Supporting Information
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KHF$_2$: A Mild and Selective Desilylating Agent for Phenol tert-Butyldimethylsilyl (TBDMS) Ethers

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General Experimental Considerations

Thin layer chromatography was performed on 200 µm aluminum-foil-backed silica gel plates, and column chromatography was performed using 100–200, 200–300, or 230–400 mesh silica gel, please see individual compound headings for details. Commercially available anhydrous DMF and anhydrous MeOH were used for the silylation and desilylation reactions, respectively. Et₂O was distilled from LiAlH₄ and then from sodium. CH₂Cl₂, EtOAc, and hexanes were distilled from anhydrous CaSO₄. ¹H NMR spectra were obtained at 500 MHz and are referenced to the residual protonated solvent resonance. ¹³C NMR spectra for new compounds were obtained at 125 MHz and are referenced to the solvent resonance. The one ¹⁹F NMR spectrum was obtained at 282 MHz in CDCl₃ and is referenced to CFCl₃. Chemical shifts (δ) are reported in parts per million (ppm) and coupling constants (J) are in hertz (Hz). Standard abbreviations are used to designate resonance multiplicities. Desilylation reactions shown in Schemes 1 and 2 were conducted using 1 mmol of the silyl ether in anhydrous MeOH (10 mL), with KHF₂ (2.5 mmol), except for the disilyl derivatives of hydroquinone, 1,1′-bi(2-naphthol), and bisphenol F where double the equivalents of KHF₂ were used (5 mmol).

p-Bromophenol (1)

Chromatographed on a 100–200 mesh silica column using hexanes followed by 25% hexanes in EtOAc to give 0.150 g (87% yield) of p-bromophenol as a crystalline, white solid.

p-Cyanophenol (2)
Chromatographed on a 100–200 mesh silica column using 50% EtOAc in hexanes, followed by EtOAc, and then 5% MeOH in CH₂Cl₂ to give 0.105 g (88% yield) of p-cyanophenol as a colorless solid.

**Acetaminophen (paracetamol, 3)**

Chromatographed on a 200–300 mesh silica column using 50% acetone in hexanes to give 0.144 g (95% yield) of acetaminophen as a free-flowing, white solid.

**Vanillin (4)**

Chromatographed on a 100–200 mesh silica column using hexanes followed by 20% EtOAc in hexanes to give 0.114 g (75% yield) of vanillin as a free-flowing, light-grey solid.

**8-Hydroxyquinoline (5)**

Chromatographed on a 200–300 mesh silica column using hexanes followed by 20% EtOAc in hexanes to give 0.129 g (89% yield) of 8-hydroxyquinoline as a crystalline, light yellow solid.

**p-Carbomethoxyphenol (6)**

Chromatographed on a 100–200 mesh silica column using hexanes, 20% EtOAc in hexanes, and 30% EtOAc in hexanes to give 0.137 g (90% yield) of p-carbomethoxyphenol as a white powder.

**2,6-Dimethylphenol (7)**

Chromatographed on a 230–400 silica column using 30% CH₂Cl₂ in pentane to give 86.7 mg (71% yield) of 2,6-dimethylphenol as a pale-yellow solid.

**Hydroquinone (8)**
Chromatographed on a 100–200 mesh silica column using hexanes, 20% EtOAc in hexanes, and 30% EtOAc in hexanes to give 73.8 mg (67% yield) of hydroquinone as a free-flowing, light-pink solid.

**1,1’-Bi(2-naphthol) (9)**
Chromatographed on a 100–200 mesh silica column using hexanes followed by 20% EtOAc in hexanes to give 0.226 g (79% yield) of 1,1’-bi(2-naphthol) as a free-flowing, white solid.

**Bisphenol F (4,4’-dihydroxydiphenylmethane, 10)**
Chromatographed on a 100–200 mesh silica column using hexanes, followed by 50% EtOAc in hexanes, and then EtOAc to give 0.169 g (84% yield) of bisphenol F as a free-flowing, white solid.

