Transition-Metal-Free Synthesis of Polysubstituted Pyrrole Derivatives via Cyclization of Methyl Isocyanocacetate with Aurone Analogues

Zhi-Peng Wang, a Yun He, a and Pan-Lin Shao*, a,b

a Chongqing Key Laboratory of Natural Product Synthesis and Drug Research, School of Pharmaceutical Sciences, Chongqing University, 55 Daxuecheng South Road, Shapingba, Chongqing 401331, P.R. China.
b College of Innovation and Entrepreneurship, Southern University of Science and Technology, Shenzhen 518000, P.R. China.

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I. General Information

$^1$H and $^{13}$C NMR spectra were recorded on an Agilent 400M NMR spectrometer at ambient temperature. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: $^1$H (chloroform δ 7.26, DMSO-$d_6$ δ 2.50), $^{13}$C (chloroform δ 77.0, DMSO-$d_6$ δ 39.52). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants (Hz) and integration. Melting point (M.P.) was obtained on SGW X-4A. For thin layer chromatography (TLC), Merck pre-coated TLC plates (Merck 60 F254) were used, and compounds were visualized with a UV light at 254 nm. High resolution mass spectra (HRMS) were obtained on a Bruker SolariX 7.0T spectrometer.

Unless otherwise noted, all the reactions were carried out in air. Dichloromethane (DCM) and acetonitrile (ACN) were distilled from calcium hydride. Deuterated solvents were purchased from Cambridge Isotope Laboratories and used as received without further purification. Other chemicals were purchased from commercial suppliers and used as received without further purification.
II. Synthesis of Aurones

General procedure. To a solution of benzofuran-3(2H)-one 1-1 (1.0 mmol) and benzaldehyde 1-2 (1.0 mmol) in dichloromethane (10 mL) was added activated basic aluminum oxide (5.0 mmol) at room temperature with vigorously stirring. After reaction completion, aluminum oxide was filtered and washed abundantly with dichloromethane, the filtrate was concentrated to afford crude product, which was purified by flash chromatography on silica gel (hexanes/ethyl acetate, 20:1) to afford the product 1a 17.8 mg as pale yellow solid.

III. Characterization of Aurones

(Z)-2-Benzylidenebenzofuran-3(2H)-one (1a)

80% yield, Rf = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, M.P. 89-90 °C. \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.93 (d, \(J = 7.3\) Hz, 2H), 7.81 (d, \(J = 7.5\) Hz, 1H), 7.66 (t, \(J = 7.8\) Hz, 1H), 7.46 (t, \(J = 7.3\) Hz, 2H), 7.40 (t, \(J = 7.1\) Hz, 1H), 7.33 (d, \(J = 8.3\) Hz, 1H), 7.22 (t, \(J = 7.5\) Hz, 1H), 6.90 (s, 1H); \(^{13}\)C NMR (101 MHz, Chloroform-d) \(\delta\) 184.78, 166.16, 146.89, 136.89, 132.30, 131.53, 129.89, 128.89, 124.67, 123.47, 121.64, 113.03, 112.94.

(Z)-2-(4-Bromobenzylidene)benzofuran-3(2H)-one (1c)

57% yield, Rf = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, M.P. 170-171 °C. \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.79 (dd, \(J = 12.4, 8.1\) Hz, 3H), 7.69 – 7.65 (m, 1H), 7.58 (d, \(J = 8.5\) Hz, 2H), 7.33 (d, \(J = 8.3\) Hz, 1H), 7.23 (t, \(J = 7.5\) Hz, 1H), 6.81 (s, 1H); \(^{13}\)C NMR (101 MHz, Chloroform-d) \(\delta\) 184.59, 166.08, 147.08, 137.04, 132.77, 132.15, 131.21, 124.74, 124.30, 123.66, 121.50, 112.93, 111.54.
(Z)-2-(4-Methoxybenzylidene)benzofuran-3(2H)-one (1d)\[^3\]

\[
\begin{align*}
\text{91\% yield, } R_f &= 0.5, \text{ (silica gel, petroleum ether:EtOAc = 5:1),} \\
\text{pale yellow solid, M.P.} &= 133-134^\circ C. \ 1^H \text{NMR (400 MHz, Chloroform-d)} \delta 7.91 - 7.87 \ (m, 2H), 7.81 \ (dd, J = 7.6, 0.8 Hz, 1H), 7.64 \ (ddd, J = 8.5, 7.3, 1.4 Hz, 1H), 7.32 \ (d, J = 8.3 Hz, 1H), 7.23 - 7.19 \ (m, 1H), 7.00 - 6.98 \ (m, 2H), 6.89 \ (s, 1H), 3.87 \ (s, 3H); \ 13^C \text{NMR (101 MHz, Chloroform-d)} \delta 184.54, 165.84, 161.07, 145.88, 136.50, 133.43, 125.06, 124.55, 123.25, 121.95, 114.50, 113.39, 112.86, 55.38.
\end{align*}
\]

(Z)-2-(3-Chlorobenzylidene)benzofuran-3(2H)-one (1e)\[^4\]

\[
\begin{align*}
\text{86\% yield, } R_f &= 0.5, \text{ (silica gel, petroleum ether:EtOAc = 5:1),} \\
\text{pale yellow solid, M.P.} &= 96-97^\circ C. \ 1^H \text{NMR (400 MHz, Chloroform-d)} \delta 7.91 \ (s, 1H), 7.78 \ (t, J = 12.5 Hz, 1H), 7.72 - 7.70 \ (m, 1H), 7.64 \ (t, J = 7.7 Hz, 1H), 7.38 - 7.32 \ (m, 3H), 7.22 \ (t, J = 7.4 Hz, 1H), 6.76 \ (s, 1H); \ 13^C \text{NMR (101 MHz, Chloroform-d)} \delta 184.55, 166.16, 147.28, 137.13, 134.80, 134.02, 130.87, 130.02, 129.70, 129.56, 124.73, 123.70, 121.37, 113.00, 111.07.
\end{align*}
\]

(Z)-2-(3-Methoxybenzylidene)benzofuran-3(2H)-one (1f)\[^2\]

\[
\begin{align*}
\text{85\% yield, } R_f &= 0.4, \text{ (silica gel, petroleum ether:EtOAc = 5:1),} \\
\text{pale yellow solid, M.P.} &= 116-117^\circ C. \ 1^H \text{NMR (400 MHz, Chloroform-d)} \delta 8.35 \ (dd, J = 7.8, 1.6 Hz, 1H), 7.66 \ (t, J = 7.8 Hz, 1H), 7.50 \ (d, J = 6.7 Hz, 2H), 7.40 - 7.32 \ (m, 2H), 7.23 \ (t, J = 7.5 Hz, 1H), 7.98 - 6.96 \ (m, 1H), 6.87 \ (s, 1H), 3.89 \ (s, 3H); \ 13^C \text{NMR (101 MHz, Chloroform-d)} \delta 184.77, 166.15, 159.77, 146.97, 136.92, 133.50, 129.83, 124.68, 124.30, 123.50, 121.61, 116.51, 115.74, 112.95, 112.93, 55.34.
\end{align*}
\]

(Z)-2-(2-Chlorobenzylidene)benzofuran-3(2H)-one (1g)\[^2\]

\[
\begin{align*}
\text{86\% yield, } R_f &= 0.5, \text{ (silica gel, petroleum ether:EtOAc = 5:1), pale} \\
\text{yellow solid, M.P.} &= 133-134^\circ C. \ 1^H \text{NMR (400 MHz, Chloroform-d)} \delta 8.35 \ (dd, J = 7.8, 1.6 Hz, 1H), 7.81 \ (d, J = 7.6 Hz, 1H), 7.68 - 7.64 \ (m, 1H), 7.46 \ (dd, J = 7.9, 1.2 Hz, 1H), 7.38 \ (dd, J = 8.7, 7.6 Hz, 2H), 7.32 - 7.29 \ (m, 2H), 7.23 \ (t, J = 7.5 Hz, 1H); \ 13^C \text{NMR (101 MHz, Chloroform-d)} \delta 184.53, 166.17,
\end{align*}
\]
147.59, 137.06, 135.94, 132.23, 130.58, 130.39, 130.00, 127.04, 124.83, 123.69, 121.49, 112.91, 107.98.

