Tuning Reactivity and Site-Selectivity of Simple Arenes in C-H Activation: Ortho-Arylation of Anisoles *Via* Arene-Metal π-Complexation

Paolo Ricci, Katrina Kramer, Igor Larrosa*

CONTENTS

General experimental details

Unless otherwise indicated, all reactions were carried out under air. THF was obtained by Grubbs type solvent purification system and stored over molecular sieves under Ar atmosphere. Di-*n*-butyl ether (99+% Extra Dry, Acroseal ®) was purchased from Acros and used without any further purification. Toluene (analytical grade) was purchased from Fisher and used without any further purification. All other starting materials and solvents were purchased from Acros, Aldrich, Alfa Aesar, Fluorochem and used without further purification. $Cr(CO)_6$ was purchased from Acros and utilized under exclusion of light. Catalysts $Pd(PPh_3)_4$, $Pd(OAc)_2$ and $Pd(dba)_2$ were purchased from Strem Chemicals and kept under Ar atmosphere. Starting O-substituted arenes have been synthesized by treatment of the corresponding phenol in presence of iodomethane,[1] 2-iodopropane[2] or chloromethyl ethyl ether[3] under previously reported conditions. Chromium complexes are photosensitive and were handled under exclusion of light as far as possible. Solid compounds were stored in an evacuated dessicator over solid dessicant under exclusion of light.

Thin layer chromatography (TLC) was performed on Merck F254 precoated silica gel plates. Visualisation was accomplished with UV light and/or $KMnO_4$ solution. Flash chromatography (FC) was performed using VWR Prolabo (45-60 μm) silica gel. Solvents for extraction and FC were analytical grade. Reported solvent mixtures for TLC and FC are volume/volume mixtures. Infrared spectra were obtained on a Bruker Tensor 37 FTIR spectrometer. Peaks are reported in cm^{-1}. High resolution mass spectra were performed at the EPSRC National Mass Spectrometry Service Centre, Swansea. ^1H and ^{13}C NMR were recorded on Bruker AV 400 MHz NMR spectrometers in the indicated deuterated solvent, which were obtained from Cambridge Isotope Labs ($CDCl_3$) or Fluorochem ($(CD_3)_2CO$). ^1H and ^{13}C NMR where referenced to the solvent peak at 7.26 or 2.05 ppm for ^1H in $CDCl_3$ and $(CD_3)_2CO$, respectively, and 77.16 or 30.6 ppm for ^{13}C. Melting points were obtained using an Electrothermal and Stanley Scientific melting point apparatus and are uncorrected.

Experimental procedures

General procedure A: preparation of arene chromium tricarbonyl complexes (1)[4]

A flame-dried round bottom flask equipped with a magnetic stirrer and a reflux condenser was charged with $Cr(CO)_6$ (6.50 mmol, 1.3 equiv), evacuated and backfilled with Ar. The required O-substituted phenol (5.00 mmol, 1.0 equiv) was added to the flask, followed by the addition of anh. nBu$_2$O and THF (9:1 v/v, 0.15 M). The resulting suspension was subjected freeze-pump-thaw cycles (3 × 30 min) and then refluxed (external temperature 150 ^{o}C) for 48 h. The solution was then cooled down to room temperature and filtered through a short pad of silica. The silica pad was washed with Et_2O (3 × 20 mL) and the organic layer was then concentrated *in vacuo*. Recrystallisation from a cold mixture of hexane/Et_2O 9:1 provided the arene tricarbonyl chromium complex **1**.

General procedure B: Direct arylation of arene tricarbonyl chromium complexes 1 with iodoarenes 2 (excess of chromium tricarbonyl complex).

To an oven-dried microwave 10 mL glass vial equipped with a round stirrer bar, the following reagents were added in this order: K_2CO_3 (172.5 mg, 1.25 mmol, 2.5 equiv), 1-AdCO_2H (45.0 mg, 0.25 mmol, 0.5 equiv), Ag_2CO_3 (70 mg, 0.25 mmol, 0.5 equiv), $Pd(PPh_3)_4$ (5 mol %, 28.9 mg, 0.01 mmol), the required arene $Cr(CO)_3$ complex **1** (0.65 mmol, 1.3 equiv) and iodoarene **2** (0.50 mmol, 1.0 equiv). $PhCH_3$ (0.3 mL, 1.7 M) and 2,2,6,6-tetramethylpiperidine (170 μL, 1.00 mmol, 2.0 equiv) were added and the glass vial was sealed with a disposable microwave cap. The resulting mixture was stirred for 48 h at 60 ^{o}C. The reaction was then cooled down and AcOH (2 mL) was slowly added with moderate stirring. After 5 min, MnO_2 (130 mg, 1.50 mmol, 3 equiv) was added in small portions and the black suspension was vigorously stirred for 30 min. The suspension was then loaded on a short silica plug (2 cm × 4 cm) and eluted with Et_2O (30 mL) before concentrating *in vacuo*. Purification via flash chromatography column on silica gel provided the required biaryl product.

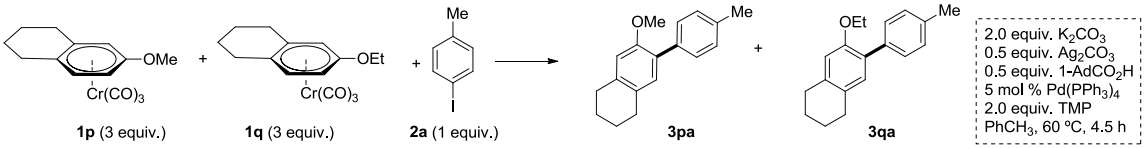
General procedure C: Direct arylation of arene tricarbonyl chromium complexes 1 with iodoarenes 2 (excess of iodoarene).

To an oven-dried microwave 10 mL glass vial equipped with a round stirrer bar, the following reagents were added in this order: K_2CO_3 (172.5 mg, 1.25 mmol, 2.5 equiv), 1-AdCO_2H (45.0 mg, 0.250 mmol, 0.5 equiv), Ag_2CO_3 (105 mg, 0.375 mmol, 0.75 equiv), $Pd(PPh_3)_4$ (5 mol%, 28.9 mg, 0.010 mmol), the required arene $Cr(CO)_3$ complex **1** (0.5 mmol, 1.0 equiv) and iodoarene **2** (0.75 mmol, 1.5 equiv). $PhCH_3$ (0.3 mL, 1.7 M) and 2,2,6,6-tetramethylpiperidine (170 μL, 1 mmol, 2.0 equiv) were added and the glass vial was sealed with a disposable microwave cap. The resulting mixture was stirred for 30 h at 60 ^{o}C. The reaction was then cooled down and AcOH (2 mL) was slowly added with moderate stirring. After 5 min, MnO_2 (130 mg, 1.5 mmol, 3 equiv) was added in

small portions and the black suspension was vigorously stirred for 30 min. The suspension was then loaded on a short silica plug (2 cm × 4 cm) and eluted with Et_2O (30 mL) before concentrating *in vacuo*. Purification via flash chromatography column on silica gel provided the required biaryl product.

Procedure for determination of the KIE by one-pot competition experiments.

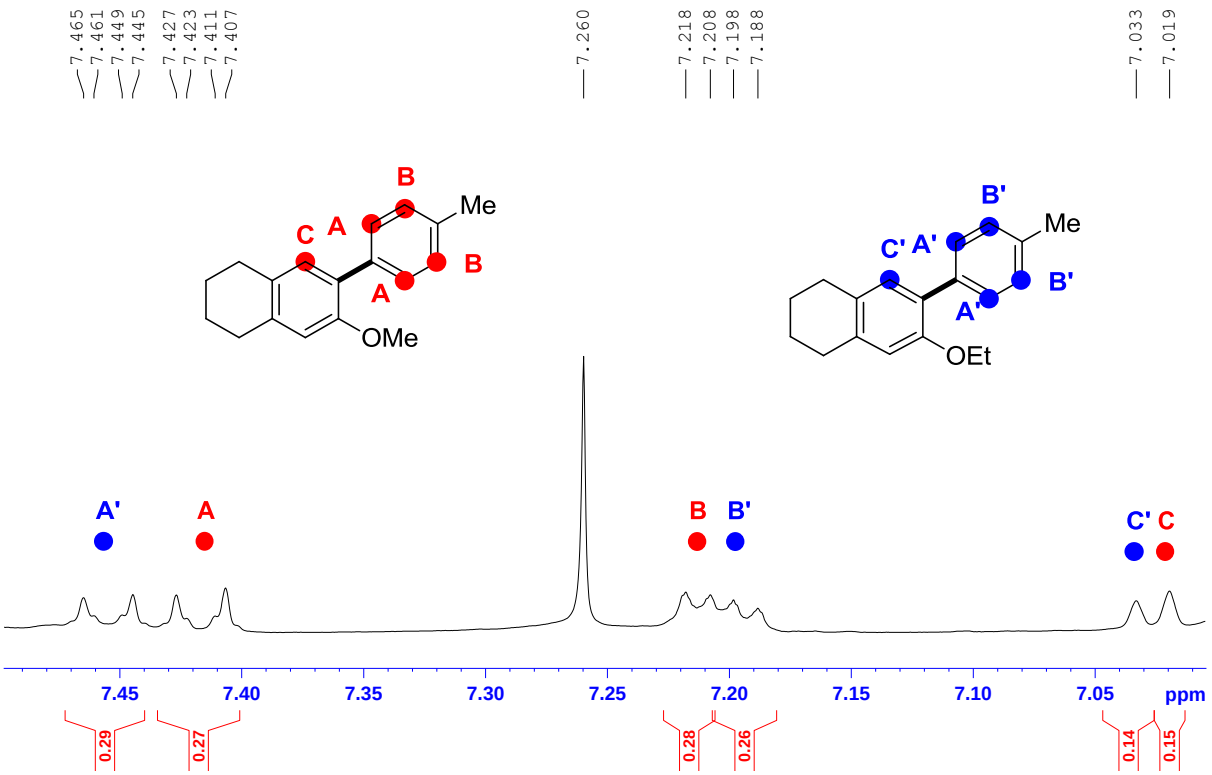
*Control experiment: Assessment of the reactivity of 6-methoxy-1,2,3,4-tetrahydronaphthalene complex **1p** versus 6-ethoxy-1,2,3,4-tetrahydronaphthalene complex **1q**.*



6-Methoxy-1,2,3,4-tetrahydronaphthalene $Cr(CO)_3$ complex (**1p**, 0.300 mmol, 89.4 mg, 3.00 equiv), 6-ethoxy-1,2,3,4-tetrahydronaphthalene $Cr(CO)_3$ (**1q**, 0.300 mmol, 93.6 mg, 3.00 equiv) and *p*-iodotoluene (**2a**, 0.100 mmol, 21.8 mg, 1.00 equiv) were subjected to direct arylation conditions for 4.5 h at 60 °C according to general procedure B. Demetallation was performed using MnO_2 (1.80 mmol, 156.5 mg, 18.0 equiv) and AcOH (5 mL) for 30 min, after which the solution was filtered through a plug of silica, which was subsequently washed three times with Et_2O.

After removal of the solvents *in vacuo*, yields were determined by ^1H NMR analysis of the crude mixture using an internal standard (1,3-dinitrobenzene, 0.100 mmol, see spectrum below). Two runs were performed. The reactivity of 6-methoxy-1,2,3,4-tetrahydronaphthalene $Cr(CO)_3$ complex **1p** and 6-ethoxy-1,2,3,4-tetrahydronaphthalene $Cr(CO)_3$ complex **1q** was determined equivalent.

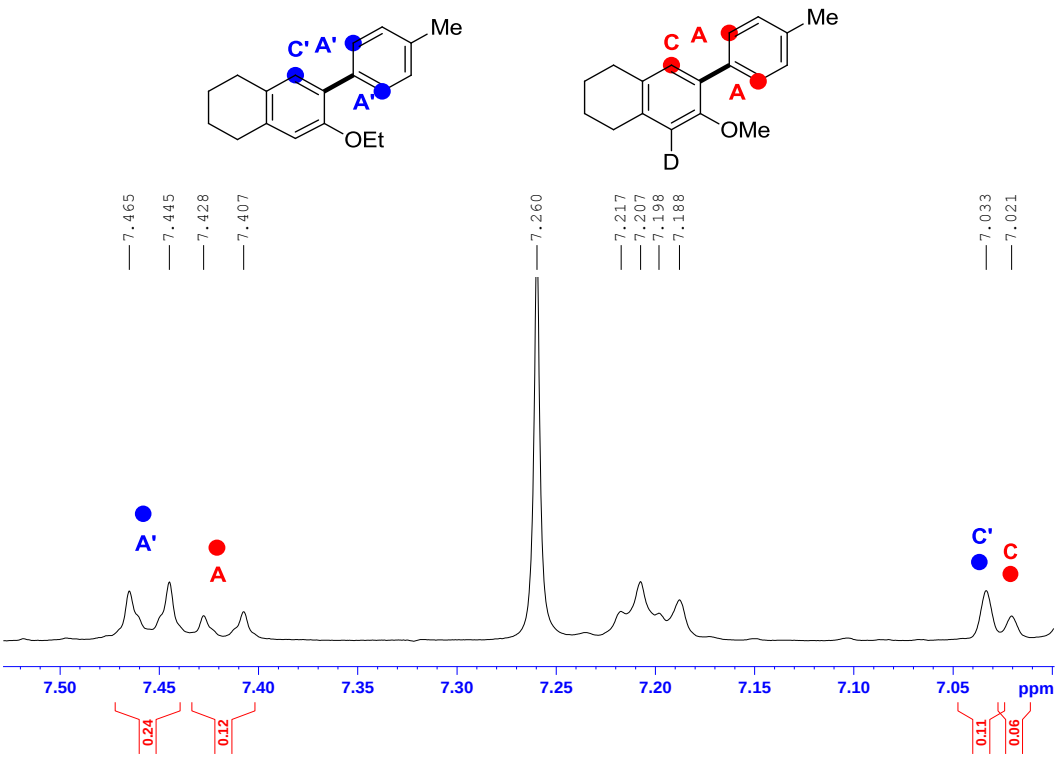
	Conv. 1p / mmol	**Average 1p /mmol**	**Conv. 1q / mmol**	**Average 1q n /mmol**
1st run	0.0287	0.0274	0.0270	0.0263
2nd run	0.0262		0.0262	



Determination of the KIE.

6-Methoxy-1,2,3,4-tetrahydronaphthalene-5,7-d_2 $Cr(CO)_3$ complex (**1p-D**, 0.300 mmol, 90.8 mg, 3.00 equiv), 6-ethoxy-1,2,3,4-tetrahydronaphthalene $Cr(CO)_3$ complex(**1q**, 0.300 mmol, 93.6 mg, 3.00 equiv) and 4-iodotoluene (**2a**, 0.100 mmol, 21.8 mg, 1.00 equiv) were subjected to direct arylation conditions for 4 h at 60 °C according to general procedure B. Demetallation was performed using MnO_2 (1.80 mmol, 156.5 mg, 18.0 equiv) and AcOH (5 mL) for 30 min, after which the solution was filtered through a plug of silica, which was subsequently washed three times with Et_2O.

After removal of the solvents *in vacuo*, yields were determined by ^{1}H NMR analysis of the crude mixture using an internal standard (1,3-dinitrobenzene, 0.100 mmol). Two runs were performed. Integration in the ^{1}H NMR was performed between protons **A** (**3p-Da**) and **A'** (**3aq**) and between protons **C** (**3p-Da**) and **C'** (**3aq**) (see spectrum below).



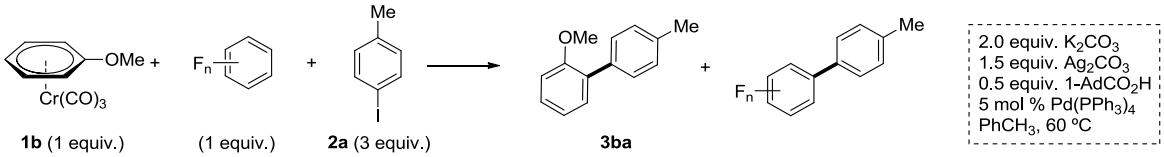
	Conv. 1p-D / mmol	Conv. 1q / mmol	Conv. 1p-D/ Conv. 1q
1st run	0.0122	0.0239	1.96
2nd run	0.0095	0.1997	2.10

$$\mathrm{KIE} = \frac{k_H}{k_D} = \frac{conversion_{\mathbf{1q}}}{conversion_{\mathbf{1p-D}}} = 2.0$$

Procedure for one-pot competition experiments between 1b and fluorinated arenes

A modification of general procedure B was applied using **1b** (24.4 mg, 0.100 mmol, 1.00 equiv), 1,3,5-trifluorobenzene or (*o*-fluorotoluene)$Cr(CO)_3$ (0.100 mmol, 1.00 equiv), **2a** (0.300 mmol, 3.00 equiv) and Ag_2CO_3 (0.150 mmol, 1.50 equiv). After the required time in each case for a moderate conversion to occur (4.5 h), the reaction was allowed to cool down to room temperature, diluted with Et_2O and filtered through silica. The yield of each arene was determined by ^1H NMR analysis of the crude mixture with an internal standard (1,3-dinitrobenzene).

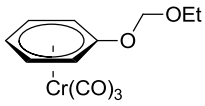
A summary of the results is shown in the table below.



1b (1 equiv.) (1 equiv.) **2a** (3 equiv.) **3ba**

Entry	Arenes	Time (h)	Yield (%)
1	**1b**	4.5	8
	(*o*-fluorotoluene)$Cr(CO)_3$		36
2	**1b**	4.5	14
	1,3,5-$C_6H_3F_3$		3

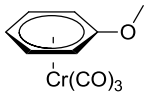
Characterization of chromium complexes and cross-coupling products



1a

(Ethoxymethoxy)benzene tricarbonyl chromium (1a).

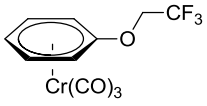
General procedure A was applied with using $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and (ethoxymethoxy)benzene (0.760 g, 5 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1a** as a yellow solid in 81% yield (1.17 g, 4.06 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.84 (app. t, *J* = 6.6 Hz, 2H), 5.54 (d, *J* = 6.4 Hz, 2H), 5.22-5.16 (m, 3H), 3.75 (q, *J* = 7.2 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 235.6, 143.2, 97.7, 95.4, 89.0, 83.2, 66.5, 16.0. IR: ν = 3096, 1949, 1843, 1531, 1226, 1082, 959 cm^{-1}. Mp: 78-80 °C. HRMS EI+ *m/z* calcd. $C_{12}H_{13}CrO_5$: $[M+H]^+$ 289.0163; found: $[M+H]^+$ 289.0162.



1b

Anisole tricarbonyl chromium (1b).

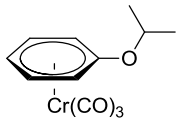
General procedure A was applied with using $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and anisole (0.640 g, 5 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1b** as a yellow solid in 79% yield (0.960 g, 3.93 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.86 (app. t, *J* = 6.0 Hz, 2H), 5.46 (d, *J* = 7.2 Hz, 2H), 5.16 (app. t, *J* = 6.0 Hz, 1H), 3.77 (s, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 235.5, 145.8, 98.1, 88.2, 81.0, 57.0. IR: ν = 3104, 1939, 1875, 1469, 1249, 991, 814 cm^{-1}. Mp: 85-87 °C. HRMS EI+ *m/z* calcd. $C_{10}H_9CrO_4$: $[M+H]^+$ 244.9900; found: $[M+H]^+$ 244.9899.



1c

(2,2,2-Trifluoroethoxy)benzene tricarbonyl chromium (1c).

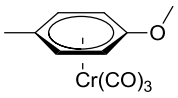
General procedure A was applied with using $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and (2,2,2-trifluoroethoxy)benzene (0.880 g, 5 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1c** as a yellow solid in 75% yield (1.156 g, 3.70 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.92 (*app* t, *J* = 6.8 Hz, 2H), 5.61 (d, *J* = 6.4 Hz, 2H), 5.25 (*app* t, *J* = 6.4 Hz, 1H), 4.65 (q, *J* = 8.4 Hz, 2H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 234.8, 142.5, 124.8 (q, $J_{C\text{-}F}$ = 276.9 Hz), 97.3, 88.9, 81.4, 66.9 (q, $J_{C\text{-}F}$ = 30.5 Hz). IR: ν = 3102, 1950, 1845, 1526, 1466, 1286, 1070 cm^{-1}. Mp: 85-87 °C.



1d

Isopropoxybenzene tricarbonyl chromium (1d).

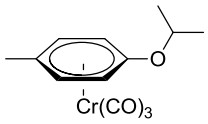
General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and isopropoxybenzene (0.682 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1d** as a yellow solid in 82% yield (1.113 g, 4.09 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.84 (*app* t, *J* = 6.8 Hz, 2H), 5.41 (d, *J* = 6.8 Hz, 2H), 5.11 (app t, *J* = 6.4 Hz, 1H), 4.51 (septet, *J* = 6.0 Hz, 1H), 1.34 (d, *J* = 6.0 Hz, 6H). ^{13}C NMR (101 MHz, (CD3)2CO): δ (ppm) = 235.0, 143.9, 98.4, 87.8, 81.1, 73.2, 23.0. IR: ν = 3100, 2980, 1946, 1853, 1527, 1461, 1251, 1105 cm^{-1}. Mp: 84-86 ^{o}C. HRMS EI+ *m/z* calcd. $C_{12}H_{13}CrO_4$: $[M+H]^+$ 273.0219; found: $[M+H]^+$ 273.0213.



1e

4-Methylanisole tricarbonyl chromium (1e).

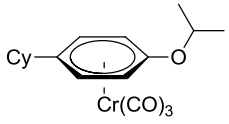
General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and *p*-methylanisole (0.610 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1e** as a yellow solid in 79% yield (1.023 g, 3.96 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.71 (br s, 2H), 5.45 (br s, 2H), 3.70 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (101 MHz, (CD3)2CO): δ (ppm) = 235.9, 143.7, 104.5, 98.3, 81.7, 57.1, 20.5. IR: ν = 3097, 1937, 1823, 1546, 1433, 1249, 1018 cm^{-1}. Mp: 57-59 ^{o}C. HRMS EI+ *m/z* calcd. $C_{11}H_{11}CrO_4$: $[M+H]^+$ 259.0057; found: $[M+H]^+$ 259.0055.



1f

1-Isopropoxy-4-methylbenzene tricarbonyl chromium (1f).

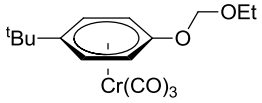
General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and 1-isopropoxy-4-methylbenzene (0.750 g, 5 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1f** as a yellow solid in 80% yield (1.142 g, 3.99 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.73 (d, *J* = 6.4 Hz, 2H), 5.43 (d, *J* = 6.4 Hz, 2H), 4.44 (septet, *J* = 6.0 Hz, 1H), 2.07 (s, 3H), 1.31 (d, *J* = 5.6 Hz, 6H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 236.1, 142.4, 103.9, 98.6, 82.4, 73.3, 22.9, 20.5. IR: ν = 3080, 2985, 1942, 1837, 1489, 1244, 936 cm^{-1}. Mp: 64-66 ^{o}C. HRMS EI+ *m/z* calcd. $C_{13}H_{15}CrO_4$: $[M+H]^+$ 287.0375; found: $[M+H]^+$ 287.0370.



1g

1-Cyclohexyl-4-isopropoxybenzene tricarbonyl chromium (1g).

General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and 1-cyclohexyl-4-isopropoxybenzene (1.09 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1g** as a yellow solid in 89% yield (1.574 g, 4.44 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.81 (d, *J* = 7.2 Hz, 2H), 5.34 (d, *J* = 7.2 Hz, 2H), 4.48 (septet, *J* = 6.0 Hz, 1H), 2.20-2.05 (m, 1H), 1.90-1.65 (m, 5H), 1.40-1.28 (m, 10H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 236.2, 144.1, 114.0, 97.7, 80.9, 73.2, 43.2, 36.1, 28.0, 27.2, 23.0. IR: ν = 2983, 2930, 1958, 1858, 1515, 1245, 931 cm^{-1}. Mp: 84-86 ^{o}C. HRMS EI+ *m/z* calcd. $C_{18}H_{23}CrO_4$: $[M+H]^+$ 355.1001; found: $[M+H]^+$ 355.0997.

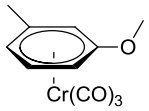


1h

1-(*Tert*-butyl)-4-(ethoxymethoxy)benzene tricarbonyl chromium (1h).

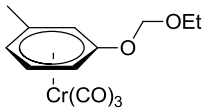
General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and 1-(*tert*-butyl)-4-(ethoxymethoxy)benzene (1.04 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1h** as a yellow solid in 89% yield (1.532 g, 4.45 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.99 (d, *J* = 6.0 Hz, 2H), 5.43 (d, *J* = 6.4 Hz, 2H), 5.19 (s, 2H), 3.75 (q, *J* = 6.8 Hz, 2H), 1.28 (s, 9H), 1.21 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 236.1, 143.2, 118.8, 96.7, 95.4, 81.5, 66.6, 35.0, 32.3, 16.1. IR: ν = 2971, 1943, 1839, 1483, 1228, 965 cm^{-1}. Mp: 75-77 ^{o}C. HRMS EI+ *m/z* calcd. $C_{16}H_{21}CrO_5$: $[M+H]^+$ 345.0788; found: $[M+H]^+$ 345.0789.

3-Methylanisole tricarbonyl chromium (1i).



1i

General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and *3*-methylanisole (0.610 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1i** as a yellow solid in 83% yield (1.074 g, 4.16 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.86 (app t, *J* = 6.4 Hz, 1H), 5.42 (s, 1H), 5.34 (d, *J* = 6.8 Hz, 1H), 5.06 (d, *J* = 6.0 Hz, 1H), 3.77 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 235.8, 146.0, 113.7, 97.9, 89.2, 82.8, 78.6, 56.9, 21.6. IR: ν = 3023, 1939, 1830, 1464, 1268, 1150, 988 cm^{-1}. Mp: 70-72 ^{o}C. HRMS EI+ *m/z* calcd. $C_{11}H_{11}CrO_4$: $[M+H]^+$ 259.0057; found: $[M+H]^+$ 259.0053.



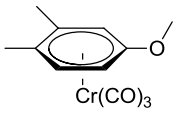
1j

1-(Ethoxymethoxy)-3-methylbenzene tricarbonyl chromium (1j).

General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and 1-(ethoxymethoxy)-3-methylbenzene (0.850 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1j** as a yellow solid in 81% yield (1.22 g,

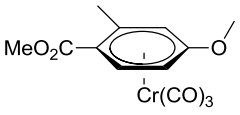
4.05 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.86 (app t, *J* = 6.8 Hz, 1H), 5.48 (s, 1H), 5.43 (d, *J* = 7.2 Hz, 1H), 5.21 (s, 2H), 5.10 (d, *J* = 6.0 Hz, 1H), 3.76 (q, *J* = 7.2 Hz, 1H), 2.28 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 235.9, 143.7, 113.6, 97.8, 95.3, 89.9, 84.8, 66.5, 21.6, 16.1. IR: ν = 3108, 1942, 1831, 1518, 1083 cm^{-1}. Mp: 72-74 ^{o}C. HRMS EI+ *m/z* calcd. $C_{13}H_{15}CrO_5$: $[M+H]^+$ 303.0319; found: $[M+H]^+$ 303.0318.

4-Methoxy-1,2-dimehtylbenzene tricarbonyl chromium (1k).



1k

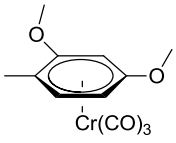
General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and 4-methoxy-1,2-dimethylbenzene (0.700 g, 5 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1k** as a yellow solid in 87% yield (1.180 g, 4.33 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.82 (d, *J* = 6.8 Hz, 1H), 5.47 (d, *J* = 2.4 Hz, 1H), 5.34 (dd, *J* = 6.8, 2.4 Hz, 1H), 3.73 (s, 3H), 2.28 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 236.2, 144.5, 112.6, 103.2, 99.6, 84.1, 79.2, 56.9, 20.0, 18.8. IR: ν = 2851, 1937, 1873, 1484, 1255, 999 cm^{-1}. Mp: 100-102 ^{o}C. HRMS EI+ *m/z* calcd. $C_{12}H_{13}CrO_4$: $[M+H]^+$ 273.0219; found: $[M+H]^+$ 273.0208.



1l

Methyl 4-methoxy-2-methylbenzoate tricarbonyl chromium (1l).

General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and methyl 4-methoxy-2-methylbenzoate (0.925 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane/ether (v:v = 9:1) gave the title product **1l** as a yellow-orange solid in 79% yield (1.253 g, 3.96 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 6.47 (d, *J* = 6.8 Hz, 1H), 5.50-5.44 (m, 2H), 3.84 (s, 3H), 3.82 (s, 3H), 2.58 (s, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 233.6, 167.2, 146.5, 114.6, 99.4, 88.0, 83.3, 78.1, 57.2, 53.5, 22.2. IR: ν = 3025, 1955, 1851, 1539, 1242, 1081 cm^{-1}. Mp: 100-102 ^{o}C. HRMS EI+ *m/z* calcd. $C_{13}H_{13}CrO_6$: $[M+H]^+$ 317.0115; found: $[M+H]^+$ 317.0112.

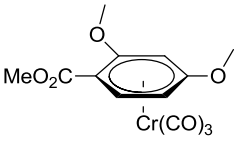


1m

2,4-Dimethoxy-1-methylbenzene tricarbonyl chromium (1m).

General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and 2,4-dimethoxy-1-methylbenzene (0.821 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1m** as a yellow solid in 78% yield (1.123 g, 3.90 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.92 (d, *J* = 6.8 Hz, 1H), 5.59 (d, *J* = 2.0 Hz,

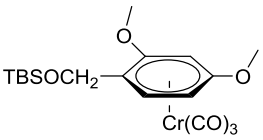
1H), 5.10 (dd, *J* = 6.4, 1.6 Hz, 1H), 3.89 (s, 3H), 3.76 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 236.1, 145.1, 144.8, 98.7, 93.9, 73.9, 69.5, 57.4, 57.1, 16.2. IR: ν = 3116, 1935, 1853, 1463, 1157, 910 cm^{-1}. Mp: 95-97 °C. HRMS EI+ *m/z* calcd. $C_{12}H_{13}CrO_5$: $[M+H]^+$ 289.0168; found: $[M+H]^+$ 289.0157.



1n

Methyl 2,4-dimethoxylbenzoate-1-methylbenzene tricarbonyl chromium (1n).

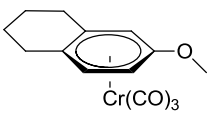
General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and methyl 2,4-dimethoxybenzoate (0.821 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane/ether (v:v = 9:1) gave the title product **1n** as a yellow solid in 82% yield (1.359 g, 4.09 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 6.44 (d, *J* = 6.8 Hz, 1H), 5.65 (s, 1H), 5.30 (d, *J* = 6.8 Hz, 1H), 3.95 (s, 3H), 3.89 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 234.0, 166.0, 146.9, 146.2, 98.1, 81.1, 74.2, 68.6, 57.9, 57.6, 53.4. IR: ν = 2952, 1955, 1730, 1246, 1086 cm^{-1}. Mp: 105-107 °C. HRMS EI+ *m/z* calcd. $C_{13}H_{12}CrO_7$: $[M+H]^+$ 333.0066; found: $[M+H]^+$ 333.0555.



1o

***Tert*-butyl(2,4-dimethoxybenzyl)oxy)dimethylsilane tricarbonyl chromium (1o).**

General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and tert-butyl((2,4-dimethoxybenzyl)oxy)dimethylsilane (1.41 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1o** as a yellow solid in 86% yield (1.788 g, 4.28 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 6.07 (d, *J* = 6.8 Hz, 1H), 5.59 (d, *J* = 2.0 Hz, 1H), 5.17 (dd, *J* = 6.8, 2.0 Hz, 1H), 4.62 (d, *J* = 12.8 Hz, 1H), 4.39 (d, *J* = 13.2 Hz, 1H), 3.89 (s, 3H), 3.79 (s, 3H), 0.96 (s, 9H), 0.16 (s, 3H), 0.15 (s, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 235.7, 145.5, 143.9, 96.9, 95.6, 73.5, 68.8, 60.6, 57.4, 57.2, 27.0, 16.6, - 4.5. IR: ν = 3104, 2927, 1940, 1843, 1523, 1210, 1084, 712, 636 cm^{-1}. Mp: 96-98 °C. HRMS EI+ *m/z* calcd. $C_{18}H_{26}CrO_6Si$: $[M]^+$ 418.0904 found: $[M]^+$ 418.0888.

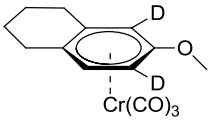


1p

2-Methoxy-1,2,3,4-tetrahydronaphthalene chromium tricarbonyl (1p).

General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and 2-methoxy-1,2,3,4-tetrahydronaphthalene (0.811 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1p** as a yellow solid in 77% yield (1.148 g,

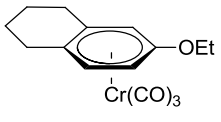
3.85 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.77 (d, J = 6.8 Hz, 1H), 5.40 (d, *J* = 6.8, 1.6 Hz, 1H), 5.37 (d, *J* = 1.6 Hz, 1H), 3.73 (s, 3H), 2.87-2.54 (m, 3H), 2.48-2.36 (m, 1H), 1.90-1.65 (m, 4H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 236.3, 144.2, 113.8, 104.9, 98.5, 81.0, 80.0, 57.0, 29.8, 28.9, 23.6, 23.3. IR: ν = 3099, 2941, 1943, 1866, 1747, 1435, 1147, 1022, 934 cm-1. Mp: 81-83 ^{o}C. HRMS EI+ *m/z* calcd. $C_{14}H_{15}CrO_4$: $[M+H]^+$ 299.0375 found: $[M+H]^+$ 299.0370.



1p-D

6-Methoxy-1,2,3,4-tetrahydronaphthalene-5,7-*d*$_2$ chromium tricarbonyl (1p-D).

n-BuLi (2.5M solution in hexane, 2 mL, 5 mmol, 2.00 equiv) was added dropwise onto a solution of complex **1p** (628 mg, 2.50 mmol) in anhydrous THF (12.0 mL) under inert atmosphere at –78 ºC. After stirring at –78 ºC for 1 h, D2O (1.5 mL, 83.3 mmol, 33.3 equiv) was added and the mixture was stirred for further 30 min while allowing it to warm up to room temperature. Then, the solvent was removed under reduced pressure. The resulting oil was taken up in Et_2O and filtered through silica. Solvent was removed *in vacuo*. Anhydrous THF (12.0 mL) was then added to the residue under inert atmosphere. The solution was cooled down at –78 ºC and n-BuLi (2.5M solution in hexane, 2 mL, 5 mmol, 2.00 equiv) was added dropwise. After stirring at –78 ºC for 1 h, D2O (1.5 mL, 83.3 mmol, 33.3 equiv) was added and the mixture was stirred for further 30 min while allowing it to warm up to room temperature. Then, the solvent was removed under reduced pressure. The resulting oil was taken up in Et_2O and filtered through silica. Solvent was removed *in vacuo* and following recrystallisation from cold hexane afforded the title product **1p-D** as a yellow solid in 81% yield (0.607 mg, 2.02 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.18 (s, 3H), 3.79 (s, 3H), 2.86-2.75 (m, 2H), 2.71-2.60 (m, 1H), 2.54-2.42 (m, 1H), 1.92-1.70 (m, 4H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 236.2, 144.3, 113.7, 104.8, 98,3, 80.8 (t, J_{C-D} = 26.5 Hz), 80.8 (t, J_{C-D} = 26.8 Hz), 29.7, 28.8, 23.6, 23.3. IR: ν = 2939, 2862, 1940, 1830, 1525, 1457, 1410 cm-1. Mp: 82-84 ^{o}C.

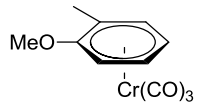


1q

2-Ethoxy-1,2,3,4-tetrahydronaphthalene chromium tricarbonyl (1q).

General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and 2-ethoxy-1,2,3,4-tetrahydronaphthalene (0.880 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1q** as a yellow solid in 80% yield (1.238 g, 3.96 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.81 (d, *J* = 6.8 Hz, 1H), 5.41 (dd, *J* = 7.2, 2.0 Hz, 1H), 5.37 (s, 1H), 4.10-3.92 (m, 2H), 2.84-2.70 (m, 2H), 2.65 (dt, *J* = 16.4, 6.0 Hz, 1H), 2.46 (dt , *J* = 16.4, 6.0 Hz, 1H), 1.92-1.68 (m, 4H), 1.36 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz,

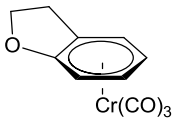
$(CD_3)_2CO$): δ (ppm) = 236.3, 143.7, 113.8, 104.6, 98.5, 81.3, 81.2, 65.9, 29.7, 28.8, 23.6, 13.3, 15.5. IR: ν = 2939, 2863, 1940, 1831, 1521, 1457, 1410, 1299 cm-1. Mp: 88-90 °C.



1r

1-Methoxy-2-methylbenzene chromium tricarbonyl (1r).

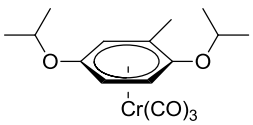
General procedure A was applied with $Cr(CO)_6$ (1.43 g, 6.5 mmol, 1.3 equiv) and 1-methoxy-2-methylbenzene (0.610 g, 5 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1r** as a yellow solid in 84% yield (1.093 g, 4.23 mmol g). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.85 (d, *J* = 6.4 Hz, 1H), 5.71 (td, *J* = 6.8, 1.2 Hz, 1H), 5.62 (d, *J* = 6.8 Hz Hz, 1H), 5.22 (*app* t, *J* = 6.4 Hz, 1H), 3.86 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 235.9, 143.7, 100.3, 99.7, 95.7, 89.1, 78.3, 57.2, 16.9. IR: ν = 2984, 1934, 1860, 1466, 1307, 1078, 957 cm-1. Mp: 85-87 °C. HRMS EI+ *m/z* calcd. $C_{11}H_9CrO_4$: $[M+H]^+$ 259.0062 found: $[M+H]^+$ 259.0057.



1s

2,3-Dihydrobenzofuran chromium tricarbonyl (1s).

General procedure A was applied with chromium hexacarbonyl (1.43 g, 6.5 mmol, 1.3 equiv) and 2,3-dihydrobenzofuran (0.601 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1s** as a yellow solid in 81% yield (1.05 g, 4.12 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 6.05 (d, *J* = 6.0 Hz, 1H), 5.67 (app dt, *J* = 6.8, 1.2 Hz, 1H), 5.51 (d, *J* = 6.8 Hz, 1H), 5.12 (app dt, *J* = 6.4, 0.4 Hz, 1H), 4.70 (ddd, *J* = 10.0, 9.2, 3.6 Hz, 1H), 4.49 (app dt, *J* = 10.4, 8.8 Hz, 1H), 3.33 (app dt, *J* = 15.2, 10.4 Hz, 1H), 3.04 (ddd, *J* = 15.2, 8.8, 3.2 Hz, 1H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 235.8, 145.6, 99.7, 96.6, 94.8, 87.8, 78.4, 73.4, 30.3. IR: ν = 2984, 1943, 1842, 1455, 1179, 931 cm^{-1}. Mp: 84-86 °C. HRMS EI+ *m/z* calcd. $C_{11}H_9CrO_4$: $[M+H]^+$ 256.9906 found: $[M+H]^+$ 256.9897.

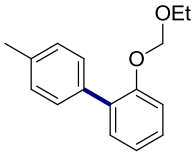


1t

1,4-Diisopropyl-2-methylbenzene tricarbonyl chromium (1t).

General procedure A was applied with chromium hexacarbonyl (1.43 g, 6.5 mmol, 1.3 equiv) and 1,4-diisopropyl-2-methylbenzene (1.06 g, 5.0 mmol, 1.0 equiv). Recrystallization from cold hexane gave the title product **1t** as a yellow solid in 84% yield (1.44 g, 4.18 mmol). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 5.70 (d, *J* = 7.2 Hz, 1H), 5.56 (s, 1H), 5.32 (d, *J* = 7.2 Hz, 1H), 4.42-4.34 (m, 2H), 2.20 (s, 3H), 1.37-1.25 (m, 12H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) 236.7, 138.4, 134.4, 103.2, 86.4, 82.3, 79.0, 74.5, 73.4, 23.4, 23.1,

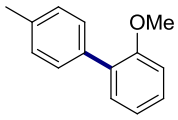
22.9 (×2), 17.4. IR: ν = 2982, 1941, 1845, 1471, 1222, 1103 cm^{-1}. Mp: 72-74 °C. HRMS EI+ *m/z* calcd. $C_{16}H_{21}CrO_5$: $[M+H]^+$ 345.0794 found: $[M+H]^+$ 345.0789.



3aa

2-(Ethoxymethoxy)-4'-methyl-1,1'-biphenyl (3aa)

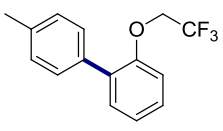
General procedure B was applied with arene chromium complex **1a** and 4-iodotoluene **2a**. Flash chromatography (gradient 1-5% Et_2O in hexane) that was performed prior to demetallation afforded the corresponding biaryl $Cr(CO)_3$ complex. AcOH (2 mL) and MnO_2 (130 mg, 1.5 mmol, 3 equiv) were then added and the black suspension was vigorously stirred for 30 min. The suspension was then loaded on a short silica plug (2 x 4 cm) and eluted with Et_2O (30 mL). Removal of solvent in vacuo afforded the title **3aa** as colourless oil in 73% yield (88.6 mg, 0.366 mmol). Crude ^1H NMR of the reaction shows an isomer ratio o:o,o:o,p = 26:1:1.7 which corresponds to a o:m:p = 95:0:5 ratio. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.43 (d, *J* = 7.6 Hz, 2H), 7.35-7.20 (m, 5H), 7.07 (app t, *J* = 6.8 Hz, 1H), 5.16 (s, 2H), 3.66 (q, *J* = 7.2 Hz, 2H), 2.40 (s, 3H), 1.19 (t, *J* = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.6, 136.7, 135.9, 131.9, 131.0, 129.6, 128.9, 128.5, 122.2, 115.8, 93.9, 64.4, 21.3, 15.2. IR: ν = 2976, 1600, 1485, 1218, 1103, 993 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{16}H_{21}O_2N$: $[M+NH_4]^+$ 260.1645; found: $[M+NH_4]^+$ 260.1647.



3ba

2-Methoxy-4'-methyl-1,1'-biphenyl (3ba).[4]

Modification of the general procedure B was applied using *p*-NMe_2PhCO_2H (0.5 equiv) instead of 1-$AdCO_2H$ with arene chromium complex **1b** and 4-iodotoluene **2a**. Flash chromatography (gradient 0.01-5% DCM in hexane) afforded the title product **3ba** as colourless oil in 69% yield (68.3 mg, 0.345 mmol). Crude ^1H NMR of the reaction shows an isomer ratio o:o.o:o.p = 18:1:1.3 which corresponds to a o:m:p = 94:0:6. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.47 (d, *J* = 8.4 Hz, 2H), 7.34 (app dt, *J* = 7.6, 1.2 Hz, 2H), 7.29-7.23 (m, 2H), 7.06 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.03-6.99 (m, 1H), 3.84 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 156.6, 136.7, 135.7, 130.9, 130.8, 129.5, 128.9, 128.5, 120.9, 111.3, 55.6, 21.3. IR: ν = 3014, 1694, 1455, 1164, 1021 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{14}H_{15}O$: $[M+H]^+$ 199.1118 found: $[M+H]^+$ 199.1117.

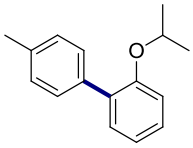


3ca

4'-methyl-2-(2,2,2-trifluoroethoxy)-1,1'-biphenyl (3ca).

Modification of the general procedure B was applied using *p*-NMe_2PhCO_2H (0.5 equiv) instead of 1-$AdCO_2H$ with arene chromium complex **1c** and 4-iodotoluene **2a**. Flash chromatography (gradient 0.01-5% DCM in hexane)

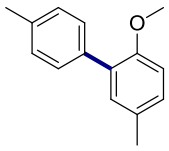
afforded the title product **3ca** as colourless oil in 80% yield (106.4 mg, 0.400 mmol). Crude ^{1}H NMR of the reaction shows an isomer ratio o: o,o: o,p = 28:1.7:1 which corresponds to a o:m:p = 97:0:3 ratio. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.44 (d, *J* = 8.0 Hz, 2H), 7.38 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.34-7.28 (m, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.15 (app t, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 4.24 (q, *J* = 8.4 Hz, 1H) , 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.7, 137.2, 134.7, 132.1, 131.5, 129.4, 129.0, 128.6, 123.5 (d, $J_{C\text{-}F}$ = 248.6 Hz), 123.4, 114.8, 67.0 (q, $J_{C\text{-}F}$ = 35.3 Hz), 21.3. IR: ν = 2930, 1488, 1229, 1163, 977 cm^{-1}.



3da

2-isopropoxy-4'-methyl-1,1'-biphenyl (3da).

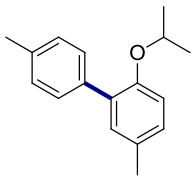
General procedure B was applied with arene chromium complex **1d** and 4-iodotoluene **2a**. Flash chromatography (gradient 1-5% Et_2O in hexane) was performed prior to demetallation affording the corresponding biaryl $Cr(CO)_3$ complex. AcOH (2 mL) and MnO_2 (130 mg, 1.5 mmol, 3 equiv) were then added and the black suspension was vigorously stirred for 30 min. The suspension was then loaded on a short silica plug (2 x 4 cm) and eluted with Et_2O (30 mL). Removal of the solvent *in vacuo* afforded the title product **3da** as colourless oil in 64% yield (72.5 mg, 0.320 mmol). Crude ^{1}H NMR of the reaction shows an isomer ratio o: o,o: o,p = 9:1:1 which corresponds to a o:m:p = 92:0:8 ratio. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.37 (d, *J* = 8.4 Hz, 2H), 7.23 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.16 (dt, *J* = 8.0, 1.6 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 6.94-6.85 (m, 2H), 4.33 (septet, *J* = 6.4 Hz, 1H), 2.30 (s, 3H), 1.16 (d, *J* = 6.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 155.0, 136.4, 136.1, 132.2, 131.2, 129.6, 128.7, 128.2, 121.2, 115.4, 71.0, 22.2, 21.3. IR: ν = 3024, 2976, 1481, 1259, 1108 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{16}H_{19}O$: $[M+H]^+$ 227.1430 found: $[M+H]^+$ 227.1432.



3ea

2-Methoxy-4',5-dimethyl-1,1'-biphenyl (3ea). [5]

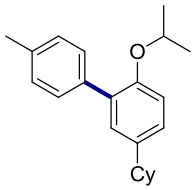
General procedure B was applied with arene chromium complex **1e** and 4-iodotoluene **2a**. Flash chromatography (gradient 0.01-5% DCM in hexane) afforded the title product **3ea** as colourless oil in 74% yield (78.4 mg, 0.370 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.33 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.05-6.97 (m, 2H), 6.78 (dd, *J* = 8.0, 2.4 Hz, 1H), 3.68 (s, 3H), 2.30 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.6, 136.6, 135.8, 131.7, 130.6, 130.1, 129.5, 128.8, 128.7, 111.5, 55.9, 21.3, 20.6. IR: ν = 3021, 2921, 1495, 1237, 1028, 820 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{15}H_{17}O$: $[M+H]^+$ 213.1274 found: $[M+H]^+$ 213.1274.



3fa

2-Isopropoxy-4',5-dimethyl-1,1'-biphenyl (3fa).