**4-[(t-Butyldimethylsilyl)oxy]phenol (11)**
In an oven-dried 100 mL round bottom flask, flushed with nitrogen gas, a mixture of imidazole (3.16 g, 46.4 mmol, 6.03 molar equiv.) and TBDMSCl (1.16 g, 7.70 mmol, 1.00 molar equiv.) in dry CH$_2$Cl$_2$ (23.2 mL) was stirred at room temperature for 10 min. Hydroquinone (2.55 g, 23.2 mmol, 3.01 molar equiv.) was added, and the reaction mixture was allowed to stir at room temperature for an additional 2 h. The reaction mixture was diluted with CH$_2$Cl$_2$, washed with deionized water, saturated aqueous NaHCO$_3$, and brine. The organic layer was dried over anhydrous Na$_2$SO$_4$, evaporated under reduced pressure, and loaded onto a 100–200 mesh silica column packed in hexanes. Sequential elution with hexanes, 3% EtOAc, and 5% EtOAc in hexanes gave 0.373 g (22% yield) of 4-[(t-butyldimethylsilyl)oxy]phenol (11) as a white solid (the disilyl derivative was isolated as well). $R_f$ (30% EtOAc in hexanes) = 0.41. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 6.72–6.68 (m, 4H,
ArH), 4.44 (br s, 1H, OH), 0.97 (s, 9H, t-Bu), 0.16 (s, 6H, SiCH$_3$). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 150.0, 149.6, 121.0, 116.2, 25.9, 18.4, -4.3. HRMS (ESI/TOF): calcd for $\text{C}_{12}\text{H}_{20}\text{O}_{2}\text{SiNa}$ [M + Na]$^+$: 247.1125; found: 247.1127. See reference 27 in the paper.

4-[(t-Butyldimethylsilyl)oxy]phenyl acetate (12)

To solution of 4-[(t-butyldimethylsilyl)oxy]phenol (11, 0.400 mg, 1.78 mmol) in CH$_2$Cl$_2$ (3.70 mL, 0.480 M) in an oven-dried 25 mL round bottom flask, DIPEA (0.465 mL, 0.345 g, 2.67 mmol, 1.50 molar equiv.) was added. The solution was allowed to stir for 5 minutes, DMAP (0.217 g, 0.178 mmol, 0.100 molar equiv.), and then acetic anhydride (0.252 mL, 0.273 g, 2.67 mmol, 1.50 molar equiv.) were added, the reaction flask was flushed with nitrogen gas, and the mixture was allowed to stir at room temperature. The reaction was monitored by TLC using 20% EtOAc in hexanes and was found to be complete within 2 hours. The reaction mixture was diluted with CH$_2$Cl$_2$, washed with deionized water, 10% aqueous NaOH, water, and brine. The organic layer was dried over anhydrous Na$_2$SO$_4$, evaporated under reduced pressure, and loaded onto a 230–400 mesh silica column packed in hexanes. Sequential elution with hexanes and 5% EtOAc in hexanes gave 0.455 g (96% yield) of 4-[(t-butyldimethylsilyl)oxy]phenyl acetate (12) as a colorless liquid. $R_f$ (20% EtOAc in hexanes) = 0.45. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 6.93 (d, $J$ = 8.8 Hz, 2H, ArH), 6.81 (d, $J$ = 8.8 Hz, 2H, ArH), 2.27 (s, 3H, CH$_3$), 0.98 (s, 9H, t-Bu), 0.19 (s, 6H, SiCH$_3$). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 169.9, 153.4, 144.9, 122.4, 120.7, 25.8, 21.3, 18.4, -4.3. HRMS (ESI/TOF): calcd for $\text{C}_{14}\text{H}_{22}\text{O}_{3}\text{SiNa}$ [M + Na]$^+$: 289.1230; found: 289.1219. See reference 28 in the paper.
Competitive desilylation reactions of the TBDMS ethers of $p$-bromophenol and 2,3-dimethoxybenzyl alcohol (14 and 15)