(Z)-2-(2-Methylbenzylidene)benzofuran-3(2H)-one (1h)[4]

82% yield, *R* = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, **M.P.** 101-102 °C. **1H NMR** (400 MHz, Chloroform-d) δ 8.27 – 8.25 (m, 1H), 7.82 (d, *J* = 7.5 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.34 – 7.20 (m, 5H), 7.14 (s, 1H), 2.52 (s, 3H); **13C NMR** (101 MHz, Chloroform-d) δ 184.76, 166.22, 146.99, 139.20, 136.84, 131.17, 130.81, 130.68, 129.83, 126.39, 124.70, 123.41, 121.73, 112.96, 109.87, 20.22.

(Z)-2-(Naphthalen-1-ylmethylene)benzofuran-3(2H)-one (1i)[2]

70% yield, *R* = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, **M.P.** 132-133 °C. **1H NMR** (400 MHz, Chloroform-d) δ 8.47 (d, *J* = 7.3 Hz, 1H), 8.32 (d, *J* = 8.5 Hz, 1H), 7.92 – 7.84 (m, 3H), 7.72 (s, 1H), 7.61 (qdd, *J* = 14.9, 11.2, 4.1 Hz, 4H), 7.34 (d, *J* = 8.3 Hz, 1H), 7.24 (dd, *J* = 11.9, 4.1 Hz, 1H); **13C NMR** (101 MHz, Chloroform-d) δ 184.61, 166.27, 147.71, 136.87, 133.73, 132.32, 130.57, 130.26, 128.96, 128.24, 127.08, 126.19, 125.58, 124.77, 123.32, 121.80, 112.99, 108.57.

(Z)-2-(Naphthalen-2-ylmethylene)benzofuran-3(2H)-one (1j)

78% yield, *R* = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), yellow solid, **M.P.** 120-121 °C. **1H NMR** (400 MHz, Chloroform-d) δ 8.30 (s, 1H), 8.06 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.85 (ddd, *J* = 14.1, 9.3, 3.4 Hz, 4H), 7.67 – 7.63 (m, 1H), 7.54 – 7.49 (m, 2H), 7.36 (d, *J* = 8.3 Hz, 1H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.03 (s, 1H); **13C NMR** (101 MHz, Chloroform-d) δ 184.63, 166.10, 147.06, 136.89, 133.72, 133.32, 132.32, 129.92, 128.73, 128.54, 127.72, 127.66, 127.47, 126.59, 124.66, 123.46, 121.70, 113.21, 112.97; **HRMS** (ESI): m/z calcd. for [C_{19}H_{13}O_{2}, M+H]^+: 273.0910; found: 273.0916.

[(Z)-(3-Oxo-2(3H)-benzofuranylidene)methyl]ferrocene (1k)[5]

74% yield, *R* = 0.4, (silica gel, petroleum ether:EtOAc = 10:1), purple solid, **M.P.** 150-151 °C. **1H NMR** (400 MHz, Chloroform-d)
δ 7.80 (d, J = 7.5 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.29 (d, J = 8.3 Hz, 1H), 7.18 (t, J = 7.4 Hz, 1H), 6.89 (s, 1H), 4.86 (s, 2H), 4.54 (s, 2H), 4.17 (s, 5H); 13C NMR (101 MHz, Chloroform-d) δ 182.87, 165.36, 145.98, 136.08, 124.45, 123.04, 122.60, 116.42, 112.91, 75.05, 71.79, 71.47, 69.93.

(Z)-2-(Thiophen-2-ylmethylene)benzofuran-3(2H)-one (1l)[6]

90% yield, Rf = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, M.P. 102-103 °C. 1H NMR (400 MHz, Chloroform-d) δ 7.79 (ddd, J = 7.6, 1.3, 0.5 Hz, 1H), 7.64 (ddd, J = 8.6, 7.3, 1.4 Hz, 1H), 7.61–7.60 (m, 2H), 7.55–7.54 (m, 1H), 7.33 (d, J = 8.3 Hz, 1H), 7.23–7.19 (m, 1H), 7.14 (dd, J = 5.1, 3.7 Hz, 1H); 13C NMR (101 MHz, Chloroform-d) δ 183.84, 165.62, 145.32, 136.64, 135.55, 133.08, 131.71, 128.05, 124.53, 123.47, 122.24, 113.00, 107.00.

(Z)-2-(Furan-2-ylmethylene)benzofuran-3(2H)-one (1m)[6]

84% yield, Rf = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), yellow solid, M.P. 119-120 °C. 1H NMR (400 MHz, Chloroform-d) δ 7.79 (d, J = 7.4 Hz, 1H), 7.66–7.62 (m, 2H), 7.31 (d, J = 8.3 Hz, 1H), 7.21 (t, J = 7.4 Hz, 1H), 7.13 (d, J = 3.3 Hz, 1H), 6.89 (s, 1H), 6.60 (d, J = 1.4 Hz, 1H); 13C NMR (101 MHz, Chloroform-d) δ 183.95, 165.72, 148.79, 145.38, 145.00, 136.65, 124.51, 123.47, 122.02, 117.24, 113.13, 112.89, 101.57.

(Z)-2-((1H-Indol-3-yl)methylene)benzofuran-3(2H)-one (1n)

48% yield, Rf = 0.2, (silica gel, petroleum ether:EtOAc = 3:1), orange solid, M.P. 232-233 °C. 1H NMR (400 MHz, DMSO-d6) δ 12.11 (br, 1H), 8.26 (d, J = 2.6 Hz, 1H), 8.06 (d, J = 7.6 Hz, 1H), 7.75 (t, J = 7.9 Hz, 2H), 7.56 (d, J = 8.1 Hz, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.36 (s, 1H), 7.23 (ddd, J = 25.2, 15.5, 7.3 Hz, 3H); 13C NMR (101 MHz, DMSO-d6) δ 182.15, 164.58, 144.58, 136.83, 136.82, 132.68, 127.12, 124.26, 123.80, 123.28, 122.70, 121.45, 119.51, 113.55, 112.81, 108.92, 107.96; HRMS (ESI): m/z calcd. for [C17H11NNaO2, M+Na]+: 284.0682; found: 284.0682.

(Z)-2-(Pyridin-3-ylmethylene)benzofuran-3(2H)-one (1o)[7]
73% yield, \( R_f = 0.2 \), (silica gel, petroleum ether:EtOAc = 5:1), yellow solid, M.P. 111-112 °C. \(^1\)H NMR (400 MHz, Chloroform-d) \( \delta \) 9.05 (s, 1H), 8.61 (d, \( J = 4.1 \) Hz, 1H), 8.29 (d, \( J = 7.9 \) Hz, 1H), 7.82 (d, \( J = 7.6 \) Hz, 1H), 7.69 (t, \( J = 7.7 \) Hz, 1H), 7.42 – 7.39 (m, 1H), 7.34 (d, \( J = 8.2 \) Hz, 1H), 7.26 (t, \( J = 7.4 \) Hz, 1H), 6.85 (s, 1H); \(^1\)C NMR (101 MHz, Chloroform-d) \( \delta \) 184.31, 166.15, 152.21, 150.06, 148.00, 137.65, 137.28, 128.55, 124.83, 123.83, 123.73, 121.31, 112.96, 108.83.

