Supporting Information

**Palladium-Catalyzed Dehydration of Amides to Nitriles**

Wandi Zhang, † Christopher W. Haskins, ‡ Yang Yang, and Mingji Dai*

Department of Chemistry and Center for Cancer Research, Purdue University, 560 Oval Drive, West Lafayette, IN 47907, United States
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Part 1. Experimental Procedure and Analytical Data

General Methods: NMR spectra were recorded on ($^1$H at 400 MHz, 500 MHz and $^{13}$C at 100 MHz, 125 MHz) spectrometers. Chemical shifts (δ) were given in ppm with reference to solvent signals ($^1$H NMR: CHCl$_3$ (7.26); $^{13}$C NMR: CDCl$_3$ (77.2)). Column chromatography was performed on silica gel. All reactions sensitive to air or moisture were carried out under argon or nitrogen atmosphere in dry and freshly distilled solvents under anhydrous conditions, unless otherwise noted. Anhydrous MeCN was distilled over calcium hydride under N$_2$. All other solvents and reagents were used as obtained from commercial sources without further purification.

General Procedure for the Synthesis of Amides

I. General Procedure for the Synthesis of Amides 1a, 1c-e.

\[ \text{LDA, PhNTf}_2, \text{THF} \xrightarrow{\text{S1}} \text{OTf} \xrightarrow{\text{Pd(PPh}_3)_2\text{Cl}_2, \text{TEA, acrylamide, DMF}} \text{NH}_2 \]

To a stirred solution of diisopropyl amine (1.1 equiv) in THF cooled to 0 °C was added n-butyllithium (1.1 equiv). The mixture was stirred at -78 °C for 30 min before ketone S1 (1.0 equiv) was added dropwise as a solution of THF to the LDA solution. The mixture was stirred at -78 °C for 1 hour. N-Phenyl-bis(trifluoromethanesulfonimide) (1.05 equiv) was added at -78 °C. The mixture was warmed to 0 °C and stirred for 2 h. The reaction was quenched with H$_2$O and extracted with Et$_2$O. The organic layers were washed with 1M aqueous NaOH, dried over MgSO$_4$, filtered and concentrated. The crude product was concentrated and purified by flash chromatography to yield the corresponding triflate S2. To a stirring solution of Pd(PPh)$_3$Cl$_2$ (0.1 equiv) in DMF, a solution of vinyl triflate S2 (1.0 equiv), triethylamine (3.4 equiv), and acrylamide (1.8 equiv) in DMF was added dropwise. The mixture was heated to 75 °C for 5 h. The mixture was diluted with H$_2$O and extracted using Et$_2$O and CH$_2$Cl$_2$. The organic layers were washed with brine and dried over Na$_2$SO$_4$. The crude product was concentrated and recrystallized using Hex:EtOAc (4:1) to yield amide 1a, 1e-e.

II. General Procedure for the Synthesis of Amides 1f and 1m.

\[ \text{S3} \xrightarrow{\text{Pd(PPh}_3)_2\text{Cl}_2, \text{TEA, acrylamide, DMF}} \text{NH}_2 \]

To a stirring solution of Pd(PPh)$_3$Cl$_2$ (0.1 equiv) in DMF, a solution of the corresponding iodide S3 (1.0 equiv), triethylamine (3.4 equiv), and acrylamide (1.8 equiv) in DMF was added dropwise.
The mixture was heated to 75 °C for 5 h. The mixture was diluted with H₂O and extracted with Et₂O and CH₂Cl₂. The organic layers were washed with brine and dried over Na₂SO₄. The crude product was concentrated and recrystallized using Hex:EtOAc (4:1) to yield amides 1f and 1m.

