Supporting Information

Vanadium-catalyzed oxidative Strecker reaction: α-C-H cyanation of para-methoxyphenyl (PMP)-protected primary amines

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1. General Information

All reactions were performed in glassware without argon protection. Commercially available reagents were used without further purification. Organic solutions were concentrated by rotary evaporator at ca. 30 mmHg. Flash column chromatography was performed as described by Still (Still, W. C.; Kahn, M.; Mitra, A. J. Org. Chem. 1978, 43, 2923), employing EMD silica gel 60 (230–400 mesh ASTM). TLC analyses were performed on EMD 250 μm Silica Gel 60 F254 plates and visualized by quenching of UV fluorescence (λmax = 254 nm), or by staining ceric ammonium molybdate. 1H and 13C NMR spectra were recorded on a Varian Inova-500 or Inova-400. Chemical shifts for 1H and 13C NMR spectra are reported in ppm (δ) relative to the 1H and 13C signals in the solvent (CDCl3: 7.26, 77.00 ppm; C6D6: δ 7.16, 128.06 ppm; CD3CN: δ 1.94 ppm) and the multiplicities are presented as follows: s = singlet, d = doublet, t = triplet, q = quartet, hept = heptet, m = multiplet. Mass spectra were acquired on an Agilent 1200 LC-MS or VG 70-VSE. Data collection on 70-VSE (purchased in part with a grant from the Division of Research Resources, National Institutes of Health RR 04648) was serviced by the Mass Spectrometry Laboratory at the University of Illinois at Urbana-Champaign.

2. General Procedures

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\begin{align*}
\text{H}^+ & \text{N}^+ \text{PMP} & 5 \text{ mol\% 3a,} \\
& 1.5 \text{ equiv TBHP,} & 1.2 \text{ equiv TMSCN} \\
& \text{CH3CN (0.2 M),} & 23 \text{ °C,} 24 \text{ h} \\
\text{H}^+ & \text{N}^+ \text{PMP}
\end{align*}
\]

PMP-protected amine (0.2 mmol) and vanadium catalyst 3a (0.01 mmol, 2.6 mg) were loaded in a reaction vial. Acetonitrile (1 mL) followed by TMSCN (0.24 mmol, 30 uL) were syringed into the mixture. Afterwards, TBHP (0.3 mmol, 44 uL) were added dropwise to the reaction which was then stirred at rt for 24 h or until the starting material had been consumed as determined by TLC. All volatiles were evaporated and the residue was purified by preparative TLC to give the α-aminonitrile product.
3. Compound Characterization

 Compound 2: 61% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.76 (s, 4H), 5.33 (s, 1H), 6.74-6.76 (m, 2H), 6.83-6.85 (m, 2H), 7.41-7.46 (m, 3H), 7.59 (dd, $J$ = 1.6, 7.2 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 51.6, 55.6, 115.0, 116.3, 118.4, 127.2, 129.2, 129.4, 134.1, 138.5, 154.1.

 Compound 4: 63% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.75 (s, 3H), 3.82 (s, 3H), 5.26 (s, 1H), 6.73-6.75 (m, 2H), 6.82-6.84 (m, 2H), 6.92-6.95 (m, 2H), 7.46-7.50 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 51.0, 55.4, 55.6, 114.5, 115.0, 116.2, 118.7, 126.2, 128.6, 138.6, 154.0, 160.3.

 Compound 5: 52% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 2.37 (s, 3H), 3.73 (s, 1H), 3.76 (s, 3H), 5.29 (d, $J$ = 6.4 Hz, 1H), 6.73-6.76 (m, 2H), 6.82-6.84 (m, 2H), 7.24 (d, $J$ = 8.0 Hz, 2H), 7.46 (d, $J$ = 8.0 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 21.2, 51.3, 55.6, 115.0, 116.2, 118.6, 127.1, 129.9, 131.2, 138.6, 139.4, 154.0.

 Compound 6: 30% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.76 (s, 3H), 3.82 (d, $J$ = 9.2 Hz, 1H), 5.41 (d, $J$ = 9.2 Hz, 1H), 6.73-6.76 (m, 2H), 6.82-6.85 (m, 2H), 7.69-7.75 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 51.3, 55.6, 115.0, 116.7, 117.8, 126.2 (q, $J_{C,F}$ = 3.8 Hz), 127.6, 131.7 (q, $J_{C,F}$ = 32.6 Hz), 138.0, 154.5.

