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Supplementary information

Palladium-Catalyzed Carbonylation of Multifunctionalized Substituted Alkynes to Quinolinone Derivatives under Mild Conditions

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1. General information

All reagents were used as received from commercial sources without further purification. Calix[6]arenes **4a-c** have been synthesized following literature procedures.[1] All solvents were dried over activated 4 Å molecular sieves for 24 h. Flash column chromatography was performed on silica gel 60 (70–230 mesh). Melting points were measured with an Electrothermal apparatus and are uncorrected. IR spectra were run on PerkinElmer Spectrum Two spectrometer paired with a Diamond Smart Orbit accessory. HRMS data were obtained with LTQ Orbitrap XL Thermo. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AVANCE 400 Hz or JEOL 600MHz ECZ600R, in deuterated chloroform, using the solvent residual signals as internal reference (7.26 and 77.00 ppm, respectively for ^{1}H and ^{13}C). ^{19}F spectra were registered on JEOL 600MHz ECZ600R at 565 Hz. Chemical shifts (δ) and coupling constants (J) are given in ppm and in Hz, respectively.

2. Experimental procedures

General procedures for the carbonylation of 1 are given in the main part of the paper.

General procedure for the reductive amination of aldehydes:[2]

A solution of 2-iodoaniline (4 mmol) in 8 mL of methanol was introduced into a 25 mL flask. An aldehyde (6 mmol) and acetic acid (6 mmol) were added, and the mixture was cooled to 0 °C. Sodium cyanoborohydrate (8 mmol) was added to the solution portionwise within 30 minutes. Once the addition was complete, the reaction was left at room temperature for 16 hours under stirring. When full conversion of the starting 2-iodoaniline was reached, the mixture was poured into a cooled 1 M Na_2CO_3 solution (25 mL). The organic phase was extracted with ethyl acetate (4x10 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was then removed under reduced pressure. The final secondary amine was purified by silica gel column chromatography using hexane/ethyl acetate mixtures as eluent.

Preparation of propargyl amides: [3]

To a cooled to 0 °C solution of a propargylamine (10 mmol) in 25 mL of DCM was added Et_3N (10.5 mmol, 1.46 mL). Aroyl chloride (10.1 mmol) was added dropwise to the solution, and the reaction mixture was stirred at room temperature for 1 h. The resulting mixture was poured into a 1 M solution of NH_4Cl (30 mL), and the organic phase was extracted with DCM (2x10 mL) and then dried over anhydrous Na_2SO_4. After filtration, the solvent was then removed under reduced pressure. The obtained propargylic amide was purified by flash chromatography on SiO_2 using hexane/ethyl acetate mixtures as eluent.

*Synthesis of substrates **1** (Sonogashira coupling):* [3]

In a 100 mL Schlenk tube under nitrogen, to a DCM solution (8 mL) containing an *N*-substituted 2-iodoaniline (1 mmol) and a propargyl amide (1.05 mmol) was added $Pd(PPh_3)_2Cl_2$ (0.02 mmol, 14 mg). Then Et_3N (57.5 mmol, 8 mL) was added, followed by the addition CuI (0.07 mmol, 13 mg). The tube was then sealed, and the reaction mixture was stirred at room temperature for 4-24 h until full conversion of the 2-iodoaniline was reached. After filtration and concentration in vacuo, the residue was diluted with ethyl acetate (40 mL) and washed with 1 M NH_4Cl solution (25 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Products **1** were isolated by flash column chromatography on SiO_2 using mixtures of hexane/ethyl acetate as eluent.

General Procedure for the Synthesis of Arylformates (TFBen[4]*, **5a-c**):*

Under N_2, acetic anhydride (265 mmol, 10 mL) and formic acid (210 mmol, 20 mL) were added to a 100 mL three-necked flask, and the mixture was stirred for an hour at 60 °C. The mixture was cooled down to room temperature, and the solution of hydroxyaryl (1 mmol) together with CH_3OONa (1.2 mmol, 1 g) in 6 mL of THF was added. The reaction was monitored by TLC using hexane/ethyl acetate mixtures as eluents. When the reaction was complete (4-72 h), a cold 2 M Na_2CO_3 solution (50 ml) was added. The organic phase was extracted with DCM (3x25 ml), washed with brine (2x15 ml) and dried over anhydrous Na_2SO_4. After filtration, the solvent was then removed under reduced pressure. The residue was

dissolved in methanol (30 mL), and the insoluble precipitate was filtered off. The evaporation of methanol afforded pure aryl formate as a white solid.

3. Characterization of compounds

***N*-(4-(2-(Benzylamino)phenyl)-2-methylbut-3-yn-2-yl)benzamide**[3] **(1a):** Yellow solid (331 mg, 90% yield); m.p. 106.5-108.5 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.74–7.66 (m, 2H), 7.55–7.47 (m, 1H), 7.46–7.37 (m, 4H), 7.34–7.20 (m, 4H), 7.15–7.07 (m, 1H), 6.58 (td, *J* = 7.4, 0.9 Hz, 1H), 6.53 (d, *J* = 8.3 Hz, 1H), 6.34 (s, 1H), 6.31 (bs, 1H), 4.58 (s, 2H), 1.85 (s, 6H).

***N*-(4-(2-(Ethylamino)phenyl)-2-methylbut-3-yn-2-yl)benzamide (1b):** Yellow solid (269 mg, 88% yield); m.p. 115.4-125.2 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.84 – 7.75 (m, 2H), 7.55 – 7.39 (m, 4H), 7.32 – 7.25 (m, 1H), 7.21 (ddd, *J* = 8.8, 7.3, 1.6 Hz, 1H), 6.66 – 6.53 (m, 2H), 6.42 (s, 1H), 5.47 (s, 1H), 3.28 (q, *J* = 7.2 Hz, 2H), 1.85 (s, 6H), 1.42 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 166.6, 150.1, 135.1, 134.9, 134.9, 131.6, 131.4, 130.9, 129.9, 128.6, 128.3, 128.2, 127.7, 127.0, 115.2, 109.1, 106.7, 97.9, 78.6, 54.5, 48.4, 38.1, 29.7, 14.7, 14.5. **HRMS (ESI)** *m/z* calcd for $C_{20}H_{22}N_2O$ $[M+H]^+$ 307.1810, found 307.1811. **IR (ATR):** ν 3348.2, 3250.0, 3059.7, 2973.4, 2855.2, 1634.6, 1600.0, 1538.5, 1509.0, 1455.3, 1312.9, 1277.6, 1160.5, 743.3, 714.2, 691.3, 533.7 cm^{-1}.

***N*-(4-(2-((3-Methylbenzyl)amino)phenyl)-2-methylbut-3-yn-2-yl)benzamide (1c):** Yellow solid (340 mg, 89% yield); m.p. 89.2-92.3 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.74 – 7.66 (m, 2H), 7.54 – 7.48 (m, 1H), 7.44 – 7.37 (m, 2H), 7.27 – 7.15 (m, 5H), 7.13 – 7.07 (m, 1H), 7.07 – 7.01 (m, 1H), 6.58 – 6.47 (m, 2H), 6.30 (s, 1H), 6.19 (d, *J* = 39.8 Hz, 1H), 4.51 (s, 2H), 2.29 (s, 3H), 1.84 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 166.7, 149.9, 140.0, 138.0, 134.8, 131.5, 131.2, 129.8, 128.6, 128.3, 127.8, 127.5, 126.9, 124.1, 115.5, 109.6, 106.8, 98.0, 78.8, 48.5, 47.3, 29.6, 21.4 ppm. **HRMS (ESI)** *m/z* calcd for $C_{26}H_{26}N_2O$ $[M+H]^+$ 383.2123, found 383.2119. **IR (ATR)** ν 3421, 3334, 3021, 2983, 2968, 2923, 2860, 1638, 1602, 1572, 1514, 1458, 1434, 1290, 1249, 1177, 1162, 742, 733, 711, 689 cm^{-1}.

***N*-(4-(2-((4-Methoxybenzyl)amino)phenyl)-2-methylbut-3-yn-2-yl)benzamide**[3] **(1d):** Yellow solid (374 mg, 94% yield); m.p. 128.5-130.0 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.73–7.67 (m, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.26 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.14–7.08 (m, 1H), 6.83 (d, *J* = 8.6 Hz, 2H), 6.60–6.50 (m, 2H), 6.33 (s, 1H), 6.18 (s, 1H), 4.49 (s, 2H), 3.79 (s, 3H), 1.84 (s, 6H).

***N*-(4-(2-((4-Nitrobenzyl)amino)phenyl)-2-methylbut-3-yn-2-yl)benzamide (1e):** Yellow solid (376 mg, 91% yield); m.p. 131.0-135.8 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.12 – 8.05 (m, 2H), 7.71 – 7.63 (m, 2H), 7.57 – 7.52 (m, 2H), 7.52 – 7.46 (m, 1H), 7.38 (dd, *J* = 8.3, 7.1 Hz, 2H), 7.28 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.09 (ddd, *J* = 8.7, 7.4, 1.6 Hz, 1H), 6.67 (t, *J* = 6.3 Hz, 1H), 6.60 (td, *J* = 7.5, 1.0 Hz, 1H), 6.46 (s, 1H), 6.39 (dd, *J* = 8.4, 1.0 Hz, 1H), 4.66 (d, *J* = 5.1 Hz, 2H), 1.85 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 167.0, 149.4, 148.4, 146.9, 134.6, 131.8, 131.1, 129.8, 128.6, 127.7, 126.8, 123.7, 116.1, 109.3, 107.4, 98.4, 48.2, 46.8, 29.7. **HRMS (ESI)** *m/z* calcd for $C_{25}H_{23}N_3O_3$ $[M+H]^+$ 414.1818, found 414.1814. **IR (ATR)** ν 3398, 3338, 3079, 2974, 2929, 2851, 1639, 1598, 1575, 1515, 1484, 1450, 1347, 1293, 1282, 741, 736, 715 cm^{-1}.

***N*-(4-(2-(Benzylamino)-5-methylphenyl)-2-methylbut-3-yn-2-yl)benzamide**[3] **(1f):** Brownish solid (306 mg, 80% yield); m.p. 129.5-131.0 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.72 – 7.67 (m, 2H), 7.53 – 7.47 (m, 1H), 7.44 – 7.37 (m, 4H), 7.32 – 7.26 (m, 2H), 7.25 – 7.18 (m, 1H), 7.09 (d, *J* = 2.0 Hz, 1H), 6.91 (dd, *J* =

8.4, 1.6 Hz, 1H), 6.43 (d, *J* = 8.4 Hz, 1H), 6.29 (br s, 1H), 6.02 (br s, 1H), 4.53 (s, 2H), 2.18 (s, 3H), 1.84 (s, 6H.

***N*-(4-(2-(Benzylamino)-5-isopropylphenyl)-2-methylbut-3-yn-2-yl)benzamide**[3] **(1g):** Yellow solid (320 mg, 78% yield); m.p. 115.3-117.9 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.74–7.69 (m, 2H), 7.54–7.48 (m, 1H), 7.46–7.38 (m, 4H), 7.34–7.28 (m, 2H), 7.27–7.22 (m, 1H), 7.17 (d, *J* = 2.1 Hz, 1H), 7.00 (dd, *J* = 8.5, 2.1 Hz, 1H), 6.49 (d, *J* = 8.5 Hz, 1H), 6.35 (bs, 1H), 6.08 (bs, 1H), 4.55 (s, 2H), 2.78 (hept, *J* = 6.9 Hz, 1H), 1.86 (s, 6H), 1.21 (d, *J* = 6.9 Hz, 6H).

***N*-(4-(2-(Benzylamino)-5-fluorophenyl)-2-methylbut-3-yn-2-yl)benzamide**[3] **(1h):** Yellow solid (363 mg, 94% yield); m.p. 150.2-150.5 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.74–7.67 (m, 2H), 7.54–7.48 (m, 1H), 7.45–7.37 (m, 4H), 7.34–7.20 (m, 3H), 6.98 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.82 (td, *J* = 8.7, 3.0 Hz, 1H), 6.41 (dd, *J* = 9.1, 4.6 Hz, 1H), 6.32 (bs, 1H), 6.22 (bs, 1H), 4.53 (s, 2H), 1.84 (s, 6H).

***N*-(4-(2-(Benzylamino)-5-bromophenyl)-2-methylbut-3-yn-2-yl)benzamide**[3] **(1i):** Brown solid (362 mg, 81% yield); m.p. 136.8-138.5 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.72–7.67 (m, 2H), 7.54–7.48 (m, 1H), 7.44–7.34 (m, 5H), 7.32–7.23 (m, 3H), 7.15 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.46 (bs, 1H), 6.37 (d, *J* = 8.9 Hz, 1H), 6.32 (bs, 1H), 4.54 (d, *J* = 2.7 Hz, 2H), 1.83 (s, 6H).