VI. General Procedure for the Synthesis of Other Amides

\[
\begin{array}{c}
\text{O} \\
\text{R} \\
\text{OH} \\
\text{i}) \text{SOCl}_2 \\
\text{OH} \\
\text{R} \\
\text{NH}_2 \\
\text{ii}) \text{NH}_2\text{OH, THF} \\
\end{array}
\]

To corresponding carboxylic acid S4 (3.0 mmol), an excess of SOCl₂ (5 mL) was added to the reaction flask. The solution was then refluxed for several hours (1-5 h) or until solution was no longer fuming. The excess SOCl₂ was removed under vacuum. The crude product was dissolved in 5 mL of THF and cooled to 0 °C. An excess amount of NH₄OH (28-30% NH₃, 15 mL) was added to the solution slowly. The solution was allowed to stir for 0.5 h after addition at 0 °C. The solution was extracted using (1x10 mL) THF and (3x10 mL) EtOAc. The product was dried over anhydrous Na₂SO₄ or MgSO₄, filtered and concentrated to give the desired amides 1g-i, and 4a-j.

Compounds 1b₁, 1j₂, 1k₂, and 1i² were synthesized according to the literature route.

**General Procedure for the Dehydration of Amides and Analytical Data**

**General Procedure A for the Dehydration of Amides**

A mixture of amide (50 mg), PdCl₂ (0.1 equiv), AgOAc (3.0 equiv), and LiCl (2.0 equiv) in MeCN (2.5 mL) in a 2 dram vial were heated at 80 °C for 24 h or until the starting material was consumed. The palladium catalyst was filtered off through a plug of celite and washed with EtOAc. The crude solution was concentrated and purified via column chromatography (Hex/EtOAc = 10/1).

**General Procedure B for Dehydration of Amides**

A mixture of amide (50 mg), Pd(PPh₃)₂Cl₂ (0.1 equiv), Cu(OAc)₂ (3.0 equiv) in MeCN (2.5 mL) in a 2 dram vial were heated at 80 °C for 24 hours or until the starting material was consumed. The palladium catalyst was filtered off through a plug of celite and washed with EtOAc. The crude solution was concentrated and purified via column chromatography (Hex/EtOAc = 10/1).

\[
\text{Ph} \\
\text{3a (96%)} \\
\text{N} \\
\]

3a was prepared using general procedure A; 96% yield. ¹H NMR (400 MHz, CDCl₃): δ = 7.33 (t, J = 7.2 Hz, 2H), 7.26-7.22 (m, 3H), 7.06 (d, J = 16.4 Hz, 1H), 6.25 (s, 1H), 5.23 (d, J = 16.4 Hz,
3b was prepared using general procedure A; 69% yield. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.46$ (dd, $J = 6.4$, 2.0 Hz, 1H), 7.40-7.34 (m, 3H), 7.15 (dd, $J = 15.6$, 12.0 Hz, 1H), 6.91-6.78 (m, 2H), 5.44 (d, $J = 16.0$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 150.4$, 141.5, 135.4, 129.8, 129.0, 127.5, 125.5, 118.4, 98.4. Our spectra are consistent with literature report.$^3$

3c was prepared using general procedure A; 82%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.34$-7.30 (m, 2H), 7.26-7.24 (m, 1H), 7.18-7.16 (m, 1H), 6.96 (d, $J = 16.8$ Hz, 1H), 6.17 (t, $J = 4.0$ Hz, 1H), 5.34 (d, $J = 16.4$ Hz, 1H), 2.87 (dd, $J = 13.2$, 2.8 Hz, 1H), 2.57-2.48 (m, 2H), 1.78-1.60 (m, 3H), 1.43 (tt, $J = 13.6$, 4.0 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta = 153.1$, 140.5, 140.4, 138.4, 129.0, 128.6, 126.4, 119.0, 92.7, 38.6, 34.3, 26.6, 24.3, 16.6; IR (film): 2936, 2215, 1622, 1599, 1266, 968 cm$^{-1}$; MS (ESI): m/z 246.0 [M+Na]$^+$. 

