Generation of 3-(1H-pyrrol-3-yl)-1H-inden-1-ones via a reaction of 1-(2-alkynylphenyl)-2-enone, 2-isocyanoacetate, with water

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Supporting Information

1. General experimental methods (S2).
2. General experimental procedure and characterization data (S2-S10).
3. $^1$H and $^{13}$C NMR spectra of compound 3 (S11–S44).
General experimental methods:

Unless otherwise stated, all commercial reagents were used as received. All solvents were dried and distilled according to standard procedures. Flash column chromatography was performed using silica gel (60-Å pore size, 32–63μm, standard grade). Analytical thin–layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at ~20 Torr at 25–35°C. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale. ¹H and ¹³C NMR spectra were recorded in CDCl₃ on a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz, respectively. All chemical shift values are quoted in ppm and coupling constants quoted in Hz. High resolution mass spectrometry (HRMS) spectra were obtained on a micrOTOF II Instrument.

General procedure of the silver(I)-catalyzed tandem reaction of the reaction of 1-(2-alkynylphenyl)-2-enone 1 with 2-isocyanoacetate 2

Silver triflate (0.02 mmol, 10 mol %), 2-isocyanoacetate 2 (0.24 mmol, 1.2 equiv), and DBU (0.1 mmol, 0.5 equiv) were added to a solution of 1-(2-alkynylphenyl)-2-enone 1 (0.20 mmol) in CH₃CN (1.0 mL). The mixture was stirred at 110 °C in a sealed tube for 4~6 hours. After completion of reaction as indicated by TLC, the mixture was purified by flash column chromatograph (EtOAc/n-hexane, 1:5) to give the desired product 3.
Ethyl 4-(1-oxo-2-phenyl-1H-inden-3-yl)-3-p-tolyl-1H-pyrrole-2-carboxylate (3a): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.70 (s, 1H), 7.45 (d, $J = 6.0$ Hz, 1H), 7.13-7.20 (m, 5H), 7.02-7.06 (m, 3H), 6.94 (d, $J = 6.8$ Hz, 2H), 6.83-6.88 (m, 3H), 4.19-4.21 (m, 2H), 2.22 (s, 3H), 1.18 (t, $J = 6.4$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 196.5, 161.0, 150.2, 145.2, 136.4, 133.3, 133.1, 131.4, 131.0, 130.8, 130.2, 129.7, 129.4, 128.6, 128.0, 127.9, 127.8, 127.2, 122.3, 121.3, 120.2, 117.7, 60.6, 21.2, 14.2; HRMS (ESI) calcd for C$_{29}$H$_{23}$NO$_3$: 434.1756 (M + H$^+$), found: 434.1737.

tert-Butyl 4-(1-oxo-2-phenyl-1H-inden-3-yl)-3-p-tolyl-1H-pyrrole-2-carboxylate (3b): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.72 (s, 1H), 7.45 (d, $J = 6.4$ Hz, 1H), 7.14-7.24 (m, 5H), 7.02-7.06 (m, 3H), 6.82-6.91 (m, 5H), 2.22 (s, 3H), 1.39 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$196.5, 160.8, 150.3, 145.4, 136.1, 133.2, 133.0, 131.5, 130.8, 130.6, 130.2, 129.8, 129.4, 128.6, 127.9, 127.8, 127.2, 122.3, 121.7, 121.6, 121.3, 117.6, 81.7, 28.3, 21.2; HRMS (ESI) calcd for C$_{37}$H$_{21}$NO$_3$: 462.2069 (M + H$^+$), found: 462.2072.

Ethyl 4-(1-oxo-2-p-tolyl-1H-inden-3-yl)-3-p-tolyl-1H-pyrrole-2-carboxylate (3c): $^1$H
NMR (400 MHz, CDCl$_3$) $\delta$ 9.53 (s, 1H), 7.44 (d, $J = 6.4$ Hz, 1H), 7.13-7.17 (m, 2H), 6.96-6.99 (m, 6H), 6.87 (d, $J = 7.2$ Hz, 2H), 6.80 (d, $J = 6.4$ Hz, 2H), 4.21 (d, $J = 6.8$ Hz, 2H), 2.29 (s, 3H), 2.23 (s, 3H), 1.20 (t, $J = 6.8$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 196.7, 160.9, 149.6, 145.3, 137.1, 136.5, 133.3, 133.2, 130.9, 130.7, 130.3, 129.7, 129.3, 128.6, 128.4, 128.0, 122.2, 121.3, 121.2, 120.1, 117.9, 60.6, 21.4, 21.2, 14.2; HRMS (ESI) calcd for C$_{30}$H$_{25}$NO$_3$: 448.1913 (M + H$^+$), found: 448.1911.

