Supporting Information

Charged Non-Classical Antifolates with Activity Against Gram-positive and Gram-negative Pathogens

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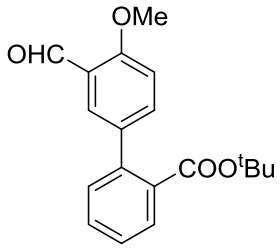
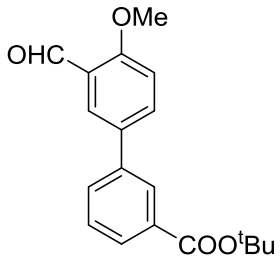
General Experimental. All reactions, unless specified, were conducted under an atmosphere of Argon in glassware that had been flame dried. Methylene chloride (CH_2Cl_2) was used from Baker Cycle-Tainers, anhydrous toluene, *tert*-butyl methyl ether (MTBE), dioxane, triethylamine and dimethylformamide (DMF) were purchased from Sigma-Aldrich. Josiphos was purchased from STREM, pyridine boronic acid from Frontier Scientific, MeMgBr (3.0 M in diethyl ether); CuBr·Me_2S from Sigma-Aldrich and was recrystallized from Me_2S prior to use. Where appropriate, control of temperature was achieved with a Neslab Cryocool CC-100 II immersion cooler, ice-bath or a heated oil bath. ^{1}H NMR spectra were recorded at 400 MHz, and/or at 500 MHz and calibrated to the $CDCl_3$ peak at 7.28 ppm. ^{13}C NMR spectra were recorded at 100MHz, and/or at 125 MHz and calibrated to the $CDCl_3$ peak at 77.23 ppm. Chemical shifts are reported in units of parts per million (ppm). High-resolution mass spectra were obtained on the JMS-AX505HA instruments and/or on an AccuTOF instrument at the University of Connecticut. Flash chromatography was performed on Silica Gel, 40 microns, 32-63 flash silica and/or -NH_2 capped spherical silica gel. Thin layer chromatography was performed on silica gel (Silica Gel 60 F_{254}) glass plates and the compounds were visualized by UV and/or potassium permanganate stain.

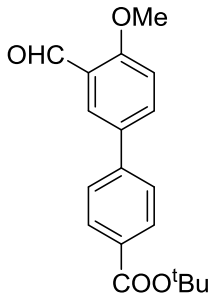
Synthetic Methods



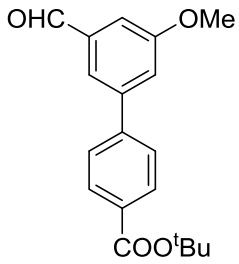
3'-Formyl-4'-methoxy-biphenyl-2-carboxylic acid *tert*-butyl ester (1a). In a screw cap pressure vessel fitted with a stir bar was added 2-(tert-Butoxycarbonylphenyl) boronic acid (1.00 g, 4.98 mmol), 3-Bromo-5-methoxybenzaldehyde (1.28 g, 4.98 mmol), $Pd(PPh_3)_4$ (0.29 g, 0.25 mmol, 5% Pd), Cs_2CO_3 (4.09 g, 12.45 mmol), anhydrous dioxane (20 mL), and water (2 mL). The mixture was degassed by bubbling argon through for 15 min, sealed, and heated to 100 °C for 4 h, when TLC showed consumption of aryl bromide. Reaction diluted with saturated brine, and extracted 3x with EtOAc. Combined organic layers dried over $NaSO_4$ and filtered. Filtrate concentrated and purified by flash column chromatography (SiO_2, 40 g, 5% EtOAc/hexanes) to afford bicyclic ester **1a** as a slightly yellow solid (1.34 g, 86%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.55 (s, 1H), 7.86 (d, *J* = 2.4 Hz, 1H), 7.84 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.57 (dd, *J* = 8.5, 2.4 Hz, 1H), 7.53 (td, *J* = 7.6, 1.5 Hz, 1H), 7.44 (td, *J* = 7.6, 1.3 Hz, 1H), 7.35 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.08 (d, *J* = 8.5 Hz, 1H), 4.03 (s, 3H), 1.38 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.5, 167.6, 161.1, 140.5, 136.0, 134.5, 132.7, 130.9, 130.6, 129.9, 128.7, 127.3, 124.4, 111.4, 81.5, 55.9, 27.8; HRMS (DART $[M+H]^+$) *m/z* 313.1433 (calculated for $C_{19}H_{21}O_4$, 313.1440).



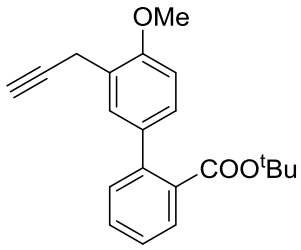
3'-Formyl-4'-methoxy-biphenyl-3-carboxylic acid *tert*-butyl ester (1b). According to the general Suzuki coupling procedure, 3-(tert-Butoxycarbonylphenyl) boronic acid (0.50 g, 2.25 mmol), 3-Bromo-5-methoxybenzaldehyde (0.48 g, 2.25 mmol), $Pd(PPh_3)_4$ (0.13 g, 0. 11 mmol, 5% Pd), Cs_2CO_3 (1.47 g, 4.5 mmol), anhydrous dioxane (10 mL), and water (1 mL) were added to 50 mL screw cap pressure vessel. The mixture was degassed by bubbling argon through for 15 min, sealed, and heated to 100 °C for 4 h, when TLC showed consumption of aryl bromide. Reaction diluted with saturated brine, and extracted 3x with EtOAc. Combined organic layers dried over $NaSO_4$ and filtered. Filtrate concentrated and purified by flash column chromatography (SiO_2, 20 g, 5% EtOAc/hexanes) to afford bicyclic ester **1b** as a slightly yellow solid (0.52 g, 74%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.57 (s, 1H), 8.23 (t, J = 1.9 Hz, 1H), 8.14 (d, J = 2.5 Hz, 1H), 8.00 (dt, J = 7.7, 1.4 Hz, 1H), 7.87 (dd, J = 8.6, 2.5 Hz, 1H), 7.77 (dt, J = 7.7, 1.4 Hz, 1H), 7.52 (t, J = 7.7 Hz, 1H), 7.14 (d, J = 8.6 Hz, 1H), 4.03 (s, 3H), 1.67 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.7, 165.7, 161.5, 139.7, 134.4, 133.0, 132.7, 130.7, 128.8, 128.3, 127.6, 127.0, 125.0, 112.3, 112.3, 81.3, 55.9, 28.2, 28.2; HRMS (DART $[M+H]^+$) *m/z* 313.1434 (calculated for $C_{19}H_{21}O_4$, 313.1440).



3'-Formyl-4'-methoxy-biphenyl-4-carboxylic acid *tert*-butyl ester (1c). According to the general Suzuki coupling procedure, 4-(tert-Butoxycarbonylphenyl) boronic acid (1.00 g, 4.98 mmol), 3-Bromo-5-methoxybenzaldehyde (1.28 g, 4.98 mmol), $Pd(PPh_3)_4$ (0.29 g, 0.25 mmol, 5% Pd), Cs_2CO_3 (4.09 g, 12.45 mmol), anhydrous dioxane (20 mL), and water (2 mL) were added to 50 mL screw cap pressure vessel. The mixture was degassed by bubbling argon through for 15 min, sealed, and heated to 100 °C for 4 h, when TLC showed consumption of aryl bromide. Reaction diluted with saturated brine, and extracted 3x with EtOAc. Combined organic layers dried over $NaSO_4$ and filtered. Filtrate concentrated and purified by flash column chromatography (SiO_2, 40 g, 5% EtOAc/hexanes) to afford bicyclic ester **1c** as a slightly yellow solid (1.23 g, 79%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.53 (s, 1H), 8.12 (d, J = 1.9 Hz, 1H), 8.06 (d, J = 8.1 Hz, 2H), 7.83 (d, J = 10.5 Hz, 1H), 7.63 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 8.7 Hz, 1H), 4.00 (s, 3H), 1.63 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.5, 165.5, 161.7, 143.3, 134.4, 132.7, 130.8, 130.0, 126.9, 126.3, 125.0, 112.3, 81.1, 55.9, 28.2; HRMS (DART $[M+H]^+$) *m/z* 313.1412 (calculated for $C_{19}H_{21}O_4$, 313.1440).



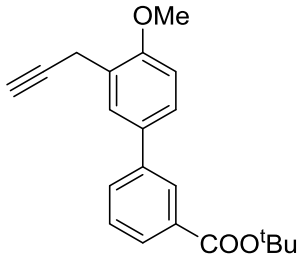
5'-Formyl-3'-methoxy-biphenyl-4-carboxylic acid *tert*-butyl ester (1d). According to the general Suzuki coupling procedure, 4-(tert-Butoxycarbonylphenyl) boronic acid (0.50 g, 2.25 mmol), 3-Bromo-4-methoxybenzaldehyde (0.48 g, 2.25 mmol), $Pd(PPh_3)_4$ (0.13 g, 0. 11 mmol, 5% Pd), Cs_2CO_3 (1.47 g, 4.5 mmol), anhydrous dioxane (10 mL), and water (1 mL) were added to 50 mL screw cap pressure vessel. The mixture was degassed by bubbling argon through for 15 min, sealed, and heated to 100 °C for 4 h, when TLC showed consumption of aryl bromide. Reaction diluted with saturated brine, and extracted 3x with EtOAc. Combined organic layers dried over $NaSO_4$ and filtered. Filtrate concentrated and purified by flash column chromatography (SiO_2, 20 g, 5% EtOAc/hexanes) to afford bicyclic ester **1d** as a slightly yellow solid (0.54 g, 77%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.09 (s, 1H), 8.12 (d, J = 8.4 Hz, 2H), 7.74 (m, 1H), 7.70 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 1.7 Hz, 2H), 3.97 (s, 3H), 1.66 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.9, 165.4, 160.7, 143.4, 142.5, 138.4, 131.7, 130.1, 126.9, 122.3, 120.2, 111.7, 81.3, 55.8, 55.7, 28.2; HRMS (DART $[M+H]^+$) *m/z* 313.1450 (calculated for $C_{19}H_{21}O_4$, 313.1440).



4'-Methoxy-3'-prop-2-ynyl-biphenyl-2-carboxylic acid *tert*-butyl ester (2a). In a dried RB flask fitted with a stir bar under argon atmosphere, methoxymethyl triphenylphosphonium chloride (1.37 g, 4.00 mmol) was dissolved in dry THF (10 mL) and cooled to 0 °C. Sodium *tert*-butoxide (0.39 g, 4.00 mmol) was added (reaction turned dark red) and stirred for 20 min. Aldehyde (0.50 g, 1.60 mmol) dissolved in dry THF (5 mL) was added (reaction turned orange). TLC showed SM consumption after 30 min. Reaction quenched with saturated NH_4Cl and extracted with EtOAc (3 x 15 mL). Combined organic layer washed with brine, dried over $NaSO_4$ and filtered. Filtrate passed through a column of silica gel (10% EtOAc in hexanes) to afford a mixture of enol ether isomers, which were immediately hydrolyzed in the subsequent step.

In a dried RB flask fitted with a stir bar under argon atmosphere was added enol ether (0.48 g, 1.41 mmol) in MeCN (20 mL). Sodium iodide (0.23 g, 1.55 mmol) added and cooled to -20 °C. TMSCl (0.17 g, 1.55 mmol) added, stirred at -20 °C for 30 min, when TLC showed SM consumption. Reaction diluted with EtOAc (20 mL) and $Na_2S_2O_3$ (10 mL), stirred until reaction warmed to rt. Organic layer separated and aqueous phase extracted with EtOAc (3 x 20 mL). Combined organic layers washed with brine, dried over $NaSO_4$ and filtered. Filtrate concentrated and used without further purification.

In a dried RB flask fitted with a stir bar under argon atmosphere was added aldehyde (0.28 g, 0.86 mmol) in MeOH (5 mL). Ohira-Bestmann reagent (0.33 g, 1.72 mmol) was added (turned yellow/green) and cooled to 0 °C. Powdered K_2CO_3 (0.36 g, 2.58 mmol) added and stirred at 0 °C for 2 h, when TLC showed consumption of SM. Reaction diluted with brine (5 mL) and extracted with EtOAc (3 x 15 mL). Combined organic layer washed with brine, dried over $NaSO_4$ and filtered. The filtrate was concentrated and purified by flash column chromatography (SiO_2, 10 g, 5% EtOAc/hexanes) to afford bicyclic alkyne **2a** as a white solid (0.20 g, 39% yield 3 steps); ^{1}H NMR (500 MHz,$CDCl_3$) δ 7.81 (dd, J = 7.7, 1.4 Hz, 1H), 7.54 (dd, J = 2.4, 1.2 Hz, 1H), 7.52 (td, J = 7.5, 1.3, 1H), 7.42 (td, J = 7.5, 1.3 Hz, 1H), 7.38 (dd, J = 7.5, 1.3 Hz, 1H), 7.25 (dd, J = 8.3, 2.3 Hz, 1H), 6.93 (d, J = 8.3 Hz, 1H), 3.93 (s, 3H), 3.66 (d, J = 2.7 Hz, 2H), 2.19 (t, J = 2.7 Hz, 1H), 1.37 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.2, 156.2, 141.8, 134.2, 133.1, 130.7, 130.6, 129.6, 129.3, 129.3, 127.9, 126.8, 124.0, 109.7, 81.7, 81.2, 70.7, 55.6, 55.6, 27.8, 19.3. HRMS (DART $[M]^+$) *m/z* 322.1573 (calculated for $C_{21}H_{23}O_3$ 322.1569).



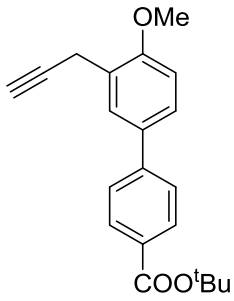
4'-Methoxy-3'-prop-2-ynyl-biphenyl-3-carboxylic acid *tert*-butyl ester (2b). In a dried RB flask fitted with a stir bar under argon atmosphere, methoxymethyl triphenylphosphonium chloride (0.88 g, 2.56 mmol) was dissolved in dry THF (8 mL) and cooled to 0 °C. Sodium *tert*-butoxide (0.25 g, 2.56 mmol) was added (reaction

turned dark red) and stirred for 20 min. Aldehyde (0.40 g, 1.28 mmol) dissolved in dry THF (4 mL) was added (reaction turned orange). TLC showed SM consumption after 30 min. Reaction quenched with saturated NH_4Cl and extracted with EtOAc (3 x 15 mL). Combined organic layer washed with brine, dried over $NaSO_4$ and filtered. Filtrate passed through a column of silica gel (10% EtOAc in hexanes) to afford a mixture of enol ether isomers, which were immediately hydrolyzed in the subsequent step.

In a dried RB flask fitted with a stir bar under argon atmosphere was added enol ether (0.39 g, 1.15 mmol) in MeCN (15 mL). Sodium iodide (0.21 g, 1.38 mmol) added and cooled to -20 °C. TMSCl (0.15 g, 1.38 mmol) added, stirred at -20 °C for 30 min, when TLC showed SM consumption. Reaction diluted with EtOAc (20 mL) and $Na_2S_2O_3$ (10 mL), stirred until reaction warmed to rt. Organic layer separated and aqueous phase extracted with EtOAc (3 x 20 mL). Combined organic layers washed with brine, dried over $NaSO_4$ and filtered. Filtrate concentrated and used without further purification.

In a dried RB flask fitted with a stir bar under argon atmosphere was added aldehyde (0.30 g, 0.92 mmol) in MeOH (5 mL). Ohira-Bestmann reagent (0.35 g, 1.84 mmol) was added (turned yellow/green) and cooled to 0 °C. Powdered K_2CO_3 (0.38 g, 2.76 mmol) added and stirred at 0 °C for 2 h, when TLC showed consumption of SM. Reaction diluted with brine (5 mL) and extracted with EtOAc (3 x 15 mL). Combined organic layer washed with brine, dried over $NaSO_4$ and filtered. The filtrate was concentrated and purified by flash column chromatography (SiO_2, 10 g, 5% EtOAc/hexanes) to afford bicyclic alkyne **2b** as a white solid (0.13 g, 31%

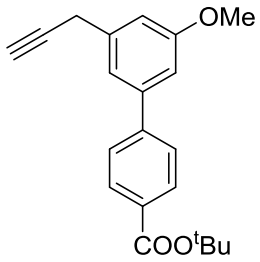
yield 3 steps); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.82 (d, J = 2.2 Hz, 1H), 7.79 – 7.74 (m, 1H), 7.53 (dd, J = 8.4, 2.2 Hz, 1H), 7.50 (t, J = 7.7 Hz, 1H), 6.96 (d, J = 8.5 Hz, 1H), 3.91 (s, 3H), 3.67 (d, J = 2.6 Hz, 2H), 2.24 (t, J = 2.6 Hz, 1H), 1.66 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.9, 156.6, 140.9, 132.7, 132.5, 130.7, 130.7, 130.7, 128.6, 127.8, 127.7, 127.7, 127.6, 127.6, 126.6, 125.0, 110.4, 81.8, 81.1, 70.7, 55.6, 28.2, 19.3; HRMS (DART $[M]^+$) *m/z* 322.1578 (calculated for $C_{21}H_{23}O_3$ 322.1569).



4'-Methoxy-3'-prop-2-ynyl-biphenyl-4-carboxylic acid *tert*-butyl ester (2c). In a dried RB flask fitted with a stir bar under argon atmosphere, methoxymethyl triphenylphosphonium chloride (1.37 g, 4.00 mmol) was dissolved in dry THF (10 mL) and cooled to 0 °C. Sodium *tert*-butoxide (0.39 g, 4.00 mmol) was added (reaction turned dark red) and stirred for 20 min. Aldehyde (0.50 g, 1.60 mmol) dissolved in dry THF (5 mL) was added (reaction turned orange). TLC showed SM consumption after 30 min. Reaction quenched with saturated NH_4Cl and extracted with EtOAc (3 x 15 mL). Combined organic layer washed with brine, dried over $NaSO_4$ and filtered. Filtrate passed through a column of silica gel (10% EtOAc in hexanes) to afford a mixture of enol ether isomers, which were immediately hydrolyzed in the subsequent step.

In a dried RB flask fitted with a stir bar under argon atmosphere was added enol ether (0.50 g, 1.47 mmol) in MeCN (20 mL). Sodium iodide (0.26 g, 1.76 mmol) added and cooled to -20 °C. TMSCl (0.19 g, 1.76 mmol) added, stirred at -20 °C for 30 min, when TLC showed SM consumption. Reaction diluted with EtOAc (20 mL) and $Na_2S_2O_3$ (10 mL), stirred until reaction warmed to rt. Organic layer separated and aqueous phase extracted with EtOAc (3 x 20 mL). Combined organic layers washed with brine, dried over $NaSO_4$ and filtered. Filtrate concentrated and used without further purification.

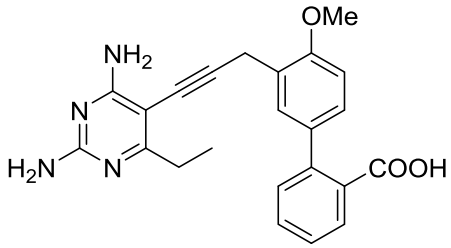
In a dried RB flask fitted with a stir bar under argon atmosphere was added aldehyde (0.34 g, 1.03 mmol) in MeOH (7 mL). Ohira-Bestmann reagent (0.40 g, 2.06 mmol) was added (turned yellow/green) and cooled to 0 °C. Powdered K_2CO_3 (0.43 g, 3.09 mmol) added and stirred at 0 °C for 2 h, when TLC showed consumption of SM. Reaction diluted with brine (5 mL) and extracted with EtOAc (3 x 15 mL). Combined organic layer washed with brine, dried over $NaSO_4$ and filtered. The filtrate was concentrated and purified by flash column chromatography (SiO_2, 12 g, 5% EtOAc/hexanes) to afford bicyclic alkyne **2c** as a white solid (0.23 g, 45% yield 3 steps); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, J = 8.2 Hz, 2H), 7.85 (d, 1H), 7.66 (d, J = 8.2 Hz, 2H), 7.52 (dd, J = 8.6, 2.4 Hz, 1H), 6.93 (d, J = 8.5 Hz, 1H), 3.89 (s, 3H), 3.67 (d, J = 2.7 Hz, 2H), 2.27 (t, J = 2.5 Hz, 1H), 1.66 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 156.9, 156.9, 144.8, 132.4, 130.2, 129.9, 129.9, 127.8, 126.7, 126.4, 125.0, 125.0, 110.4, 81.7, 77.4, 77.1, 76.9, 70.9, 55.5, 28.3, 19.4; HRMS (DART $[M]^+$) *m/z* 322.1539 (calculated for $C_{21}H_{23}O_3$ 322.1569).



3'-Methoxy-5'-prop-2-ynyl-biphenyl-4-carboxylic acid *tert*-butyl ester (2d). In a dried RB flask fitted with a stir bar under argon atmosphere, methoxymethyl triphenylphosphonium chloride (1.76 g, 5.12 mmol) was dissolved in dry THF (12 mL) and cooled to 0 °C. Sodium *tert*-butoxide (0.49 g, 5.12 mmol) was added (reaction turned dark red) and stirred for 20 min. Aldehyde (0.64 g, 2.05 mmol) dissolved in dry THF (7 mL) was added (reaction turned orange). TLC showed SM consumption after 30 min. Reaction quenched with saturated NH_4Cl and extracted with EtOAc (3 x 15 mL). Combined organic layer washed with brine, dried over $NaSO_4$ and filtered. Filtrate passed through a column of silica gel (10% EtOAc in hexanes) to afford a mixture of enol ether isomers, which were immediately hydrolyzed in the subsequent step.

In a dried RB flask fitted with a stir bar under argon atmosphere was added enol ether (0.56 g, 1.64 mmol) in MeCN (20 mL). Sodium iodide (0.27 g, 1.80 mmol) added and cooled to -20 °C. TMSCl (0.20 g, 1.80 mmol) added, stirred at -20 °C for 30 min, when TLC showed SM consumption. Reaction diluted with EtOAc (20 mL) and $Na_2S_2O_3$ (10 mL), stirred until reaction warmed to rt. Organic layer separated and aqueous phase extracted with EtOAc (3 x 20 mL). Combined organic layers washed with brine, dried over $NaSO_4$ and filtered. Filtrate concentrated and used without further purification.

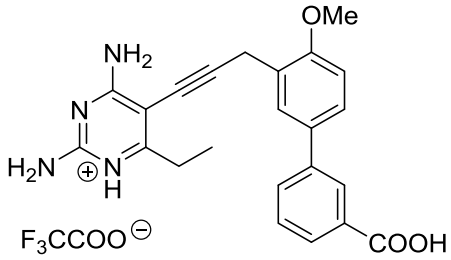
In a dried RB flask fitted with a stir bar under argon atmosphere was added aldehyde (0.38 g, 1.15 mmol) in MeOH (7 mL). Ohira-Bestmann reagent (0.44 g, 2.30 mmol) was added (turned yellow/green) and cooled to 0 °C. Powdered K_2CO_3 (0.48 g, 3.45 mmol) added and stirred at 0 °C for 2 h, when TLC showed consumption of SM. Reaction diluted with brine (5 mL) and extracted with EtOAc (3 x 15 mL). Combined organic layer washed with brine, dried over $NaSO_4$ and filtered. The filtrate was concentrated and purified by flash column chromatography (SiO_2, 12 g, 5% EtOAc/hexanes) to afford bicyclic alkyne **2d** as a white solid (0.22 g, 34% yield 3 steps); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, J = 8.5 Hz, 2H), 7.67 (d, J = 8.5 Hz, 2H), 7.23 (s, 1H), 7.07 (s, 1H), 7.00 (s, 1H), 3.92 (s, 3H), 3.71 (d, J = 2.6 Hz, 2H), 2.27 (t, J = 2.7 Hz, 1H), 1.66 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 160.3, 144.9, 141.9, 138.3, 131.1, 129.9, 127.0, 119.4, 113.1, 111.6, 81.6, 81.1, 70.9, 55.5, 28.3, 25.0. HRMS (DART $[M]^+$) *m/z* 322.1572 (calculated for $C_{21}H_{23}O_3$ 322.1569).



6-Ethyl-5-[3-(2-methoxy-5-(2-carboxyphenyl)-phenyl)-prop-1-ynyl]-pyrimidine-2,4-diamine (3a). In a screw cap vial fitted with a stir bar and a septum, was added alkyne (0.10 g, 0.31 mmol), iodo-ethylpyrimidine (0.06 mg, 0.24 mmol), $Pd(PPh_3)_2Cl_2$ previously doped with 10% CuI by weight (0.01 g, 0.02 mmol), and KOAc (0.23 g, 2.38 mmol). DMF (3 mL) added and argon bubbled through the stirring solution for

10 min. Vial sealed and heated to 50 °C until complete by TLC (2-3 h). Dried in vacuo using toluene as an azeotrope. Residue washed with saturated sodium bicarbonate, extracted 3x with EtOAc. Organic layer washed with brine, dried over sodium sulfate, and filtered. Filtrate concentrated and purified by flash column chromatography (coupled product eluted with 90% EtOAc in hexanes). Material carried forward with no further purification.

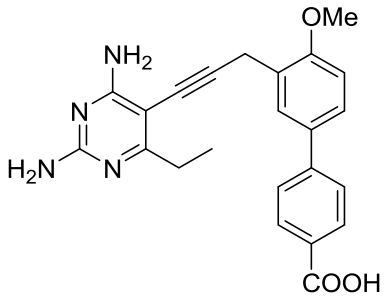
TFA (0.5 mL) added to ester dissolved in DCM (1 mL). Stirred until complete by TLC (30 min). Reaction dried in vacuo to remove excess TFA. Column run on residue. Carboxylic acid eluted with 8% MeOH in DCM to give a white solid (0.043 g, 42% 2 step yield); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.71 (d, J = 7.3 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 7.50 – 7.46 (m, 1H), 7.43 (t, J = 7.5 Hz, 1H), 7.36 (d, J = 7.6 Hz, 1H), 7.23 (dd, J = 8.3, 2.0 Hz, 1H), 7.06 (d, J = 8.4 Hz, 1H), 6.38 (bs, 2H), 6.21 (bs, 2H), 3.88 (s, 3H), 3.85 (s, 2H), 2.55 (q, J = 7.5 Hz, 2H), 1.04 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 170.3, 164.9, 156.4, 141.2, 133.5, 132.8, 131.2, 130.8, 129.5, 129.2, 128.2, 127.3, 125.1, 110.7, 95.7, 88.6, 76.7, 56.0, 29.1, 21.1, 12.8; HRMS (DART [M+H]$^+$) *m/z* 403.1744 (calculated for $C_{23}H_{23}N_4O_3$ 403.1770).



6-Ethyl-5-[3-(2-methoxy-5-(3-carboxyphenyl)-phenyl)-prop-1-ynyl]-pyrimidine-2,4-diamine-trifluoroacetate salt (3b). In a screw cap vial fitted with a stir bar and a septum, was added alkyne (0.10 g, 0.31 mmol), iodo-ethylpyrimidine (0.06 mg, 0.24

mmol), $Pd(PPh_3)_2Cl_2$ previously doped with 10% CuI by weight (0.01 g, 0.02 mmol), and KOAc (0.23 g, 2.38 mmol). DMF (3 mL) added and argon bubbled through the stirring solution for 10 min. Vial sealed and heated to 50 °C until complete by TLC (2-3 h). Dried in vacuo using toluene as an azeotrope. Residue washed with saturated sodium bicarbonate, extracted 3x with EtOAc. Organic layer washed with brine, dried over sodium sulfate, and filtered. Filtrate concentrated and purified by flash column chromatography (coupled product eluted with 90% EtOAc in hexanes). Material carried forward with no further purification.

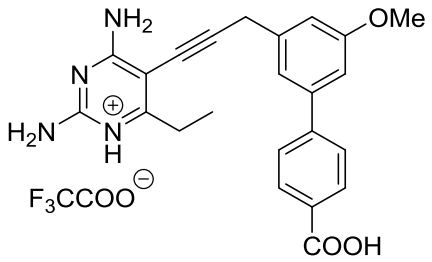
TFA (0.5 mL) added to ester dissolved in DCM (1 mL). Stirred until complete by TLC (30 min). Reaction dried in vacuo to remove excess TFA. Column run on residue. Carboxylic acid eluted with 8% MeOH in DCM to give a white solid (0.48 g, 53% yield 2 steps). Compound isolated as the TFA salt; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.48 (s, 1H), 8.16 (s, 1H), 7.91 (d, *J* = 7.7 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.78 – 7.75 (m, 1H), 7.73 (s, 1H), 7.67 – 7.63 (m, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.17 (d, *J* = 8.5 Hz, 1H), 3.93 (s, 2H), 3.91 (s, 3H), 2.71 (q, *J* = 7.5 Hz, 2H), 1.18 (t, *J* = 7.6 Hz, 3H)**;** ^{13}C NMR (126 MHz, DMSO) δ 167.7, 164.9, 164.9, 159.0 (q, *J* = 31.3), 157.0, 154.5, 140.6, 131.9, 131.0, 129.8, 128.1, 127.6, 127.2, 127.0, 125.3, 111.8, 98.6, 91.8, 72.2, 56.2, 25.6, 21.0, 12.4; HRMS (DART $[M+H]^+$) *m/z* 403.1748 (calculated for $C_{23}H_{23}N_4O_3$ 403.1770).



6-Ethyl-5-[3-(2-methoxy-5-(4-carboxyphenyl)-phenyl)-prop-1-ynyl]-pyrimidine-2,4-diamine (3c). In a screw cap vial fitted with a stir bar and a septum, was added alkyne (0.10 g, 0.31 mmol), iodo-ethylpyrimidine (0.06 mg, 0.24 mmol), $Pd(PPh_3)_2Cl_2$ previously doped with 10% CuI by weight (0.01 g, 0.02 mmol), and KOAc (0.23 g, 2.38 mmol). DMF (3 mL) added and argon bubbled through the stirring solution for 10 min. Vial sealed and heated to 50 °C until complete by TLC (2-3 h). Dried in vacuo using toluene as an azeotrope. Residue washed with saturated sodium bicarbonate, extracted 3x with EtOAc. Organic layer washed with brine, dried over sodium sulfate, and filtered. Filtrate concentrated and purified by flash column chromatography (coupled product eluted with 90% EtOAc in hexanes). Material carried forward with no further purification.

TFA (1 mL) added to ester dissolved in DCM (1 mL). Stirred until complete by TLC (30 min). Reaction dried in vacuo to remove excess TFA. Column run on residue. Carboxylic acid eluted with 8% MeOH in DCM to give a white solid (0.039 g, 43% yield 2 steps); ^{1}H NMR (500 MHz, $CDCl_3$: Methanol-d_4) δ 8.08 (d, *J* = 8.4 Hz, 2H), 7.76 (d, *J* = 2.3 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.61 (dd, *J* = 8.5, 2.4 Hz, 1H), 7.10 (d, *J* = 8.6 Hz, 1H), 3.95 (s, 3H), 3.95 (s, 2H), 2.79 (q, *J* = 7.6 Hz, 2H), 1.28 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (126 MHz, DMSO) δ 171.8, 165.0, 161.6, 157.3, 144.2, 131.7,

130.4, 127.9, 127.7, 127.0, 126.5, 126.3, 111.7, 95.7, 88.5, 76.9, 56.2, 29.3, 21.1, 11.0**;** HRMS (DART $[M+H]^+$) *m/z* 403.1746 (calculated for $C_{23}H_{23}N_4O_3$ 403.1770).

