

Supporting Information

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

Chen Zhu, Ji-Bao Xia and Chuo Chen*

*Division of Chemistry, Department of Biochemistry, The University of Texas Southwestern
Medical Center, Dallas, USA*

Email: Chuo.Chen@UTSouthwestern.edu

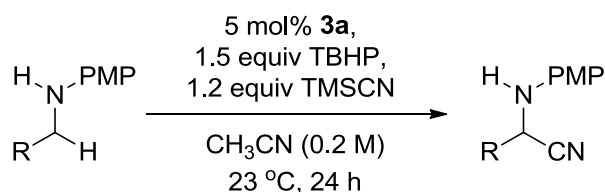
Table of Contents

1. General Information	S2
2. General Procedures	S2
3. Compound Characterization	S3-S6
4. ^1H and ^{13}C Spectra	S7-S20

1. General Information

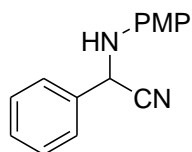
All reactions were performed in glassware without argon protection. Commercially available reagents were used without further purification. Organic solutions were concentrated by rotary evaporator at ca. 30 mmHg. Flash column chromatography was performed as described by Still (Still, W. C.; Kahn, M.; 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 ($\lambda_{\text{max}} = 254 \text{ nm}$), or by staining ceric ammonium molybdate. ^1H and ^{13}C NMR spectra were recorded on a Varian Inova-500 or Inova-400. Chemical shifts for ^1H and ^{13}C NMR spectra are reported in ppm (δ) relative to the ^1H and ^{13}C signals in the solvent (CDCl_3 : 7.26, 77.00 ppm; C_6D_6 : δ 7.16, 128.06 ppm; CD_3CN : 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

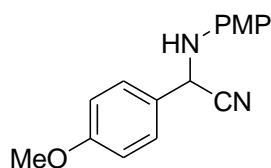


PMP-protected amine (0.2 mmol) and vanadium catalyst **3a** (0.01 mmol, 2.6 mg) were loaded in a reaction vial. Acetonitrile (1 mL) followed by TMSCN (0.24 mmol, 30 μL) were syringed into the mixture. Afterwards, TBHP (0.3 mmol, 44 μL) were added dropwise to the reaction which was then stirred at rt 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.

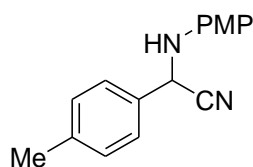
3. Compound Characterization



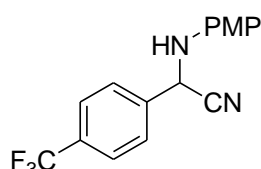
Compound **2**:¹ 61% yield. ¹H NMR (400 MHz, CDCl₃) δ 3.76 (s, 4H), 5.33 (s, 1H), 6.74-6.76 (m, 2H), 6.83-6.85 (m, 2H), 7.41-7.46 (m, 3H), 7.59 (dd, *J* = 1.6, 7.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 51.6, 55.6, 115.0, 116.3, 118.4, 127.2, 129.2, 129.4, 134.1, 138.5, 154.1.



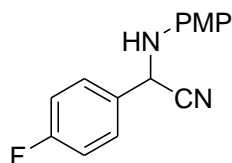
Compound **4**:¹ 63% yield. ¹H NMR (400 MHz, CDCl₃) δ 3.75 (s, 3H), 3.82 (s, 3H), 5.26 (s, 1H), 6.73-6.75 (m, 2H), 6.82-6.84 (m, 2H), 6.92-6.95 (m, 2H), 7.46-7.50 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 51.0, 55.4, 55.6, 114.5, 115.0, 116.2, 118.7, 126.2, 128.6, 138.6, 154.0, 160.3.



Compound **5**:² 52% yield. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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**:³ 30% yield. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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.