Ethyl

4-(2-(4-methoxyphenyl)-1-oxo-1H-inden-3-yl)-3-p-tolyl-1H-pyrrole-2-carboxylate (3d): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.62 (s, 1H), 7.43 (d, $J = 6.4$ Hz, 1H), 7.12-7.19 (m, 3H), 7.04 (d, $J = 7.2$ Hz, 2H), 6.98 (d, $J = 6.8$ Hz, 2H), 6.82-6.87 (m, 3H), 6.69 (d, $J = 8.0$ Hz, 2H), 4.21 (d, $J = 6.8$ Hz, 2H), 3.77 (s, 3H), 2.23 (s, 3H), 1.19 (t, $J = 6.8$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 197.0, 161.0, 159.0, 148.8, 145.5, 136.5, 133.3, 132.8, 130.9, 130.8, 130.7, 130.3, 129.7, 128.3, 128.0, 123.9, 122.3, 122.2, 121.0, 120.1, 117.9, 60.6, 55.3, 21.2, 14.2; HRMS (ESI) calcd for C$_{30}$H$_{25}$NO$_4$: 464.1862 (M + H$^+$), found: 464.1854.

Ethyl

4-(2-(4-chlorophenyl)-1-oxo-1H-inden-3-yl)-3-p-tolyl-1H-pyrrole-2-carboxylate (3e): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.52 (s, 1H), 7.46-7.48 (d, $J = 6.8$ Hz, 1H), 7.19-7.27 (m, 2H), 7.13 (s, 1H), 7.06 (d, $J = 7.2$ Hz, 2H), 6.98 (d, $J = 6.8$ Hz, 1H), 6.91 (d, $J = 6.8$ Hz, 2H), 6.85-6.88 (m, 4H), 4.21 (d, $J = 6.8$ Hz, 2H), 2.23 (s, 3H), 1.18 (t, $J = 6.8$ Hz, 2H), 2.23 (s, 3H), 1.18 (t, $J = 6.8$ Hz, 2H).
Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 196.1, 160.8, 145.0, 136.5, 133.4, 133.1, 130.8, 130.7, 130.6, 129.9, 129.8, 128.9, 128.0, 127.9, 127.8, 122.5, 122.1, 122.0, 121.2, 120.5, 117.4, 60.7, 21.2, 14.2; HRMS (ESI) calcd for C$_{29}$H$_{22}$ClNO$_3$: 468.1366 (M + H$^+$), found: 468.1352.

Ethyl 3-(4-methoxyphenyl)-4-(1-oxo-2-phenyl-1H-inden-3-yl)-1H-pyrrole-2-carboxylate (3f): $^1$H NMR (400 MHz, CDCl$_3$) δ 9.63 (s, 1H), 7.46 (d, $J = 6.4$ Hz, 1H), 7.13-7.24 (m, 5H), 7.04-7.06 (m, 3H), 6.97 (d, $J = 7.6$ Hz, 2H), 6.88 (d, $J = 6.8$ Hz, 1H), 6.59 (d, $J = 7.6$ Hz, 2H), 4.20 (d, $J = 6.8$ Hz, 2H), 3.72 (s, 3H), 1.19 (t, $J = 6.8$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 196.5, 161.0, 158.6, 150.1, 145.2, 133.3, 131.4, 131.0, 130.8, 130.6, 129.4, 128.6, 127.8, 127.3, 125.7, 122.4, 122.3, 121.2, 120.1, 117.7, 112.9, 60.6, 55.2, 14.2; HRMS (ESI) calcd for C$_{29}$H$_{23}$NO$_4$: 450.1705 (M + H$^+$), found: 450.1686.

