Efficient Synthesis of Acylsilanes from Morpholine Amides

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Supporting Information

General Information. All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring. THF, Et₂O, DMF, and CH₂Cl₂, were purified by passage through a bed of activated alumina.¹ HMPA, triethylamine, and diisopropylethylamine were distilled over calcium hydride prior to use. Morpholine was used as received from Sigma-Aldrich. Reagents were purified prior to use unless otherwise stated following the guidelines of Perrin and Armarego.² Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and anisaldehyde, ceric ammonium nitrate stain, potassium permanganate, or phosphomolybic acid followed by heating. Infrared spectra were recorded on a Bio-Rad FTS 4000 FT-IR spectrometer. ¹H-NMR spectra were recorded on a Varian Inova 500 (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 7.26 ppm). Data are reported as (ap = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ¹³C-NMR spectra were recorded on a Varian Inova 500 (125 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 77.0 ppm). Mass spectra data were obtained on a

(1) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520.

(2) Perrin, D. D. and Armarego, W. L. *Purification of Laboratory Chemicals*; 3rd ed., Pergamon Press, Oxford. 1988.

Voyager-DE Pro and a Thermo Finnigan LCQ Advantage. Dimethylphenylsilyllithium was synthesized according to the procedure of Fleming and coworkers.³

General Experimental Procedure for the Synthesis of Morpholine Amides from Acid

Chlorides: The acid chloride (1 equiv) was added to a flask containing CH₂Cl₂ (enough to make a 1M solution of the acid chloride). The flask was cooled to 0 °C, and morpholine (3 equiv) was added. The reaction was allowed to warm to 23 °C and stirred for 30 minutes at which time it was diluted with EtOAc, then washed with 1M hydrochloric acid, saturated sodium bicarbonate, and brine. The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated *in vacuo*. The resulting amide compounds were used without further purification.

General Experimental Procedure for the Synthesis of Acylsilanes from Morpholine

Amides: The morpholine amide (2 mmol) was added to a flame-dried 50 mL round-bottomed flask under dry nitrogen. To this amide, THF (3 mL) was added, and the solution was then cooled to –78 °C. Dimethylphenylsilyllithium (1.0 M solution in THF, 3 mL) was added dropwise *via* syringe, and the reaction was allowed to stir for 1.5 hours, at which time, it was quenched at –78 °C (**very important to prevent decomposition**) by the addition of 4 mL of saturated aqueous ammonium chloride. The resulting heterogeneous mixture was allowed to warm to room temperature and then stirred for an additional 30 minutes. The reaction was then partitioned between water (5 mL) and ether (5 mL), the phases were separated, and the aqueous phase was extracted with ether (2x5 mL). The combined organics were washed with water (2x20 mL) and once with brine (20 mL), dried over anhydrous MgSO₄, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography using silica gel and the indicated solvent systems to yield pure acylsilane. This procedure has been successfully used at up to 50 mmol scale with care taken to control the internal temperature of the reaction.

(3) Fleming, I.; Newton, T. W.; Roessler, F. J. *Chem. Soc., Perkin Trans I* **1981**, 2527-2532.

1-(Dimethyl(phenyl)silyl)pent-4-en-1-one (3a): Purified with 4% EtOAc/hexanes, yielding **3a** in a 73% yield as a light yellow oil. $R_f = 0.48$ (5% EtOAc/hexanes); IR (film) 3072, 2962, 2911, 1642, 1427, 1251, 1111, 911, 733, 649 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.57 (d, $J = 6$ Hz, 2H), 7.41 (m, 3H), 5.73 (m, 1H), 4.93 (m, 2H), 2.69 (t, $J = 7$ Hz, 2H), 2.23 (td, $J = 7, 7$ Hz, 2H), 0.52 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 244.9, 137.3, 134.2, 133.9, 129.8, 128.1, 114.7, 47.6, 26.1, -4.9 . LRMS (electrospray): Mass calcd for $\text{C}_{13}\text{H}_{18}\text{NaOSi}$ $[\text{M}+\text{Na}]^+$, 241.10. Found 241.