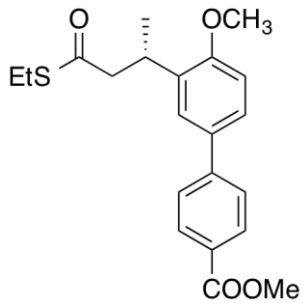


6-Ethyl-5-[3-(3-methoxy-5-(4-carboxyphenyl)-phenyl)-prop-1-ynyl]-pyrimidine-2,4-diamine-trifluoroacetate salt (3d). In a screw cap vial fitted with a stir bar and a septum, was added alkyne (0.10 g, 0.31 mmol), iodo-ethylpyrimidine (0.06 mg, 0.24 mmol), $Pd(PPh_3)_2Cl_2$ previously doped with 10% CuI by weight (0.01 g, 0.02 mmol), and KOAc (0.23 g, 2.38 mmol). DMF (3 mL) added and argon bubbled through the stirring solution for 10 min. Vial sealed and heated to 50 °C until complete by TLC (2-3 h). Dried in vacuo using toluene as an azeotrope. Residue washed with saturated sodium bicarbonate, extracted 3x with EtOAc. Organic layer washed with brine, dried over sodium sulfate, and filtered. Filtrate concentrated and purified by flash column chromatography (coupled product eluted with 90% EtOAc in hexanes). Material carried forward with no further purification.

TFA (1 mL) added to ester dissolved in DCM (1 mL). Stirred until complete by TLC (30 min). Reaction dried in vacuo to remove excess TFA. Column run on residue. Carboxylic acid eluted with 8% MeOH in DCM to give as a white solid (0.045 g, 49% yield 2 steps). Compound isolated as the TFA salt; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.5-7.0 (bs, 4H), 8.04 (d, *J* = 7.7 Hz, 2H), 7.81 (d, *J* = 7.7 Hz, 2H), 7.36 (s, 1H), 7.18 (s, 1H), 7.06 (s, 1H), 4.01 (s, 2H), 3.86 (s, 3H), 2.75 – 2.61 (m, 2H), 1.18 (t, *J* = 7.4

Hz, 3H)**;** ^{13}C NMR (126 MHz, DMSO) δ 167.6, 164.9, 160.5, 158.6 (q, *J* = 31.3), 144.6, 141.1, 139.5, 130.4, 127.4, 119.5, 114.1, 111.1, 98.0, 90.8, 73.4, 55.8, 26.5, 26.0, 12.6**;** HRMS (DART [M+H]$^+$) *m/z* 403.1777 (calculated for $C_{23}H_{23}N_4O_3$ 403.1770).

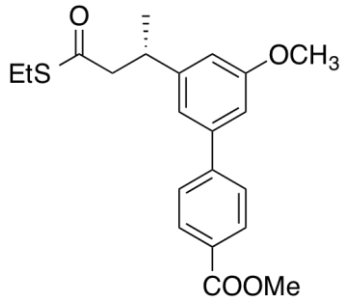
***Synthesis of* 3*S*-(2-Methoxy-5-(4-carbomethoxyphenyl)-phenyl)-thiobutyric acid S-ethyl ester**



To 4-(Methoxycarbonyl)phenylboronic acid (680 mg, 3.78 mmol), $Pd(PPh_3)_4$ (291 mg, 0.252 mmol), and Cs_2CO_3 (1.06 g, 3.78 mmol) was added followed by 3*S*-(5-Bromo-2-methoxy-phenyl)-thiobutyric acid S-ethyl ester **4*S*** (400 mg, 1.26 mmol) dissolved in dioxane (9 mL). To the reaction mixture was added water (2.5 mL) and stirred at 89 ^{o}C for 14 h. Later the reaction mixture was quenched with water (10 mL) and extracted with EtOAc (3 x 30 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated. Purification by flash chromatography on silica gel (Hexane/EtOAc 80:20) provided 3*S*-(2-Methoxy-5-(4-carbomethoxyphenyl)-phenyl)-thiobutyric acid S-ethyl ester as a colorless semi-solid (390 mg, 83% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.4, 2.5 Hz, 1H), 7.46 (d, *J* = 2.2 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 3.98 (s, 3H), 3.94 (s, 3H), 3.79 (sextet, *J* = 7.0 Hz, 1H), 3.02 (dd, *J* = 14.7, 5.9 Hz, 1H), 2.90 (q, *J* = 7.4

Hz, 2H), 2.84 (dd, *J* = 14.6, 8.7 Hz, 1H), 1.38 (d, *J* = 6.9 Hz, 3H), 1.25 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.6, 167.1, 157.3, 145.5, 134.0, 132.2, 130.1, 128.2, 126.6, 126.2, 126.1, 111.0, 55.5, 52.1, 50.5, 31.2, 23.3, 19.7, 14.8; HRMS (DART, M^++H) *m/z* 373.1456 (calculated for $C_{21}H_{25}O_4S$, 373.1474).

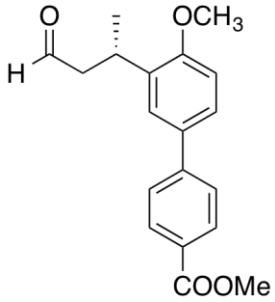
***Synthesis of* 3*S*-(3-Methoxy-5-(4-carbomethoxyphenyl)-phenyl)-thiobutyric acid S-ethyl ester**



To 4-(Methoxycarbonyl)phenylboronic acid (680 mg, 3.78 mmol), $Pd(PPh_3)_4$ (291 mg, 0.252 mmol), and Cs_2CO_3 (1.06 g, 3.78 mmol) was added followed by 3*S*-(5-Bromo-3-methoxy-phenyl)-thiobutyric acid S-ethyl ester **5*S*** (400 mg, 1.26 mmol) dissolved in dioxane (9 mL). To the reaction mixture was added water (2.5 mL) and stirred at 89 ^{o}C for 14 h. Later the reaction mixture was quenched with water (10 mL) and extracted with EtOAc (3 x 30 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated. Purification by flash chromatography on silica gel (Hexane/EtOAc 80:20) provided 3*S*-(3-Methoxy-5-(4-carbomethoxyphenyl)-phenyl)-thiobutyric acid S-ethyl ester as a colorless semi-solid (402 mg, 86% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 2H), 7.08 (s, 1H), 7.00 (s, 1H), 6.82 (s, 1H), 3.93 (s, 3H), 3.85 (s, 3H), 3.42 (sextet, *J* = 7.0 Hz, 1H), 2.87 (m, 4H), 1.36 (d, *J* = 7.0 Hz, 3H), 1.21 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz,

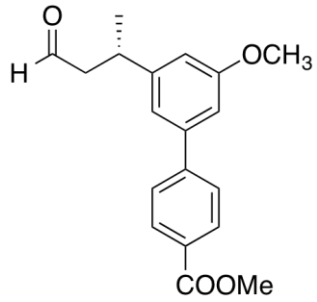
$CDCl_3$) δ 197.9, 166.8, 160.2, 147.7, 145.6, 141.5, 130.0, 129.0, 127.1, 118.4, 112.4, 110.9, 55.3, 52.0, 37.1, 23.3, 21.5, 14.8; HRMS (DART, M^++H) *m/z* 373.1483 (calculated for $C_{21}H_{25}O_4S$, 373.1474).

***Synthesis of* 3*S*-(2-Methoxy-5-(4-carbomethoxyphenyl)-phenyl)-butyraldehyde (6*S*)**



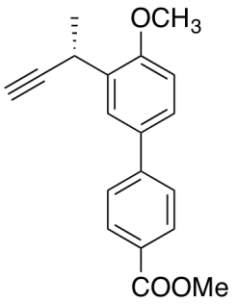
To 3*S*-(2-Methoxy-5-(4-carbomethoxyphenyl)-phenyl)-thiobutyric acid S-ethyl ester (203 mg, 0.649 mmol) dissolved in CH_2Cl_2 (3 mL) was added 10% Pd/C (687 mg, 0.649 mmol Pd) followed by Et_3SiH (0.310 mL, 1.95 mmol) and stirred vigorously at rt for 30-40 min. The reaction monitored by TLC and filtered through the celite and washed with CH_2Cl_2 (2 x 20 mL). The solution was concentrated and purified by flash chromatography on silica gel (hexane/EtOAc 60:40) to yield **6*S*** as colorless oil (172 mg, 85% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.77 (t, *J* = 2.2 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.48 (m, *2*H), 6.97 (d, *J* = 8.3 Hz), 3.96 (s, 3H), 3.91 (s, 3H), 3.83 (sextet, *J* = 7.0 Hz, 1H), 2.82 (ddd, *J* = 16.3, 6.5, 2.1 Hz, 1H), 2.70 (ddd, *J* = 16.3, 7.8, 2.4 Hz, 1H), 1.40 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.3, 167.0, 157.0, 145.4, 133.9, 132.4, 130.1, 128.3, 126.5, 126.3, 125.9, 111.0, 55.5, 52.0, 50.5, 28.0, 20.3; HRMS (DART, M^++H) *m/z* 313.1431 (calculated for $C_{19}H_{21}O_4$, 313.1440).

***Synthesis of* 3*S*-(3-Methoxy-5-(4-carbomethoxyphenyl)-phenyl)-butyraldehyde (7*S*)**



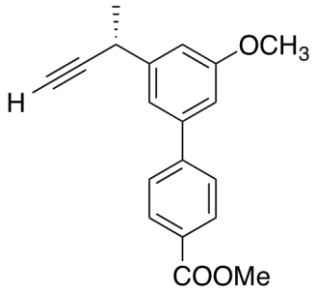
To 3*S*-(2-Methoxy-5-(4-carbomethoxyphenyl)-phenyl)-thiobutyric acid S-ethyl ester (400 mg, 1.07 mmol) dissolved in CH_2Cl_2 (6 mL) was added 10% Pd/C (1.13 g, 1.07 mmol Pd) followed by Et_3SiH (0.62 mL, 3.22 mmol) and stirred vigorously at rt for 30-40 min. The reaction monitored by TLC and filtered through the celite and washed with CH_2Cl_2 (2 x 30 mL). The solution was concentrated and purified by flash chromatography on silica gel (hexane/EtOAc 60:40) to yield **7*S*** as colorless oil (300 mg, 89% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.76 (t, *J* = 1.8 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.09 (dd, *J* = 1.3, 1.3 Hz, 1H), 7.01 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.84 (dd, *J* = 1.7, 1.7 Hz, 1H), 3.96 (s, 3H), 3.88 (s, 3H), 3.44 (sextet, *J* = 7.0 Hz, 1H), 2.84 (ddd, *J* = 16.8, 6.8, 1.7 Hz, 1H), 2.72 (ddd, *J* = 16.8, 7.7, 2.0 Hz, 1H), 1.38 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.5, 166.9, 160.3, 147.9, 145.5, 141.8, 130.1, 129.1, 127.2, 118.4, 112.5, 110.8, 55.4, 52.1, 51.6, 34.4, 22.1; HRMS (DART, M^++H) *m/z* 313.1430 (calculated for $C_{19}H_{21}O_4$, 313.1440).

***Synthesis of* 4-[4-Methoxy-3-(1*S*-methyl-prop-2-ynyl)-phenyl]-methylbenzoate (8*S*)**



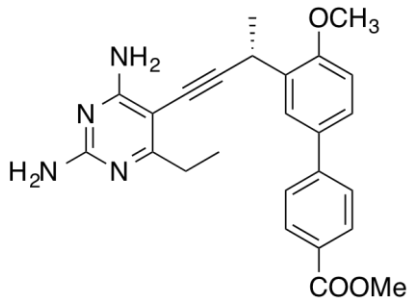
To (S)-aldehyde **6*S*** (0.14 g, 0.45 mmol) dissolved in DMF (2 mL) was added NfF (0.30 mL, 1.68 mmol) at -15 ^{o}C followed by the phosphazene base (0.75 mL, 2.46 mmol) and stirred vigorously at rt for 18 h. The reaction mixture was quenched with water (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated. Purification by flash chromatography on silica gel (hexane/EtOAc 70:30) provided (S)-alkyne **8*S*** as white solid (0.11 g, 83 % yield); R-isomer $[\alpha]_D^{21}$ = - 83.9 (*c*, 1.36, $CHCl_3$)/ S-isomer $[\alpha]_D^{21}$ = + 81.9 (*c*, 1.30, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.5 Hz, 2H), 7.92 (d, *J* = 2.4 Hz, 1H), 7.70 (d, *J* = 8.5 Hz, 2H), 7.54 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.97 (d, *J* = 8.5 Hz, 1H), 4.29 (dq, *J* = 7.0, 2.5 Hz, 1H), 3.98 (s, 3H), 3.93 (s, 3H), 2.32 (d, *J* = 2.5 Hz, 1H), 1.54 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 156.4, 145.4, 132.4, 131.6, 130.1, 128.3, 126.7, 126.6, 110.8, 87.3, 69.9, 55.6, 52.1, 25.6, 22.7; HRMS (DART, M^++H) *m/z* 295.1321 (calculated for $C_{19}H_{19}O_3$, 295.1334).

***Synthesis of* 4-[5-Methoxy-3-(1*S*-methyl-prop-2-ynyl)-phenyl]-methylbenzoate (9*R*)**



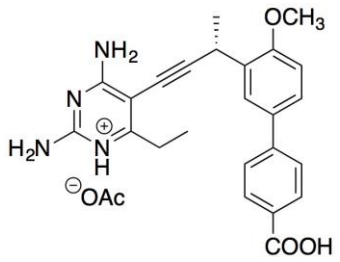
To (S)-aldehyde **7*S*** (0.30 g, 0.96 mmol) dissolved in DMF (4 mL) was added NfF (0.64 mL, 3.60 mmol) at -15 ^{o}C followed by the phosphazene base (1.60 mL, 5.28 mmol) and stirred vigorously at rt for 12 h. The reaction mixture was quenched with water (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated. Purification by flash chromatography on silica gel (hexane/EtOAc 70:30) provided (R)-alkyne **9*R*** as white solid (197 mg, 70 % yield); R-isomer $[\alpha]_D^{21}$ = + 13.4 (*c*, 1.09, $CHCl_3$)/ S-isomer $[\alpha]_D^{21}$ = - 8.7 (*c*, 1.17, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.27 (dd, *J* = 1.3, 1.3 Hz, 1H), 7.06 (dd, *J* = 1.6, 1.6 Hz, 1H), 7.05 (dd, *J* = 1.6, 1.6 Hz, 1H), 3.98 (s, 3H), 3.92 (s, 3H), 3.86 (dq, *J* = 7.1, 2.5 Hz, 1H), 2.35 (d, *J* = 2.5 Hz, 1H), 1.61 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 160.3, 145.5, 144.9, 141.7, 130.1, 129.1, 127.2, 118.5, 112.4, 111.4, 86.7, 70.6, 55.4, 52.1, 31.8, 24.2; HRMS (DART, M^++H) *m/z* 295.1316 (calculated for $C_{19}H_{19}O_3$, 295.1334).

Synthesis of 6-Ethyl-5-[3*S*-(2-methoxy-5-(4-carbomethoxyphenyl)-phenyl)-but-1-ynyl]-pyrimidine-2,4-diamine



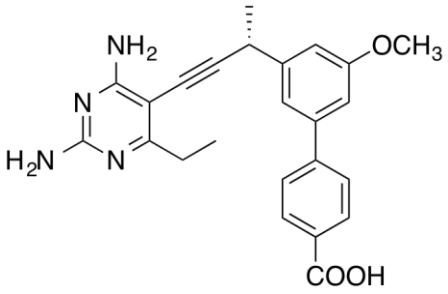
To (S)-alkyne **8*S*** (0.040 g, 0.136 mmol), iodo-ethyl pyrimidine (0.027 g, 0.104 mmol), KOAc (102 mg, 1.04 mmol) and $PdCl_2(PPh_3)_2$ (6.0 mg, 0.0083 mmol) previously doped with 10% CuI was added followed by DMF (2.0 mL) and stirred at 70 ^{0}C for 6 h. The reaction mixture was quenched with saturated $NaHCO_3$ (5 mL) and extracted with (4 x 10 mL) EtOAc. The combined organic layers concentrated by azeotroping with toluene (3 x 10 mL) and purified by gradient flash chromatography (100 % EtOAc followed by 1% MeOH in CH_2Cl_2) to yield coupled pyrimidine as pale yellow solid (30 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.4 Hz, 2H), 7.89 (d, *J* = 2.4 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.56 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.01 (d, *J* = 8.5 Hz, 1H), 5.16 (br s, 2H), 4.84 (br s, 2H), 4.51 (q, *J* = 7.0 Hz, 1H), 3.98 (s, 3H), 3.97 (s, 3H), 2.76 (q, *J* = 7.6 Hz, 2H), 1.62 (d, *J* = 7.0 Hz, 3H), 1.27 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3, 167.0, 164.4, 160.7, 156.4, 145.2, 132.5, 132.1, 130.1, 128.4, 126.7, 126.6, 126.5, 110.9, 101.8, 90.8, 74.8, 55.6, 52.1, 29.7, 27.1, 22.9, 12.5; HRMS (DART, M^++H) *m/z* 431.2078 (calculated for $C_{25}H_{27}N_4O_3$, 431.2083).

Synthesis of 6-Ethyl-5-[3*S*-(2-methoxy-5-(4-carboxyphenyl)-phenyl)-but-1-ynyl]-pyrimidine-2,4-diamine-acetate salt (10*S*)



To coupled pyrimidine (30 mg, 0.069 mmol) dissolved in MeOH (1.4 mL) and THF (0.15 mL) was added LiOH (10.0 mg, 0.418 mmol) dissolved in water (0.45 mL) and stirred at 32 ^{o}C for 24 h. The reaction mixture was quenched with saturated NH_4Cl and extracted with EtOAc (4 x 10 mL). The combined organic layers concentrated and purified by gradient flash chromatography (5-10% MeOH in CH_2Cl_2 followed by 1% AcOH + 9 % MeOH in CH_2Cl_2) to yield acid **10*S*** as white solid (12 mg, 28% over 2 steps); R-isomer $[\alpha]_D^{21}$ = - 63.2 (*c*, 0.33, DMSO-d_6)/ S-isomer $[\alpha]_D^{21}$ = + 59.1 (*c*, 0.30, DMSO-d_6); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.97 (d, *J* = 8.0 Hz, 2H), 7.85 (d, *J* = 2.2 Hz, 1H), 7.57 (m, 3H), 7.12 (d, *J* = 8.5 Hz, 1H), 6.19 (br s, 2H), 6.04 (s, 2H), 4.42 (q, *J* = 7.0 Hz, 1H), 3.91 (s, 3H), 2.61 (q, *J* = 7.5 Hz, 2H), 1.52 (d, *J* = 7.0 Hz, 3H), 1.14 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 176.6, 172.1, 164.8, 161.7, 156.1, 141.3, 133.0, 132.2, 130.2, 126.6, 126.4, 125.5, 112.1, 101.2, 88.6, 75.9, 56.2, 29.3, 27.1, 24.2, 23.4, 12.8; HRMS (DART, M^++H) *m/z* 417.1908 (calculated for $C_{24}H_{25}N_4O_3$, 417.1927).

Synthesis of 6-Ethyl-5-[3*S*-(3-methoxy-5-(4-carboxyphenyl)-phenyl)-but-1-ynyl]-pyrimidine-2,4-diamine (11*R*)



To (R)-alkyne **9*R*** (0.040 g, 0.136 mmol), iodo-ethyl pyrimidine (0.027 g, 0.104 mmol), KOAc (102 mg, 1.04 mmol) and $PdCl_2(PPh_3)_2$ (6.0 mg, 0.0083 mmol) previously doped with 10% CuI was added followed by DMF (2.0 mL) and stirred at 70 ^{0}C for 6 h. The reaction mixture was quenched with saturated $NaHCO_3$ (5 mL) and extracted with (4 x 10 mL) EtOAc. The combined organic layers concentrated by azeotroping with toluene (3 x 10 mL) and purified by gradient flash chromatography (100 % EtOAc followed by 1% MeOH in CH_2Cl_2) to yield coupled pyrimidine as pale yellow solid (40 mg); To coupled pyrimidine (40 mg, 0.093 mmol) dissolved in MeOH (1.6 mL) and THF (0.2 mL) was added LiOH (13.4 mg, 0.56 mmol) dissolved in water (0.6 mL) and stirred at 32 ^{o}C for 24 h. The reaction mixture was quenched with saturated NH_4Cl and extracted with EtOAc (4 x 10 mL). The combined organic layers concentrated and purified by gradient flash chromatography (5-10% MeOH in CH_2Cl_2 followed by 1% AcOH + 9 % MeOH in CH_2Cl_2) to yield acid **11*R*** as white solid (24 mg, 55% over 2 steps); R-isomer $[\alpha]_D^{22}$ = - 6.6 (*c*, 0.85, DMSO-d_6)/ S-isomer $[\alpha]_D^{22}$ = + 5.83 (*c*, 0.19, DMSO-d_6); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.5 Hz, 2H), 7.67 (d, *J* = 7.5 Hz, 2H), 7.37 (s, 1H), 7.11 (s, 1H), 7.05 (s, 1H), 6.24 (br

s, 2H), 6.16 (br s, 2H), 4.16 (q, *J* = 7.0 Hz, 1H), 3.85 (s, 3H), 2.58 (q, *J* = 7.5 Hz, 2H), 1.56 (d, *J* = 7.0 Hz, 3H), 1.13 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 164.7, 161.7, 160.4, 146.4, 141.9, 130.3, 126.5, 118.2, 112.4, 110.9, 100.9, 88.3, 76.6, 55.7, 32.8, 29.4, 25.1, 12.9; HRMS (DART, M^++H) *m/z* 417.1973 (calculated for $C_{24}H_{25}N_4O_3$, 417.1927).

HPLC Purity

Purity analysis were performed with a reversed phase high performance liquid chromatography on a Shimadzu Prominence 20 instrument fitted with a Luna 5μ C18(2) 100 Å column (5 μM, 4.6 mm x 250 mm, Phenomenex) and using UV diode array detection at 254 nm. Two separate determinations (Method A: isocratic: 40/60/0.1 MeCN/H_2O/TFA and Method B: isocratic: 60/40/0.1 MeOH/H_2O/TFA or 80/20/0.1 MeOH/H_2O/TFA) were made to determine compound purity. Flow rate was 1.0 mL/min for Method A and 1.0 mL/min for Method B. Compounds were diluted in HPLC grade methanol and filtered prior to analysis. Sample concentrations were 1 mg/ml. All final tested compounds were at least 95% pure according to both methods.

Biological Supplemental Information

Table S1. Enzyme Inhibition Values with Standard Deviations

Cmpd	R_P	R_1	R_2	Ar	Sa K_i (nM)	Ec K_i (nM)	Hu K_i (nM)
3a	H	OCH_3	H	*o*-COOH	53.47 ± 4.5	2.12±0.09	2494±46
3b	H	OCH_3	H	*m*-COOH	23.38±1.2	5.72±0.22	346±13
3c	H	OCH_3	H	*p*-COOH	4.8 ±1.5	0.979±0.07	200±7
3d	H	H	OCH_3	*p*-COOH	1.64±0.09	5.52±0.09	158±9
10*S*	S-CH_3	OCH_3	H	*p*-COOH	5.51±0.3	1.93±0.22	376.6±21
10*R*	R-CH_3	OCH_3	H	*p*-COOH	32.2±2.9	3.14±0.44	451±11
11*R*	R-CH_3	H	OCH_3	*p*-COOH	1.34±0.10	0.914±0.02	234.2±14
11*S*	S- CH_3	H	OCH_3	*p*-COOH	2.09±0.15	1.81±0.11	388±23
TMP					3.43 ±0.45	0.22±02	45738.5±0.6

Table S2. Data collection and structure refinement statistics

	Sa(WT):NADPH:**3c**	Sa(WT):NADPH:**3d**
PDB ID	5HF0	5HF2
Space group	*$P6_122$*	*$P6_122$*
No. monomers in asymmetric unit	1	1
Unit cell (*a, b, c* in Å)	79.09, 79.09, 107.93 90.0, 90.0, 120.0	79.02, 79.02, 108.25 90.0, 90.0, 120.0
Resolution (Å)	32.65-2.24 (2.28-2.24)	25.15-1.81 (1.87-1.81)
Completeness % (last shell, %)	100 (99.9)	99.8 (100)
Unique reflections	10,059	18,798
Redundancy (last shell)	14 (14.2)	12.32 (12.03)
Rsym, (last shell)	0.055 (0.144)	0.110 (0.644)
$\langle I/\sigma \rangle$ (last shell)	68.5 (31.9)	11.7 (2.3)
R-factor/Rfree	0.1703/ 0.2167	0.1991/0.2322
No. of atoms (protein, ligands, solvent)	1,499	1,489
Rms deviation bond lengths (Å), angles (deg)	0.008, 1.912	0.009. 1.810
Average B factor for protein (Å2)	22.34	28.01
Average B factor for ligand (Å2)	17.46 α-NADPH 16.91 β-NADPH 31.29 Inhibitor	24.65 α-NADPH 24.93 Inhibitor
Average B factor for solvent molecules (Å2)	25.25	35.10
Residues in most favored regions (%)[a]	96.86	98.73
Residues in additional allowed regions (%)[a]	3.14	1.27
Residues in disallowed regions (%)[a]	0	0
Collection Location	SSRL Beamline 7-1	Rigaku HighFlux-007

Table S3. Minimum Bactericidal Concentrations

Compound	*S. aureus* MIC (µg/mL)	*S. aureus* MBC (µg/mL)
3d	0.0195	0.0391
11*R*	0.0098	0.0195
11*S*	0.0098	0.0195

Table S4. MIC values (µg/mL) in *E. coli* wild-type and *E. coli* Δ*acrB*

Compound	*E. coli BW25113*	*JW0451*
3a	>32	>32
3b	>20	>20
3c	>20	>20
3d	>20	>20
10*S*	>20	>20
10*R*	20	20
11*R*	10	5
11*S*	10	10
TMP	0.3125	0.0391
MTX	>40	>40

In order to examine whether the COOH-PLAs are subject to efflux by the common AcrB efflux pump, we compared MIC values in a parent *E. coli* strain with those in a strain in which AcrB is deleted (JW0451) (Table S4). As the MIC values against the JW0451 strain are similar to the parent strain and not the NR698 strain (Table 1), it is likely that the compounds are not subject to efflux by AcrB.

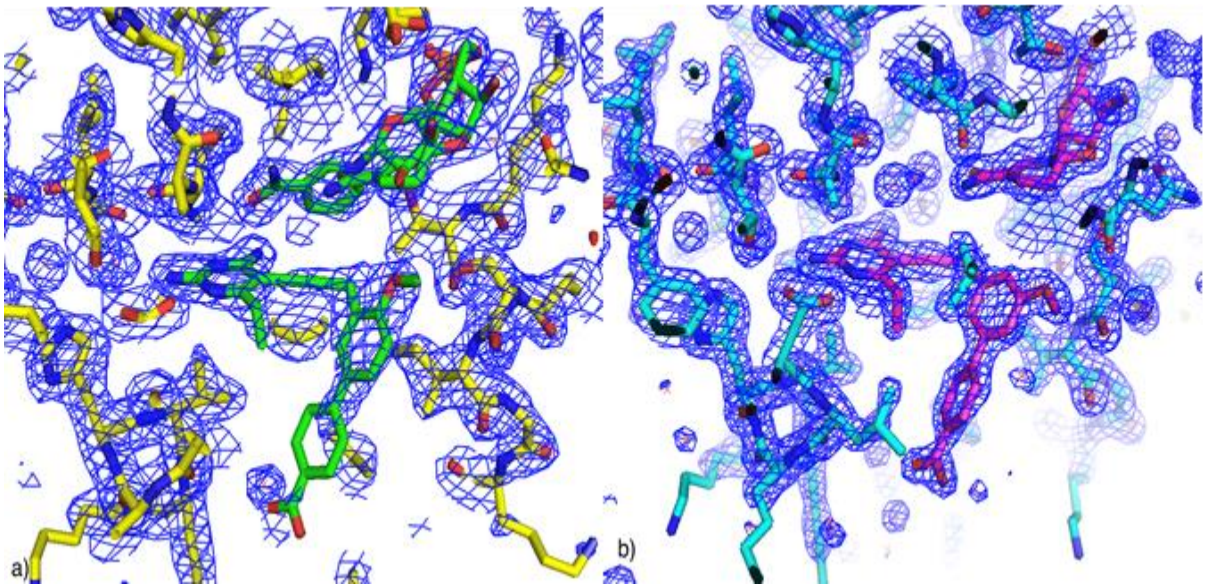


Figure S1: Electron density (2Fo-Fc) of the active site residues. Panel a) shows density for the Sa(WT)DHFR:NADPH:**3c**, shown at 1.0σ and panel b) density for the Sa(WT)DHFR:NADPH:**3d**, shown at 1.5σ.

Materials and Methods

Protein Expression and Purification

Recombinant *Sa*DHFR and *Ec*DHFR in PET-41a(+) were over-expressed in *E. coli* BL21 (DE3) (Invitrogen) cells and purified using nickel affinity chromatography (5Prime) using previously reported conditions.[1] Protein was desalted using a PD-10 column (GE Healthcare) into buffer containing 20 mM Tris pH 7.0, 20 % glycerol, 0.1 mM EDTA, 2 mM DTT, the protein was flash frozen and stored in aliquots at -80 ^{o}C.

Recombinant HuDHFR purified using methotrexate affinity chromatography according to previously reported conditions.[2]

Enzymatic Assays

Sa, Ec, and human *DHFR Assays*

IC_{50} values for *Sa, Ec* and human DHFR enzymes were determined using enzyme inhibition assays by monitoring the rate of NADPH oxidation by DHFR via absorbance at 340 nM. The reaction was performed at room temperature in buffer containing 20 mM TES pH 7.0, 50 mM KCl, 0.5 mM EDTA, 10 mM β-ME and 1mg/mL BSA with 0.1 mM NADPH and 2 µg/mL enzyme. Inhibitor in DMSO was added to the enzyme/NADPH mixture and incubated for 5 minutes prior to the addition of 0.1 mM dihydrofolate in 50 mM TES. The enzymatic activity is determined via Equation 1 and the IC_{50} is determined using Equation 2.

[1] Frey, K. M., et al. (2009) Crystal Structure of Wild-type and Mutant Methicillin-resistant Staphyloccocus aureus Dihydrofolate Reductase Reveal an Alternate Conformation of NADPH That May Be Linked to Trimethoprim Resistance. *J. Mol. Bill.* 387, 1289-1309.