Ethyl 4-(1-oxo-2-phenyl-1H-inden-3-yl)-3-phenyl-1H-pyrrole-2-carboxylate (3g): $^1$H NMR (400 MHz, CDCl$_3$) δ 9.66 (s, 1H), 7.46 (d, $J = 6.4$ Hz, 1H), 7.13-7.24 (m, 5H), 7.04-7.10 (m, 8H), 6.88 (d, $J = 6.8$ Hz, 1H), 4.19 (d, $J = 6.8$ Hz, 2H), 1.16 (t, $J = 6.8$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 196.4, 161.0, 149.9, 145.2, 133.2, 131.3, 130.8, 130.7, 129.9, 129.4, 129.3, 128.7, 127.9, 127.2, 126.8, 122.4, 122.3, 121.2, 120.4, 119.4, 118.6, 117.7, 60.7, 14.1; HRMS (ESI) calcd for C$_{28}$H$_{31}$NO$_3$: 420.1600 (M + H$^+$), found: 420.1586.
Ethyl

3-(4-chlorophenyl)-4-(1-oxo-2-phenyl-1H-inden-3-yl)-1H-pyrrole-2-carboxylate (3h):
$^1{H}$ NMR (400 MHz, CDCl$_3$) $\delta$ 9.80 (s, 1H), 7.49 (d, $J = 6.4$ Hz, 1H), 7.30 (t, $J = 6.8$ Hz, 1H), 7.22 (t, $J = 7.2$ Hz, 1H), 7.11-7.16 (m, 4H), 6.95-7.01 (m, 5H), 6.84 (d, $J = 7.2$ Hz, 2H), 4.19 (d, $J = 6.8$ Hz, 2H), 1.16 (t, $J = 6.8$ Hz, 3H); $^{13}{C}$ NMR (100 MHz, CDCl$_3$) $\delta$ 196.2, 160.8, 149.1, 145.1, 133.4, 133.1, 132.7, 131.6, 131.3, 131.0, 130.8, 129.5, 129.3, 128.9, 127.8, 127.4, 122.6, 122.4, 120.9, 120.5, 117.5, 60.8, 14.1; HRMS (ESI) calcd for C$_{28}$H$_{20}$ClNO$_3$: 454.1210 (M + H$^+$), found: 454.1194.

Ethyl

4-(1-oxo-2-phenyl-1H-inden-3-yl)-3-(4-(trifluoromethyl)phenyl)-1H-pyrrole-2-carboxylate (3i):
$^1{H}$ NMR (400 MHz, CDCl$_3$) $\delta$ 9.69 (s, 1H), 7.51 (d, $J = 6.8$ Hz, 1H), 7.34 (t, $J = 7.2$ Hz, 1H), 7.20-7.27 (m, 4H), 7.03-7.10 (m, 4H), 6.94 (d, $J = 7.6$ Hz, 2H), 6.81 (d, $J = 7.6$ Hz, 2H), 4.17 (d, $J = 6.8$ Hz, 2H), 1.13 (t, $J = 6.8$ Hz, 3H); $^{13}{C}$ NMR (100 MHz, CDCl$_3$) $\delta$ 196.0, 160.6, 148.5, 145.1, 136.8, 133.4, 133.2, 131.1, 130.7, 130.0, 129.1, 129.0, 128.3, 127.9, 127.2, 125.8, 124.0 (f, $^1{J}_{CF} = 2.8$Hz), 122.8, 122.3, 120.8, 120.7, 117.6, 60.9, 14.0; HRMS (ESI) calcd for C$_{29}$H$_{20}$F$_3$NO$_3$: 488.1474 (M + H$^+$), found: 488.1451.
Ethyl 4-(1-oxo-2-phenyl-1H-inden-3-yl)-3-(thiophen-2-yl)-1H-pyrrole-2-carboxylate (3j): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.59 (s, 1H), 7.47 (d, $J = 5.6$ Hz, 1H), 7.13-7.24 (m, 8H), 6.90-6.96 (m, 2H), 6.76-6.80 (m, 2H), 4.28 (d, $J = 7.2$ Hz, 2H), 1.27 (t, $J = 6.8$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 196.5, 160.6, 150.1, 145.3, 134.1, 133.6, 133.4, 131.2, 130.5, 129.6, 128.6, 128.5, 128.0, 127.5, 126.5, 126.2, 123.0, 122.4, 122.1, 121.1, 120.5, 118.6, 60.9, 14.2; HRMS (ESI) calcd for C$_{26}$H$_{19}$NO$_3$S: 426.1164 (M + H$^+$), found: 426.1140.

