Palladium-Catalyzed Reaction of 2-Alkynylhalobenzene with 2-Alkynylbenzamide: An Efficient Approach to Indeno[1,2-c]azepin-3(2H)-ones

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Supporting Information

1. General experimental methods (S2).
2. General experimental procedure and characterization data (S2-S9).
3. $^1$H and $^{13}$C NMR spectra of compound 3 (S10-S51).
4. X-ray ORTEP illustration of compound 3a (S52)
General experimental methods:

All reactions were performed in reaction tubes under nitrogen atmosphere. Flash column chromatography was performed using silica gel (60-Å pore size, 32–63 µm, 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 (house vacuum) at 25–35°C. Commercial reagents and solvents were used as received. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale.

General procedure for the synthesis of indeno[1,2-c]azepin-3(2H)-ones via a Pd-catalyzed reaction of 2-alkynylbromobenzene 1 with 2-alkynylbenzamide 2.

2-Alkynylhalobenzene (0.24 mmol) was added to a mixture of Pd(OAc)₂ (0.01 mmol, 5 mol%), PCy₃ or PPh₃ (0.02 mmol, 10 mol%), K₂CO₃ (0.4 mmol), and 2-alkynylbenzamide (0.20 mmol) in 1,4-dioxane (2.0 mL). The reaction was stirred under reflux conditions. After completion of the reaction as indicated by TLC (usually 3-6 hours), the reaction was cooled and the mixture was purified immediately by flash chromatography on silica gel to give products 3.
7,12-Diphenylbenzo[\textit{c}]{\textit{inden}}o\textit{[2,1-\textit{e}]}azepin-5(6\textit{H})-one 3\textit{a}. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.21 (d, $J = 8.0$ Hz, 1H), 7.94 (br, 1H), 7.63-7.59 (m, 5H), 7.47-7.33 (m, 7H), 7.27 (t, $J = 7.8$ Hz, 1H), 7.19-7.14 (m, 2H), 6.89 (t, $J = 8.0$ Hz, 1H), 6.08 (d, $J = 8.0$ Hz, 1H). $^{13}$C NMR (100 MHz) $\delta$ 168.0, 140.9, 140.2, 138.9, 137.6, 136.4, 135.2, 134.8, 132.7, 132.3, 131.9, 130.2, 129.8, 129.7, 129.0, 128.5, 127.6, 127.1, 125.9, 124.8, 122.2, 121.4, 120.1. HRMS (ESI) calculated for C$_{29}$H$_{19}$NO [M+Na]$^+$ requires 420.1364, found 420.1369.

7-(4-Methoxyphenyl)-12-phenylbenzo[\textit{c}]{\textit{inden}}o\textit{[2,1-\textit{e}]}azepin-5(6\textit{H})-one 3\textit{b}. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.22 (d, $J = 7.6$ Hz, 1H), 7.88 (br, 1H), 7.51-7.49 (m, 2H), 7.46-7.35 (m, 7H), 7.9-7.25 (m, 1H), 7.20-7.16 (m, 2H), 7.12-7.09 (m, 2H), 6.93 (t, $J = 7.6$ Hz, 1H), 6.23 (d, $J = 8.0$ Hz, 1H), 3.94 (s, 3H). $^{13}$C NMR (100 MHz) $\delta$ 168.0, 160.9, 147.3, 140.8, 139.9, 139.1, 136.5, 134.8, 132.7, 132.2, 131.8, 130.0, 129.9, 129.8, 129.7, 129.0, 127.6, 127.1, 125.8, 124.9, 122.3, 121.4, 120.1, 114.9, 55.5. HRMS (ESI) calculated for C$_{30}$H$_{21}$NO$_2$ [M+H]$^+$ requires 428.1651, found 428.1648.

