Palladium-Catalyzed Methylation and Arylation of sp^2 and sp^3 C-H Bonds in Simple Carboxylic Acids

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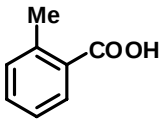
General Information: Solvents were obtained from Acros and used directly without further purification. Infrared spectra were recorded on a Perkin Elmer FT-IR Spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian instrument (400 MHz and 100 MHz, respectively) and internally referenced to $SiMe_4$ signal. High resolution mass spectra for new compounds were recorded at Mass Spectrometry Facilities, Harvard University.

Carboxylic acids were purchased from Acros, Sigma-Aldrich and Alfa-Aesar. Carboxylic acid **9** was prepared by alkylation of methyl isobutyrate with benzyl 3-bromopropyl ether and subsequent basic hydrolysis.[1] Carboxylic acid **10** was prepared from 2,2-dimethylglutaric acid by selectively esterifying the less hindered carboxyl group by converting it first to acid chloride and then reacting with MeOH.

Sodium or potassium carboxylates were prepared by treating the corresponding carboxylic acids with 0.8 equivalent of aqueous sodium or potassium hydroxide. Water was removed in a rotary evaporator and the excess of carboxylic acids was removed by washing with diethyl ether. The metal carboxylates were dried under high vacuum for 24 h at 110 °C.

Substrate Structure



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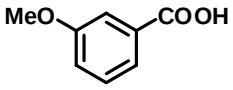

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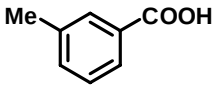

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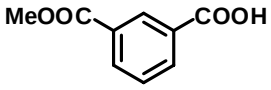

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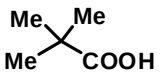

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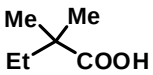

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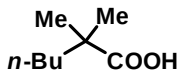

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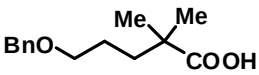

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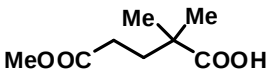

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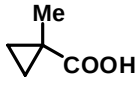

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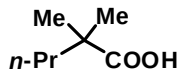

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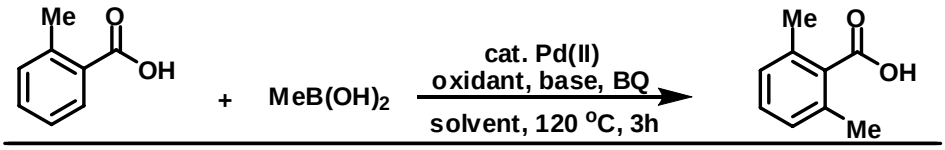
[1]Pei, T.; Wang, X.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2003**, *125*, 648.

Experimental Section

A. Methylation of benzoic acid derivatives

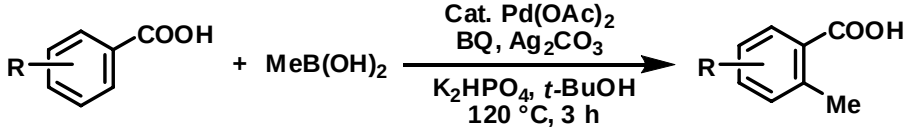
Optimization of reaction condition[a]



entry	Pd(II)	oxidant/base/benzoquinone(BQ)	yield (%)[b]
1	$Pd(OAc)_2$	None/K_2HPO_4/BQ	10
2	$Pd(OAc)_2$	Ag_2CO_3/K_2HPO_4/BQ	55
3	$Pd(OAc)_2$	Ag_2CO_3/K_2HPO_4/none	25
4	$Pd(OAc)_2$	Ag_2CO_3/K_2HPO_4(1.5eq)/BQ	60
5	$Pd(OAc)_2$	Ag_2CO_3/K_2HPO_4(1.5eq)/BQ(0.5eq)	75[c]
6	$Pd(OAc)_2$	Ag_2CO_3/K_2HPO_4(1.5eq)/BQ(0.5eq)	70[d]
7	$Pd(OAc)_2$	Ag_2CO_3/K_2HPO_4(1.5eq)/BQ(0.5eq)	15[e]
8	$Pd(OAc)_2$	Ag_2CO_3/K_2HPO_4(2eq)/BQ(0.5eq)	64
9	$Pd(OAc)_2$	Ag_2CO_3(0.5eq)/K_2HPO_4(1.5eq)/BQ(0.5eq)	38
10	$Pd(OAc)_2$	Ag_2CO_3(1.5eq)/K_2HPO_4(1.5eq)/BQ(0.5eq)	70
11	$Pd(OAc)_2$	Ag_2CO_3/K_3PO_4 (1.5 eq)/BQ(0.5eq)	52
12	$Pd(OAc)_2$	Ag_2CO_3/Na_2CO_3(1.5eq)/BQ (0.5 eq)	40[c]
13	$PdCl_2$	Ag_2CO_3/K_2HPO_4(1.5eq)/BQ(0.5eq)	20

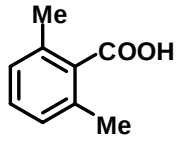
[a]10 mol% $Pd(OAc)_2$, 1 equiv of Ag_2CO_3, 1 equiv of base, 1 equiv of benzoquinone, 3 equiv of methylboronic acid in 1 mL of *tert*-butanol were used for a 0.2 mmol scale reaction, unless specified otherwise.
[b]Yields were determined by ^1H NMR.
[c]Isolated yield from a 0.3 mmol scale reaction.
[d]2 equiv of $MeB(OH)_2$ was used.
[e]1 equiv of $MeB(OH)_2$ was used.

General reaction scheme



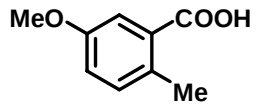
General procedure: Carboxylic acid (0.3 mmol), Ag_2CO_3 (82.7 mg, 0.3 mmol), benzoquinone (16.2 mg, 0.15 mmol), K_2HPO_4 (78.3 mg, 0.45 mmol) and methylboronic

acid (53.8 mg, 0.9 mmol) were dissolved in *tert*-butanol (1.5 mL) in a 25 mL glass pressure vessel. $Pd(OAc)_2$ (6.7 mg, 0.03 mmol) was added to the reaction mixture, tightly capped and heated to 120 °C with vigorous stirring. The reaction was stopped after it completely turned black (typically 3h). The reaction mixture was basified with 0.5 N NaOH and *tert*-butanol was removed in a rotary evaporator. The aqueous fraction was washed with diethyl ether (3 mL× 3), acidified with 2N HCl and extracted with ethyl acetate (3 mL ×3). The combined ethyl acetate fraction was washed with brine (3 mL), dried over Na_2SO_4 and the solvent was removed in a rotary evaporator. The product was purified by silica gel column chromatography using 5:1:94/EtOAc:HOAc:hexane as an eluting solvent.



1b

2,6-Dimethylbenzoic acid (1b): The title compound **1b** was obtained as a white solid (34 mg, 75% yield). The title compound **1b** is also obtained in 50% or 48% isolated yield when sodium or potassium carboxylate is used as the substrate in absence of K_2HPO_4 under similar conditions. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 6H), 7.08 (d, *J* = 7.9 Hz, 2H), 7.24 (t, *J* = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.54, 128.24, 130.30, 132.63, 136.01, 176.37; IR (neat) ν 2966, 1692, 1465, 1430, 1301, 918, 757 cm^{-1}; HRMS (EI) Calcd for $C_9H_9O_2$ $(M-H)^+$ 149.0603, found 149.0610.

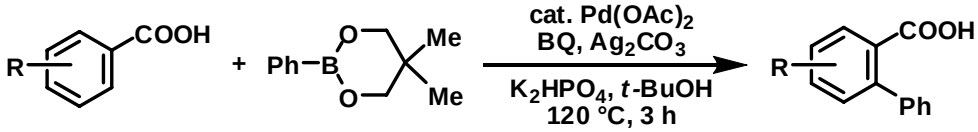


3a

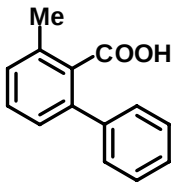
5-Methoxy-2-methylbenzoic acid (3a): The title compound **3a** was obtained as a white solid (35 mg, 71% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.59 (s, 3H), 3.84 (s, 3H), 7.03 (dd, *J* = 7.9, 2.4 Hz, 1H), 7.18 (d, *J* = 8.5 Hz, 1H), 7.6 (d, *J* = 3.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.58, 55.81, 115.95, 120.02, 129.16, 133.30, 133.82, 157.77, 173.46; IR (neat) ν 2916, 1693, 1438, 1283, 1238, 1045, 892, 817 cm^{-1}; GC-MS (M^+) 166.

B. Arylation of benzoic acid derivatives

General reaction scheme



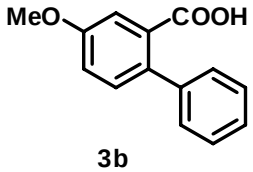
General procedure: Carboxylic acid (0.3 mmol), Ag_2CO_3 (82.7 mg, 0.3 mmol), benzoquinone (16.2 mg, 0.15 mmol), K_2HPO_4 (78.3 mg, 0.45 mmol) and 5,5-dimethyl-2-phenyl-1,2,3-dioxaborinane (57 mg, 0.3 mmol) were dissolved in *tert*-butanol (1.5 mL) in a 25 mL glass pressure vessel. $Pd(OAc)_2$ (6.7 mg, 0.03 mmol) was added to the reaction mixture, tightly capped and heated to 120 °C with vigorous stirring. The reaction was stopped after it completely turned black (typically 3h). The reaction mixture was basified with 0.5 N NaOH and *tert*-butanol was removed in a rotary evaporator. The aqueous fraction was washed with diethyl ether (3 mL× 3), acidified with 2N HCl and extracted with ethyl acetate (3 mL ×3). The combined ethyl acetate fraction was washed with brine (5 mL), dried over Na_2SO_4 and the solvent was removed in a rotary evaporator. The product was purified by silica gel column chromatography using 5:1:94/EtOAc:HOAc:hexane as an eluting solvent.



1c

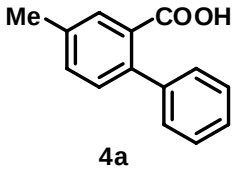
3-Methylbiphenyl-2-carboxylic acid (1c): The title compound **1c** was obtained as a white solid (40 mg, 63% yield). The title compound **1c** is also obtained in 45% isolated yield when sodium carboxylate is used as the substrate in absence of K_2HPO_4 under similar conditions. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), 7.22 (d, J = 7.9 Hz, 2H), 7.36-7.41 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.27, 127.81, 127.86, 128.65, 128.71, 129.54, 130.09, 132.43, 135.75, 140.50, 140.94, 175.97; IR (neat) ν 3030, 2916, 2651, 1697, 1461, 1293, 940, 758 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{13}O_2$ (MH^+) 213.0916, found 213.0910.

Compound **1c** was also obtained by arylating *o*-toluic acid with iodobenzene (see page S8). *O*-toluic acid (68 mg, 0.5 mmol), iodobenzene (112 μL, 1 mmol), Ag_2CO_3 (275.7 mg, 1 mmol), K_2HPO_4 (87.1 mg, 0.5 mmol) and sodium acetate (82 mg, 1 mmol) were dissolved in *tert*-butanol (2.5 mL) in a 25 mL glass pressure vessel. $Pd(OAc)_2$ (11.2 mg, 0.05 mmol) was added to the reaction mixture, tightly capped and heated to 120 °C with vigorous stirring. The reaction was stopped after it completely turned black (typically 3h). The black solid was filtered off, the filtrate was basified with 0.5 N NaOH and *tert*-butanol was removed in a rotary evaporator. The aqueous fraction was washed with diethyl ether (2 mL× 3), acidified with 2N HCl and extracted with ethyl acetate (5 mL ×5). The combined ethyl acetate fraction was washed with brine (10 mL), dried over Na_2SO_4 and the solvent was removed in a rotary evaporator. The product **1c** was obtained as a white solid (100.7 mg, 95% yield) after purification by silica gel column chromatography using 5:1:94/EtOAc:HOAc:hexane as an eluting solvent.



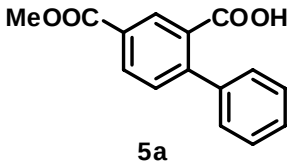
3b

4-Methoxybiphenyl-2-carboxylic acid (3b): The title compound **3b** was obtained as a white solid (32 mg, 46% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 3H), 7.09 (dd, *J* = 8.5, 2.4 Hz, 1H), 7.28-7.37 (m, 6H), 7.45 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.89, 115.43, 118.81, 127.34, 128.36, 128.93, 130.38, 132.76, 136.25, 141.06, 158.83, 173.97; IR (neat) ν 2963, 2666, 1697, 1454, 1285, 1033, 910, 759 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{16}NO_3$ (MNH_4^+) 246.1130, found 246.1139.



4a

4-Methylbiphenyl-2-carboxylic acid (4a): The title compound **4a** was obtained as a white solid (32 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.25 (d, *J* = 7.3 Hz, 1H), 7.30-7.37 (m, 6H), 7.75 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.24, 127.49, 128.37, 128.84, 129.36, 131.48, 131.49, 133.21, 137.41, 140.88, 141.29, 174.24; IR (neat) ν 3028, 2674, 1694, 1436, 1310, 1215, 954, 770, 704 cm^{-1}; GC-MS (M^+) 212.



5a

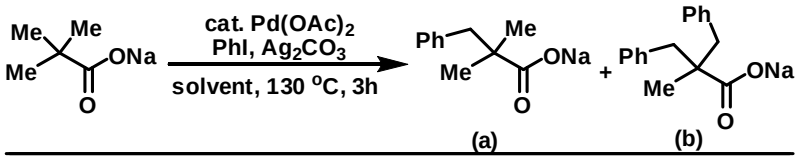
4-(Methoxycarbonyl)biphenyl-2-carboxylic acid (5a): The title compound **5a** was obtained as a white solid (31 mg, 40% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.96 (s, 3H), 7.34-7.41 (m, 5H), 7.46 (d, *J* = 7.9 Hz, 1H), 8.21 (dd, *J* = 7.9, 1.8 Hz, 1H), 8.61 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.80, 128.36, 128.59, 128.62, 129.48, 129.94, 131.85, 132.31, 133.19, 140.28, 147.94, 166.36, 172.93; IR (neat) ν 3027, 2636, 1725, 1698, 1437, 1303, 1117, 756 cm^{-1}; HRMS (EI) Calcd for $C_{15}H_{13}O_4$ (MH^+) 257.0814, found 257.0806.

C. Arylation of β-C-H bonds in sp^3 carboxylic acids

The arylated carboxylic acids (**6a**,**b**-**8a**,**b**; **10a**,**b**,**c**,**d**; **11a**; and **12a**,**b**,**c**,**d**) were purified and characterized as their corresponding methyl esters (**6c**,**d**-**8c**,**d**; **10e**,**f**,**g**,**h**; **11b**; and **12e**,**f**,**g**,**h**), respectively. The arylated carboxylic acids (**9a**,**b**) were purified and characterized as their corresponding lactones (**9c**,**d**), respectively.

C1. Using aryl iodide as a coupling reagent

Solvent screening[a]

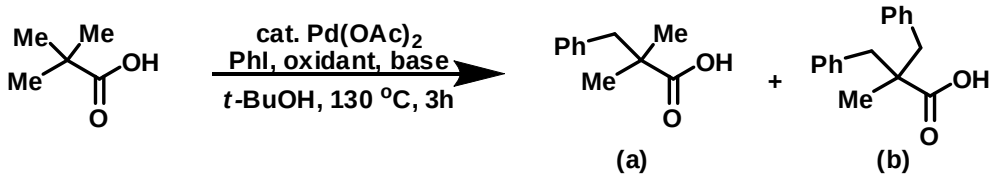


(a) (b)

entry	solvent	yield (%)/ratio (a:b)[b]
1	MeCN	2
2	DCE	10/3:1
3	CH_2Cl_2	26/2:1
4	EtOAc	37/3:1
5	C_6H_6	2
6	Dioxane	3
7	*t*-BuOH	38/3:1
8	DMSO	0
9	DMF	10/3:1
10	NMP	0

[a]10 mol% $Pd(OAc)_2$, 1 equiv of PhI, 1 equiv of Ag_2CO_3 and 1.5 mL of solvent for a 0.3 mmol scale reaction were used.
[b]Yields and the ratios of the caboxylic acid products were determined by ^{1}H NMR.

Optimization of reaction condition[a]



(a) (b)

entry	oxidant/base/additive[a]	yield (%)/ratio (a:b)[b]
1	Ag_2CO_3/K_2HPO_4/none	42/3:1
2	AgOAc/K_2HPO_4/none	40/3:1
3	None/K_2HPO_4/none	10/3:1
4	AgOAc/Na_2CO_3/none	41/3:1
5	Ag_2CO_3/DABCO/none	5
6	Ag_2CO_3/K_2HPO_4 (2 equiv)/none	40/3:1
7	Ag_2CO_3 (2 equiv)/K_2HPO_4/none	55(40)/5:2[c]
8	Ag_2CO_3 (2 equiv)/K_2HPO_4 (2 equiv)/none	53/5:2
9	Ag_2CO_3 (2 equiv)/K_2HPO_4/NaOAc	71/5:2
10	Ag_2CO_3 (2 equiv)/K_2HPO_4/NaOAc (2 equiv)	82(70)/5:2[c]

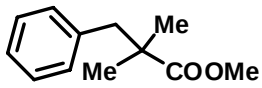
[a]10 mol % $Pd(OAc)_2$, 1 equiv of oxidant, 2 equiv of aryl iodide, 1 equiv of base, 1equiv of additive and 1.5 mL of *tert*-butanol were used for a 0.3 mmol scale reaction unless specified otherwise. Reactions were run for 3 h.
[b]Yields and ratios of the caboxylic acid products were determined by ^{1}H NMR.
[c]Isolated yield of the corresponding methyl ester from a 0.5 mmol scale reaction is given in paranthesis.

General procedure: Carboxylic acid (0.5 mmol), aryl iodide (1 mmol), Ag_2CO_3 (275.7 mg, 1 mmol), K_2HPO_4 (87.1 mg, 0.5 mmol) and sodium acetate (82 mg, 1 mmol) were dissolved in *tert*-butanol (2.5 mL) in a 25 mL glass pressure vessel. $Pd(OAc)_2$ (11.2 mg, 0.05 mmol) was added to the reaction mixture, tightly capped and heated to 120 °C with vigorous stirring. The reaction was stopped after it completely turned black (typically 3h). The black solid was filtered off, the filtrate was basified with 0.5 N NaOH and *tert*-butanol was removed in a rotary evaporator. The aqueous fraction was washed with diethyl ether (2 mL× 3), acidified with 2N HCl and extracted with ethyl acetate (5 mL ×5). The combined ethyl acetate fraction was dried over Na_2SO_4 and the solvent was removed in a rotary evaporator.

Oxalyl chloride (95.2 mg, 375 μL from a 2 M solution in methylene chloride, 0.75 mmol) was slowly added at 0 °C to a stirred solution of the crude carboxylic acid mixture in methylene chloride (1 mL) and allowed to slowly warm up to room temperature. The

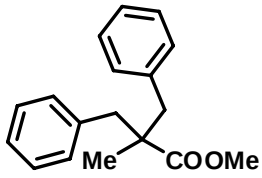
reaction was stopped after the gas was no longer produced and the excess oxalyl chloride was removed in a rotary evaporator. The crude carboxylic acid chloride was slowly added at 0 °C to a stirred solution of methanol (405 μL, 10 mmol) and triethylamine (140.5 μL, 1 mmol) in methylene chloride (1 mL), allowed to slowly warm up to room temperature. After 8 h, the reaction mixture was washed with saturated aqueous $NaHCO_3$ (1 mL ×2), $NaHCO_3$ fraction was extracted with methylene chloride (2 mL × 2), the combined methylene chloride fraction was dried over Na_2SO_4 and the solvent was removed in a rotary evaporator. The crude methyl carboxylate was purified by silica gel column chromatography using 1-5% diethyl ether/hexane as an eluting solvent.

The arylating conditions for sp^3 carboxylic acids are also applicable to the arylation of benzoic acid derivatives (see page S6).



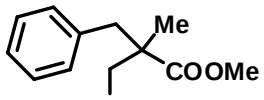
6c

Methyl 2,2-dimethyl-3-phenylpropanoate (6c): The title compound **6c** was obtained as a colorless oil (48 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (s, 6H), 2.85 (s, 3H), 3.66 (s, 3H), 7.09 (d, *J* = 7.3 Hz, 2H), 7.19-7.28 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.21, 43.92, 46.64, 51.93, 126.73, 128.27, 130.36, 138.14, 178.17; IR (neat) ν 2973, 1733, 1472, 1193, 1124, 742, 702 cm^{-1}; HRMS (EI) Calcd for $C_{12}H_{17}O_2$ (MH^+) 193.1228, found 193.1223.



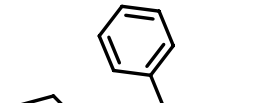
6d

Methyl 2-benzyl-2-methyl-3-phenylpropanoate (6d): The title compound **6d** was obtained as a colorless oil (27 mg, 20% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (s, 3H), 2.68 (d, *J* = 13.4 Mz, 2H), 3.22 (d, *J* = 13.4 Mz, 2H), 3.60 (s, 3H), 7.11 (d, *J* = 7.3 Hz, 4H), 7.19-7.28 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.18, 46.59, 49.44, 51.78, 126.90, 128.42, 130.49, 137.83, 176.71; IR (neat) ν 3028, 2946, 1732, 1455, 1193, 1100, 746, 702 cm^{-1}; HRMS (EI) Calcd for $C_{18}H_{21}O_2$ (MH^+) 269.1541, found 269.1537.



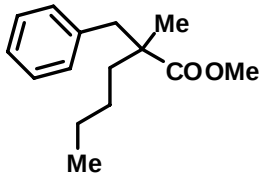
7c

Methyl 2-benzyl-2-methylbutanoate (7c): The title compound **7c** was obtained as a colorless oil (60 mg, 58% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.9 Hz, 3H), 1.08 (s, 3H), 1.41-1.50 (m, 1H), 1.76-1.85 (m, 1H), 2.69 (d, *J* = 13.4 Hz, 1H), 3.02 (d, *J* = 13.4 Hz, 1H), 3.66 (s, 3H), 7.09 (d, *J* = 6.7 Hz, 2H), 7.18-7.27 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.48, 20.49, 32.44, 45.58, 48.22, 51.76, 126.70, 128.28, 130.38, 138.11, 177.45; IR (neat) ν 2971, 1732, 1455, 1230, 1186, 1130, 1015, 741, 702 cm^{-1}; HRMS (EI) Calcd for $C_{13}H_{19}O_2$ (MH^+) 207.1385, found 207.1390.



7d

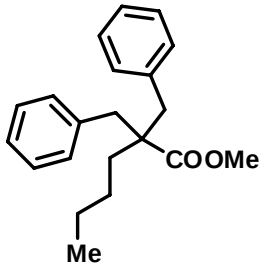
Methyl 2,2-dibenzylbutanoate (7d): The title compound **7d** was obtained as a colorless oil (20 mg, 14% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (t, *J* = 7.3 Hz, 3H), 1.53 (q, *J* = 7.3 Hz, 2H), 2.87 (d, *J* = 14 Hz, 2H), 3.06 (d, *J* = 14 Hz, 2H), 3.61 (s, 3H), 7.10 (d, *J* = 7.3 Hz, 4H), 7.18-7.27 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.97, 24.33, 41.51, 51.64, 52.66, 126.79, 128.45, 130.28, 137.94, 176.66; IR (neat) ν 3029, 2946, 1731, 1454, 1204, 1177, 739, 701 cm^{-1}; GC-MS (M^+) 282.



