Electronic Supplementary Material (ESI) for Chemical Communications

Simultaneous Control of Regioselectivity and Enantioselectivity in the Hydroxycarbonylation and Methoxycarbonylation of Vinyl arenes.

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Supporting Information

A range of further experiments using the parent phanephos systems were carried out as mentioned in the main paper. The most informative results are presented in Tables ESI1 and ESI2.

Table ESI 1: Hydroxycarbonylation of styrene under a range of conditions.

Entry	Catalyst [a]	T (°C)	Time (h)	[LiCl] (%)	[acid] (%)	b/l	e.e.[b] (%)	Yield [c] (%)
1	(*S*)-2di	50	40	20	20	1.1	79(*S*)	56
2	(*R*)-1di	50	42	20	20	1.1	69(*R*)	35
3	(*S*)-2di	50	42	20	20	1.1	80(*S*)	71
4	(*S*)-2mo	50	42	20	20	0.43	50(*S*)	8
5	(*R*)-1mo	50	42	20	20	0.75	62(*R*)	4
6	(*R*)-1di	45	17	20	20	1.2	59(*R*)	13
7	(*R*)-1di	45	17	20	20	1.3	57(*R*)	18
8	(*S*)-2di	45	17	20	20	1.3	80(*S*)	7
9	(*S*)-2di	45	17	20	20	1.2	81(*S*)	15
10	(*R*)-1di	60	44	20	20	1.2	67(*R*)	55
11	(*R*)-1di	60	16	20	20	1.1	63(*R*)	32
12	(*R*)-1di	60	17	20	20	1.2	59(*R*)	29
13	(*S*)-2di	60	16	20	20	1	76(*S*)	58
14	(*R*)-1mo	60	17	20	20	1.2	55(*R*)	4
15	(*S*)-2mo	60	17	20	20	0.73	66(*S*)	14
16	(*R*)-1di	70	17	20	20	1.10	52(*R*)	73
17	(*R*)-1di	70	17	20	20	0.47	31 (*R*)	7[d]
18	(*S*)-2di	70	17	20	20	0.84	63(*S*)	77
19	(*R*)-1mo	70	17	20	20	0.60	38(*R*)	10
20	(*R*)-2mo	70	17	20	20	0.36	34(*R*)	7
21	(*R*)-1mo	100	18	5	5	0.28	8(*R*)	51
22	(*R*)-1mo	100	18	20	20	0.26	8(*R*)	51
23	(*R*)-1di	100	18	20	20	0.68	18(*R*)	53
24	(*R*)-1di	100	16	5	5	0.40	5(*R*)	59
25	(*R*)-1di	100	4	20	20	0.43	10(*R*)	56
26	(*S*)-2di	100	17	20	20	0.30	18(*S*)	67
27	(*S*)-2mo	100	17	20	20	0.25	16(*S*)	60

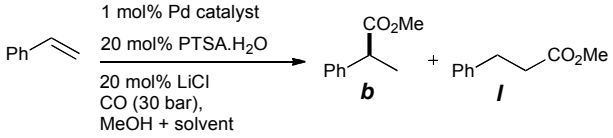
a: Reactions were carried out using 1 mol% catalyst at 30 bar CO in 1.5 mL of degassed butanone as solvent, 20 mol% LiCl and 20 mol% *p*-toluene sulfonic acid hydrate co-catalyst unless otherwise stated. b: e.e. determined by chiral HPLC. Absolute configuration in brackets; b/ l determined by ^{1}H NMR spectroscopy. c: Yield refers to yield of pure acid isolated after acid/base extraction. [d]: 20 bar of CO used.

Table ESI 2: Analysis of acidic medium and co-catalyst for the hydroxycarbonylation of styrene using shortened reaction times (5 hours).

Entry	Catalyst [a]	T (°C)	[Co-catalyst] [b]	[Acid] [b]	Conversion (%)[c]	(%) Product (Yield)[c]	b/l[c]	e.e.[d] (%)
1	(*R*)-2di	70	-	-	13	11 (7)	1.2	58(*R*)
2	(*R*)-2di	70	LiCl	-	8	8 (2)	1.3	72(*R*)
3	(*R*)-2di	70	-	*p*-TsOH	13	12 (2)	0.6	38(*R*)
4	(*R*)-2di	70	LiCl	*p*-TsOH	26	26 (9)	1.0	74(*R*)
5	(*R*)-2di	70	-	TFA	18	18 (3)	0.8	53(*R*)
6	(*R*)-2di	70	LiCl	TFA	18	14 (10)	1.0	69(*R*)
7	(*R*)-2di	70	-	H_2SO_4	15	15 (7)	0.5	24(*R*)
8	(*R*)-2di	70	LiCl	H_2SO_4	16	16 (7)	1.0	64(*R*)
9	(*R*)-2di	70	-	H_3PO_4	12	12 (3)	0.8	44(*R*)
10	(*R*)-2di	70	LiCl	H_3PO_4	12	12 (5)	1.0	62(*R*)
11	(*R*)-2di	70	-	$Al(OTf)_3$	14	14 (6)	0.2	5(*R*)
12	(*R*)-2di	70	LiCl	$Al(OTf)_3$	17	17 (11)	1.0	50(*R*)
13	(*R*)-2di	70	NaCl	-	9	5 (2)	1.1	56(*R*)
14	(*R*)-2di	70	NaCl	*p*-TsOH	10	8 (2)	0.7	46(*R*)
15	(*R*)-2di	70	NH_4Cl	-	12	12 (6)	0.9	56(*R*)
16	(*R*)-2di	70	NH_4Cl	*p*-TsOH	10	10 (6)	0.8	56(*R*)
17	(*R*)-2di	70	CsCl	-	14	13 (8)	1.8	41(*R*)
18	(*R*)-2di	70	CsCl	*p*-TsOH	32	28 (11)	1.0	60(*R*)
19	(*R*)-2di	70	LiBr	-	7	6 (2)	1.3	33(*R*)
20	(*R*)-2di	70	LiBr	*p*-TsOH	7	3 (3)	1.3	38(*R*)
21	(*R*)-2di	70	LiBr	TFA	3	1 (1)	1.2	51(*R*)

a: Reactions were carried out on 0.5 mmol of styrene, 1.25 mmol water, using 1 mol% catalyst (see scheme 2 of main paper for structures) at 30 bar CO in 1.5 mL of degassed butanone as solvent for 5 hours. b: 20 mol % co-catalyst and acid used. c: Conversion, (%) product and b/l determined by ^{1}H NMR spectroscopy and comparison with an internal standard. d: e.e. determined by chiral HPLC. Absolute configuration in brackets.

Table ESI 3: Enantioselective and regioselective alkoxycarbonylation of styrene.



Entry[a]	Catalyst	T (°C)	Time (h)	% ester {yield}[c]	b/l [c]	e.e. [d]
1	2mo	60	20	>99	0.7	79
2	2di	60	20	>99	0.7	79
3	3mo	60	20	60	1.3	35
4 [b]	3mo	60	20	49	32	15
5 [f]	**3mo**	**35**	**71**	**72**	**4.0**	**93**
6 [b]	3mo	35	72	34	19	38
7 [e]	3di	60	20	58	1.5	27
8 [e,f]	3di	35	71	42	3.5	93
9	4mo	60	20	>99	2.2	48
10	4mo	50	20	95 {83}	1.8	57
11	4di	60	20	99	2.1	47
12	4di	50	20	87 {77}	1.7	51
13 [b]	4di	50	20	>99	14	61
14	5mo	60	20	>99 {51}	1.9	54
15	5di	60	20	>99 {60}	1.3	63
16 [b]	5di	60	20	>99	5.4	33
17	5di	40	24	81 {76}	1.9	76
18 [b]	6mo	60	22	92	>100	56
19 [b]	**6di**	**60**	**22**	**>99**	**>100**	**79**
20	6di	60	22	71	>100	68
21 [b]	7mo	60	22	>99	17	55
22 [b]	7di	60	22	>99	23	61

a: Reactions were carried out using 1 mol% catalyst, 1 mmol styrene at 30 bar CO in 1.5 mL of MeOH, 20 mol% LiCl and 20 mol% 4-$MeC_6H_4SO_3H.H_2O$, unless otherwise stated. b: Reactions were carried out using 2.5 mmol MeOH in 1.5 mL of butanone. c: % ester against internal standard. d: e.e. determined by chiral HPLC or chiral GC; b/ l determined by 1H NMR spectroscopy. (R) catalyst gives (R) product and vice versa. e: Dipalladium complex formed from monomer in situ. f: 0.5 mol% catalyst loading.

Instrumentation and Chemicals

Unless otherwise stated all reactions were carried out under inert atmosphere using standard Schlenk techniques.

NMR All ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded either on a Bruker Avance 300 spectrometer (^{1}H at 300 MHz, ^{13}C at 75 MHz, ^{31}P at 121 MHz) or Bruker Avance II 400 (^{1}H at 400 MHz, ^{13}C at 100 MHz, ^{31}P at 161 MHz) spectrometer. Chemical shift values are given in parts per million and were referenced to external standards (^{1}H and ^{13}C were referenced to tetramethylsilane and ^{31}P spectra to phosphoric acid). All deuterated solvents were purchased from Deuterio GmbH. Proton signals multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br s (broad singlet) or a combination of them.

EA and MS Elemental analyses were carried out by the Elemental Analysis Service at the London Metropolitan University. Mass spectroscopy was carried out by the EPSRC National Mass Spectroscopy Service Centre, Swansea.

Solvents Dichloromethane, hexane, toluene and ether were dried and purified via an Innovative Technologies Puresolve 400 solvent purification system, and degassed by purging with nitrogen. Methanol was dried over $CaCl_2$ and tetrahydrofuran was dried over Na wires (benzophenone as indicator). Other solvents were bought and used as received without further purification other than degassing by purging with nitrogen.

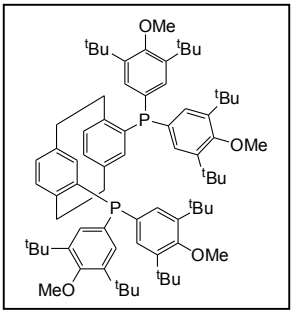
OR Optical rotations were measured on a Perkin Elmer 341 polarimeter using a 1 mL cell with a 1 dm path length at 20 ^{o}C using the sodium d line.

Materials (*R*)- and (*S*)-4,12-dibromo[2.2]-*p*-cyclophane was donated by Chirotech and used as received. 4,12-Bis(diphenylphosphino)-[2.2]-paracyclophane ((*R*)-(–)- and (*S*)-(+)-PHANEPHOS) and 4,12-Bis[di(3,5-xylyl)phosphino]-[2.2]-paracyclophane ((*R*)-(–)- and (*S*)-(+)- Xylyl-PHANEPHOS) were purchased from Aldrich chemical company or donated by Chirotech and used as received without further purification, after checking optical rotation data with the literature.[1] $[PdCl_2(PhCN)_2]$, LiCl, PTSA monohydrate, styrene, 4-chlorostyrene and 4-*tert*-butylstyrene were obtained from Aldrich and used as received. Carbon monoxide was obtained from BOC. Flash column chromatography was performed using Davasil silica gel 40-63µm and normal grade solvents.

Catalyst **1mo/di** and **2mo/di** were prepared as reported in literature.[2]

Synthesis of ligands and complexes

(*S*)-(+)-4,12-bis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino)-[2.2]-*para*-cyclophane, L3



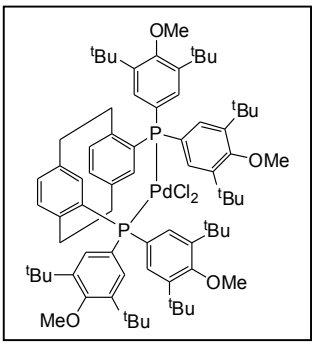
(*S*)-(+)-4,12-Dibromo-*para*-cyclophane (181.2 mg, 0.495 mmol) was placed in a dry Schlenk flask under inert atmosphere, Et_2O (15 ml) added and n-BuLi (0.40 ml, 0.990 mmol, 2.5 M in hexane) was slowly added. The resulting solution was stirred for 3 hours and then bis(3,5-di-*tert*-butyl-4-methoxyphenyl)chlorophosphine (500 mg, 0.990 mmol) was added in one portion and stirred overnight. A small sample (0.5ml) was taken and analysed by ^{31}P $\{^{1}H\}$ NMR spectroscopy confirming the reaction has gone to completion. MeOH (1 ml) was added and the solvent was removed under vacuum. The product was then dissolved in hexane, the precipitate filtered off and solvent removed leaving the title compound in 81% yield (456 mg, 0.3980 mmol).

^{1}H NMR (300MHz, CD_2Cl_2) δ_H 1.30 (br s, 72H), 2.5-3.00 (m, 8H), 3.58 (br s, 12H), 6.34-6.46 (m, 5H), 6.64 (d, J = 2.37, 1H), 7.18-7.26 (m, 2H), 7.39-7.56 (m, 6H). ^{31}P $\{^{1}H\}$ NMR (161MHz; $CDCl_3$) δ_P 0.21 (s).

MS (CI): m/z calcd. for $C_{76}H_{106}O_4P_2$: 1144.76; found 1145.76. (Good agreement was found between measured and theoretical isotope patterns).

Anal.calcd. for $C_{76}H_{106}O_4P_2$: C 79.68, H 9.33 Found : C 79.56, H 9.26.

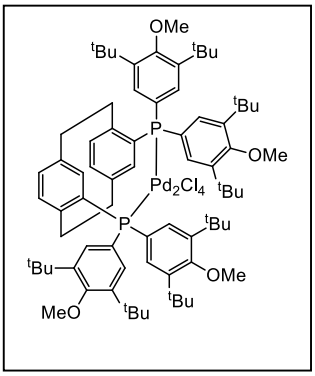
{{(*S*)-(+)-4,12-bis[bis-(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-[2.2]-*para*-cyclophane}palladium(II)chloride}, 3mo



(*S*)-(+)-4,12-Bis[bis (3,5 di-*tert*-butyl-4-methoxyphenyl) phosphino]-[2.2]-*para*-cyclophane (142 mg, 0.124 mmol) was put under inert atmosphere and dissolved in CH_2Cl_2. One equivalent of $[PdCl_2(PhCN)_2]$ (48 mg, 0.124 mmol) was added. The solution was stirred overnight. A small sample was taken for ^{31}P $\{^1H\}$ NMR confirming the reaction has gone to completion. The solvent was removed and the complex washed with hexane (3 x 20 ml). The solid obtained was dried under vacuum, yielding the desired compound as a bright yellow solid in 88% yield (144 mg, 0.109 mmol).

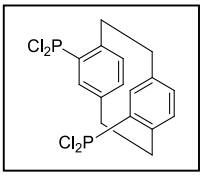
^1H NMR (300MHz, $CDCl_3$) δ_H 1.23 (bs, 54H), 1.38 (bs, 18H), 2.26-2.33 (m, 2H), 2.37-2.51 (m, 4H), 3.01 (s, 2H), 3.56 (s, 6H), 3.64 (s, 6H), 6.26-6.37 (m, 4H), 6.41 (s, 2H), 6.91-7.01 (m, 2H), 7.23 (d, J = 6.0 Hz, 1H), 7.87-7.91 (m, 3H), 8.53-8.58 (m, 2H). ^{13}C-NMR, (75MHz, CD_2Cl_2) δ_C 31.64 (s, CH_2), 31.88 (s,CH_3), 32.06 (s, CH_3), 32.40 (s, CH_3), 36.40 (s, CH_2), 64.66 (s, CH_2), 66.28 (s, CH_2), 124.28 (s, C_q), 124.82 (s, C_q), 127.06 (s, C_q), 127.52 (s, C_q), 130.45 (s, CH), 134.76 (s, CH), 136.42 (m, CH), 136.70 (m, CH), 137.49 (t, *J* = 8.1Hz, CH), 139.97 (t, *J* = 4.4Hz, C_q), 143.16 (t, *J*=4.0Hz, C_q), 144.60 (s, C_q),163.14 (s, C_q), 163.22 (s, C_q). ^{31}P $\{^1H\}$ NMR (161MHz; $CDCl_3$): δ_P 45.67 ppm (s).
MS (CI): m/z calcd. for $C_{76}H_{106}O_4P_2PdCH_3COO$ $[M\text{-}2Cl+CH_3CO_2]^+$: 1309.67; found 1309.67. (Good agreement was found between measured and theoretical isotope patterns).
Anal.calcd. for $C_{76}H_{106}Cl_2O_4P_2Pd$: C 69.0, H 8.08 Found : C 69.14, H 8.17.
$[\alpha]_D$= -132.3 (c = 0.065, $CHCl_3$). 168 °C (decomposition).