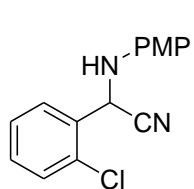
Compound **7**:⁴ 45% yield. ¹H NMR (400 MHz, CDCl₃) δ 3.76 (s, 4H), 5.31 (d, *J* = 8.4 Hz, 1H), 6.73-6.75 (m, 2H), 6.82-6.85 (m, 2H), 7.10-7.14 (m, 2H), 7.56-7.59 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 51.0, 55.6, 115.0, 116.2 (d, *J*_{C-F} = 21.9 Hz), 116.5, 118.2, 129.1 (d, *J*_{C-F} = 8.5 Hz), 130.0 (d, *J*_{C-F} = 3.4 Hz), 138.3, 154.3, 163.2 (d, *J*_{C-F} = 247.9 Hz).

¹ Xie, Z.; Li, G.; Zhao, G.; Wang, J. *Synthesis* **2009**, 2035.

² Pan, F.; Chen, J.-M.; Qin, T.-Y.; Zhang, S. X.-A.; Liao, W.-W. *Eur. J. Org. Chem.* **2012**, 5324.

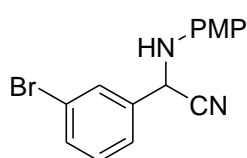
³ Seayad, A. M.; Ramalingam, B.; Yoshinaga, K.; Nagata, T.; Chai, C. L. L. *Org. Lett.* **2010**, *12*, 264.

⁴ Csongar, Ch.; Mueller, I.; Slezak, H.; Klebsch, H.-J.; Tomaschewski, G. *J. Prakt. Chem.* **1988**, *330*, 1006.



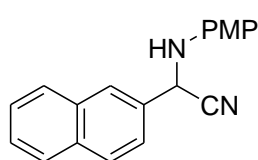
Compound **8**: 37% yield. ^1H NMR (400 MHz, CDCl_3) δ 3.75 (s, 4H), 5.61 (s, 1H), 6.77-6.80 (m, 2H), 6.82-6.85 (m, 2H), 7.36-7.38 (m, 2H), 7.45-7.47 (m, 1H), 7.69-7.71 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 49.6, 55.6, 115.0, 116.8, 118.0, 127.7, 129.0, 130.4, 130.9, 131.9, 133.5, 138.3, 154.4. HRMS

(EI): m/z calcd for $\text{C}_{15}\text{H}_{13}\text{N}_2\text{OCl}$: 272.0716; found: 272.0710.



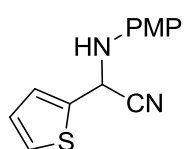
Compound **9**: 47% yield. ^1H NMR (400 MHz, CDCl_3) δ 3.76 (s, 3H), 3.80 (d, $J = 8.8$ Hz, 1H), 5.32 (d, $J = 8.8$ Hz, 1H), 6.72-6.75 (m, 2H), 6.81-6.84 (m, 2H), 7.31 (dd, $J = 8.0, 8.0$ Hz, 1H), 7.52-7.56 (m, 2H),

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 $\text{C}_{15}\text{H}_{13}\text{N}_2\text{OBr}$: 316.0211; found: 316.0212.



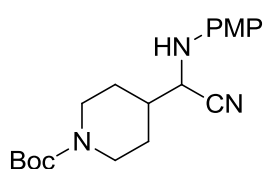
Compound **10**: 58% yield. ^1H NMR (400 MHz, CDCl_3) δ 3.76 (s, 3H), 3.86 (s, 1H), 5.49 (s, 1H), 6.77-6.80 (m, 2H), 6.83-6.86 (m, 2H), 7.53-7.56 (m, 2H), 7.61 (dd, $J = 2.0, 8.4$ Hz, 1H), 7.85-7.92 (m, 3H), 8.10 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 51.8, 55.6, 115.0, 116.4, 118.4,

124.5, 126.5, 126.9, 127.1, 127.8, 128.2, 129.3, 131.4, 133.1, 133.4, 138.6, 154.2.