***N*-(4-(2-(Benzylamino)-5-(trifluoromethyl)phenyl)-2-methylbut-3-yn-2-yl)benzamide**[3] **(1j):** Yellow solid (375 mg, 86% yield); m.p. 133.5-134.5 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.69 (d, *J* = 7.4 Hz, 2H), 7.55–7.47 (m, 2H), 7.45–7.37 (m, 4H), 7.33–7.21 (m, 4H), 6.93 (bs, 1H), 6.51 (d, *J* = 8.8 Hz, 1H), 6.31 (bs, 1H), 4.61 (d, *J* = 5.3 Hz, 2H), 1.84 (s, 6H).

Methyl 3-(3-benzamido-3-methylbut-1-yn-1-yl)-4-(benzylamino)benzoate[3] **(1k):** Yellow solid (320 mg, 75% yield); m.p. 161.2-163.0 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.96 (d, *J* = 1.9 Hz, 1H), 7.77 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.68 (d, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.1 Hz, 1H), 7.42–7.35 (m, 4H), 7.32–7.21 (m, 3H), 7.08 (b t, *J* = 5.9 Hz, 1H), 6.49 (d, *J* = 8.8 Hz, 1H), 6.42 (bs, 1H), 4.63 (d, *J* = 5.9 Hz, 2H), 3.83 (s, 3H), 1.83 (s, 6H).

***N*-(4-(2-(Benzylamino)-4-chlorophenyl)-2-methylbut-3-yn-2-yl)benzamide**[3] **(1l):** Yellow solid (282 mg, 70% yield); m.p. 128.0-128.5 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.68 (d, *J* = 8.0 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.43 – 7.37 (m, 4H), 7.34 – 7.22 (m, 3H), 7.15 (d, *J* = 8.0 Hz, 1H), 6.55 – 6.48 (m, 3H), 6.31 (br s, 1H), 4.54 (s, 2H), 1.82 (s, 6H).

***N*-(4-(2-(Benzylamino)-3,5-dimethylphenyl)-2-methylbut-3-yn-2-yl)benzamide**[3] **(1m):** Yellow solid (320 mg, 75% yield); m.p. 79.0-80.0 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.76 – 7.72 (m, 2H), 7.51 – 7.43 (m, 3H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.34 – 7.27 (m, 2H), 7.26 – 7.22 (m, 1H), 7.11 (d, *J* = 1.6 Hz, 1H), 6.93 (d, *J* = 1.5 Hz, 1H), 6.55 (br s, 1H), 4.46 (m, 3H), 2.35 (s, 3H), 2.26 (s, 3H), 1.83 (s, 6H).

***N*-(1-((2-((4-Methoxybenzyl)amino)phenyl)ethynyl)cyclohexyl)benzamide (1n):** Yellow solid (346 mg, 79% yield); m.p. 96.1-102.3 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.75 – 7.65 (m, 2H), 7.53 – 7.46 (m, 1H), 7.41 (ddt, *J* = 8.2, 6.5, 1.2 Hz, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), 7.29 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.11 (ddd, *J* = 8.8, 7.4, 1.6 Hz, 1H), 6.86 – 6.79 (m, 2H), 6.60 – 6.49 (m, 2H), 6.24 (m, 2H), 4.47 (s, 2H), 3.79 (s, 3H), 2.39 (dd, *J* = 10.8, 6.0 Hz, 2H), 2.43 – 2.29 (m, 2H), 1.96 – 1.51 (m, 7H), 1.46 – 1.28 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 166.6, 158.5, 149.8, 135.1, 132.0, 131.5, 131.3, 129.6, 128.6 (2C), 128.4 (2C), 126.9 (2C), 115.4, 113.8

(2C), 109.5, 107.2, 96.6, 80.9, 55.3, 52.7, 46.7, 37.5, 25.4, 22.7. **HRMS (ESI)** *m/z* calcd for $C_{29}H_{30}N_2O_2$ $[M+H]^+$ 439.2386, found 439.2383. **IR (ATR)** ν 3393, 3346, 3335, 3061, 2930, 2845, 1646, 1600, 1574, 1508, 1483, 1301, 1247, 1172, 1030, 819, 739, 710 cm^{-1}.

***N*-(4-(2-(Benzylamino)phenyl)-2-methylbut-3-yn-2-yl)-4-fluorobenzamide**[3] **(1o):** Yellow solid (355 mg, 92% yield); m.p. 100.1-101.0 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.73–7.67 (m, 2H), 7.45 (d, *J* = 7.2 Hz, 2H), 7.36–7.25 (m, 4H), 7.18–7.11 (m, 1H), 7.09–7.02 (m, 2H), 6.62 (td, *J* = 7.5, 0.9 Hz, 1H), 6.58 (d, *J* = 8.3 Hz, 1H), 6.48 (bs, 1H), 6.31 (bs, 1H), 4.60 (s, 2H), 1.86 (s, 6H).

***N*-(4-(2-(Benzylamino)phenyl)-2-methylbut-3-yn-2-yl)-4-chlorobenzamide**[3] **(1p):** Yellow solid (355 mg, 92% yield); m.p. 130.2-131.0 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.63 – 7.58 (m, 2H), 7.46 – 7.42 (m, 2H), 7.38 – 7.25 (m, 6H), 7.15 (ddd, *J* = 8.4, 7.4, 1.6 Hz, 1H), 6.62 (td, *J* = 7.5, 1.0 Hz, 1H), 6.58 (d, *J* = 8.3 Hz, 1H), 6.42 (br s, 1H), 6.25 (br s, 1H), 4.59 (s, 2H), 1.86 (s, 6H).

***N*-(4-(2-(Benzylamino)phenyl)-2-methylbut-3-yn-2-yl)-4-nitrobenzamide**[3] **(1q):** Yellow solid (355 mg, 92% yield); m.p. 125.1-126.5 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.16 (d, *J* = 8.8 Hz, 2H), 7.77 (d, *J* = 8.8 Hz, 2H), 7.42 (d, *J* = 7.1 Hz, 2H), 7.37 – 7.23 (m, 4H), 7.18 – 7.11 (m, 1H), 6.65 (br s, 1H), 6.63 – 6.55 (m, 2H), 6.13 (br s, 1H), 4.56 (s, 2H), 1.87 (s, 6H).

***N*-(4-(2-(benzylamino)phenyl)-2-methylbut-3-yn-2-yl)furan-2-carboxamide (1r):** Light yellow solid (332 mg, 93%); m.p. 114.0-114.9 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.45 – 7.38 (m, 3H), 7.33 – 7.27 (m, 2H), 7.27 – 7.20 (m, 2H), 7.09 (ddd, *J* = 8.2, 7.3, 1.6 Hz, 1H), 7.02 (dd, *J* = 3.5, 0.9 Hz, 1H), 6.55 (td, *J* = 7.4, 1.1 Hz, 2H), 6.52 – 6.46 (m, 2H), 6.19 (br s, 1H), 4.53 (s, 2H), 1.83 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 157.6, 149.8, 148.1, 143.7, 140.0, 131.2, 129.8, 128.4 (2C), 127.1 (2C), 126.7, 115.5, 114.4, 112.2, 109.6, 106.8, 97.8, 78.9, 48.1, 47.3, 29.7 (2C). **HRMS (ESI)** *m/z* calcd for $C_{23}H_{22}N_2O_2$ $[M+H]^+$ 359.1760, found 359.1760. **IR (ATR):** ν 3414.6, 3350.5, 3250.2, 3029.7, 2985.6, 2929.5, 2857.3, 1655.4, 1600.0, 1589.6, 1573.4, 1538.5, 1509.0, 1470.2, 1451.4, 1322.8, 1295.2, 1188.7, 1162.3, 1008.9, 909.1, 744.1 730.6 cm^{-1}.

***N*-(4-(2-(benzylamino)phenyl)-2-methylbut-3-yn-2-yl)thiophene-2-carboxamide (1s):** Light yellow solid (295 mg, 79%); m.p. 153.3-155.8 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.49 – 7.39 (m, 4H), 7.34 – 7.28 (m, 2H), 7.28 – 7.20 (m, 2H), 7.12 – 7.03 (m, 2H), 6.56 (td, *J* = 7.5, 1.1 Hz, 1H), 6.51 (dd, *J* = 8.4, 1.0 Hz, 1H), 6.21 (br s, 1H), 6.19 (br s, 1H), 4.54 (s, 2H), 1.83 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 161.3, 149.8, 140.0, 139.4, 131.2, 130.1, 129.8, 128.4 (2C), 128.1, 127.6, 127.1 (2C), 126.7, 115.5, 109.7, 106.8, 97.9, 78.9, 48.7, 47.3, 29.6 (2C). **HRMS (ESI)** *m/z* calcd for $C_{23}H_{22}N_2OS$ $[M+H]^+$ 389.1688, found 389.1690. **IR (ATR):** ν 3387.8, 3285.1, 3084.8, 3071.5, 3027.2, 2984.2, 2830.7, 1622.3, 1600.7, 1574.2, 1532.7, 1505.3, 1470.9, 1454.6, 1433.4, 1305.8, 1182.0, 1163.2, 858.0, 743.0, 728.2, 698.5 cm^{-1}.

6-Benzyl-4,4-dimethyl-2-phenyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one[3] **(2a):** White solid (106 mg, 90% yield); m.p. 211.2-212.0 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.20 (dd, *J* = 7.9, 1.7 Hz, 2H), 8.12 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.56–7.45 (m, 4H), 7.36–7.22 (m, 7H), 5.59 (br s, 2H), 1.86 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 161.0, 150.4, 146.1, 138.7, 136.6, 131.9, 131.2, 131.1, 128.9 (2C), 128.4 (2C), 127.5 (2C), 127.3, 126.5 (2C), 122.9, 122.1, 114.9, 114.0, 112.0, 52.9, 45.9, 30.1 (2C). **HRMS (ESI)** *m/z* calcd for $C_{26}H_{22}N_2O_2$ $[M+H]^+$ 395.1760, found 395.1762. **IR (ATR)** ν 3013, 2948, 1684, 1631, 1512, 1452, 1297, 1262, 1247, 1136, 1018, 743 cm^{-1}.

6-Ethyl-4,4-dimethyl-2-phenyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one (2b): White solid (80 mg, 84% yield); m.p. 142.2-145.7 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.18 – 8.15 (m, 2H), 8.10 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.63 (ddd, *J* = 8.7, 7.1, 1.6 Hz, 1H), 7.58 – 7.44 (m, 3H), 7.41 (d, *J* = 8.6 Hz, 1H), 7.33 (ddd, *J* = 8.1, 7.1, 0.9 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.82 (s, 6H), 1.40 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 160.3, 150.0, 146.1, 138.1, 131.9, 131.3, 131.1, 128.4 (2C), 127.5 (2C), 123.0, 121.8, 113.9 (2C), 112.0, 52.9, 37.4, 30.0 (2C), 12.9. **HRMS (ESI)** *m/z* calcd for $C_{21}H_{20}N_2O_2$ $[M+H]^+$ 333.1603, found 333.1603. **IR (ATR)** ν 3660, 3366, 2988, 2968, 2923, 2900, 1692, 1627, 1597, 1579, 1366, 1316, 1276, 1249, 1147, 1110, 1074, 1042, 1022, 761, 695, 686 cm^{-1}.

6-(3-Methylbenzyl)-4,4-dimethyl-2-phenyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one (2c): White solid (115 mg, 94% yield); m.p. 144.2-149.6 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.28 – 8.16 (m, 2H), 8.13 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.62 – 7.45 (m, 4H), 7.36 – 7.27 (m, 2H), 7.27 – 7.18 (m, 1H), 7.12 – 6.98 (m, 3H), 5.56 (br s, 2H), 2.34 (s, 3H), 1.89 (s, 6H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 161.0, 150.4, 146.1, 138.7, 138.5, 136.6, 131.8, 131.2, 131.2, 128.8, 128.5 (2C), 128.1, 127.5 (2C), 127.2, 123.5, 122.8, 122.1, 114.9, 113.9, 112.0, 53.0, 45.9, 30.1 (2C), 21.6 ppm. **HRMS (ESI)** *m/z* calcd for $C_{27}H_{24}N_2O_2$ $[M+H]^+$ 409.1916, found 409.1413. **IR (ATR)** ν 3368, 3177, 2928, 2847, 1641, 1600, 1569, 1505, 1448, 1351, 1313, 1239, 754, 739, 682 cm^{-1}.

