

Supporting information

for

Construction of Spirocycles Containing Highly Substituted Pyrrolidine and 1-Indanone Motifs with Spiro Quaternary Stereogenic Centers via 1,3-Dipolar Cycloaddition of 2-Alkylidene-1-Indanone and Azomethine Ylides Prompted by Simple Imidazolium Salts

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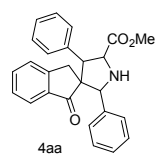
General information

All reagents were obtained from commercial supplier without further purification. Commercial grade solvent was dried and purified by standard procedures as specified in Purification of Laboratory Chemicals, 4th Ed (Armarego, W. L. F.; Perrin, D. D. Butterworth Heinemann: 1997). NMR spectra were recorded with tetramethylsilane as the internal standard. ^1H NMR spectra were recorded at 400 MHz, and ^{13}C NMR spectra were recorded at 100 MHz (Bruker Avance). Chemical shifts (δ) are reported in ppm downfield from CDCl_3 ($\delta = 7.26$ ppm) for ^1H NMR and relative to the central CDCl_3 resonance ($\delta = 77.0$ ppm) for ^{13}C NMR spectroscopy. The following abbreviations were used to describe peak patterns where appropriate: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants were reported in Hertz (Hz). Flash column chromatography was carried out using silica gel eluting with ethyl acetate and petroleum ether. Reactions were monitored by TLC and visualized with ultraviolet light.

General procedure for 2-Alkylidene-1-Indanone with Azomethine Ylides Promted by Imidazolium Salts.

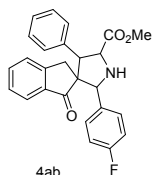
Typical experimental procedure for the Methyl 1-oxo-2',4'-diphenyl-1,3-dihydrospiro [indene-2,3'-pyrrolidine]-5'-carboxylate (4aa): A stirred solution of 2-alkylidene-1-indanone (**1a**, 0.20 mmol, 1.0 equiv), azomethine ylide (**2a**, 0.2 mmol, 1.0 equiv) and catalyst **3g** (20 mmol%) in CH_3CN (1.0 mL) was stirred at 40 °C. After the 2-alkylidene-1-indanone was consumed as indicated monitored by TLC, the reaction solution was added H_2O (20 mL), then extracted with CH_2Cl_2 (25 mL \times 3). The organic phase was dried with anhydrous MgSO_4 , filtered and concentrated *in-vacuo*. The residue was purified by column chromatography on silica gel (eluent PE: EtOAc = 200:1 to 40:1) to afford pure products **4aa**. All known products were identified by spectroscopic data (^1H NMR) which are in good agreement with those reported.^[6]

Methyl-1-oxo-2',4'-diphenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate (4aa):



79.0 mg, 99% yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm): 2.79 (d, $J = 17.6$ Hz, 1H), 2.88 (d, $J = 17.6$ Hz, 1H), 3.85 (s, 3H), 3.99 (d, $J = 5.8$ Hz, 1H), 4.36 (d, $J = 5.9$ Hz, 1H), 4.57 (s, 1H), 7.03 – 7.12 (m, 5H), 7.15 (dd, $J = 7.6, 1.7$ Hz, 2H), 7.28 – 7.34 (m, 5H), 7.37 – 7.41 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 35.5, 52.4, 56.1, 65.7, 67.6, 74.1, 123.2, 125.4, 126.6, 127.1, 127.3, 127.8, 128.0, 128.7, 128.9, 134.4, 135.9, 136.1, 141.3, 151.8, 173.2, 207.9. IR (KBr, cm^{-1}): 3430, 3063, 3032, 3003, 2950, 2840, 1741, 1704, 1609, 1513, 1461, 1440, 1382, 1328, 1285, 1252, 1215, 1182, 1121, 1034, 959, 919, 834, 756, 703, 673, 555, 521. HRMS (ESI-TOF) calcd for $\text{C}_{26}\text{H}_{24}\text{NO}_3$ ($[\text{M}+\text{H}]^+$): 398.1751, found: 398.1768.

Methyl-2'-(4-fluorophenyl)-1-oxo-4'-phenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate (4ab):

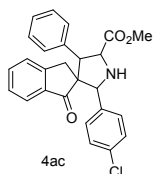


70.9 mg, 85% yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm): 2.76 (d, $J = 17.6$ Hz, 1H), 2.88 (d, $J = 17.6$ Hz, 1H), 3.85 (s, 3H), 3.99 (d, $J = 5.9$ Hz, 1H), 4.35 (d, $J = 5.9$ Hz, 1H), 4.55 (s, 1H), 6.75 (t, $J = 8.7$ Hz, 2H), 7.07 – 7.18 (m, 4H), 7.29 – 7.41 (m, 7H). ^{13}C NMR (100

MHz, CDCl₃) δ (ppm): 35.6, 52.4, 55.8, 65.6, 67.4, 73.4, 114.8, 115.0, 123.3, 125.5, 127.3, 128.3, 128.4, 128.7, 128.9, 132.2, 134.6, 135.9, 141.1, 151.7, 161.0, 163.5, 173.1, 207.7. IR (KBr, cm⁻¹): 3425, 3066, 3034, 2951, 2924, 2851, 1737, 1704, 1606, 1508, 1461, 1435, 1377, 1329, 1287, 1220, 1153, 1096, 1024, 913, 841, 764, 703, 639, 522. **HRMS (ESI-TOF)** calcd for C₂₆H₂₃FNO₃ ([M+H]⁺): 416.1656, found: 416.1653.