[2] Kristen Lamb, et al. (2013) Elucidating Features that Drive the Design of Selective Antifolates Using Crystal Structures of Human Dihydrofolate Reductase. *Biochemistry*, 52(41), 7318-7326.

$$Activity = \left(\frac{(A_2 - A_1) * 0.041}{(T_2 - T_1)}\right)/60 \quad (1)$$

Where 0.041 is a term derived by the absorbance coefficient of NADPH, ε=6.2x10^3 Lmol^{-1}cm^{-1}.

$$IC_{50}(nM) = \left(\frac{(Ink.Volume/(100 - \% Activity)) * 50}{(550)}\right) * Inh\ Conc. \quad (2)$$

The assay was preformed in triplication and average IC_{50} and the standard deviation from the mean are reported. The IC_{50} values were converted to K_i using K_M values of Sa DHFR of 17.5μM[3], Ec DHFR of 1.1μM[4] and Human DHFR of 30μM[5].

Cell Based Assays

S. aureus MICs

Minimum inhibitory concentrations were determined according to Clinical and Laboratory Standards Institute's guideline for Standard Micro-dilution broth assay using a final inoculum of 5 x 10^5 CFU/mL of ATCC strain 43300 in Isosensitest Broth (Oxoid). The MIC was defined as the lowest concentration of inhibitor to visually inhibit growth. Growth was monitored at A_{600} after 18h of incubation at 37^{o}C. MICs were confirmed, colorimetrically, using Presto Blue (Life Technologies).

E. coli

Minimum inhibitory concentrations were determined using *E. coli* (ATCC 25922) and the microdilution broth assay with an inoculum of 1 x 10^5 CFU/mL in Isosensitest Broth (Oxoid). Growth was monitored at A_{600} using the Alamar Blue assay; the MIC

[3] Reeve, S. M., et al. (2015) Protein Design and algorithms predict viable resistance to an experimental antifolate. *PNAS*, *112(3)*, 749-754.
[4] Iwakura, M., Tanaka, T. (1992) Dihydrofolate Reductase from Bacillus subtilis and its Artificial Derivatives: Expression, Purification, and Characterization. *J. Biochem. 111*, 638-642.
[5] Blakely, R. L. (1995) Eukaryotic dihydrofolate reductase. *Adv. Enzymol. Relat. Mol. Biol., 70,* 23-102.

is defined as the lowest concentration of inhibitor to completely inhibit growth. Strains *E. coli* BW25113 and JW0451 were obtained from the Coli Genetic Stock Center, Yale University; strain NR698 was a gift from Dr. Thomas Silhavy (Princeton) and Dr. Daniel Kahne (Harvard); cell growth inhibition was evaluated using similar procedures as *E. coli* ATCC 25922.

CYP Inhibition

Human Cytochrome P450 3A4 and 2D6 inhibition assays were run in 96-well microtiter plates using CYP3A4/BQ and CYP2D6/AMMC High Throughput Inhibitor Screening Kits (Gentest, Woburn, MA). Briefly, the ability to inhibit CYP catalytic activity was measured by following the presence of a fluorescent substrate. Inhibitor concentrations ranged from 0.02 to 50 µM. Reactions were terminated after 30 minutes by addition of 75 µL of a 4:1 acetonitrile/0.5 M Tris base solution. The BQ (CYP3A4 substrate) metabolite 7-hydroxyquinoline was measured at 409 nm excitation and 530 nm. The AMMC (CYP2D6 substrate) metabolite 3-[-2-(N,N-diethylamino)ethyl]-7-hydroxy-4-methylcoumarin hydrochloride metabolite was measured at 390 nm excitation and 460 nm emission. IC_{50} values were calculated via linear interpolation with inhibitor concentrations and corresponding percent inhibition values.

Microsomal stability

Compounds (0.5 µg/ml) were incubated with mouse liver microsomes (0.5 mg/mL; MLM; BD Biosciences, San Jose, CA) in 0.1 M potassium phosphate buffer (pH 7.4) and 200 µg/ml HPMC A4M in the presence of an NADPH regenerating system at 37°C. The NADPH regenerating system consisted of NADP+ (1.3 mM), glucose 6-

phosphate (3.3 mM), and glucose-6-phosphate dehydrogenase (0.5 U/mL). The metabolic reaction was initiated by the addition of microsomes and quenched by the addition of an equal volume of ice-cold acetonitrile at seven time points: 0, 10, 20, 30, 40, 60, and 90 minutes. Samples were centrifuged at 15,000 rpm for 10 minutes, supernantants were collected and spiked with an internal standard (diltiazem, 500 ng/mL) then analyzed using a Shimadzu Prominence 20 high-performance liquid chromatography (HPLC) instrument (Shimadzu, Kyoto, Japan) fitted with a Luna 5 µm C18(2) 100Å column (5 µM, 4.6 × 250 mm; Phenomenex, Torrance, CA) and a UV diode array detection at 254 nm. The area under the curve for the parent compound determined and normalized using the internal standard. The amount of parent compound remaining was determined using a standard curve. Data was plotted and the metabolic half-life was calculated following first order kinetics.

SaDHFR Crystallization

*SaDHFR:NADPH:**3c***

Purified SaDHFR at18 mg/mL protein was co-crystallized with 2 mM NADPH and 1 mM **3c** in DMSO via the hanging drop method. The mixture of protein and cofactor was incubated on ice for 3 hours. Equal volumes of protein solution were added to an optimized buffer solution containing 0.1 M MES, pH 5.5, 0.2 M sodium acetate, 17% PEG 10,000 and 12.5% gamma-butyrolactone. When stored at 4^{o}C, crystals typically formed within 7 days. Crystals were harvested and frozen in cryo-protectant buffer containing 25% glycerol. Data were collected remotely on beamline 7-1 at Stanford Synchrotron Radiation Lightsource, SLAC National Accelerator Laboratory. Data were indexed and scaled using HKL2000. Phaser was used to identify

molecular replacement solutions using PDB ID: 3F0Q as a probe. Coot and Phenix were used for structure refinement until acceptable R_{Work} and R_{Free} were achieved.

*SaDHFR:NADPH:**3d***

Purified SaDHFR was co-crystallized with 2 mM NADPH and 1mM **3d** in DMSO via hanging drop method. Crystallization details were similar to those used above except for a change in buffer to 0.1M MES, pH 5.0. Data were collected on the Rigaku Highflux Homelab system at the University of Connecticut's Protein X–Ray Crystallography Facility. Data were indexed and scaled using Structure Studio (d*Trek). Similar to above, Phaser[6] was used for molecular replacement; Coot and Phenix[7] were used for structure refinement.

Bacteriostatic/Bactericidal Determination

The minimum bactericidal concentrations were determined by plating 20 µL of culture on non-antibiotic LB agar at 1x, 2x, 4x and 8x MIC when MIC was determined using an inoculum of 1x10^5 CFU/mL. The MBC is defined as the concentration there is a $\geq$ 99% decrease of bacteria. Compounds with a MBC/MIC <4 are considered bactericidal.[8]

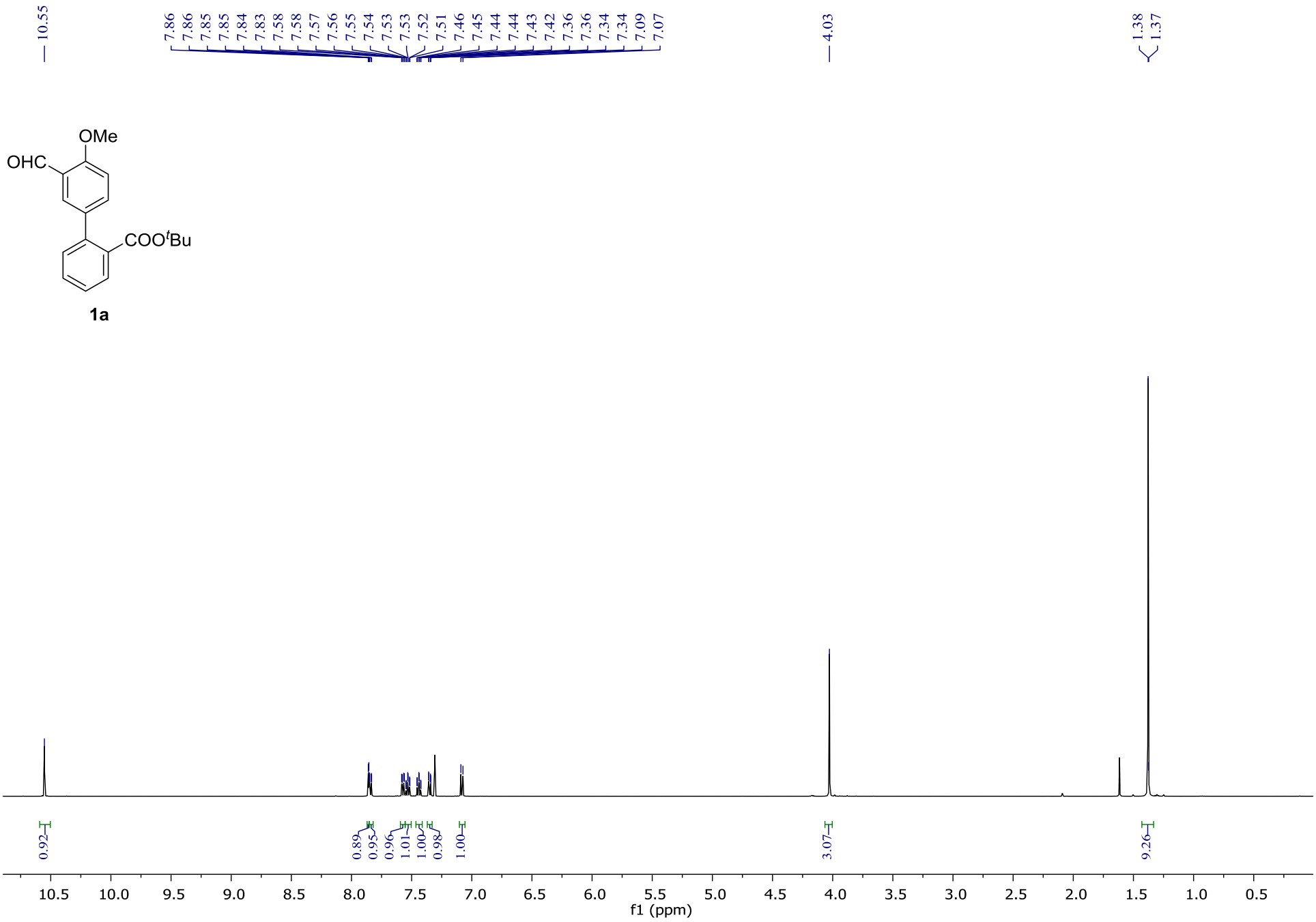
[6] McCoy A. J. (2007) Solving structures of protein complexes by molecular replacement with Phaser *Acta Crystallogr. D. Biol. Crystallogr.* 63 (pt1): 32-41.

[7] Adams P. D., et al. (2010) PHENIX: A comprehensive Python-based system for macromolecular structure solution. *Acta Crystallogr. D. Biol. Crystallogr.* 66 (Pt 2): 213-221.

[8] Pankey GA and Sabath LD. (2004) Clinical Relevance of Bacteriostatic versus Bactericidal Mechanisms of Action its Treatment of Gram-Positive Bacterial Infections. *Clinical Infectious Diseases*, 38:864-70.

Human cell toxicity assays

Adherent cell lines were maintained in Eagle's Minimal Essential Media with 2 mM glutamine and Earle's Balanced Salt Solution adjusted to contain 1.5 g/L sodium bicarbonate, 0.1 mM non-essential amino acids, 1 mM sodium pyruvate and 10 % fetal calf serum. Fetal calf serum used in these assays was lot matched throughout. All cultures were maintained under a humidified 5 % CO_2 atmosphere at 37 °C, had media refreshed twice weekly and were subcultured by trypsinization and resuspension at a ratio of 1:5 each week. Toxicity assays were conducted between passages 10 – 20. Target compound toxicity was measured by incubating the test compound with the cells for four hours, washing the cells and finally treating the cells with Alamar Blue. After 12 – 24 hours the fluorescence of the reduced dye was measured. Fluorescence intensity as a function of test compound concentration was fit to the Fermi equation to estimate IC_{50} values.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7.07
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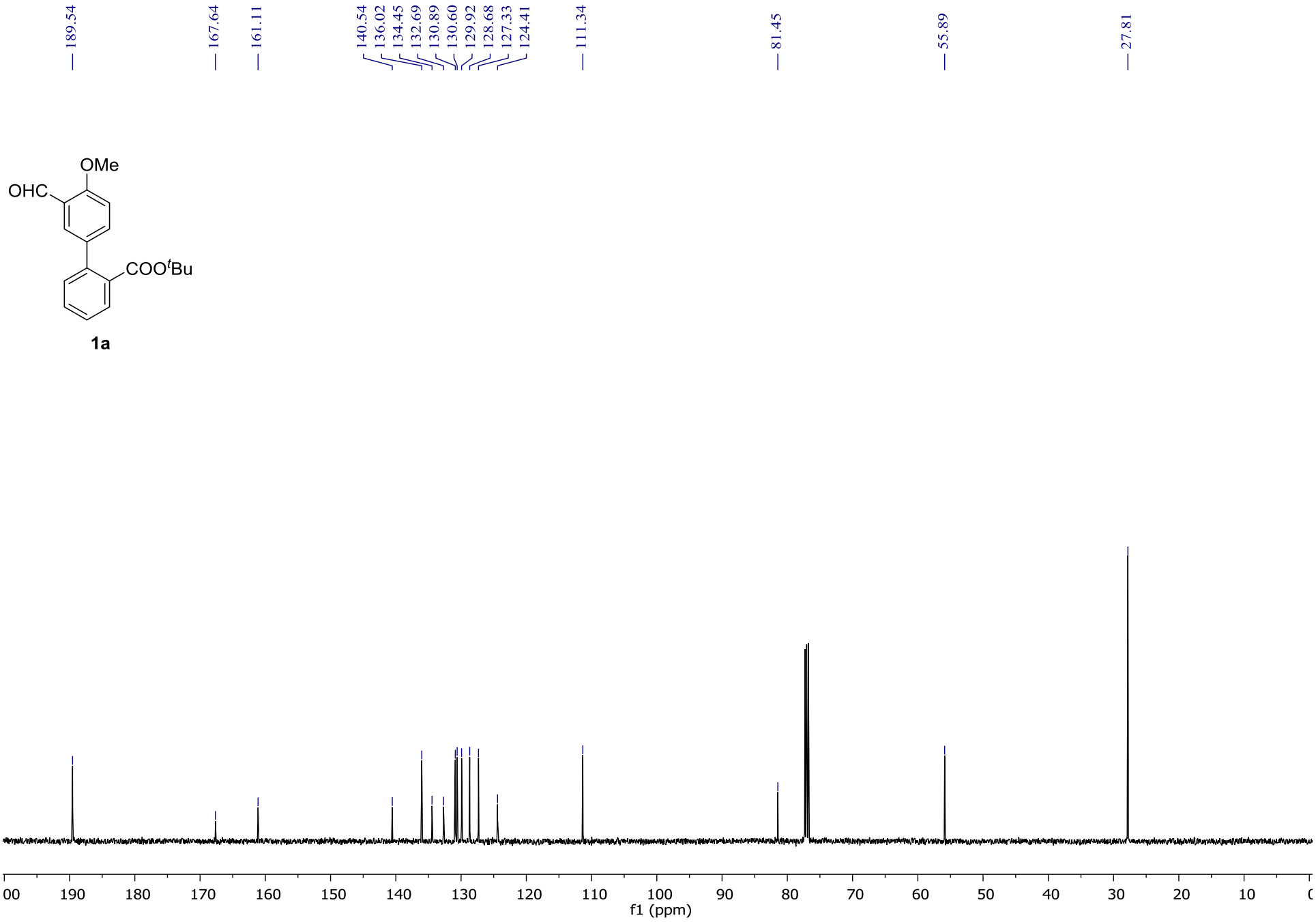
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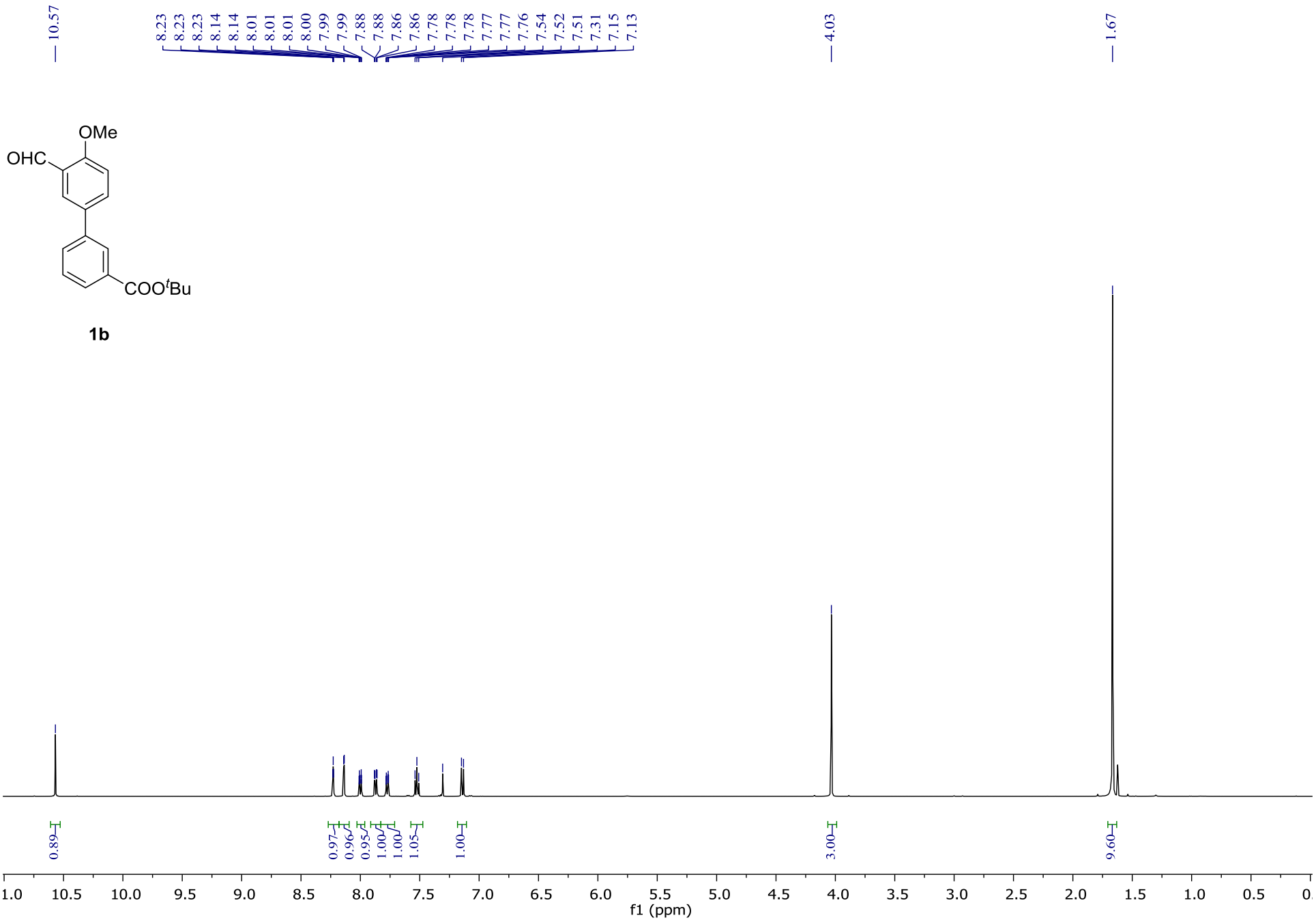
f1 (ppm)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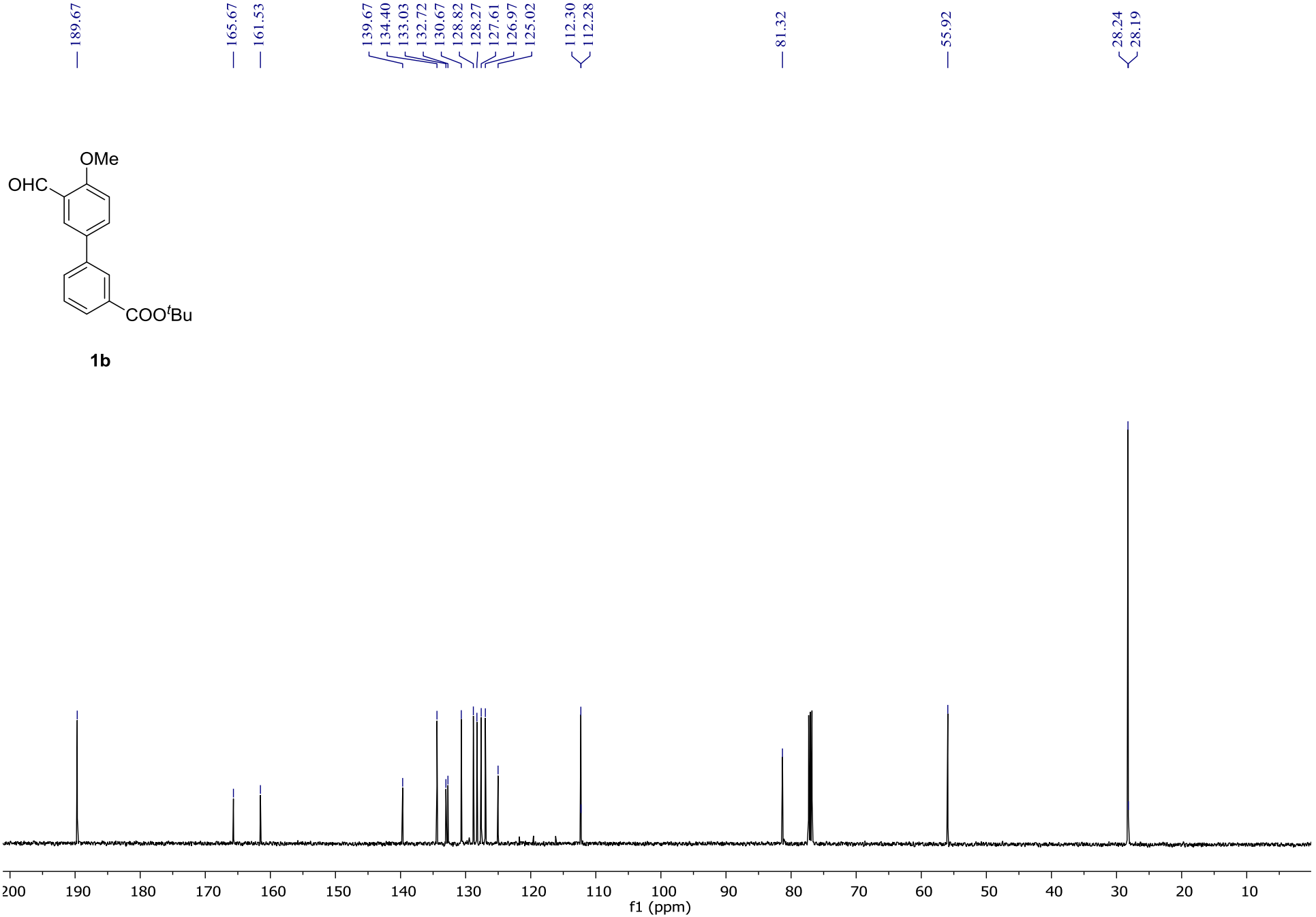
1b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50
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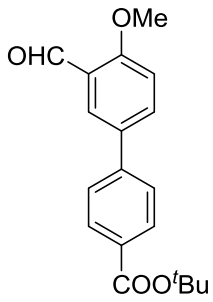
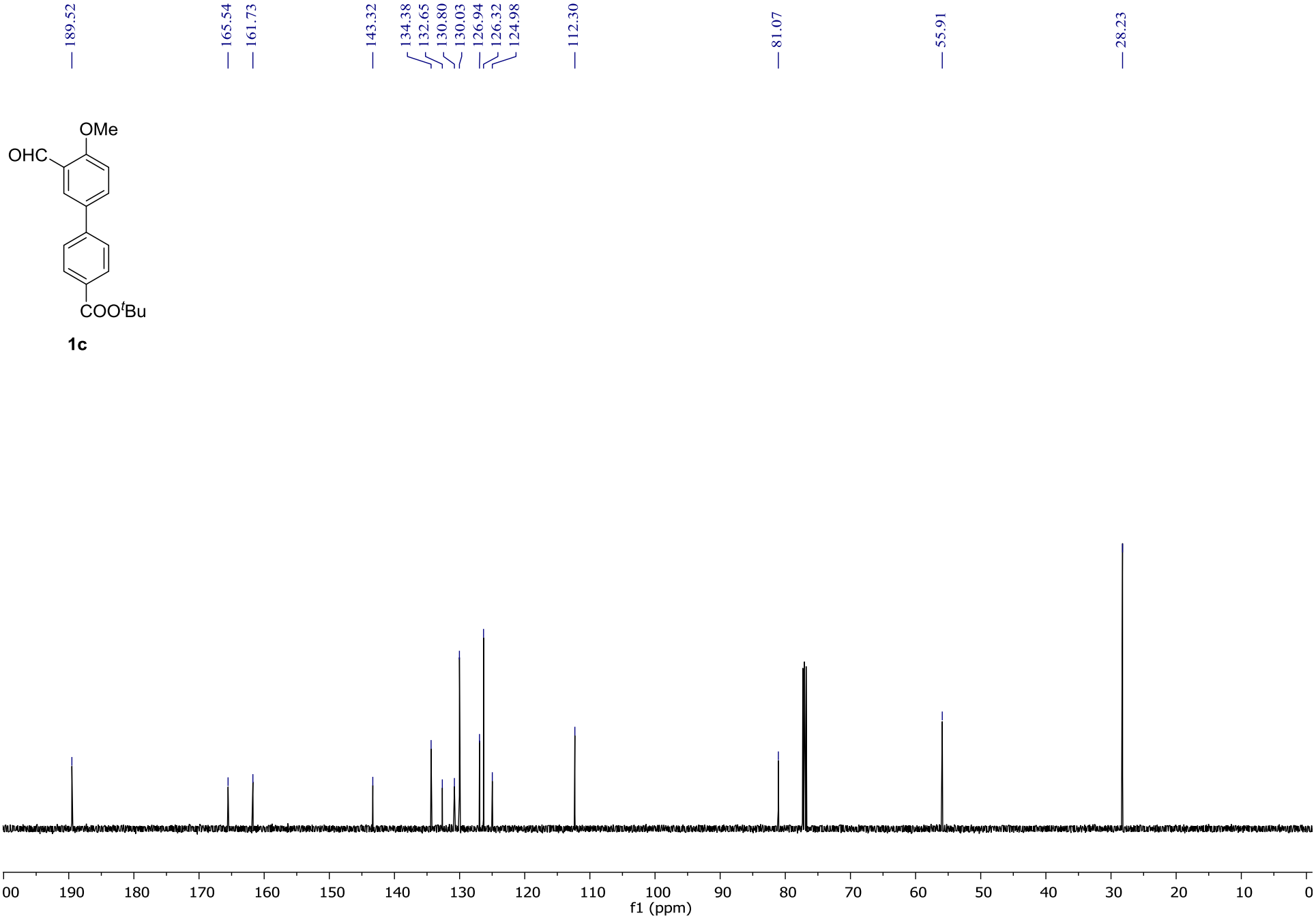
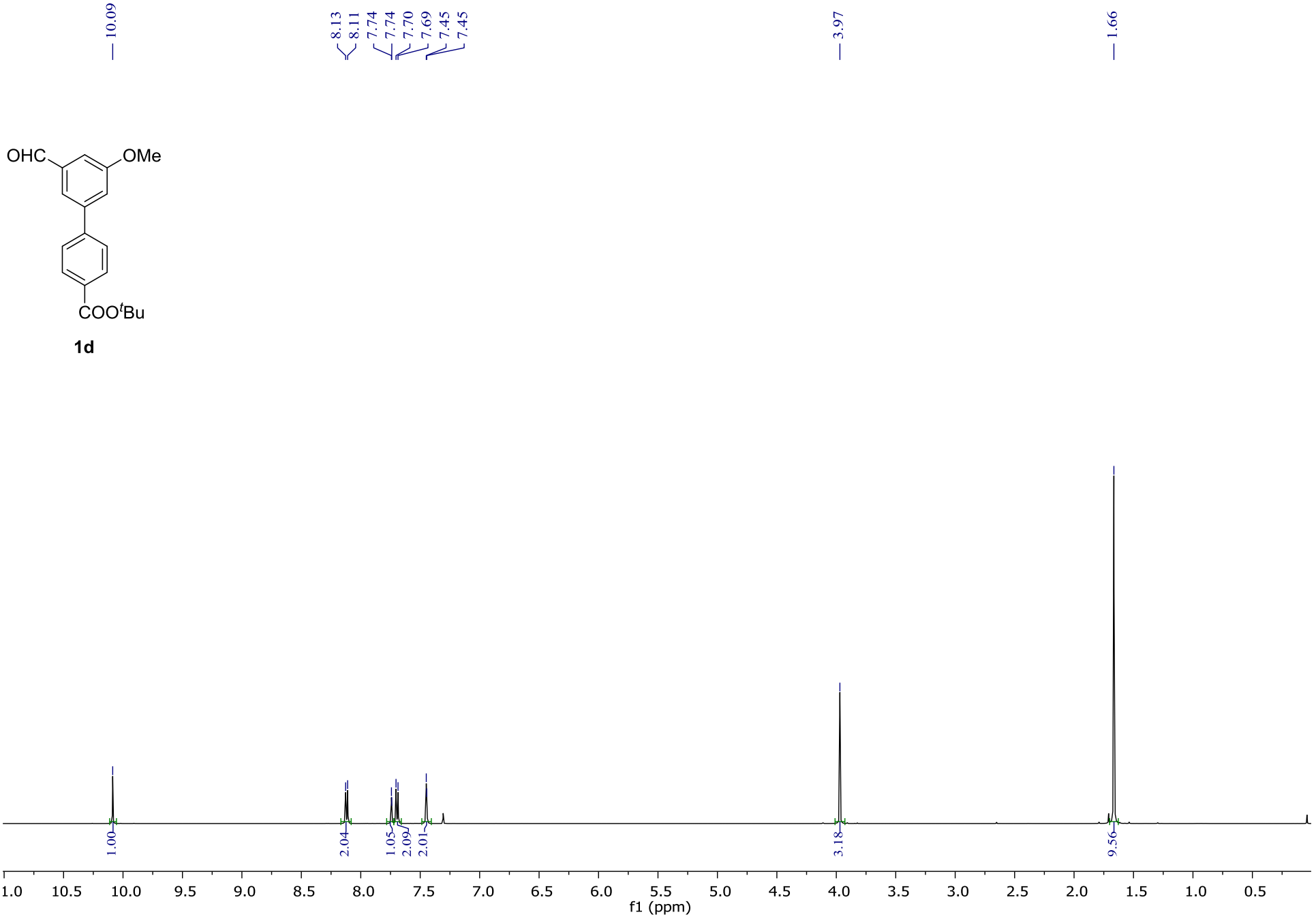
30
20
10
f1 (ppm)