3d was prepared using general procedure A; 49%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.00$ (d, $J = 16.0$ Hz, 1H), 5.99 (t, $J = 4.4$ Hz, 1H), 5.20 (d, $J = 16.4$ Hz, 1H), 3.57 (d, $J = 11.2$ Hz, 2H), 2.56 (s, 2H), 2.22-2.20 (m, 2H), 2.03 (t, $J = 6.4$ Hz, 2H), 1.03 (s, 3H), 0.93 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 152.4$, 135.6, 134.1, 118.1, 96.6, 93.8, 70.5, 35.9, 30.3, 26.9, 22.8, 22.6, 21.9; IR (film): 2959, 2217, 1633, 1266, 1039, 968 cm$^{-1}$; MS (ESI): m/z 256.1 [M+Na]$^+$. 

3e was prepared using general procedure A; 51%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 6.93$ (dd, $J = 16.8$, 1.2 Hz, 1H), 6.42 (d, $J = 3.2$ Hz, 1H), 5.46 (dd, $J = 16.4$, 1.2 Hz, 1H), 2.41 (t, $J = 3.6$ Hz, 1H), 1.96-1.90 (m, 1H), 1.64-1.59 (m, 1H), 1.14 (s, 3H), 1.09-0.95 (m, 2H), 0.08 (s, 3H), 0.76 (s,
13C NMR (100 MHz, CDCl3): δ = 146.2, 145.5, 142.8, 119.2, 94.0, 57.6, 54.2, 52.3, 31.4, 25.0, 19.5, 19.3, 12.6; IR (film): 2959, 2214, 1606, 1265, 966, 910 cm⁻¹; MS (ESI): m/z 210.1 [M+Na]⁺.

3f was prepared using general procedure A; 59%. 1H NMR (500 MHz, CDCl3): δ = 7.28 (d, J = 16.5 Hz, 1H), 6.93-6.92 (m, 2H), 6.82 (dd, J = 7.0, 1.0 Hz, 1H), 6.02 (s, 2H), 5.67 (d, J = 16.5 Hz, 1H); 13C NMR (100 MHz, CDCl3): δ = 150.5, 150.1, 148.7, 128.1, 124.2, 118.6, 108.8, 105.7, 101.9, 94.0. Our spectra are consistent with literature report.⁴

3g was prepared using general procedure A; 80%. 1H NMR (400 MHz, CDCl3): δ = 8.28 (d, J = 8.8 Hz, 2H), 7.63 (dd, J = 6.8, 2.0 Hz, 2H), 7.47 (d, J = 16.8 Hz, 1H) 6.05 (d, J = 16.8 Hz, 1H); 13C NMR (100 MHz, CDCl3): δ = 149.2, 147.9, 139.3, 128.3, 124.5, 117.1, 101.2. Our spectra are consistent with literature report.⁵

3h was prepared using general procedure A; 87%. 1H NMR (500 MHz, CDCl3): δ = 7.29 (d, J = 16.5 Hz, 1H), 6.64 (s, 2H), 5.78 (d, J = 16.5 Hz, 1H), 3.86 (s, 9H); 13C NMR (100 MHz, CDCl3): δ = 153.7, 150.5, 141.0, 129.1, 118.3, 104.8, 95.5, 61.1, 56.3. Our spectra are consistent with literature report.⁶