Methyl-2'-(4-chlorophenyl)-1-oxo-4'-phenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate

(4ac):

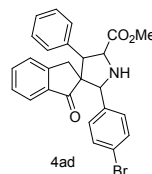


71.6 mg, 83% yield. **¹H NMR** (400 MHz, CDCl₃) δ (ppm): 2.77 (d, *J* = 17.6 Hz, 1H), 2.89 (d, *J* = 17.6 Hz, 1H), 3.85 (s, 3H), 3.99 (d, *J* = 6.0 Hz, 1H), 4.36 (d, *J* = 6.0 Hz, 1H), 4.54 (s, 1H), 7.04 (d, *J* = 8.5 Hz, 2H), 7.08 – 7.16 (m, 4H), 7.27 – 7.41 (m, 7H). **¹³C NMR** (100 MHz, CDCl₃) δ (ppm): 35.6, 52.4, 55.8, 65.6, 67.3, 73.4, 123.4, 125.5, 127.3, 127.4, 128.1,

128.1, 128.7, 128.9, 135.6, 134.7, 135.1, 135.9, 140.9, 151.7, 173.1, 207.5. IR (KBr, cm⁻¹): 3337, 3061, 3033, 2950, 2922, 2849, 1737, 1704, 1603, 1490, 1461, 1439, 1329, 1287, 1215, 1136, 1093, 1041, 1017, 912, 829, 764, 705, 638, 512, 473, 416.

Methyl-2'-(4-bromophenyl)-1-oxo-4'-phenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate

(4ad):

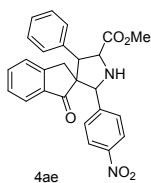


82.7 mg, 87% yield. The ratio of **4ad-A/4ad-B/4ad-C** was 1:0.27:0.15 as determined by ¹H NMR. **¹H NMR** (400 MHz, CDCl₃, a mixture of three isomers) δ (ppm): 2.56 (dd, *J* = 36.0, 18.0 Hz, 2H, isomer B), 2.76 (dd, *J* = 21.6, 18.0 Hz, 2H, isomer A), 2.88 (d, *J* = 14.0 Hz, 2H, isomer C), 3.30 (s, 3H, isomer C), 3.42 (s, 3H, isomer B), 3.69 (s, 3H, isomer A), 3.88

(d, *J* = 7.6 Hz, 1H, isomer C), 4.14 (d, *J* = 8.4 Hz, 1H, isomer B), 4.32 (d, *J* = 9.2 Hz, 1H, isomer A), 4.51 (d, *J* = 9.2 Hz, 1H, isomer A), 4.63 (d, *J* = 8.4 Hz, 1H, isomer B), 4.67 (s, 1H, isomer B), 4.92 (s, 1H, isomer C), 5.02 (s, 1H, isomer A), 5.33 (d, *J* = 7.6 Hz, 1H, isomer C), 6.88 (t, *J* = 1.0 Hz, isomer A), 7.06 - 7.25 (m, 15H, for isomer A and isomer B and isomer C, overlapped), 7.31 (d, *J* = 7.2 Hz, 1H, isomer B), 7.36 (t, *J* = 7.2 Hz, 1H, isomer A), 7.62 (d, *J* = 7.6 Hz, 1H, isomer A), 7.71 (d, *J* = 7.2 Hz, 1H, isomer B). **¹³C NMR** (100 MHz, CDCl₃) δ (ppm): 29.6, 33.4, 35.1, 51.5, 51.5, 52.5, 54.7, 56.7, 58.4, 60.6, 63.6, 64.1, 64.7, 65.3, 65.4, 68.7, 68.9, 70.2, 121.1, 121.3, 121.4, 123.3, 123.5, 123.7, 125.4, 125.7, 127.0, 127.1, 127.2, 127.3, 128.0, 128.2, 128.2, 128.4, 128.6, 128.8, 128.8, 128.9, 129.2, 130.8, 130.9, 130.9, 134.8, 134.9, 135.1, 135.7, 135.9, 136.2, 137.0, 137.4, 138.2, 139.2, 151.2, 153.5, 153.7, 172.5, 173.7, 175.2, 207.1, 207.2, 208.9. IR (KBr, cm⁻¹): 3342, 3062, 3032, 2951, 2925, 2851, 1738, 1704, 1605, 1489, 1459, 1436, 1407, 1326, 1285, 1214, 1134, 1073, 1010, 914, 822, 764, 705, 510, 472, 401. **HRMS (ESI-TOF)** calcd for C₂₆H₂₃BrNO₃ ([M+H]⁺): 476.0856, found: 476.0850.

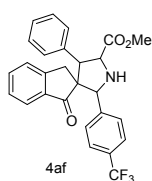
Methyl-2'-(4-nitrophenyl)-1-oxo-4'-phenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate

(4ae):



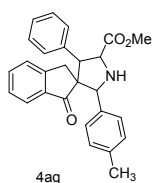
75.8 mg, 86% yield. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ (ppm): 2.91 (d, $J = 17.8$ Hz, 1H), 2.99 (d, $J = 17.8$ Hz, 1H), 3.32 (s, 3H), 3.89 (d, $J = 7.7$ Hz, 1H), 5.09 (s, 1H), 5.33 (d, $J = 7.6$ Hz, 1H), 7.09 – 7.16 (m, 2H), 7.22 (d, $J = 6.8$ Hz, 2H), 7.30 – 7.39 (m, 5H), 7.47 (d, $J = 8.7$ Hz, 2H), 7.90 (d, $J = 8.8$ Hz, 2H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ (ppm): 35.5, 51.7, 54.7, 64.8, 65.9, 70.0, 122.9, 123.6, 125.5, 127.6, 127.7, 128.0, 128.7, 128.9, 135.1, 135.7, 139.0, 146.9, 147.3, 150.9, 173.6, 206.4. IR (KBr, cm^{-1}): 3427, 3065, 3031, 2952, 2925, 2853, 1740, 1709, 1607, 1562, 1467, 1438, 1406, 1363, 1325, 1210, 1128, 1068, 1030, 883, 826, 748, 703, 674, 514, 448. **HRMS (ESI-TOF)** calcd for $\text{C}_{26}\text{H}_{23}\text{N}_2\text{O}_5$ ($[\text{M}+\text{H}]^+$): 443.1601, found: 443.1593.

