Supporting Information

Direct Carboxylation of Simple Arenes with CO₂ through a Rhodium-Catalyzed C-H Bond Activation
Takuya Suga, Hajime Mizuno, Jun Takaya and Nobuharu Iwasawa*
Department of Chemistry, Tokyo Institute of Technology, O-okayama, Meguro-ku, Tokyo 152-8551, Japan

Table of Contents

p2-p3  1) General information
p3    2) Preparation of aluminum reagents
p3-p5  3) Preparation of rhodium complexes
p5-p6  4) Rhodium-catalyzed carboxylation of simple aromatic compounds
p6-p7  5) Mechanistic studies
p7-p8  6) Appendix for optimization of the reaction conditions
p8-p9  7) References
1) General information

All operations were performed under an argon atmosphere. $^1$H, $^{13}$C, $^{27}$Al, $^{31}$P-NMR spectra were recorded on JEOL ECX-500 (500MHz for $^1$H, 125 MHz for $^{13}$C, 130 MHz for $^{27}$Al, and 200 MHz for $^{31}$P) or Bruker DRX-500 (125 MHz for $^{13}$C) using tetramethylsilane ($^1$H, $\delta = 0.00$), $C_6D_6$ ($^1$H, $\delta = 7.15$), C$_6D_6$ ($^{13}$C, $\delta = 77.0$), C$_6D_6$ ($^{13}$C, $\delta = 128.0$) as internal standards and 1.5 mol/L Al(NO$_3$)$_3$ aq. ($^{27}$Al, $\delta = 0.00$), 85 % H$_3$PO$_4$ aq. ($^{31}$P, $\delta = 0.00$) as an external standard. IR spectra were recorded on an FT/IR-460 plus (JASCO Co., Ltd.) with ATR PRO450-S accessory (JASCO Co., Ltd.). Mass spectra were recorded on a JEOL JMS-700. Elemental analyses were performed on an elementar vario MICRO. Silica Gel 60 (Kanto Chemical Co., Inc.) was used for column chromatography. Merck Kieselgel 60 F254 plate (0.25 mm thickness, coated on glass 20x20 cm$^2$) was used for analytical thin layer chromatography (TLC), and Wakogel B-5F coated on glass in a thickness of 0.9 mm was used for preparative TLC.

Dehydrated dimethylacetamide was purchased from Sigma-Aldrich co., LLC. Tetramethyleurea was purchased from Tokyo Chemical Industry co. LTD. Ethanol was distilled according to the usual procedure and stored over Molecular Sieves. AlMe$_3$ (solution in hexane) was purchased from Sigma-Aldrich co. LLC. and Tokyo Chemical Industry co., LTD.

Xylenes 3d, 3e, 3f, anisole (99.8+ %, dehydrated) 3l, $\alpha,\alpha,\alpha$-trifluorotoluene 3j and 1,2-bis(dicyclohexylphosphino)ethane were purchased from Sigma-Aldrich co., LLC. 1,2-Bis(diethylphosphino)ethane, benzene 3a and cumene 3c were purchased from Wako Chemical Pure Industries, LTD. Fluorobenzene 3i, benzo-1,4-dioxane 3o, 2-chloro-$m$-xylene 3p, $N,N$-dimethylaniline 3m, 2,3-benzofuran 3q, 1-methylindole 3r, 1,3-bis(trifluoromethyl)benzene 3n and phenyl(trimethyl)silane 3k were purchased from Tokyo Chemical Industry co., LTD. Toluene 3b, naphthalene 3h and ferrocene 3s were purchased from Kanto Chemical Co., Inc.

All the liquid materials were distilled, degassed by argon bubbling, and stored in the glovebox. [RhCl(coe)$_2$]; and [RhCl(cod)]$_2$ were prepared by the known procedure. 1-(Trimethylsilyl)benzene carboxylic acid $\beta$-4k, $^x$-4-(trimethylsilyl)benzene carboxylic acid $\gamma$-4k, $^x$ benzo[b]furan-2-carboxylic acid 4q, $^x$ 1-methylindole-2-carboxylic acid $\alpha$-4r, $^x$ 1-methylindole-3-carboxylic acid $\beta$-4r, $^x$ and ferrocene carboxylic acid 4s$^{xii}$ were characterized by comparing their spectral data with literature values after isolation as their corresponding methyl esters.
3-(Dimethylamino)benzenecarboxylic acidβ-4m was identified by comparing its spectral data with those of the authentic sample purchased from Kanto Chemical Co., Inc.

