Supporting Information to Accompany

Metal-Free Functionalization of \(N,N\)-Dialkylanilines via Temporary Oxidation to \(N,N\)-Dialkylaniline-\(N\)-Oxides and Group Transfer

Robert S. Lewis, Michael F. Wisthoff, J. Grissmerson, and William J. Chain

Department of Chemistry, University of Hawaii at Manoa
**General Information:** All reactions were performed in single-neck oven- or flame-dried round-bottom flasks fitted with rubber septa under a positive pressure of argon, unless otherwise noted. Air- and moisture-sensitive liquids were transferred via syringe or stainless steel cannula. Organic solutions were concentrated by rotary evaporation below 35 °C at 10 Torr (diaphragm vacuum pump) unless otherwise noted. Analytical thin-layer chromatography (TLC) was performed using glass plates pre-coated with silica gel (0.25 mm, 60-Å pore size, 5–20 μm, Silicycle) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light (UV), then were stained by submersion in aqueous ceric ammonium molybdate solution (CAM), ethanolic phosphomolybdic acid solution (PMA), acidic ethanolic p-anisaldehyde solution (anisaldehyde), or aqueous potassium permanganate solution (KMnO$_4$), followed by brief heating on a hot plate (215 °C, 10–15 s). Flash chromatography was performed as described by Still et al.$^1$, employing silica gel (60-Å pore size, 40–63 μm, standard grade, Silicycle) or basic alumina (60-Å pore size, 50–200 μm, Brockmann I, Sorbent Technologies or Acros Organics).

**Materials:** Commercial reagents and solvents were used as received with the following exceptions. Triethylamine, dichloromethane, ethyl ether, dimethylsulfoxide, tetrahydrofuran, hexane, toluene, and benzene were purified by the method of Pangborn, et. al.$^2$ $N,N$-dimethylformamide (DMF) was distilled from calcium hydride under reduced pressure (0.1 Torr) and stored under argon. Iodomethane was filtered through a column of basic alumina, neat, immediately prior to use. 3-Chloroperbenzoic acid was dissolved in benzene and washed with an aqueous solution buffered at pH 7.4 (NaH$_2$PO$_4$/NaOH). The organic layer was dried over anhydrous magnesium sulfate and the dried solution was carefully concentrated to give a white solid. The solid was recrystallized from dichloromethane/diethyl ether and the recrystallized solid was stored in a plastic bottle under an atmosphere of argon. Where noted, solvents were deoxygenated before use by bubbling with argon for 20 minutes.

**Instrumentation:** Proton nuclear magnetic resonance ($^1$H NMR) spectra and carbon nuclear magnetic resonance ($^{13}$C NMR) spectra were recorded on Varian Mercury Plus 300 MHz/75 MHz or Varian Unity INOVA 500 MHz/125 MHz NMR spectrometers at 23 °C. Fluorine nuclear magnetic resonance ($^{19}$F NMR) spectra were recorded on a Varian Mercury Plus 282 MHz spectrometer at 23 °C. Proton chemical shifts are expressed in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent.

---

$^1$ Still, W. C.; Kahn, M.; Mitra, A. J. Org. Chem. 1978, 43, 2923–2925.

$^2$ Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. Organometallics 1996, 15, 1518–1520.
(CHCl₃: δ 7.26, CD₂HOD: δ 3.31, CD₃SOCD₂H: δ 2.50, C₆D₅H: δ 7.16). Carbon chemical shifts are expressed in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to the carbon resonance of the NMR solvent (CDCl₃: δ 77.16, CD₃OD: δ 49.00, CD₃SOCD₃: δ 39.52, C₆D₆: δ 128.00). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent), integration, and coupling constant (J) in Hertz (Hz). Infrared (IR) spectra were obtained using a Shimadzu IRAffinity-1 FT-IR spectrophotometer referenced to a polystyrene standard and data are represented as frequency of absorption (cm⁻¹). Accurate mass measurements were obtained on a Waters LCT premier (ESI source, flow injection analysis) or a Waters GCT premier (GC-MS fitted with an EI or CI source) at the Mass Spectrometry Facility at the University of California at Irvine.

(For clarity, intermediates that have not been assigned numbers in the text are numbered sequentially in the supplemental information beginning with 7a.)

Experimental Procedures:

General procedure for the Synthesis of N,N-Dimethylanilines

Iodomethane (3.97 mL, 63.8 mmol, 2.19 equiv) was added dropwise to a stirred suspension of 2-bromoaniline (5.00 g, 29.1 mmol, 1 equiv) and potassium carbonate (12.0 g, 86.8 mmol, 2.98 equiv) in 100 mL of N,N-dimethylformamide (DMF) under argon. The reaction mixture was stirred at 23 °C for 18 h, then was filtered and diluted with water (100 mL). The resultant solution was extracted diethyl ether (3 × 50 mL) and the combined organic extracts were washed with water (3 × 30 mL) and then with saturated aqueous sodium chloride solution (3 × 30 mL). The combined organic layers were dried over anhydrous sodium sulfate and the dried solution was concentrated. Purification of the residue by flash column chromatography (2% ethyl acetate–hexanes), afforded 7b (4.08 g, 70%) as a clear, yellow oil.
2-bromo-N,N-dimethylaniline 7b: TLC: 5% ethyl acetate–hexanes, $R_f = 0.42$ (UV, KMnO$_4$). $^1$H NMR (300 MHz, CDCl$_3$), $\delta$: 7.55 (m, 1H), 7.26 (m, 1H), 7.09 (dd, $J_1 = 8.1$ Hz, $J_2 = 1.4$ Hz, 1H), 6.89 (m, 1H), 2.80 (s, 6H).

![Image of 7b](image)

4-methyl-N,N-dimethylaniline 7c: TLC: 5% ethyl acetate–hexanes, $R_f = 0.34$ (UV, KMnO$_4$). $^1$H NMR (300 MHz, CDCl$_3$), $\delta$: 7.07 (m, 2H), 6.70 (m, 2H), 2.91 (s, 6H), 2.27 (s, 3H).

![Image of 7c](image)

methyl 3-(N,N-dimethylamino)benzoate 7d: TLC: 5% ethyl acetate–hexanes, $R_f = 0.20$ (UV, KMnO$_4$). $^1$H NMR (300 MHz, CDCl$_3$), $\delta$: 7.41–7.35 (m, 2H), 7.28 (t, $J = 7.9$ Hz, 1H), 6.90 (m, 1H), 3.90 (s, 3H), 3.00 (s, 6H). $^{13}$C NMR (75 MHz, CDCl$_3$), $\delta$: 167.9, 150.6, 130.9, 129.1, 117.6, 116.8, 113.3, 52.2, 40.7. FTIR (NaCl, thin film), cm$^{-1}$: 2950, 2808, 1724, 1603, 1438, 1354, 1113, 1008, 784. HRMS: ES$^+$ [M + Na]$^+$ Calcd. for C$_{10}$H$_{13}$NO$_2$Na: 202.0844. Found: 202.0840.

![Image of 7d](image)

1-(N,N-dimethylamino)naphthalene 7e: TLC: 5% ethyl acetate–hexanes, $R_f = 0.41$ (UV, KMnO$_4$). $^1$H NMR (300 MHz, CDCl$_3$), $\delta$: 8.24 (m, 1H), 7.83 (m, 1H), 7.57–7.43 (m, 3H), 7.40

![Image of 7e](image)

---

3. I. Bonnaventure, A. Charette, *J. Org. Chem.* 2008, 73, 6330–6340.
4. R. Lundgren, A. Sappong-Kumankumah, M. Stradiotto, *Chem. Eur. J.*, 2010, 16, 1983–1991.
5. N. Shohji, T. Kawaji, S. Okamoto, *Org. Lett.*, 2011, 13, 2626–2629.
(m, 1H), 7.08 (m, 1H), 2.91 (s, 6H). FTIR (NaCl, thin film), cm⁻¹: 3047, 2939, 2785, 1575, 1395, 1305, 773. HRMS: El⁺ [M]⁺ Calcd. for C₁₂H₁₃N: 171.1048. Found: 171.1040.

3-methyl-\(\text{N,N-dimethylaniline}\) 7f: TLC: 5% ethyl acetate-hexanes, \(R_f = 0.41\) (UV, KMnO₄). \(^1\)H NMR (300MHz, CDCl₃), δ: 7.16 (m, 1H), 6.59 (m, 3H), 2.95 (s, 6H), 2.34 (s, 3H).

4-chloro-\(\text{N,N-dimethylaniline}\) 7g: TLC: 5% ethyl acetate-hexanes, \(R_f = 0.37\) (UV, KMnO₄). \(^1\)H NMR (500 MHz, CDCl₃), δ: 7.18 (d, \(J = 9.0\) Hz, 2H), 6.63 (d, \(J = 9.0\) Hz, 2H), 2.93 (s, 6H).