Methyl-1-oxo-4'-phenyl-2'-(4-(trifluoromethyl)phenyl)-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate (4af):



79.4 mg, 85% yield. The ratio of **4af-A**/**4af-B**/**4af-C** was 1:0.31:0.24 as determined by $^1\text{H NMR}$. $^1\text{H NMR}$ (400 MHz, CDCl_3 , a mixture of three isomers) δ (ppm): 2.49 (d, $J = 17.6$ Hz, 1H, isomer C), 2.60 (d, $J = 17.6$ Hz, 1H, isomer C), 2.71 (d, $J = 17.2$ Hz, 1H, isomer B), 2.80 (d, $J = 17.2$ Hz, 1H, isomer B), 2.84 (d, $J = 17.6$ Hz, 1H, isomer A), 2.93 (d, $J = 17.6$ Hz, 1H, isomer A), 3.30 (s, 3H, isomer A), 3.43 (s, 3H, isomer C), 3.70 (s, 3H, isomer B), 3.87 (d, $J = 8.0$ Hz, 1H, isomer A), 4.12 (d, $J = 8.4$ Hz, 1H, isomer C), 4.31 (d, $J = 9.6$ Hz, 1H, isomer B), 4.51 (d, $J = 9.6$ Hz, 1H, isomer B), 4.63 (d, $J = 8.4$ Hz, 1H, isomer C), 4.65 (s, 1H, isomer C), 4.92 (s, 1H, isomer A), 5.00 (s, 1H, isomer B), 5.30 (d, $J = 8.0$ Hz, 1H, isomer A), 6.90 – 6.96 (m, 1H, isomer A), 7.09 – 7.22 (m, 10H, for isomer A and isomer B and isomer C, overlapped), 7.29 – 7.43 (m, 8H, for isomer A and isomer B and isomer C, overlapped), 7.48 (d, $J = 1.6$ Hz, 1H, isomer B), 7.64 (d, $J = 7.6$ Hz, 1H, isomer B), 7.75 (d, $J = 7.6$ Hz, 1H, isomer C). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ (ppm): 29.7, 33.5, 35.3, 51.6, 51.7, 52.3, 54.4, 56.6, 60.6, 63.6, 64.1, 64.6, 65.3, 65.6, 68.1, 68.3, 68.6, 123.4, 123.6, 123.9, 125.5, 125.8, 126.2, 126.4, 126.6, 127.2, 127.2, 127.3, 127.4, 127.5, 128.1, 128.3, 128.7, 128.7, 128.9, 129.1, 129.2, 129.7, 129.7, 129.8, 131.1, 131.3, 131.4, 131.9, 132.0, 134.9, 135.1, 135.3, 136.0, 137.0, 138.2, 138.9, 139.0, 139.1, 151.0, 153.4, 153.5, 172.3, 173.7, 175.1, 206.6, 206.9. IR (KBr, cm^{-1}): 3372, 3065, 3033, 2953, 2926, 2854, 1741, 1705, 1611, 1497, 1462, 1437, 1327, 1276, 1212, 1167, 1124, 1069, 1019, 981, 925, 839, 756, 704, 676, 607, 551, 472, 411. **HRMS (ESI-TOF)** calcd for $\text{C}_{27}\text{H}_{23}\text{F}_3\text{NO}_3$ ($[\text{M}+\text{H}]^+$): 466.1625, found: 466.1631.

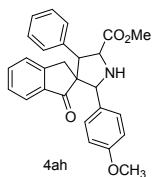
Methyl-1-oxo-4'-phenyl-2'-(p-tolyl)-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate (4ag):



76.6 mg, 93% yield. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ (ppm): 2.14 (s, 3H), 2.83 (q, $J = 17.6$ Hz, 2H), 3.85 (s, 3H), 3.97 (d, $J = 5.9$ Hz, 1H), 4.37 (d, $J = 5.9$ Hz, 1H), 4.54 (s, 1H), 6.86 (d, $J = 7.5$ Hz, 2H), 7.04 (d, $J = 7.7$ Hz, 2H), 7.10 (d, $J = 7.6$ Hz, 2H), 7.29 – 7.33 (m, 5H), 7.36 – 7.42 (m, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ (ppm): 20.9, 35.5, 52.4, 56.2, 65.6, 67.5, 73.9, 123.3, 125.5, 126.6, 127.1, 127.2, 128.7, 128.8, 128.8, 133.0, 134.4, 136.1, 137.4, 141.2, 151.9, 173.2, 208.0. IR (KBr, cm^{-1}): 3340, 3062, 3030, 2950, 2923, 2855, 1738, 1704, 1606, 1509, 1459, 1435, 1377, 1328, 1284, 1214, 1139, 1029, 913, 871, 820, 762, 704, 674, 515, 470. **HRMS (ESI-TOF)** calcd for $\text{C}_{27}\text{H}_{26}\text{NO}_3$ ($[\text{M}+\text{H}]^+$): 412.1907, found: 412.1909.