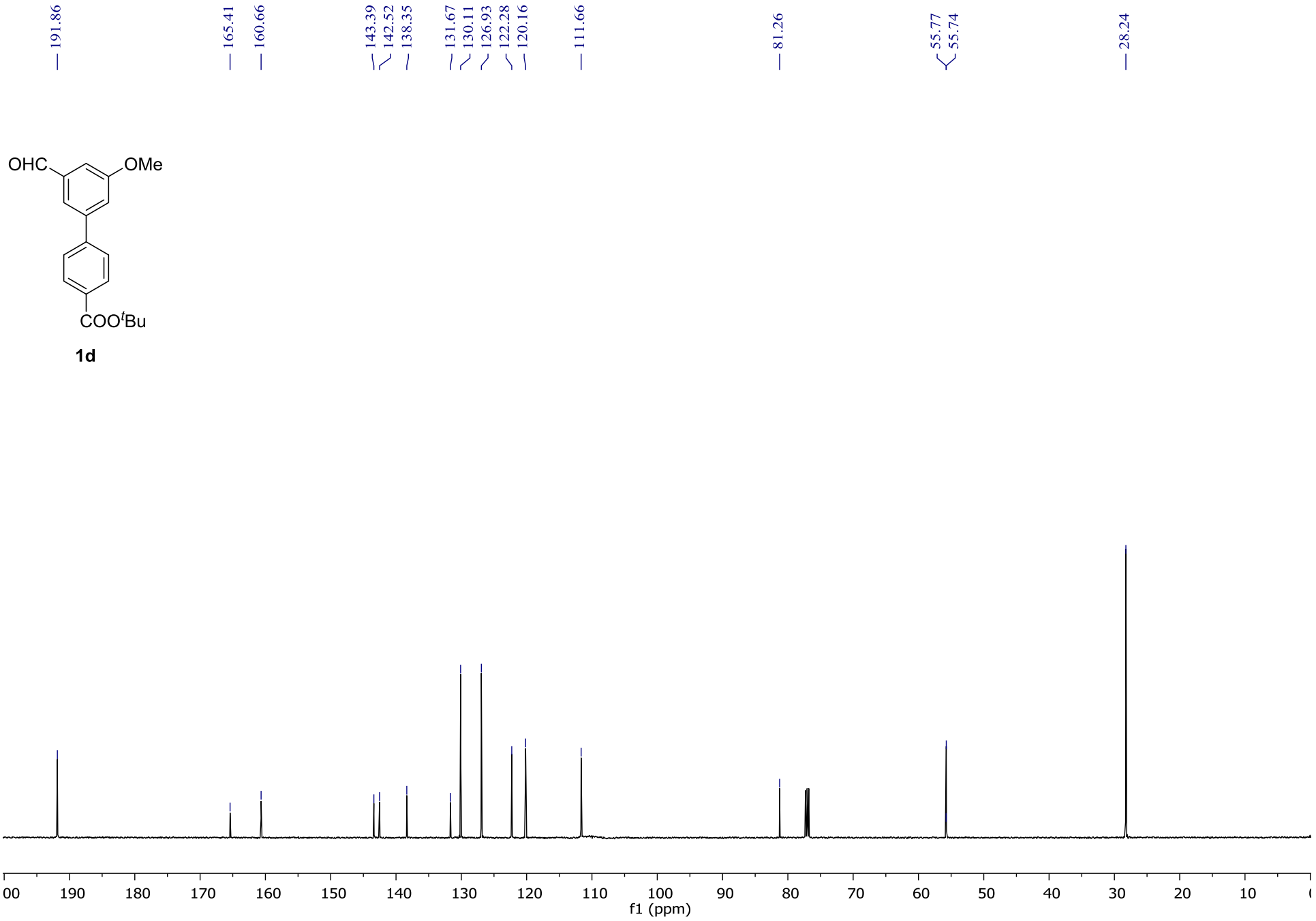

OMe
OHC
COO^{t}Bu

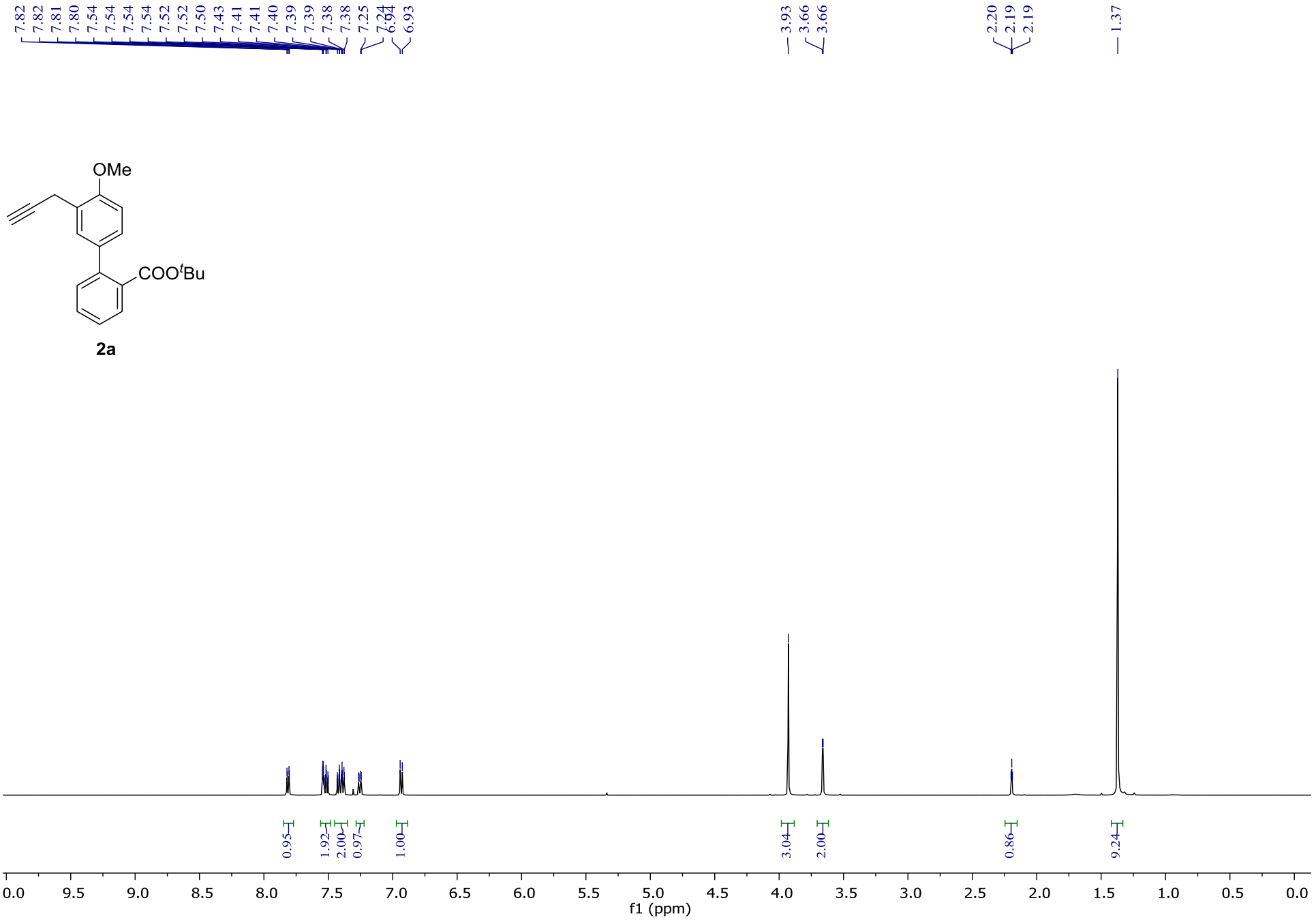
1c

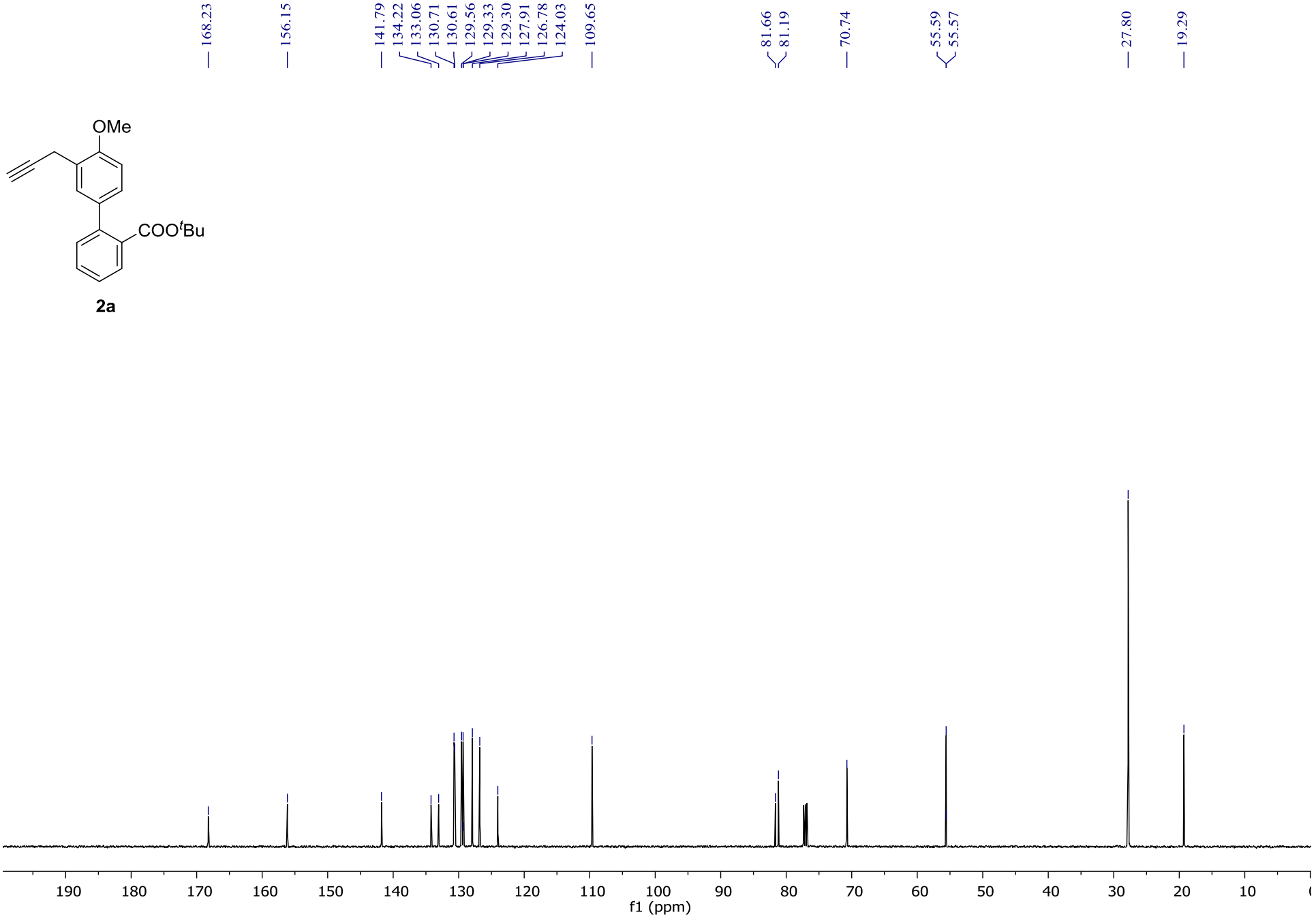
10.53
8.12
8.11
8.06
8.05
7.84
7.82
7.63
7.62
7.11
7.09
4.00
1.63
0.90
0.94
1.92
0.99
1.99
1.00
3.03
9.10
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

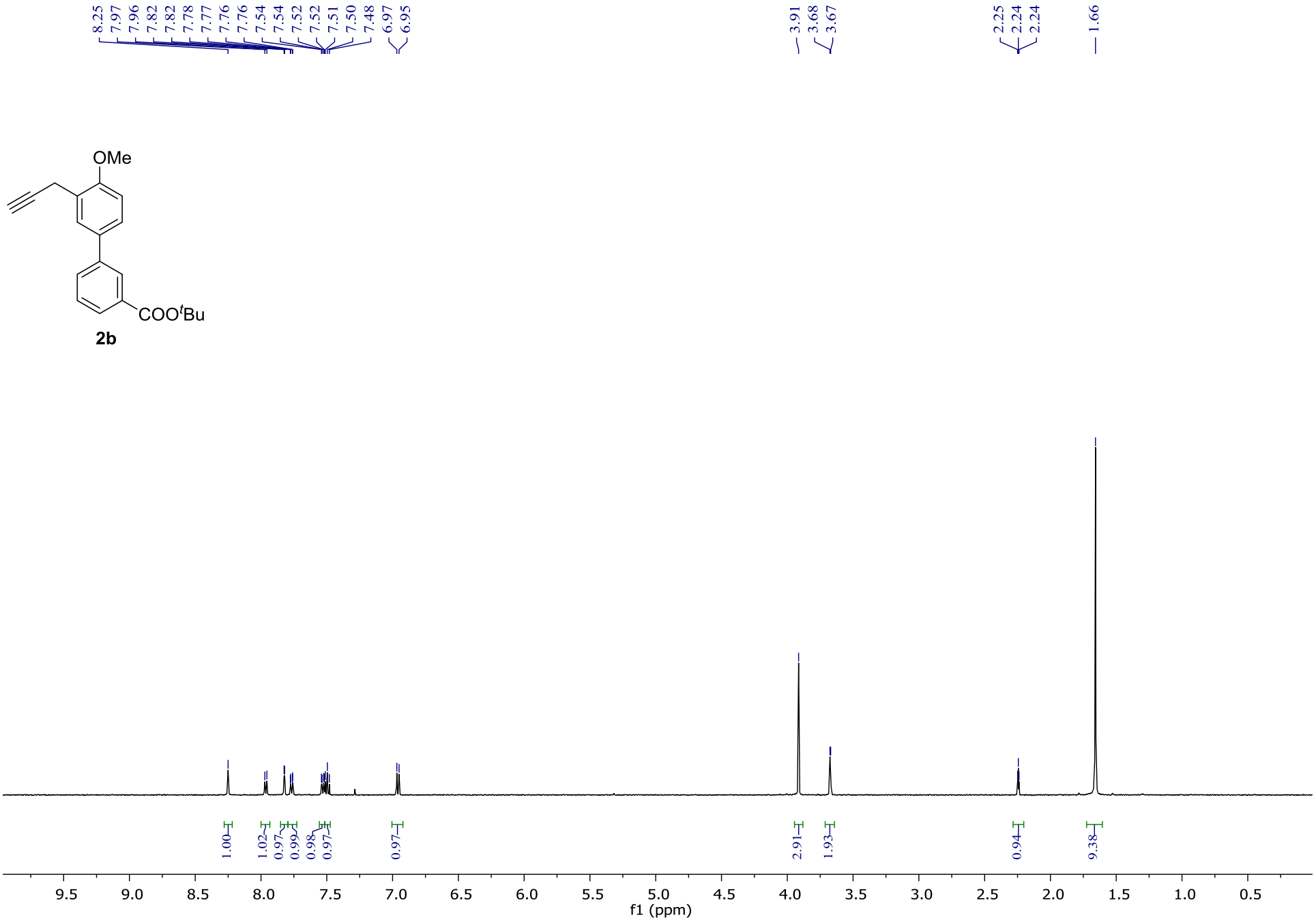

189.52
165.54
161.73
143.32
134.38
132.65
130.80
130.03
126.94
126.32
124.98
112.30
81.07
55.91
28.23
OMe
OHC
COO^{t}Bu
1c
f1 (ppm)

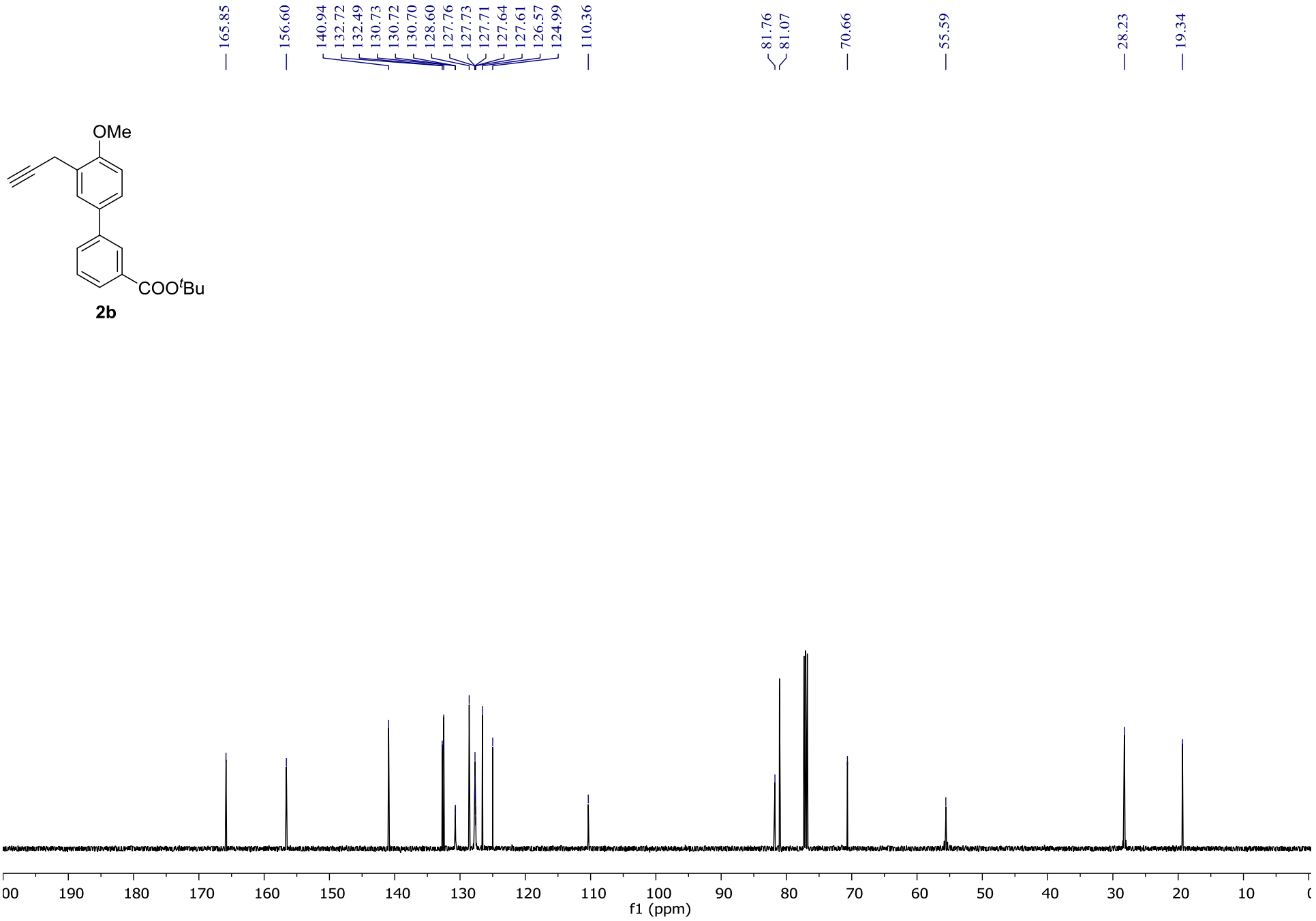

10.09
8.13
8.11
7.74
7.74
7.70
7.69
7.45
7.45
3.97
1.66
OHC
OMe
COO^{t}Bu
1d
1.00
2.04
1.05
2.09
2.01
3.18
9.56
f1 (ppm)

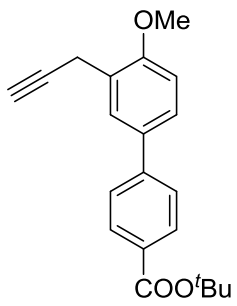

191.86
165.41
160.66
143.39
142.52
138.35
131.67
130.11
126.93
122.28
120.16
111.66
81.26
55.77
55.74
28.24
OHC
OMe
COO^{t}Bu
1d
f1 (ppm)


7.82
7.82
7.81
7.80
7.54
7.54
7.54
7.54
7.52
7.52
7.50
7.43
7.41
7.41
7.40
7.39
7.39
7.38
7.38
7.25
7.24
6.94
6.93
3.93
3.66
3.66
2.20
2.19
2.19
1.37
OMe
COO^{t}Bu
2a
0.95
1.92
2.00
0.97
1.00
3.04
2.00
0.86
9.24
0.0
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)


168.23
156.15
141.79
134.22
133.06
130.71
130.61
129.56
129.33
129.30
127.91
126.78
124.03
109.65
81.66
81.19
70.74
55.59
55.57
27.80
19.29
OMe
COO^{t}Bu
2a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

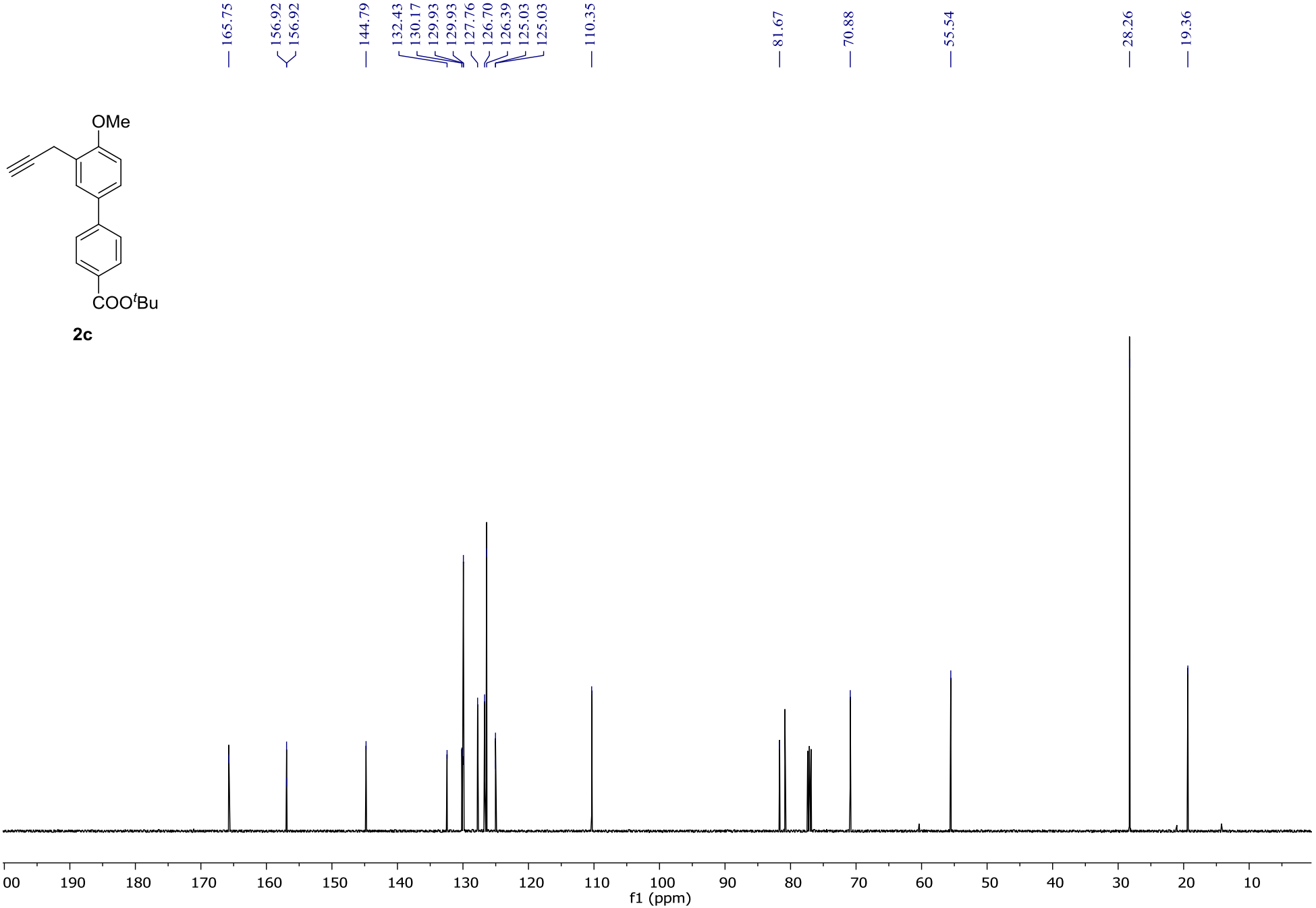

8.25
7.97
7.96
7.82
7.82
7.78
7.77
7.76
7.76
7.54
7.54
7.52
7.52
7.51
7.50
7.48
6.97
6.95
3.91
3.68
3.67
2.25
2.24
2.24
1.66
OMe
COO^{t}Bu
2b
1.00
1.02
0.97
0.99
0.98
0.97
0.97
2.91
1.93
0.94
9.38
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

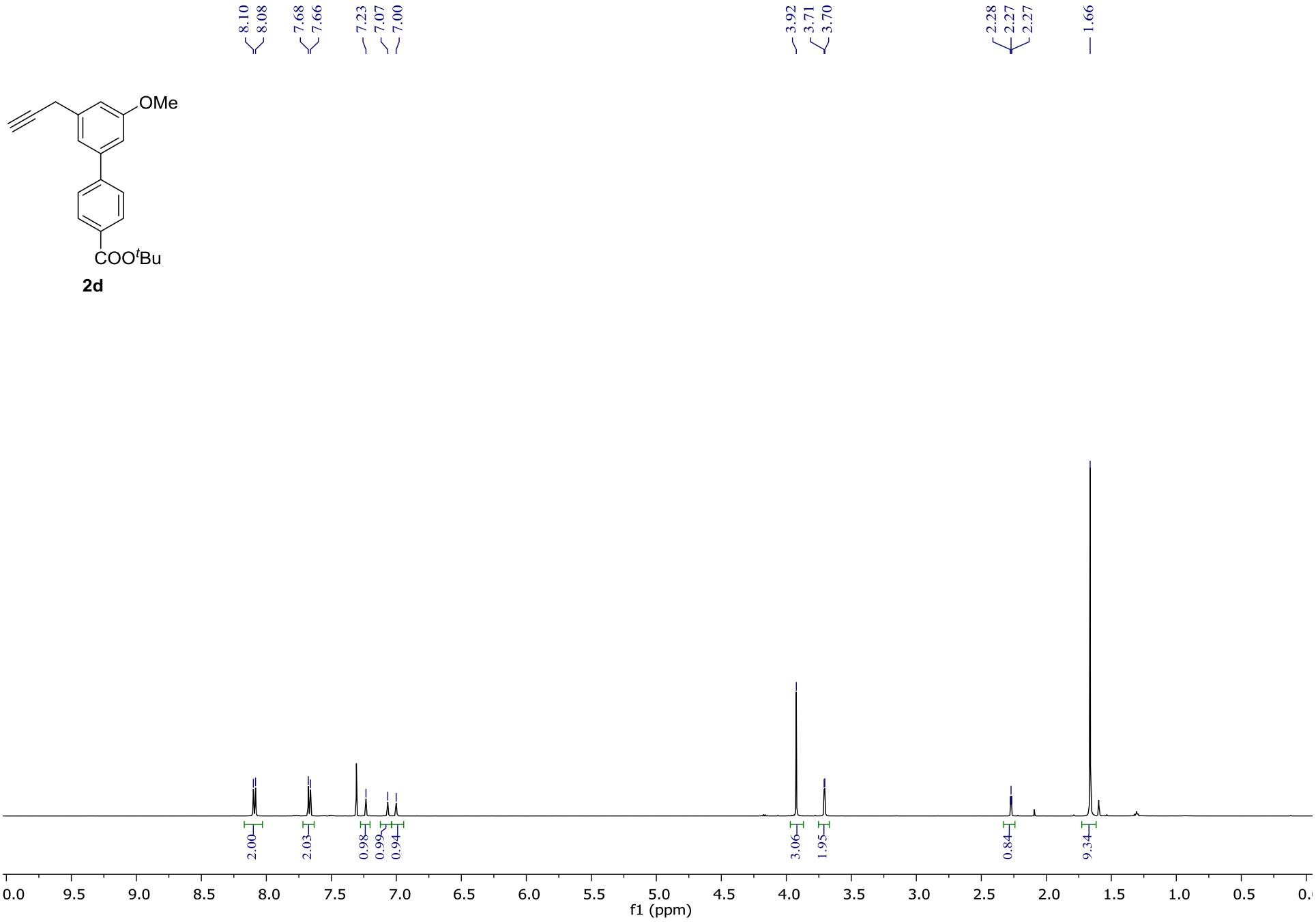

165.85
156.60
140.94
132.72
132.49
130.73
130.72
130.70
128.60
127.76
127.73
127.71
127.64
127.61
126.57
124.99
110.36
81.76
81.07
70.66
55.59
28.23
19.34
OMe
COO^{t}Bu
2b
f1 (ppm)

