

Supporting Information

Direct Carboxylation of Simple Arenes with CO₂ through a Rhodium-Catalyzed C-H Bond Activation

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1) General information

All operations were performed under an argon atmosphere. ^1H , ^{13}C , ^{27}Al , ^{31}P -NMR spectra were recorded on JEOL ECX-500 (500MHz for ^1H , 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 (^1H , $\delta = 0.00$), C_6D_6 (^1H , $\delta = 7.15$), CDCl_3 (^{13}C , $\delta = 77.0$), C_6D_6 (^{13}C , $\delta = 128.0$) as internal standards and 1.5 mol/L $\text{Al}(\text{NO}_3)_3$ aq. (^{27}Al , $\delta = 0.00$), 85 % H_3PO_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 elemental 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 cm²) 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. Tetramethylurea 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**, α,α,α -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. $[\text{RhCl}(\text{coe})_2]_2$ and $[\text{RhCl}(\text{cod})]_2$ were prepared by the known procedure.ⁱ

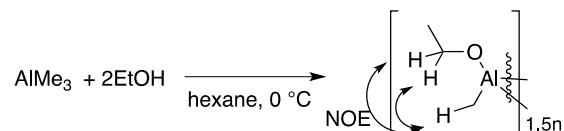
Compounds **4a**ⁱⁱ, **4b**^{ii,vi}, **4c**ⁱⁱⁱ, **4d**^{iva}, **4e**^{iva,vi}, **4f**^v, **4g**^v, **4h**^{vi}, **4i**^{iv}, **4j**^{vii}, **4l**ⁱⁱ, γ -**4m**^{viii}, **4n**^{viii} were known compounds and their spectral data were in good agreement with literature values. 3-(Trimethylsilyl)benzene carboxylic acid β -**4k**,^{ix} 4-(trimethylsilyl)benzene carboxylic acid γ -**4k**,^{ix} benzo[b]furan-2-carboxylic acid **4q**,^x 1-methylindole-2-carboxylic acid α -**4r**,^{xi} 1-methylindole-3-carboxylic acid β -**4r**^{xi} 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 acid **β-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 $\text{AlMe}_n(\text{OEt})_{3-n}$

$\text{AlMe}_{1.5}(\text{OEt})_{1.5}$ was prepared by the following procedure.



To a solution of AlMe_3 (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.

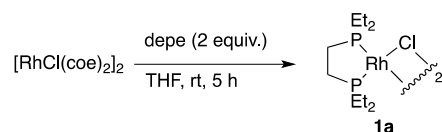
Based on its $^1\text{H-NMR}$, the ratio of methyl group and ethoxy group was determined to be almost 1 : 1. 23.2 mg of this reagent contained 0.306 mmol of methyl group based on $^1\text{H-NMR}$ with mesitylene (benzylic 9H) as an internal standard. This value is consistent with that of $\text{AlMe}_{1.5}(\text{OEt})_{1.5}$, 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 $\text{AlMe}_3 : \text{Al}(\text{OEt})_3 = 1 : 1$. $^{27}\text{Al-NMR}$ suggested the presence of the 4-coordinated aluminum ($\delta = 155.6$ ppm) and 6-coordinated aluminum ($\delta = 7.30$ ppm)^{xiii}.

The spectra of the major product was as follows; $^1\text{H-NMR}$ (500 MHz, C_6D_6) δ 3.74–3.83 (m, 1.5H), 3.50–3.60 (m, 1.5H), 1.08 (t, $J = 7.2$ Hz, 4.5H), -0.50 (s, 3H); $^{27}\text{Al-NMR}$ (130 MHz, C_6D_6) δ 155.6 (broad), 7.30 (s).

A mixture of $\text{AlMe}_3 : \text{EtOH} = 1 : 1$ 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**

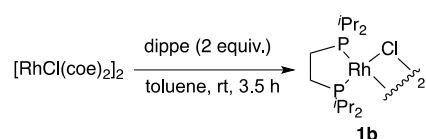


In a glovebox, a solution of 1,2-bis(diethylphosphino)ethane (124 mg, 0.6 mmol) in THF (30 mL) was added dropwise to a solution of $[\text{RhCl}(\text{coe})_2]_2$ (217 mg, 0.3 mmol) in THF (30 mL) and the

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 MHz, C_6D_6) δ 1.75–1.86 (m, 4H), 1.36–1.46 (m, 4H), 1.19–1.27 (m, 12H), 0.96 (d, $J = 14.3$ Hz, 4H); $^{13}\text{C-NMR}$ (125 MHz, C_6D_6) δ 25.2 (td, $J = 23.3, 6.0$ Hz), 22.8 (t, $J = 23.7$ Hz), 9.86 (s); $^{31}\text{P-NMR}$ (200 MHz, C_6D_6) δ 85.1 (d, $J = 194$ Hz); HR-MS (FAB $^+$): Calcd for $\text{C}_{20}\text{H}_{48}\text{Cl}_2\text{P}_4\text{Rh}_2$ $[\text{M}]^+$: 688.0194; Found: 688.0191.

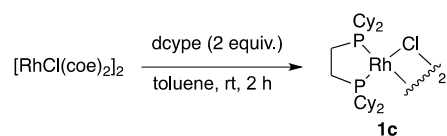
Synthesis of [1,2-bis(diisopropylphosphino)ethane]rhodium(I) chloride dimer **1b**



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

$^1\text{H-NMR}$ (500 MHz, C_6D_6) δ 1.99–2.08 (m, 4H), 1.49 (dd, $J = 14.6, 7.2$ Hz, 12H), 1.02 (dd, $J = 12.6, 6.9$ Hz, 12H), 0.94 (d, $J = 11.5$ Hz, 4H); $^{13}\text{C-NMR}$ (125 MHz, C_6D_6) δ 26.7 (t, $J = 11.5$ Hz), 22.0 (td, $J = 21.2, 6.1$ Hz), 20.5 (s), 18.8 (s); $^{31}\text{P-NMR}$ (200 MHz, C_6D_6) δ 102.6 (d, $J = 194$ Hz); HR-MS (FAB $^+$): Calcd for $\text{C}_{28}\text{H}_{64}\text{Cl}_2\text{P}_4\text{Rh}_2$ $[\text{M}]^+$: 800.1446; 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 $[\text{RhCl}(\text{coe})_2]_2$ (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. Recrystallization from toluene/pentane in a refrigerator gave the title compound in 69 % yield (320 mg, 0.29 mmol) as an orange-yellow powder.

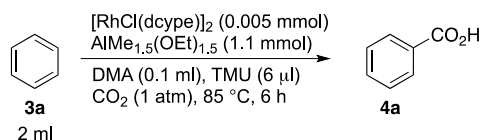
$^1\text{H-NMR}$ (500 MHz, C_6D_6) δ 2.62 (d, $J = 12.6$ Hz, 8H), 1.83–1.99 (m, 16H), 1.49–1.83 (m, 40H), 1.13–1.43 (m, 24H), 1.05 (d, $J = 11.5$ Hz, 8H); $^{13}\text{C-NMR}$ (125 MHz, C_6D_6) δ 36.4 (t, $J = 11.3$ Hz), 29.8 (d, $J = 83.5$ Hz), 27.8 (broad d, $J = 45.3$ Hz), 26.9, 22.8–23.2 (m); $^{31}\text{P-NMR}$ (200 MHz, C_6D_6) δ 95.5 (d, $J = 199$ Hz); $^{31}\text{P-NMR}$ (200 MHz, CDCl_2) δ 94.6 (d, $J = 200$ Hz);

Anal. Calcd for C₅₂H₉₆Cl₂P₄Rh₂: 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.

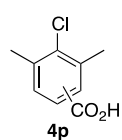


A solution of [RhCl(dcppe)]₂ **1c** (5.6 mg, 0.005 mmol), DMA (0.1 mL), TMU (6 μL, 0.05 mmol) and AlMe_{1.5}(OEt)_{1.5} (132 mg, 1.1 mmol) in benzene **3a** (2 mL) was stirred in a glass tube (φ = 2.0 cm, 18 cm) at room temperature for a few minutes, and then the system was purged with an atmospheric pressure of CO₂. 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 MgSO₄. After removal of solvent under reduced pressure, the residue was purified by silica-gel column chromatography (CH₂Cl₂ : 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 CO₂ 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.

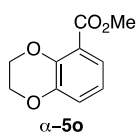
A mixture of 3-chloro-2,4-dimethylbenzenecarboxylic acid α-4p and 4-chloro-3,5-dimethylbenzenecarboxylic acid β-4p



¹H-NMR (500 MHz, CDCl₃) 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); ¹³C-NMR (125 MHz, CDCl₃) 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⁺) : Calcd for C₉H₉ClO₂ [M]⁺ : 184.0291; Found: 184.0266; White solid.

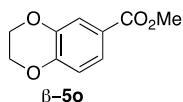
The compounds shown below were characterized after isolation as their corresponding methyl esters by treatment with TMSCHN₂ (2.0 M sol. in Et₂O, 1.0 ml, 2.0 mmol) in Et₂O-MeOH (4:1, 7.5 ml) at 0 °C in 50 ml one-necked flask under nitrogen, followed by purification by PTLC.

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



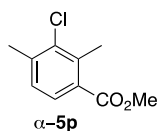
¹H-NMR (500 MHz, CDCl₃) δ 7.39 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.02 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 6.85 (t, J = 8.0 Hz, 1H), 4.35-4.38 (m, 2H), 4.29-4.31 (m, 2H), 3.89 (s, 3H); ¹³C-NMR (125 MHz, CDCl₃) δ 166.0, 144.1, 144.0, 123.7, 121.3, 120.3, 120.0, 64.6, 63.8, 52.0; IR (ATR) 1714, 1435, 1317, 1285, 1223, 1047, 770 cm⁻¹; HR-MS (EI⁺) : Calcd for C₁₀H₁₀O₄ [M]⁺ : 194.0579; Found: 194.0544; White solid.

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



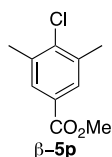
¹H-NMR (500 MHz, CDCl₃) δ 7.56 (s, 1H), 7.55 (d, J = 8.4 Hz, 1H), 6.88 (d, J = 8.4 Hz, 1H), 4.33-4.25 (m, 4H), 3.87 (s, 3H); ¹³C-NMR (125 MHz, CDCl₃) δ 166.6, 147.7, 143.1, 123.4, 118.9, 117.1, 64.6, 64.0, 51.9, one aromatic carbon overlaps; IR (ATR) 1703, 1584, 1440, 1287, 1201, 1061, 880, 766 cm⁻¹; HR-MS (EI⁺) : Calcd for C₁₀H₁₀O₄ [M]⁺ : 194.0579; Found: 194.0547; White solid.

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



¹H-NMR (500 MHz, CDCl₃) 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); ¹³C-NMR (125 MHz, CDCl₃) 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 C₁₀H₁₁ClO₂ [M]⁺ : 198.0448; Found: 194.0416; White solid.

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



¹H-NMR (500 MHz, CDCl₃) δ 7.75 (s, 2H), 3.90 (s, 3H), 2.41 (s, 6H); ¹³C-NMR (125 MHz, CDCl₃) 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 C₁₀H₁₁ClO₂ [M]⁺ : 198.0448; Found: 194.0418; White solid.

5) Mechanistic studies

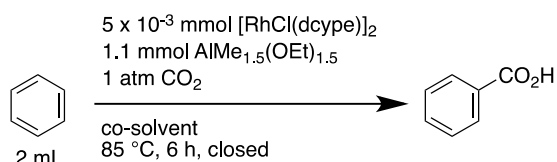
Procedure for the KIE experiment



The KIE of the reaction between benzene-*d*₀ **3a-d₀** and benzene-*d*₆ **3a-d₆** was estimated by ¹H-NMR after esterification with benzyl bromide according to the known procedure.^{xvi} A mixture of benzoic acid **4a** and benzoic acid-*d*₅ **4a-d₅** 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-d₅** prepared (which contained total of ca. 0.1 mmol of products based on weight), DMF (1 mL), K₂CO₃ (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 NH₄Cl. The organic layer was washed with water three times, dried over MgSO₄, 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-d₅**. KIE ([**6a-d₀**]/[**6a-d₆**]) 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



entry	co-solvents (0.1 mL)	TON
1	DMA	29
2	DMSO	0
3	DMF	trace
4	THF	10

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

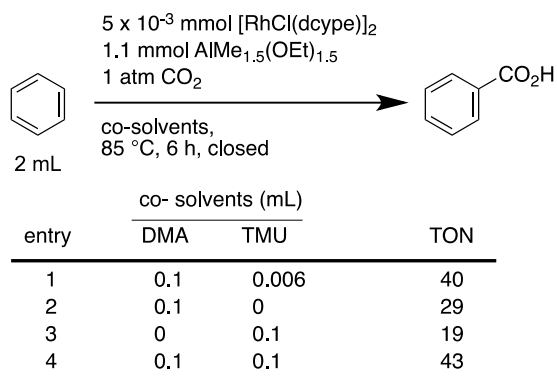


Table S2. The effects of concentrations of co-solvents.

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