1-(Dimethyl(phenyl)silyl)octan-1-one (3b): Purified with 4% EtOAc/hexanes, yielding **3b** in a 81% yield as a light yellow oil. IR (film) 2927, 2856, 1641, 1427, 1250, 1111, 833, 781, 735, 700 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.57 (m, 2H), 7.40 (m, 3H), 2.57 (t, $J = 7$ Hz, 2H), 1.44 (tt, $J = 7, 7$ Hz, 2H), 1.28-1.15 (m, 8H), 0.87 (t, $J = 7$ Hz, 3H), 0.50 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 246.7, 134.6, 133.9, 129.8, 128.1, 48.8, 31.6, 29.1, 29.0, 22.5, 22.1, 14.0, -4.8 .⁴

1-(Dimethyl(phenyl)silyl)ethanone (3c): Purified with 5% EtOAc/hexanes, yielding **3c** in a 76% yield as a light yellow oil. IR (film) 3090, 2962, 2903, 1644, 1425, 1340, 1251, 1111, 814, 781, 736, 701 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.57 (m, 2H), 7.41 (m, 3H), 2.26 (s, 3H), 0.52 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 245.3, 134.1, 133.8, 129.8, 128.1, 35.8, -5.0 .⁵

1-(Dimethyl(phenyl)silyl)propan-1-one (3d): Purified with 4% EtOAc/hexanes, yielding **3d** as a colorless oil. IR (film) 2970, 2897, 1644, 1427, 1250, 1111, 816, 735, 701 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.57 (d, $J = 6$ Hz, 2H), 7.40 (m, 3H), 2.61 (q, $J = 7$ Hz, 2H), 0.93 (t, $J = 7$ Hz, 3H), 0.51 (s, 6H); ^{13}C NMR

(4) Identical to previously reported spectra for this compound reported in Katritzky, A. R.; Lang, H.; Wang, Z.; Zhu, L. *J. Org. Chem.* **1996**, 61, 7551-7557.

(5) Identical to previously reported spectra for this compound in Tacke, R.; Wagner, S. A.; Brakmann, S.; Wuttke, F.; Eilert, U. *J. Organomet. Chem.* **1993**, 458, 13-18.

(125 MHz, CDCl_3) δ 246.2, 134.6, 133.9, 129.8, 128.1, 41.9, 6.1, -4.8. LRMS (MALDI-TOF): Mass calcd for $\text{C}_{11}\text{H}_{17}\text{OSi}$, 193.10. Found 193.⁶

1-(Dimethyl(phenyl)silyl)-3-phenylpropan-1-one (3e): Purified with 4% EtOAc/hexanes, yielding **3e** in a 80% yield as a colorless oil. IR (film) 3065, 3027, 2957, 1641, 1427, 1251, 1111, 814, 782, 736, 699 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.53 (d, $J = 7$ Hz, 2H), 7.41 (m, 3H), 7.24 (m, 2H), 7.16 (t, $J = 8$ Hz, 1H), 7.08 (d, $J = 8$ Hz, 2H), 2.90 (t, $J = 8$ Hz, 2H), 2.78 (t, $J = 8$ Hz, 2H), 0.48 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 245.1, 141.5, 134.2, 134.0, 129.9, 128.4, 128.3, 128.2, 125.9, 50.4, 28.2, -4.9.⁷

2-Methyl-1-(dimethyl(phenyl)silyl)propan-1-one (3f): Purified with 3% EtOAc/hexanes, yielding **3f** in a 60% yield as a light yellow oil. IR (film) 3083, 2967, 1638, 1425, 1250, 1112, 813, 781, 736, 702 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.58 (m, 2H), 7.40 (m, 3H), 2.92 (m, 1H), 0.93 (d, $J = 7$ Hz, 6H), 0.52 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 248.6, 135.0, 133.9, 129.7, 128.1, 45.3, 16.4, -4.1.⁸

2,2-Dimethyl-1-(dimethyl(phenyl)silyl)propan-1-one (3g): Purified with 5% EtOAc/hexanes, yielding **3g** in a 65% yield as a light yellow oil. IR (film) 3090, 2965, 1632, 1469, 1425, 1249, 1109, 818, 780, 702 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.58 (d, $J = 6$ Hz, 2H), 7.39 (m, 3H), 1.01 (s, 9H), 0.56 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 247.9, 136.0, 134.0, 129.6, 128.0, 49.4, 24.7, -2.4.⁹

Cyclopropyl(dimethyl(phenyl)silyl)methanone (3h): Purified with 5% EtOAc/hexanes, yielding **3h** in a 82% yield as a light yellow oil. IR (film) 3104,

(6) Identical to previously reported spectra for this compound in Fujiwara, T.; Sawabe, K.; Takeda, T. *Tetrahedron*. **1997**, 53, 8349-8370.

