Supplementary Material (ESI) for Chemical Communications

Nucleophilic Aromatic Substitution Using Et_3SiH/ cat. *t*-Bu-P4 as a System for Nucleophile Activation

Masahiro Ueno, Misato Yonemoto, Masahiro Hashimoto, Andrew E. H. Wheatley, Hiroshi Naka and Yoshinori Kondo

General comment

1H-NMR spectra were recorded on a JEOL AL-400 using tetramethylsilane as an internal standard. Chemical shifts are expressed in d(ppm) values, and coupling constants are expressed in herts (Hz). The following abbreviations are used: s = singlet, d = doublet, m = multiplet, t = triplet, brs = broad

singlet, dd = double-doublet, dt = double-triplet and ddd = double-doublet-doublet. Mass spectra were recorded on JEOL JMS-DX303 or JEOL JMS-AX500 spectrometer. IR spectra were measured with SensIR ATR FT-IR. All the reactions dealing with air or moisture sensitive compounds were carried out in a dry reaction vessel under argon atmosphere unless otherwise noted. Flash column chromatography was carried out using Kanto Chemical Silica gel 60N (70-230 mesh). Triethylsilane was purchased from ACROS. Dry DMSO and dry DMF were purchased from Kanto Chemical Company and used as supplied. *tert*-Butyl P4 base 1.0 *M* solution in *n*-hexane was purchased from Fulka Chemie and used as supplied.

General procedure for the S_NAr reaction of alcohols using Et_3SiH/cat. *t*-Bu-P4

A mixture of aryl fluoride (0.50 mmol), alcohol (1.20 mmol), triethylsilane (120 mg, 1.03 mmol) and dry DMSO (1 mL) was placed in a 20-mL flask equipped with a magnetic stirring bar under argon atmosphere. *t*-Bu-P4 base, *1.0 M* solution in *n*-hexane (50 mL, 0.05 mmol) was added to the solution. The reaction mixture was stirred for 2 h at 100 ^oC. The mixture was quenched with MeOH (2.0 mL) and stirred for several hours (Table 1). Brine was added to the solution and extracted with AcOEt. The combined organic extracts were dried over $MgSO_4$, filtrated, and concentrated under reduced pressure. The crude product was purified with SiO_2 column chromatography.

1-Hexyloxy-2-nitrobenzene

Yield: 100 %, yellow oil.

^{1}H-NMR($CDCl_3$)δ(ppm): 0.90 (t, 3 H, *J* = 7.4 Hz), 1.31-1.36 (m, 4 H), 1.44-1.56 (m, 2 H), 1.83 (td, 2 H, *J* = 6.8Hz, 7.4 Hz), 4.09 (t, 2 H, *J* = 6.8 Hz), 6.99 (dt, 1 H, *J* = 1.0 Hz, 7.8 Hz), 7.05 (dd, 1 H, *J* = 1.0 Hz, 7.8 Hz), 7.49 (dt, 1 H, *J* = 1.6 Hz, 7.8 Hz), 7.8 Hz (dd, 1 H, *J* = 1.6 Hz, 7.8 Hz); IR(neat) 2929, 1607, 1351, 1277, 1254, 1005 cm^{-1}; LRMS(EI) m/z: 223 (M^+) HRMS: calcd for $C_{12}H_{17}NO_3$ 223.1208, found 223.1190.

1-Butoxy-2-nitrobenzene

Yield: 97 %, yellow oil.

^{1}H-NMR($CDCl_3$)δ(ppm): 0.97 (t, 3 H, *J* = 7.5 Hz), 1.46-1.59 (m, 2 H), 1.78-1.87 (m, 2 H), 4.11 (t, 2 H, *J* = 6.5 Hz), 7.00 (t, 1 H, *J* = 8.0 Hz), 7.07 (d, 1 H, *J* = 8.0 Hz), 7.51 (dt, 1 H, *J* = 1.9 Hz, 8.0 Hz), 7.82 (dd, 1 H, *J* = 1.9 Hz, 8.0 Hz); IR(neat) 2960, 1607, 1522, 1351, 1279, 1254, 1165 cm^{-1}; MS(EI) m/z: 243 (M^+); HRMS calcd for $C_{10}H_{13}NO_3$ 195.0895, found 195.0878.

1-Nitro-2-(1-phenylethoxy)benzene

Yield: 92 %, yellow oil.