6-(4-Methoxybenzyl)-4,4-dimethyl-2-phenyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one[3] **(2d):** White solid (104 mg, 82% yield); m.p. 155.1-158.8 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.21 – 8.16 (m, 2H), 8.11 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.59 – 7.48 (m, 4H), 7.38 – 7.26 (m, 2H), 7.24 – 7.16 (m, 2H), 6.91 – 6.83 (m, 2H), 5.52 (br s, 2H), 3.78 (s, 3H), 1.87 (s, 6H).

6-(4-Nitrobenzyl)-4,4-dimethyl-2-phenyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one (2e): White solid (128 mg, 97% yield); m.p. 224.5-233.4 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.27 – 8.10 (m, 5H), 7.61 – 7.49 (m, 4H), 7.43 – 7.31 (m, 3H), 7.17 (d, *J* = 8.5 Hz, 1H), 5.67 (s, 2H), 1.85 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 160.9, 150.8, 147.3, 146.0, 144.2, 138.2, 131.6, 131.5, 131.4, 128.5 (2C), 127.5 (2C), 127.4 (2C), 124.2 (2C), 123.3, 122.7, 114.3, 114.1, 111.9, 52.9, 45.6, 30.1 (2C). **HRMS (ESI)** *m/z* calcd for $C_{26}H_{21}N_3O_4$ $[M+H]^+$ 440.1610, found 440.1607. **IR (ATR)** ν 3393, 3335, 3184, 2973, 2930, 2845, 1692, 1641, 1600, 1575, 1511, 1483, 1484, 1455, 1343, 1313, 1246, 739, 710, 690 cm^{-1}.

6-Benzyl-4,4,9-trimethyl-2-phenyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one[3] **(2f):** White solid (116 mg, 95% yield); m.p. 192.0-193.0 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ δ 8.23 – 8.17 (m, 2H), 7.87 (dd, *J* = 2.0, 1.0 Hz, 1H), 7.60 – 7.51 (m, 3H), 7.37 – 7.16 (m, 7H), 5.58 (br s, 2H), 2.49 (s, 3H), 1.86 (s, 6H).

6-Benzyl-9-isopropyl-4,4-dimethyl-2-phenyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one[3] **(2g):** White solid (102 mg, 78% yield); m.p. 183.5-183.9 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.23–8.19 (m, 2H), 7.94 (d, *J* = 2.0 Hz, 1H), 7.61–7.52 (m, 3H), 7.40 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.35 (t, *J* = 7.3 Hz, 2H), 7.31–7.24 (m, 4H), 5.59 (bs, 2H), 3.08 (hept, *J* = 6.9 Hz, 1H), 1.87 (s, 6H), 1.36 (s, 3H), 1.34 (s, 3H).

6-Benzyl-9-fluoro-4,4-dimethyl-2-phenyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one[3] **(2h):** White solid (114 mg, 92% yield); m.p. 219.7-220.1 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.20–8.15 (m, 2H), 7.75 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.60–7.50 (m, 3H), 7.37–7.32 (m, 2H), 7.31–7.19 (m, 5H), 5.58 (bs, 2H), 1.86 (s, 6H).

6-Benzyl-9-bromo-4,4-dimethyl-2-phenyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one[3] **(2i):** White solid (125 mg, 88% yield); m.p. 209.1-211.5 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.21–8.14 (m, 3H), 7.60–7.51 (m, 4H), 7.36–7.26 (m, 3H), 7.24–7.19 (m, 2H), 7.16 (d, *J* = 9.0 Hz, 1H), 5.55 (bs, 2H), 1.86 (s, 6H).

6-Benzyl-4,4-dimethyl-2-phenyl-9-(trifluoromethyl)-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one[3] **(2j):** White solid (90 mg, 65% yield); m.p. 222.1-224.2 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.35 (d, *J* = 1.2 Hz, 1H), 8.19 (dd, *J* = 7.8, 1.8 Hz, 2H), 7.72 (dd, *J* = 8.9, 1.9 Hz, 1H), 7.62–7.52 (m, 3H), 7.43–7.34 (m, 3H), 7.33–7.27 (m, 1H), 7.24 (d, *J* = 7.2 Hz, 2H), 5.61 (bs, 2H), 1.87 (s, 6H).

Methyl 6-benzyl-4,4-dimethyl-5-oxo-2-phenyl-5,6-dihydro-4*H*-[1,3]oxazino[5,6-c]quinoline-9-carboxylate[3] **(2k):** White solid (31 mg, 23% yield); m.p. 258.1-259.9 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.78 (d, *J* = 2.0 Hz, 1H), 8.23–8.18 (m, 2H), 8.12 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.61–7.51 (m, 3H), 7.37–7.25 (m, 4H), 7.23 (d, *J* = 7.1 Hz, 2H), 5.60 (bs, 2H), 3.99 (s, 3H), 1.84 (s, 6H).

6-Benzyl-8-chloro-4,4-dimethyl-2-phenyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one[3] **(2l):** White solid (114 mg, 89% yield); m.p. 188.2-189.5 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.20 – 8.13 (m, 2H), 8.02 (d, *J* = 8.5 Hz, 1H), 7.60 – 7.48 (m, 3H), 7.36 (dd, *J* = 8.2, 6.6 Hz, 2H), 7.33 – 7.19 (m, 5H), 5.53 (br s, 2H), 1.84 (s, 6H).

6-Benzyl-4,4,7,9-tetramethyl-2-phenyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one[3] **(2m):** White solid (92 mg, 73% yield); m.p. 188.2-189.5 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.24 – 8.14 (m, 2H), 7.81 (d, *J* = 2.2 Hz, 1H), 7.60 – 7.49 (m, 3H), 7.32 (dd, *J* = 8.3, 6.8 Hz, 2H), 7.27 – 7.20 (m, 1H), 7.19 (d, *J* = 2.2 Hz, 1H), 7.12 – 7.05 (m, 2H), 5.70 (br s, 2H), 2.55 (s, 3H), 2.46 (s, 3H), 1.80 (s, 6H).

6'-(4-Methoxybenzyl)-2'-phenylspiro[cyclohexane-1,4'-[1,3]oxazino[5,6-c]quinolin]-5'(6'*H*)-one (2n): White solid (89 mg, 64% yield); m.p. 206.5-209.6 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.24 (d, *J* = 7.0 Hz, 2H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.61 – 7.47 (m, 4H), 7.32 (ddd, *J* = 15.6, 7.7, 3.7 Hz, 2H), 7.20 (dd, *J* = 8.6, 2.1 Hz, 2H), 6.92 – 6.84 (m, 2H), 5.51 (s, 2H), 3.79 (d, *J* = 2.1 Hz, 3H), 3.01 – 2.88 (m, 2H), 2.19 (q, *J* = 13.5, 13.1 Hz, 2H), 1.73 (td, *J* = 49.5, 49.0, 13.3 Hz, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 161.1, 158.8, 151.3, 144.0, 138.8, 132.1, 131.1, 131.0, 128.7, 128.4 (2C), 127.9 (2C), 127.5 (2C), 122.8, 122.0, 114.8, 114.3 (2C), 114.1, 111.7, 55.3, 45.4, 36.5 (2C), 25.8, 20.8 (2C). **HRMS (ESI)** *m/z* calcd for $C_{30}H_{28}N_2O_3$ $[M+H]^+$ 465.2178, found 465.2173. **IR (ATR)** ν 3675, 2958, 2925, 2907, 2850, 1692, 1629, 1597, 1510, 1251, 1172, 1130, 1107, 1039, 1020, 737, 688, 680 cm^{-1}.

6-Benzyl-2-(4-fluorophenyl)-4,4-dimethyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one[3] **(2o):** White solid (111 mg, 90% yield); m.p. 225.7-226.8 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.24–8.15 (m, 2H), 8.08 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.55–7.47 (m, 1H), 7.38–7.16 (m, 9H), 5.59 (bs, 2H), 1.84 (s, 6H).

6-Benzyl-2-(4-chlorophenyl)-4,4-dimethyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one[3] **(2p):** White solid (113 mg, 88% yield); m.p. 195.6-197.3 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.17 – 8.10 (m, 2H), 8.07 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.54 – 7.46 (m, 3H), 7.37 – 7.20 (m, 7H), 5.59 (br s, 2H), 1.85 (s, 6H).

6-Benzyl-2-(4-nitrophenyl)-4,4-dimethyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one[3] **(2q):** Yellow solid (112 mg, 85% yield); m.p. 204.2-206.4 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.37 (s, 4H), 8.07 (dd,

J = 8.2, 1.6 Hz, 1H), 7.53 (ddd, *J* = 8.8, 7.2, 1.6 Hz, 1H), 7.34 (tq, *J* = 6.9, 1.5 Hz, 4H), 7.30 – 7.26 (m, 1H), 7.26 – 7.22 (m, 2H), 5.59 (br s, 2H), 1.86 (s, 6H).

6-Benzyl-2-(furan-2-yl)-4,4-dimethyl-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one (2r): White solid (77 mg, 67%); m.p. 205.4-206.5 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.04 – 7.97 (m, 1H), 7.63 (dd, *J* = 1.7, 0.9 Hz, 1H), 7.48 (ddd, *J* = 8.7, 7.4, 1.6 Hz, 1H), 7.35 – 7.19 (m, 7H), 7.16 (dd, *J* = 3.4, 0.9 Hz, 1H), 6.58 (dd, *J* = 3.4, 1.8 Hz, 1H), 5.56 (br s, 2H), 1.88 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 160.8, 150.0, 145.4, 145.0, 140.0, 138.6, 136.5, 131.3, 128.9 (2C), 127.3, 126.5 (2C), 122.7, 122.1, 114.9, 113.6, 113.5, 112.0, 111.5, 52.8, 45.9, 30.0 (2C). **HRMS (ESI)** *m/z* calcd for $C_{24}H_{20}N_2O_3$ $[M+H]^+$ 385.1552, found 385.1553. **IR (ATR):** ν 3112.7, 2972.8, 2928.2, 2856.9, 1694.0, 1636.9, 1596.9, 1575.8, 1482.8, 1454.4, 1378.0, 1366.0, 1303.5, 1173.6, 1130.4, 1053.4, 1011.6, 776.9, 749.5, 738.2 cm^{-1}.

6-Benzyl-4,4-dimethyl-2-(thiophen-2-yl)-4,6-dihydro-5*H*-[1,3]oxazino[5,6-c]quinolin-5-one (2s): White solid (106 mg, 85%); m.p. 202.7-204.2 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.07 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.84 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.37 – 7.21 (m, 7H), 7.17 (dd, *J* = 5.0, 3.7 Hz, 1H), 5.58 (br s, 2H), 1.84 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 160.9, 150.2, 142.9, 138.6, 136.5, 135.6, 131.2, 129.5, 129.0, 128.9 (2C), 127.5, 127.3, 126.5 (2C), 122.8, 122.4, 122.1, 114.8, 112.0, 53.1, 45.9, 29.9 (2C). **HRMS (ESI)** *m/z* calcd for $C_{24}H_{20}N_2O_2S$ $[M+H]^+$ 415.1480, found 415.1482. **IR (ATR):** ν 3116.7, 3088.7, 3024.8, 2968.8, 2928.8, 2856.9, 1689.4, 1637.4, 1597.1, 1574.1, 1494.7, 1432.9, 1385.6, 1355.6, 1260.6, 1238.8, 1128.8, 1080.4, 1018.5, 979.5, 751.4, 739.0, 723.5, 692.3 cm^{-1}.

***N*-(4-(2-(N-benzylformamido)phenyl)-2-methylbut-3-yn-2-yl)benzamide** (*mixture of rotamers 13/1*) **(3a):** Colorless oil (43 mg, 36% yield, Table 2, entry 2); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.37 (s, 1H), 7.86 – 7.79 (m, 2H), 7.55 – 7.40 (m, 4H), 7.30 – 7.15 (m, 7H), 7.03 – 6.97 (m, 1H), 6.42 (s, 1H), 5.00 (s, 2H), 1.82 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 166.6, 163.2, 141.8, 136.5, 134.9, 133.4, 131.5, 129.2, 128.8 (2C), 128.5 (2C), 128.4 (2C), 127.6, 127.5, 127.5, 127.1 (2C), 121.7, 98.2, 77.7, 49.2, 48.8, 28.9 (2C). **HRMS (ESI)** *m/z* calcd for $C_{26}H_{24}N_2O_2$ $[M+H]^+$ 397.1916, found 397.1917. **IR (ATR)** ν 3313, 3061, 3030, 2981, 2934, 2869, 2244, 1660, 1525, 1488, 1451, 1358, 1290, 1192, 1078, 909, 715, 728, 696 cm^{-1}.