8c

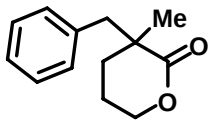
Methyl 2-benzyl-2-methylhexanoate (8c): The title compound **8c** was obtained as a colorless oil (58.5 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, *J* = 7.3 Hz, 3H), 1.08 (s, 3H), 1.14-1.18 (m, 1H), 1.24-1.31 (m, 3H), 1.37-1.44 (m, 1H), 1.70-1.77 (m, 1H), 2.68 (d, *J* = 13.4 Hz, 1H), 3.02 (d, *J* = 13.4 Hz, 1H), 3.65 (s, 3H), 7.08 (d, *J* =

6.7 Hz, 2H), 7.18-7.27 (3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.38, 21.06, 23.50, 27.33, 39.67, 45.91, 47.83, 51.83, 126.34, 128.32, 130.45, 138.15, 177.67; IR (neat) ν 2952, 1731, 1454, 1204, 1154, 741, 702 cm^{-1}; HRMS (EI) Calcd for $C_{15}C_{23}O_2$ (MH^+) 235.1698, found 235.1697.



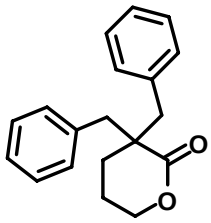
8d

Methyl 2,2-dibenzylhexanoate (8d): The title compound **8d** was obtained as a white solid (18.5 mg, 12% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.3 Hz, 3H), 1.26-1.33 (m, 2H), 1.40-1.46 (m, 4H), 2.88 (d, *J* = 13.4 Hz, 2H), 3.05 (d, *J* = 13.4 Hz, 2H), 3.62 (s, 3H), 7.10 (d, *J* = 7.3 Hz, 4H), 7.19-7.28 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.48, 23.39, 26.57, 31.83, 41.94, 51.67, 52.34, 126.80, 128.46, 130.30, 138.01, 176.78; IR (neat) ν 2952, 1724, 1495, 1454, 1207, 1176, 740, 701 cm^{-1}; HRMS (EI) Calcd for $C_{21}H_{27}O_2$ (MH^+) 311.2011, found 311.2003.



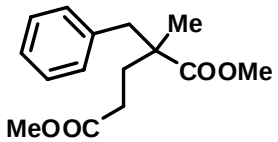
9c

3-Benzyl-3-methyltetrahydro-2*H*-pyran-2-one (9c): The crude carboxylic acid **9a** debenzylates under acidic condition during the preparation of carboxylic acid chloride using oxalyl chloride and cyclizes to form the six-membered lactone **9c**. The title compound **9c** was obtained as a colorless oil (37.5 mg, 37% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 3H), 1.51-1.58 (m, 1H), 1.64-1.72 (m, 1H), 1.81-1.93 (m, 2H), 2.68 (d, *J* = 13.4 Hz, 1H), 3.31 (d, *J* = 13.4 Hz, 1H), 4.03-4.08 (m, 1H), 4.27-4.31 (m, 1H), 7.18 ((d, *J* = 7.3 Hz, 2H), 7.22-7.31 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.89, 27.64, 31.49, 44.19, 46.24, 70.79, 127.09, 128.61, 130.83, 137.42, 176.71; IR (neat) ν 2964, 1722, 1454, 1264, 1126, 1072, 705 cm^{-1}; GC-MS (M^+) 204.



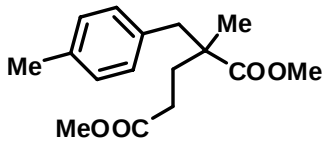
9d

3,3-Dibenzyltetrahydro-2*H*-pyran-2-one (9d): The crude carboxylic acid **9b** debenzylates under acidic condition during the preparation of carboxylic acid chloride using oxalyl chloride and cyclizes to form the six-membered lactone **9d**. The title compound **9d** was obtained as a colorless oil (11.5 mg, 8% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22-1.29 (m, 2H), 1.82 (t, *J* = 6.1 Hz, 2H), 2.63 (d, *J* = 12.8 Hz, 2H), 3.48 (d, *J* = 12.8 Hz, 2H), 3.75 (t, *J* = 5.5 Hz, 2H), 7.21 (d, *J* = 7.3 Hz, 4H), 7.25-7.32 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.43, 27.46, 47.06, 49.74, 70.33, 127.24, 128.75, 130.85, 137.27, 176.05; IR (neat) ν 3026, 2945, 1716, 1451, 1156, 705 cm^{-1}; GC-MS (M^+) 280.



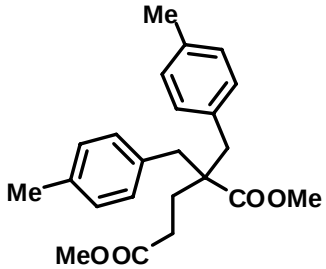
10e

Dimethyl 2-benzyl-2-methylpentanedioate (10e): During the reaction of substrate **10**, the methyl ester is hydrolyzed in the reaction giving **10e** as a dicarboxylic acid in the crude mixture. The dicarboxylic acid was converted to dimethyl ester **10e**. The title compound **10e** was obtained as a colorless oil (55.5 mg, 42% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (s, 3H), 1.74-1.82 (m, 1H), 2.08-2.16 (m, 1H), 2.23-2.40 (m, 2H), 2.73 (d, *J* = 12.8 Hz, 1H), 3.02 (d, *J* = 12.8 Hz, 1H), 3.66 (s, 3H), 3.67 (s, 3H), 7.08 (d, *J* = 7.3 Hz, 2H), 7.20-7.28 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.01, 30.16, 34.17, 45.91, 47.19, 52.05, 126.98, 128.44, 130.41, 137.41, 174.06, 176.74; IR (neat) ν 2950, 1734, 1495, 1435, 1381, 1196, 1107, 993, 743, 703 cm^{-1}; HRMS (EI) Calcd for $C_{15}H_{21}O_4$ (MH^+) 265.1440, found 265.1435.



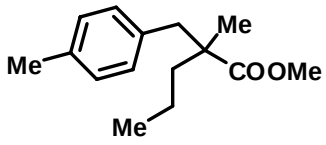
10g

Dimethyl 2-methyl-2-(4-methylbenzyl)pentanedioate (10g): During the reaction of substrate **10**, the methyl ester is hydrolyzed in the reaction giving **10g** as a dicarboxylic acid in the crude mixture. The dicarboxylic acid was converted to dimethyl ester **10g**. The title compound **10g** was obtained as a colorless oil (50 mg, 36% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (s, 3H), 1.72-1.80 (m, 1H), 2.07-2.14 (m, 1H), 2.22-2.41 (m, 2H), 2.31 (s, 3H), 2.69 (d, *J* = 13.4 Hz, 1H), 2.97 (d, *J* = 13.4 Hz, 1H), 3.66 (s, 3H), 3.67 (s, 3H), 6.96 (d, *J* = 7.9 Hz, 2H), 7.07 (d, *J* = 7.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.99, 21.37, 30.17, 34.10, 45.53, 47.20, 52.04, 129.16, 130.27, 134.26, 136.50, 174.11, 176.84; IR (neat) ν 3451, 2950, 1732, 1514, 1435, 1380, 1195, 996, 820, 782 cm^{-1}; HRMS (EI) Calcd for $C_{16}C_{23}O_4$ (MH^+) 279.1596, found 279.1586.



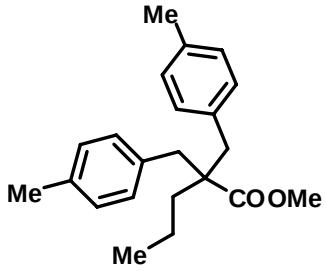
10h

Dimethyl 2,2-bis(4-methylbenzyl)pentanedioate (10h): During the reaction of substrate **10**, the methyl ester is hydrolyzed in the reaction giving **10h** as a dicarboxylic acid in the crude mixture. The dicarboxylic acid was converted to dimethyl ester **10h**. The title compound **10h** was obtained as a colorless oil (13 mg, 7% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.82-1.86 (m, 2H), 2.31 (s, 6H), 2.41-2.45 (m, 2H), 2.79 (d, *J* = 14.0 Hz, 2H), 3.03 (d, *J* = 14.0 Hz, 2H), 3.63 (s, 3H), 3.65 (s, 3H), 6.99 (d, *J* = 7.9 Hz, 4H), 7.07 (d, *J* = 7.9 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.38, 27.49, 29.83, 41.94, 51.74, 51.84, 52.02, 129.32, 130.19, 134.10, 136.56, 174.05, 176.08; IR (neat) ν 2949, 1736, 1514, 1453, 1188, 1082, 812 cm^{-1}; HRMS (EI) Calcd for $C_{23}H_{29}O_4$ (MH^+) 369.2066, found 369.2060.



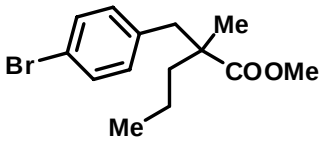
12e

Methyl 2-methyl-2-(4-methylbenzyl)pentanoate (12e): The title compound **12e** was obtained as a colorless oil (52.5 mg, 45% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, *J* = 6.7 Hz, 3H), 1.07 (s, 3H), 1.14-1.24 (m, 1H), 1.30-1.41 (m, 2H), 1.67-1.74 (m, 1H), 2.31 (s, 3H), 2.65 (d, *J* = 13.4 Hz, 1H), 2.98 (d, *J* = 13.4 Hz, 1H), 3.65 (s, 3H), 6.97 (d, *J* = 7.9 Hz, 2H), 7.06 (d, *J* = 7.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.88, 18.41, 21.03, 21.37, 42.10, 45.53, 47.87, 51.79, 129.03, 130.30, 134.96, 136.20, 177.73; IR (neat) ν 2958, 1732, 1464, 1213, 1132, 818 cm^{-1}; GC-MS (M^+) 234.



12f

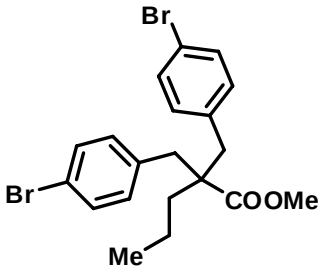
Methyl 2,2-bis(4-methylbenzyl)pentanoate (12f): The title compound **12f** was obtained as a colorless oil (24.5 mg, 15% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.3 Hz, 3H), 1.39-1.51 (m, 4H), 2.31 (s, 6H), 2.82 (d, *J* = 14.0 Hz, 2H), 3.01 (d, *J* = 14.0 Hz, 2H), 3.62 (s, 3H), 6.98 (d, *J* = 7.9 Hz, 4H), 7.06 (d, *J* = 7.9 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.68, 17.62, 21.38, 34.09, 41.53, 51.61, 52.49, 129.16, 130.13, 134.89, 136.24, 176.86; IR (neat) ν 2957, 1735, 1514, 1452, 1264, 1174, 1118, 1042, 824, 788 cm^{-1}; HRMS (EI) Calcd for $C_2H_{29}O_2$ (MH^+) 325.2167, found 325.2170.



12g

Methyl 2-methyl-2-(4-bromobenzyl) pentanoate (12g): The title compound **12g** was obtained as a colorless oil (70 mg, 47% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.3 Hz, 3H), 1.05 (s, 3H), 1.14-1.39 (m, 3H), 1.63-1.70 (m, 1H), 2.60 (d, *J* = 13.4 Hz, 1H), 2.95 (d, *J* = 13.4 Hz, 1H), 3.62 (s, 3H), 6.93 (d, *J* = 7.9 Hz, 2H), 7.35 (d, *J* = 7.9 Hz,

2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.84, 18.36, 21.03, 42.19, 45.22, 47.77, 51.92, 120.76, 131.43, 132.14, 137.12, 177.37; IR (neat) ν 2958, 1731, 1488, 1466, 1214, 1073, 1012, 837 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{23}BrNO_2$ (MNH_4^+) 316.0912, found 316.0906.

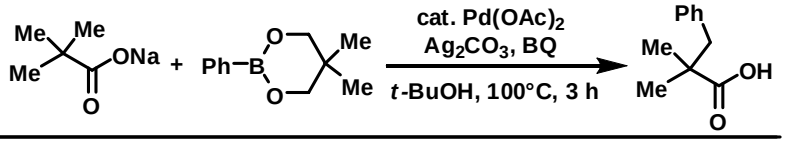


12h

Methyl 2,2-bis(4-bromobenzyl)pentanoate (12h): The title compound **12h** was obtained as a colorless oil (36.5 mg, 16% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, *J* = 6.7 Hz, 3H), 1.39-1.43 (m, 4H), 2.81 (d, *J* = 12.4 Hz, 2H), 2.97 (d, *J* = 12.4 Hz, 2H), 3.61 (s, 3H), 6.95 (d, *J* = 7.9 H, 4H), 7.38 (d, *J* = 7.9 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.63, 17.64, 34.19, 41.37, 51.86, 52.21, 120.90, 131.62, 131.92, 136.71, 176.29; IR (neat) ν 2957, 1732, 1488, 1465, 1213, 1074, 1012, 828 cm^{-1}; HRMS (EI) Calcd for $C_{20}H_{26}Br_2NO_2$ (MNH_4^+) 470.0330, found 470.0337.

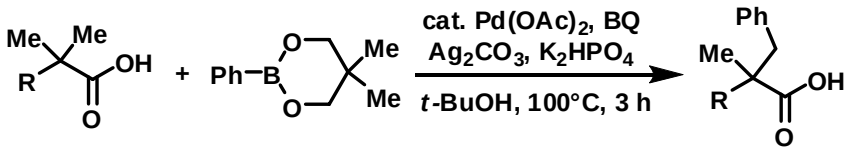
C2. Using phenylboronate as a coupling reagent

Reaction optimization



entry	oxidant/base[a]	yield (%)[b]
1	Ag_2CO_3/none	30[c]
2	AgOAc/none	5
3	Ag_2O/none	4
4[d]	Ag_2CO_3/Na_2CO_3	0
5[d]	Ag_2CO_3/K_2HPO_4	38[c]

[a]10 mol % $Pd(OAc)_2$, 1equiv of oxidant, 0.5 equiv of benzoquinone (BQ) and 1.5 equiv of base in 1.5 mL of *tert*-butanol were used for a 0.3 mmol scale reaction unless specified otherwise. Reactions were run for 3 h.
[b]Yields of the caboxylic acid products were determined by ^{1}H NMR.
[c]Isolated yield of the corresponding methyl ester from a 0.5 mmol scale reaction. Less than 2% diarylated product was observed by ^{1}H NMR.
[d]Carboxylic acid was used instead of sodium carboxylate.



General procedure: Carboxylic acid (0.5 mmol), benzoquinone (27 mg, 0.25 mmol), Ag_2CO_3 (138 mg, 0.5 mmol), K_2HPO_4 (130.7 mg, 0.75 mmol) and 5,5-dimethyl-2-phenyl-1,2,3-dioxaborinane (95 mg, 0.5 mmol) were dissolved in *tert*-butanol (2.5 mL) in a 25 mL glass pressure vessel. $Pd(OAc)_2$ (11.2 mg, 0.05 mmol) was added to the reaction mixture, tightly capped and heated to 120 °C with vigorous stirring. The reaction was stopped after it completely turned black (typically 3h). The black solid was filtered off, the filtrate was basified with 0.5 N NaOH and *tert*-butanol was removed in a rotary evaporator. The aqueous fraction was washed with diethyl ether (2 mL× 3), acidified with 2N HCl and extracted with ethyl acetate (5 mL ×5). The combined ethyl acetate fraction was dried over Na_2SO_4 and the solvent was removed in a rotary evaporator.

Oxalyl chloride (95.2 mg, 375 μL from a 2 M solution in methylene chloride, 0.75 mmol) was slowly added at 0 °C to a stirred solution of the crude carboxylic acid mixture in methylene chloride (1 mL) and allowed to slowly warm up to room temperature. The reaction was stopped after the gas was no longer produced and the excess oxalyl chloride was removed in a rotary evaporator. The crude carboxylic acid chloride was slowly added at 0 °C to a stirred solution of methanol (405 μL, 10 mmol) and triethylamine (141 μL, 1 mmol) methylene chloride (1 mL), allowed to slowly warm up to room temperature. After 8 h, the reaction mixture was washed with saturated aqueous $NaHCO_3$ (1 mL ×2), $NaHCO_3$ fraction was extracted with methylene chloride (2 mL × 2), the combined methylene chloride fraction was dried over Na_2SO_4 and the solvent was removed in a rotary evaporator. The crude methyl carboxylate was purified by silica gel column chromatography using 1-5% diethyl ether/hexane as an eluting solvent.

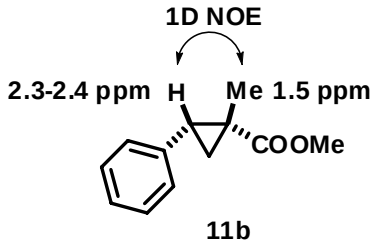
Methyl 2,2-dimethyl-3-phenylpropanoate (6c): The title compound **6c** was obtained as a colorless oil (36.5 mg, 38% yield). The title compound **6c** is also obtained in 30% isolated yield when sodium carboxylate is used as the substrate in absence of K_2HPO_4 under similar conditions. See Section C1 for spectral characterization.

Methyl 2-benzyl-2-methylbutanoate (7c): The title compound **7c** was obtained as a colorless oil (31 mg, 30% yield). See Section C1 for spectral characterization.

Methyl 2-benzyl-2-methylhexanoate (8c): The title compound **8c** was obtained as a colorless oil (32.5 mg, 28% yield). See Section C1 for spectral characterization.

3-Benzyl-3-methyltetrahydro-2*H*-pyran-2-one (9c): The crude carboxylic acid **9a** debenzylates under acidic condition during the preparation of carboxylic acid chloride using oxalyl chloride and cyclizes to form the six-membered lactone **9c**. The title compound **9c** was obtained as a colorless oil (49 mg, 30% yield). See Section C1 for spectral characterization.

Dimethyl 2-benzyl-2-methylpentanedioate (10e): During the reaction of substrate **10**, the methyl ester is hydrolyzed in the reaction giving **10e** as a dicarboxylic acid in the crude mixture. The dicarboxylic acid was converted to dimethyl ester **10e**. The title compound **10e** was obtained as a colorless oil (39.5 mg, 30% yield). See Section C1 for spectral characterization.



11b

Methyl 1-methyl-2-phenylcyclopropanecarboxylate (11b): The title compound **11b** was obtained as a colorless oil (19 mg, 20% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12-1.15 (m, 1H), 1.50 (s, 3H), 1.93-1.96 (m, 1H), 2.32-2.36 (m, 1H), 3.31 (s, 3H), 7.16-7.26 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.25, 21.63, 28.12, 34.14, 51.69, 126.78, 128.16, 129.32, 137.58, 173.30; IR (neat) ν 2950, 1722, 1460, 1332, 1193, 1156, 765, 776, 723, 697 cm^{-1}; HRMS (EI) Calcd for $C_{12}H_{15}O_2$ (MH^+) 191.1072, found 191.1081.

The *cis*-geometry of the phenyl group to the ester group in **11b** was confirmed by 1D NOE experiment.

D. Preparation of Palladium *O*-Toluate[2] and Its Reactions

Palladium acetate (224 mg, 1 mmol) was dissolved in benzene (8 mL), stirred for 1 hour and filtered through a Whatman No.1 filter paper. *O*-Toluic acid (408 mg, 3 mmol) was added to the filtrate and stirred for 10 hours. Benzene was removed in a rotary evaporator and the remaining solid was washed with hexane to obtain palladium *o*-toluate (332 mg, 88% yield based on palladium acetate) as a brown powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.54 (s, 3H), 7.07-7.13 (m, 2H), 7.26 (t, *J* = 7.9 Hz, 1H), 7.76 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.54, 125.65, 131.10, 131.19, 131.52, 132.04, 139.69, 184.75.

Palladium *o*-toluate (37.7 mg, 0.1 mmol), benzoquinone (5.4 mg, 0.05 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol) and 5,5-dimethyl-2-phenyl-1,2,3-dioxaborinane (19 mg, 0.1 mmol) were dissolved in *tert*-butanol (0.5 mL) in a 10 mL glass pressure vessel. The vessel was tightly capped and heated to 120 °C with vigorous stirring for 3h. The reaction mixture was basified with 0.5 N NaOH and *tert*-butanol was removed in a rotary evaporator. The aqueous fraction was washed with diethyl ether (1 mL× 2), acidified with 2N HCl and extracted with ethyl acetate (1 mL ×3). The combined ethyl acetate fraction was dried over Na_2SO_4 and the solvent was removed in a rotary evaporator. ^{1}NMR analysis of the crude product revealed that the arylated product **1c** was formed in 35% yield based on palladium. When K_2HPO_4 was omitted from the reaction mixture, no product was observed, suggesting that the base is crucial for the reaction and the C-H activation would less likely proceed through o-anion binding to the palladium.

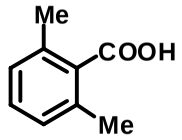
[2]Hermans, S.; Wenkin, M; Devillers, M. *J. Mol. Catal. A: Chemical* **1998**, *136*, 59.