^{1}H-NMR($CDCl_3$)δ(ppm): 1.68 (d, 3 H, *J* = 6.6 Hz), 5.45 (q, 1 H, *J* = 6.6 Hz), 6.90 (d, 1 H, *J* = 8.1 Hz), 6.94 (t, 1 H, *J* = 8.1 Hz), 7.23-7.42 (m, 6 H), 7.77 (dd, 1 H, *J* = 1.6 Hz, 8.1 Hz)
IR(neat) 2981, 1605, 1520, 1449, 1351, 1275, 1252, 1065, 853 cm^{-1}; MS(EI) m/z: 243 (M^+); HRMS calcd for $C_{14}H_{13}NO_3$ 243.0895, found 243.0911.

1-*sec*-Butoxy-2-nitrobenzene

Yield: 71 %, yellow oil.
^{1}H-NMR($CDCl_3$)δ(ppm): 1.00 (t, 3 H, *J* = 7.5 Hz), 1.35 (d, 3 H, *J* = 6.0 Hz), 1.62-1.88 (m, 2 H), 4.45 (sext, 1 H, *J* = 6.0 Hz), 6.98 (t, 1 H, *J* = 8.1 Hz), 7.06 (d, 1 H, *J* = 8.1 Hz), 7.48 (dt, 1 H, *J* = 1.5 Hz, 8.1 Hz), 7.77 (dd, 1 H, *J* = 1.5 Hz, 8.1 Hz); IR(neat) 2975, 1605, 1522, 1351, 1277, 1252, 922, 854 cm^{-1}; MS(EI) m/z: 243 (M^+); HRMS calcd for $C_{10}H_{13}NO_3$ 195.0895, found 195.0883.

4-Butoxybenzonitrile

Yield: 98 %, colorless oil.
^{1}H-NMR($CDCl_3$)δ(ppm): 0.98 (t, 3 H, *J* = 7.1 Hz), 1.49 (sext, 2 H, *J* = 7.1 Hz), 1.75-1.82 (m, 2 H), 4.00 (t, 2 H, *J* = 7.1 Hz), 6.93 (d, 2 H, *J* = 9.2 Hz), 7.57 (d, 2 H, *J* = 9.2 Hz); IR(neat) 2958, 2223, 1605, 1507, 1256, 1171, 834 cm^{-1}; MS(EI) m/z: 175 (M^+), HRMS calcd for $C_{11}H_{13}NO$ 175.0997, found 175.0991

1-Butoxy-4-(trifluoromethyl)benzene

Yield: 58 %, colorless oil.
^{1}H-NMR($CDCl_3$)δ(ppm): 0.92 (t, 3 H, *J* = 7.6 Hz), 1.45-1.54 (m, 2 H), 1.74-1.82 (m, 2 H), 3.99 (t, 2 H, *J* = 6.6 Hz), 6.94 (d, 2 H, 8.8 Hz), 7.52 (d, 2 H, *J* = 8.8 Hz)
IR(neat) 2937, 1617, 1520, 1328, 1256, 1119, 1067, 1009, 836 cm^{-1}
MS(EI) m/z: 218 (M^+). HRMS: calcd. for $C_{11}H_{13}F_3O$ 218.0918, found 218.0900

2-(4-Methoxyphenoxy)nitrobenzene

Yield: 76 %, yellow crystal
m.p. 73-75°C; ^{1}H-NMR($CDCl_3$)δ(ppm): 3.81 (s, 3 H), 6.88-6.93 (m, 3 H), 7.02 (d, 2H, *J* = 9.3 Hz), 7.09-7.15 (m, 1 H), 7.44 (ddd, 1 H, *J* = 1.7 Hz, *J* = 7.5 Hz, *J* = 8.3 Hz), 7.91 (dd, 1 H, *J* = 1.7 Hz, *J* = 8.3 Hz) ; IR (crystal) 3;101, 3012, 2840, 1600, 1497, 1345, 1229 cm^{-1} ; MS(EI) m/s: 245 (M^+); HRMS calcd for $C_{13}H_{11}NO_4$ 245.0688, found 245.0688.

General procedure for silylation of alcohols using Et_3SiH/cat. *t*-Bu-P4

A mixture of an alcohol (2 mmol), triethylsilane (2.4 mmol), DMF (2 mL), *t*-Bu-P4 base 1.0 *M* solution in *n*-hexane (0.02 mmol) was stirred using the conditions listed in Table 2. The mixture

was treated with saturated aq. NH_4Cl and H_2O and the mixture was extracted with AcOEt. The extract was washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and afforded the crude product, which was purified by SiO_2 column chromatography using n-hexane-AcOEt as an eluent. The silyl ethers were obtained as colorless oils or white solids.

