Supporting Information

Polymer-supported PPh₃ as a reusable organocatalyst for the Mukaiyama aldol reaction of aldehydes and imines

Satoru Matsukawa,* Kazuki Fukazawa, and Junya Kimura

Department of Science Education, Faculty of Education, Ibaraki University

Mito, Ibaraki 310-8512, Japan

Instrumentation and Chemicals	S2
Experimental procedure	82
Copies of ¹ H and ¹³ C NMR Spectra of products	87
References	S27

General

All reactions were performed under an argon atmosphere using oven-dried glassware. Flash column chromatography was performed using silica gel Wakogel C-200. Preparative thin-layer chromatography was carried out on silica gel Wakogel B-5F. Dehydrate DMF, THF, toluene and CH₃CN were purchased from Wako Chemical. Other commercially available reagents was used as received without further purification. Yields refer to isolated compounds estimated to be >95% pure, as determined by ¹H NMR spectroscopy. IR spectra were recorded on a JUSCO FT/IR-430 spectrometer. ¹H and ¹³C NMR spectra were determined for solutions in CDCl₃ with Me₄Si as internal standard on a Bruker Avance III instrument. HRMS data were measured on a JEOL JMS-700 mass spectrometer.

General procedure for PS-PPh₃ catalyzed Mukaiyama aldol reaction of aldehyde with silyl ketene acetals

To a solution of PS-PPh₃ (0.05mmol) in DMF (1 mL) was added aldehyde 1 (1.0 mmol) and silvl ketene acetal (1.25 mmol) at room temperature. After the reaction was complete (as determined by TLC), EtOAc (5 ml) was added to the mixture and PS-PPh₃ was separated by filtration. The filtrate was concentrated under vacuum and purified by column chromatography on silica gel (EtOAc:hexane = 1:3) to give the corresponding product. The recovered catalyst is reusable after washing (acetone, NH₄OH and water) and drying in vacuo.

General procedure for PS-PPh₃ catalyzed Mukaiyama aldol reaction of imine with silyl ketene acetals

To a solution of PS-PPh₃ (0.10 mmol) in DMF (1 mL) was added aldehyde 1 (1.0 mmol) and silvl ketene acetal (1.25 mmol) at room temperature or 30 °C. After the reaction was complete (as determined by TLC), EtOAc (15 ml) was added to the mixture and PS-PPh₃ was separated by filtration. The filtrate was washed with brine and water and dried over anhydrous Na₂SO₄, then evaporated. The crude mixture was purified by preparative TLC (EtOAc:hexane = 1:3) to afford the corresponding product.

Methyl 3-(4-methoxyphenyl)-2,2-dimethyl-3-trimethyl-silyloxypropionate (3a)¹: Colorless oil; yield: 303 mg (94 %); ¹H NMR (500 MHz, CDCl3): δ 0.09 (s, 9H), 0.93 (s, 3H), 1.06 (s, 3H), 3.63 (s, 3H), 3.75 (s, 3H), 4.88 (s, 1H), 6.77 (d, *J* = 8.6 Hz, 5H), 7.13 (d, *J* = 8.6 Hz, 5H); ¹³C NMR (125 MHz, CDCl3) δ =0.0, 19.1, 21.7, 49.1, 51.6, 55.2, 78.8, 112.8, 128.8, 133.0, 158.9, 177.4; HRMS (FAB): *m/z*: calcd for C₁₆H₂₇O₄Si: 323.1679; found: 323.1961 [M + H]⁺.

Methyl 2,2-dimethyl-3-phenyl-3-trimethylsilyloxypropionate (3b)²: Colorless oil; yield: 255 mg (91 %); ¹H NMR (500 MHz, CDCl3): δ 0.04 (s, 9H), 0.97 (s, 3H), 1.11 (s, 3H), 3.66 (s, 3H), 4.96 (s, 1H), 4.92 (s, 1H), 7.22-7.32 (m, 5H); ¹³C NMR (125 MHz, CDCl3) δ = 0.0, 19.0, 22.0, 49.1, 51.7, 79.2, 127.4, 127.8, 140.7, 177.3; HRMS (FAB): *m/z*: calcd for C₁₅H₂₅O₃Si: 281.1573; found: 281.1568 [M + H]⁺.