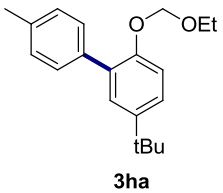
General procedure C was applied with arene chromium complex **1f** and 4-iodotoluene **2a**. Flash chromatography (gradient 0.01-5% DCM in hexane) afforded the title product **3fa** as colourless oil in 64% yield (77.1 mg, 0.321 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.49 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 7.6 Hz, 2H), 7.18 (d, *J* = 2.0 Hz, 1H), 7.09 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 4.35 (septet, *J* = 6.0 Hz, 1H), 2.42 (s, 3H), 2.36 (s, 3H), 1.25 (d, *J* = 6.0 Hz, 6H) . ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 152.9, 136.3, 136.2, 132.2, 131.8, 130.6, 129.5, 128.9, 128.7, 116.2, 71.4, 22.2, 21.3, 20.7. IR: ν = 3021, 2975, 1492, 1230, 1110, 953 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{17}H_{21}O$: $[M+H]^+$ 241.1587 found: $[M+H]^+$ 241.1587.



3ga

5-Cyclohexyl-2-isopropoxy-4'-methyl-1,1'-biphenyl (3ga).

General procedure C was applied with arene chromium complex **1g** and 4-iodotoluene **2a**. Flash chromatography (gradient 1-5% Et_2O in hexane) was performed prior to demetallation affording the corresponding biaryl $Cr(CO)_3$ complex. AcOH (2 mL) and MnO_2 (130 mg, 1.5 mmol, 3 equiv) were then added and the black suspension was vigorously stirred for 30 min. The suspension was then loaded on a short silica plug (2 x 4 cm) and eluted with Et_2O (30 mL) before concentrating *in vacuo* and afford the title product **3ga** as colourless oil in 76% yield (117.1 mg, 0.380 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.38 (d, *J* = 8.0 Hz, 2H), 7.14-7.05 (m, 3H), 6.99 (dd, *J* = 8.0, 2.4 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 4.27 (septet, *J* = 6.0 Hz, 1H), 2.48-2.32 (m, 1H), 2.30 (s, 3H), 1.85-1.60 (m, 5H), 1.14-1.15 (m, 5H), 1.14 (d, *J* = 6.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 153.1, 140.8, 136.5, 136.2, 131.8, 129.6, 129.6, 128.6, 126.3, 115.4, 71.1, 43.9, 34.8, 27.1, 26.3, 22.3, 21.3. IR: ν = 3022, 2922, 1488, 1235, 1111 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{22}H_{29}O$: $[M+H]^+$ 309.2213 found: $[M+H]^+$ 309.2213.

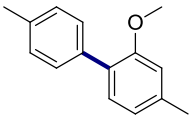


3ha

5-(Tert-butyl)-2-(ethoxymethoxy)-4'-methyl-1,1'-biphenyl (3ha).

General procedure C was applied with arene chromium complex **1h** and 4-iodotoluene **2a**. Flash chromatography (gradient 1-5% DCM in hexane) afforded the title product **3ha** as colourless oil in 81% yield (120.7 mg, 0.404 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.50 (d, *J* = 7.2 Hz, 2H), 7.42-7.34 (m, 2H), 7.29 (d, *J* = 7.2 Hz, 2H), 7.24 (dd, *J* = 8.4, 1.2 Hz, 1H), 5.20 (s, 2H), 3.67 (q, *J* = 7.2 Hz, 2H), 2.47 (s, 3H), 1.40 (s, 9H), 1.21 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 152.4, 144.9, 136.6, 136.4, 131.3,

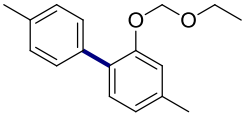
129.6, 128.8, 128.1, 125.3, 115.6, 94.1, 64.3, 34.4, 31.7, 21.3, 15.2. IR: ν = 3025, 2960, 1517, 1493, 1223, 1104, 994 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{19}H_{25}O_2$: $[M+H]^+$ 285.1855; found: $[M+H]^+$ 285.1883.



3ia

2-Methoxy-4,4'-dimethyl-1,1'-biphenyl (3ia).

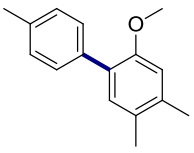
General procedure B was applied with arene chromium complex **1i** and 4-iodotoluene **2a**. Flash chromatography (gradient 2-10% DCM in hexane) afforded the title product **3ia** as colourless oil in 69% yield (73.5 mg, 0.346 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.32 (d, *J* = 8.4 Hz, 2H), 7.15-7.06 (m, 3H), 6.74 (d, *J* = 7.6 Hz, 1H), 6.70 (s, 1H), 3.69 (s, 3H), 2.30 (s, 3H), 2.29 (s, 3H) ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 156.5, 138.5, 136.4, 135.8, 130.7, 129.5, 128.8, 128.0, 121.6, 112.3, 55.6, 21.7, 21.3. IR: ν = 2919, 1610, 1495, 1275, 1005, 804 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{15}H_{17}O$: $[M+H]^+$ 213.1274; found: $[M+H]^+$ 213.1271.



3ja

2-(Ethoxymethoxy)-4,4'-dimethyl-1,1'-biphenyl (3ja).

General procedure B was applied with arene chromium complex **1j** and 4-iodotoluene **2a**. Flash chromatography (gradient 2-10% DCM in hexane) afforded the title product **3ja** as colourless oil in 73% yield (93.5 mg, 0.365 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.42 (d, *J* = 8.0 Hz, 2H), 7.25-7.20 (m, 3H), 7.08 (d, *J* = 0.4 Hz, 1H), 6.91 (ddd, *J* = 7.6, 1.6, 0.4 Hz, 1H), 5.17 (s, 2H), 3.67 (q, *J* = 7.1 Hz, 2H), 2.41 (s, 3H), 2.40 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.4, 138.6, 136.4, 135.9, 130.7, 129.5, 129.0, 128.8, 123.0, 116.6, 93.9, 64.4, 21.5, 21.3, 15.2. IR: ν = 3023, 2976, 1578, 1494, 1162, 1104, 999 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{17}H_{24}O_2N$: $[M+NH_4]^+$ 274.1800; found: $[M+NH_4]^+$ 274.1788.

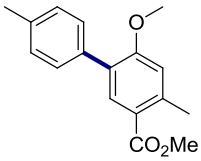


3ka

2-Methoxy-4,4',5-trimethyl-1,1'-biphenyl (3ka).

General procedure C was applied with arene chromium complex **1k** and 4-iodotoluene **2a**. Flash chromatography (gradient 2-10% DCM in hexane) afforded the title product **3ka** as colourless oil in 93% yield (104.9 mg, 0.463 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.32 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.98 (s, 1H), 6.68 (s, 1H), 3.66 (s, 3H), 2.27 (s, 3H), 2.20 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ

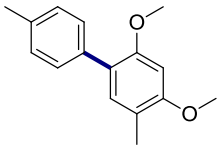
(ppm) = 154.6, 136.6, 136.3, 135.8, 132.1, 129.5, 128.8, 128.6, 128.2, 113.2, 55.9, 21.3, 20.0, 18.8 IR: ν = 3020, 2920, 1612, 1497, 1203, 820 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{16}H_{19}O$: $[M+H]^+$ 227.1430; found: $[M+H]^+$ 227.1430.



3la

Methyl 6-methoxy-4,4'-dimethyl-[1,1'-biphenyl]-3-carboxylate (3la).

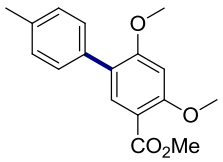
General procedure C was applied with arene chromium complex **1l** and 4-iodotoluene **2a**. Flash chromatography (gradient 10-20% Et_2O in hexane) afforded the title product **3la** as colourless oil in 88% yield (119.1 mg, 0.441 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.97 (s, 1H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.81 (s, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 2.69 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 167.7, 159.2, 142.3, 137.0, 134.5, 134.7, 133.8, 128.9, 128.2, 121.7, 114.1, 55.7, 51.6, 22.4, 21.3. IR: ν = 2996, 1713, 1469, 1300, 1205, 823 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{17}H_{18}O_3Na_1$: $[M+Na]^+$ 293.1148; found: $[M+Na]^+$ 293.1143.



3ma

2,4-Dimethoxy-4',5-dimethyl-1,1'-biphenyl (3ma).

General procedure C was applied with arene chromium complex **1m** and 4-iodotoluene **2a**. Flash chromatography (gradient 1-5% Et_2O in hexane) afforded the title product **3ma** as colourless oil in 92% yield (111.4 mg, 0.460 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.30 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.99 (s, 1H), 6.43 (s, 1H), 3.78 (s, 3H), 3.69 (s, 3H), 2.28 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 157.8, 155.6, 136.1, 135.7, 132.6, 129.4, 128.8, 122.6, 118.7, 96.0, 56.2, 55.7, 21.3, 15.4. IR: ν = 2923, 2833, 1612, 1504, 1306, 1204, 819 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{16}H_{19}O_2$: $[M+H]^+$ 243.1380; found: $[M+H]^+$ 243.1378.

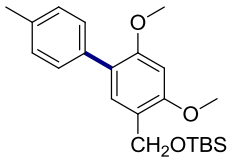


3na

Methyl 4,6-dimethoxy-4'-methyl-[1,1'-biphenyl]-3-carboxylate (3na).

General procedure C was applied with arene chromium complex **1n** and 4-iodotoluene **2a**. Flash chromatography (gradient 10-20% Et_2O in hexane) afforded the title product **3na** as colourless oil in 86% yield (123.3 mg, 0.431 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.88 (s, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.56 (s, 1H), 3.98 (s, 3H), 3.88 (s, 3H), 3.87 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 166.1, 161.0, 160.9, 136.7, 134.5, 134.4, 129.4, 128.9, 123.0, 111.9, 95.9, 56.4,

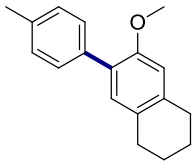
55.8, 51.8, 21.3. IR: ν = 2996, 1713, 1563, 1300, 1205, 822 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{17}H_{19}O_4$: $[M+H]^+$ 287.1278; found: $[M+H]^+$ 287.1279.



3oa

tert-Butyl((4,6-dimethoxy-4'-methyl-[1,1'-biphenyl]-3-yl)methoxy)dimethylsilane (3oa).

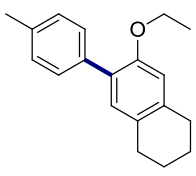
General procedure C was applied with arene chromium complex **1o** and 4-iodotoluene **2a**. Flash chromatography (gradient 1-5% Et_2O in hexane) afforded the title product **3oa** as colourless oil in 89% yield (166.0 mg, 0.446 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.45 (d, *J* = 8.0 Hz, 2H), 7.43 (s, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.55 (s, 1H), 4.77 (s, 2H), 3.90 (s, 3H), 3.83 (s, 3H), 2.41 (s, 3H), 0.97 (s, 9H), 0.14 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 156.6, 156.5, 136.0, 135.8, 129.9, 129.4, 128.8, 122.7, 122.1, 95.6, 60.1, 56.1, 55.6, 26.2, 21.3, 18.6, -5.1 IR: ν = 2984, 2855, 1614, 1461, 1274, 1141, 819 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{22}H_{33}O_3Si$: $[M+H]^+$ 373.2193; found: $[M+H]^+$ 373.2004.



3pa

6-Methoxy-7-(p-tolyl)-1,2,3,4-tetrahydronaphthalene (3pa).

General procedure C was applied with arene chromium complex **1p** and 4-iodotoluene **2a**. Flash chromatography (gradient 2-10% DCM in hexane) afforded the title product **3pa** as colourless oil in 90% yield (113.8 mg, 0.451 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.31 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.91 (s, 1H), 6.57 (s, 1H), 3.66 (s, 3H), 2.75-2.58 (m, 4H), 2.28 (s, 3H), 1.78-1.62 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.5., 137.2, 136.4, 135.8, 131.4, 129.5, 129.3, 128.8, 128.5, 111.8, 55.8, 29.7, 28.7, 23.6, 23.4, 21.3. IR: ν = 2923, 1610, 1496, 1224, 1038, 730 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{18}H_{21}O_1$: $[M+H]^+$ 253.1587; found: $[M+H]^+$ 253.1587.

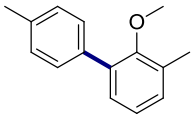


3qa

6-Ethoxy-7-(p-tolyl)-1,2,3,4-tetrahydronaphthalene (3qa).

General procedure C was applied with arene chromium complex **1q** and 4-iodotoluene **2a**. Flash chromatography (gradient 2-10% DCM in hexane) afforded the title product **3qa** as colourless oil in 88% yield (117.1 mg, 0.440 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.45 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 7.2 Hz, 2H), 7.03 (s, 1H), 6.68 (s, 1H), 3.99 (q, *J* = 6.8 Hz, 2H), 2.84-2.70 (m, 4H), 2.40 (s, 3H), 1.92-1.70 (m, 4H). ^{13}C NMR

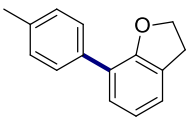
(101 MHz, $CDCl_3$): δ (ppm) = 153.8, 137.1, 136.2, 135.9, 131.5, 129.5, 129.4, 128.7, 113.5, 64.4, 29.7, 28.7, 23.6, 23.4, 21.3, 15.0. IR: ν = 2923, 1611, 1496, 1392, 1065, 820 cm^{-1}.



3ra

2-Methoxy-3,4'-dimethyl-1,1'-biphenyl (3ra).

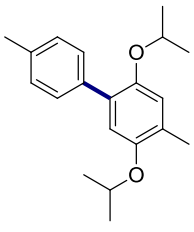
General procedure B was applied with arene chromium complex **1r** and 4-iodotoluene **2a**. Flash chromatography (gradient 1-5% Et_2O in hexane) was performed prior to demetallation and afforded the corresponding biaryl $Cr(CO)_3$ complex. AcOH (2 mL) and MnO_2 (130 mg, 1.5 mmol, 3 equiv) were then added and the black suspension was vigorously stirred for 30 min. The suspension was then loaded on a short silica plug (2 x 4 cm) and eluted with Et_2O (30 mL). Removal of the solvent *in vacuo* afforded the title product **3ra** as colourless oil in 12% yield. Crude ^1H NMR of the reaction shows an isomer ratio o:p= 4:1. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.49 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.20-7.14 (m, 2H), 7.06 (*app* t, J = 7.6 Hz, 1H), 3.39 (s, 3H), 2.40 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 156.1, 136.7, 136.0, 134.9, 131.6, 130.2, 129.1, 129.1, 128.9, 124.0. 59.9, 21.3, 16.4. IR: ν = 2967, 1613, 1421, 1234, 1039, 960 cm^{-1}.



3sa

7-(*p*-Tolyl)-2,3-dihydrobenzofuran (3sa).

General procedure B was applied with arene chromium complex **1s** and 4-iodotoluene **2a** without the employment of 2,2,6,6-tetramethylpiperidine and for longer reaction time (60h). Flash chromatography (gradient 2-10% DCM in hexane) afforded the title product **3sa** as colourless oil in 72% yield. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.50 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.83 (*app* t, *J* = 7.6 Hz, 1H), 4.50 (t, *J* = 8.8 Hz, 2H), 3.16 (t, *J* = 8.8 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 157.3, 136.9, 134.6, 129.2, 128.3, 127.8, 123.8, 123.7, 120.9, 71.1, 30.0, 21.3. IR: ν = 2975, 1517, 1450, 1201, 986, 821 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{15}H_{15}O$: $[M+H]^+$ 211.1117; found: $[M+H]^+$ 211.1117.

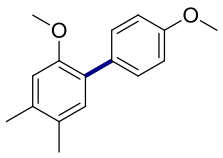


3ta

2,5-Diisopropoxy-4,4'-dimethyl-1,1'-biphenyl (ta).

General procedure C was applied with arene chromium complex **1t** and 4-iodotoluene **2a**. Flash chromatography (gradient 1-5% Et_2O in hexane) that was performed prior to demetallation afforded the corresponding biaryl $Cr(CO)_3$

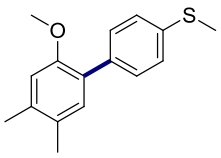
complex. AcOH (2 mL) and MnO_2 (130 mg, 1.5 mmol, 3 equiv) were then added and the black suspension was vigorously stirred for 30 min. The suspension was then loaded on a short silica plug (2 x 4 cm) and eluted with Et_2O (30 mL) before concentrating *in vacuo* and afford the title product **3ta** as colourless oil in 81% yield (120.7 mg, 0.404 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.49 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.87 (s, 1H), 6.84 (s, 1H), 4.46 (septet, *J* = 6.0 Hz, 1H), 4.21 (septet, *J* = 6.0 Hz, 1H), 2.42 (s, 3H), 2.27 (s, 3H), 1.37 (d, *J* = 6.0 Hz, 6H), 1.20 (d, *J* = 6.0 Hz, 6H) ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 150.9, 148.7, 136.4, 136.2, 130.7, 129.5, 128.7, 128.0, 120.3, 117.1, 72.4, 71.5, 22.5, 22.3, 21.3, 16.5. IR: ν = 2974, 1492, 1381, 1196, 957, 820 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{20}H_{27}O_2$: $[M+H]^+$ 299.2006; found: $[M+H]^+$ 299.2006.



3kb

2,4'-Dimethoxy-4,5-dimethyl-1,1'-biphenyl (3kb).

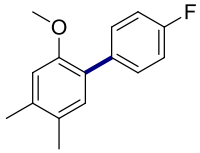
General procedure C was applied with arene chromium complex **1k** and 4-iodoanisole **2b**. Flash chromatography (gradient 2-20% DCM in hexane) afforded the title product **3kb** as colourless oil in 91% yield (110.2 mg, 0.455 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.59 (d, *J* = 8.8 Hz, 2H), 7.21 (s, 1H), 7.06 (d, *J* = 8.8 Hz, 2H), 6.90 (s, 1H), 3.93 (s, 3H), 3.89 (s, 3H), 2.42 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 158.5, 154.5, 136.3, 131.9, 131.1, 130.6, 128.6, 127.7, 113.5, 113.2, 55.8, 55.2, 19.9, 18.8. IR: ν = 2835, 2863, 1578, 1497, 1243, 831 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{16}H_{19}O_2$: $[M+H]^+$ 243.1380; found: $[M+H]^+$ 243.1378.



3kc

(2'-Methoxy-4',5'-dimethyl-[1,1'-biphenyl]-4-yl)(methyl)sulfane (3kc).

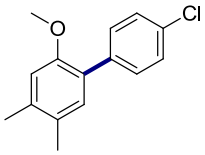
General procedure C was applied with arene chromium complex **1k** and 4-iodothioanisole **2c**. Flash chromatography (gradient 2-15% DCM in hexane) afforded the title product **3kc** as colourless oil in 90% yield (116.4 mg, 0.450 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.53 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.15 (s, 1H), 6.85 (s, 1H), 3.84 (s, 3H), 2.56 (s, 3H), 2.38 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.5, 136.9, 136.6, 135.6, 131.9, 129.9, 128.7, 127.4, 126.5, 113.3, 55.9, 20.0, 18.8, 16.1 IR: ν = 2918, 1899, 1463, 1487, 1204, 1043, 823 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{16}H_{19}OS$: $[M+H]^+$ 259.1151; found: $[M+H]^+$ 259.1148.



3kd

4'-Fluoro-2-methoxy-4,5-dimethyl-1,1'-biphenyl (3kd).

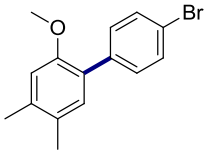
General procedure C was applied with arene chromium complex **1k** and 1-fluoro-4-iodobenzene **2d**. Flash chromatography (gradient 2-10% DCM in hexane) afforded the title product **3kd** as colourless oil in 90% yield (103.9 mg, 0.451 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.40-7.33 (m, 2H), 6.99-6.91 (m, 3H), 6.67 (s, 1H), 3.66 (s, 3H), 2.19 (s, 3H), 2.13 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 162.3 (d, *J* = 246.1 Hz), 154.5, 137.0, 134.6, 132.0, 131.1 (d, *J* = 8.0 Hz, 1H), 128.7, 127.1, 114.9 (d, *J* = 21.2 Hz), 113.3, 55.9, 20.0, 18.8. IR: ν = 2936, 2862, 1603, 1497, 1219, 1045, 835 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{15}H_{16}OF$: $[M+H]^+$ 231.1180; found: $[M+H]^+$ 231.1177.



3ke

4'-Chloro-2-methoxy-4,5-dimethyl-1,1'-biphenyl (3ke).

General procedure C was applied with arene chromium complex **1k** and 1-chloro-4-iodobenzene **2e**. Flash chromatography (gradient 2-10% DCM in hexane) afforded the title product **3ke** as colourless oil in 91% yield (112.1 mg, 0.454 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.51 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.12 (s, 1H), 6.84 (s, 1H), 3.83 (s, 3H), 2.37 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.5, 137.3, 137.1, 132.6, 131.9, 130.9, 128.8, 128.2, 126.8, 113.3, 55.9, 20.1, 18.8 IR: ν = 2936, 2838, 1613, 1486, 1295, 1090, 830 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{15}H_{16}OCl$: $[M+H]^+$ 247.0084; found: $[M+H]^+$ 247.0880.

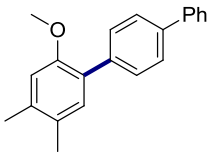


3kf

4'-Bromo-2-methoxy-4,5-dimethyl-1,1'-biphenyl (3kf).

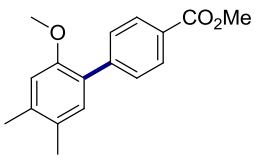
General procedure C was applied with arene chromium complex **1k** and 1-bromo-4-iodobenzene **2f**. Flash chromatography (gradient 2-10% DCM in hexane) afforded the title product **3kf** as colourless oil in 91% yield (132.7 mg, 0.456 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.59 (d, *J* = 8.8 Hz, 2H), 7.49 (d, *J* = 8.8 Hz, 2H), 7.15 (s, 1H), 6.87 (s, 1H), 3.86 (s, 3H), 2.40 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.4, 137.6, 137.4, 131.8, 131.2, 128.8, 126.8, 120.8, 113.3, 55.8, 20.1, 18.8. IR: 2935, 1611, 1484, 1205, 1044, 826 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{15}H_{16}OBr$: $[M+H]^+$ 291.0379; found: $[M+H]^+$ 291.0378.

2-Methoxy-4,5-dimethyl-1,1':4',1''-terphenyl (3kg).



3kg

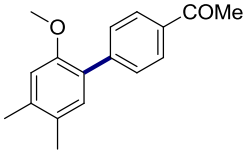
General procedure C was applied with arene chromium complex **1k** and 4-iodo-1,1'-biphenyl **2g**. Flash chromatography (gradient 3-15% DCM in hexane) afforded the title product **3kg** as colourless oil in 89% yield (128.5 mg, 0.446 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.52-7.48 (m, 6H), 7.35-7.29 (m, 2H), 7.24-7.12 (m, 1H), 7.04 (s, 1H), 6.60 (s, 1H), 3.68 (s, 3H), 2.20 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.7, 141.2, 139.5, 137.7, 137.0, 132.1, 130.0, 128.8, 128.7, 127.6, 127.2 (x2), 126.8, 113.3, 55.9, 20.1, 18.9. IR: ν = 3057, 2935, 1601, 1484, 1204, 1127, 841 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{21}H_{21}O$: $[M+H]^+$ 288.1509; found: $[M+H]^+$ 288.1506.



3kh

Methyl 2'-methoxy-4',5'-dimethyl-[1,1'-biphenyl]-4-carboxylate (3kh).

General procedure C was applied with arene chromium complex **1k** and 4-methyl iodobenzoate **2h**. Flash chromatography (gradient 1-5% Et_2O in hexane) afforded the title product **3kh** as colourless oil in 89% yield (120.1 mg, 0.445 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.10 (d, *J* = 8.8 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.15 (s, 1H), 6.84 (s, 1H), 3.96 (s, 3H), 3.81 (s, 3H), 2.35 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 167.2, 154.6, 143.5, 137.8, 131.9, 129.5, 129.3, 128.8, 128.2, 126.9, 113.3, 55.8, 52.0, 20.0, 18.8 IR: ν = 2949, 1718, 1607, 1274, 1101, 706 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{17}H_{19}O_3$: $[M+H]^+$ 271.1329; found: $[M+H]^+$ 271.1328.

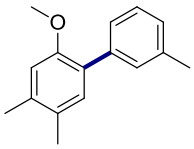


3ki

1-(2'-Methoxy-4',5'-dimethyl-[1,1'-biphenyl]-4-yl)ethanone (**3ki).**

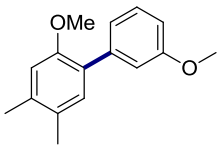
General procedure B was applied with arene chromium complex **1k** and 4'-iodoacetophenone **2i**. Flash chromatography (gradient 1-5% Et_2O in hexane) afforded the title product **3ki** as colourless oil in 89% yield (113.0 mg, 0.445 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.00 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.12 (s, 1H), 6.82 (s, 1H), 3.81 (s, 3H), 2.63 (s, 3H), 2.34 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 197.9, 154.6, 143.8, 138.0, 135.3, 131.9, 129.7, 128.9, 128.1, 126.8, 113.3, 55.9, 26.7, 20.1, 18.8 IR: ν = 2999, 1678, 1603, 1265, 1101, 842 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{17}H_{19}O_2$: $[M+H]^+$ 255.1380; found: $[M+H]^+$ 255.1373.

2-Methoxy-3',4,5-trimethyl-1,1'-biphenyl (3kj).



3kj

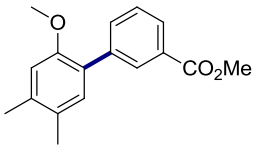
General procedure C was applied with arene chromium complex **1k** and 3-iodotoluene **2j**. Flash chromatography (gradient 2-5% DCM in hexane) afforded the title product **3kj** as colourless oil in 89% yield (100.6 mg, 0.445 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.42-7.31 (m, 3H), 7.18 (d, *J* = 7.2 Hz, 1H), 7.15 (s, 1H), 6.85 (s, 1H), 3.83 (s, 3H), 2.46 (s, 3H), 2.37 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.6, 138.7, 137.5, 136.8, 132.2, 130.3, 128.6, 128.3, 127.9, 127.5, 126.8, 113.3, 59.9, 21.7, 20.1, 18.9. IR: ν = 2920, 1605, 1301, 1250, 1052, 843 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{16}H_{19}O$: $[M+H]^+$ 227.1430; found: $[M+H]^+$ 227.1428.



3kk

2,3'-Dimethoxy-4,5-dimethyl-1,1'-biphenyl (3kk).

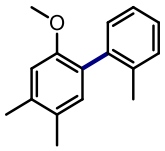
General procedure C was applied with arene chromium complex **1k** and 3-iodoanisole **2k**. Flash chromatography (gradient 2-5% Et_2O in hexane) afforded the title product **3kk** as colourless oil in 87% yield (105.3 mg, 0.435 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.37 (app t, *J* = 8.0 Hz, 1H), 7.20-7.13 (m, 3H), 6.92 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.84 (s, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 2.37 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) =159.4, 154.6, 140.1, 137.0, 132.1, 129.0, 128.7, 128.0, 122.1, 115.4, 113.3, 112.3, 55.9, 55.3, 20.1, 18.8. IR: ν = 2936, 1599, 1480, 1460, 1248, 1040 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{16}H_{19}O_2$: $[M+H]^+$ 243.1380; found: $[M+H]^+$ 243.1379.



3kl

Methyl 2'-methoxy- 4',5'-dimethyl-[1,1'-biphenyl]-3-carboxylate (3kl).

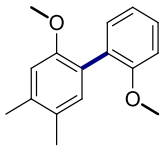
General procedure C was applied with arene chromium complex **1k** and methyl 3-iodobenzoate **2l**. Flash chromatography (gradient 10-25% Et_2O in hexane) afforded the title product **3kl** as colourless oil in 85% yield (115.0 mg, 0.425 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.20 (s, 1H), 7.98 (d, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.46 (*app* t, *J* = 7.6 Hz, 1H), 7.12 (s, 1H), 6.81 (s, 1H), 3.94 (s, 3H), 3.80 (s, 3H), 2.33 (s, 3H), 2.27 (s, 3H) ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 167.4, 154.6, 139.0, 137.5, 134.2, 132.0, 130.7, 130.1, 128.9, 128.0, 127.9, 127.0, 113.3, 59.9, 52.2, 20.1, 18.9 IR: ν = 2950, 1721, 1509, 1305, 1108, 761 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{17}H_{22}O_3N$: $[M+NH_4]^+$ 288.1594; found: $[M+NH_4]^+$ 288.1591.



3km

2-Methoxy-2',4,5-trimethyl-1,1'-biphenyl (3km).

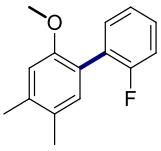
Modification of the general procedure C was applied (2 equiv of iodoarene and 1.0 equiv of Ag_2CO_3 were employed, reaction time = 40 h) with complex **1k** and 2-iodotoluene **2m**. Flash chromatography (gradient 2-5% DCM in hexane) afforded the title product **3km** as colourless oil in 71% yield (80.3 mg, 0.355 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.18-7.06 (m, 4H), 6.83 (s, 1H), 6.68 (s, 1H), 3.64 (s, 3H), 2.24 (s, 3H), 2.15 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.8, 138.8, 137.1, 136.7, 132.4, 130.3, 129.7, 128.3, 128.2, 127.2, 125.5, 112.7, 55.8, 20.2, 20.1, 18.9 IR: ν = 2924, 1614, 1453, 1204, 757 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{16}H_{19}O$: $[M+H]^+$ 227.1430; found: $[M+H]^+$ 227.1428.



3kn

2,2'-Dimethoxy-4,5-dimethyl-1,1'-biphenyl (3kn).

Modification of the general procedure C was applied (2 equiv of iodoarene and 1.0 equiv of Ag_2CO_3 were employed, reaction time = 40h) with complex **1k** and 2-iodoanisole **3n**. Flash chromatography (gradient 2-10% DCM in hexane) afforded the title product **3kn** as colourless oil in 64% yield (77.7 mg, 0.321 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.33 (dt, *J* = 8.0, 1.6 Hz, 1H), 7.24 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.04-6.94 (m, 3H), 6.79 (s, 1H), 3.79 (s, 3H), 3.75 (s, 3H), 2.31 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 157.3, 155.2, 136.9, 132.7, 131.7, 128.5, 128.3, 128.0, 125.3, 120.5, 113.3, 111.1, 56.1, 55.8, 20.2, 18.9 IR: ν = 2935, 1600, 1488, 1242, 1053 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{16}H_{19}O_2$: $[M+H]^+$ 243.1380; found: $[M+H]^+$ 243.1379.

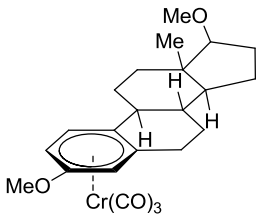


3ko

2'-Fluoro-2-methoxy-4,5-dimethyl-1,1'-biphenyl (3ko).

Modification of the general procedure C was applied (2 equiv of iodoarene and 1.0 equiv of Ag_2CO_3 were employed, reaction time = 40h) with complex **1k** and 2-fluoro iodobenzene **3o**. Flash chromatography (gradient 2-10% DCM in hexane) afforded the title product **3ko** as colourless oil in 59% yield (67.8 mg, 0.295 mmol), . ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.37-7.27 (m, 2H), 7.16 (dt, J = 7.6, 1.6 Hz, 1H), 7.10 (ddd, J = 8.4, 7.6, 1.2 Hz, 1H), 7.04 (s, 1H), 3.78 (s, 3H), 2.32 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 160.2 (d, *J* = 248.1 Hz), 155.1, 137.8, 132.5, 132.1 (d, *J* = 3.6 Hz), 128.8 (d, *J* = 8.2 Hz), 128.5, 126.4 (d, *J* = 16.0 Hz), 123.8 (d, *J* = 3.5 Hz), 122.3, 115.5 (d, *J* = 22.7 Hz), 113.1, 56.0, 20.2, 18.9 IR: ν = 2928, 1514, 1487, 1307, 1233, 1131, 824 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{15}H_{16}OF$: $[M+H]^+$ 231.1185; found: $[M+H]^+$ 231.1174.

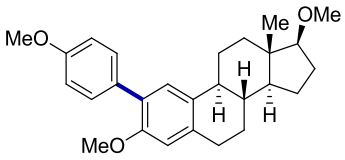
Synthesis, direct arylation and derivatization of $Cr(CO)_3$ estradiol complex 1u



1u

(8*R*,9*S*,13*S*,14*S*,17*S*)-3,17-Dimethoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[*a*]phenanthrene chromium tricarbonyl (1u).

General procedure A was applied with chromium hexacarbonyl (1.43 g, 6.5 mmol, 1.3 equiv) and **4** (8*R*,9*S*,13*S*,14*S*,17*S*)-3,17-dimethoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene (1.50 g, 5.0 mmol, 1.0 equiv).[6] Recrystallization from cold hexane gave the title product **1u** as a yellow solid (2.03 g, 93% yield) as a facial mixture of diastereoisomers (1.1:1). ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 6.08 (minor, d, *J* = 7.2 Hz, 1H), 5.94 (major, d, *J* = 7.2 Hz, 1H), 5.41 (minor, dd, *J* = 7.2 Hz, 1H), 5.35 (major + minor, app d, *J* = 2.4 Hz, 2H), 5.23 (major, dd, *J* = 7.2, 2.4 Hz, 1H), 3.77 (major, s, 3H), 3.73 (minor, s, 3H), 3.33-3.24 (major + minor, m, 8H), 3.10-2.75 (major + minor, m, 4H), 2.30-1.80 (major + minor, m, 8H), 1.77-1.10 (major + minor, m, 18H), 0.81 (major, s, 3H), 0.77 (minor, s, 3H). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 235.9 (major), 235.4 (minor), 144.7 (major), 144.1 (minor), 113.8 (major), 113.4 (minor), 109.0 (major), 106.6 (minor), 95.7 (minor), 94.8 (major), 91.1 (major), 91.0 (minor), 80.5 (major), 80.1 (minor), 79.2 (minor), 77.7 (major), 57.9 (major), 57.9 (minor), 56.2 (major + minor, 2C), 50.6 (major), 50.3 (minor), 44.2 (minor), 43.9 (major + minor, 2C), 43.3 (minor), 39.4 (minor), 38.7 (major), 38.3 (minor), 38.2 (major), 30.7 (major + minor, 2C), 28.4 (minor), 28.3 (major), 27.3 (minor), 27.1 (major), 26.7 (major), 26.6 (minor), 23.7 (minor), 23.6 (minor), 12.0 (minor), 11.9 (major). IR: ν = 2934, 1933, 1861, 1475, 1541, 1381, 1272, 1105, 932 cm^{-1}. Mp: 134-136 °C. HRMS EI+ *m/z* calcd. $C_{23}H_{29}O_5Cr$: $[M+H]^+$ 437.1420; found: $[M+H]^+$ 437.1415.

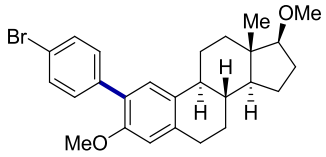


3ub

(8R,9S,13S,14S,17S)-3,17-Dimethoxy-2-(4-methoxyphenyl)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene (3ub).

General procedure C was applied with arene chromium complex **1u** and 4-iodoanisole **2b**. Flash chromatography (gradient 1-10% Et_2O in hexane) afforded the title product **3ub** as colourless oil in 88% yield (178.5 mg, 0.439 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.36 (d, *J* = 8.4 Hz, 2H), 7.13 (s, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.59 (s, 1H), 3.74 (s, 3H), 3.68 (s, 3H), 3.28 (s, 3H), 3.22 (t, *J* = 8.0 Hz, 1H), 2.90-2.72 (m, 2H), 2.28-2.08 (m, 2H), 2.10-1.90 (m, 2H), 1.90-1.75 (m, 1H), 1.67-1.08 (m, 8H), 0.71 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 158.6, 154.4, 136.8, 132.7, 131.4, 130.7, 128.0, 127.9, 113.6, 111.7, 90.9,

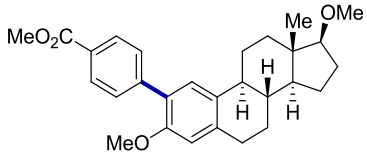
58.0, 55.7, 55.4, 50.4, 44.1, 43.4, 38.8, 38.2, 29.9, 27.9, 27.4, 26.6, 23.2, 11.7. IR: ν = 2838, 1609, 1495, 1356, 904, 727 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{27}H_{34}O_3$: $[M]^+$ 406.2502; found: $[M]^+$ 406.2493.



3uf

(8R,9S,13S,14S,17S)-2-(4-Bromophenyl)-3,17-dimethoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene (3uf).

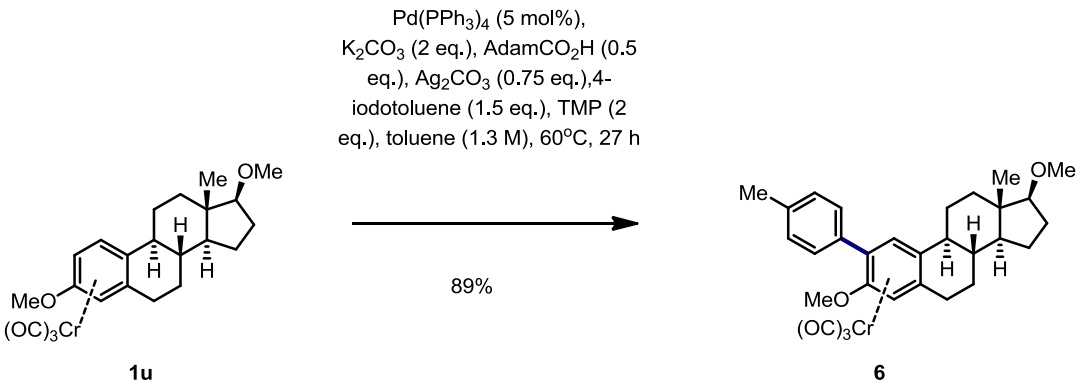
General procedure C was applied with arene chromium complex **1u** and 4-bromo iodobenzene **2f**. Flash chromatography (gradient 1-10% Et_2O in hexane) afforded the title product **3uf** as a white solid in 86% yield (195.4 mg, 0.430 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.54 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.24 (s, 1H), 6.74 (s, 1H), 3.80 (s, 3H), 3.42 (s, 3H), 3.35 (t, *J* = 8.0 Hz, 1H), 3.05-2.80 (m, 2H), 2.39-2.2 (m, 2H), 2.18-2.05 (m, 2H), 2.00-1.91 (m, 1H), 1.80-1.68 (m, 1H), 1.67-1.20 (m, 7H), 0.84 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 154.4, 137.9, 137.7, 132.9, 131.3, 131.1, 127.8, 126.9, 120.8, 111.8, 90.8, 58.0, 55.7, 50.4, 44.0, 43.3, 38.7, 38.1, 29.9, 27.9, 27.4, 26.6, 23.2, 11.7. IR: ν = 2867, 1610, 1482, 1356, 1127, 905, 728 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{26}H_{32}O_2Br$: $[M+H]^+$ 455.1580; found: $[M+H]^+$ 455.1568.



3uh

Methyl 4-((8R,9S,13S,14S,17S)-3,17-dimethoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-2-yl)benzoate (3uh).

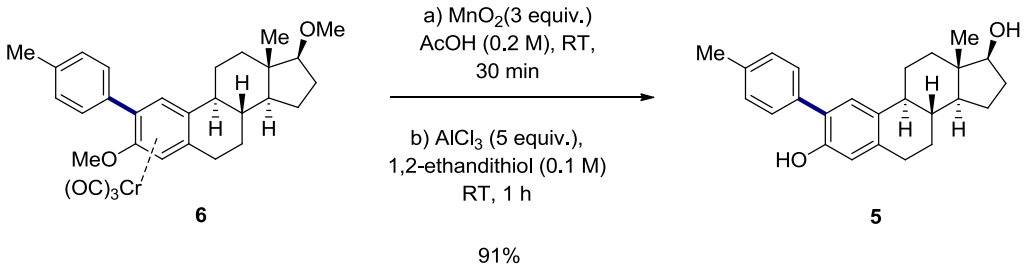
General procedure C was applied with arene chromium complex **1t** and 4-methyl iodobenzoate **2h**. Flash chromatography (gradient 1-10% Et_2O in hexane) afforded the title product **3uh** as colourless oil in 90% yield (195.5 mg, 0.450 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.95 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.14 (s, 1H), 6.60 (s, 1H), 3.82 (s, 3H), 3.67 (s, 3H), 3.27 (s, 3H), 3.21 (t, *J* = 8.4 Hz, 1H), 2.84-2.75 (m, 2H), 2.30-1.90 (m, 4H), 1.86-1.75 (m, 1H), 1.68-1.51 (m, 1H), 1.50-1.05 (m, 7H), 0.70 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 167.2, 154.4, 143.9, 138.2, 132.9, 129.5, 129.2, 128.2, 127.9, 127.1, 111.8, 90.8, 57.9, 55.7, 52.0, 50.3, 43.9, 43.3, 38.7, 38.1, 29.9, 27.8, 27.6, 26.6, 23.1, 11.7. IR: ν = 2932, 1716, 1609, 1277, 905, 727 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{28}H_{35}O_4$: $[M+H]^+$ 435.2530; found: $[M+H]^+$ 435.2525.



(8R,9S,13S,14S,17S)-3,17-Dimethoxy-13-methyl-2-(*p*-tolyl)-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene tricarbonyl chromium (6).

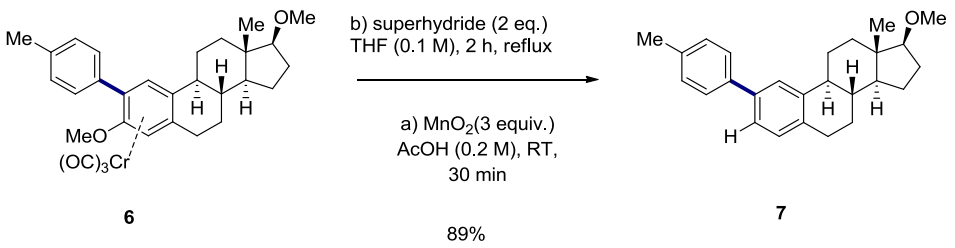
To an oven-dried microwave 10 mL glass vial equipped with a round stirrer bar, the following reagents were added in this order: K_2CO_3 (172.5 mg, 1.25 mmol, 2.5 equiv), 1-AdCO_2H (45.0 mg, 0.250 mmol, 0.5 equiv), Ag_2CO_3 (70 mg, 0.25 mmol, 0.5 equiv), $Pd(PPh_3)_4$ (5 mol%, 28.9 mg, 0.010 mmol), complex **1u** (218 mg, 0.50 mmol, 1.0 equiv) and 4-iodotoluene (163.5 mg, 0.75 mmol, 1.5 equiv). $PhCH_3$ (0.3 mL, 1M) and 2,2,6,6-tetramethylpiperidine (170 µL, 1 mmol, 2.0 equiv) were added and the glass vial was sealed with a disposable microwave cap. The resulting mixture was stirred for 27 h at 60 °C. The reaction was then cooled down and Et_2O (5 mL) was added and the suspension was then loaded on a short silica plug (2 x 4 cm) and eluted with Et_2O (30 mL) before concentrating *in vacuo*. Purification via flash chromatography column on silica gel (Hexane:Et_2O 9:1) provided the title product **6** in 89% yield (234.1 mg, 0.445 mmol) as an equimolar mixture of facial diastereoisomers . ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ (ppm) = 7.48 (d, *J* = 7.6 Hz, 2H, diast. A), 7.44 (d, *J* = 7.6 Hz, 2H, diast. B), 7.23-7.16 (m, 2H + 2H, diast. A+B), 6.18 (s, 1H, diast. A), 6.06 (s, 1H, diast. B), 5.50 (s, 1H + 1H, diast. A+B), 3.83 (s, 3H, diast. A), 3.76 (s, 3H, diast. B), 3.29 (s, 3H + 3H, diast. A+B), 3.20-2.71 (m, 2H, diast. A+B), 2.35 (s, 3H + 3H, diast. A+B), 2.32-1.80 (m, 7H, diast. A+B), 1.80-1.21 (21H, diast. A+B), 1.00-0.81 (m, 2H, diast. A+B), 0.82 (s, 3H, diast. A), 0.79 (s, 3H, diast. B). ^{13}C NMR (101 MHz, $(CD_3)_2CO$): δ (ppm) = 236.6 (diast. A), 236.0 (diast. B), 143.5 (diast. A), 143.0 (diast. B), 139.5 (diast. A), 139.4 (diast. B). 133.5 (diast. A+B), 131.9 (diast. B), 131.8 (diast. A), 130.1 (diast. A+B), 114.0 (diast. B), 113.6 (diast. A), 108.9 (diast. A), 106.4 (diast. B), 102.4 (diast. B), 101.2 (diast. A), 99.4 (diast. B), 98.8 (diast. A), 91.8 (diast. B), 91.7 (diast. A), 77.6 (diast. B), 77.5 (diast. A), 58.6 (diast. A), 57.3 (diast. B), 51.3 (diast. A+B), 51.0 (diast. A+B), 45.0 (diast. B), 44.7 (diast. B), 44.6 (diast. A), 44.0 (diast. A), 40.2 (diast. B), 39.4 (diast. A), 39.1 (diast. A), 39.0 (diast. B), 31.3 (diast. A+B), 29.0 (diast. A), 29.0 (diast. B), 28.0 (diast. A), 27.9 (diast. B), 27.4 (diast. A+B), 24.5 (diast. A), 24.3 (diast. B), 21.9 (diast. A+B), 12.7 (diast. A), 12.6 (diast. B).

142.7, 119.1, 110.8, 95.5, 94.1, 82.4, 80.6, 66.4, 33.2, 32.4, 25.6, 16.1 IR: ν = 2935, 1943, 1853, 1700, 1474, 1245, 1102 cm^{-1}. Mp: 104-106 °C. HRMS EI+ *m/z* calcd. $C_{30}H_{35}O_5Cr$: $[M+H]^+$ 527.1890; found: $[M+H]^+$ 527.1873.



(8R,9S,13S,14S,17S)-13-Methyl-2-(*p*-tolyl)-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene-3,17-diol (5)[7].

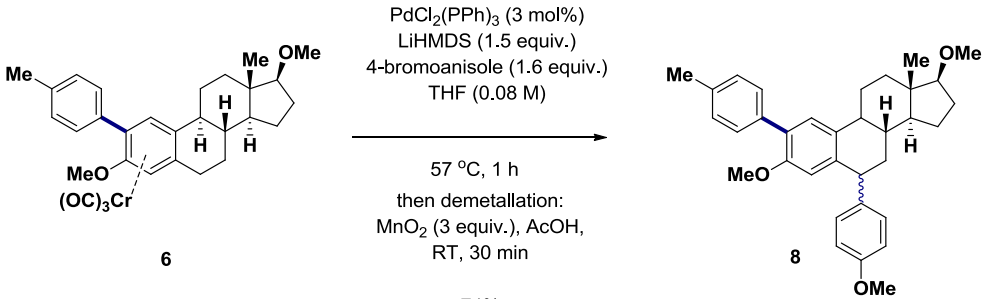
In an oven-dried microwave 10 mL glass vial containing complex **6** (mixture of facial diastereoisomers, 104 mg, 0.2 mmol), AcOH (2 mL) was slowly added with moderate stirring. After 5 min, MnO_2 (90 mg, 0.6 mmol, 3 equiv) was added in small portions and the black suspension was vigorously stirred for 30 min. The suspension was then loaded on a short silica plug (2 x 4 cm) and eluted with Et_2O (30 mL) before concentrating *in vacuo*. To the crude mixture $AlCl_3$ (133 mg, 1.0 mmol) was added and the flask placed under Ar atmosphere. 1,2-ethandithiol (2 mL) was added and the mixture stirred for 1 h at RT. The reaction was then concentrated *in vacuo*. Purification via flash chromatography column (gradient hexane/Et_2O 90:10 to 60:40) on silica gel provided the title product **5** as a white solid in 91% yield (68 mg, 0.181 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.36 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.16 (s, 1H), 6.72 (s, 1H), 5.14 (*br* s, 1H), 3.73 (t, *J* = 8.4 Hz, 1H), 2.98-2.80 (m, 2H), 2.41 (s, 3H), 2.35-2.09 (m, 3H), 1.98-1.85 (m, 2H), 1.80-1.14 (m, 9H), 0.79 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 150.4, 137.9, 137.5, 134.7, 132.9, 130.0, 129.1, 127.3, 125.7, 115.7, 82.1, 50.2, 44.1, 43.4, 39.0, 36.8, 30.7, 29.5, 27.4, 26.5, 23.3, 21.3, 11.2. IR: ν = 3320, 3024, 2923, 1501, 906, 730 cm^{-1}. Mp: 154-156 °C. . HRMS EI+ *m/z* calcd. $C_{25}H_{31}O_2$: $[M+H]^+$ 363.2310; found: $[M+H]^+$ 363.2312.



