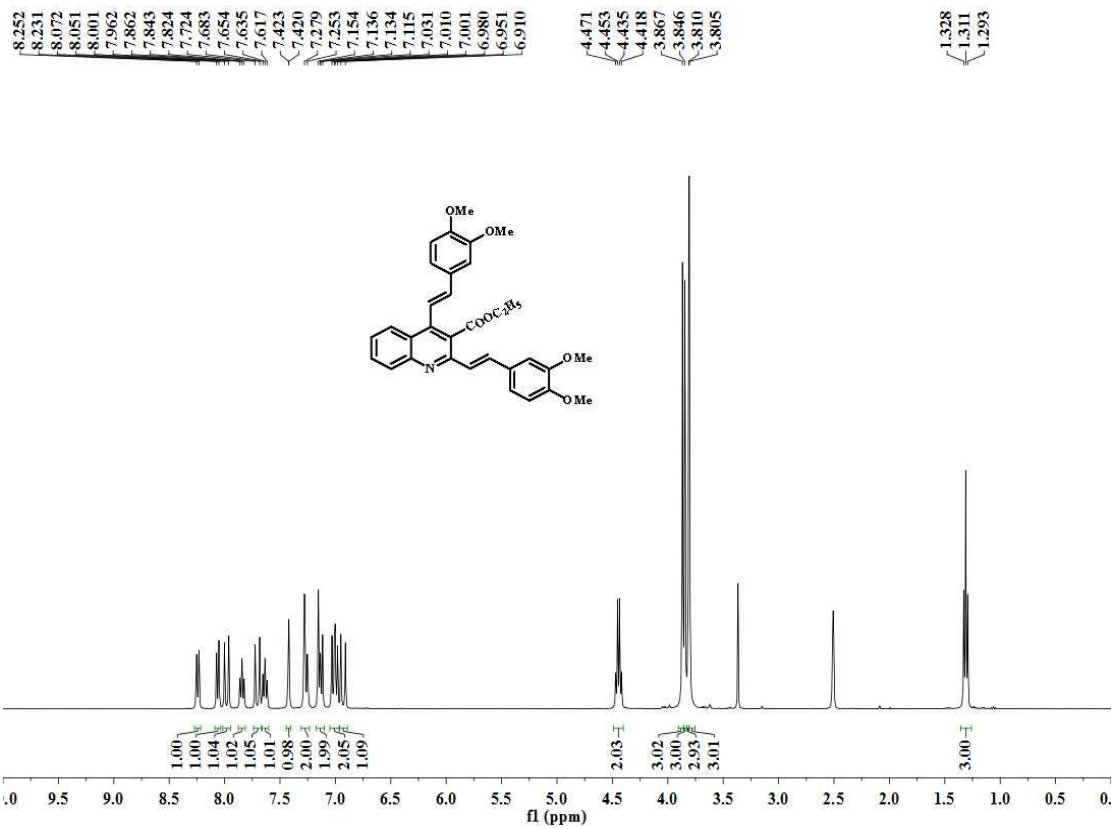

Fig. S17 ^{1}H NMR spectrum of **3h**

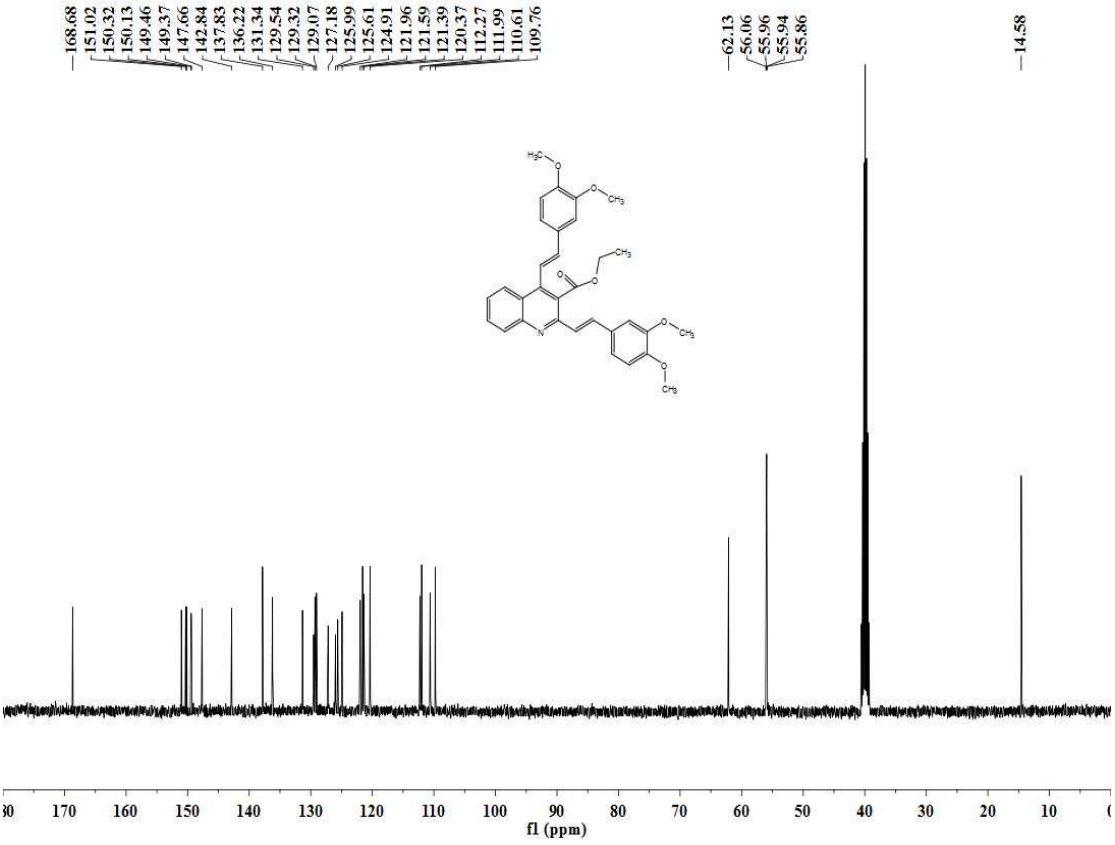

Fig. S18 ^{13}C NMR spectrum of **3h**

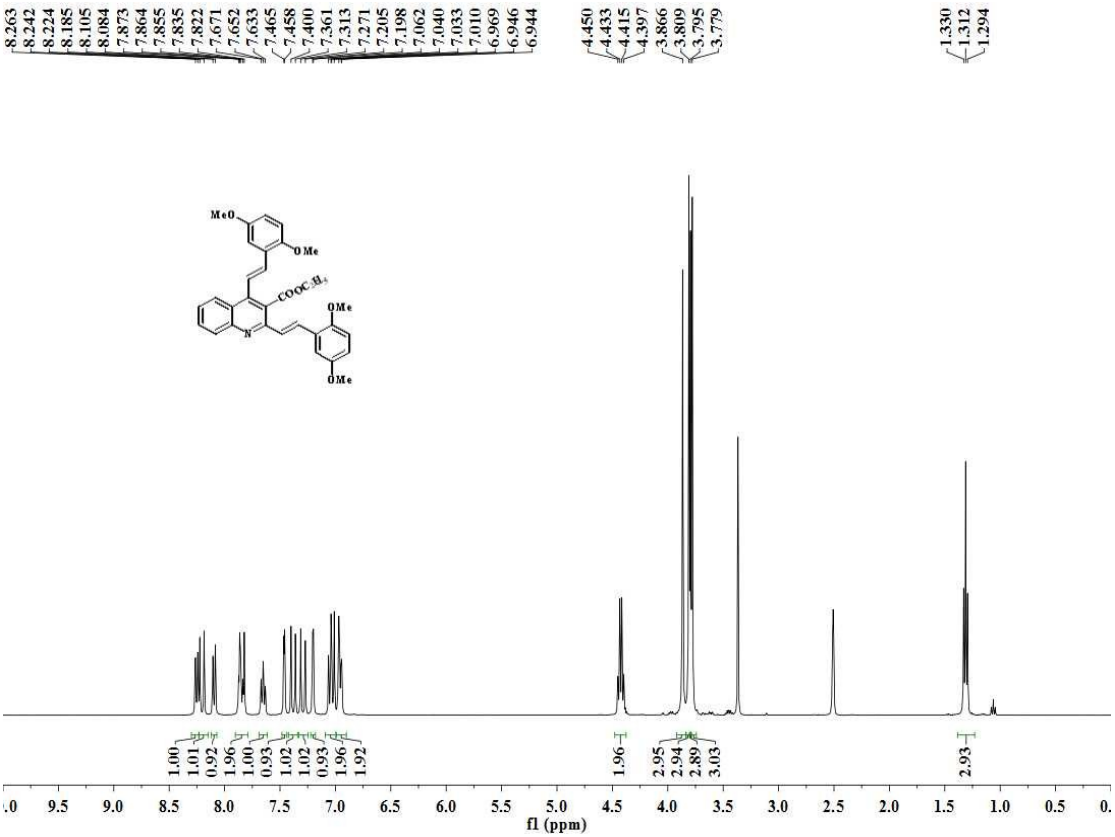

Fig. S19 ^{1}H NMR spectrum of **3i**