Triethylnon-8-enyloxysilane

Colorless oil 500mg (98%)

^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 0.60 (q, *J* = 8.0 Hz, 6 H), 0.96 (t, *J* = 8.0 Hz, 9 H), 1.30-1.33 (m, 8 H), 1.49-1.56 (m, 2 H), 2.04 (dt, *J* = 6.4, 8.0 Hz, 2 H), 3.59 (t, *J* = 6.4 Hz, 2 H), 4.92 (ddt, *J* = 1.6, 2.0, 10.4 Hz, 1 H), 4.99 (dq, *J* = 1.6, 17.2 Hz, 1 H), 5.81 (ddt, *J* = 6.4, 10.4, 17.2 Hz, 1 H)

IR(neat) 2927, 2346, 1640, 1459, 1414, 1239, 1098, 1005, 909, 745

LRMS (EI) m/z 227 $(M-29)^+$

HRMS calcd for $C_{13}H_{27}O$ Si 227.1830, found 227.1826.

Benzyloxytriethylsilane

Colorless oil 423 mg (95%)

^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 0.65 (q, *J*= 7.6 Hz, 6 H), 0.98 (t, *J*= 7.6 Hz, 9 H), 4.73 (s, 2 H), 7.25 (m, 1 H), 7.32-7.33 (m, 4 H)

IR(neat) 2954, 2875, 2360, 2117, 1740, 1495, 1455, 1414, 1376, 1239, 1206, 1096, 1069, 1007, 810, 799, 731, 697

LRMS (EI) m/z 222 (M^+)

HRMS calcd for $C_{13}H_{22}OSi$ 222.1440, found 222.1455.

Triethyl(1-phenylethoxy)silane

Colorless oil 458 mg (97%)

^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 0.57 (m, 6 H), 0.91 (t, *J*= 8.0 Hz, 9 H), 1.42 (d, *J*= 6.4 Hz, 3 H), 4.86 (q, *J*= 6.4 Hz, 1 H), 7.21 (m, 1 H), 7.23-7.35 (m, 4 H)

IR(neat) 2954, 2875, 2362, 2115, 1492, 1455, 1414, 1358, 1239, 1206, 1094, 1034, 955, 793, 743, 699

LRMS (EI) m/z 236 (M^+)

HRMS calcd for $C_{14}H_{24}OSi$ 236.1596, found 236.1601.

Triethyl(1-propylheptyloxy)silane

Colorless oil 534 mg (98%)

^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 0.59 (q, *J*= 8.0 Hz, 6 H), 0.88 (t, *J*= 6.8 Hz, 3 H), 0.90 (t, *J*= 6.8 Hz, 3 H), 0.96 (t, *J*= 8.0 Hz, 9 H), 1.27 (brs, 10 H), 1.40-1.41 (m, 4 H), 3.63 (quint, *J*= 6.0 Hz, 1 H)

IR(neat) 2956, 2931, 2875, 1459, 1378, 1237, 1125, 1071, 1040, 1005, 724

LRMS (EI) m/z 243 $(M-29)^+$

HRMS calcd for $C_{14}H_{31}OSi$ 243.2143, found 243.2153.

Triethyl(1-methyl-1-phenylethoxy)silane

Colorless oil 476 mg (95%)

^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 0.59 (q, *J*= 8.0 Hz, 6 H), 0.94 (t, *J*= 8.0 Hz, 9 H), 1.57 (s, 6 H), 7.19 (tt, *J*=1.6, 7.6 Hz, 1 H), 7.30 (t, *J*= 7.6 Hz, 2 H), 7.46 (dd, *J*= 1.6, 7.6 Hz, 2 H)

IR(neat) 2954, 2875, 2362, 2117, 1737, 1493, 1459, 1380, 1258, 1173, 1040, 741, 699

LRMS (EI) m/z 221 $(M-29)^+$

HRMS calcd for $C_{13}H_{21}OSi$ 221.1361, found 221.1350.

Triethyltrityloxysilane

White solid 653 mg (87%)

^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 0.29 (q, *J*= 8.0 Hz, 6 H), 0.83 (t, *J*= 8.0 Hz, 9H), 7.20-7.29 (m, 9 H), 7.41-7.44 (m, 6 H)

IR(neat) 2954, 2904, 2871, 1488, 1445, 1241, 1158, 1088, 1061, 1001, 905, 851, 741, 724,695, 673

LRMS (EI) m/z 374 (M^+)

HRMS calcd for $C_{24}H_{22}O_3Si$ 374.2066, found 374.2048.