A mixture of $p$-bromophenol TBDMS ether 14 (71.8 mg, 0.25 mmol), 2,3-dimethoxybenzyl alcohol TBDMS ether 15 (70.6 mg, 0.25 mmol), and KHF$_2$ (48.8 mg, 0.625 mmol) in anhydrous MeOH (5 mL) was stirred for 30 minutes. TLC analysis (20% EtOAc in hexanes to observe the silyl ethers and 80% EtOAc in hexanes to observe the deprotected products) after 30 minutes revealed that the phenol silyl ether 14 was completely deprotected whereas the benzylic alcohol silyl ether 15 remained unaffected. The reaction flask was resealed and the mixture was stirred for an additional 30 minutes at which time TLC indicated that no additional change had occurred. The mixture was evaporated and the crude material was loaded onto a 200–300 mesh silica column. Gradient elution with 20% EtOAc in hexanes gradually progressing to 80% EtOAc in hexanes gave 39.5 mg (91% yield) of $p$-bromophenol (1) and 68.3 mg (97% recovered) of 2,3-dimethoxybenzyl alcohol TBDMS ether (15).

Competitive desilylation reactions of the TBDMS ethers of $p$-bromophenol and $p$-bromobenzyl alcohol (14 and 16)

A mixture of $p$-bromophenol TBDMS ether 14 (71.8 mg, 0.25 mmol), $p$-bromobenzyl alcohol TBDMS ether 16 (75.3 mg, 0.25 mmol), and KHF$_2$ (48.8 mg, 0.625 mmol) in anhydrous MeOH (5 mL) was stirred for 30 minutes. TLC analysis ($\text{CH}_2\text{Cl}_2$ to observe the silyl ethers) after 30 minutes revealed that the phenol silyl ether 14 was completely deprotected whereas the benzylic alcohol silyl ether 16 remained unaffected. The reaction flask was resealed and the mixture was stirred for an additional 30 minutes at which time TLC indicated that no additional change had occurred. The mixture was evaporated and
the crude material was loaded onto a 200–300 mesh silica column. Gradient elution with 20% EtOAc in hexanes gradually progressing to 80% EtOAc in hexanes gave 37.8 mg (87% yield) of p-bromophenol (1) and 68.2 mg (91% recovered) of p-bromobenzyl alcohol TBDMS ether (16).

**{4-[[t-Butyldimethylsilyl]oxy]phenyl}(2,3-dimethoxyphenyl)methanol (17)**

In a clean, dry, 50 mL round-bottom flask, a solution of (4-bromophenoxy)(t-butyl)dimethylsilane (14, 0.574 g, 2 mmol) in anhydrous Et₂O (10 mL) was cooled to 0 °C, under a nitrogen atmosphere. To this stirring solution was added nBuLi in hexanes (1.87 mL of 1.6 M, 3 mmol), dropwise, with vigorous stirring. The mixture was warmed to room temperature, stirred for 1 h, and then recooled to 0 °C. A solution of 2,3-dimethoxybenzaldehyde (0.565 g, 3.4 mmol) in anhydrous Et₂O (2 mL) was added dropwise. The mixture was warmed to room temperature, stirred for 20 h, and quenched by the addition of saturated aq. NH₄Cl. The organic layer was separated, washed with water, dried over anhydrous Na₂SO₄, and evaporated under reduced pressure. Flash chromatography of the crude material on a 230–400 mesh silica gel column eluted with hexanes, 5% and then 10% acetone in hexanes to give 0.499 g (67% yield) of compound 17 as a pale-yellow, syrupy material. \( R_f \) (10% acetone in hexanes) = 0.28. \(^1\)H NMR (500 MHz, CDCl₃): \( \delta = 7.23 \) (d, \( J = 8.3 \) Hz, 2H, ArH), 7.06 (t, \( J = 7.8 \) Hz, 1H, ArH), 6.97 (d, \( J = 7.8 \) Hz, 1H, ArH), 6.87 (d, \( J = 7.8 \) Hz, 1H, ArH), 6.79 (d, \( J = 8.3 \) Hz, 2H, ArH), 5.96 (d, \( J = 5.3 \) Hz, 1H, CH), 3.85 (s, 3H, OCH₃), 3.56 (s, 3H, OCH₃), 2.89 (d, \( J = 5.8 \) Hz, 1H, OH), 0.97 (s, 9H, t-Bu), 0.17 (s, 6H, SiCH₃). \(^{13}\)C NMR (125 MHz, CDCl₃): \( \delta = 154.9, 152.8, 146.5, 138.0, 127.8, 124.1, 120.0, 119.8, 112.0, 72.43, 72.4, 60.54, 60.5, 55.9, 55.88, 25.8, 18.4, -4.2. \) HRMS (ESI/TOF): calcd for C₂₁H₃₀O₄SiNa [M + Na]⁺: 397.1806; found: 397.1809.
**t-Butyl{4-[(t-butyldimethylsilyl)oxy](2,3-dimethoxyphenyl)methyl]phenoxyl}dimethylsilane (18)**