(7) Identical to previously reported spectra for this compound in Fleming, I.; Mwankiki, J. *J. Chem. Soc. Perkin Trans. I*. **1998**, 1237-1248.

(8) Identical to previously reported spectra for this compound reported in Fleming, I.; Ghosh, U. *J. Chem. Soc. Perkin Trans. I*. **1994**, 257-262.

(9) Identical to previously reported spectra for this compound reported in Fleming, I.; Ghosh, U. *J. Chem. Soc. Perkin Trans. I*. **1994**, 257-262.

3005, 2961, 1622, 1425, 1357, 1250, 1111, 1003, 781, 736, 701 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.61 (m, 2H), 7.42 (m, 3H), 2.48 (ap tt, $J = 3, 4$ Hz, 1H), 1.07 (m, 2H), 0.80 (m, 2H), 0.54 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 244.8, 134.7, 134.0, 129.7, 128.1, 25.7, 11.5, -4.7 .¹⁰

Cyclohexyl(dimethyl(phenyl)silyl)methanone (3i): Purified with 5% EtOAc/hexanes, yielding **3i** in a 65% yield as a colorless oil. IR (film) 2930, 2854, 1634, 1250, 1111, 822, 780, 701 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3)

δ 7.56 (d, $J = 6$ Hz, 2H), 7.40 (m, 3H), 2.69 (m, 1H), 1.65 (m, 5H), 1.15 (m, 5H), 0.51 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 248.5, 135.0, 133.9, 129.7, 128.0, 55.6, 26.7, 25.9, 25.6, -4.1 .¹¹

(2,4-Dimethoxyphenyl)(dimethyl(phenyl)silyl)methanone (16): Purified with 10% EtOAc/hexanes, yielding **16** in a 35% yield as a bright yellow oil. $R_f = 0.35$ (10% EtOAc/hexanes); IR (film) 3004, 2963, 2840, 1611,

1570, 1462, 1254, 1213, 1161, 1111, 1028, 813, 732, 702 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.58 (d, $J = 8$ Hz, 1H), 7.49 (m, 2H), 7.33 (m, 3H), 6.52 (dd, $J = 2, 8$ Hz, 1H), 6.30 (d, $J = 2$ Hz, 1H), 3.82 (s, 3H), 3.46 (s, 3H), 0.50 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 231.1, 164.6, 161.0, 137.2, 133.2, 128.9, 128.8, 128.4, 127.6, 105.3, 97.4, 55.4, 54.0, -3.1 . LRMS (MALDI-TOF): Mass calcd for $\text{C}_{17}\text{H}_{24}\text{O}_3\text{Si}$ $[\text{M}+\text{H}]^+$, 301.13. Found 302.

(Furan-2-yl)(dimethyl(phenyl)silyl)methanone (17): Purified with 10% EtOAc/hexanes, yielding **17** in a 62% yield as a bright yellow oil. IR (film) 3129, 2962, 2901, 1590, 1460, 1456, 1249, 111, 1082, 837, 806, 784, 736, 702

cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.63 (d, $J = 6$ Hz, 2H), 7.55 (ap s, 1H), 7.42 (m, 3H), 6.88 (d, $J = 3$ Hz, 1H), 6.44 (m, 1H), 0.64 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 218.8, 157.7, 146.0,

(10) Identical to previously reported spectra for this compound reported in Bonini, B. F.; Busi, F.; Laet, R. C.; Mazzanti, G.; Thuring, J.-W. *J. F. J. Chem. Soc. Perkin Trans. I.* **1993**, 1011-1018.

(11) Identical to previously reported spectra for this compound reported in Bonini, B. F.; Busi, F.; Laet, R. C.; Mazzanti, G.; Thuring, J.-W. *J. F. J. Chem. Soc. Perkin Trans. I.* **1993**, 1011-1018.