6 **7**

(8R,9S,13S,14S,17S)-17-Methoxy-13-methyl-2-(*p*-tolyl)-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene (7)[8].

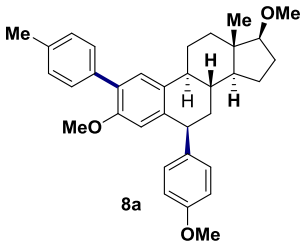
An oven-dried microwave 10 mL glass vial was charged with complex **6** (1:1 mixture of facial diastereoisomers, 104 mg, 0.2 mmol, 1.0 equiv) under Ar atmosphere. THF (2 mL) was added, followed by superhydride (1M in THF, 0.4 mL, 0.4 mmol, 2 equiv). The resulting solution was refluxed for 2 h and then cooled down in an ice bath. AcOH (2 mL) was slowly added with moderate stirring. After 5 min, MnO_2 (90 mg, 0.6 mmol, 3 equiv) was added in small portions and the black suspension was vigorously stirred for 30 min. The suspension was then loaded on a short silica plug (2 x 4 cm) and eluted with Et_2O (30 mL) before concentrating *in vacuo*. Purification via flash chromatography column (Hexane/Et_2O 90:10) on silica gel provided the required product **7** as colourless oil in 89% yield (64.1 mg, 0.178 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.54 (*br* s, 1H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.36 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 3.41 (s, 3H), 3.35 (t, *J* =8.0 Hz, 1H), 2.98-2.90 (m, 2H), 2.49-2.27 (m, 5H), 2.18-2.04 (m, 2H), 1.80-1.20 (m, 9H), 0.83 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 140.8, 139.0, 138.7, 136.7, 135.7, 129.5, 127.1, 124.4, 124.2, 90.9, 58.0, 50.6, 44.7, 43.4, 38.6, 38.2, 29.4, 27.9, 27.4, 26.4, 23.2, 21.2, 11.7. IR: ν = 3021, 2924, 1490, 1103, 976, 805 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{26}H_{33}O$: $[M+H]^+$ 361.2526; found: $[M+H]^+$ 361.2526.



6 **8**

(8R,13S,14S,17S)-3,17-Dimethoxy-6-(4-methoxyphenyl)-13-methyl-2-(*p*-tolyl)-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene (8)[9].

An oven-dried microwave 10 mL glass vial was charged with $PdCl_2(PPh_3)_2$ (3.5 mg, 0.006 mmol, 3 mol %), placed under vacuum and refilled with an Ar balloon. Then THF (1 mL), LiHMDS (1.0 M in THF/ethylbenzene, 0.32 mmol, 1.6 equiv) and finally 4-bromoanisole (60 mg, 0.32 mmol, 1.6 equiv) were added. The resulting mixture was stirred for 10 min and was then transferred by syringe to an oven-dried microwave 10 mL glass vial under Ar, containing complex **6** (mixture of facial diastereoisomers, 104 mg, 0.2 mmol, 1.0 equiv). The orange suspension was stirred for 16 h at 60 ^oC and then quenched with AcOH (1 mL). MnO_2 (90 mg, 0.6 mmol, 3 equiv) was added in small portions and the black suspension was vigorously stirred for 30 min. The suspension was then loaded on a short silica plug (2 x 4 cm) and eluted with Et_2O (30 mL) before concentrating *in vacuo*. Analysis on the crude ^1H NMR showed the product as a mixture of diastereoisomers **8a: 8b** in a 3:1 ratio (42% yield for **8a** and 15% yield for **8b**). Purification via flash chromatography (gradient hexane/Et_2O 98:2 to 95:5) afforded a pure sample of the main diastereoisomer **8a** in order to assign its absolute configuration. ^1H NMR, ^{13}C NMR, HSQC and NOESY analysis allowed the tentative assignment of the benzylic configuration for compound **8a** as shown below.



^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.45 (d, *J* = 7.5 Hz, 2H), 7.31 (s, 1H), 7.22 (d, *J* = 7.6, 2H), 7.00 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 7.9 Hz, 2H), 6.52 (s, 1H), 4.27-4.21 (m, 1H), 3.81 (s, 3H), 3.62 (s, 3H), 3.36 (s, 3H), 3.29 (t, *J* = 8.2 Hz, 1H), 2.40 (s, 3H), 2.37-2.20 (m, 2H), 2.12-1.92 (m, 2H), 1.90-1.75 (m, 2H), 1.68-1.32 (m, 6H), 1.32-1.00 (m, 2H), 0.72 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) = 157.7, 154.6, 140.4, 138.8, 136.5, 136.0, 133.6, 129.9, 129.5, 128.9, 128.8, 127.8, 113.6, 113.2, 90.9, 58.0, 55.8, 55.3, 50.1, 44.4, 43.8, 43.6, 38.3, 36.3, 33.0, 27.8, 26.7, 23.0, 21.3, 11.8. IR: ν = 2930, 2847, 1609, 1508, 977, 832 cm^{-1}. HRMS EI+ *m/z* calcd. $C_{34}H_{41}O_3$: $[M+H]^+$ 497.3050; found: $[M+H]^+$ 497.3050.

References

[1] Khenkin, M. A.; Weiner, L.; Wang, Y.; Neumann, R. *J. Am. Chem. Soc.*, 2001, 123, 8531.

[2] Morgan, D. L.; Martinez-Castro, N.; Storey, R. F. *Macromolecules*, **2010**, *43*, 8274.

[3] Harrowven, D. C.; Lucas, M. C.; Howes, P. D. *Tetrahedron*, **2001**, *57*, 791.

[4] Kingston, Jesudoss, V.; Verkade, J. G. *J. Org. Chem.* **2007**, *72*, 2816.

[5] Jacquesy, J.-C.; Jounnetaud, M.-P. *Bull. Chem. Soc. Fr.* **1980**, 2, 295.

[6] Wang, B.; Qin, L.; Neumann, K.; ShriHarsha, U.; Cerny, L. R.; DiMagno *Org. Lett.* **2010,** *12*, 3352.

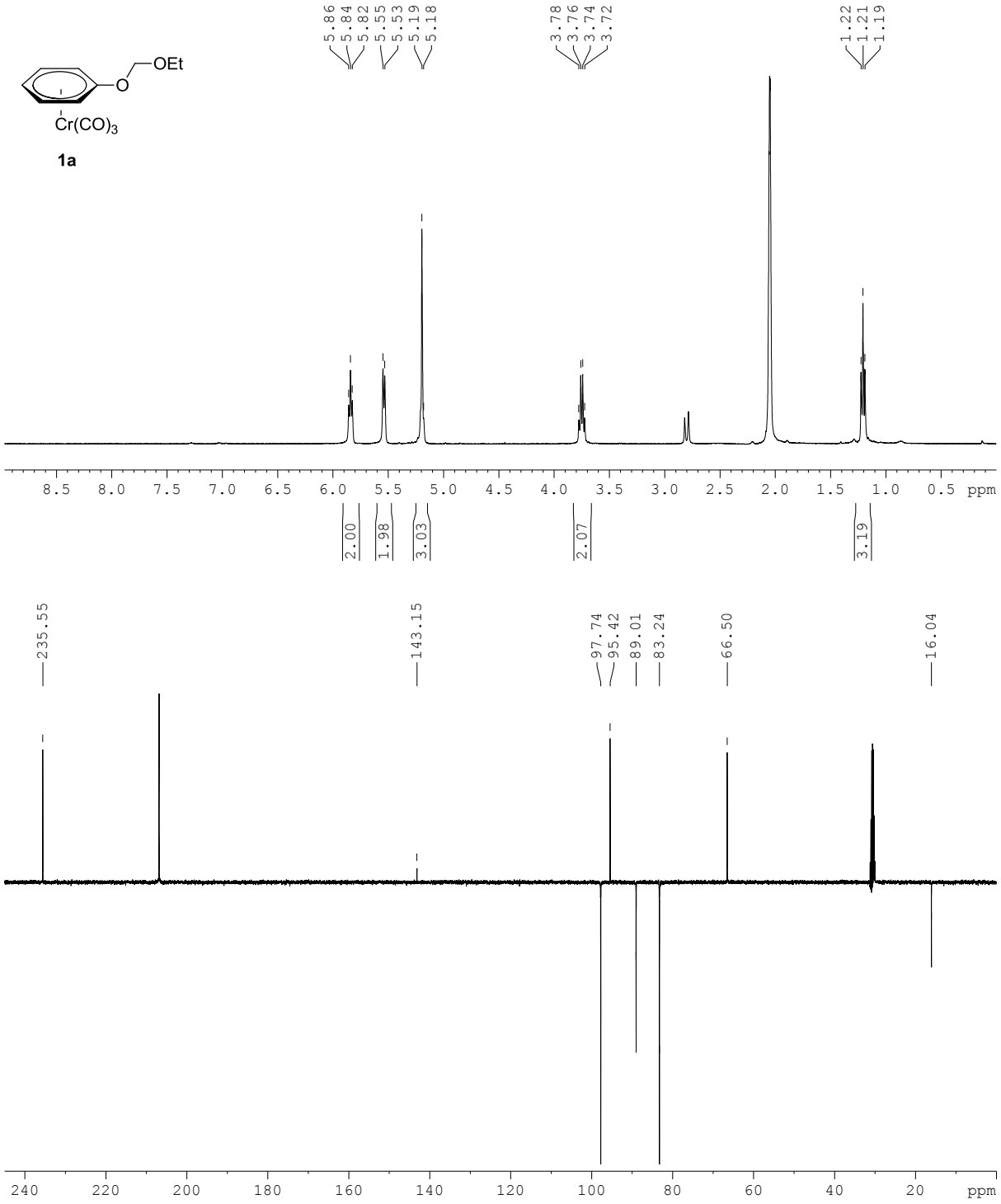
[7] Inaba, T.; Umezawa, Yuasa, M.; Inoue, T.; Mihashi, S.; Itokawa, H.; Ogura, K. *J. Org. Chem.* **1980**, *45*, 4275.

[8] Djukic, J. P.; Rose-Munch, Rose, E. *J. Am. Chem. Soc.* **1993**, *115*, 6434.

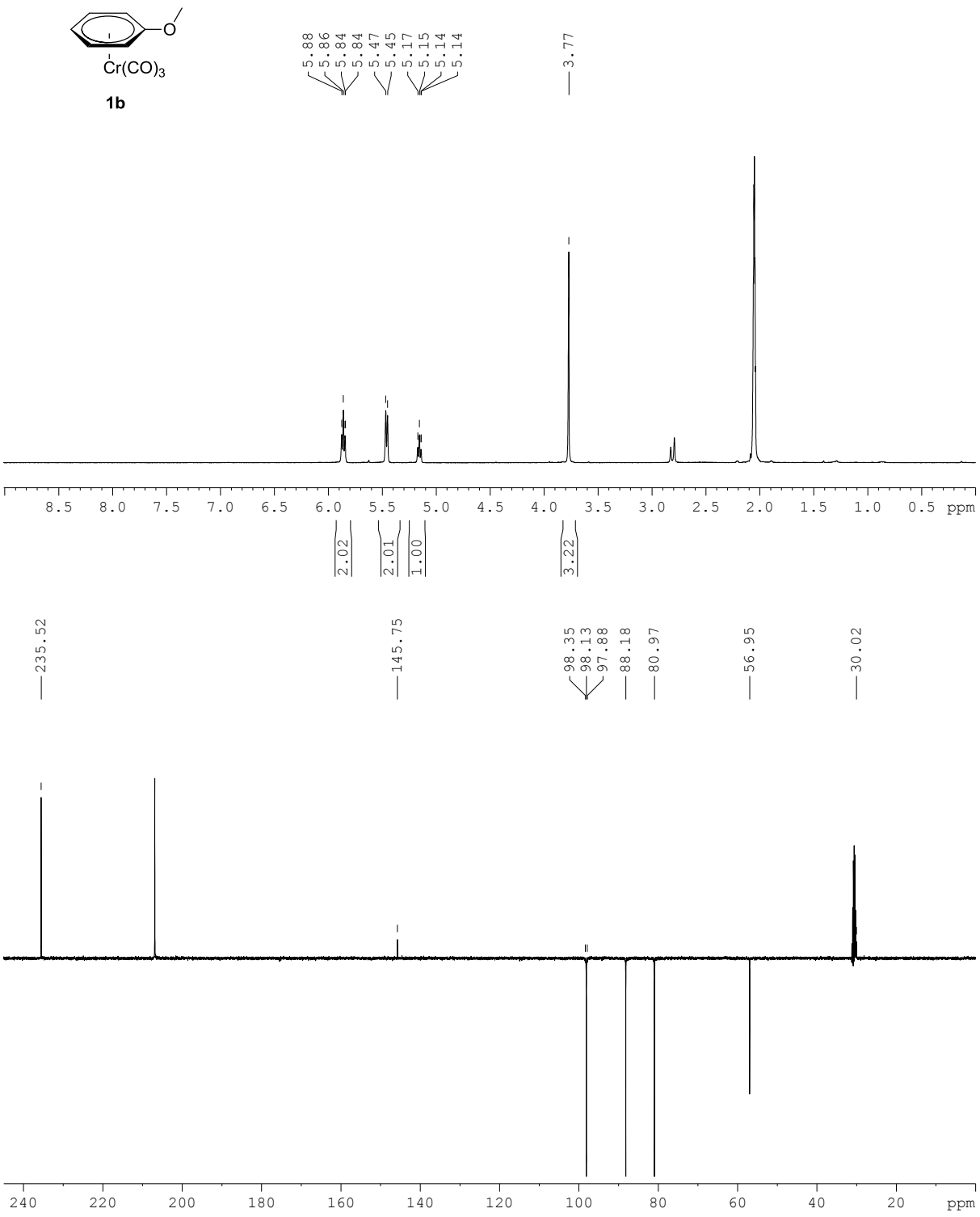
[9] McGrew, G. I.; Stanciu, C.; Zhang, J.; Carroll, P. J.; Spencer, D. D.; Walsh, P. J. *Angew. Chem. Int. Ed.* **2012**, *51*, 11510.

^{1}H and ^{13}C NMR spectra of arene chromium complexes 1 and arylation products 3-6.

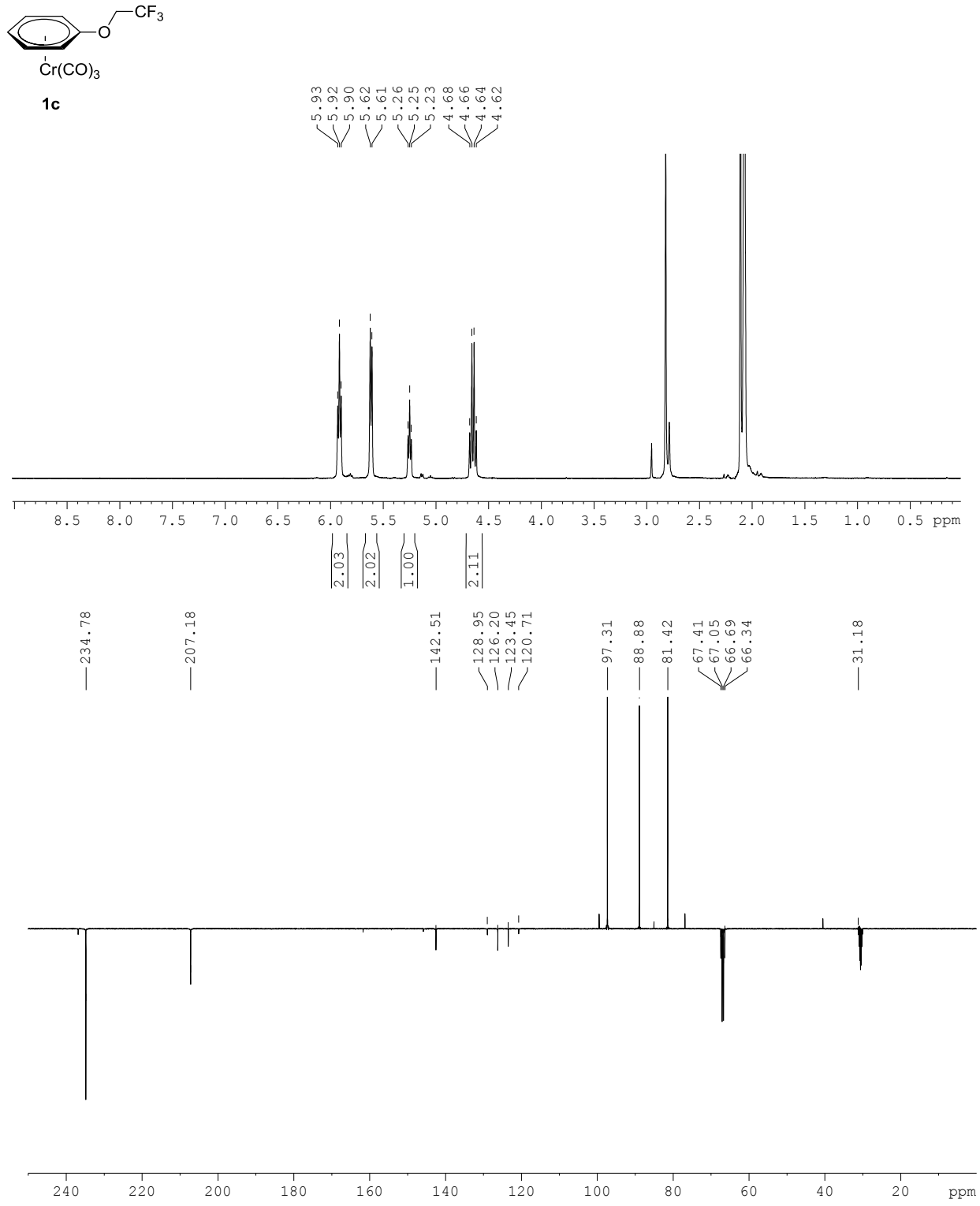
(Ethoxymethoxy)benzene tricarbonyl chromium (1a).



Anisole tricarbonyl chromium (1b).

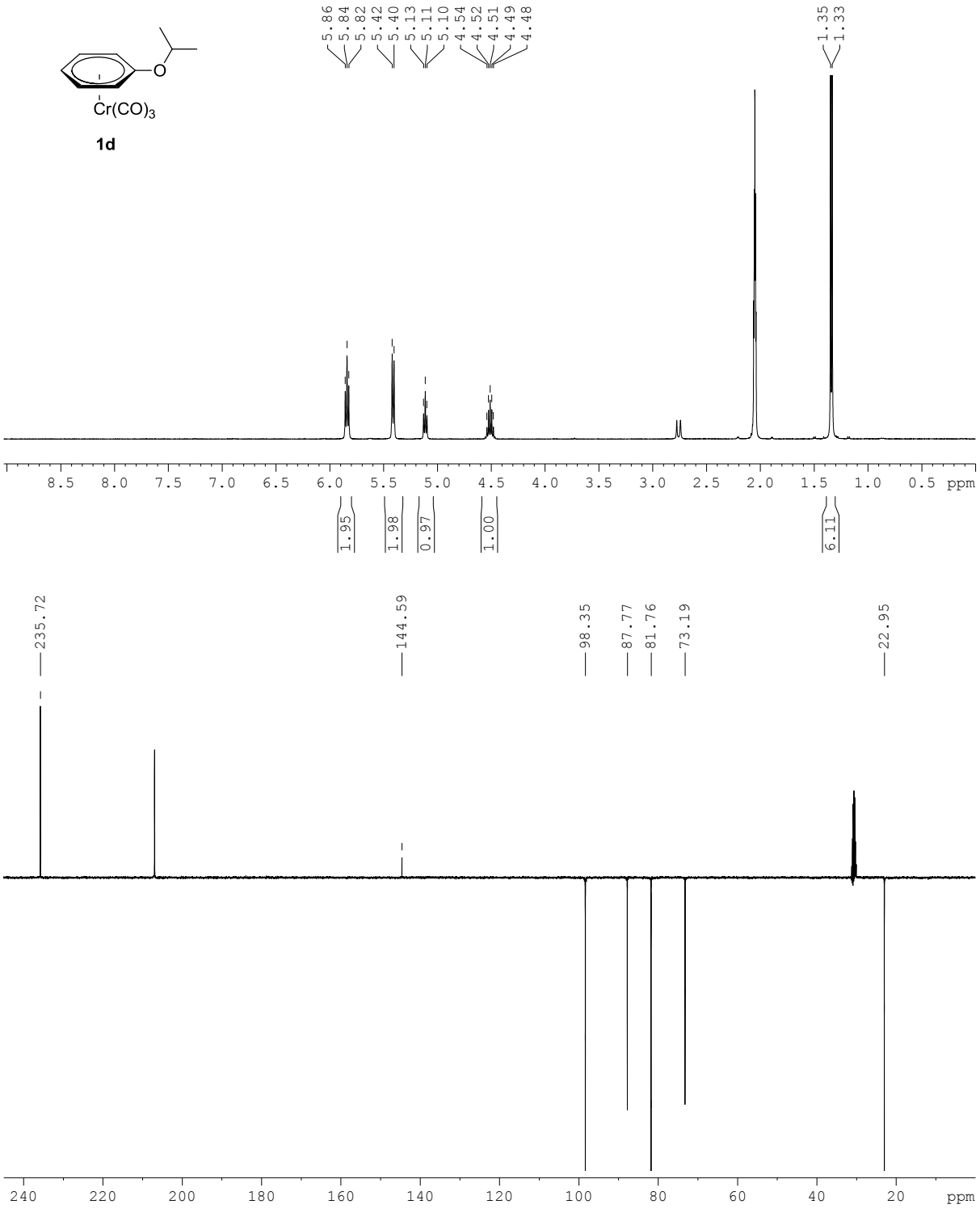


(2,2,2-Trifluoroethoxy)benzene tricarbonyl chromium (1c).

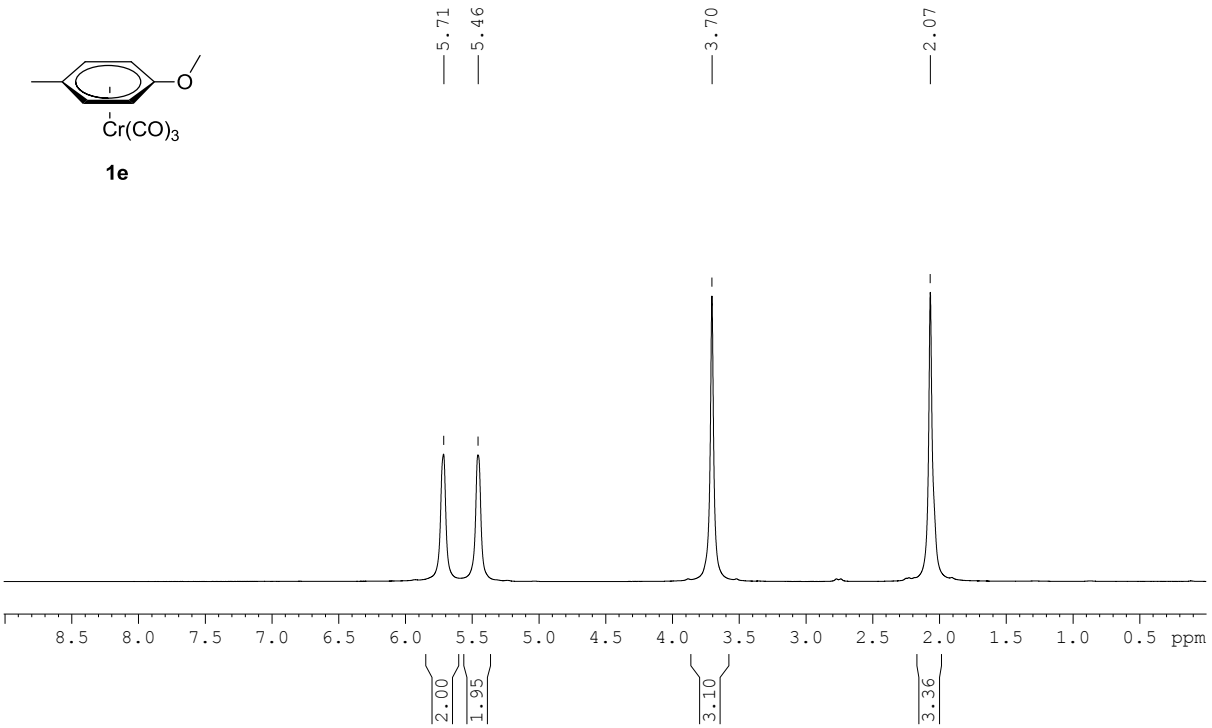


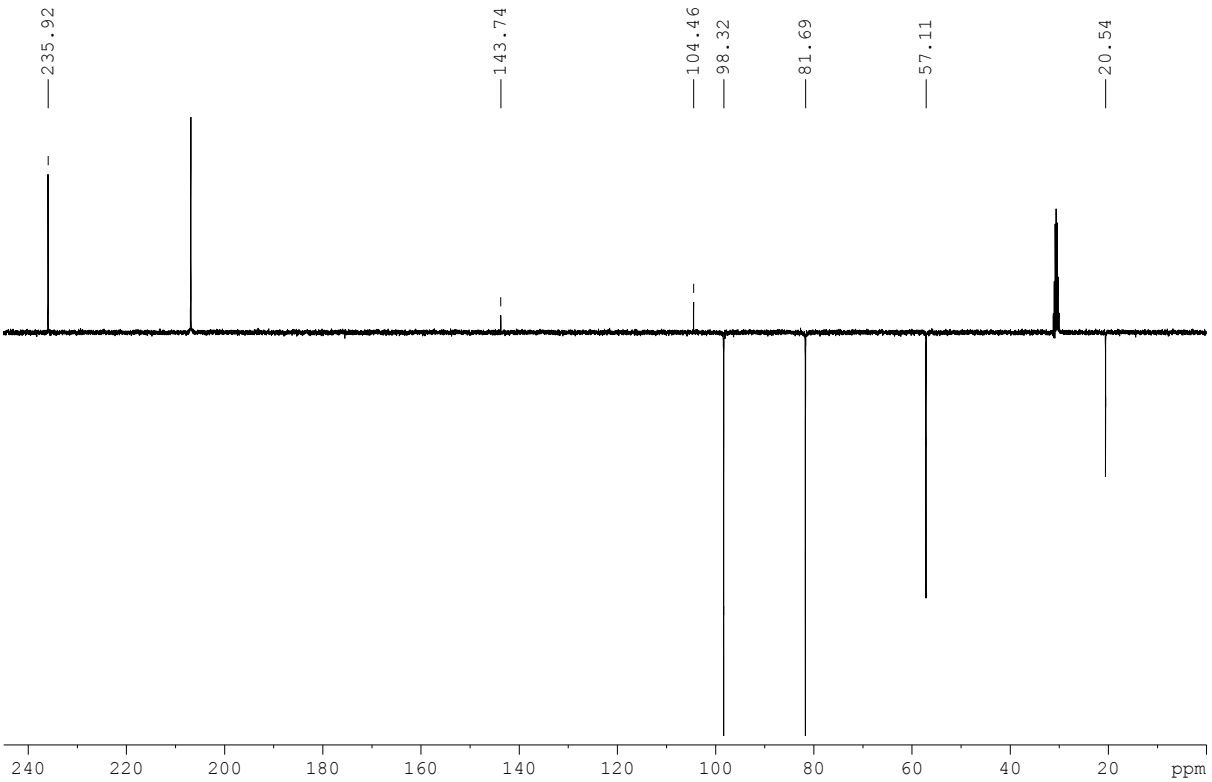
Isop

ropoxybenzene tricarbonyl chromium (1d).

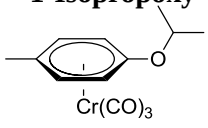


4-Methylanisole tricarbonyl chromium (1e).

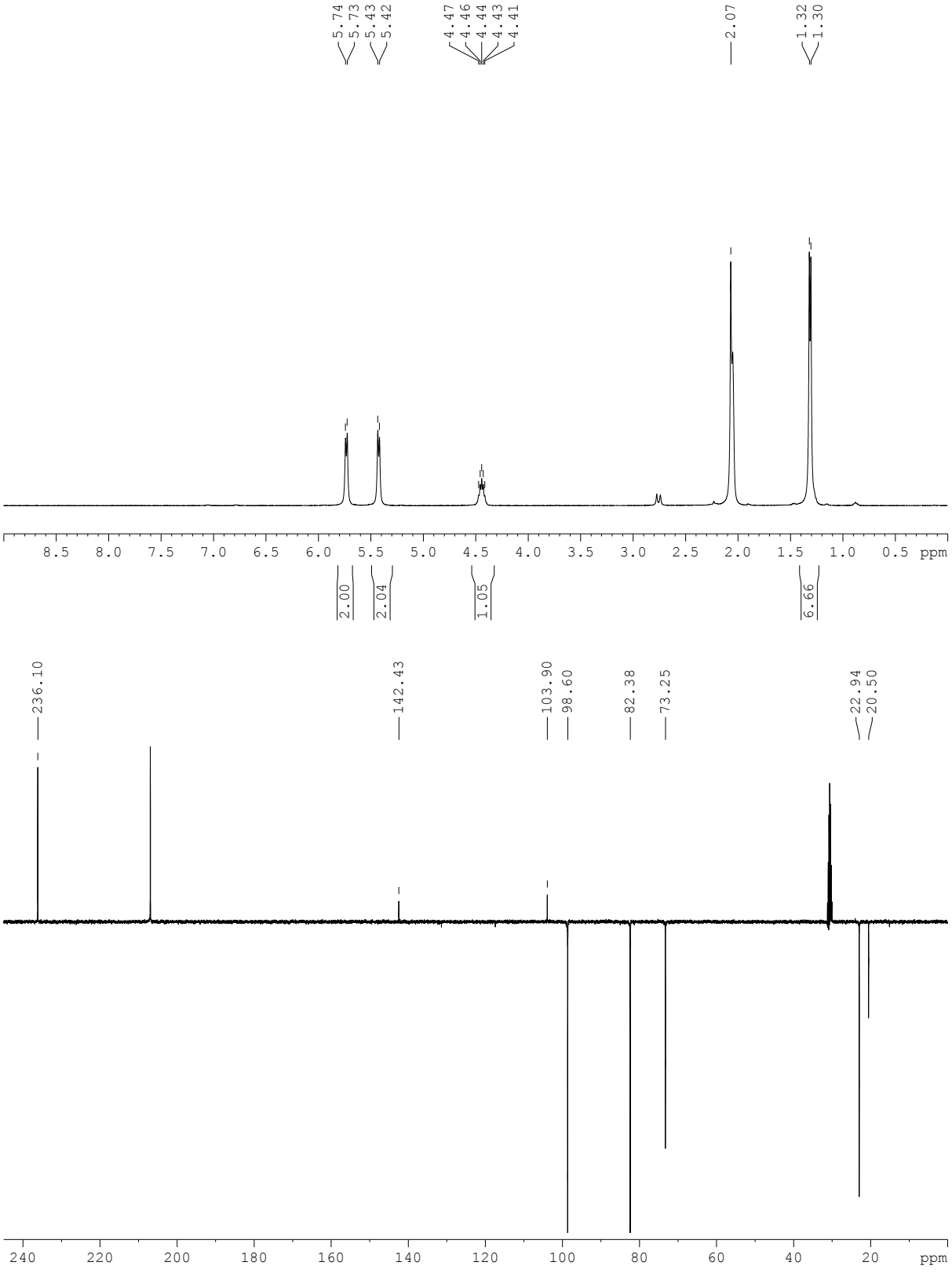




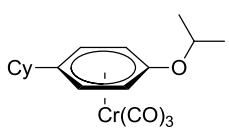
1-Isopropoxy-4-methylbenzene tricarbonyl chromium (1f).



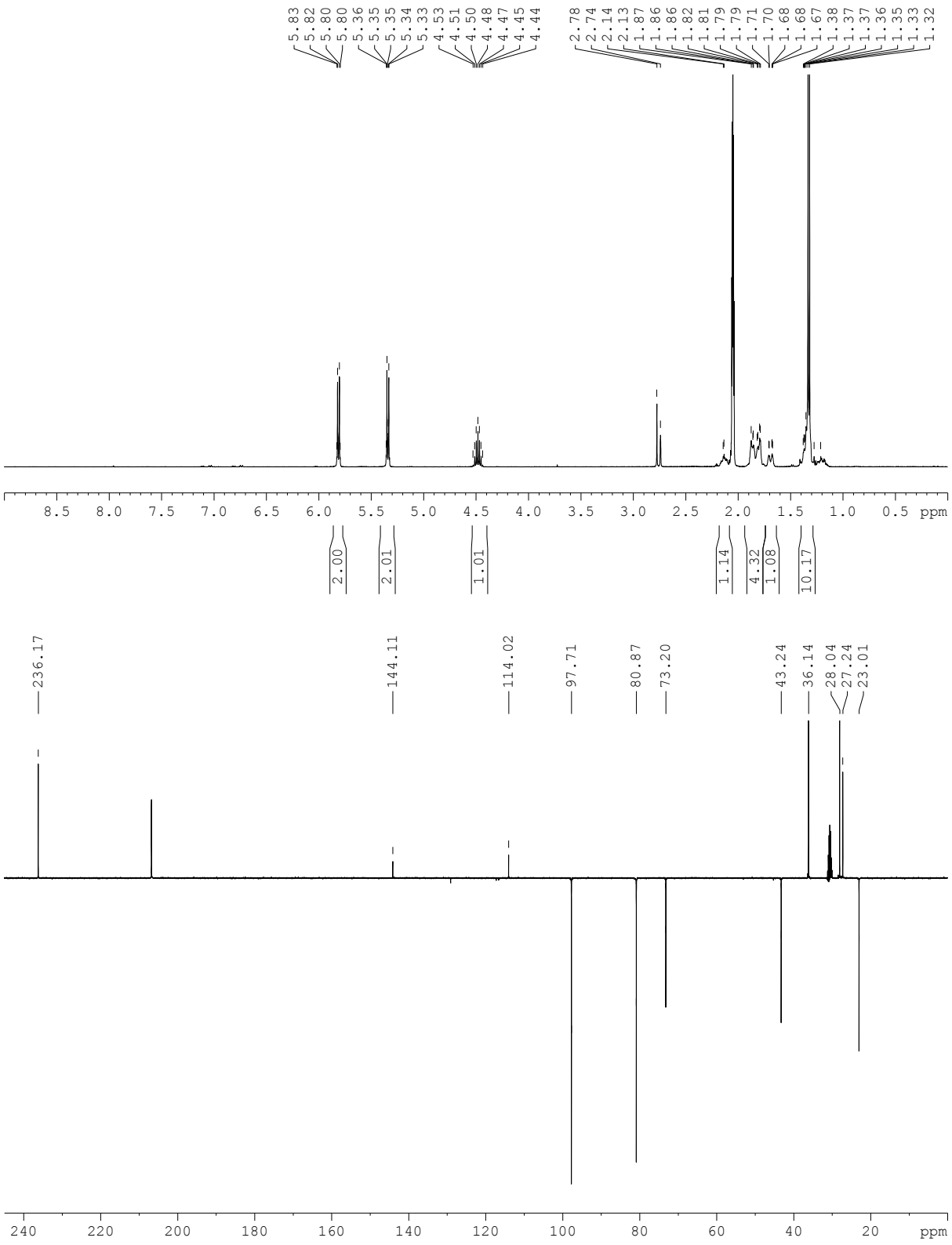
1f



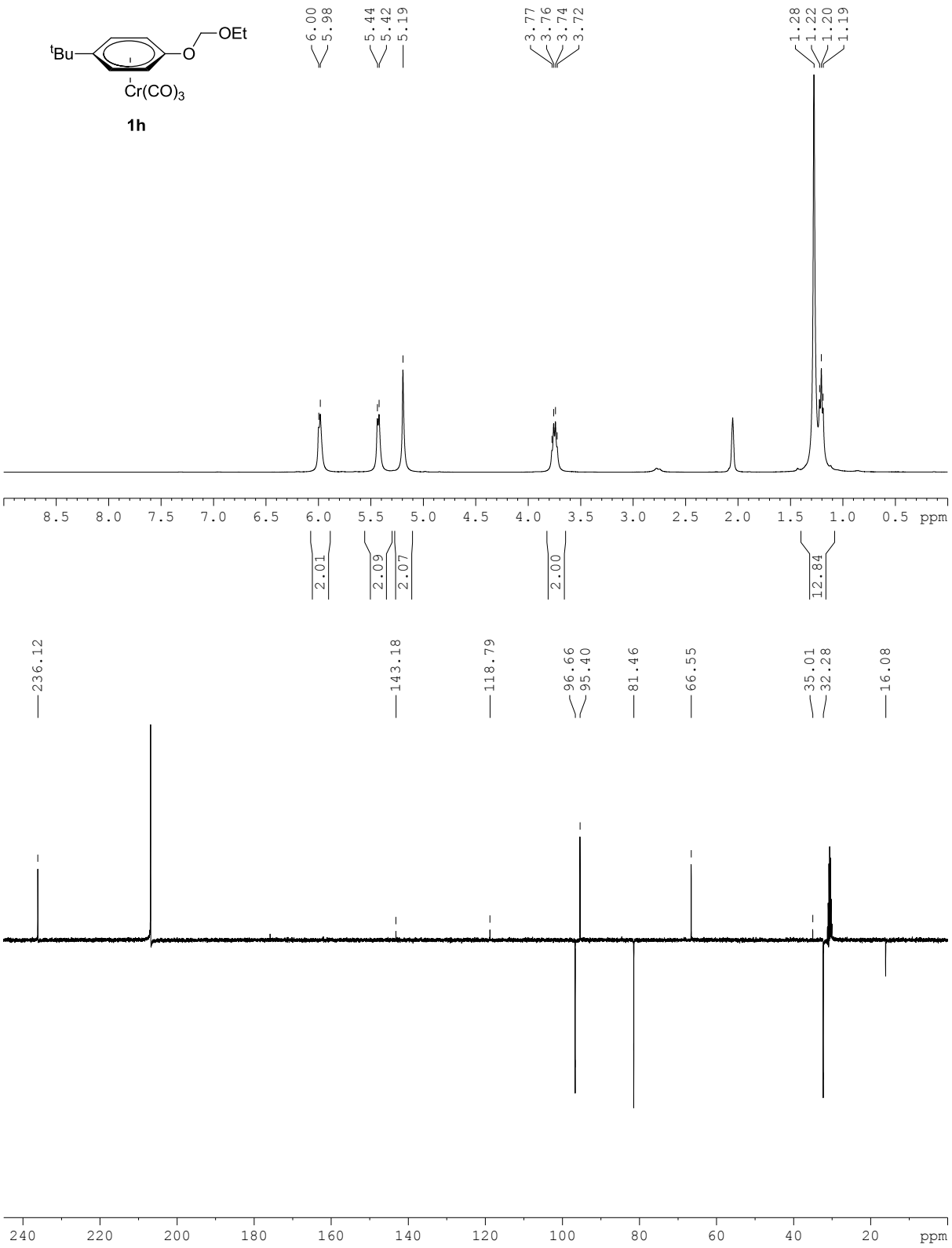
1-cyclohexyl-4-isopropoxybenzene tricarbonyl chromium (1g).



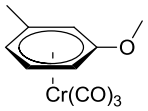
1g



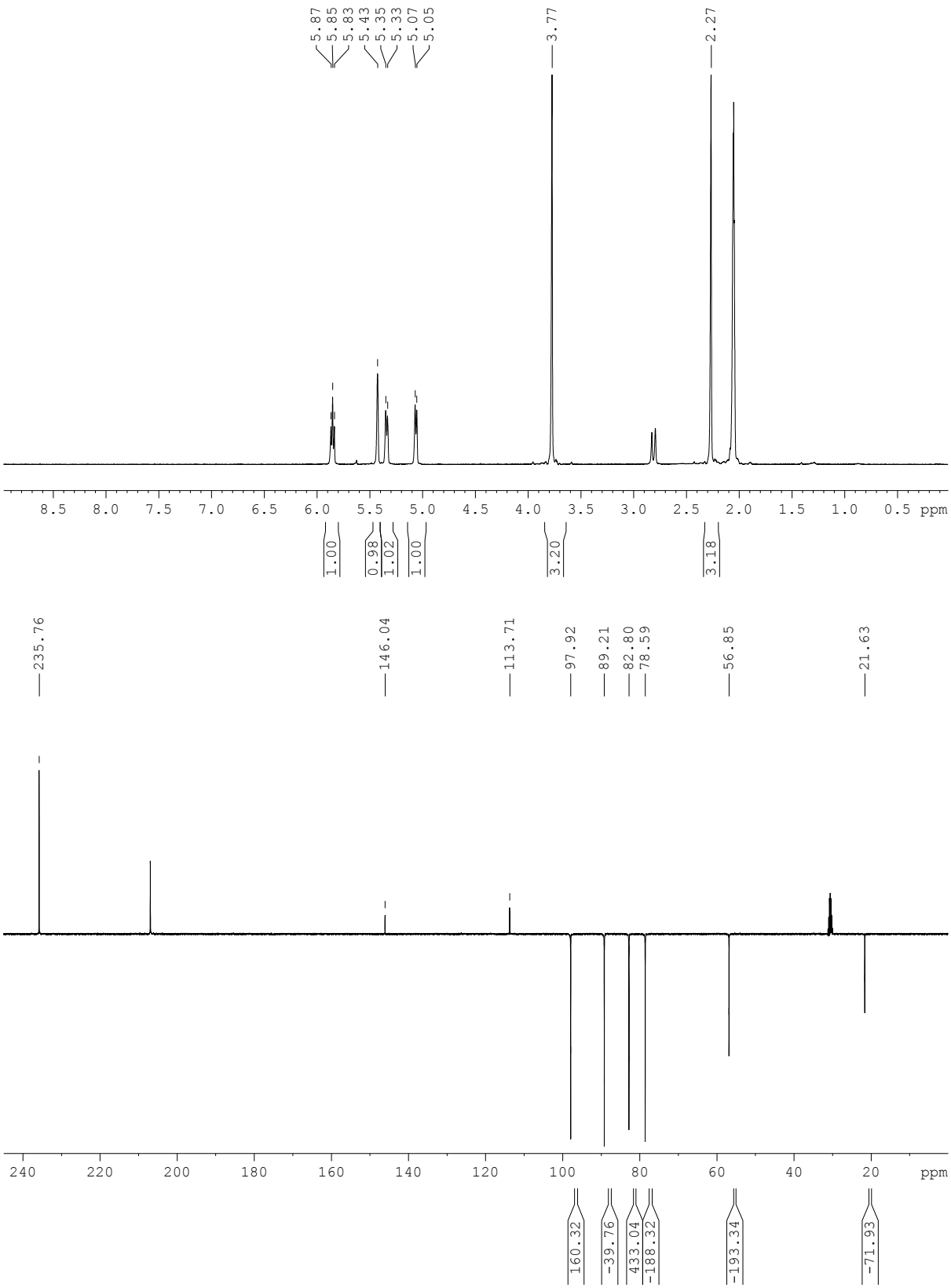
1-(*Tert*-butyl)-4-(ethoxymethoxy)benzene tricarbonyl chromium (1h).



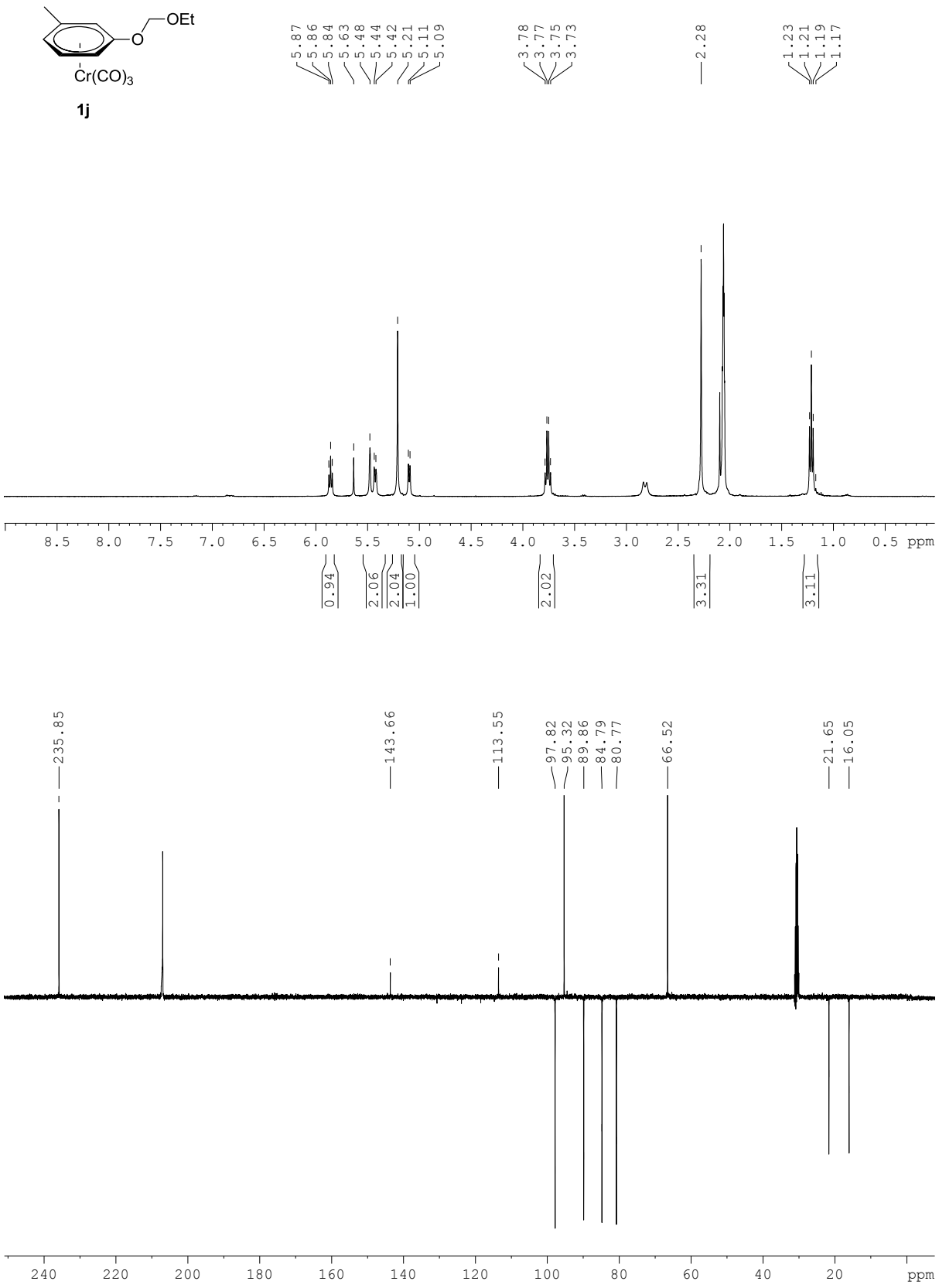
3-Methylanisole tricarbonyl chromium (1i).