Methyl-2'-(4-methoxyphenyl)-1-oxo-4'-phenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-

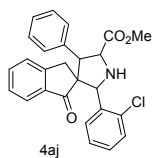
carboxylate (4ah):



83.6 mg, 98% yield. The ratio of **4ah-A**/**4ah-B** was 1:0.87 as determined by ^1H NMR. ^1H NMR (400MHz, CDCl_3 , a mixture of two isomers) δ (ppm): 2.74 (d, $J = 17.2$ Hz, 1H, isomer A), 2.81 (d, $J = 11.2$ Hz, 1H, isomer B), 2.85 (d, $J = 11.2$ Hz, 1H, isomer B), 2.99 (d, $J = 17.2$ Hz, 1H, isomer A), 3.30 (s, 3H, isomer B), 3.64 (s, 3H, isomer B), 3.67 (s, 3H, isomer A), 3.70 (s, 3H, isomer A), 3.89 (d, $J = 7.9$ Hz, 1H, isomer B), 4.34 (d, $J = 9.1$ Hz, 1H, isomer A), 4.50 (d, $J = 9.1$ Hz, 1H, isomer A), 4.89 (s, 1H, isomer B), 5.01 (s, 1H, isomer A), 5.35 (d, $J = 7.9$ Hz, 1H, isomer B), 6.60 (dd, $J = 14.1, 8.7$ Hz, 1H, for isomer A and isomer B, overlapped), 7.10 (d, $J = 7.2$ Hz, 3H, for isomer A and isomer B, overlapped), 7.13 – 7.15 (m, 5H, for isomer A and isomer B, overlapped), 7.16 – 7.24 (m, 7H, for isomer A and isomer B, overlapped), 7.29 – 7.39 (m, 6H, for isomer A and isomer B, overlapped), 7.61 (d, $J = 7.6$ Hz, 1H, isomer A). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 29.7, 35.0, 51.5, 52.4, 54.8, 55.1, 55.1, 56.6, 60.7, 64.8, 65.3, 65.6, 69.1, 70.7, 113.1, 113.3, 113.8, 113.9, 123.2, 123.4, 125.4, 125.7, 126.8, 127.1, 127.1, 127.2, 127.8, 128.1, 128.2, 128.5, 129.1, 130.2, 134.5, 134.6, 136.2, 136.7, 137.2, 136.7, 137.2, 139.5, 151.5, 153.8, 158.7, 159.0, 173.9, 175.4, 207.6, 207.7. IR (KBr, cm^{-1}): 3429, 3063, 3032, 3002, 2928, 2844, 1736, 1704, 1608, 1512, 1461, 1439, 1379, 1290, 1250, 1214, 1178, 1144, 1033, 958, 914, 836, 762, 704, 622, 535, 472. HRMS (ESI-TOF) calcd for $\text{C}_{27}\text{H}_{26}\text{NO}_4$ ($[\text{M}+\text{H}]^+$): 428.1856, found: 428.1860.

Methyl-2'-(2-chlorophenyl)-1-oxo-4'-phenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate

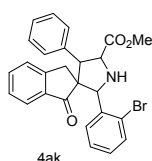
(4aj):



56.2 mg, 65% yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm): 2.89 (d, $J = 17.3$ Hz, 1H), 3.23 (d, $J = 17.3$ Hz, 1H), 3.82 (s, 3H), 4.09 (d, $J = 7.4$ Hz, 1H), 4.44 (d, $J = 7.4$ Hz, 1H), 5.25 (s, 1H), 7.00 – 7.12 (m, 3H), 7.18 (dd, $J = 13.2, 7.2$ Hz, 2H), 7.28 – 7.36 (m, 7H), 7.64 (d, $J = 7.8$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 35.9, 52.4, 55.2, 66.1, 66.5, 68.2, 123.2, 125.6, 126.8, 127.1, 127.3, 128.6, 128.6, 128.7, 128.7, 129.1, 133.4, 134.4, 135.5, 136.1, 139.4, 151.9, 173.3, 206.9. IR (KBr, cm^{-1}): 3363, 3062, 3030, 2949, 2923, 2850, 1740, 1702, 1606, 1496, 1462, 1440, 1382, 1331, 1244, 1207, 1179, 1094, 1040, 961, 920, 870, 760, 700, 670, 575, 466. HRMS (ESI-TOF) calcd for $\text{C}_{26}\text{H}_{23}\text{ClNO}_3$ ($[\text{M}+\text{H}]^+$): 432.1361, found: 432.1358.

Methyl-2'-(2-bromophenyl)-1-oxo-4'-phenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate

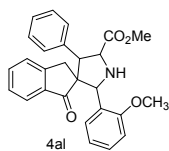
(4ak)



81.1 mg, 85% yield. ^1H NMR (400 MHz, CDCl_3) δ (ppm): 2.91 (d, $J = 17.2$ Hz, 1H), 3.29 (d, $J = 17.2$ Hz, 1H), 3.80 (s, 3H), 4.10 (d, $J = 7.5$ Hz, 1H), 4.45 (d, $J = 7.5$ Hz, 1H), 5.22 (s, 1H), 6.95 (t, $J = 7.5$ Hz, 1H), 7.10 (t, $J = 7.2$ Hz, 1H), 7.17 (d, $J = 7.5$ Hz, 1H), 7.22 – 7.39 (m, 9H), 7.67 (d, $J = 7.7$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): 35.9, 52.3, 55.0, 65.8, 66.4, 70.6, 123.2, 124.2, 125.6, 127.1, 127.2, 127.3, 128.6, 128.7, 128.9, 129.0, 132.4, 134.4, 136.3, 137.4, 139.1, 151.9, 173.3, 206.8. IR (KBr, cm^{-1}): 3380, 3062, 3032, 2951, 2924, 2852, 1739, 1707, 1606,

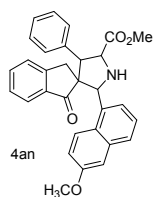
1496, 1464, 1436, 1379, 1328, 1272, 1211, 1105, 1075, 1023, 920, 868, 758, 703, 660, 523, 459. **HRMS (ESI-TOF)** calcd for $C_{26}H_{23}BrNO_3$ ($[M+H]^+$): 476.0856, found: 476.0852.