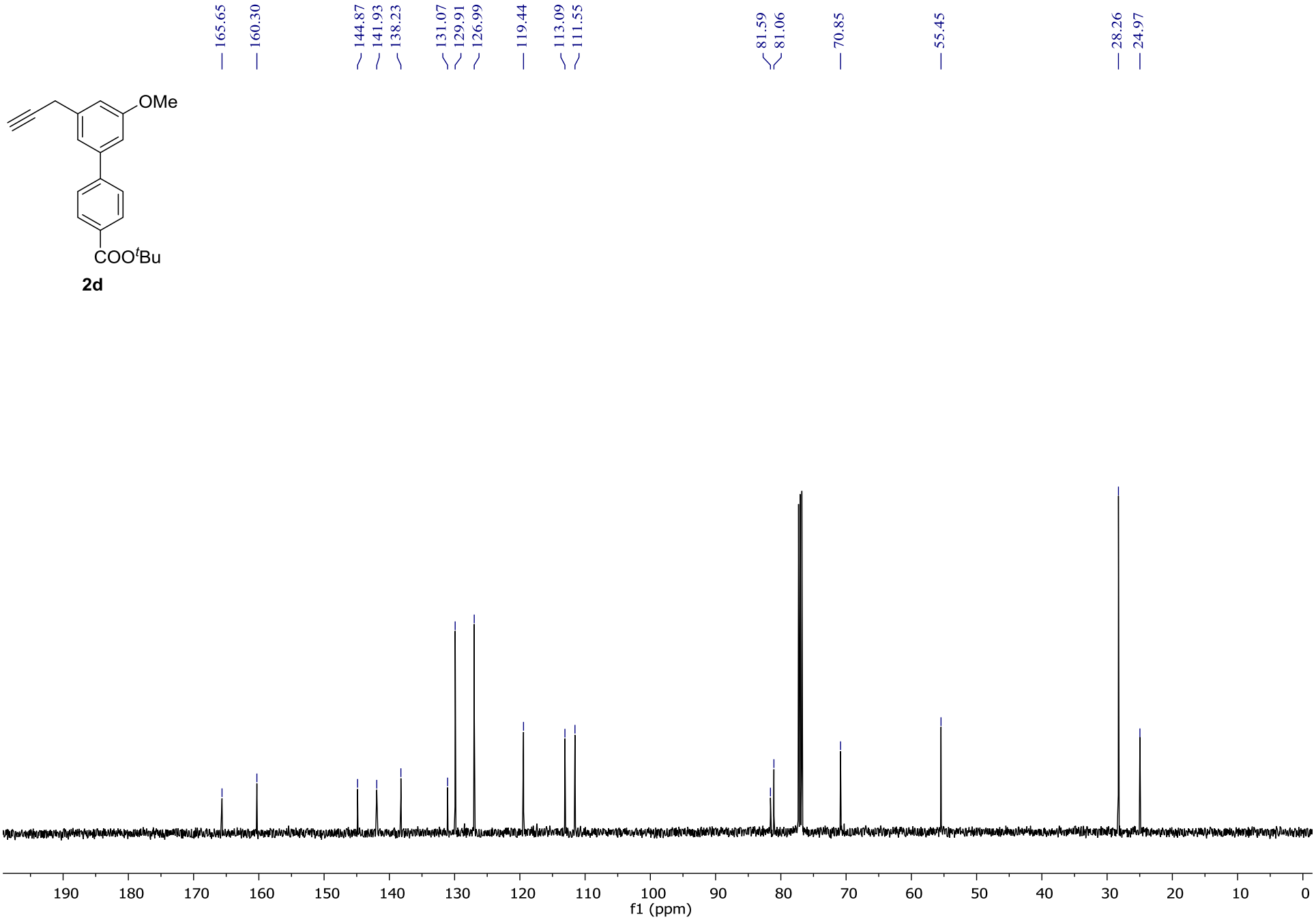

OMe
COO^{t}Bu

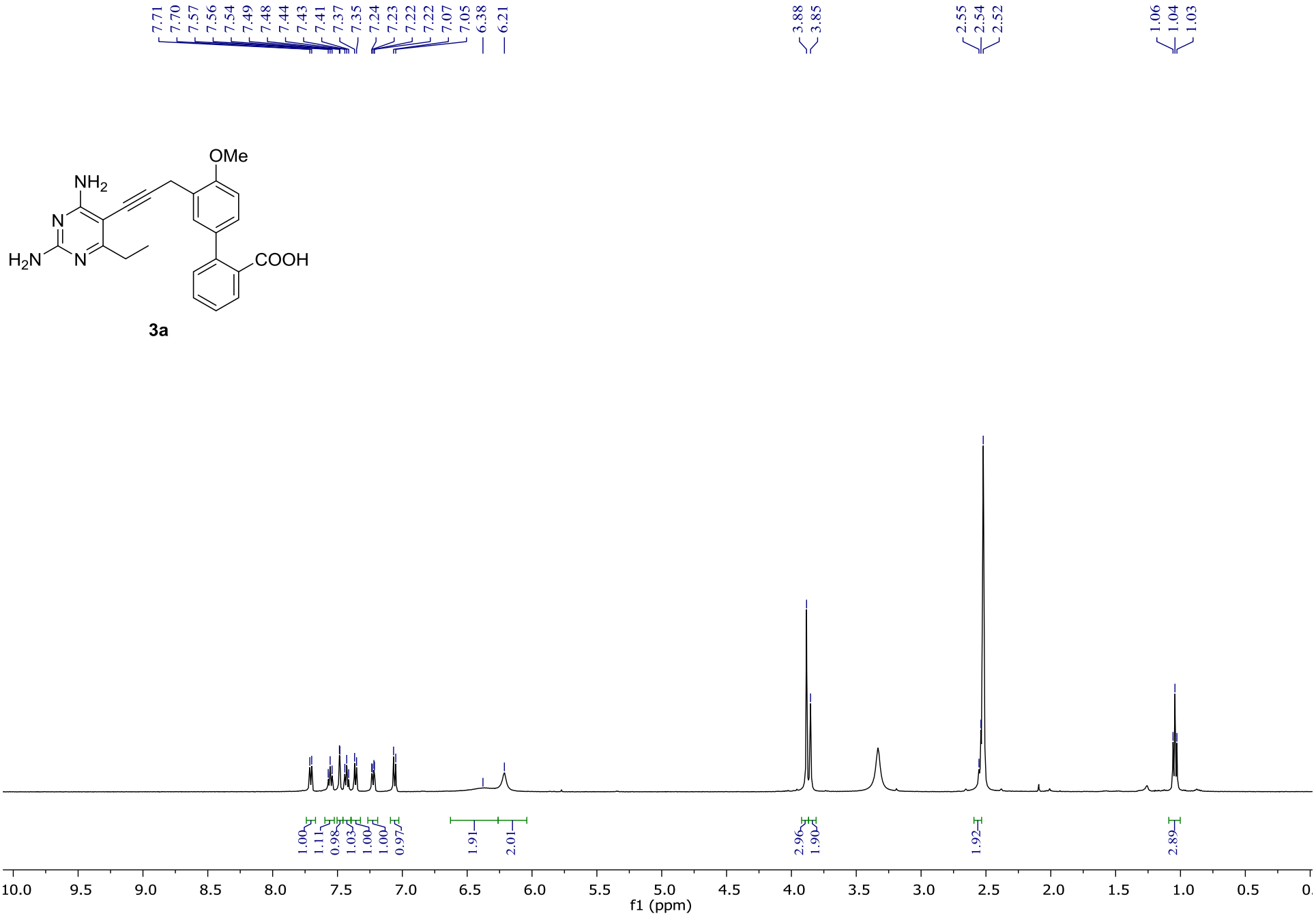
2c

8.09
8.08
7.85
7.85
7.67
7.65
7.53
7.53
7.51
7.51
6.94
6.92
3.89
3.67
3.67
2.28
2.27
2.27
1.66
2.00
1.01
2.12
1.06
1.05
3.13
2.03
0.66
9.69
0.0
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
f1 (ppm)

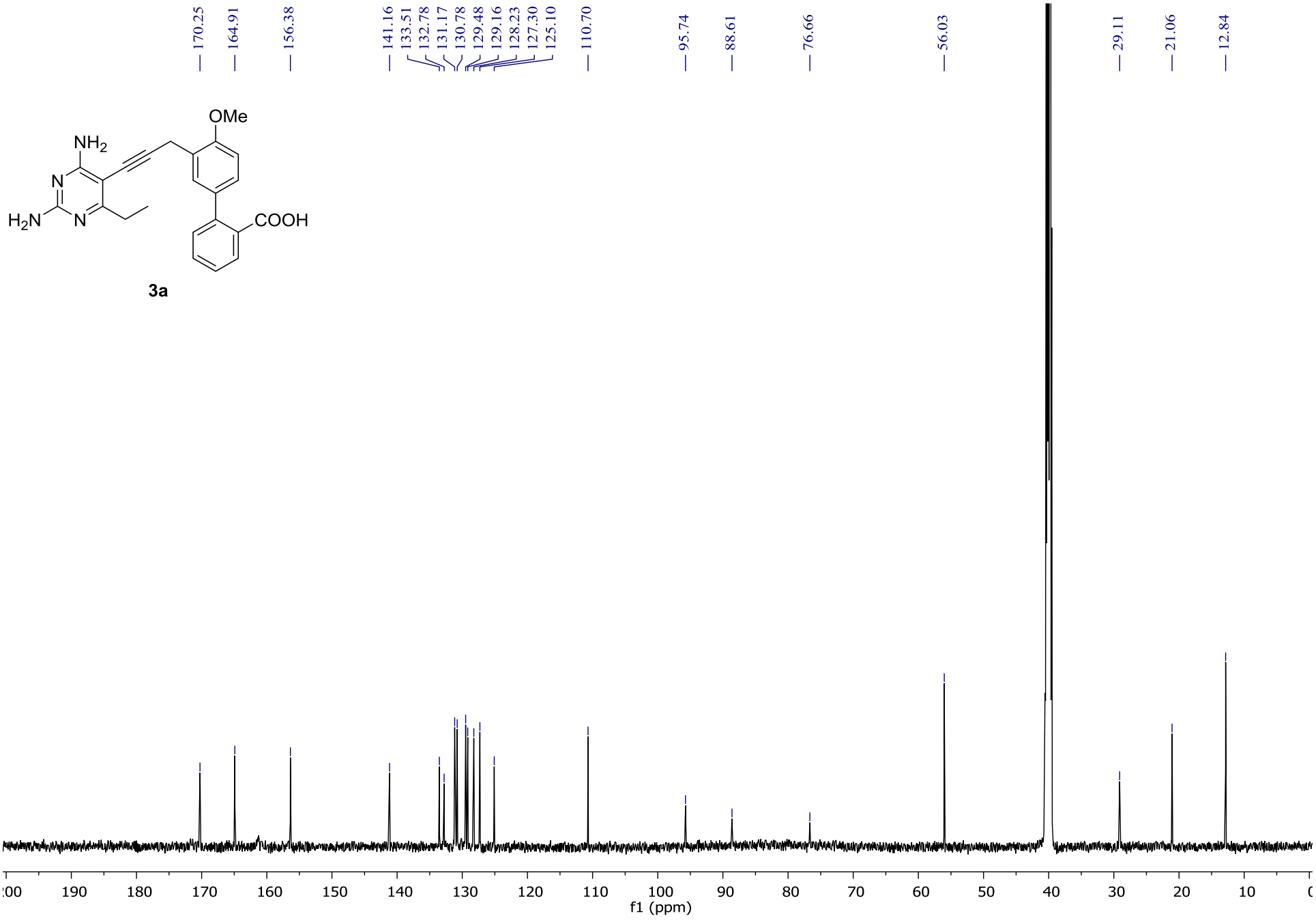

165.75
156.92
156.92
144.79
132.43
130.17
129.93
129.93
127.76
126.70
126.39
125.03
125.03
110.35
81.67
70.88
55.54
28.26
19.36
OMe
COO^{t}Bu
2c
f1 (ppm)

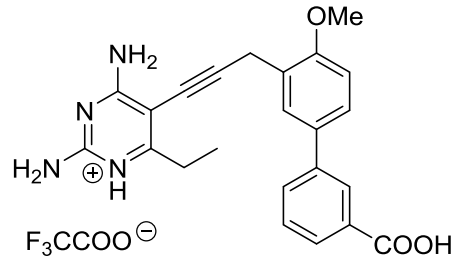

8.10
8.08
7.68
7.66
7.23
7.07
7.00
3.92
3.71
3.70
2.28
2.27
2.27
1.66
OMe
COO^{t}Bu
2d
2.00
2.03
0.98
0.99
0.94
3.06
1.95
0.84
9.34
f1 (ppm)


165.65
160.30
144.87
141.93
138.23
131.07
129.91
126.99
119.44
113.09
111.55
81.59
81.06
70.85
55.45
28.26
24.97
OMe
COO'Bu
2d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.71
7.70
7.57
7.56
7.54
7.49
7.48
7.44
7.43
7.41
7.37
7.35
7.24
7.23
7.22
7.22
7.07
7.05
6.38
6.21
3.88
3.85
2.55
2.54
2.52
1.06
1.04
1.03
OMe
NH2
N
H2N
N
COOH
1.00
1.11
0.98
1.03
1.00
1.00
0.97
1.91
2.01
2.96
1.90
1.92
2.89
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
f1 (ppm)

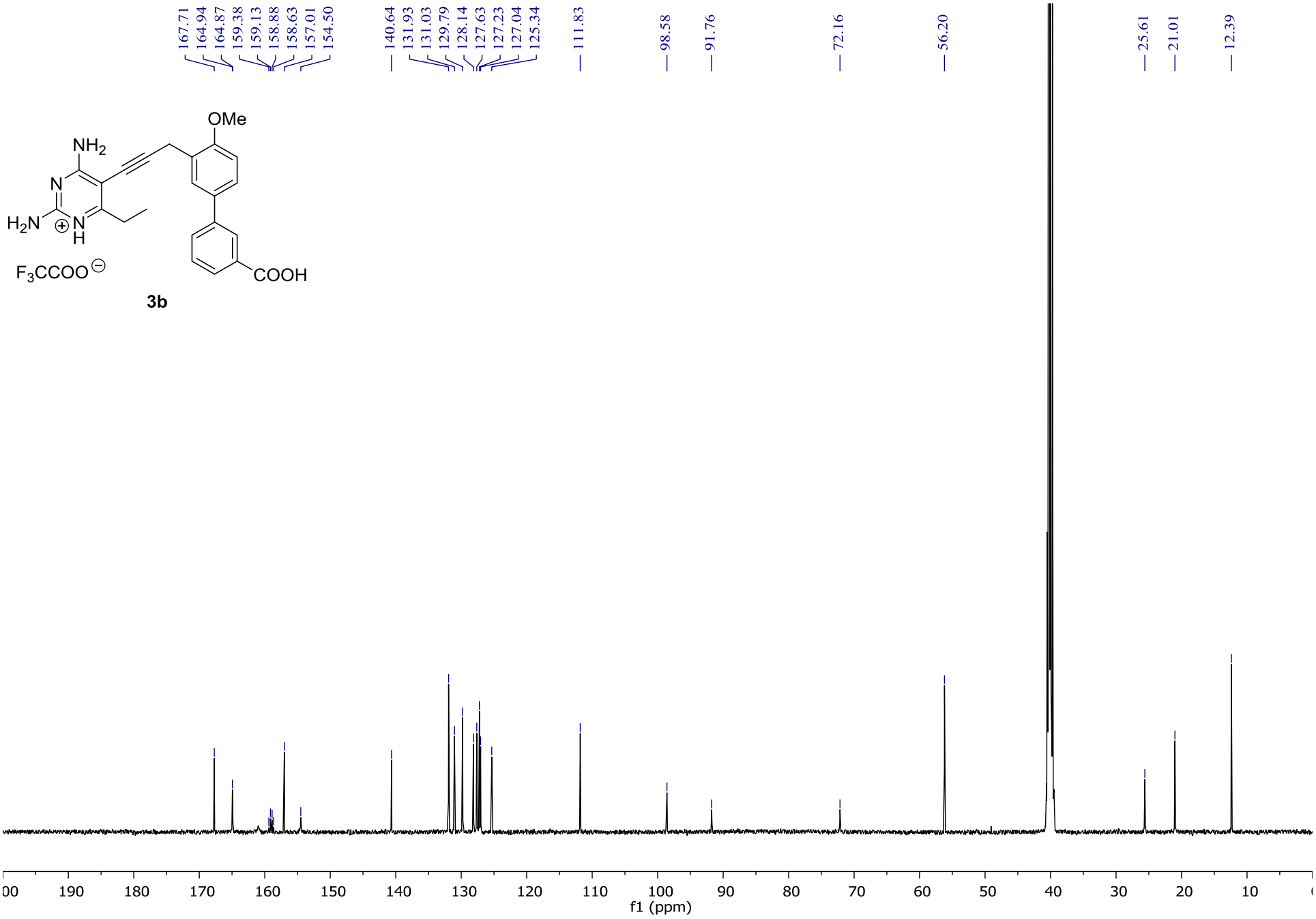
3a

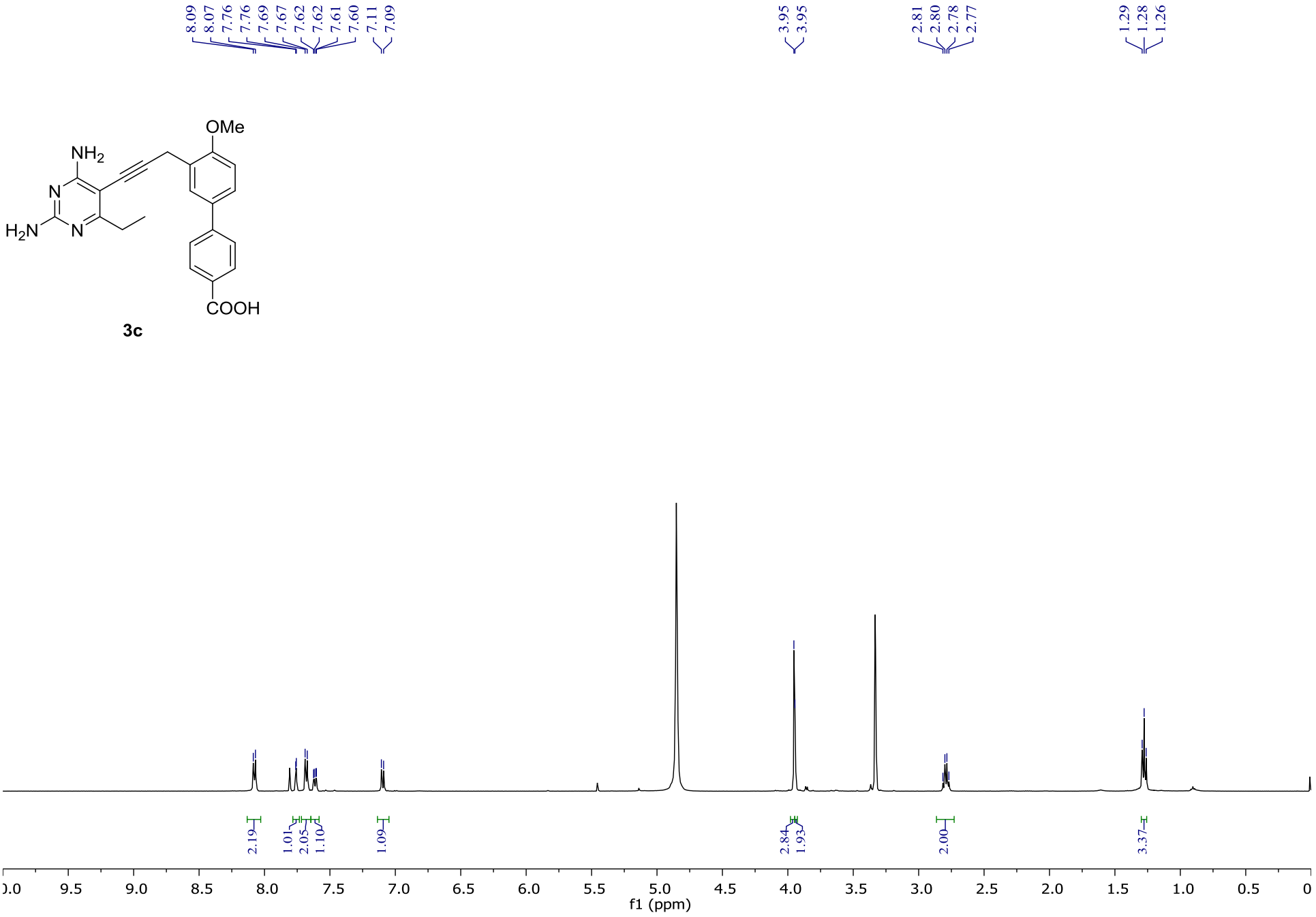

170.25
164.91
156.38
141.16
133.51
132.78
131.17
130.78
129.48
129.16
128.23
127.30
125.10
110.70
95.74
88.61
76.66
56.03
29.11
21.06
12.84
OMe
NH2
N
H2N
N
COOH
3a
f1 (ppm)


OMe
NH2
N
H2N
N
H
F3CCOO
COOH

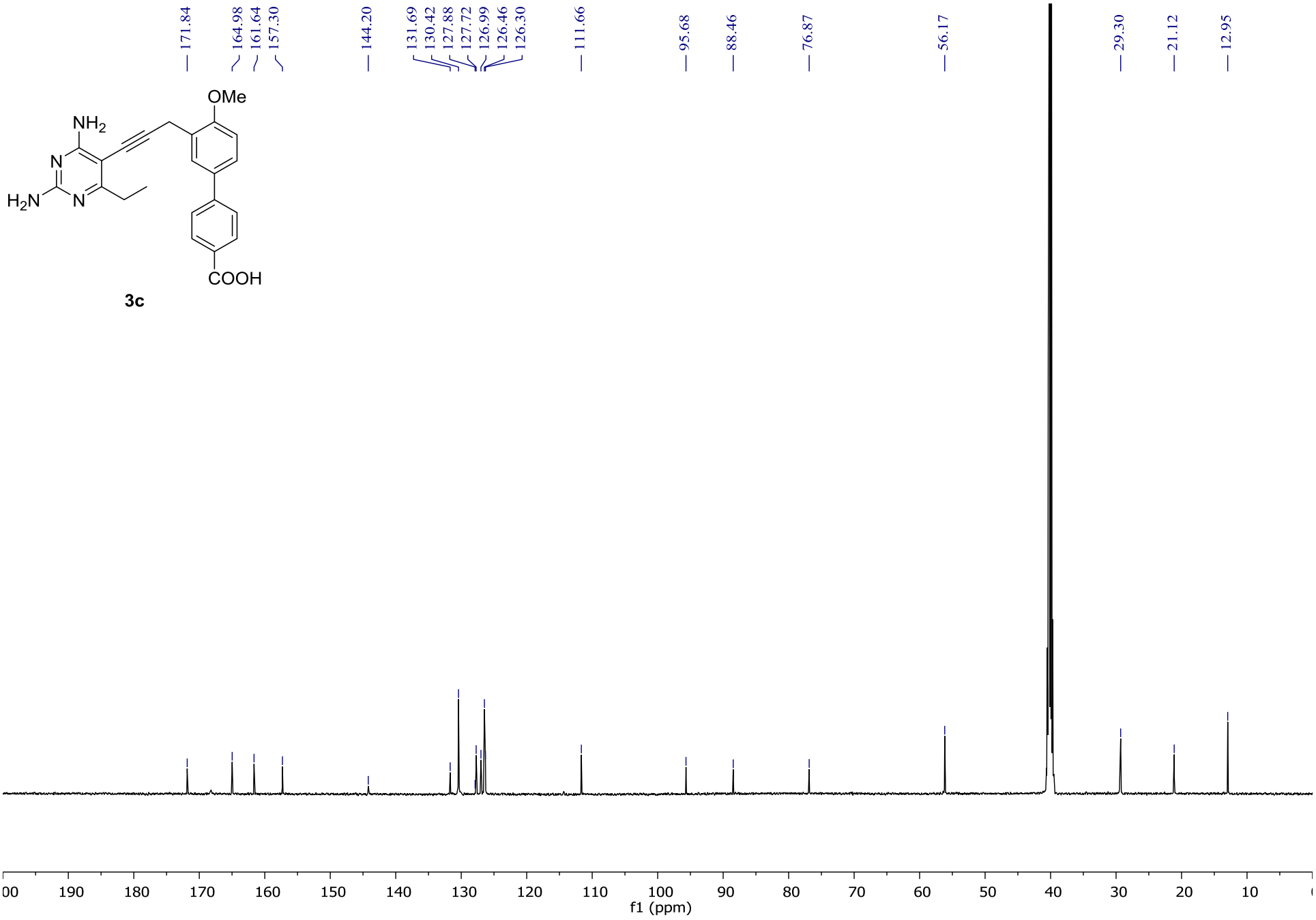
3b

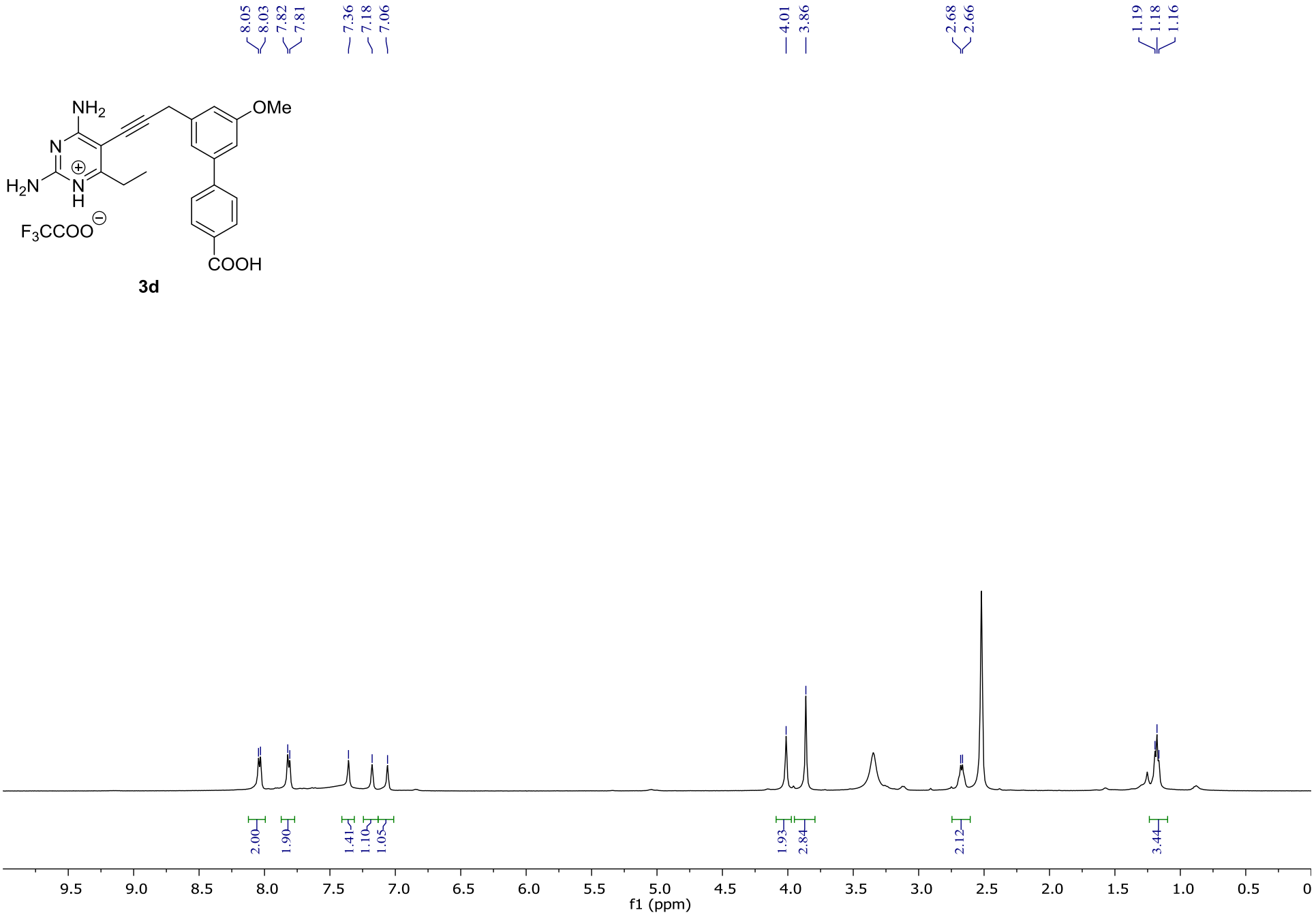
8.48
8.16
7.92
7.91
7.89
7.87
7.76
7.76
7.66
7.65
7.64
7.64
7.61
7.59
7.58
3.93
3.91
2.73
2.72
2.70
2.68
1.20
1.18
1.17
0.65
1.00
0.97
1.07
1.17
1.05
1.17
1.29
1.06
1.87
3.07
1.94
3.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

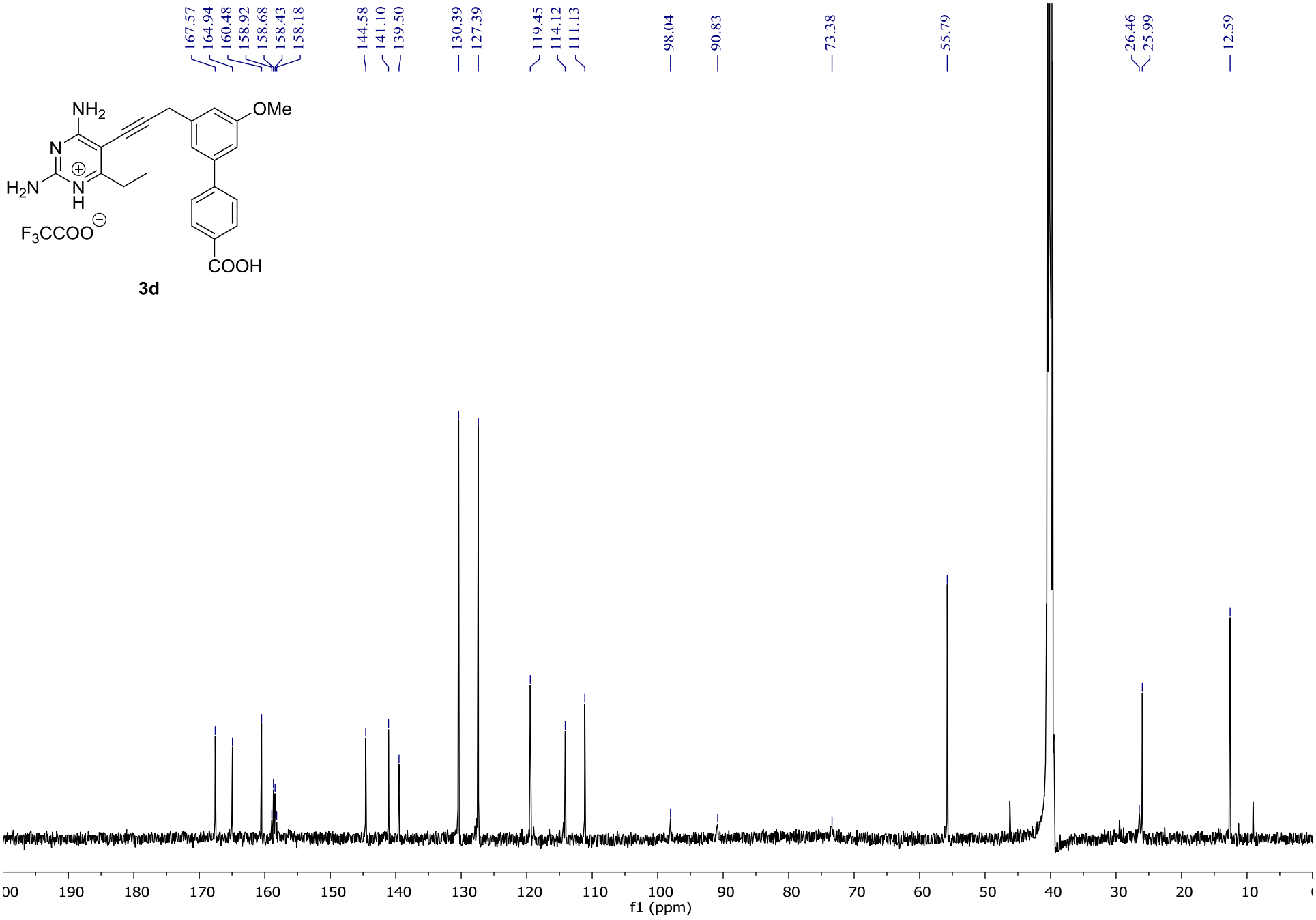

167.71
164.94
164.87
159.38
159.13
158.88
158.63
157.01
154.50
140.64
131.93
131.03
129.79
128.14
127.63
127.23
127.04
125.34
111.83
98.58
91.76
72.16
56.20
25.61
21.01
12.39
OMe
NH2
N
H2N
N
H
F3CCOO
COOH
3b
f1 (ppm)