2) Preparation of aluminum reagents

Preparation of AlMe₅(OEt)₃-n

AlMe₁.₅(OEt)₁.₅ was prepared by the following procedure.

\[
\text{AlMe}_3 + 2 \text{EtOH} \rightarrow \text{AlMe}_{1.5}(\text{OEt})_{1.5}
\]

To a solution of AlMe₃ (15w% in hexane, 100 mL, 137 mmol) was carefully added EtOH (16.0 mL, 274 mmol) dropwise at 0 °C under nitrogen. (Caution: methane gas evolved intensively.) After evolution of the gas ceased, the mixture was concentrated in vacuo at room temperature and the residual sticky solid was collected in a glovebox.

Based on its \(^1\)H-NMR, the ratio of methyl group and ethoxy group was determined to be almost 1 : 1. 23.2 mg of this reagent contained 0.306 mmol of methyl group based on \(^1\)H-NMR with mesitylene (benzylic 9H) as an internal standard. This value is consistent with that of AlMe₁.₅(OEt)₁.₅, 23.2 mg of which should contain 0.297 mmol of methyl group. NOE between protons of a methyl group and those of a methylene group of ethoxy moiety suggests this is a discrete complex, not a mixture such as AlMe₃ : Al(OEt)₃ = 1 : 1. \(^{27}\)Al-NMR suggested the presence of the 4-coordinated aluminum (\(\delta = 155.6 \text{ ppm} \)) and 6-coordinated aluminum (\(\delta = 7.30 \text{ ppm} \))\(^{xiii}\).

The spectra of the major product was as follows; \(^1\)H-NMR (500 MHz, C₆D₆) \(\delta = 3.74\)–3.83 (m, 1.5H), 3.50–3.60 (m, 1.5H), 1.08 (t, \(J = 7.2 \text{ Hz} \), 4.5H), -0.50 (s, 3H); \(^{27}\)Al-NMR (130 MHz, C₆D₆) \(\delta = 155.6 \text{ (broad), } 7.30 (s) \).

A mixture of AlMe₃ : EtOH = 1 : 1 was also prepared as a colorless oil according to this procedure except 1 equiv. of EtOH was used instead of 2 equiv.

3) Preparation of rhodium complexes

Synthesis of [1,2-bis(diethylphosphino)ethane]rhodium(I) chloride dimer 1a

\[
[RhCl(coe)]_2 \rightarrow [1,2\text{-bis(diethylphosphino)ethane}]\text{Rhodium(I) chloride dimer }1a
\]

In a glovebox, a solution of 1,2-bis(diethylphosphino)ethane (124 mg, 0.6 mmol) in THF (30 mL) was added dropwise to a solution of [RhCl(coe)]₂ (217 mg, 0.3 mmol) in THF (30 mL) and the
mixture was stirred for 5 h at room temperature. The mixture was concentrated to ca. 15 mL and pentane (ca. 60 mL) was added. After 1 day, a brown precipitate was filtered off and the filtrate was concentrated to give the title compound in 69 % yield (143 mg, 0.42 mmol) as a yellow powder.

\[^1\text{H-NMR}\ (500 \text{ MHz}, \text{C}_6\text{D}_6) \delta 1.75–1.86 \text{ (m, 4H)}, 1.36–1.46 \text{ (m, 4H)}, 1.19–1.27 \text{ (m, 12H)}, 0.96 \text{ (d, } J = 14.3 \text{ Hz, 4H}); \[^{13}\text{C-NMR}\ (125 \text{ MHz}, \text{C}_6\text{D}_6) \delta 25.2 \text{ (td, } t = 23.3, 6.0 \text{ Hz)}, 22.8 \text{ (t, } t = 23.7 \text{ Hz)}, 9.86 \text{ (s);} \[^{31}\text{P-NMR}\ (200 \text{ MHz}, \text{C}_6\text{D}_6) \delta 85.1 \text{ (d, } J = 194 \text{ Hz)}; \text{HR-MS (FAB\(^{+}\))}: \text{Calcd for C}_{20}\text{H}_{48}\text{Cl}_2\text{P}_4\text{Rh}_2 [M]^{+}: 688.0194; \text{Found: 688.0191.}\]