37,38,39,40,41,42-Hexa-*O*-formylcalix[6]arene (5a): White solid (675 mg, 84% yield); m.p. 239.7-240.2 °C; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.75 (br s, 6H), 7.13 (t, *J* = 7.5 Hz, 6H), 7.05 (d, *J* = 7.5 Hz, 12H), 3.68 (s, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 158.7 (6C), 146.6 (6C), 132.4 (12C), 129.8 (12C), 126.7 (12C), 31.8 (6C). **IR (ATR)** ν 1730.51 cm^{-1}.

5,11,17,23,29,35-Hexa-(*tert*-butyl)-37,38,39,40,41,42-hexa-*O*-formylcalix[6]arene (5b): White solid (1048 mg, 92% yield); m.p. 221.8-222.4 °C (deg.); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 (br s, 6H), 7.02 (s, 12H), 3.63 (s, 12H), 1.22 (m, 54H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 158.9 (6C), 149.3 (12C), 144.3 (6C), 131.4 (12C), 126.7 (12C), 34.4 (6C), 32.0 (6C), 31.4 (18C). **ESI-MS** *m/z* calcd for $C_{72}H_{84}O_{12}$ $[M+Na]^+$ 1163.586, found 1163.778. **IR (ATR)** ν 2955, 1733 cm^{-1}.

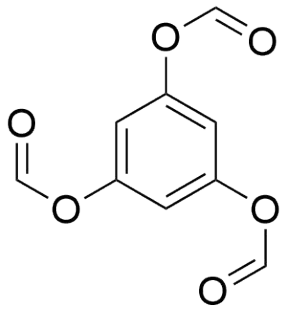
5,11,17,23,29,35-Hexabromo-37,38,39,40,41,42-hexa-*O*-formylcalix[6]arene (5c): White solid (664 mg, 52% yield); m.p. 300.2-301.8 °C (deg.); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.86 (br s, 6H), 7.18 (s, 12H), 3.61 (s, 12H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 159.1 (6C), 145.1 (6C), 134.4 (12C), 131.9 (6C), 118.9 (12C), 29.6 (6C). **IR (ATR)** ν 2971, 1740 cm^{-1}.

References

1. (a) Gutsche, C. D.; Lin, L.-G. *Tetrahedron* 1986, *42*, 1633–1640; (b) C.D. Gutsche. J.D. White (Ed.), Org. Syntheses, 68 (1989), pp. 234-246; (c) Clark, T. E.; Makha, M.; Sobolev, A. N.; Su, D.; Rohrs, H.; Gross, M. L.; Atwood, J. L.; Raston, C. L. *New J. Chem.* 2008, *32*, 1478.
2. Pound, S.M.; Underwood, S.J.; Douglas, C.J. *Eur. J. Org. Chem*., 2020, *2020*, 2448-2453.
3. Pancrazzi, F.; Sarti, N.; Della Ca', N. et al. *Org. Lett.,* 2020, *22*, 1569−1574.
4. Ying, J.; Wang, H.; Qi, X.; Peng, J.-B.; Wu, X.-F. *Eur. J. Org. Chem.*, 2018, 688-692.

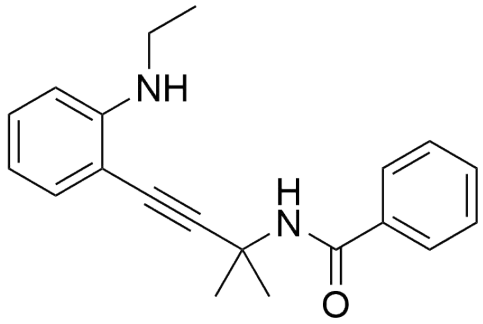
5. Copy of NMR spectra

^{1}H, $CDCl_3$



TFBen

^1H, $CDCl_3$

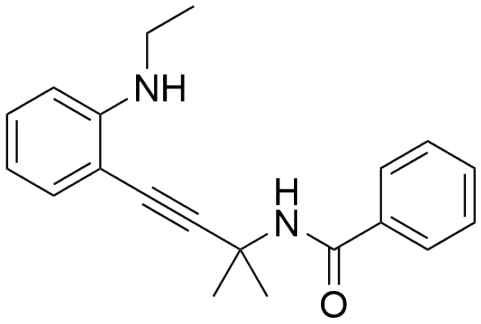


1b

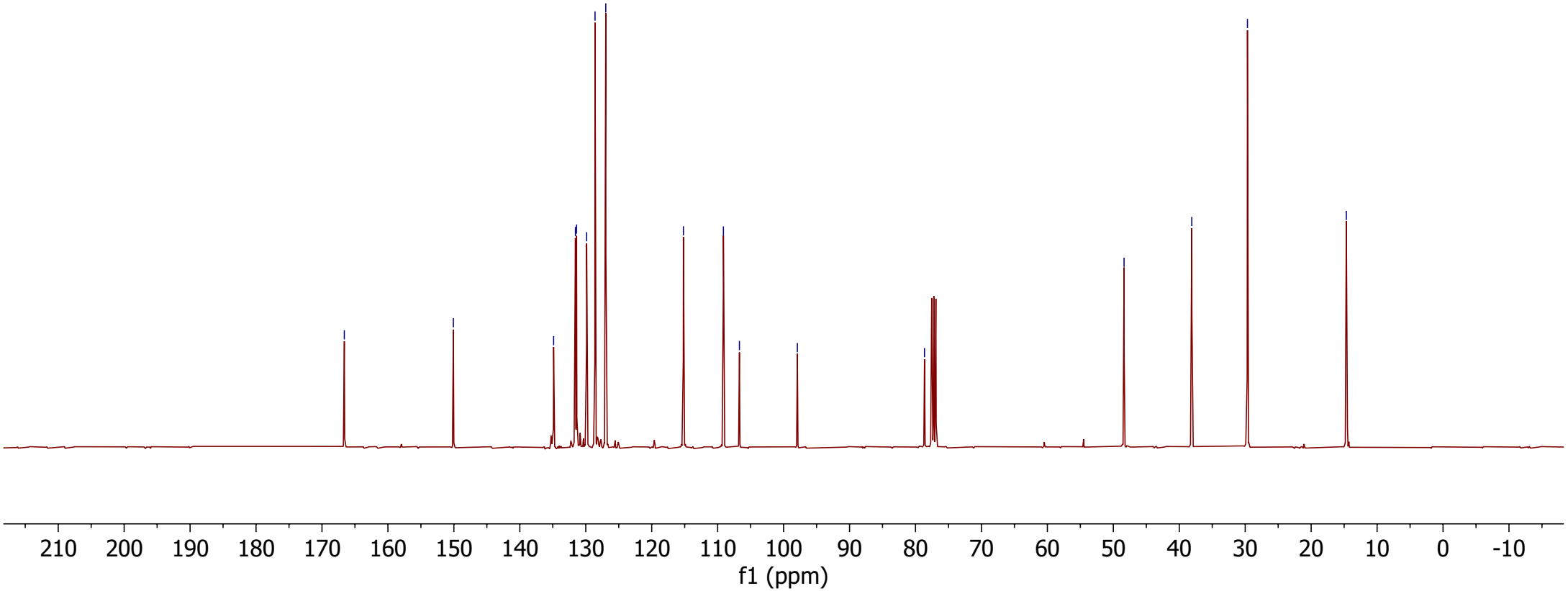
f1 (ppm)

^{13}C, $CDCl_3$

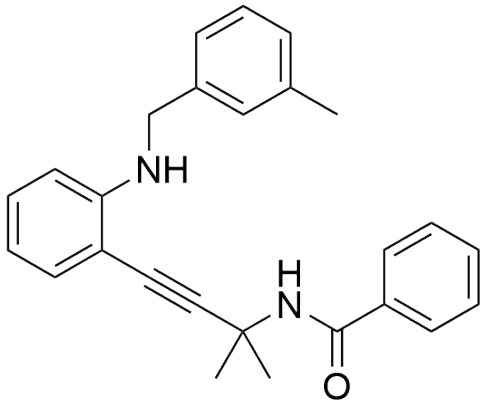
166.61
150.08
134.88
131.57
131.39
129.87
128.59
126.97
115.19
109.13
106.70
97.91
78.63
48.37
38.10
29.66
14.67



1b



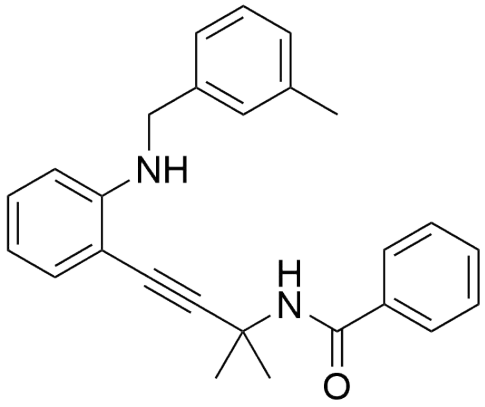
^{1}H, $CDCl_3$


NH
H
N
O

1c

7.71
7.70
7.68
7.52
7.50
7.49
7.42
7.41
7.39
7.26
7.24
7.23
7.22
7.20
7.18
7.12
7.10
7.08
7.05
7.03
6.57
6.56
6.53
6.51
6.30
6.24
4.51
2.29
1.84
2.05
1.13
2.44
4.58
1.15
1.04
2.00
1.80
1.97
3.01
6.04
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

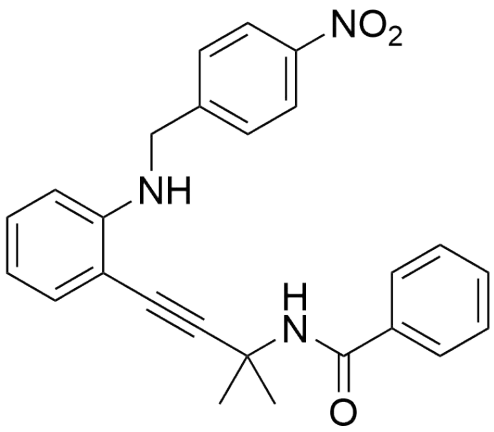
^{13}C, $CDCl_3$


NH
H
N
O

1c

166.72
149.91
139.97
138.01
134.83
131.53
131.15
129.79
128.56
128.30
127.76
127.53
126.87
124.13
115.47
109.61
106.83
98.04
78.78
48.46
47.32
29.57
21.43
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

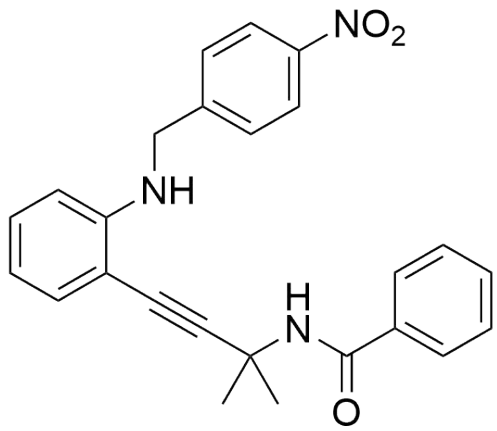
^1H, $CDCl_3$


NO2
NH
H
N
O

1e

8.10
8.07
7.69
7.67
7.55
7.53
7.49
7.47
7.40
7.38
7.36
7.29
7.29
7.27
7.11
7.09
7.07
6.69
6.67
6.66
6.62
6.60
6.58
6.46
6.40
6.38
4.67
4.65
1.85
1.91
1.97
3.31
2.05
1.47
1.00
0.91
1.02
0.96
1.00
1.94
5.97
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

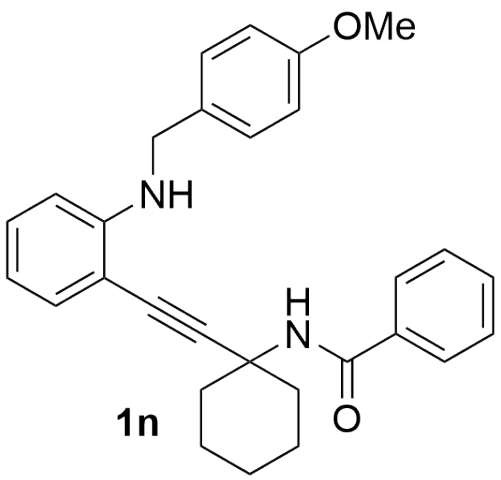
^{13}C, $CDCl_3$


NO2
NH
H
N
O

1e

167.00
149.43
148.37
146.87
134.56
131.77
131.13
129.79
128.61
127.73
126.81
123.69
116.08
109.30
107.41
98.39
78.59
48.22
46.76
29.66
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