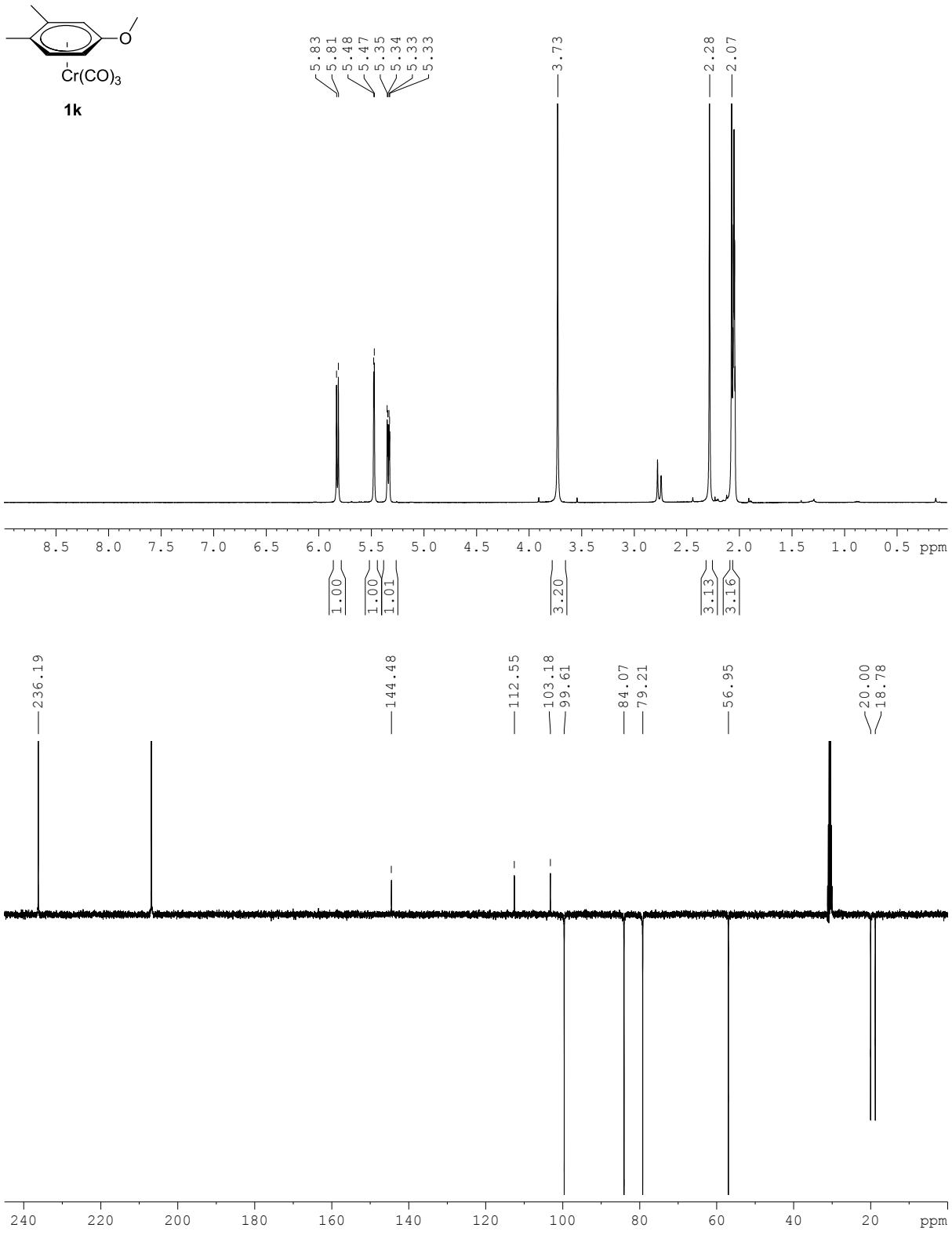
1i



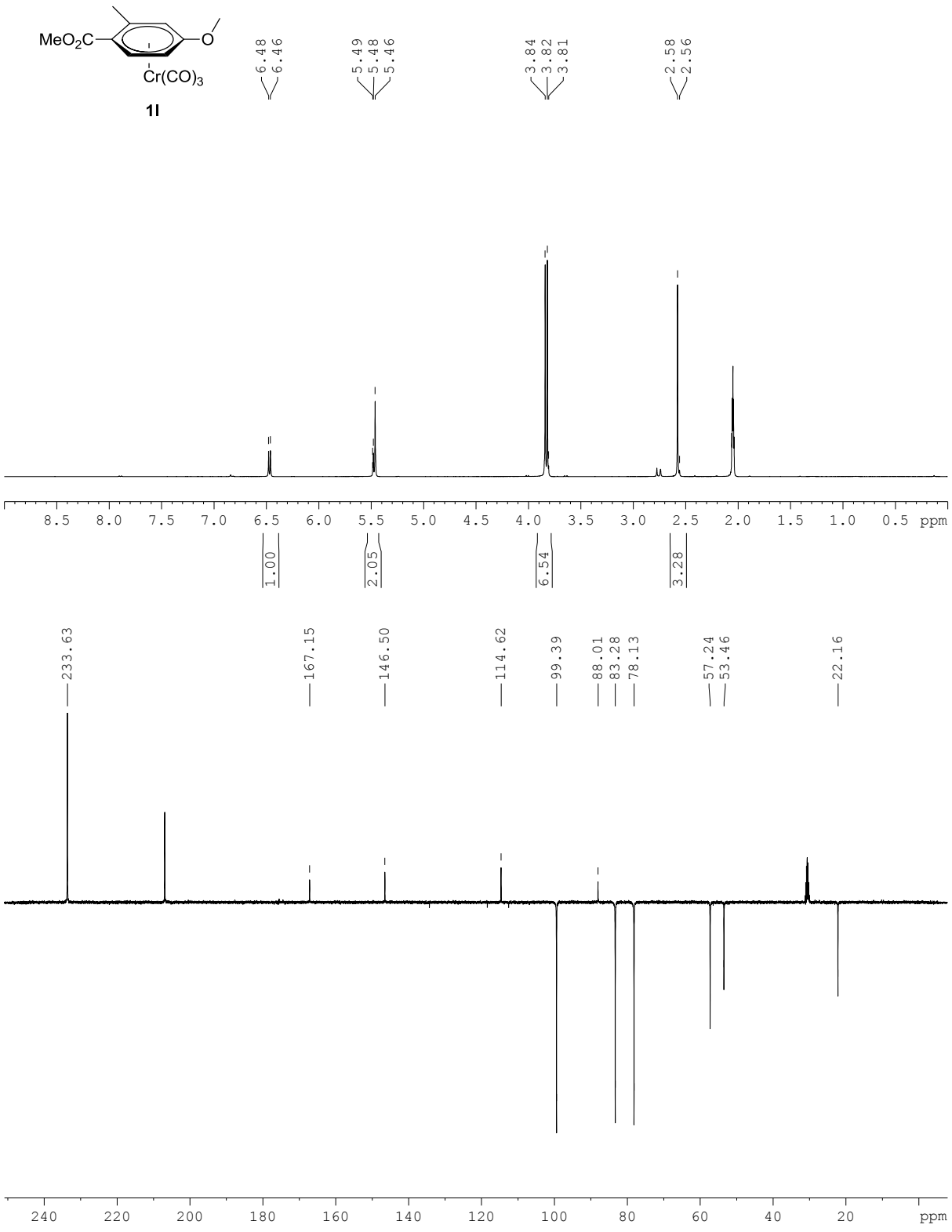
1-(Ethoxymethoxy)-3-methylbenzene tricarbonyl chromium (1j).



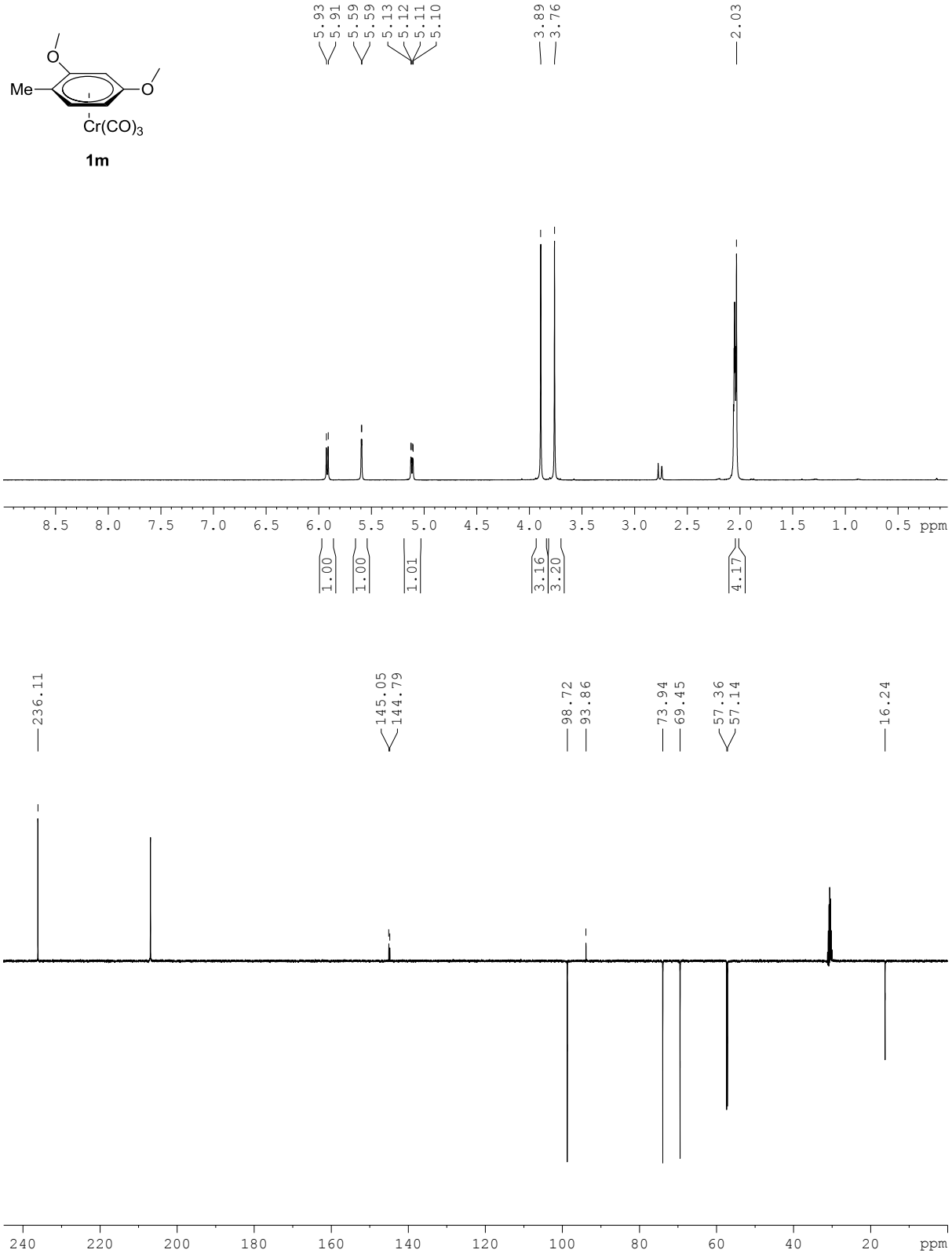
4-Methoxy-1,2-dimehtylbenzene tricarbonyl chromium (1k)



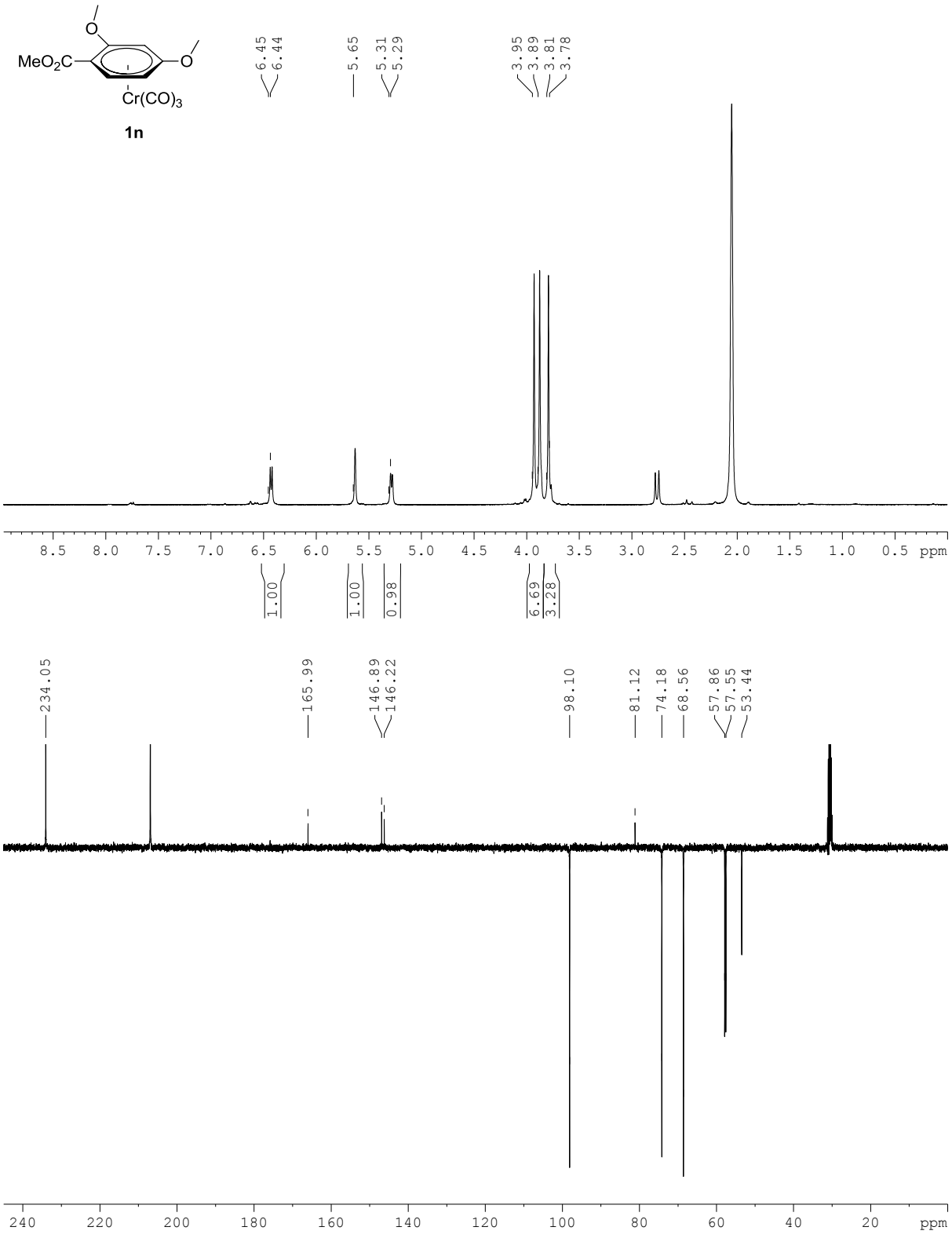
Methyl 4-methoxy-2-methylbenzoate tricarbonyl chromium (1l)



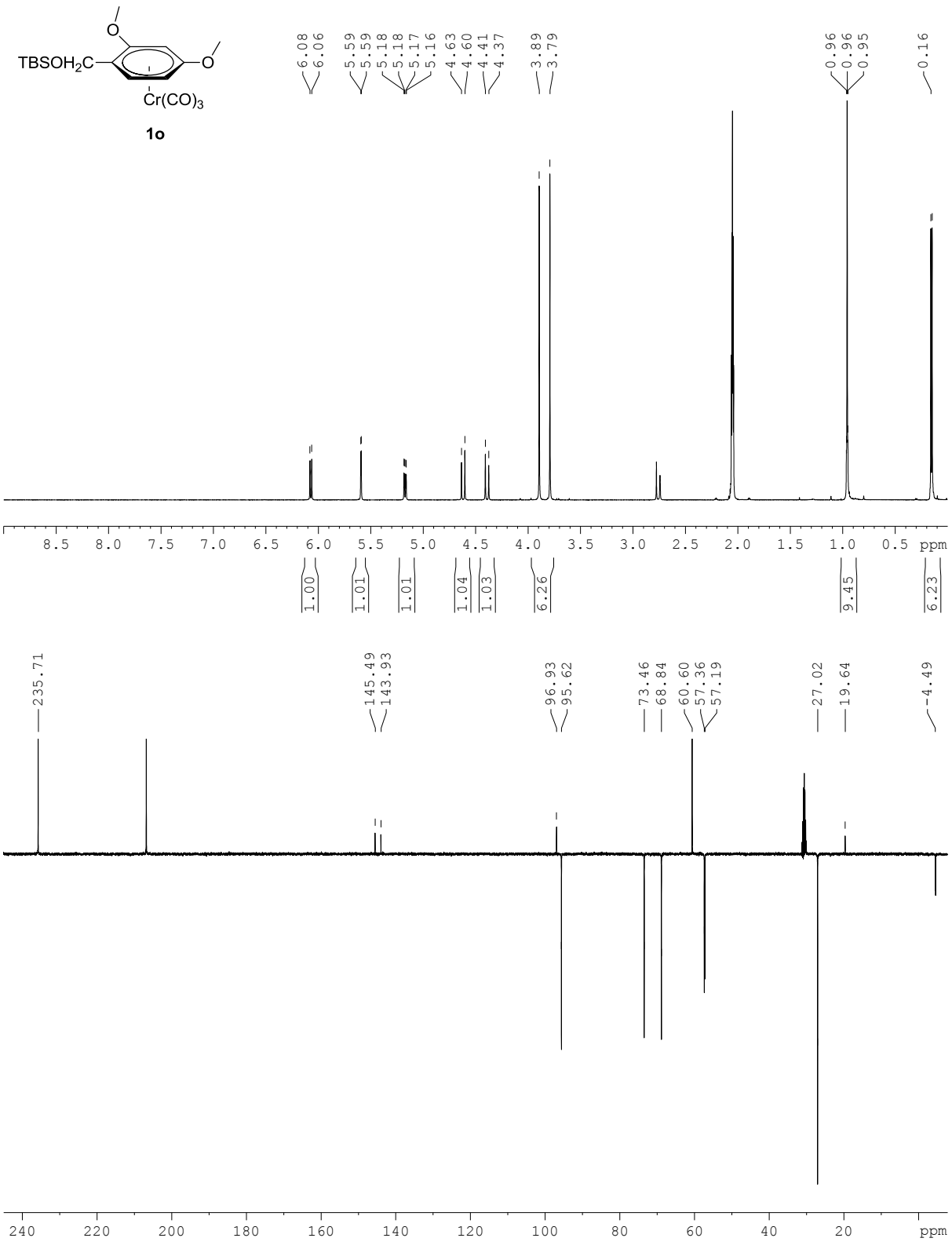
2,4-Dimethoxy-1-methylbenzene tricarbonyl chromium (1m).



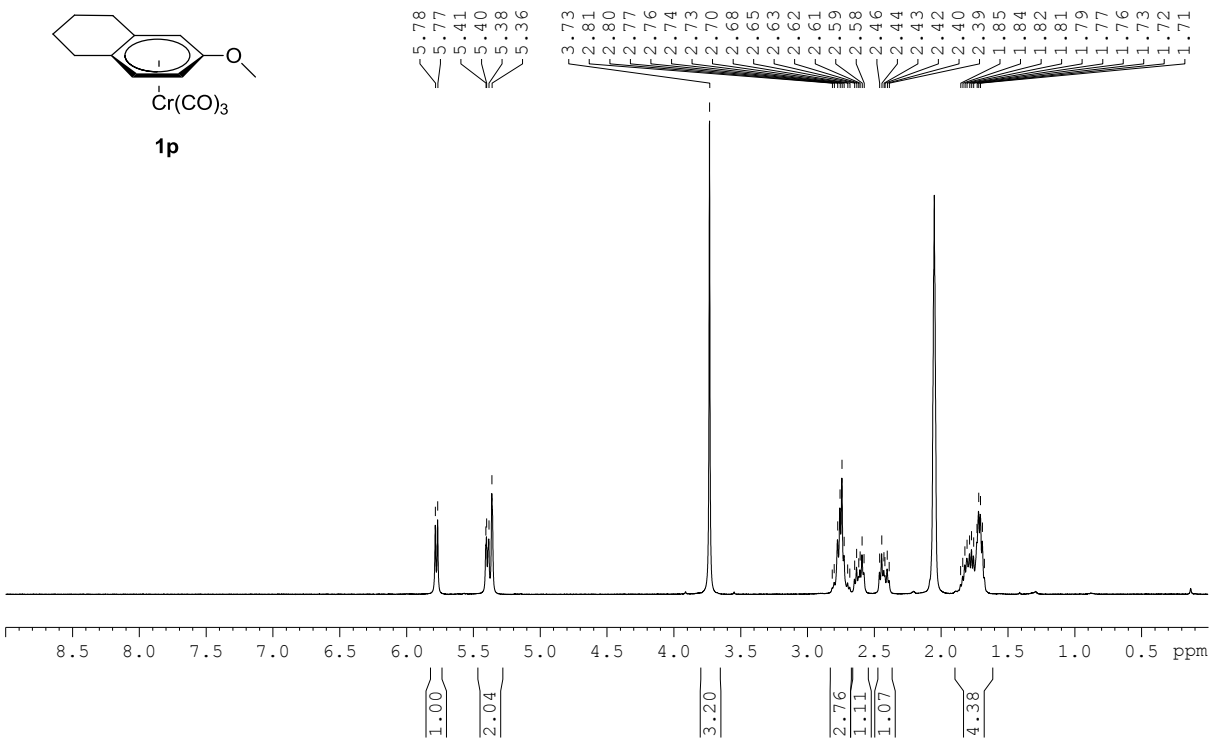
Methyl 2,4-dimethoxylbenzoate -1-methylbenzene tricarbonyl chromium (1n).

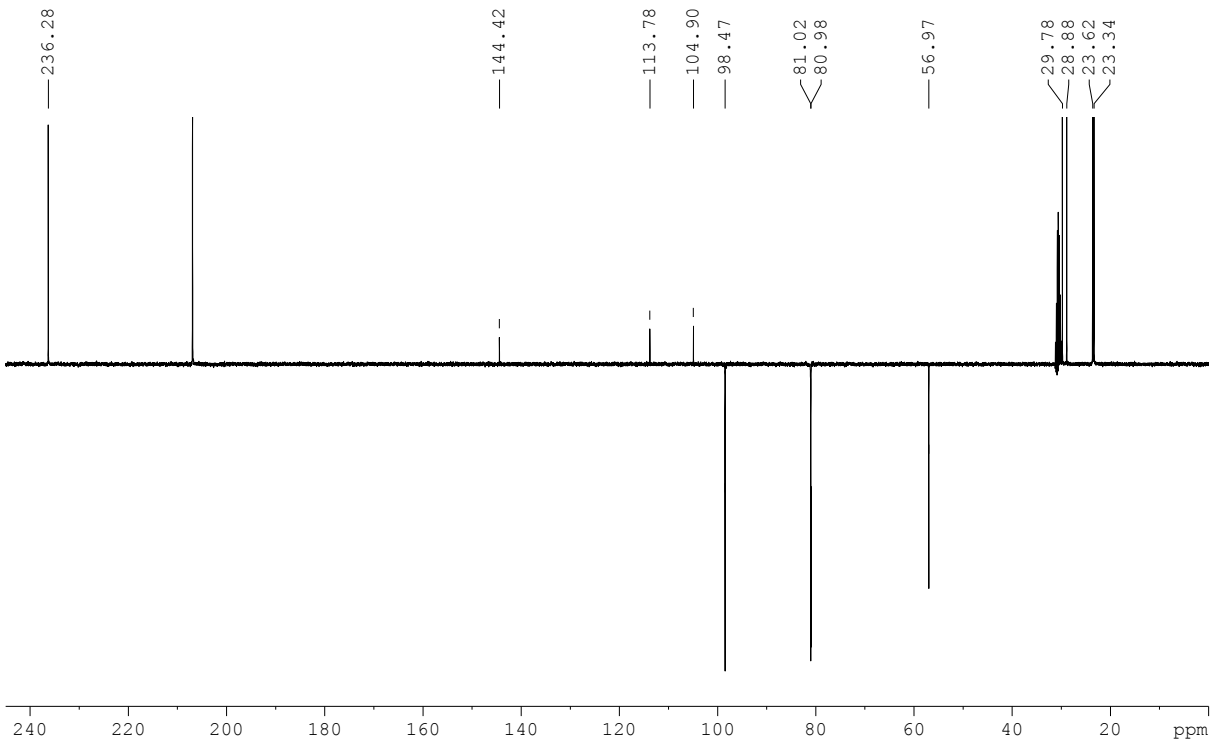


***Tert*-butyl(2,4-dimethoxybenzyl)oxy)dimethylsilane tricarbonyl chromium (1o).**

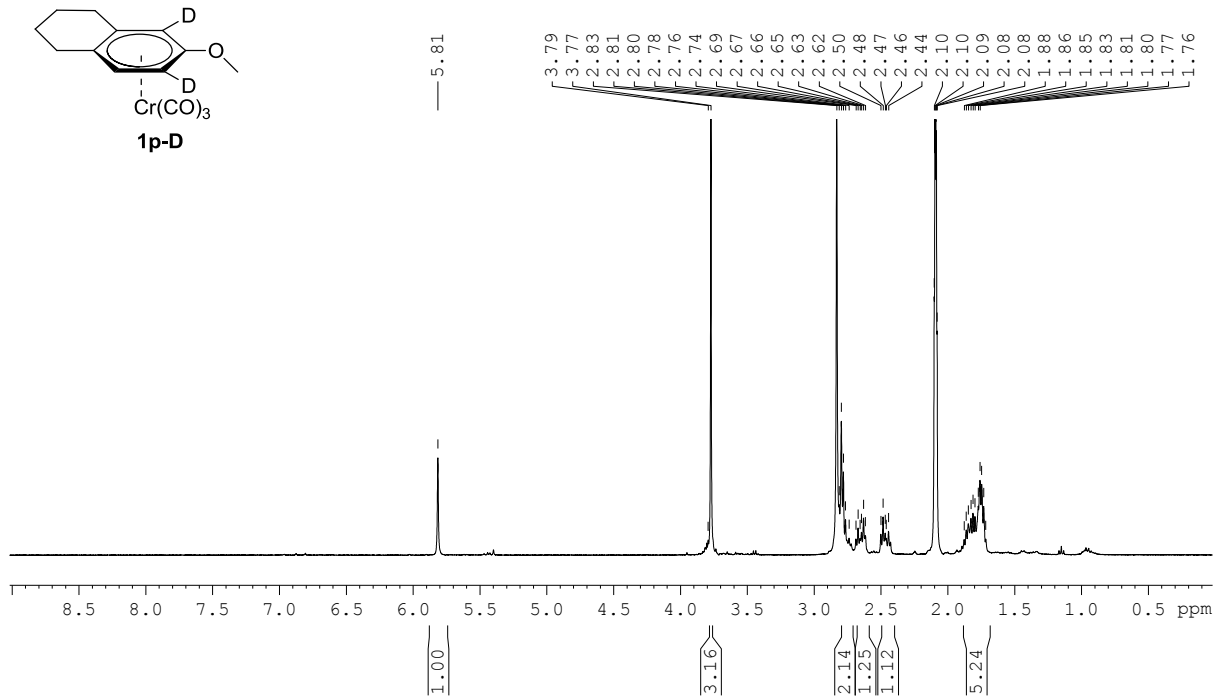


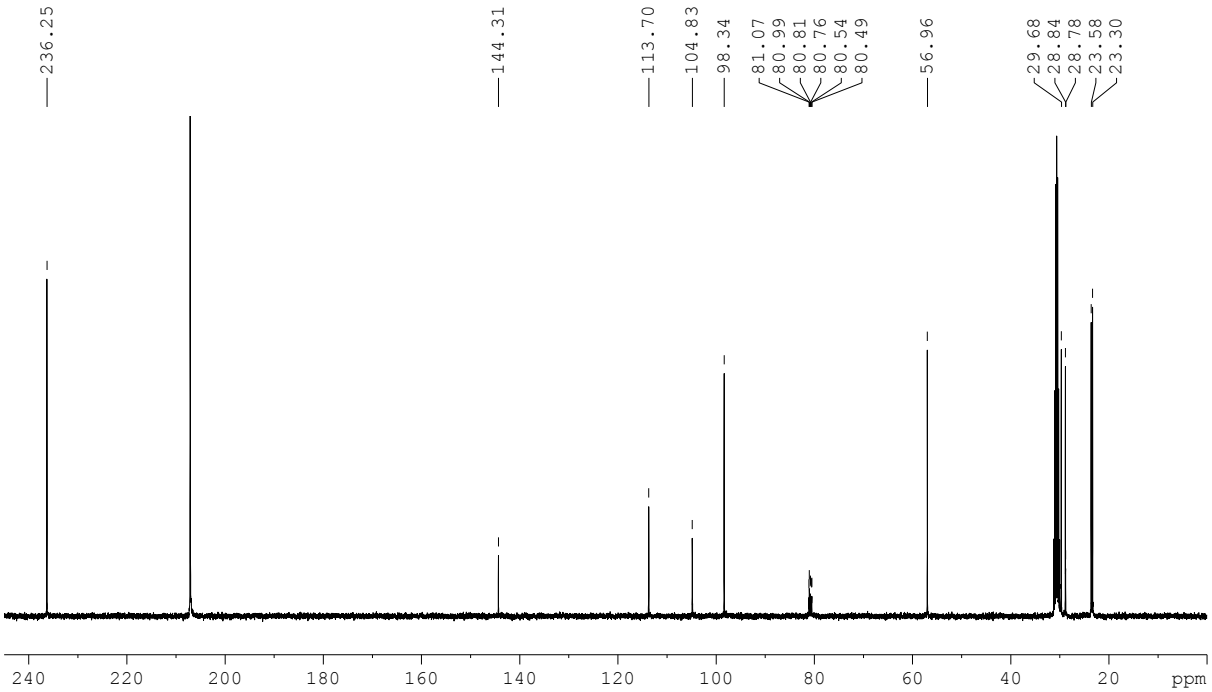
2-Methoxy-1,2,3,4-tetrahydronaphthalene chromium tricarbonyl (1p).


Cr(CO)3
O
1p
5.78
5.77
5.41
5.40
5.38
5.36
3.73
2.81
2.80
2.77
2.76
2.74
2.73
2.70
2.68
2.65
2.63
2.62
2.61
2.59
2.58
2.46
2.44
2.43
2.42
2.40
2.39
1.85
1.84
1.82
1.81
1.79
1.77
1.76
1.73
1.72
1.71
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 ppm
1.00
2.04
3.20
2.76
1.11
1.07
4.38

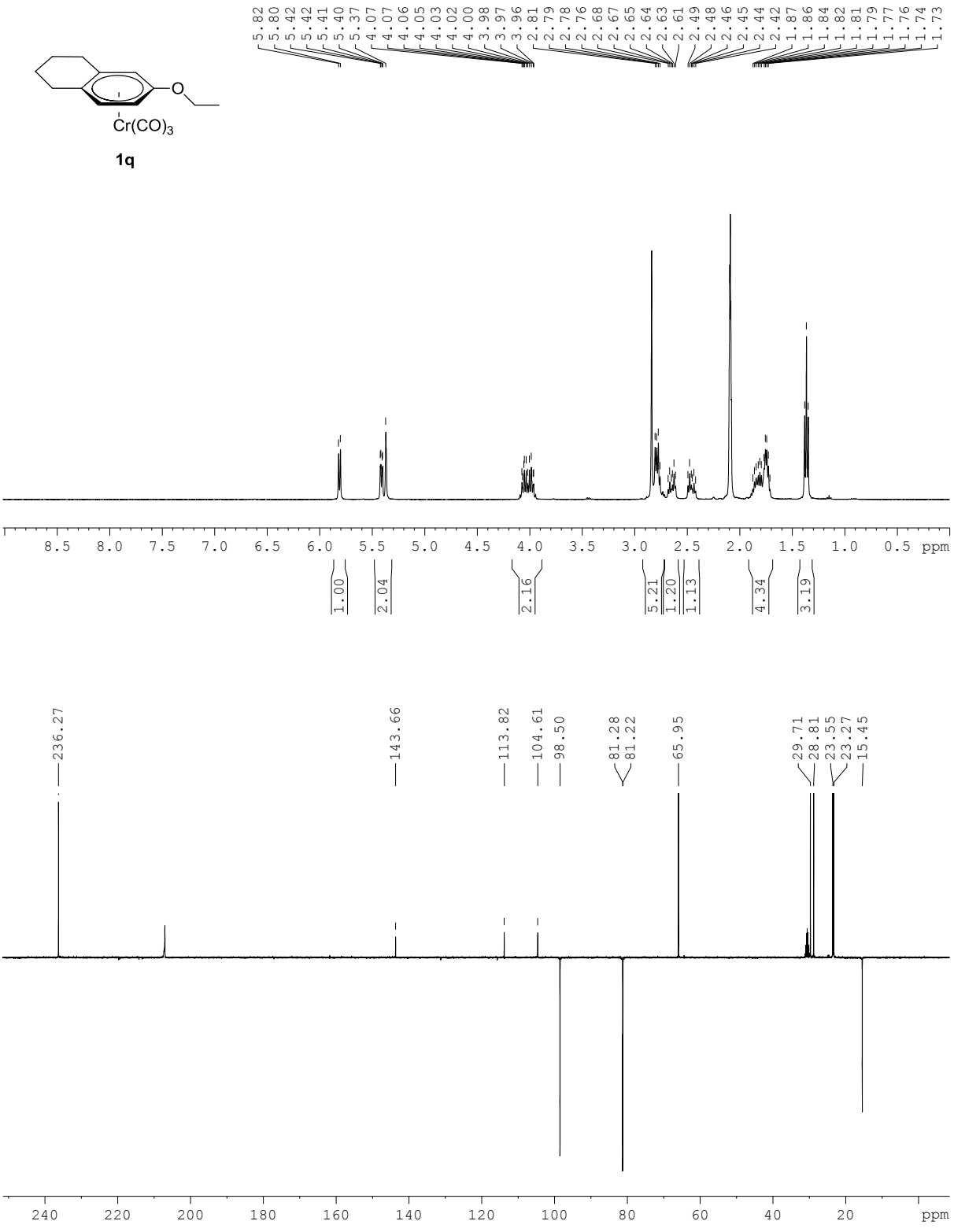

236.28
144.42
113.78
104.90
98.47
81.02
80.98
56.97
29.78
28.88
23.62
23.34
240 220 200 180 160 140 120 100 80 60 40 20 ppm

6-Methoxy-1,2,3,4-tetrahydronaphthalene-5,7-d_2 chromium tricarbonyl (1p-D).

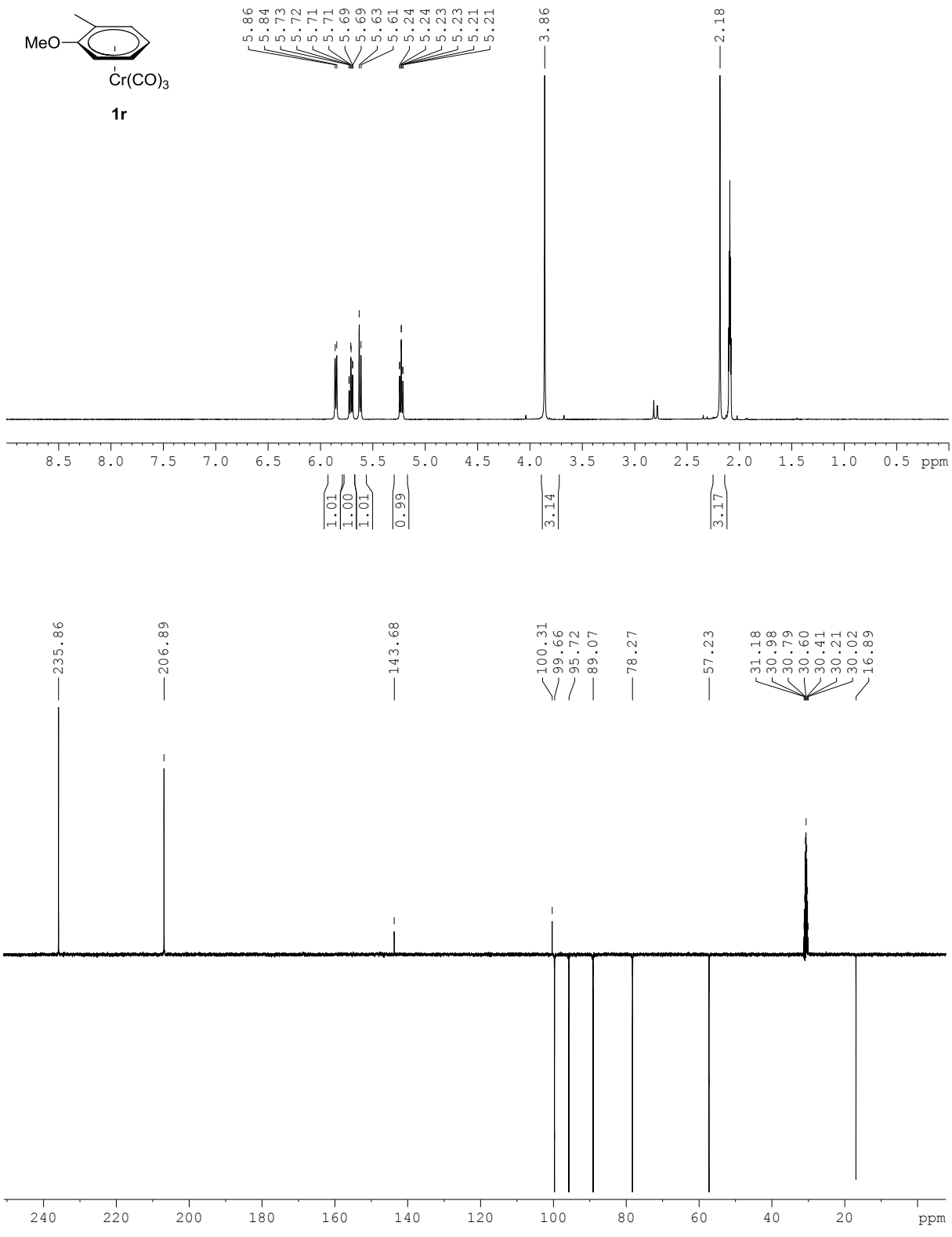




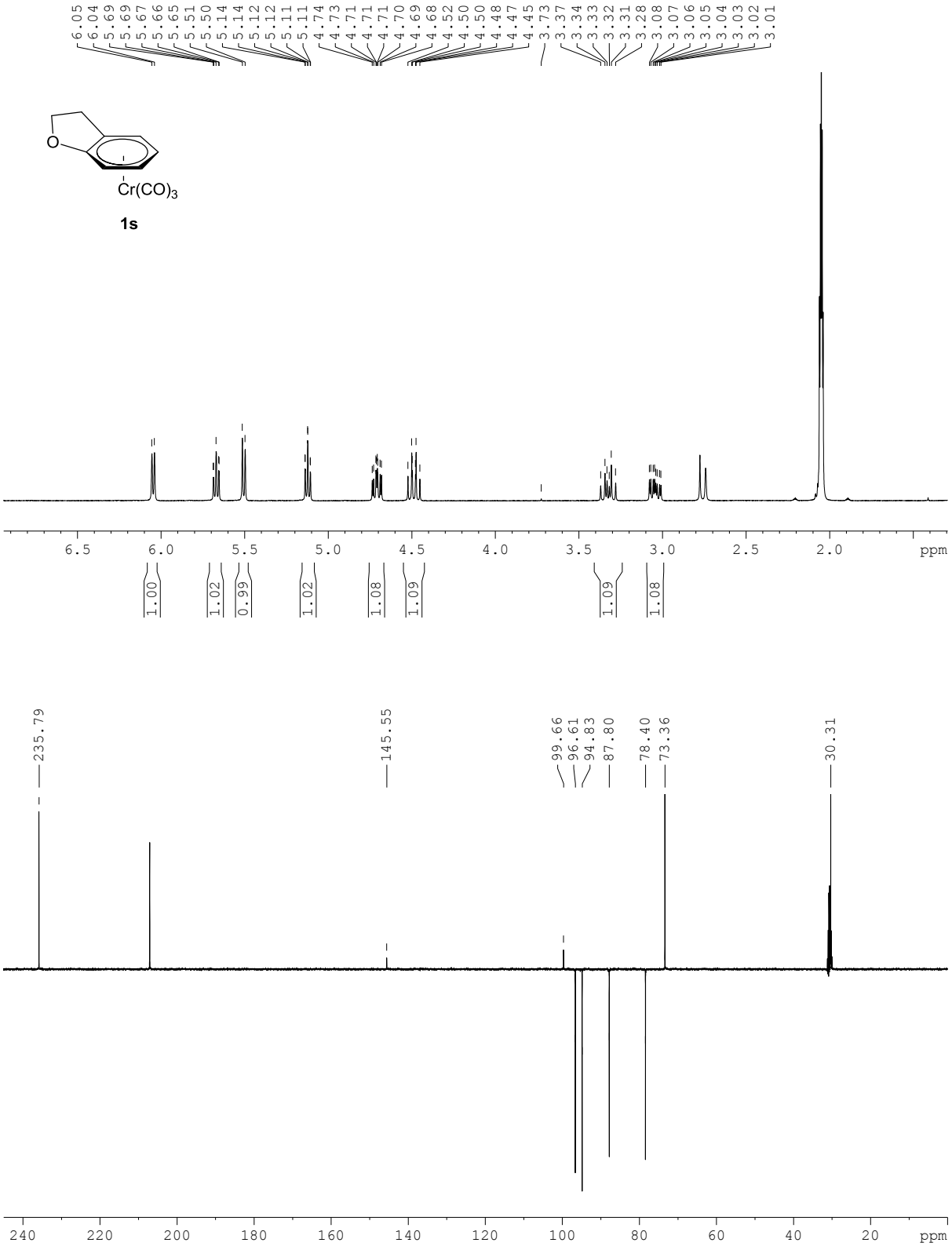
2-Ethoxy-1,2,3,4-tetrahydronaphthalene chromium tricarbonyl (1q).



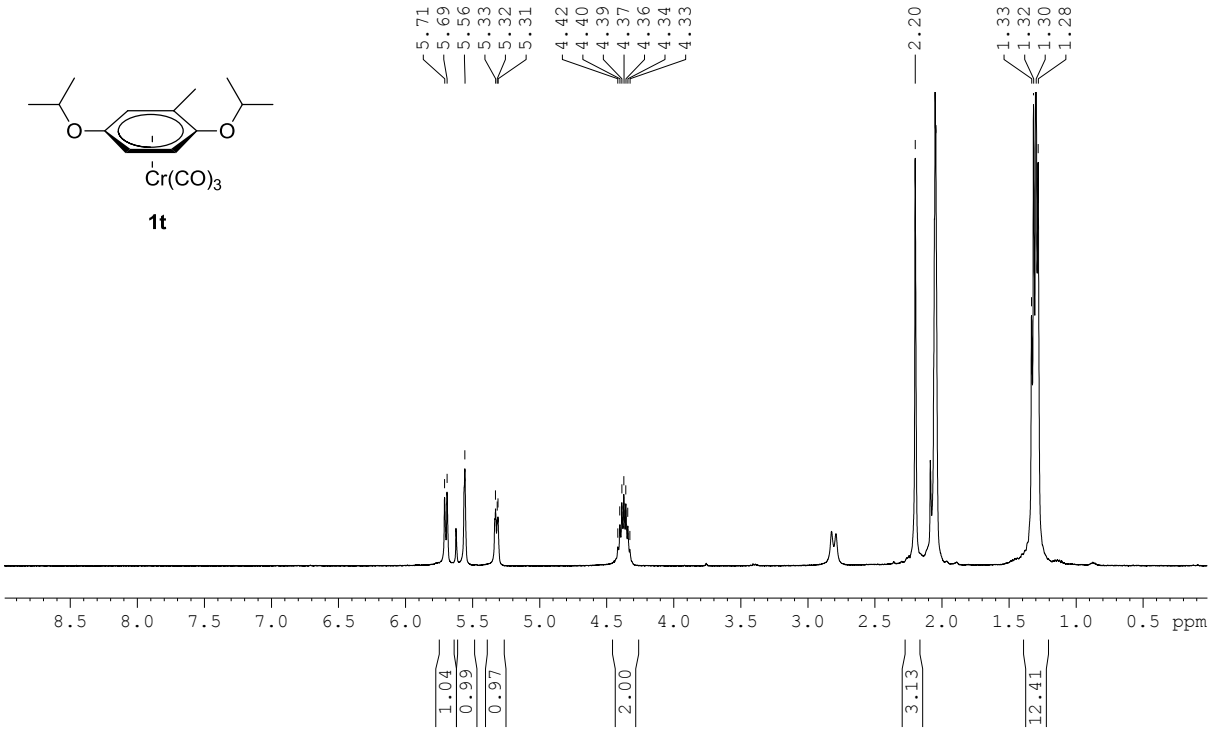
1-Methoxy-2-methylbenzene chromium tricarbonyl (1r).

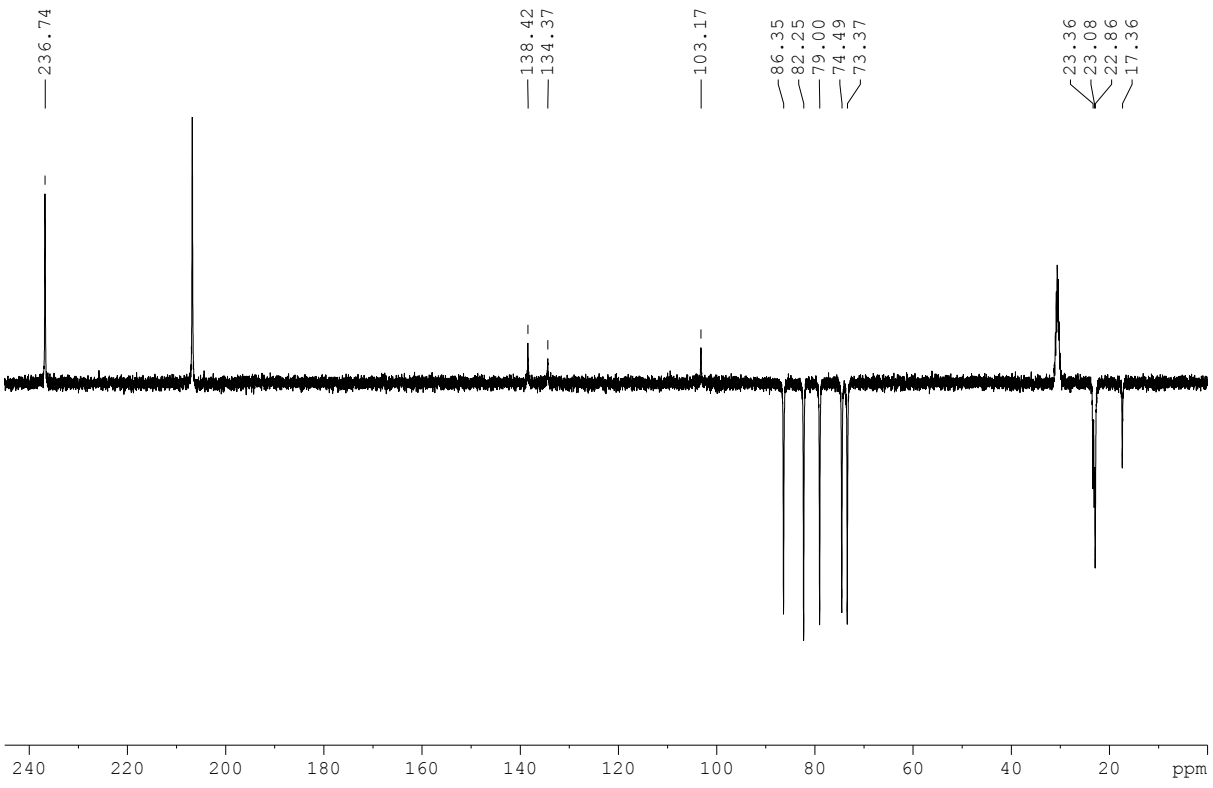


2,3-Dihydrobenzofuran chromium tricarbonyl (1s).