### Synthesis of [1,2-bis(diisopropylphosphino)ethane]rhodium(I) chloride dimer 1b

[1,2-Bis(diisopropylphosphino)ethane]rhodium(I) chloride dimer 1b was prepared according to the procedure for the synthesis of [RhCl(dcype)]\(_2\) 1c except 1,2-bis(diisopropylphosphino)ethane was used instead of dcype (61 % yield).

\[^1\text{H-NMR}\ (500 \text{ MHz}, \text{C}_6\text{D}_6) \delta 1.99–2.08 \text{ (m, 4H)}, 1.49 \text{ (dd, } J = 14.6, 7.2 \text{ Hz, 12H)}, 1.02 \text{ (dd, } J = 12.6, 6.9 \text{ Hz, 12H)}, 0.94 \text{ (d, } J = 11.5 \text{ Hz, 4H}); \[^{13}\text{C-NMR}\ (125 \text{ MHz}, \text{C}_6\text{D}_6) \delta 26.7 \text{ (t, } t = 11.5 \text{ Hz)}, 22.0 \text{ (td, } J = 21.2, 6.1 \text{ Hz)}, 20.5 \text{ (s), 18.8 (s);} \[^{31}\text{P-NMR}\ (200 \text{ MHz}, \text{C}_6\text{D}_6) \delta 102.6 \text{ (d, } J = 194 \text{ Hz);} \text{HR-MS (FAB\(^{+}\))}: \text{Calcd for C}_{28}\text{H}_{64}\text{Cl}_2\text{P}_4\text{Rh}_2 [M]^{+}: 800.1446; \text{Found: 800.1456.}\]

### Synthesis of [1,2-bis(dicyclohexylphosphino)ethane]rhodium(I) chloride dimer 1c

In a glovebox, 1,2-bis(dicyclohexylphosphino)ethane (353 mg, 0.84 mmol) was added to a suspension of [RhCl(coe)]\(_2\) (300 mg, 0.42 mmol) in toluene (15 mL) and the mixture was stirred for 2 h. The resulting mixture was filtered through Celite and the filtrate was concentrated in vacuo. Recrystalization from toluene/pentane in a refrigerator gave the title compound in 69 % yield (320 mg, 0.29 mmol) as an orange-yellow powder.

\[^1\text{H-NMR}\ (500 \text{ MHz}, \text{C}_6\text{D}_6) \delta 2.62 \text{ (d, } J = 12.6 \text{ Hz, 8H)}, 1.83–1.99 \text{ (m, 16H)}, 1.49–1.83 \text{ (m, 40H), 1.13–1.43 \text{ (m, 24H)}, 1.05 \text{ (d, } J = 11.5 \text{ Hz, 8H});} \[^{13}\text{C-NMR}\ (125 \text{ MHz}, \text{C}_6\text{D}_6) \delta 36.4 \text{ (t, } t = 11.3 \text{ Hz)}, 29.8 \text{ (d, } J = 83.5 \text{ Hz), 27.8 (broad d, } J = 45.3 \text{ Hz) 26.9, 22.8–23.2 (m);} \[^{31}\text{P-NMR}\ (200 \text{ MHz}, \text{C}_6\text{D}_6) \delta 95.5 \text{ (d, } J = 199 \text{ Hz)}; \[^{31}\text{P-NMR}\ (200 \text{ MHz, CDCl}_2) \delta 94.6 \text{ (d, } J = 200 \text{ Hz);}\]
Anal. Calcd for C_{52}H_{96}Cl_{2}P_{4}Rh_{2}: C, 55.67; H, 8.62; Found: C, 55.76; H, 8.51.
NMR spectra of the product were consistent with the literature values.xiv

4) Rhodium-catalyzed carboxylation of simple aromatic compounds

Procedure for the preparation of benzoic acid derivatives: a typical procedure was described

for the reaction of benzene.