134.7, 134.1, 129.9, 128.1, 116.8, 111.9, -4.0. LRMS (MALDI-TOF): Mass calcd for $C_{13}H_{15}O_2Si [M+H]^+$, 231.08. Found 232.¹²

4-(Benzyloxy)-1-(dimethyl(phenyl)silyl)butan-1-one (18):

Purified with 10% EtOAc/hexanes, yielding **18** in a 85% yield as a colorless oil. R_f = 0.34 (10% EtOAc/hexanes); IR (film) 3029, 2957, 2860, 1706, 1642, 1427, 1251, 1112, 831, 782, 736, 700 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J = 6 Hz, 2H), 7.44-7.31 (m, 8H), 4.45 (s, 2H), 3.42 (t, J = 6 Hz, 2H), 2.74 (t, J = 7 Hz, 2H), 1.85 (ap tt, J = 6, 7 Hz, 2H), 0.53 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 245.7, 138.6, 134.6, 134.2, 130.0, 128.5, 128.3, 127.8, 127.6, 72.8, 69.5, 45.5, 22.4, -4.6. LRMS (MALDI-TOF): Mass calcd for $C_{19}H_{24}NaO_2Si [M+Na]^+$, 335.14. Found 336.

4-((2-Methoxyethoxy)methoxy)-1-(dimethyl(phenyl)silyl)butan-1-one (19):

Purified with 20% EtOAc/hexanes, yielding **19** in a 67% yield as a colorless oil. R_f = 0.23 (20% EtOAc/hexanes); IR (film) 3093, 2930, 2880, 1641, 1429, 1250, 1041, 833, 781, 736, 702 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, J = 6 Hz, 2H), 7.38 (m, 3H), 4.61 (s, 2H), 3.60 (t, J = 5 Hz, 2H), 3.51 (t, J = 5 Hz, 2H), 3.44 (t, J = 6 Hz, 2H), 3.37 (s, 3H), 2.66 (t, J = 7 Hz, 2H), 1.75 (ap tt, J = 6, 7 Hz, 2H), 0.48 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 245.3, 134.3, 133.9, 129.8, 128.1, 95.2, 71.7, 66.8, 66.6, 58.9, 45.2, 22.0, -4.9. LRMS (MALDI-TOF): Mass calcd for $C_{16}H_{26}NaO_4Si [M+Na]^+$, 333.15. Found 334.

1-(Dimethyl(phenyl)silyl)-4-(trityloxy)butan-1-one (20):

Purified with 5% EtOAc/hexanes, yielding **20** in a 75% yield as a colorless oil. R_f = 0.34 (5% EtOAc/hexanes); IR (film) 3058, 2955, 2872, 1642, 1489, 1445, 1250, 1073, 908, 734 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 7 Hz, 2H), 7.38 (m, 9H), 7.27 (m, 9H), 2.99 (t, J = 6 Hz, 2H), 2.68 (t, J = 7 Hz, 2H), 1.80 (ap tt, J = 6, 7 Hz, 2H), 0.49 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 245.6, 144.3, 134.5, 134.0, 129.8, 128.6,

(12) Identical to previously reported spectra for this compound in Bonini, B. F.; Comes-Franchini, M.; Mazzanti, G.; Passamonti, U.; Ricci, A.; Zani, P. *Synthesis*. **1995**, 92-96.

128.1, 127.7, 126.8, 86.3, 62.8, 45.5, 22.5, -4.8. LRMS (MALDI-TOF): Mass calcd for $C_{31}H_{32}NaO_2Si$ $[M]^+$, 487.21. Found 489.

4-(tert-Butyldiphenylsiloxy)-1-(dimethyl(phenyl)silyl)butan-1-one (21): Purified with 5% EtOAc/hexanes, yielding **21** in a 60% yield as a colorless oil. $R_f = 0.52$ (10% EtOAc/hexanes); IR (film)

2957, 2857, 1711, 1639, 1425, 1252, 1113, 1061, 831, 782, 734, 700 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, $J = 7$ Hz, 4H), 7.57 (m, 2H), 7.43-7.37 (m, 9H), 3.60 (t, $J = 6$ Hz, 2H), 2.73 (t, $J = 7$ Hz, 2H), 1.74 (ap tt, $J = 6, 7$ Hz, 2H), 1.03 (s, 9H), 0.51 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 245.9, 135.5, 134.5, 133.9, 129.8, 129.6, 129.5, 128.1, 127.7, 127.6, 63.0, 45.2, 26.8, 24.9, 19.2, -4.8. LRMS (electrospray): Mass calcd for $C_{28}H_{37}O_2Si_2$ $[M+H]^+$, 461.24. Found 461.