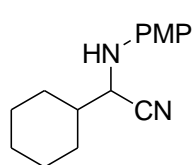
Compound **11**: 30% yield. ^1H NMR (400 MHz, CDCl_3) δ 3.76 (s, 3H), 3.91 (d, $J = 9.6$ Hz, 1H), 5.53 (d, $J = 9.6$ Hz, 1H), 6.76-6.79 (m, 2H), 6.83-6.86 (m, 2H), 7.03 (dd, $J = 3.6, 5.2$ Hz, 1H), 7.34 (ddd, $J = 1.2, 1.2, 3.6$ Hz, 1H),

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 $\text{C}_{13}\text{H}_{12}\text{N}_2\text{OS}$: 244.0670; found: 244.0665.

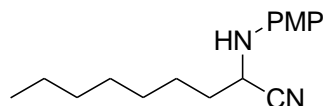


Compound **12**: 41% yield. ^1H NMR (400 MHz, CDCl_3) δ 1.33-1.38 (m, 1H), 1.45 (s, 9H), 1.88-2.00 (m, 3H), 2.60-2.80 (m, 2H), 3.48 (d, $J = 10.8$ Hz, 1H), 3.74 (s, 3H), 3.95 (dd, $J = 6.8, 10.0$ Hz, 1H), 4.15-4.25 (m, 2H), 6.66-6.71 (m, 2H), 6.79-6.84 (m, 2H); ^{13}C NMR (100 MHz,

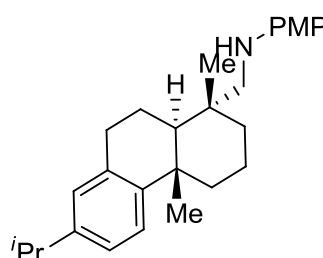
CDCl_3) δ 28.4, 39.6, 52.8, 55.6, 79.8, 115.0, 116.5, 118.6, 138.6, 154.1, 154.6. HRMS (EI): m/z calcd for $\text{C}_{19}\text{H}_{27}\text{N}_3\text{O}_3$: 345.2052; found: 345.2056.



Compound **13**:⁵ 64% yield. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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.

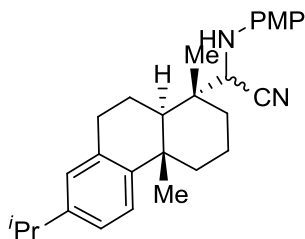


Compound **14**: 70% yield. ¹H NMR (400 MHz, CDCl₃) δ 0.87 (t, *J* = 2.8 Hz, 3H), 1.27-1.33 (m, 8H), 1.55-1.60 (m, 2H), 1.87-1.94 (m, 2H), 3.44 (d, *J* = 9.2 Hz, 1H), 3.75 (s, 3H), 4.06-4.12 (m, 1H), 6.67-6.70 (m, 2H), 6.81-6.83 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 14.0, 22.6, 25.6, 28.9, 29.0, 31.6, 33.6, 47.4, 55.6, 115.0, 116.1, 119.9, 138.8, 153.9. HRMS (EI): *m/z* calcd for C₁₆H₂₄N₂O: 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 Cs₂CO₃ (1.0 mmol, 326 mg) were loaded in a dry vial, which was then evacuated and flushed with N₂ 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 H₂O. The reaction was extracted with 3×100 mL EtOAc. The organic layer was combined and washed with 3×50 mL H₂O and 50 mL brine. After drying with anhydrous Na₂SO₄ and concentration, the residue was purified by column chromatography (EtOAc/hexanes 1:4 and then CH₂Cl₂/hexanes 1:1) to give product 97 mg (50% yield) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 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); ¹³C NMR (100 MHz, CDCl₃) δ 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 C₂₇H₃₈NO (M+H)⁺ 392.3, found 392.3.

⁵ Sonobe, T.; Oisaki, K.; Kanai, M. *Chem. Sci.* **2012**, *3*, 3249.



Compound **16**: 61% yield, 2:1 isomers. ^1H 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 $\text{C}_{28}\text{H}_{36}\text{N}_2\text{O}$: 416.2828; found: 416.2828.