Methyl-2'-(2-methoxyphenyl)-1-oxo-4'-phenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate (4al):



57.6 mg, 67% yield. The ratio of **4al-A/4al-B/4al-C** was 1:0.7:0.52 as determined by 1H NMR. 1H NMR (400 MHz, $CDCl_3$, a mixture of three isomers) δ (ppm): 2.38 (d, $J = 17.6$ Hz, 1H, isomer A), 2.46 (d, $J = 17.6$ Hz, 1H, isomer A), 2.56 (d, $J = 17.2$ Hz, 1H, isomer B), 2.75 (d, $J = 17.2$ Hz, 1H, isomer B), 2.82 (d, $J = 15.6$ Hz, 1H, isomer C), 2.90 (d, $J = 15.6$ Hz, 1H, isomer C), 3.04 (s, 3H, isomer A), 3.27 (s, 3H, isomer C), 3.33 (s, 3H, isomer B), 3.37 (s, 3H, isomer A), 3.45 (s, 3H, isomer C), 3.72 (s, 3H, isomer B), 3.79 (d, $J = 7.6$ Hz, 1H, isomer C), 3.92 (d, $J = 1.6$ Hz, 1H, isomer B), 3.94 (d, $J = 1.6$ Hz, 1H, isomer B), 4.45 (d, $J = 8.0$ Hz, 1H, isomer A), 4.74 (d, $J = 8.0$ Hz, 1H, isomer A), 4.96 (s, 1H, isomer A), 5.12 (s, 1H, isomer B), 5.28 (d, $J = 7.6$ Hz, 1H, isomer C), 5.54 (s, 1H, isomer C), 6.33 (d, $J = 7.9$ Hz, 1H, isomer C), 6.38 (d, $J = 7.9$ Hz, 1H, isomer C), 6.52 (d, $J = 7.9$ Hz, 1H, isomer A), 6.78 – 6.83 (m, 1H, for isomer A and isomer B and isomer C, overlapped), 6.88 – 6.96 (m, 2H, for isomer A and isomer B and isomer C, overlapped), 7.00 – 7.08 (m, 3H, for isomer A and isomer B and isomer C, overlapped), 7.13 – 7.23 (m, 10H, for isomer A and isomer B and isomer C, overlapped), 7.25 – 7.30 (m, 4H, for isomer A and isomer B and isomer C, overlapped), 7.33 – 7.37 (m, 3H, for isomer A and isomer B and isomer C, overlapped), 7.50 (dd, $J = 7.7$, 1.5 Hz, 1H, isomer B), 7.62 (d, $J = 7.3$ Hz, 1H, isomer B), 7.78 (t, $J = 6.2$ Hz, 2H, for isomer A and isomer B), 7.91 (d, $J = 7.5$ Hz, 1H, isomer A). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 31.0, 34.6, 36.5, 51.3, 51.4, 52.4, 53.6, 54.6, 55.3, 55.4, 56.1, 58.4, 61.9, 62.8, 63.5, 64.0, 64.3, 64.3, 65.0, 65.3, 65.9, 108.6, 109.1, 119.7, 120.2, 120.3, 122.8, 123.1, 123.5, 125.1, 125.4, 125.5, 126.3, 126.7, 126.8, 126.9, 126.9, 127.1, 127.3, 127.4, 127.4, 127.7, 127.8, 127.9, 127.9, 128.0, 128.2, 128.2, 128.4, 128.5, 128.7, 128.7, 129.2, 129.7, 133.9, 134.0, 134.2, 135.5, 136.0, 136.9, 137.9, 139.3, 139.5, 152.2, 152.6, 153.6, 156.4, 156.5, 156.5, 172.1, 173.6, 175.2, 206.4, 208.0, 209.7. IR (KBr, cm^{-1}): 3424, 3065, 3033, 3003, 2950, 2842, 1740, 1708, 1604, 1492, 1462, 1438, 1328, 1280, 1244, 1207, 1177, 1104, 1028, 913, 869, 756, 703, 665, 575, 471. **HRMS (ESI-TOF)** calcd for $C_{27}H_{26}NO_4$ ($[M+H]^+$): 428.1856, found: 428.1853.