(Z)-6-Benzylidene-[1,3]dioxolo[4,5-f]benzofuran-7(6H)-one (1p)

94% yield, \( R_f = 0.6 \), (silica gel, petroleum ether:EtOAc = 10:1), yellow solid, M.P. 189-191 °C. \(^1\)H NMR (400 MHz, Chloroform-d) \( \delta \) 7.86 (d, \( J = 7.3 \) Hz, 2H), 7.41 (dt, \( J = 23.3, 7.2 \) Hz, 3H), 7.09 (s, 1H), 6.80 (s, 1H), 6.76 (s, 1H), 6.09 (s, 2H); \(^1\)C NMR (101 MHz, Chloroform-d) \( \delta \) 183.13, 164.58, 155.84, 148.00, 145.05, 132.28, 131.40, 129.75, 128.87, 114.75, 112.35, 102.72, 101.81, 94.41. HRMS (ESI): m/z calcd. for \([\text{C}_{16}\text{H}_{10}\text{NaO}_4, \text{M}+\text{Na}]^+\): 289.0471; found: 289.0471.

(Z)-2-Benzylidene-6-methoxybenzofuran-3(2H)-one (1q)\(^8\)

85% yield, \( R_f = 0.5 \), (silica gel, petroleum ether:EtOAc = 5:1), white scaly solid, M.P. 132-133 °C. \(^1\)H NMR (400 MHz, Chloroform-d) \( \delta \) 7.90 – 7.88 (m, 2H), 7.69 (t, \( J = 5.9 \) Hz, 1H), 7.45 (dd, \( J = 10.1, 4.6 \) Hz, 2H), 7.40 – 7.36 (m, 1H), 6.81 (s, 1H), 6.76 (dt, \( J = 8.4, 2.0 \) Hz, 2H), 3.92 (s, 3H); \(^1\)C NMR (101 MHz, Chloroform-d) \( \delta \) 183.02, 168.58, 167.45, 147.83, 132.43, 131.30, 129.59, 128.83, 125.83, 114.84, 112.18, 111.85, 96.65, 56.02.

(Z)-2-Benzylidene-6-bromobenzofuran-3(2H)-one (1r)\(^9\)

95% yield, \( R_f = 0.3 \), (silica gel, petroleum ether:EtOAc = 10:1), pale yellow solid, M.P. 168-170 °C. \(^1\)H NMR (400 MHz, Chloroform-d) \( \delta \) 7.88 (d, \( J = 7.1 \) Hz, 2H), 7.65 (d, \( J = 8.1 \) Hz, 1H), 7.54 (s, 1H), 7.43 (dq, \( J = 14.3, 7.0 \) Hz, 3H), 7.35 (d, \( J = 8.1 \) Hz, 1H), 6.90 (s, 1H); \(^1\)C NMR (101 MHz, Chloroform-d) \( \delta \) 183.48, 166.08, 146.76, 131.93, 131.64, 131.34, 130.23, 128.97, 127.20, 125.51, 120.65, 116.62, 113.99.
(Z)-2-Benzylidene-4-methylbenzofuran-3(2H)-one (1s)

84% yield, Rf = 0.3, (silica gel, petroleum ether:EtOAc = 40:1), white solid, M.P. 108-109 °C. \( ^1H \) NMR (400 MHz, Chloroform-d) \( \delta \) 7.90 (d, \( J = 7.3 \) Hz, 2H), 7.45 (dq, \( J = 14.8, 7.5 \) Hz, 3H), 7.38 (t, \( J = 7.3 \) Hz, 1H), 7.11 (d, \( J = 8.2 \) Hz, 1H), 6.94 (d, \( J = 7.5 \) Hz, 1H), 6.81 (s, 1H), 2.68 (s, 3H); \( ^13C \) NMR (101 MHz, Chloroform-d) \( \delta \) 185.5, 166.4, 146.9, 140.1, 136.2, 132.4, 131.3, 129.5, 128.8, 124.8, 119.7, 111.90, 109.89, 17.79; HRMS (ESI): m/z calcd. for \([C_{16}H_{12}NaO_2]^+\): 259.0730; found: 259.0731.

(Z)-2-Benzylidene-6-((10-((tert-butyldimethylsilyl)oxy)decyl)oxy)benzofuran-3(2H)-one (1t)

90% yield, Rf = 0.6, (silica gel, petroleum ether:EtOAc = 10:1), white solid, M.P. 58-59 °C. \( ^1H \) NMR (400 MHz, Chloroform-d) \( \delta \) 7.88 (d, \( J = 7.8 \) Hz, 2H), 7.68 (d, \( J = 8.1 \) Hz, 1H), 7.44 (t, \( J = 7.5 \) Hz, 2H), 7.37 (t, \( J = 7.3 \) Hz, 1H), 6.80 (s, 1H), 6.73 (d, \( J = 8.0 \) Hz, 2H), 4.05 (t, \( J = 6.5 \) Hz, 2H), 3.59 (t, \( J = 6.6 \) Hz, 2H), 1.86 – 1.79 (m, 2H), 1.47 (dt, \( J = 15.2, 6.6 \) Hz, 4H), 1.40 – 1.25 (m, 10H), 0.88 (s, 9H), 0.04 (s, 6H); \( ^13C \) NMR (101 MHz, Chloroform-d) \( \delta \) 183.0, 168.63, 167.09, 147.89, 132.46, 131.29, 129.55, 128.83, 125.78, 114.54, 112.66, 111.74, 96.95, 68.98, 63.31, 32.86, 29.53, 29.47, 29.41, 29.29, 28.91, 25.98, 25.92, 25.78, 18.38, -5.26. HRMS (ESI): m/z calcd. for \([C_{31}H_{45}O_4Si, M+H]^+\): 509.3082; found: 509.3079.

IV. Preparation of d\(^1\)-1a and d\(^2\)-2c

**Procedure:**\(^{[10]}\) To a flame-dried reaction tube equipped with a condenser was added NaBD\(_4\) 126.0 mg (3.0 equiv.) and 10 mL anhydrous THF, then 1,2-ethanediethyl 376.0 mg (4.0 equiv.) and methyl benzoate 136.0 mg (1.0 equiv.) were added sequentially, then this mixture was refluxed at 80 °C overnight. After the reaction
completion, quenched with 10 mL saturated NH₄Cl solution, and the aqueous phase was extracted with ethyl acetate (20 mL×3). The combined organic layer was dried over sodium sulfate. The solvent was evaporated, and the residue was purified by a flash silica gel column chromatography (eluent: PE/EtOAc = 5:1) to give d-benzyl alcohol in 95% yield. The product was then dissolved in a 10 ml flask with 3 mL DCM, 2.5 equivalents of Dess-Martin periodinane was added and the reaction was stirred at r.t. for 5 hrs. After reaction completion, sodium thiosulfate aqueous solution was added to quench the reaction, the aqueous layer was extracted with CH₂Cl₂ (10 mL×3), and then the organic layers were combined, dried over sodium sulfate, and washed with saturated aq. NaHCO₃ (10 mL). Flash column chromatography (silica gel, PE/EtOAc = 50:1) yielded d-benzaldehyde d¹-1a-2 in 90% yield with 88% deuterium labeling. To a round-bottom flask was added the obtained aldehyde and 5.0 equivalents of Al₂O₃ (basic), dissolved in 5.0 mL DCM, then the benzofuranone 1-1 (1.0 equiv.) was added, and the mixture was stirred at r.t. After 10 h the reaction was diluted with CH₂Cl₂ and filtered through a short pad of celite and washed with CH₂Cl₂, the solvent was concentrated and the residue was purified by flash column chromatography (silica gel, PE/EtOAc = 20:1) to give product d¹-1a in 90% yield with 88% deuterium labeling. Rf = 0.3, (silica gel, petroleum ether:EtOAc = 20:1), pale yellow solid, M.P. 105-107 °C. ¹H NMR (400 MHz, Chloroform-d) δ 7.93 – 7.91 (m, 2H), 7.80 (d, J = 7.6 Hz, 1H), 7.65 (dd, J = 11.3, 4.3 Hz, 1H), 7.46 (dd, J = 11.4, 4.4 Hz, 2H), 7.39 (dd, J = 8.7, 5.8 Hz, 1H), 7.33 (d, J = 8.3 Hz, 1H), 7.21 (t, J = 7.5 Hz, 1H), 6.89 (s, 0.12H); ¹³C NMR (101 MHz, Chloroform-d) δ184.78, 166.14, 146.84, 136.88, 132.23, 131.51, 129.89, 128.88, 124.65, 123.45, 121.63, 112.96, 112.93; HRMS (ESI): m/z calcd. for [C₁₅H₉DNaO₂, M+Na]⁺: 246.0636; found: 246.0629.