12-Phenyl-7-(\textit{p}-tolyl)benzo[\textit{c}]{\textit{inden}}o\textit{[2,1-\textit{e}]}azepin-5(6\textit{H})-one 3\textit{c}. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.24 (d, $J = 7.2$ Hz, 1H), 7.77 (br, 1H), 7.47-7.27 (m, 11H), 7.28 (t, $J = 7.2$ Hz, 1H), 7.20-7.16 (m, 2H), 6.92 (t, $J = 7.6$ Hz, 1H), 6.19 (d, $J = 8.0$ Hz, 1H), 2.52 (s, 3H). $^{13}$C NMR (100 MHz) $\delta$ 168.0, 147.3, 140.9, 140.4, 140.0, 139.2, 136.5, 135.3, 134.9,
134.7, 132.8, 132.3, 131.9, 130.4, 129.9, 129.0, 128.4, 127.6, 127.1, 125.8, 124.8, 121.4, 120.1, 21.6. HRMS (ESI) calculated for C_{30}H_{21}NO [M+H]^+ requires 412.1701, found 412.1703.

![Structure](https://example.com/structure.png)

7-(4-Chlorophenyl)-12-phenylbenzo[c]indeno[2,1-e]azepin-5(6H)-one 3d. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.22 (d, $J$ = 8.0 Hz, 1H), 7.78 (br, 1H), 7.61-7.51 (m, 4H), 7.45-7.40 (m, 6H), 7.35-7.27 (m, 2H), 7.23-7.17 (m, 2H), 6.95 (t, $J$ = 7.2 Hz, 1H), 6.16 (d, $J$ = 8.0 Hz, 1H). $^{13}$C NMR (100 MHz) $\delta$ 168.0, 141.1, 140.6, 137.4, 136.4, 136.2, 135.9, 135.0, 134.7, 132.7, 132.3, 132.0, 131.8, 130.2, 130.1, 130.0, 129.8, 129.7, 129.1, 127.8, 127.2, 126.2, 125.0, 121.3, 120.3. HRMS (ESI) calculated for C$_{29}$H$_{18}$ClNO [M+Na]$^+$ requires 454.0975, found 454.0983.

![Structure](https://example.com/structure.png)

7-Butyl-12-phenylbenzo[c]indeno[2,1-e]azepin-5(6H)-one 3e. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.40 (br, 1H), 8.25-8.23 (m, 1H), 7.72-7.70 (m, 1H), 7.53-7.51 (m, 1H), 7.46-7.40 (m, 4H), 7.37-7.31 (m, 3H), 7.27-7.24 (m, 2H), 7.14-7.10 (m, 1H), 3.02 (t, $J$ = 8.4 Hz, 2H), 1.94-1.90 (m, 2H), 1.66-1.60 (m, 2H), 1.07-1.03 (t, $J$ = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz) $\delta$ 169.0, 147.4, 141.2, 141.0, 136.4, 135.2, 134.9, 132.9, 132.6, 131.9, 131.8, 130.0, 129.4, 128.9, 127.5, 126.9, 125.7, 125.2, 121.7, 121.5, 120.6, 35.9, 30.7, 22.8, 13.9. HRMS (ESI) calculated for C$_{27}$H$_{23}$NO [M+H]$^+$ requires 378.1858, found 378.1865.
9-Methyl-7,12-diphenylbenzo[c]indenol2,1-e]azepin-5(6H)-one 3f. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.25 (d, $J = 8.0$ Hz, 1H), 7.70 (br, 1H), 7.64-7.55 (m, 5H), 7.47-7.41 (m, 4H), 7.39-7.32 (m, 2H), 7.29-7.27 (m, 2H), 7.17-7.15 (m, 1H), 7.00 (d, $J = 8.0$ Hz, 1H), 5.83 (s, 1H), 2.08 (s, 3H). $^{13}$C NMR (100 MHz) $\delta$ 168.0, 138.7, 138.4 137.7, 136.6, 134.5, 132.7, 132.3, 131.9, 130.1, 129.8, 129.6, 129.0, 128.6, 127.6, 126.9, 126.8, 122.2, 119.8, 21.8. HRMS (ESI) calculated for C$_{30}$H$_{21}$NO [M+Na]$^+$ requires 434.1521, found 434.1527.