{{(*S*)-(+)-4,12-bis[bis(3,5-di-*tert*-butyl-4-methoxy-phenyl)phosphino]-[2.2]-*para*-cyclophane} dipalladium(II)tetrachloride}, 3di



(*S*)-(+)-4,12-bis[bis(3,5 di-*tert*-butyl-4-methoxyphenyl)phosphino]-[2.2]-*para*-cyclophane (45 mg, 0.040 mmol) was weighed into a dry schlenk flask and dissolved in CH_2Cl_2 (10 ml). Two equivalents of $[PdCl_2(PhCN)_2]$ (30.4 mg, 0.079 mmol) added to the solution and stirred overnight. A dark brown/orange solid was formed over night.
The compound was purified by removing solvent and washing with hexane (2 x 20 ml). The solution was filtered off and the precipitate dried under vacuum, giving a dark red/brown solid in 95% yield (57mg, 0.038 mmol).
An attempt to dissolve a small sample was taken for ^{31}P $\{^1H\}$ NMR spectroscopy but no signal could be found. Due to the insolubility of the compound, this could not be characterized, but MS gives the same type of spectra as the characterised dipalladium species of other ligands.
MS (CI): m/z calcd. for $C_{76}H_{106}Cl_4O_4P_2Pd_2$ $[M^-+NH_3]^+$: 1500.4; found 1500.6.

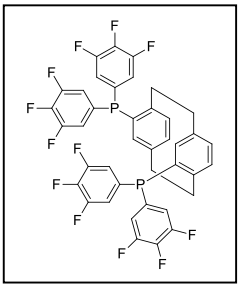
Literature: (*R*)-(-)-4,12-bis(dichlorophosphino)-[2.2]-*para*-cyclophane[3]



(*R*)-(-)-4,12-dibromo-*para*-cyclophane (3.02 g, 8.249 mmol) was placed in a dry Schlenk flask under argon atmosphere and partly dissolved in dry Et_2O (40 ml). *n*-BuLi (14 ml, 35.00 mmol, 2.5 M in hexane) was added slowly under room temperature and stirred for 3 hours. Bis(di-*iso*-propylamino)chlorophosphine (5 g, 0.019 mol) was added in one portion and the solution stirred overnight. Anhydrous MeOH (30 ml) was

added and some solvent was removed under vacuum, until half the solvent was removed, then more MeOH (100 ml) was added. The solution was filtered off by cannula filtration and the white precipitate dried under vacuum, resulting in (*R*)-(-)-4, 12-bis[bis(di-*iso*-propylamino)phosphino]-[2.2]-*para*-cyclophane in 87% yield (4.80 g, 7.172 mmol). (^{31}P {^{1}H} NMR in $CDCl_3$ 72.3 ppm).
A solution of HCl in Et_2O (2 M, 100 ml, 0.200 mol) was added to the solid (*R*)-(-)-4,12-bis[bis(di-*iso*-propylamino)phosphino]-[2.2]-*para*-cyclophane and stirred overnight at room temperature. The solvent was removed and hexane (100 ml) was added. The solution was filtered through a cannula and the solvent removed. More hexane (100 ml) was added and the solution again filtered off and the solvent removed. Hexane (100 ml) was added and the cloudy solution was filtered again. The solvent was evaporated resulting in the product (*R*)-(-)-4,12-bis(dichlorophosphino)-[2.2]-*para*-cyclophane as a white powder in 31% yield (908 mg, 2.214 mmol). (^{31}P {^{1}H} NMR in $CDCl_3$ 166.0 ppm).

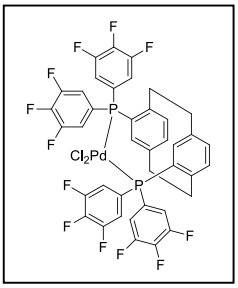
(*R*)-(-)-4,12-bis[bis(3,4,5-trifluorophenyl)phosphino]-[2.2]-*para*-cyclophane, L4



(*R*)-(-)-4, 12-bis(dichlorophosphino)-[2.2]-*para*-cyclophane (385.0 mg, 0.939 mmol) was dissolved in THF (5 ml) and 3,4,5 trifluorophenylmagnesiumbromide (16 ml, 4.695 mmol, 0.3 M in THF) was added slowly. After stirring for 2 hours at room temperature the solution was heated to 50 °C for one hour and cooled to room temperature. After checking the completion of the reaction using ^{31}P {^{1}H} NMR MeOH (1 ml) was added and stirred, the solvent removed and hexane added and the solution was filtered off. After removing the solvent under reduced pressure, the crude product was obtained as brownish solid. The solid was dissolved in hexane (30 ml) and charcoal (spatula point) was added. The solution was filtered though celite under argon. After removing the solvent under reduced pressure the product was obtained in 33% yield (348 mg, 0.3103 mmol) as a white solid.

^{1}H NMR (400MHz, CD_2Cl_2) δ_H 2.61-3.28 (m, 8H), 6.29-6.80 (m, 6H), 6.87-7.01 (m, 4H), 7.05-7.23 (m, 4H). ^{31}P {^{1}H} NMR (121MHz; $CDCl_3$) δ_P 2.09 (s).
MS (CI): m/z calcd. for $C_{40}H_{22}F_{12}P_2$ $[M\text{-}F]^+$: 774.54; found 774.0. (Good agreement was found between measured and theoretical isotope patterns).
Anal. calcd. For $C_{40}H_{22}F_{12}P_2$: C, 60.62; H, 2.80 ; Found : C, 60.53; H 2.93,.
$[\alpha]_D$= -27.1 (c = 0.16, $CHCl_3$).

{{(*R*)-(-)-4,12-bis[bis-(3,4,5-trifluorophenyl)phosphino]-[2.2]-*para*-cyclophane}palladium(II) dichloride}, 4mo

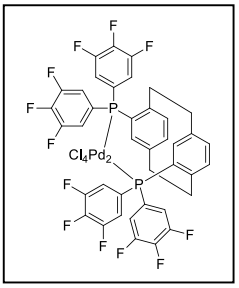


(*R*)-(-)-4,12-Bis[bis(3,4,5-trifluorophenyl)phosphino]-[2.2]-paracyclophane (103 mg, 0.1300 mmol) was dissolved in DCM (10 ml) before adding one equivalent $[PdCl_2(PhCN)_2]$ (50 mg, 0.130 mmol). The solution was stirred overnight. Taking a small sample (0.5 ml) for ^{31}P {^{1}H} NMR spectroscopy confirmed the reaction had gone to completion. The solvent was removed under vacuum, until a few ml were left and then hexane (20 ml) was added. The yellowish precipitate was washed 3 times with hexane before dried under vacuum, yielding the palladium complex as a bright yellow powder in 70% yield (88 mg, 0.091 mmol).

^{1}H NMR (400MHz, CD_2Cl_2) δ_H 2.59-2.82 (m, 6H), 2. 87-3.33 (m, 2H), 6.51-6.54 (m, 2H), 6.60-6.69 (m, 2H), 6.76-6.80 (m, 2H), 6.99-7.12 (m, 1H), 7.16-7.26 (m, 1H), 7.41 (t, *J*=7.6, 1H), 7.52-7.62 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 32.77 (s, CH_2), 36.32 (s, CH_2), 117.00 (s, C_{qu}), 121.77-122.12 (m, CH), 127.59 (s, C_{qu}), 128.20 (s, C_{qu}), 137.01 (s, CH), 137.15 (s, CH), 137.28 (d, CH, *J*=4.42), 137.37 (s, CH), 137.49 (t, *J*=4.5, CH), 140.77-140.91 (m, C_{qu}), 144.72 (s, C_{qu}), 149.49-149.77 (m, C_{qu}), 150.15-150.62 (m,
MS (CI (NH3)): m/z calcd. for $C_{40}H_{22}Cl_2F_{12}P_2Pd$ (NH_3) : 969.9; found 969.8. (Good agreement was found between measured and theoretical isotope patterns).

C_{qu}), 152.08-152.49 (m, C_{qu}), 152.70-153.06 (m, C_{qu}). ^{31}P {^{1}H} NMR (161 MHz; $CDCl_3$) δ_P 40.8 (s).
Anal. calcd. for $C_{40}H_{22}Cl_2F_{12}P_2Pd$: C, 49.54; H, 2.29; Found : C, 49.62; H 2.39,.
$[\alpha]_D$= +12.0 (c = 0.075, $CHCl_3$). m.p. 180 °C (decomposition).

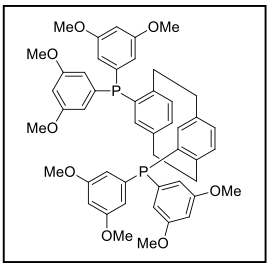
{{(*R*)-(-)-4,12-bis[bis(3,4,5-trifluorophenyl)phosphino]-[2.2]-*para*-cyclophane}dipalladium(II) tetrachloride}, 4di



(*R*)-(-)-4,12-Bis[bis (3,4,5-trifluorophenyl) phosphino]-[2.2]- *para*-cyclophane (193 mg, 0.244 mmol) was weighed into an dry schlenk flask and put under argon. The compound was dissolved in CH_2Cl_2 (30 ml) before adding 2 equivalent of [$PdCl_2(PhCN)_2$] (187 mg, 0.488 mmol). The resulting solution was then stirred overnight. A small sample (0.5 ml) was taken for ^{31}P {^{1}H} NMR spectroscopy confirming the reaction has gone to completion. Then the solvent was removed until a few ml were left and the reddish precipitate obtained washed 5 times with hexane. After cannula filtration the precipitate was dried under vacuum, yielding the title compound as an orange solid in 43% yield (126 mg, 0.110 mmol).

^{1}H NMR (300MHz, CD_2Cl_2) δ_H 2.87-3.33 (m, 8H), 6.55 (br s, 4H), 7.04-7.13 (m, 4H), 7.38-7.44 (m, 3H), 7.52-7.61 (m, 3H).). ^{13}C NMR (75 MHz, CD_2Cl_2) δ_C 33.68 (s, CH_2), 35.25 (s, CH_2), 115.69 (s, CH), 116.11 (s, CH), 128.29 (s, CH), 131.40 (s, CH), 131.97 (s, CH), 135.06 (d, *J*=2.7, CH), 139.51 (s, CH), 148.18 (s, C_{qu}), 151.32 (s, C_{qu}), 151.63 (s, C_{qu}). ^{31}P {^{1}H} NMR (121MHz; $CDCl_3$) δ_P 36.06 (s).
MS (CI): m/z calcd. for $C_{40}H_{22}Cl_4F_{12}P_2Pd_2$: 1147.8; found 1147.7. (Good agreement was found between measured and theoretical isotope patterns).
Anal. calcd. For $C_{40}H_{22}Cl_4F_{12}P_2Pd_2$: C, 41.88; H, 1.93; Found : C, 41.95; H, 1.86.
$[\alpha]_D$= +691.7 (c = 0.06, $CHCl_3$). m.p. 172 °C (decomposition).

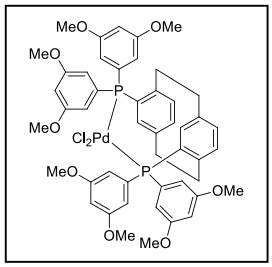
(*R*)-(-)-4,12-bis[bis(3,5-dimethoxyphenyl)phosphino]-[2.2]-*para*-cyclophane, L5



(*R*)-(-)-4,12-bis(dichlorophosphino)-[2.2]-*para*-cyclophane (600 mg, 1.463 mmol) was dissolved in THF (10 ml) and 3,5 dimethoxyphenylmagnesiumbromide (7.5 ml, 7.316 mmol, 1M in THF) slowly added. The solution was heated to 68 °C for 3 hours, then cooled to room temperature and stirred overnight. The completion of the reaction was checked using ^{31}P {^{1}H} NMR spectroscopy. MeOH (5 ml) was added to quench the rest of the unreacted grignard. The solvent was removed, hexane added and the solution filtered via cannula filtration. After removing the solvent under reduced pressure, the product was obtained in 79% yield (943 mg, 1.154 mmol) as a white sticky solid.

^{1}H NMR (400MHz, $CDCl_3$) δ_H 3.67-3.76 (m, 32H), 6.38-6.45 (m, 14H), 7.11 (t, J = 8.2, 4H). ^{31}P {^{1}H} NMR (161MHz; $CDCl_3$) δ_P 3.87 (s).
MS (CI): m/z calcd. for $[C_{48}H_{50}O_8P_2+H]^+$: 817.30 found 817.30. (Good agreement was found between measured and theoretical isotope patterns).
Anal. calcd. for $C_{48}H_{50}O_8P_2$: C, 70.58; H, 6.17; Found : C, 70.39; H 6.05.
$[\alpha]_D$= -32.1 (c = 0.28, $CHCl_3$).

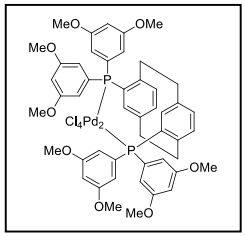
{{(*R*)-(-)-4,12-bis[bis(3,5-dimethoxyphenyl)phosphino]-[2.2]-*para*-cyclophane}palladium(II) dichloride}, 5mo



(*R*)-(-)-4,12-Bis[bis(3,5-dimethoxyphenyl)phosphino]-[2.2]-*para*-cyclophane (262 mg, 0.3208 mmol) was dissolved in CH_2Cl_2 (10 ml) and $[PdCl_2(PhCN)_2]$ (123 mg, 0.3208 mmol) added in one portion and stirred overnight. A small sample (0.5 ml) was taken for ^{31}P $\{^1H\}$ NMR spectroscopy confirming the reaction has gone to completion. The solution was removed leaving a yellowish oily residue, which was then washed with hexane resulting in a yellow precipitate. Filtering off the solution and drying the yellow precipitate under vacuum resulted in a yellow sticky solid. In order to have the compound washed thoroughly this solid was dissolved again in CH_2Cl_2 (6 ml) and then precipitated with hexane (20 ml). About one third of the solution was removed prior to cannula filtration. The residue was dried under vacuum again leaving a yellow sticky solid in 73% yield (233.3 mg, 0.235 mmol).

^1H NMR (400MHz, $CDCl_3$) δ_H 3.54-3.84 (m, 32H), 6.36-6.44 (m, 6H), 6.63 (d, *J*=2.2, 4H), 7.09 (t, J = 8.1, 2H), 7.47-7.51 (m, 2H), 7.66-7.73 (m, 4H). ^{13}C NMR (75 MHz, CD_2Cl_2) δ_C 30.92 (s, CH_2), 35.10 (s, CH_2), 54.24 (s, OMe), 54.42 (s, OMe), 54.57 (s, OMe), 98.46 (s, CH), 99.50 (s, CH), 102.59 (s, CH), 103.24 (s, CH), 104.51 (s, CH), 105.40 (s, CH), 114.52 (t, *J*=5.25, CH), 128.86 (s, CH), 130.78 (d, *J*=11.25, C_{qu}), 131.50 (d, *J*=8.25, C_{qu}), 133.22 (d, *J*=7.5, C_{qu}), 133.93 (s, CH), 134.75 (d, *J*=7.5, C_{qu}), 135.58 (t, *J*=5.25, CH), 136.28 (t, *J*=11.25, CH), 138.66 (t, *J*=7.5, C_{qu}), 142.43 (s, C_{qu}), 143.10 (s, C_{qu}), 158.82 (t, *J*=7.5, C_{qu}), 159.55 (t, *J*=8.25, C_{qu}), 159.96 (s, C_{qu}). ^{31}P $\{^1H\}$ NMR (161MHz; CD_2Cl_2) δ_P 45.65 (s).
MS (EI): m/z calcd. for $[C_{48}H_{50}Cl_2O_8P_2Pd]$: 994.1; found 994.2. (Good agreement was found between measured and theoretical isotope patterns).
Anal. calcd. for $C_{48}H_{50}Cl_2O_8P_2Pd$: C, 57.99; H, 5.07; Found : C, 58.18; H, 4.99.
$[\alpha]_D$= +134.3 (c = 2.69, $CHCl_3$).