^1H, $CDCl_3$

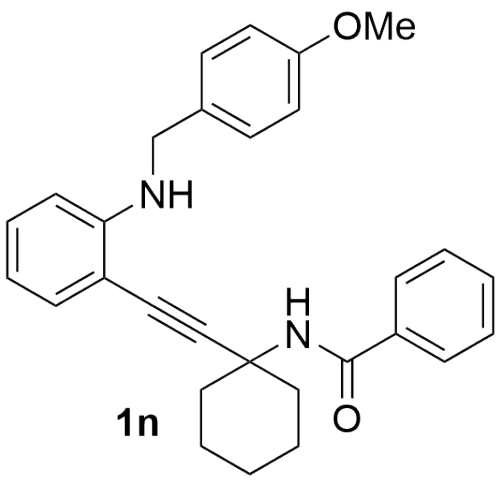

OMe
NH
H
N
O

1n

7.71
7.69
7.52
7.50
7.48
7.43
7.41
7.39
7.34
7.32
7.29
7.27
7.13
7.11
7.09
6.84
6.81
6.58
6.57
6.56
6.54
6.24
4.47
3.79
2.40
2.36
1.94
1.91
1.89
1.83
1.81
1.72
1.68
1.66
1.40
1.37
2.04
1.07
2.13
1.97
1.21
1.00
1.88
1.90
1.76
1.86
2.92
1.87
4.09
3.22
1.02
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

^{13}C, $CDCl_3$

166.57
158.49
149.84
135.07
132.03
131.47
131.31
129.65
128.55
128.36
126.89
115.41
113.82
109.53
107.21
96.63
80.90
55.26
52.67
46.74
37.53
25.42
22.74

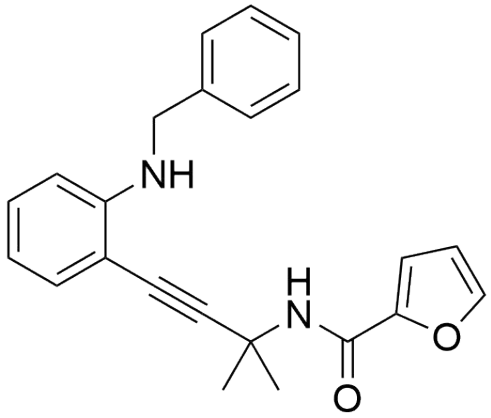


1n

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

^1H, $CDCl_3$

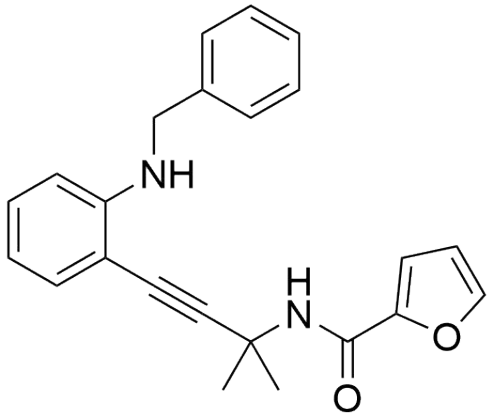

NH
H
N
O
O

1r

7.43
7.42
7.40
7.32
7.30
7.28
7.26
7.25
7.24
7.24
7.23
7.21
7.11
7.09
7.07
7.02
7.02
6.57
6.55
6.53
6.51
6.49
6.48
6.48
6.19
4.53
1.83
2.97
2.57
2.00
1.00
0.95
1.91
2.02
0.85
2.00
6.21
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

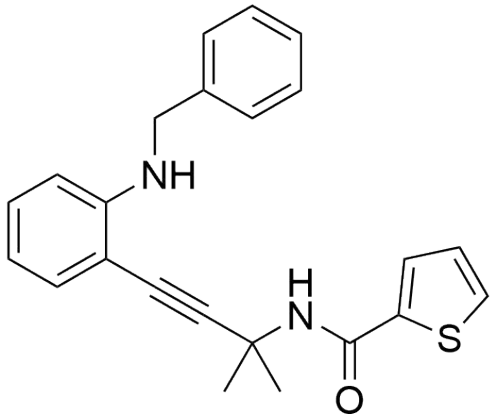
^{13}C, $CDCl_3$

157.60
149.77
148.14
143.73
140.02
131.22
129.78
128.41
127.07
126.71
115.53
114.38
112.24
109.62
106.84
97.78
78.90
48.15
47.26
29.66



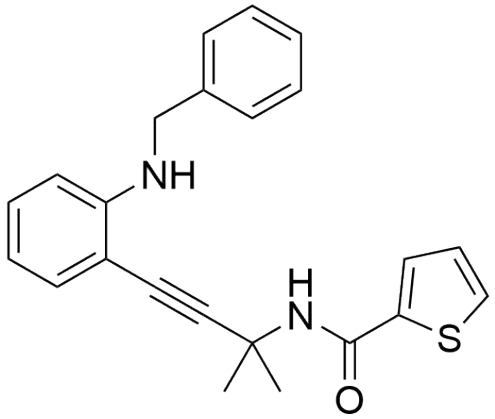
1r

^1H, $CDCl_3$



1s

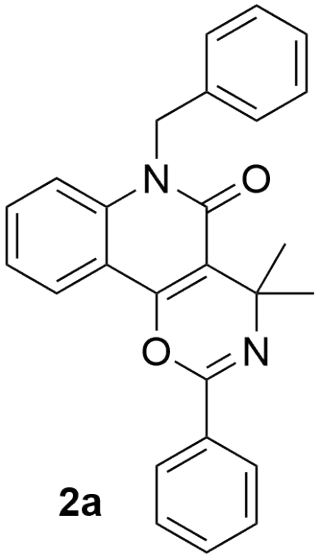
^{13}C, $CDCl_3$


NH
H
N
O
S

1s

161.25
149.82
140.01
139.36
131.19
130.13
129.81
128.42
128.12
127.60
127.09
126.72
115.53
109.66
106.82
97.86
78.94
48.70
47.30
29.64
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

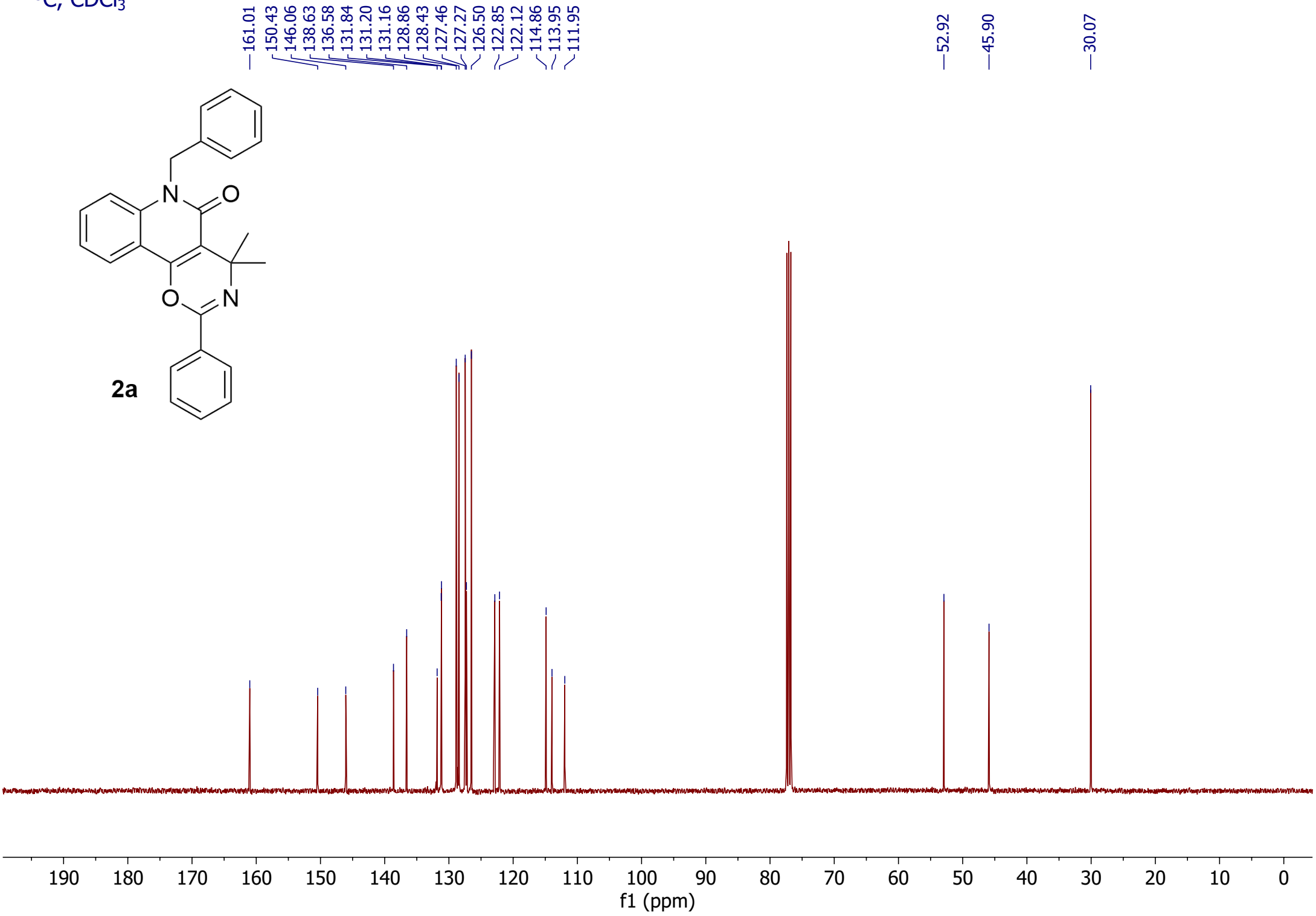
^1H, $CDCl_3$


N
O
O
N

2a

8.21
8.21
8.19
8.19
8.13
8.12
8.11
8.10
7.56
7.54
7.52
7.50
7.48
7.36
7.34
7.32
7.31
7.29
7.28
7.25
7.23
5.59
1.86
2.07
1.00
4.28
7.36
1.91
6.20
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^{13}C, $CDCl_3$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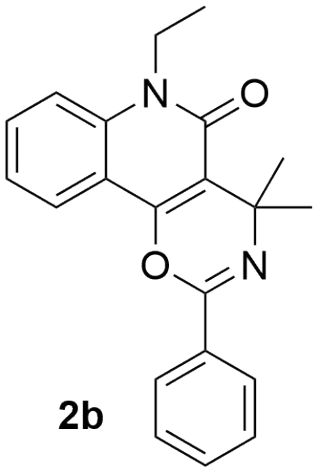
150.43
146.06
138.63
136.58
131.84
131.20
131.16
128.86
128.43
127.46
127.27
126.50
122.85
122.12
114.86
113.95
111.95
52.92
45.90
30.07
N
O
O
N
2a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

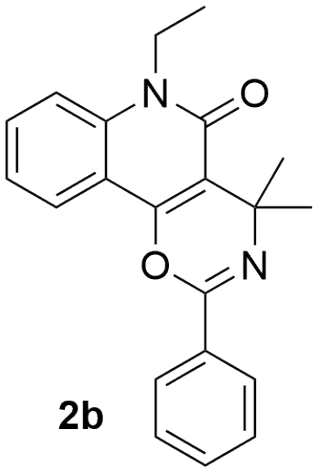
^1H, $CDCl_3$


N
O
O
N

2b

8.18
8.16
8.11
8.10
7.65
7.63
7.61
7.54
7.52
7.50
7.49
7.42
7.40
7.35
7.33
7.31
4.41
4.39
4.37
4.35
1.82
1.41
1.40
1.38
2.00
1.00
1.03
3.13
1.01
1.02
2.03
6.17
3.11
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

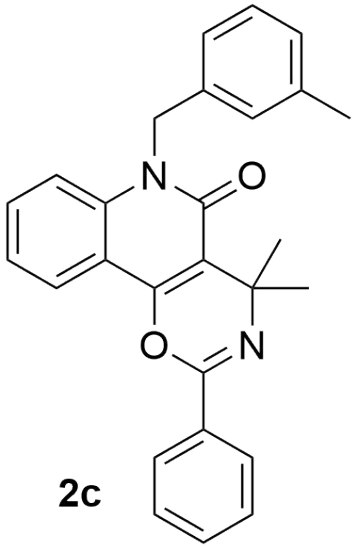
^{13}C, $CDCl_3$


N
O
O
N

2b

160.32
149.96
146.14
138.14
131.85
131.16
131.10
128.40
127.45
122.98
121.78
113.86
111.97
52.88
37.39
30.01
12.93
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