Procedure:¹ To 20 mL of deuterium oxide in a Schlenk tube, which was previously rinsed with deuterium oxide and dried, was added sequentially a solution of 1.1 mL (10 mmol) of d²-2c-1 in 10 mL of deuteriochloroform and 50 µL
triethylamine. The reaction mixture was stirred at room temperature, and the exchange reaction was monitored by the disappearance of the methylene group protons at 4.18 in the $^1$H NMR spectrum. After the exchange reaction was complete, the organic phase was separated and then was stirred for an additional 1 h with 20 mL of fresh deuterium oxide. The aqueous phase was separated, and the organic phase was dried over anhydrous sodium sulfate. The solvent was removed in vacuo, and the residue was distilled, to give 0.87 g of a colorless liquid with 99% deuterium labeling of α protons. $^1$H NMR (400 MHz, Chloroform-d) δ 4.20 (q, $J = 7.2$ Hz, 2H), 1.24 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 163.98, 160.86, 62.65, 43.25, 13.90.

V. Synthesis of Pyrrole Derivatives with Isocyanatoacetate and Aurores

\[
\begin{align*}
\text{Ph} & \quad \text{Ph} \\
\text{1a} & \quad \text{2a} \\
\text{NaOH (cat.)} & \quad \text{MeOH, RT} \\
\text{3a} & \quad \text{MeOH} \\
\end{align*}
\]

**General procedure:** To a solution of aurone 1a (22.2 mg, 0.1 mmol) in 1.0 mL MeOH was added isocyanatoacetate 2a (11.9 mg, 0.12 mmol), and then a solution of NaOH (1.0 M in MeOH) 20 μL (20 mol%) was added. The reaction was stirred at ambient temperature for 12 h. After completion, the reaction was quenched with 20 μL HCl solution (1.0 N in MeOH), the solvent was removed under reduced pressure and then purified by flash chromatography on silica gel (hexanes/ethyl acetate, 5:1) to afford the product 3a 31.8 mg.

VI. Characterization of Pyrroles

**Methyl 4-(2-hydroxybenzoyl)-3-phenyl-1H-pyrrole-2-carboxylate (3a)**

\[
\begin{align*}
\text{Ph} & \quad \text{Ph} \\
\text{3a} & \quad \text{MeOH} \\
\end{align*}
\]

99% yield, $R_f = 0.2$, (silica gel, petroleum ether:EtOAc = 5:1), white solid, **M.P. 53-54 °C.** $^1$H NMR (400 MHz, Chloroform-d) δ 11.89 (s, 1H), 9.70 (br, 1H), 7.64 (dd, $J = 8.0, 1.5$ Hz, 1H), 7.42 –
7.38 (m, 1H), 7.35–7.26 (m, 6H), 6.95 (d, \( J = 8.4 \) Hz, 1H), 6.78–6.74 (m, 1H), 3.75 (s, 3H); \( ^{13}\text{C NMR} \) (101 MHz, Chloroform-d) \( \delta \) 195.54, 162.52, 161.23, 135.78, 132.80, 132.69, 132.08, 130.20, 127.57, 127.49, 126.28, 124.46, 120.41, 118.49, 117.98, 51.76. \text{HRMS (ESI): } m/z\text{ calcd. for } [C_{19}H_{15}NNaO_4, M+Na]^+: 344.0893;\text{ found: 344.0894.}

(2-Hydroxyphenyl)(4-phenyl-5-tosyl-1H-pyrrol-3-yl)methanone (3b)

94% yield, \( R_f = 0.1 \), (silica gel, petroleum ether:EtOAc = 5:1), white solid, \text{M.P.} 179-181 \degree C. \( ^{1}H \text{NMR} \) (400 MHz, Chloroform-d) \( \delta \) 11.77 (s, 1H), 10.21 (br, 1H), 7.59 (d, \( J = 8.0 \) Hz, 1H), 7.39–7.26 (m, 6H), 7.20 (d, \( J = 7.8 \) Hz, 2H), 6.95 (d, \( J = 8.4 \) Hz, 1H), 6.78 (t, \( J = 7.6 \) Hz, 1H), 2.34 (s, 3H); \( ^{13}\text{C NMR} \) (101 MHz, Chloroform-d) \( \delta \) 195.54, 162.52, 161.23, 135.78, 132.80, 132.08, 130.20, 127.57, 127.49, 126.28, 124.46, 120.41, 118.49, 117.98, 51.76. \text{HRMS (ESI): } m/z\text{ calcd. for } [C_{19}H_{15}NNaO_4, M+Na]^+: 344.0893;\text{ found: 344.0894.}

Methyl 3-(4-bromophenyl)-4-(2-hydroxybenzoyl)-1H-pyrrole-2-carboxylate (3c)

99% yield, \( R_f = 0.2 \), (silica gel, petroleum ether:EtOAc = 5:1), white solid, \text{M.P.} 80-81 \degree C. \( ^{1}H \text{NMR} \) (400 MHz, Chloroform-d) \( \delta \) 11.81 (s, 1H), 9.62 (br, 1H), 7.64 (d, \( J = 7.6 \) Hz, 1H), 7.43 (d, \( J = 7.9 \) Hz, 3H), 7.33 (d, \( J = 2.5 \) Hz, 1H), 7.21 (d, \( J = 8.0 \) Hz, 2H), 6.97 (d, \( J = 8.3 \) Hz, 1H), 6.78 (t, \( J = 7.5 \) Hz, 1H), 3.76 (s, 3H); \( ^{13}\text{C NMR} \) (101 MHz, Chloroform-d) \( \delta \) 195.19, 162.47, 144.50, 137.72, 135.96, 132.70, 131.00, 130.48, 130.31, 129.46, 128.02, 127.76, 127.69, 127.21, 125.48, 124.82, 120.03, 118.56, 117.97, 21.54. \text{HRMS (ESI): } m/z\text{ calcd. for } [C_{24}H_{19}NNaO_4S, M+Na]^+: 440.0927;\text{ found: 440.0926.}

Methyl 4-(2-hydroxybenzoyl)-3-(4-methoxyphenyl)-1H-pyrrole-2-carboxylate (3d)

91% yield, \( R_f = 0.2 \), (silica gel, petroleum ether:EtOAc = 5:1), white solid, \text{M.P.} 65-67 \degree C. \( ^{1}H \text{NMR} \) (400 MHz, Chloroform-d) \( \delta \) 11.93 (s, 1H), 9.68 (br, 1H), 7.64 (dd, \( J = 7.9, 1.3 \) Hz, 1H), 7.40
(t, J = 7.8 Hz, 1H), 7.29 (dd, J = 9.7, 6.0 Hz, 3H), 6.96 (d, J = 8.3 Hz, 1H), 6.84 (d, J = 8.6 Hz, 2H), 6.76 (t, J = 7.6 Hz, 1H), 3.79 (s, 3H), 3.76 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 195.79, 162.53, 161.30, 158.97, 135.78, 132.77, 132.00, 131.43, 126.54, 124.95, 124.22, 120.47, 120.23, 118.55, 117.97, 113.11, 55.13, 51.73. HRMS (ESI): m/z calcd. for [C$_{20}$H$_{17}$NNaO$_5$, M+Na]$^+$: 374.0999; found: 374.0998.