 Compound 7: 45% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.76 (s, 4H), 5.31 (d, $J$ = 8.4 Hz, 1H), 6.73-6.75 (m, 2H), 6.82-6.85 (m, 2H), 7.10-7.14 (m, 2H), 7.56-7.59 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 51.0, 55.6, 115.0, 116.2 (d, $J_{C,F}$ = 21.9 Hz), 116.5, 118.2, 129.1 (d, $J_{C,F}$ = 8.5 Hz), 130.0 (d, $J_{C,F}$ = 3.4 Hz), 138.3, 154.3, 163.2 (d, $J_{C,F}$ = 247.9 Hz).

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1 Xie, Z.; Li, G.; Zhao, G.; Wang, J. Synthesis 2009, 2035.
Compound 8: 37% yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 3.75 (s, 4H), 5.61 (s, 1H), 6.77-6.80 (m, 2H), 6.82-6.85 (m, 2H), 7.36-7.38 (m, 2H), 7.45-7.47 (m, 1H), 7.69-7.71 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 49.6, 55.6, 115.0, 116.8, 118.0, 127.7, 129.0, 130.4, 130.9, 131.9, 133.5, 138.3, 154.4. HRMS (EI): m/z calcd for C$_{13}$H$_{13}$N$_2$OCl: 272.0716; found: 272.0710.

 Compound 9: 47% yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 3.76 (s, 3H), 3.80 (d, $J = 8.8$ Hz, 1H), 5.32 (d, $J = 8.8$ Hz, 1H), 6.72-6.75 (m, 2H), 6.81-6.84 (m, 2H), 7.31 (dd, $J = 8.0$, 8.0 Hz, 1H), 7.52-7.56 (m, 2H), 7.76 (dd, $J = 1.6$, 1.6 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 51.0, 55.6, 115.0, 116.6, 117.9, 123.2, 125.8, 130.3, 130.7, 132.6, 136.2, 138.1, 154.4. HRMS (EI): m/z calcd for C$_{15}$H$_{13}$N$_2$OBr: 316.0211; found: 316.0212.

 Compound 10: 58% yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 3.76 (s, 3H), 3.86 (s, 1H), 5.49 (s, 1H), 6.77-6.80 (m, 2H), 6.83-6.86 (m, 2H), 7.53-7.56 (m, 2H), 7.61 (dd, $J = 2.0$, 8.4 Hz, 1H), 7.85-7.92 (m, 3H), 8.10 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 51.8, 55.6, 115.0, 116.4, 118.4, 124.5, 126.5, 126.9, 127.1, 127.8, 128.2, 129.3, 131.4, 133.1, 133.4, 138.6, 154.2.

 Compound 11: 30% yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 3.76 (s, 3H), 3.91 (d, $J = 9.6$ Hz, 1H), 5.53 (d, $J = 9.6$ Hz, 1H), 6.76-6.79 (m, 2H), 6.83-6.86 (m, 2H), 7.03 (dd, $J = 3.6$, 5.2 Hz, 1H), 7.34 (ddd, $J = 1.2$, 1.2, 3.6 Hz, 1H), 7.37 (dd, $J = 1.2$, 5.2 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 47.8, 55.6, 115.0, 117.0, 117.7, 126.9, 127.0, 127.1, 137.1, 137.9, 154.5. HRMS (EI): m/z calcd for C$_{13}$H$_{12}$N$_2$O$_2$: 244.0670; found: 244.0665.

 Compound 12: 41% yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 1.33-1.38 (m, 1H), 1.45 (s, 9H), 1.88-2.00 (m, 3H), 2.60-2.80 (m, 2H), 3.48 (d, $J = 10.8$ Hz, 1H), 3.74 (s, 3H), 3.95 (dd, $J = 6.8$, 10.0 Hz, 1H), 4.15-4.25 (m, 2H), 6.66-6.71 (m, 2H), 6.79-6.84 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 28.4, 39.6, 52.8, 55.6, 79.8, 115.0, 116.5, 118.6, 138.6, 154.1, 154.6. HRMS (EI): m/z calcd for C$_{10}$H$_{27}$N$_3$O$_3$: 345.2052; found: 345.2056.
Compound 13: 64% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.19-1.31 (m, 5H), 1.70-1.73 (m, 1H), 1.80-1.83 (m, 3H), 1.93-1.96 (m, 2H), 3.48 (s, 1H), 3.75 (s, 3H), 3.92-3.96 (m, 1H), 6.67-6.70 (m, 2H), 6.79-6.82 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 25.5, 25.6, 25.9, 28.9, 29.7, 40.8, 53.3, 55.6, 115.0, 116.1, 119.1, 139.0, 153.9.

Compound 14: 70% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 0.87 (t, $J = 2.8$ Hz, 3H), 1.27-1.33 (m, 8H), 1.55-1.60 (m, 2H), 1.87-1.94 (m, 2H), 3.44 (d, $J = 9.2$ Hz, 1H), 3.75 (s, 3H), 6.67-6.70 (m, 2H), 6.81-6.83 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 14.0, 22.6, 25.6, 28.9, 29.0, 31.6, 33.6, 47.4, 55.6, 115.0, 116.1, 119.9, 138.8, 153.9. HRMS (EI): m/z calcd for C$_{16}$H$_{24}$N$_2$O: 260.1889; found: 260.1890.