8.09
8.07
7.76
7.76
7.69
7.67
7.62
7.62
7.61
7.60
7.11
7.09
3.95
3.95
2.81
2.80
2.78
2.77
1.29
1.28
1.26
OMe
NH2
N
H2N
N
COOH
2.19
1.01
2.05
1.10
1.09
2.84
1.93
2.00
3.37
f1 (ppm)

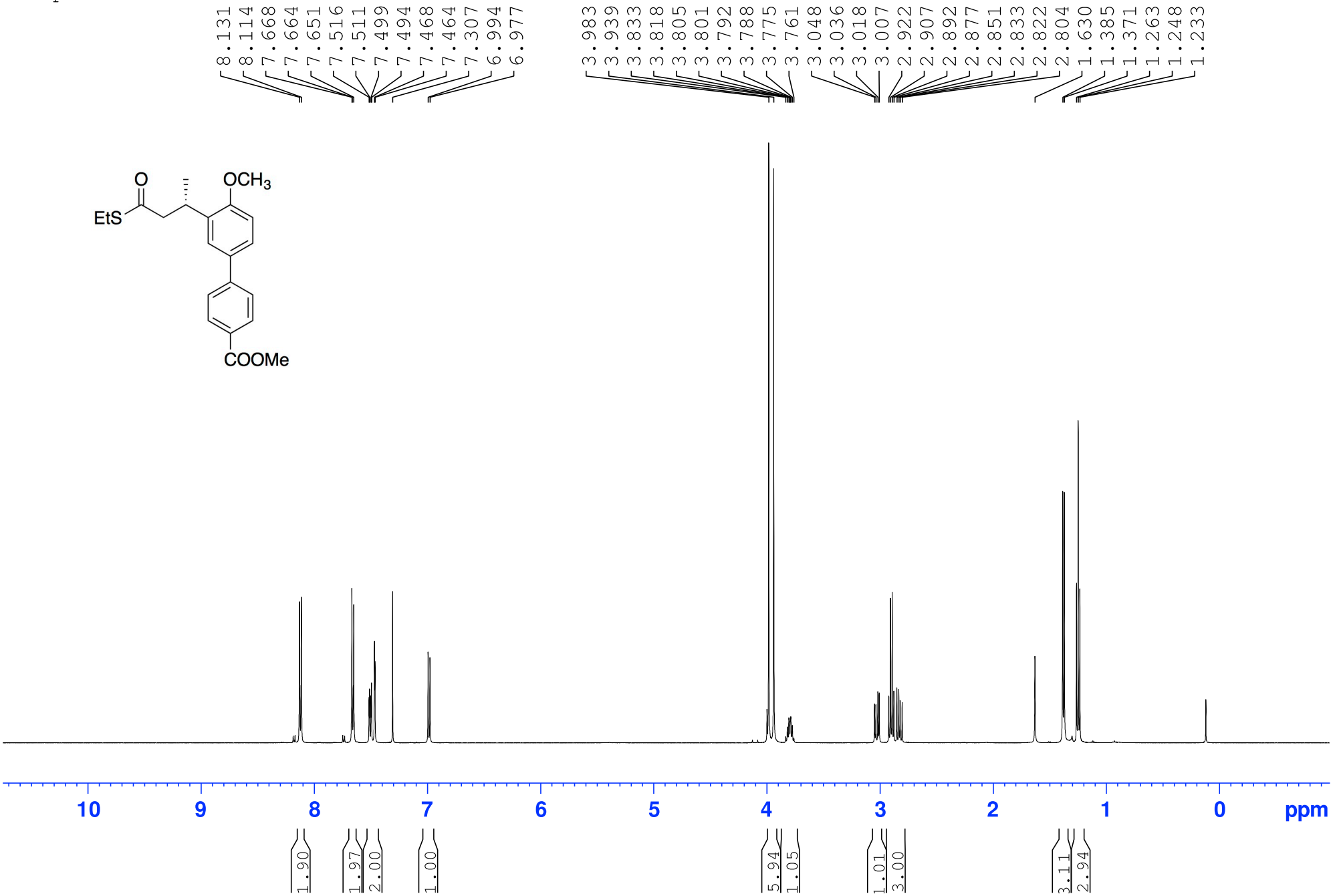
3c


171.84
164.98
161.64
157.30
144.20
131.69
130.42
127.88
127.72
126.99
126.46
126.30
111.66
95.68
88.46
76.87
56.17
29.30
21.12
12.95
OMe
NH2
N
H2N
N
COOH
3c
f1 (ppm)


8.05
8.03
7.82
7.81
7.36
7.18
7.06
4.01
3.86
2.68
2.66
1.19
1.18
1.16
NH2
OMe
N
H2N
N
H
F3CCOO
COOH
3d
2.00
1.90
1.41
1.10
1.05
1.93
2.84
2.12
3.44
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
f1 (ppm)

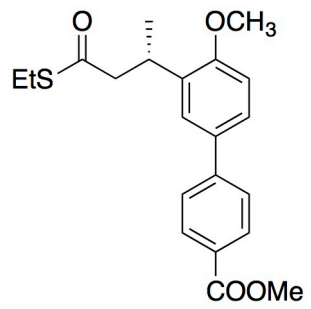

167.57
164.94
160.48
158.92
158.68
158.43
158.18
144.58
141.10
139.50
130.39
127.39
119.45
114.12
111.13
98.04
90.83
73.38
55.79
26.46
25.99
12.59
NH2
OMe
N
H2N
N
H
F3CCOO
COOH
3d
f1 (ppm)

1H spectrum


8.131
8.114
7.668
7.664
7.651
7.516
7.511
7.499
7.494
7.468
7.464
7.307
6.994
6.977
3.983
3.939
3.833
3.818
3.805
3.801
3.792
3.788
3.775
3.761
3.048
3.036
3.018
3.007
2.922
2.907
2.892
2.877
2.851
2.833
2.822
2.804
1.630
1.385
1.371
1.263
1.248
1.233
O
OCH3
EtS
COOMe
10
9
8
7
6
5
4
3
2
1
0
ppm
1.90
1.97
2.00
1.00
5.94
1.05
1.01
3.00
3.11
2.94

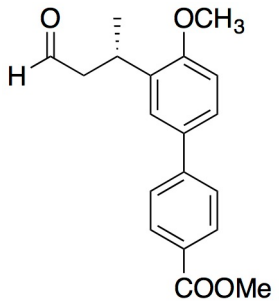
1D 13C spectrum
Probe: 5 mm PABBO BB-1H/D Z-GRD Z113652/0192

198.595
167.118
157.295
145.518
134.005
132.256
130.102
128.235
126.562
126.228
126.186
111.005
55.557
52.089
50.492
31.234
23.319
19.755
14.796

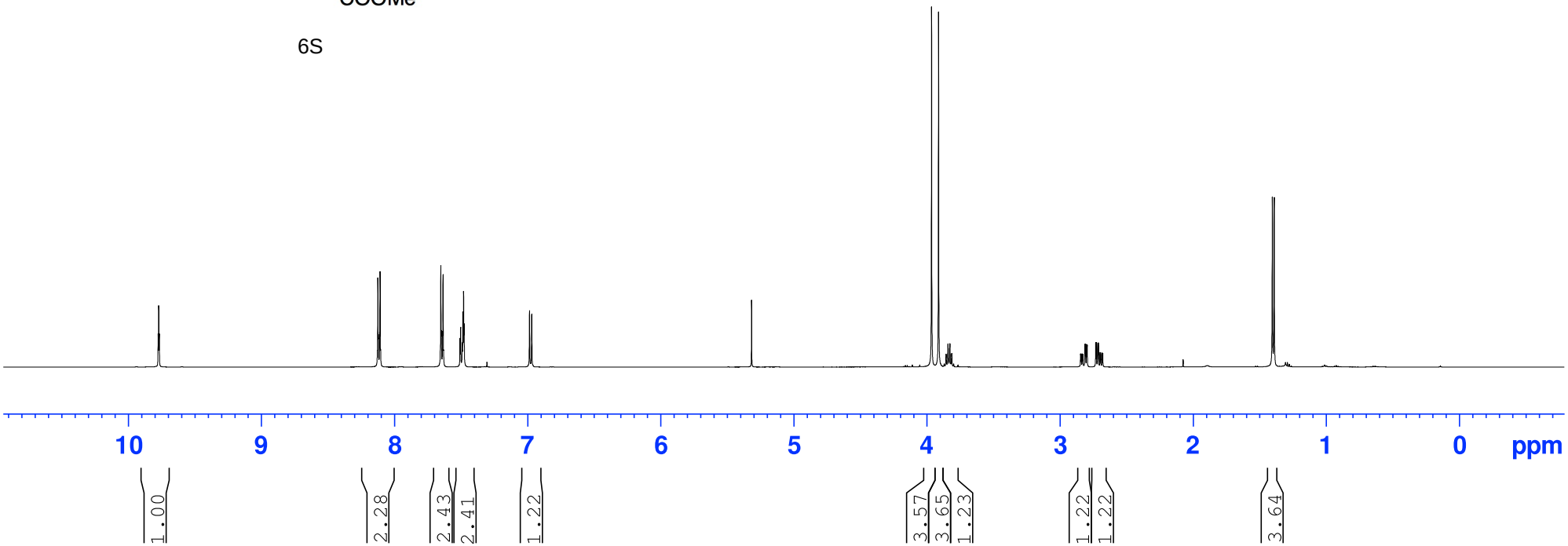


1H spectrum

9.772
8.126
8.122
8.112
8.109
8.105
7.656
7.652
7.649
7.639
7.635
7.632
7.508
7.504
7.492
7.487
7.482
7.477
6.986
6.969
3.965
3.913
3.856
3.842
3.828
3.813
2.846
2.841
2.833
2.829
2.813
2.809
2.800
2.796
2.732
2.727
2.716
2.711
2.699
2.694
2.684
2.679
1.405
1.391

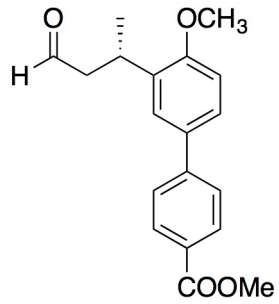


6S



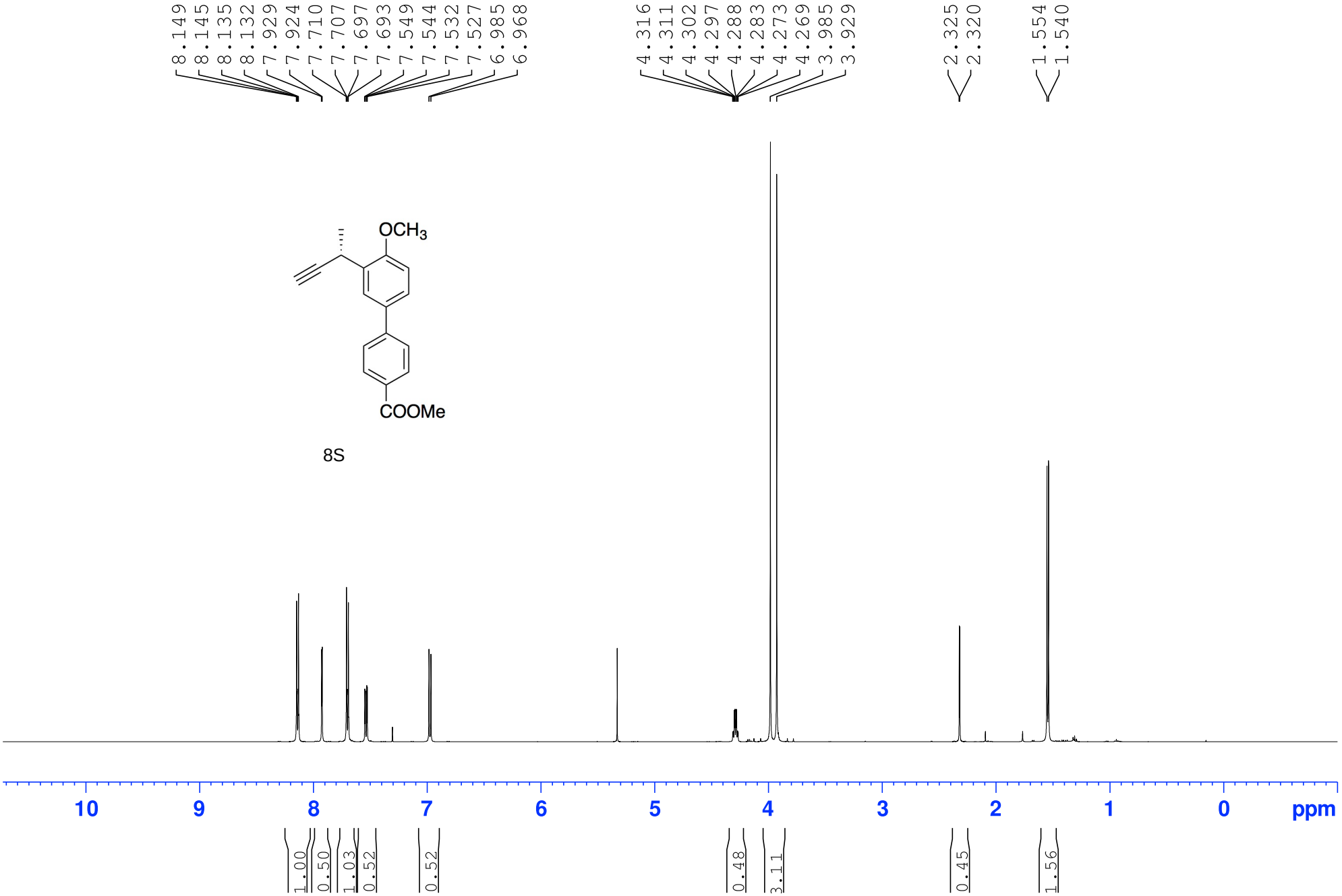
1D 13C spectrum
Probe: 5 mm PABBO BB-1H/D Z-GRD Z113652/0192

202.265
167.041
157.063
145.398
133.956
132.453
130.119
128.319
126.560
126.350
125.999
111.026
55.487
52.065
50.588
28.077
20.351



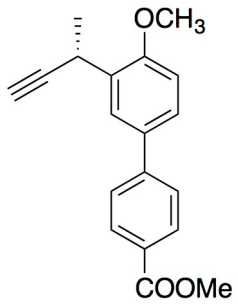
6S

1H spectrum


8.149
8.145
8.135
8.132
7.929
7.924
7.710
7.707
7.697
7.693
7.549
7.544
7.532
7.527
6.985
6.968
4.316
4.311
4.302
4.297
4.288
4.283
4.273
4.269
3.985
3.929
2.325
2.320
1.554
1.540
OCH3
COOMe
8S
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.50
1.03
0.52
0.52
0.48
3.11
0.45
1.56

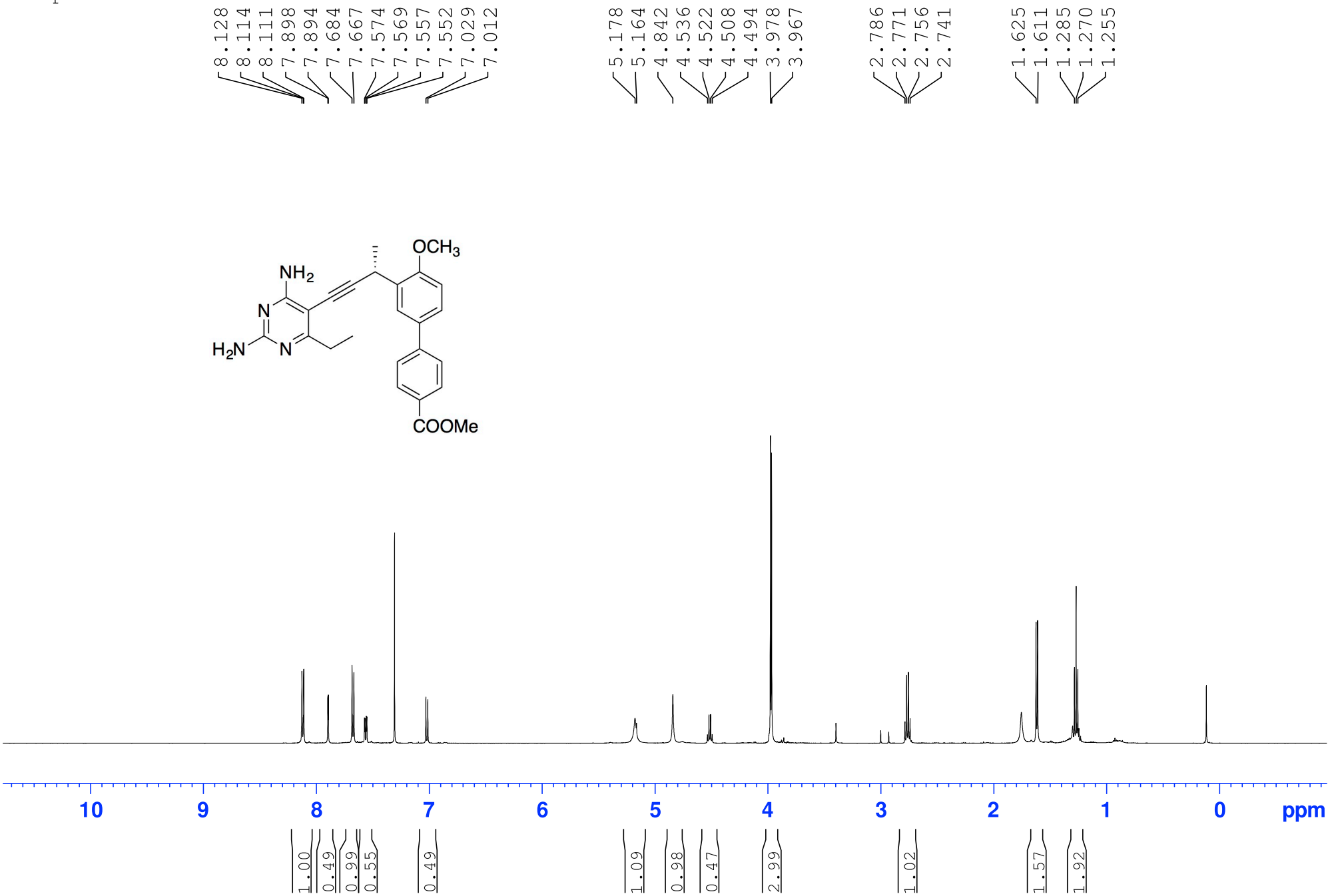
1D 13C spectrum
Probe: 5 mm PABBO BB-1H/D Z-GRD Z113652/0192

167.095
156.361
145.391
132.438
131.559
130.120
128.291
126.713
126.587
110.844
87.291
77.368
77.114
76.859
69.890
55.611
52.076
25.563
22.749

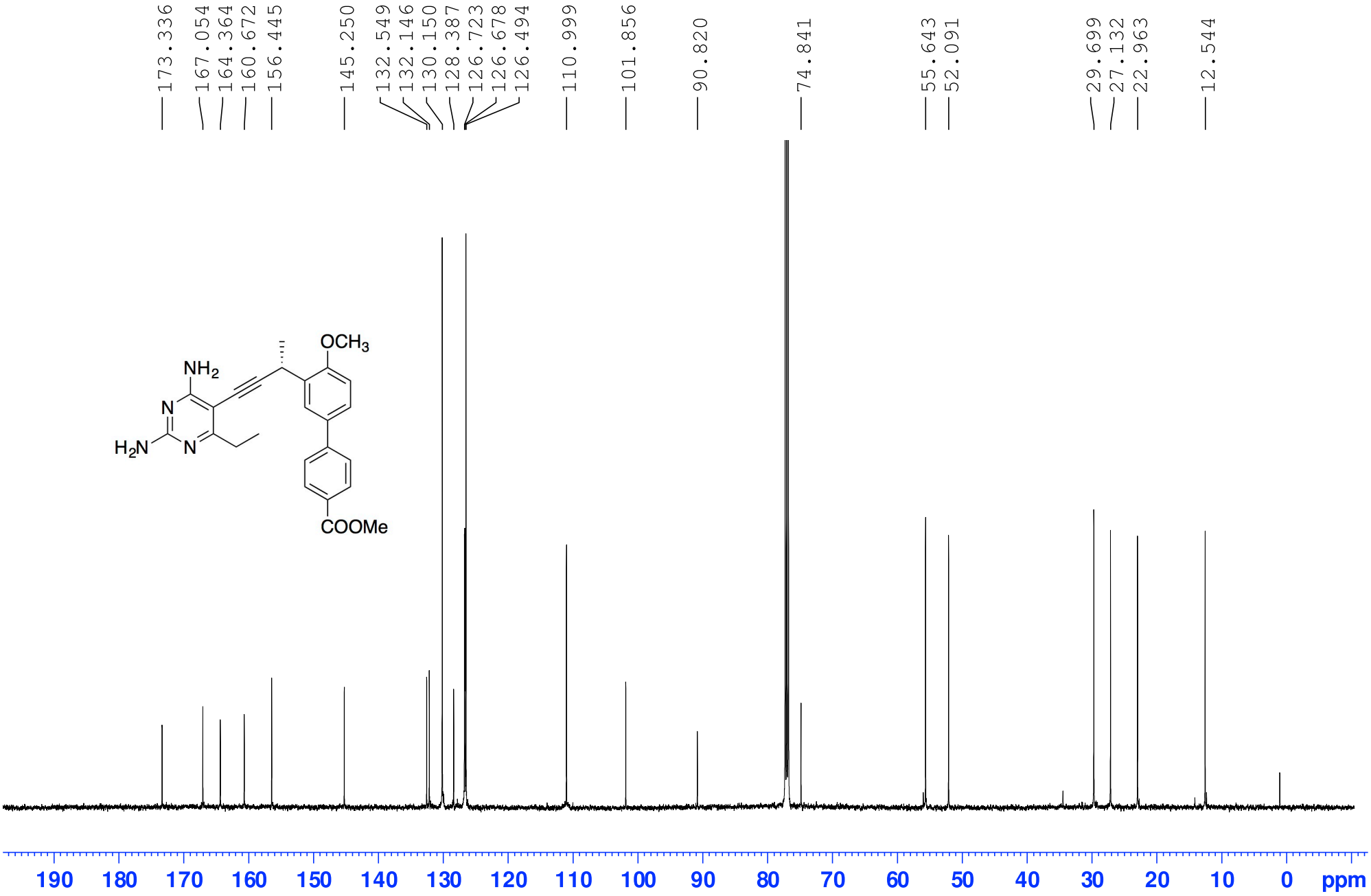


8S

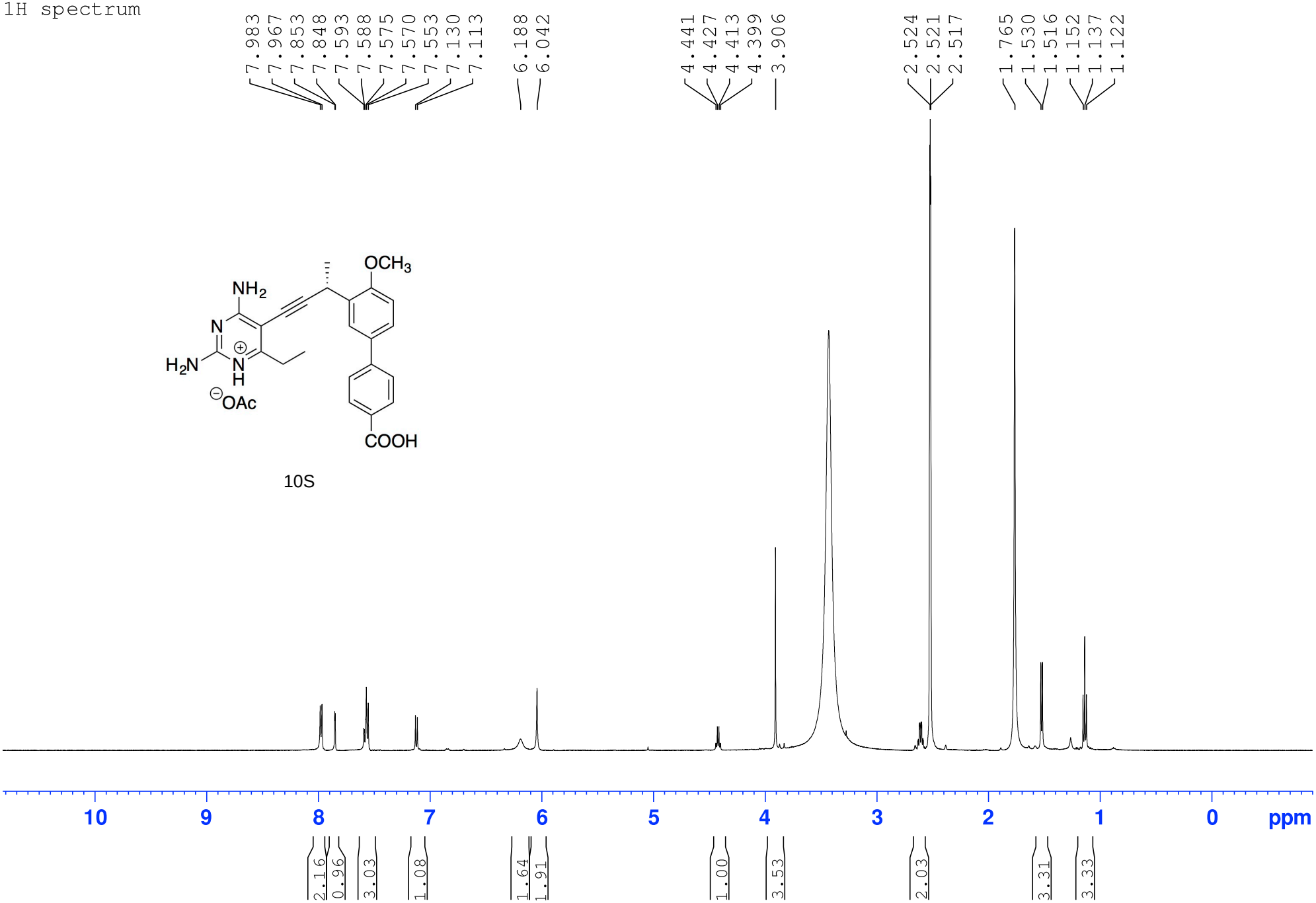
1H spectrum


8.128
8.114
8.111
7.898
7.894
7.684
7.667
7.574
7.569
7.557
7.552
7.029
7.012
5.178
5.164
4.842
4.536
4.522
4.508
4.494
3.978
3.967
2.786
2.771
2.756
2.741
1.625
1.611
1.285
1.270
1.255
OCH3
NH2
N
H2N
N
COOMe
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.49
0.99
0.55
0.49
1.09
0.98
0.47
2.99
1.02
1.57
1.92

1D 13C spectrum
Probe: 5 mm PABBO BB-1H/D Z-GRD Z113652/0192



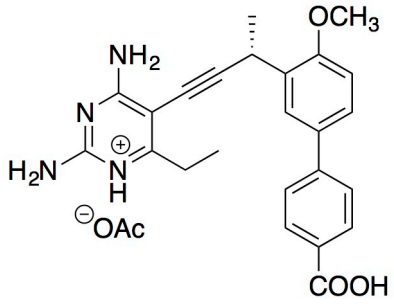
1H spectrum



10S

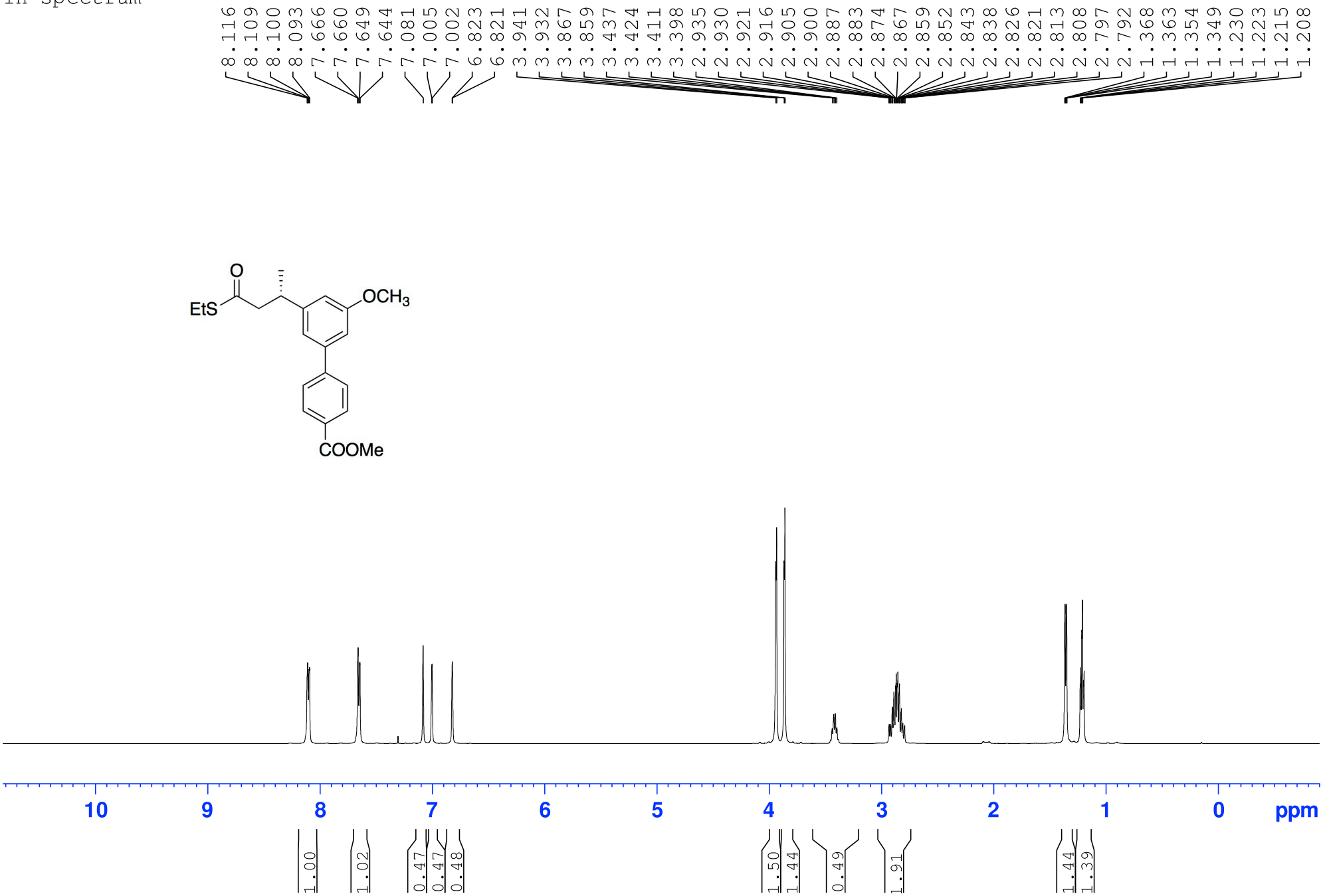
1D 13C spectrum
Probe: 5 mm PABBO BB-1H/D Z-GRD Z113652/0192