Methyl 3-(4-chlorophenyl)-2,2-dimethyl-3-trimethylsilyloxy-propionate (3c)²: White solid; m.p. 53 °C; yield: 299 mg (95 %); ¹H NMR (500 MHz, CDCl3): δ 0.06 (s, 9H), 0.94 (s, 3H), 1.08 (s, 3H), 3.64 (s, 3H), 7.18 (d, J = 8.4 Hz, 5H), 7.23 (d, J = 8.6 Hz, 5H); ¹³C NMR (125 MHz, CDCl3) $\delta = 0.0$, 19.2, 21.4, 48.9, 51.7, 78.5, 127.6, 129.2, 133.1, 139.5, 177.0; HRMS (FAB): m/z: calcd for C₁₅H₂₄ClO₃Si: 315.1183; found: 315.1175 [M + H]⁺.

Methyl 3-(4-methylphenyl)-2,2-dimethyl-3-trimethylsilyloxy-propionate (3d)³: Colorless oil; yield: 259 mg (88 %); ¹H NMR (500 MHz, CDCl3): δ 0.07 (s, 9H), 0.96 (s, 3H), 1.09 (s, 3H), 2.30 (s, 3H), 3.65 (s, 3H), 4.91 (s, 1H), 7.05 (d, *J* = 8.0 Hz, 5H), 7.13 (d, *J* = 8.0 Hz, 5H); ¹³C NMR (125 MHz, CDCl3) δ = 0.0, 19.1, 21.1, 21.7, 49.0, 51.6, 79.0, 127.7, 128.1, 136.9, 137.8, 177.5; HRMS (FAB): *m/z*: calcd for C₁₆H₂₇O₃Si: 295.1729; found: 295.1727[M + H]⁺.

Methyl 2,2-dimethyl-3-(4-Nitromethoxyphenyl)-3-trimethyl-silyloxypropionate (3e)³: White solid; m.p. 116 °C; yield: 275 mg (85 %); ¹H NMR (500 MHz, CDCl3): δ 0.04 (s, 9H), 0.97 (s, 3H), 1.11 (s, 3H), 3.65 (s, 3H), 5.03 (s, 1H), 7.43 (d, J = 8.5 Hz, 5H), 8.13 (d, J = 8.5 Hz, 5H); ¹³C NMR (125 MHz, CDCl3) δ = 0.0, 19.7, 21.3, 49.1, 52.0, 78.3, 122.8, 128.5, 147.4, 148.7, 176.5.; HRMS (FAB): m/z: calcd for C₁₅H₂₄NO₅Si: 326.1424; found: 326.1417 [M + H]⁺.

Methyl 3-[4-(dimethylamino)phenyl]-2,2-dimethyl-3-trimethylsilyloxypropionate (3f)²: White solid; m.p. 76 °C; yield: 291 mg (90 %); ¹H NMR (500 MHz, CDCl3): δ 0.08 (s, 9H), 0.94 (s, 3H), 1.07 (s, 3H), 2.92 (S, 6H), 3.64 (s, 3H), 4.86 (s, 1H), 6.55-6.70 (m, 2H), 7.05-7.15 (m, 2H); ¹³C NMR (125 MHz, CDCl3) δ = 0.0, 18.9, 21.9, 40.7, 49.2, 51.7, 79.1, 111.4, 128.7, 149.8, 177.6; HRMS (FAB): *m/z*: calcd for C₁₇H₃₀NO₃Si: 324.1995; found: 324.2007 [M + H]⁺..