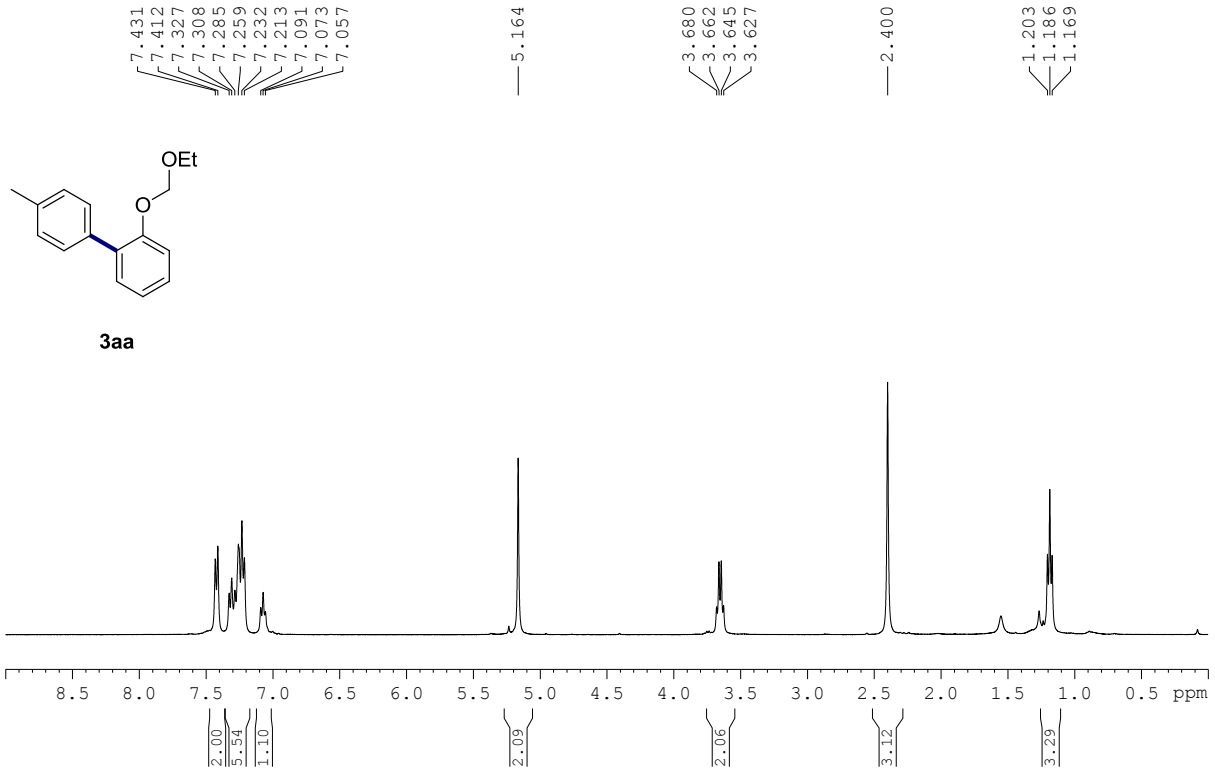


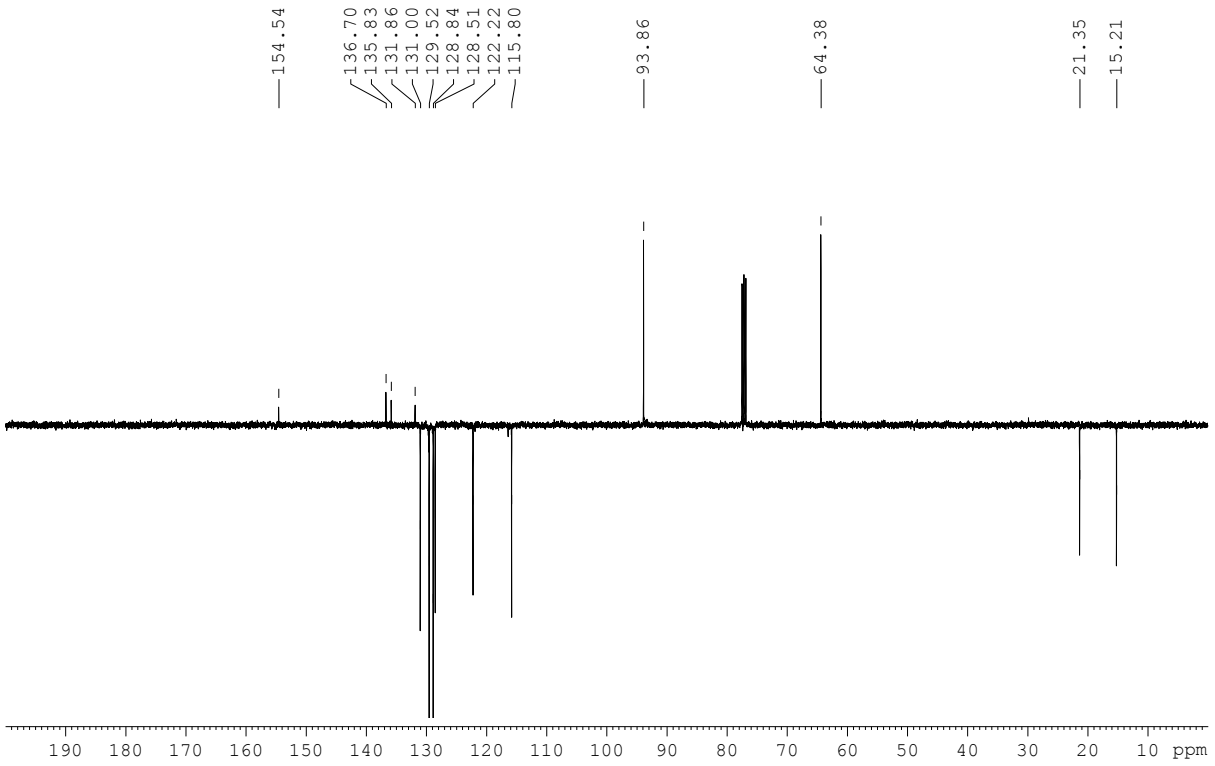
1,4-Diisopropyl-2-methylbenzene tricarbonyl chromium (1t).



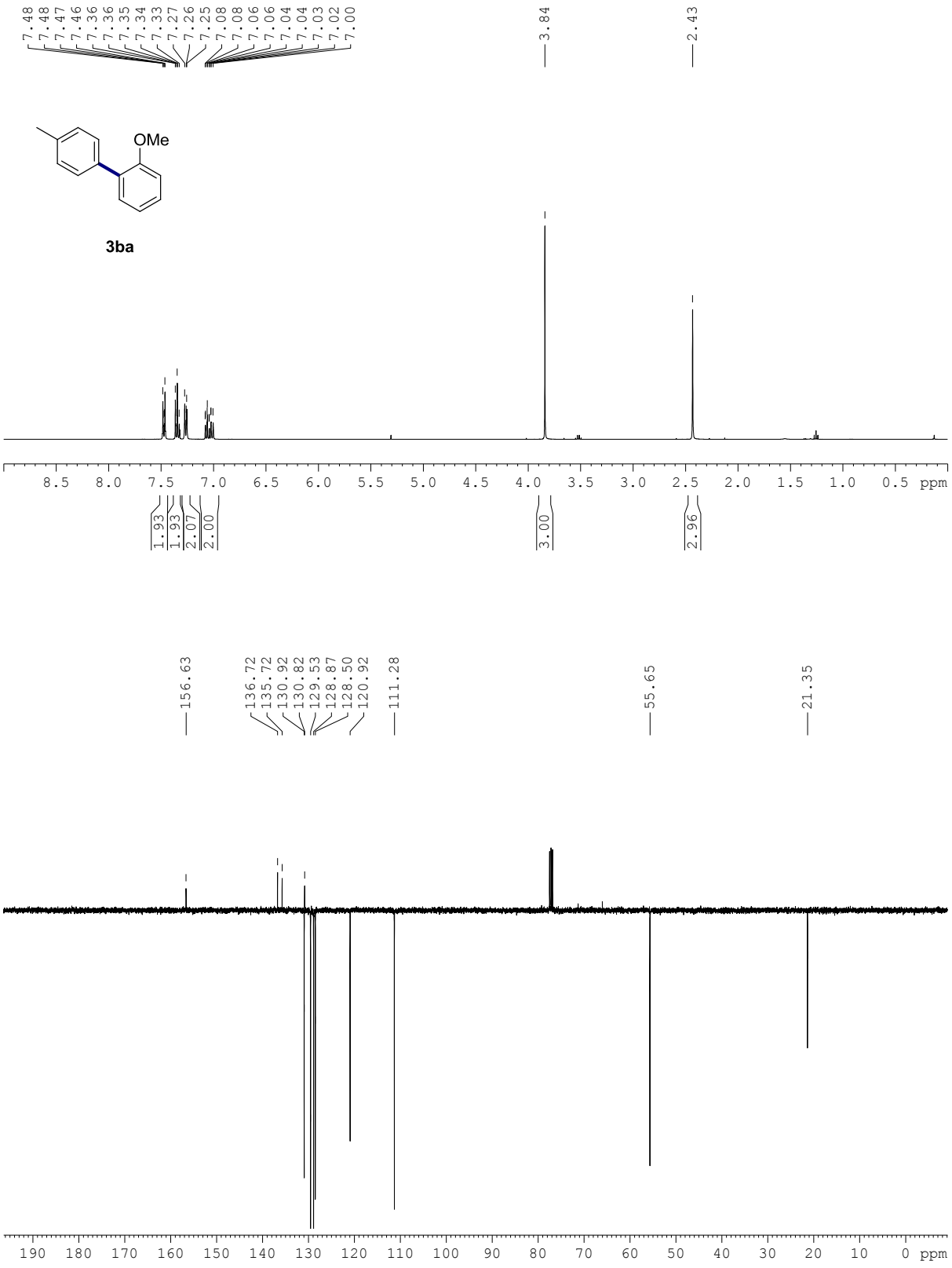


2-(Ethoxymethoxy)-4'-methyl-1,1'-biphenyl (3aa)

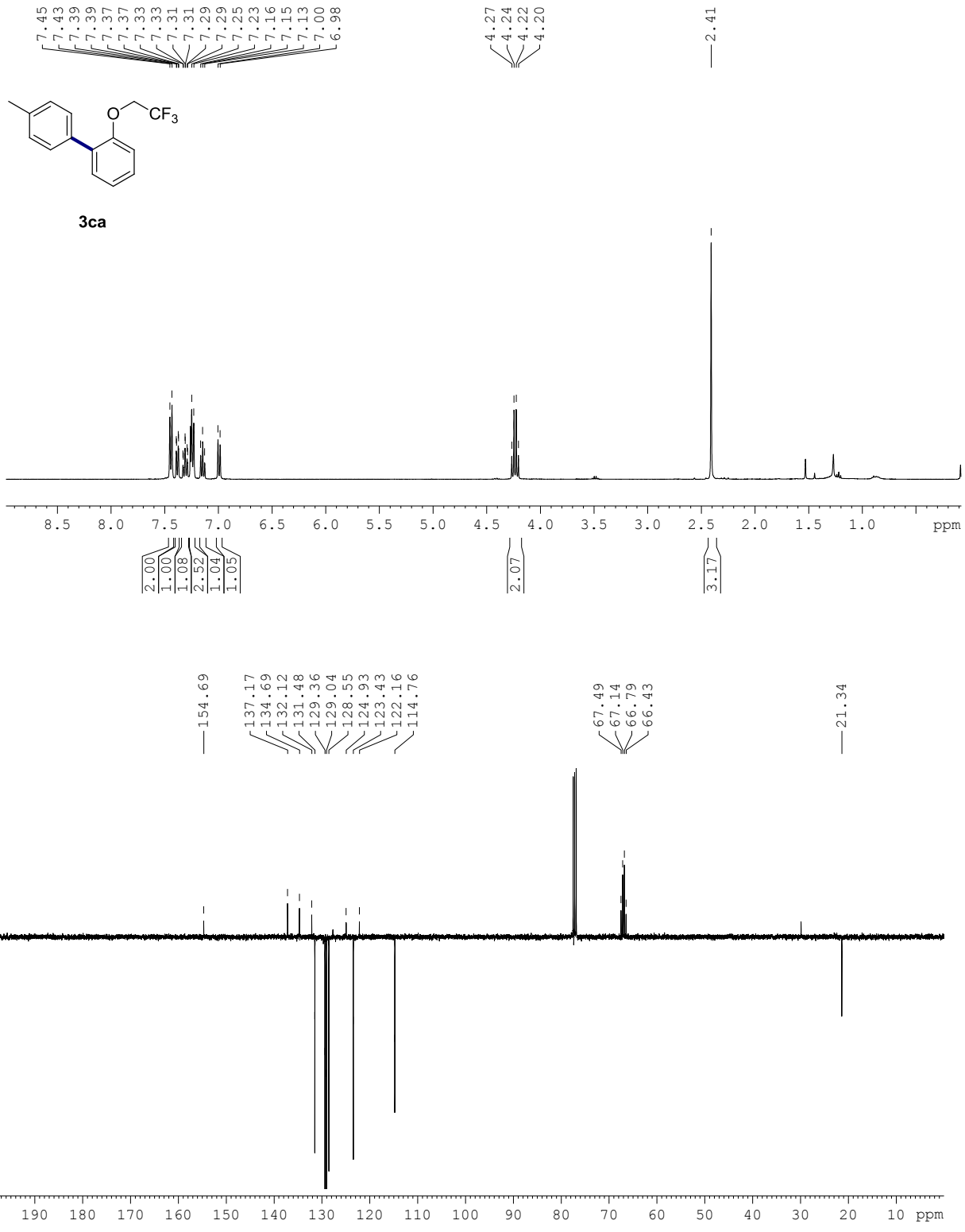




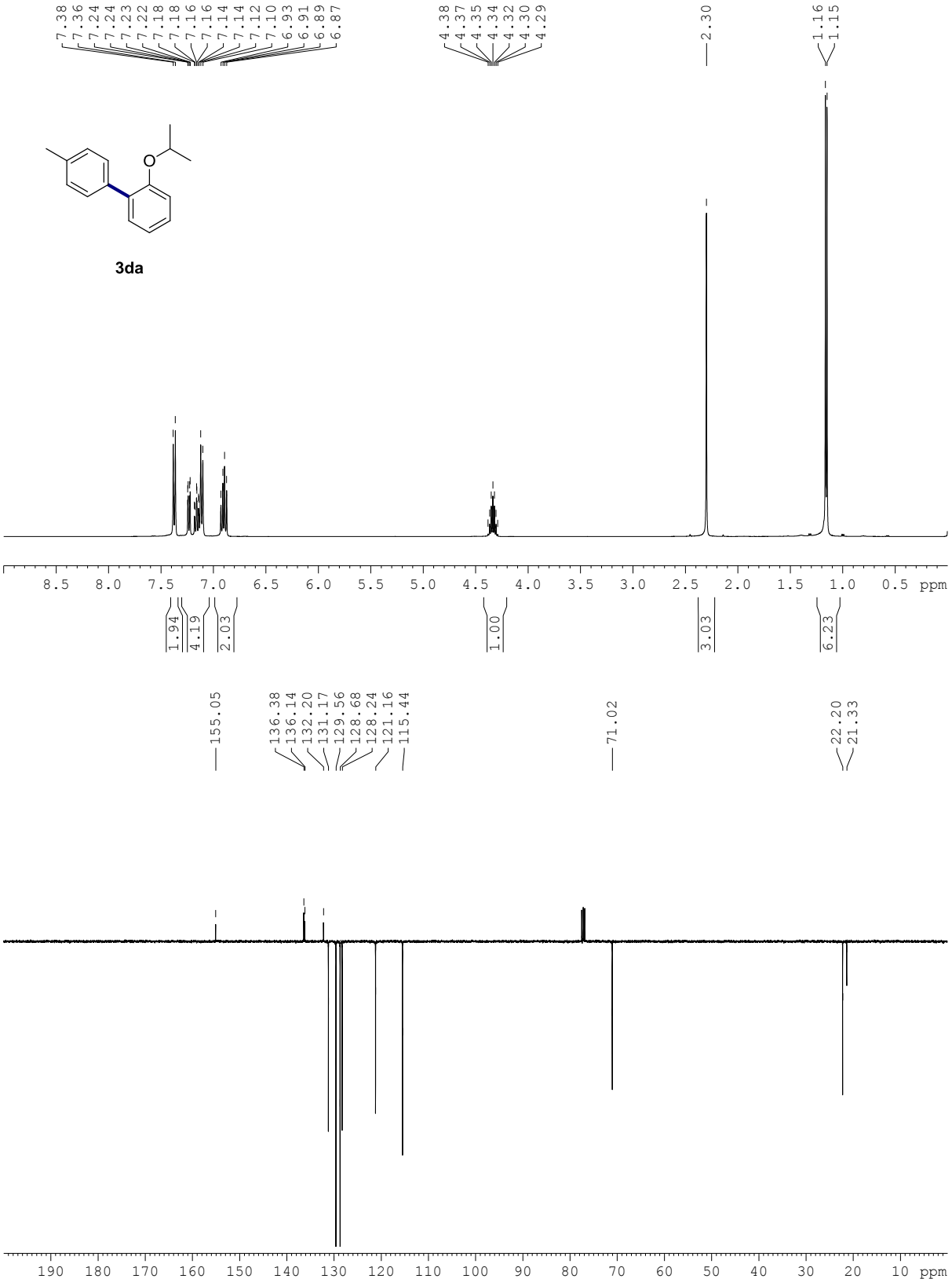
2-Methoxy-4'-methyl-1,1'-biphenyl (3ba).



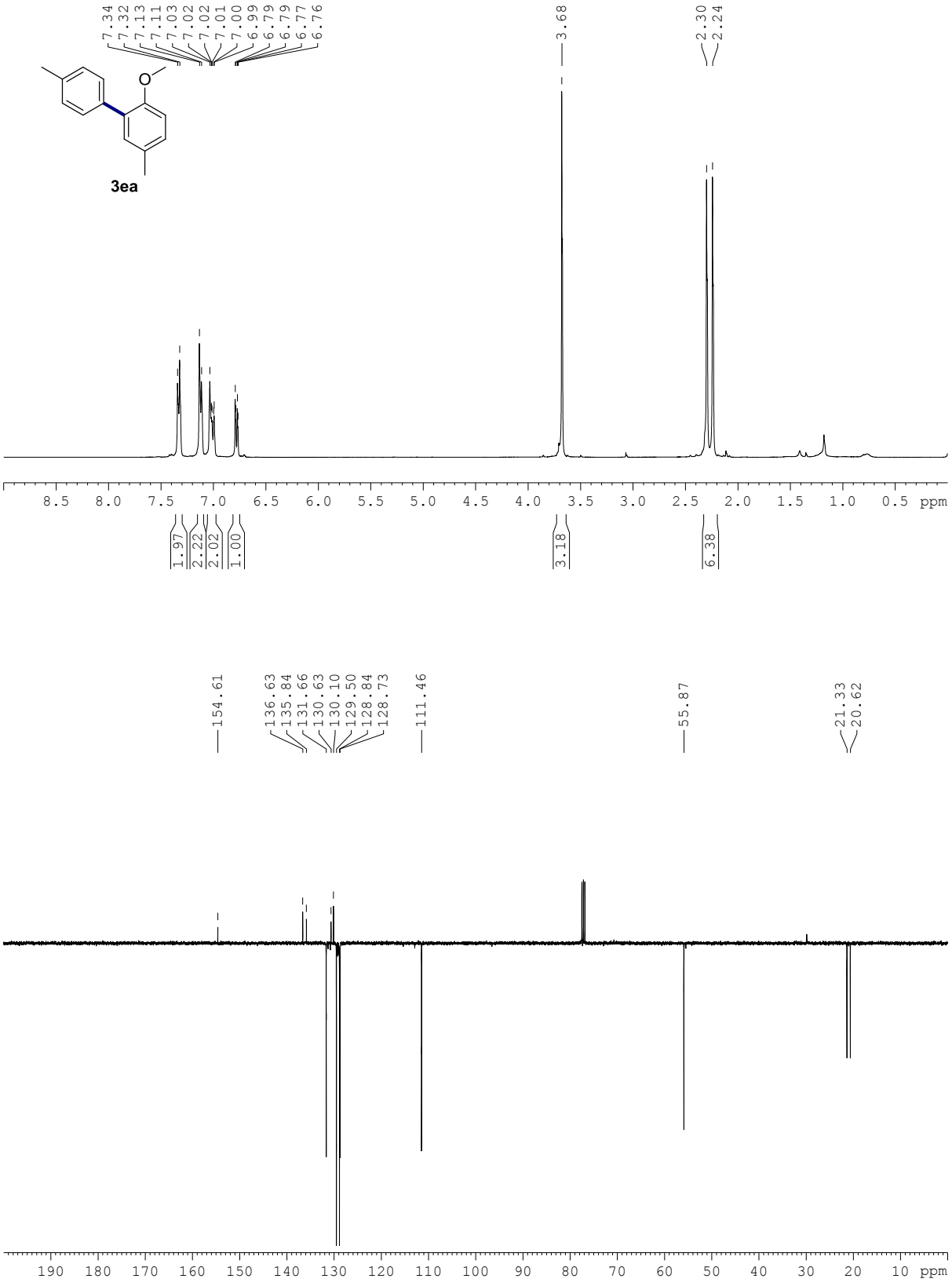
4'-methyl-2-(2,2,2-trifluoroethoxy)-1,1'-biphenyl (3ca).



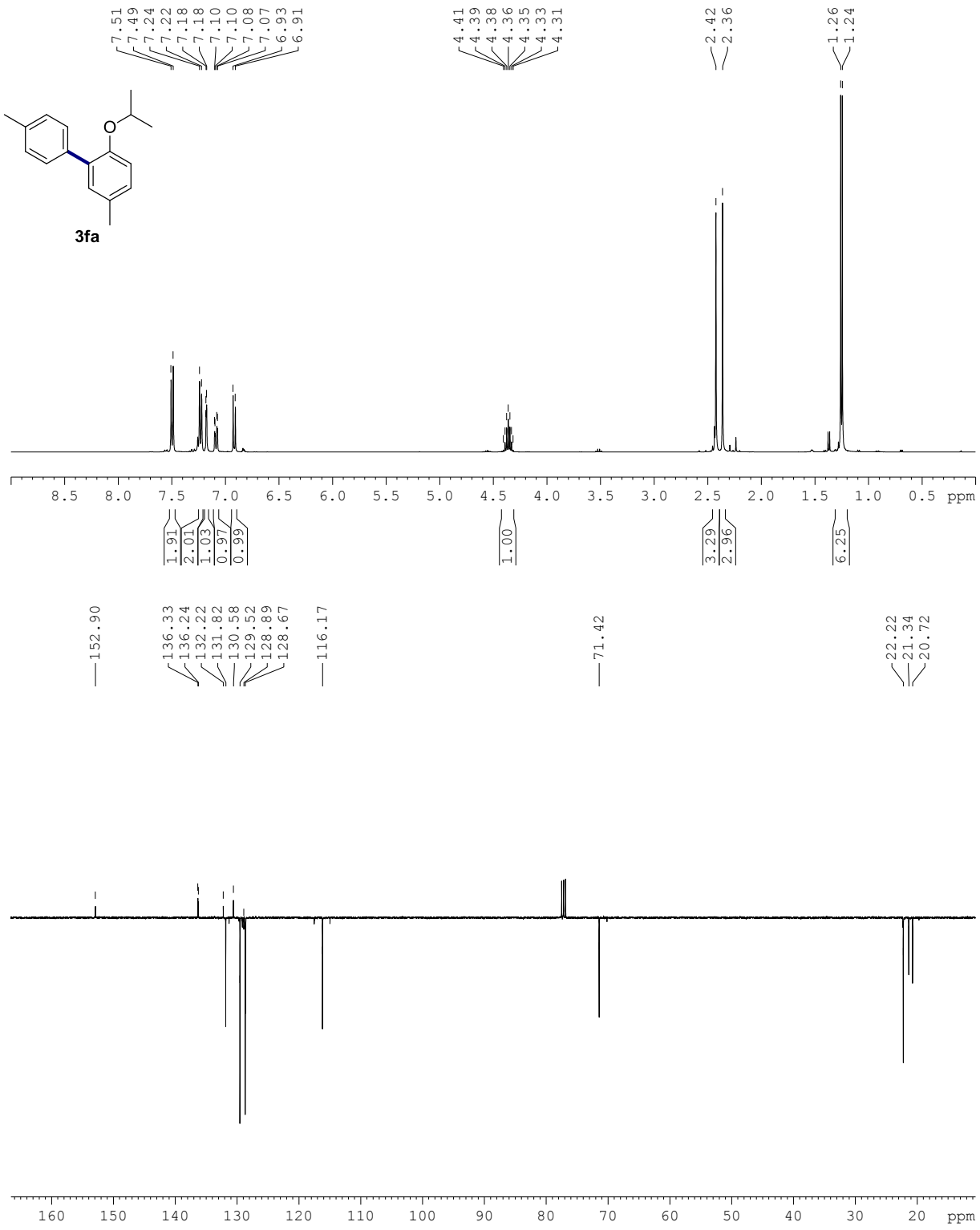
2-Isopropoxy-4'-methyl-1,1'-biphenyl (3da).



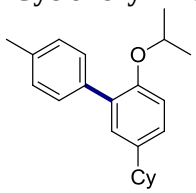
2-Methoxy-4',5-dimethyl-1,1'-biphenyl (3ea).



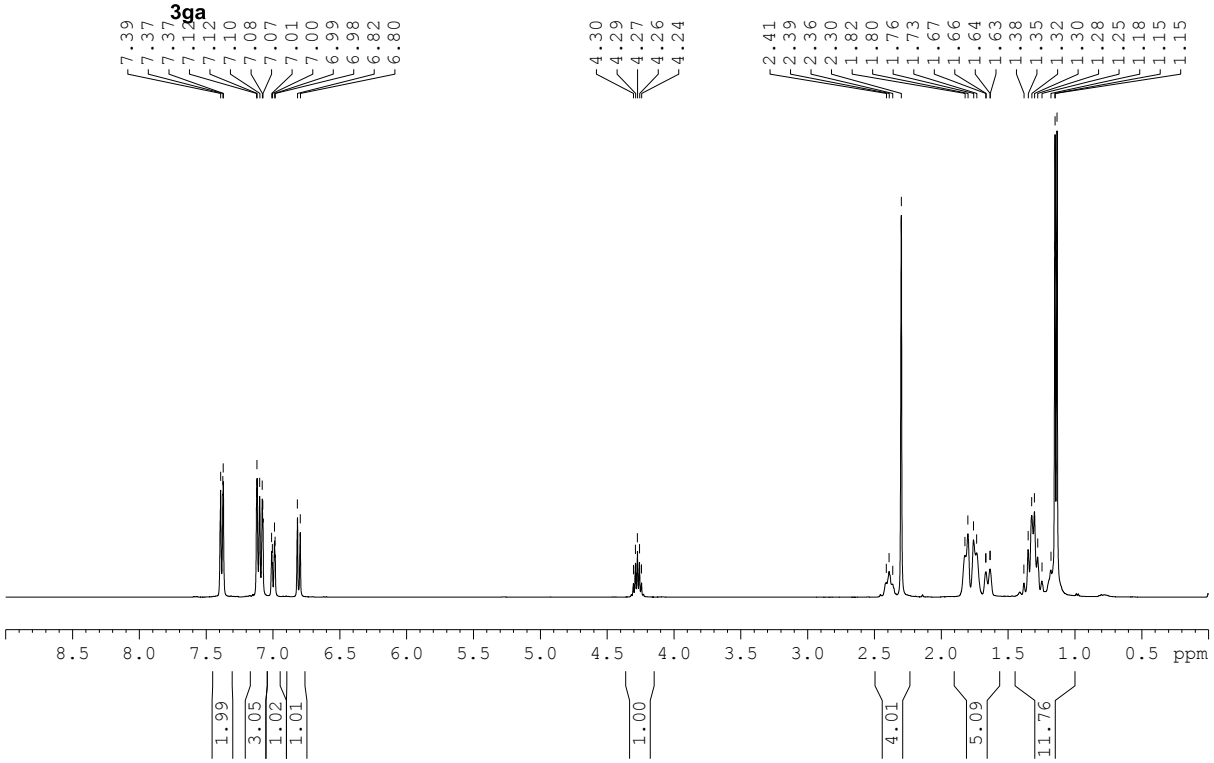
2-Isopropoxy-4',5-dimethyl-1,1'-biphenyl (3fa).

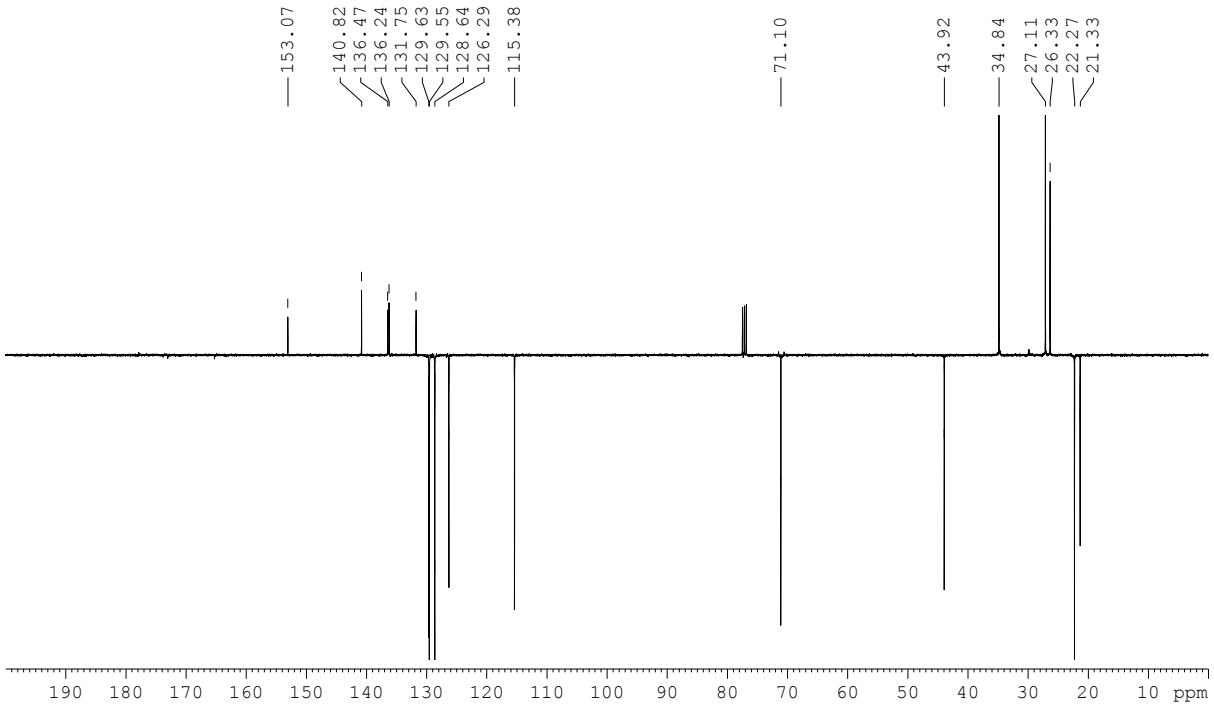


5-Cyclohexyl-2-isopropoxy-4'-methyl-1,1'-biphenyl (3ga).

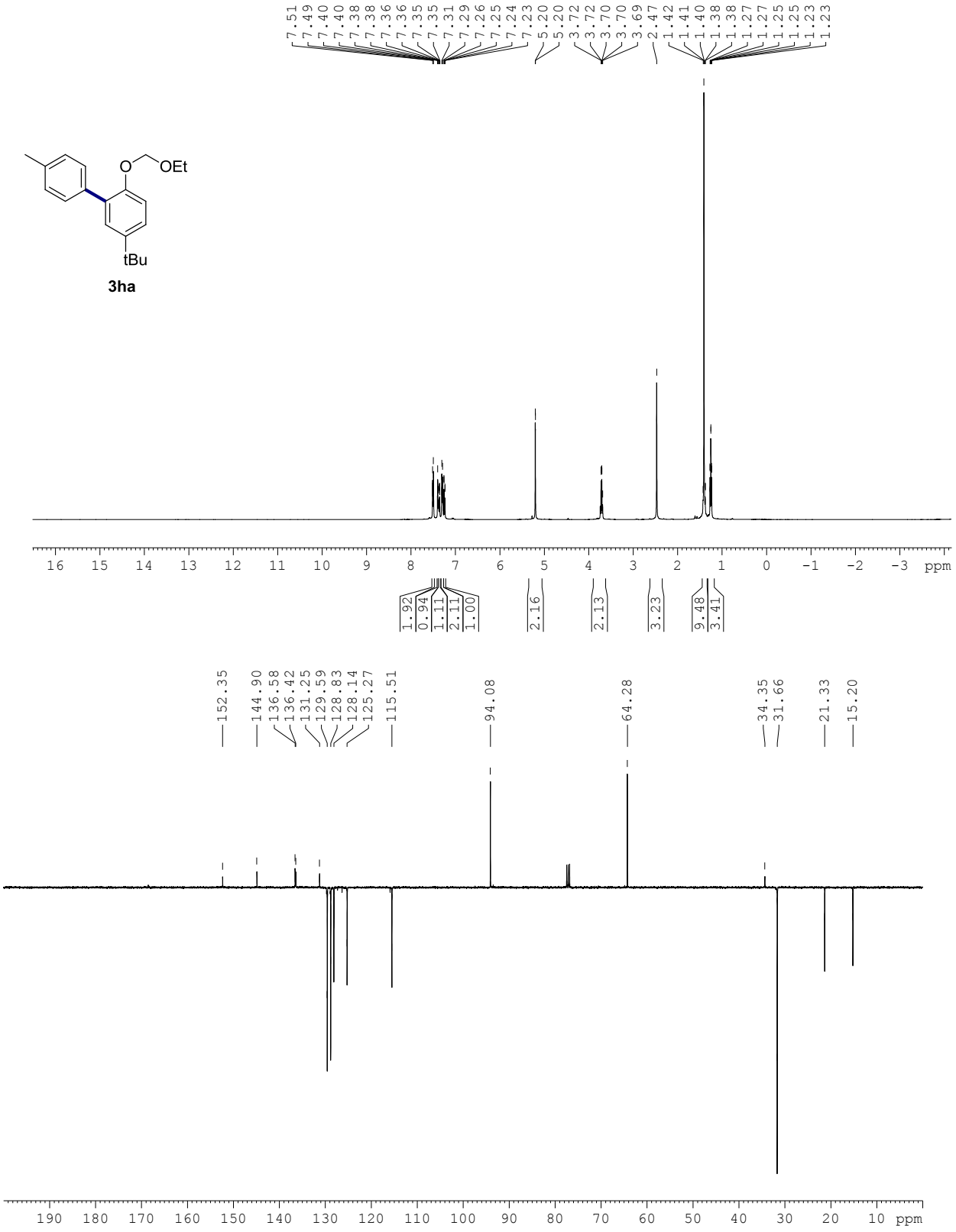


3ga

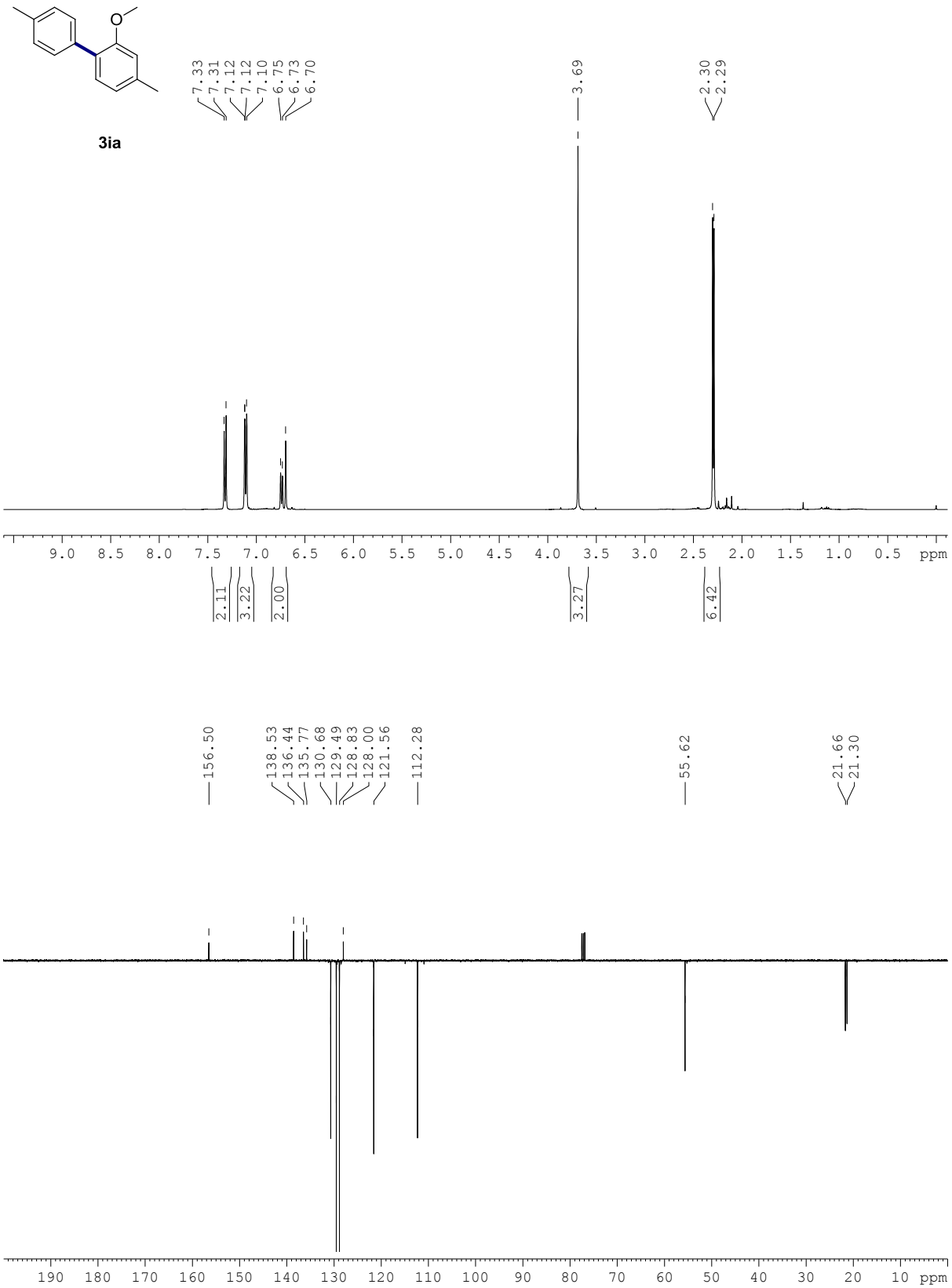




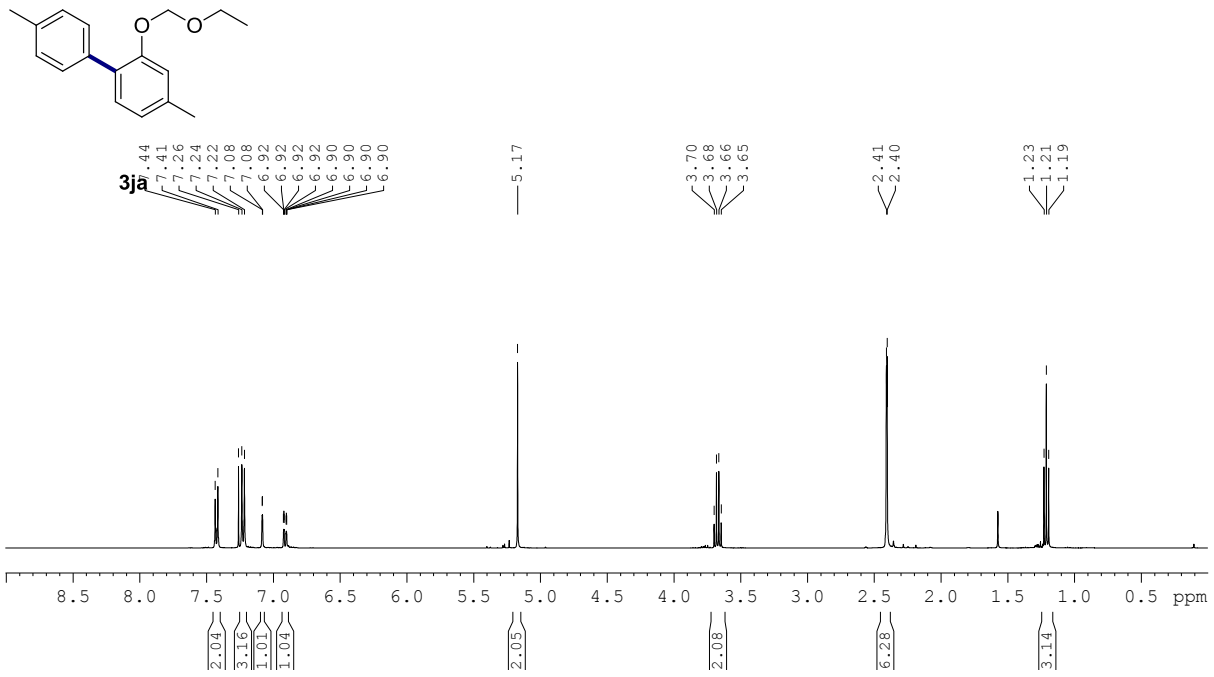
5-(Tert-butyl)-2-(ethoxymethoxy)-4'-methyl-1,1'-biphenyl (3ha).

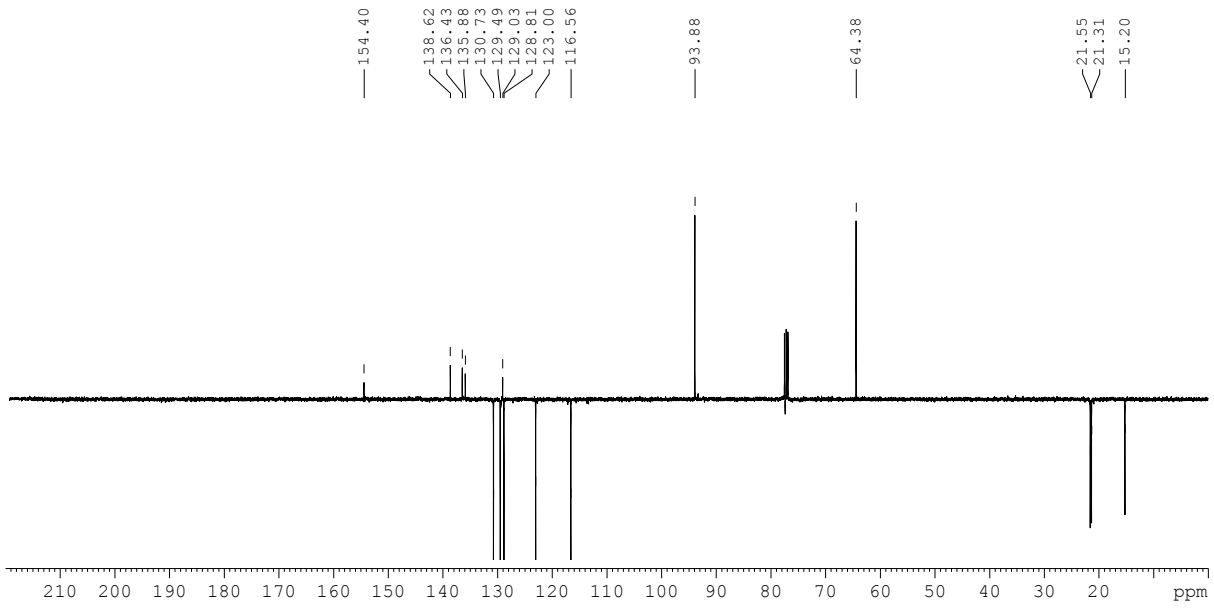


2-Methoxy-4,4'-dimethyl-1,1'-biphenyl (3ia).

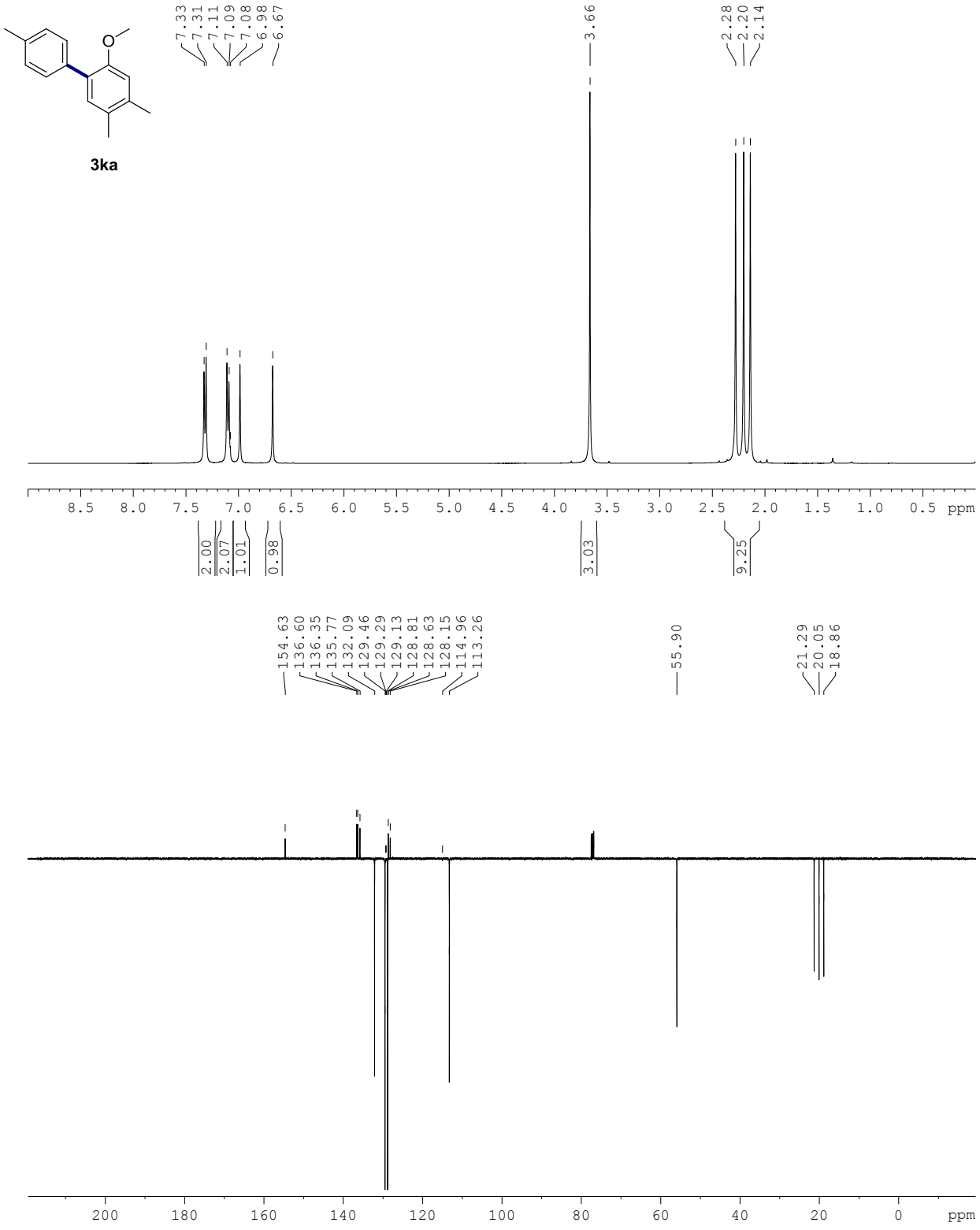


2-(Ethoxymethoxy)-4,4'-dimethyl-1,1'-biphenyl (3ja).