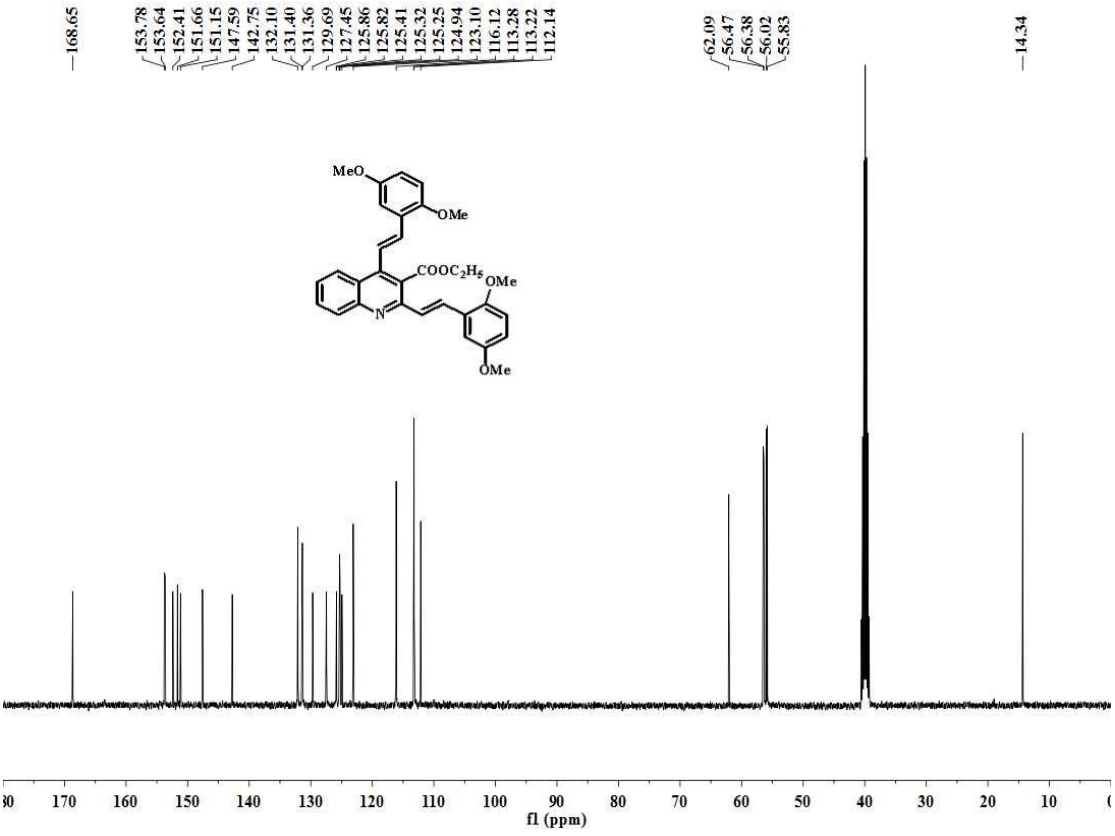

Fig. S20 ^{13}C NMR spectrum of **3i**

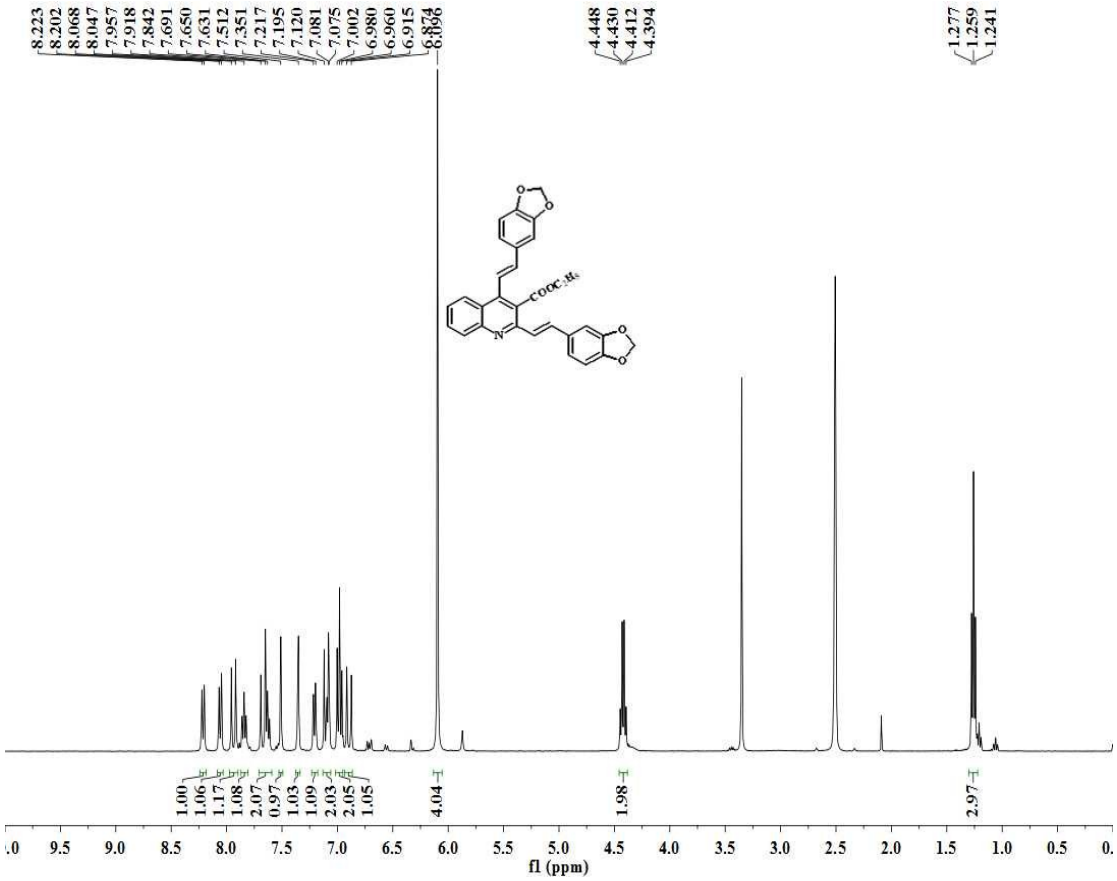

Fig. S21 ^{1}H NMR spectrum of **3j**

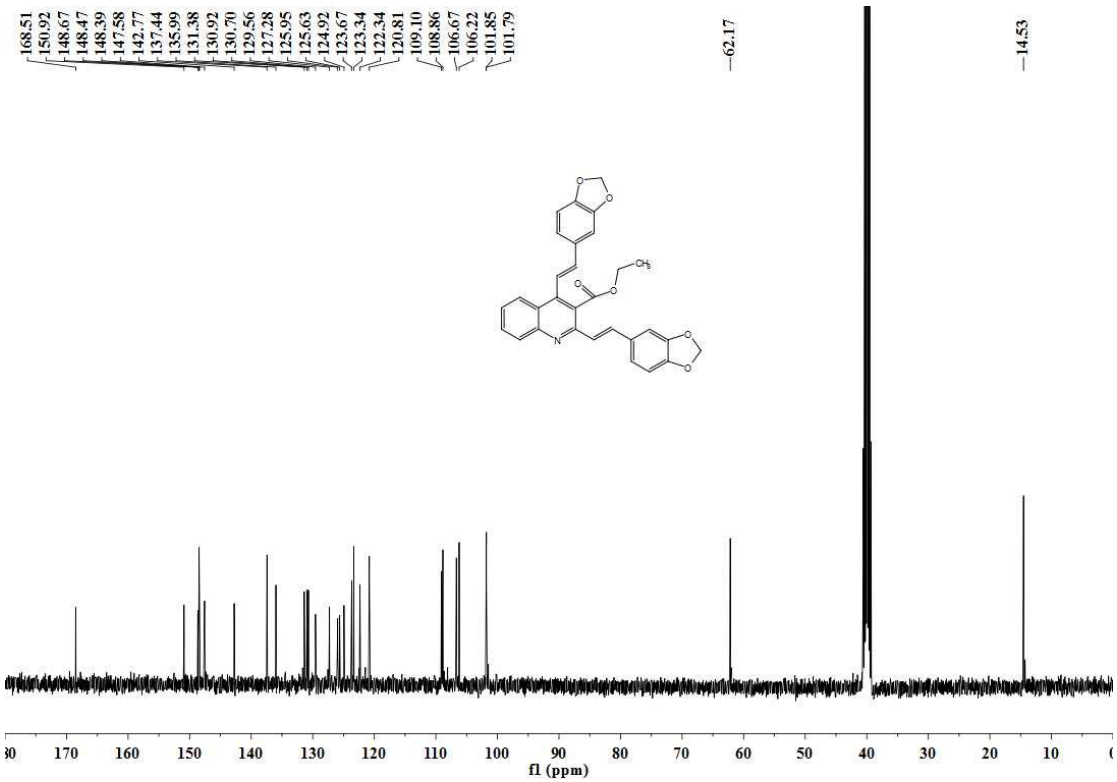

Fig. S22 ^{13}C NMR spectrum of **3j**

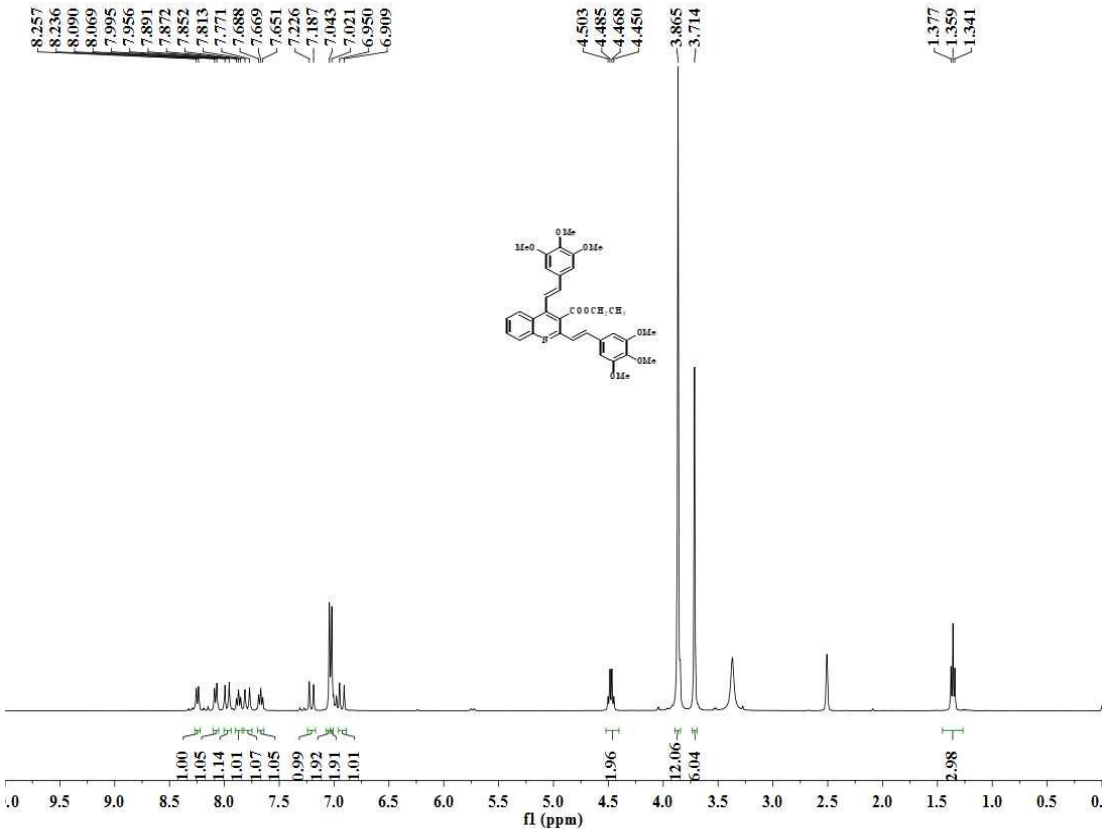

Fig. S23 ^{1}H NMR spectrum of **3k**

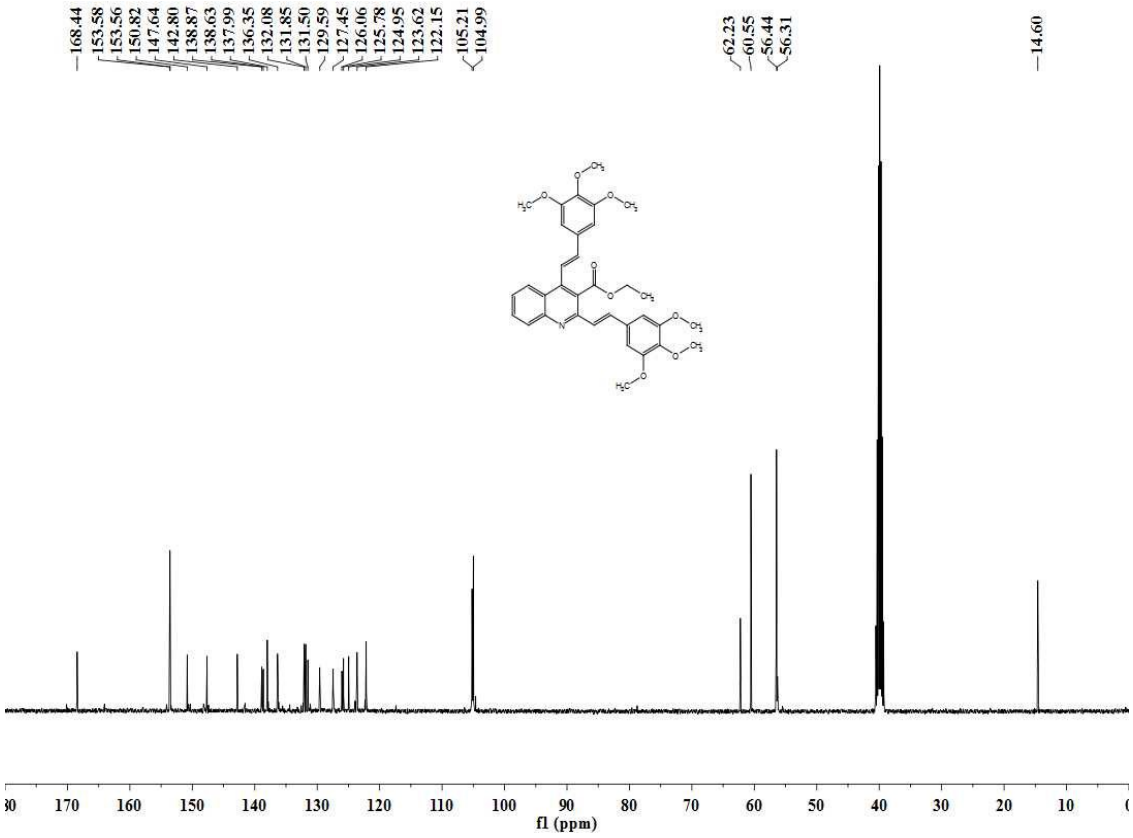

Fig. S24 ^{13}C NMR spectrum of **3k**

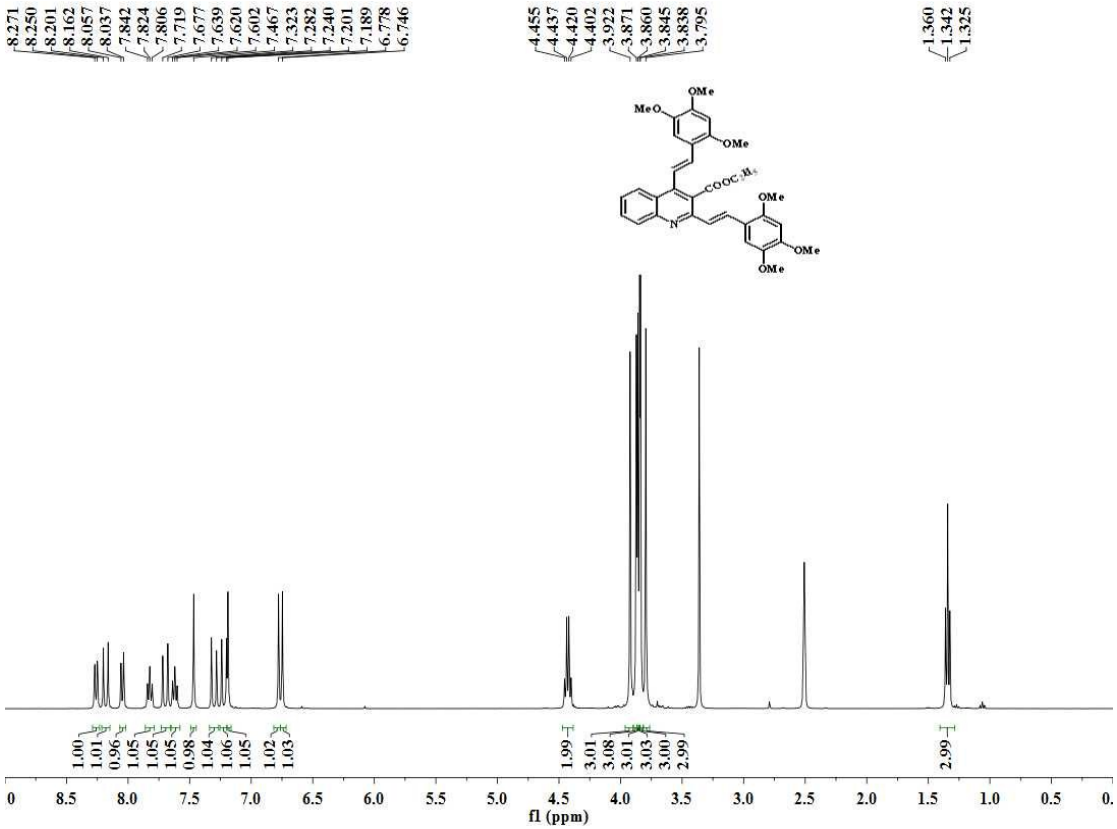

Fig. S25 ^{1}H NMR spectrum of **3l**

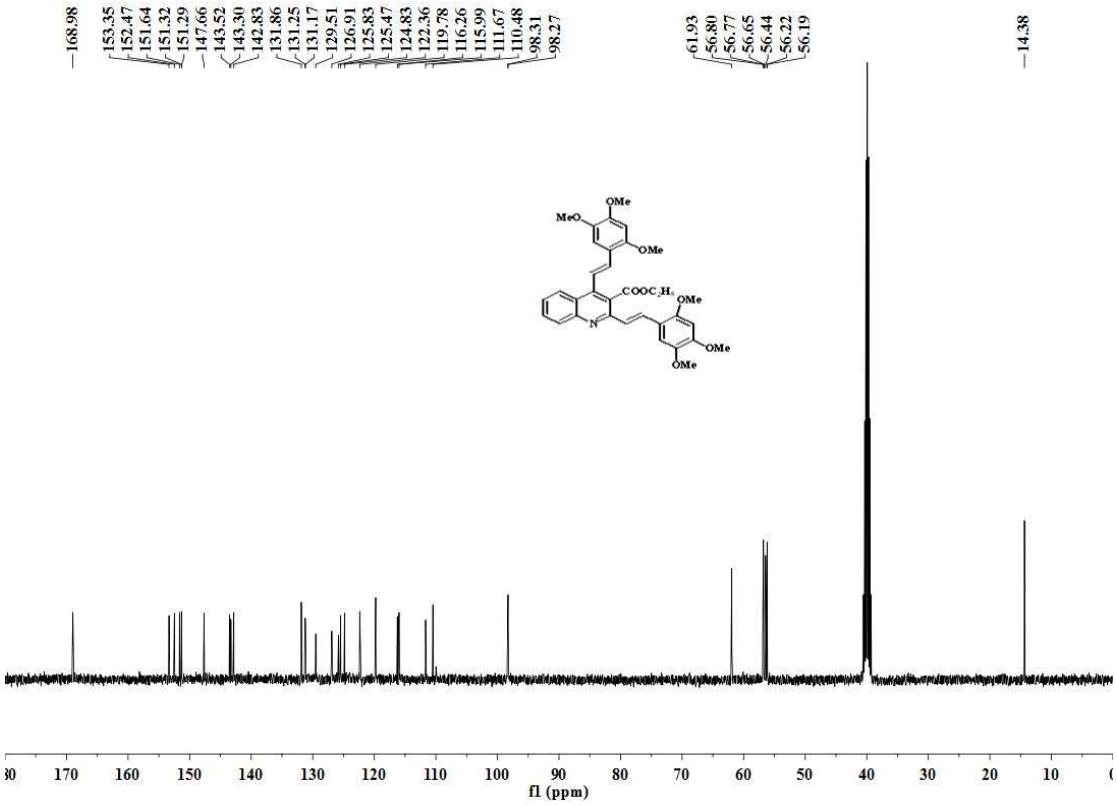

Fig. S26 ^{13}C NMR spectrum of **3l**

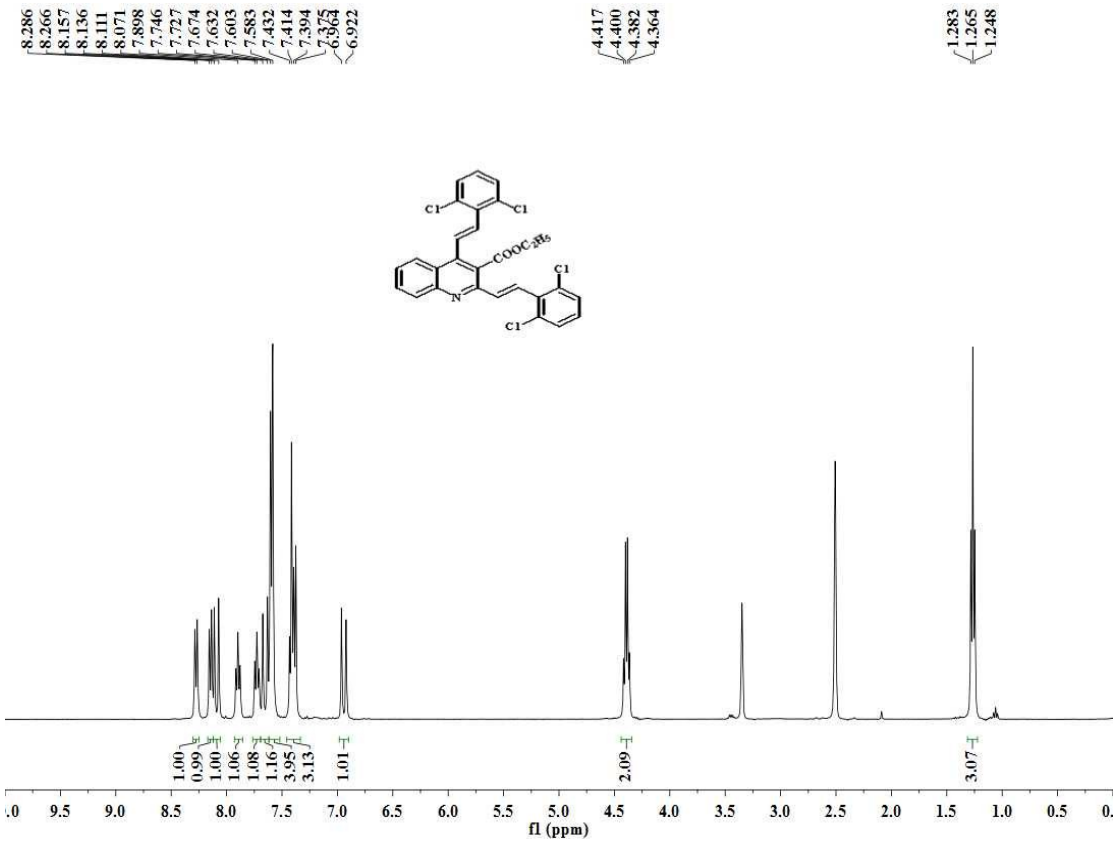

Fig. S27 [1]H NMR spectrum of **3m**

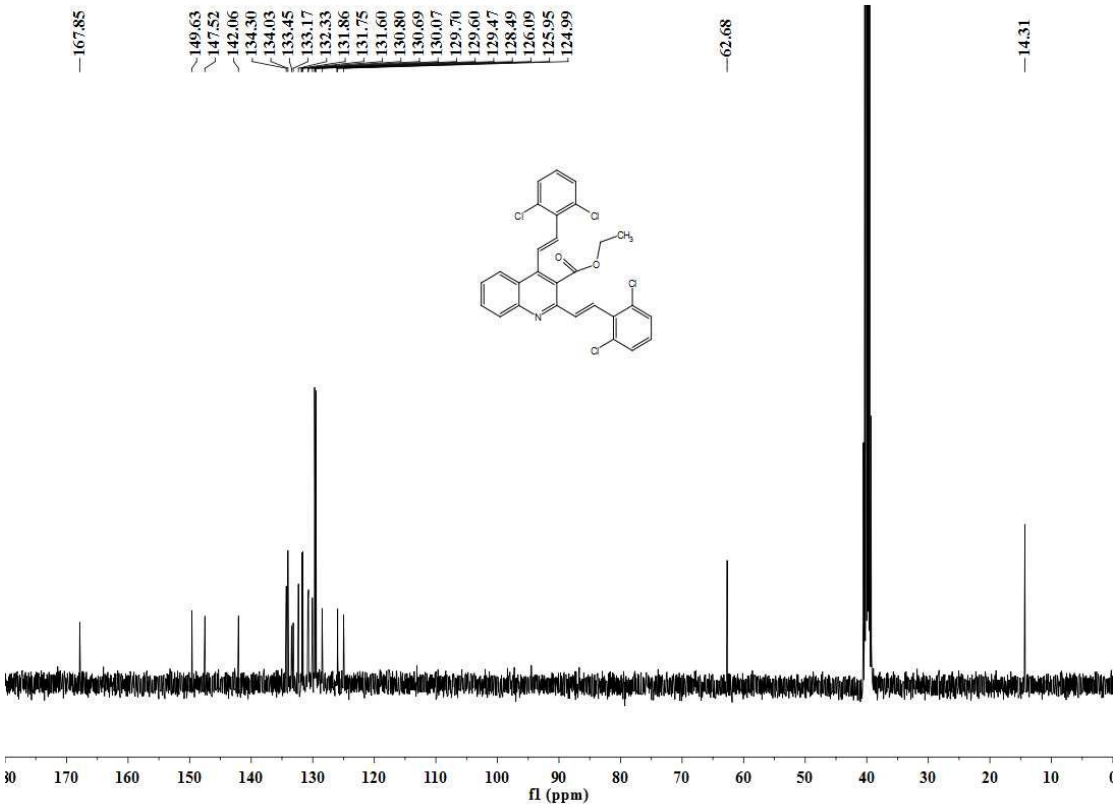

Fig. S28 [13]C NMR spectrum of **3m**

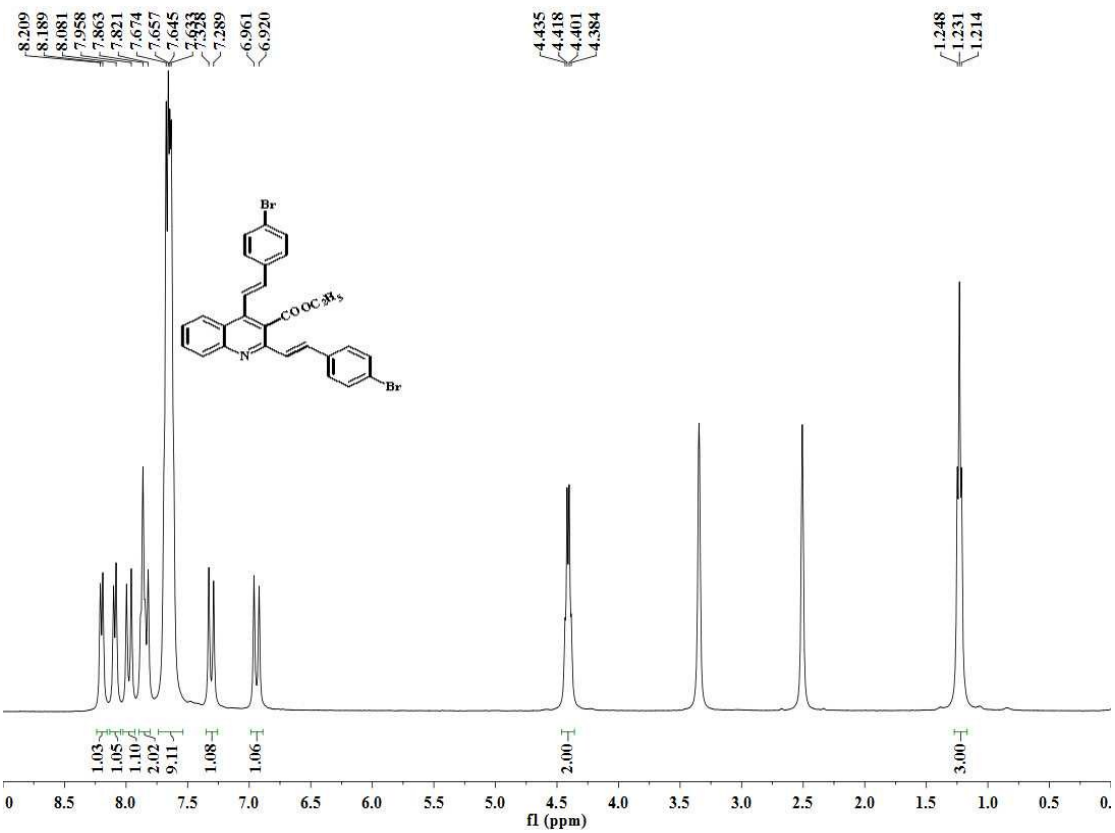

Fig. S29 ^{1}H NMR spectrum of **3n**

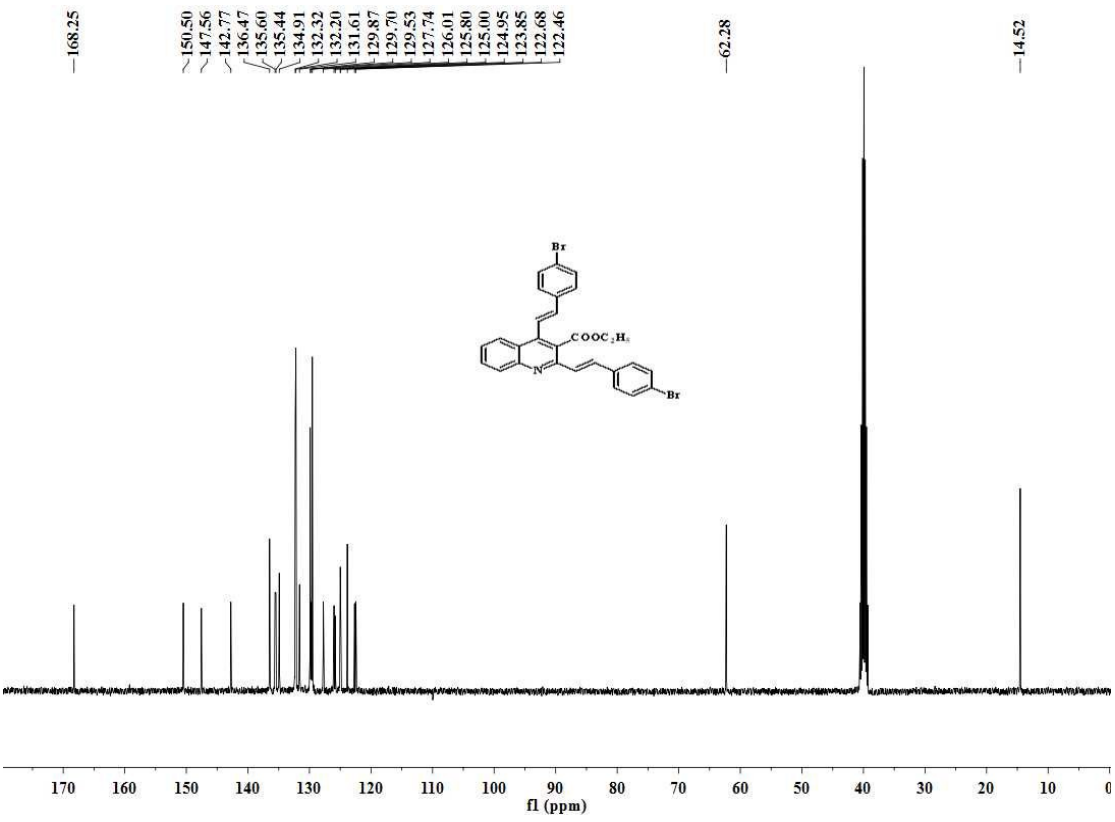

Fig. S30 ^{13}C NMR spectrum of **3n**

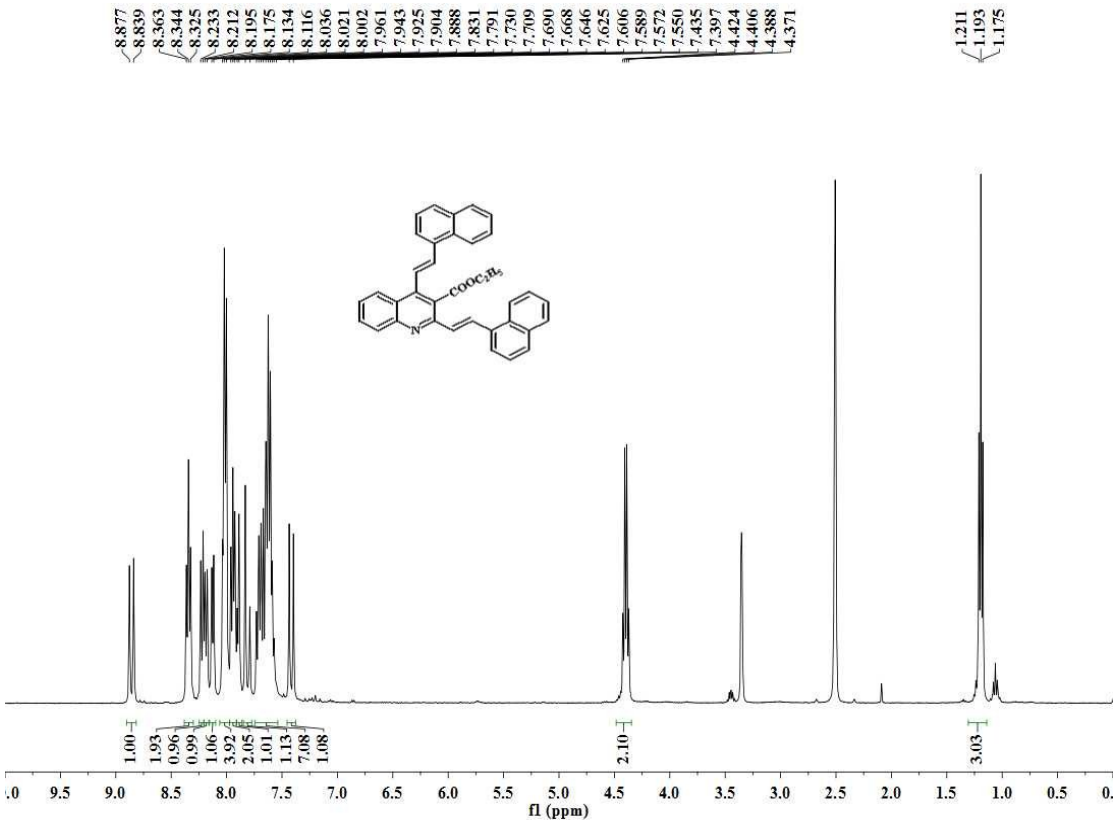

Fig. S31 ^{1}H NMR spectrum of **3o**

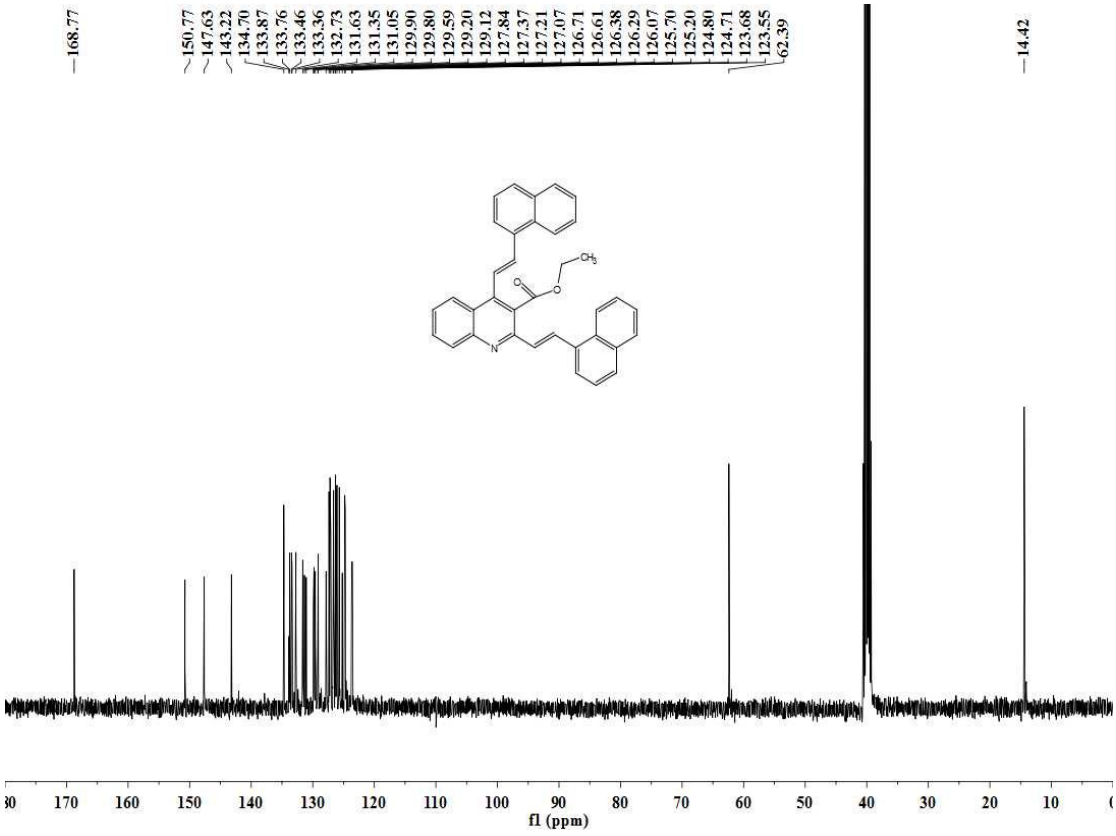

Fig. S32 ^{13}C NMR spectrum of **3o**

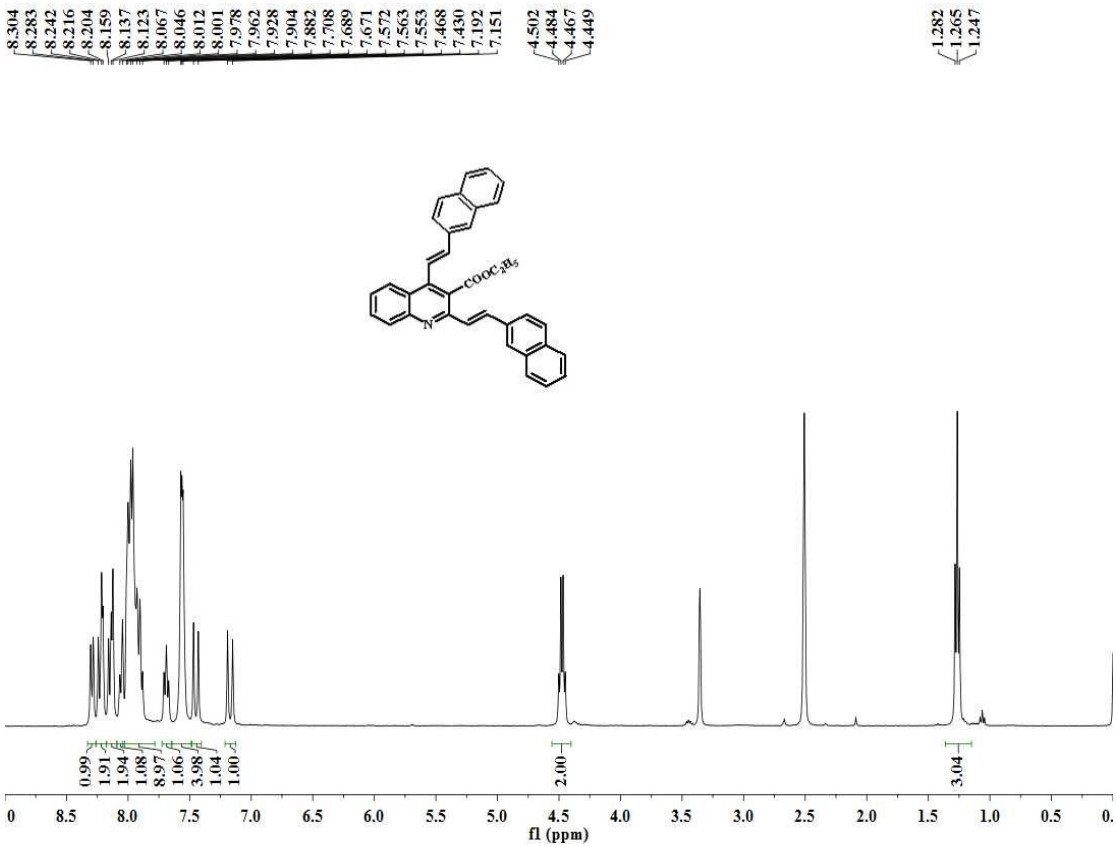

Fig. S33 ^{1}H NMR spectrum of **3p**

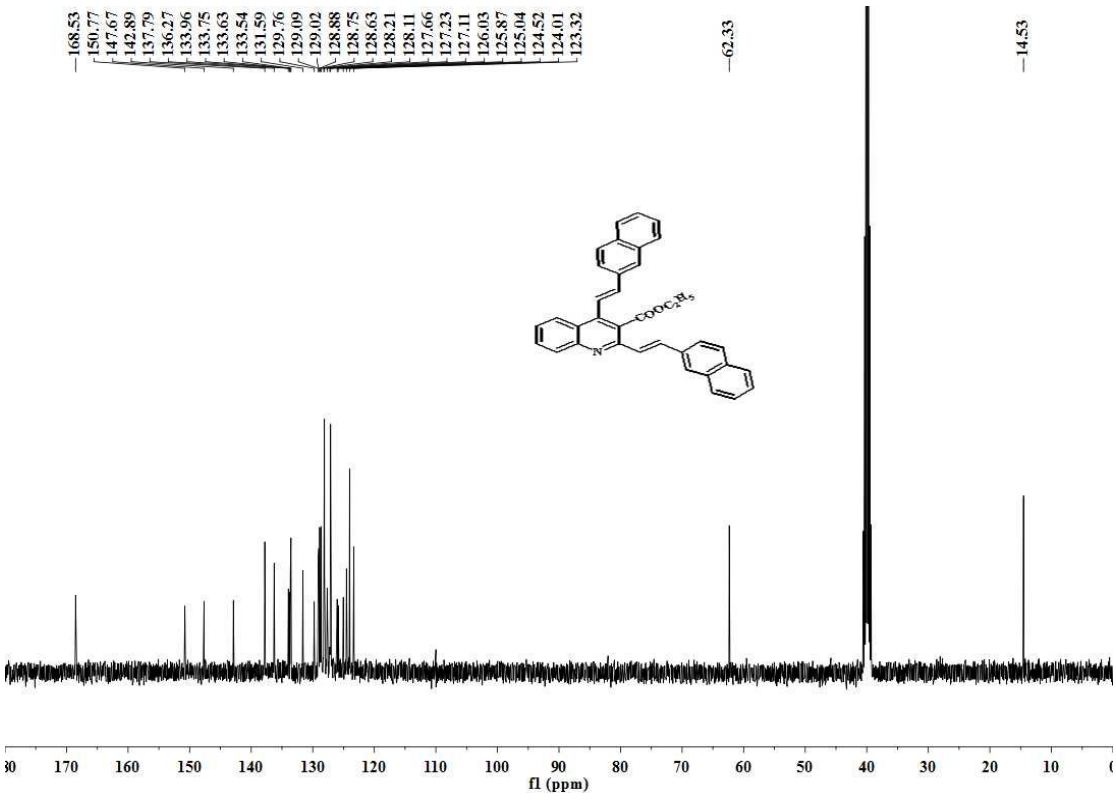

Fig. S34 ^{13}C NMR spectrum of **3p**

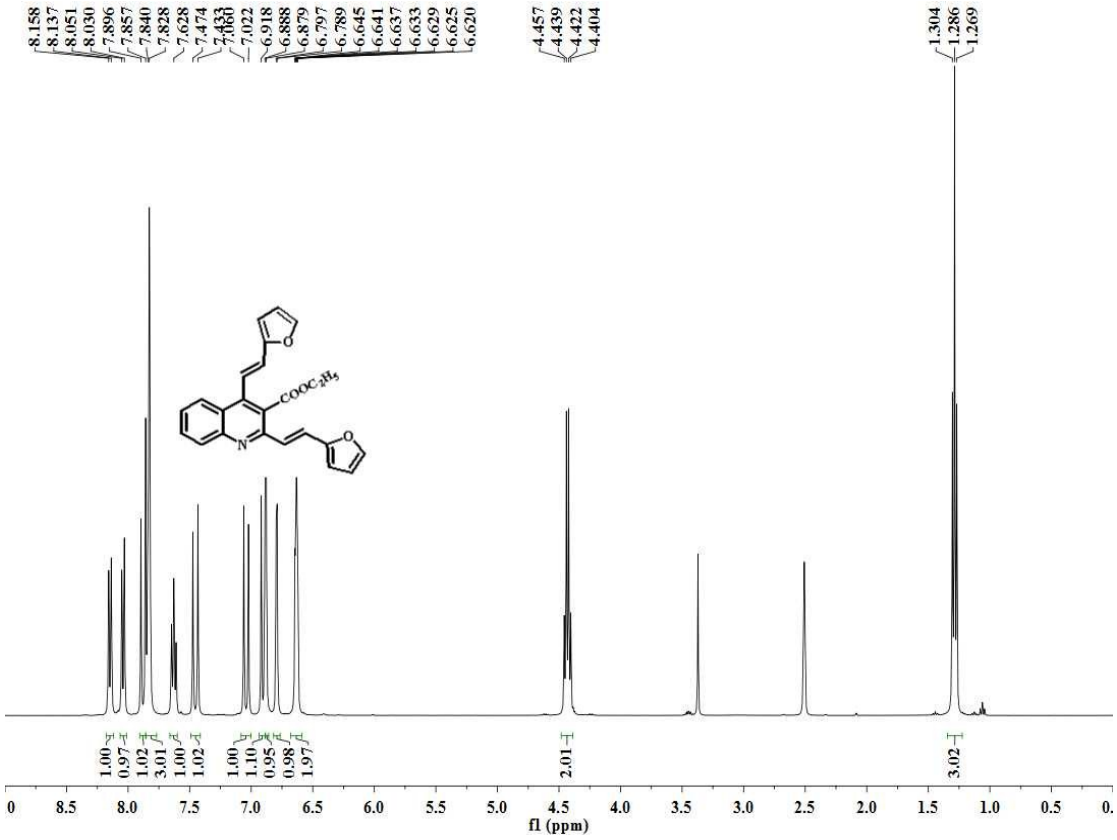

Fig. S35 ^{1}H NMR spectrum of **3q**

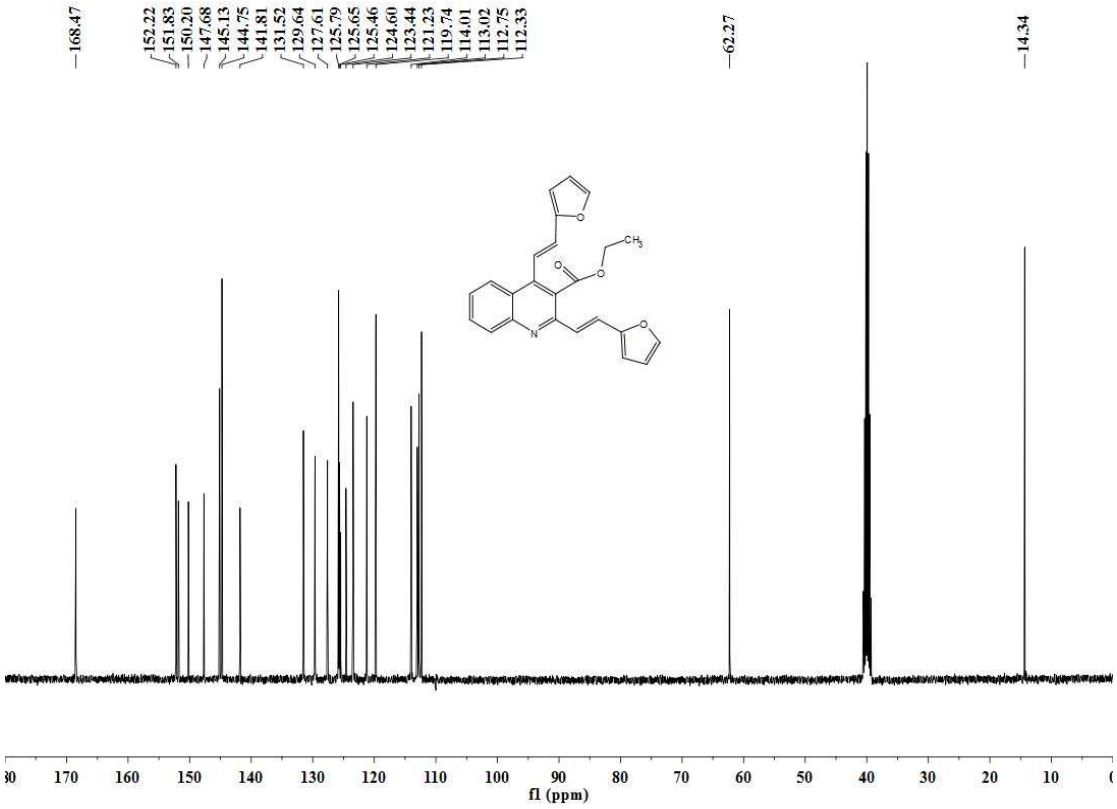