STANDARD 1H OBSERVE

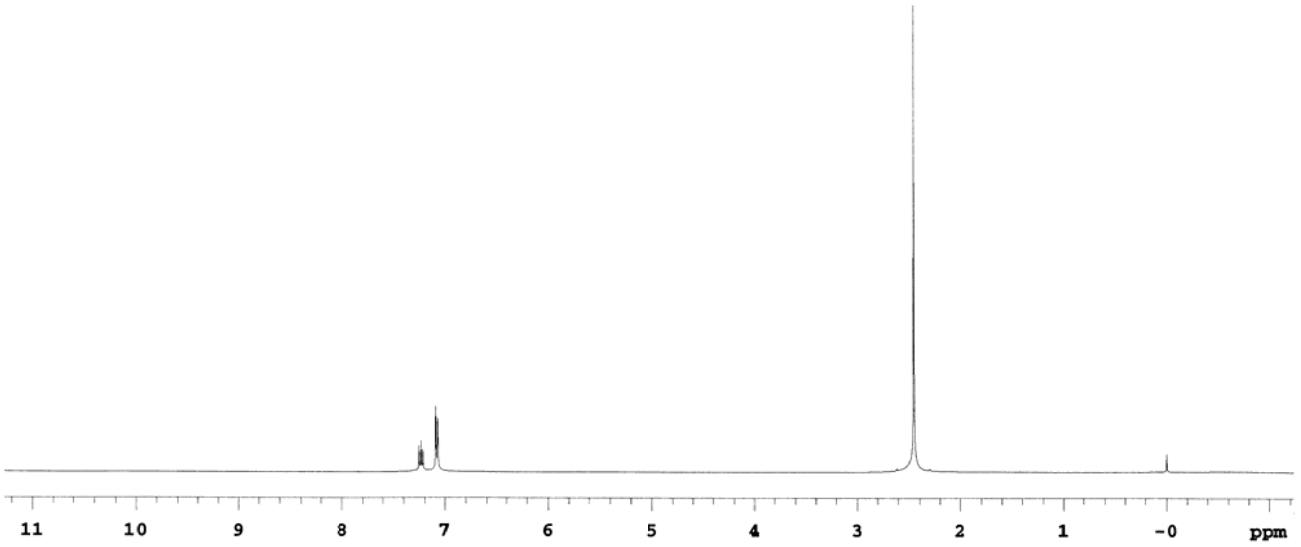
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: nm3-77-1H1
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
30 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 7 min, 2 sec



1b

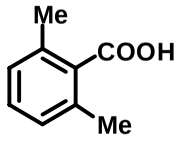


13C OBSERVE

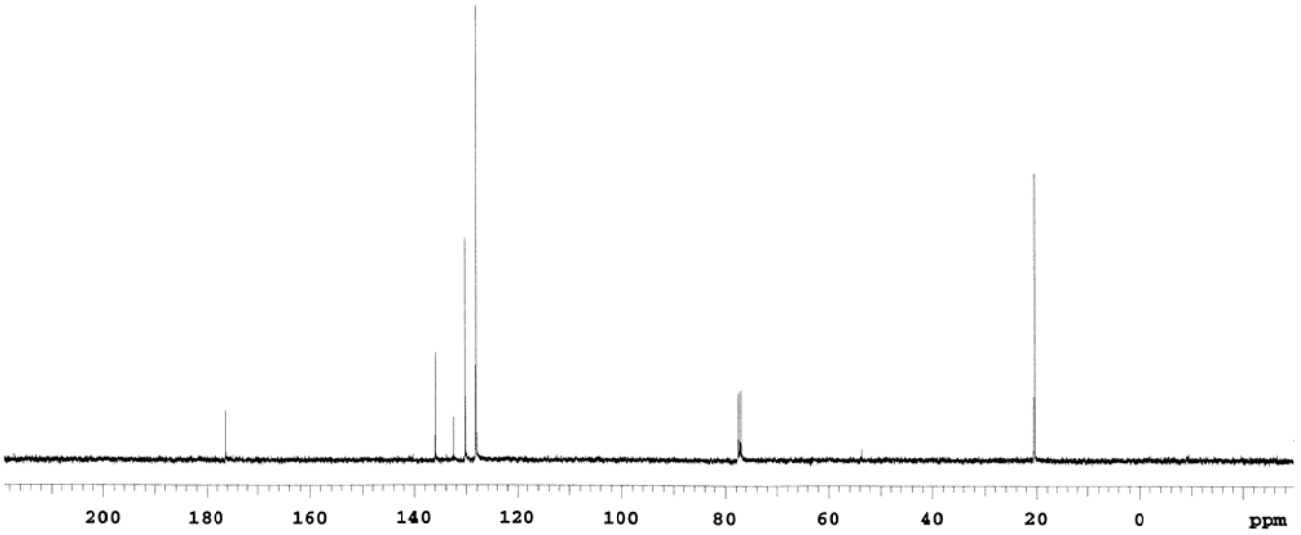
Pulse Sequence: s2pul

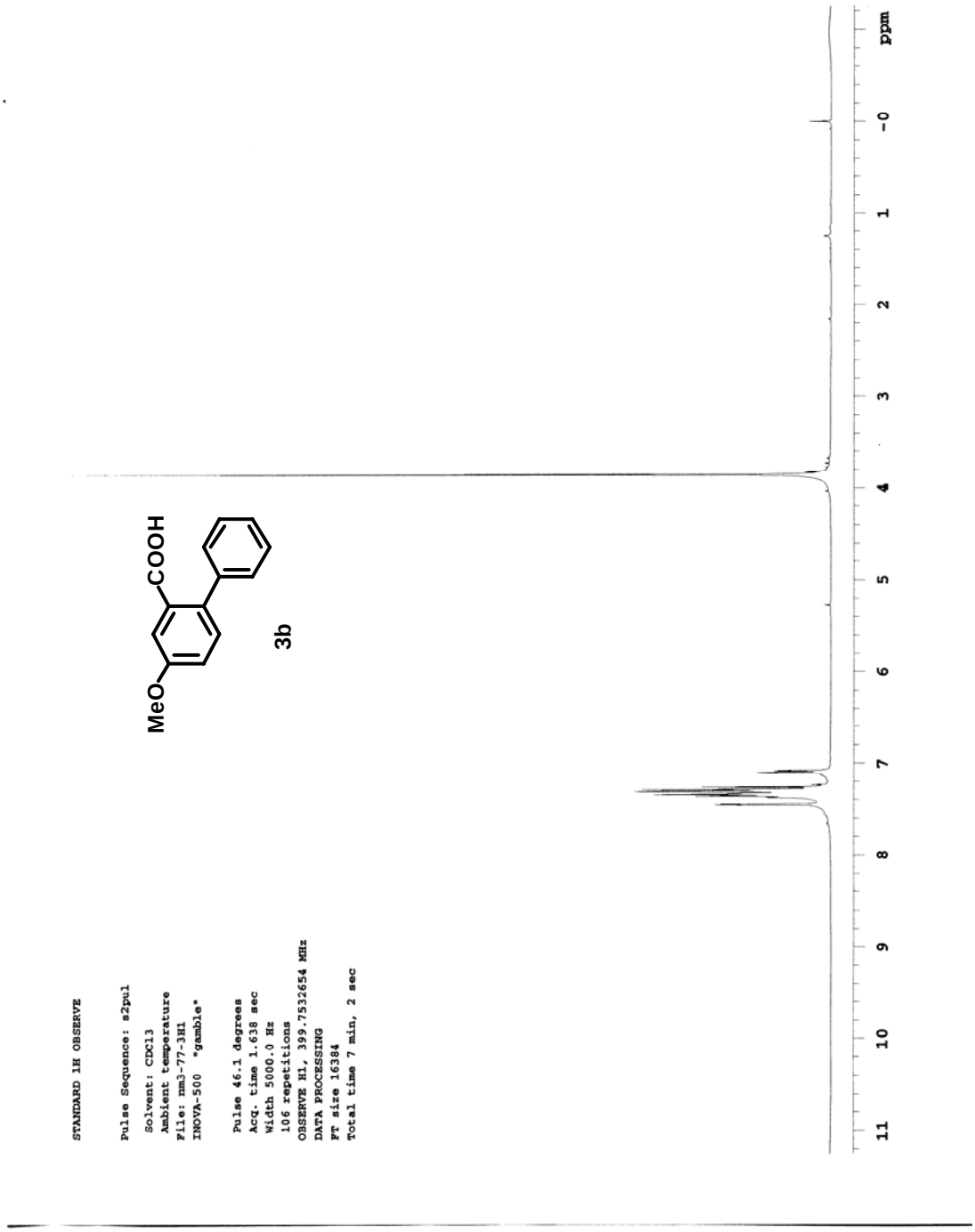
Solvent: CDCl3
Ambient temperature
File: nm3-77-1C13
INOVA-500 "gamble"

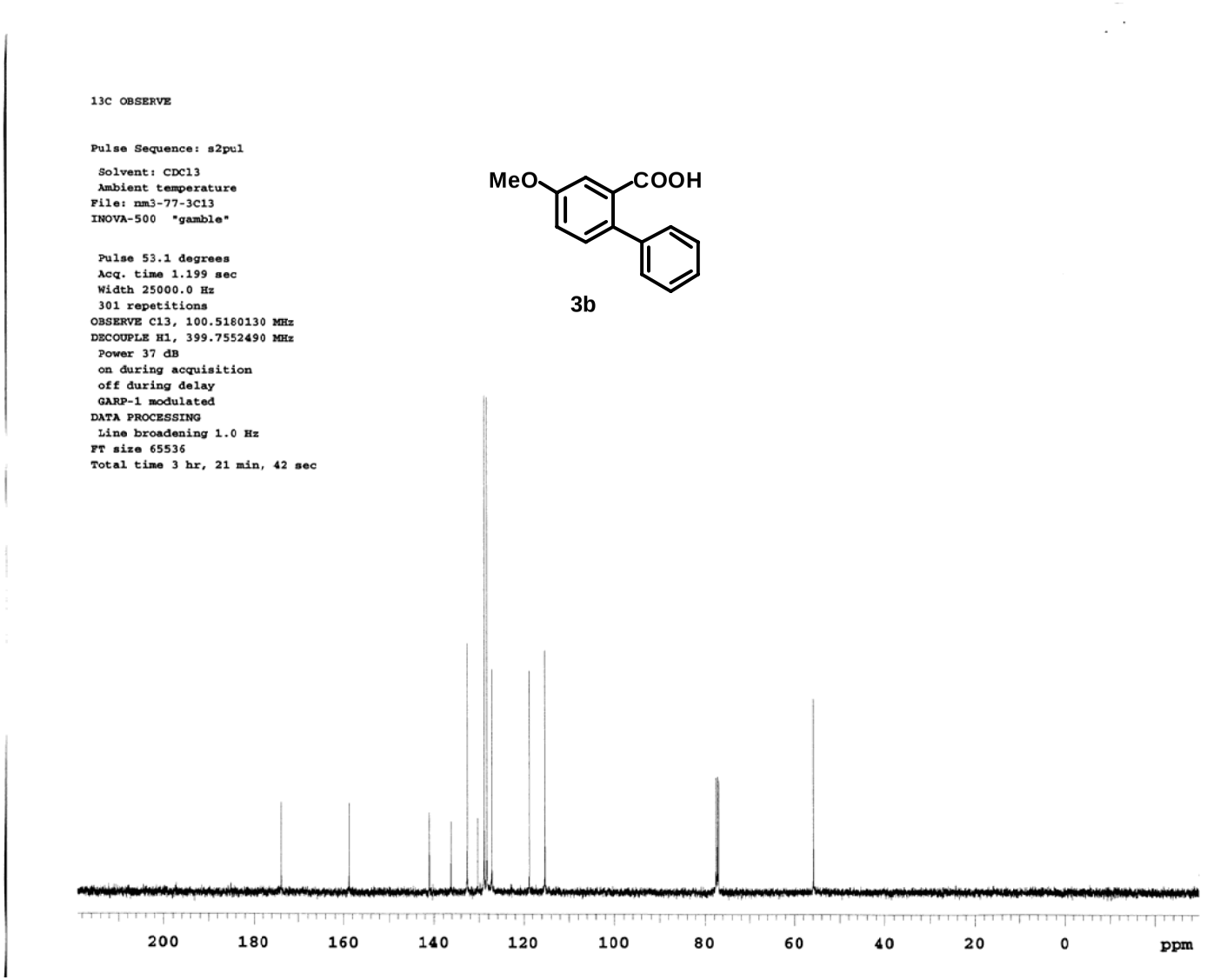
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
303 repetitions
OBSERVE C13, 100.5180130 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3 hr, 21 min, 42 sec



1b




STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: nm3-77-3H1
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
106 repetitions
OBSERVE H1, 399.7532654 MHz
DATA PROCESSING
FT size 16384
Total time 7 min, 2 sec
COOH
MeO
3b
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

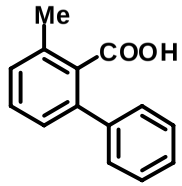

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: nm3-77-3C13
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
301 repetitions
OBSERVE C13, 100.5180130 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3 hr, 21 min, 42 sec
MeO
COOH
3b
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD 1H OBSERVE

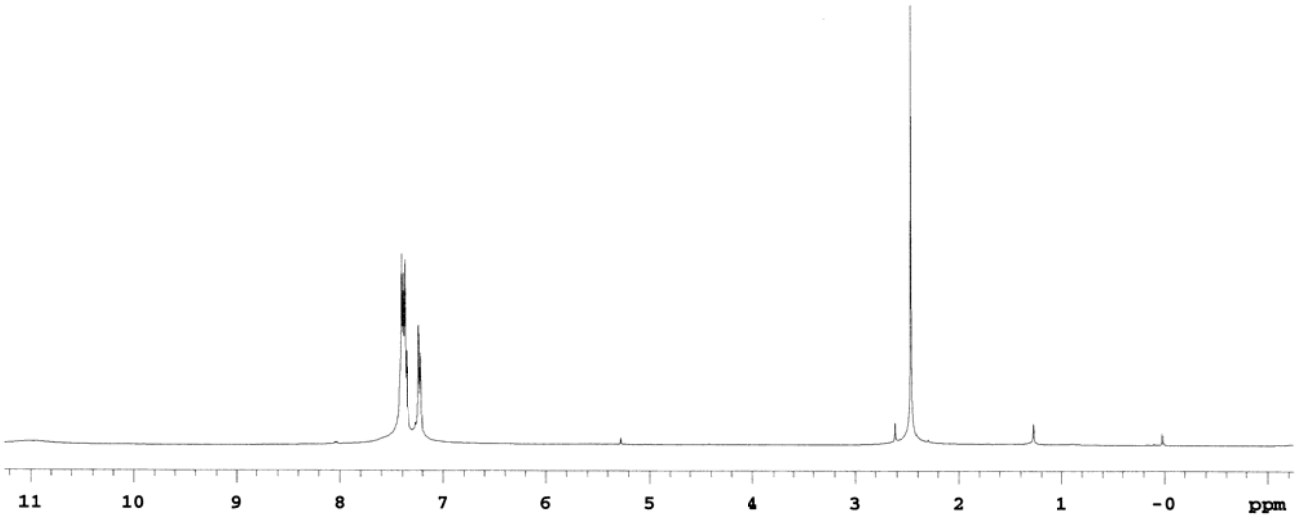
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: nm3-77-2H1
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
35 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 7 min, 2 sec



1c

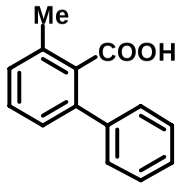


13C OBSERVE

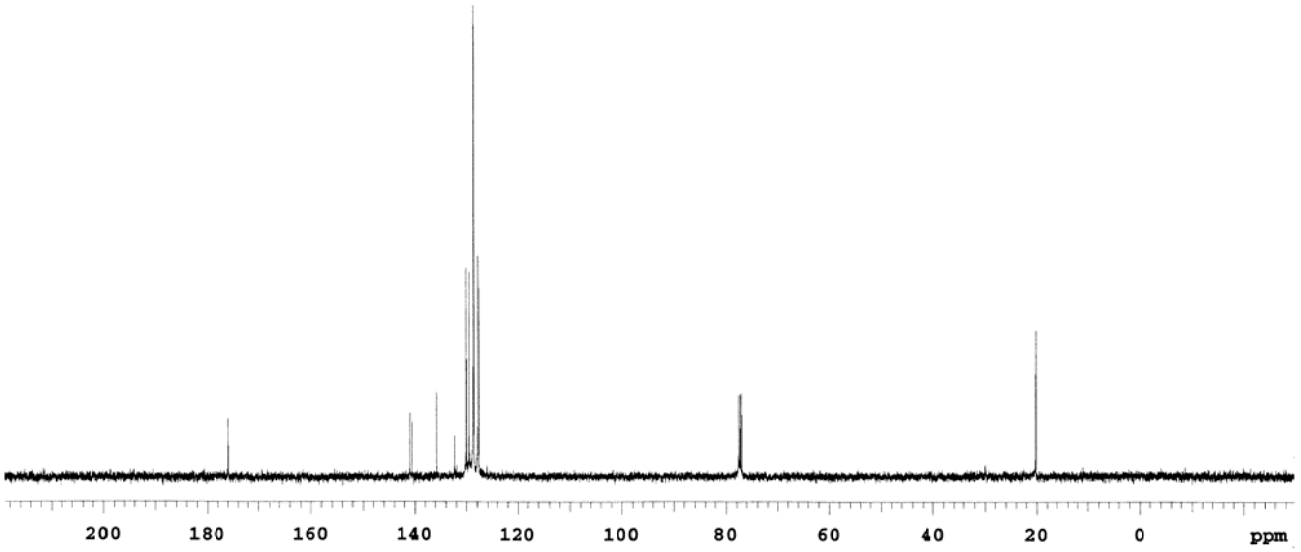
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: nm3-77-2C13
INOVA-500 "gamble"

Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
304 repetitions
OBSERVE C13, 100.5180130 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3 hr, 21 min, 42 sec



1c

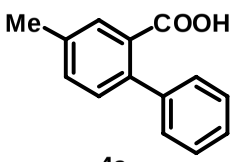


STANDARD 1H OBSERVE

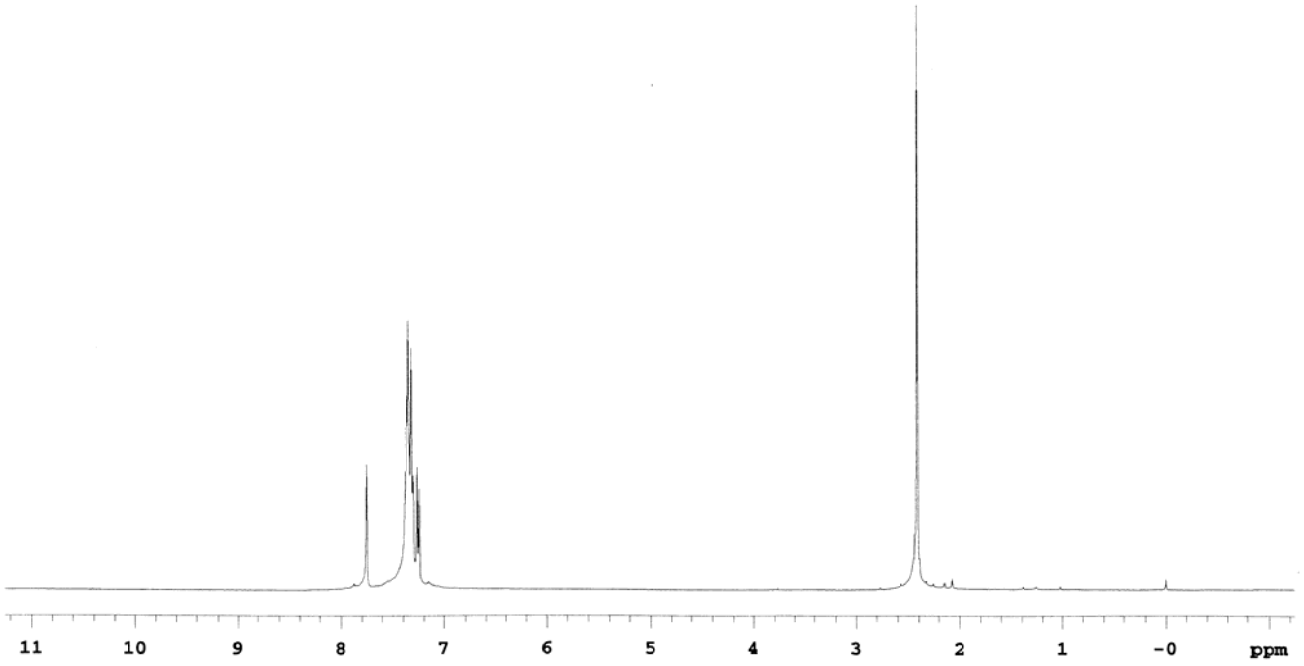
Pulse Sequence: s2pul

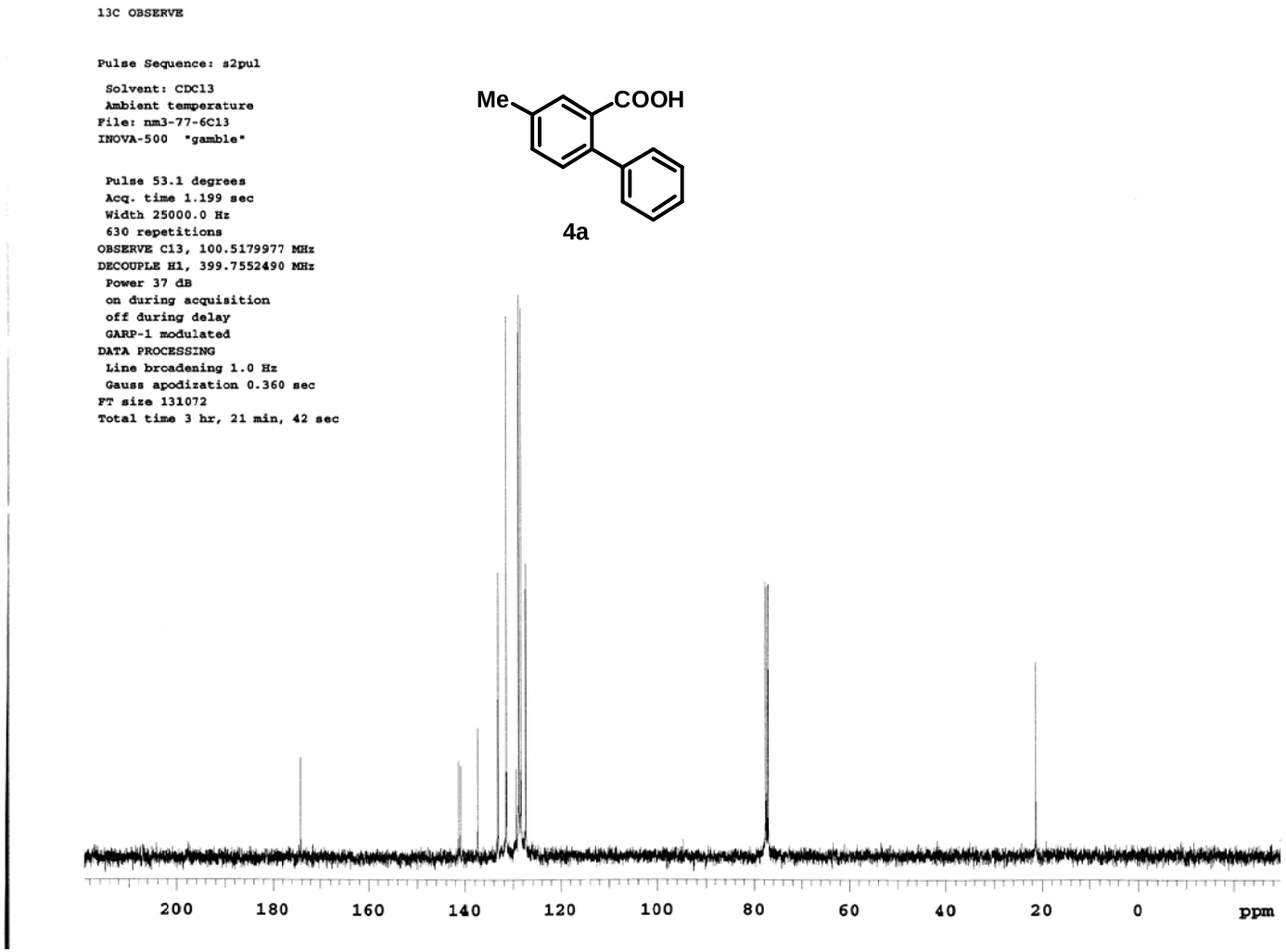
Solvent: CDCl3
Ambient temperature
File: nm3-77-6H1
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
31 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 7 min, 2 sec



4a



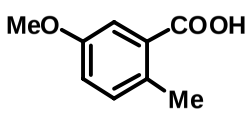

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: nm3-77-6C13
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
630 repetitions
OBSERVE C13, 100.5179977 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
Gauss apodization 0.360 sec
FT size 131072
Total time 3 hr, 21 min, 42 sec
Me
COOH
4a
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD 1H OBSERVE

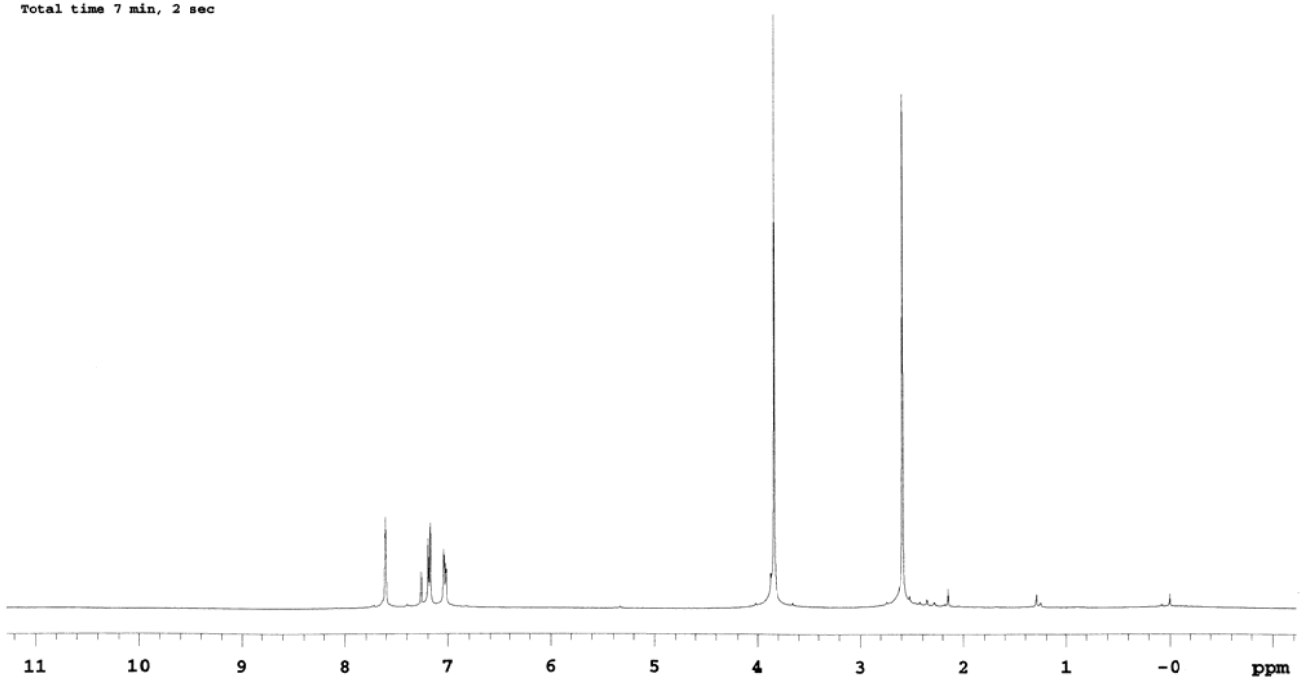
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: nm3-77-5
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
44 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 7 min, 2 sec