General procedure for the S_NAr reaction of C-nucleophiles using Et_3SiH/cat. *t*-Bu-P4

A mixture of aryl fluoride (0.50 mmol), C-nucleophiles (0.75 mmol), triethylsilane (87 mg, 0.75 mmol) and dry DMF (0.5 mL) was placed in a 10-mL flask equipped with a magnetic stirring bar under argon atmosphere. *t*-Bu-P4 base, *1.0 M* solution in *n*-hexane (50 μL, 0.05 mmol) was added to the solution. The reaction mixture was stirred for 1-24 h at 80 °C. The mixture was treated with saturated aq. NH_4Cl and H_2O and the mixture was extracted with AcOEt. The extract was washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and afforded the crude product, which was purified by SiO_2 column chromatography using n-hexane-AcOEt as an eluent.

Diethyl methyl(2-nitrophenyl)malonate

Yellow oil 146 mg (99%)

^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 1.23 (t, *J*= 7.2 Hz, 6 H), 1.56 (s, 3H), 4.15-4.30 (m, 4H), 7.33 (dd, *J*= 1.2 Hz, 8.0 Hz, 1H), 7.48 (dt, *J*= 1.2 Hz, 8.0 Hz, 1H), 7.59 (dt, *J*= 1.2 Hz, 8.0 Hz, 1H), 8.02 (dd, *J*= 1.2 Hz, 8.0 Hz, 1H)

IR(neat) 2983, 1746, 1528, 1355, 1260, 1204, 1106, 1015, 856, 748

LRMS (EI) m/z 296 $(M+1)^+$

HRMS calcd for $C_{14}H_{18}NO_6$ 296.1134, found 296.1122.

Diethyl 2-nitrophenylmalonate

Colorless oil 79 mg (56%)

^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 1.29 (t, *J*= 7.1 Hz, 6 H), 4.27 (q, *J*= 7.1 Hz, 4H), 5.30 (s, 1H), 7.48-7.58 (m, 2H), 7.66 (t, *J*= 7.3 Hz, 1H), 8.08 (d, *J*= 7.3 Hz, 1H)

IR(neat) 2983, 1748, 1530, 1349, 1223, 1030, 856, 787

LRMS (EI) m/z 282 $(M+1)^+$

HRMS calcd for $C_{13}H_{16}NO_6$ 282.0978, found 282.0939.

Diethyl *n*-hexyl(2-nitrophenyl)malonate

Orange oil 139 mg (76%)

^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 0.86 (t, *J*= 6.8Hz, 3H), 1.19-1.55 (m, 14H), 2.44-2.49 (m, 2H), 7.34 (dd, *J*= 1.2 Hz, 7.8 Hz, 1H), 7.47 (dt, *J*= 1.2 Hz, 7.8 Hz, 1H), 7.60 (dt, *J*= 1.5 Hz, 7.8 Hz, 1H), 8.01 (dd, *J*= 1.5 Hz, 7.8 Hz, 1H)

^{13}C-NMR (100MHz, $CDCl_3$)δ(ppm): 13.69, 13.83, 22.40, 25.37, 29.33, 31.31, 35.41, 61.82, 62.75, 125.53, 128.26, 130.35, 132.41 (2C), 149.47, 169.10

IR(neat) 2931, 1748, 1735, 1530, 1355, 1246, 1196, 1023, 857, 714

LRMS (EI) m/z 365 $(M)^+$

HRMS calcd for $C_{19}H_{27}NO_6$ 365.1838, found 365.1869.

Diethyl 2-nitrophenyl(2-propenyl)malonate

Yellow oil 152 mg (95%)

^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 1.22 (t, *J*= 7.2 Hz, 6 H), 3.27 (dt, *J*= 1.6 Hz, 7.2 Hz, 2H), 4.17-4.28 (m, 4H), 4.98 (d, *J*= 10.4 Hz, 1H), 5.00 (dd, *J*= 1.2 Hz, 17.6 Hz, 1H), 5.70-5.81 (m, 1H), 7.32 (dd, *J*= 1.2 Hz, 8.0 Hz, 1H), 7.46 (dt, *J*= 1.2 Hz, 8.0 Hz, 1H), 7.57 (dt, *J*= 1.2 Hz, 8.0 Hz, 1H), 8.01 (dd, *J*= 1.2 Hz, 8.0 Hz, 1H)

^{13}C-NMR (100MHz, $CDCl_3$)δ(ppm): 13.86, 39.75, 62.15, 63.07, 119.01, 125.60, 128.39, 130.87, 132.01, 132.35, 133.01, 149.17, 168.62

IR(neat) 2983, 1733, 1530, 1356, 1241, 1202, 1027, 857, 717

LRMS (EI) m/z 322 $(M+1)^+$

HRMS calcd for $C_{16}H_{20}NO_6$ 322.1291, found 322.1286.