176.631
172.063
164.805
161.699
156.091
141.273
133.015
132.254
130.256
126.604
126.360
125.492
112.120
101.189
88.576
75.964
56.247
29.346
27.150
24.189
23.399
12.768

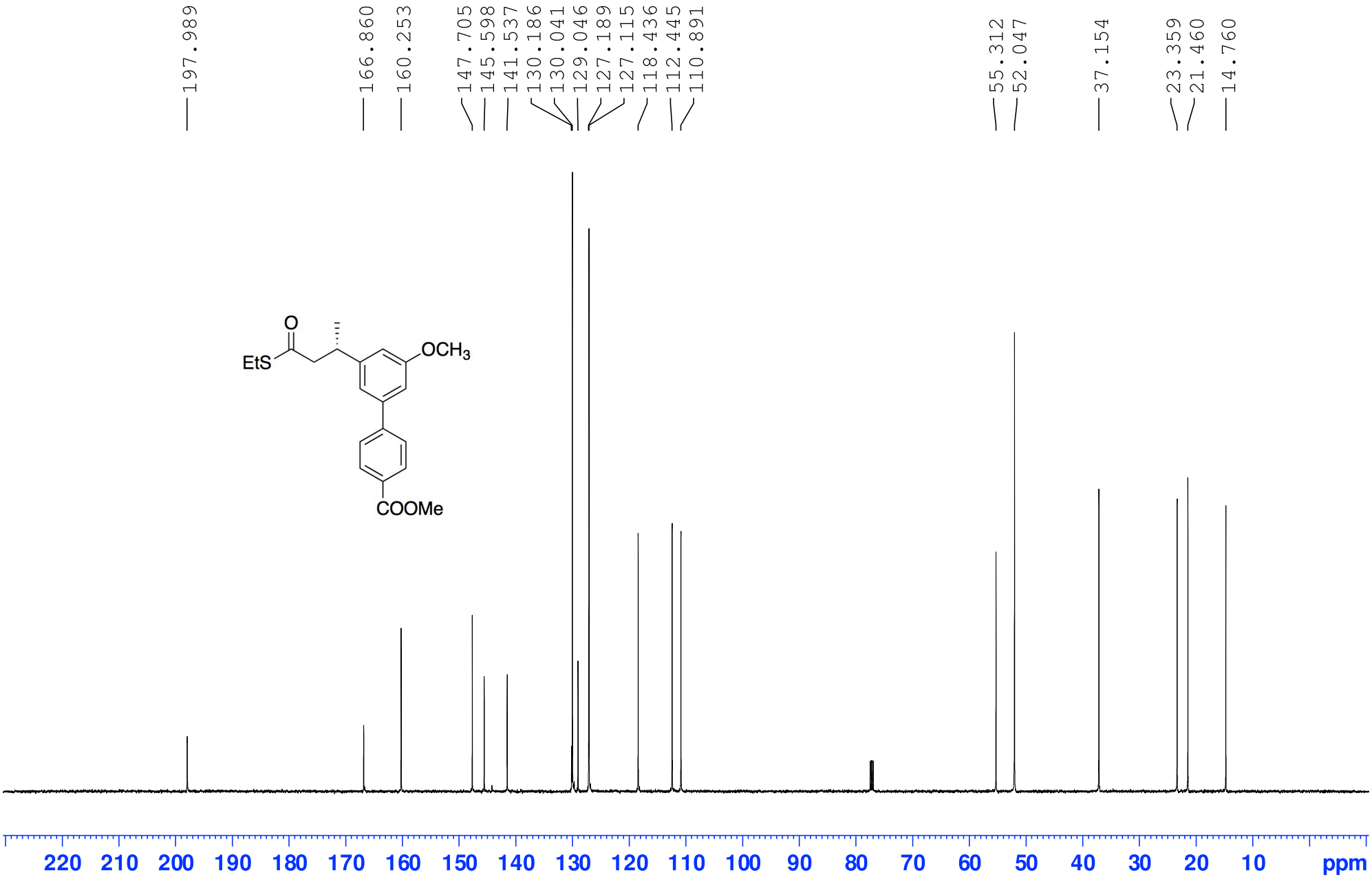


10S

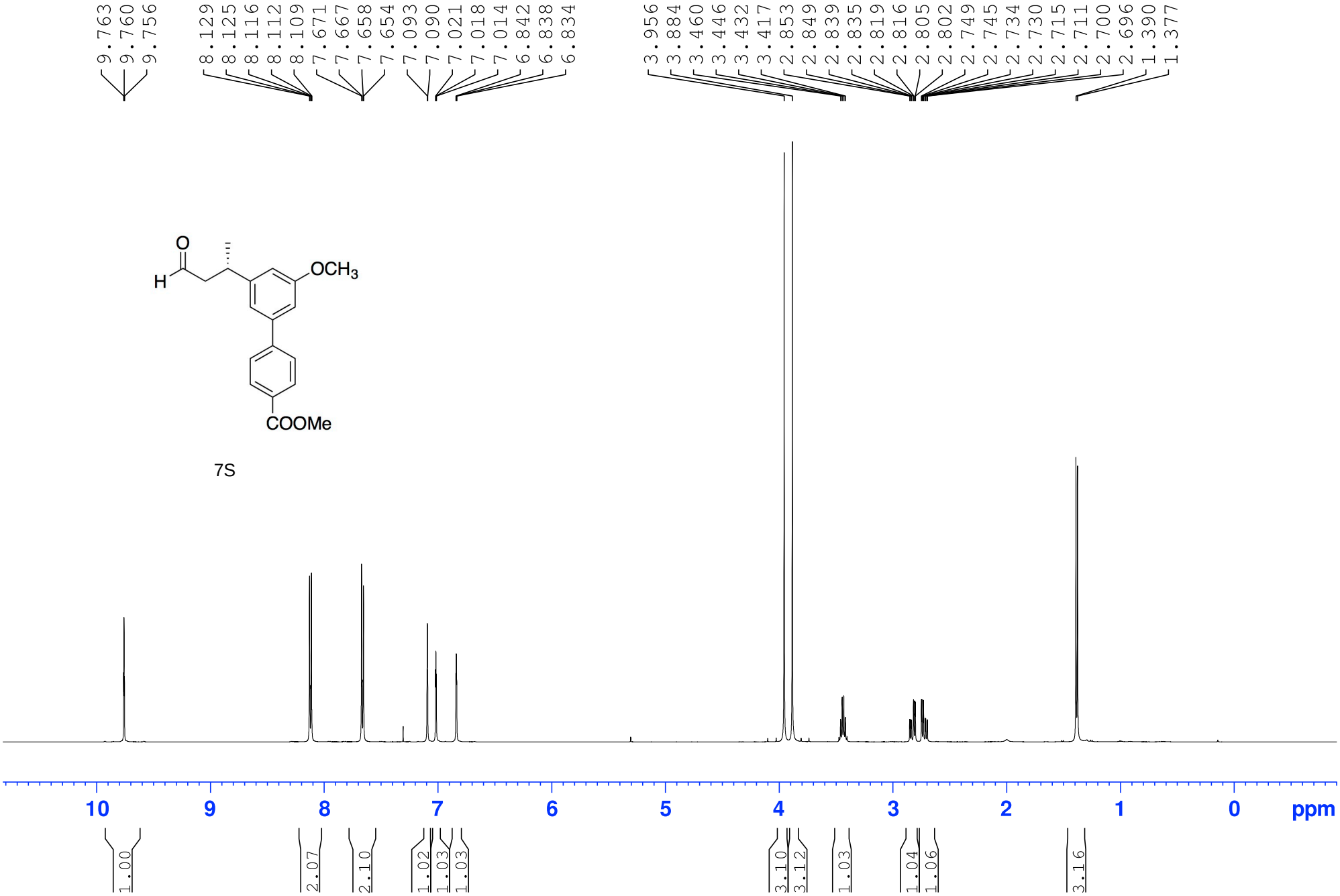
1H spectrum


8.116
8.109
8.100
8.093
7.666
7.660
7.649
7.644
7.081
7.005
7.002
6.823
6.821
3.941
3.932
3.867
3.859
3.437
3.424
3.411
3.398
2.935
2.930
2.921
2.916
2.905
2.900
2.887
2.883
2.874
2.867
2.859
2.852
2.843
2.838
2.826
2.821
2.813
2.808
2.797
2.792
1.368
1.363
1.354
1.349
1.230
1.223
1.215
1.208
O
EtS
OCH3
COOMe
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.02
0.47
0.47
0.48
1.50
1.44
0.49
1.91
1.44
1.39

1D 13C spectrum
Probe: 5 mm PABBO BB-1H/D Z-GRD Z113652/0192

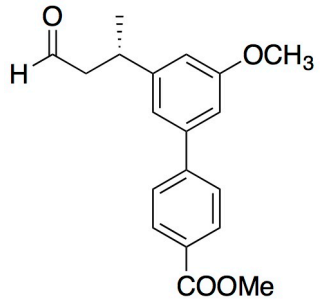


1H spectrum


9.763
9.760
9.756
8.129
8.125
8.116
8.112
8.109
7.671
7.667
7.658
7.654
7.093
7.090
7.021
7.018
7.014
6.842
6.838
6.834
3.956
3.884
3.460
3.446
3.432
3.417
2.853
2.849
2.839
2.835
2.819
2.816
2.805
2.802
2.749
2.745
2.734
2.730
2.715
2.711
2.700
2.696
1.390
1.377
O
H
OCH3
COOMe
7S
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
2.07
2.10
1.02
1.03
1.03
3.10
3.12
1.03
1.04
1.06
3.16

1D 13C spectrum
Probe: 5 mm PABBO BB-1H/D Z-GRD Z113652/0192

201.481
166.910
160.351
147.887
145.542
141.795
130.076
129.119
127.160
118.406
112.541
110.816
55.368
52.124
51.645
34.431
22.130



7S

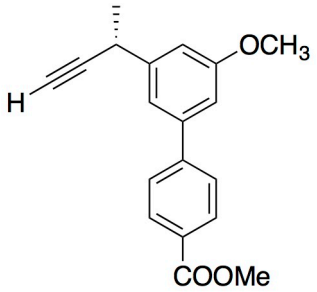
1H spectrum

8.155
8.151
8.142
8.138
8.135
7.708
7.705
7.695
7.691
7.688
7.277
7.274
7.073
7.069
7.065
7.053
7.050
7.046

3.985
3.922
3.912
3.887
3.883
3.873
3.868
3.859
3.854
3.845
3.840

2.365
2.360

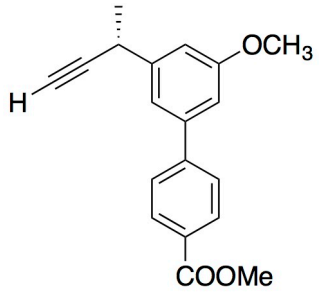
1.797
1.615
1.601



9R

1D 13C spectrum
Probe: 5 mm PABBO BB-1H/D Z-GRD Z113652/0192

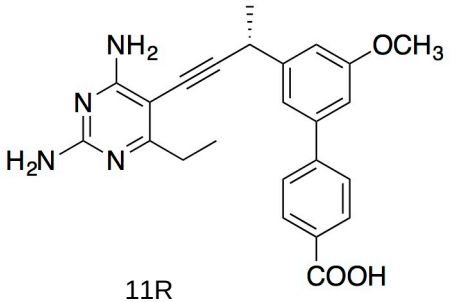
166.965
160.307
145.514
144.938
141.735
130.089
129.126
127.195
118.464
112.432
111.369
86.758
70.615
55.439
52.149
31.823
24.247



9R

1H spectrum

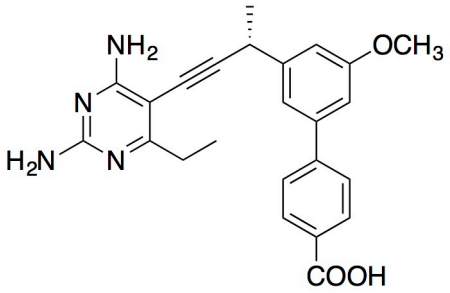
8.047
8.032
7.684
7.668
7.366
7.112
7.053
6.242
6.156
4.183
4.169
4.155
4.141
3.853
2.601
2.586
2.571
2.556
1.578
1.564
1.146
1.131
1.115



11R

1D 13C spectrum
Probe: 5 mm PABBO BB-1H/D Z-GRD Z113652/0192

172.140
164.704
161.701
160.387
146.382
141.945
130.265
126.466
118.253
112.456
110.860
100.924
88.266
76.613
55.694
32.801
29.378
25.074
12.907

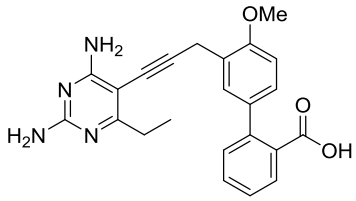


11R

==== Shimadzu LCsolution Analysis Report ====

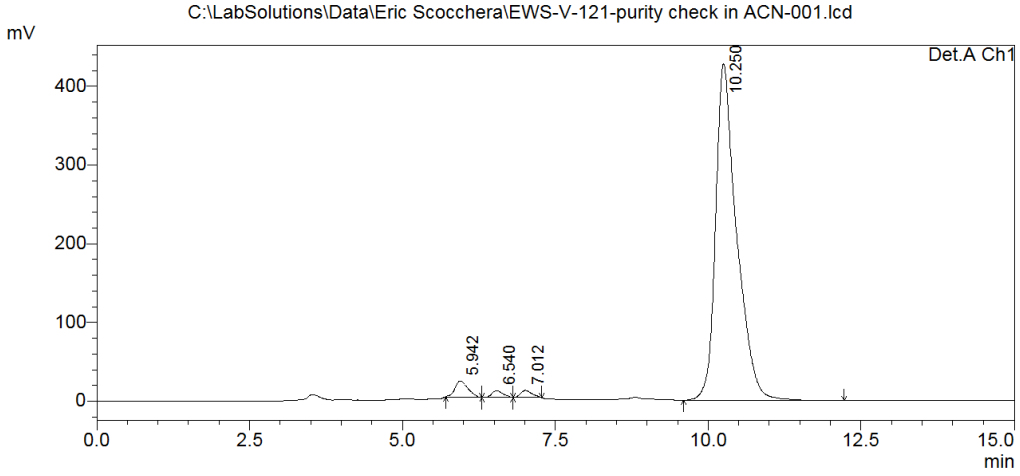
C:\LabSolutions\Data\Eric Scocchera\EWS-V-121-purity check in ACN-001.lcd

Acquired by	: Admin
Sample Name	: EWS-V-121 purity
Sample ID	: EWS-V-121 purity
Tray#	: 1
Vail #	: 10
Injection Volume	: 10 uL
Data File Name	: EWS-V-121-purity check in ACN-001.lcd
Method File Name	: 1106_DTZ.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 2/21/2016 8:07:07 AM
Data Processed	: 2/26/2016 1:40:33 PM



3a

<Chromatogram>



PeakTable

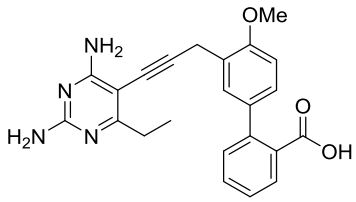
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.942	304835	20664	2.827	4.442
2	6.540	109298	8562	1.014	1.841
3	7.012	114365	8850	1.061	1.903
4	10.250	10252632	427101	95.098	91.815
Total		10781130	465177	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Eric Scocchera\EWS-V-121-purity check in MeOH-001.lcd

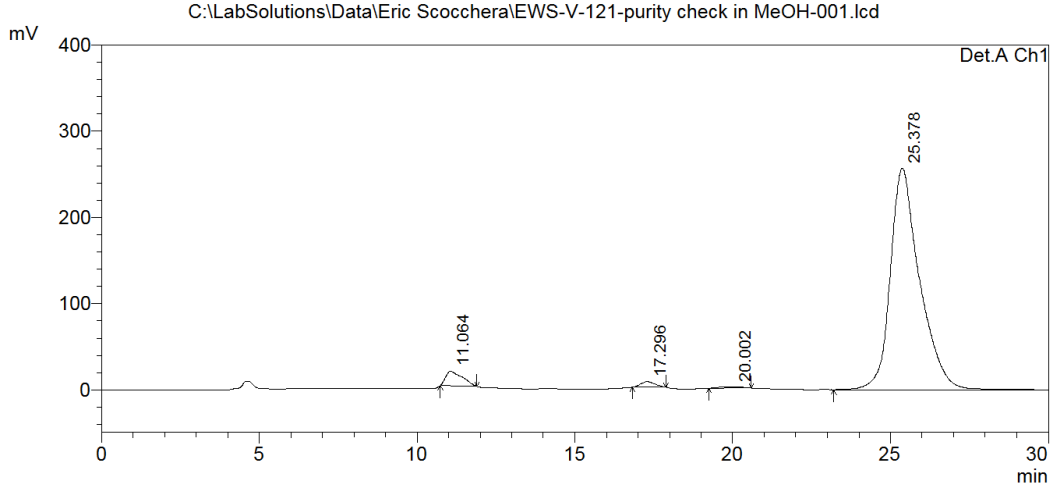
Acquired by	: Admin
Sample Name	: EWS-V-121 purity in MeOH
Sample ID	: EWS-V-121 purity in MeOH
Tray#	: 1
Vail #	: 10
Injection Volume	: 10 uL
Data File Name	: EWS-V-121-purity check in MeOH-001.lcd
Method File Name	: 1106_DTZ.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 2/21/2016 3:12:53 PM
Data Processed	: 2/21/2016 4:14:43 PM



3a

<Chromatogram>

C:\LabSolutions\Data\Eric Scocchera\EWS-V-121-purity check in MeOH-001.lcd



PeakTable

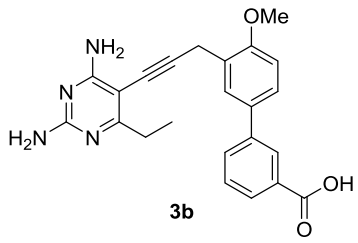
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.064	622304	17018	3.559	6.044
2	17.296	203796	6203	1.166	2.203
3	20.002	64018	1317	0.366	0.468
4	25.378	16593874	257055	94.909	91.286
Total		17483992	281594	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

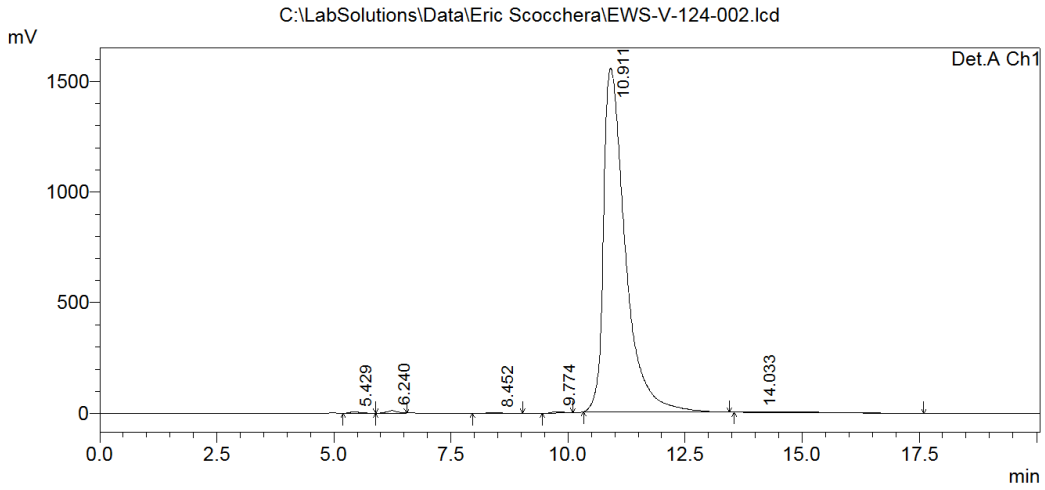
C:\LabSolutions\Data\Eric Scocchera\EWS-V-124-002.lcd

Acquired by	: Admin
Sample Name	: EWS-V-124
Sample ID	: EWS-V-124
Tray#	: 1
Vail #	: 10
Injection Volume	: 30 uL
Data File Name	: EWS-V-124-002.lcd
Method File Name	: Test1.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 2/24/2016 2:36:36 PM
Data Processed	: 2/24/2016 3:03:36 PM



3b

<Chromatogram>



PeakTable

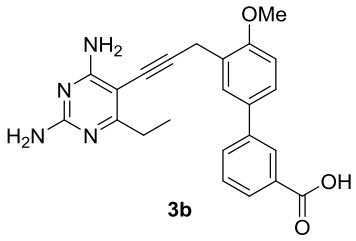
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.429	117820	6384	0.230	0.403
2	6.240	205350	11598	0.402	0.732
3	8.452	70045	2878	0.137	0.181
4	9.774	93959	6185	0.184	0.390
5	10.911	50465823	1555769	98.705	98.128
6	14.033	175142	2640	0.343	0.166
Total		51128139	1585454	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Eric Scocchera\EWS-V-124-in MeOH-003.lcd

Acquired by	: Admin
Sample Name	: EWS-V-124-in MeOH
Sample ID	: EWS-V-124-in MeOH
Tray#	: 1
Vail #	: 10
Injection Volume	: 30 uL
Data File Name	: EWS-V-124-in MeOH-003.lcd
Method File Name	: Test1.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 2/24/2016 4:43:29 PM
Data Processed	: 2/24/2016 6:32:00 PM



3b

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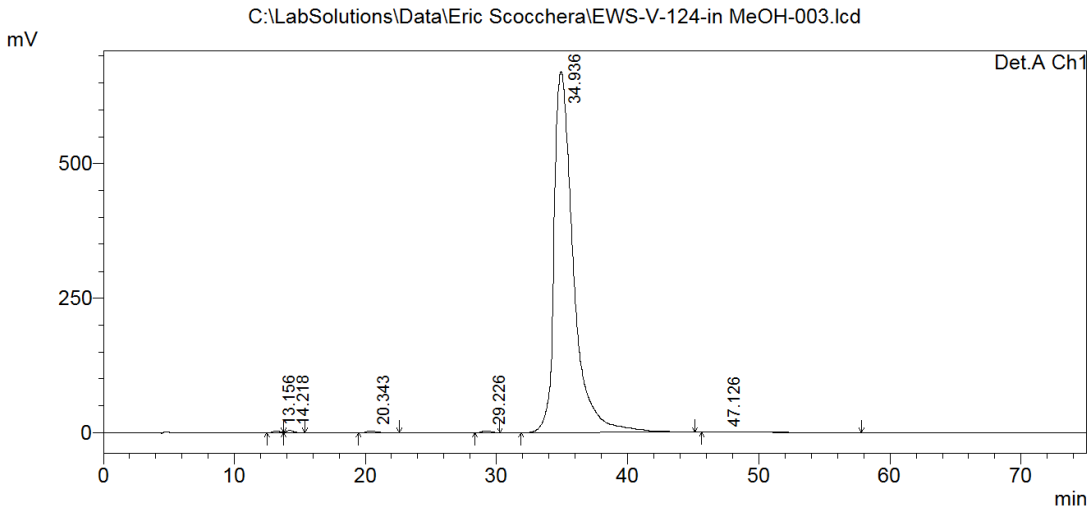


PeakTable

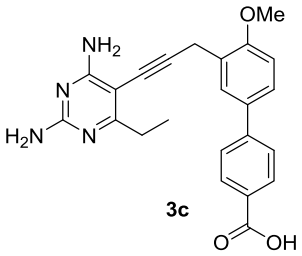
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.156	104356	3261	0.150	0.476
2	14.218	138297	4215	0.199	0.615
3	20.343	180182	3021	0.259	0.441
4	29.226	166584	3216	0.240	0.469
5	34.936	68733445	671150	98.958	97.930
6	47.126	134293	472	0.193	0.069
Total		69457157	685336	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Eric Scocchera\EWS-V-170-005.lcd

Acquired by	: Admin
Sample Name	: EWS-V-170-good
Sample ID	: EWS-V-170
Tray#	: 1
Vail #	: 69
Injection Volume	: 40 uL
Data File Name	: EWS-V-170-005.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/11/2015 12:46:34 PM
Data Processed	: 12/11/2015 1:08:30 PM



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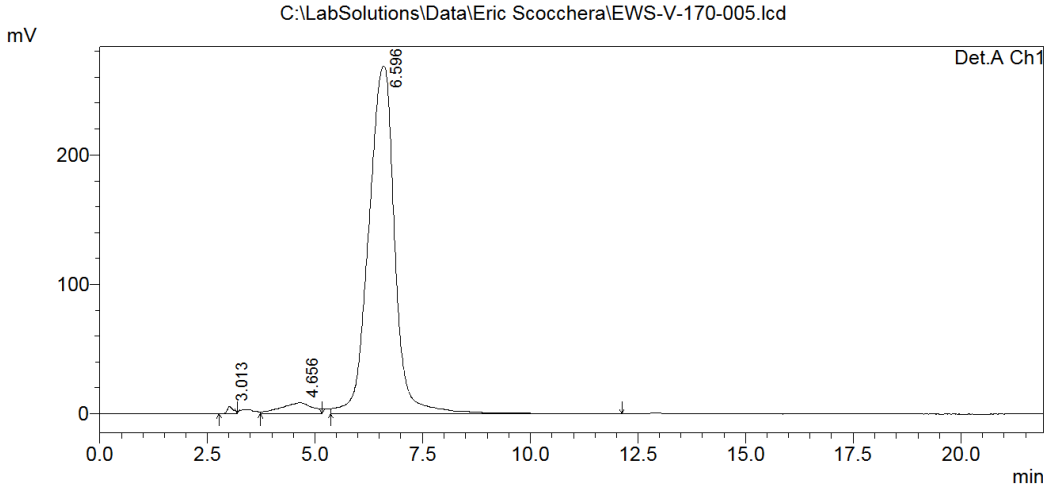


PeakTable

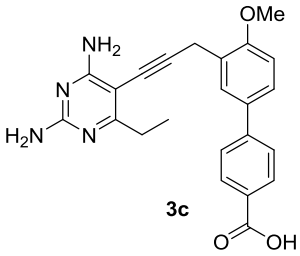
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	3.013	57844	5655	0.493	2.001
2	4.656	438677	8450	3.739	2.990
3	6.596	11236471	268471	95.768	95.008
Total		11732992	282577	100.000	100.000

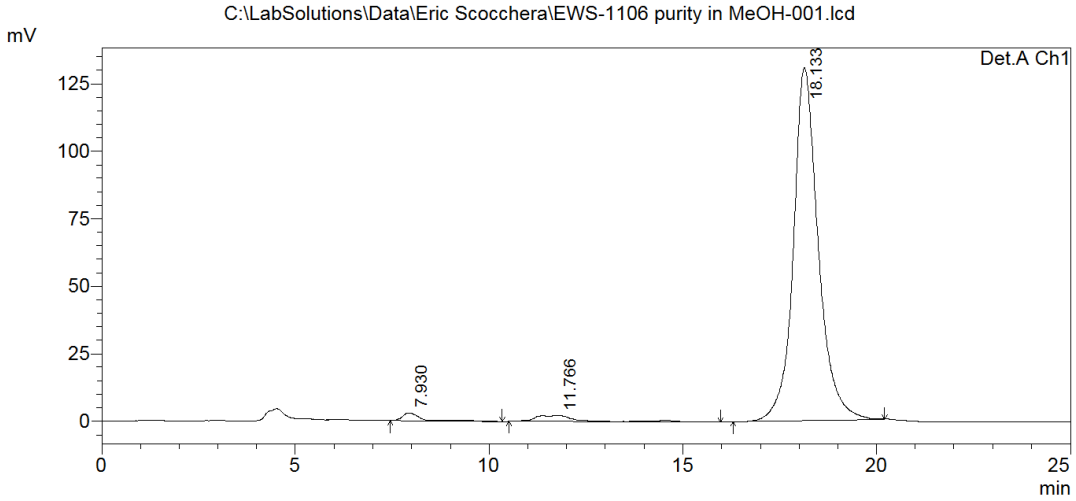
==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Eric Scocchera\EWS-1106 purity in MeOH-001.lcd

Acquired by	: Admin
Sample Name	: EWS-1106 purity check methanol
Sample ID	: ucp-1106 Methanol
Tray#	: 1
Vail #	: 69
Injection Volume	: 25 uL
Data File Name	: EWS-1106 purity in MeOH-001.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/18/2015 5:38:44 PM
Data Processed	: 12/18/2015 6:13:50 PM



<Chromatogram>



PeakTable

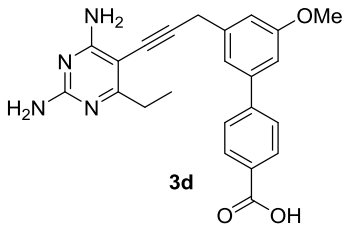
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.930	86543	2909	1.413	2.139
2	11.766	169834	2270	2.773	1.670
3	18.133	5867404	130799	95.813	96.191
Total		6123782	135979	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

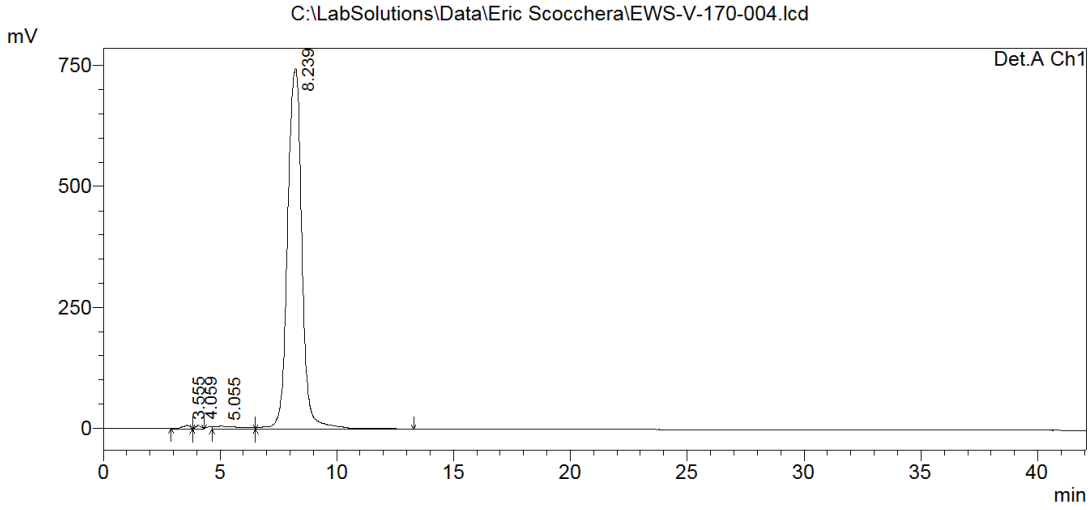
C:\LabSolutions\Data\Eric Scocchera\EWS-V-170-004.lcd