{{(*R*)-(-)-4,12-bis[bis(3,5-dimethoxyphenyl)phosphino]-[2.2]-*para*-cyclophane}dipalladium(II) tetrachloride}, 5di

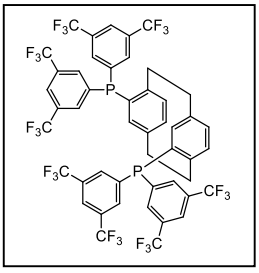


{{(*R*)-(-)-4,12-bis[bis(3,5-dimethoxyphenyl)phosphino]-[2.2]-*para*-cyclophane}palladium(II)chloride} (233 mg, 0.235 mmol) was dissolved in CH_2Cl_2 (15 ml) and $[PdCl_2(PhCN)_2]$ (90 mg, 0.235 mmol) added and stirred overnight. A small sample (0.5ml) was taken ^{31}P $\{^1H\}$ NMR spectroscopy confirming the reaction has gone to completion. Solvent was removed until a few ml of CH_2Cl_2 left and hexane (2 x 20 ml) added to precipitate and wash the complex. After cannula filtration the solution was dried under vacuum, leaving a red crystalline powder in 55% yield (150.2 mg, 0.129 mmol).

^1H NMR (400MHz, $CDCl_3$) δ_H 3.54-3.75 (m, 32H), 6.10-6.14 (m, 3H), 6.23-6.24 (m, 2H), 6.32-6.46 (m, 4H), 6.63 (d, *J*=2.32, 2H), 6.88-7.03 (m, 6H), 7.92-7.97 (m, 1H). ^{13}C NMR (75 MHz, CD_2Cl_2) δ_C 34.78 (s, CH_2), 36.64 (s, CH_2), 55.96 (s, OMe, CH_3), 55.78 (s, OMe, CH_3), 102.49 (s, CH), 103.42 (s, CH), 110.74 (d, *J*=12.75, CH), 125.05 (s, C_{qu}), 125.84 (s, C_{qu}), 131.89 (s, C_{qu}), 132.75 (s, C_{qu}), 135.20 (d, *J*=9.0, CH), 136.83 (d, *J*=12.8, CH), 139.58 (s, CH), 139.85 (s, C_{qu}), 147.26 (s, C_{qu}), 160.23 (d, *J*=12.0, C_{qu}), 160.47 (d, *J*=12.0, C_{qu}). $^{31}P\{^1H\}$ NMR (161MHz; CD_2Cl_2) δ_P 38.69 (s).

MS (CI) (NH_3): m/z calcd. for [$C_{48}H_{50}Cl_4O_8P_2Pd2$] $[M-2Cl]^+$: 1100.04; found 1100.1; $[M-3Cl]^+$ 1066.08; found 1066.07. (Good agreement was found between measured and theoretical isotope patterns).
Anal. calcd. for $C_{48}H_{50}Cl_4O_8P_2Pd_2$: C, 49.21; H, 4.30; Found : C, 49.29; H, 4.24.
$[\alpha]_D$= +708.4 (c = 0.22, $CHCl_3$, 20 °C).

[(R)-(-)-4, 12-Bis(bis (3,5-trifluoromethylphenyl)phosphino)-[2,2]-*para*-cyclophane], L6

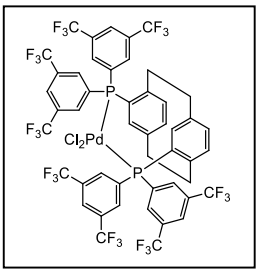


(*R*)-(-)-4, 12-dibromo-[2,2]-*para*-cyclophane (185.8 mg, 0.5075 mmol) was dissolved in dry and degassed Et_2O (25 ml). *n*-BuLi (1.6M in hexane) (3.25 ml, 2.030 mmol) was added dropwise and the reaction stirred for 2.5 hours. Bis(3,5-di(trifluoromethyl)phenyl)chlorophosphine (500 mg, 1.015 mmol) was dissolved in Et_2O (4 ml) and added in one portion added and the reaction stirred overnight. MeOH (5 ml) was added to quench the reaction. Solvents were removed under vacuum. The crude product was washed with MeOH (2 x 20 ml). The product was then dissolved in hexane (10 ml) and degassed water (15 ml) added. The organic layer was collected and solvents removed under vacuum to give the product as an off-white solid in 52 % yield (295.7 mg, 0.2639 mmol).*

*This synthesis worked very well on several occasions but also failed on several occasions. Therefore, this compound was often prepared via the tetrachloride in a highly reproducible manner using the same procedure as given for **L7**.

^{1}H NMR, (300 MHz, $CDCl_3$): δ_H 2.45-2.60 (m, 2H), 2.65-2.82 (m, 2H), 2.82-2.99 (m, 4H), 6.39 (d, J = 10.5, 2H), 6.67-6.74 (m, 4H), 7.86 (s, 2H), 7.91 (d, J = 7.2, 4H), 7.94-8.01 (m, 6H). ^{19}F {^{1}H} NMR (282 MHz, $CDCl_3$) δ_F -63.38 (s, 12F), -63.52 (s, 12F). ^{31}P {^{1}H} NMR (121 MHz, $CDCl_3$) δ_P 0.6 (s).
MS EI+ m/z 1120.1 (M^+ requires 1120.1) (Good agreement was found between measured and theoretical isotope patterns).

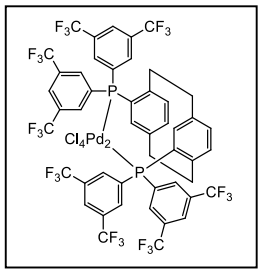
[((R)-(-)-4, 12-Bis(bis (3,5-trifluoromethylphenyl)phosphino)-[2,2]-*para*-cyclophane)palladium]dichloride], 6mo



[(*R*)-(-)-4, 12-Bis(bis (3,5-trifluoromethylphenyl)phosphino)-[2,2]-paracyclophane] (143.0 mg, 0.1276 mmol) was dissolved in CH_2Cl_2 (15 ml) and $[PdCl_2(PhCN)_2]$ (48.9 mg, 0.1276 mmol) added and stirred overnight. A sample was taken for analysis by ^{31}P {^{1}H} NMR to ensure that the reaction had reached completion. Solvent was removed until a few ml of CH_2Cl_2 left and hexane (2 x 20 ml) added to precipitate and wash the complex. The product was collected on a scintered disc (pore size 4) and further washed with hexane (3 x 20 ml) leaving the product as a yellow powder in 91 % yield (146.7 mg, 0.1161 mmol).

^{1}H NMR, (300 MHz, $CDCl_3$): δ_H 2.56-2.80 (m, 8H), 6.64-6.76 (m, 6H), 7.05-7.14 (m, 2H), 8.01 (s, 3H), 8.17 (s, 2H), 8.37 (d, J = 9.1, 5H). ^{19}F NMR {^{1}H} (282 MHz, $CDCl_3$) δ_F -63.59 (s, 12F), -63.67 (s, 12F). ^{31}P {^{1}H} NMR (121 MHz, $CDCl_3$) δ_P 38.9 (s).
MS MALDI$^+$ m/z 1263.0 ($(M-Cl)^+$ requires 1263.0) (Good agreement was found between measured and theoretical isotope patterns).
Anal. calcd. $C_{48}H_{26}F_{24}Cl_2P_2Pd$: C, 44.42; H, 2.02; Found : C, 44.52; H, 2.09. $[\alpha]_D$= +32.9 (c = 0.413, $CHCl_3$).

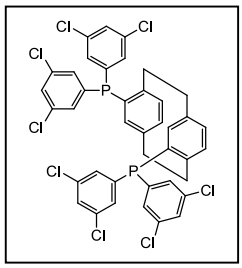
[[(R)-(-)-4, 12-Bis(bis (3,5-trifluoromethylphenyl)phosphino)-[2,2]-*para*-cyclophane)dipalladium]tetrachloride], 6di



[(*R*)-(-)-4, 12-Bis(bis (3,5-trifluoromethylphenyl)phosphino)-[2,2]-paracyclophane] (375.0 mg, 0.3346 mmol) was dissolved in CH_2Cl_2 (8 ml) and $[PdCl_2(PhCN)_2]$ (256.7 mg, 0.6692 mmol) added and stirred overnight. A sample was taken for analysis by ^{31}P $\{^1H\}$ NMR to ensure that the reaction had reached completion. Solvent was removed until a few ml of CH_2Cl_2 left and hexane (2 x 20 ml) added to precipitate and wash the complex. The product was collected on a scintered disc (pore size 4) and further washed with hexane (3 x 20 ml) leaving the product as a red powder in 90 % yield (444.4 mg, 0.3012 mmol).

^1H NMR, (400 MHz, $CDCl_3$): δ_H 2.84-3.11 (m, 6H), 3.32-3.47 (m 2H), 7.19-7.25 (m, 2H), 7.41-7.57 (m, 6H), 7.59-7.82 (m, 5H) 7.87-8.02 (m, 5H). ^{19}F $\{^1H\}$ NMR (282 MHz, $CDCl_3$) δ_F -63.62 (s, 12F), -63.75 (s, 12F). ^{31}P $\{^1H\}$ NMR (161 MHz, $CDCl_3$) δ_P 35.8 (s).
MS EI^+: m/z 1475.9 (M+ requires 1475.8) (Good agreement was found between measured and theoretical isotope patterns).
Anal. calcd. $C_{48}H_{26}F_{24}Cl_4P_2Pd_2$: C, 39.04; H, 1.78; Found : C, 39.14; H, 2.00. $[\alpha]_D$= +113.5 (c = 0.467, $CHCl_3$).

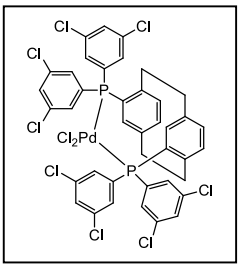
[(R)-(-)-4, 12-Bis(3,5-dichlorophenyl)phosphino)-[2,2]-*para*-cyclophane)], L7



(*R*)-(-)-4, 12-dibromo-[2,2]-paracyclophane (2 g, 5.4631 mmol) was dissolved in dry and degassed Et_2O (50 ml). *n*-BuLi (1.6M in hexane) (8.5 ml, 13.6578 mmol) was added dropwise and the reaction stirred for 1 hour. Bis(diisopropylamino)chlorophosphine (2.915 g, 10.9262 mmol) was added in one portion and the reaction stirred for 30 min. Anhydrous MeOH (20 ml) was added, and the Et_2O removed under vacuum. The precipitate was collected and dried under vacuum. HCl (2M in Et_2O, 50 ml) was added and the reaction stirred for 18 hours. The solvent was removed under vacuum and the solid residue suspended in Et_2O (45 ml). Salts were removed by filtration. The solvent was removed under vacuum and Et_2O (20 ml) and hexane (25 ml) added and the resulting cloudy solution filtered. The solvent was removed and hexane (40 ml) added and the reaction heated to 70 ºC for 10 min. The solution was cooled to rt, filtered and the solvent removed under vacuum to give a tetrachloride species in 38 % yield (0.861 g, 2.099 mmol) as a white solid. The tetrachloride was dissolved in THF (20 ml) and 3,5-dichlorophenylmagnesium bromide solution (0.5M in THF) (16.8 ml, 8.417 mmol) was added dropwise. The reaction was heated to 50 ºC and stirred for 2 hours. The reaction was cooled to rt and a sample was taken for ^{31}P $\{^1H\}$ NMR analysis to assure that the reaction had gone to completion. This sample was returned to the bulk reaction mixture, and the reaction was quenched with MeOH (5 ml). Solvents were removed under vacuum. Hexane (40 ml) was added and the product collected by cannula filtration. Hexane was removed to give the product as a white powder in 47 % yield (18 % overall yield) (838.6 mg, 0.984 mmol).

^1H $\{^{31}P\}$ NMR (400 MHz, $CDCl_3$) 2.57-2.77 (m, 4H), 2.84-2.97 (m, 4H), 6.37 (s, 1H), 6.48-6.62 (m, 4H), 7.14-7.24 (m, 6H), 7.30 (d, J = 1.8, 3H), 7.32-7.41 (m, 2H), 7.45-7.63 (m, 2H). ^{31}P $\{^1H\}$ NMR (121 MHz, $CDCl_3$) δ_P 2.2.
MS EI^+ m/z 851.9 (M^+ requires 851.9) (Good agreement was found between measured and theoretical isotope patterns).

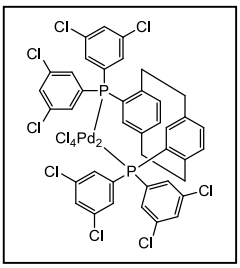
[((R)-(-)-4, 12-Bis(3,5-dichlorophenyl)phosphino)-[2,2]-*para*-cyclophane)palladium]dichloride], 7mo



[((*R*)-(-)-4, 12-Bis(3,5-dichlorophenyl)phosphino)-[2,2]-p*ara*-cyclophane)] (377.5 mg, 0.443 mmol) was dissolved in CH_2Cl_2 (8 ml) and $[PdCl_2(PhCN)_2]$ (170.0 mg, 0.443 mmol) added and stirred overnight. A sample was analysed by ^{31}P $\{^1H\}$ NMR to confirm completion of the reaction. Solvent was removed until a few ml of CH_2Cl_2left and hexane (2 x 20 ml) added to precipitate and wash the complex. The product was collected on a sintered disc (pore size 4) and further washed with hexane (3 x 20 ml) leaving the product as a yellow powder in 42 % yield (191.5 mg, 0.186 mmol).

^1H NMR, (400 MHz, $CDCl_3$): δ_H 1.91-2.09 (m, 2H), 2.55-2.80 (m 6H), 6.50-6.71 (m, 5H), 6.99-7.08 (m, 2H), 7.45 (s, 2H) 7.62 (s, 2H), 7.77 (d, J =9.2, 4H), 7.87-7.90 (m, 3H). ^{31}P $\{^1H\}$ NMR (121 MHz, $CDCl_3$) δ_P 40.6.
MS MALDI$^+$: m/z 992.7 ($(M\text{-}Cl)^+$ requires 992.8) (Good agreement was found between measured and theoretical isotope patterns).
Anal. calcd. $C_{40}H_{26}Cl_{10}P_2Pd$: C, 46.66; H, 2.55; Found : C, 46.44; H, 2.56. $[\alpha]_D$= +79.3 (c = 0.347, $CHCl_3$).

[((R)-(-)-4, 12-Bis(3,5-dichlorophenyl)phosphino)-[2,2]-*para*-cyclophane)dipalladium]tetrachloroide], 7di



[((*R*)-(-)-4, 12-Bis(3,5-dichlorophenyl)phosphino)-[2,2]-*para*-cyclophane)] (244.6 mg, 0.287 mmol) was dissolved in CH_2Cl_2 (8 ml) and $[PdCl_2(PhCN)_2]$ (210.1 mg, 0.574 mmol) added and stirred overnight. A ^{31}P $\{^1H\}$ NMR was taken to confirm completion of the reaction. Solvent was removed until a few ml of CH_2Cl_2 left and hexane (2 x 20 ml) added to precipitate and wash the complex. The product was collected on a sintered disc (pore size 4) and further washed with hexane (3 x 20 ml) leaving the product as a red powder in 49 % yield (116.5 mg, 0.141 mmol).

^1H NMR, (300 MHz, $CDCl_3$): δ_H 2.85-3.12 (m, 6H), 3.38-3.56 (m, 2H), 6.88 (d, J = 11.8, 6H), 7.09-7.19 (m, 4H), 7.24 (s, 2H), 7.39 (s, 2H), 7.51-7.61 (m, 2H), 7.94 (d, J = 16.1, 2H). ^{31}P {H} NMR (121 MHz, $CDCl_3$) δ_P 35.8.
MS MALDI$^-$: m/z 1207.6 (M^- requires 1207.6) (Good agreement was found between measured and theoretical isotope patterns).
Anal. calcd. $C_{40}H_{26}Cl_{12}P_2Pd_2$: C, 39.81; H, 2.17; Found : C, 40.02; H, 2.30. $[\alpha]_D$= +632.9 (c = 0.353, $CHCl_3$).

General procedure for hydroxycarbonylation of styrene

Lithium chloride (8.4 mg, 0.20 mmol), *para*-toluenesulfonic acid (34.4 mg, 0.20 mmol) and $[LPd_xCl_y]$ (L = diphosphine) (0.01mmol) were weighed into a Biotage 5 ml microwave vial. A magnetic stirrer bar was added and the vial was sealed with a crimp cap and put under an inert atmosphere. Styrene (114 µl, 1 mmol), degassed water (45 µl, 2.5 mmol), degassed 2-butanone (1.5 ml) and in most instances an internal standard (approximately 10µl of either tetraethylsilane or more commonly 1-methylnaphtalene) were added using a syringe. The solution was mixed before 20 µl of the solution was diluted in $CDCl_3$ and analysed using ^1H NMR (to give a t_0 spectra that calibrates the internal standard against starting material). The caps were pierced with two needles and quickly placed in an autoclave that had previously been placed under an argon atmosphere before being opened under a flow of argon. The autoclave was sealed, purged three times with CO and then pressurised to 30 bar and heated in a preheated oil bath or heating jacket with constant magnetic stirring. After the desired time, the autoclave was cooled to room temperature and the pressure released slowly. The mixture was then analysed by taking a sample, diluting with $CDCl_3$ and obtaining a ^1H NMR spectrum. The solvent was carefully removed from the reaction mixture and the residue was dissolved in toluene and extracted 3 times with saturated $NaHCO_3$ solution

and the combined extracts were acidified with conc. HCl. The solution was then extracted 3 times with ethyl acetate and the combined organic layers were dried over $MgSO_4$, filtered and the solvent removed to give chemically pure regio-isomers 2-phenylpropanoic and 3-phenylpropanoic acid. The enantiomeric excess was determined by HPLC, using a Chiracel OD-H column, 250 x 4.6 mm, 5 μm with guard cartridge, 0.5 mL min^{-1}, 97:3:0.1 hexane : *iso*-propanol: trifluoroacetic acid, t_R[(+)-*S*] = 19 min, t_R[(–)-*R*] = 17 min, t_R[linear] = 21 min.