9-Chloro-7,12-diphenylbenzo[c]indenol2,1-e]azepin-5(6H)-one 3g. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.26 (d, $J = 7.6$ Hz, 1H), 7.75 (br, 1H), 7.68-7.62 (m, 3H), 7.58-7.56 (m, 2H), 7.45-7.43 (m, 5H), 7.35-7.29 (m, 3H), 7.20-7.12 (m, 2H), 5.95 (s, 1H). $^{13}$C NMR (100 MHz) $\delta$ 132.7, 132.5, 132.1, 130.6, 129.9, 129.8, 129.6, 128.4, 128.9, 127.4, 125.8, 121.6, 120.9. HRMS (ESI) calculated for C$_{28}$H$_{18}$ClNO [M+H]$^+$ requires 432.1155, found 432.1178.

12-(4-Methoxyphenyl)-7-phenylbenzo[c]indenol2,1-e]azepin-5(6H)-one 3h. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.25(dd, $J = 7.6$, 1.2 Hz, 1H), 7.69 (br, 1H), 7.63-7.55 (m, 5H), 7.43-7.39 (m, 4H), 7.31-7.29 (m, 1H), 7.22-7.17 (m, 2H), 6.99-6.90 (m, 2H), 6.88 (t, $J = 7.6$ Hz, 1H), 6.08 (d, $J = 8.0$ Hz, 1H), 3.88 (s, 3H). $^{13}$C NMR (100 MHz) $\delta$ 168.1, 137.7, 132.6, 132.3, 131.9, 131.0, 130.2, 129.7, 128.5, 127.0, 125.9, 124.8, 121.4, 120.2, 114.5. HRMS (ESI) calculated for C$_{30}$H$_{21}$NO$_2$ [M+Na]$^+$ requires 450.1470, found 450.1485.
7-Phenyl-12-(p-tolyl)benzo[c]indeno[2,1-e]azepin-5(6H)-one 3i. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.25 (d, $J = 7.6$ Hz, 1H), 7.72 (br, 1H), 7.63-7.55 (m, 5H), 7.42-7.34 (m, 4H), 7.31-7.23 (m, 3H), 7.20-7.16 (m, 2H), 6.88 (t, $J = 7.6$ Hz, 1H), 6.08 (d, $J = 7.6$ Hz, 1H), 2.43 (s, 3H). $^{13}$C NMR (100 MHz) $\delta$ 168.0, 141.1, 140.3, 138.5, 137.6, 137.4, 135.2, 135.0, 133.3, 132.7, 132.3, 131.9, 130.2, 129.8, 129.73, 129.70, 128.5, 127.0, 125.9, 124.8, 121.3, 120.2, 21.4. HRMS (ESI) calculated for C$_{30}$H$_{21}$NO [M+H]$^+$ requires 412.1701, found 412.1715.

12-(4-Chlorophenyl)-7-phenylbenzo[c]indeno[2,1-e]azepin-5(6H)-one 3j. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.26 (d, $J = 7.6$ Hz, 1H), 7.78 (br, 1H), 7.63-7.56 (m, 4H), 7.46-7.41 (m, 5H), 7.37-7.31 (m, 4H), 7.25-7.17 (m, 1H), 6.90 (t, $J = 7.6$ Hz, 1H), 6.09 (d, $J = 8.0$ Hz, 1H). $^{13}$C NMR (100 MHz) $\delta$ 167.9, 140.5, 139.3, 138.7, 137.5, 135.2, 134.9, 134.5, 133.6, 133.4, 132.7, 132.4, 132.1, 131.2, 130.3, 129.9, 129.8, 129.4, 128.9, 128.5, 127.4, 126.0, 125.0, 121.4, 119.9. HRMS (ESI) calculated for C$_{29}$H$_{18}$ClNO [M+H]$^+$ requires 432.1155, found 432.1138.