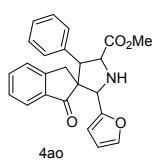
Methyl-2'-(6-methoxynaphthalen-1-yl)-1-oxo-4'-phenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate (4am):



85.5 mg, 90% yield. The ratio of **4am-A/4am-B** was 1:0.32 as determined by 1H NMR. 1H NMR (400 MHz, $CDCl_3$, a mixture of two isomers) δ (ppm): 2.79 (d, $J = 17.9$ Hz, 1H, isomer B), 2.88 (d, $J = 17.9$ Hz, 1H, isomer B), 2.91 (d, $J = 18.2$ Hz, 1H, isomer A), 2.96 (d, $J = 18.2$ Hz, 1H, isomer A), 3.32 (s, 3H, isomer A), 3.72 (s, 3H, isomer B), 3.84 (s, 3H, isomer A), 3.84 (s, 3H, isomer B), 3.93 (d, $J = 7.8$ Hz, 1H, isomer A), 4.39 (d, $J = 9.2$ Hz, 1H, isomer B), 4.57 (d, $J = 9.2$ Hz, 1H, isomer B), 5.07 (s, 1H, isomer A), 5.22 (s, 1H, isomer B), 5.42 (d, $J = 7.8$ Hz, 1H, isomer A), 6.76 (d, $J = 7.6$ Hz, 1H, isomer B), 6.93 – 7.04 (m, 3H, for isomer A and

isomer B, overlapped), 7.07 – 7.15 (m, 3H, for isomer A and isomer B, overlapped), 7.28 – 7.43 (m, 10H, for isomer A and isomer B, overlapped), 7.56 (d, $J = 8.8$ Hz, 1H, isomer A), 7.62 – 7.64 (m, 2H, for isomer A and isomer B, overlapped), 7.81 (s, 1H, isomer B). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ (ppm): 30.5, 35.1, 51.5, 52.5, 54.9, 55.1, 57.1, 58.4, 60.8, 64.8, 65.5, 65.5, 69.3, 71.1, 105.3, 105.4, 118.5, 118.6, 123.2, 123.4, 125.3, 125.4, 125.6, 125.6, 125.7, 126.2, 126.2, 126.4, 126.8, 127.1, 127.1, 127.3, 128.1, 128.2, 128.3, 128.4, 128.6, 128.8, 129.1, 129.3, 129.4, 130.9, 133.0, 133.8, 134.0, 134.5, 134.7, 136.0, 136.4, 137.1, 139.5, 151.4, 157.4, 173.9, 207.6. IR (KBr, cm^{-1}): 3432, 3060, 3031, 3002, 2949, 2845, 1740, 1705, 1632, 1607, 1487, 1461, 1437, 1386, 1327, 1267, 1214, 1175, 1120, 1032, 955, 906, 855, 811, 763, 705, 672, 564, 476. **HRMS (ESI-TOF)** calcd for $\text{C}_{31}\text{H}_{28}\text{NO}_4$ ($[\text{M}+\text{H}]^+$): 478.2013, found: 478.2025.

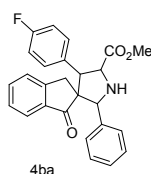
Methyl-2'-(furan-2-yl)-1-oxo-4'-phenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate (4an):



46.3 mg, 61% yield. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ (ppm): 2.72 (d, $J = 17.7$ Hz, 1H), 2.78 (d, $J = 17.7$ Hz, 1H), 3.43 (s, 3H), 4.08 (d, $J = 8.6$ Hz, 1H), 4.61 (d, $J = 8.6$ Hz, 1H), 4.72 (s, 1H), 6.20 (s, 2H), 7.07 (d, $J = 7.6$ Hz, 1H), 7.16 – 7.25 (m, 6H), 7.29 (d, $J = 7.5$ Hz, 1H), 7.42 (t, $J = 7.4$ Hz, 1H), 7.71 (d, $J = 7.4$ Hz, 1H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ (ppm):

33.4, 51.6, 55.8, 64.1, 64.5, 64.9, 108.0, 110.0, 124.0, 125.7, 127.2, 127.3, 128.2, 129.5, 134.9, 135.3, 137.4, 142.0, 152.1, 153.6, 172.4, 208.2. IR (KBr, cm^{-1}): 3344, 3062, 3031, 2949, 2924, 2852, 1960, 1895, 1817, 1740, 1704, 1606, 1494, 1458, 1435, 1371, 1326, 1291, 1212, 1150, 1114, 1075, 1036, 928, 869, 843, 759, 703, 665, 581, 544, 469. **HRMS (ESI-TOF)** calcd for $\text{C}_{24}\text{H}_{22}\text{NO}_4$ ($[\text{M}+\text{H}]^+$): 388.1543, found: 388.1536.

Methyl-4'-(4-fluorophenyl)-1-oxo-2'-phenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate (4ba):

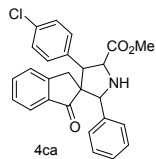


66.2 mg, 80% yield. The ratio of **4ba-A/4ba-B/4ba-C** was 1:0.24:0.23 as determined by $^1\text{H NMR}$. $^1\text{H NMR}$ (400 MHz, CDCl_3 , a mixture of three isomers) δ (ppm): 2.68 (d, $J = 11.6$ Hz, 2H, isomer C), 2.73 (d, $J = 10.8$ Hz, 1H, isomer A), 2.79 (d, $J = 21.2$ Hz, 1H, isomer A), 2.87 (s, 2H, isomer B), 3.35 (s, 3H, isomer C), 3.67 (s, 3H, isomer B), 3.70 (s,