**Methyl 3-(3-chlorophenyl)-4-(2-hydroxybenzoyl)-1H-pyrrole-2-carboxylate (3e)**

98% yield, R$_f$ = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, M.P. 57-59 °C. $^1$H NMR (400 MHz, Chloroform-d) δ 11.80 (s, 1H), 9.69 (br, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 7.8 Hz, 1H), 7.36 – 7.33 (m, 2H), 7.27 – 7.18 (m, 3H), 6.96 (d, J = 8.4 Hz, 1H), 6.79 (t, J = 7.6 Hz, 1H), 3.76 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 195.00, 162.56, 160.96, 135.93, 134.67, 133.33, 132.45, 130.41, 130.27, 128.73, 128.45, 127.58, 126.39, 124.30, 120.78, 120.33, 118.57, 118.13, 51.89. HRMS (ESI): m/z calcd. for [C$_{19}$H$_{14}$ClNNaO$_4$, M+Na]$^+$: 378.0504; found: 378.050.

**Methyl 4-(2-hydroxybenzoyl)-3-(3-methoxyphenyl)-1H-pyrrole-2-carboxylate (3f)**

99% yield, R$_f$ = 0.2, (silica gel, petroleum ether:EtOAc = 4:1), white solid, M.P. 50-52 °C. $^1$H NMR (400 MHz, Chloroform-d) δ 11.89 (s, 1H), 9.77 (br, 1H), 7.62 (dd, J = 7.9, 1.5 Hz, 1H), 7.41 – 7.37 (m, 1H), 7.30 (d, J = 3.2 Hz, 1H), 7.20 (t, J = 7.9 Hz, 1H), 6.95 – 6.89 (m, 3H), 6.82 – 6.80 (m, 1H), 6.74 (t, J = 7.6 Hz, 1H), 3.75 (s, 3H), 3.74 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 195.61, 162.46, 161.21, 158.80, 135.80, 134.08, 132.66, 131.73, 128.52, 126.21, 124.46, 122.81, 120.44, 120.39, 118.50, 117.94, 115.97, 113.11, 55.17, 51.78. HRMS (ESI): m/z calcd. for [C$_{20}$H$_{17}$NClNaO$_5$, M+Na]$^+$: 378.0504; found: 378.050.

**Methyl 3-(2-chlorophenyl)-4-(2-hydroxybenzoyl)-1H-pyrrole-2-carboxylate (3g)**

98% yield, R$_f$ = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, M.P. 163-165 °C. $^1$H NMR (400 MHz, Chloroform-d) δ 11.67 (s, 1H), 9.67 (br, 1H), 7.72 (d, J = 7.6 Hz, 1H), 7.38 (dd, J = 22.9, 14.9 Hz, 4H), 7.25 (s, 2H), 6.95 (d, J = 8.3 Hz, 1H), 6.80 (t, J = 7.4 Hz, 1H), 6.74 (t, J = 7.8 Hz, 1H), 6.96 (d, J = 8.3 Hz, 1H), 6.84 (d, J = 8.6 Hz, 2H), 6.76 (t, J = 7.6 Hz, 1H), 3.79 (s, 3H), 3.76 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 195.79, 162.53, 161.30, 158.97, 135.78, 132.77, 132.00, 131.43, 126.54, 124.95, 124.22, 120.47, 120.23, 118.55, 117.97, 113.11, 55.13, 51.73. HRMS (ESI): m/z calcd. for [C$_{20}$H$_{17}$NNaO$_5$, M+Na]$^+$: 374.0999; found: 374.1001.
3.72 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 194.62, 162.32, 161.02, 135.64, 133.67, 132.54, 132.44, 131.98, 129.04, 128.90, 128.48, 126.40, 126.05, 124.59, 121.50, 120.25, 118.53, 117.99, 51.87. HRMS (ESI): m/z calcd. for [C$_{10}$H$_{14}$ClNNaO$_4$, M+Na]$^+$: 378.0504; found: 378.0501.

Methyl 4-(2-hydroxybenzoyl)-3-(o-tolyl)-1H-pyrrole-2-carboxylate (3h)

98% yield, R$_f$ = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, M.P. 65-66 °C. $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 11.75 (s, 1H), 9.61 (br, 1H), 7.70 (d, $J$ = 7.5 Hz, 1H), 7.40 (dd, $J$ = 15.7, 8.0 Hz, 2H), 7.17 (d, $J$ = 17.6 Hz, 4H), 6.94 (d, $J$ = 8.1 Hz, 1H), 6.81 (t, $J$ = 7.3 Hz, 1H), 3.68 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 194.73, 162.37, 161.27, 136.58, 135.58, 133.08, 132.28, 131.50, 130.02, 129.38, 127.61, 126.67, 124.97, 124.36, 121.08, 120.43, 118.47, 118.07, 51.78, 20.19. HRMS (ESI): m/z calcd. for [C$_{20}$H$_{17}$NNaO$_4$, M+Na]$^+$: 358.1050; found: 358.1051.

Methyl 4-(2-hydroxybenzoyl)-3-(naphthalen-1-yl)-1H-pyrrole-2-carboxylate (3i)

98% yield, R$_f$ = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), pale yellow solid, M.P. 57-59 °C. $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 11.62 (s, 1H), 9.94 (br, 1H), 7.82 (t, $J$ = 8.8 Hz, 2H), 7.17 (d, $J$ = 8.3 Hz, 2H), 7.44 (dd, $J$ = 16.1, 6.6 Hz, 4H), 7.33 (dd, $J$ = 21.2, 12.7 Hz, 2H), 6.87 (d, $J$ = 8.2 Hz, 1H), 6.68 (t, $J$ = 7.5 Hz, 1H), 3.51 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 194.81, 162.19, 161.29, 135.58, 133.08, 132.28, 131.50, 130.02, 129.38, 127.61, 126.67, 124.97, 124.36, 121.08, 120.43, 118.47, 118.07, 51.78, 20.19. HRMS (ESI): m/z calcd. for [C$_{23}$H$_{17}$NNaO$_4$, M+Na]$^+$: 394.1050; found: 394.1047.

Methyl 4-(2-hydroxybenzoyl)-3-(naphthalen-2-yl)-1H-pyrrole-2-carboxylate (3j)

98% yield, R$_f$ = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), yellow solid, M.P. 63-64 °C. $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 11.85 (s, 1H), 9.71 (br, 1H), 7.79 (dd, $J$ = 13.7, 4.6 Hz, 4H), 7.71 (dd, $J$ = 7.9, 1.1 Hz, 1H), 7.48 – 7.43 (m, 3H), 7.38 (dd, $J$ = 13.4, 6.1 Hz, 2H), 6.94 (d, $J$ = 8.3 Hz, 1H), 6.76 (t, $J$ = 7.6 Hz, 1H), 3.72 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 195.41, 162.55, 161.27, 135.80, 132.94, 132.63,
132.60, 132.03, 130.36, 129.17, 128.40, 128.10, 127.65, 126.95, 126.48, 125.96, 125.88, 124.51, 120.76, 120.47, 118.52, 118.05, 51.79. HRMS (ESI): m/z calcd. for [C_{23}H_{17}NNaO_4, M+Na]^+: 394.1050; found: 394.1049.

**Methyl 4-(2-hydroxybenzoyl)-3-ferrocene-1H-pyrrole-2-carboxylate (3k)**

90% yield, R_f = 0.5, (silica gel, petroleum ether:EtOAc = 5:1), white solid, M.P. 58-59 °C. ^1H NMR (400 MHz, Chloroform-d) \( \delta \) 12.41 (s, 1H), 9.49 (br, 1H), 7.63 (dd, \( J = 7.9, 1.2 \) Hz, 1H), 7.45 (dd, \( J = 11.3, 4.2 \) Hz, 1H), 7.11 (s, 1H), 7.02 (d, \( J = 8.3 \) Hz, 1H), 6.79 (t, \( J = 7.6 \) Hz, 1H), 4.74 – 4.73 (m, 2H), 4.20 – 4.19 (m, 2H), 3.94 (s, 5H), 3.89 (s, 3H); ^13C NMR (101 MHz, Chloroform-d) \( \delta \) 197.06, 162.97, 160.75, 136.18, 133.16, 129.73, 125.17, 125.03, 120.68, 120.46, 118.66, 118.19, 71.76, 69.33, 68.07, 51.72. HRMS (ESI): m/z calcd. for [C_{23}H_{19}FeNNaO_4, M+Na]^+: 452.0556; found: 452.0557.