12-butyl-7-phenylbenzo[c]indeno[2,1-e]azepin-5(6H)-one 3k. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.32 (d, $J = 8.0$ Hz, 1H), 7.73-7.71 (m, 1H), 7.66-7.62 (m, 2H), 7.60-7.51 (m, 5H), 7.48-7.44 (m, 2H), 7.24-7.20 (m, 1H), 6.85 (t, $J = 7.6$ Hz, 1H), 6.02 (d, $J = 8.0$ Hz,
1H), 2.99 (t, J = 8.0 Hz, 2H), 1.84-1.80 (m, 2H), 1.54-1.48 (m, 2H), 0.99 (t, J = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz) δ 167.9, 147.3, 141.4, 140.6, 137.7, 136.8, 135.3, 135.2, 132.5, 132.46, 132.43, 132.1, 130.7, 130.0, 129.6, 128.7, 127.1, 124.4, 125.6, 121.1, 119.2, 31.5, 27.3, 23.3, 13.9. HRMS (ESI) calculated for C$_{27}$H$_{23}$NO [M+H]$^+$ requires 378.1858, found 378.1827.

3-Methoxy-7,12-diphenylbenzo[c]inden[2,1-e]azepin-5(6H)-one 3l. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.90 (s, 1H), 7.74 (br, 1H), 7.61-7.58 (m, 5H), 7.45-7.37 (m, 6H), 7.30-7.25 (m, 1H), 7.17 (d, J = 7.6 Hz, 1H), 6.87 (t, J = 7.6 Hz, 1H), 6.75 (dd, J = 8.8, 2.4 Hz, 1H), 6.07 (d, J = 7.6 Hz, 1H), 3.85 (s, 3H). $^{13}$C NMR (100 MHz) δ 167.6, 158.3, 147.3, 141.2, 138.6, 138.3, 137.6, 136.6, 134.9, 134.4, 131.7, 130.8, 130.2, 129.8, 129.7, 129.0, 128.6, 127.5, 125.9, 124.5, 122.5, 121.4, 120.2, 119.8, 114.2, 55.5. HRMS (ESI) calculated for C$_{30}$H$_{21}$NO$_2$ [M+H]$^+$ requires 428.1651, found 428.1623.

3-Fluoro-7,12-diphenylbenzo[c]inden[2,1-e]azepin-5(6H)-one 3m. $^1$H NMR (400 MHz, CDCl$_3$): δ 8.07 (br, 1H), 7.87 (dd, J = 10, 2.8 Hz, 1H), 7.65-7.57 (m, 5H), 7.45-7.44 (m, 4H), 7.40-7.38 (m, 2H), 7.37-7.32 (m, 1H), 7.18 (t, J = 7.2 Hz, 1H), 6.91-6.87 (m, 2H), 6.09 (t, J = 8.0 Hz, 1H). $^{13}$C NMR (100 MHz) δ 166.6, 161.1 (d, J$_{(C,F)}$ = 247.3 Hz), 140.9, 140.1, 138.6, 137.3, 136.1, 135.0, 134.9 (d, J$_{(C,F)}$ = 7.2 Hz), 131.6 (d, J$_{(C,F)}$ = 7.1 Hz), 131.2, 130.8, 130.3, 129.8, 129.2, 128.5, 127.8, 126.1, 125.0, 122.5, 121.5, 120.1, 119.6, (d, J$_{(C,F)}$ = 21.4 Hz), 118.0 (d, J$_{(C,F)}$ = 23.8 Hz). HRMS (ESI) calculated for C$_{29}$H$_{19}$FNO [M+H]$^+$ requires 416.1451, found 416.1434.
Ethyl 4-(5-oxo-7,12-diphenylbenzo[c]indeno[2,1-e]azepin-6(5H)-yl)benzoate 3n. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.04 (d, $J = 7.6$ Hz, 1H), 7.90 (d, $J = 8.0$ Hz, 2H), 7.58 (m, 2H), 7.48-7.40 (m, 4H), 7.27-7.20 (m, 5H), 7.17-7.12 (m, 4H), 7.05-7.03 (m, 2H), 6.77 (t, $J = 8.0$ Hz, 1H), 5.47 (t, $J = 8.0$ Hz, 1H), 4.33 (q, $J = 7.2$ Hz, 2H), 1.36 (t, $J = 7.2$ Hz, 3H).