Ethyl 3-(naphthalen-1-yl)-4-(1-oxo-2-phenyl-1H-inden-3-yl)-1H-pyrrole-2-carboxylate (3k): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.65 (s, 1H), 7.68 (d, $J = 7.6$ Hz, 1H), 7.59 (d, $J = 8.0$ Hz, 1H), 7.53 (d, $J = 8.8$ Hz, 1H), 7.37-7.39 (m, 1H), 7.24-7.30 (m, 2H), 7.09-7.13 (m, 4H), 6.87-6.99 (m, 7H), 3.89 (d, $J = 6.8$ Hz, 2H), 0.61 (t, $J = 6.8$ Hz, 3H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 196.1, 160.5, 151.3, 145.4, 134.2, 133.1, 132.7, 132.3, 132.0, 131.5, 130.1, 129.4, 129.2, 128.2, 128.1, 127.5, 127.3, 126.2, 125.4, 125.2, 124.7, 122.3, 121.8, 121.6, 117.3, 59.9, 13.8; HRMS (ESI) calcd for C$_{32}$H$_{23}$NO$_3$: 470.1756 (M + H$^+$), found: 470.1734.
Ethyl 4-(6-fluoro-1-oxo-2-phenyl-1H-inden-3-yl)-3-p-tolyl-1H-pyrrole-2-carboxylate (3l): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.58 (s, 1H), 7.10-7.15 (m, 6H), 6.98-7.00 (m, 3H), 6.74-6.89 (m, 4H), 4.22 (m, 2H), 2.24 (s, 3H), 1.19 (t, $J = 6.4$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 194.8, 163.4 (d, $^1$J$_{CF}$ = 247.9 Hz), 160.9, 150.4, 140.4, 136.7, 133.4, 133.1 (d, $^3$J$_{CF}$ = 7.6 Hz), 131.1, 130.8, 130.1, 129.7, 129.4, 128.1, 127.9, 127.4, 122.5, 122.4 (d, $^3$J$_{CF}$ = 10.0 Hz), 120.2, 118.4 (d, $^2$J$_{CF}$ = 22.9 Hz), 117.6, 110.9 (d, $^2$J$_{CF}$ = 24.8 Hz), 60.7, 21.2, 14.2; HRMS (ESI) calcd for C$_{29}$H$_{22}$FNO$_3$: 452.1662 (M + H$^+$), found: 452.1633.

Ethyl 4-(5-methyl-1-oxo-2-phenyl-1H-inden-3-yl)-3-p-tolyl-1H-pyrrole-2-carboxylate (3m): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.72 (s, 1H), 7.35 (d, $J = 6.8$ Hz, 1H), 7.02-7.13 (m, 6H), 6.94-6.96 (m, 3H), 6.86 (d, $J = 8.0$ Hz, 2H), 6.68 (s, 1H), 4.20 (d, $J = 6.4$ Hz, 2H), 2.24 (s, 3H), 2.23 (s, 3H), 1.19 (t, $J = 6.8$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 196.3, 161.0, 149.7, 145.6, 144.1, 136.4, 133.5, 131.5, 131.0, 130.3, 129.8, 129.4, 128.6, 128.4, 128.0, 127.8, 127.2, 122.7, 122.4, 120.1, 117.8, 60.6, 21.9, 21.2, 14.2; HRMS (ESI) calcd for C$_{30}$H$_{25}$NO$_3$: 448.1913 (M + H$^+$), found: 448.1884.