NMR data for catalysis products

2-phenylpropanoic acid[4] :

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (3H, d, J = 7.2, CH_3), 3.7 (1H, q, J = 7.2, CH), 7.2 (5H, m, ArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3, 45.5, 127.5, 127.7, 128.8, 139.8, 181.2.

3-phenylpropanoic acid[5] :

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.6 (2H, t, J = 7.7, CO-CH_2), 2.9 (2H, t, J = 7.7, CH_2), 7.2 (5H, m, ArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.6, 35.7, 126.4, 128.3, 128.6, 140.2, 179.6.

GC-MS: MS (EI): m/z calcd. for [$C_9H_{10}O_2$] : 150.17; found 149.0.

General procedure for methoxycarbonylation of styrene

Lithium chloride (8.4 mg, 0.20 mmol), *para*-toluenesulfonic acid (34.4 mg, 0.20 mmol) and [LPd_xCl_y] (L = diphosphine) (0.01mmol) were weighed into a Biotage 5 ml microwave vial. A magnetic stirrer bar was added and the vial was sealed with a crimp cap and put under inert atmosphere. Styrene (1 mmol), dry and degassed methanol (1.5 ml) and an internal standard (approximately 10µl of either tetraethylsilane or 1-methylnaphtalene) were added using a syringe. The solution was mixed before 20 µl of the solution was diluted in $CDCl_3$ and analysed using ^{1}H NMR (to give a t_0 spectra that calibrates the internal standard against starting material). The caps were pierced with two needles and quickly placed in an autoclave that had previously been placed under an argon atmosphere before being opened under a flow of argon. The autoclave was sealed, purged three times with CO and then pressurised to 30 bar and heated in a preheated oil bath or heating jacket with constant magnetic stirring. After the desired time, the autoclave was cooled to room temperature and the pressure released slowly. The mixture was then analysed by taking a sample, diluting with $CDCl_3$ and obtaining a ^{1}H NMR spectrum. The solvent was carefully removed from the reaction mixture and the crude product was filtered through a small column packed with SiO_2 eluting with hexane: ethylacetate 8:1. The solvent was removed to give colourless chemically pure mixture of linear methyl-3-phenylpropanoate and branched methyl-2-phenylpropanoate. The enantiomeric excess was determined by HPLC, using a Chirapak AD-H, 250 x 4.6 mm, 5 μm with guard cartridge, *n*-hexane 100%, 0.5 mL min^{-1}, 210 nm, t_R[(+)-*S*] = 17.9 min, t_R[(–)-*R*] = 20.0 min, t_R[linear] = 25.1 min.

The absolute configuration of the ester was determined by comparison of the sign of the optical rotation with the literature values.[4b] In some cases, the enantiomeric excess was determined by chiral GC, using a MEGA-DEX DMP Beta (stationary phase), 0.25 µl filmthickness, 0.25 mm internal diameter, 25 m length. Linear methyl-3 phenylpropanoate t_R[linear] = 20.00 min; branched methyl-2-phenylpropanoate t_R[(+)-S] = 17.24 min, t_R[(+)-R] = 17.38 min, t_R[linear] = 19.9 min.

NMR data for catalysis products

Methyl-2-phenylpropanoate[6] :

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.42 (d, J = 9, CH_3, 3H), 3.57 (s, CH_3, 3H), 3.65 (q, J = 9 Hz, CH, 1H), 7.07-7.28 (m, ArH, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.6, 45.5, 52.1, 127.2, 127.5, 128.7, 140.5, 175.1.

Methyl-3-phenylpropanoate[7] :

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.55 (t, J = 7.5, CH_2, 2H), 2.87 (t, J = 7.5, CH_2, 2H), 3.58 (s, OCH_3, 3H), 7.07-7.28 (m, ArH, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.0, 35.7, 51.7, 126.3, 128.3, 128.5, 173.4.

GC-MS: MS (EI): m/z calcd. for [$C_{10}H_{12}O_2$] : 164.20; found 164.0.

General procedure for hydroxycarbonylation of aryl-alkenes

Lithium chloride (4.2 mg, 0.10 mmol), *para*-toluenesulfonic acid (17.2 mg, 0.10 mmol), [LPd_xCl_y] (L = diphosphine) (0.005 mmol) and the aryl-alkene (0.5 mmol) were weighed into a Biotage 5 ml microwave vial. A magnetic stirrer bar was added and the vial was sealed with a crimp cap and put under inert atmosphere. Degassed water (22.5 µl, 1.25 mmol), degassed 2-butanone (1.5 ml) and internal standard (approximately 10µl of 1-methylnaphtalene or tetraethylsilane) were added using a syringe. The solution was mixed before taking a crude ^{1}H NMR sample (for t_0 NMR approximately 20 µl of solution were

taken). The caps were pierced with two needles and placed in the autoclave that was put under inert atmosphere and opened under argon flow before quickly sealed. The autoclave was purged three times with CO and then pressurised to 30 bar and heated in a preheated oil bath or heating jacket. After the desired time, the autoclave was cooled to room temperature and the pressure released slowly. The mixture was stirred before taking another ^{1}H NMR sample (for t_1 NMR approximately 20 µl of solution were taken for calculating % product). The solvent was carefully removed from the reaction mixture and the residue was dissolved in toluene and filtered to remove precipitate. The toluene filtrate was extracted 3 times with saturated $NaHCO_3$ solution and the combined extracts were acidified with conc. HCl. The solution was then extracted 3 times with ethyl acetate and the combined organic layers were dried over $MgSO_4$, filtered and the solvent removed to give a mixture of branched and linear acids.

2-(4-Chlorophenyl)propionoic acid
^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.42 (d, J = 7.2, 3H), 3.63 (q, J = 7.2, 1H), 7.17 (d, J = 8.6, 2H), 7.22 (d, J = 8.6, 2H), 11.00 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 18.1 (CH_3), 44.8 (CH), 128.8 (2CH), 129.0 (2CH), 133.3 (C_{qu}), 138.1 (CCl), 180.6 (CO_2H). MS CI$^+$: m/z 139.0 (100%), 184.0 (12%, M^+), 185.0 (20%, $M+H^+$). HPLC Chiralpak AD-H, 0.7 ml/min, 98:2:0.1 hexane:iso-propanol:TFA. R_t: 32 min [(*R*)-enantiomer], 36 min [(*S*)-enantiomer]. $[\alpha]_D$ = -30.4 (c = 4.0, $CHCl_3$, ee = 66%(*R*)) {lit.[8] $[\alpha]_D$ = +48.5 (c = 4.0, $CHCl_3$, ee = 98%(*S*)}.

3-(4-Chlorophenyl)propionoic acid[9]
^{1}H NMR (300 MHz, $CDCl_3$): δ_H 2.65 (t, J = 7.5, 2H), 2.91 (t, J = 7.5, 2H), 7.13 (d, J = 8.5, 2H), 7.25 (d, J = 8.5, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 30.3 (CH_2), 35.4 (CH_2), 128.6 (2CH), 130.1 (2CH), 132.0 (C_{qu}), 139.5 (CCl), 175.0 (CO_2H). GC MS: MS (EI): m/z calcd. for [$C_9H_9O_2Cl$]: 184.03 found 184.0.

2-(4-*tert*-butylphenyl)propionoic acid[2]
^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.32 (s, 9H), 1.51 (d, J = 7.2, 3H), 3.72 (q, J = 7.2, 1H), 7.26 (d, J = 8.4, 2H), 7.36 (d, J = 8.4, 2H), 10.24 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 18.1 (CH_3), 31.3 ($3CH_3$) 34.5 (C_{qu}) 44.8 (CH) 125.6 (2CH), 127.2 (2CH), 136.6 (C_{qu}), 150.3 (C_{qu}) 180.7 (CO_2H). MS CI$^+$: m/z 191.10 (100%), 206.1 (20%, M^+) 207.14 (10%, $M+H^+$). HPLC Chiralpak AD-H, 0.5 ml/min, 95:5:0.1 hexane:iso-propanol:TFA. R_t: 21 min [(*R*)-enantiomer], 23 min [(*S*)-enantiomer].

3-(4-*tert*-butylphenyl)propionoic acid[2]
^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.33 (s, 9H), 2.69 (t, J = 8.0, 2H), 2.95 (t, J = 8.0, 2H), 7.21 (d, J = 8.5, 2H), 7.29 (d, J = 8.5, 2H). ^{13}C NMR (75 MHz, CDCl3): δ_C 30.0 (CH_2), 31.4 ($3CH_3$), 34.5 (C_{qu}), 35.6 (CH_2), 125.5 (2CH), 128.0 (2CH), 137.3 (C_{qu}) 149.2 (C_{qu}), 179.6 (CO_2H). GC MS: MS (EI): m/z calcd. for [$C_{13}H_{18}O_2$]: 206.1 found 206.0.

***para*-(1-carboxy-ethyl)benzoic acid**
^{1}H NMR (300 MHz, CD_2Cl_2*): δ_H 1.42 (d, J = 7.2, 3H), 3.70 (q, J = 7.2, 1H), 7.35 (d, J = 8.2, 2H), 7.92 (d, J = 8.2, 2H). ^{13}C NMR (100 MHz, $CDCl_3$*): δ_C 18.3 (CH_3), 45.4 (CH) 127.5 (2CH), 129.5 (C_{qu}) 130.0 (2CH), 145.9 (C_{qu}), 168.3 (CO_2H) 175.9 (CO_2H). MS ES$^-$: m/z calcd. for [$(M-H^+)^-$] : 193.05; found 193.05. HPLC Chiralcel OD-H, 0.5 ml/min, 95:5:0.1 hexane:iso-propanol:TFA. R_t: 29 min [(*S*)-enantiomer], 34 min [(*R*)-enantiomer]. $[\alpha]_D$ = -28.5 (c = 0.533, MeOH, ee = 66%).
*A drop of deuterated DMSO was added for solubility purposes.

***para*-(2-carboxy-ethyl)benzoic acid**
^{1}H NMR (300 MHz, $CDCl_3$): δ_H 2.54 (t, J = 7.5, 2H), 2.91 (t, J = 7.5, 2H), 7.22 (d, J = 8.1, 2H), 7.87 (d, J = 8.1, 2H). MS ES$^-$: m/z calcd. for [$(M-H^+)^-$] : 193.05; found 193.05.

2-(2-Chlorophenyl)propionoic acid
^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.54 (d, J = 7.2, 3H), 4.28 (q, J = 7.2, 1H), 7.18-7.31 (m, 2H), 7.33-7.42 (m, 2H), 11.42 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 17.6 (CH_3), 42.3 (CH), 127.5 (CH), 128.8 (CH), 128.9 (CH), 130.0 (CH), 134.2 (C_{qu}), 137.9 (CCl), 180.7 (CO_2H). MS NESI$^-$: m/z calcd. for [$(M-H^+)^-$] : 183.02; found 183.02. HPLC Chiralpak IC, 0.5 ml/min, 100:1:0.1 hexane:iso-propanol:TFA. R_t: 29 min [(*S*)-enantiomer], 37 min [(*R*)-enantiomer]. $[\alpha]_D$ = -33.2 (c = 1.0, $CHCl_3$, ee = 60%(*R*)) {lit.[10] $[\alpha]_D$ = +32.8 (c = 1.31, $CHCl_3$, ee = 55%(*S*)}.

2-(3-Fluorophenyl)propionoic acid
^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.39 (d, J = 7.2, 3H), 3.61 (q, J = 7.2, 1H), 6.80-7.00 (m, 3H), 7.10-7.22 (m, 1H), 11.33 (br s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ_C 18.3 (CH_3), 45.4 (CH), 114.9 (app. t, J = 21.3, 2CH), 123.7 (d, J = 2.8, CH), 130.5 (d, J = 8.4, CH), 142.3 (d, J = 7.4, C_{qu}), 163.2 (d, J = 246.4, CF), 180.8 (CO_2H).
MS NESI$^-$: m/z calcd. for $[(M\text{-}H^+)^-]$: 167.05; found 167.05.
HPLC Chiralcel OD-H, 0.5 ml/min, 95:5:0.1 hexane:iso-propanol:TFA. R_t: 19 min [(*R*)-enantiomer], 24 min [(*S*)-enantiomer].
$[\alpha]_D$ = -29.0 (c = 0.42, $CHCl_3$, ee = 73%(*R*)) {lit.[11] $[\alpha]_D$ = -68 (c = unknown, $CHCl_3$, ee = 97%(*R*)}.

2-(4-Biphenylyl)propionoic acid
^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.57 (d, J = 7.2, 3H), 3.81 (q, J = 7.2, 1H), 7.31-7.38 (m, 1H), 7.39-7.48 (m, 4H), 7.54-7.61 (m, 4H).
^{13}C NMR (100 MHz, $CDCl_3$): δ_C 18.5 (CH_3), 45.3 (CH), 127.4 (CH), 127.7 (CH), 127.8 (CH), 128.4 (CH), 129.1 (CH), 139.1 (C_{qu}), 140.8 (C_{qu}), 141.1 (C_{qu}), 180.3 (CO_2H).
MS NESI$^-$: m/z calcd. for $[(M\text{-}H^+)^-]$: 225.09; found 225.09. HPLC Chiralcel OD-H, 0.5 ml/min, 95:5:0.1 hexane:iso-propanol:TFA. R_t: 33 min [(*R*)-enantiomer], 40 min [(*S*)-enantiomer]. $[\alpha]_D$ = -32.8 (c = 0.80, $CHCl_3$, ee = 62%(*R*)) {lit.[12] $[\alpha]_D$ = +46.7 (c = 1.0, $CHCl_3$, ee = 91%(*S*)}.

Synthesis of 4-Phenylstyrene

4-Vinylphenylboronic acid (443.9 mg, 3 mmol), K_2CO_3 (552.8 mg, 4 mmol) and [$PdCl_2$(Phanephos)] (6.0 mg, 0.008 mmol) were weighed out into a dry schlenk flask, which was placed under an inert atmosphere. Dry and degassed toluene (8 ml) was added via syringe, followed by bromobenzene (210 µl, 2.0 mmol). The reaction was heated to 100 °C and stirred overnight. The reaction mixture was then cooled to room temperature and concentrated under vacuum. Purification by column chromatography (hexane : EtOAc, 4:1) gave the white solid product in 80 % yield (289.2 mg, 1.60 mmol %).
^{1}H NMR (300 MHz, $CDCl_3$): δ_H 5.28 (dd, J = 0.9, 10.9, 1H), 5.80 (dd, J = 0.9, 17.6, 1H), 6.77 (dd, J = 10.9, 17.6, 1H) 7.31-7.38 (m, 1H), 7.41-7.52 (m, 4H), 7.55-7.64 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 114.3 (CH_2), 127.0 (2CH), 127.3 (2CH), 127.6 (2CH), 127.7 (CH), 129.1 (2CH), 136.7 (C_{qu}), 136.9 (C_{qu}), 140.9 (C_{qu}), 141.0 (C_{qu}). MS CI$^+$: m/z calcd. for $[(M+H^+)^+]$: 181.10; found 181.10.