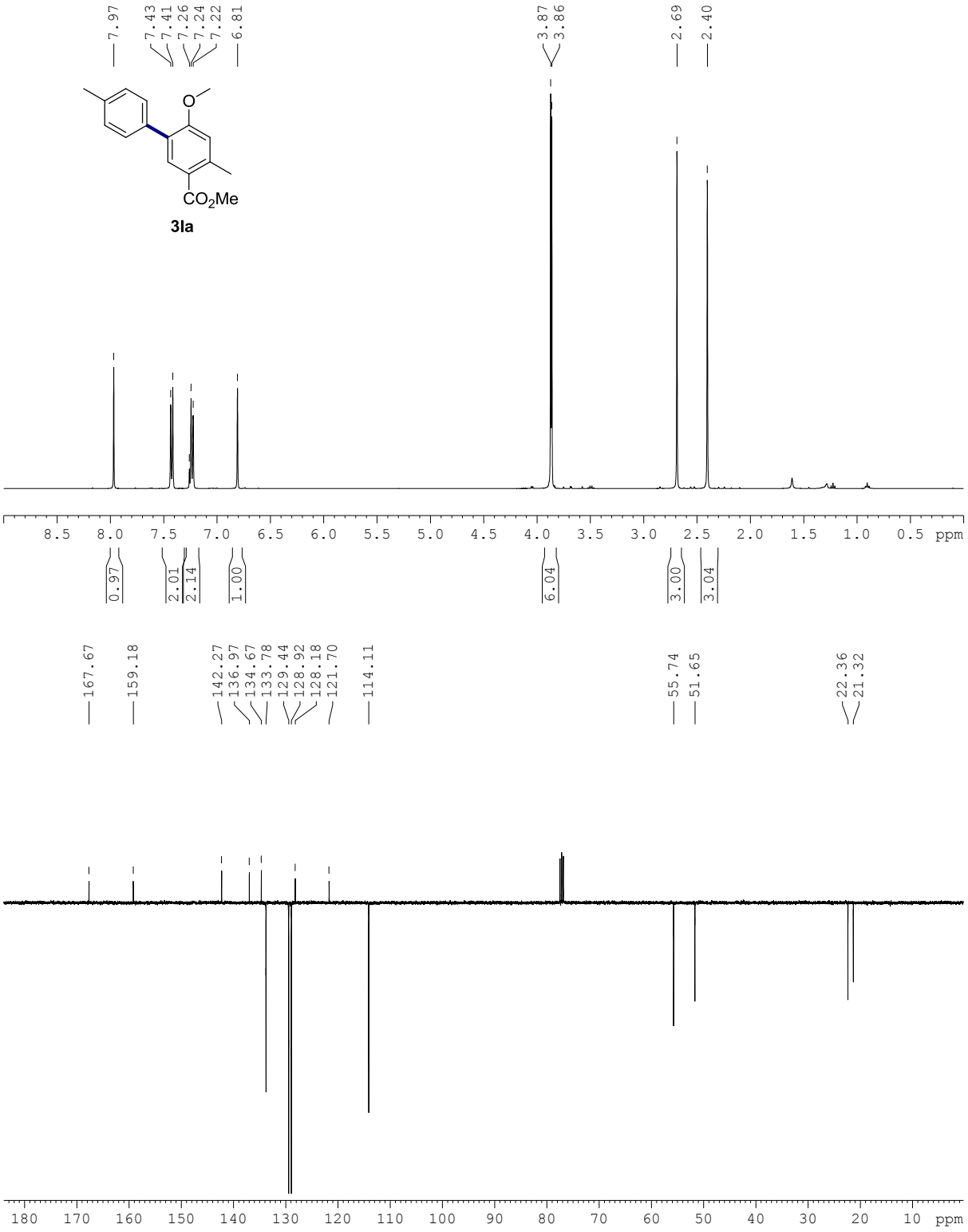




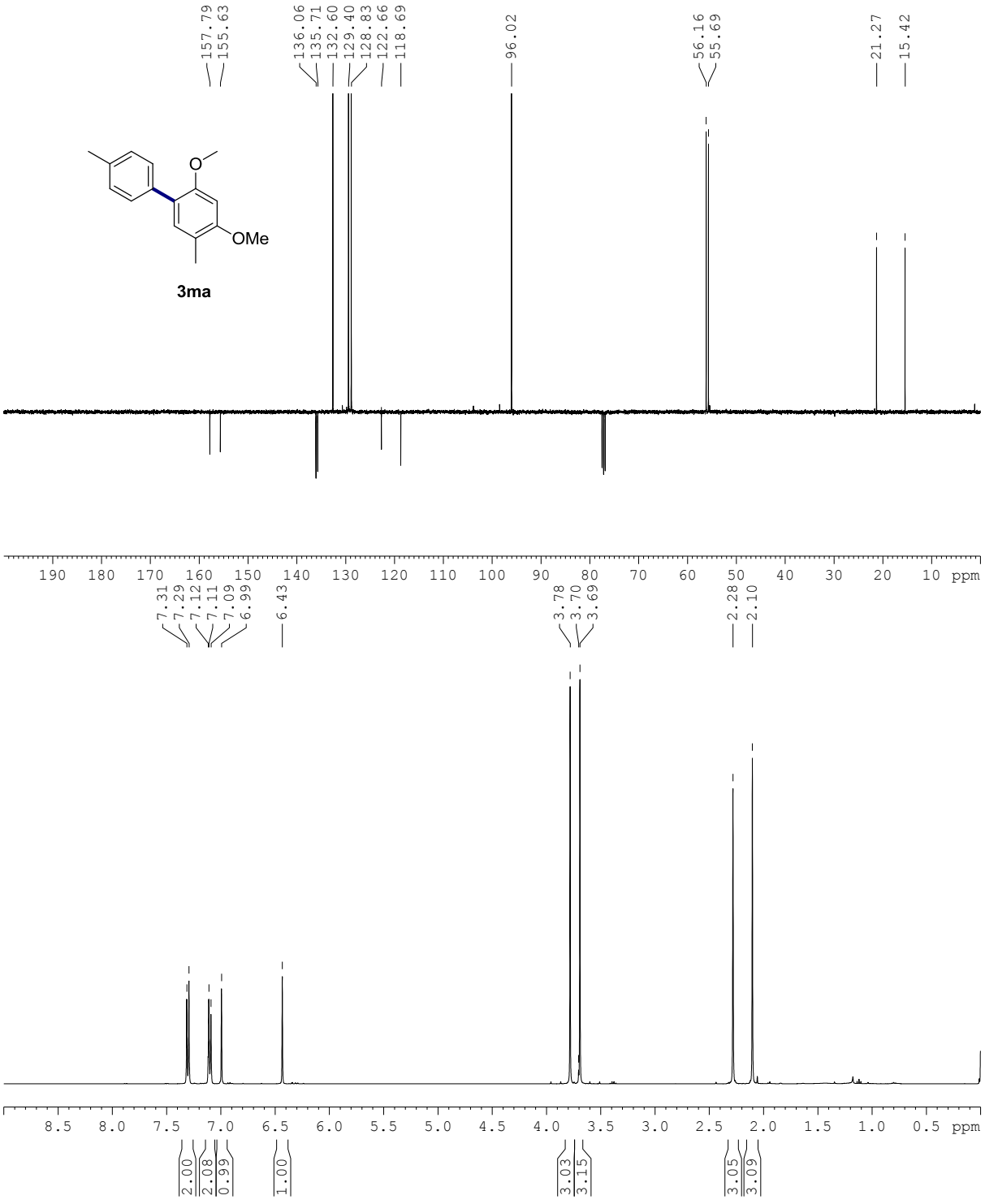
2-Methoxy-4,4',5-trimethyl-1,1'-biphenyl (3ka)



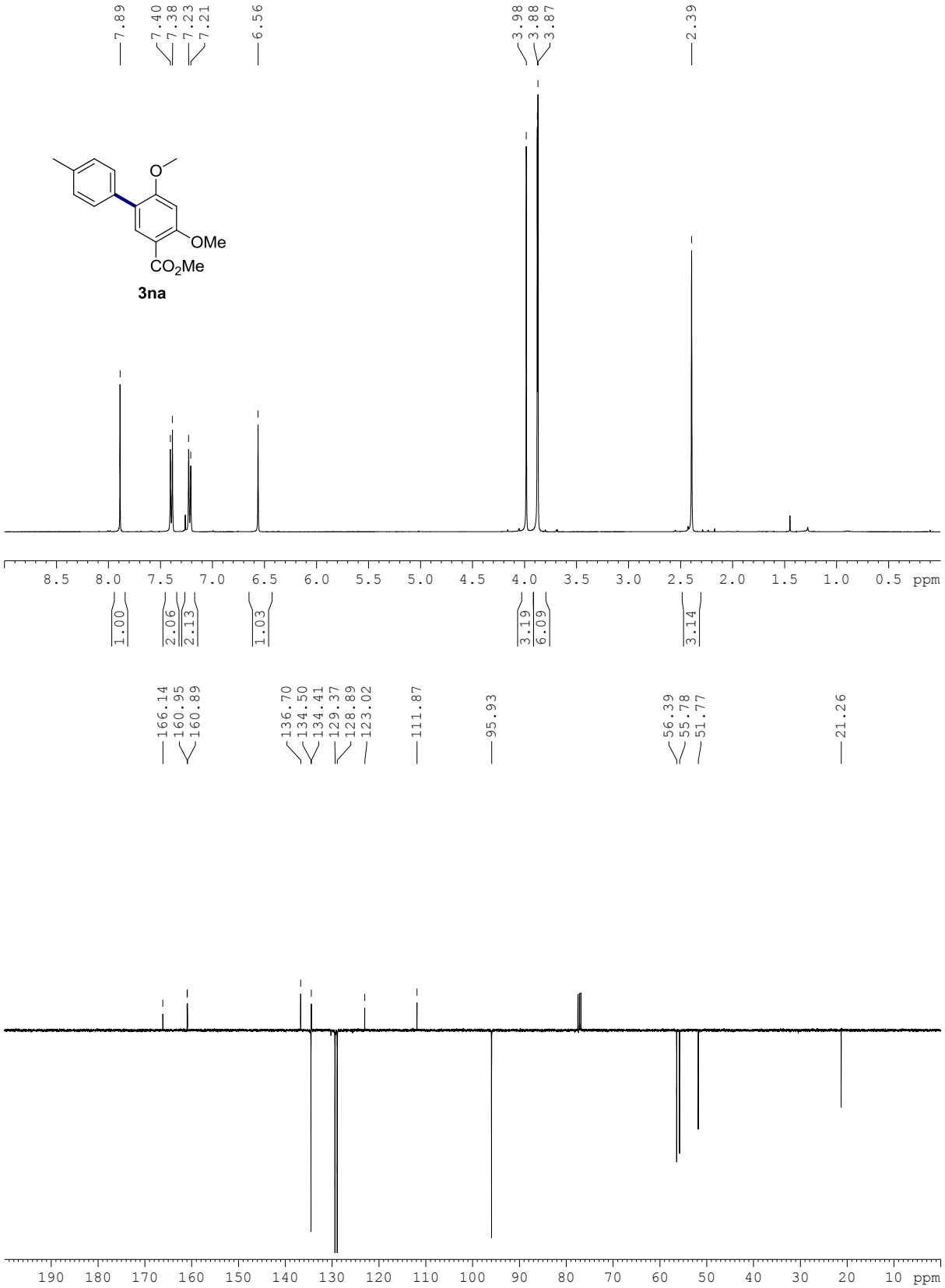
Methyl 6-methoxy-4,4'-dimethyl-[1,1'-biphenyl]-3-carboxylate (3la).



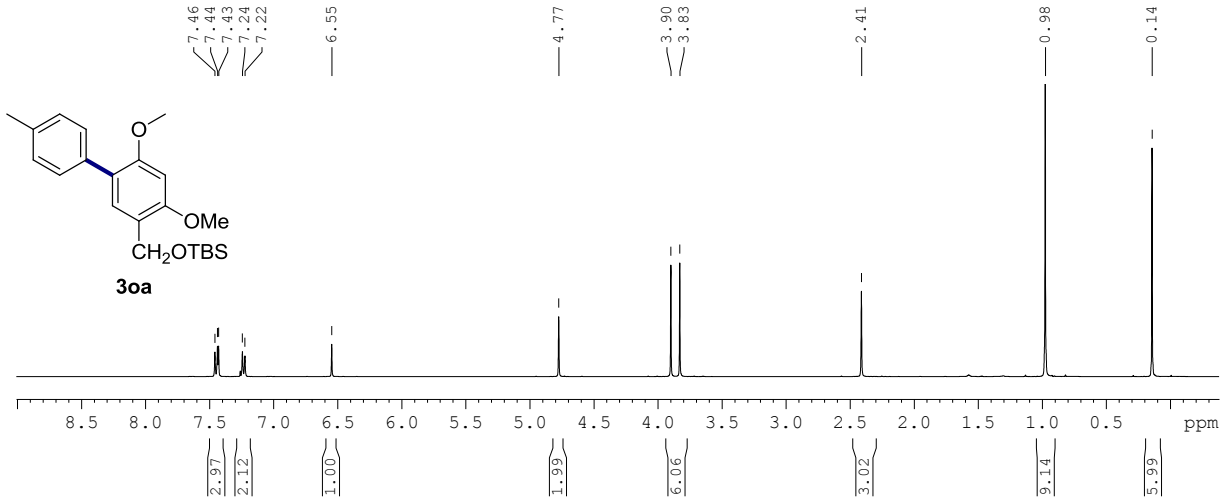
2,4-Dimethoxy-4',5-dimethyl-1,1'-biphenyl (3ma).

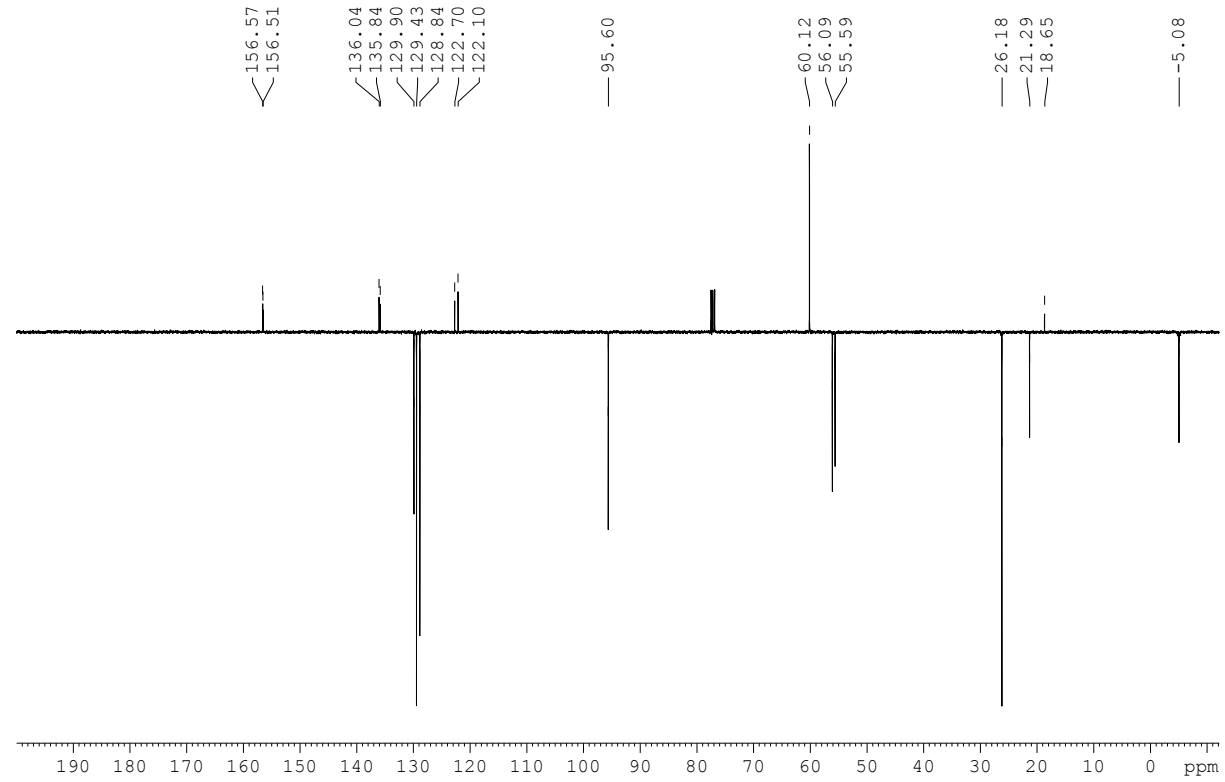


Methyl 4,6-dimethoxy-4'-methyl-[1,1'-biphenyl]-3-carboxylate (3na).

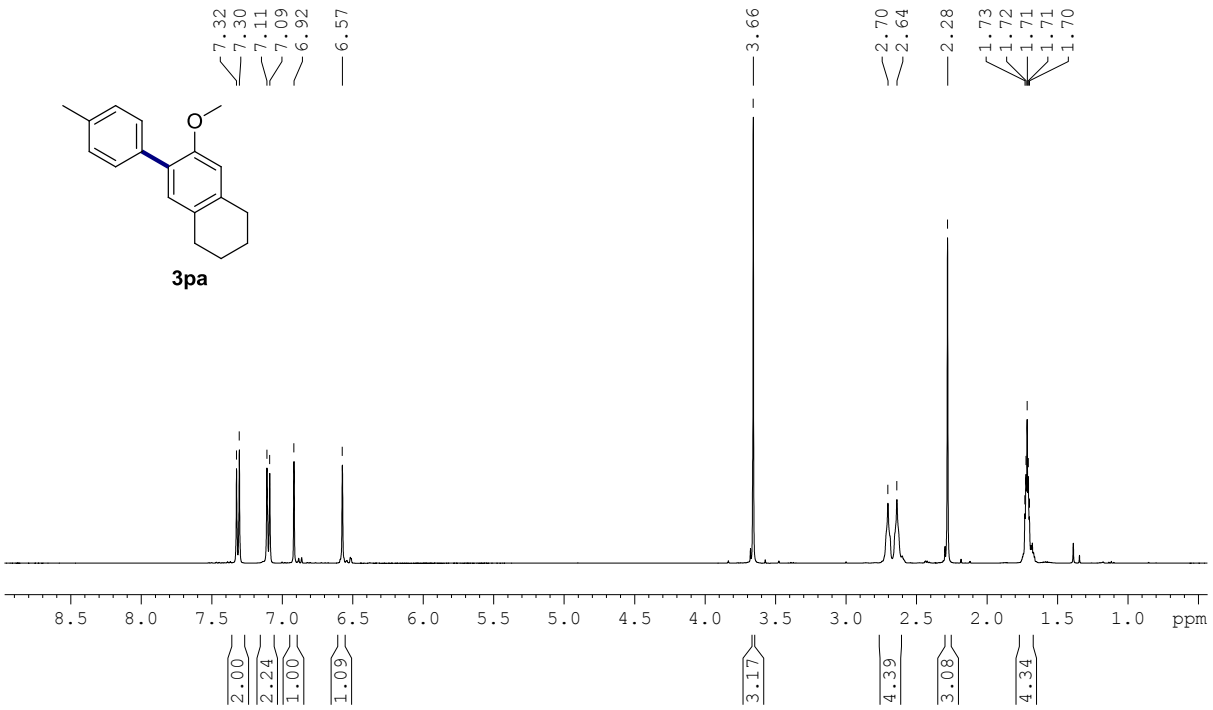


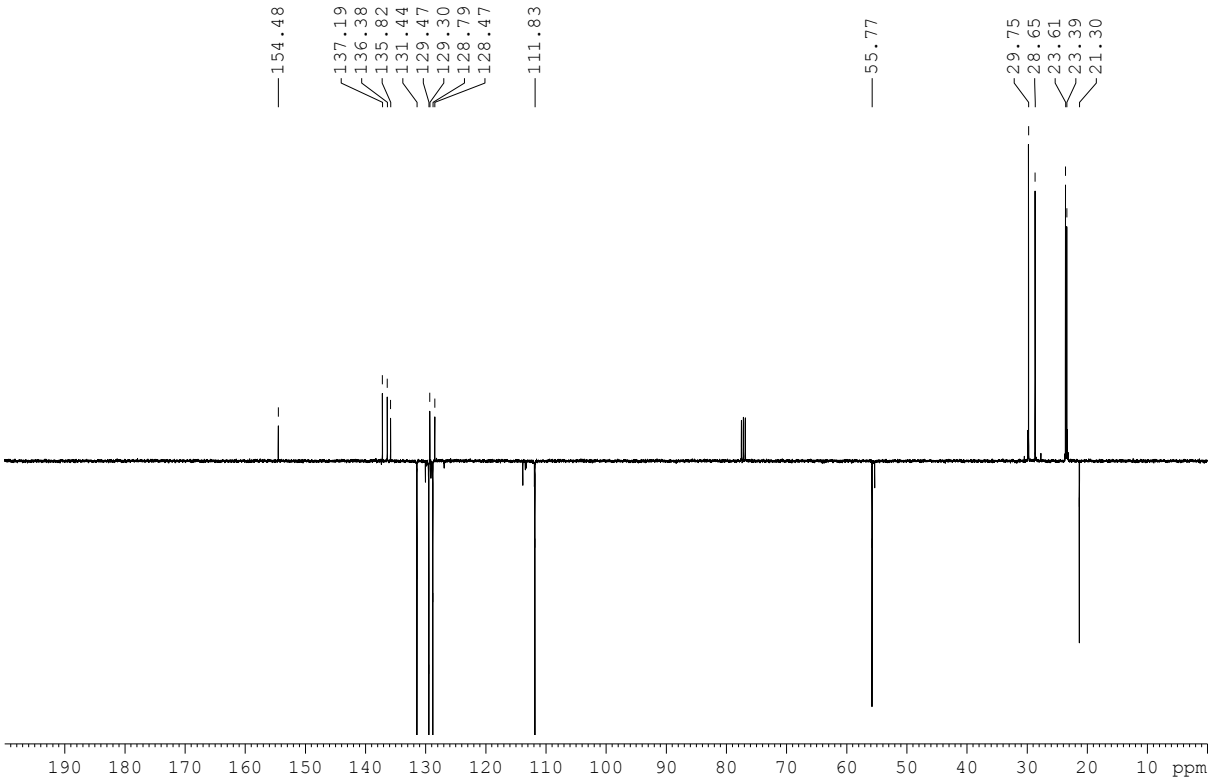
Tert-butyl((4,6-dimethoxy-4'-methyl-[1,1'-biphenyl]-3-yl)methoxy)dimethylsilane (3oa).



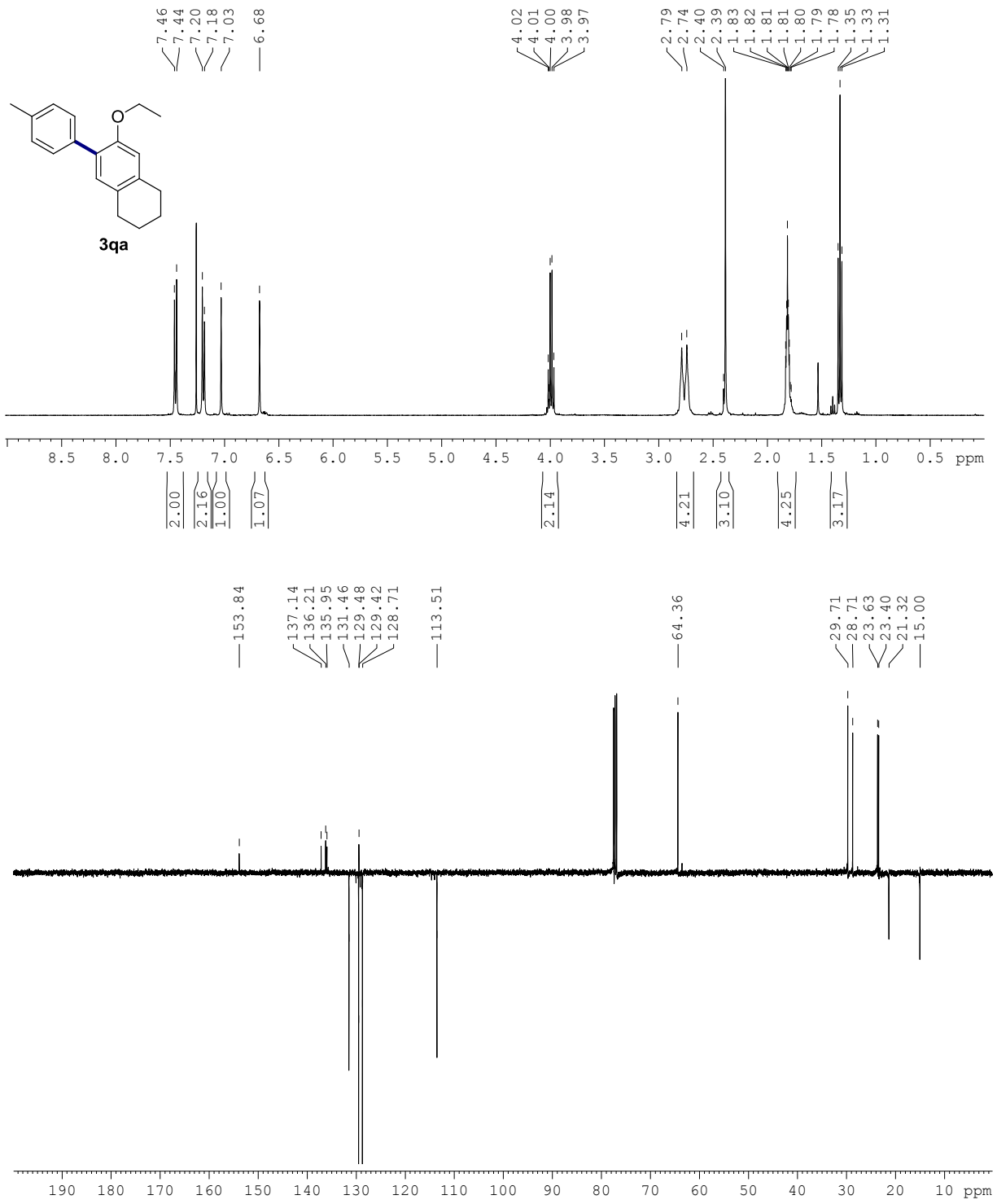


6-Methoxy-7-(p-tolyl)-1,2,3,4-tetrahydronaphthalene (3pa).

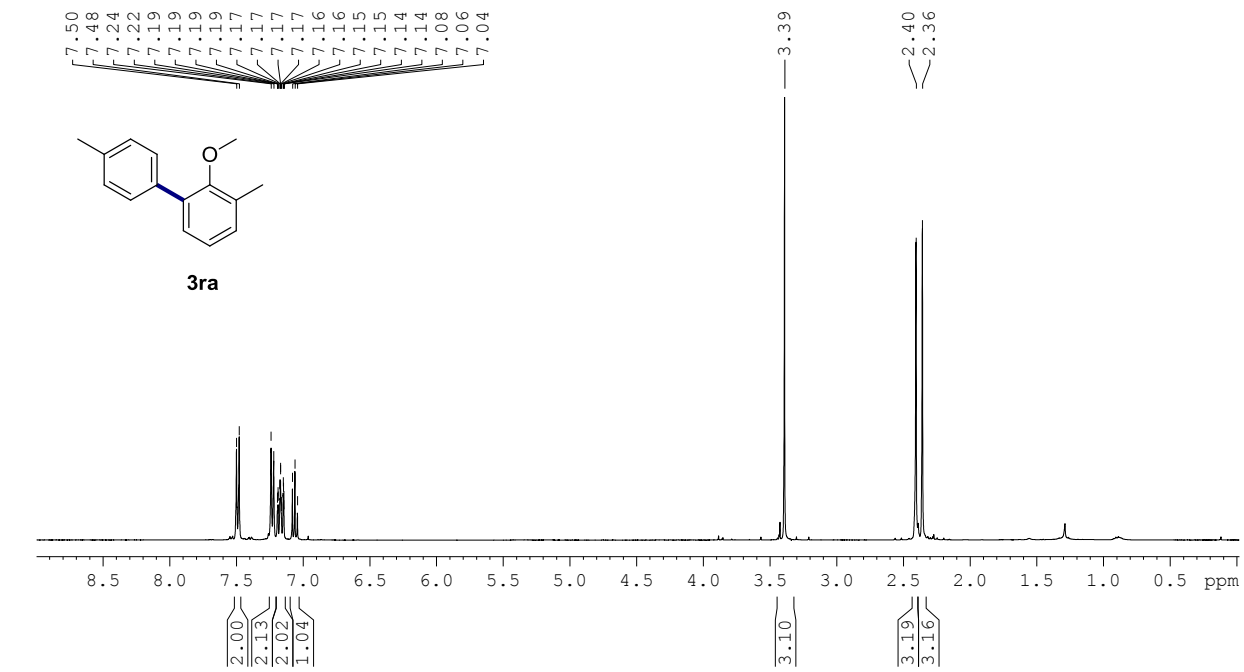


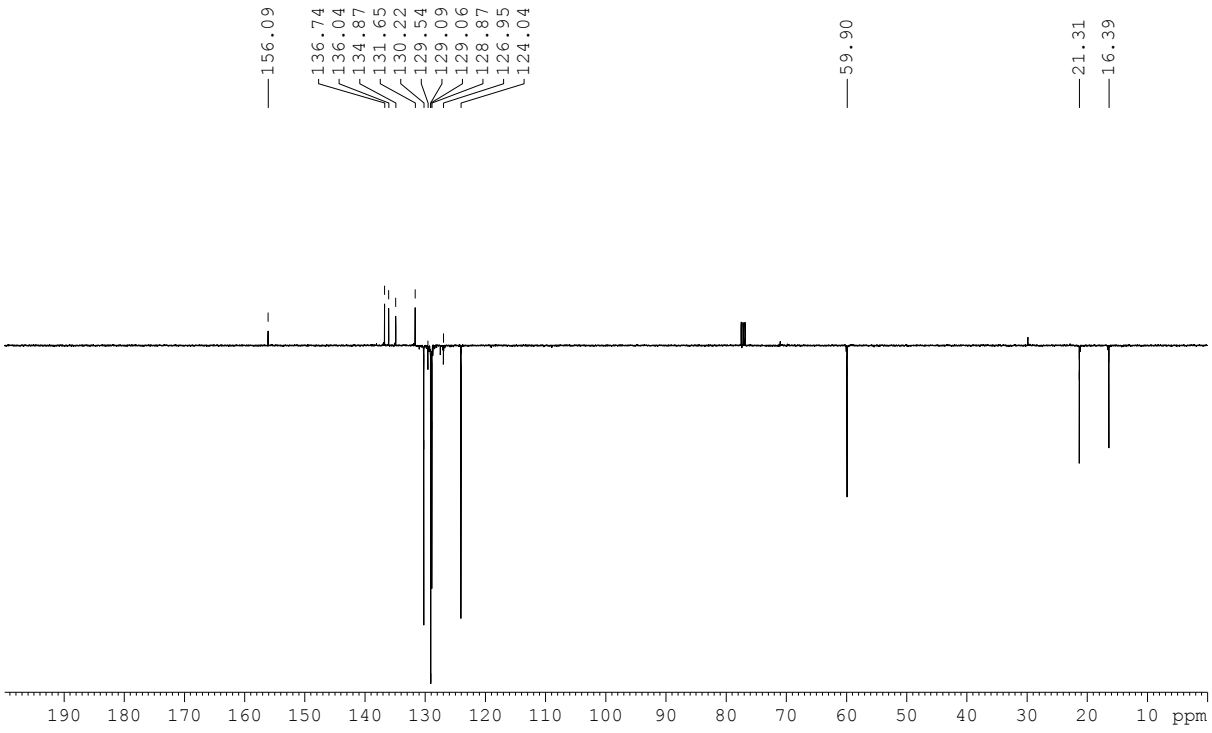


6-Ethoxy-7-(p-tolyl)-1,2,3,4-tetrahydronaphthalene (3qa).

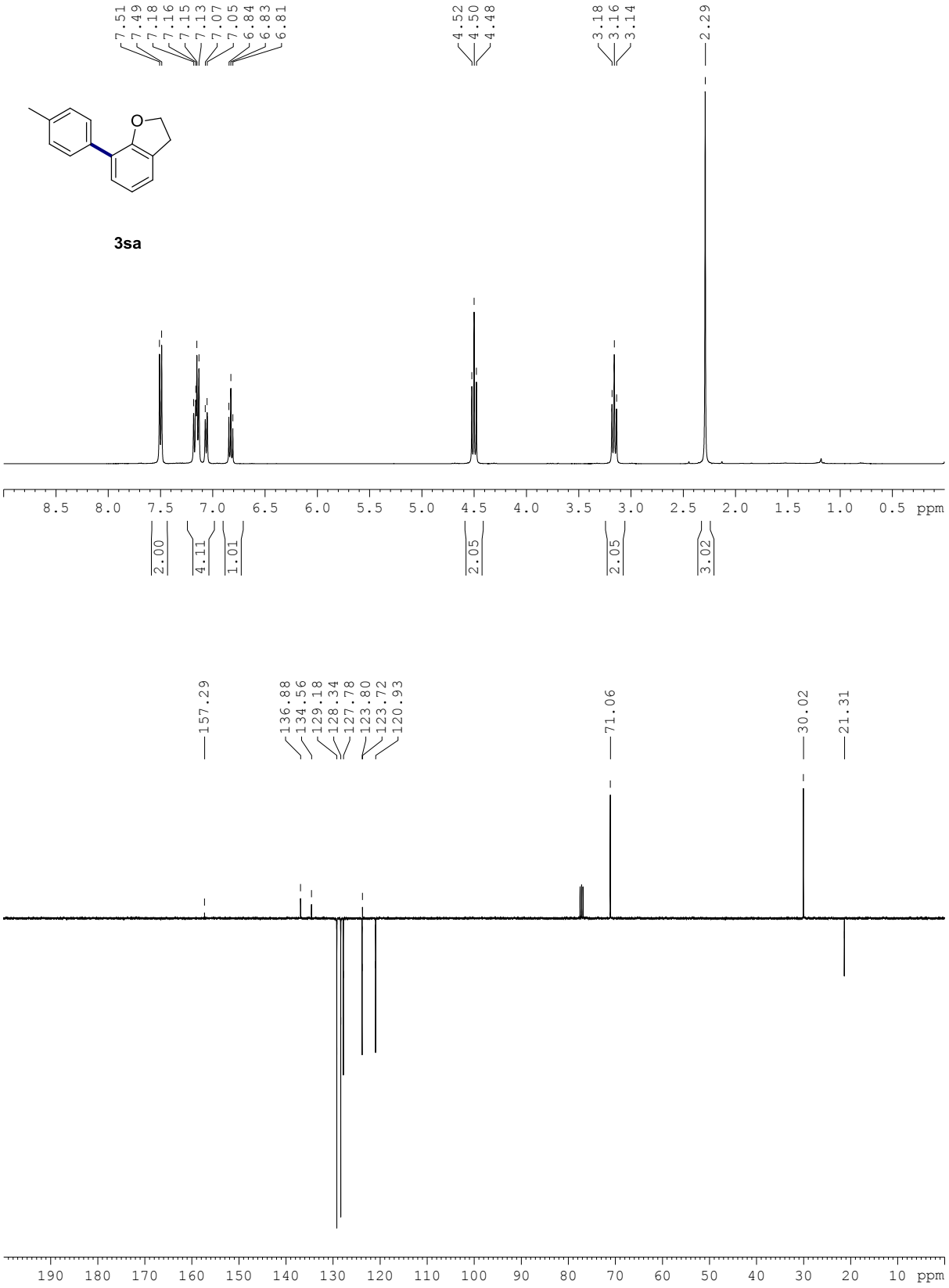


2-Methoxy-3,4'-dimethyl-1,1'-biphenyl (3ra).

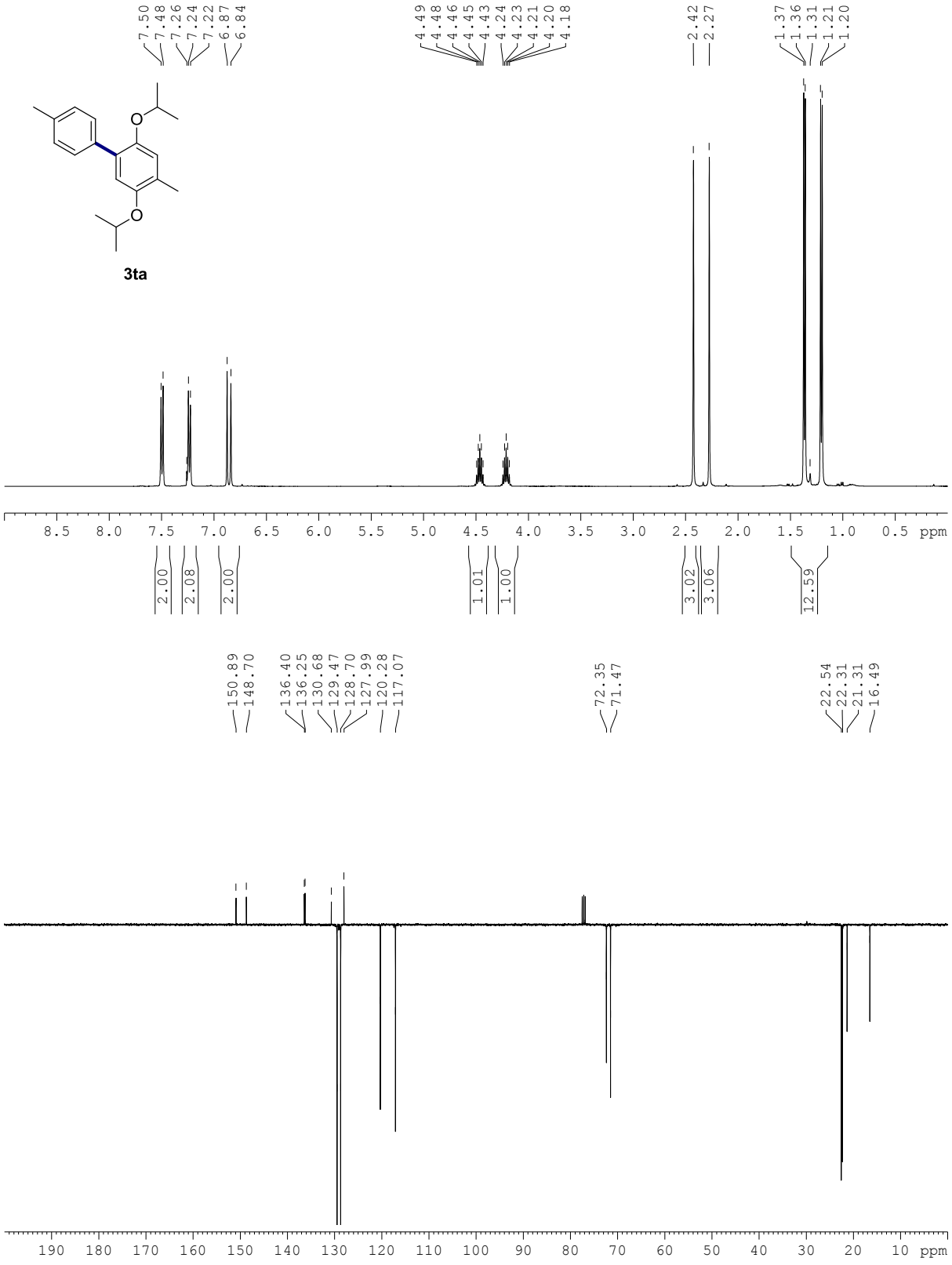




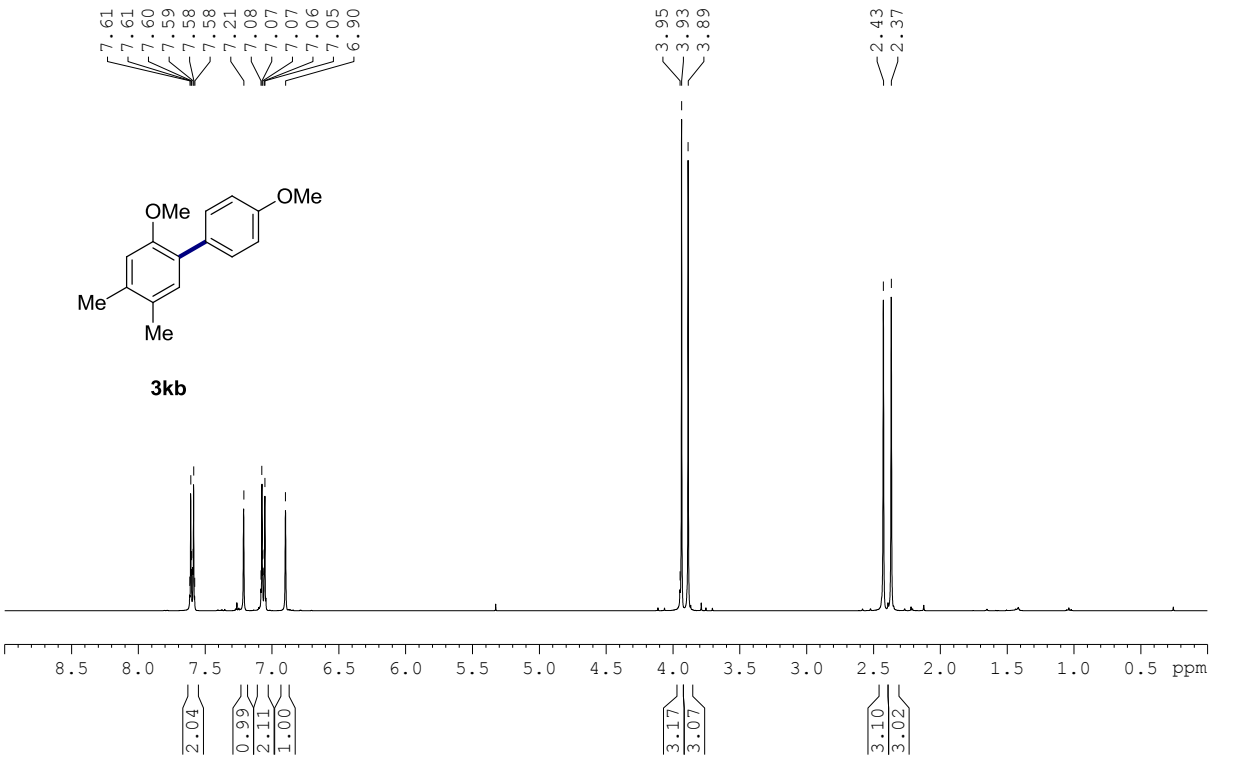
7-(*p*-Tolyl)-2,3-dihydrobenzofuran (3sa).

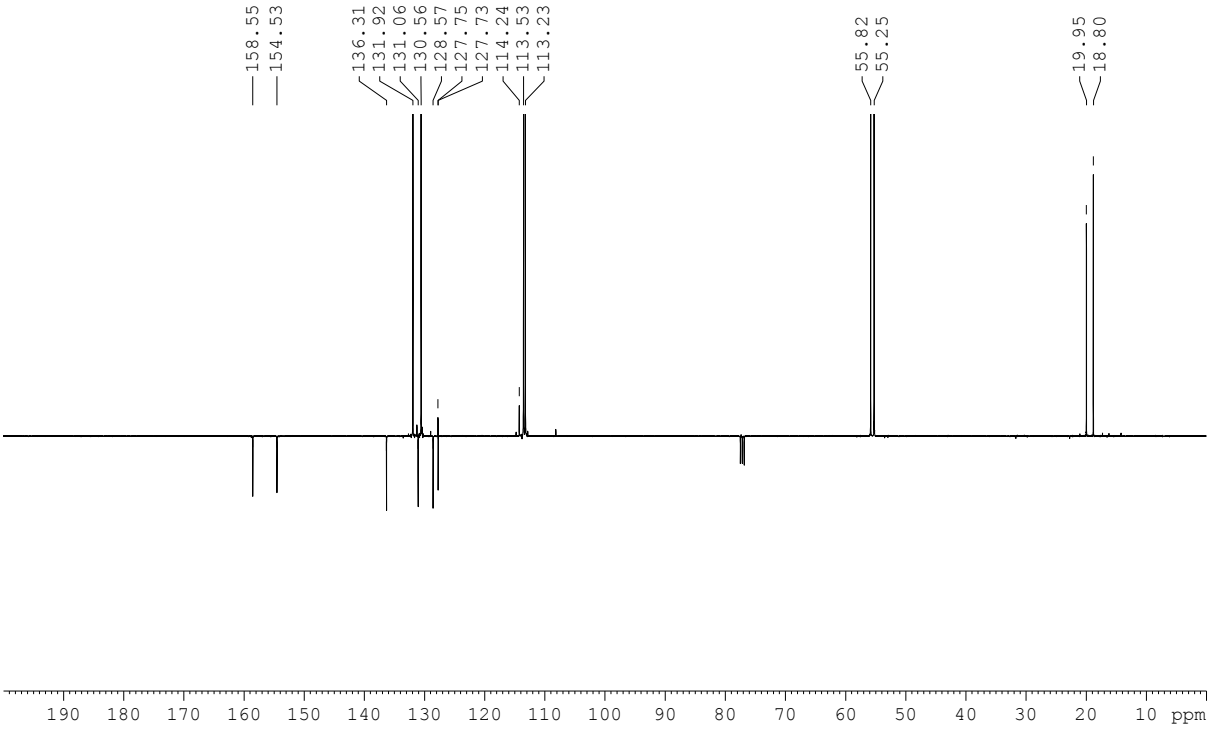


2,5-Diisopropoxy-4,4'-dimethyl-1,1'-biphenyl (3ta).

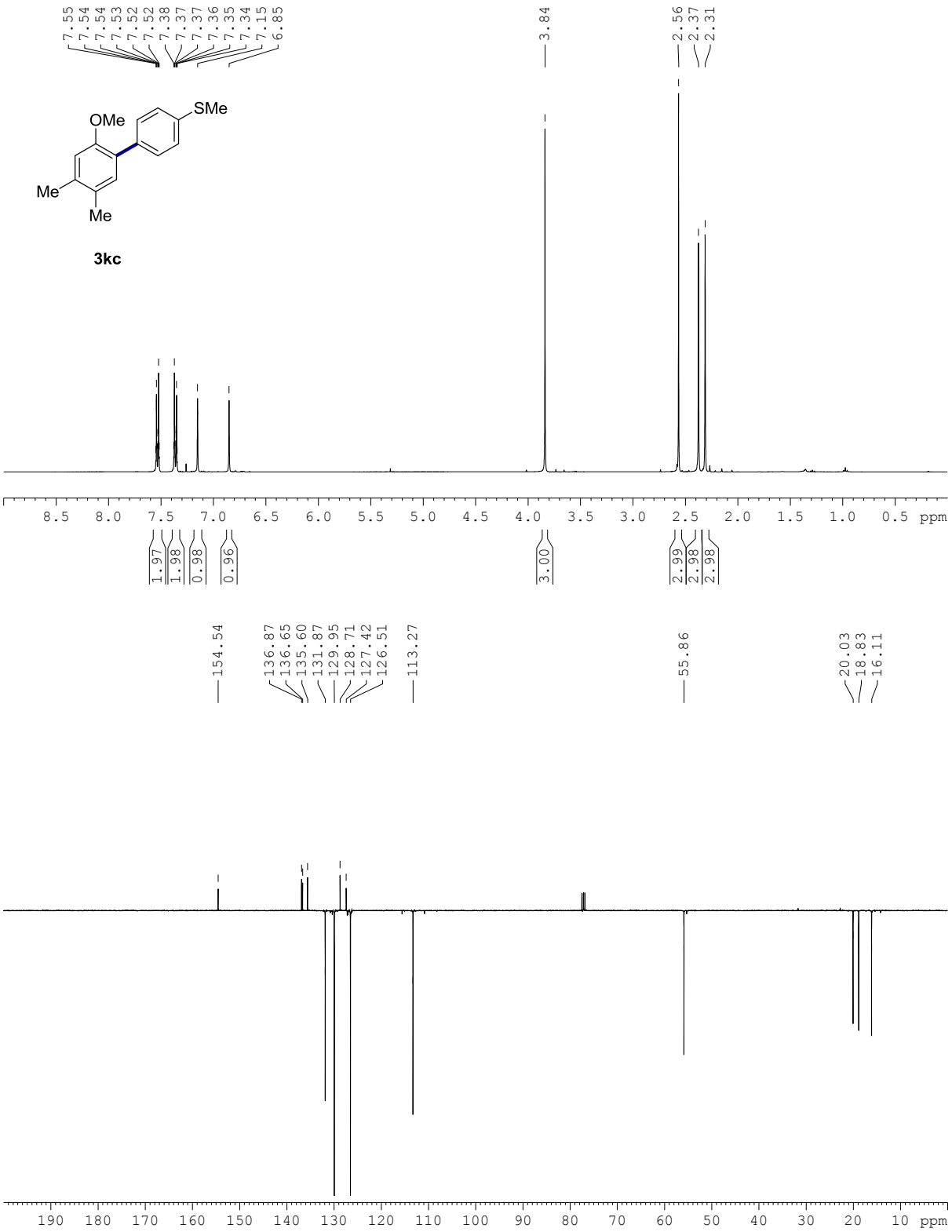


2,4'-Dimethoxy-4,5-dimethyl-1,1'-biphenyl (3kb).