Ethyl 4-(5-fluoro-1-oxo-2-phenyl-1H-inden-3-yl)-3-p-tolyl-1H-pyrrole-2-carboxylate (3n): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.70 (s, 1H), 7.43 (t, $J = 5.2$ Hz, 1H), 7.09-7.15 (m, 5H), 6.95-6.99 (m, 3H), 6.87 (d, $J = 7.2$ Hz, 2H), 6.79 (t, $J = 8.4$ Hz, 1H), 6.56 (d, $J = 8.4$ Hz, 1H), 4.21 (d, $J = 7.2$ Hz, 2H), 2.24 (s, 3H), 1.19 (t, $J = 6.4$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 194.8, 166.5 (d, $^1$J$_{CF}$ = 251.7 Hz), 160.9, 148.7 (d, $^3$J$_{CF}$ =
(9.5Hz), 148.1, 136.6, 134.5, 131.0, 130.8, 130.1, 129.7, 129.4, 128.1, 127.9, 127.6, 126.5 (d, \(^4J_{CF} = 2.9\) Hz), 124.1 (d, \(^3J_{CF} = 8.6\) Hz), 122.2 (d, \(^4J_{CF} = 1.9\) Hz), 120.3, 117.3, 114.1 (d, \(^2J_{CF} = 22.9\) Hz), 110.2 (d, \(^2J_{CF} = 24.8\) Hz), 60.7, 21.2, 14.2; HRMS (ESI) calcd for C\(_{29}\)H\(_{22}\)FNO\(_3\): 452.1662 (M + H\(^+\)), found: 452.1643.

![Chemical structure](image)

Ethyl 4-(5-chloro-1-oxo-2-phenyl-1H-inden-3-yl)-3-p-tolyl-1H-pyrrole-2-carboxylate (3o): \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.72 (s, 1H), 7.37 (d, \(J = 7.2\) Hz, 1H), 7.08-7.15 (m, 6H), 7.01 (s, 1H), 6.94 (d, \(J = 7.2\) Hz, 2H), 6.87 (d, \(J = 7.6\) Hz, 2H), 6.82 (s, 1H), 4.21 (d, \(J = 7.2\) Hz, 2H), 2.24 (s, 3H), 1.19 (t, \(J = 6.4\) Hz, 3H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 195.0, 160.9, 148.9, 147.2, 139.5, 136.7, 134.2, 131.0, 130.8, 130.1, 129.7, 129.4, 128.9, 128.1, 128.0, 127.9, 127.6, 123.2, 122.4, 122.1, 120.3, 117.2, 60.7, 21.2, 14.2; HRMS (ESI) calcd for C\(_{30}\)H\(_{22}\)ClNO\(_3\): 468.1366 (M + H\(^+\)), found: 468.1342.

![Chemical structure](image)

Ethyl 4-(6-methoxy-1-oxo-2-phenyl-1H-inden-3-yl)-3-p-tolyl-1H-pyrrole-2-carboxylate (3p): \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.65 (s, 1H), 7.06-7.12 (m, 6H), 6.95-7.00 (m, 3H), 6.86 (d, \(J = 7.2\) Hz, 2H), 6.73 (d, \(J = 7.6\) Hz, 1H), 6.62 (d, \(J = 7.6\) Hz, 1H), 4.21 (d, \(J = 6.4\) Hz, 2H), 3.78 (s, 3H), 2.24 (s, 3H), 1.19 (t, \(J = 6.4\) Hz, 3H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 195.0, 160.9, 148.9, 147.2, 139.5, 136.7, 134.2, 131.0, 130.8, 130.1, 129.7, 129.4, 128.9, 128.1, 128.0, 127.9, 127.6, 123.2, 122.4, 122.1, 120.3, 117.2, 60.7, 21.2, 14.2; HRMS (ESI) calcd for C\(_{30}\)H\(_{25}\)NO\(_4\): 464.1862 (M + H\(^+\)), found: 464.1842.
Ethyl 4-(2-(phenylethynyl)benzoyl)-3-p-tolyl-2,3-dihydro-1H-pyrrole-2-carboxylate (B1): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.52 (d, $J = 6.8$ Hz, 1H), 7.23-7.34 (m, 10H), 7.08 (d, $J = 6.8$ Hz, 1H), 6.91 (d, $J = 7.6$ Hz, 2H), 5.39 (s, 1H), 4.68 (d, $J = 4.4$ Hz, 1H), 4.19-4.22 (m, 3H), 2.22 (s, 1H), 1.28 (t, $J = 6.8$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 189.1, 172.1, 153.5, 143.7, 140.2, 136.2, 132.7, 131.9, 129.4, 128.7, 128.3, 128.1, 127.9, 127.6, 127.0, 123.1, 120.6, 118.1, 93.0, 87.8, 69.7, 61.9, 49.3, 21.1, 14.2; HRMS (ESI) calcd for C$_{29}$H$_{26}$NO$_3$: 436.1907 (M + H$^+$), found: 436.1906.
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