4-fluoro-\(\text{N,N-dimethylaniline}\) 7h: TLC: 5% ethyl acetate-hexanes, \(R_f = 0.37\) (UV, KMnO₄). \(^1\)H NMR (500 MHz, CDCl₃), δ: 6.97 (m, 2H), 6.68 (m, 2H), 2.91 (s, 6H). \(^{13}\)C NMR (125 MHz, CDCl₃), δ: 155.7 (d, \(J = 235.1\) Hz), 147.6, 115.4 (d, \(J = 21.8\) Hz), 114.0 (d, \(J = 7.3\) Hz), 41.5. FTIR (NaCl, thin film), cm⁻¹: 2886, 1848, 1526, 1448, 1225, 814. HRMS: El⁺ [M]⁺ Calcd. for C₈H₁₀FN: 139.0797. Found: 139.0800.

---

6 V. Dichiarante, M. Fagnoni, A. Albini, J. Org. Chem. 2010, 75, 2171–2176.
7 L. Huang, T. Niu, J. Wu, Y. Zhang, J. Org. Chem., 2011, 76, 1739–1776.
4-methoxy-\(N,N\)-dimethylaniline 7i: TLC: 5% ethyl acetate–hexanes, \(R_f = 0.16\) (UV, KMnO\(_4\)).
\(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 6.88–6.72 (m, 4H), 3.78 (s, 3H), 2.87 (s, 6H).

![Structure of 4-methoxy-\(N,N\)-dimethylaniline 7i]

3-methoxy-\(N,N\)-dimethylaniline 7j: TLC: 5% ethyl acetate–hexanes, \(R_f = 0.26\) (UV, KMnO\(_4\)).
\(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 7.17 (m, 1H), 6.39 (m, 1H), 6.35–6.27 (m, 2H), 3.81 (s, 3H), 2.95 (s, 6H).
\(^{13}\)C NMR (75 MHz, CDCl\(_3\)), \(\delta\): 160.8, 152.1, 129.8, 105.9, 101.5, 99.2, 55.2, 40.7.
HRMS: ES\(^+\) [M + H]\(^+\) Calcd. for C\(_9\)H\(_{14}\)NO: 152.1075. Found: 152.1075.

![Structure of 3-methoxy-\(N,N\)-dimethylaniline 7j]

2-iso-propyl-\(N,N\)-dimethylaniline 7k: TLC 5% ethyl acetate-hexanes, \(R_f = 0.68\) (UV, KMnO\(_4\)).
\(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 7.28 (m, 1H), 7.10 (m, 3H), 3.55 (hept, \(J = 6.8\) Hz, 1H), 2.67 (s, 6H), 1.24 (d, \(J = 0.7\) Hz, 3H), 1.22 (d, \(J = 0.7\) Hz, 3H).
\(^{13}\)C NMR (75 MHz, CDCl\(_3\)), \(\delta\): 152.0, 144.3, 126.6, 126.3, 124.0, 119.7, 46.0, 26.8, 24.3.
FTIR (NaCl, thin film), cm\(^{-1}\): 2964, 2824, 1490, 1448, 946, 764.
HRMS: ES\(^+\) [M + H]\(^+\) Calcd. for C\(_{11}\)H\(_{17}\)N: 164.1439. Found: 164.1433.

\(^8\) B. Lee, M. Biscoe, S. Buchwald, *Tetrahedron Letters*, 2009, 50, 3672–3674.
General procedure for the Synthesis of N,N-Dimethylaniline-N-Oxides

A solution of 2-bromo-N,N-dimethylaniline (4.08 g, 20.4 mmol, 1 equiv) in dichloromethane (50 mL) was transferred via cannula to a stirred solution of 3-chloroperbenzoic acid (70% w/w, 5.03 g, 20.4 mmol, 1.00 equiv) in dichloromethane (50 mL). The resultant solution was stirred for 4 h at 23 °C then was loaded directly onto a basic alumina column and eluted with 25% methanol–chloroform. The combined filtrates were concentrated to give 2-bromo-N,N-dimethylaniline-N-oxide 1b (4.19 g, 95% yield) as a crystalline orange-yellow solid.

2-bromo-N,N-dimethylaniline-N-oxide 1b: TLC: 2-15% ethyl acetate-hexanes, R_f = 0.0 (UV, KMnO_4). ^1H NMR (300 MHz, CDCl_3), δ: 9.14 (dd, J_1 = 8.4 Hz, J_2 = 1.7 Hz, 1H), 7.62 (dd, J_1 = 7.8 Hz, J_2 = 1.5 Hz, 1H), 7.48 (ddd, J_1 = 8.6 Hz, J_2 = 7.3 Hz, J_3 = 1.5 Hz, 1H), 7.29–7.18 (m, 1H), 3.80 (s, 6H). ^13C NMR (125 MHz, CDCl_3), δ: 152.6, 135.4, 131.1, 129.2, 125.8, 112.7, 60.9, 50.7. FTIR (NaCl, thin film), cm⁻¹: 3100, 1644, 1451, 1436. HRMS: EI+ [M]+ Calcd. for C_8H_10BrNO: 214.9945. Found: 214.9955.

N,N-dimethylaniline-N-oxide 1a: TLC: 2-15% ethyl acetate-hexanes, R_f = 0.0 (UV, KMnO_4). ^1H NMR (300 MHz, CDCl_3), δ: 7.98 (m, 2H), 7.53–7.42 (m, 3H), 3.59 (s, 6H).

---

9 Y. Imada, H. Iida, S. Ono, S. Murahashi, J. Am. Chem. Soc. 2003, 125, 2868–2869.
4-methyl-\(N,N\)-dimethylaniline-\(N\)-oxide \(1c\)^{10}: TLC: 2-15% ethyl acetate-hexanes, \(R_f = 0.0\) (UV, KMnO\(_4\)). \(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 7.81 (m, 2H), 7.25 (m, 2H), 3.55 (s, 6H), 2.37 (s, 3H).

\[ \text{H} \]

\[ \text{O} \]

\[ \text{N} \]

\[ \text{CH}_3 \]

\[ \text{CH}_3 \]

\[ \text{O} \]

\[ \text{N} \]

\[ \text{CH}_3 \]

\[ \text{CH}_3 \]

\[ \text{O} \]

\[ \text{N} \]

\[ \text{CH}_3 \]

methyl 3-(\(N,N\)-dimethylamino)benzoate-\(N\)-oxide \(1d\): TLC: 2-15% ethyl acetate-hexanes, \(R_f = 0.0\) (UV, KMnO\(_4\)). \(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 8.49-8.37 (m, 2H), 8.07 (m, 1H), 7.57 (m, 1H), 3.93 (s, 3H), 3.60 (s, 6H). \(^1\)\(^3\)C NMR (75 MHz, CDCl\(_3\)), \(\delta\): 166.0, 155.0, 131.2, 130.2, 129.8 125.2, 120.9, 63.6, 52.7. FTIR (NaCl, thin film), cm\(^{-1}\): 3103, 2952, 1671, 1441, 1344, 1292, 1243, 1209. HRMS: ES\(^+\) [M + Na]\(^+\) Calcd. for C\(_{10}\)H\(_{13}\)NO\(_3\)Na: 218.0793. Found: 218.0788.

\[ \text{H} \]

\[ \text{O} \]

\[ \text{N} \]

\[ \text{CH}_3 \]

\[ \text{CH}_3 \]

\[ \text{O} \]

\[ \text{N} \]

\[ \text{CH}_3 \]

\[ \text{CH}_3 \]

\[ \text{O} \]

\[ \text{N} \]

\[ \text{CH}_3 \]

1-(\(N,N\)-dimethylamino)naphthalene-\(N\)-oxide \(1e\): TLC: 2-15% ethyl acetate-hexanes, \(R_f = 0.0\) (UV, KMnO\(_4\)). \(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 9.08 (m, 1H), 8.31 (m, 1H), 7.92 (m, 2H), 7.69–7.52 (m, 2H), 7.49 (m, 1H), 3.91 (s, 6H). \(^1\)\(^3\)C NMR (125 MHz, CDCl\(_3\)), \(\delta\): 135.8, 131.0, 129.6, 127.1, 126.2, 125.8, 125.4, 124.5, 118.4, 62.7. FTIR (NaCl, thin film), cm\(^{-1}\): 3325, 3057, 2360, 2313, 1506. HRMS: EI\(^+\) [M]\(^+\) Calcd. for C\(_{12}\)H\(_{13}\)NO: 187.0997. Found: 187.0995.

\[ \text{H} \]

\[ \text{O} \]

\[ \text{N} \]

\[ \text{CH}_3 \]

\[ \text{CH}_3 \]

\[ \text{O} \]

\[ \text{N} \]

\[ \text{CH}_3 \]

\[ \text{CH}_3 \]

3-methyl-\(N,N\)-dimethylaniline-\(N\)-oxide \(1f\): TLC: 2-15% ethyl acetate-hexanes, \(R_f = 0.0\) (UV, KMnO\(_4\)). \(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 7.86 (s, 1H), 7.60 (m, 1H), 7.30 (m, 1H), 7.17 (m, 1H), 6.98 (m, 2H), 3.55 (s, 6H), 2.37 (s, 3H).