4-(Triisopropylsiloxy)-1-(dimethyl(phenyl)silyl)butan-1-one (22): Purified with 4% EtOAc/hexanes, yielding **22** in a 79% yield as a colorless oil. $R_f = 0.44$ (5% EtOAc/hexanes); IR (film) 2944,

2866, 1643, 1464, 1249, 1109, 883 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, $J = 7$ Hz, 2H), 7.38 (m, 3H), 3.60 (t, $J = 6$ Hz, 2H), 2.71 (t, $J = 7$ Hz, 2H), 1.70 (ap tt, $J = 6, 7$ Hz, 2H), 1.02 (m, 21H), 0.49 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 246.0, 134.5, 133.9, 129.8, 128.1, 62.3, 45.1, 25.3, 18.0, 11.9, -4.8. LRMS (MALDI-TOF): Mass calcd for $C_{21}H_{36}NaO_2Si_2$ $[M+Na]^+$, 401.23. Found 402.

4-(Benzyloxy)-1-morpholinobutan-1-one (23): To a suspension of sodium hydride (60% dispersion in mineral oil, 400 mg, 10 mmol) in tetrahydrofuran (40 mL) at 0 °C was added 4-hydroxy-

1-morpholinobutan-1-one (1.732 g, 10 mmol) in tetrahydrofuran (50 mL) *via* cannulation. The reaction was allowed to stir at this temperature for 1 h. Benzyl bromide (1.19 mL, 10 mmol) was added *via* syringe, and the reaction all allowed to warm to 23 °C and then stirred for 14 h. Water (40 mL) was added, and the reaction mixture was extracted with EtOAc (2x50 mL). The combined organics were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel,

eluted with 40% EtOAc/hexanes, yielding 1.53 g (58%) of pure 4-(benzyloxy)-1-morpholinobutan-1-one as a colorless oil. $R_f = 0.17$ (50% EtOAc/hexanes); IR (film) 3497, 2960, 2924, 2858, 1643, 1437, 1269, 1116, 1032, 741, 700 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.33 (m, 5H), 4.51 (s, 2H), 3.66 (m, 4H), 3.62 (m, 2H), 3.56 (t, $J = 6$ Hz, 2H), 3.48 (m, 2H), 2.45 (t, $J = 7$ Hz, 2H), 1.98 (ap tt, $J = 6, 7$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.3, 138.3, 128.3, 127.6, 127.5, 72.8, 69.3, 66.8, 66.6, 45.8, 41.8, 29.5, 25.2. LRMS (electrospray): Mass calcd for $\text{C}_{15}\text{H}_{22}\text{NO}_3$ $[\text{M}+\text{H}]^+$, 264.16. Found 264.

4-((2-Methoxyethoxy)methoxy)-1-morpholinobutan-1-one (24): Methoxyethoxymethyl chloride (0.628 mL, 5.5 mmol) as added to stirring solution of 4-hydroxy-1-

morpholinobutan-1-one (0.866 g, 5.0 mmol) and diisopropylethylamine (1.02 mL, 5.8 mmol) in dichloromethane (7 mL) at rt. The reaction was allowed to stir for 16 h, and then it was diluted with dichloromethane and washed three times with saturated sodium bicarbonate. The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo* to give 662 mg (51%) of pure 4-((2-methoxyethoxy)methoxy)-1-morpholinobutan-1-one as a colorless oil. $R_f = 0.33$ (10% methanol/ CH_2Cl_2); IR (film) 2926, 2874, 1647, 1435, 1271, 1116, 1042, 850, 733 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 4.68 (s, 2H), 3.64-3.45 (m, 14H), 3.37 (s, 3H), 2.39 (t, $J = 7$ Hz, 2H), 1.91 (ap tt, $J = 6, 7$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.1, 95.4, 71.7, 66.9, 66.8, 66.7, 66.5, 58.9, 45.8, 41.8, 29.5, 25.1. LRMS (MALDI-TOF): Mass calcd for $\text{C}_{12}\text{H}_{24}\text{NO}_5$ $[\text{M}+\text{H}]^+$, 262.17. Found 263.