$^{13}$C NMR (100 MHz) $\delta$ 170.2, 165.8, 145.2, 141.4, 141.1, 140.8, 137.1, 136.4, 135.8, 134.7, 132.5, 132.3, 131.9, 131.5, 131.2, 130.34, 130.30, 130.0, 129.9, 129.4, 129.0, 128.6, 128.5, 128.0, 127.1, 127.0, 126.1, 124.9, 122.1, 120.3, 61.1, 14.2. HRMS (ESI) calculated for C$_{38}$H$_{27}$NO$_3$ [M+H]$^+$ requires 546.2069, found 546.2054.

Ethyl 4-(5-oxo-12-phenyl-7-(p-tolyl)benzo[c]indeno[2,1-e]azepin-6(5H)-yl)benzoate 3o.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.03 (d, $J = 8.0$ Hz, 1H), 7.91 (d, $J = 8.4$ Hz, 2H), 7.59-7.57 (m, 2H), 7.47-7.39 (m, 4H), 7.26-7.12 (m, 6H), 7.03-7.01 (m, 2H), 6.92-6.90 (m, 2H), 6.80 (t, $J = 7.6$ Hz, 1H), 5.53 (d, $J = 8.0$ Hz, 1H), 4.34 (q, $J = 7.2$ Hz, 2H), 2.32 (s, 3H), 1.37 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (100 MHz) $\delta$ 170.3, 165.9, 147.2, 145.2, 141.7, 141.0, 140.6, 138.5, 137.3, 135.9, 134.7, 133.4, 132.4, 132.2, 132.0, 131.4, 131.2, 130.3, 130.1, 129.98, 129.93, 129.3, 129.2, 129.0, 127.9, 127.0, 126.0, 124.9, 122.1, 120.3, 21.4, 14.2. HRMS (ESI) calculated for C$_{39}$H$_{29}$NO$_3$ [M+H]$^+$ requires 560.2226, found 560.2189.
Ethyl 4-(7-butyl-5-oxo-12-phenylbenzo[c]indeno[2,1-\(\text{e}\)]azepin-6(5H)-yl)benzoate 3p. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta \) 8.16 (d, \(J = 8.4\) Hz, 2H), 7.97 (d, \(J = 8.0\) Hz, 1H), 7.62 (d, \(J = 6.8\) Hz, 1H), 7.58-7.55 (m, 3H), 7.46-7.39 (m, 5H), 7.35-7.32 (m, 2H), 7.25-7.22 (m, 1H), 7.11 (t, \(J = 8.0\) Hz, 1H), 7.04-7.02 (m, 1H), 4.41 (q, \(J = 7.6\) Hz, 2H), 2.69 (t, \(J = 8.0\) Hz, 2H), 1.65-1.62 (m, 2H), 1.42 (t, \(J = 6.8\) Hz, 3H), 0.88-0.84 (m, 2H), 0.79 (t, \(J = 7.6\) Hz, 3H). \(^{13}\)C NMR (100 MHz) \(\delta \) 169.9, 165.8, 147.3, 146.4, 145.4, 141.6, 140.9, 136.6, 135.5, 134.9, 133.2, 131.9, 131.8, 131.7, 131.1, 130.7, 130.1, 130.0, 129.0, 128.9, 128.1, 127.0, 126.4, 125.9, 121.9, 121.4, 61.2, 34.3, 32.5, 22.4, 14.3, 13.8. HRMS (ESI) calculated for C\(_{36}\)H\(_{31}\)NO\(_3\) [M+H]\(^+\) requires 526.2382, found 526.2368.