3H, isomer A), 3.74 (d, $J = 10.2$ Hz, 1H, isomer C), 3.91 (d, $J = 7.8$ Hz, 1H, isomer B), 4.32 (d, $J = 9.3$ Hz, 1H, isomer A), 4.46 (d, $J = 9.3$ Hz, 1H, isomer A), 4.75 (s, 1H, isomer C), 4.83 (d, $J = 10.2$ Hz, 1H, isomer C), 4.90 (s, 1H, isomer B), 5.06 (s, 1H, isomer A), 5.37 (d, $J = 7.8$ Hz, 1H, isomer B), 6.76 – 6.88 (m, 3H, for isomer A, isomer B and isomer C, overlapped), 7.00 – 7.26 (m, 13H, for isomer A, isomer B and isomer C, overlapped), 7.32 – 7.40 (m, 2H, for isomer A, isomer B and isomer C, overlapped), 7.51 (d, $J = 7.8$ Hz, 1H, isomer B), 7.62 (d, $J = 7.6$ Hz, 1H, isomer A). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ (ppm): 29.6, 35.2, 35.9, 51.5, 52.1, 52.4, 54.0, 56.0, 57.3, 61.0, 62.6, 64.8, 65.0, 65.4, 65.4, 66.8, 69.3, 71.2, 115.0, 115.2, 115.3, 115.5, 123.3, 123.4, 123.6, 125.4, 125.7, 126.7, 126.9, 127.2, 127.4, 127.5, 127.6, 127.7, 127.9, 128.5, 129.6, 129.6, 130.3, 130.4, 130.6, 130.7, 132.2, 132.3, 134.5, 134.8, 134.8, 135.2, 136.0, 137.1, 138.1, 151.1, 152.1, 153.6, 160.5, 163.0, 173.6, 173.9, 175.0, 207.3. IR (KBr, cm^{-1}): 3428, 3064, 3033, 2950, 2854, 1737, 1704, 1608, 1493, 1460, 1434, 1328, 1286, 1227, 1104, 1096, 1013, 910, 872, 841, 759, 701, 649, 586, 471. **HRMS (ESI-TOF)** calcd for $\text{C}_{26}\text{H}_{23}\text{FNO}_3$ ($[\text{M}+\text{H}]^+$): 416.1656, found: 416.1653.

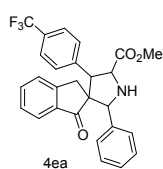
Methyl-4'-(4-chlorophenyl)-1-oxo-2'-phenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate

(4ca):



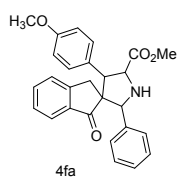
65.6mg, 76% yield. The ratio of **4ca-A/4ca-B/4ca-C** was 1:0.29:0.16 as determined by ¹H NMR. ¹H NMR (400 MHz, CDCl₃, a mixture of three isomers) δ (ppm): 2.69 (d, *J* = 17.6 Hz, 1H, isomer A), 2.79 (d, *J* = 17.6 Hz, 2H, isomer C), 2.85 (d, *J* = 17.6 Hz, 1H, isomer A), 2.86 (s, 2H, isomer B), 3.37 (s, 3H, isomer C), 3.68 (s, 3H, isomer B), 3.71 (s, 3H, isomer A), 3.82 (d, *J* = 10.2 Hz, 1H, isomer B), 3.89 (d, *J* = 7.7 Hz, 1H, isomer C), 4.32 (d, *J* = 9.2 Hz, 1H, isomer A), 4.46 (d, *J* = 9.2 Hz, 1H, isomer A), 4.74 (s, 1H, isomer B), 4.83 (d, *J* = 10.2 Hz, 1H, isomer B), 4.88 (s, 1H, isomer C), 5.04 (s, 1H, isomer A), 5.39 (d, *J* = 7.7 Hz, 1H, isomer C), 6.87 (d, *J* = 7.7 Hz, 1H, isomer A), 7.06 – 7.17 (m, 10H, for isomer A and isomer B and isomer C, overlapped), 7.21 – 7.25 (m, 4H, for isomer A and isomer B and isomer C, overlapped), 7.33 – 7.40 (m, 2H, for isomer A and isomer B and isomer C, overlapped), 7.53 (d, *J* = 7.6 Hz, 1H, isomer B), 7.62 (d, *J* = 7.6 Hz, 1H, isomer A). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 29.6, 35.2, 35.8, 51.6, 52.2, 52.5, 54.1, 55.9, 57.3, 60.9, 62.6, 64.7, 65.0, 65.3, 65.4, 67.0, 69.5, 71.2, 123.3, 123.4, 123.7, 125.4, 125.7, 125.7, 126.7, 126.9, 127.0, 127.2, 127.4, 127.6, 127.6, 127.7, 127.9, 128.3, 128.4, 128.6, 128.7, 129.5, 130.2, 130.4, 132.9, 133.3, 133.7, 134.6, 134.8, 134.9, 135.2, 136.0, 137.0, 138.0, 142.5, 151.1, 152.1, 153.3, 160.8, 173.6, 175.0, 207.2. IR (KBr, cm⁻¹): 3388, 3070, 3033, 2952, 2926, 2853, 1738, 1707, 1631, 1602, 1521, 1439, 1346, 1275, 1212, 1109, 1015, 921, 854, 800, 757, 701, 632, 510, 472. HRMS (ESI-TOF) calcd for C₂₆H₂₃ClNO₃ ([M+H]⁺): 432.1361, found: 432.1359.