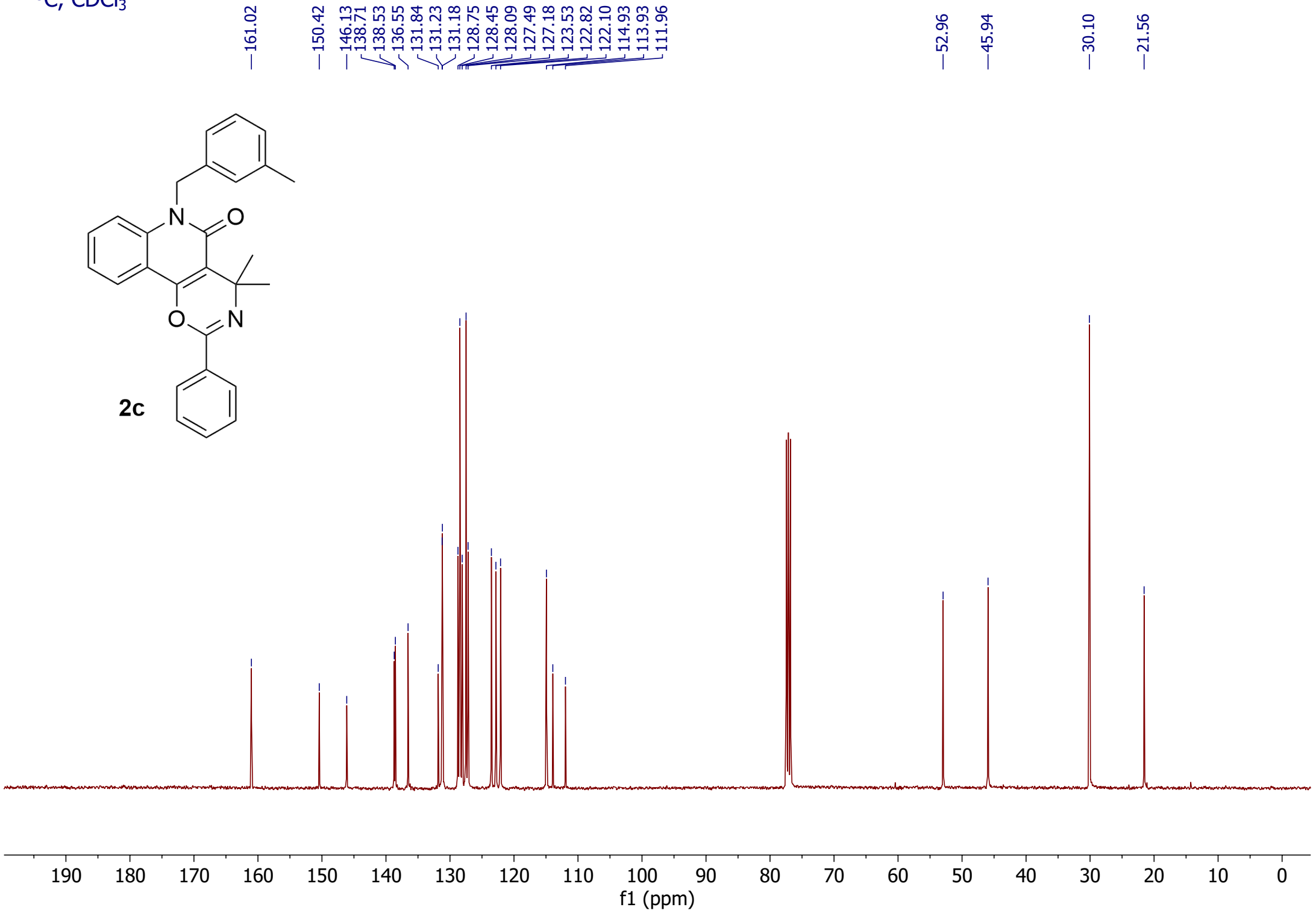
^1H, $CDCl_3$


N
O
O
N

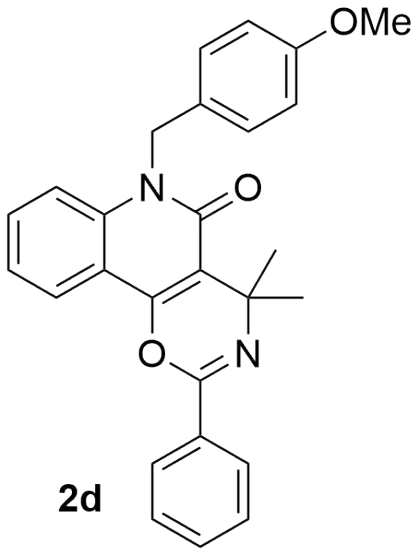
2c

8.23
8.21
8.14
8.11
7.57
7.55
7.53
7.51
7.33
7.31
7.28
7.25
7.23
7.21
7.10
7.08
7.05
7.03
5.56
2.34
1.89
2.00
1.00
4.07
2.26
1.04
3.04
1.77
3.05
6.09
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^{13}C, $CDCl_3$


161.02
150.42
146.13
138.71
138.53
136.55
131.84
131.23
131.18
128.75
128.45
128.09
127.49
127.18
123.53
122.82
122.10
114.93
113.93
111.96
52.96
45.94
30.10
21.56
N
O
O
N
2c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

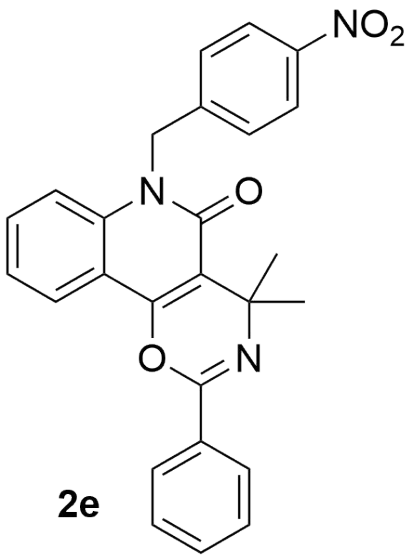
^1H, $CDCl_3$


OMe
N
O
O
N

2d

8.21
8.19
8.12
8.10
7.56
7.54
7.52
7.51
7.36
7.34
7.32
7.30
7.28
7.21
7.19
6.89
6.86
5.52
3.78
1.87
2.00
1.00
4.10
1.02
1.12
2.04
2.04
1.78
3.07
6.19
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

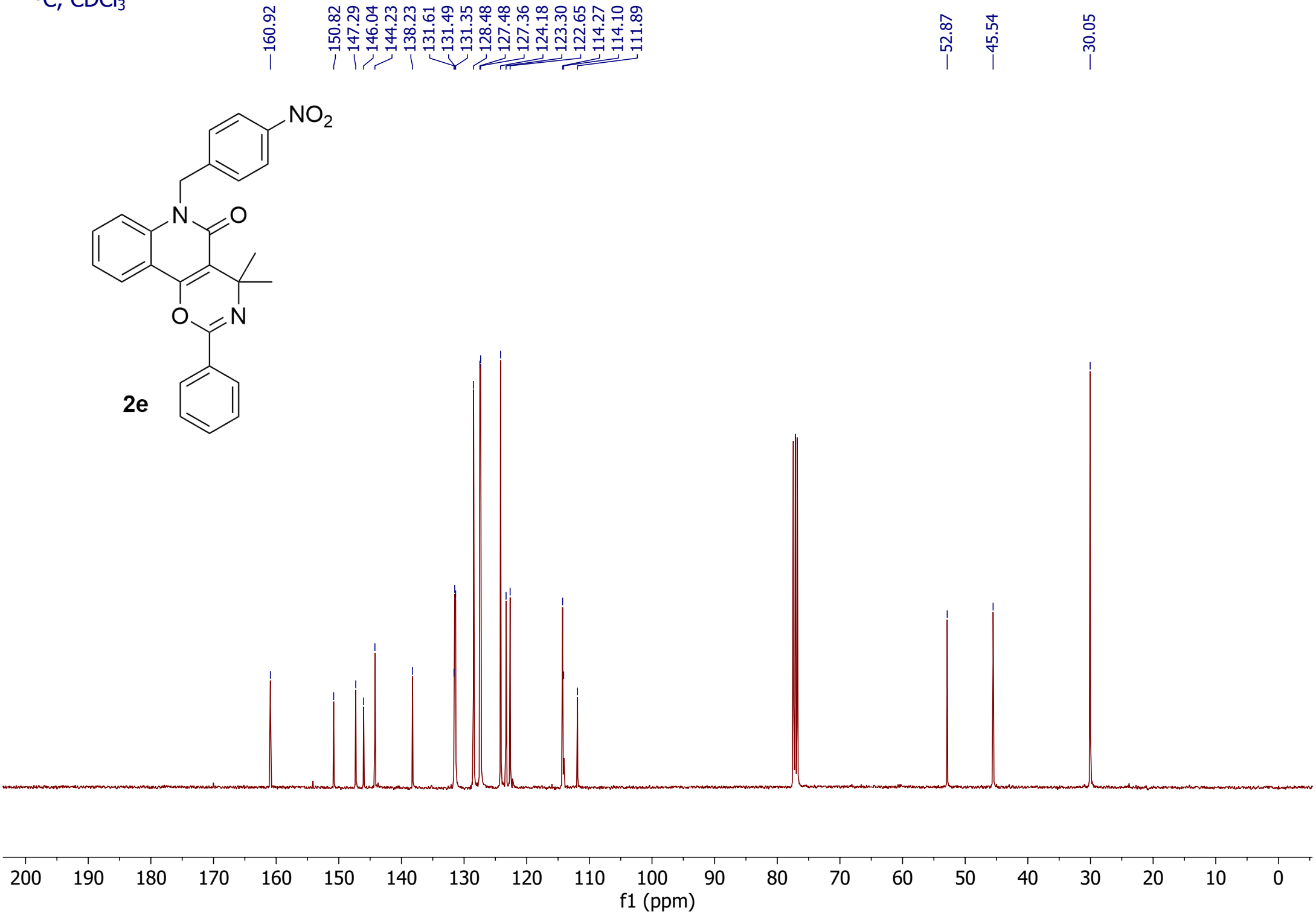
^1H, $CDCl_3$


NO2
N
O
O
N

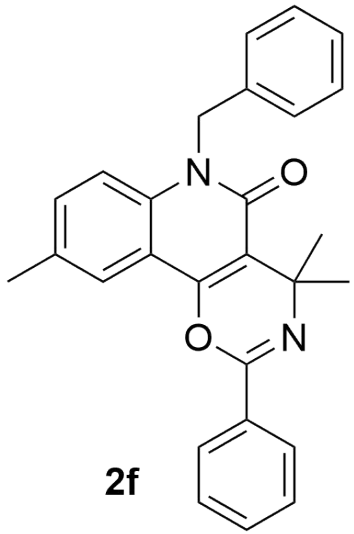
2e

8.20
8.18
8.17
8.15
7.54
7.53
7.51
7.40
7.38
7.35
7.18
7.16
5.67
1.85
4.96
4.06
3.11
1.00
1.77
6.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^{13}C, $CDCl_3$


160.92
150.82
147.29
146.04
144.23
138.23
131.61
131.49
131.35
128.48
127.48
127.36
124.18
123.30
122.65
114.27
114.10
111.89
52.87
45.54
30.05
NO2
N
O
O
N
2e
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

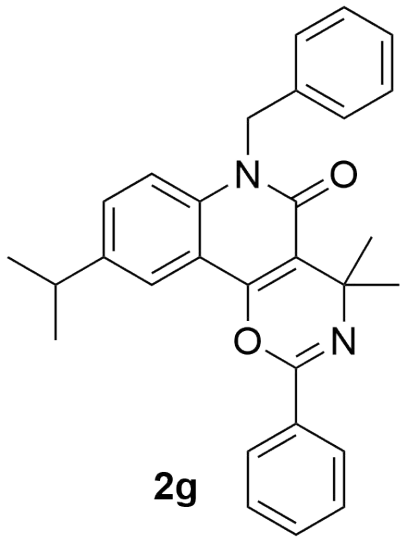
^1H, $CDCl_3$


N
O
O
N

2f

8.21
8.19
7.87
7.57
7.56
7.54
7.35
7.34
7.32
7.28
7.26
7.24
7.22
7.21
7.19
5.58
2.49
1.86
2.02
1.00
3.09
7.46
1.81
3.08
6.17
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