To a solution of {4-[(t-butyldimethylsilyl)oxy]phenyl}(2,3-dimethoxyphenyl)methanol (17, 0.420 g, 1.12 mmol) in DMF (3.0 mL), were added TBDMSI (0.202 g, 1.34 mmol) and imidazole (0.183 g, 2.69 mmol), and the mixture was stirred at room temperature for 20 h. The mixture was diluted with EtOAc and washed with water. The organic layer was dried over anhydrous Na\textsubscript{2}SO\textsubscript{4} and evaporated under reduced pressure. Flash chromatography of the crude material on a 230–400 mesh silica column eluted with hexanes followed by 5% EtOAc in hexanes gave 0.526 g (96% yield) of silyl ether 18 as a colorless, syrupy material. 

\(R_f\) (20% EtOAc in hexanes) = 0.87. \(^1\)H NMR (500 MHz, CDCl\textsubscript{3}): \(\delta = 7.24\) (t, \(J = 6.6\) Hz, 3H, ArH), 7.04 (t, \(J = 8.0\) Hz, 1H, ArH), 6.79 (d, \(J = 8.3\) Hz, 1H, ArH), 6.72 (d, \(J = 8.3\) Hz, 2H, ArH), 6.08 (s, 1H, CH), 3.83 (s, 3H, OCH\textsubscript{3}), 3.60 (s, 3H, OCH\textsubscript{3}), 0.95 and 0.89 (2s, 18H, t-Bu), 0.14, −0.02, and −0.05 (2s, 12H, SiCH\textsubscript{3}). \(^{13}\)C NMR (125 MHz, CDCl\textsubscript{3}): \(\delta = 154.4, 152.2, 145.2, 139.4, 138.2, 127.9, 123.7, 119.5, 118.2, 110.8, 70.5, 60.1, 55.6, 25.9, 25.7, 18.3, 18.2, −4.4, −4.83, −4.81. HRMS (ESI/TOF): calcld for C\textsubscript{27}H\textsubscript{44}O\textsubscript{4}Si\textsubscript{2}Na [M + Na]⁺: 511.2670; found: 511.2674.

**4-{{(t-Butyldimethylsilyl)oxy}(2,3-dimethoxyphenyl)methyl}phenol (19)**

In a 25 mL oven dried round bottom flask, a mixture of t-butyl{4-{{(t-butyldimethylsilyl)oxy}(2,3-dimethoxyphenyl)methyl}phenoxy}dimethylsilane (18, 0.489 g, 1 mmol) and KHF\textsubscript{2} (0.195 g, 2.5 mmol) in anhydrous MeOH (10 mL) was stirred at room temperature. The reaction was monitored by TLC using 20% EtOAc in hexanes and was found to be complete within 2 hours. The mixture was evaporated under reduced pressure and loaded onto a 230–400 mesh silica column packed in hexanes (adequate caution was exercised to ensure complete transfer of the crude material). Sequential elution with
hexanes and 10% EtOAc in hexanes gave 0.360 g (96% yield) of 19 as a yellow, syrupy material. \( R_f \) (20% EtOAc in hexanes) = 0.46. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta = 7.24–7.20 \) (m, 3H, ArH), 7.04 (t, \( J = 7.3 \) Hz, 1H, ArH), 6.79 (d, \( J = 7.3 \) Hz, 1H, ArH), 6.70 (d, \( J = 7.8 \) Hz, 2H, ArH), 6.09 (s, 1H, CH), 4.66 (s, 1H, OH), 3.83 (s, 3H, OCH\(_3\)), 3.67 (s, 3H, OCH\(_3\)), 0.90 (s, 9H, t-Bu), –0.018 and –0.024 (2s, 6H, SiCH\(_3\)). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta = 154.4, 152.3, 145.2, 139.5, 138.0, 128.1, 124.0, 119.0, 114.9, 110.9, 70.4, 60.4, 55.8, 26.0, 18.4, –4.7. \) HRMS (ESI/TOF): calcd for \( \text{C}_{21}\text{H}_{30}\text{O}_{4}\text{SiNa}[\text{M}+\text{Na}]^+ \): 397.1806; found: 397.1803.