\(^{10}\) F. Chen, B. Qiu, X. Feng, G, Zhang, Y. Jiang, Tetrahedron, 2004, 60, 10449–10460.
3.54 (s, 6H), 2.39 (s, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$), $\delta$: 139.8, 129.7, 129.0, 120.8, 116.7, 110.1, 63.3, 21.7. FTIR (NaCl, thin film), cm$^{-1}$: 2935, 2856, 2353, 1550, 1264, 1218, 1008, 987, 748. HRMS: ES$^+$ [M + Na]$^+$ Calcd. for C$_9$H$_{13}$NONa: 174.0895. Found: 174.0894.

4-chloro-$N,N$-dimethylaniline-$N$-oxide 1g: TLC: 2-15% ethyl acetate-hexanes, $R_f$ = 0.0 (UV, KMnO$_4$). $^1$H NMR (300 MHz, CDCl$_3$), $\delta$: 7.93 (m, 2H), 7.43 (m, 2H), 3.57 (s, 6H). $^{13}$C NMR (125 MHz, CDCl$_3$), $\delta$: 153.2, 135.1, 129.3, 121.8, 63.6. FTIR (NaCl, thin film), cm$^{-1}$: 3340, 1661, 1485, 1459. HRMS: EI$^+$ [M]$^+$ Calcd. for C$_8$H$_{10}$ClNO: 171.0451. Found: 171.0449.

4-fluoro-$N,N$-dimethylaniline-$N$-oxide 1h: TLC: 2-15% ethyl acetate-hexanes, $R_f$ = 0.0 (UV, KMnO$_4$). $^1$H NMR (300 MHz, CDCl$_3$), $\delta$: 7.88 (m, 2H), 7.12–6.89 (m, 2H), 3.47 (s, 6H). $^{13}$C NMR (75 MHz, CDCl$_3$), $\delta$: 162.2 (d, $J$ = 248.9 Hz), 150.3, 122.1 (d, $J$ = 8.5 Hz), 115.8 (d, $J$ = 22.9 Hz), 63.5. $^{19}$F NMR (282 MHz, CDCl$_3$), $\delta$: -112.9. FTIR (NaCl, thin film), cm$^{-1}$: 1647, 1600, 1501, 562. HRMS: ES$^+$ [M + Na]$^+$ Calcd. for C$_8$H$_{10}$FNONa: 178.0644. Found: 178.0637.
4-methoxy-\(N,N\)-dimethylaniline-\(N\)-oxide 1i: TLC: 2-15% ethyl acetate-hexanes, \(R_f = 0.0\) (UV, KMnO\(_4\)). \(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 7.93–7.79 (m, 2H), 6.99–6.86 (m, 2H), 3.83 (s, 3H), 3.56 (s, 6H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)), \(\delta\): 159.7, 147.5, 121.3, 114.1, 63.7, 55.8. FTIR (NaCl, thin film), cm\(^{-1}\): 2958, 2842, 1593, 1505. HRMS: EI+ [M]+ Calcd. for C\(_9\)H\(_{13}\)NO\(_2\): 167.0946. Found: 167.0942.

![1j](image)

3-methoxy-\(N,N\)-dimethylaniline-\(N\)-oxide 1j: TLC: 2-15% ethyl acetate–hexanes, \(R_f = 0.0\) (UV, KMnO\(_4\)). \(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 7.71 (m, 1H), 7.25–7.10 (m, 2H), 6.80 (m, 1H), 3.74 (s, 3H), 3.44 (s, 6H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)), \(\delta\): 160.2, 155.7, 129.5, 114.9, 111.2, 106.1, 63.2, 55.6. FTIR (NaCl, thin film), cm\(^{-1}\): 3044, 2940, 2410, 1610, 1484, 1259, 1036. HRMS: ES+ [M + Na]+ Calcd. for C\(_9\)H\(_{13}\)NO\(_2\)Na: 190.0844. Found: 190.0836.

![1k](image)

2-iso-propyl-\(N,N\)-dimethylaniline-\(N\)-oxide 1k: TLC: 2-15% ethyl acetate–hexanes, \(R_f = 0.0\) (UV, KMnO\(_4\)). \(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 8.19 (m , 1H), 7.43 (m, 1H), 7.35 (m, 1H), 7.32–7.21 (m, 1H), 4.11 (hept, \(J = 6.8\) Hz, 1H), 3.68 (s, 6H), 1.35 (d, \(J = 0.8\) Hz, 3H), 1.32 (d, \(J = 0.8\) Hz, 3H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\): 141.9, 129.5, 129.3, 126.5, 120.2, 62.8, 29.6, 24.4. FTIR (NaCl, thin film), cm\(^{-1}\): 3052, 2986, 2357, 1422, 1265, 896, 738. HRMS: ES+ [M + H]+ Calcd. for C\(_{11}\)H\(_{17}\)NOH: 180.1388. Found: 180.1379.
General procedure for the Synthesis of Hydroxylated N,N-Dimethylanilines (1 mmol scale)

A stirred solution of \( \text{N},\text{N}-\text{dimethylaniline-N-oxide} \ 1\text{a} \) (0.137 g, 1.00 mmol, 1 equiv, dried by azeotropic distillation with benzene) in dichloromethane (10 mL) was cooled to –78 °C whereupon trifluoroacetic anhydride (0.155 mL, 1.10 mmol, 1.10 equiv) was added dropwise via syringe. The resultant solution was stirred for 1 h whereupon triethylamine (0.276 mL, 2.00 mmol, 2.00 equiv) was added. The reaction mixture was stirred for 15 min, then was quenched by the addition of three drops of acetic acid. The resultant mixture was warmed to 23 °C, then was concentrated. Purification of the residue by flash column chromatography (gradient elution 1 → 5% ethyl acetate–hexanes) afforded \( 2\text{a} \) (0.0916 g, 67%) as a pale yellow oil.

General procedure for the Synthesis of Hydroxylated N,N-Dimethylanilines (10 mmol scale)

A stirred solution of \( \text{N},\text{N}-\text{dimethylaniline-N-oxide} \ 1\text{a} \) (1.37 g, 10.0 mmol, 1 equiv, dried by azeotropic distillation with benzene) in dichloromethane (100 mL) was cooled to –78 °C whereupon trifluoroacetic anhydride (1.55 mL, 11.0 mmol, 1.10 equiv) was added dropwise via syringe (addition time approximately two minutes). The resultant solution was stirred for 1 h whereupon triethylamine (2.76 mL, 20.0 mmol, 2.00 equiv) was added. The reaction mixture was stirred for 15 min, then was warmed to 0 °C for 45 minutes before being quenched by the addition of water (1.0 mL) and silica gel (4 g). The resultant mixture was concentrated to a volume of 20 mL, then was diluted with hexanes (20 mL). The resultant mixture was filtered through a 1” by 1” plug of silica gel topped with 0.5 cm of anhydrous sodium sulfate. The plug was further eluted with 10% ethyl acetate–hexanes (100 mL). The filtrate was concentrated to give \( 2\text{a} \) (0.880 g, 64%) as an orange oil which slowly solidified.

2-Hydroxy-\( \text{N},\text{N}-\text{dimethylaniline} \ 2\text{a} \): TLC: 10% ethyl acetate–hexanes, \( R_f = 0.26 \) (UV, KMnO\textsubscript{4}). \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}), \( \delta \): 7.67 (s, 1H), 7.18 (dd, \( J_1 = 7.9, J_2 = 1.5 \) Hz, 1H), 7.13–7.02 (m, 1H), 6.96 (dd, \( J_1 = 8.1, J_2 = 1.5 \) Hz, 1H), 6.92–6.80 (m, 1H), 2.69 (s, 6H). \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}), \( \delta \): 151.5, 140.1, 126.4, 120.8, 120.1, 114.6, 45.2. FTIR (NaCl, thin film), cm\textsuperscript{-1}: 3325, 2945, 2888, 2789, 2358, 1741, 1589. HRMS: ES+ [M + H\textsuperscript{+}] Calcd. for C\textsubscript{8}H\textsubscript{12}NO: 138.0919. Found: 138.0920.
3-bromo-4-\((N,N\text{-dimethylamino})\)phenol 2b: TLC: 10\% ethyl acetate–hexanes, \(R_f = 0.32\) (UV, KMnO\(_4\)). \(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 7.09 (dd, \(J_1 = 2.0\ Hz, J_2 = 0.5\ Hz, 1H\)), 7.01 (s, 1H), 6.99 (dd, \(J_1 = 2.1\ Hz, J_2 = 0.6\ Hz, 1H\)), 2.62 (s, 6H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)), \(\delta\): 152.6, 139.9, 123.1, 122.3, 118.8, 117.6, 45.2. FTIR (NaCl, thin film), cm\(^{-1}\): 3262, 2938, 2873, 1573, 1446. HRMS: TOF MS CI- [M - H] - Calcd. for C\(_8\)H\(_9\)BrNO: 213.9868. Found: 213.9861.