3i was prepared using general procedure A; 78%. 1H NMR (400 MHz, CDCl3): δ = 7.45-7.37(m, 3H), 7.34 (d, J = 1.7 Hz, 1H), 7.32 (s, 1H), 7.22 (s, 1H), 2.15 (d, J = 1.6 Hz, 3H); 13C NMR (100 MHz, CDCl3): δ = 144.3, 134.0, 129.2, 129.2, 128.6, 121.2, 109.6, 16.7. Our spectra are consistent with literature report.⁷
3j was prepared using general procedure A; 59%. $^1$H NMR (400 MHz, CDCl$_3$): δ = 7.74 (s, 1H), 7.70 (d, $J = 7.89$ Hz, 1H), 7.35 (d, $J = 7.80$ Hz, 1H), 7.21 (d, $J = 6.10$, 1H), 7.1 (t, $J = 7.83$, 1H), 5.8 (d, $J = 16.6$, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 148.7, 139.8, 135.9, 135.4, 130.6, 126.4, 117.5, 97.79, 94.71; IR(film): 2957, 2931, 2220, 1620, 1560, 1409 cm$^{-1}$; MS (ESI): $m/z$ 277.9 [M+Na]$^+$. 

3k was prepared using general procedure A; 60%. $^1$H NMR (400 MHz, CDCl$_3$): δ = 7.60 (t, $J = 1.8$ Hz, 1H), 7.57 (d, $J = 7.93$ Hz, 1H), 7.38-7.27 (m, 3H), 5.89 (d, $J = 16.7$, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 149.0, 135.6, 134.1, 130.7, 130.2, 126.1, 123.4, 117.7, 98.2. Our spectra are consistent with literature report. 

3l was prepared using general procedure A; 56%. $^1$H NMR (400 MHz, CDCl$_3$): δ = 7.55 (d, $J = 17.0$, 1H), 7.38 (d, $J = 8.1$ Hz, 2H), 7.24 (t, $J = 8.4$ Hz, 1H), 6.19 (d, $J = 17.0$, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 144.3, 134.9, 130.9, 130.6, 129.2, 117.3, 105.9. Our spectra are consistent with literature report.

3m was prepared using general procedure A; 91%. $^1$H NMR (500 MHz, CDCl$_3$): δ = 7.46-7.38 (m, 6H), 5.88 (d, $J = 17.0$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 150.7, 133.6, 131.3, 129.2, 127.4, 118.3, 96.4. Our spectra are consistent with literature report.

5a was prepared using general procedure B; 87%. $^1$H NMR (400 MHz, CDCl$_3$): δ = 7.36 (t, $J = 8.48$ Hz, 1H), 7.23(t, $J = 10.57$ Hz, 1H), 7.12 (br s, 2H), 3.82 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 159.5, 130.2,124.4, 119.2, 118.6, 116.7, 113.1, 55.4. Our spectra are consistent with
5b was prepared using general procedure B; 83%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.14$-$7.04$ (m, 3H), 4.00 (s, 3H), 3.88 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 152.6$, 151.6, 124.3, 116.9, 116.2, 106.9, 61.6, 56.0. Our spectra are consistent with literature report.\(^{11}\)

5c was prepared using general procedure B; 53%. $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 7.87$ (d, $J = 7.5$ Hz, 2H), 7.80-7.78 (m, 4H), 7.64 (t, $J = 7.5$ Hz, 1H), 7.51 (t, $J = 7.5$ Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta = 195.2$, 141.3, 136.4, 133.5, 132.3, 130.4, 130.2, 128.8, 118.1, 115.8. Our spectra are consistent with literature report.\(^{12}\)

5d was prepared using general procedure B; 77%. $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 8.26$ (d, $J = 2.0$ Hz, 1H), 7.78 (dd, $J = 3.0$, 2.0 Hz, 1H), 7.51 (d, $J = 8.0$ Hz, 1H), 2.68 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 149.4$, 139.1, 135.8, 134.1, 128.5, 116.7, 111.5. Our spectra are consistent with literature report.\(^{13}\)

5e was prepared using general procedure B; 77%. $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 8.02$ (d, $J = 8.5$ Hz, 1H), 7.68-7.65 (m, 2H), 2.62 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 151.6$, 136.6, 134.7, 130.8, 125.3, 117.0, 116.7, 20.0. Our spectra are consistent with literature report.\(^{14}\)

5f was prepared using general procedure B; 88%. $^1$H NMR (CDCl$_3$, 400 MHz) $\delta = 7.36$ (t, $J = 6.85$ Hz, 2H), 7.29 (m, 1H), 7.26 (d, $J = 6.91$ Hz, 2H), 2.97 (t, $J = 7.09$ Hz, 2H), 2.62 (t, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta = 138.0$, 128.8, 128.2, 127.1, 119.1, 31.5, 19.2. Our spectra are
consistent with literature report.\textsuperscript{15}

\textbf{5g} was prepared using general procedure B; 95%. \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 400 MHz) $\delta$ = 7.30 (t, $J$ = 7.17 Hz, 2H), 7.19 (m, 3H), 2.67 (t, $J$ = 7.23 Hz, 2H), 2.35 (t, $J$ = 7.09 Hz, 2H), 2.27 (s, 3H), 1.80 (m, 2H), 1.71 (m, 2H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 100 MHz) $\delta$ = 141.1, 128.4, 128.3, 126.0, 119.5, 34.9, 30.2, 24.7, 17.0. Our spectra are consistent with literature report.\textsuperscript{15}

\textbf{5h} was prepared using general procedure B; 93%. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): $\delta$ = 7.38-7.34 (m, 4H), 7.31-7.25 (m, 6H), 4.40 (t, $J$ = 9.5 Hz, 1H), 3.04 (d, $J$ = 9.5 Hz, 2H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): $\delta$ = 141.3, 129.0, 127.6, 127.5, 47.2, 24.3. Our spectra are consistent with literature report.\textsuperscript{16}

\textbf{5i} was prepared using general procedure B; 93%. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): $\delta$ = 3.09 (t, $J$ = 7.28 Hz, 2H), 2.68 (t, $J$ = 7.32 2H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): $\delta$ = 146.7, 144.2, 142.3, 139.8, 139.2, 136.7, 117.9, 111.2, 109.0, 19.1, 17.4; \textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}): -144.68, -155.95, -162.75; IR (film): 2252, 1522, 1502, 1040, 941, 876 cm\textsuperscript{-1}; MS (ESI): m/z 244.0 [M+Na]\textsuperscript{+}.

\textbf{5j} was prepared using general procedure B; 78%. \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): $\delta$ = 2.33 (t, $J$ = 7.0 Hz, 2H), 1.68-1.62 (m, 2H), 1.47-1.41 (m, 2H), 1.31-1.25 (m, 22H), 0.88 (t, $J$ = 7.0 Hz, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): $\delta$ = 120.0, 32.0, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 28.9, 28.8, 25.5, 22.8, 17.2, 14.2. Our spectra are consistent with literature report.\textsuperscript{17}
References


Part 2. X–Ray Structure of 6a

Figure S1. X–Ray Structure of 3a
Part 3. NMR Spectra of New Compounds

Figure S2. $^1$H NMR of 3a (400 MHz, CDCl$_3$)

Figure S3. $^{13}$C NMR of 3a (100 MHz, CDCl$_3$)
Figure S4. $^1$H NMR of 3c (400 MHz, CDCl$_3$)

Figure S5. $^{13}$C NMR of 3c (125 MHz, CDCl$_3$)
Figure S6. $^1$H NMR of 3d (400 MHz, CDCl$_3$)

Figure S7. $^{13}$C NMR of 3d (100 MHz, CDCl$_3$)
Figure S8. $^1$H NMR of 3e (400 MHz, CDCl$_3$)

Figure S9. $^{13}$C NMR of 3e (100 MHz, CDCl$_3$)
Figure S10. $^1$H NMR of 3j (400 MHz, CDCl$_3$)

Figure S11. $^{13}$C NMR of 3j (125 MHz, CDCl$_3$)
Figure S12. $^1$H NMR of 5i (400 MHz, CDCl$_3$)

Figure S13. $^{13}$C NMR of 5i (100 MHz, CDCl$_3$)