A solution of [RhCl(dcyype)]_2 1c (5.6 mg, 0.005 mmol), DMA (0.1 mL), TMU (6 µL, 0.05 mmol) and AlMe_{1.5}(OEt)_{1.5} (132 mg, 1.1 mmol) in benzene 3a (2 mL) was stirred in a glass tube (φ = 2.0 cm, 18 cm) at room temperature for a few minutes, and then the system was purged with an atomospheric pressure of CO_2. The mixture was heated at 85 °C (outer temperature) for 6 h in the closed system. 2N HCl aq. and diethyl ether were added and the mixture was vigorously stirred for a few minutes. The mixture was filtered, extracted with diethyl ether three times, and the combined organic layer was extracted with NaOH aq. three times. The combined aqueous layer was acidified with HCl aq., then extracted with diethyl ether three times, and the extract was dried over MgSO_4. After removal of solvent under reduced pressure, the residue was purified by silica-gel column chromatography (CH_2Cl_2 : AcOEt = 9 : 1) to give benzoic acid 4a as a white solid (44.5 mg, 0.37 mmol).

Formation of acetic acid was also detected. As the rate-determining step is the C-H activation step, the amount of CO_2 such as the volume of the reaction vessel might affect the formation of acetic acid and the desired aryl carboxylic acid. So the use of the indicated apparatus is recommended. Detailed analysis is now in progress.

A mixture of 3-chloro-2,4-dimethylbenzenecarboxylic acid α-4p and 4-chloro-3,5-dimethylbenzenecarboxylic acid β-4p

$^1$H-NMR (500 MHz, CDCl_3) for α-4p : δ 7.82-7.81 (d, J = 8.0 Hz, 1H), 7.16 (d, J = 8.0 Hz, 1H), 2.71 (3H, s), 2.44 (3H, s); for β-4p : δ 7.82 (s, 2H), 2.43 (s, 6H); $^{13}$C-NMR (125 MHz, CDCl_3) δ 173.0, 171.9, 141.9, 140.9, 138.8, 136.9, 136.6, 130.0, 129.2, 128.5, 127.9, 126.9, 21.7, 20.8, 18.1; IR (ATR) 1685, 1424, 1251, 1047, 769 cm\(^{-1}\); HR-MS (EI\(^+\)) : Caled for C_9H_9ClO_2 [M] \(^+\) : 184.0291; Found: 184.0266; White solid.
The compounds shown below were characterized after isolation as their corresponding methyl esters by treatment with TMSCHN$_2$ (2.0 M sol. in Et$_2$O, 1.0 ml, 2.0 mmol) in Et$_2$O-MeOH (4:1, 7.5 ml) at 0 °C in 50 ml one-necked flask under nitrogen, followed by purification by PTLC.

**Methyl-1,4-benzodioxane-5-carboxylate α-5o**

![Structure](image)

$^1$H-NMR (500 MHz, CDCl$_3$) δ 7.39 (dd, $J = 8.0$ Hz, 1.6 Hz, 1H), 7.02 (dd, $J = 8.0$ Hz, 3H); $^{13}$C-NMR (125 MHz, CDCl$_3$) δ 166.0, 144.1, 144.0, 123.7, 121.3, 120.3, 120.0, 64.6, 63.8, 52.0; IR (ATR) 1714, 1435, 1317, 1285, 1223, 1047, 770 cm$^{-1}$; HR-MS (EI$^+$): Calcd for C$_{10}$H$_{10}$O$_4$ [M$^+$]: 194.0579; Found: 194.0544; White solid.

**Methyl-1,4-benzodioxane-6-carboxylate β-5o**

![Structure](image)

$^1$H-NMR (500 MHz, CDCl$_3$) δ 7.56 (s, 1H), 7.55 (d, $J = 8.4$ Hz, 1H), 6.88 (d, $J = 8.4$ Hz, 1H), 4.33-4.25 (m, 4H), 3.87 (s, 3H); $^{13}$C-NMR (125 MHz, CDCl$_3$) δ 166.6, 147.7, 143.1, 123.4, 118.9, 117.1, 64.6, 64.0, 51.9, one aromatic carbon overlaps; IR (ATR) 1703, 1584, 1440, 1287, 1201, 1061, 880, 766 cm$^{-1}$; HR-MS (EI$^+$): Calcd for C$_{10}$H$_{10}$O$_4$ [M$^+$]: 194.0579; Found: 194.0547; White solid.