**Methyl 4-(2-hydroxybenzoyl)-3-(thiophen-2-yl)-1H-pyrrole-2-carboxylate (3l)**

99% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, M.P. 107-109 °C. ^1H NMR (400 MHz, Chloroform-d) \( \delta \) 11.92 (s, 1H), 9.65 (br, 1H), 7.58 (dd, \( J = 8.0, 1.4 \) Hz, 1H), 7.41 – 7.37 (m, 1H), 7.31 – 7.27 (m, 2H), 7.07 (dd, \( J = 3.5, 1.0 \) Hz, 1H), 6.96 – 6.94 (m, 2H), 6.76 – 6.72 (m, 1H), 3.81 (s, 3H); ^13C NMR (101 MHz, Chloroform-d) \( \delta \) 195.65, 162.53, 160.87, 135.91, 132.86, 132.61, 129.06, 126.57, 126.49, 125.67, 125.26, 123.55, 120.97, 120.41, 118.54, 117.96, 51.87. HRMS (ESI): m/z calcd. for [C_{17}H_{13}NNaO_4S, M+Na]^+: 350.0457; found: 350.0458.

**Methyl 3-(furan-2-yl)-4-(2-hydroxybenzoyl)-1H-pyrrole-2-carboxylate (3m)**

99% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, M.P. 48-50 °C. ^1H NMR (400 MHz, Chloroform-d) \( \delta \) 12.04 (s, 1H), 9.55 (br, 1H), 7.50 (dd, \( J = 8.0, 1.5 \) Hz, 1H), 7.42 – 7.38 (m, 1H), 7.29 (d, \( J = 3.2 \) Hz, 1H), 7.25 – 7.24 (m, 1H), 6.98 (d, \( J = 8.4 \) Hz, 1H), 6.85 (d, \( J = 3.4 \) Hz, 1H), 6.73 – 6.70 (m, 1H), 6.39 (dd, \( J = 3.3, 1.8 \) Hz, 1H), 3.89 (s, 3H); ^13C NMR (101 MHz, Chloroform-d) \( \delta \) 196.11, 162.46, 160.53, 145.69, 142.28, 135.78, 132.40, 125.24, 124.00, 120.45, 120.31, 119.57, 118.57, 117.93, 111.42, 111.22, 51.94. HRMS (ESI): m/z calcd. for [C_{17}H_{13}NNaO_5, M+Na]^+: 334.0686;
found: 334.0685.

**Methyl 4-(2-hydroxybenzoyl)-3-(1H-indol-3-yl)-1H-pyrrole-2-carboxylate (3n)**

95% yield, R$_f$ = 0.3, (silica gel, petroleum ether:EtOAc = 2:1), orange solid, **M.P.** 232-233 °C. $^1$H NMR (400 MHz, DMSO-d$_6$) δ 12.45 (br, 1H), 11.37 (br, 1H), 11.04 (s, 1H), 7.56 (dd, $J = 7.8$, 1.4 Hz, 1H), 7.39 (s, 1H), 7.37 – 7.36 (m, 2H), 7.30 (d, $J = 8.1$ Hz, 1H), 7.11 (d, $J = 7.9$ Hz, 1H), 6.98 (t, $J = 7.5$ Hz, 1H), 6.74 (t, $J = 7.5$ Hz, 1H), 3.60 (s, 3H); $^{13}$C NMR (101 MHz, DMSO-d$_6$) δ 194.74, 161.11, 160.33, 136.11, 134.92, 132.27, 129.13, 127.56, 124.58, 124.13, 122.77, 120.93, 120.56, 119.44, 119.05, 118.97, 117.43, 111.77, 107.40, 51.49. **HRMS** (ESI): m/z calcd. for [C$_{21}$H$_{16}$N$_2$NaO$_4$, M$+$Na]$^+$: 383.1002; found: 383.1005.

**Methyl 4-(2-hydroxybenzoyl)-3-(pyridin-3-yl)-1H-pyrrole-2-carboxylate (3o)**

81% yield, R$_f$ = 0.1, (silica gel, petroleum ether:EtOAc = 1:1), pale yellow solid, **M.P.** 88-90 °C. $^1$H NMR (400 MHz, Chloroform-d) δ 11.77 (s, 1H), 10.56 (br, 1H), 8.59 (s, 1H), 8.53 (d, $J = 4.3$ Hz, 1H), 7.73 (d, $J = 7.8$ Hz, 1H), 7.67 (d, $J = 7.9$ Hz, 1H), 7.41 (dd, $J = 8.5$, 5.5 Hz, 2H), 7.28 (dd, $J = 7.7$, 5.0 Hz, 1H), 6.95 (d, $J = 8.3$ Hz, 1H), 6.79 (t, $J = 7.6$ Hz, 1H), 3.72 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 194.77, 162.59, 160.90, 150.34, 147.88, 138.06, 135.97, 132.38, 129.46, 127.96, 126.99, 124.18, 122.55, 121.36, 120.26, 118.66, 118.21, 51.87. **HRMS** (ESI): m/z calcd. for [C$_{18}$H$_{14}$N$_2$NaO$_4$, M$+$Na]$^+$: 345.0846; found: 345.0843.

**Methyl 4-(6-hydroxybenzo[1,3]dioxole-5-carbonyl)-3-phenyl-1H-pyrrole-2-carboxylate (3p)**

99% yield, R$_f$ = 0.2, (silica gel, petroleum ether:EtOAc = 4:1), pale yellow solid, **M.P.** 172-173 °C. $^1$H NMR (400 MHz, Chloroform-d) δ 12.82 (s, 1H), 9.60 (br, 1H), 7.34 – 7.27 (m, 6H), 6.95 (s, 1H), 6.42 (s, 1H), 5.90 (s, 2H), 3.75 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 193.88, 162.39, 161.23, 154.05, 140.01, 132.87, 131.63, 130.21, 127.59, 127.42, 125.12, 124.61, 120.07, 112.90, 109.52, 101.76, 98.48, 51.71. **HRMS** (ESI): m/z calcd. for [C$_{20}$H$_{15}$NNaO$_6$, M$+$Na]$^+$: 388.0792; found: 388.0787.
Methyl 4-(2-hydroxy-4-methoxybenzoyl)-3-phenyl-1H-pyrrole-2-carboxylate (3q)

93% yield, R_f = 0.3, (silica gel, petroleum ether:EtOAc = 5:1), white solid, M.P. 61-63 °C. ^1H NMR (400 MHz, Chloroform-d) δ 12.59 (s, 1H), 9.84 (br, 1H), 7.53 (d, J = 8.9 Hz, 1H), 7.35 – 7.24 (m, 6H), 6.41 (d, J = 2.3 Hz, 1H), 6.28 (dd, J = 8.9, 2.4 Hz, 1H), 3.80 (s, 3H), 3.74 (s, 3H); ^13C NMR (101 MHz, Chloroform-d) δ 194.2, 165.8, 165.5, 161.3, 134.5, 132.9, 131.8, 130.2, 127.5, 127.4, 125.6, 124.5, 121.9, 119.7, 51.7. HRMS (ESI): m/z calcd. for [C_{20}H_{17}NNaO_5, M+Na]^+: 374.0999; found: 374.1000.

Methyl 4-(4-bromo-2-hydroxybenzoyl)-3-phenyl-1H-pyrrole-2-carboxylate (3r)

98% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 5:1), white solid, M.P. 64-66 °C. ^1H NMR (400 MHz, Chloroform-d) δ 12.00 (s, 1H), 9.67 (br, 1H), 7.44 (d, J = 8.5 Hz, 1H), 7.30 – 7.4 (m, 6H), 7.12 (d, J = 1.9 Hz, 1H), 6.85 (dd, J = 8.5, 1.9 Hz, 1H), 3.74 (s, 3H); ^13C NMR (101 MHz, Chloroform-d) δ 194.9, 162.9, 161.1, 133.5, 132.6, 131.9, 130.1, 127.6, 127.4, 126.1, 124.2, 121.9, 121.1, 119.1, 51.8. HRMS (ESI): m/z calcd. for [C_{19}H_{14}BrNNaO_4, M+Na]^+: 421.9998; found: 421.9996.