Methyl 2,2-dimethyl-3-(naphthalene-1-yl)-3-trimethylsilyloxy-propionate (3g)⁴: Colorless oil; yield: 285 mg (86 %); ¹H NMR (500 MHz, CDCl3): δ -0.11 (s, 9H), 0.93 (s, 3H), 1.21 (s, 3H), 3.64 (s, 3H), 6.00 (s, 1H), 7.40-7.51 (m, 3H), 7.69 (d, J = 7.4 Hz, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.82 (d, J = 7.4 Hz, 1H), 8.15 (d, J = 8.2 Hz, 1H); ¹³C NMR (125 MHz, CDCl3) δ = -0.1, 18.5, 23.0, 50.0, 51.8, 72.9, 123.2, 124.8, 125.0,

125.7, 127.0, 127.9, 128.8, 131.6, 133.2, 136.8, 177.5; HRMS (FAB): *m*/*z*: calcd for C₁₉H₂₇O₃Si: 331.1729; found: 331.1736 [M + H]⁺.

Methyl 2,2-dimethyl-3-(naphthalene-2-yl)-3-trimethylsilyloxy-propionate (3h)⁵: White solid; m.p. 70 °C; yield: 315 mg (95 %); ¹H NMR (500 MHz, CDCl3): δ -0.05 (s, 9H), 1.02 (s, 3H), 1.15 (s, 3H), 3.67 (s, 3H), 5.13 (s, 1H), 7.40-7.47 (m, 3H), 7.67 (d, *J* = 4.4 Hz, 1H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.81 (d, *J* = 7.4 Hz, 2H); ¹³C NMR (125 MHz, CDCl3) δ = 0.0, 19.2, 21.8, 49.3, 51.7, 79.3, 125.7, 125.9, 126.1, 126.6, 127.0, 127.6, 128.0, 132.8, 133.0, 138.5, 177.3; HRMS (FAB): *m/z*: calcd for C₁₉H₂₇O₃Si: 331.1729; found: 331.1715 [M + H]⁺.

Methyl (4*E***)-2,2-dimethyl-5-phenyl-3-trimethylsilyloxypent-4-enoate (3i)³:** Colorless oil; yield: 285 mg (93 %); ¹H NMR (500 MHz, CDCl3): δ 0.00 (s, 9H), 1.02 (s, 3H), 1.11 (s, 3H), 3.59 (s, 3H), 4.40 (d, *J* = 7.0 Hz, 1H), 6.03 (dd, *J* = 7.0, 16.0 Hz, 1H), 6.41 (d, *J* = 16.0 Hz, 1H), 7.16 (d, *J* = 7.4 Hz, 1H), 7.24 (dd, *J* = 7.2, 7.5 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 2H); ¹³C NMR (125 MHz, CDCl3) δ = 0.3, 19.8, 21.2, 48.5, 51.8, 78.5, 126.4, 127.6, 128.6, 128.8, 132.0, 136.8, 177.1; HRMS (FAB): *m/z*: calcd for C₁₇H₂₇O₃Si: 307.1729; found: 307.1740 [M + H]⁺.

Methyl 2,2-dimethyl-5-phenyl-3-trimethylsilyloxypentanoate (3j)³: Colorless oil; yield: 268 mg (87 %); ¹H NMR (500 MHz, CDCl3): δ 0.14 (s, 9H), 1.08 (s, 3H), 1.16 (s, 3H), 1.61-1.66 (m, 2H), 2.40-2.55 (m, 2H), 3.64 (s, 3H), 3.97 (d, J = 12.0 Hz, 1H), 7.16-7.22 (m, 2H), 7.24-7.29 (m, 2H); ¹³C NMR (125 MHz, CDCl3) δ =0.9, 20.3, 21.6, 33.5, 35.2, 48.4, 51.8, 77.5, 125.8, 128.3, 128.4, 142.2, 177.6; HRMS (FAB): m/z: calcd for C₁₇H₂₉O₃Si: 309.1886; found: 309.1876 [M]⁺.