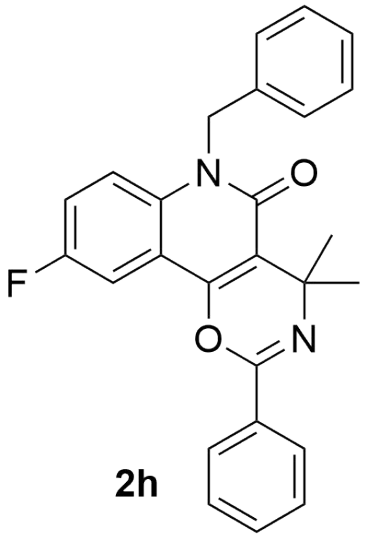
^1H, $CDCl_3$


N
O
O
N

2g

8.22
8.20
7.94
7.57
7.55
7.41
7.39
7.37
7.35
7.33
7.29
7.27
7.25
5.59
3.11
3.10
3.08
3.06
3.04
1.87
1.87
1.87
1.36
1.34
2.01
1.00
3.08
3.08
4.18
1.80
0.98
6.25
3.07
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^1H, $CDCl_3$



2h

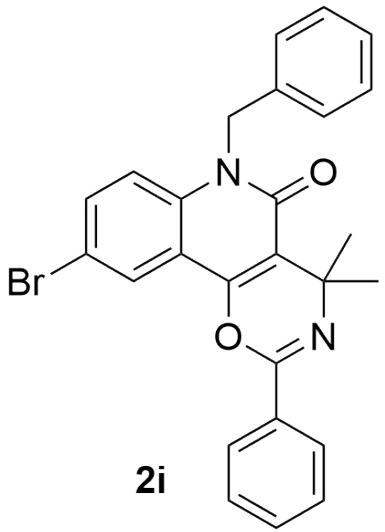
8.18 8.16 7.76 7.74 7.57 7.56 7.55 7.53 7.36 7.35 7.33 7.29 7.28 7.28 7.26 7.25 7.23 7.21 5.57 1.85

1.99 1.00 3.06 2.04 5.31 1.85 6.13

11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

f1 (ppm)

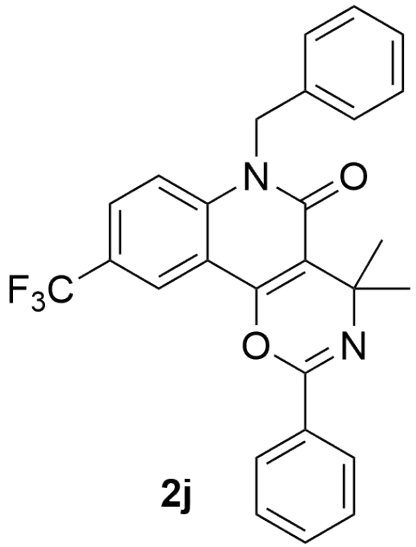
^1H, $CDCl_3$


N
O
Br
O
N

2i

8.18
8.17
8.17
8.16
7.57
7.56
7.54
7.36
7.35
7.33
7.30
7.28
7.22
7.20
7.18
7.15
5.55
1.85
3.11
4.28
3.51
2.09
1.00
1.86
6.16
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

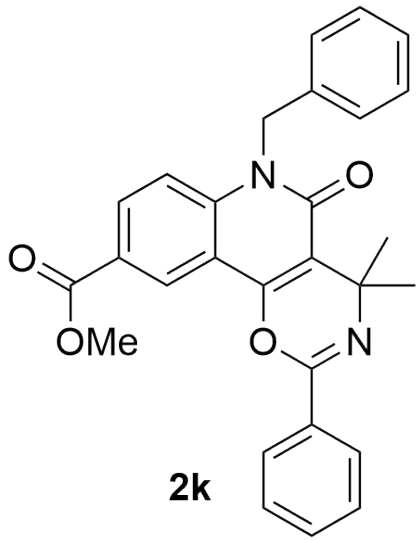
^1H, $CDCl_3$


N
O
F3C
O
N

2j

8.34
8.34
8.19
8.16
7.72
7.70
7.57
7.55
7.41
7.38
7.36
7.34
7.31
7.29
7.28
7.24
7.23
5.61
1.86
1.00
2.03
1.01
3.15
3.17
1.30
2.02
1.88
6.22
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

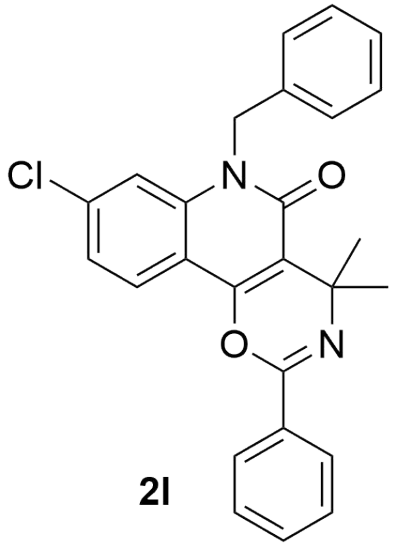
^1H, $CDCl_3$


N
O
O
OMe
O
N

2k

8.78
8.22
8.20
8.14
8.12
7.58
7.56
7.54
7.34
7.32
7.29
7.28
7.27
7.24
7.22
5.60
3.99
1.84
1.02
2.16
1.00
3.34
6.85
1.84
3.02
6.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

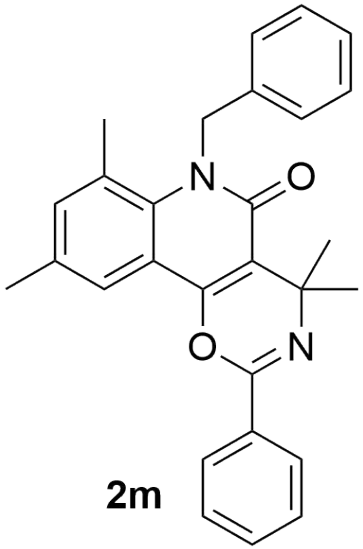
^1H, $CDCl_3$


Cl
N
O
O
N

2l

8.17
8.16
8.03
8.01
7.57
7.54
7.52
7.51
7.38
7.36
7.34
7.31
7.28
7.27
7.25
7.23
5.53
1.84
2.02
1.00
3.13
2.16
5.54
1.88
6.13
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^1H, $CDCl_3$



2m

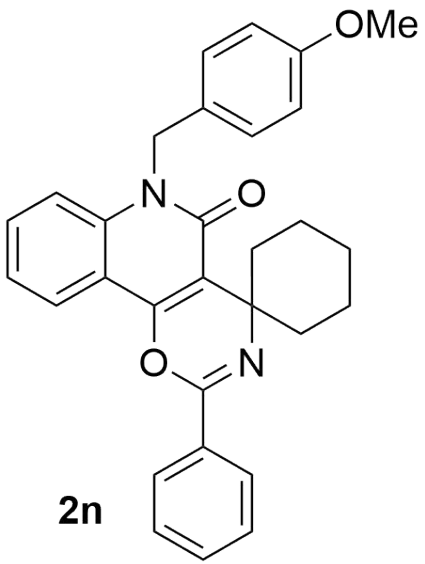
8.21 8.19 7.81 7.56 7.54 7.34 7.32 7.30 7.25 7.23 7.22 7.19 7.10 7.08 5.70 2.55 2.46 1.80

2.02 1.00 3.10 2.05 1.05 1.01 2.08 1.71 3.06 3.07 6.20

11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

f1 (ppm)

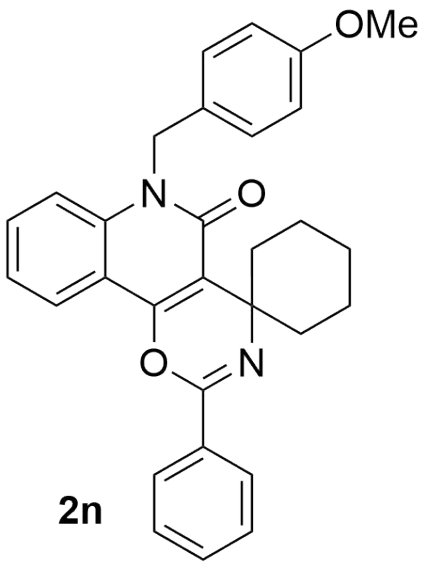
^1H, $CDCl_3$


OMe
N
O
O
N

2n

8.25
8.23
8.13
8.11
7.54
7.52
7.51
7.49
7.34
7.32
7.30
7.28
7.20
7.19
6.88
6.86
5.51
3.79
2.98
2.95
2.92
2.23
2.20
2.17
2.14
1.87
1.84
1.74
1.71
1.62
1.59
1.55
2.03
1.00
4.18
2.28
2.05
2.08
1.71
3.16
1.99
1.99
6.83
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

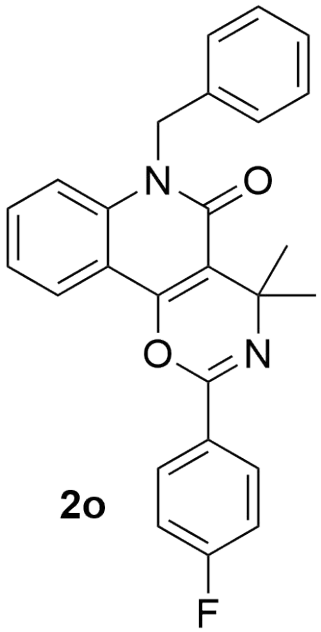
^{13}C, $CDCl_3$


OMe
N
O
O
N

2n

161.08
158.78
151.27
144.00
138.78
132.13
131.07
131.04
128.69
128.37
127.87
127.46
122.84
121.99
114.75
114.25
114.08
111.67
55.28
45.39
36.45
25.79
20.84
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

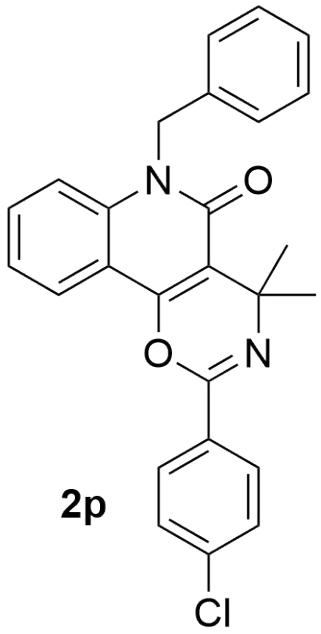
^1H, $CDCl_3$


N
O
O
N
F

2o

8.22
8.20
8.19
8.18
8.09
8.07
7.52
7.50
7.48
7.35
7.34
7.32
7.28
7.26
7.25
7.22
7.20
7.18
5.59
1.84
2.00
1.00
1.05
9.65
1.82
6.19
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

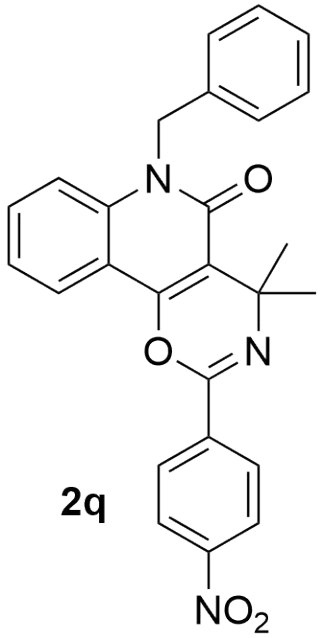
^1H, $CDCl_3$


N
O
O
N
Cl

2p

8.14
8.12
8.08
8.06
7.52
7.50
7.48
7.36
7.34
7.32
7.28
7.25
7.23
5.59
1.85
1.96
1.00
2.98
7.53
1.80
6.03
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

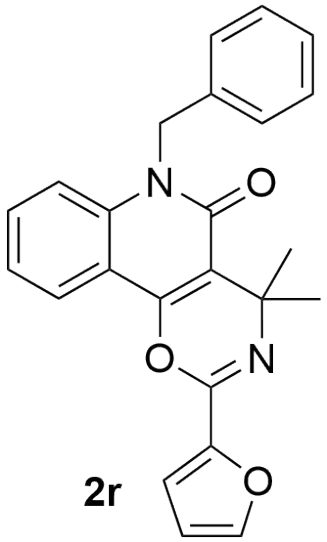
^1H, $CDCl_3$


N
O
O
N
NO2

2q

8.37
8.08
8.07
7.55
7.53
7.51
7.35
7.34
7.32
7.27
7.24
7.23
5.59
1.86
4.00
1.00
1.03
4.10
1.23
2.12
1.84
6.11
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

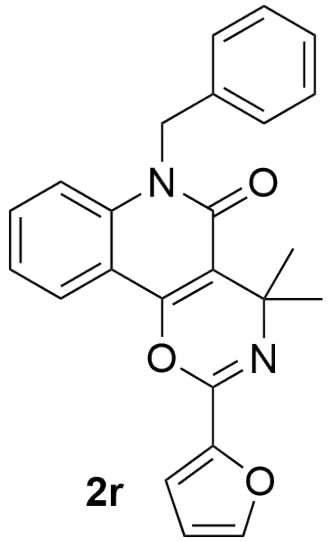
^1H, $CDCl_3$


N
O
O
N
O

2r

8.02
8.00
7.64
7.63
7.50
7.48
7.46
7.34
7.32
7.30
7.29
7.27
7.25
7.23
7.21
7.17
7.16
6.59
6.58
5.56
1.88
1.00
0.97
1.05
7.30
1.00
1.00
1.76
6.08
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