2-\((N,N\text{-dimethylamino})\)-5-methylphenol 2c: TLC: 20\% ethyl acetate–hexanes, \(R_f = 0.58\) (UV, KMnO\(_4\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)), \(\delta\): 7.09 (d, \(J = 8.0\ Hz, 1H\)), 6.814 (s, 1H), 6.71 (d, \(J = 8.0\ Hz, 1H\)), 2.66 (s, 6H), 2.32 (s, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)), \(\delta\): 151.3, 138.0, 136.1, 120.6, 120.5, 114.7, 45.4, 21.3. FTIR (NaCl, thin film), cm\(^{-1}\): 3085, 2961, 2797, 2658, 1615, 1447. HRMS: ES+ [M + H]\(^+\) Calcd. for C\(_9\)H\(_{14}\)NO: 152.1075. Found: 152.1075.

methyl 3-(dimethylamino)-4-hydroxybenzoate 2d: TLC: 10\% ethyl acetate–hexanes, \(R_f = 0.37\) (UV, KMnO\(_4\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)), \(\delta\): 7.87 (d, \(J = 2.0\ Hz, 1H\)), 7.78 (dd, \(J_1 = 8.4\ Hz, J_2 = 2.0\ Hz, 1H\)), 6.94 (d, \(J = 8.4\ Hz, 1H\)), 3.87 (s, 3H), 2.66 (s, 6H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)), \(\delta\): 167.0, 156.0, 140.5, 128.6, 123.0, 122.2, 113.9, 52.0, 45.2. FTIR (NaCl, thin film), cm\(^{-1}\):
methyl 3-(dimethylamino)-2-hydroxybenzoate 2d: TLC: 10% ethyl acetate–hexanes, R_f = 0.16 (UV, KMnO_4). \(^1\)H NMR (500 MHz, CDCl_3), \(\delta\): 11.35 (s, 1H), 7.47 (dd, \(J_1 = 8.0 \text{ Hz}, J_2 = 1.6 \text{ Hz}, 1H\)), 7.07 (dd, \(J_1 = 7.8 \text{ Hz}, J_2 = 1.6 \text{ Hz}, 2H\)), 6.81 (t, \(J = 7.9 \text{ Hz}, 1H\)), 3.93 (s, 3H), 2.82 (s, 6H). \(^{13}\)C NMR (125 MHz, CDCl_3), \(\delta\): 171.5, 155.4, 142.2, 123.5, 122.5, 118.8, 112.3, 52.4, 43.1. FTIR (NaCl, thin film), cm\(^{-1}\): 3103, 3081, 2952, 2832, 2784, 1671, 1441. HRMS: ES\(^+\) [M + H]\(^+\) Calcd. for C\(_{10}\)H\(_{14}\)NO\(_3\): 196.0974. Found: 196.0970.

1-(N,N-dimethylamino)naphthalen-2-ol 2e: TLC: 20% ethyl acetate–hexanes, R_f = 0.72 (UV, KMnO_4). \(^1\)H NMR (500 MHz, CDCl_3), \(\delta\): 8.11 (s, 1H), 7.90 (d, \(J = 8.4 \text{ Hz}, 1H\)), 7.82 (d, \(J = 8.6 \text{ Hz}, 1H\)), 7.65 (d, \(J = 9.0 \text{ Hz}, 1H\)), 7.47 (t, \(J = 7.0 \text{ Hz}, 2H\)), 7.29 (m, 2H), 3.059 (s, 6H). \(^{13}\)C NMR (75 MHz, CDCl_3), \(\delta\): 151.8, 131.7, 129.8, 129.6, 128.2, 126.0, 122.5, 122.0, 116.1, 44.0. FTIR (NaCl, thin film), cm\(^{-1}\): 3275, 2973, 2936, 2873, 1623, 1598, 1519, 1206. HRMS: ES\(^+\) [M + H]\(^+\) Calcd. for C\(_{12}\)H\(_{14}\)NO: 188.1075. Found: 188.1071.

2-(N,N-dimethylamino)-4-methylphenol 2f (isolated as a mixture of regioisomers, asterisk denotes minor peaks): TLC: 20% ethyl acetate–hexanes, R_f = 0.30 (UV, KMnO_4). \(^1\)H NMR (500 MHz, CDCl_3), \(\delta\): 7.48* (s, 1H), 7.08* (dd, \(J_1 = 7.9 \text{ Hz}, J_2 = 1.5 \text{ Hz}, 1H\)), 7.04 (s, 1H), 6.98* (d, \(J = 7.5 \text{ Hz}, 1H\)), 6.91 (s, 2H), 6.82* (t, \(J = 7.7 \text{ Hz}, 1H\)), 2.73 (s, 6H), 2.69* (s, 3H), 2.34* (s,
3H), 2.32 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$), δ: 149.8, 149.0, 139.9, 139.4, 129.3, 127.5, 126.7, 123.5, 121.2, 119.2, 118.0, 114.2, 45.3, 45.1, 20.8, 15.9. FTIR (NaCl, thin film), cm$^{-1}$: 3383, 2944, 2831, 2789, 1474. HRMS: ESI+ [M + H]$^+$ Calcd. for C$_9$H$_{14}$NO: 152.1075. Found: 152.1073.

![Image](image.png)

5-chloro-2-(N,N-dimethylamino)phenol 2g: TLC: 10% ethyl acetate–hexanes, R$_f$ = 0.26 (UV, KMnO$_4$). $^1$H NMR (500 MHz, CDCl$_3$), δ: 7.07 (d, J = 8.5 Hz, 1H), 6.94 (s, 1H), 6.824 (d, J = 8.5 Hz, 1H), 2.62 (s, 6H). $^{13}$C NMR (125 MHz, CDCl$_3$), δ: 152.3, 139.4, 131.1, 121.8, 120.1, 114.7, 45.2. FTIR (NaCl, thin film), cm$^{-1}$: 2999, 2879, 2840, 1509, 1464. HRMS: EI+ [M]$^+$ Calcd. for C$_8$H$_{10}$ClNO: 171.0451. Found: 171.0452.

![Image](image.png)

2-(N,N-dimethylamino)-4-methoxyphenol 2h: TLC: 10% ethyl acetate–hexanes, R$_f$ = 0.21 (UV, KMnO$_4$). $^1$H NMR (300 MHz, CDCl$_3$), δ: 6.85 (d, J = 8.4 Hz, 1H), 6.74 (d, J = 3.0 Hz, 1H), 6.60 (dd, $J_1$ = 8.7 Hz, $J_2$ = 3.0 Hz, 1H), 3.75 (s, 3H), 2.64 (s, 6H). $^{13}$C NMR (75 MHz, CDCl$_3$), δ: 153.3, 145.4, 141.2, 114.2, 110.2, 107.6, 55.9, 45.1. FTIR (NaCl, thin film), cm$^{-1}$: 3369, 2945, 2833, 1761, 1611, 1505, 1456. HRMS: ESI+ [M + H]$^+$ Calcd. for C$_9$H$_{14}$NO$_2$: 168.1024. Found: 168.1026.
2-(N,N-dimethylamino)-5-methoxyphenol 2i: TLC: 10% ethyl acetate–hexanes, R_f = 0.32 (UV, KMnO_4). ^1H NMR (500 MHz, CDCl_3), δ: 7.09 (d, J = 8.5 Hz, 1H), 6.53 (d, J = 2.5 Hz, 1H), 6.41 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 3.76 (s, 3H), 2.61 (s, 6H). ^13C NMR (125 MHz, CDCl_3), δ: 158.0, 152.5, 133.6, 121.4, 105.2, 105.2, 99.8, 55.3, 45.6. FTIR (NaCl, thin film), cm^{-1}: 3362, 2947, 2867, 2833, 1623, 1509, 1507. HRMS: EI+ [M]^+ Calcd. for C_9H_13NO_2: 167.0946. Found: 167.0942.

General procedure for the Synthesis of Sulfonylated N,N-Dimethylanilines (1.0 mmol scale)

A stirred solution of N,N-dimethylaniline-N-oxide 1a (0.137 g, 1.00 mmol, 1 equiv, dried by azeotropic distillation with benzene) in dichloromethane (10 mL) was cooled to −78 °C whereupon trifluoromethanesulfonic anhydride (0.190 mL, 1.10 mmol, 1.10 equiv) was added dropwise via syringe. The resultant solution was stirred for 1 h whereupon triethylamine (0.276 mL, 2.00 mmol, 2.00 equiv) was added. The reaction mixture was stirred for 15 min, then was diluted with hexanes (10 mL) before addition of silica gel (ca. 3 mL). The resultant biphasic mixture was warmed to 23 °C, then was concentrated. Immediate purification of the residue by flash column chromatography (gradient elution 1 → 2% ethyl acetate–hexanes) afforded 3a (0.246 g, 91%) as a clear, yellow oil.