Methyl 2,2-dimethyl-3-trimethylsilyloxy-dodecanoate (3k)²: Colorless oil; yield: 288 mg (91 %); ¹H NMR (500 MHz, CDCl3): δ 0.09 (s, 9H), 0.85 (t, J = 8.1 Hz, 3H), 1.04 (s, 3H), 1.11 (s, 3H), 1.11-1.45 (m, 12H), 1.53-1.64 (m, 2H), 3.64 (s, 3H), 3.83 (d, J = 9.1 Hz, 1H); ¹³C NMR (125 MHz, CDCl3) $\delta = 0.7$, 14.1, 20.1, 21.6, 22.6, 27.0, 29.2, 29.5, 29.7, 31.8, 32.8, 48.2, 51.5, 77.7, 177.8; HRMS (FAB): m/z: calcd for C₁₇H₃₇O₃Si: 317.2512; found: 317.2523 [M + H]⁺.

Methyl 3-(2-furyl)-2,2-dimethyl-3-trimethylsilyloxy-propionate (31)²: Colorless oil; yield: 242 mg (84 %); ¹H NMR (500 MHz, CDCl3): δ 0.00 (s, 9H), 1.04 (s, 3H), 1.23 (s, 3H), 3.68 (s, 3H), 5.00 (s, 1H), 6.20 (d, *J* = 3.2 Hz, 1H), 6.31 (d, *J* = 3.2 Hz, 1H), 7.32-7.34 (m, 1H); ¹³C NMR (125 MHz, CDCl3) δ = -0.3, 19.6,

21.2, 48.6, 51.8, 73.5, 107.9, 109.9, 141.5, 154.4, 176.8; HRMS (FAB): m/z: calcd for C₁₃H₂₃O₄Si: 271.1366; found: 271.1363 [M + H]⁺.

Ethyl 3-3-hydroxy-3-phenylpropionate (5a)³: Colorless oil; yield: 165 mg (85 %); ¹H NMR (500 MHz, CDCl3): δ 1.26 (t, J = 7.2 Hz, 3H), 2.70 (dd, J = 3.9, 16.4 Hz, 1H), 2.76 (dd, J = 9.0, 16.4 Hz, 1H), 3.30-3.34 (brs, 3H), 4.18 (q, J = 7.2 Hz, 2H), 5.13 (dd, J = 2.8, 8.8 Hz, 1H), 7.28-7.31 (m, 1H), 7.35-7.39 (m, 4H); ¹³C NMR (125 MHz, CDCl3) δ = 14.1, 43.2, 60.9, 70.3, 125.6, 127.8, 128.5, 142.4, 172.4; HRMS (FAB): *m/z*: calcd for C₁₁H₁₅O₃: 195.1021; found: 195.1010 [M + H]⁺.

Methyl 3-3-hydroxy-2-methyl-3-phenylpropionate (5b)²: *syn / anti* mixture: Colorless oil; yield: 175 mg (90 %); HRMS (FAB): *m/z*: calcd for C₁₁H₁₅O₃: 195.1021; found: 195.1033 [M + H]⁺. *syn* Isomer: ¹H NMR (500 MHz, CDCl3): δ 1.12 (d, *J* = 7.2 Hz, 3H), 2.78 (dq, *J* = 4.1, 7.2 Hz, 1H), 2.93-2.98 (brs, 3H), 3.67 (s, 3H), 5.10 (d, *J* = 4.0 Hz, 1H), 7.23-7.30 (m, 1H), 7.31-7.39 (m, 4H); ¹³C NMR (125 MHz, CDCl3): δ 1.00 (d, *J* = 7.2 Hz, 3H), 2.83 (dq, *J* = 7.2, 8.4 Hz, 1H), 2.90-3.05 (brs, 3H), 3.72 (s, 3H), 4.74 (d, *J* = 8.4 Hz, 1H), 7.25-7.30 (m, 1H), 7.31-7.42 (m, 4H); ¹³C NMR (125 MHz, CDCl3) δ = 14.4, 47.1, 51.8, 76.4, 126.6, 128.1, 128.5, 141.5, 176.3.