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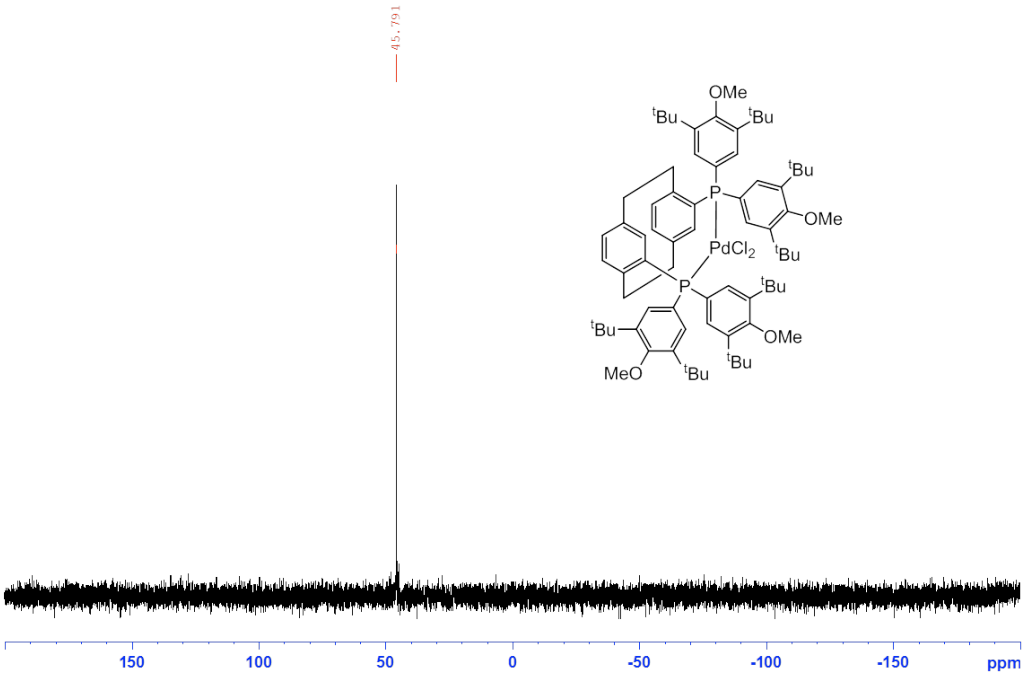
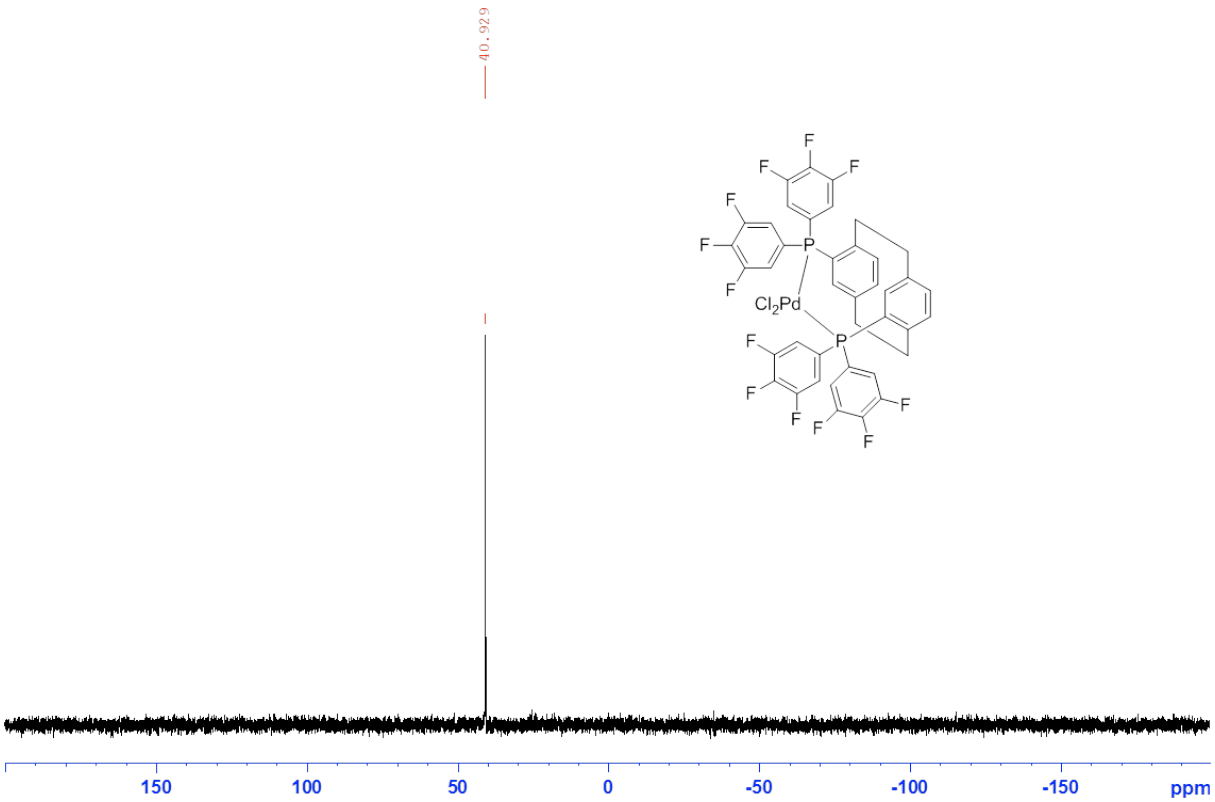
{{(*S*)-(+)-4,12-bis[bis-(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-[2.2]-*para*-cyclophane}palladium(II)chloride}, 3mo

^{31}P {H} NMR



{{(*R*)-(-)-4,12-bis[bis-(3,4,5-trifluorophenyl)phosphino]-[2.2]-*para*-cyclophane}palladium(II) dichloride}, 4mo

^{31}P {H} NMR



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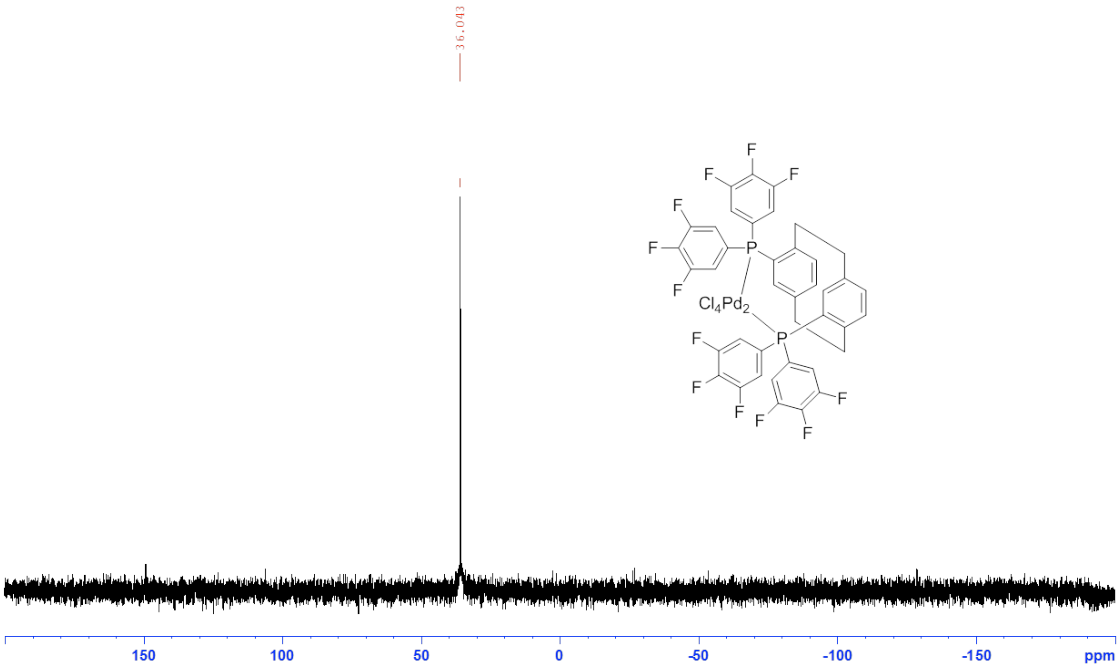
^{31}P {H} NMR



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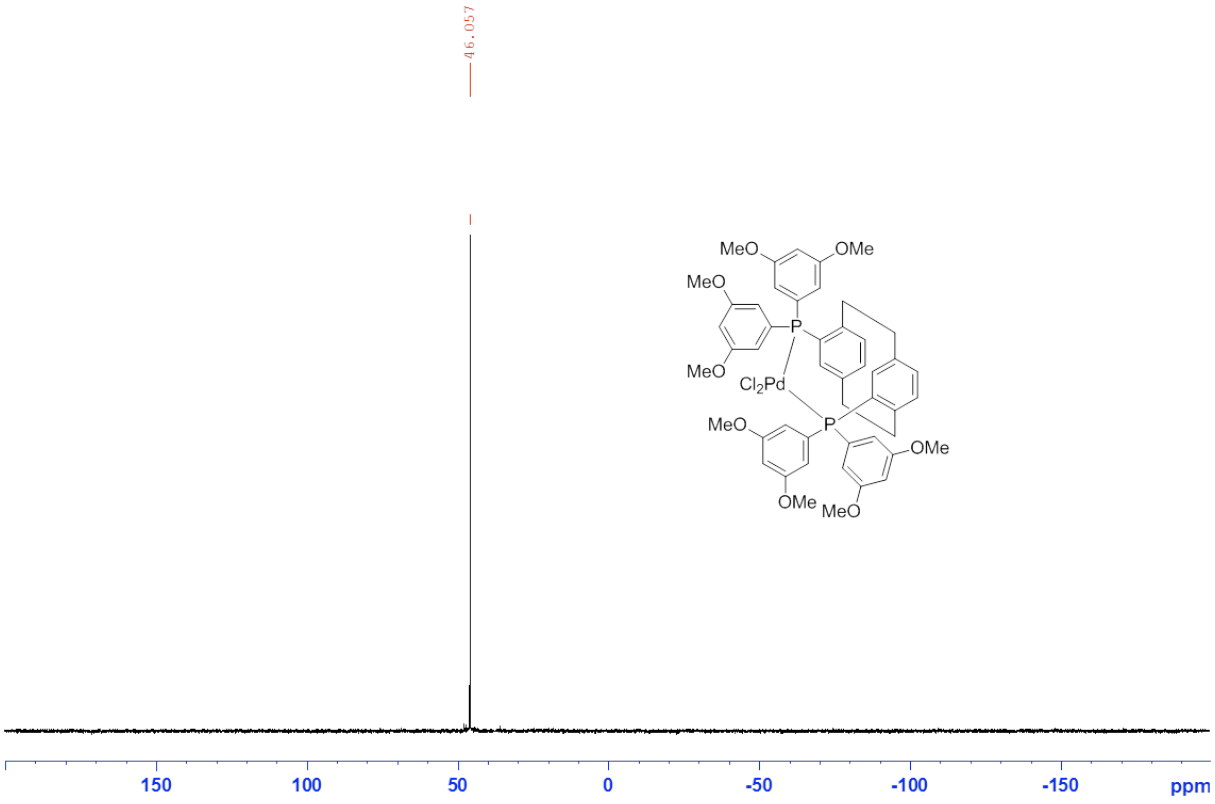
^{31}P {H} NMR



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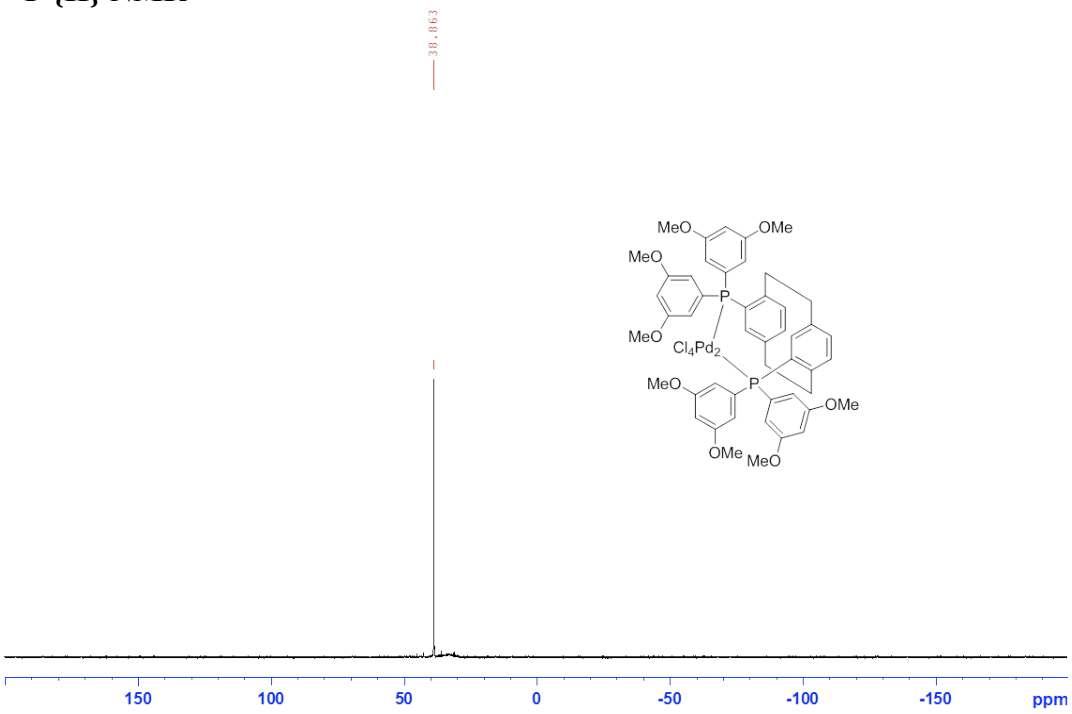
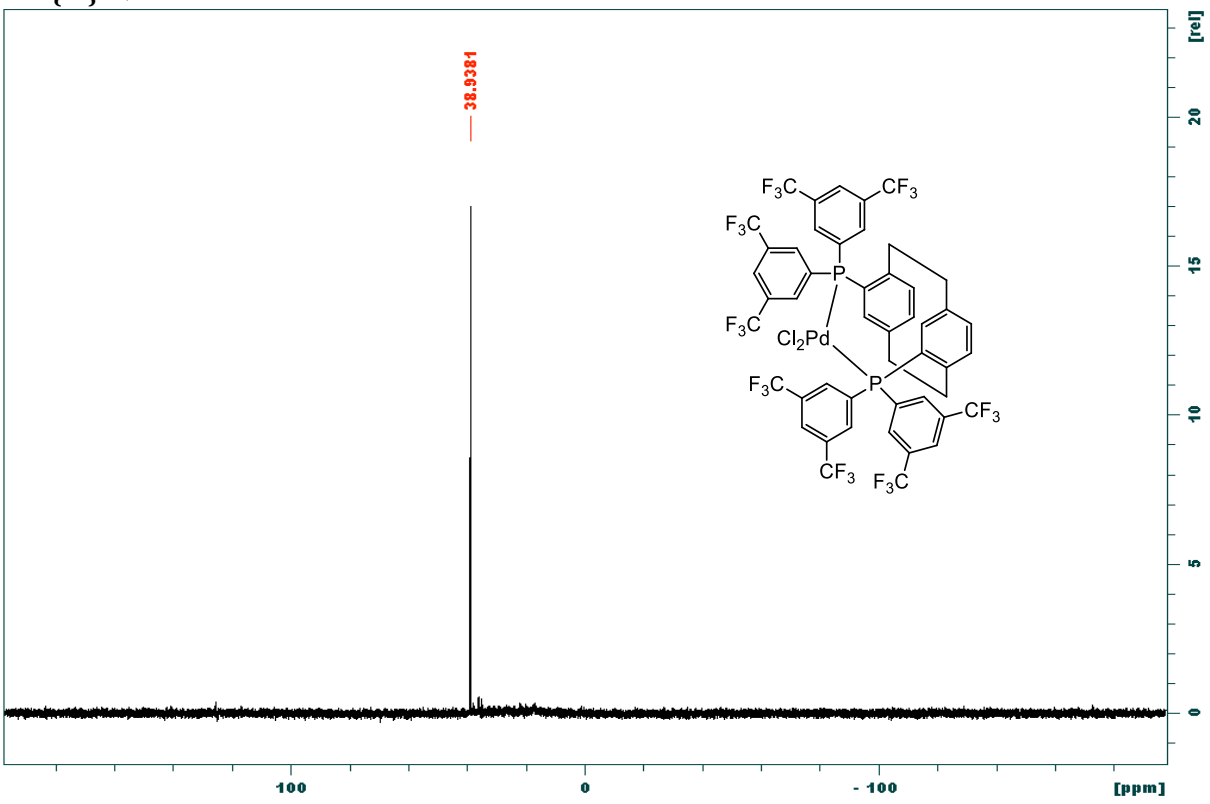
^{31}P {H} NMR