General procedure for the Synthesis of Sulfonylated N,N-Dimethylanilines (10 mmol scale)

A stirred solution of N,N-dimethylaniline-N-oxide 1a (1.37 g, 10.0 mmol, 1 equiv, dried by azeotropic distillation with benzene) in dichloromethane (100 mL) was cooled to −78 °C whereupon trifluoromethanesulfonic anhydride (1.90 mL, 11.0 mmol, 1.10 equiv) was added
dropwise via syringe (addition time approximately two minutes). The resultant solution was stirred for 1 h whereupon triethylamine (2.76 mL, 20.0 mmol, 2.00 equiv) was added. The reaction mixture was stirred for 15 min, then was warmed to 0 °C for 45 minutes, then was quenched by the addition of water (1.0 mL) and silica gel (4 g). The resultant mixture was concentrated to a volume of 20 mL, then was diluted with hexanes (20 mL). The resultant mixture was filtered through a 1” by 1” plug of silica gel topped with 0.5 cm of anhydrous sodium sulfate. The plug was further eluted with 10% ethyl acetate–hexanes (100 mL). The filtrate was concentrated to give 3a (2.157 g, 80%) as a pale yellow oil.

2-(N,N-dimethylamino)phenyl trifluoromethanesulfonate 3a: TLC: 10% ethyl acetate–hexanes, Rf = 0.68 (UV, KMnO₄). ¹H NMR (300 MHz, CDCl₃), δ: 7.34–7.25 (m, 1H), 7.17 (dd, J₁ = 8.1, J₂ = 1.5 Hz, 1H), 7.11 (dd, J₁ = 8.1, J₂ = 1.6 Hz, 1H), 7.00 (dd, J₁ = 8.0, J₂ = 7.3, J₃ = 1.7 Hz, 1H), 2.81 (s, 6H). ¹³C NMR (75 MHz, CDCl₃), δ: 146.7, 143.4, 129.0, 122.5, 122.3, 120.5, 118.7 (q, J = 318 Hz), 43.1. ¹⁹F NMR (282 MHz, CDCl₃), δ: -74.7. FTIR (NaCl, thin film), cm⁻¹: 2954, 2841, 2792, 1609, 1499. HRMS: ES⁺ [M + H]⁺ Calcd. for C₉H₁₁F₃NO₃S: 270.0412. Found: 270.0407.

3-bromo-4-(N,N-dimethylamino)phenyl trifluoromethanesulfonate 3b: TLC: 10% ethyl acetate–hexanes, Rf = 0.59 (UV, KMnO₄). ¹H NMR (300 MHz, CDCl₃), δ: 7.48 (d, J = 2.9 Hz, 1H), 7.19 (dd, J₁ = 8.9, J₂ = 2.8 Hz, 1H), 7.08 (d, J = 8.9 Hz, 1H), 2.81 (s, 6H). ¹³C NMR (125 MHz, CDCl₃), δ: 152.3, 143.9, 127.0, 121.0, 120.9, 119.0, 118.8 (q, J = 318 Hz), 44.1. ¹⁹F NMR (282 MHz, CDCl₃), δ: -72.7. FTIR (NaCl, thin film), cm⁻¹: 2951, 2839, 2790, 1490, 1425. HRMS: ES⁺ [M + H]⁺ Calcd. for C₉H₁₀BrF₃NO₃S: 347.9517. Found: 347.9510.
3-isopropyl-4-(N,N-dimethylamino)phenyl trifluoromethanesulfonate \textit{para-3c}: TLC: 10% ethyl acetate–hexanes, \(R_f = 0.72\) (UV, KMnO\(_4\)). \(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 7.14–7.08 (m, 2H), 7.03 (dd, \(J = 8.8\) Hz, 3.0 Hz, 1H), 3.52 (hept, \(J = 6.8\) Hz, 1H), 2.68 (s, 6H), 1.21 (d, \(J = 6.9\) Hz, 6H). \(^13\)C NMR (75 MHz, CDCl\(_3\)), \(\delta\): 152.0, 146.9, 146.0, 121.2, 119.5, 119.0 (q, \(J = 319\) Hz), 118.9, 45.7, 27.2, 24.0. \(^19\)F NMR (282 MHz, CDCl\(_3\)), \(\delta\): -72.9. FTIR (NaCl, thin film), cm\(^{-1}\): 2967, 2870, 2830, 1602, 1492, 1423. HRMS: EI+ \([M]^+\) Calcd. for C\(_{12}\)H\(_{16}\)F\(_3\)NO\(_3\)S: 311.0803. Found: 311.0794.

3-isopropyl-2-(N,N-dimethylamino)phenyl trifluoromethanesulfonate \textit{ortho-3c}: TLC: 10% ethyl acetate–hexanes, \(R_f = 0.81\) (UV, KMnO\(_4\)). \(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 7.13 (dd, \(J_1 = 7.8, J_2 = 1.6\) Hz, 1H), 7.05 (t, \(J = 7.9\) Hz, 1H), 6.91 (dd, \(J_1 = 8.0\) Hz, \(J_2 = 1.7\) Hz, 1H), 3.21 (hept, \(J = 6.9\) Hz, 1H), 2.73 (d, \(J = 0.5\) Hz, 6H), 1.13 (d, \(J = 6.9\) Hz, 6H). \(^13\)C NMR (125 MHz, CDCl\(_3\)), \(\delta\): 151.2, 148.8, 142.7, 126.7, 126.4, 118.6 (q, \(J = 319\) Hz), 118.5, 43.5, 28.4, 24.2. \(^19\)F NMR (282 MHz, CDCl\(_3\)), \(\delta\): -75.0. FTIR (NaCl, thin film), cm\(^{-1}\): 2969, 2871, 2797, 1454, 1417. HRMS: EI+ \([M]^+\) Calcd. for C\(_{12}\)H\(_{16}\)F\(_3\)NO\(_3\)S: 311.0803. Found: 311.0799.

methyl 3-(N,N-dimethylamino)-4-(trifluoromethanesulfonate)benzoate \textit{3d}: TLC: 10% ethyl acetate–hexanes, \(R_f = 0.45\) (UV, KMnO\(_4\)). \(^1\)H NMR (300 MHz, CDCl\(_3\)), \(\delta\): 7.76 (d, \(J = 2.0\) Hz, 1H), 7.67 (ddd, \(J_1 = 8.4\) Hz, \(J_2 = 2.1\) Hz, \(J_3 = 1.1\) Hz, 1H), 7.28–7.16 (m, 1H), 3.92 (d, \(J = 1.1\) Hz, 3H), 2.83 (d, \(J = 1.1\) Hz, 6H). \(^13\)C NMR (125 MHz, CDCl\(_3\)), \(\delta\): 166.1, 146.7, 146.1, 130.8, 123.8, 122.5, 121.8, 118.8 (q, \(J = 320\) Hz), 52.6, 43.1. \(^19\)F NMR (282 MHz, CDCl\(_3\)), \(\delta\): -74.5. FTIR
NaCl, thin film), cm⁻¹: 2956, 2845, 2796, 1730, 1499, 1424. HRMS: ES+ [M + Na]⁺ Calcd. for C₁₁H₁₂F₃NO₅SNa: 350.0286. Found: 350.0281.

methyl 3-((N,N-dimethylamino)-2-(trifluoromethanesulfonate)benzoate 3d: TLC: 10% ethyl acetate–hexanes, Rₚ = 0.55 (UV, KMnO₄). ¹H NMR (500 MHz, CDCl₃), δ: 7.59 (dd, J₁ = 7.5 Hz, J₂ = 2.0 Hz, 1H), 7.38–7.27 (m, 2H), 3.93 (s, 3H), 2.78 (s, 6H). ¹³C NMR (125 MHz, CDCl₃), δ: 165.0, 147.6, 142.3, 128.3, 125.5, 125.3, 124.9, 118.8 (q, J = 319 Hz), 52.8, 43.4. ¹⁹F NMR (282 MHz, CDCl₃), δ: -74.9. FTIR (NaCl, thin film), cm⁻¹: 2957, 2876, 2844, 1735, 1421. HRMS: ES+ [M + Na]⁺ Calcd. for C₁₁H₁₂F₃NO₅SNa: 350.0286. Found: 350.0287.

H₃C
\[\text{N} \quad \text{CH₃} \quad \text{OTf} \]
3d

73%

1-(N,N-dimethylamino)naphthalene-2-trifluoromethanesulfonate 3e: TLC: 20% ethyl acetate–hexanes, Rₚ = 0.73 (UV, KMnO₄). ¹H NMR (500 MHz, CDCl₃), δ: 8.29 (dd, J₁ = 8.1 Hz, J₂ = 1.9 Hz, 1H), 8.11–8.03 (d, 1H), 7.67–7.57 (m, 2H), 7.38 (dd, J₁ = 8.5 Hz, J₂ = 1.9 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 2.92 (s, 6H). ¹³C NMR (125 MHz, CDCl₃), δ: 151.5, 141.1, 129.9, 127.7, 127.6, 126.5, 124.9, 121.3, 118.9 (q, J = 320 Hz), 117.9, 112.8, 45.2. ¹⁹F NMR (282 MHz, CDCl₃), δ: -73.80. FTIR (NaCl, thin film), cm⁻¹: 2984, 2945, 2835, 2790, 1599, 1575, 1419, 600. HRMS: ES+ [M + H]⁺ Calcd. for C₁₄H₁₃F₃NO₃S: 320.0568. Found: 320.0575.