Methyl 4-chlorophenyl-2,2-Dimethyl-3-(tosylamino)propionate (7a)⁶: White solid; m.p. 145 °C; yield: 332 mg (84 %); ¹H NMR (500 MHz, CDCl3): δ 1.03 (s, 3H), 1.31 (s, 3H), 2.30 (s, 3H), 3.58 (s, 3H), 4.27 (d, J = 9.5 Hz, 1H), 6.13 (d, J = 9.5 Hz, 1H), 6.82 (d, J = 8.5 Hz, 2H), 6.94-7.00 (m, 4H), 7.35 (d, J = 8.5 Hz, 2H); ¹³C NMR (125 MHz, CDCl3) $\delta = 21.3$, 22.5, 24.9, 46.9, 52.2, 64.3, 126.8, 128.0, 129.1, 129.3, 135.7, 137.5, 143.0, 176.4; HRMS (FAB): m/z: calcd for C₁₉H₂₃ClNO₄S: 396.1036; found: 396.1022 [M + H]⁺.

Methyl 2,2-dimethyl-3-phenyl-3-(tosylamino)propionate (7b)⁶: White solid; m.p. 130 °C; yield: 285 mg (82 %); ¹H NMR (500 MHz, CDCl3): δ 1.08 (s, 3H), 1.26 (s, 3H), 2.24 (s, 3H), 3.60 (s, 3H), 4.38 (d, *J* = 9.9 Hz, 1H), 6.30 (d, *J* = 9.9 Hz, 1H), 6.88 (d, *J* = 7.0 Hz, 2H), 6.93 (d, *J* = 8.0 Hz, 2H), 9.68-7.10 (m, 5H), 7.39 (d, *J* = 8.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl3) δ = 21.2, 221., 24.2, 41.3, 52.0, 64.5, 126.7, 127.2, 127.7, 127.8, 128.9, 136.9, 137.4, 142.5, 176.4; HRMS (FAB): *m/z*: calcd for C₁₉H₂₄NO₄S: 362.1426; found: 362.1429 [M + H]⁺.

Methyl 2,2-dimethyl-3-(4-nitrophenyl)-3-(tosylamino)propionate (7c)⁶: White solid; m.p. 180 °C; yield: 365 mg (90 %); ¹H NMR (500 MHz, CDCl3): δ 1.05 (s, 3H), 1.33 (s, 3H), 2.26 (s, 3H), 3.59 (s, 3H), 4.39 (d,

J = 9.3 Hz, 1H), 6.30 (d, J = 9.3 Hz, 1H), 6.98 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.5 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.88 (d, J = 8.5 Hz, 2H); ¹³C NMR (125 MHz, CDCl3) $\delta = 21.4$, 22.5, 24.9, 46.8, 52.4, 64.2, 123.0, 126.8, 129.0, 129.2, 137.3, 143.4, 144.7, 147.1, 176.1; HRMS (FAB): m/z: calcd for C₁₉H₂₃N₂O₆S: 407.1277; found: 407.1273 [M + H]⁺.