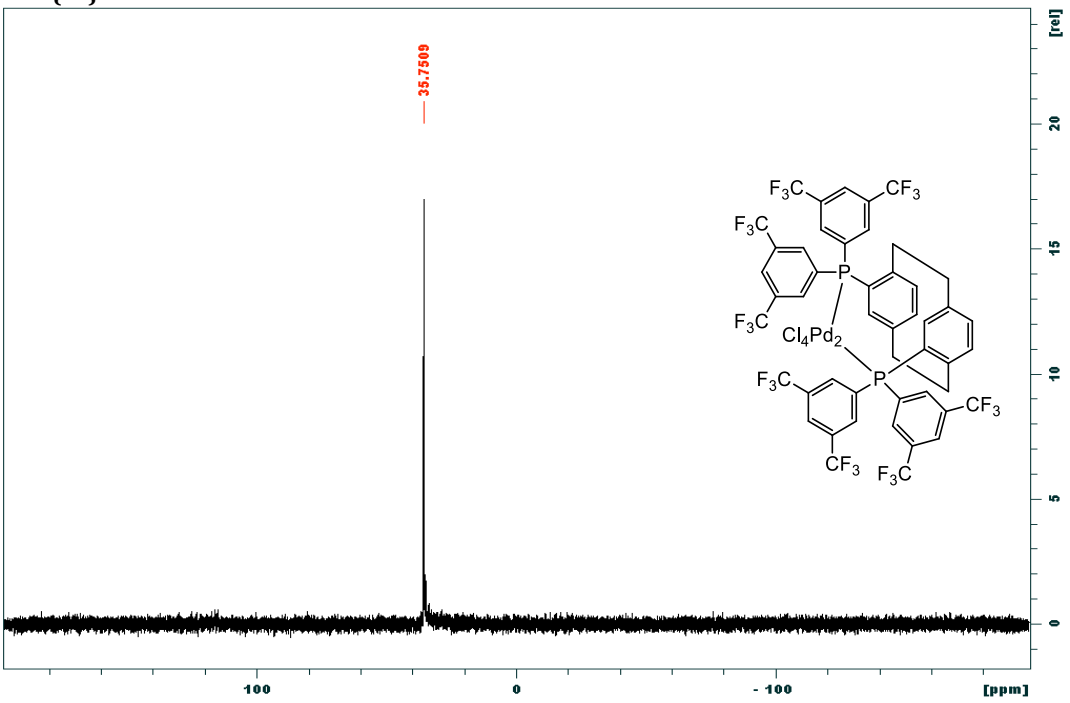
[((R)-(-)-4, 12-Bis(bis (3,5-trifluoromethylphenyl)phosphino)-[2,2]-*para*-cyclophane)palladium]dichloride], 6mo

^{31}P {H} NMR



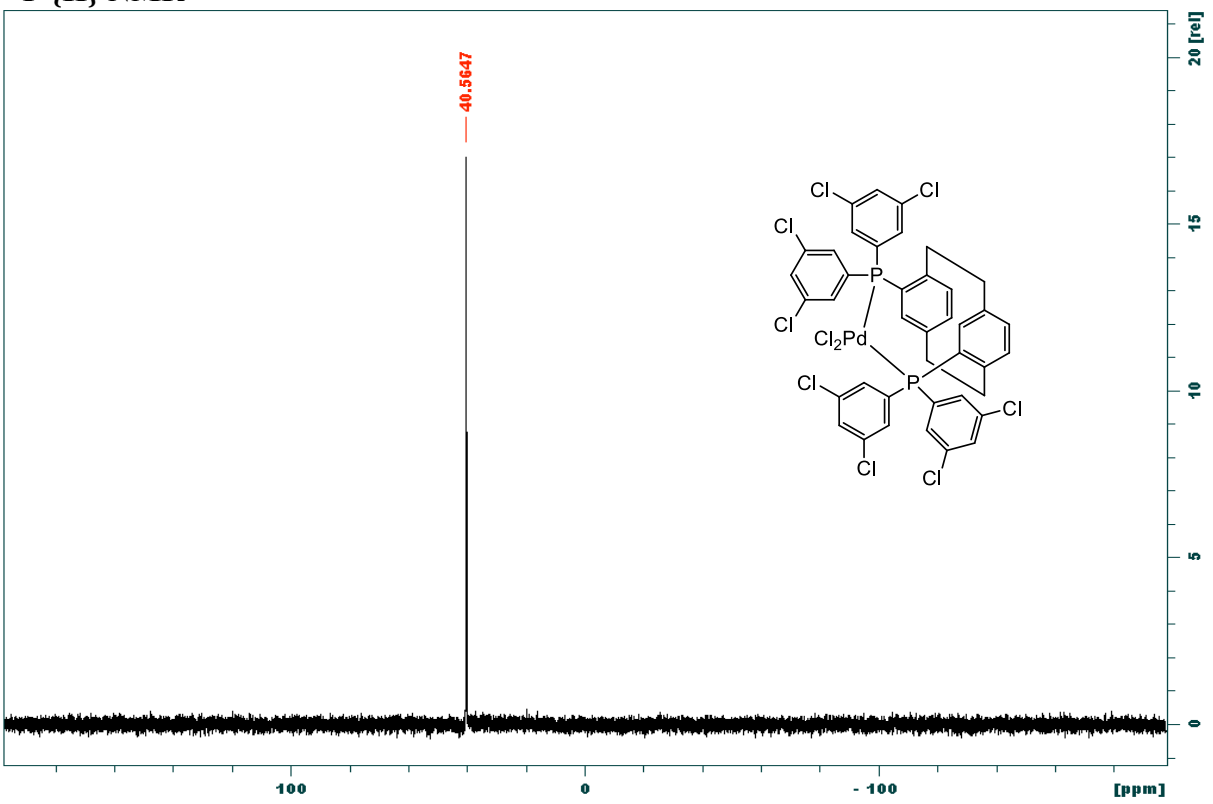
[[(R)-(-)-4, 12-Bis(bis (3,5-trifluoromethylphenyl)phosphino)-[2,2]-*para*-cyclophane)dipalladium]tetrachloride], 6di

^{31}P {H} NMR



[(R)-(-)-4, 12-Bis(3,5-dichlorophenyl)phosphino)-[2,2]-*para*-cyclophane)palladium]dichloride], 7mo

^{31}P {H} NMR



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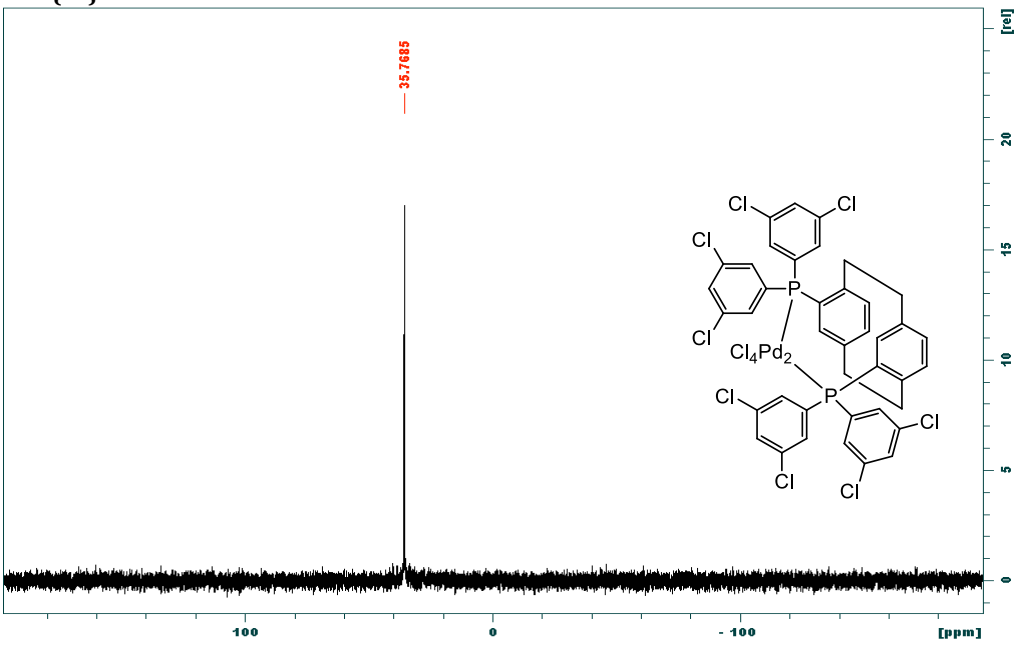
^{31}P {H} NMR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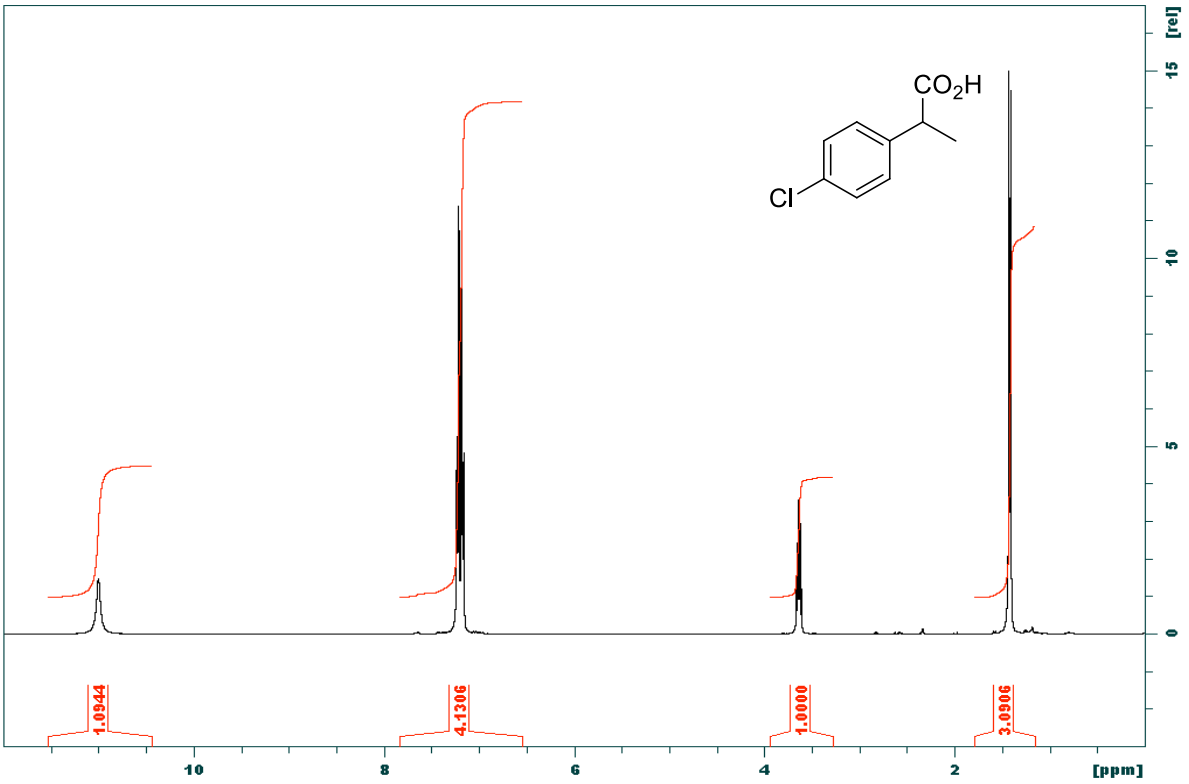
2-(4-Chlorophenyl)propionoic acid

^{1}H NMR



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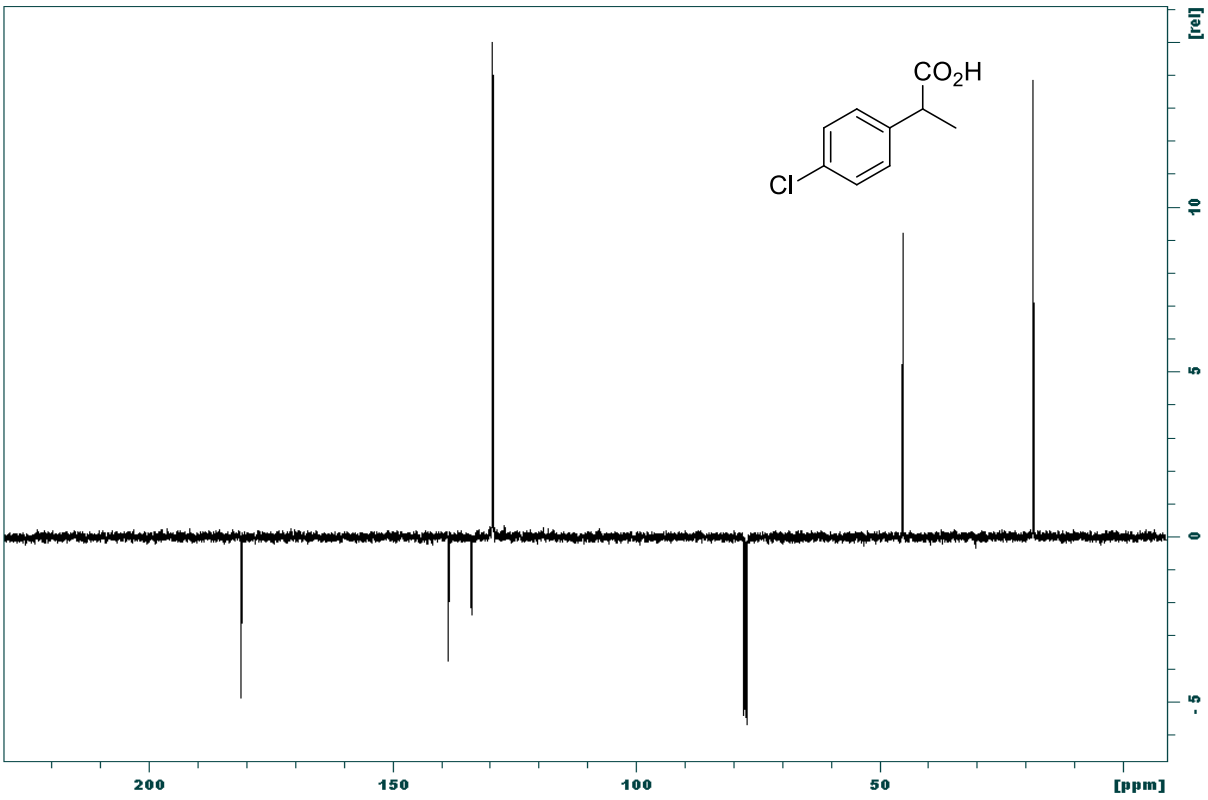
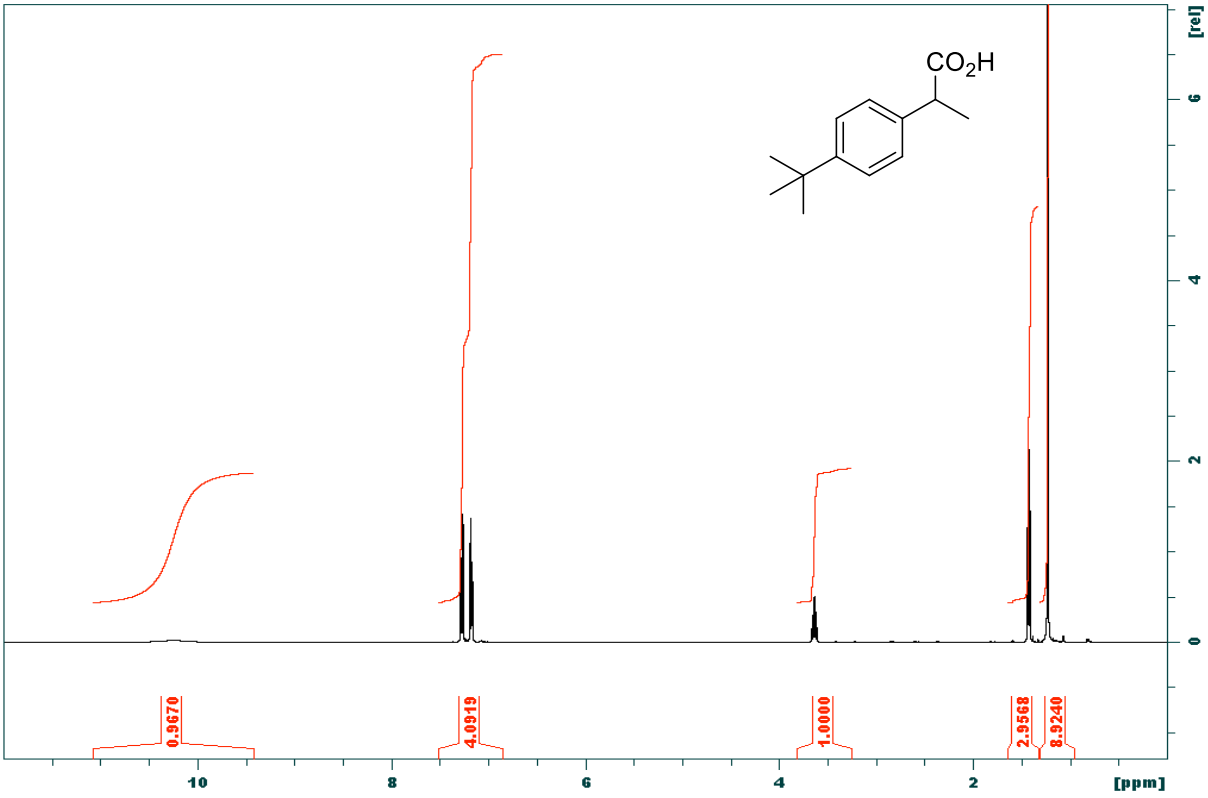
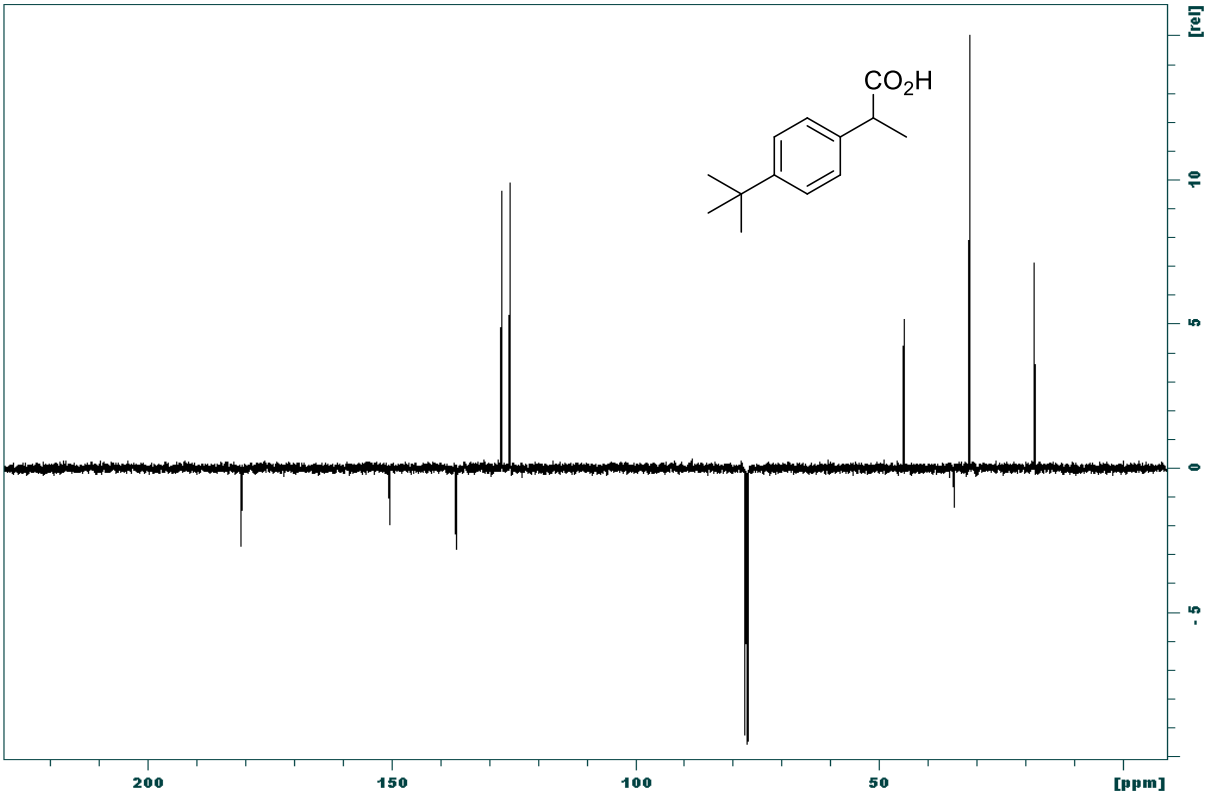