3a

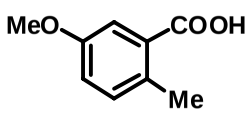


13C OBSERVE

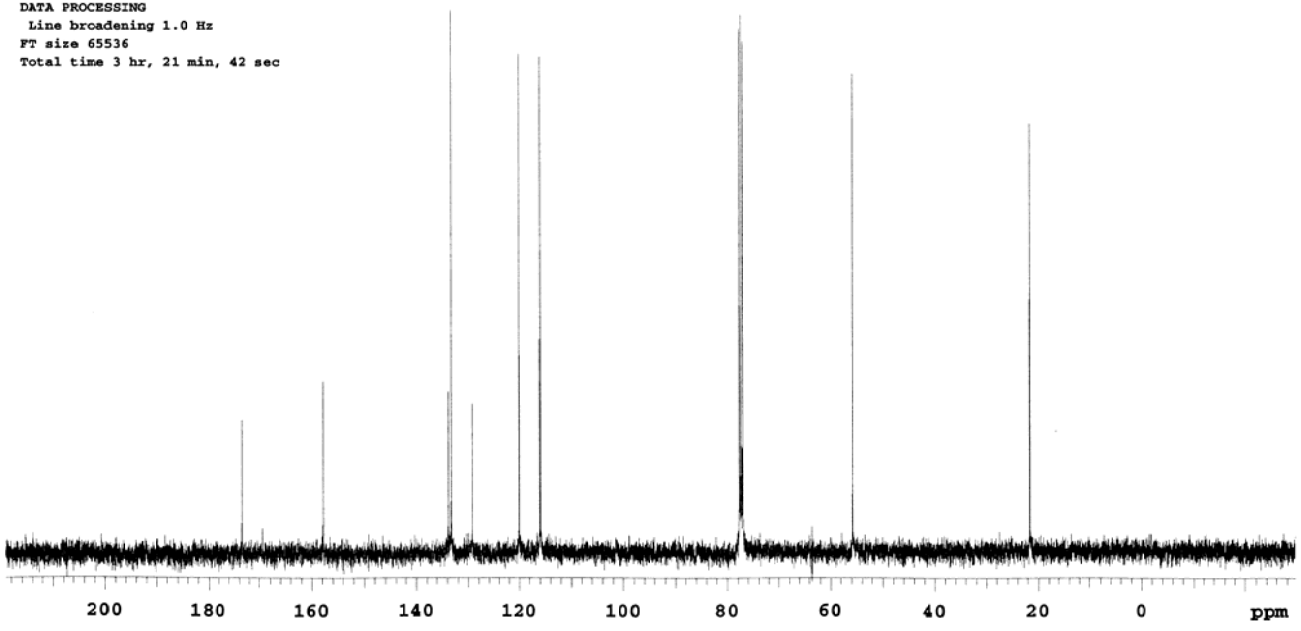
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: nm3-77-5C13
INOVA-500 "gamble"

Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1543 repetitions
OBSERVE C13, 100.5179977 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3 hr, 21 min, 42 sec



3a

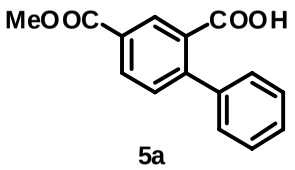


STANDARD 1H OBSERVE

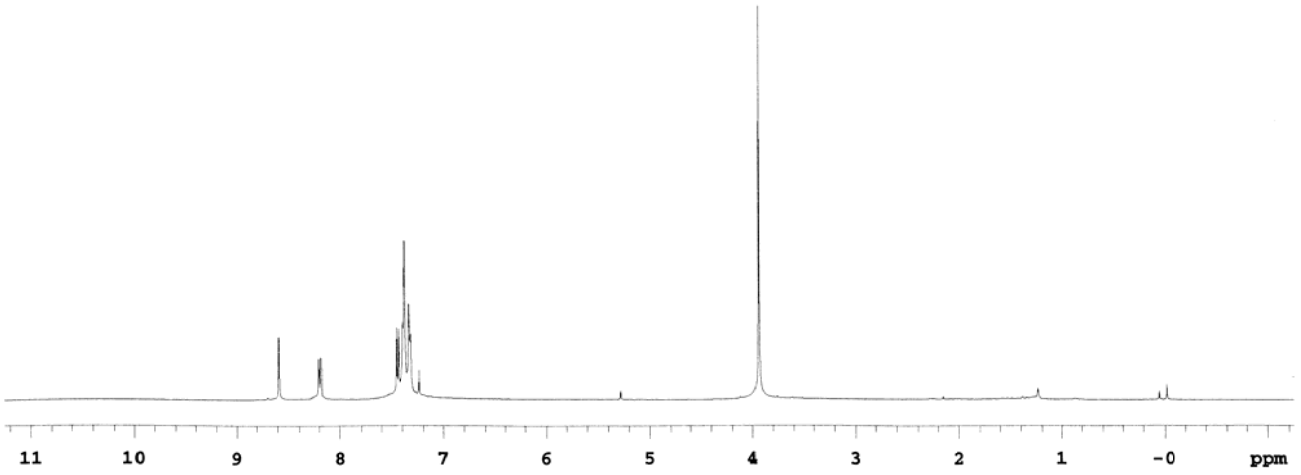
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: nm3-77-4H1
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
15 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 7 min, 2 sec



5a

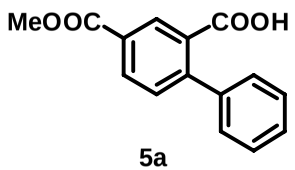


13C OBSERVE

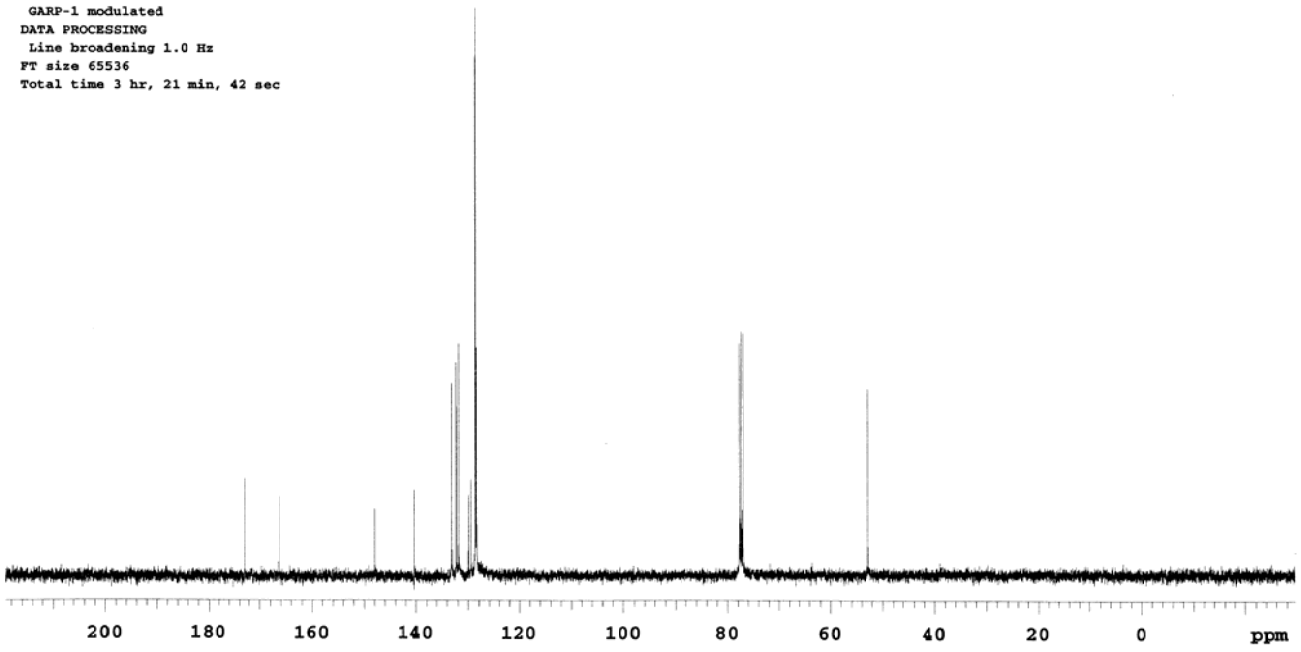
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: nm3-77-4C13
INOVA-500 "gamble"

Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1176 repetitions
OBSERVE C13, 100.5179977 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3 hr, 21 min, 42 sec



5a

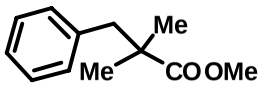


wdh-6-14-1

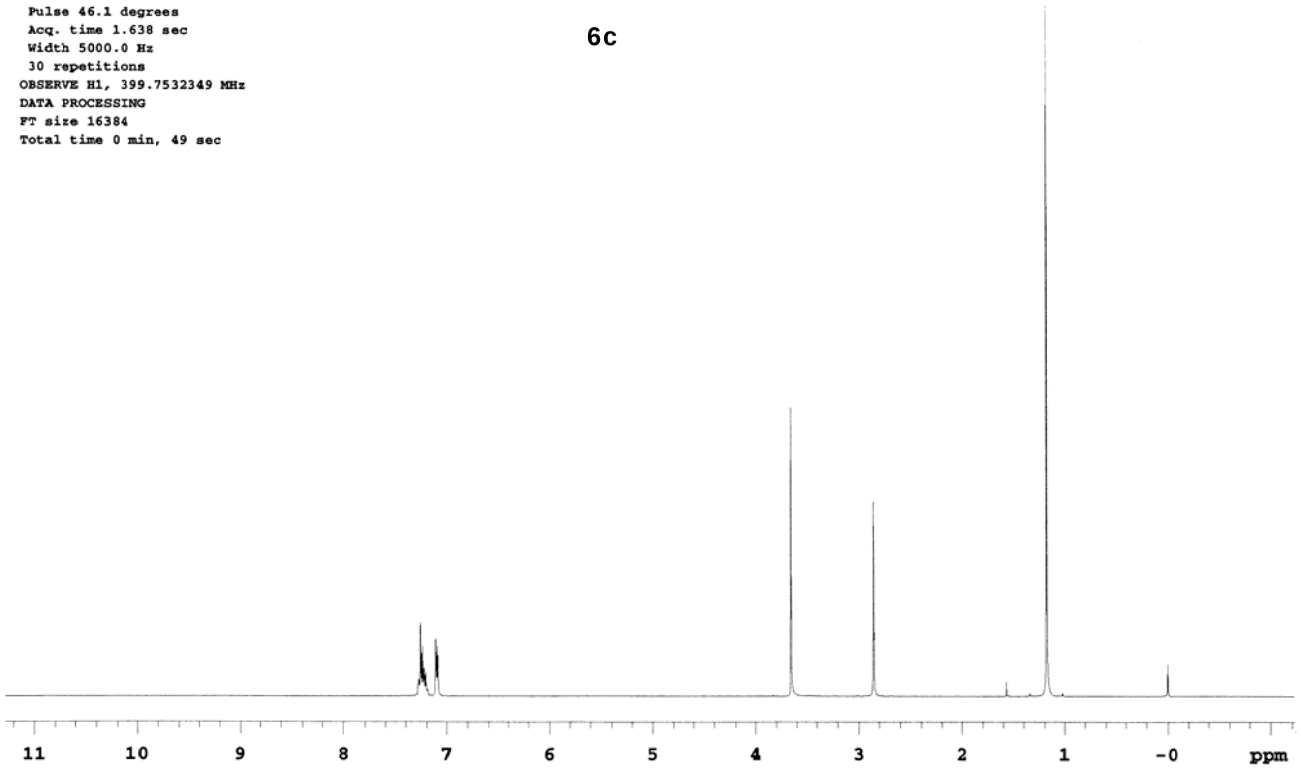
Pulse Sequence: s2pul

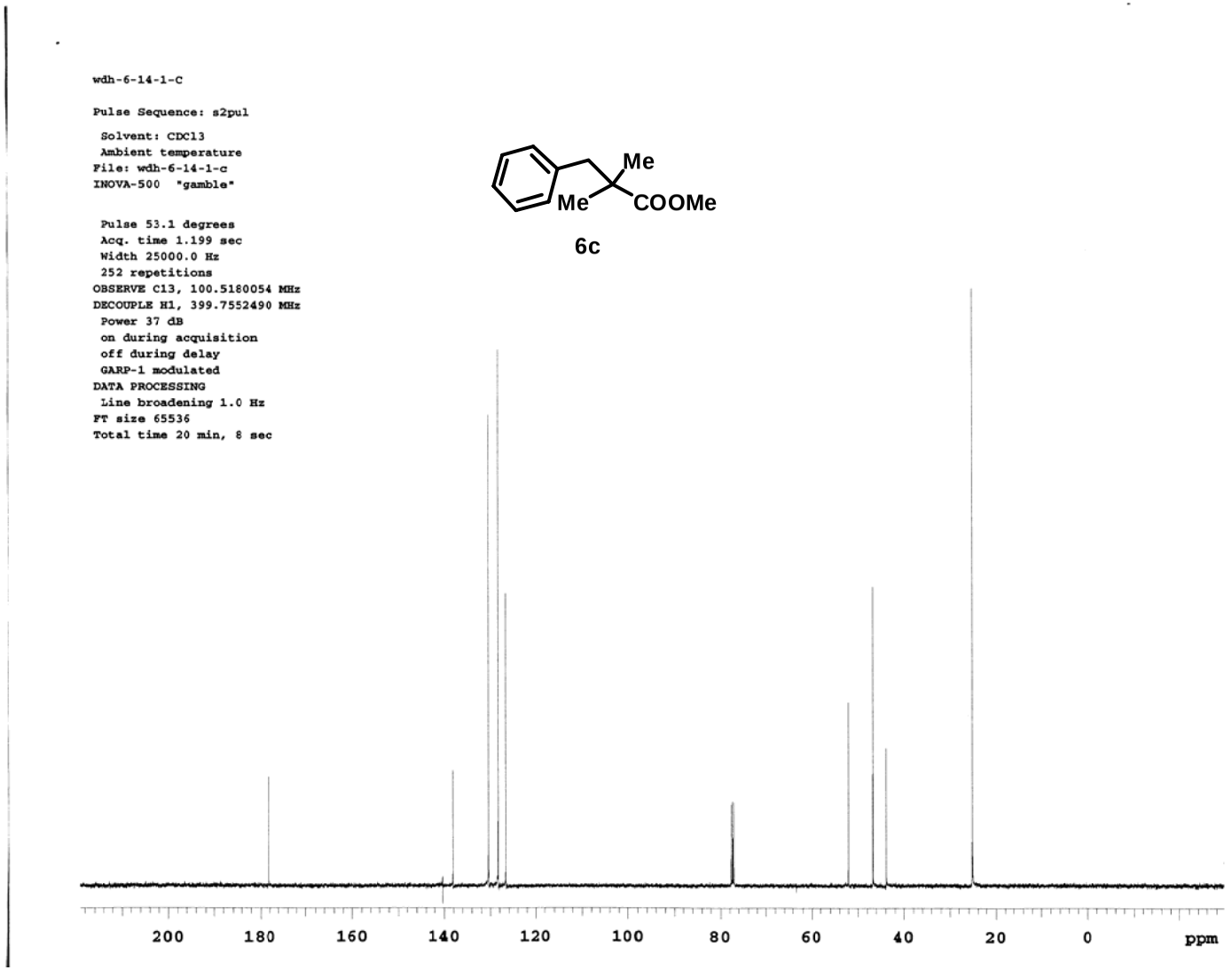
Solvent: CDCl3
Ambient temperature
File: wdh-6-14-1
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
30 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 49 sec



6c



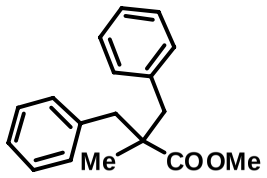

wdh-6-14-1-C
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: wdh-6-14-1-c
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
252 repetitions
OBSERVE C13, 100.5180054 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 20 min, 8 sec
Me
Me
COOMe
6c
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD 1H OBSERVE

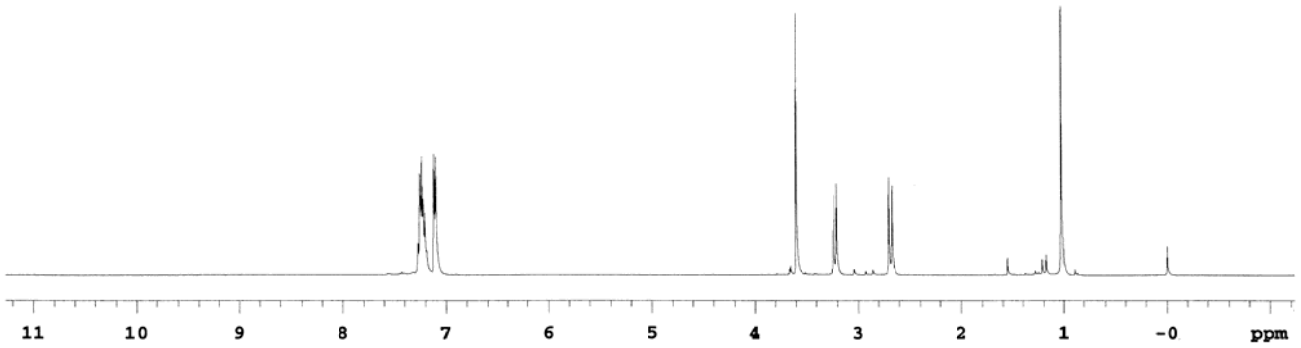
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: wdh-6-14-2
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
20 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 32 sec



6d

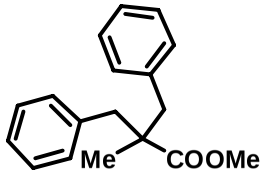


wdh-6-14-2-C

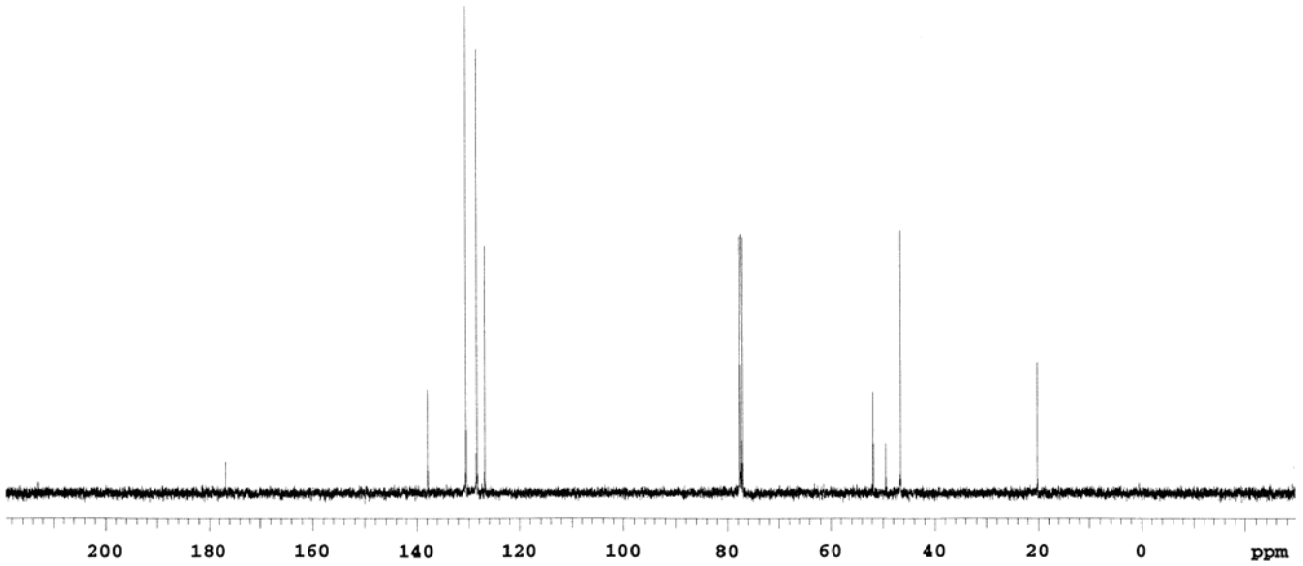
Pulse Sequence: s2pul

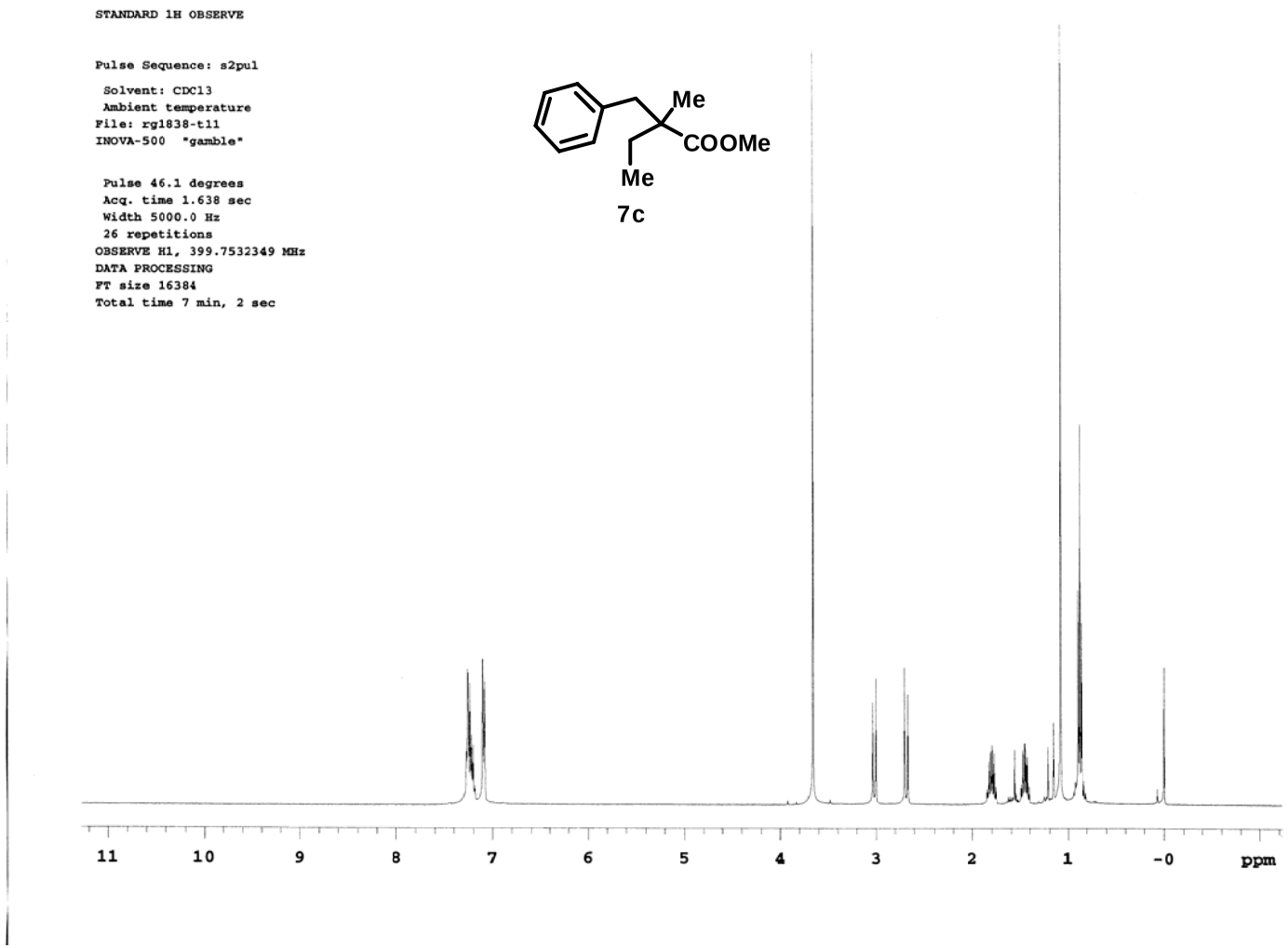
Solvent: CDCl3
Ambient temperature
File: wdh-6-14-2-C
INOVA-500 "gamble"