Fig. S36 ^{13}C NMR spectrum of **3q**

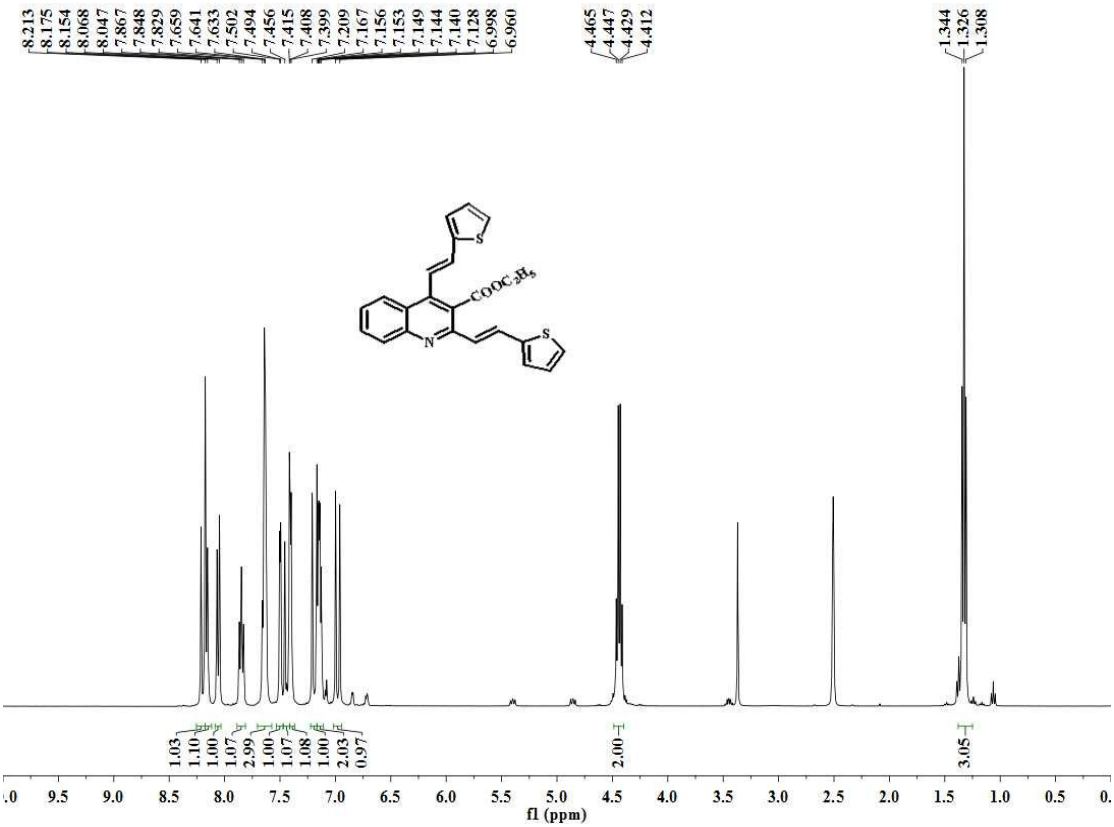

Fig. S37 ^{1}H NMR spectrum of **3r**

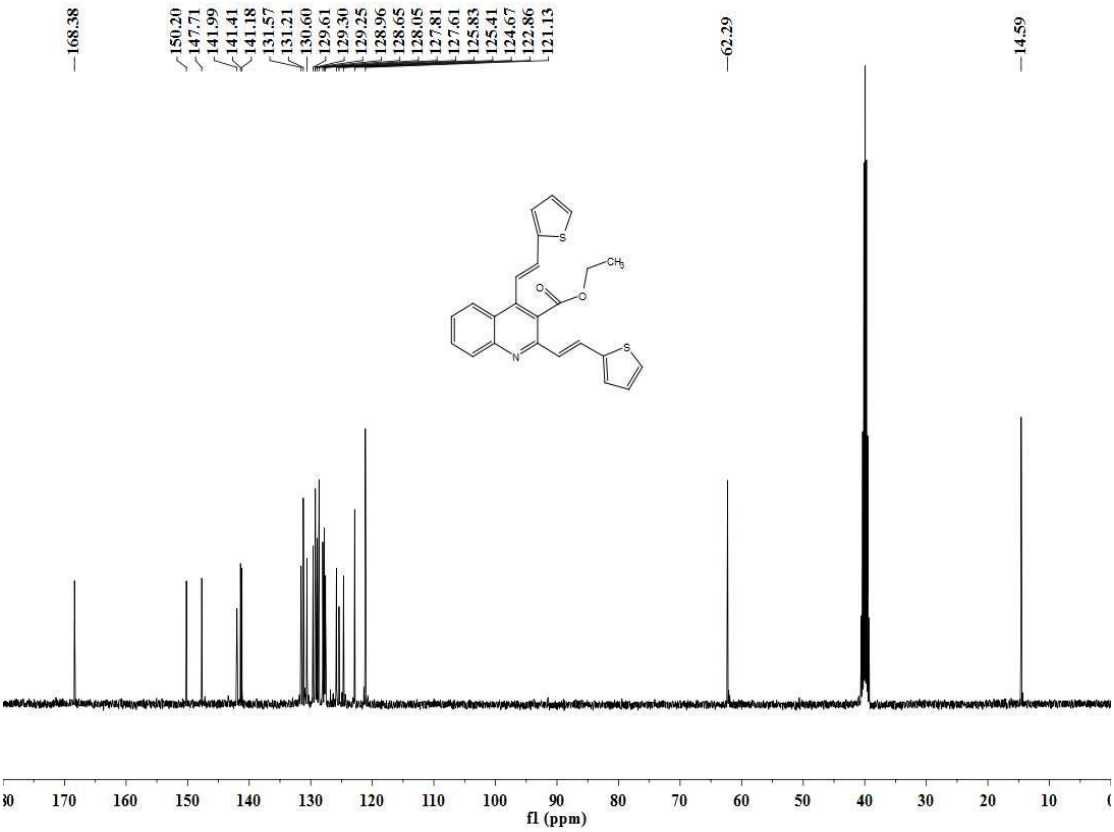

Fig. S38 ^{13}C NMR spectrum of **3r**

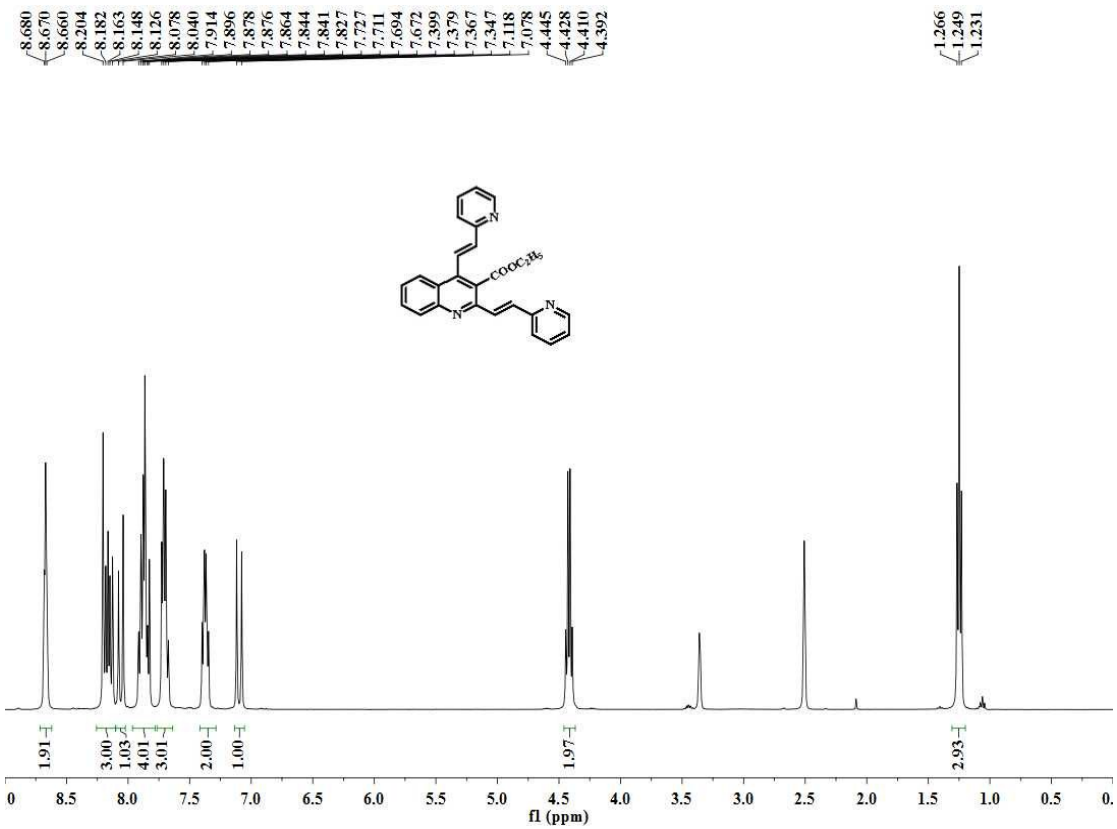