2-(4-*tert*-butylphenyl)propionoic acid[2]

^{1}H NMR

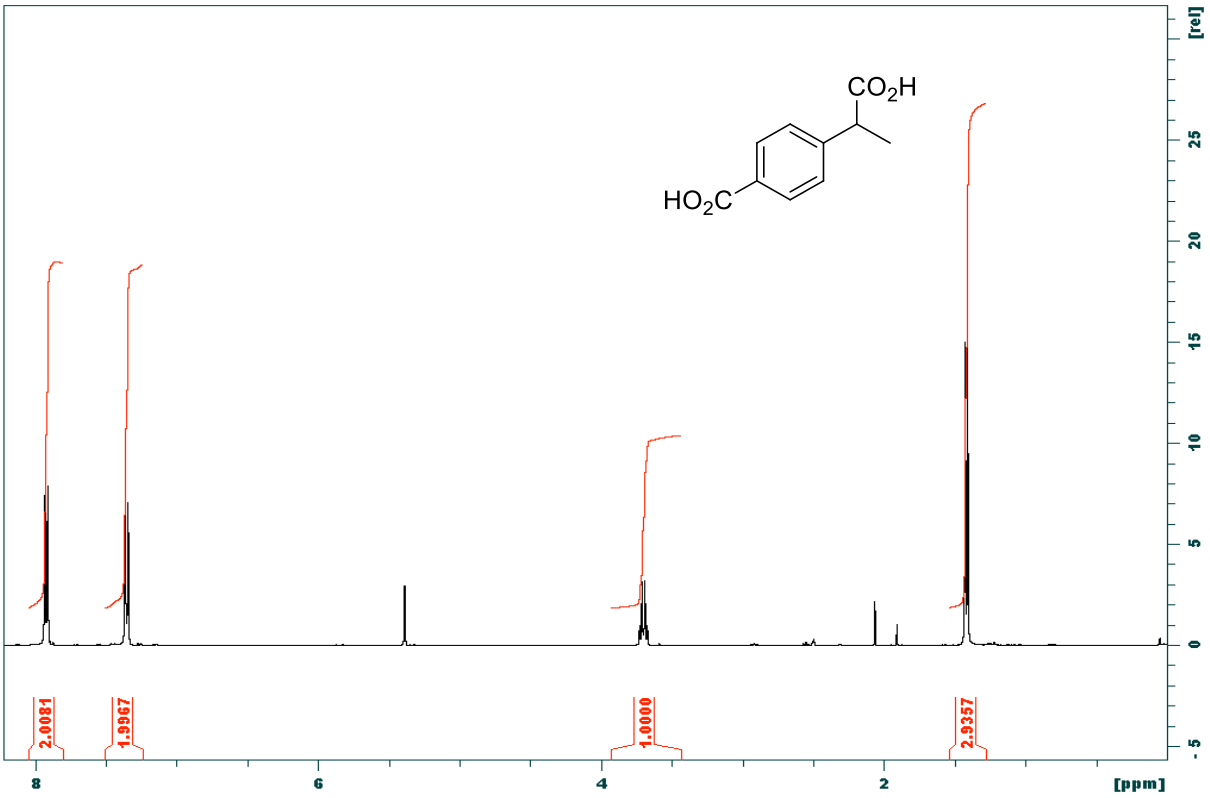


^{13}C NMR

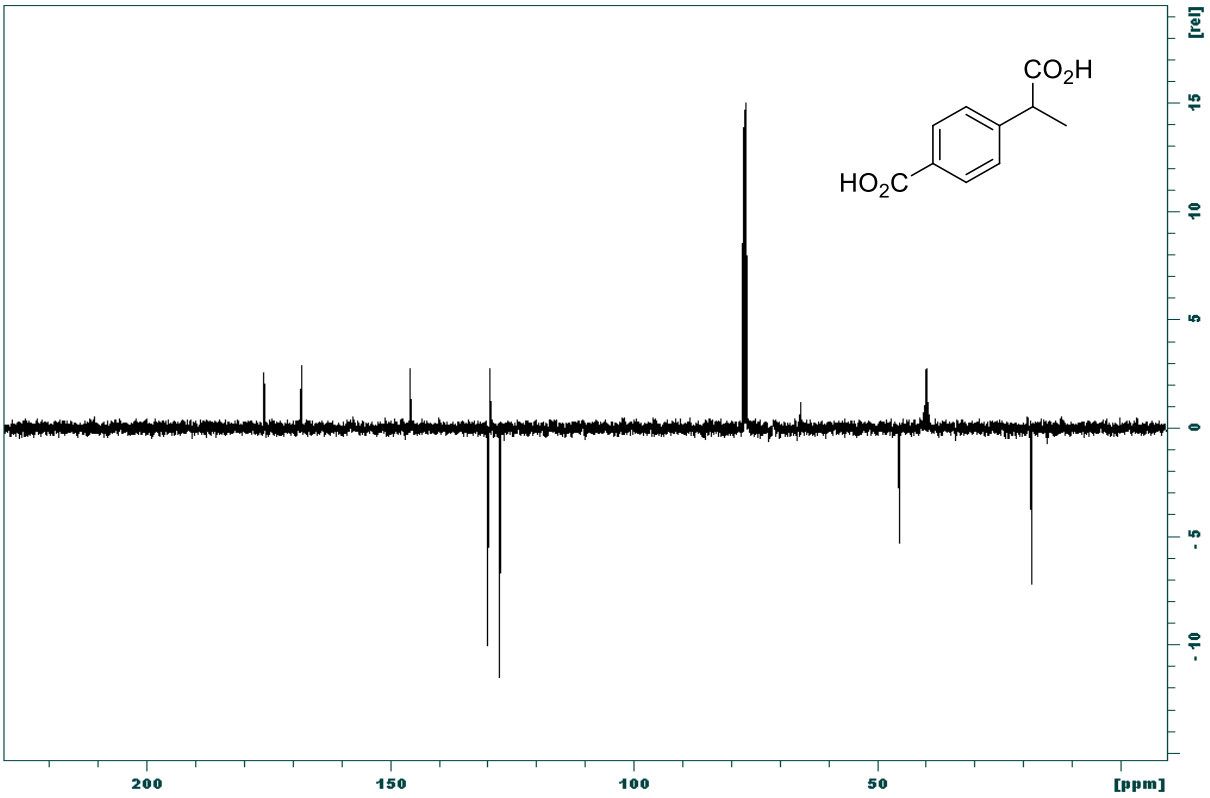


para-(1-carboxy-ethyl)benzoic acid

^{1}H NMR

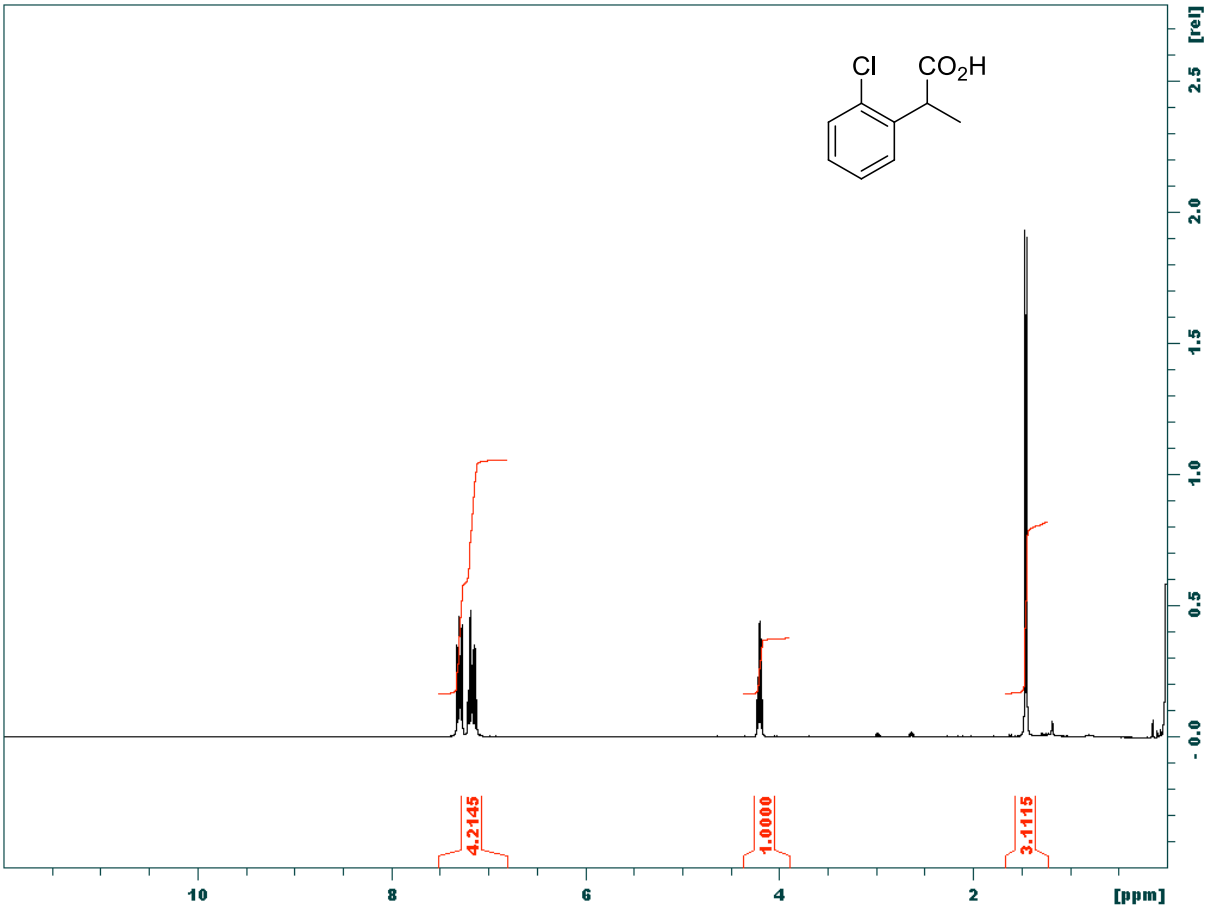


^{13}C NMR

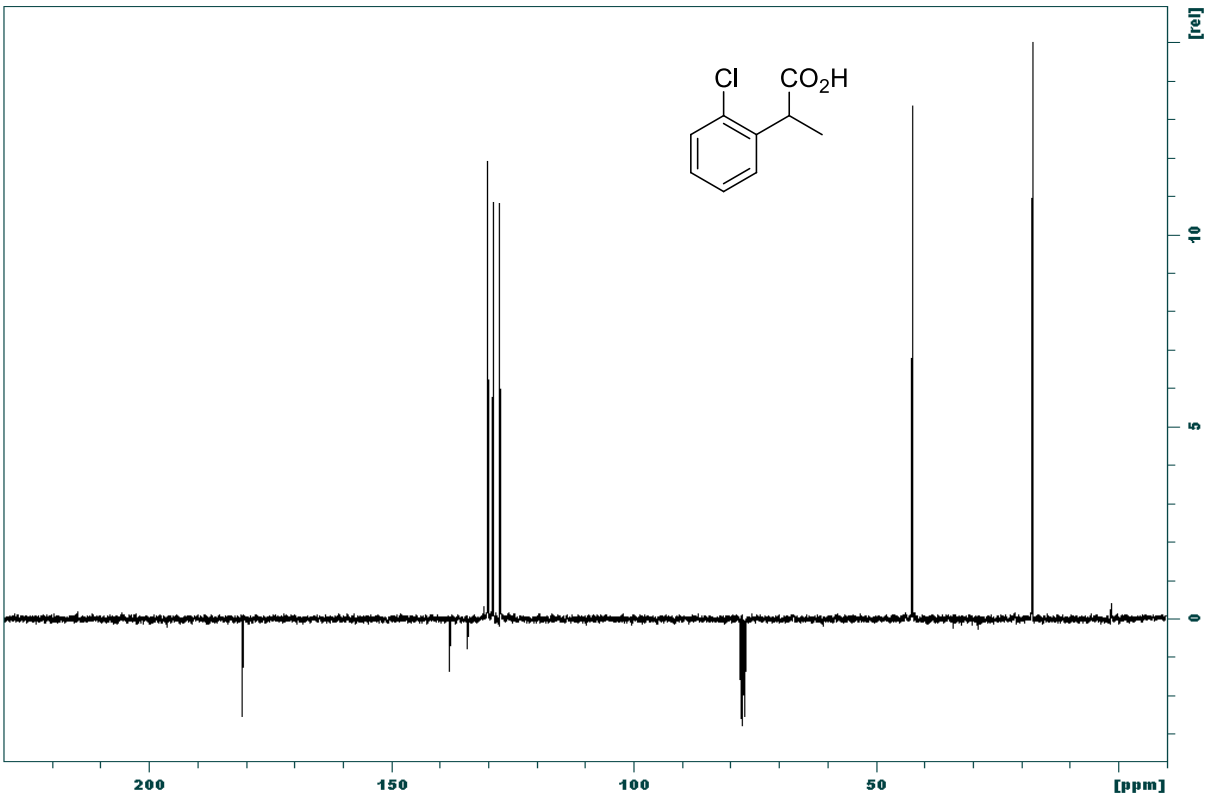


2-(2-Chlorophenyl)propionoic acid

^{1}H NMR

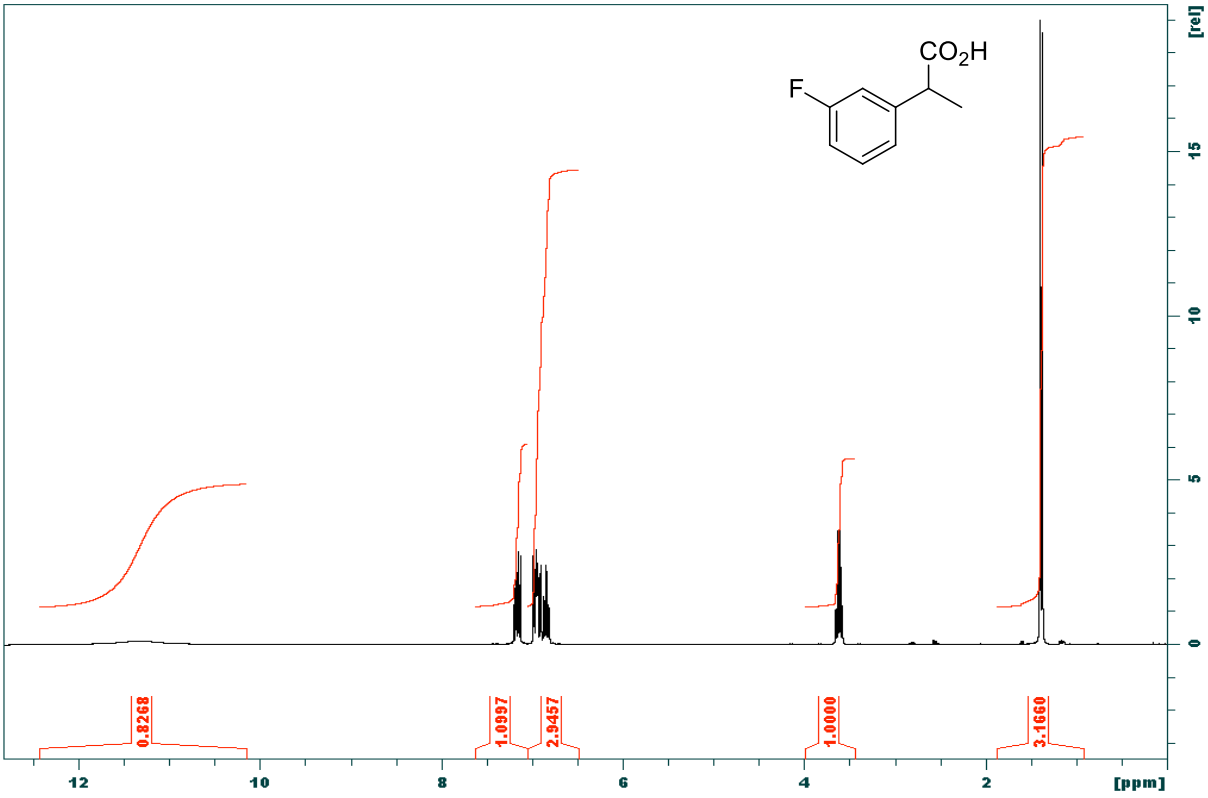


^{13}C NMR