Methyl 3-(4-methoxyphenyl)- 2,2-dimethyl-3-(tosylamino)propionate (7d)⁶: White solid; m.p. 114 °C; yield: 250 mg (64 %); ¹H NMR (500 MHz, CDCl3): δ 1.04 (s, 3H), 1.25 (s, 3H), 2.25 (s, 3H), 3.57 (s, 3H), 3.68 (s, 3H), 4.29 (d, J = 9.2 Hz, 1H), 6.12 (d, J = 9.2 Hz, 1H), 6.53 (d, J = 8.8 Hz, 2H), 6.78 (d, J = 8.5 Hz, 2H), 7.36 (d, J = 8.8 Hz, 2H), 7.81 (dd, J = 8.5, 8.8 Hz, 2H); ¹³C NMR (125 MHz, CDCl3) $\delta = 21.5$, 22.5, 24.6, 47.6, 52.2, 55.4, 64.3, 113.1, 126.9, 129.0, 129.1, 129.4, 137.7, 142.4, 158.8, 176.4; HRMS (FAB): m/z: calcd for C₂₀H₂₆NO₅S: 392.1532; found: 392.1540 [M + H]⁺.

Methyl 3-[4-(dimethylamino)phenyl]-2,2-dimethyl-3-(tosylamino)propionate (7e)⁶: White solid; m.p. 155 °C; yield: 226 mg (56 %); ¹H NMR (500 MHz, CDCl3): δ 1.04 (s, 3H), 1.25 (s, 3H), 2.23 (s, 3H), 2.82 (s, 6H), 3.57 (s, 3H), 4.23 (d, J = 9.6 Hz, 1H), 5.99 (d, J = 9.6 Hz, 1H), 6.34 (d, J = 7.1 Hz, 2H), 6.68 (d, J = 8.6 Hz, 2H), 6.91 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.6 Hz, 2H); ¹³C NMR (125 MHz, CDCl3) δ = 21.3, 22.2, 24.5, 40.4, 47.3, 51.9, 64.4, 111.9, 126.9, 128.6, 128.8, 142.0, 149.7, 162.5, 176.8; HRMS (FAB): *m/z*: calcd for C₂₀H₂₆NO₅S: 392.1532; found: 392.1540 [M + H]⁺.

Methyl 2,2-dimethyl-3-phenyl-3-(phenylamino)propionate (7f)⁶: Colorless oil; yield: 234 mg (82 %); ¹H NMR (500 MHz, CDCl3): δ 1.13 (s, 3H), 1.24 (s, 3H), 2.23 (s, 3H), 3.62 (s, 3H), 4.46 (s, 1H), 4.70 (br, 1H), 6.46 (d, J = 8.5 Hz, 2H), 6.56 (dd, J = 8.5, 8.8 Hz, 1H), 7.00 (d, J = 8.5, 8.8 Hz, 2H), 7.20-7.28 (m, 5H). ¹³C NMR (125 MHz, CDCl3) δ = 20.7, 24.5, 47.0, 52.0, 64.3, 113.3, 117.2, 127.4, 128.0, 128.2, 129.0, 139.2, 146.9, 177.0; HRMS (FAB): *m/z*: calcd for C₁₈H₂₂NO₂: 284.1651; found: 286.1648 [M + H]⁺









`CH₃





NMe₂

MeO



















CI





⁻ S22 -









References

1. N. Giuseppone, P. Van de Weghe, M. Mellah, J. Collin Tetrahedron, 1998, 54, 13129-13148.

- 2. T. Nakagawa, H. Fujisawa, Y. Nagata, T. Mukaiyama Bull. Chem. Soc. Jpn, 2004, 77, 1555-1567.
- 3. G. Onodera, T TOeda, N. Toda, D. Shibagishi, R. Takeuchi Tetrahedron, 2010, 66, 9021-9031.
- 4. K. Gedrich, M. Heitbaum, A. Notzon, I. Senkovska, R. Fröhlich, J. Getzschmann, U. Mueller, F. Glorius,
- S. Kaskel Chem. Euro. J., 2011, 17, 2099-2106.
- 5. M. Abe, M. Ikeda, Y. Shirodai, M. Nojima Tetrahedron Lett. 1996, 37, 5901-5904.
- 6. H. Fujisawa, E. Takahashi, T. Mukaiyama Chem. Eur. J. 2006, 12, 5082-5093.