1-Morpholino-4-(trityloxy)butan-1-one (25): To a solution of 4-hydroxy-1-morpholinobutan-1-one (0.866 g, 5.0 mmol), trityl chloride (1.533 g, 5.5 mmol), and triethylamine (1.14 mL, 8.2 mmol)

in dimethylformamide (25 mL) was added 4-(dimethylamino)pyridine (30.5 mg, 0.25 mmol). The reaction was allowed to stir for 15 h at 23 $^\circ\text{C}$, then poured over ice water and extracted with dichloromethane (2x50 mL). The combined organic layers were washed with saturated aqueous ammonium chloride and water, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel using 40%

EtOAc/hexanes, yielding 1.85 g (89%) of pure 1-morpholino-4-(trityloxy)butan-1-one as a light yellow solid. R_f = 0.52 (50% EtOAc/hexanes); IR (film) 3057, 2963, 2960, 2922, 1646, 1441, 1269, 1223, 1116, 1070, 1032, 736, 704, 633 cm^{-1} ; mp = 108-110 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.43 (d, J = 8 Hz, 6H), 7.30 (m, 6H), 7.24 (m, 3H), 3.63 (m, 6H), 3.43 (m, 2H), 3.15 (t, J = 6 Hz, 2H), 2.40 (t, J = 7 Hz, 2H), 1.97 (ap tt, J = 6, 7 Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.5, 144.2, 128.6, 127.7, 126.9, 86.5, 66.9, 66.6, 62.8, 45.9, 41.8, 29.8, 25.8. LRMS (MALDI-TOF): Mass calcd for $\text{C}_{27}\text{H}_{29}\text{NNaO}_3$ $[\text{M}+\text{Na}]^+$, 438.20. Found 439.

4-(*tert*-Butyldiphenylsiloxy)-1-morpholinobutan-1-one (26): To

a solution of 4-hydroxy-1-morpholinobutan-1-one (1.00 g, 5.77 mmol), imidazole (825 mg, 12.1 mmol), and 4-(dimethylamino)pyridine (70 mg, 0.58 mmol) in dichloromethane (45 mL) at 0 °C was added *tert*-butyldiphenylchlorosilane (1.62 mL, 6.35 mmol) *via* syringe slowly over 15 min. It was allowed to warm to 23 °C and then stirred for additional 1 h. After that time, the reaction was filtered over celite was washed with 1M hydrochloric acid (2x10 mL), water (2x10 mL), and brine (10 mL). The organic layer was then dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The resulting oil was purified by flash chromatography on silica gel with 45% EtOAc/hexanes, yielding 2.26 g (99%) of pure 4-(*tert*-butyldiphenylsiloxy)-1-morpholinobutan-1-one as a colorless oil. R_f = 0.45 (50% EtOAc/hexanes); IR (film) 2110, 2960, 2931, 2857, 1649, 1428, 1111, 737, 704, 611 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.69 (d, J = 7 Hz, 4H), 7.42 (m, 6H), 3.78 (t, J = 6 Hz, 2H), 3.65 (m, 6H), 3.46 (m, 2H), 2.45 (t, J = 7 Hz, 2H), 1.93 (ap tt, J = 6, 7 Hz, 2H), 1.09 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.4, 135.4, 133.6, 127.5, 66.6, 66.5, 63.0, 45.8, 41.7, 29.3, 28.0, 26.8, 19.1. LRMS (MALDI-TOF): Mass calcd for $\text{C}_{24}\text{H}_{34}\text{NO}_3\text{Si}$ $[\text{M}+\text{H}]^+$, 412.23. Found 413.

4-(Triisopropylsiloxy)-1-morpholinobutan-1-one (27): 4-

(Dimethylamino)pyridine (733 mg, 6.0 mmol) was added to a stirring solution of 4-hydroxy-1-morpholinobutan-1-one (866 mg, 5.0 mmol), triisopropylchlorosilane (1.17 mL, 5.5 mmol), and triethylamine (0.906 mL, 6.5 mmol) in dichloromethane (39 mL) at 0 °C. The reaction was allowed to warm to 23 °C and then