Fig. S39 ^{1}H NMR spectrum of **3s**

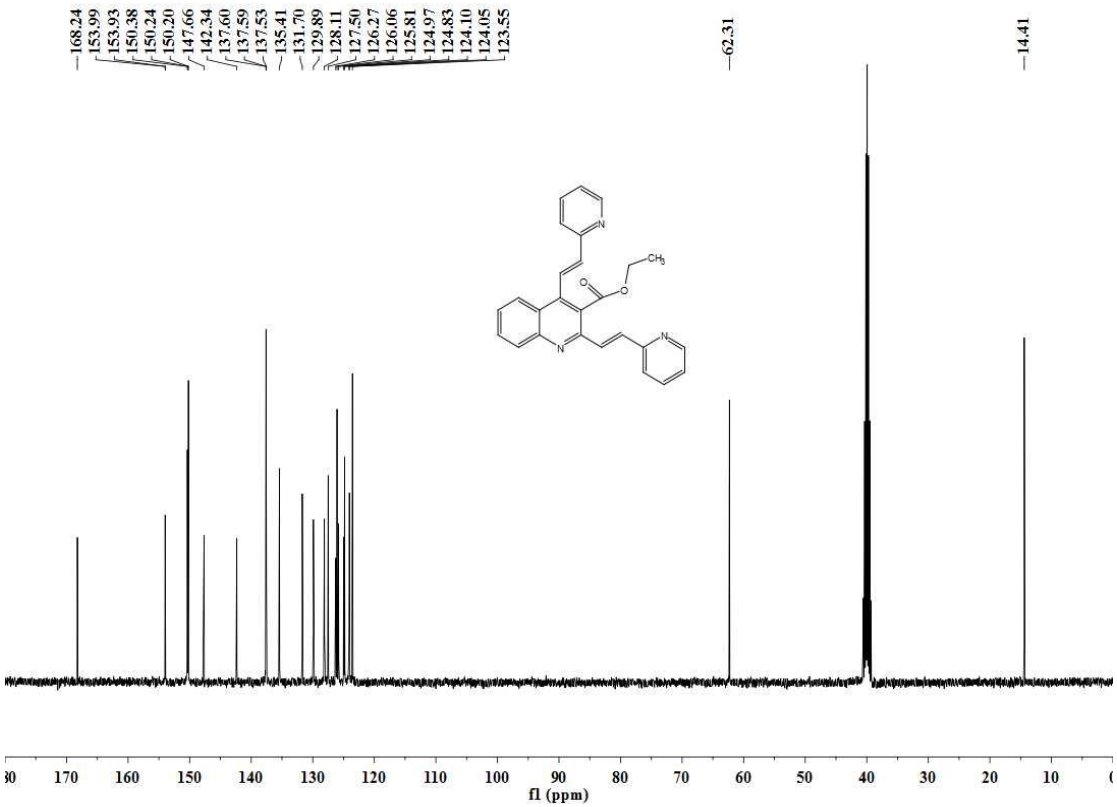

Fig. S40 ^{13}C NMR spectrum of **3s**

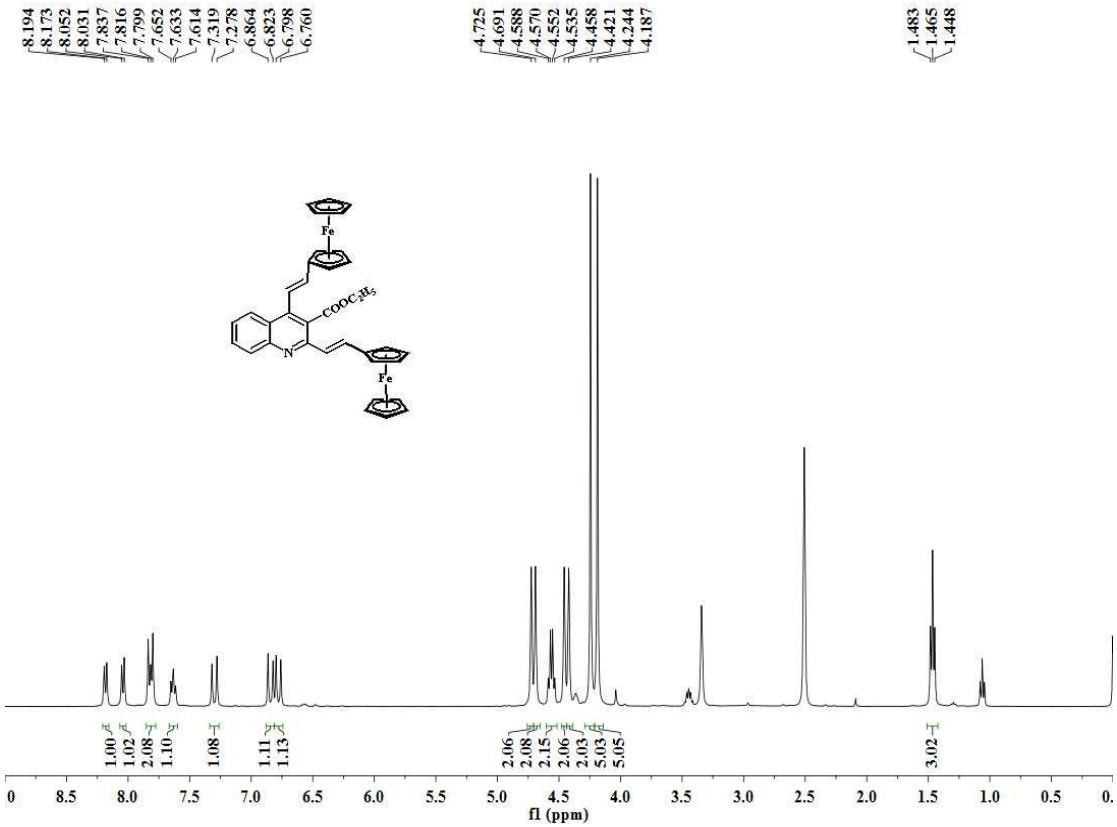

Fig. S41 ^{1}H NMR spectrum of **3t**

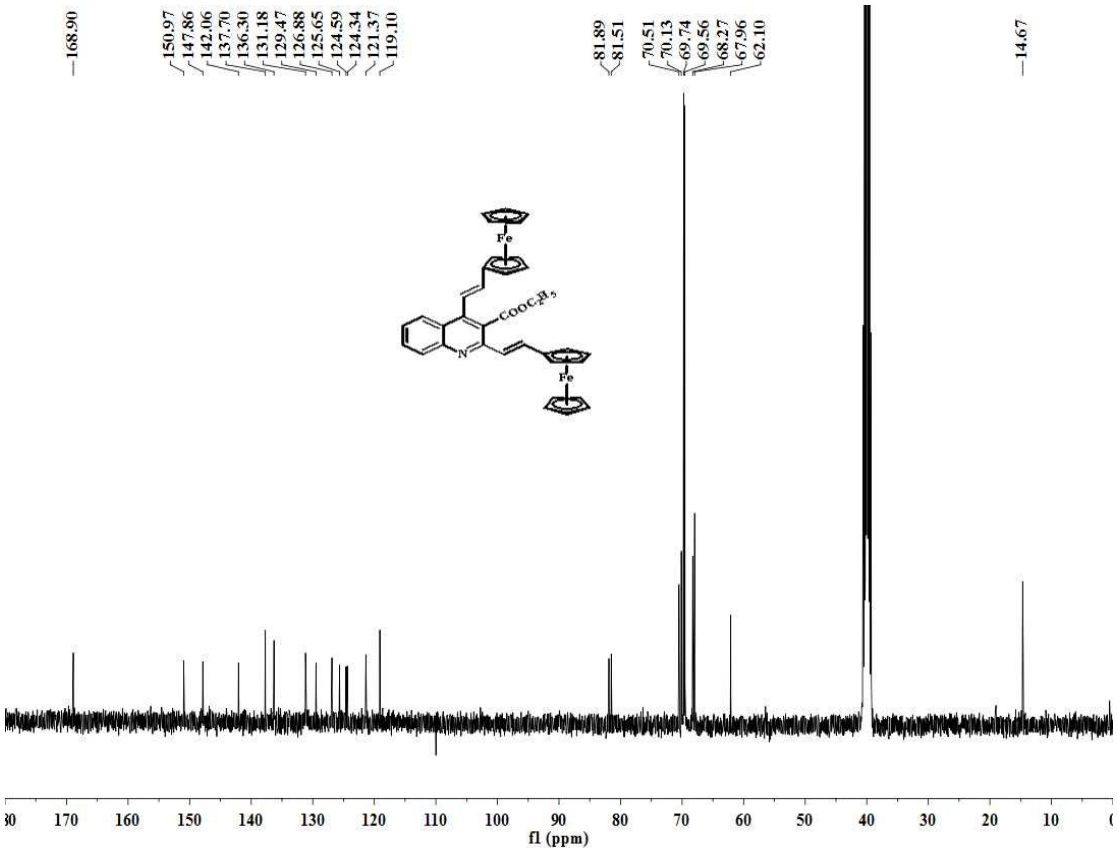

Fig. S42 ^{13}C NMR spectrum of **3t**