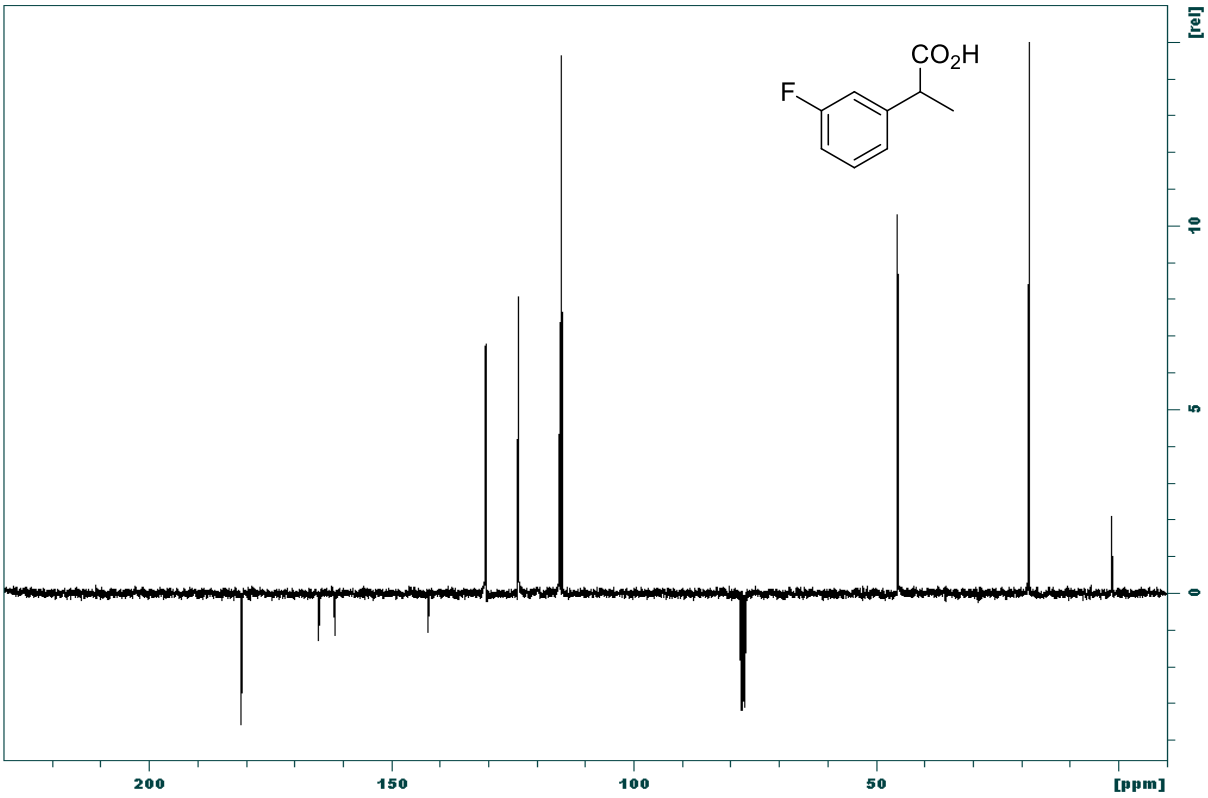


2-(3-Fluorophenyl)propionoic acid

^{1}H NMR

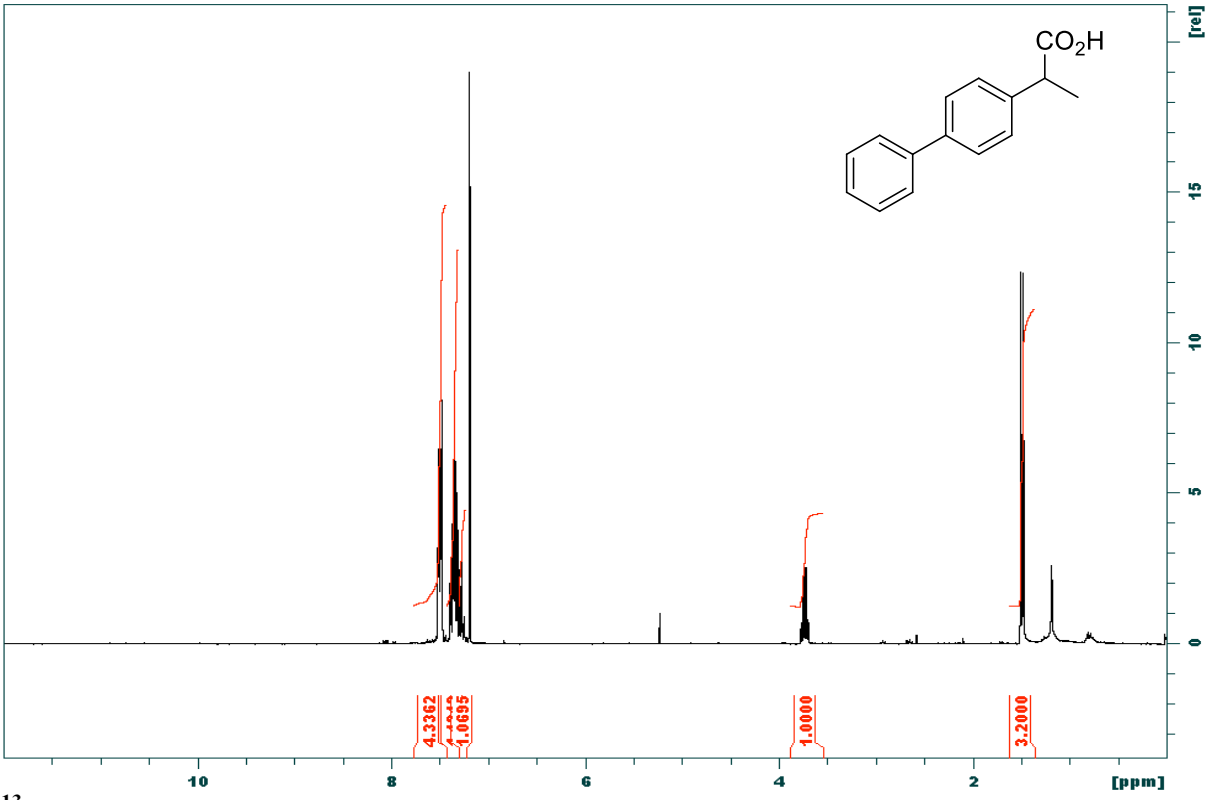


^{13}C NMR

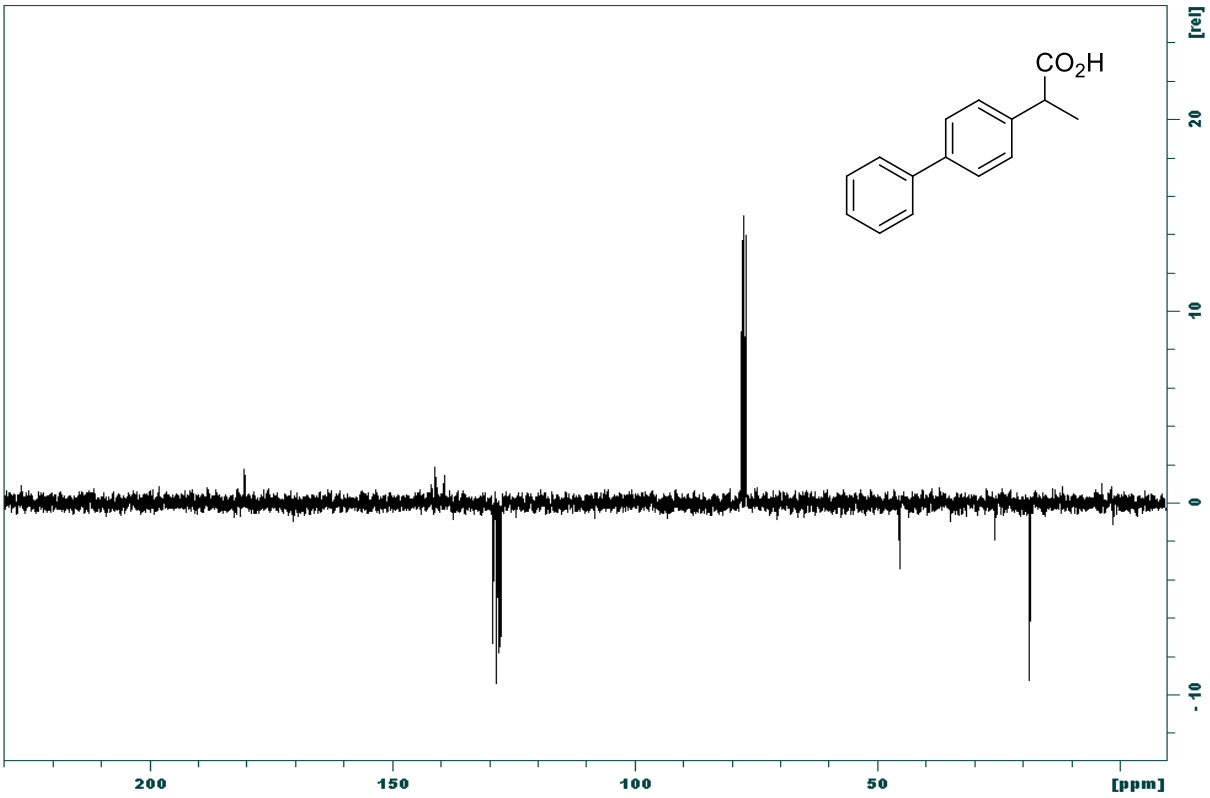


2-(4-Biphenylyl)propionoic acid

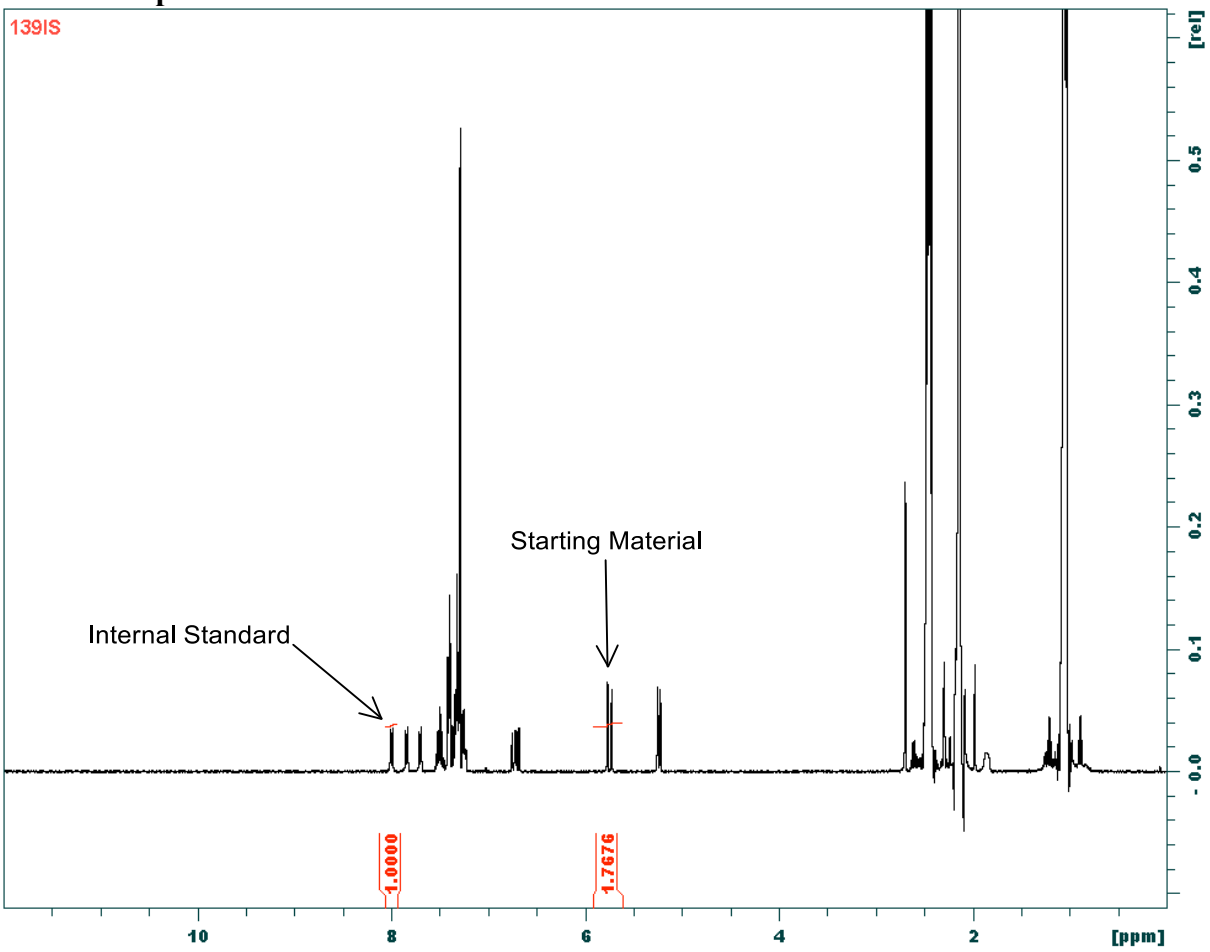
^{1}H NMR



^{13}C NMR



Example crude ^{1}H NMR for determination of conversion in hydroxycarbonylation reaction of styrene.
Before CO pressurization:



After pressure release: