Cross-coupling of benzylic acetates with arylboronic acids: one-pot transformation of benzylic alcohols to diarylmethanes

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Supplementary Information

General and Materials. NMR spectra were measured with Bruker AVANCE 400 (9.4 T magnet) spectrometer. IR spectra were measured with Nicolet Magna 560. Elemental analyses were performed by Service Centre of Elementary Analysis of Organic Compounds in Kyushu University. Flash column chromatographies were performed with silica gel 60 (230–400 mesh, Merck).

tert-Amyl alcohol was distilled from calcium hydride. All benzylic acetates were prepared from acetylation of the corresponding alcohols with acetic anhydride in the presence of pyridine, and were purified with vacuum distillation. [Pd(η³-C₃H₅)Cl]₂ was prepared according to literatures,¹ but was commercially available. All boronic acids and DPEphos were commercially available.

General Procedure for Cross-Coupling of Benzylic Acetates with Arylboronic Acids: Procedure 1. Under a nitrogen atmosphere, a benzylic acetate 4 (1.0 mmol) was added to a suspension of an arylboronic acid 2 (1.1 mmol), potassium carbonate (304 mg, 2.2 mmol), [Pd(η³-C₃H₅)Cl]₂ (3.6 mg, 10 µmol), and DPEphos (11.8 mg, 22 µmol) in tert-amyl alcohol (1.0 cm³). The suspension was stirred at 80 °C until 4 was completely consumed (monitored by GC). After brine was added, the mixture was extracted several times with hexane. The combined organic layer was dried with MgSO₄, and was evaporated under reduced pressure. The residue was purified by a flash column chromatography (EtOAc/hexane) to give the desired product.

Procedure 2. Under a nitrogen atmosphere, a benzylic acetate 4 (1.0 mmol) was added to a suspension of potassium carbonate (304 mg, 2.2 mmol), [Pd(η³-C₃H₅)Cl]₂ (3.6 mg, 10 µmol), and DPEphos (11.8 mg, 22 µmol) in tert-amyl alcohol (1.0 cm³), and then the mixture was stirred at room temperature for 10 min. An arylboronic acid 2 (1.1 mmol) and additional tert-amyl alcohol (1.0 cm³) were added to the mixture. The mixture was stirred at 80 °C until 4 was completely consumed (monitored by GC). After brine was added, the mixture was extracted several times with hexane. The combined organic layer was dried with MgSO₄, and was evaporated under reduced pressure. The residue was purified by a flash column chromatography (EtOAc/hexane) to give the desired product.

4-Benzylanisole (3a) (Entry 7 in Table 1).² The procedure 1 was followed with 4-methoxybenzyl acetate (4a) (180 mg, 1.00 mmol) and phenylboronic acid (2a) (134 mg, 1.10 mmol). The crude product was purified by a flash column chromatography (EtOAc/hexane = 1/50) to give 3a (186 mg, 94%) as colorless oil.

3a: ¹H NMR (400 MHz, CDCl₃, TMS) δ 3.77 (s, 3H), 3.92 (s, 2H), 6.82 (d, J = 8.5 Hz, 2H), 7.10 (d, J = 8.5 Hz, 2H), 7.15–7.20 (m, 3H), 7.27 (t, J = 7.3 Hz, 2H);¹³C {¹H} NMR (100 MHz, CDCl₃) δ 41.0, 55.2, 113.9, 125.9, 128.4, 128.8, 129.8, 133.2, 141.6, 157.9.

Diphenylmethane (3b) (Entry 1 in Table 2).³ The procedure 1 was followed with benzyl acetate (4b) (151 mg, 1.01 mmol) and 2a (134 mg, 1.10 mmol). The crude product was purified by a flash column chromatography (hexane) to give 3b (139 mg, 83%) as colorless oil:

3b: ¹H NMR (400 MHz, CDCl₃, TMS) δ 3.97 (s, 2H), 7.16–7.21 (m, 6H), 7.27 (t, J = 7.5 Hz, 4H);¹³C {¹H} NMR (100 MHz, CDCl₃) δ 41.9, 126.0, 128.4, 128.9, 141.1.
4-Benzyl-1-(trifluoromethyl)benzene (3c) (Entry 2 in Table 2). The procedure 1 was followed with 4-(trifluoromethyl)benzyl acetate (4c) (218 mg, 1.00 mmol) and 2a (135 mg, 1.10 mmol). The crude product was purified by a flash column chromatography (hexane) to give 3c (202 mg, 86%) as colorless oil: \(^1H\) NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\) 4.02 (s, 2H), 7.15–7.33 (m, 7H), 7.53 (d, \(J = 8.1\) Hz, 2H); \(^13C\) \((^1H)\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 41.7, 124.3 (q, \(J = 272\) Hz), 125.4 (q, \(J = 4\) Hz), 126.5, 128.5 (q, \(J = 33\)Hz), 128.6, 128.9, 129.2, 140.0, 145.2.

Methyl 4-Benzylbenzoate (3d) (Entry 3 in Table 2). The procedure 1 was followed with 4-(methoxycarbonyl)benzyl acetate (4d) (206 mg, 0.99 mmol) and 2a (137 mg, 1.12 mmol). The crude product was purified by flash column chromatography (EtOAc/hexane = 1/20) to give 3d (192 mg, 85%) as colorless oil: \(^1H\) NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\) 3.89 (s, 3H), 4.03 (s, 2H), 7.17 (d, \(J = 7.3\) Hz, 2H), 7.19–7.32 (m, 5H), 7.95 (d, \(J = 8.2\) Hz, 2H); \(^13C\) \((^1H)\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 41.9, 52.0, 126.4, 128.1, 128.6, 128.9, 129.8, 140.1, 146.5, 167.0.

4-Benzyl-1-chlorobenzene (3e) (Entry 4 in Table 2). The procedure 1 was followed with 4-chlorobenzyl acetate (4e) (95 mg, 0.51 mmol), 2a (91 mg, 0.75 mmol), potassium carbonate (212 mg, 1.54 mmol), [Pd(\(\eta^2\rceilC,H_3\)_2]Cl\(_2\)) (4.7 mg, 13 \(\mu\)mol), DPEphos (15 mg, 28 \(\mu\)mol), and tert-amyl alcohol (1.0 cm\(^3\)). The crude product was purified by a flash column chromatography (EtOAc/hexane = 1/100) to give 3e (69 mg, 65%) as colorless oil: \(^1H\) NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\) 3.94 (s, 2H), 7.10 (d, \(J = 8.3\) Hz, 2H), 7.15 (d, \(J = 7.2\) Hz, 2H), 7.17–7.31 (m, 5H); \(^13C\) \((^1H)\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 41.2, 126.3, 128.5, 128.8, 130.2, 131.9, 139.6, 140.5.

2-Benzyltoluene (3f) (Entry 5 in Table 2). The procedure 2 was followed with 2-methylbenzyl acetate (4f) (165 mg, 1.01 mmol) and 2a (135 mg, 1.10 mmol). The crude product was purified by a flash column chromatography (EtOAc/hexane = 1/20) to give 3f (147 mg, 80%) as colorless oil: \(^1H\) NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\) 2.23 (s, 3H), 3.98 (s, 2H), 7.07–7.20 (m, 7H), 7.26 (t, \(J = 7.4\) Hz, 2H); \(^13C\) \((^1H)\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 19.6, 39.4, 125.9, 126.0, 126.4, 128.4, 128.7, 129.9, 130.3, 136.6, 138.9, 140.4.

Bis(4-methoxyphenyl)methane (3g) (Entry 6 in Table 2). The procedure 1 was followed with 4a (181 mg, 1.00 mmol), 4-methoxyphenylboronic acid (2b) (168 mg, 1.10 mmol), and 2.0 cm\(^3\) of tert-amyl alcohol. The crude product was purified by a flash column chromatography (EtOAc/hexane = 1/20) to give 3g (211 mg, 92%) as colorless oil: \(^1H\) NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\) 3.76 (s, 6H), 3.85 (s, 2H), 6.81 (d, \(J = 8.6\) Hz, 4H), 7.08 (d, \(J = 8.6\) Hz, 4H); \(^13C\) \((^1H)\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 40.1, 55.2, 113.8, 129.7, 133.7, 157.9.

4-[4-(trifluoromethyl)benzyl]anisole (3h) (Entry 7 in Table 2). The procedure 2 was followed with 4a (180 mg, 1.00 mmol) and 4-(trifluoromethyl)phenylboronic acid (2c) (219 mg, 1.15 mmol). The crude product was purified by a flash column chromatography (EtOAc/hexane = 20/1) to give 3h (238 mg, 89%) as colorless oil: \(^1H\) NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\) 3.78 (s, 3H), 3.96 (s, 2H), 6.84 (d, \(J = 8.6\) Hz, 2H), 7.08 (d, \(J = 8.6\) Hz, 2H), 7.27 (d, \(J = 8.1\) Hz, 2H), 7.52 (d, \(J = 8.1\) Hz, 2H); \(^13C\) \((^1H)\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 40.8, 55.2, 114.0, 124.3 (q, \(J = 272\) Hz), 125.3 (q, \(J = 4\) Hz), 128.4 (q, \(J = 32\) Hz), 129.0, 129.9, 132.0, 145.7, 158.2.

3-(4-Methoxybenzy1)phenyl)methanol (3i) (Entry 8 in Table 2). Under a nitrogen atmosphere, 4a (179 mg, 1.00 mmol) was added to a suspension of potassium carbonate (304 mg, 2.20 mmol), [Pd(\(\eta^2\rceilC,H_3\)_2]Cl\(_2\)) (3.7 mg, 10 \(\mu\)mol), and DPEphos (11.6 mg, 22 \(\mu\)mol) in tert-amyl alcohol (1.0 cm\(^3\)), and then the mixture was stirred at room temperature for 10 min. 3-(Hydroxymethyl)phenylboronic acid (2d) (169 mg, 1.11 mmol), additional tert-amyl alcohol (2.0 cm\(^3\)), and DMF (0.5 cm\(^3\)) were added to the mixture. The mixture was stirred at 80 °C for 48 h. After brine was added, the mixture was extracted four times with EtOAc. The combined organic layer was dried with Na\(_2\)SO\(_4\), and was evaporated under reduced pressure. The residue was purified by a flash column chromatography (EtOAc/hexane = 2/1) to give 3i (209 mg, 92%) as a pale yellow solid: \(^1H\) NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\) 1.63 (br t, \(J = 4.9\) Hz, 1H), 3.78 (s, 3H), 3.92 (s, 2H), 4.65 (d, \(J = 4.9\) Hz, 2H), 6.83 (d, \(J = 8.6\) Hz, 2H), 7.08–7.13 (m, 3H), 7.19 (d, \(J = 7.9\) Hz, 2H), 7.27 (t, \(J = 7.7\) Hz, 1H); \(^13C\) \((^1H)\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 41.0, 55.2, 65.4, 113.9, 124.7, 127.4, 128.1, 128.7, 129.8, 133.1, 141.0, 142.0, 158.0.
(3j) (Entry 9 in Table 2). The procedure 1 was followed with 4a (181 mg, 1.00 mmol) and 2-biphenylboronic acid (2e) (218 mg, 1.10 mmol). The crude product was purified by a flash column chromatography (hexane) to give 3j (237 mg, 86%) as colorless oil: \(^1\)H NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\) 7.35 (s, 3H), 3.85 (s, 2H), 6.75 (d, \(J = 8.5\) Hz, 2H), 6.82 (d, \(J = 8.7\) Hz, 2H), 7.18–7.38 (m, 9H); \(^1\)C \{\(^1\)H\} NMR (100 MHz, CDCl\(_3\)) \(\delta\) 137.4, 127.4, 128.0, 129.3, 129.7, 130.06, 130.13, 133.5, 138.6, 141.7, 142.1, 157.7; IR (KBr) 1580 cm\(^{-1}\); Anal. Calcd for C\(_{18}\)H\(_{18}\)O: C, 87.56; H, 6.61. Found: C, 87.67; H, 6.63.

Generl Procedures for One-Pot Transformation of Benzylic Alcohols into Diarylmethanes.

Under a nitrogen atmosphere, acetic anhydride (103 mg, 1.02 mmol) was added to a solution of a benzylic alcohol 5 (1.0 mmol) and triethylamine (104 mg, 1.02 mmol) in tert-amyl alcohol (1.0 cm\(^3\)) at 0 °C. The mixture was stirred at room temperature for 12 h. [Pd(η\(^3\)-C\(_5\)H\(_5\))Cl\(_2\)] (3.6 mg, 10 μmol), DPEphos (11.8 mg, 22 μmol), and potassium carbonate (304 mg, 2.20 mmol) were added to the mixture containing 4, and then the mixture was stirred for 10 min. After 2a (134 mg, 1.1 mmol) was added, the mixture was stirred at 80 °C until 4 was completely consumed (monitored by GC). After brine was added, the mixture was extracted several times with hexane. The combined organic layer was dried with MgSO\(_4\), and was evaporated under reduced pressure. The residue was purified by a flash column chromatography (EtOAc/hexane) to give the desired product.

4-Benzylanisole (3a) (Scheme 2). The general procedure was followed with 4-methoxybenzyl alcohol (5a) (139 mg, 1.00 mmol). The reaction mixture was heated at 80°C for 48 h. The crude product was purified by a flash column chromatography (EtOAc/hexane = 1/50) to give 3a (150 mg, 75%) as colorless oil: \(^1\)H NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\) 7.38 (m, 9H); \(\delta\) 7.32 (m, 5H), 7.95 (d, \(J = 8.5\) Hz, 2H), 7.10 (d, \(J = 8.2\) Hz, 2H), 6.86 (d, \(J = 8.7\) Hz, 2H), 6.82 (d, \(J = 8.5\) Hz, 2H), 7.18–7.38 (m, 9H); \(^1\)C \{\(^1\)H\} NMR (100 MHz, CDCl\(_3\)) \(\delta\) 41.6, 55.2, 113.6, 126.0, 126.8, 127.4, 128.0, 129.3, 129.7, 130.06, 130.13, 133.5, 138.6, 141.7, 142.1, 157.7; IR (KBr) 3076, 1580 cm\(^{-1}\); Anal. Calcd for C\(_{18}\)H\(_{18}\)O: C, 87.56; H, 6.61. Found: C, 87.67; H, 6.63.

4-Benzyl-1-((trifluoromethyl)benzene (3c) (Scheme 2). The general procedure was followed with 4-(trifluoromethyl)benzyl alcohol (5b) (177 mg, 1.01 mmol). The reaction mixture was heated at 80°C for 2 h. The crude product was purified by a flash column chromatography (hexane) to give 3c (181 mg, 75%) as colorless oil: \(^1\)H NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\) 7.35 (s, 3H), 3.85 (s, 2H), 6.75 (d, \(J = 8.1\) Hz, 2H), 7.15–7.33 (m, 7H), 7.53 (d, \(J = 8.1\) Hz, 2H); \(^1\)C \{\(^1\)H\} NMR (100 MHz, CDCl\(_3\)) \(\delta\) 128.4, 128.8, 128.9, 132.3, 141.6, 157.9.

Methyl 4-Benzylbenzoate (3d) (Scheme 2). The general procedure was followed with 4-(methoxycarbonyl)benzyl alcohol (5c) (166 mg, 1.00 mmol). The reaction mixture was heated at 80°C for 72 h. The crude product was purified by a flash column chromatography (hexane) to give 3d (168 mg, 74%) as colorless oil: \(^1\)H NMR (400 MHz, CDCl\(_3\), TMS) \(\delta\) 3.89 (s, 3H), 4.03 (s, 3H), 7.17 (d, \(J = 7.3\) Hz, 2H), 7.19–7.32 (m, 5H), 7.95 (d, \(J = 8.2\) Hz, 2H); \(^1\)C \{\(^1\)H\} NMR (100 MHz, CDCl\(_3\)) \(\delta\) 41.9, 52.0, 126.4, 128.1, 128.6, 128.9, 129.8, 140.1, 164.5, 167.0.

References