Acquired by	: Admin
Sample Name	: EWS-V-170
Sample ID	: EWS-V-170
Tray#	: 1
Vail #	: 57
Injection Volume	: 30 uL
Data File Name	: EWS-V-170-004.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/9/2015 2:19:34 PM
Data Processed	: 12/9/2015 3:01:40 PM



3d

<Chromatogram>



PeakTable

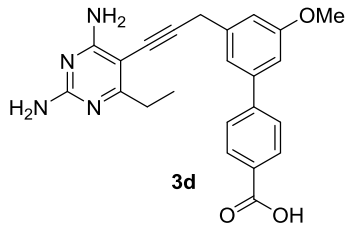
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	3.555	170534	6981	0.525	0.911
2	4.059	123746	7893	0.381	1.030
3	5.055	469975	6027	1.448	0.786
4	8.239	31702936	745370	97.646	97.272
Total		32467191	766270	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Eric Scocchera\EWS-1175 purity in MeOH-004.lcd

Acquired by	: Admin
Sample Name	: EWS-1175 purity check
Sample ID	: ucp-1175
Tray#	: 1
Vail #	: 70
Injection Volume	: 25 uL
Data File Name	: EWS-1175 purity in MeOH-004.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/18/2015 5:04:09 PM
Data Processed	: 2/26/2016 2:08:58 PM



3d

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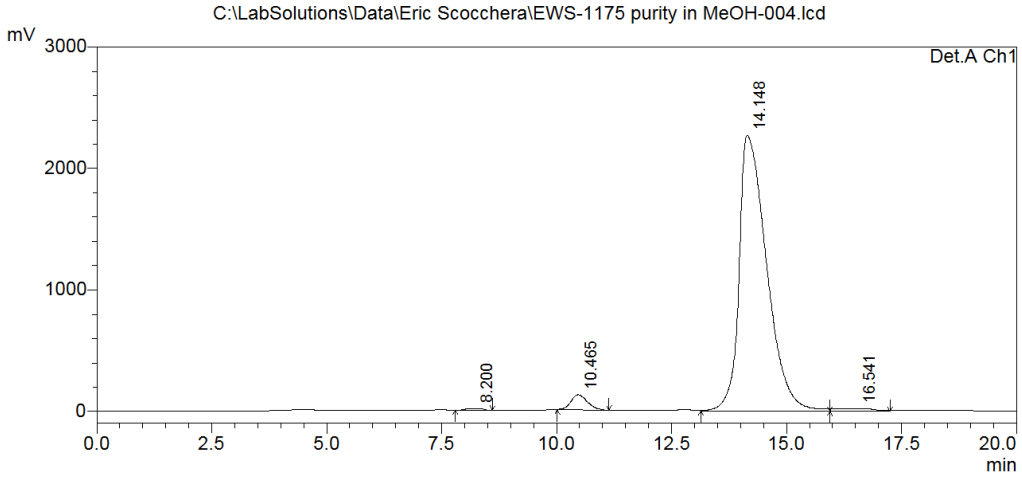


PeakTable

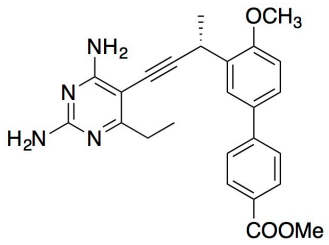
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.200	385597	16155	0.388	0.664
2	10.465	3089120	124922	3.107	5.136
3	14.148	94823379	2270390	95.371	93.344
4	16.541	1128084	20804	1.135	0.855
Total		99426180	2432271	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Santosh\zwitterions final\skk-nb4-134-004.lcd

Acquired by	: Admin
Sample Name	: skk-nb4-134
Sample ID	: skk-nb4-134
Tray#	: 1
Vail #	: 41
Injection Volume	: 40 uL
Data File Name	: skk-nb4-134-004.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/9/2015 5:15:09 PM
Data Processed	: 12/9/2015 6:02:03 PM



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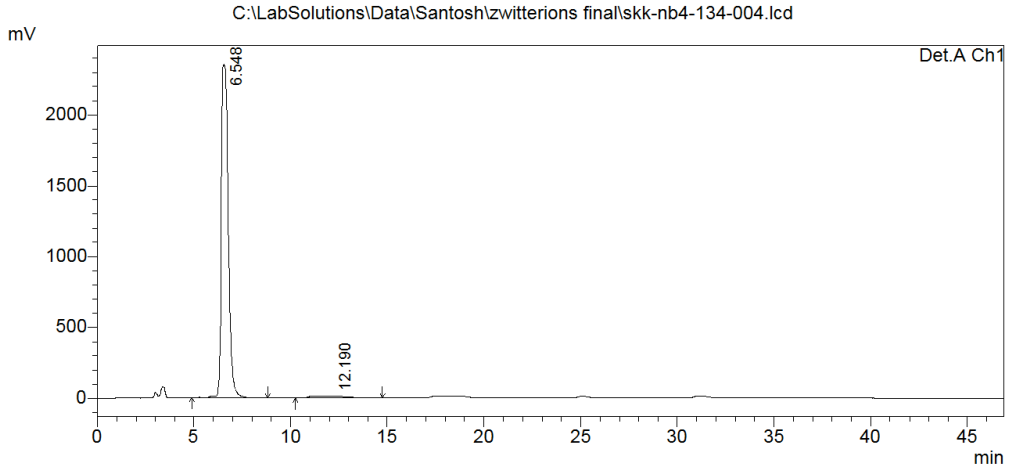


PeakTable

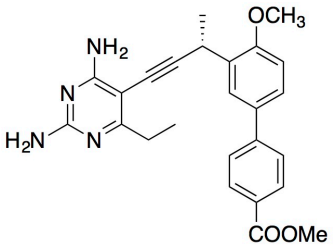
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.548	59135238	2352052	97.269	99.349
2	12.190	1660436	15401	2.731	0.651
Total		60795674	2367453	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1179-010.lcd

Acquired by	: Admin
Sample Name	: ucp-1179
Sample ID	: ucp-1179
Tray#	: 1
Vail #	: 44
Injection Volume	: 10 uL
Data File Name	: ucp-1179-010.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/16/2015 3:58:45 PM
Data Processed	: 12/16/2015 4:29:53 PM



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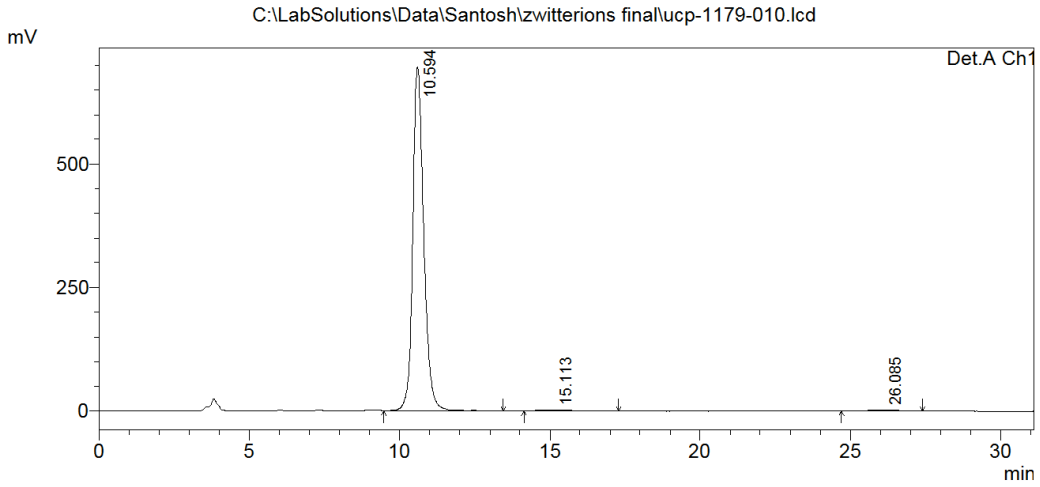
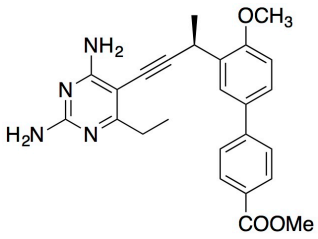


Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.594	17490881	695753	98.569	99.598
2	15.113	109883	1253	0.619	0.179
3	26.085	144129	1553	0.812	0.222
Total		17744893	698559	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

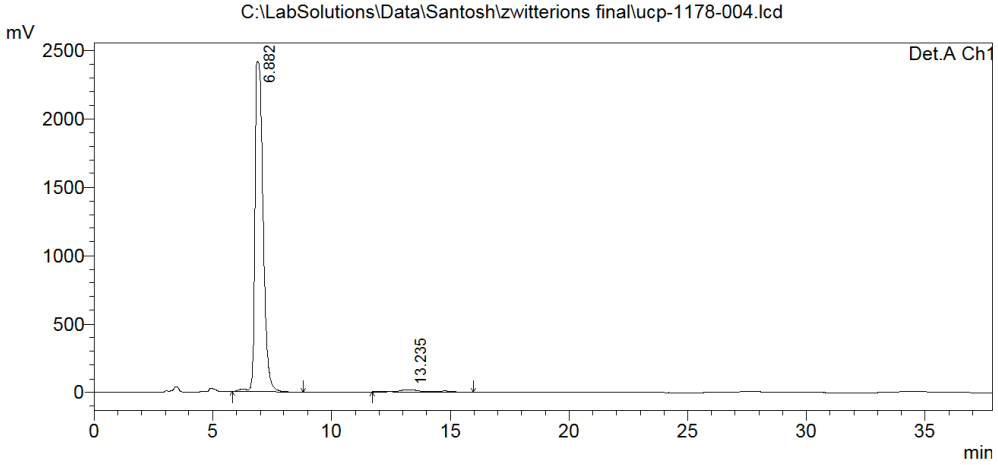


C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1178-004.lcd

Acquired by	: Admin
Sample Name	: ucp-1178
Sample ID	: ucp-1178
Tray#	: 1
Vail #	: 43
Injection Volume	: 30 uL
Data File Name	: ucp-1178-004.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/15/2015 7:35:51 PM
Data Processed	: 12/15/2015 8:13:43 PM

<Chromatogram>

C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1178-004.lcd



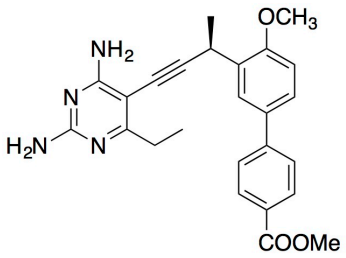
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.882	57240718	2414401	98.065	99.312
2	13.235	1129429	16728	1.935	0.688
Total		58370147	2431129	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1178-010.lcd

Acquired by	: Admin
Sample Name	: ucp-1178
Sample ID	: ucp-1178
Tray#	: 1
Vail #	: 43
Injection Volume	: 10 uL
Data File Name	: ucp-1178-010.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/16/2015 3:27:44 PM
Data Processed	: 12/16/2015 3:57:58 PM



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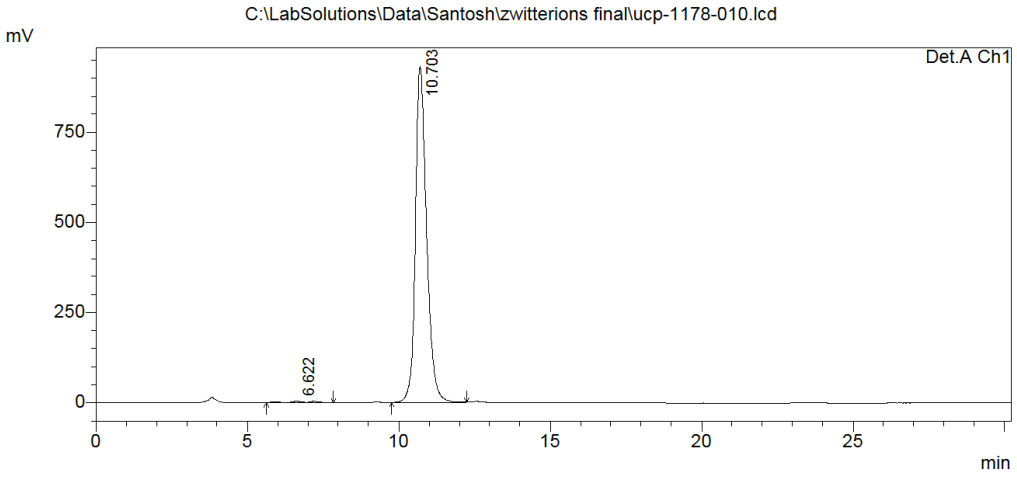


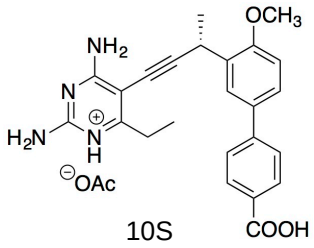
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.622	166295	4605	0.689	0.492
2	10.703	23980730	931521	99.311	99.508
Total		24147026	936126	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1163-001.lcd

Acquired by	: Admin
Sample Name	: ucp-1163
Sample ID	: ucp-1163
Tray#	: 1
Vail #	: 43
Injection Volume	: 40 uL
Data File Name	: ucp-1163-001.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/14/2015 12:42:46 PM
Data Processed	: 12/14/2015 1:18:54 PM



10S

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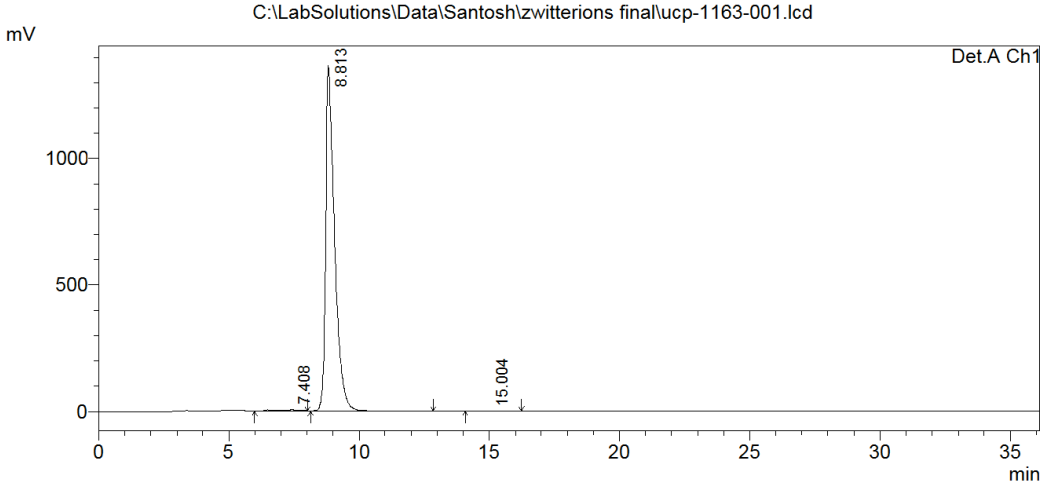


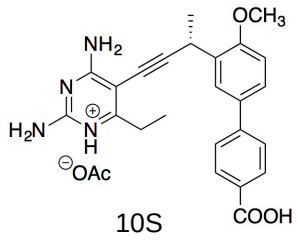
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.408	335859	6538	1.019	0.474
2	8.813	32587903	1370135	98.856	99.417
3	15.004	41273	1491	0.125	0.108
Total		32965034	1378163	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1163-010.lcd

Acquired by	: Admin
Sample Name	: ucp-1163
Sample ID	: ucp-1163
Tray#	: 1
Vail #	: 45
Injection Volume	: 20 uL
Data File Name	: ucp-1163-010.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/16/2015 4:35:14 PM
Data Processed	: 12/16/2015 5:06:16 PM



10S

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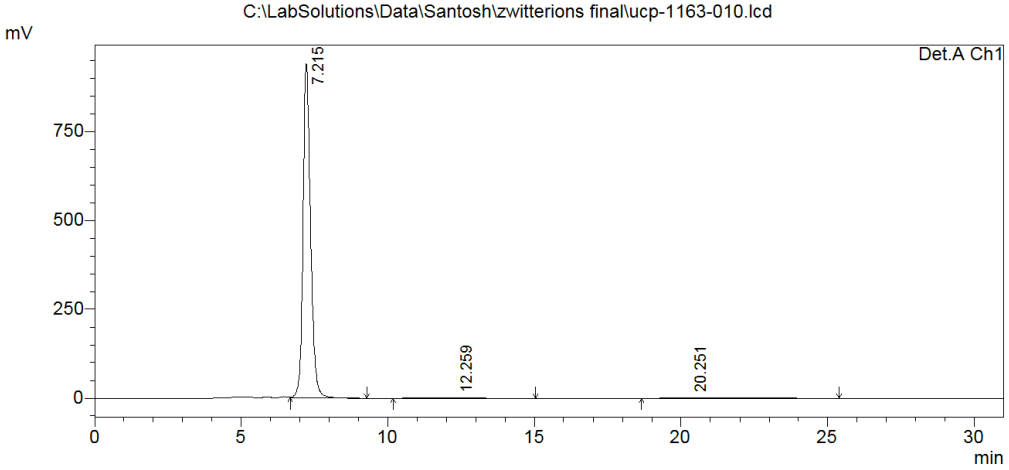
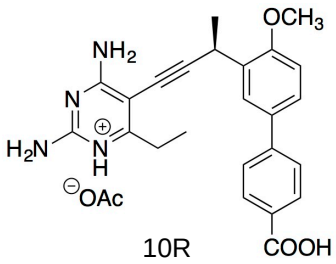
C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1163-010.lcd



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.215	16832483	939672	97.558	99.738
2	12.259	180747	1190	1.048	0.126
3	20.251	240628	1280	1.395	0.136
Total		17253858	942142	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

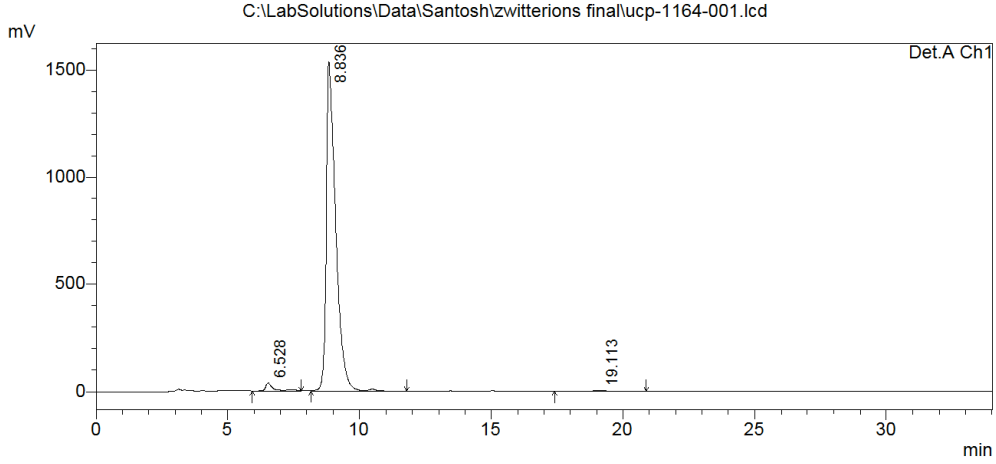


C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1164-001.lcd

Acquired by	: Admin
Sample Name	: ucp-1164
Sample ID	: ucp-1164
Tray#	: 1
Vail #	: 44
Injection Volume	: 40 uL
Data File Name	: ucp-1164-001.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/14/2015 1:19:45 PM
Data Processed	: 12/14/2015 1:53:47 PM

<Chromatogram>

C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1164-001.lcd



PeakTable

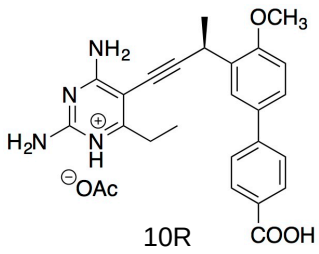
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.528	1002068	38826	2.535	2.458
2	8.836	38315402	1537068	96.912	97.294
3	19.113	218907	3918	0.554	0.248
Total		39536376	1579812	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1164-010.lcd

Acquired by	: Admin
Sample Name	: ucp-1164
Sample ID	: ucp-1164
Tray#	: 1
Vail #	: 46
Injection Volume	: 20 uL
Data File Name	: ucp-1164-010.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/16/2015 5:08:03 PM
Data Processed	: 12/16/2015 5:41:06 PM



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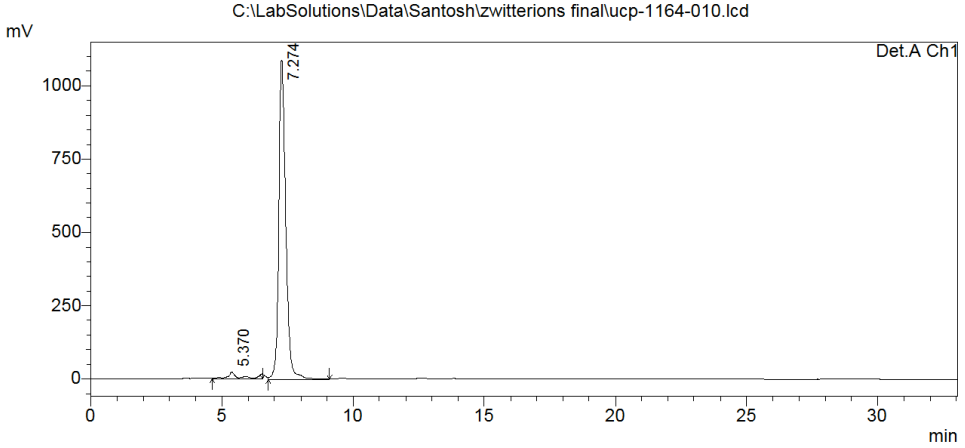
C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1164-010.lcd



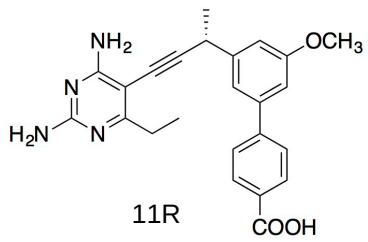
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.370	762844	22995	3.685	2.070
2	7.274	19941162	1088070	96.315	97.930
Total		20704006	1111065	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1172-001.lcd

Acquired by	: Admin
Sample Name	: ucp-1172
Sample ID	: ucp-1172
Tray#	: 1
Vail #	: 45
Injection Volume	: 40 uL
Data File Name	: ucp-1172-001.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/14/2015 1:54:49 PM
Data Processed	: 12/14/2015 3:00:21 PM



11R

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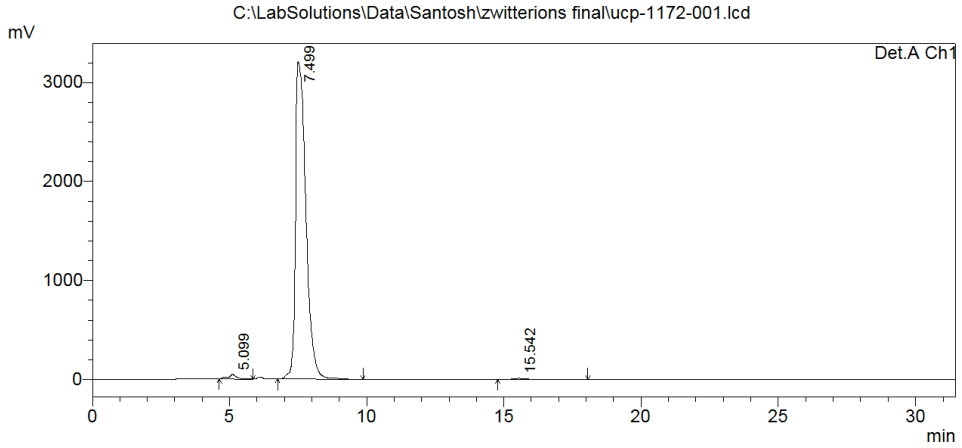


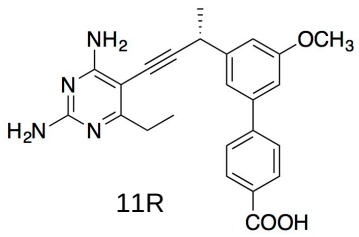
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.099	1107205	46099	1.280	1.412
2	7.499	84943012	3203897	98.217	98.143
3	15.542	434618	14522	0.503	0.445
Total		86484834	3264518	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1172-021.lcd

Acquired by	: Admin
Sample Name	: ucp-1172
Sample ID	: ucp-1172
Tray#	: 1
Vail #	: 47
Injection Volume	: 5 uL
Data File Name	: ucp-1172-021.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/16/2015 7:17:15 PM
Data Processed	: 12/16/2015 7:45:30 PM



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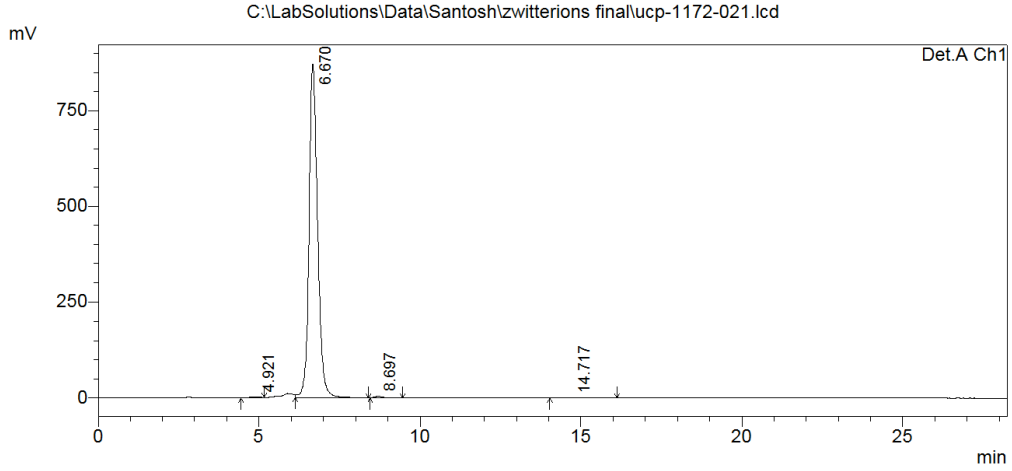
C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1172-021.lcd



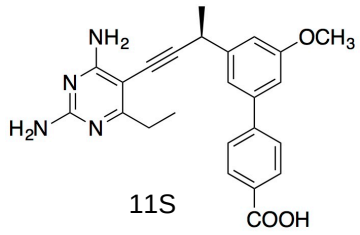
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.921	68872	2737	0.422	0.312
2	6.670	16167208	870906	98.969	99.200
3	8.697	82997	3588	0.508	0.409
4	14.717	16550	697	0.101	0.079
Total		16335627	877928	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1173-001.lcd

Acquired by	: Admin
Sample Name	: ucp-1173
Sample ID	: ucp-1173
Tray#	: 1
Vail #	: 46
Injection Volume	: 40 uL
Data File Name	: ucp-1173-001.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/14/2015 2:27:10 PM
Data Processed	: 12/14/2015 3:31:42 PM



11S

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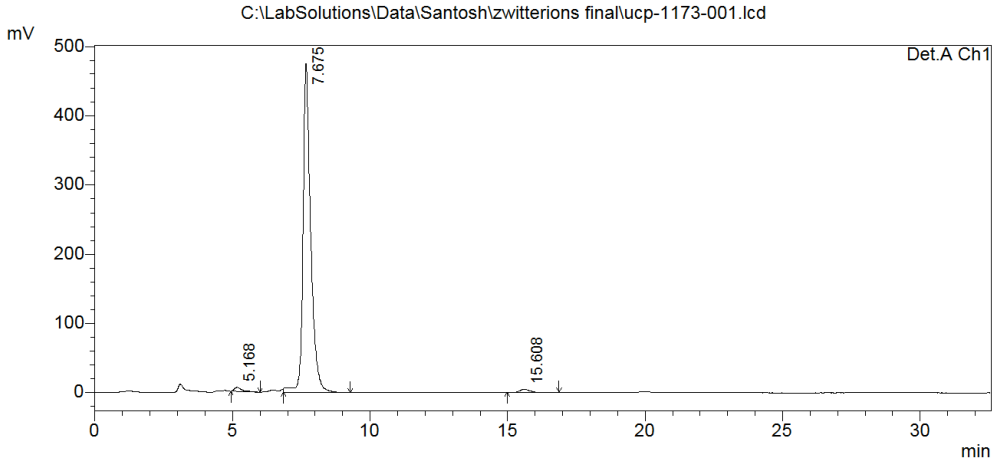


PeakTable

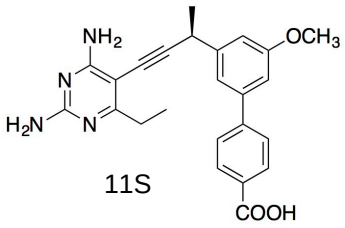
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.168	101096	5913	1.082	1.223
2	7.675	9160298	473314	98.040	97.867
3	15.608	81995	4403	0.878	0.910
Total		9343388	483629	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1173-020.lcd

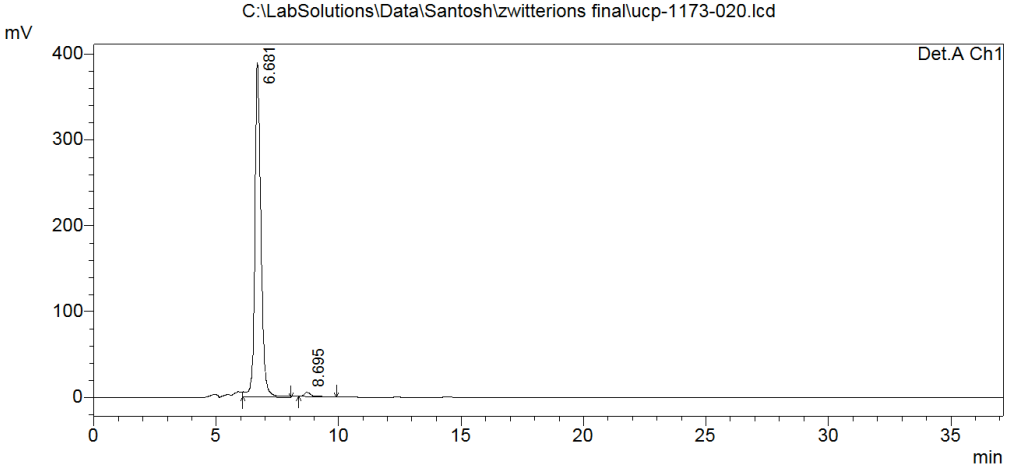
Acquired by	: Admin
Sample Name	: ucp-1173
Sample ID	: ucp-1173
Tray#	: 1
Vail #	: 48
Injection Volume	: 20 uL
Data File Name	: ucp-1173-020.lcd
Method File Name	: Test.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/16/2015 7:46:24 PM
Data Processed	: 12/16/2015 8:23:32 PM



11S

<Chromatogram>

C:\LabSolutions\Data\Santosh\zwitterions final\ucp-1173-020.lcd



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.681	6693252	388581	98.608	98.773
2	8.695	94473	4829	1.392	1.227
Total		6787724	393410	100.000	100.000