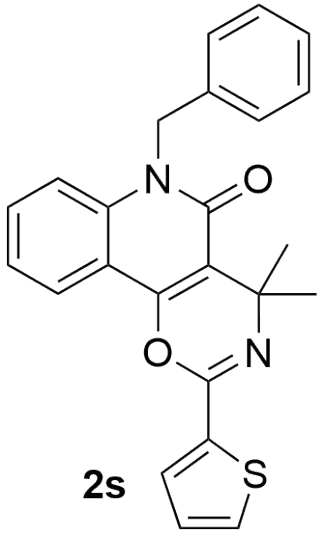
^{13}C, $CDCl_3$



2r

160.77
150.00
145.40
145.02
140.03
138.59
136.47
131.30
128.86
127.30
126.48
122.74
122.15
114.86
113.63
113.51
112.03
111.54
52.79
45.93
29.97

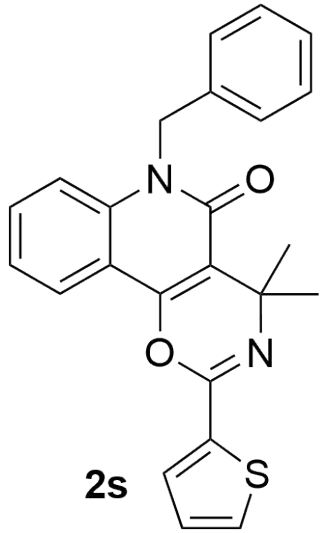
^1H, $CDCl_3$


N
O
O
N
S

2s

8.08
8.06
7.84
7.83
7.52
7.51
7.50
7.48
7.35
7.34
7.32
7.29
7.26
7.24
7.22
7.22
7.18
7.17
7.16
5.58
1.84
1.05
1.00
2.04
8.13
1.03
1.88
6.22
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

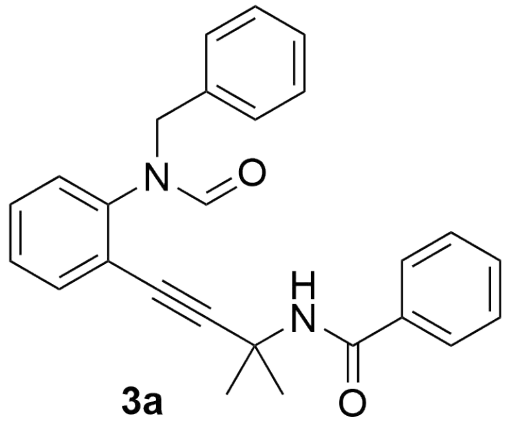
^{13}C, $CDCl_3$


N
O
O
N
S

2s

160.88
150.25
142.88
138.61
136.53
135.60
131.22
129.49
128.98
128.85
127.55
127.28
126.49
122.82
122.41
122.14
114.84
112.01
53.06
45.91
29.91
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

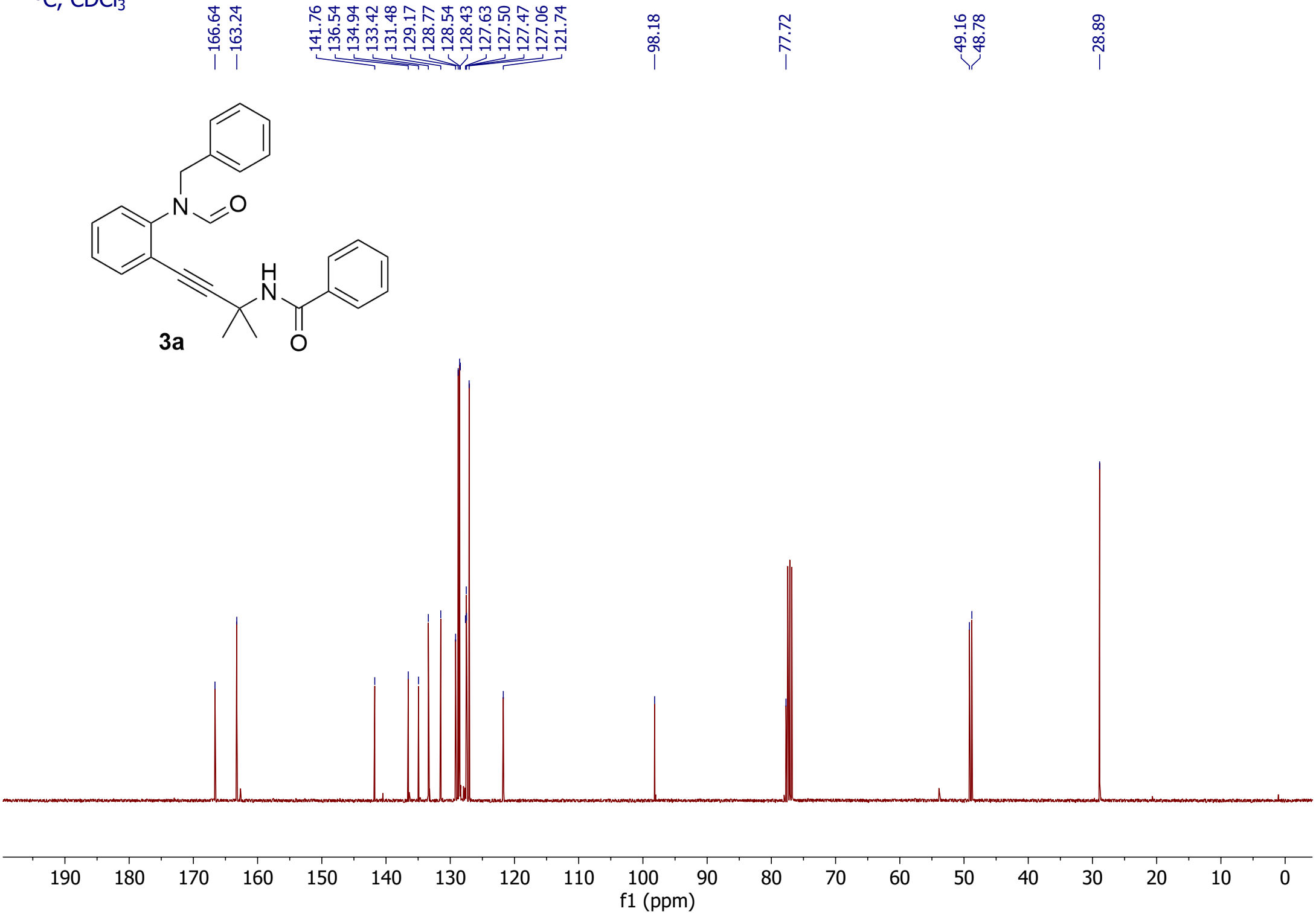
^1H, $CDCl_3$



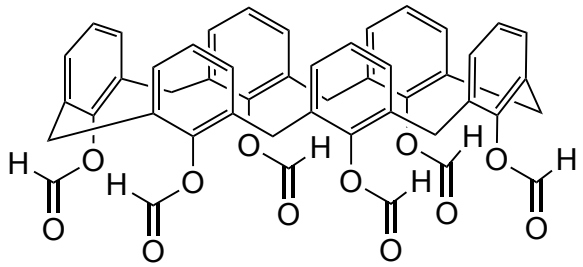
3a

f1 (ppm)

^{13}C, $CDCl_3$


166.64
163.24
141.76
136.54
134.94
133.42
131.48
129.17
128.77
128.54
128.43
127.63
127.50
127.47
127.06
121.74
98.18
77.72
49.16
48.78
28.89
N
O
H
N
O
3a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

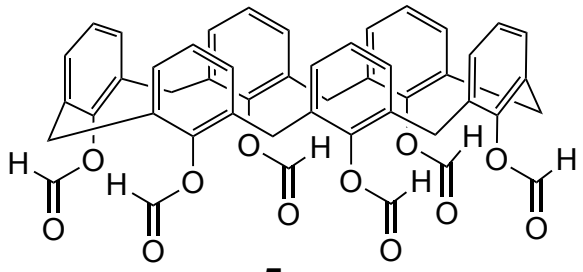
^{1}H, $CDCl_3$



5a

7.75
7.15
7.13
7.11
7.05
7.04
3.68
5.67
6.75
11.66
12.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

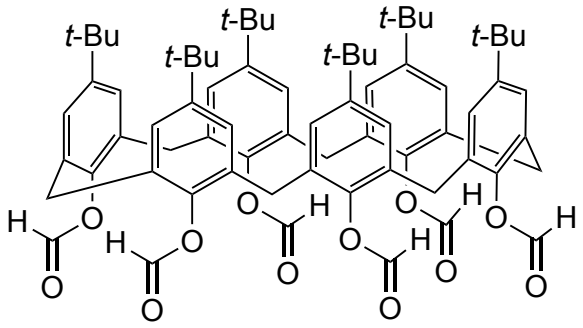
^{13}C, $CDCl_3$



5a

158.67
146.58
132.38
129.78
126.72
31.82
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

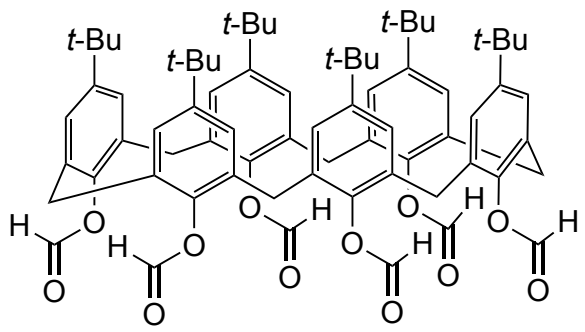
^1H, $CDCl_3$


t-Bu
t-Bu
t-Bu
t-Bu
t-Bu
t-Bu
H
O
O
H
O
O
H
O
O
H
O
O
H
O
O
H
O
O

5b

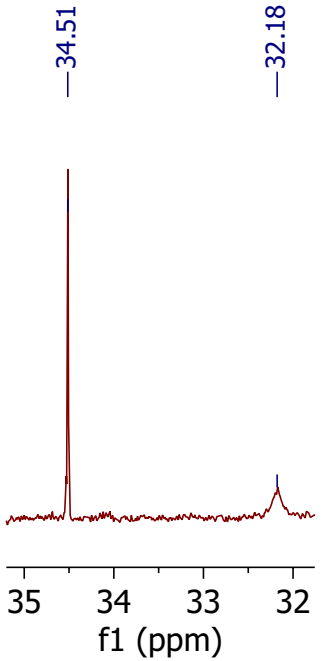
7.65
7.02
3.63
1.22
5.89
12.04
12.15
54.22
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^{13}C, $CDCl_3$



5b

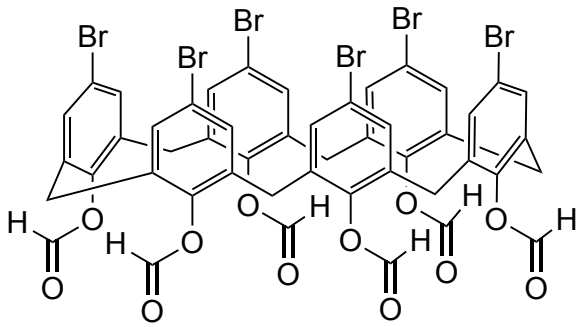
158.87
149.27
144.28
131.40
126.69
34.51
32.18
31.35



190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

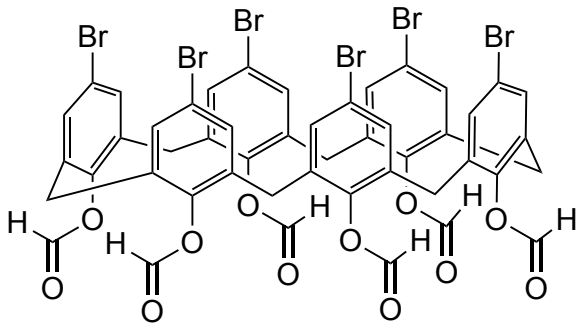
^1H, $CDCl_3$


Br
Br
Br
Br
Br
Br
H
O
O
H
O
O
H
O
O
H
O
O
H
O
O
H
O
O

5c

7.86
7.18
3.61
6.00
12.29
12.17
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^{13}C, $CDCl_3$



5c

159.07
145.06
134.42
131.92
118.88
29.56

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)