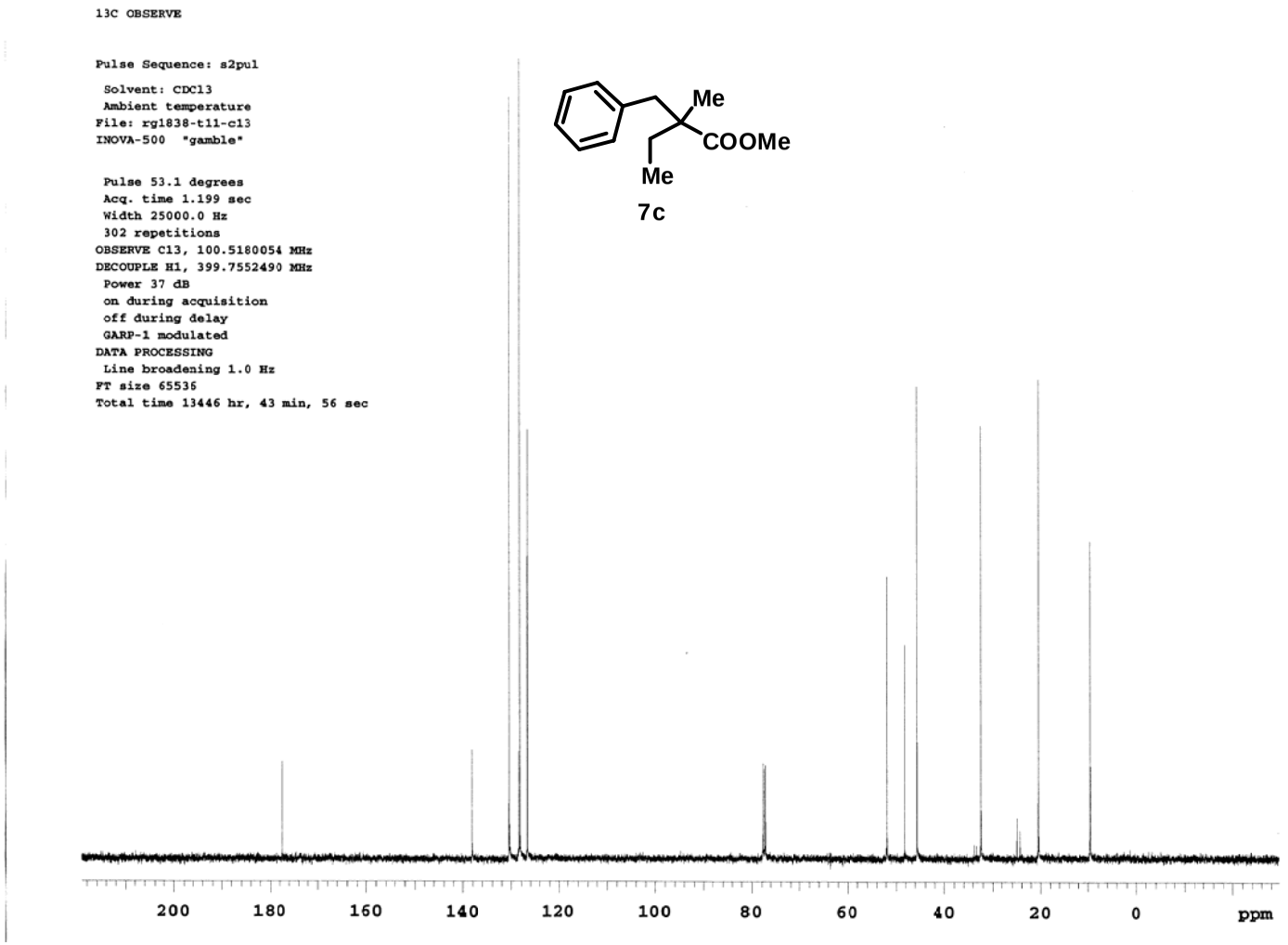
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
642 repetitions
OBSERVE C13, 100.5179977 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3 hr, 21 min, 40 sec



6d




STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: rg1838-t11
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
26 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 7 min, 2 sec
Me
COOMe
Me
7c
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

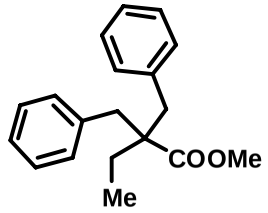

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: rg1838-t11-c13
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
302 repetitions
OBSERVE C13, 100.5180054 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 13446 hr, 43 min, 56 sec
Me
COOMe
Me
7c
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD 1H OBSERVE

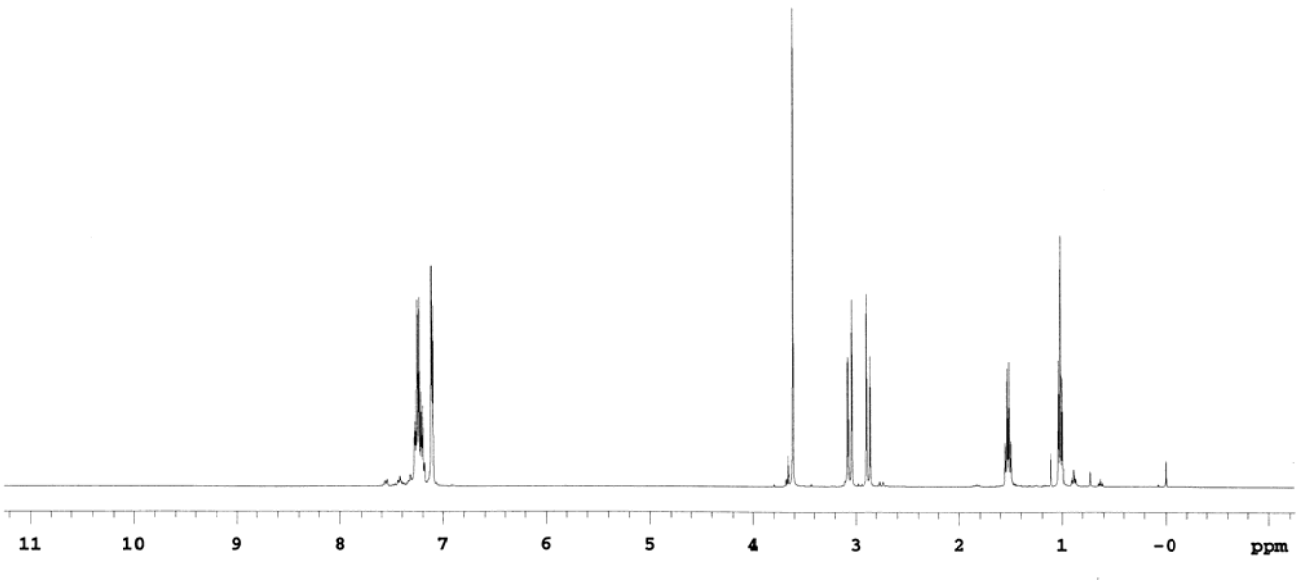
Pulse Sequence: s2pul

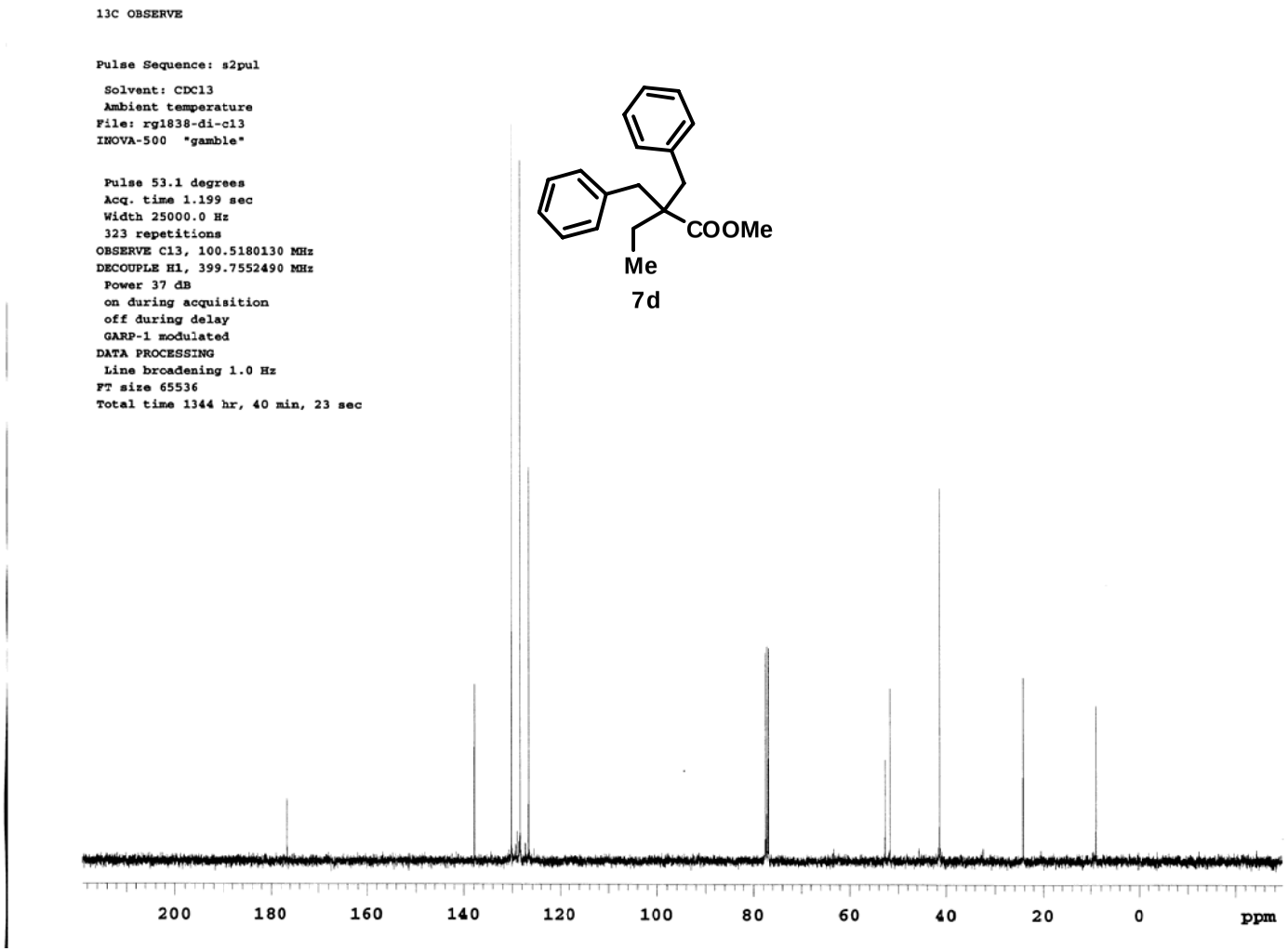
Solvent: CDCl3
Ambient temperature
File: rg1838-di-1H
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
25 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 7 min, 2 sec



7d



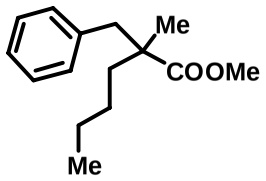

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: rg1838-di-c13
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
323 repetitions
OBSERVE C13, 100.5180130 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1344 hr, 40 min, 23 sec
COOMe
Me
7d
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD 1H OBSERVE

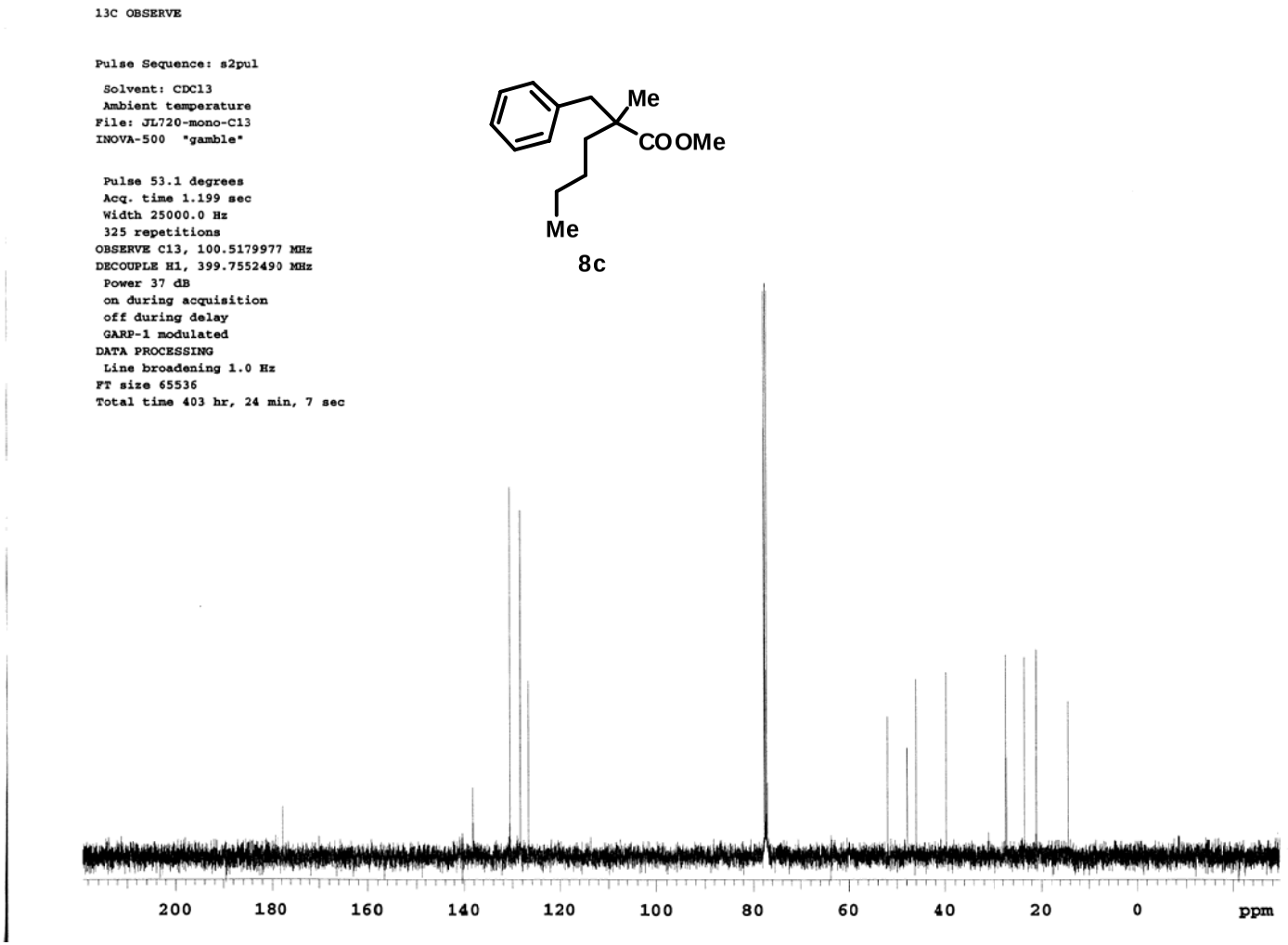
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: JL720-mono
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
34 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 549 hr, 44 min, 36 sec



8c

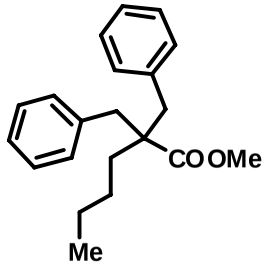

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: JL720-mono-C13
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
325 repetitions
OBSERVE C13, 100.5179977 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 403 hr, 24 min, 7 sec
Me
COOMe
Me
8c
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD 1H OBSERVE

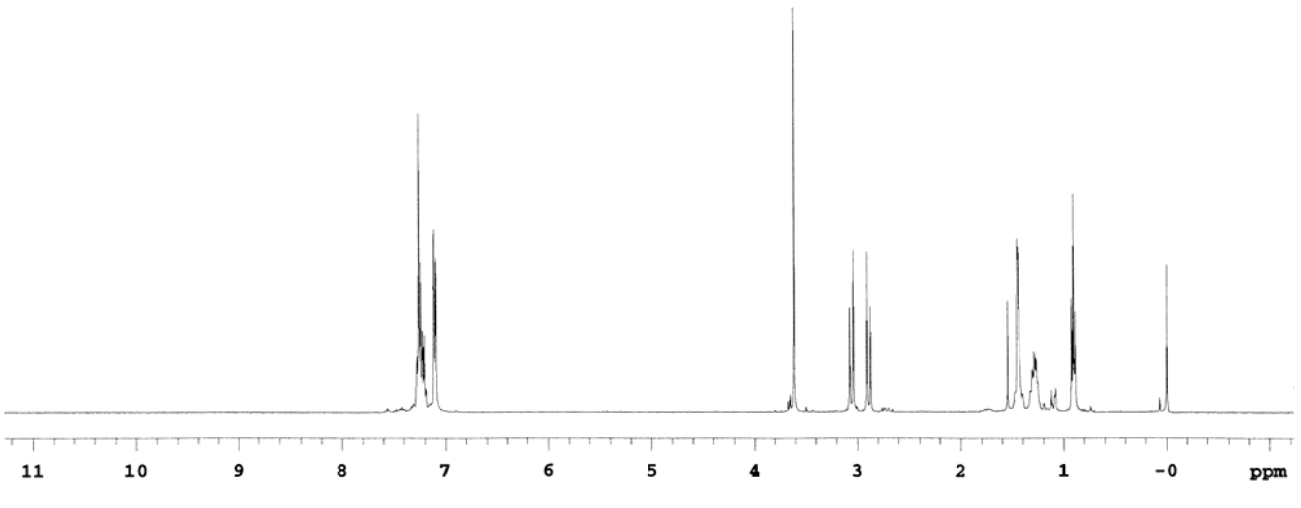
Pulse Sequence: s2pul

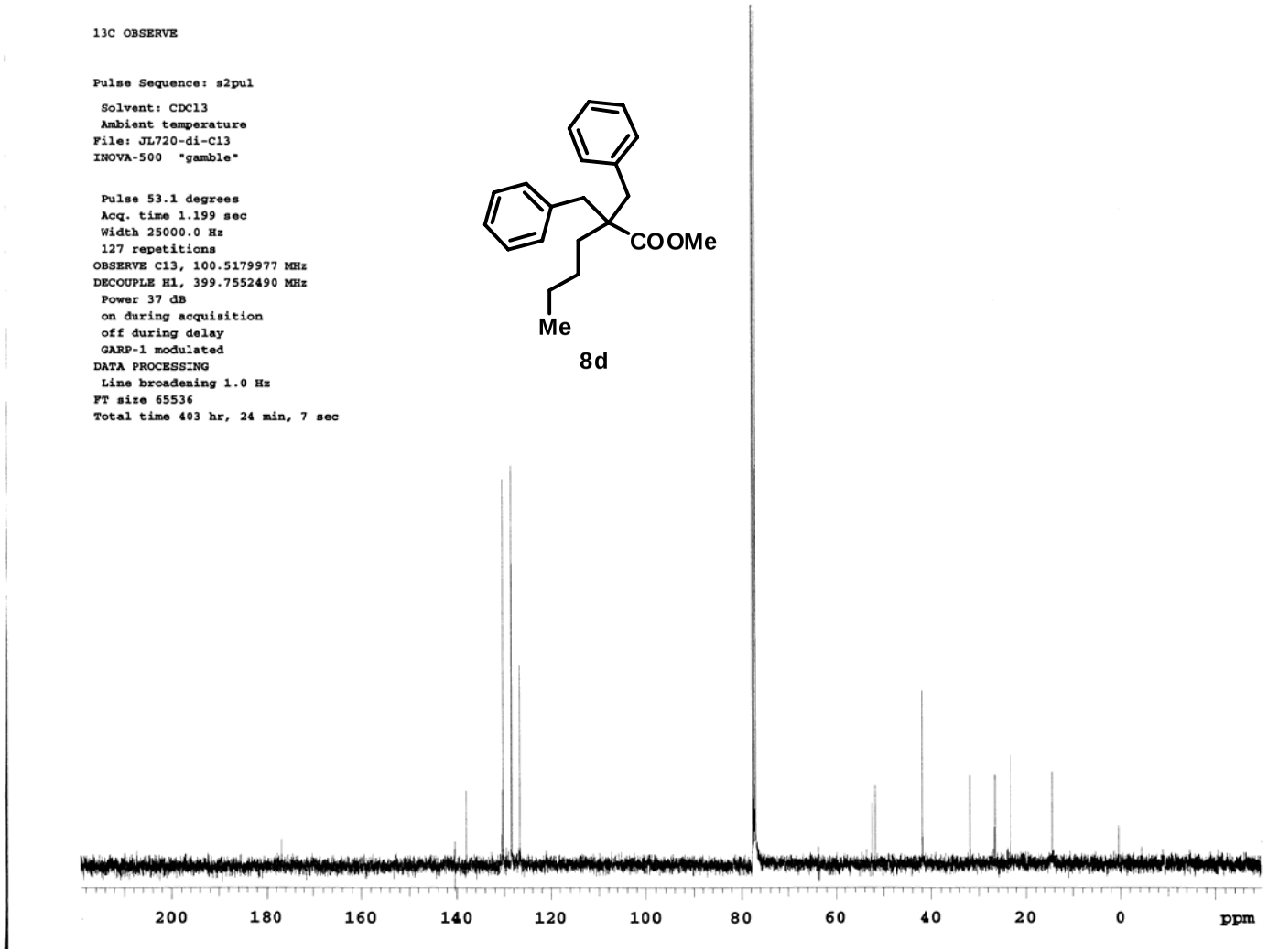
Solvent: CDCl3
Ambient temperature
File: JL720-di
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
32 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 54 hr, 58 min, 27 sec