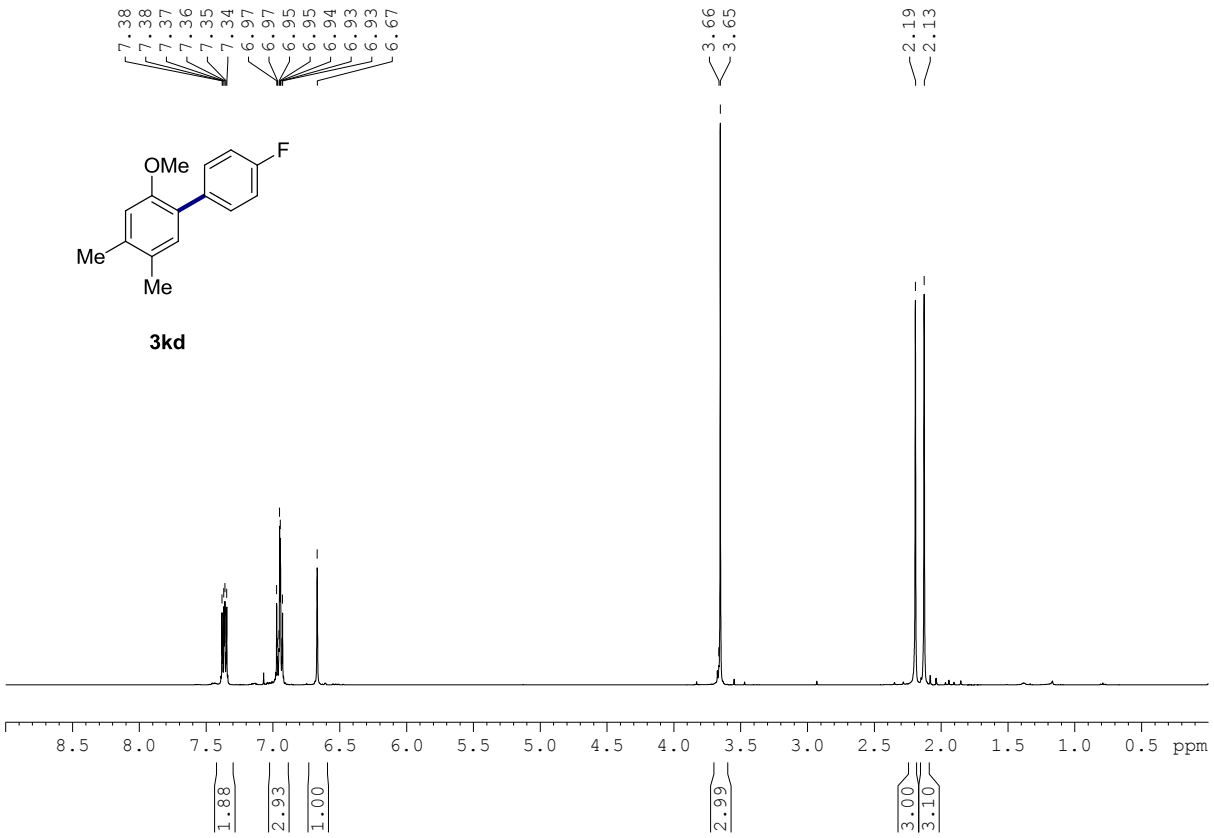


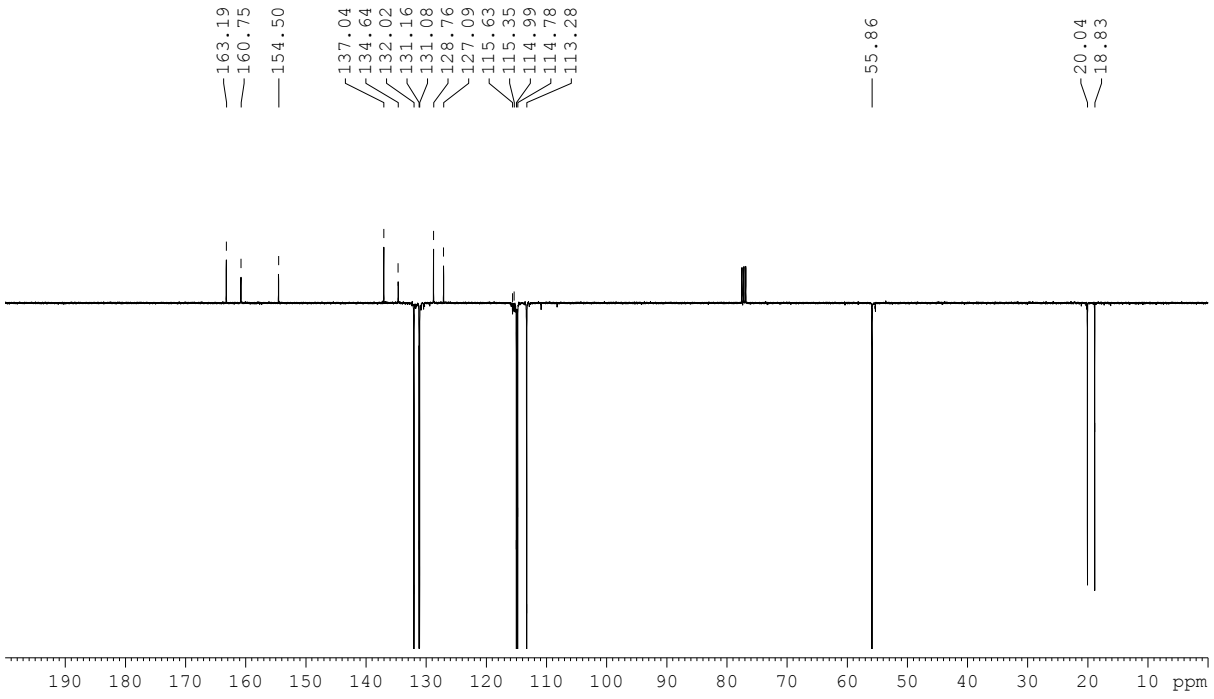


(2'-Methoxy-4',5'-dimethyl-[1,1'-biphenyl]-4-yl)(methyl)sulfane (3kc).

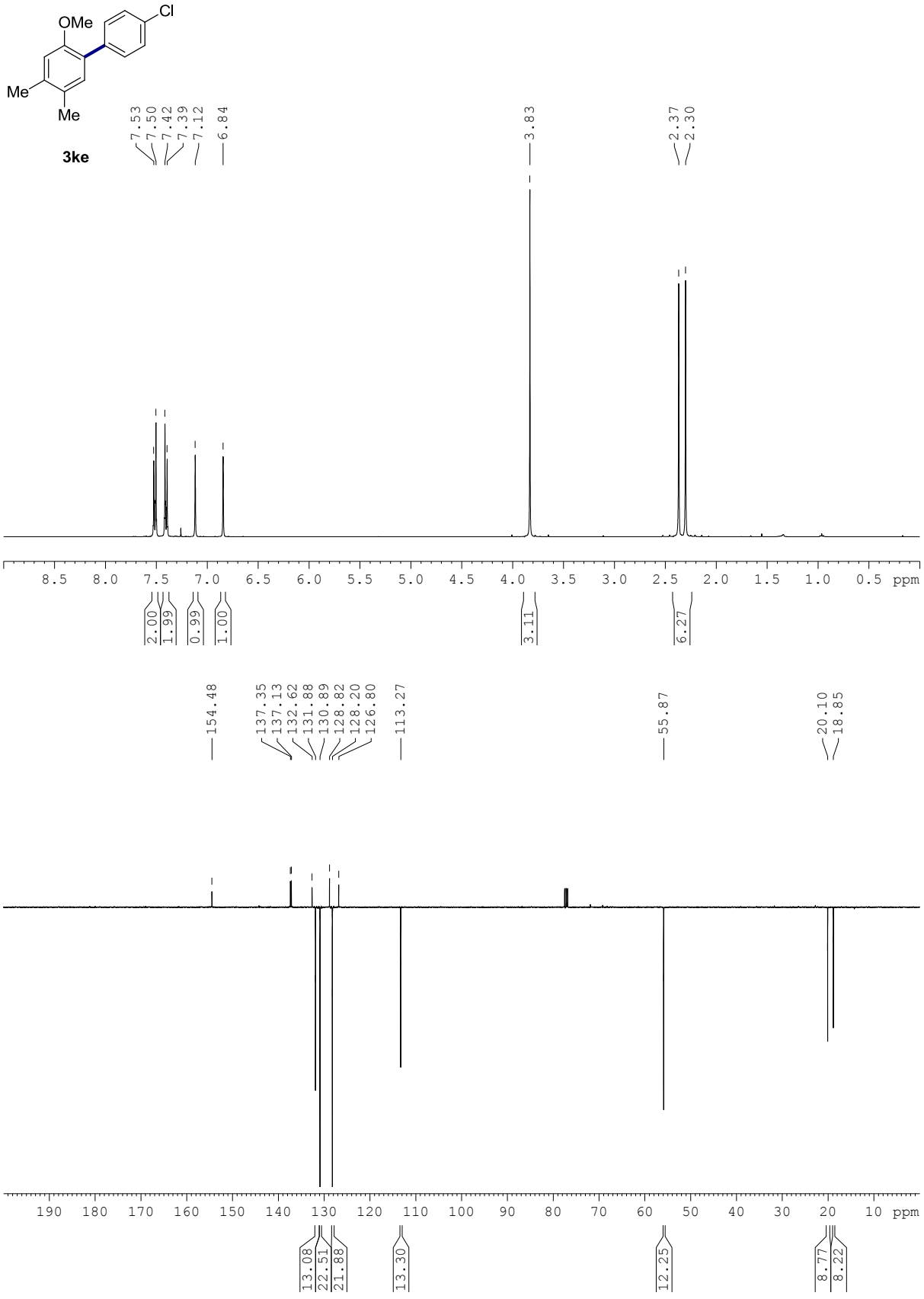


4'-Fluoro-2-methoxy-4,5-dimethyl-1,1'-biphenyl (3kd).

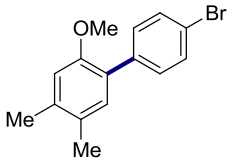




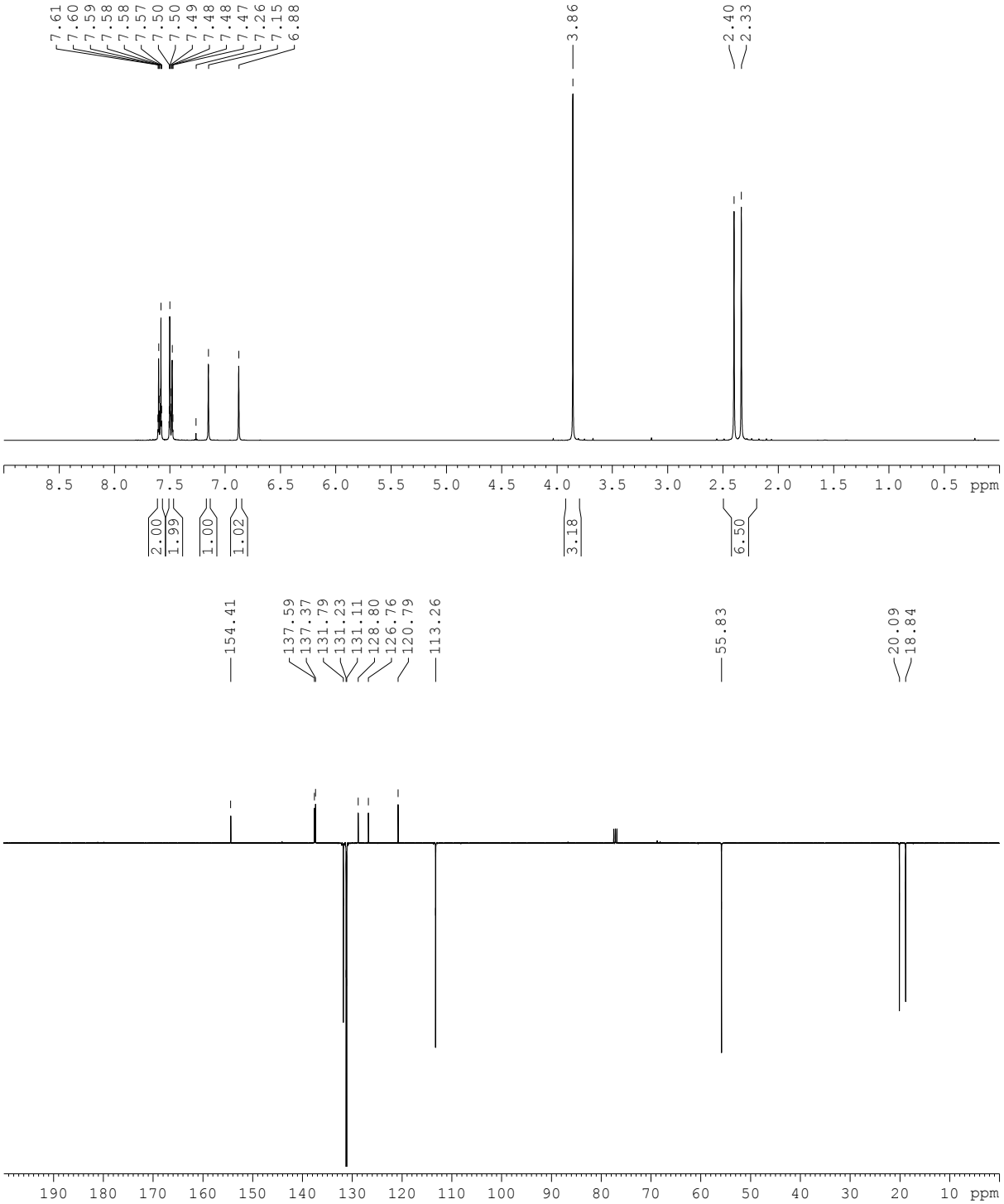
4'-Chloro-2-methoxy-4,5-dimethyl-1,1'-biphenyl (3ke).



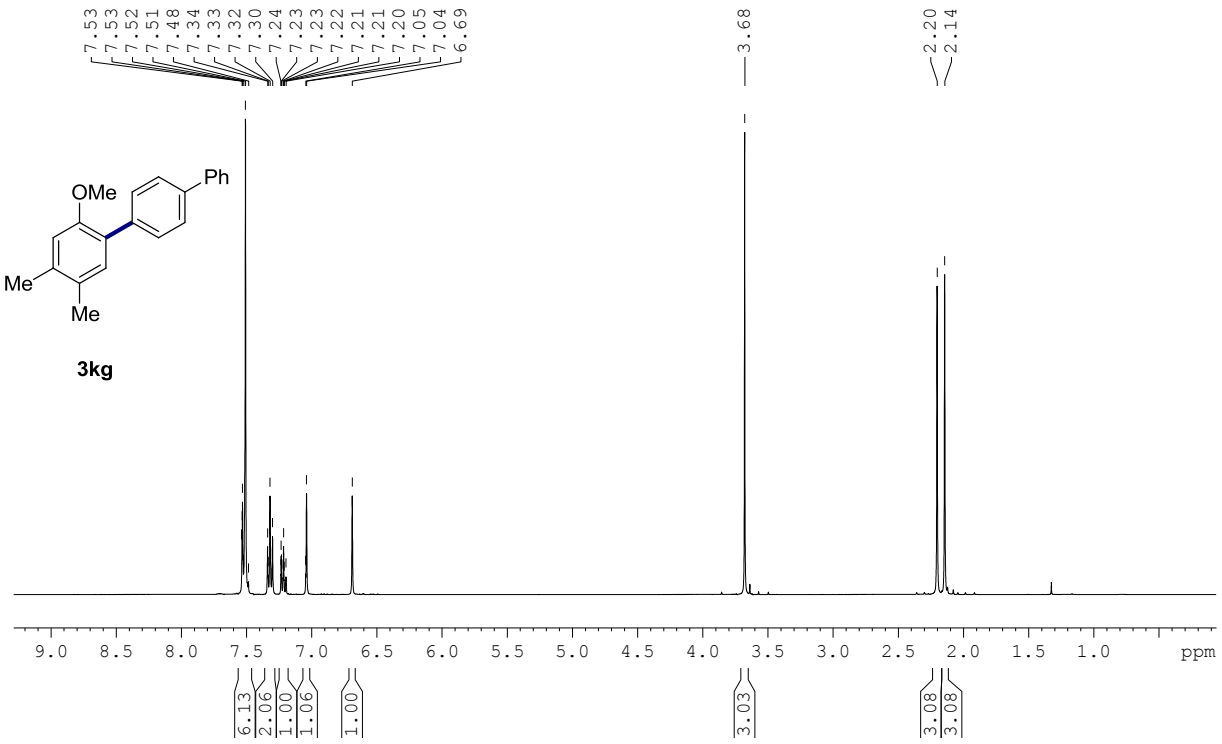
4'-Bromo-2-methoxy-4,5-dimethyl-1,1'-biphenyl (3kf).

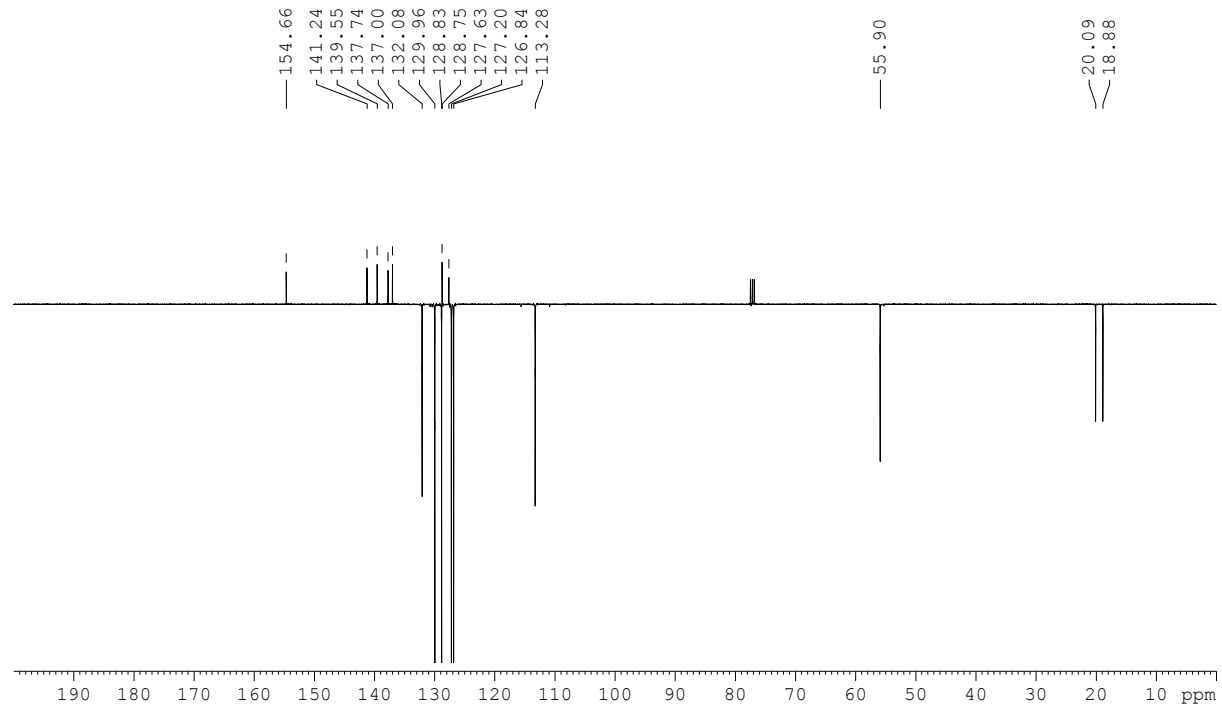


3kf

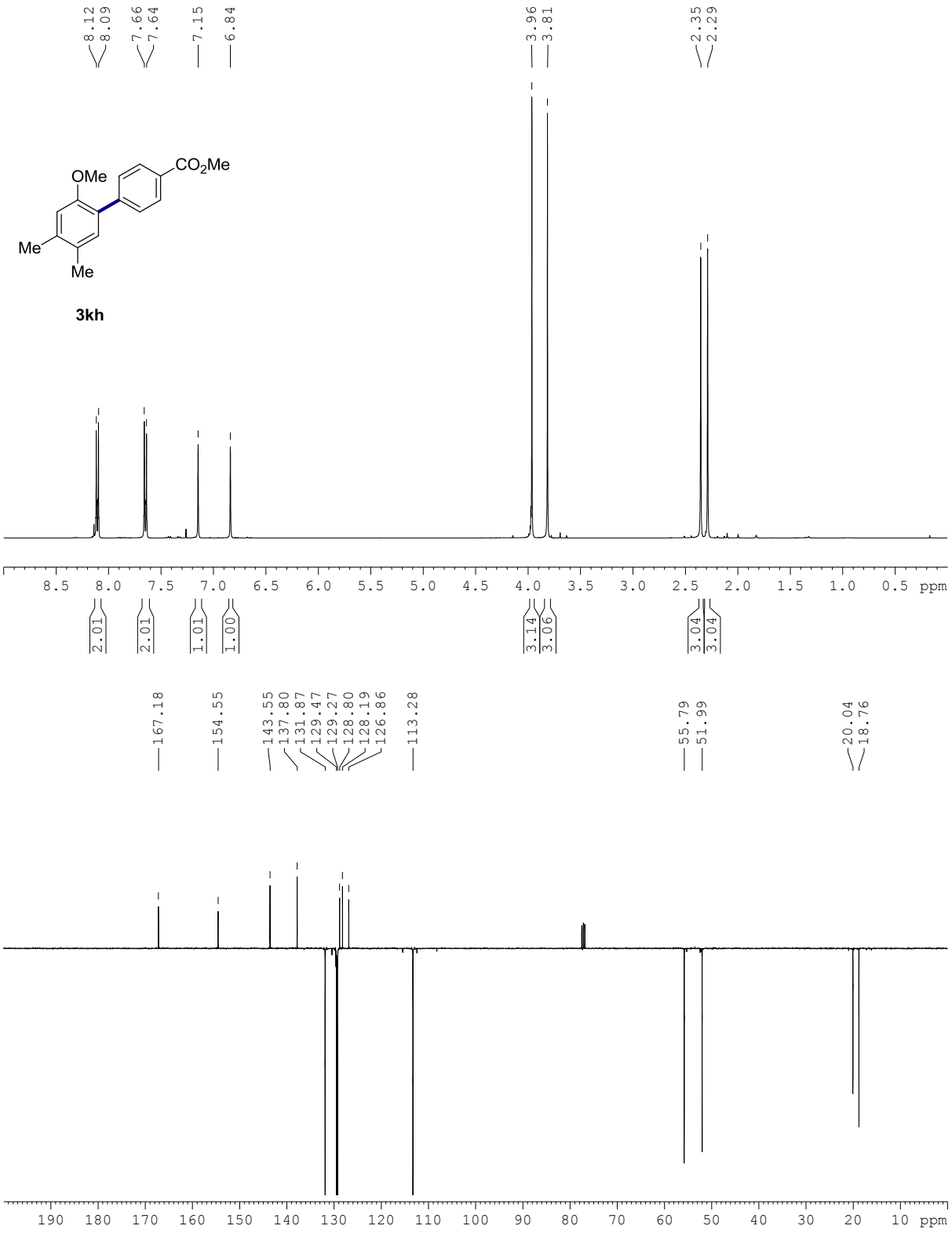


2-Methoxy-4,5-dimethyl-1,1':4',1''-terphenyl (3kg).

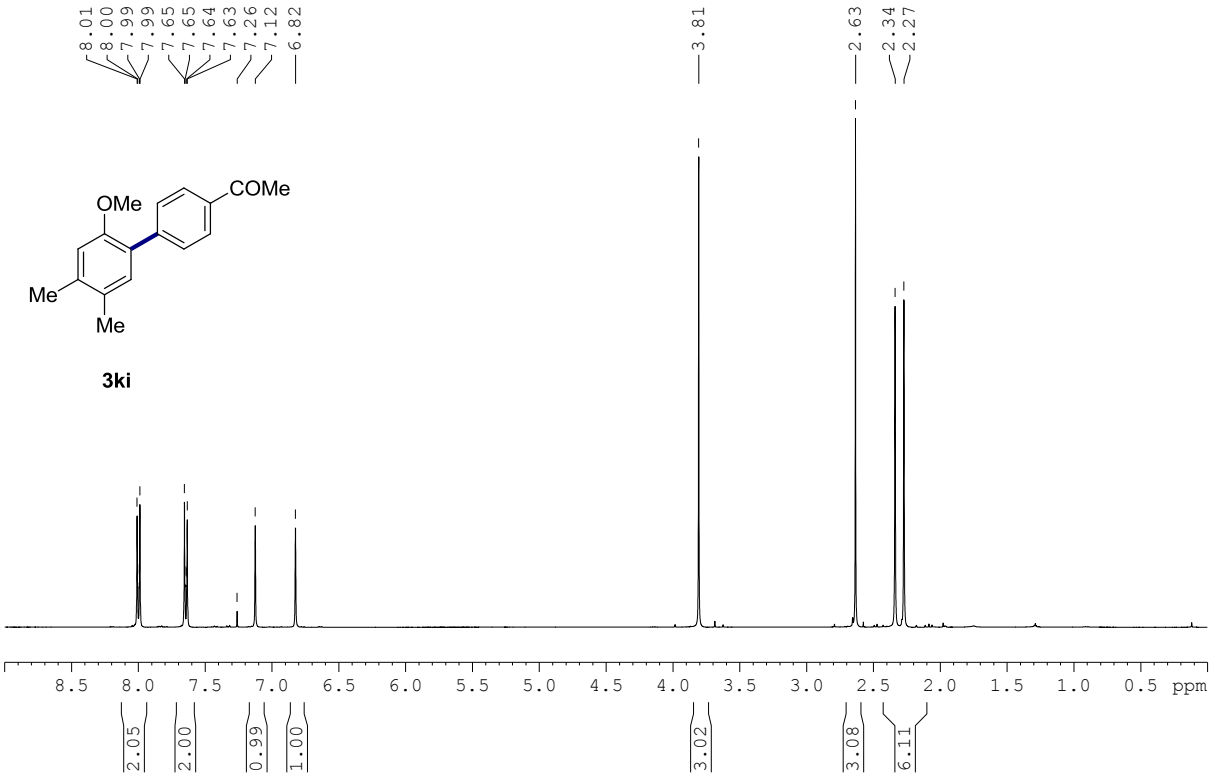


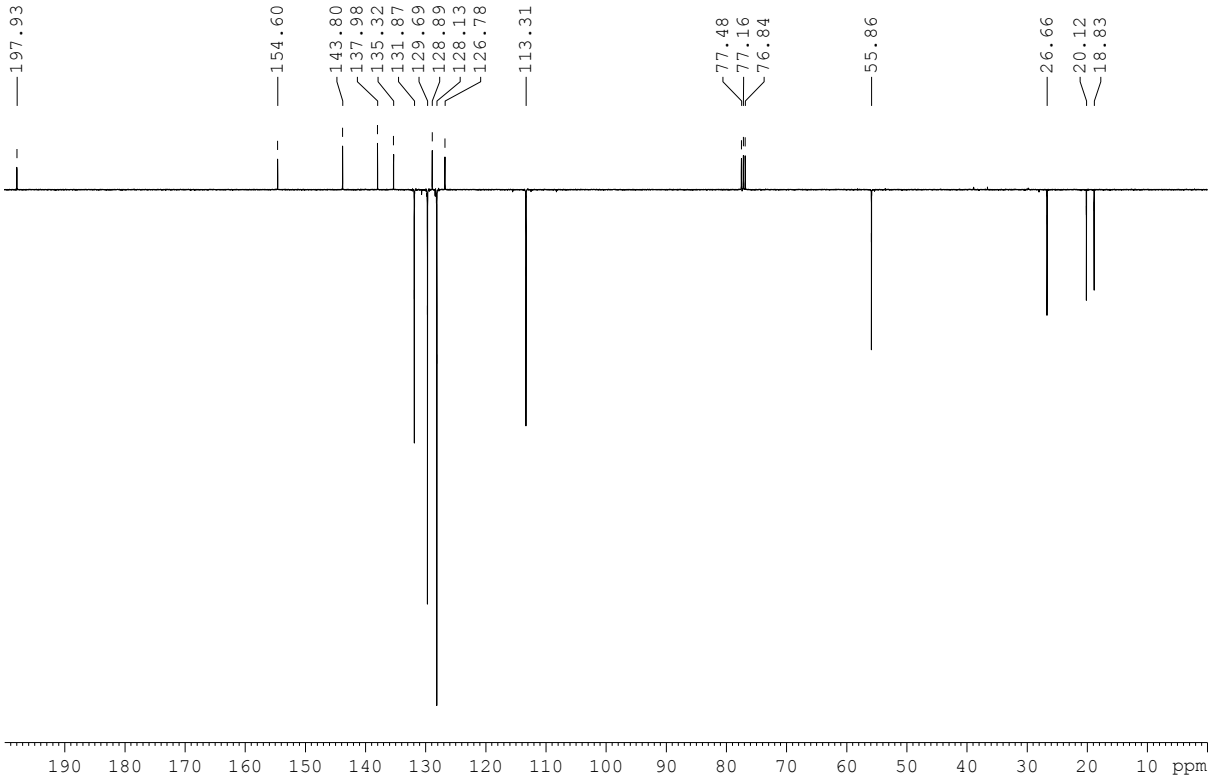


Methyl 2'-methoxy-4',5'-dimethyl-[1,1'-biphenyl]-4-carboxylate (3kh)

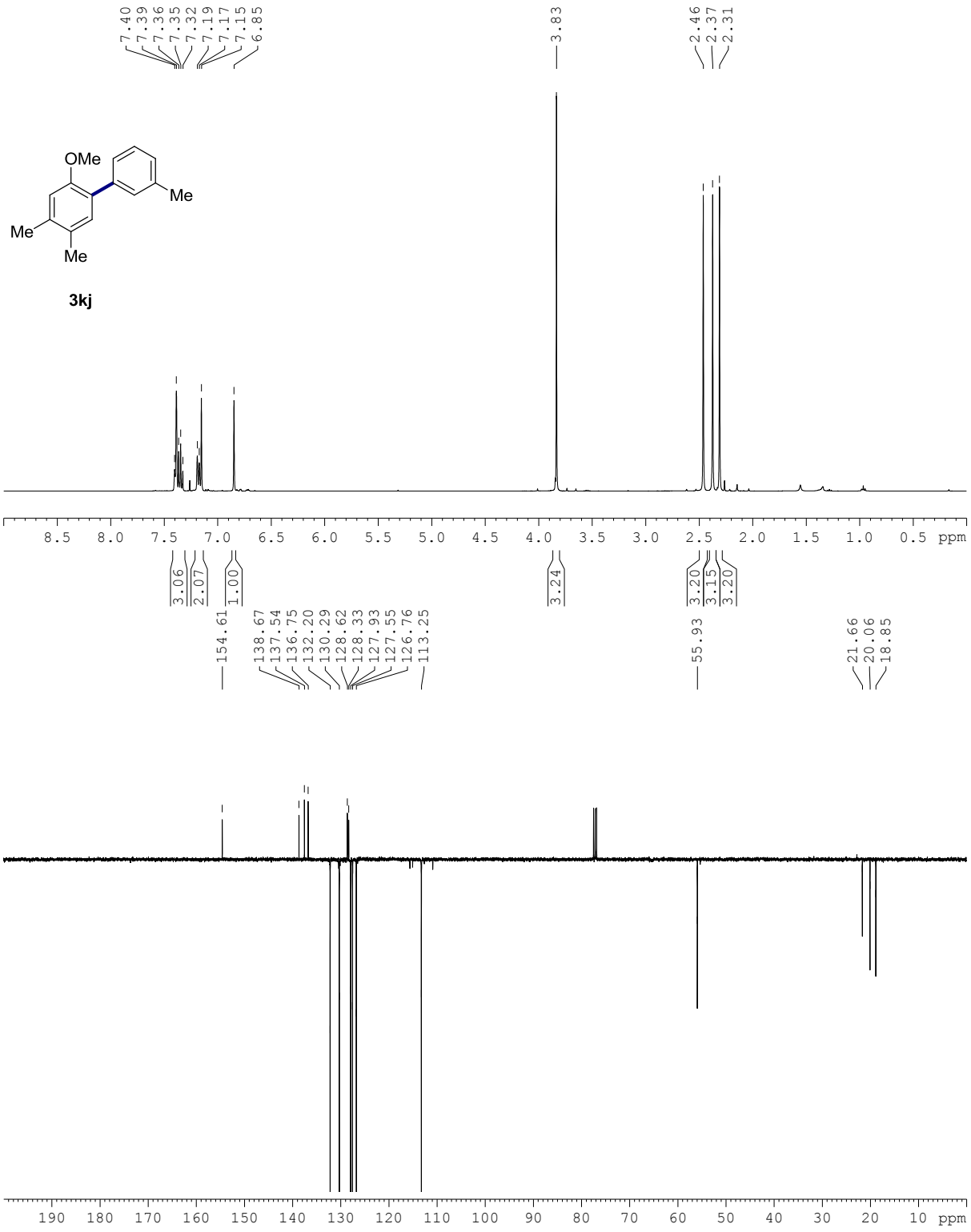


1-(2'-methoxy-4',5'-dimethyl-[1,1'-biphenyl]-4-yl)ethanone (3ki).

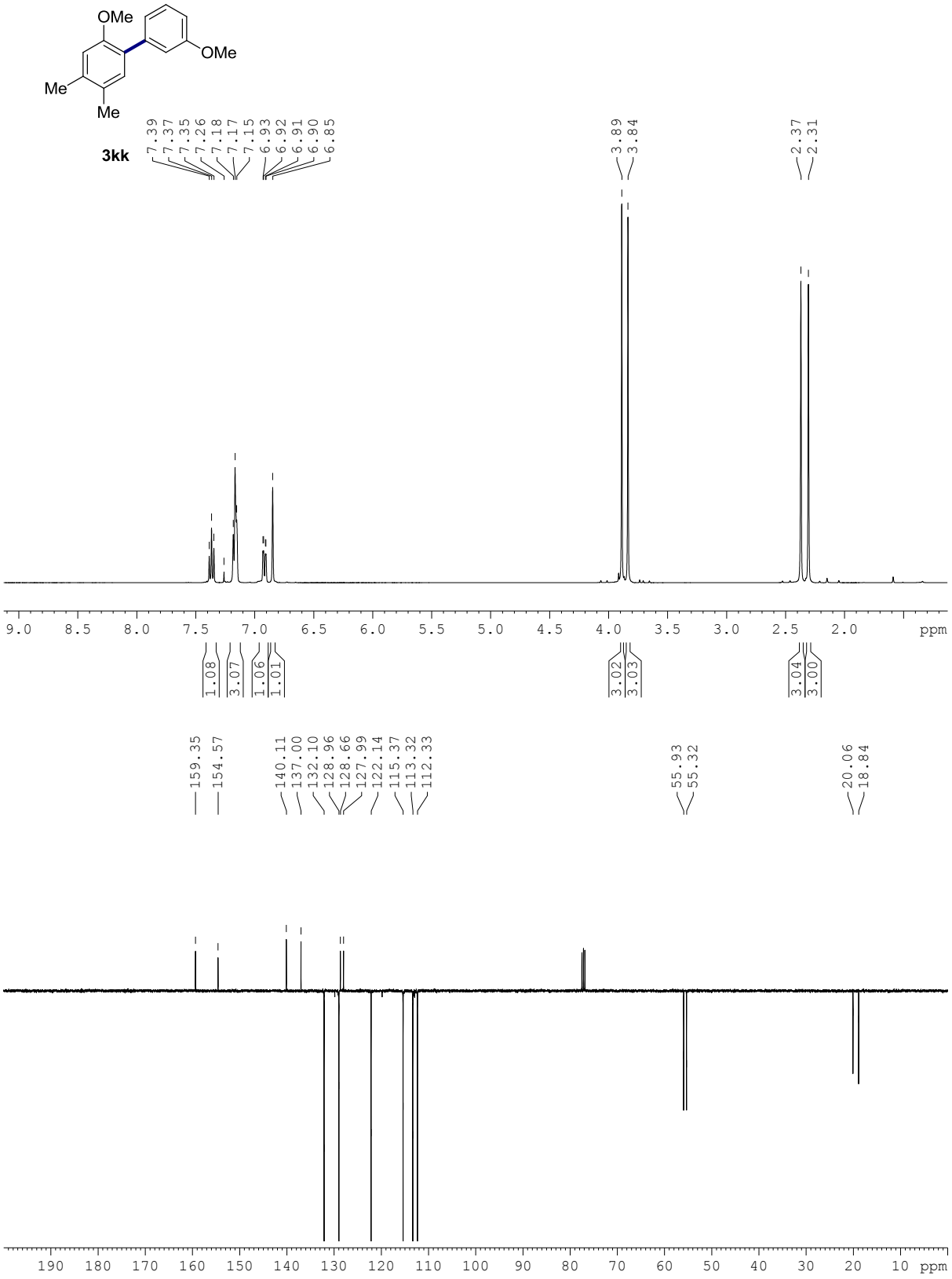




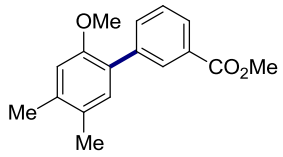
2-Methoxy-3',4,5-trimethyl-1,1'-biphenyl (3kj).



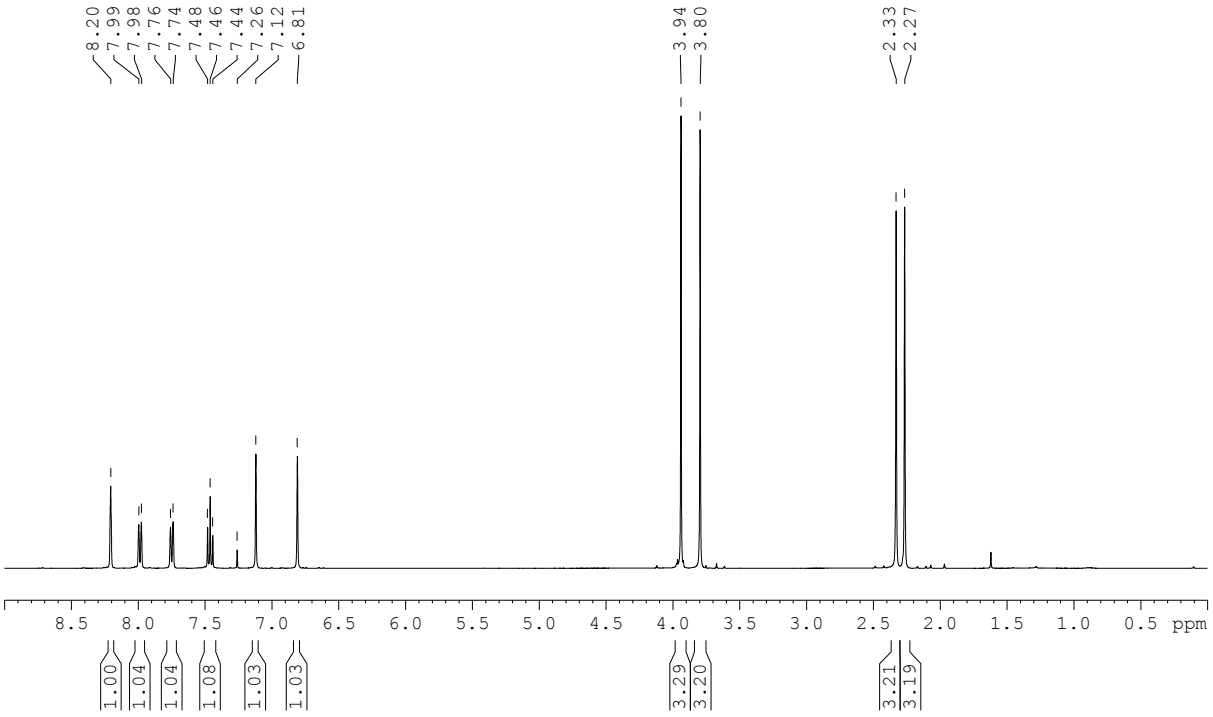
2,3'-Dimethoxy-4,5-dimethyl-1,1'-biphenyl (3kk).

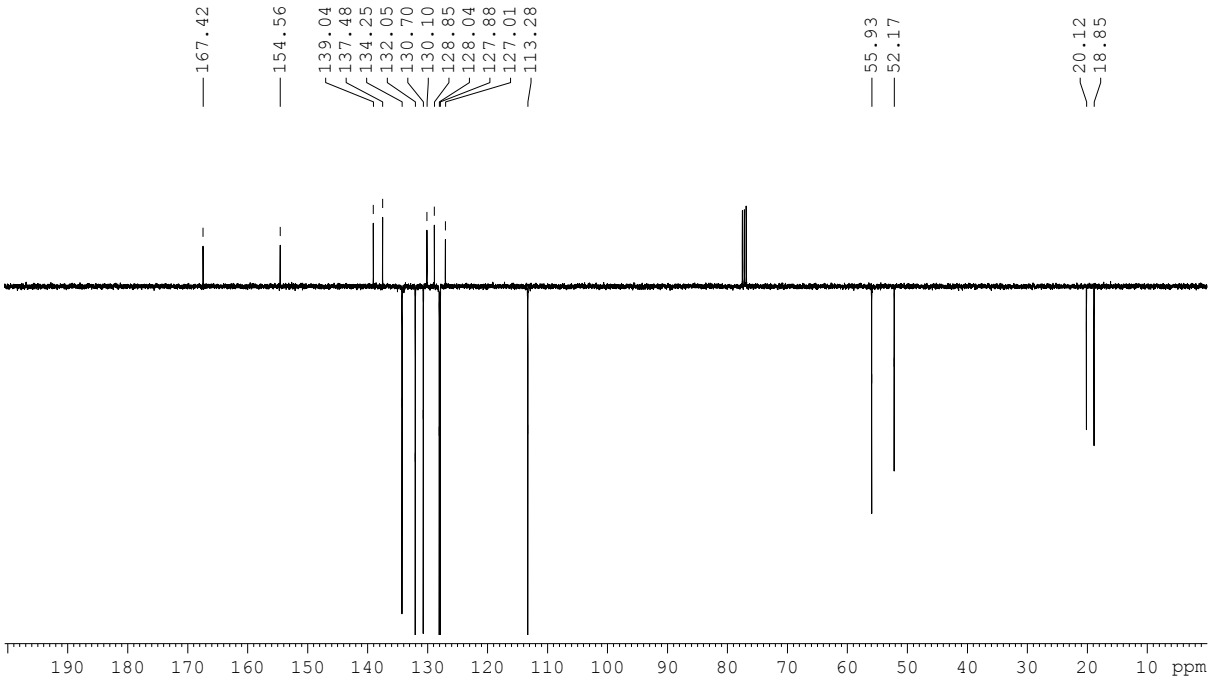


Methyl 2'-methoxy- 4',5'-dimethyl-[1,1'-biphenyl]-3-carboxylate (3kl)

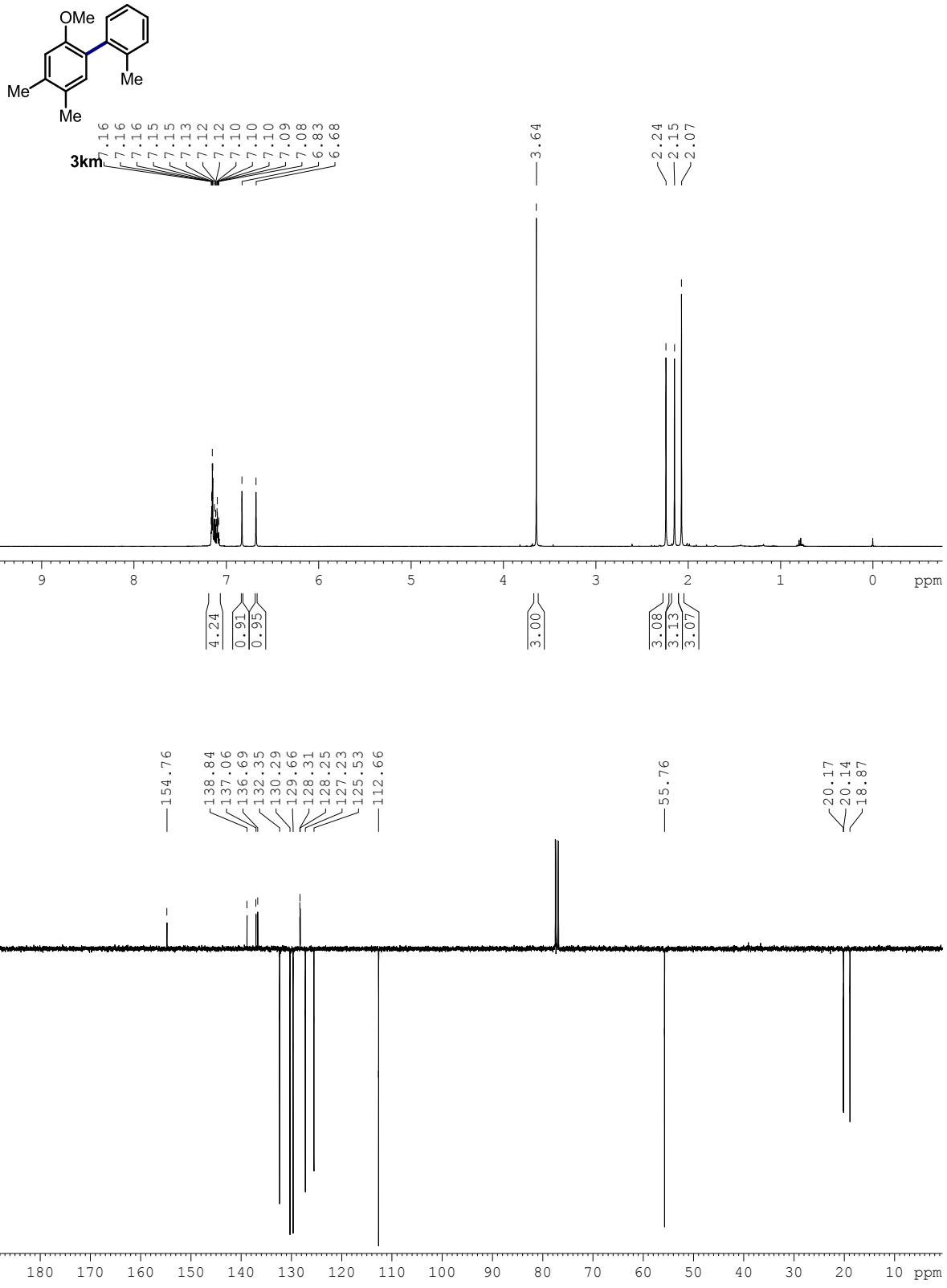


3kl

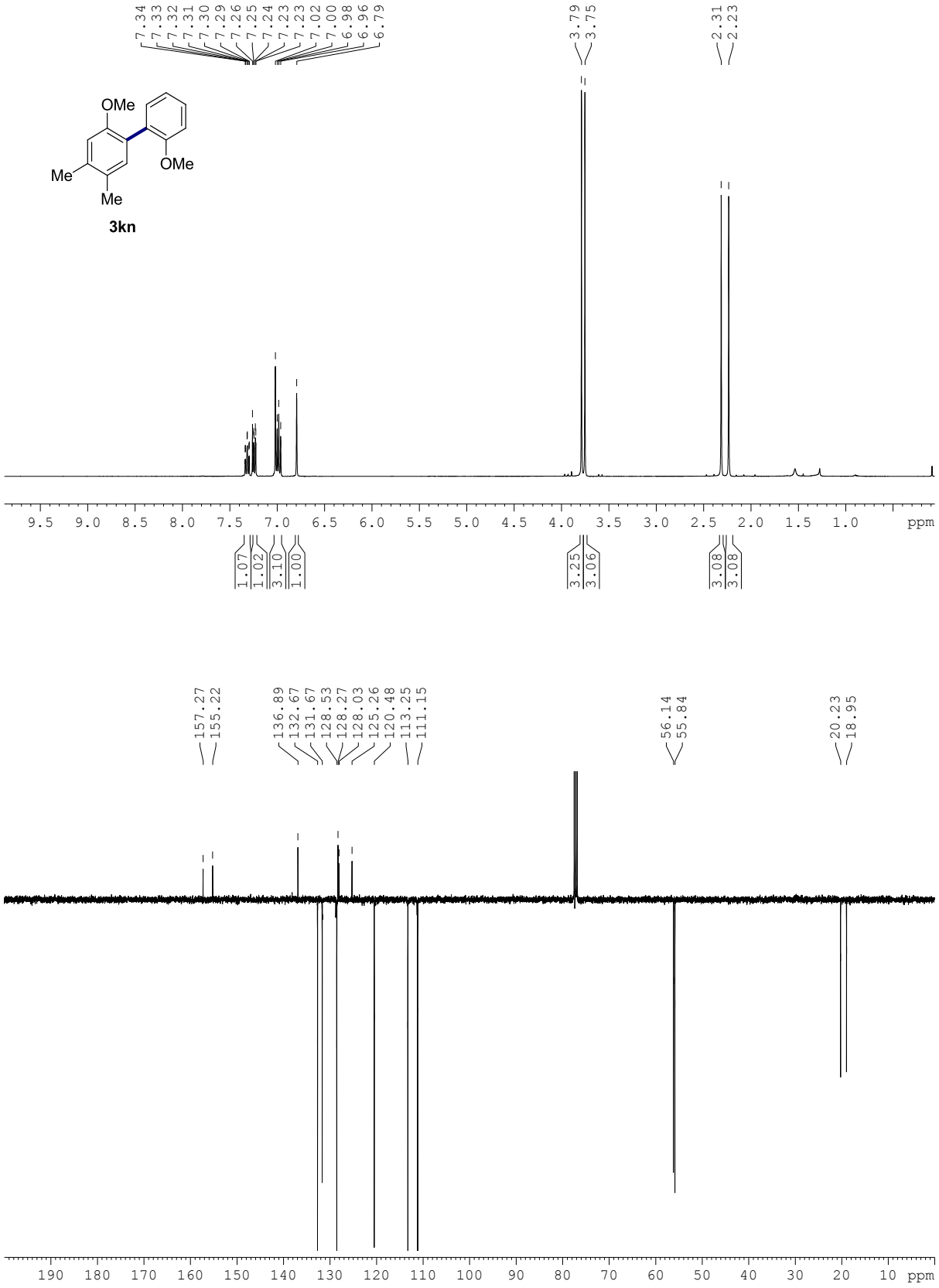




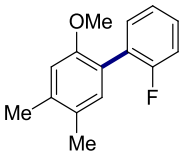
2-Methoxy-2',4,5-trimethyl-1,1'-biphenyl (3km).