**Comparative evaluation of the desilylation reactions of \( p \)-bromophenol TBDMS, TBDPS, and TIPS ethers (14, 20, and 21)**

(a) In a reaction vial, TBDMS-protected \( p \)-bromophenol (14, 143.6 mg, 0.5 mmol) and KHF\(_2\) (97.6 mg, 1.25 mmol) were stirred in anhydrous MeOH (5 mL) at room temperature for 15 minutes. TLC analysis (hexanes) revealed two spots: a faint spot with \( R_f = 0.49 \) and a dark spot at the baseline. The mixture was allowed to stir for an additional 15 min (30 min total) at which time TLC analysis (hexanes) revealed only one dark spot at the baseline. Evaporation of the reaction mixture and chromatography on a 200–300 mesh silica gel column eluted with 10% EtOAc in hexanes afforded 82.1 mg (95% yield) of \( p \)-bromophenol (1) as white crystalline material.

(b) In a reaction vial, TBDPS-protected \( p \)-bromophenol (20, 205.7 mg, 0.5 mmol) and KHF\(_2\) (97.6 mg, 1.25 mmol) were stirred in anhydrous MeOH (5 mL) at room temperature for 15 minutes. TLC analysis (hexanes) revealed two dark spots: one with \( R_f = 0.47 \) and another spot at the baseline. The mixture was allowed to stir for an additional 15 min (30 min total) at which time TLC analysis (hexanes) revealed two dark spots: one with \( R_f = 0.47 \) and another spot at the baseline. Evaporation of the reaction mixture and chromatography on a
200–300 mesh silica gel column sequentially eluted with hexanes and 10% EtOAc in hexanes afforded 79.3 mg (92% yield) of p-bromophenol (1) as a white crystalline product. In addition, 51.5 mg of a byproduct, \( R_f = 0.47 \) (hexanes), was also isolated. \(^1\)H NMR spectrum showed this byproduct to only contain the \( t\)-butyl and phenyl resonances from the TBDPS group (the spectrum was identical to that of the non-polar material obtained from the competitive desilylation of TBDMS and TBDPS ethers of \( p\)-bromophenol, see pages S-35 and S-36).

(c) In a reaction vial, TIPS-protected \( p\)-bromophenol (21, 164.6 mg, 0.5 mmol) and KHF\(_2\) (97.6 mg, 1.25 mmol) were stirred in anhydrous MeOH (5 mL) at room temperature for 15 minutes. TLC analysis (hexanes) revealed two spots: one dark spot with \( R_f = 0.49 \) and a faint spot at the baseline. The mixture was allowed to stir for an additional 15 min (30 min total). TLC analysis (hexanes) revealed two spots: one dark spot with \( R_f = 0.49 \) and a faint spot at the baseline. Evaporation of the reaction mixture and chromatography on a 200–300 mesh silica gel column sequentially eluted with hexanes and 10% EtOAc in hexanes afforded 23.1 mg (25% yield) of \( p\)-bromophenol (1) as a white crystalline product. In addition, 107.4 mg (65%) of \( p\)-bromophenol TIPS ether (21) was recovered.