8d



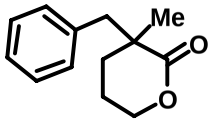

13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: JL720-di-C13
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
127 repetitions
OBSERVE C13, 100.5179977 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 403 hr, 24 min, 7 sec
COOMe
Me
8d
200
180
160
140
120
100
80
60
40
20
0
ppm

s-355-T-rack4-11

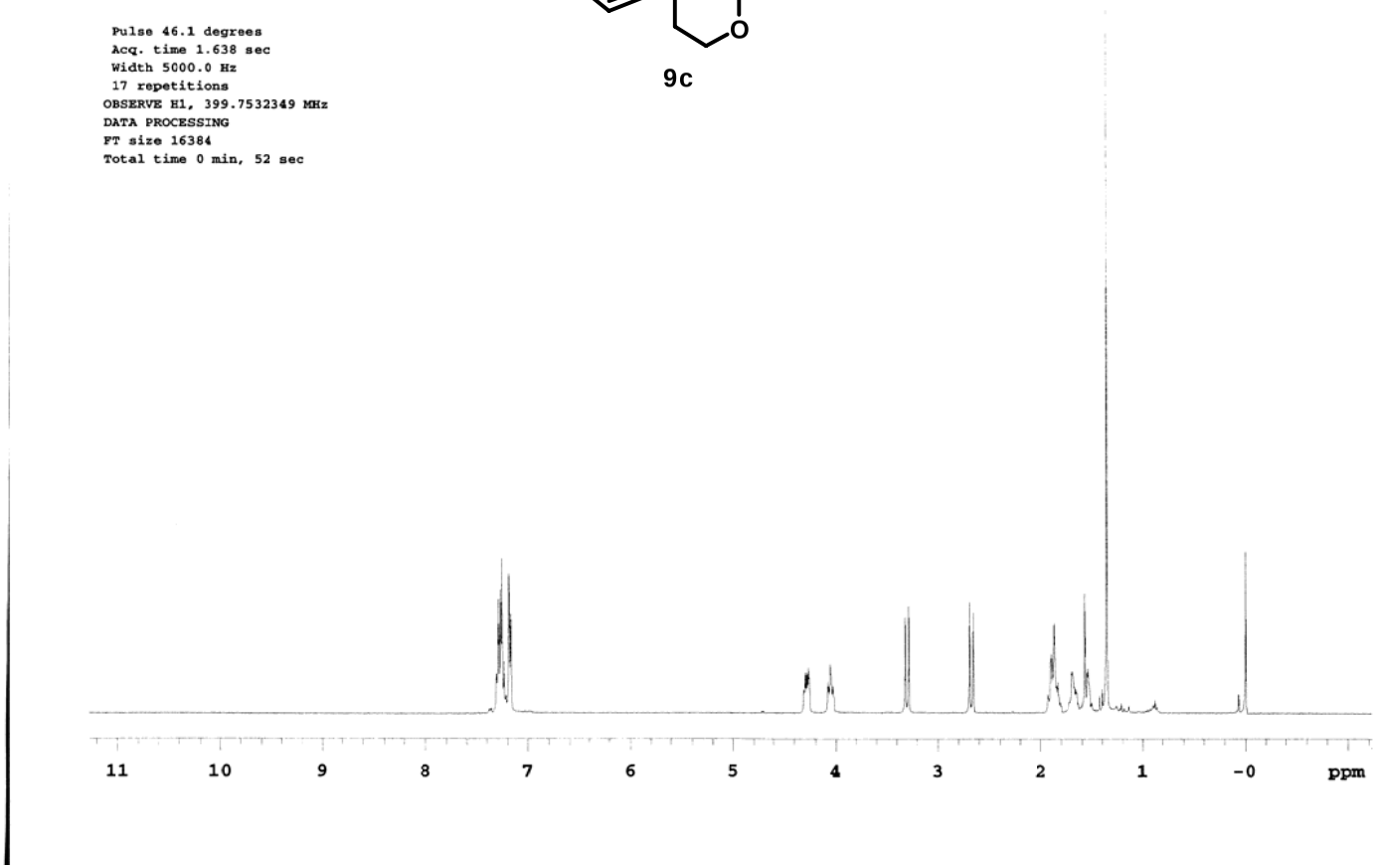
Pulse Sequence: s2pul

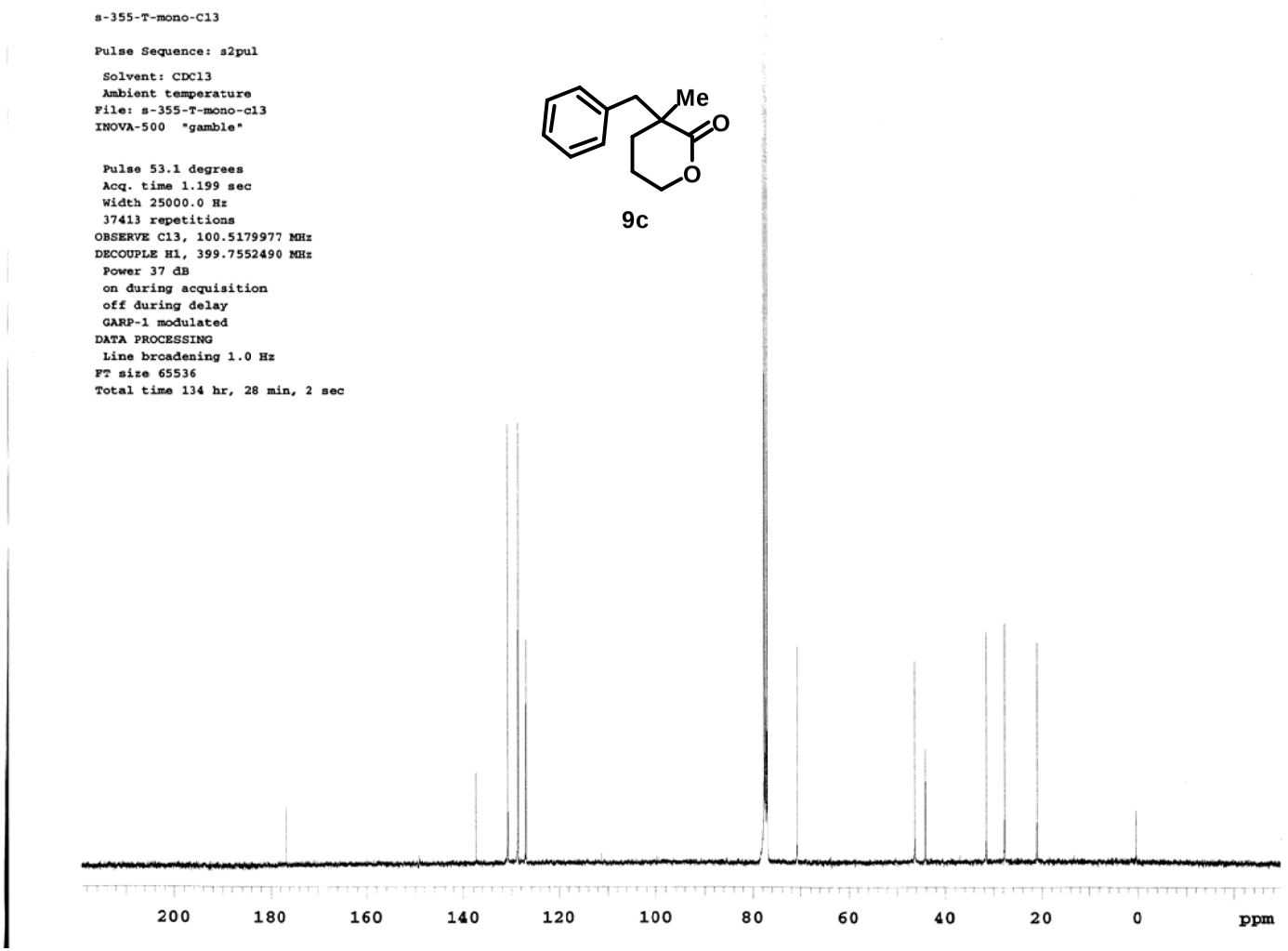
Solvent: CDCl3
Ambient temperature
File: s-355-T-rack4-11
INOVA-500 "gamble"

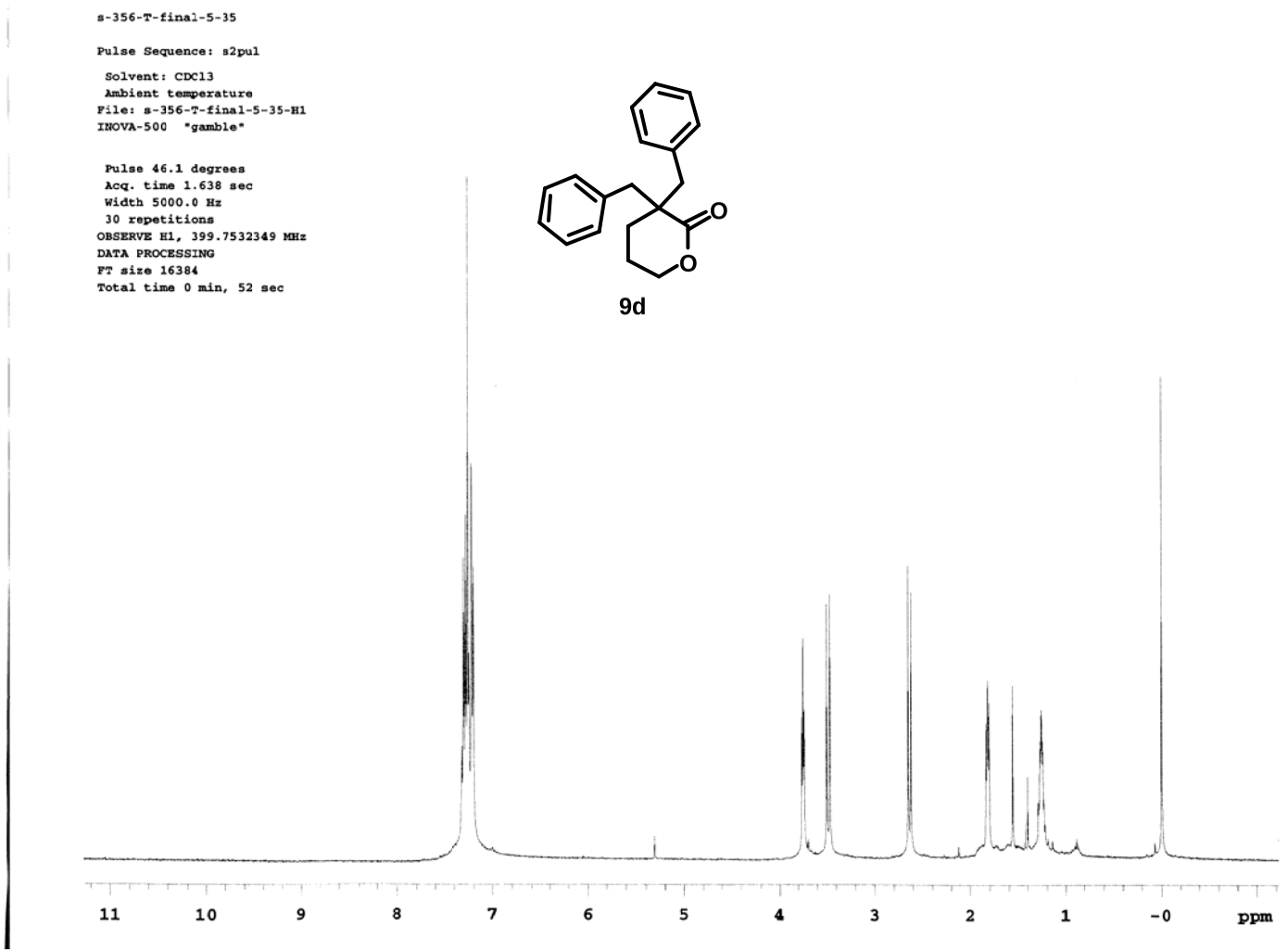
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
17 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 52 sec



9c




s-355-T-mono-C13
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: s-355-T-mono-c13
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
37413 repetitions
OBSERVE C13, 100.5179977 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 134 hr, 28 min, 2 sec
Me
O
O
9c
200
180
160
140
120
100
80
60
40
20
0
ppm

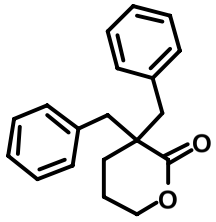

s-356-T-final-5-35
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: s-356-T-final-5-35-H1
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
30 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 52 sec
O
O
9d
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

s-365-C13

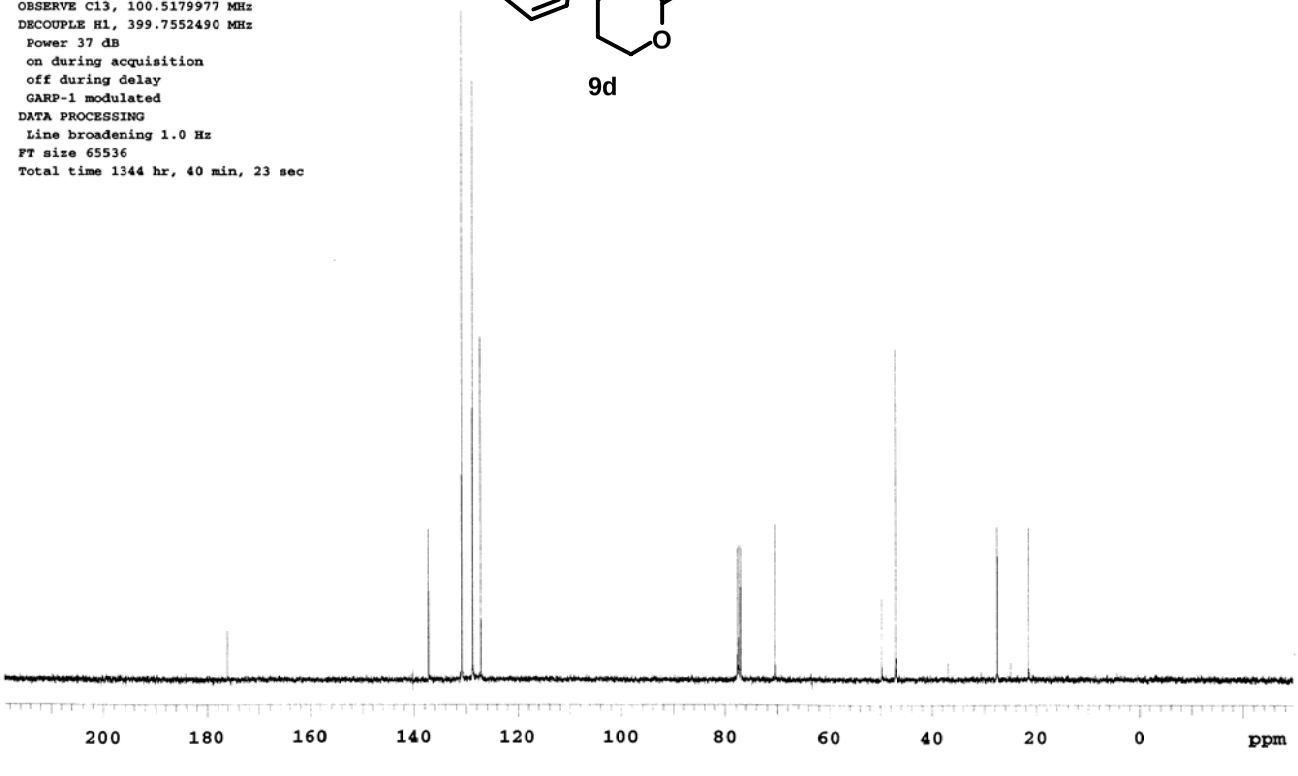
Pulse Sequence: s2pul

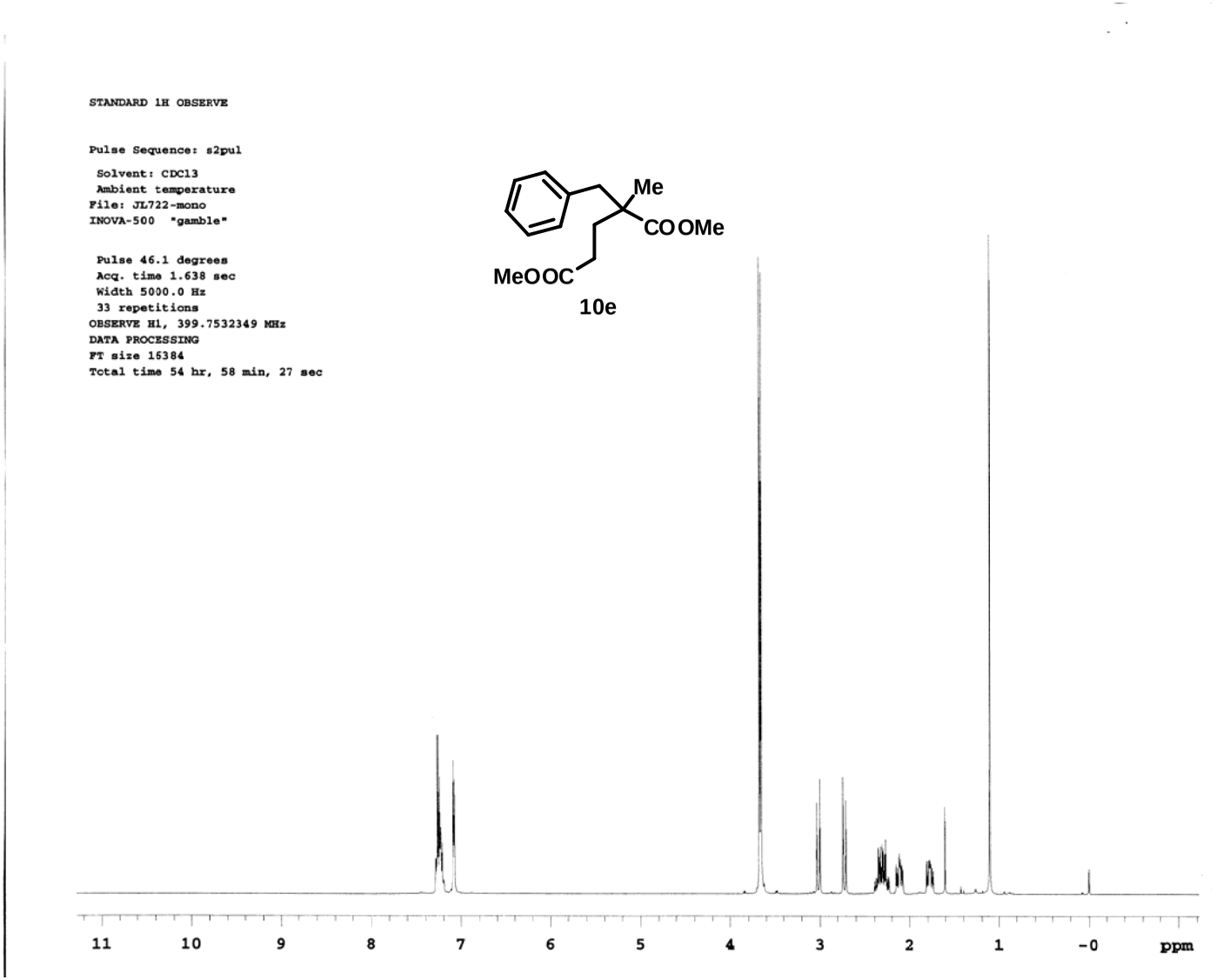
Solvent: CDCl3
Ambient temperature
File: s-356-di-C13
INOVA-500 "gamble"

Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
576 repetitions
OBSERVE C13, 100.5179977 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 1344 hr, 40 min, 23 sec



9d



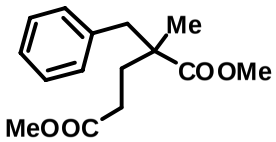

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: JL722-mono
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
33 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 54 hr, 58 min, 27 sec
Me
COOMe
MeOOC
10e
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

13C OBSERVE

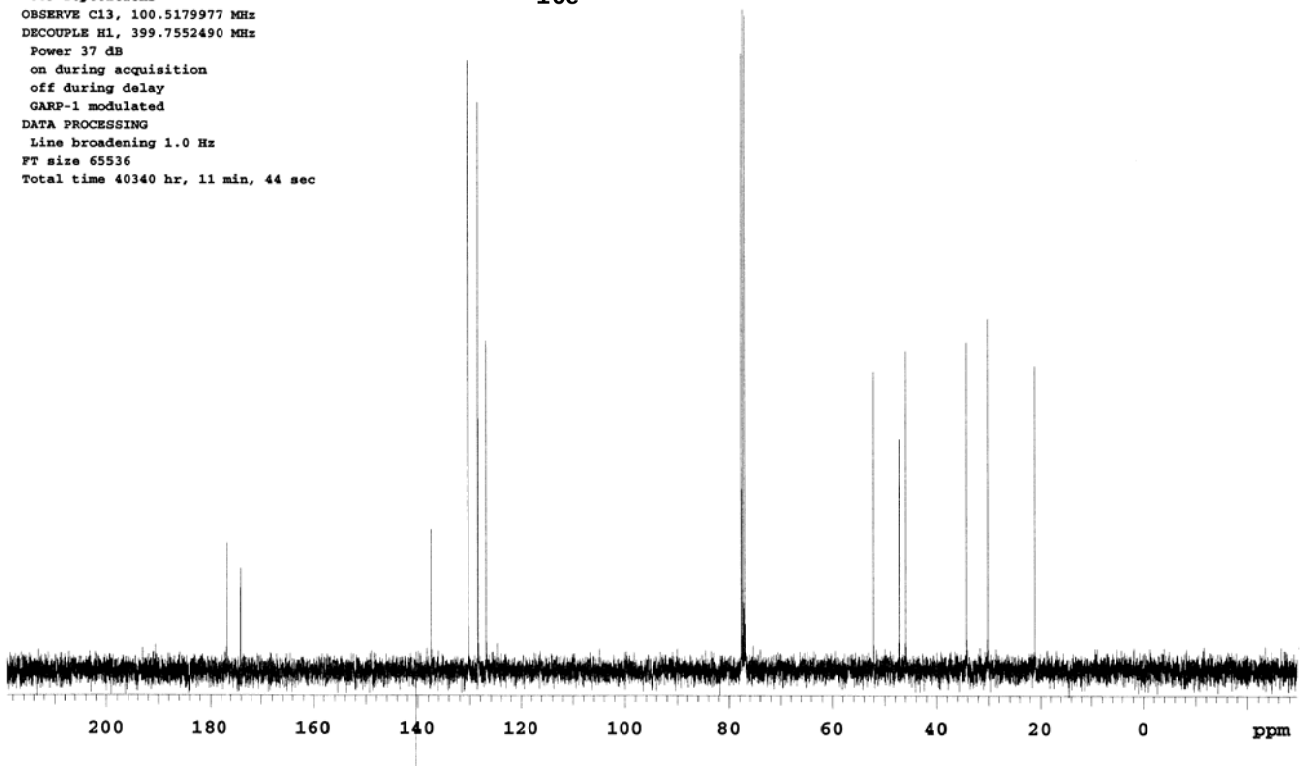
Pulse Sequence: s2pul

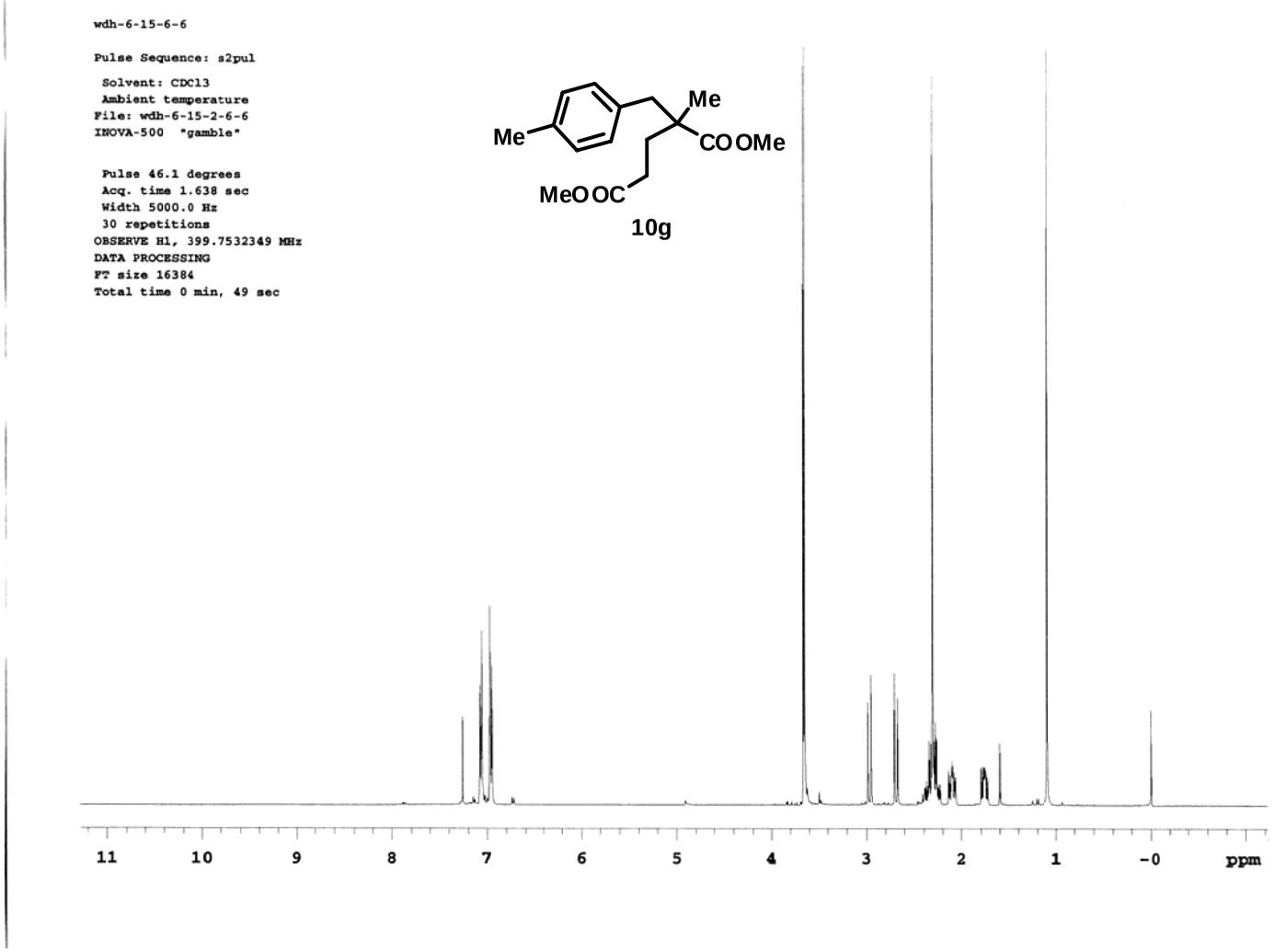
Solvent: CDCl3
Ambient temperature
File: JL722-mono-C13
INOVA-500 "gamble"

Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
369 repetitions
OBSERVE C13, 100.5179977 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 40340 hr, 11 min, 44 sec



10e



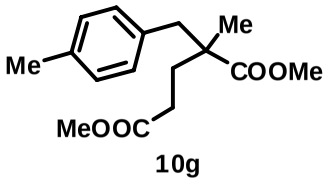

wdh-6-15-6-6
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: wdh-6-15-2-6-6
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
30 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 49 sec
Me
Me
COOMe
MeOOC
10g
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

wdh-6-15-2-6-6

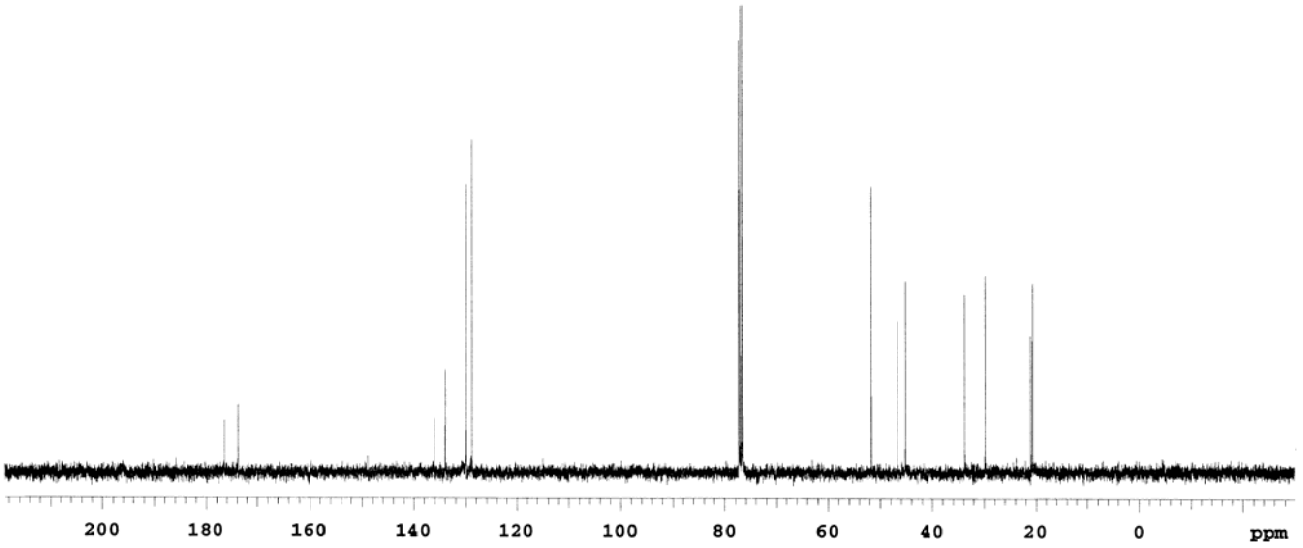
Pulse Sequence: s2pul

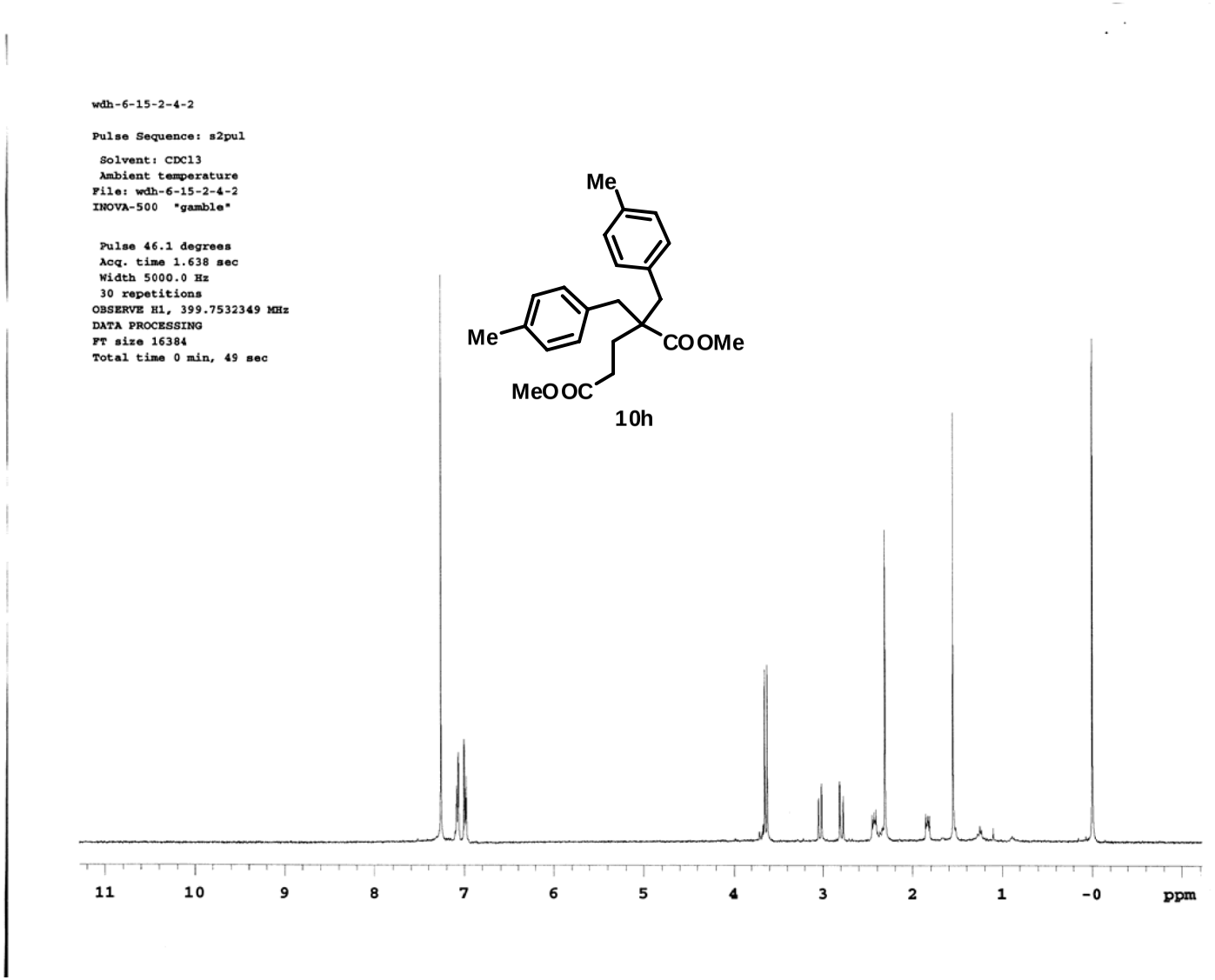
Solvent: CDCl3
Ambient temperature
File: wdh-6-15-2-6-6-c
INOVA-500 "gamble"

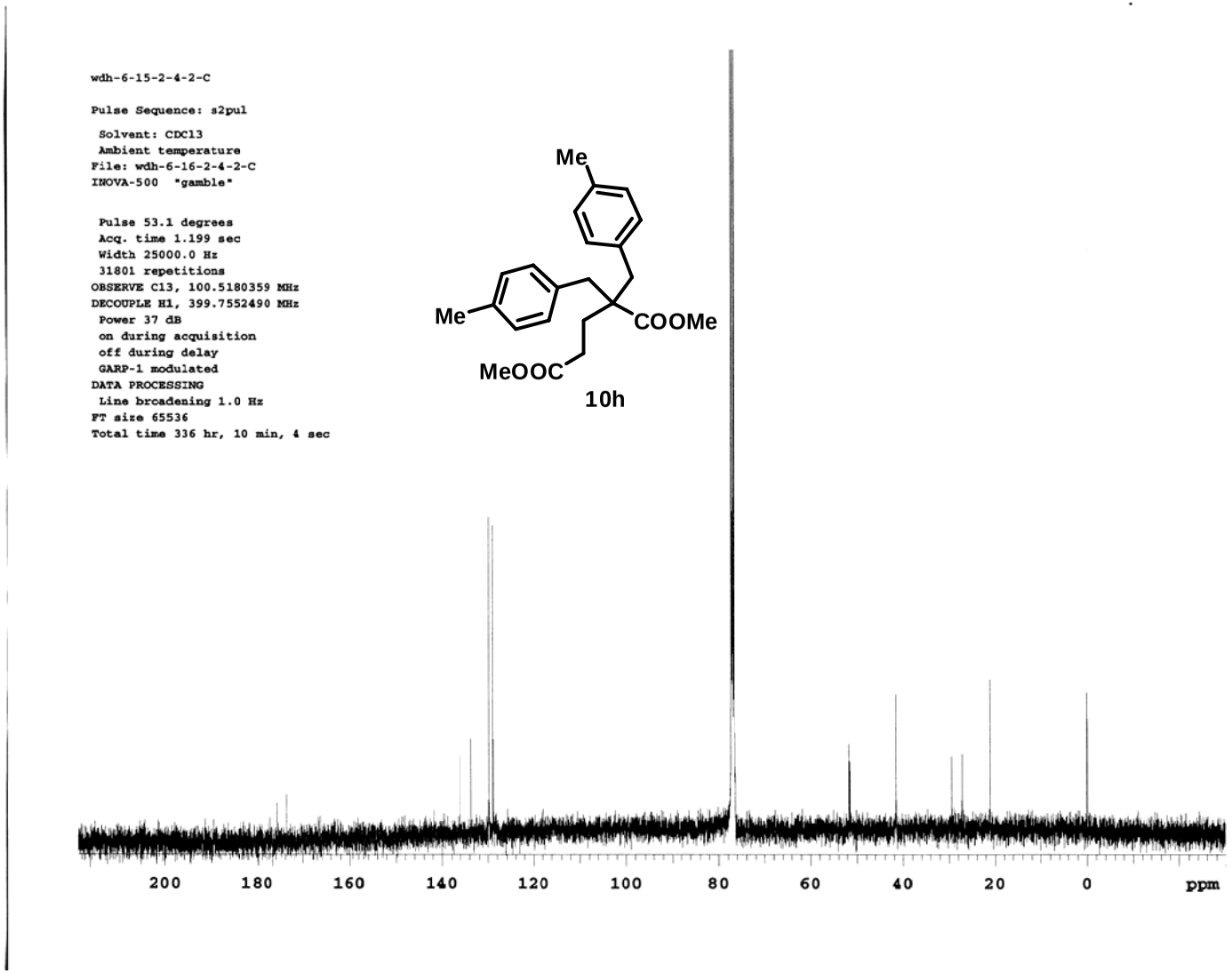
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
630 repetitions
OBSERVE C13, 100.5180359 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3 hr, 21 min, 40 sec



10g




wdh-6-15-2-4-2
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: wdh-6-15-2-4-2
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
30 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 49 sec
Me
Me
COOMe
MeOOC
10h
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

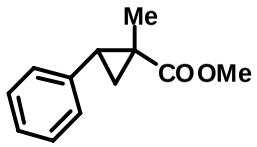

wdh-6-15-2-4-2-C
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: wdh-6-16-2-4-2-C
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
31801 repetitions
OBSERVE C13, 100.5180359 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 336 hr, 10 min, 4 sec
Me
Me
COOMe
MeOOC
10h
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD 1H OBSERVE

Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: JL721-H1
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
107 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 5 hr, 29 min, 50 sec



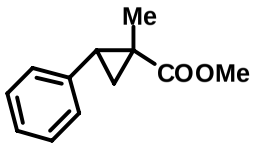
11b

13C OBSERVE

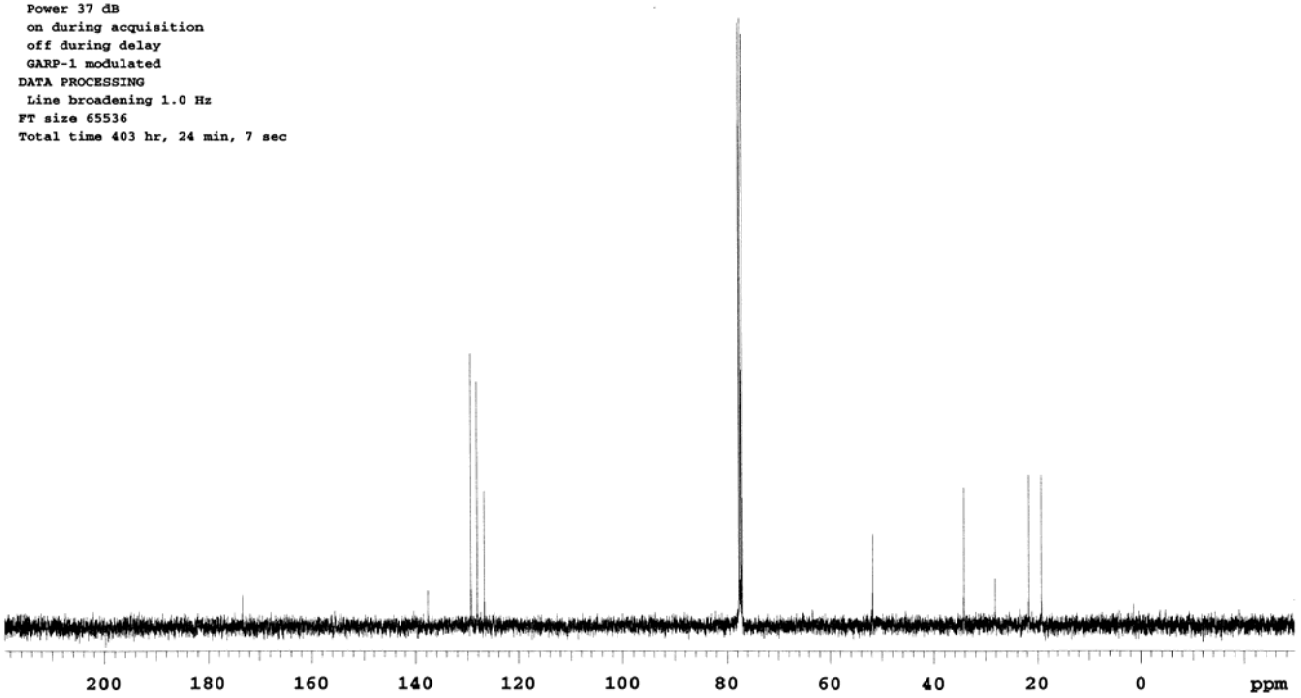
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: JL721-C13
INOVA-500 "gamble"

Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
657 repetitions
OBSERVE C13, 100.5179977 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 403 hr, 24 min, 7 sec



11b

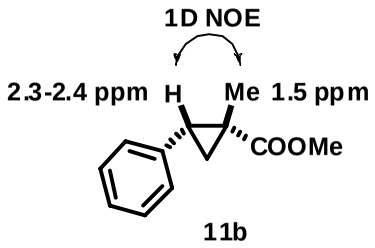


STANDARD 1H OBSERVE

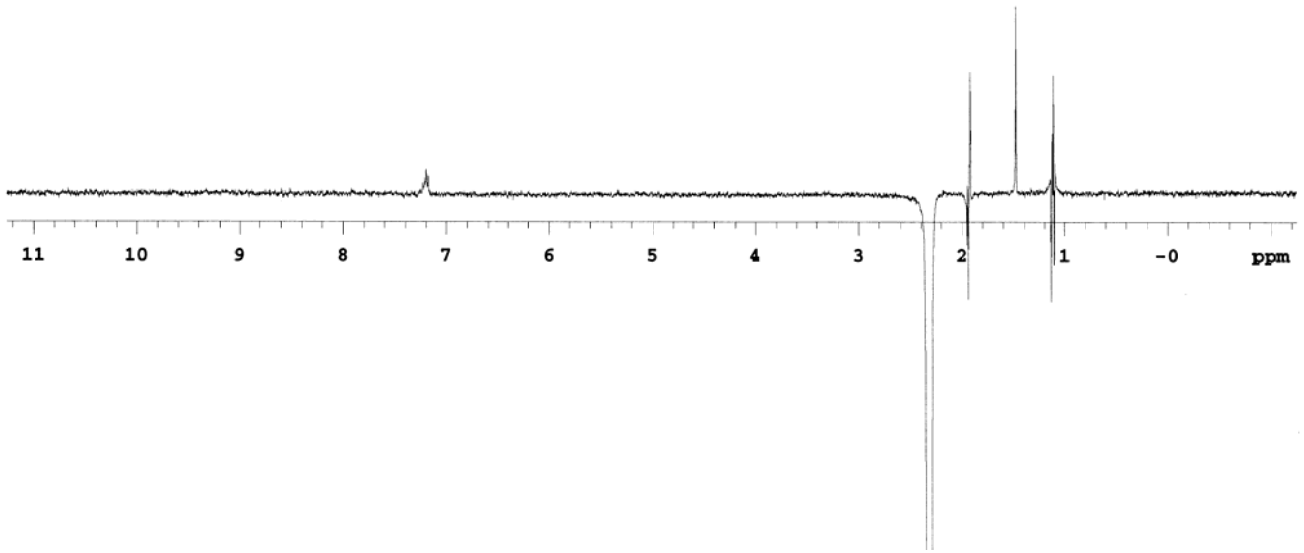
Pulse Sequence: NOESY1D

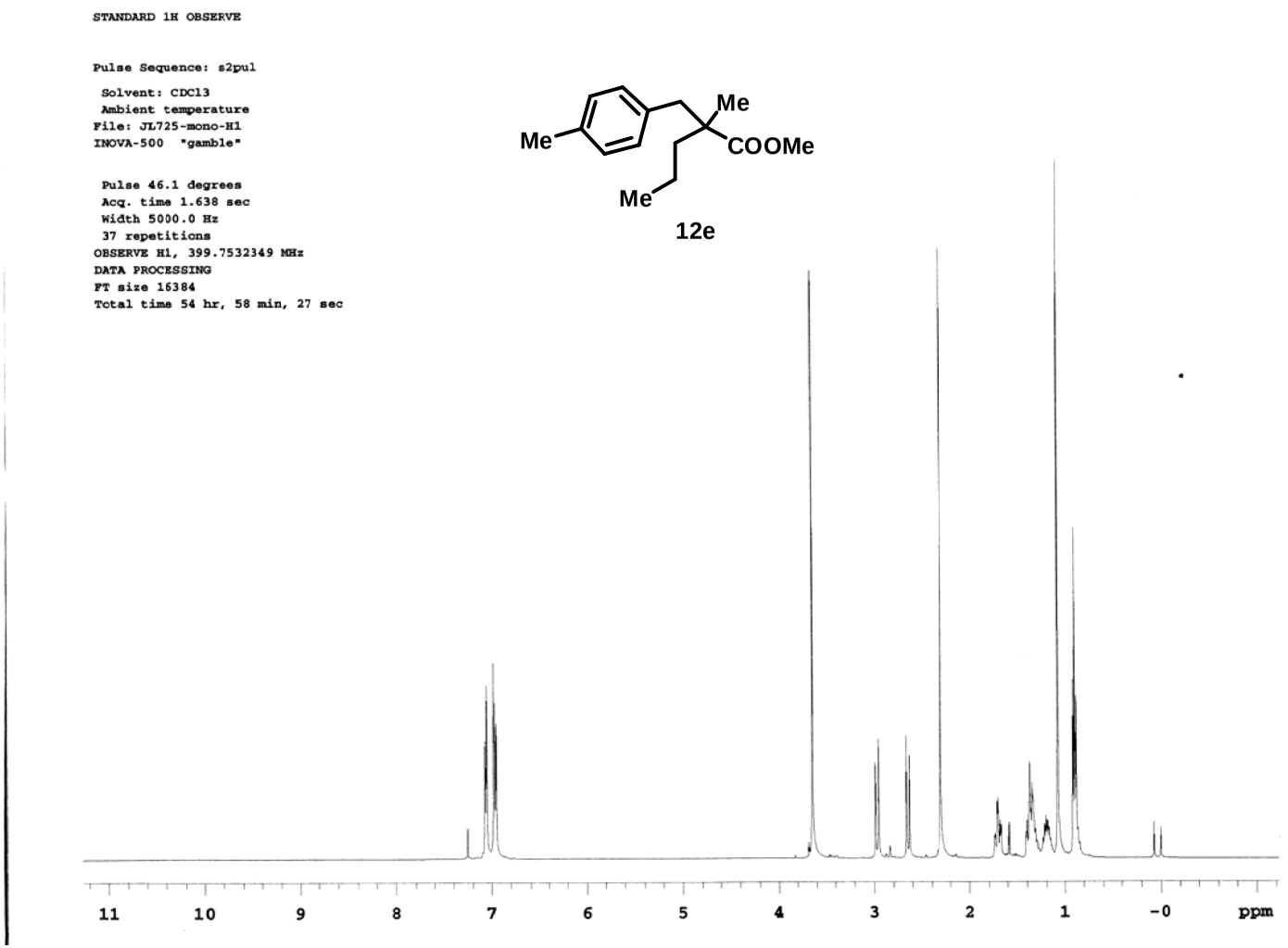
Solvent: CDCl3
Ambient temperature
File: JL-720-1DNOE-1
INOVA-500 "gamble"

Relax. delay 1.000 sec
Pulse 78.3 degrees
Mixing 0.500 sec
Acq. time 1.638 sec
Width 5000.0 Hz
600 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
Line broadening 0.6 Hz
FT size 16384
Total time 34 min, 9 sec



11b



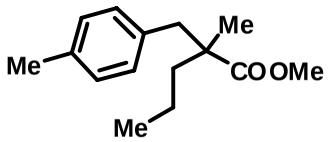

STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: JL725-mono-H1
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
37 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 54 hr, 58 min, 27 sec
Me
Me
COOMe
Me
12e
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