H₃C
\[\text{N} \quad \text{CH₃} \quad \text{OTf} \]
3e

73%

2-(N,N-dimethylamino)-4-methylphenyl trifluoromethanesulfonate 3f (isolated as a mixture of regioisomers, asterisk denotes minor peaks): TLC: 20% ethyl acetate–hexanes, Rₚ = 0.73 (UV, KMnO₄). ¹H NMR (500 MHz, CDCl₃), δ: 7.20* (t, J = 7.8 Hz, 1H), 7.08 (d, J = 8.2 Hz, 1H),
7.06–7.03* (m, 1H), 6.96* (ddd, J1 = 7.6 Hz, J2 = 1.7 Hz, J3 = 0.8 Hz, 1H), 6.93 (d, J = 2.2 Hz, 1H), 6.85–6.78 (m, 1H), 2.81 (s, 6H), 2.74* (s, 6H), 2.37 (d, J = 3.7 Hz, 3H), 2.37* (d, J = 3.7 Hz, 3H). 13C NMR (125 MHz, CDCl3), δ: 146.9, 146.2, 143.7, 141.4, 139.2, 131.1, 129.0, 128.1, 126.0, 123.0, 121.9, 121.0, 120.1, 118.8, 117.8, 117.6, 117.5, 114.5, 113.6, 110.5, 34% 5-chloro-2-(N,N-dimethylamino)phenyl trifluoromethanesulfonate 3g: TLC: 10% ethyl acetate–hexanes, Rf = 0.73 (UV, KMnO4). 1H NMR (300 MHz, CDCl3), δ: 7.25 (dd, J1 = 8.7 Hz, J2 = 2.4 Hz, 1H), 7.16 (d, J = 2.4 Hz, 1H), 7.02 (d, J = 8.7 Hz, 1H), 2.78 (s, 6H). 13C NMR (75 MHz, CDCl3), δ: 145.6, 143.0, 129.1, 127.0, 122.8, 121.2, 118.8 (q, J = 318 Hz), 43.1. 19F NMR (282 MHz, CDCl3), δ: -74.9. FTIR (NaCl, thin film), cm⁻¹: 2956, 2844, 2794, 1497, 1424. HRMS: EI+ [M]+ Calcd. for C9H9ClF3NO3S: 302.9943. Found: 302.9938.

2-(N,N-dimethylamino)-4-methoxyphenyl trifluoromethanesulfonate 3h: TLC: 10% ethyl acetate–hexanes, Rf = 0.59 (UV, KMnO4). 1H NMR (300 MHz, CDCl3), δ: 7.08 (d, J = 8.9 Hz, 1H), 6.59 (d, J = 2.9 Hz, 1H), 6.47 (dd, J1 = 8.9 Hz, J2 = 2.9 Hz, 1H), 3.80 (s, 3H), 2.79 (s, 6H). 13C NMR (75 MHz, CDCl3), δ: 159.7, 147.6, 137.0, 122.9, 118.8 (q, J = 320 Hz), 106.6, 105.9, 55.7, 43.0. 19F NMR (282 MHz, CDCl3), δ: -74.5. FTIR (NaCl, thin film), cm⁻¹: 2951, 2841,
2795, 1615, 1504, 1418. HRMS: ES+ [M + H]^+ Calcd. for C_{10}H_{13}NO_{4}S: 300.0517. Found: 300.0522.

A solution of p-toluenesulfonyl chloride (220 mg, 1.15 mmol, 1.15 equiv) in dichloromethane (4 mL) was added dropwise to a stirred solution of N,N-dimethylaniline-N-oxide 1a (137 mg, 1.00 mmol, dried by azeotropic distillation with benzene) in dichloromethane (10 mL) at –78 °C. The resultant mixture was warmed to 23 °C and was stirred at that temperature for 2 h before being cooled to –78 °C. Triethylamine (0.276 mL, 2.00 mmol, 2.00 equiv) was added dropwise via syringe and the resultant mixture was warmed to 23 °C, stirred for 15 min, then was diluted with hexanes (10 mL). The resultant mixture was filtered through a plug of silica gel (hexanes) and concentrated. Purification of the residue by flash column chromatography (2% ethyl acetate–hexanes) afforded 4a (0.111 g, 38%) as a yellow oil.

2-(N,N-dimethylamino)phenyl (4-methylbenzene)sulfonate 4a: TLC: 10% ethyl acetate–hexanes, R_f = 0.48 (UV, KMnO_4). 1H NMR (300 MHz, CDCl_3), δ: 7.69 (d, J = 8.1 Hz, 5H), 7.28–7.18 (m, 3H), 7.17–7.07 (m, 1H), 6.95–6.81 (m, 1H), 6.78 (dd, J_1 = 8.1 Hz, J_2 = 1.6 Hz, 1H), 2.52 (s, 6H), 2.43 (s, 3H). 13C NMR (75 MHz, CDCl_3), δ: 145.8, 144.9, 141.9, 133.5, 129.1, 128.7, 127.8, 124.4, 121.1, 118.9, 42.5, 21.8. FTIR (NaCl, thin film), cm⁻¹: 2944, 2837, 2788, 1600, 1499, 1370. HRMS: ES+ [M + Na]^+ Calcd. for C_{15}H_{17}NO_{3}SNa: 314.0827. Found: 314.0823.
2-((N,N-dimethylamino)-4-methoxyphenyl (4-methylbenzene)sulfonate 4b:  TLC:  10% ethyl acetate–hexanes, 
\( R_f = 0.33 \) (UV, KMnO₄).  \(^1\)H NMR (300 MHz, CDCl₃), \( \delta \):  7.64 (d, \( J = 8.3 \) Hz, 2H), 7.21 (d, \( J = 8.0 \) Hz, 2H), 7.09 (d, \( J = 8.8 \) Hz, 1H), 6.35 (dd, \( J_1 = 8.8 \) Hz, \( J_2 = 2.9 \) Hz, 1H), 6.25 (d, \( J = 2.9 \) Hz, 1H), 3.72 (s, 3H), 2.46 (s, 6H), 2.39 (s, 3H).  \(^1^3\)C NMR (75 MHz, CDCl₃), \( \delta \): 158.7, 146.6, 144.8, 135.4, 133.3, 129.0, 128.5, 124.8, 105.1, 104.4, 55.4, 42.1, 21.6.  FTIR (NaCl, thin film), \( \text{cm}^{-1} \):  2943, 2838, 2790, 1600, 1505, 1366.  HRMS:  ES + [M + Na]⁺ Calcd. for C₁₆H₁₉NO₄SNa: 344.0933.  Found: 344.0923.

![Structure of 4b](image)

2-((N,N-dimethylamino)-3-isopropylphenyl (4-methylbenzene)sulfonate 4c:  TLC:  10% ethyl acetate–hexanes, 
\( R_f = 0.67 \) (UV, KMnO₄).  \(^1\)H NMR (300 MHz, CDCl₃), \( \delta \):  7.87 (d, \( J =8.4 \) Hz, 2H), 7.38 (d, \( J = 8.4 \) Hz, 2H), 7.15 (dd, \( J_1 = 7.9 \) Hz, \( J_2 = 1.7 \) Hz, 1H), 7.02 (t, \( J = 7.9 \) Hz, 1H), 6.89 (dd, \( J_1 = 8.1 \) Hz, \( J_2 = 1.6 \) Hz, 1H), 3.48 (hept, \( J = 7.0 \) Hz, 1H), 2.75 (s, 6H), 2.48 (s, 3H), 1.20 (d, \( J = 7.0 \) Hz, 6H).  \(^1^3\)C NMR (75 MHz, CDCl₃), \( \delta \): 150.1, 148.5, 145.2, 142.8, 134.4, 129.9, 128.3, 125.3, 124.7, 119.2, 43.9, 27.9, 24.0, 21.8.  FTIR (NaCl, thin film), \( \text{cm}^{-1} \):  2964, 2927, 2360, 2331, 1455, 1373.  HRMS:  ES+ [M + Na]⁺ Calcd. for C₁₈H₂₃NO₃SNa: 356.1296.  Found: 356.1294.