Compound 15: Amine (0.6 mmol, 171 mg), iodoanisole (0.5 mmol, 117 mg), CuI (0.1 mmol, 19 mg), L-proline (0.2 mmol, 21 mg), and Cs$_2$CO$_3$ (1.0 mmol, 326 mg) were loaded in a dry via, which was then evacuated and flushed with N$_2$ for 3 times. DMSO (3 mL) was syringed into the vial. The reaction was stirred at 90 °C for 24 h until most of the starting material was consumed monitored by TLC. The reaction was cooled down to room temperature, and quenched with 5 mL H$_2$O. The reaction was extracted with 3×100 mL EtOAc. The organic layer was combined and washed with 3×50 mL H$_2$O and 50 mL brine. After drying with anhydrous Na$_2$SO$_4$ and concentration, the residue was purified by column chromatography (EtOAc/hexanes 1:4 and then CH$_2$Cl$_2$/hexanes 1:1) to give product 97 mg (50% yield) as yellow oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.00 (s, 3H), 1.22 (d, $J = 6.8$ Hz, 6H), 1.23 (s, 3H), 1.36-1.46 (m, 3H), 1.60-1.85 (m, 5H), 2.30 (dt, $J = 2.8$, 12.4 Hz, 1H), 2.76-2.93 (m, 4H), 3.00 (d, $J = 12.4$ Hz, 1H), 3.74 (s, 3H), 6.54-6.59 (m, 2H), 6.74-6.79 (m, 2H), 6.89 (d, $J = 1.6$ Hz, 1H), 7.00 (dd, $J = 1.6$, 8.4 Hz, 1H), 7.19 (d, $J = 8.4$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 18.7, 18.8, 19.3, 24.0, 25.3, 30.1, 33.4, 36.3, 37.4, 37.5, 38.4, 45.3, 55.9, 56.1, 113.8, 114.9, 123.9, 124.2, 126.8, 134.7, 143.4, 145.6, 147.3, 151.7. MS (ESI)$^+$ calcd for C$_{27}$H$_{36}$NO (M+H)$^+$ 392.3, found 392.3.

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Compound 16: 61% yield, 2:1 isomers. $^1$H NMR (400 MHz, CDCl$_3$) δ 1.19 (s, 3H, major), 1.20 (d, $J = 7.2$ Hz, 3H, minor), 1.22 (d, $J = 7.2$ Hz, 6H, major), 1.24 (s, 1.5H, minor), 1.26 (s, 1.5H, minor), 1.27 (s, 3H, major), 1.40-1.60 (m, 4.5H, major and minor), 1.75-1.90 (m, 6H, major and minor), 1.96-2.01 (m, 1H, major), 2.03-2.08 (m, 0.5H, minor), 2.30-2.37 (m, 1.5H, major and minor), 2.67-3.05 (m, 4.5H, major and minor), 3.40 (d, $J = 11.2$ Hz, 0.5H, minor), 3.45 (d, $J = 11.2$ Hz, 1H, major), 3.75 (s, 1.5H, minor), 3.76 (s, 3H, major), 4.13 (d, $J = 11.2$ Hz, 1H, major), 4.21 (d, $J = 11.2$ Hz, 0.5H, minor), 6.66-6.71 (m, 1H, minor), 6.72-6.76 (m, 2H, major), 6.78-6.86 (m, 3H, major and minor), 6.87-6.90 (m, 1.5H, major and minor), 6.97-7.03 (m, 1.5H, major and minor), 7.15-7.19 (m, 1.5H, major and minor); $^{13}$C NMR (100 MHz, CDCl$_3$) (major) δ 17.0, 18.4, 19.2, 23.9, 24.0, 25.2, 30.1, 33.0, 33.5, 37.7, 37.8, 40.6, 46.1, 55.7, 58.5, 115.0, 117.0, 119.0, 124.1, 124.4, 126.8, 134.2, 139.6, 145.9, 146.3, 154.2; (minor) δ 18.4, 18.8, 19.2, 23.9, 24.0, 25.3, 29.7, 32.8, 33.4, 37.6, 38.1, 40.3, 42.5, 55.6, 57.1, 115.0, 116.5, 119.6, 124.0, 124.1, 126.8, 134.4, 139.0, 145.9, 146.8, 154.0. HRMS (EI): m/z calcd for C$_{28}$H$_{36}$N$_2$O: 416.2828; found: 416.2828.