Methyl 4-(2-hydroxy-6-methylbenzoyl)-3-phenyl-1H-pyrrole-2-carboxylate (3s)

90% yield, R_f = 0.2, (silica gel, petroleum ether:EtOAc = 2:1), white solid, M.P. 62-63 °C. ^1H NMR (400 MHz, Chloroform-d) δ 9.71 (br, 1H), 8.60 (s, 1H), 7.30 – 7.20 (m, 6H), 7.09 (t, J = 7.9 Hz, 1H), 6.70 (d, J = 8.2 Hz, 1H), 6.52 (d, J = 7.5 Hz, 1H), 3.70 (s, 3H), 2.14 (s, 3H); ^13C NMR (101 MHz, Chloroform-d) δ 194.8, 161.2, 157.4, 137.6, 137.6, 132.5, 132.2, 131.4, 127.6, 126.1, 124.2, 121.9, 121.1, 114.5, 51.7, 21.7; HRMS (ESI): m/z calcd. for [C_{20}H_{17}NNaO_4, M+Na]^+: 358.1050; found: 358.1053.

Methyl 4-(4-((10-((tert-butyldimethylsilyl)oxy)decyl)oxy)-2-hydroxybenzoyl)-3-phenyl-1H-pyrrole-2-carboxylate (3t)
91% yield, $R_f = 0.2$, (silica gel, petroleum ether:EtOAc = 5:1), colorless oil. $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 12.56 (s, 1H), 9.61 (br, 2H), 7.52 (d, $J = 8.9$ Hz, 1H), 7.35 – 7.26 (m, 6H), 6.38 (d, $J = 2.3$ Hz, 1H), 6.27 (dd, $J = 8.9$, 2.4 Hz, 1H), 3.95 (t, $J = 6.5$ Hz, 2H), 3.74 (s, 3H), 3.60 (t, $J = 6.6$ Hz, 2H), 1.78 – 1.72 (m, 2H), 1.52 – 1.49 (m, 2H), 1.42 (dt, $J = 14.2$, 7.2 Hz, 2H), 1.34 – 1.26 (m, 10H), 0.90 (s, 9H), 0.05 (s, 6H); $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 194.13, 165.61, 165.44, 161.23, 134.40, 132.89, 131.72, 130.21, 127.55, 127.42, 125.30, 124.70, 120.09, 114.19, 107.45, 101.22, 68.36, 63.32, 51.67, 32.86, 29.53, 29.46, 29.40, 28.93, 25.98, 25.91, 25.78, 18.37, -5.26. HRMS (ESI): m/z calcd. for $[\text{C}_{35}\text{H}_{49}\text{NNaO}_6\text{Si}, \text{M+Na}^+]$: 630.3221; found: 630.3218.

**Ethyl 4-(2-hydroxybenzoyl)-3-phenyl-1H-pyrrole-2-carboxylate (3u)**

93% yield, $R_f = 0.2$, (silica gel, petroleum ether: EtOAc = 5:1), white solid, M.P. 53-55 °C. $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 11.90 (s, 1H), 9.74 (br, 1H), 7.65 (d, $J = 8.0$ Hz, 1H), 7.39 (t, $J = 7.8$ Hz, 1H), 7.35 – 7.28 (m, 6H), 6.95 (d, $J = 8.3$ Hz, 1H), 6.76 (t, $J = 7.6$ Hz, 1H), 4.21 (q, $J = 7.1$ Hz, 2H), 1.15 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 194.13, 165.61, 165.44, 161.23, 134.40, 132.89, 131.72, 130.21, 127.55, 127.42, 125.30, 124.70, 120.09, 114.19, 107.45, 101.22, 68.36, 63.32, 51.67, 32.86, 29.53, 29.46, 29.40, 28.93, 25.98, 25.91, 25.78, 18.37, -5.26. HRMS (ESI): m/z calcd. for $[\text{C}_{20}\text{H}_{17}\text{NNaO}_4, \text{M+Na}^+]$: 358.1050; found: 358.1041.

**Methyl 3-oxo-4'-phenyl-4',5'-dihydro-3H-spiro[benzofuran-2,3'-pyrrole]-5'-carboxylate (4)**

Colorless oil, $R_f = 0.2$ (silica gel, petroleum ether: EtOAc = 5:1). 31% yield. $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.60 (d, $J = 7.7$ Hz, 1H), 7.50 (dd, $J = 9.2$, 5.1 Hz, 2H), 7.19 – 7.16 (m, 5H), 7.03 (t, $J = 7.5$ Hz, 1H), 6.91 (d, $J = 8.4$ Hz, 1H), 5.22 (dd, $J = 7.9$, 2.9 Hz, 1H), 4.12 (d, $J = 8.0$ Hz, 1H), 3.77 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 197.47, 171.28, 170.06, 161.65, 138.72, 132.08, 129.21, 128.33, 127.93, 124.53, 122.78, 120.40, 113.27, 98.01, 79.65, 54.38, 52.73; HRMS (ESI): m/z calcd. for $[\text{C}_{19}\text{H}_{15}\text{NNaO}_4, \text{M+Na}^+]$: 344.0893; found: 344.0892.
VII. Deuterium Labelling Experiments

a. Deuterium Labelling of Substrates

\[
\begin{align*}
d^1-1a, \, 86\% \, D & \quad + \quad \text{CN}^-\text{CO}_2\text{Me} & \quad \text{NaOH} \, (20 \text{ mol\%}) & \quad \text{CH}_3\text{OH}, \, 12 \, h, \, RT \\
& \quad \rightarrow & \quad \text{3a}, \, 99\% \, \text{yield}
\end{align*}
\]

\[
\begin{align*}
d^2-2a, \, 99\% \, D & \quad + \quad \text{CN}^-\text{CO}_2\text{Et} & \quad \text{NaOH} \, (20 \text{ mol\%}) & \quad \text{CH}_3\text{CN} \, (\text{anhyd}), \, 12 \, h, \, RT \\
& \quad \rightarrow & \quad \text{3u}, \, 93\% \, \text{yield}
\end{align*}
\]

b. Deuterium Solvents

\[
\begin{align*}
1a & \quad + \quad \text{CN}^-\text{CO}_2\text{Me} & \quad \text{NaOH} \, (20 \text{ mol\%}) & \quad \text{CO}_2\text{MeD}, \, 12 \, h, \, RT \\
& \quad \rightarrow & \quad \text{d}^3-3a, \, 99\% \, \text{yield}
\end{align*}
\]

\[
\begin{align*}
1a & \quad + \quad \text{CN}^-\text{CO}_2\text{Me} & \quad \text{NaOH} \, (20 \text{ mol\%}) & \quad \text{CH}_3\text{CN}, \, \text{D}_2\text{O} \, (3.0 \text{ equiv}) \quad 24 \, h, \, RT \\
& \quad \rightarrow & \quad \text{d}^4-3a, \, 95\% \, \text{yield}
\end{align*}
\]

**Procedure for eq. (1):** To a solution of aurone d\(^1\)-1\(a\) (22.3 mg, 0.1 mmol) in 1.0 mL MeOH was added isocyanatoacetate 2\(a\) (11.9 mg, 0.12 mmol), then a solution of NaOH (1.0 M in MeOH) 20 μL (20 mol%) was added. The reaction was stirred at ambient temperature for 12h. After completion, the solvent was removed under reduced pressure and then purified by flash chromatography on silica gel (hexanes/ethyl acetate = 5:1) to afford the product 3\(a\).

**Procedure for eq. (2):** To a flame-dried flask was added aurone 1\(a\) (22.2 mg, 0.1 mmol), anhydrous MeCN 1.0 mL, and NaOH solid (0.8 mg, 20 mol%), then isocyanatoacetate d\(^2\)-2\(c\) (13.8 mg, 0.12 mmol) was added dropwise, the reaction was stirred under argon atmosphere for 12h at room temperature. After completion, the solvent was removed under reduced pressure and then purified by flash chromatography on silica gel (hexanes/ethyl acetate = 5:1) to afford the product 3\(u\).

**Procedure for eq. (3):** To a solution of aurone 1\(a\) (22.2 mg, 0.1 mmol) in 1.0 mL MeOD was added isocyanatoacetate 2\(a\) (11.9 mg, 0.12 mmol), and then NaOH solid (0.8 mg, 20 mol%) was added. The reaction was stirred at ambient temperature for
12h. After completion, monitoring the deuterium labeling percentage by NMR directly, the pure product was obtained by flash chromatography on silica gel (hexanes/ethyl acetate = 5:1).

**Procedure for eq. (4):** To a flame-dried flask was added aurone 1a (22.2 mg, 0.1 mmol), anhydrous MeCN 1.0 mL, and NaOH solid (0.8 mg, 20 mol%), then 3.0 equivalents of D$_2$O and isocyanacetate d$_2$-2c (13.8 mg, 0.12 mmol) were added sequentially, the reaction was stirred under argon atmosphere for 12h at room temperature. After completion, the solvent was removed under reduced pressure and then purified by flash chromatography on silica gel (hexanes/ethyl acetate = 5:1) to afford the product d$_4$-3a.

### VIII. Synthesis of Chromanone Fused Pyrrole 5

**Procedure A:**[12] To a 50 mL sealed tube was added the phenol derivative 3a (642.6 mg, 2.0 mmol), potassium carbonate (276.4 mg, 2.0 mmol), CuI (38.1 mg, 0.2 mmol), DMF (10 mL) in sequence. This mixture was heated to 120 °C with stirring. After the reaction finished, the mixture was cooled down to ambient temperature, and concentrated in vacuo. This residue was diluted with 50 mL water, extracted with ethyl acetate (10 mLx3), washed with brine (20 mL), dried over anhydrous Na$_2$SO$_4$, filtered and concentrated in vacuo to give the crude product, which was further purified by flash chromatography on silica gel (hexanes/ethyl acetate, 2:1) to afford the product 5 434.2 mg (68% yield).

**Procedure B:** To a 50 mL sealed tube was added the aurone 1a (88.8 mg, 0.4 mmol), sodium hydroxide (32.0 mg, 0.8 mmol), CuI (22.9 mg, 0.12 mmol), DMF (8 mL) and...
isocyanatoacetate 2a (79.2 mg, 0.8 mmol) in sequence. This mixture was heated to 120 °C with stirring. After the reaction finished, the mixture was cooled down to ambient temperature, and concentrated in vacuo. This residue was diluted with water 30 mL, extracted with ethyl acetate (50 mL× 3), washed with brine (20 mL), dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo to give the crude product, which was further purified by flash chromatography on silica gel (hexanes/ethyl acetate = 2:1) to afford the product 5 99.6 mg (78% yield).

**Methyl 4-oxo-3-phenyl-1,4-dihydrochromeno[2,3-b]pyrrole-2-carboxylate (5)**

White solid, M.P. 263-265 °C, Rf = 0.2 (silica gel, petroleum ether: EtOAc = 2 : 1). ¹H NMR (400 MHz, DMSO-d₆) δ 13.34 (br, 1H), 8.03 (t, J = 28.8 Hz, 1H), 7.75 (t, J = 7.6 Hz, 1H), 7.62 (d, J = 8.3 Hz, 1H), 7.46 – 7.42 (m, 3H), 7.34 (s, 3H), 3.65 (s, 3H); ¹³C NMR (101 MHz, DMSO-d₆) δ 172.78, 161.05, 153.99, 151.15, 134.05, 132.56, 131.33, 127.71, 127.65, 127.21, 126.41, 125.16, 123.30, 117.98, 114.73, 105.51, 51.87; HRMS (ESI): m/z calcd. for [C₁₉H₁₃NNaO₄, M+Na]⁺: 342.0737; found: 342.0738.

**IX. Preparation of the Single Crystal Compounds**

**Methyl 4-(2-((4-nitrobenzoyl)oxy)benzoyl)-3-phenyl-1H-pyrrole-2-carboxylate (3a’)**

To a solution of phenol derivative 3a (160.5 mg, 0.5mmol) in dry DCM was added 4-nitrobenzoyl chloride (101.8 mg, 0.55 mmol) in 2 mL DCM dropwise, and then triethylamine (101.2 mg, 1.0 mmol) was added at room temperature. The reaction was stirred at room temperature until the phenol was completed, then quenched with aqueous NH₄Cl solution, the aqueous layer was extracted with CH₂Cl₂ (3×20 mL), the combined organic layers were washed with brine, dried over sodium sulfate and
concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel to afford pure product 3a´ as pale yellow solid. **M.P.** 193-194 °C, R_f = 0.2 (silica gel, petroleum ether: EtOAc = 5 : 1). 81% yield. **¹H NMR** (400 MHz, Chloroform-d) δ 9.58 (br, 1H), 8.27 (d, J = 8.8 Hz, 2H), 8.19 (d, J = 8.8 Hz, 2H), 7.47 (d, J = 7.6 Hz, 1H), 7.43 (td, J = 7.9, 1.4 Hz, 1H), 7.31 (d, J = 3.5 Hz, 1H), 7.21 (ddd, J = 20.9, 9.7, 4.8 Hz, 7H), 3.67 (s, 3H); **¹³C NMR** (101 MHz, Chloroform-d) δ 188.66, 163.11, 161.08, 150.81, 147.95, 134.55, 132.57, 132.33, 131.93, 131.88, 131.23, 130.44, 130.25, 128.30, 127.36, 127.21, 125.91, 125.70, 123.57, 122.65, 120.58, 51.69; **HRMS** (ESI): m/z calcd. for [C_{26}H_{18}N_{2}NaO_{7}, M+Na]^+: 493.1006; found: 493.1005.

**X. X-ray Crystallographic Analysis**

The crystal 3a´ was prepared from a solution of ethyl acetate/hexane at ambient temperature.

![X-ray structure of 3a´](image)

**Figure 1. X-ray structure of 3a´**

**Table 1.** Crystal data and structure refinement for C_{26}H_{18}N_{2}O_{7} (CCDC 1833509)

<table>
<thead>
<tr>
<th>Identification code</th>
<th>WZP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C_{26}H_{18}N_{2}O_{7}</td>
</tr>
<tr>
<td>Formula weight</td>
<td>470.42</td>
</tr>
<tr>
<td>Temperature/K</td>
<td>293(2)</td>
</tr>
</tbody>
</table>
Crystal system triclinic
Space group P-1
a/Å 7.4307(5)
b/Å 10.8091(7)
c/Å 14.3220(8)
α/° 88.506(5)
β/° 89.846(5)
γ/° 83.022(5)
Volume/Å³ 1141.42(12)
Z 2
ρcalc g/cm³ 1.369
μ/mm⁻¹ 0.101
F(000) 488.0
Crystal size/mm³ 0.35 × 0.25 × 0.23
Radiation MoKα (λ = 0.71073)
2Θ range for data collection/° 6.76 to 52.734
Index ranges -9 ≤ h ≤ 9, -13 ≤ k ≤ 12, -16 ≤ l ≤ 17
Reflections collected 8044
Independent reflections 4665 [Rint = 0.0188, Rsigma = 0.0395]
Data/restraints/parameters 4665/0/317
Goodness-of-fit on F² 1.047
Final R indexes [I>=2σ (I)] R₁ = 0.0525, wR₂ = 0.1201
Final R indexes [all data] R₁ = 0.0776, wR₂ = 0.1387
Largest diff. peak/hole / e Å⁻³ 0.19/-0.25

XI. References

XII. NMR Spectra of the Products

1a
S53