![Structure of 4c](image)

methyl 3-((N,N-dimethylamino)-4-((p-toluenesulfonate)benzoate 4d:  TLC:  10% ethyl acetate–hexanes, 
\( R_f = 0.30 \) (UV, KMnO₄).  \(^1\)H NMR (300 MHz, CDCl₃), \( \delta \):  7.67 (dd, \( J_1 = 8.4 \) Hz, \( J_2 = 1.6 \) Hz, 2H), 7.53 (dd, \( J_1 = 8.4 \) Hz, \( J_2 = 2.1 \) Hz, 1H), 7.44 (d, \( J = 2.0 \) Hz, 1H), 7.29–7.20 (m, 3H), 3.89 (s, 3H), 2.56 (s, 6H), 2.41 (s, 3H).  \(^1^3\)C NMR (75 MHz, CDCl₃), \( \delta \):  166.6, 145.7, 145.3, 145.0, 133.2, 129.4, 129.3, 128.6, 124.3, 122.4, 120.2, 52.4, 42.4, 21.8.  FTIR (NaCl, thin film),
cm⁻¹: 2951, 2842, 1723, 1596, 1501, 1375. HRMS: ES⁺ [M + Na]+ Calcd. for C₁₇H₁₉NO₅SNa: 372.0882. Found: 372.0884.

**General procedure for the Synthesis of Alkylated N,N-Dimethylanilines (1.0 mmol scale)**

A stirred solution of N,N-dimethylaniline-N-oxide 1a (0.137 g, 1.00 mmol, 1 equiv, dried by azeotropic distillation with benzene) in dichloromethane (20 mL) was cooled to −78 °C whereupon ethyl malonyl chloride (0.140 mL, 1.10 mmol, 1.10 equiv) was added dropwise via syringe. The resultant solution was stirred for 1 h whereupon triethylamine (0.237 mL, 1.10 mmol, 2.00 equiv) was added. The reaction mixture was stirred for 15 min, then was warmed to 23 °C, stirred at that temperature for 8 h, then was concentrated. Purification of the residue by flash column chromatography (gradient elution 1 → 2% ethyl acetate–hexanes) afforded 5a (0.136 g, 67%) as a pale yellow oil.

**General procedure for the Synthesis of Alkylated N,N-Dimethylanilines (10 mmol scale)**

A stirred solution of N,N-dimethylaniline-N-oxide 1a (1.37 g, 10.0 mmol, 1 equiv, dried by azeotropic distillation with benzene) in dichloromethane (200 mL) was cooled to −78 °C whereupon ethyl malonyl chloride (1.40 mL, 11.0 mmol, 1.10 equiv) was added dropwise via syringe (addition time approximately two minutes). The resultant solution was stirred for 1 h whereupon triethylamine (2.37 mL, 20.0 mmol, 2.00 equiv) was added. The reaction mixture was stirred for 15 min, then was warmed to 23 °C, stirred at that temperature for 8 h, then was concentrated. Purification of the residue by flash column chromatography (2% ethyl acetate–hexanes) afforded 5a (1.13 g, 55%) as a pale yellow.

Ethyl [2-(N,N-dimethylamino)phenyl]acetate 5a: TLC: 10% ethyl acetate–hexanes, Rₚ = 0.48 (UV, KMnO₄). ¹H NMR: (300 MHz, CDCl₃), δ: 7.25–7.20 (m, 2H), 7.18–7.11 (m, 1H), 7.05 (td, J₁ = 7.4, J₂ = 1.4 Hz, 1H), 4.16 (q, J = 7.2 Hz, 2H), 3.73 (s, 2H), 2.64 (s, 6H), 1.25 (t, J = 7.1 Hz, 4H). ¹³C NMR (75 MHz, CDCl₃), δ: 172.6, 153.2, 131.0, 130.5, 128.1, 123.9, 120.3, 60.7, 45.1,
37.3, 14.4. FTIR (NaCl, thin film), cm⁻¹: 2980, 2939, 2877, 2785, 1735, 1495. HRMS: ES⁺ [M + Na]⁺ Calcd. for C₁₂H₁₇NO₂Na: 230.1157. Found: 230.1152.

Ethyl [4-(N,N-dimethylamino)-3-isopropylphenyl]acetate para-5b. TLC: 10% ethyl acetate–hexanes, Rf = 0.57 (UV, KMnO₄). ¹H NMR (500 MHz, CDCl₃), δ: 7.15 (d, J = 1.4 Hz, 1H), 7.06 (d, J = 1.3 Hz, 2H), 4.15 (q, J = 7.1 Hz, 2H), 3.56 (s, 2H), 3.50 (hept, J = 6.9 Hz, 1H), 2.66 (s, 6H), 1.31–1.17 (m, 9H). ¹³C NMR (125 MHz, CDCl₃), δ: 171.9, 150.7, 144.1, 129.3, 127.4, 126.9, 119.7, 60.7, 45.8, 41.0, 26.6, 24.1, 14.2. FTIR (NaCl, thin film), cm⁻¹: 2963, 2935, 2868, 1735, 1501. HRMS: ES⁺ [M + Na]⁺ Calcd. for C₁₅H₂₃NO₂Na: 272.1627. Found: 272.1620.

Ethyl [2-(N,N-dimethylamino)-3-isopropylphenyl]acetate ortho-5b. TLC: 10% ethyl acetate–hexanes, Rf = 0.61 (UV, KMnO₄). ¹H NMR (500 MHz, CDCl₃), δ: 7.17 (d, J = 7.5 Hz, 1H), 7.12 (t, J = 7.5 Hz, 1H), 7.05 (d, J = 7.5 Hz, 1H), 4.17 (q, J = 7.0 Hz, 2H), 3.61 (s, 2H), 3.18 (m, 1H), 2.76 (s, 6H), 1.27–1.21 (m, 9H). ¹³C NMR (125 MHz, CDCl₃), δ: 172.1, 150.9, 144.3, 129.5, 127.6, 127.1, 119.8, 60.9, 46.0, 41.2, 26.8, 24.3, 14.4. FTIR (NaCl, thin film), cm⁻¹: 2963, 2868, 2784, 1735, 1447. HRMS: ES⁺ [M + Na]⁺ Calcd. for C₁₅H₂₃NO₂Na: 272.1627. Found: 272.1621.

ethyl (2-(N,N-dimethylamino)-5-fluorophenyl)acetate 5c: TLC: 10% ethyl acetate–hexanes, Rf = 0.48 (UV, KMnO₄). ¹H NMR (500 MHz, CDCl₃), δ: 7.12 (dd, J₁ = 8.8 Hz, J₂ = 5.2 Hz, 1H), 7.00–6.87 (m, 2H), 4.17 (q, J = 7.0 Hz, 2H), 3.71 (s, 2H), 2.60 (s, 6H), 1.26 (t, J = 7.1, 3H). ¹³C
NMR (125 MHz, CDCl₃), δ: 172.0, 159.3 (d, J = 242 Hz), 149.3, 132.8, 121.9 (d, J = 7.6 Hz), 117.4 (d, J = 22.1 Hz), 114.6 (d, J = 22.1 Hz), 60.9, 45.4, 37.1, 14.4. ¹⁹F NMR (470 MHz, CDCl₃), δ: -118.3. FTIR (NaCl, thin film), cm⁻¹: 2982, 2940, 2828, 1735, 1499. HRMS: EI⁺ [M]⁺ Calcd. for C₁₂H₁₈FNO₂: 225.1165. Found: 225.1168.

![Structure 5d]

ethyl (2-(N,N-dimethylamino)-5-methylphenyl)acetate 5d: TLC: 20% ethyl acetate–hexanes, R₆ = 0.66 (UV, KMnO₄). ¹H NMR (300 MHz, CDCl₃), δ: 7.07 (s, 3H), 4.18 (dd, J₁ = 7.1 Hz, J₂ = 0.6 Hz, 2H), 3.71 (s, 2H), 2.62 (d, J = 0.6 Hz, 6H), 2.30 (s, 3H), 1.50–1.07 (m, 3H). ¹³C NMR (75 MHz, CDCl₃), δ: 172.7, 150.7, 133.4, 131.5, 130.4, 128.7, 120.2, 60.6, 45.2, 37.2, 20.9, 14.4. FTIR (NaCl, thin film), cm⁻¹: 2979, 2930, 2858, 1735, 1503, 1454. HRMS: ES⁺ [M + Na]⁺ Calcd. for C₁₃H₁₉NO₂Na: 244.1313. Found: 244.1311.