**Methyl 3-chloro-2,4-dimethylbenzenecarboxylate α-5p**

![Structure](image)

$^1$H-NMR (500 MHz, CDCl$_3$) δ 7.62 (d, 1H, $J = 8.0$ Hz), 7.12 (d, 1H, $J = 8.0$ Hz), 3.89 (s, 3H), 2.63(s, 3H), 2.42(s, 3H); $^{13}$C-NMR (125 MHz, CDCl$_3$) δ 168.0, 140.5, 137.5, 136.3, 129.9, 128.0, 127.7, 52.1, 21.4, 17.9; IR (ATR) 1717, 1435, 1267, 1241, 1210, 1101, 1013, 765 cm$^{-1}$; HR-MS (EI$^+$): Calcd for C$_{10}$H$_{11}$ClO$_2$ [M$^+$]: 198.0448; Found: 194.0416; White solid.

**Methyl 4-chloro-3,5-dimethylbenzenecarboxylate β-5p**

![Structure](image)

$^1$H-NMR (500 MHz, CDCl$_3$) δ 7.75 (s, 2H), 3.90 (s, 3H), 2.41 (s, 6H); $^{13}$C-NMR (125 MHz, CDCl$_3$) δ 166.7, 139.7, 136.5, 129.3, 127.7, 52.1, 20.7; IR (ATR) 1715, 1594, 1435, 1315, 1223, 1044, 769 cm$^{-1}$; HR-MS (EI$^+$): Calcd for C$_{10}$H$_{11}$ClO$_2$ [M$^+$]: 198.0448; Found: 194.0418; White solid.

5) Mechanistic studies

**Procedure for the KIE experiment**
The KIE of the reaction between benzene-$d_0$ 3a-$d_0$ and benzene-$d_6$ 3a-$d_6$ was estimated by $^1$H-NMR after esterification with benzyl bromide according to the known procedure. A mixture of benzoic acid 4a and benzoic acid-$d_5$ 4a-$d_5$ was prepared according to the general procedure, except that the reaction time was 1 h and a mixed solution of each substrate (1 mL : 1 mL) was used.

To a 10 mL bial, a crude mixture of 4a and 4a-$d_5$ prepared (which contained total of ca. 0.1 mmol of products based on weight), DMF (1 mL), K$_2$CO$_3$ (21 mg, 0.15 mmol) and NaI (6 mg, 0.04 mmol) were added at room temperature. After a few minutes, benzyl bromide (18 µL, 0.15 mmol) was added and the mixture was stirred for 18 h. The reaction mixture was diluted with diethyl ether, and then quenched with aqueous NH$_4$Cl. The organic layer was washed with water three times, dried over MgSO$_4$, and concentrated in vacuo. The crude mixture was purified by preparative TLC (hexane : ethyl acetate = 19 : 1) to give a mixture of 6a and 6a-$d_5$. KIE ([6a-$d_0$]/[6a-$d_6$]) was calculated to be 5.5 on average of two sets of reactions by comparing integration of benzylic 2H (5.36 ppm) and 2H at ortho-positions of carboxy group (8.08 ppm) to those of authentic 6a. Authentic 6a was prepared as above from commercially available benzoic acid 4a (12.2 mg, 0.10 mmol). The yield was 80 % after purification.

6) Appendix for optimization of the reaction conditions

<table>
<thead>
<tr>
<th>entry</th>
<th>co-solvents (0.1 mL)</th>
<th>TON</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DMA</td>
<td>29</td>
</tr>
<tr>
<td>2</td>
<td>DMSO</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>DMF</td>
<td>trace</td>
</tr>
<tr>
<td>4</td>
<td>THF</td>
<td>10</td>
</tr>
</tbody>
</table>

Table S1. The effects of co-solvents. Other co-solvents were not as effective as DMA.
Table S2. The effects of concentrations of co-solvents.

References:


