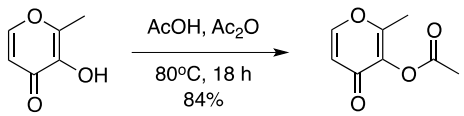
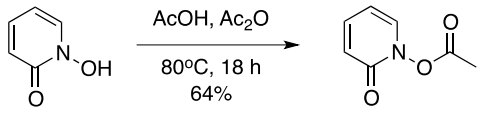
Synthesis



1

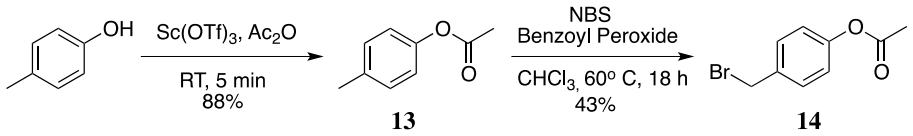
2-methyl-4-oxo-4*H*-pyran-3-yl acetate (1). 3-hydroxy-2-methyl-4*H*-pyran-4-one (maltol) (0.20 g, 1.6 mmol) was reacted with acetic anhydride (15 mL, 158.9 mmol) and glacial acetic acid (3 mL, 52.4 mmol). The reaction was held at 80°C for 18 h under nitrogen. The solution was concentrated and the resulting residue was dissolved in CH_2Cl_2 (20 mL) and washed with brine (2×20 mL). The organic layer was collected, dried over $MgSO_4$, and filtered. Co-evaporation with MeOH afforded **1** in 84% yield (0.23 g, 1.3 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 6.0 Hz, 1H), 6.41 (d, J = 6.0 Hz, 1H), 2.34 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 167.7, 159.3, 154.5, 138.8, 117.0, 20.5, 12.5. ESI-MS(+): *m/z* 168.95 $[M+H]^+$, 191.02 $[M+Na]^+$.



4

2-oxopyridin-1(2*H*)-yl acetate (4). 1-hydroxypyridin-2(1*H*)-one (1,2-HOPO) (0.20 g, 1.8 mmol) was reacted with acetic anhydride (15 mL, 158.9 mmol) and glacial acetic acid (3 mL, 52.4 mmol). The reaction was held at 80°C for 18 h under nitrogen. The solution was concentrated and the resulting residue was dissolved in CH_2Cl_2 (20 mL) and washed with brine (2×20 mL). The organic layer was collected, dried over $MgSO_4$, and filtered. Co-evaporation with MeOH afforded **4** in 64% yield (0.18 g, 1.2 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 5.6 Hz, 1H), 7.19 (d, J = 5.6 Hz, 1H), 2.36 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (100 MHz,

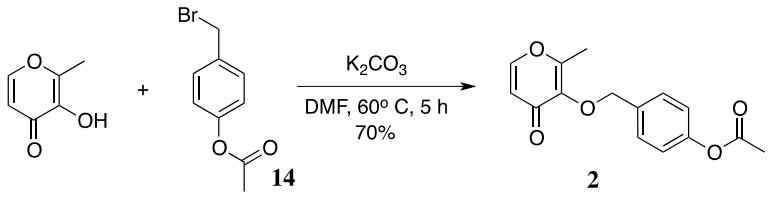
$CDCl_3$) δ 166.7, 146.4, 139.6, 135.4, 123.1, 105.3, 18.2. ESI-MS(+): *m/z* 153.89 $[M+H]^+$, 175.94 $[M+Na]^+$.



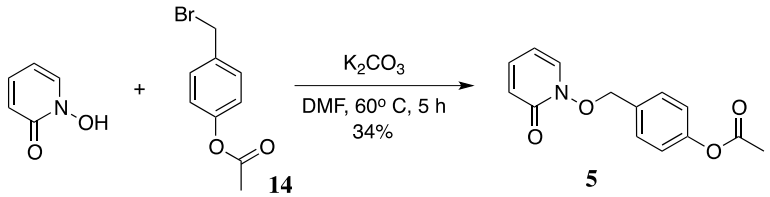
13 **14**

***p*-Tolyl acetate (13).** *p*-Cresol (1.50 g, 13.9 mmol) was dissolved in CH_2Cl_2 (140 mL) and acetic anhydride (4 mL, 41.6 mmol). To this was added scandium(III) triflate (0.13 g, 0.3 mmol) at room temperature and stirred for 5 min. The mixture was washed with a saturated $NaHCO_3$ solution (2×50 mL). The organic layer was collected, dried over $MgSO_4$, filtered and co-evaporated with MeOH to afford **5** in 88% yield (1.82 g, 12.2 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (d, J = 8.4 Hz, 2H), 6.98 (d, J = 8.4 Hz, 2H), 2.35 (s, 3H), 2.29 (s, 3H). ESI-MS(+): *m/z* 167.95 $[M+NH_4]^+$, 172.96 $[M+Na]^+$.

4-(bromomethyl)phenyl acetate (14). **13** (1.82 g, 12.1 mmol) was dissolved in $CHCl_3$ (50 mL) and reacted with *N*-bromosuccinimide (2.91 g, 16.4 mmol) and benzoyl peroxide (0.59 g, 2.4 mmol) in a flame dried vessel. The reaction was held at reflux under nitrogen gas for 18 h. The mixture was cooled to RT, concentrated, brought up in CH_2Cl_2 (50 mL) and washed with brine (2×50 mL). The organic layer was collected, dried over $MgSO_4$ and filtered. The resulting residue was purified via silica gel chromatography eluting 5% EtOAc in hexanes to afford **14** in 43% yield (1.20 g, 5.2 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 7.2 Hz, 2H), 7.07 (d, J = 7.2 Hz, 2H), 4.46 (s, 2H), 2.28 (s, 3H). ESI-MS(+): *m/z* 245.93 $[M+NH_4]^+$, 250.91 $[M+Na]^+$.



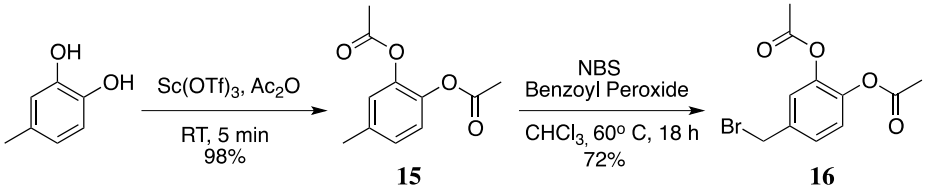
4-(((2-methyl-4-oxo-4*H*-pyran-3-yl)oxy)methyl)phenyl acetate (2). Maltol (0.10 g, 0.8 mmol) was dissolved in dry DMF (25 mL). To this was added K_2CO_3 (0.33 g, 2.4 mmol) followed by **14** (0.54 g, 2.4 mmol), and the reaction was held at 60°C under nitrogen for 5 h. The reaction was cooled to RT, and concentrated via rotary evaporation. The resulting residue was brought up in CH_2Cl_2 (30 mL) and washed with brine (2×20 mL). The organic layer was collected, dried over $MgSO_4$ and filtered. The crude product was purified via silica gel chromatography eluting 70% EtOAc in hexanes to afford the desired purified product **2** in 70% yield (0.15 g, 0.6 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 5.6 Hz, 1H), 7.37 (d, J = 8.8 Hz, 2H), 7.03 (d, J = 8.8 Hz, 2H), 6.31 (d, J = 5.6 Hz, 1H), 5.08 (s, 2H), 2.22 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 162.8, 153.7, 150.8, 146.4, 140.4, 134.7, 130.3, 121.8, 117.39, 73.0, 21.4, 15.1. ESI-MS(+): *m/z* 274.95 $[M+H]^+$, 297.06 $[M+Na]^+$.



4-(((2-oxopyridin-1(2*H*)-yl)oxy)methyl)phenyl acetate (5).

1,2-HOPO (0.10 g, 0.9 mmol) was dissolved in dry DMF (10 mL). To this was added K_2CO_3 (0.37 g, 2.7 mmol) followed by **14** (0.21 g, 0.9 mmol), and the reaction was held at 60°C under nitrogen for 5 h. The mixture was cooled to RT, and concentrated via rotary evaporation. The resulting residue was dissolved in CH_2Cl_2 (20 mL) and washed with brine (2×20 mL). The

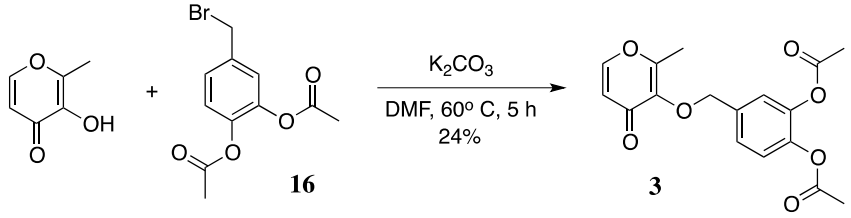
organic layer was collected, dried over $MgSO_4$ and filtered. The crude product was purified via silica gel chromatography eluting 70% EtOAc in hexanes to afford the desired product **5** in 34% yield (0.08 g, 0.3 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.6 Hz, 2H), 7.23 (td, J_1 = 6.8 Hz, J_2 = 2.0 Hz, 1H), 7.12 (dd, J_1 = 7.6 Hz, J_2 = 2.0 Hz, 1H), 7.09 (d, J = 8.6 Hz, 2H), 6.68 (dd, J_1 = 7.6 Hz, J_2 = 1.0 Hz, 1H), 5.96 (td, J_1 = 6.8 Hz, J_2 = 2.0 Hz, 1H), 5.25 (s, 2H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 159.1, 151.6, 146.4, 138.9, 136.8, 131.4, 122.9, 122.1, 104.8, 77.8, 21.3. ESI-MS(+): *m/z* 260.0 $[M+H]^+$, 282.0 $[M+Na]^+$.



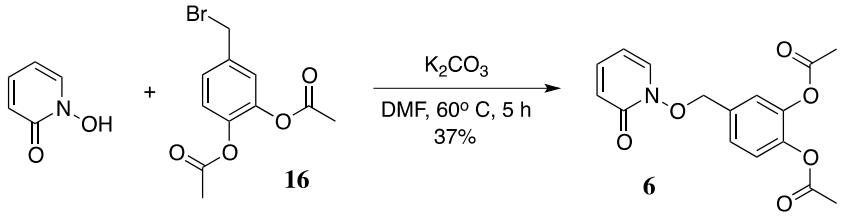
4-methyl-1,2-phenylene diacetate (15). 4-methylcatechol (0.50 g, 4.0 mmol) was dissolved in CH_2Cl_2 (40 mL). To this was added acetic anhydride (1.5 mL, 16.1 mmol) and scandium (III) triflate (0.04 g, 0.08 mmol) at RT. After 5 min, the reaction was complete via TLC and the resulting solution was washed with saturated $NaHCO_3$ (2×50 mL). The organic layer was collected, dried over $MgSO_4$, filtered and co-evaporated with MeOH to afford **15** in a 98% yield (0.82 g, 3.9 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07-7.02 (m, 2H), 6.99 (s, 1H), 2.33 (s, 3H), 2.26 (s, 3H). ESI-MS(+): *m/z* 226.0 $[M+NH_4]^+$, 231.0 $[M+Na]^+$, 247.0 $[M+K]^+$.

4-(bromomethyl)-1,2-phenylene diacetate (16). **15** (0.82 g, 3.9 mmol) was dissolved in $CHCl_3$ (50 mL) and reacted with *N*-bromosuccinimide (0.95 g, 5.3 mmol) and benzoyl peroxide (0.19 g, 0.80 mmol) in a flame-dried vessel. The reaction was held at reflux for 18 h. The mixture was cooled to RT and concentrated. The resulting residue was brought up in CH_2Cl_2 (20 mL) and

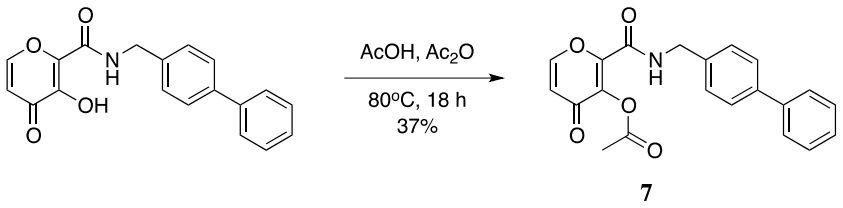
washed with brine (2×50 mL). The organic layer was collected, dried over $MgSO_4$ and filtered. The crude product was purified via silica gel chromatography eluting 15% EtOAc in hexanes to afford **16** in 72% yield (0.82 g, 2.8 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.13 (m, 3H), 4.43 (s, 2H), 2.26 (s, 6H). ESI-MS(+): *m/z* 306.01 $[M+NH_4]^+$.



4-(((2-methyl-4-oxo-4*H*-pyran-3-yl)oxy)methyl)-1,2-phenylene diacetate (3). Maltol (0.10 g, 0.8 mmol) was dissolved in dry DMF (10 mL). To this was added K_2CO_3 (0.33 g, 2.4 mmol) followed by **16** (0.68 g, 2.4 mmol), and the reaction was held at 60°C under nitrogen for 5 h. The mixture was then concentrated, dissolved in CH_2Cl_2 (20 mL) and washed with brine (2×20 mL). The organic layer was collected, dried over $MgSO_4$ and filtered. The resulting residue was purified via silica gel chromatography eluting 60% EtOAc in hexanes to afford **3** in 24% yield (0.06 g, 0.2 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 5.6 Hz, 1H), 7.29-7.15 (m, 3H), 6.48 (d, J = 5.6 Hz, 1H), 5.16 (s, 2H), 2.29 (s, 6H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 168.4, 160.4, 153.9, 142.2, 135.9, 127.1, 124.1, 123.5, 122.8, 120.8, 117.2, 72.5, 20.8, 15.1. ESI-MS(+): *m/z* 333.10 $[M+H]^+$, 355.08 $[M+Na]^+$.

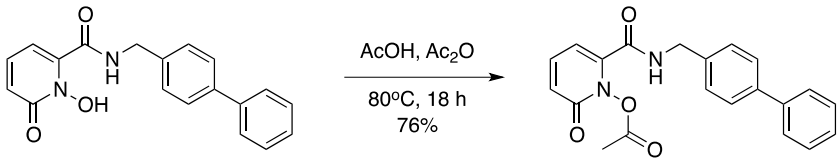


4-(((2-oxopyridin-1(2*H*)-yl)oxy)methyl)-1,2-phenylene diacetate (6). 1,2-HOPO (0.10 g, 0.9 mmol) was dissolved in dry DMF (10 mL). To this was added K_2CO_3 (0.37 g, 2.7 mmol) followed by **16** (0.77 g, 2.7 mmol), and the reaction was held at 60°C under nitrogen for 5 h. The mixture was then concentrated via rotary evaporation, dissolved in CH_2Cl_2 (20 mL) and washed with brine (2×20 mL). The organic layer was collected, dried over $MgSO_4$ and filtered. The resulting residue was purified via silica gel chromatography eluting 60% EtOAc in hexanes to afford **6** in 37% yield (0.11 g, 0.3 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (J = 1.9 Hz, 1H), 7.28-7.16 (m, 4H), 6.65 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 5.95 (td, J_1 = 6.7 Hz, J_2 = 1.7 Hz, 1H), 5.25 (s, 2H), 2.28 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 168.2, 159.0, 143.1, 142.4, 139.1, 136.7, 132.7, 128.2, 125.2, 123.9, 122.9, 105.0, 77.3, 20.9, 20.8. ESI-MS(+): *m/z* 318.12 $[M+H]^+$, 335.02 $[M+NH_4]^+$, 340.15 $[M+Na]^+$.



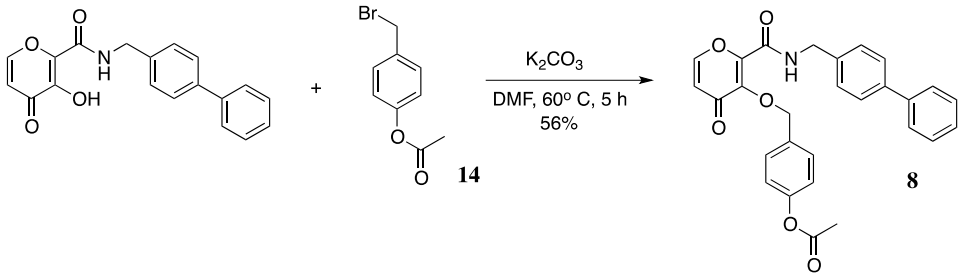
2-(([1,1'-biphenyl]-4-ylmethyl)carbamoyl)-4-oxo-4*H*-pyran-3-yl acetate (7). PY-2 [1] (0.05 g, 0.2 mmol) was reacted with acetic anhydride (15 mL, 158.9 mmol) and glacial acetic acid (3 mL, 52.4 mmol), and the reaction was held at 80°C for 18 h under nitrogen. The solution was concentrated and the resulting residue was dissolved in CH_2Cl_2 (20 mL) and washed with brine (2×20 mL). The organic layer was collected, dried over $MgSO_4$, and filtered. The resulting

residue was purified via silica gel chromatography eluting 70% EtOAc in hexanes to afford **7** in 37% yield (0.02 g, 0.06 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.48 (s, 1H), 8.29 (d, J = 5.6 Hz, 1H), 7.65-7.63 (m, 4H), 7.45-7.35 (m, 5H), 6.62 (d, J = 5.6 Hz, 1H), 4.68 (d, J = 6.0 Hz, 2H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.0, 167.9, 158.4, 156.6, 149.7, 140.5, 139.7, 138.2, 129.6, 128.6, 128.0, 127.4, 127.2, 117.5, 42.7, 20.7. HRMS calcd for $C_{21}H_{17}NO_5Na$: 386.0999; Found: 386.1000.

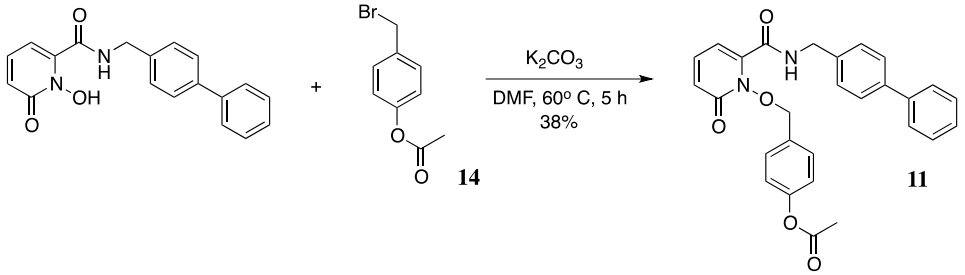


10

6-(([1,1'-biphenyl]-4-ylmethyl)carbamoyl)-2-oxopyridin-1(2*H*)-yl acetate (10). 1,2-HOPO-2 [1] (0.10 g, 0.3 mmol) was reacted with acetic anhydride (15 mL, 158.9 mmol) and glacial acetic acid (3 mL, 52.4 mmol), and the reaction was held at 80°C for 18 h under nitrogen. The solution was concentrated and the resulting residue was dissolved in CH_2Cl_2 (20 mL) and washed with brine (2×20 mL). The organic layer was collected, dried over $MgSO_4$, and filtered. The resulting residue was purified via silica gel chromatography eluting 70% EtOAc in hexanes to afford **10** in 76% yield (0.09 g, 0.2 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61-7.30 (m, 10H), 6.70 (d, J = 9.2 Hz, 1H), 6.56 (d, J = 6.5 Hz, 1H), 4.50 (s, 2H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 166.2, 160.4, 158.0, 141.3, 140.7, 140.5, 140.0, 137.1, 128.7, 128.1, 127.2, 127.0, 122.9, 106.2, 42.9, 16.3. ESI-MS (+): m/z 384.98 $[M+Na]^+$.

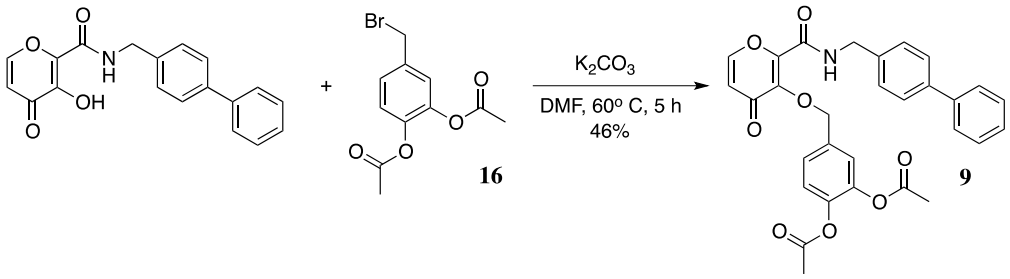


4-(((2-(([1,1'-biphenyl]-4-ylmethyl)carbamoyl)-4-oxo-4*H*-pyran-3yl)oxy)methyl)phenyl acetate (8). PY-2 (0.10 g, 0.3 mmol) was dissolved in dry DMF (10 mL). To this was added K_2CO_3 (0.13 g, 0.9 mmol) followed by **14** (0.21 g, 0.9 mmol), and the reaction was held at 60°C under nitrogen for 5 h. The mixture was then cooled to RT and concentrated. MeOH was added to crude which caused the formation of a white precipitate. The precipitate was filtered afford the desired product **8** in 56% yield (0.08 g, 0.2 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.18 (t, J = 5.6 Hz, 1H), 8.22 (d, J = 5.6 Hz, 1H), 7.63 (d, J = 7.2 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H), 7.47 (t, J = 7.2 Hz, 2H), 7.38-7.33 (m, 4H), 7.05 (d, J = 8.4 Hz, 2H), 6.54 (d, J = 5.6 Hz, 1H), 5.14 (s, 2H), 4.45 (d, J = 6 Hz, 2H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 175.7, 169.7, 159.5, 156.2, 150.9, 150.8, 145.3, 140.5, 139.5, 138.2, 134.5, 130.3, 129.6, 128.7, 128.0, 127.3, 127.2, 122.3, 117.7, 73.7, 42.9, 21.5. HRMS calcd for $C_{28}H_{23}NO_6Na$: 492.1418; Found: 492.1419.



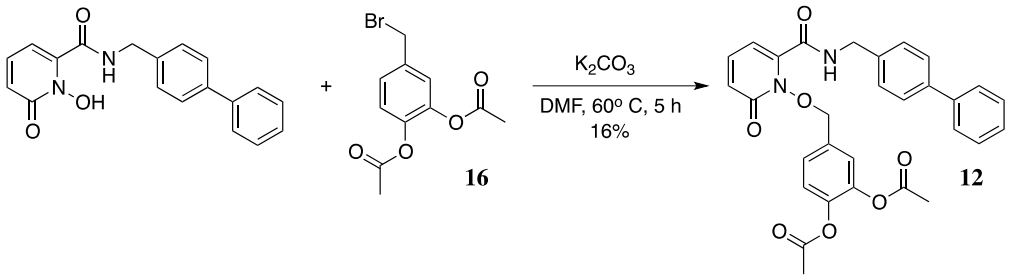
4-(((6-(([1,1'-biphenyl]-4-ylmethyl)carbamoyl)-2-oxopyridin-1(2*H*)-yl)oxy)methyl)phenyl acetate (11). 1,2-HOPO-2 (0.15 g, 0.5 mmol) was dissolved in dry DMF (10 mL). To this was

added K_2CO_3 (0.19 g, 1.4 mmol) followed by **14** (0.32 g, 1.4 mmol), and the reaction was held at 60°C under nitrogen for 5 h. The mixture was then cooled to RT and concentrated. MeOH was added to crude which caused the formation of a white precipitate. The precipitate was filtered to afford the desired product **11** in 38% yield (0.08 g, 0.2 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.46 (*br*, s, 1H) 7.62 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 7.6 Hz, 2H), 7.50-7.43 (m, 3H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.38-7.36 (m, 3H), 7.08 (d, *J* = 7.2 Hz, 2H), 6.68 (d, *J* = 7.2 Hz, 1H), 6.38 (d, *J* = 6.8 Hz, 1H), 5.24 (s, 2H), 4.48 (d, *J* = 6.0 Hz, 2H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.2, 160.9, 158.1, 155.3, 151.5, 144,6 139.7, 139.5, 138.2, 132.0, 131.5, 129.6, 128.0, 127.3, 127.2, 123.1, 122.5, 104.6, 78.3, 42.9, 21.5. HRMS calcd for $C_{28}H_{24}N_2O_5Na$: 491.1577; Found: 491.1578.



4-(((2-(([1,1'-biphenyl]-4-ylmethyl)carbamoyl)-4-oxo-4*H*-pyran-3-yl)oxy)methyl)-1,2-phenylene diacetate (9). PY-2 (0.10 g, 0.3 mmol) was dissolved in dry DMF (10 mL). To this was added K_2CO_3 (0.129 g, 0.9 mmol) followed by **16** (0.27 g, 0.9 mmol), and the reaction was held at 60°C under nitrogen for 5 h. The mixture was then cooled to RT, concentrated, brought up in CH_2Cl_2 (20 mL), and washed with brine (2×50 mL). The organic layer was collected, dried over $MgSO_4$ and filtered. The resulting residue was purified via silica gel chromatography eluting 70% EtOAc in hexanes to afford the desired product **9** in 46% yield (0.08 g, 0.2 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.21 (*br*, s, 1H), 8.24 (d, *J* = 5.6 Hz, 1H), 7.64-7.56 (m, 4H),

7.47 (t, *J* = 7.2 Hz, 2H), 7.36-7.30 (m, 5H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.56 (d, *J* = 5.6 Hz, 1H), 5.13 (s, 2H), 4.46 (*J* = 6.0 Hz, 2H), 2.25 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 175.7, 168.8, 159.5, 156.3, 151.0, 145.2, 142.4, 140.5, 139.6, 138.2, 136.0, 129.5, 128.6, 128.0, 127.3, 127.2, 127.0, 124.1, 123.9, 117.8, 73.3, 42.8, 21.0, 20.9. HRMS calcd. for $C_{30}H_{25}NO_8Na$: 550.1472; Found: 550.1471.



4-(((6-(([1,1'-biphenyl]-4-ylmethyl)carbamoyl)-2-oxopyridin-1(2*H*)-yl)oxy)methyl)-1,2-phenylenediacetate (12). 1,2-HOPO-2 (0.10 g, 0.3 mmol) was dissolved in dry DMF (10 mL). To this was added K_2CO_3 (0.129 g, 0.9 mmol) followed by **16** (0.267 g, 0.933mmol), and the reaction was held at 60°C under nitrogen for 5 h. The mixture was then cooled to RT, concentrated, brought up in CH_2Cl_2 (40 mL) and washed with brine (2×50 mL). The organic layer was collected, dried over $MgSO_4$ and filtered. The resulting residue was purified via silica gel chromatography eluting 70% EtOAc in hexanes to afford the desired product **12** was obtained in 16% yield (0.03 g, 0.05 mmol). ^{1}H NMR (400Hz, DMSO-d_6) δ 7.58-7.52 (m, 5H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.37-7.33 (m, 3H), 7.23 (td, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 2H), 7.16 (s, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.48 (d, *J* = 8.4 Hz, 1H), 6.35 (d, *J* = 5.6 Hz, 1H), 5.15 (s, 2H), 4.53 (d, *J* = 6.0 Hz, 2H), 2.26 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.5, 168.2, 160.5, 158.8, 143.2, 142.8, 142.1, 140.8, 140.7, 138.5, 136.7, 132.2, 129.1, 129.0, 128.7, 127.8,

127.7, 127.3, 125.7, 124.1, 123.9, 106.5, 64.3, 43.7, 20.8, 20. 7. HRMS calcd. for $C_{30}H_{26}N_2O_7Na$: 549.1632; Found: 549.1631.

UV-Vis Spectroscopy

The dashed curve represents the initial absorbance spectrum, while the red curve depicts the absorbance of an authentic sample of the MBG/MMPi. Absorbance curves coinciding with the unprotected red curve are indicative of the deprotection of the proMBG/proMMPi by esterase. Arrows indicate the direction of change over time.

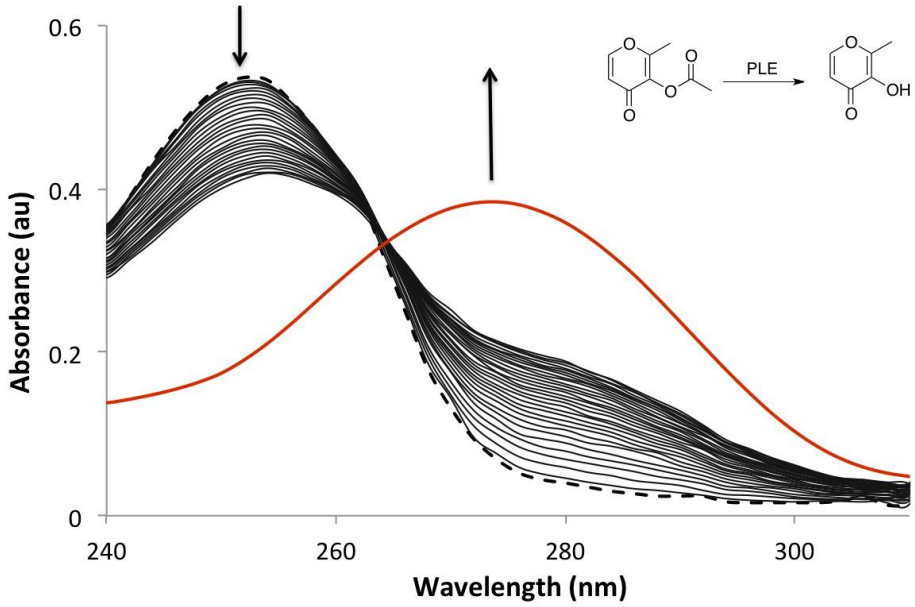


Figure S1. Absorption spectra of **1** (50 μM) in 50 mM HEPES (pH 7.5) the presence of PLE (3.57 U) monitored every 1 min for 60 min.

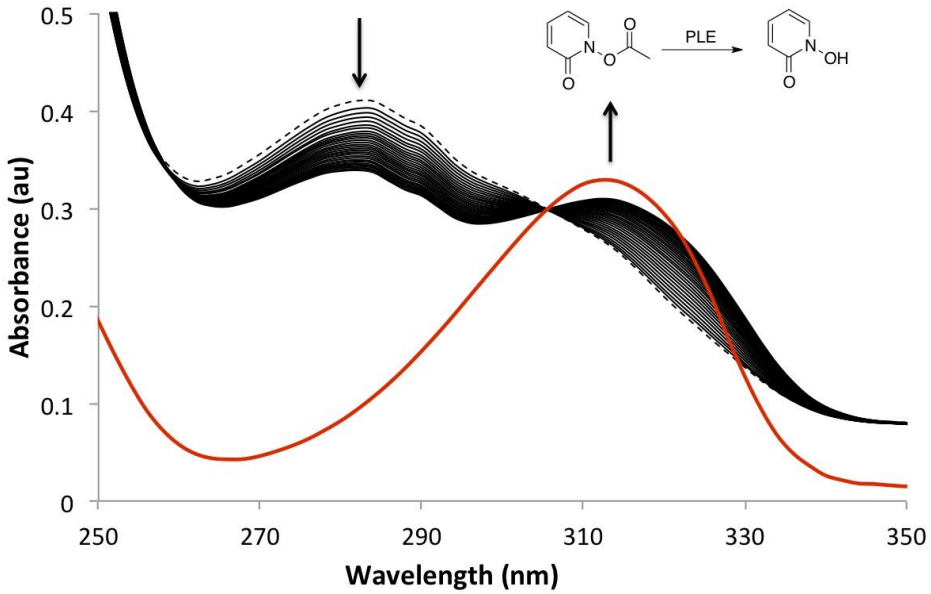


Figure S2. Absorption spectra of **4** (50 μM) in 50 mM HEPES (pH 7.5) the presence of PLE (3.57 U) monitored every 30 sec for 30 min.

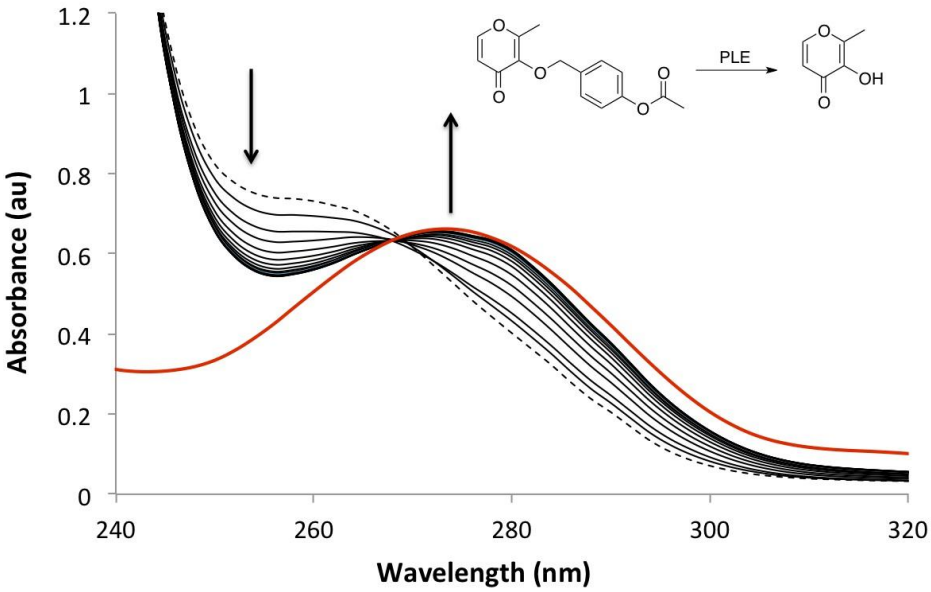


Figure S3. Absorption spectra of **2** (50 μM) in 50 mM HEPES (pH 7.5) the presence of PLE (3.57 U) monitored every 15 sec for 4.5 min.

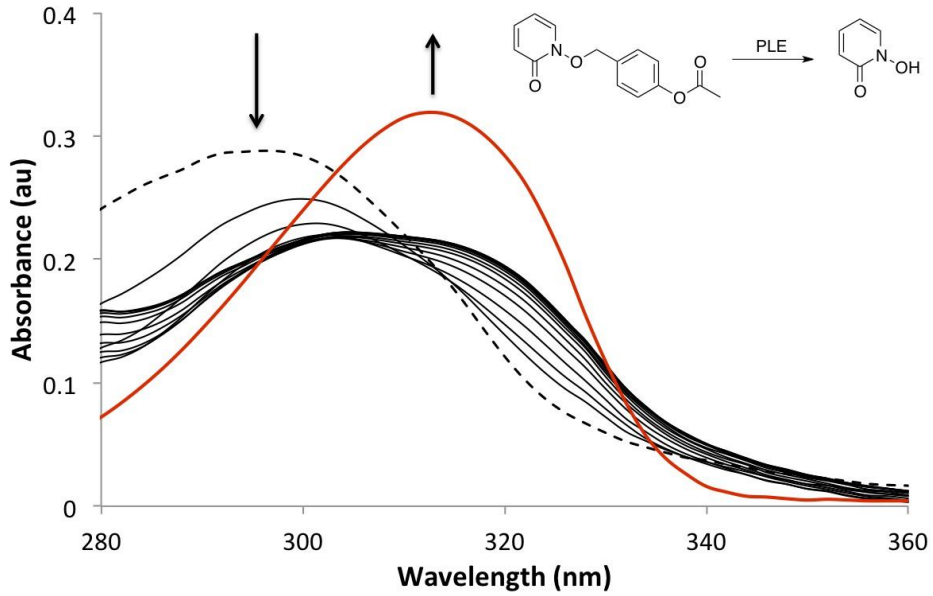


Figure S4. Absorption spectra of **4** (50 μM) in 50 mM HEPES (pH 7.5) the presence of PLE (3.57 U) monitored every 30 sec for 9 min.

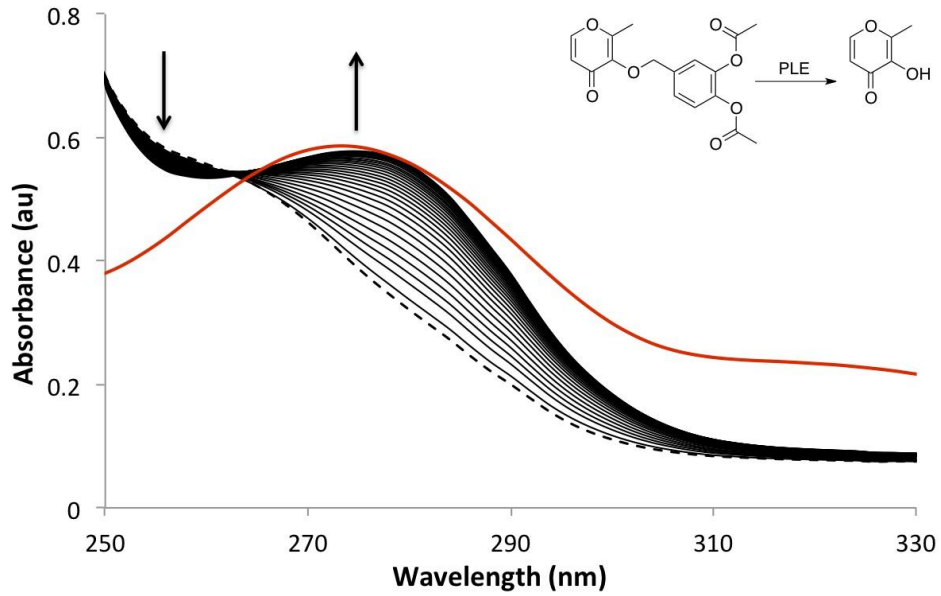


Figure S5. Absorption spectra of **5** (50 μM) in 50 mM HEPES (pH 7.5) the presence of PLE (3.57 U) monitored every 30 sec for 15 min.

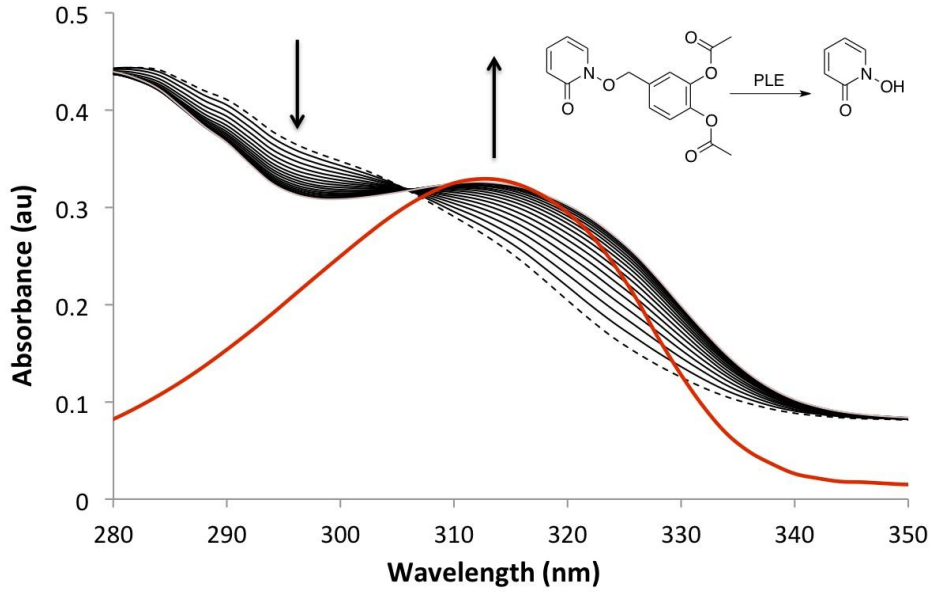


Figure S6. Absorption spectra of **6** (50 μM) in 50 mM HEPES (pH 7.5) the presence of PLE (3.57 U) monitored every 30 sec for 10 min.

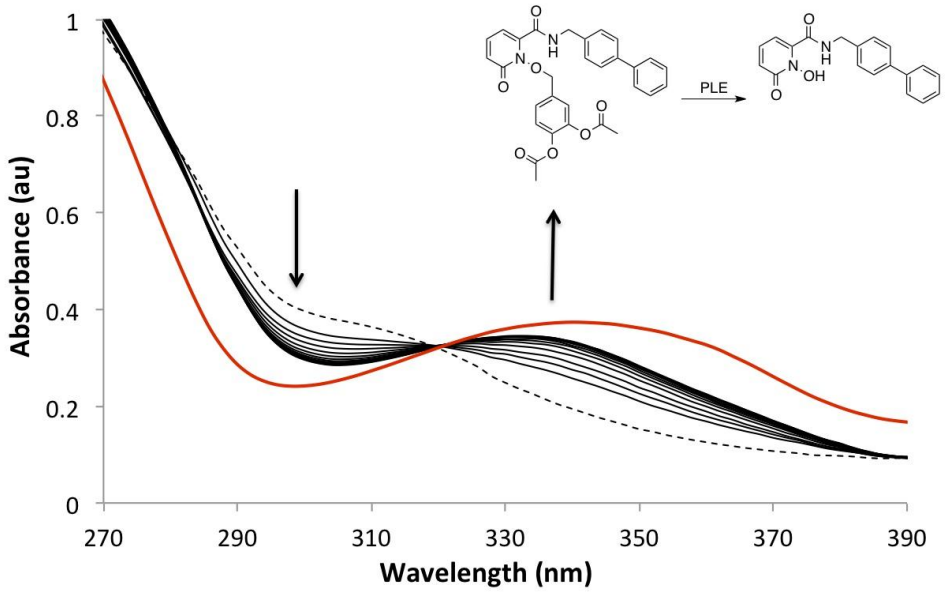


Figure S7. Absorption spectra of **12** (50 μM) in 50 mM HEPES (pH 7.5) the presence of PLE (3.57 U) monitored every 30 sec for 6.5 min.

HPLC Analysis

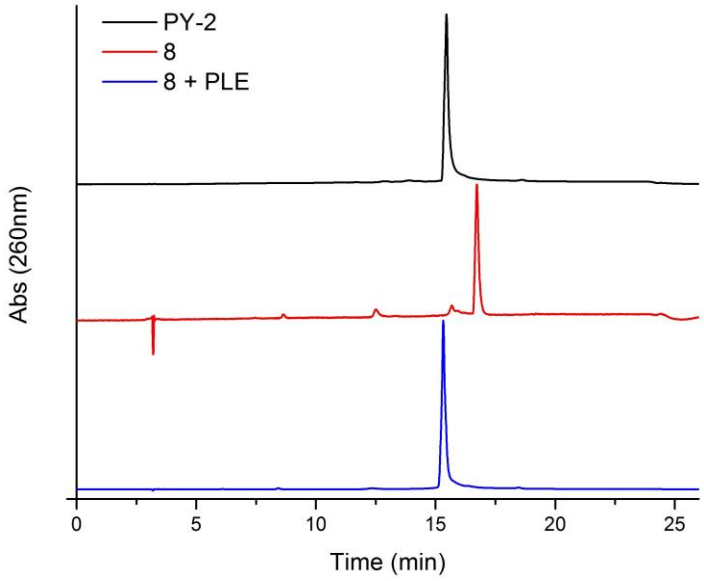


Figure S8. HPLC trace of **PY-2** (black), **8** (red) and **8** after the reaction with PLE (50 U) for 1 h (blue). Retention times are 15.4 min for **PY-2**, 16.7 min for **8**, and 15.4 min for **8** with PLE.

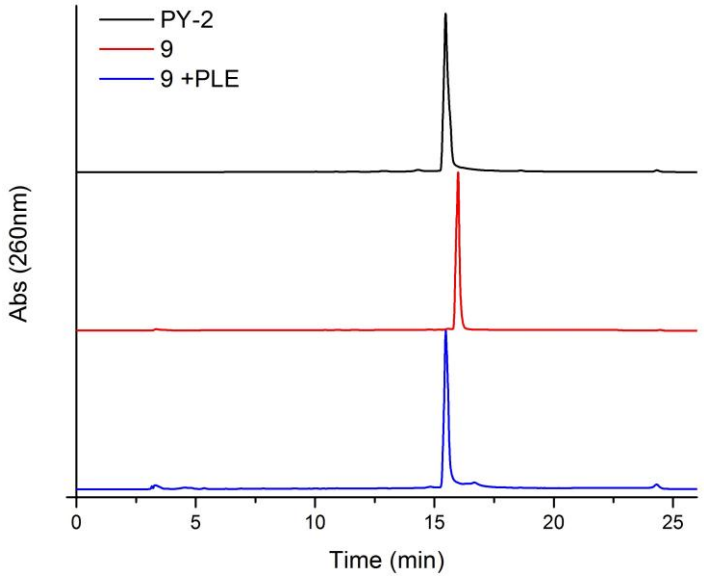


Figure S9. HPLC trace of **PY-2** (black), **9** (red) and **9** after the reaction with PLE (50 U) for 1 h (blue). Retention times are 15.4 min for **PY-2**, 16 min for **9**, and 15.4 min for **9** with PLE.

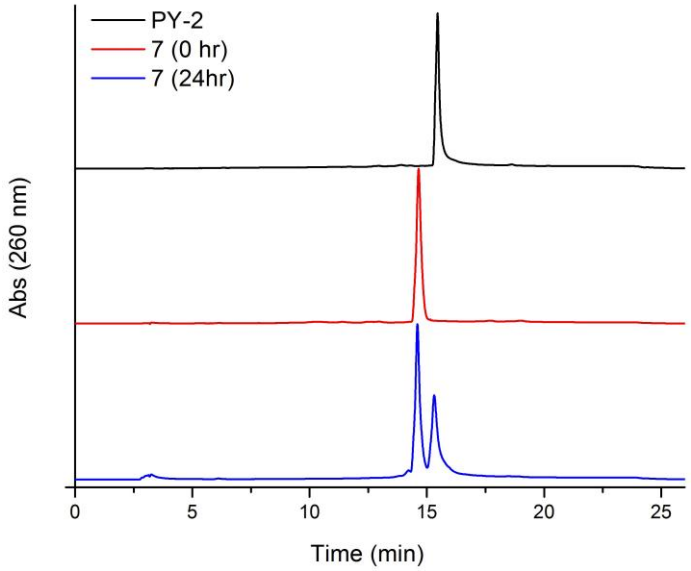


Figure S10. HPLC trace of **PY-2** (black), **7** in HEPES (50 mM, pH 7.4) at 0 h (red) and after a 24 h incubation in HEPES buffer at 37°C (blue). Retention times are 15.4 min for **PY-2**, 14.5 min for **7** (0 h), and 14.5 min and 15.4 for **7** (24 h).

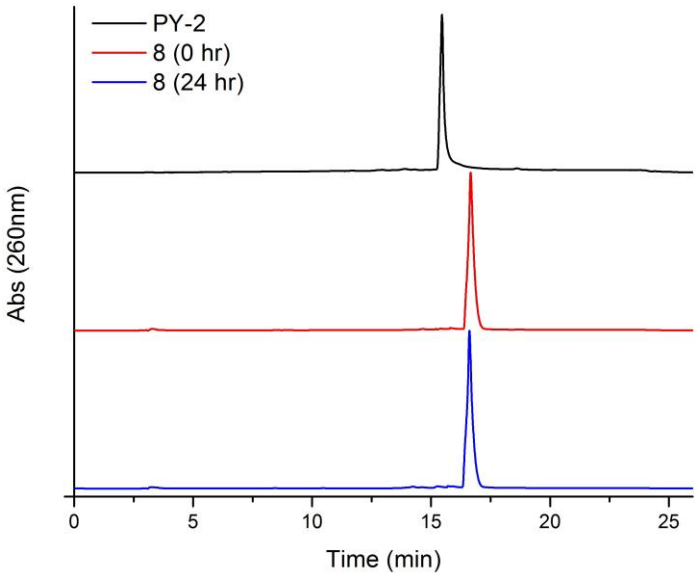


Figure S11. HPLC trace of **PY-2** (black), **8** in HEPES (50 mM, pH 7.4) at 0 h (red) and after a 24 h incubation in HEPES buffer at 37°C (blue). Retention times are 15.4 min for **PY-2**, 16.7 min for **8** (0 h), and 16.7 min for **8** (24 h).

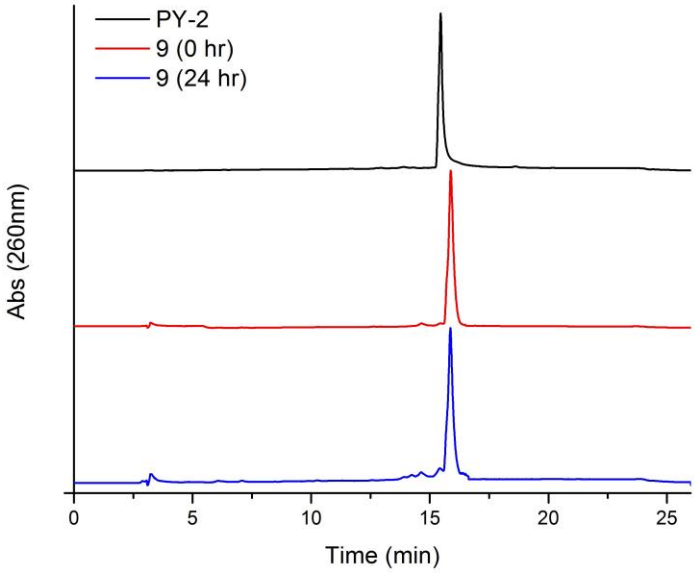


Figure S12. HPLC trace of **PY-2** (black), **9** in HEPES (50 mM, pH 7.4) at 0 h (red) and after a 24 h incubation in HEPES buffer at 37°C (blue). Retention times are 15.4 min for **PY-2**, 16 min for **9** (0 h), and 16 min for **9** (24 h).

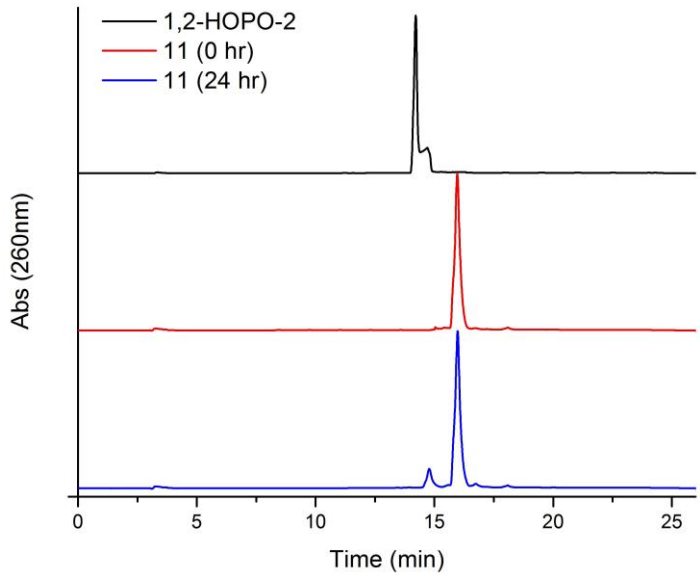


Figure S13. HPLC trace of **1,2-HOPO-2** (black), **11** in HEPES (50 mM, pH 7.4) at 0 h (red) and after a 24 h incubation in HEPES buffer at 37°C (blue). Retention times are 14.2 min for **1,2-HOPO**, 15.9 min for **11** (0 h), and 14.8 min and 15.9 min for **11** (24 h).

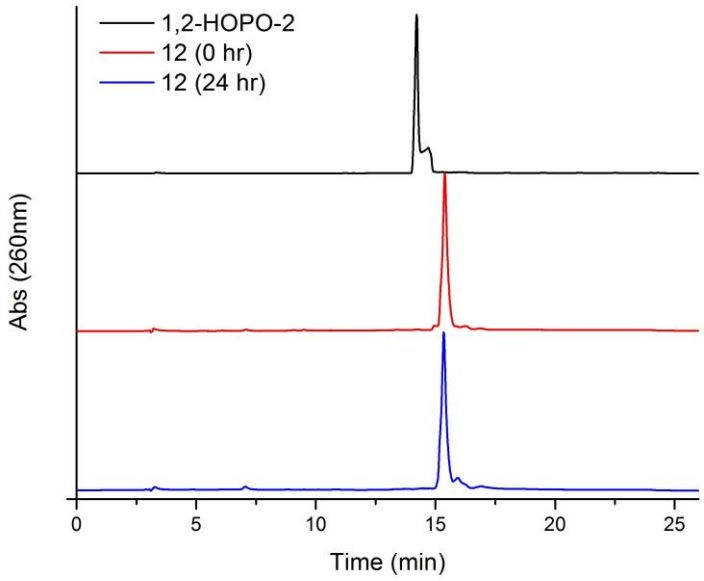


Figure S14. HPLC trace of **1,2-HOPO-2** (black), **12** in HEPES (50 mM, pH 7.4) at 0 h (red) and after a 24 h incubation in HEPES buffer at 37°C (blue). Retention times are 14.2 min for **1,2-HOPO**, 15.4 min for **12** (0 h), and 15.4 min for **12** (24 h).

Reference:

(1) Agrawal, A.; Romero-Perez, D.; Jacobsen, J. A.; Villarreal, F. J.; Cohen, S. M. *ChemMedChem* **2008**, *3*, 812-820.