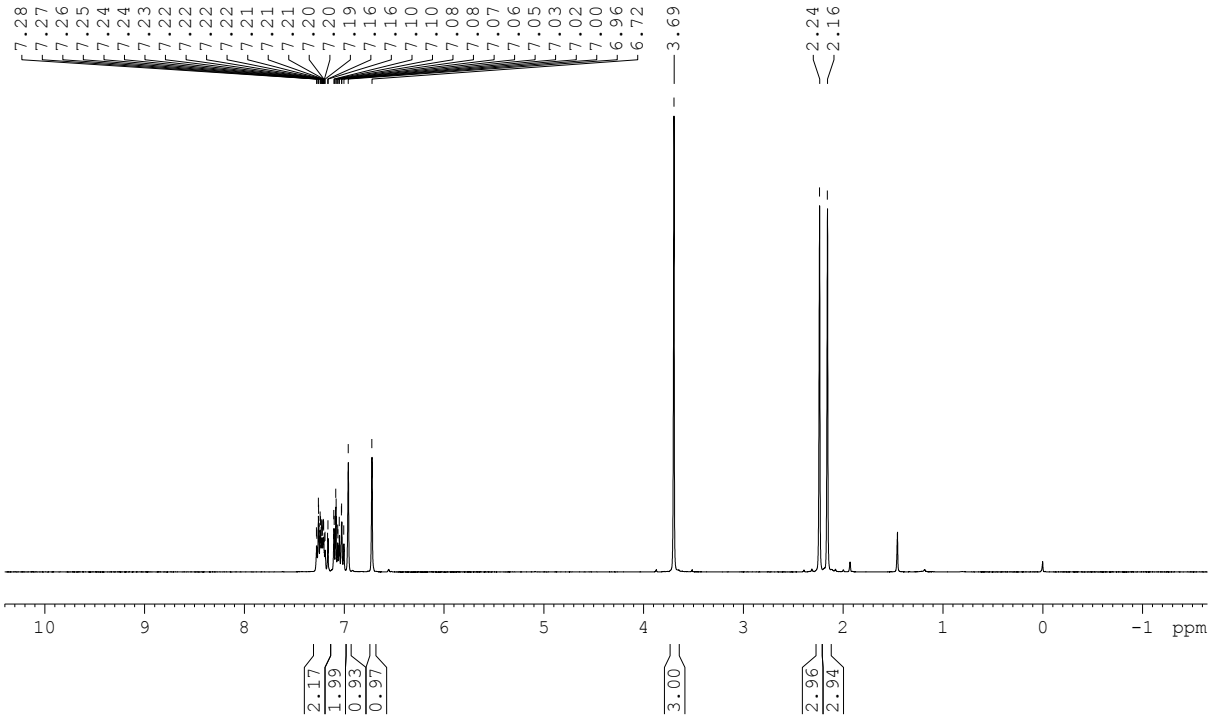
2,2'-Dimethoxy-4,5-dimethyl-1,1'-biphenyl (3kn).

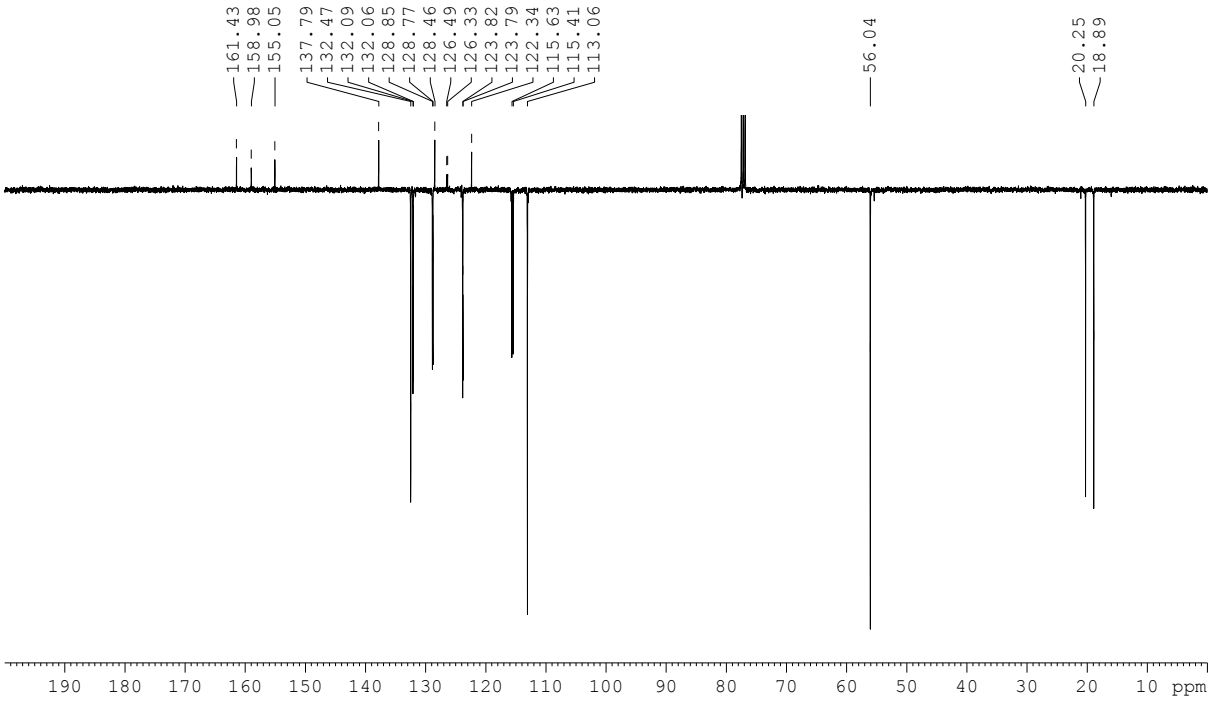


2'-Fluoro-2-methoxy-4,5-dimethyl-1,1'-biphenyl (3ko).

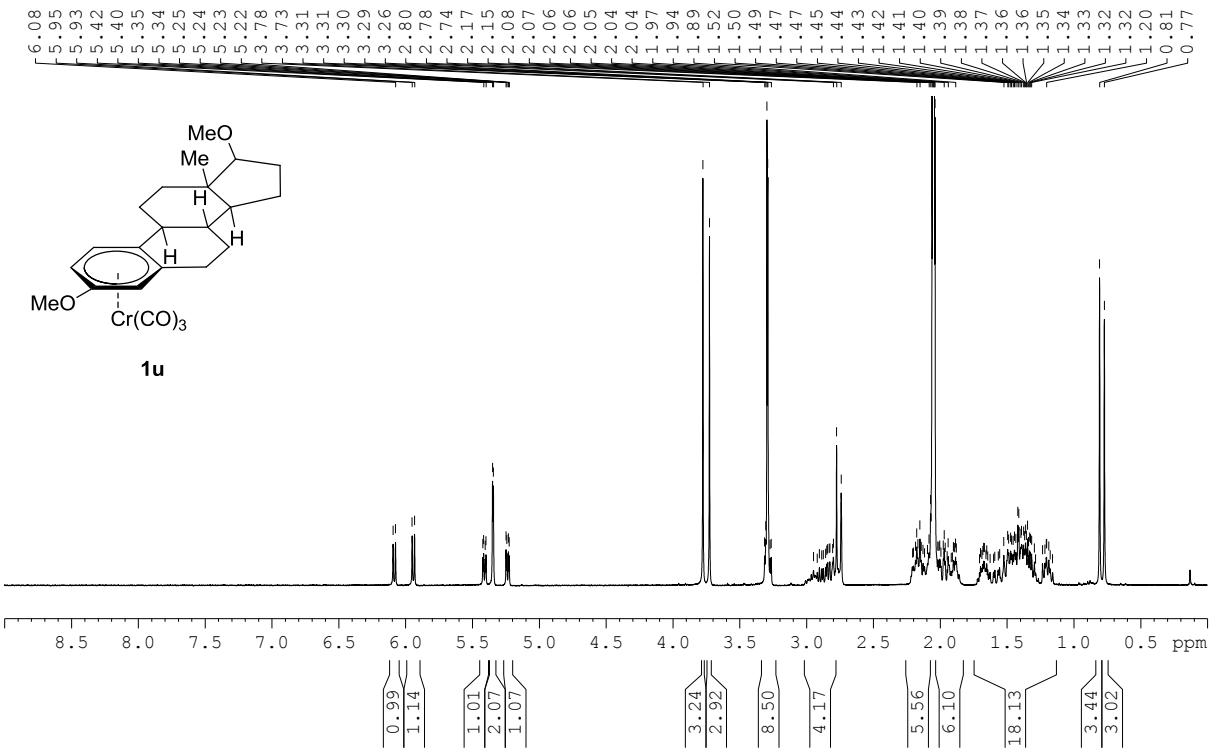


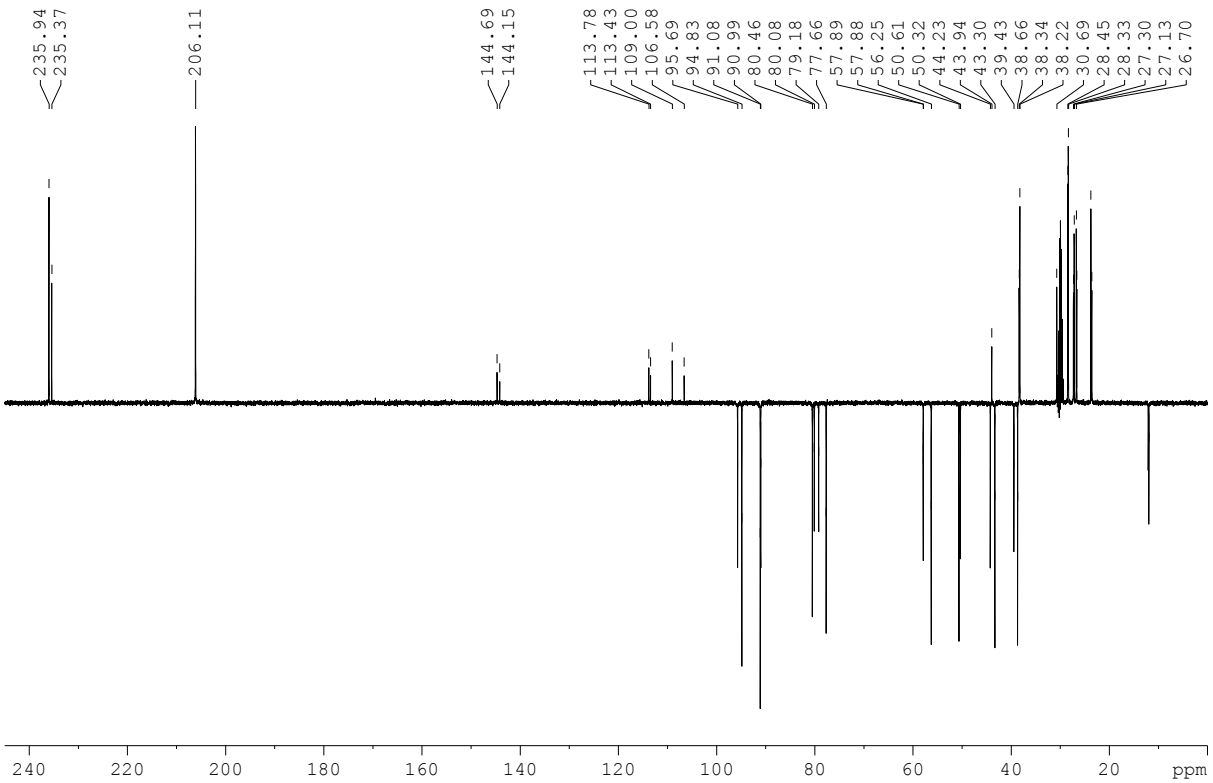
3ko



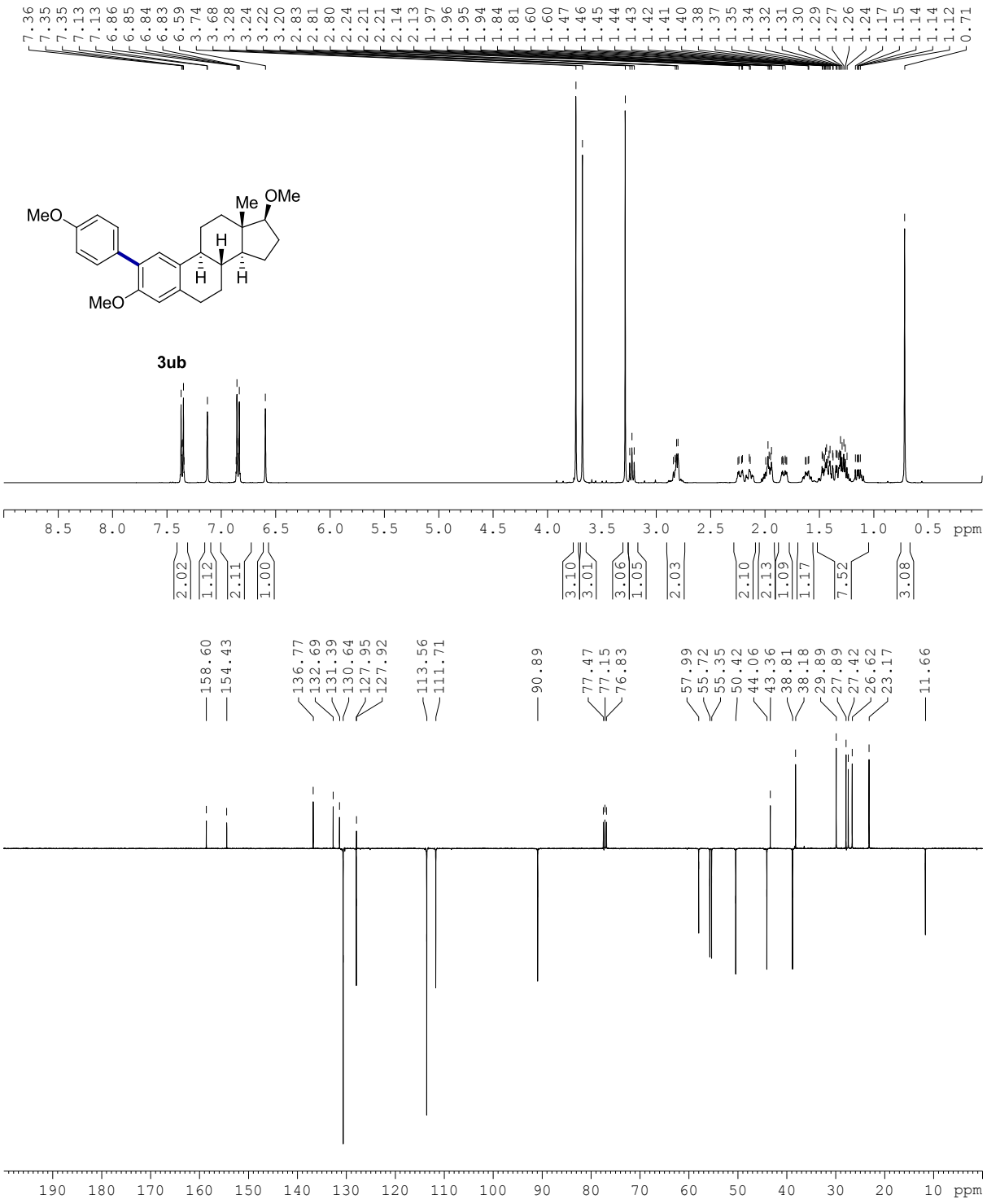


(8*R*,9*S*,13*S*,14*S*,17*S*)-3,17-Dimethoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[*a*]phenanthrene chromium tricarbonyl (1u).

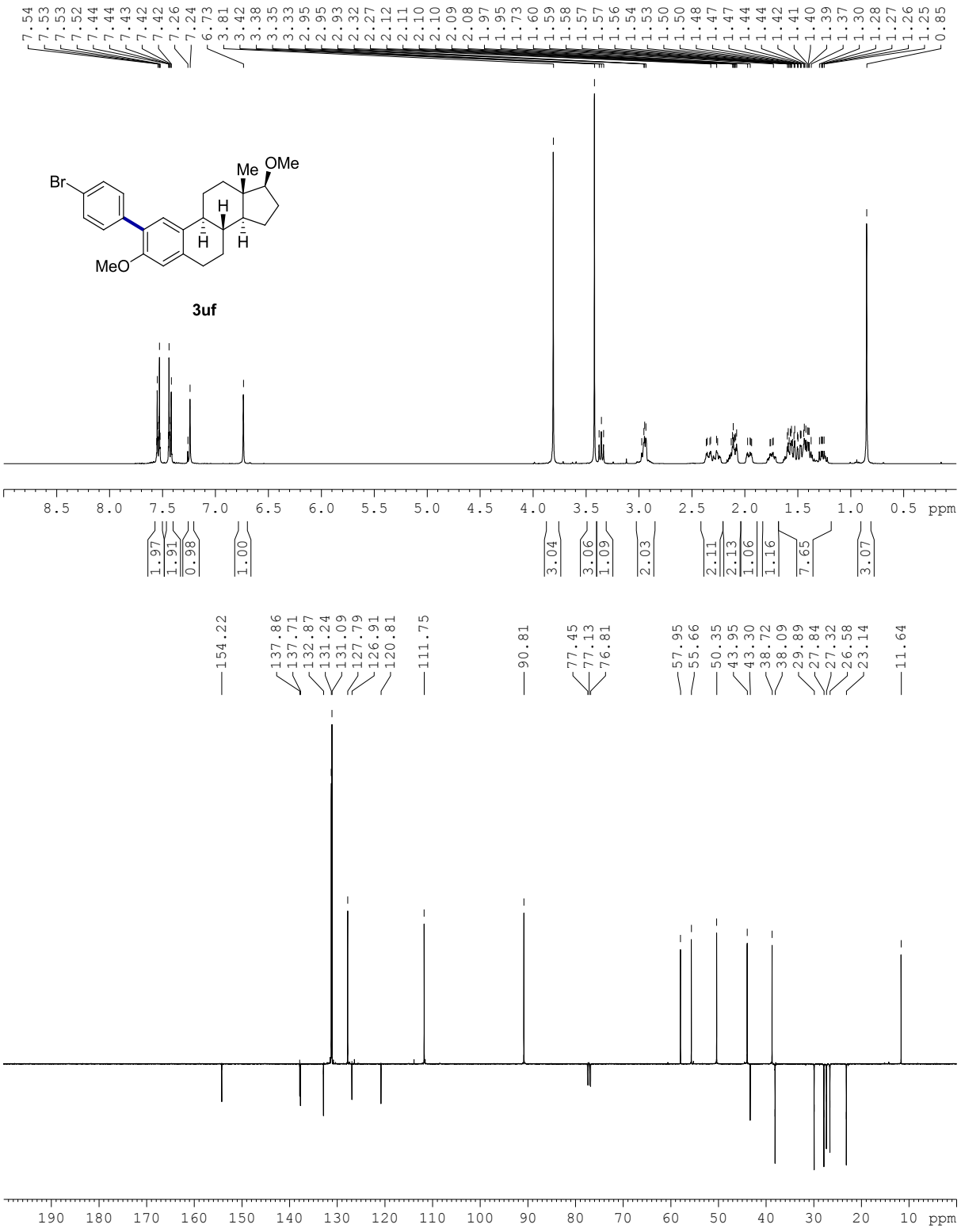




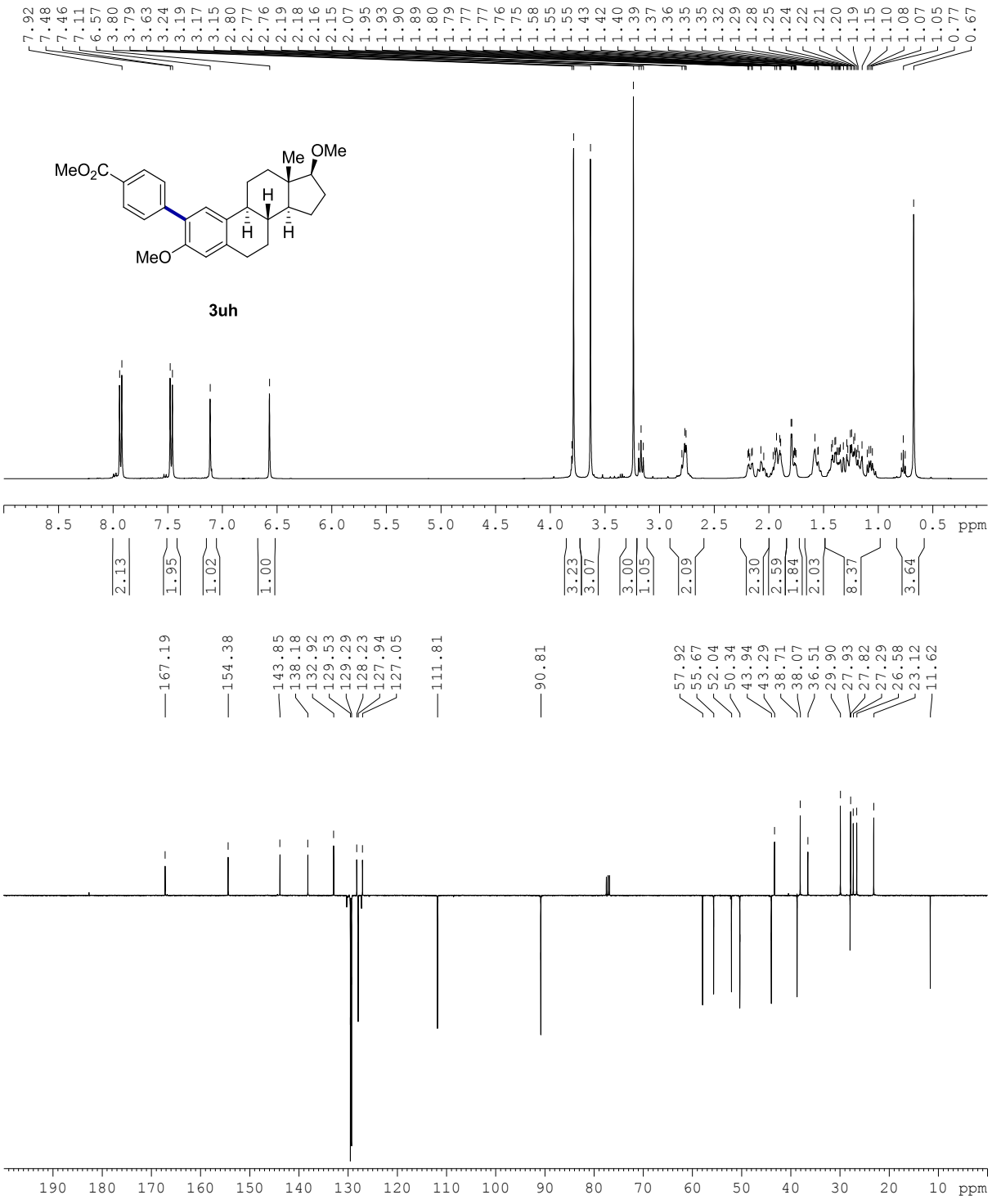
(8R,9S,13S,14S,17S)-3,17-Dimethoxy-2-(4-methoxyphenyl)-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene (3ub).



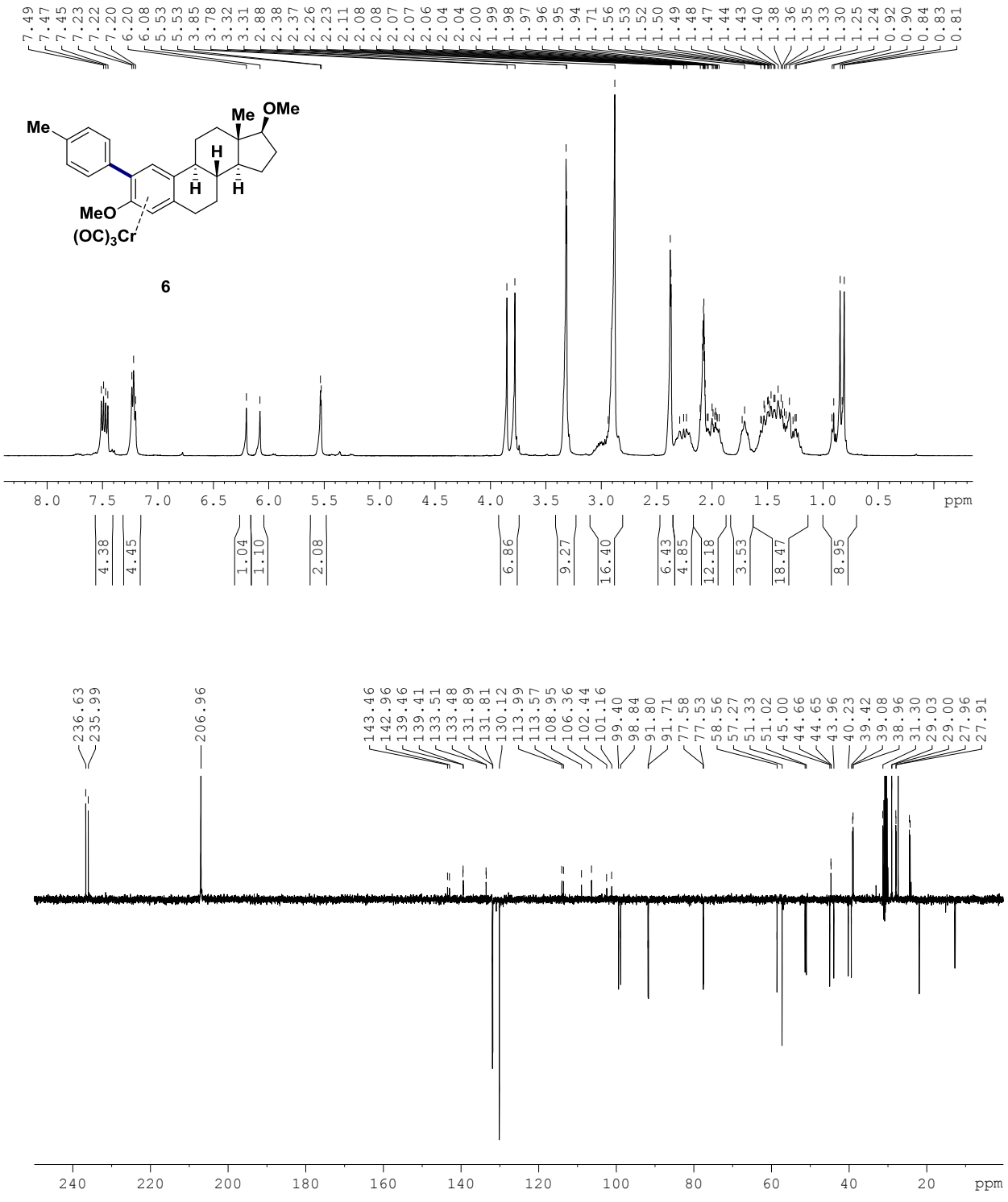
(8R,9S,13S,14S,17S)-2-(4-Bromophenyl)-3,17-dimethoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene (3uf).



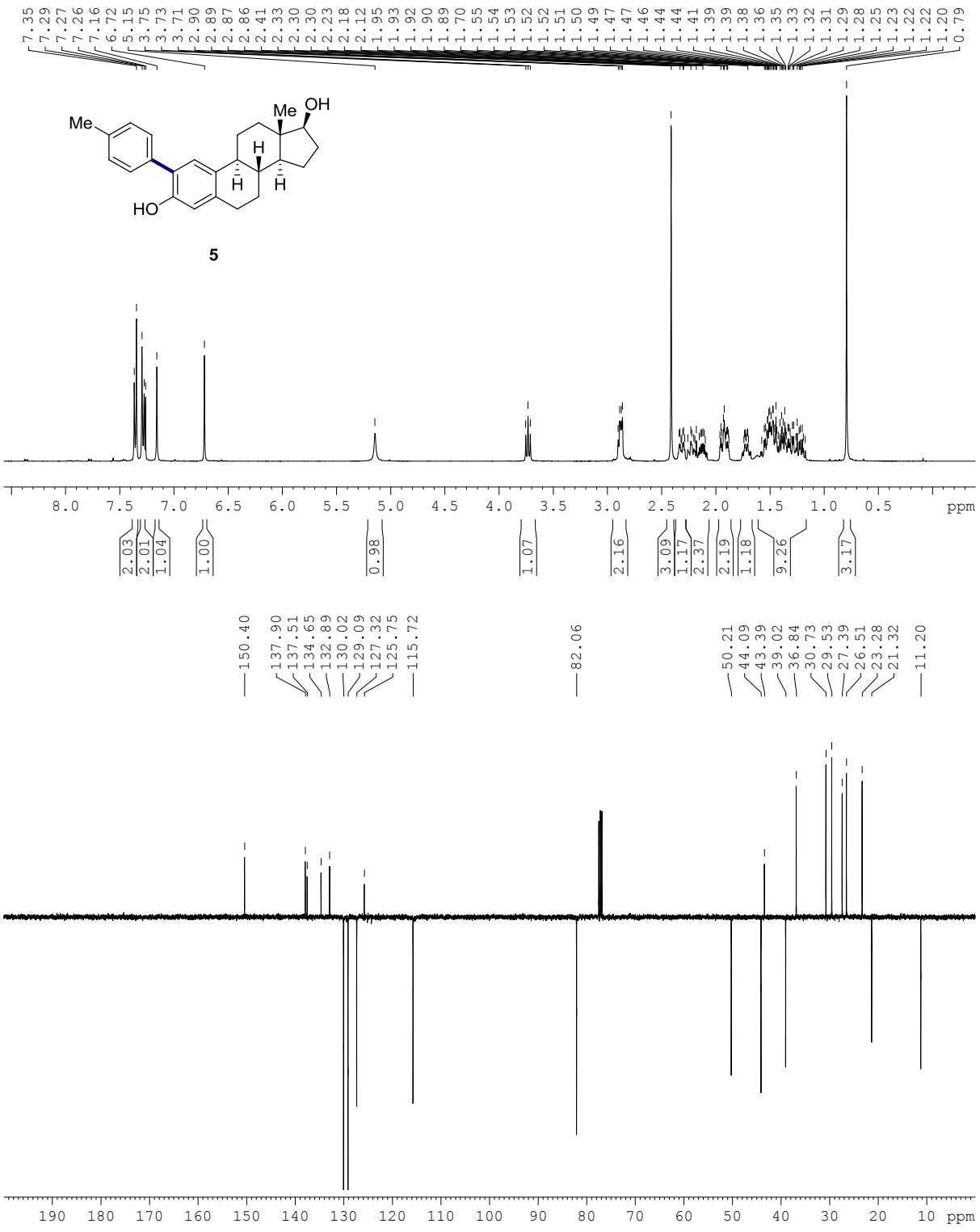
Methyl 4-((8R,9S,13S,14S,17S)-3,17-dimethoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-2-yl)benzoate (3uh).



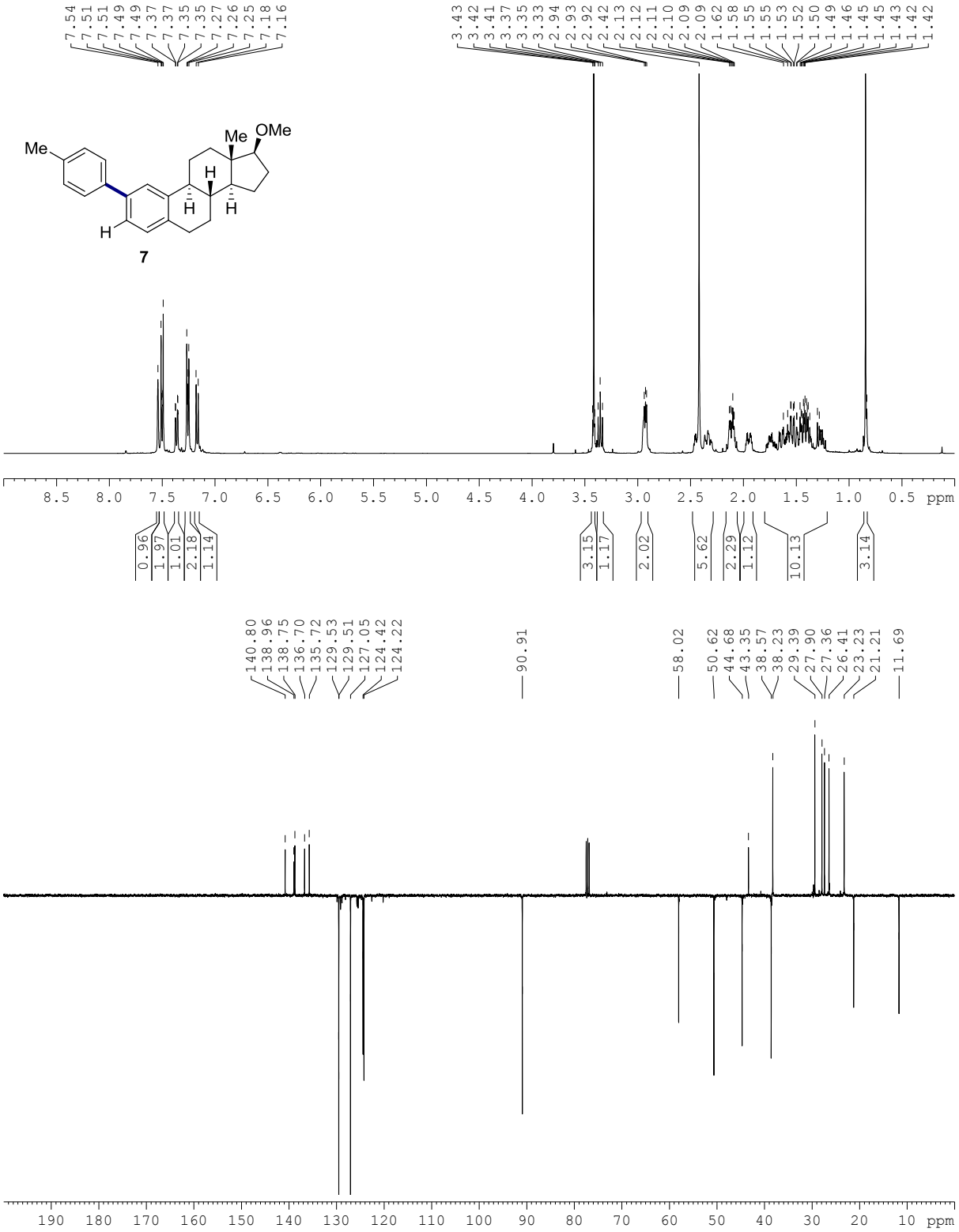
(8R,9S,13S,14S,17S)-3,17-Dimethoxy-13-methyl-2-(*p*-tolyl)-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene tricarbonyl chromium (6).



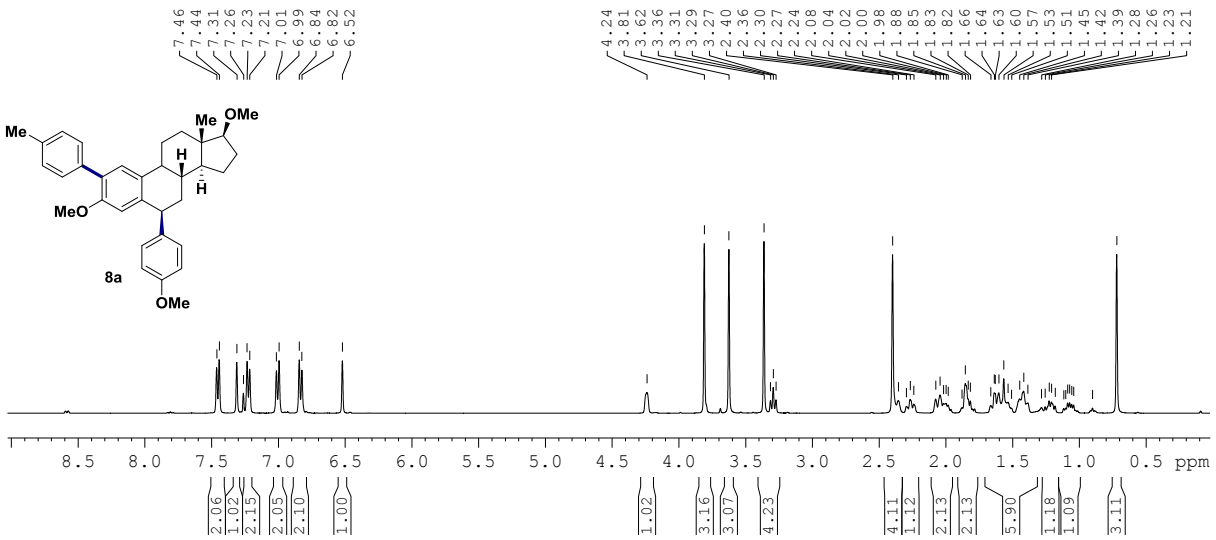
(8R,9S,13S,14S,17S)-13-Methyl-2-(*p*-tolyl)-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene-3,17-diol (5).

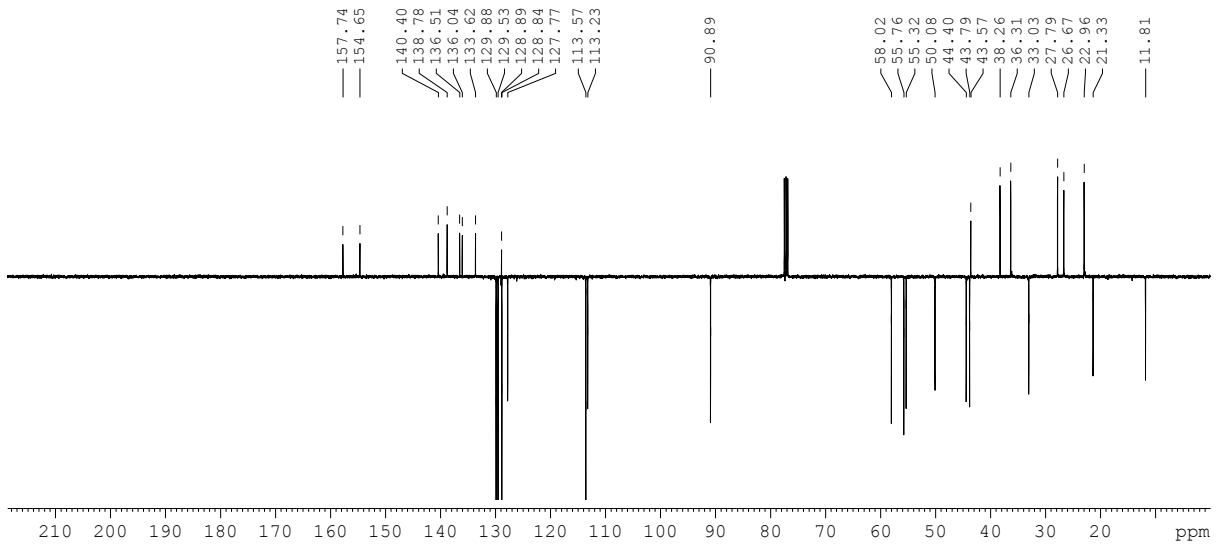


(8R,9S,13S,14S,17S)-17-Methoxy-13-methyl-2-(*p*-tolyl)-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene (7).

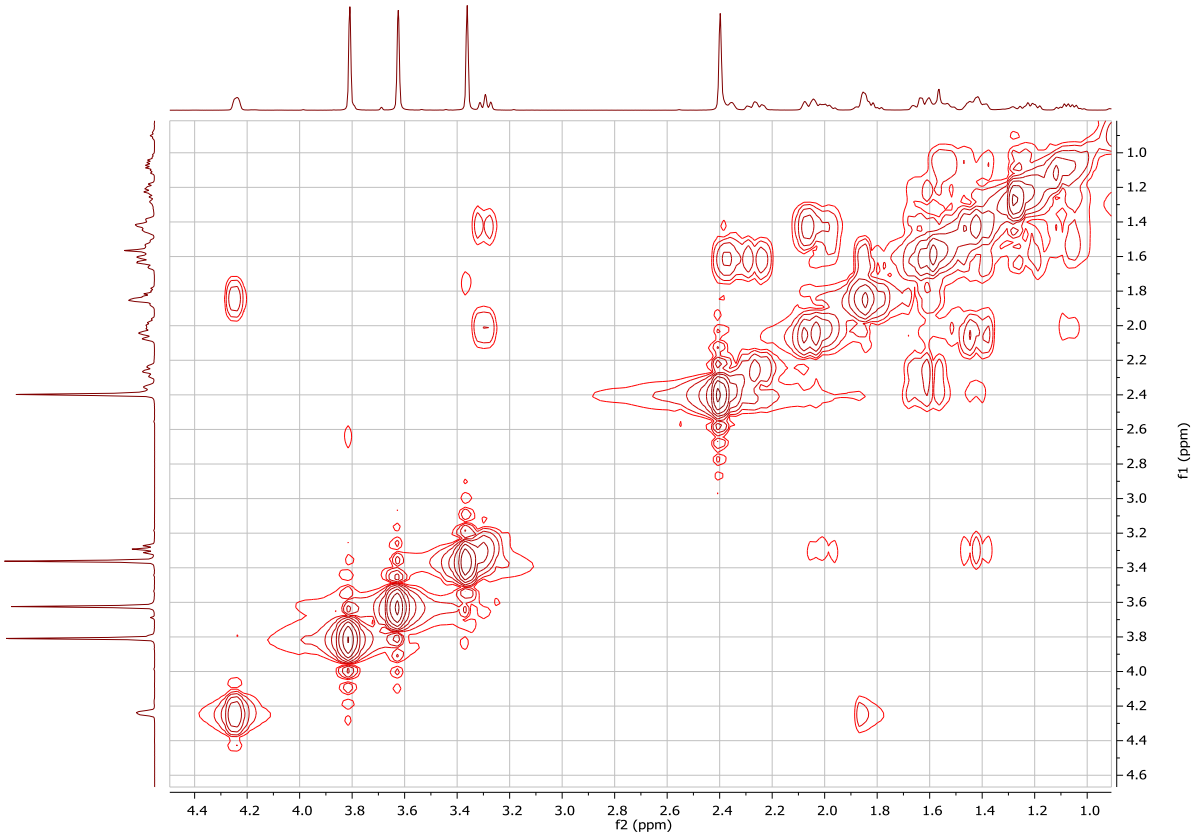


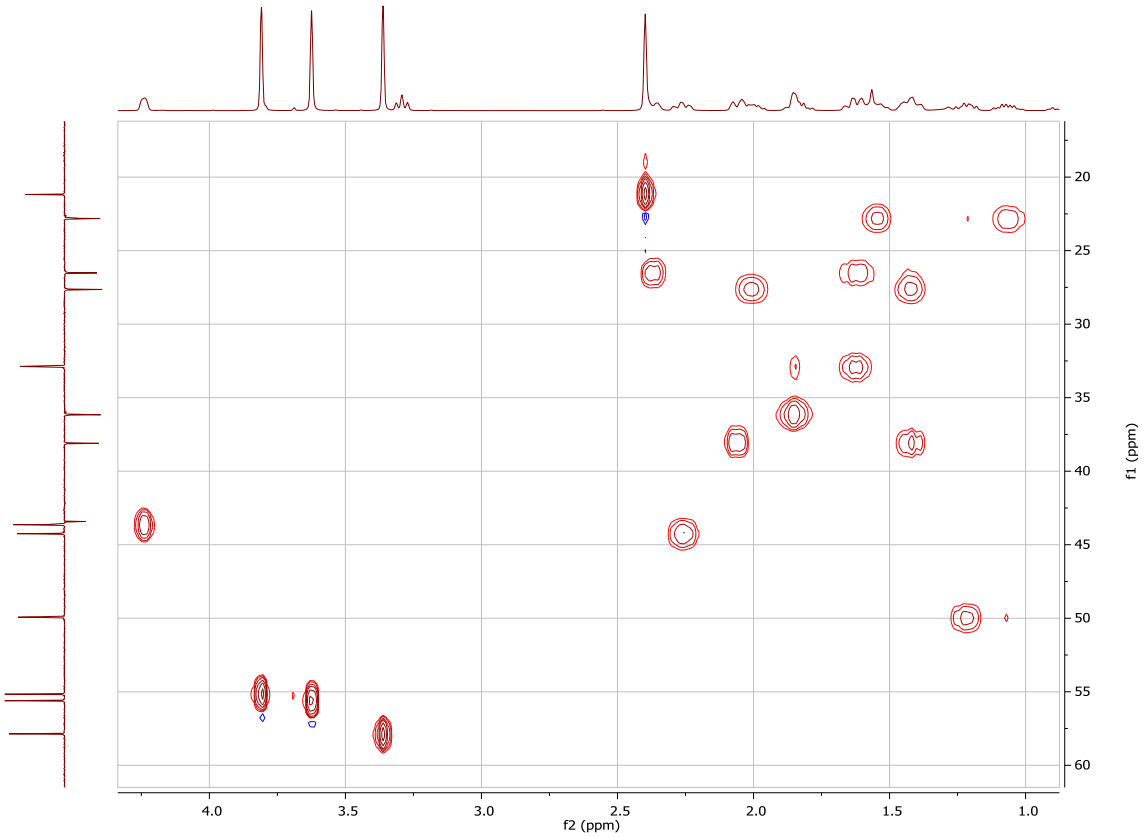
(6S,8R,9S,13S,14S,17S)-3,17-dimethoxy-6-(4-methoxyphenyl)-13-methyl-2-(p-tolyl)-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene (8a).





COSY and HSQC of 8a





NOESY analysis on 8a