Ethyl 2-cyano-2-(2-nitrophenyl)-4-pentenoate

Yellow oil 122 mg (89%)

^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 1.30 (t, *J*= 7.3 Hz, 3 H), 3.19 (dd, *J*= 7.3 Hz, 14.4 Hz, 1H), 3.32 (dd, *J*= 7.3 Hz, 14.4 Hz, 1H), 4.29 (q, *J*= 7.3 Hz, 2H), 5.18-5.22 (m, 2H), 5.69-5.80 (m, 1H), 7.60 (d, *J*= 7.6 Hz, 1H), 7.72 (t, *J*= 7.6 Hz, 1H), 7.79 (d, *J*= 7.6 Hz, 1H), 8.13 (d, *J*= 7.6 Hz, 1H)
IR(neat) 3085, 2985, 2248, 1742, 1530, 1351, 1219, 1027, 932, 853, 753, 731
LRMS (EI) m/z 274 $(M)^+$
HRMS calcd for $C_{14}H_{14}N_2O_4$ 274.0945, found 296.0975.

2-Nitrophenyl(2-propenyl)malononitrile
Orange oil 101 mg (89%)
^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 3.32 (d, *J*= 7.2 Hz, 2H), 5.44-5.49 (m, 2H), 5.87-5.98 (m, 1H), 7.69 (dt, *J*= 1.6 Hz, 7.2 Hz, 1H), 7.78 (dt, *J*= 1.6 Hz, 7.2 Hz, 1H), 7.87 (dd, *J*= 1.6 Hz, 7.2 Hz, 1H), 8.06 (dd, *J*= 1.6 Hz, 7.2 Hz, 1H)
^{13}C-NMR (100MHz, $CDCl_3$)δ(ppm): 41.60, 43.64, 112.98, 124.15, 124.28, 126.67, 127.97, 129.66, 131.53, 133.93, 147.86
IR(neat) 2925, 2252, 1739, 1530, 1351, 940, 849, 745, 720
LRMS (EI) m/z 227 $(M)^+$
HRMS calcd for $C_{12}H_9N_3O_2$ 227.0695, found 227.0675.

Diethyl methyl(4-nitrophenyl)malonate
Yellow oil 143 mg (97%)
^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 1.27 (t, *J*= 6.8 Hz, 6 H), 1.90 (s, 3H), 4.25 (q, *J*= 6.8 Hz, 2H), 4.26 (q, *J*= 6.8 Hz, 2H), 7.57 (d, *J*= 9.2 Hz, 2H), 8.20 (d, *J*= 9.2 Hz, 2H)
IR(neat) 2985, 1721, 1520, 1349, 1252, 1208, 1094, 1013, 855, 710
LRMS (EI) m/z 295 $(M)^+$
HRMS calcd for $C_{14}H_{17}NO_6$ 295.1056, found 295.1043.

Diethyl methyl(2-cyanophenyl)malonate
Yellow oil 63 mg (46%)
^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 1.32 (t, *J*= 7.2 Hz, 6 H), 1.97 (m, 3H), 4.24-4.39 (m, 4H), 7.28 (dd, *J*= 1.2 Hz, 7.6 Hz, 1H), 7.40 (dt, *J*= 1.2 Hz, 7.6 Hz, 1H), 7.56 (dt, *J*= 1.6 Hz, 7.6 Hz, 1H), 7.73 (dd, *J*= 1.6 Hz, 7.6 Hz, 1H)
^{13}C-NMR (100MHz, $CDCl_3$)δ(ppm): 13.85, 22.74, 59.76, 62.38, 112.96, 117.93, 127.32, 127.66, 132.48, 132.52, 142.26, 169.74
IR(neat) 2985, 2225, 1727, 1258, 1214, 1110, 1015, 859, 760
LRMS (EI) m/z 275 $(M)^+$
HRMS calcd for $C_{15}H_{17}NO_4$ 275.1158, found 275.1174.

Diethyl methyl(4-cyanophenyl)malonate

Yellow oil 91 mg (66%)

^{1}H-NMR (400MHz, $CDCl_3$)δ(ppm): 1.26 (t, *J*= 7.1 Hz, 6H), 1.87 (s, 3H), 4.20-4.30 (m, 4H), 7.50 (d, *J*= 8.4 Hz, 2H), 7.64 (d, *J*= 8.4 Hz, 2H)

IR(neat) 2985, 2229, 1727, 1250, 1208, 1094, 1017, 858, 841

LRMS (EI) m/z 275 $(M)^+$

HRMS calcd for $C_{15}H_{17}NO_4$ 275.1158, found 275.1172.