![Structure 5e]

ethyl (2-(N,N-dimethylamino)-5-methoxyphenyl)acetate 5e: TLC: 10% ethyl acetate–hexanes, R₆ = 0.39 (UV, KMnO₄). ¹H NMR (500 MHz, CDCl₃), δ: 7.12 (d, J = 8.5 Hz, 1H), 6.80 (m, 2H), 4.17 (q, J = 7 Hz, 2H), 3.76 (s, 3H), 3.71 (s, 2H), 2.59 (s, 6H), 1.26 (t, J = 7.1, 3H). ¹³C NMR (125 MHz, CDCl₃), δ: 172.2, 156.0, 146.3, 132.1, 121.5, 115.9, 113.2, 60.5, 55.3, 45.5, 37.2, 14.3. FTIR (NaCl, thin film), cm⁻¹: 2980, 2938, 2826, 2781, 1738, 1608, 1506. HRMS: EI⁺ [M]⁺ Calcd. for C₁₃H₁₉NO₃: 237.1364. Found: 237.1366.
ethyl (1-(N,N-dimethylamino)naphthalen-2-yl)acetate ortho-5f: TLC: 20% ethyl acetate–hexanes, R_f = 0.63 (UV, KMnO_4). \(^1\)H NMR (300 MHz, CDCl_3), δ: 8.13–8.02 (d, 1H), 7.93–7.82 (m, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.55–7.43 (m, 2H), 7.40 (d, J = 8.4 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.88 (s, 2H), 3.05 (s, 6H), 1.29 (t, J = 7.1 Hz, 3H). \(^1\)^13C NMR (75 MHz, CDCl_3), δ: 172.2, 147.2, 134.8, 132.8, 131.6, 128.9, 128.8, 126.1, 125.6, 125.4, 124.5, 60.7, 43.8, 38.6, 14.4. FTIR (NaCl, thin film), cm\(^{-1}\): 3050, 2979, 2926, 2832, 1733, 1386. HRMS: ES+ [M + Na]^+ Calcd. for C\(_{16}\)H\(_{19}\)NO\(_2\)Na: 280.1313. Found: 280.1306.

ethyl (4-(N,N-dimethylamino)naphthalen-1-yl)acetate para-5f: TLC: 20% ethyl acetate–hexanes, R_f = 0.54 (UV, KMnO_4). \(^1\)H NMR (300 MHz, CDCl_3), δ: 8.36–8.24 (m, 1H), 8.03–7.92 (m, 1H), 7.58–7.45 (m, 2H), 7.34 (dt, J\(_1\) = 7.7 Hz, J\(_2\) = 0.6 Hz, 1H), 7.05 (d, J = 7.6 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 4.01 (d, J = 0.6 Hz, 2H), 2.90 (s, 6H), 1.25 (t, J = 7.1 Hz, 3H). \(^1\)^13C NMR (75 MHz, CDCl_3), δ: 172.1, 150.9, 133.4, 129.3, 128.0, 126.2, 125.3, 125.1, 124.9, 124.4, 113.8, 61.0, 45.4, 39.2, 14.4. FTIR (NaCl, thin film), cm\(^{-1}\): 3050, 2979, 2926, 2832, 1733, 1386. HRMS: ES+ [M + Na]^+ Calcd. for C\(_{16}\)H\(_{19}\)NO\(_2\)Na: 280.1313. Found: 280.1306.

ethyl (2-(N,N-dimethylamino)-4-methylphenyl)acetate 5g (isolated as a mixture of regioisomers, asterisk denotes minor peaks): TLC: 20% ethyl acetate–hexanes, R_f = 0.57 (UV, KMnO_4). \(^1\)H NMR (500 MHz, CDCl_3), δ: 7.19* (t, J = 7.8 Hz, 1H), 7.16 d, J = 8.1 Hz, 1H), 7.07* (d, J = 8.2 Hz, 1H), 6.99 (s, 1H), 6.97* (d, J = 7.8 Hz, 1H), 6.90 (d, J = 7.6 Hz, 1H), 4.19 (q, J = 7.1 Hz,
2H), 4.19* (q, J = 7.1 Hz, 2H), 3.90* (s, 2H), 3.73 (s, 2H), 2.66 (s, 6H), 2.66* (s, 6H), 2.35 (s, 3H), 2.29* (s, 3H), 1.28 (t, J = 7.1 Hz, 3H), 1.28* (t, J = 7.1 Hz, 3H). 13C NMR (125 MHz, CDCl3), δ: 172.7, 172.6, 153.6, 152.9, 138.4, 137.7, 130.7, 129.6, 129.1, 127.6, 127.2, 125.9, 124.5, 120.9, 118.2, 117.9, 113.2, 109.7, 60.5, 45.4, 36.9, 34.0, 21.4, 20.2, 14.3. FTIR (NaCl, thin film), cm⁻¹: 2979, 2937, 2826, 2781, 1732, 1609, 1507. HRMS: ES+ [M + Na]⁺ Calcd. for C13H19NO2Na: 244.1313. Found: 244.1309.

![Diagram of compound 5h](image)

ethyl (5-chloro-2-(N,N-dimethylamino)phenyl)acetate 5h: TLC: 10% ethyl acetate–hexanes, Rf = 0.46 (UV, KMnO4). 1H NMR (300 MHz, CDCl3), δ: 7.24–7.16 (m, 2H), 7.06 (d, J = 8.4 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.68 (s, 2H), 2.61 (s, 6H), 1.25 (t, J = 7.1 Hz, 3H). 13C NMR (75 MHz, CDCl3), δ: 171.9, 151.8, 130.8, 129.1, 128.0, 121.6, 113.5, 60.9, 45.0, 37.0, 14.4. FTIR (NaCl, thin film), cm⁻¹: 2982, 2941, 2787, 1734, 1490. HRMS: EI+ [M]⁺ Calcd. for C12H16ClNO2: 241.0869. Found: 241.0859.

![Diagram of compound 5i](image)

ethyl (2-(N,N-dimethylamino)-4-methoxyphenyl)acetate 5i (isolated as a mixture of regioisomers, asterisk denotes minor peaks): TLC: 10% ethyl acetate–hexanes, Rf = 0.35 (UV, KMnO4). 1H NMR (300 MHz, CDCl3), δ: 7.21* (t, J = 8.2 Hz, 1H), 7.16 (d, J = 8.4 Hz, 1H), 6.80* (d, J = 8.1 Hz, 1H), 6.71 (d, J = 2.6 Hz, 1H), 6.65* (d, J = 8.3 Hz, 1H), 6.61 (dd, J₁ = 8.3 Hz, J₂ = 2.7 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 4.17* (d, J = 7.1 Hz, 2H), 3.79 (s, 2H), 3.79* (s, 2H), 3.78* (s, 2H), 3.67, (s, 2H), 2.66* (s, 6H), 2.64 (s, 6H), 1.26 (t, J = 7.1 Hz, 3H), 1.26* (t, J = 7.1 Hz, 2H).
A solution of phenyl isocyanate (0.150 mL, 1.20 mmol, 1.2 equiv) in DCM (50 mL) was added dropwise over six hours to a stirred, cooled solution of N,N-dimethylaniline-N-oxide 1a (137 mg, 1.00 mmol, dried by azeotropic distillation with benzene) in dichloromethane (50 mL) at 0 °C. The resultant solution slowly turned red and was stirred 0 °C for 6 h whereupon the solution was allowed to slowly rise to 22 °C over the next 8 h. After this period, silica gel (ca. 3 mL) was added. The resultant suspension was stirred for 30 min, allowed to settle, then the yellow solution was filtered and concentrated. The crude product mixture was suspended in hexanes such that a solid white byproduct is removed and the yellow extract passed through a small plug of silica gel (hexane) to afford the amine 6a (83.9 mg, 40%) after concentration as an orange solid.

\( N'N'\text{-dimethyl-N}^2\text{-phenylbenzene-1,2-diamine 6a:} \) TLC: 10% ethyl acetate–hexanes, \( R_f = 0.63 \) (UV, KMnO₄). \(^1\)H NMR (500 MHz, CDCl₃), \( \delta: \) 7.37–7.26 (m, 3H), 7.19–7.13 (m, 2H), 7.11 (dd, \( J_1 = 7.8 \text{ Hz}, J_2 = 1.5 \text{ Hz}, 1\text{H} \)), 7.03–6.89 (m, 2H), 6.85 (td, \( J_1 = 7.6 \text{ Hz}, J_2 = 1.5 \text{ Hz}, 1\text{H} \)), 6.57 (s, 1H), 2.68 (s, 6H). \(^{13}\)C NMR (125 MHz, CDCl₃), \( \delta: \) 129.4, 129.2, 124.2, 120.9, 120.0, 119.8, 118.4, 116.8, 114.5, 112.8, 44.3, 40.8. FTIR (NaCl, thin film), cm⁻¹: 3354, 3040, 2939, 2826, 2360, 1592, 1512. HRMS: ES+ [M + H]^+ Calcd. for C₁₄H₁₇N₂: 213.1392. Found: 213.1387.
2f
2:1
(6-OH:2-OH)
(6-OH:2-OH)
$\text{H}_3\text{C}-\text{N}-\text{CH}_3$

$\text{O Tf}$

$\text{3a}$
$\text{H}_3\text{C}-\text{N}-\text{CH}_3$

$\text{CH}_3$

$\text{CH}_3$

3c

6-OTf
\[
\text{H}_3\text{C} - \text{N} - \text{CH}_3
\]

\[
\begin{array}{c}
\text{3f} \\
2.5:1 \\
(6\text{-OTf}:2\text{-OTf})
\end{array}
\]
S-100

H₃C-\text{N}-\text{CH₃}

2.5:1

(6-OTf:2-OTf)
$\text{EtO}_2\text{C}$

5b
6-alk
5g
2:1
(6-alk:2:alk)
$\text{H}_3\text{C-N-CH}_3$

```
5g
2:1
(6-alk:2:alk)
```
5i
2:1
(6-alk:2-alk)
5i
2:1
(6-alk:2-alk)