**Competitive desilylation of the TBDMS and TBDPS ethers of \( p\)-bromophenol (14 and 20)**

In a reaction vial, a mixture of TBDMS-protected \( p\)-bromophenol (14, 71.8 mg, 0.25 mmol), TBDPS-protected \( p\)-bromophenol (20, 102.8 g, 0.25 mmol), and KHF\(_2\) (48.8 mg, 0.625 mmol) was stirred in anhydrous MeOH (5 mL) at room temperature for 30 minutes. TLC analysis (hexanes) revealed two dark spots: one with \( R_f = 0.47 \) and another spot at the baseline. Evaporation of the reaction mixture and chromatography on a 200–300 mesh
silica gel column sequentially eluted with hexanes and 10% EtOAc in hexanes afforded 81.9 mg (95% yield) of \( p \)-bromophenol (1) as white crystalline solid. In addition, 23.1 mg of a byproduct, \( R_f = 0.47 \), was also isolated. \(^1\)H NMR spectrum revealed this byproduct to only contain the \( t \)-butyl and phenyl resonances from the TBDPS group, and \(^19\)F NMR indicated presence of a fluorine atom (see pages S-35 and S-36).

**Representative procedure for desilylation of alkanol TBDMS ethers: 2,3-dimethoxybenzyl alcohol (22)**

In an oven dried 25 mL round-bottom flask, a mixture of TBDMS-protected 2,3-dimethoxybenzyl alcohol (0.282 g, 1 mmol) and \( \text{KHF}_2 \) (0.195 g, 2.5 mmol) in anhydrous MeOH (10 mL) was stirred at 60 °C. The reaction was monitored by TLC using 25% EtOAc in hexanes and was found to be complete within 15 hours. The mixture was evaporated under reduced pressure and loaded onto a 100–200 mesh silica column packed in 50% EtOAc in hexanes (adequate caution was exercised to ensure complete transfer of the crude material). Elution with 50% EtOAc in hexanes gave 0.143 g (85% yield) of 2,3-dimethoxybenzyl alcohol as a white solid. \( R_f(25\% \text{ EtOAc in hexanes}) = 0.20 \).

**\( p \)-Bromobenzyl alcohol (23)**

Chromatographed on a 200–300 mesh silica gel column using 10% EtOAc in hexanes to give 0.175 g (94% yield) of \( p \)-bromobenzyl alcohol as a white solid.

**Cinnamyl alcohol (24)**

Chromatographed on a 100–200 mesh silica gel column using 50% EtOAc in hexanes to give 0.101 g (75% yield) of cinnamyl alcohol as a white solid.

**2-(4-Methylthiazol-5-yl)ethan-1-ol (25)**
Chromatographed on a 100–200 mesh silica column using 50% EtOAc in hexanes followed by EtOAc, and then 5% MeOH in CH₂Cl₂ to give 0.108 g (75% yield) of 2-(4-methylthiazol-5-yl)ethan-1-ol as a yellow, oily syrup.
OH

OHC

OMe

4
Sample Name: EthylBenzene-18-070214
Data Collected on: capella500.scl.ccny.cuny.edu-inova500
Archive directory: /home/vmarl/vmarlys/data
Sample directory: EthylBenzene-18-070214_20140702_01
FID File: TK-1205-01-35-binaphthol-5hdrying+3hdrying@50C-harisolvent-cdcl3-H1

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 3 2016

Temp. 25.0 C / 298.1 K
Operator: mhl

Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.732 sec
Width 5997.5 Hz
64 repetitions

OBSERVE HI, 499.7707206 MHz
DATA PROCESSING
FT size 32768
Total time 10 min
Sample Name: Compound_10
Data Collected on: capella500.sci.cuny.edu-inova500
Archive directory:
Sample directory:
File: MB-1222-01-02-pure-y-1H-CDCl3
Pulse Sequence: PROTON (m2pul)
Solvent: cdc13
Data collected on: Jan 29 2016
Sample Name:

Data Collected on:

capella500.soil.cuny.edu-inova500

Archive directory:

Sample directory:

FidFile: 1203_VB_02_54_13C

Pulse Sequence: CARBON (z2pul)

Solvent: cdc13

Data collected on: Dec 31 2015
$^1$H NMR spectrum of the non-polar material obtained from the competitive desilylation of $p$-bromophenol TBDMS and TBDPS ethers.
$^{19}$F NMR spectrum of the non-polar material obtained from the competitive desilylation of $p$-bromophenol TBDMS and TBDPS ethers.