stirred for 18 h. After this time, the reaction was quenched by the addition of 30 mL of saturated aqueous ammonium chloride. The reaction was diluted with EtOAc, and the organic layer was separated and washed with saturated aqueous citric acid, saturated aqueous sodium bicarbonate, and brine. The organic layer was then dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel with 40% EtOAc/hexanes, yielding 1.24 g (76%) of pure 4-(triisopropylsiloxy)-1-morpholinobutan-1-one was a colorless oil. R_f = 0.52 (50% EtOAc/hexanes); IR (film) 2943, 2864, 1654, 1431, 1241, 1113, 883, 681 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 3.74 (t, J = 6 Hz, 2H), 3.63 (m, 6H), 3.49 (m, 2H), 2.44 (t, J = 7 Hz, 2H), 1.87 (ap tt, J = 7, 7 Hz, 2H), 1.05 (m, 21H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.7, 66.9, 66.6, 62.3, 45.9, 41.8, 29.2, 28.4, 18.0, 11.9. LRMS (MALDI-TOF): Mass calcd for $\text{C}_{17}\text{H}_{36}\text{NO}_3\text{Si}$ $[\text{M}+\text{H}]^+$, 330.25. Found 331.

Selected ^1H NMR Spectra:

H1 stdgar N2 DB_8va 1nov2000

Pulse Sequence: zgpg30

Solvent: CDCl3

Ambient temperature

User: 1-11-87

File: 2-4-dimethoxy

NOVA-500 "wztko"

PULSE SEQUENCE

Relax. delay 1.000 sec

Pulse 65.5 degrees

Acq. time 1.003 sec

Width 8997.0 Hz

16 repetitions

OBSERVE N1. 499.5181506 MHz

DATA PROCESSING

Time broadening 1.6 Hz

FT size 65536

Total time 0 min, 32 sec

H1 sddpqr NF D8_5mm 1aovv860

Pulse Sequence: zgpg30

Solvent: CDCl3

Ambient temperature

User: 1-18-87

File: IN-CHC-BenzylAS

NOVA-100 "vaks"

PULSE SEQUENCE

Relax. delay 1.000 sec

Pulse 68.5 degrees

Acq. time 1.003 sec

Width 5997.0 Hz

16 repetitions

OBSERVE H1, 499.8387985 MHz

DATA PROCESSING

Line broadening 1.0 Hz

FT size 65536

Total time 0 min, 32 sec

18

h1 stdgar N2 DB_8mm innova600

Pulse Sequence: zgpg30

Solvent: CDCl3

Ambient temperature

User: 1-13-87

File: 18-CHC-trityl18

INSTR-500 "vnmr"

PULSE SEQUENCE

Relax. delay 1.000 sec

Pulse 68.3 degrees

Acq. time 1.003 sec

Width 8997.0 Hz

16 repetitions

OBSERVE F1. 499.8187506 MHz

DATA PROCESSING

Line broadening 1.0 Hz

FT size 65536

Total time 0 min, 32 sec

h1 st4par NT 05_5mm inovas00

Pulse Sequence: zgpg30

Solvent: CDCl3

Acquire temperature

User: j-18-87

File: IN-CTC-INDP34E

NOVA-500 "vnmr"

PULSE SEQUENCE

Relax. delay 1.000 sec

Pulse 63.5 degrees

Acq. time 1.003 sec

Width 5997.0 Hz

16 repetitions

OBSERVE F1. 499.518795 MHz

DATA PROCESSING

Line broadening 1.0 Hz

FT size 65536

Total time 0 min, 32 sec

H1 stüper XT DS_5mm.inova500

Pulse Sequence: zgpg30

Solvent: CDCl₃

Ambient temperature

User: 1-18-87

File: UK-CCC-TMSAE

INOVA-500 "ukae"

PULSE SEQUENCE

Relax. delay 1.000 sec

Pulse 68.8 degrees

Acq. time 1.001 sec

Width 8997.0 Hz

16 repetitions

CONVERT M1. 499.8388044 MHz

DATA PROCESSING

Line broadening 1.0 Hz

FT size 65536

Total time 0 min, 32 sec

h1 ntldgar N2 DB_5mm isova500

Pulse Sequence: zgpg30

Solvent: CDCl₃

Ambient temperature

User: 1-12-27

File: 12-CTC-TRIMYANIDE

INOVA-500 "walle"

PULSE SEQUENCE

Relax. delay 1.000 sec

Pulse 68.5 degrees

Acq. time 1.003 sec

Width 5997.0 Hz

16 repetitions

OBSERVE M1. 499.5287985 MHz

DATA PROCESSING

Time Broadening 1.0 Hz

FT size 65536

Total time 0 min, 32 sec