13C OBSERVE

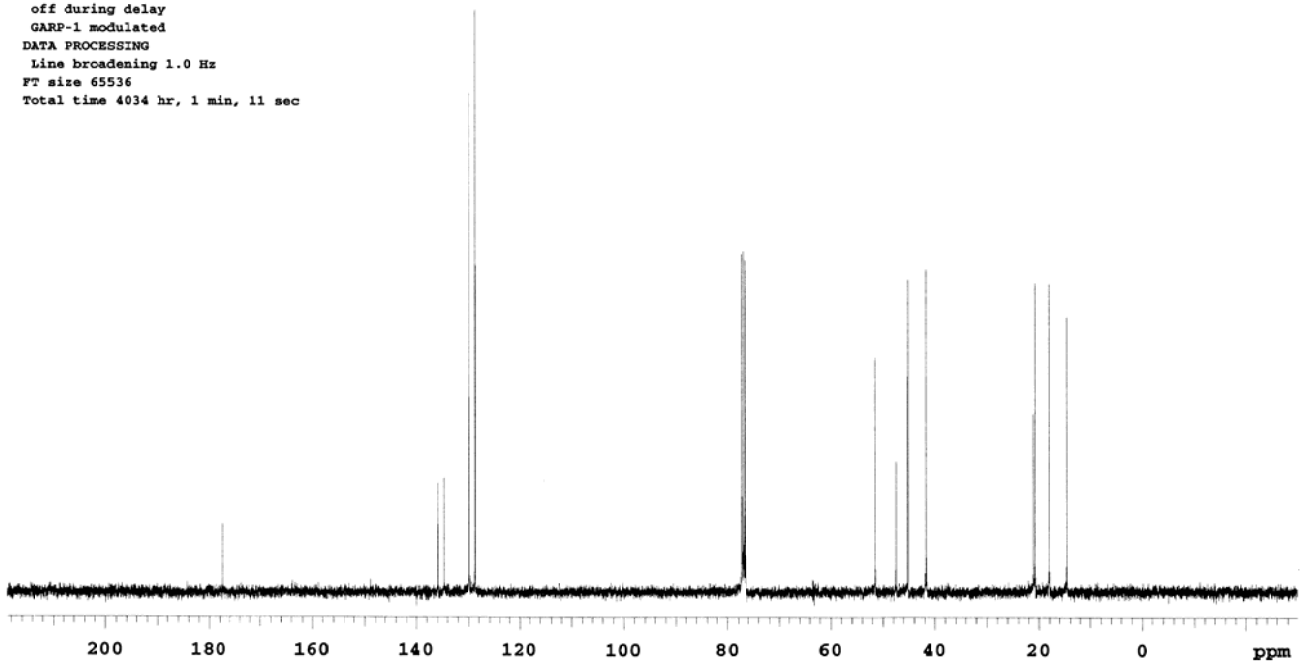
Pulse Sequence: s2pul

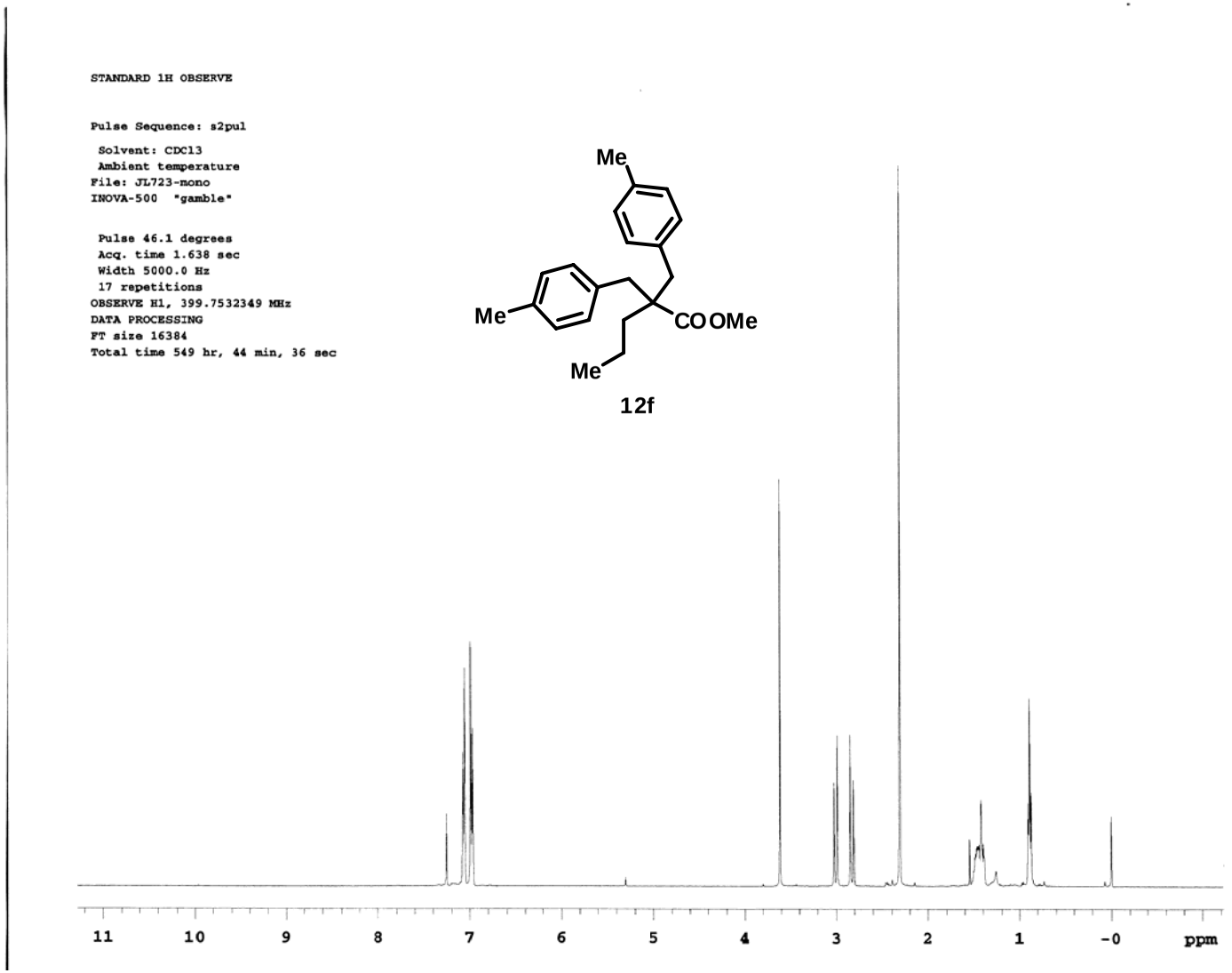
Solvent: CDCl3
Ambient temperature
File: JL725-mono-C13
INOVA-500 "gamble"

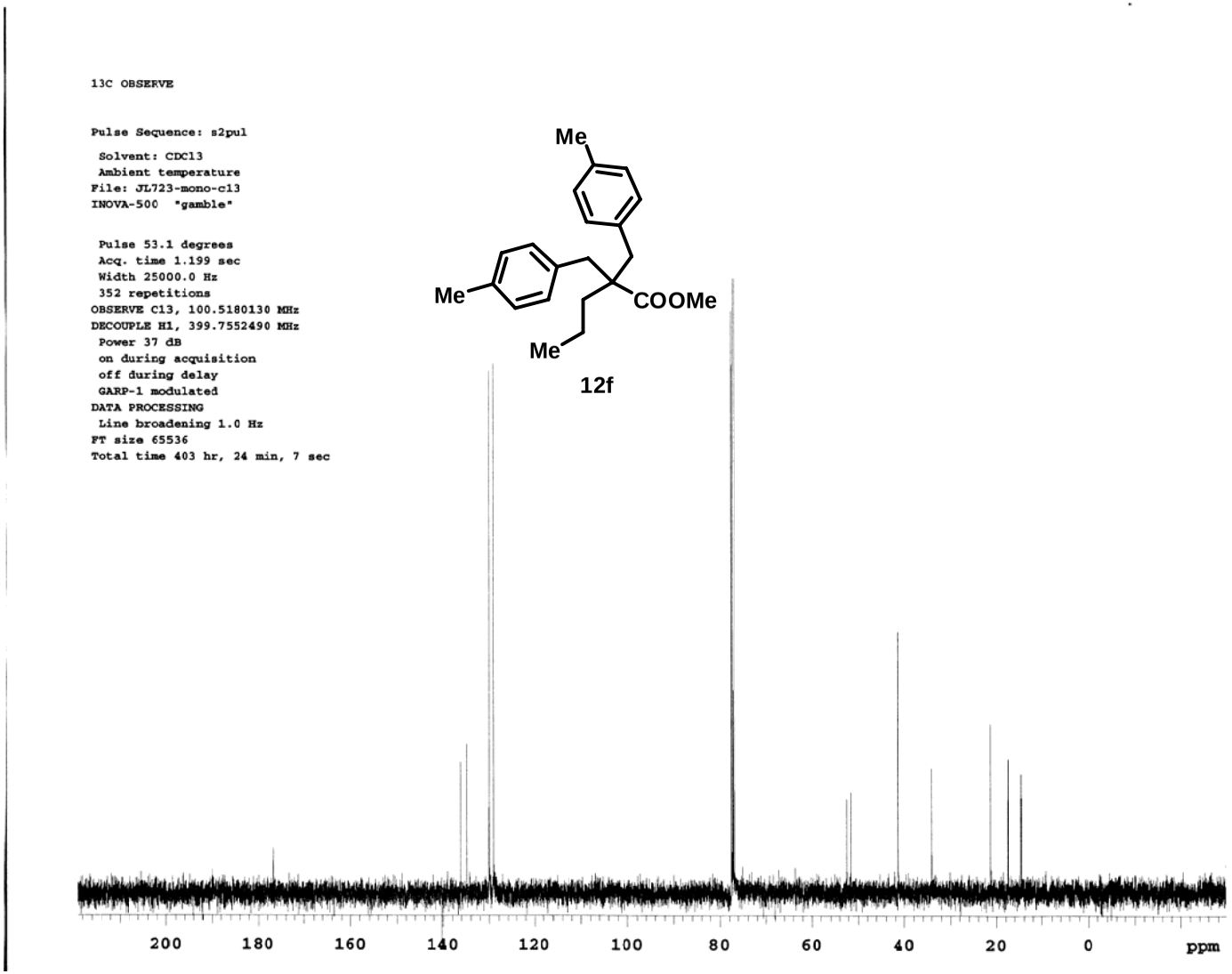
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
890 repetitions
OBSERVE C13, 100.5180359 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 4034 hr, 1 min, 11 sec

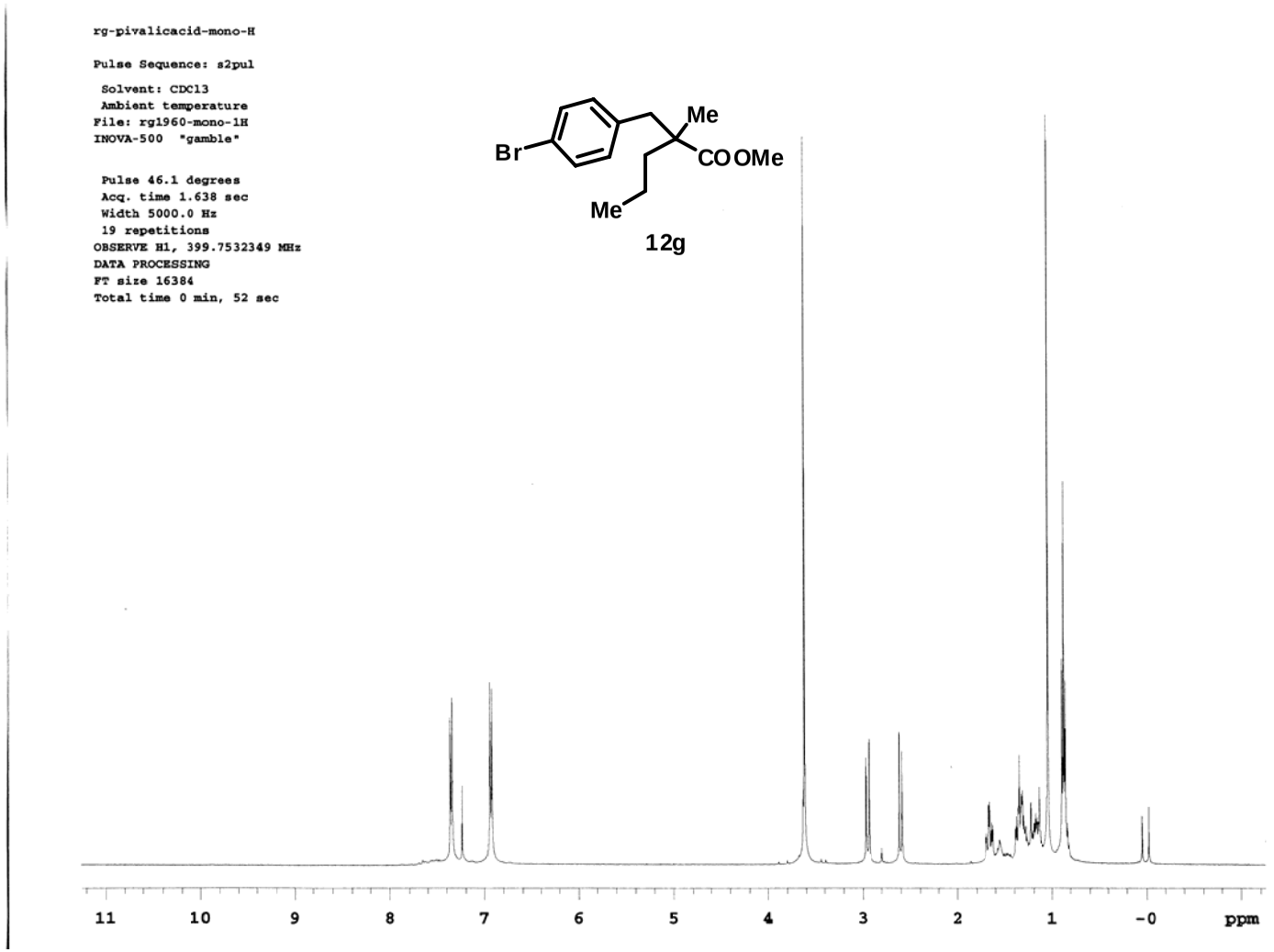


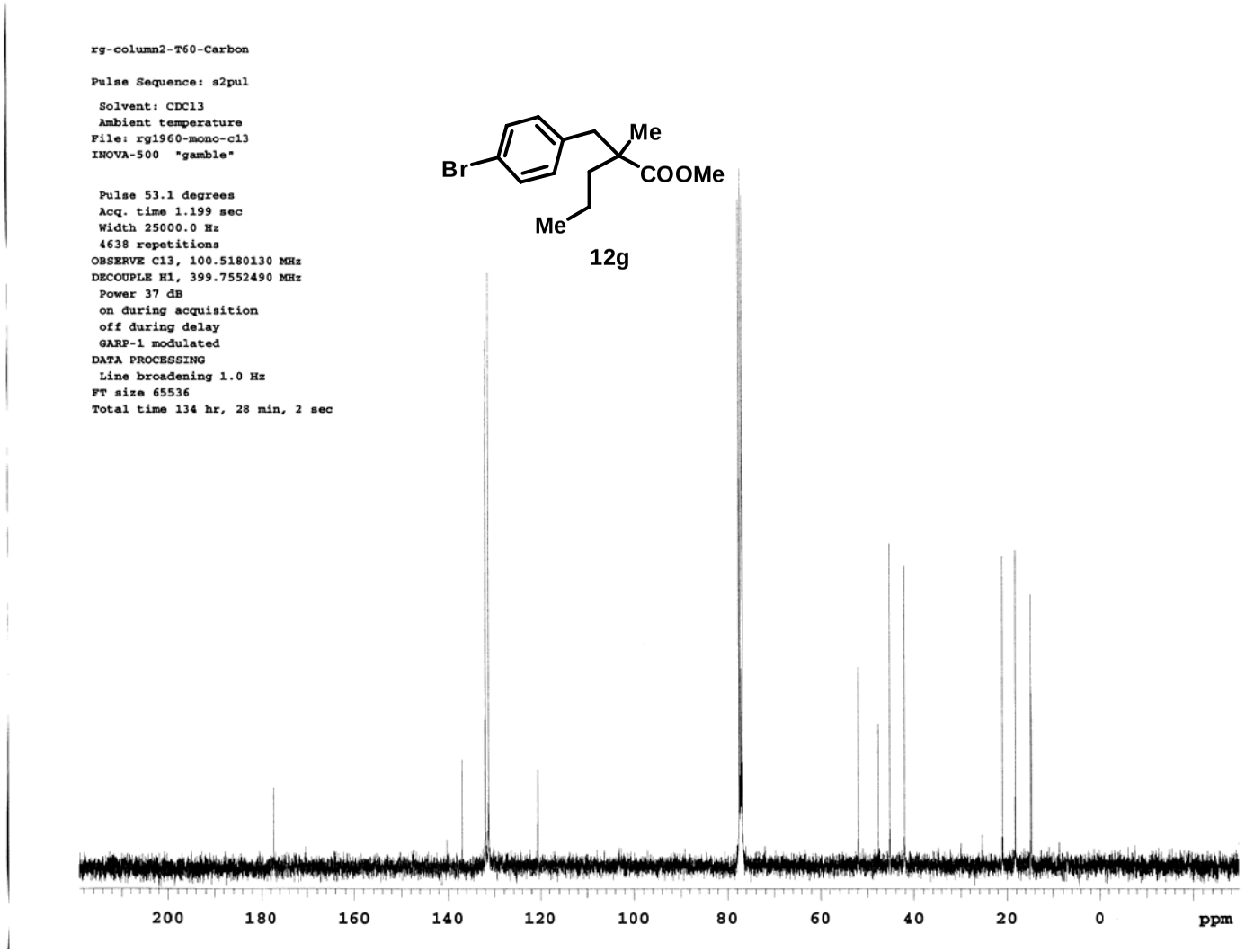
12e




STANDARD 1H OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: JL723-mono
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
17 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 549 hr, 44 min, 36 sec
Me
Me
COOMe
Me
12f
11
10
9
8
7
6
5
4
3
2
1
-0
ppm


13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: JL723-mono-c13
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
352 repetitions
OBSERVE C13, 100.5180130 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 403 hr, 24 min, 7 sec
Me
Me
COOMe
Me
12f
200
180
160
140
120
100
80
60
40
20
0
ppm


rg-pivalicacid-mono-H
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: rg1960-mono-1H
INOVA-500 "gamble"
Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
19 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 0 min, 52 sec
Br
Me
COOMe
Me
12g
11
10
9
8
7
6
5
4
3
2
1
-0
ppm

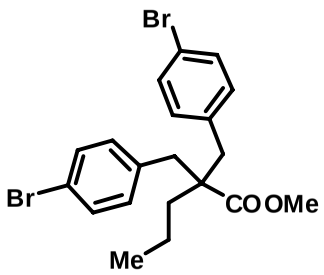

rg-column2-T60-Carbon
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: rg1960-mono-c13
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
4638 repetitions
OBSERVE C13, 100.5180130 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 134 hr, 28 min, 2 sec
Br
Me
COOMe
Me
12g
200
180
160
140
120
100
80
60
40
20
0
ppm

STANDARD 1H OBSERVE

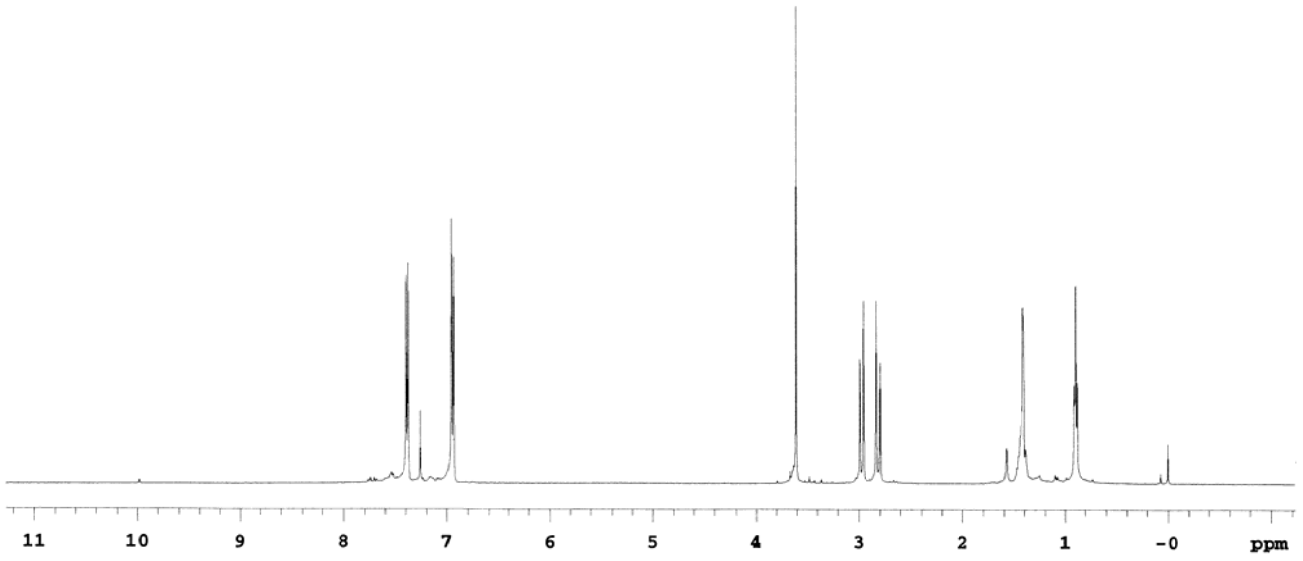
Pulse Sequence: s2pul

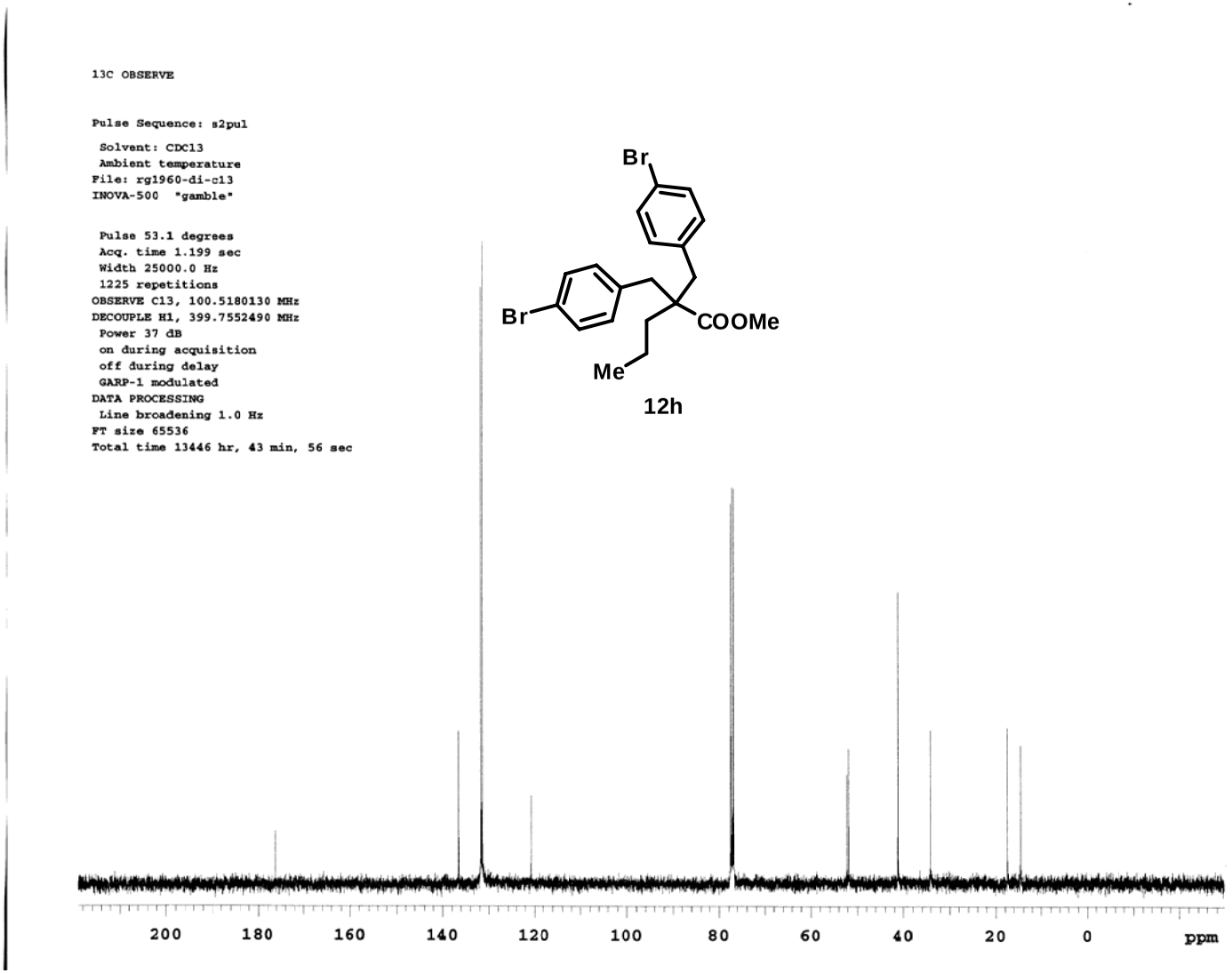
Solvent: CDCl3
Ambient temperature
File: rg1960-di-H1
INOVA-500 "gamble"

Pulse 46.1 degrees
Acq. time 1.638 sec
Width 5000.0 Hz
41 repetitions
OBSERVE H1, 399.7532349 MHz
DATA PROCESSING
FT size 16384
Total time 7 min, 2 sec



12h




13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: rg1960-di-c13
INOVA-500 "gamble"
Pulse 53.1 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
1225 repetitions
OBSERVE C13, 100.5180130 MHz
DECOUPLE H1, 399.7552490 MHz
Power 37 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 13446 hr, 43 min, 56 sec
Br
Br
COOMe
Me
12h
200
180
160
140
120
100
80
60
40
20
0
ppm