Methyl-1-oxo-2'-phenyl-4'-(4-(trifluoromethyl)phenyl)-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate (4ea)



72.7 mg, 78% yield. The ratio of **4ea-A/4ea-B** was 1:0.31 as determined by ¹H NMR. ¹H NMR (400 MHz, CDCl₃, a mixture of two isomers) δ (ppm): 2.65 (d, *J* = 17.2 Hz, 1H, isomer A), 2.72 (d, *J* = 18.0 Hz, 1H, isomer B), 2.82 (d, *J* = 18.0 Hz, 1H, isomer B), 2.87 (d, *J* = 17.2 Hz, 1H, isomer A), 3.69 (s, 3H, isomer B), 3.72 (s, 3H, isomer A), 3.82 (d, *J* = 10.0 Hz, 1H, isomer B), 4.41 (d, *J* = 8.8 Hz, 1H, isomer A), 4.53 (d, *J* = 8.8 Hz, 1H, isomer A), 4.78 (s, 1H, isomer B), 4.89 (d, *J* = 10.0 Hz, 1H, isomer B), 5.04 (s, 1H, isomer A), 6.85 (d, *J* = 7.6 Hz, 1H, isomer A), 7.04 – 7.18 (m, 5H, for isomer A and isomer B, overlapped), 7.18 – 7.24 (m, 4H, for isomer A and isomer B, overlapped), 7.27 – 7.39 (m, 6H, for isomer A and isomer B, overlapped), 7.43 (d, *J* = 8.2 Hz, 2H, isomer A), 7.51 (d, *J* = 7.8 Hz, 1H, isomer B), 7.63 (d, *J* = 7.6 Hz, 1H, isomer A). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 29.7, 35.9, 52.2, 52.5, 56.0, 57.6, 60.8, 62.6, 65.2, 65.4, 67.0, 69.6, 122.5, 123.4, 123.7, 125.2, 125.2, 125.7, 126.7, 126.9, 127.1, 127.5, 127.5, 127.6, 127.6, 127.8, 128.5, 128.6, 129.2, 134.9, 135.0, 135.9, 137.0, 137.8, 139.6, 141.0, 142.3, 152.0, 153.4, 173.6, 174.9, 206.9, 207.6. IR (KBr, cm⁻¹): 3431, 3062, 3032, 2949, 2925, 2852, 1740, 1705, 1606, 1488, 1460, 1436, 1379, 1327, 1279, 1214, 1123, 1074, 1012, 922, 828, 799, 757, 703, 671, 513, 471. HRMS (ESI-TOF) calcd for C₂₇H₂₃F₃NO₃ ([M+H]⁺): 466.1625, found: 466.1627.

Methyl-4'-(4-methoxyphenyl)-1-oxo-2'-phenyl-1,3-dihydrospiro[indene-2,3'-pyrrolidine]-5'-carboxylate (4fa):



54.5 mg, 64% yield. The ratio of **4fa-A**/**4fa-B**/**4fa-C** was 1:0.43:0.17 as determined by $^1\text{H NMR}$. $^1\text{H NMR}$ (400 MHz, CDCl_3 , a mixture of three isomers) δ (ppm): 2.74 (d, $J = 8.4$ Hz, 2H, isomer A), 2.80 (d, $J = 8.0$ Hz, 2H, isomer C), 2.83 (d, $J = 8.0$ Hz, 2H, isomer B), 3.35 (s, 3H, isomer B), 3.66 (s, 3H, isomer C), 3.67 (s, 3H, isomer C), 3.69 (s, 3H, isomer A), 3.70 (s, 3H, isomer A), 3.82 (s, 3H, isomer B), 3.87 (d, $J = 7.9$ Hz, 1H, isomer B), 4.31 (d, $J = 9.3$ Hz, 1H, isomer A), 4.46 (d, $J = 9.3$ Hz, 1H, isomer A), 4.72 (s, 1H, isomer C), 4.84 (d, $J = 10.2$ Hz, 1H, isomer C), 4.92 (s, 1H, isomer B), 5.05 (s, 1H, isomer A), 5.34 (d, $J = 7.9$ Hz, 1H, isomer B), 6.63 (d, $J = 8.7$ Hz, 1H, isomer B), 6.69 (d, $J = 8.7$ Hz, 2H, isomer A), 6.87 (t, $J = 7.5$ Hz, 2H, isomer A), 7.00 – 7.10 (m, 5H, for isomer A and isomer B and isomer C, overlapped), 7.12 – 7.15 (m, 3H, for isomer A and isomer B and isomer C, overlapped), 7.18 – 7.24 (m, 5H, for isomer A and isomer B and isomer C, overlapped), 7.32 – 7.40 (m, 2H, for isomer A and isomer B and isomer C, overlapped), 7.53 (d, $J = 7.7$ Hz, 1H, isomer C), 7.61 (d, $J = 7.6$ Hz, 1H, isomer A). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ (ppm): 29.3, 35.0, 35.6, 45.7, 51.2, 52.1, 54.0, 54.8, 54.8, 55.0, 56.1, 60.8, 61.2, 62.6, 64.7, 64.8, 65.3, 65.4, 66.7, 69.2, 70.8, 113.3, 113.3, 113.6, 122.9, 123.0, 123.2, 125.3, 125.5, 126.6, 126.9, 127.0, 127.1, 127.2, 127.3, 127.5, 127.6, 128.3, 128.3, 129.0, 129.7, 130.0, 130.2, 131.2, 134.2, 134.4, 136.0, 136.0, 137.0, 138.1, 138.2, 151.3, 152.1, 153.6, 158.3, 158.5, 173.6, 175.1, 207.2. IR (KBr, cm^{-1}): 3425, 3330, 3063, 3033, 2926, 2854, 1741, 1706, 1607, 1498, 1462, 1437, 1377, 1326, 1281, 1219, 1152, 1122, 1069, 1015, 957, 887, 813, 759, 706, 677, 602, 557. **HRMS (ESI-TOF)** calcd for $\text{C}_{27}\text{H}_{26}\text{NO}_3$ ($[\text{M}+\text{H}]^+$): 428.1856, found: 428.1854.

Selected NMR spectra

