Construction of pyrrolidinyl spirooxindoles via a 1,3-dipolar cycloaddition reaction of (*E*)-*N*-Boc-3-alkylidene-indolin-2(3*H*)ones with azomethine ylides

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General Experimental Information

Reagents and starting materials obtained from commercial suppliers were used without further purification unless otherwise stated. All reactions were conducted in a closed system with an atmosphere of air and were monitored by TLC. ^1H NMR and ^{13}C NMR spectra were performed on a Bruker-300 MHz spectrometer for products dissolved by CDCl_3 with tetramethylsilane (TMS) as an internal standard. Data for ^1H are reported as follows: chemical shift (in ppm) and multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Splitting patterns that could not be clearly distinguished are designated as multiplets (m). Data for ^{13}C NMR are reported in ppm. High-resolution mass spectral analyses (HRMS) were measured using ESI ionization. The bacterial strains *Staphylococcus aureus* (ATCC-25825) was procured from Guizhou Provincial Institute for Drug, Guizhou, China.

General Experimental Procedures for Construction of Pyrrolidinyl Spirooxindoles via a 1,3-dipolar Cycloaddition Reaction of (*E*)-*N*-Boc-3-alkyl- idene-indolin-2(3*H*)ones with Azomethine ylides

A solution of compound **2** (0.5 mmol), paraformaldehyde (4 mmol), sarcosine (2 mmol) in CCl_3CH_3 (8 mL) at 75 °C for 8 h. After completion of the reaction, as indicated by TLC, the reaction mixture was directly subjected to flash column chromatography on silica gel (petroleum ether/EtOAc = 5:1~3:1) to furnish the corresponding products **4** as an orange oil. The two diastereomers pyrrolidinyl spirooxindoles can be separated chromatographically, and the dr values were determined by ^1H NMR analysis of the crude products.

Characterization Data for Compounds 4b-4z

tert-butyl 1'-methyl-2-oxo-4'-phenylspiro[indoline-3,3'-pyrrolidine]-1-carboxylate (**4b**). light orange oil; 13.0:1 dr, yield 82%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.64 (s, 9H), 2.56 (s, 3H), 2.97 (d, J = 9.6 Hz, 1H), 3.21-3.29 (m, 2H), 3.39-3.45 (m, 1H), 4.04-4.09 (m, 1H), 6.88-7.14 (m, 8H), 7.59 (d, J = 8.1 Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 28.1, 42.2, 55.1, 59.5, 59.9, 66.6, 84.2, 114.1, 123.8, 125.1, 126.8, 127.7, 127.8, 130.1, 137.6, 138.8, 149.1, 178.3; ^1H NMR (CDCl_3 , 300 MHz) δ (minor): 1.42 (s, 9H), 2.60 (s, 3H), 3.09 (d, J = 10.2 Hz, 1H), 3.24-3.29 (m, 1H), 3.33-3.46 (m, 2H), 3.72-3.78 (m, 1H), 6.80-6.86 (m, 2H), 7.11 (d, J = 6.4 Hz, 3H), 7.25-7.31

(m, 2H), 7.54-7.56 (m, 1H), 7.65 (d, $J = 7.2$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (minor): 27.8, 42.1, 58.6, 59.0, 59.8, 64.4, 83.5, 114.6, 122.4, 124.9, 127.4, 127.6, 127.9, 128.3, 131.8, 134.8, 139.4, 148.6, 176.9; HRMS (ESI) Calcd. for $\text{C}_{23}\text{H}_{27}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 379.1943; Found: 379.1951.

1-benzyl-1'-methyl-4'-phenylspiro[indoline-3,3'-pyrrolidin]-2-one (4c). light orange oil; 7.2:1 dr, yield 36%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 2.62 (s, 3H), 3.01 (d, $J = 9.3$ Hz, 1H), 3.23-3.29 (m, 1H), 3.34 (d, $J = 9.3$ Hz, 1H), 3.48-3.55 (m, 1H), 4.11-4.15 (m, 1H), 4.66 (d, $J = 15.6$ Hz, 1H), 5.09 (d, $J = 15.6$ Hz, 1H), 6.47 (d, $J = 7.5$ Hz, 1H), 6.88-7.06 (m, 9H), 7.21-7.24 (m, 3H), 7.35 (d, $J = 7.2$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 42.5, 43.7, 54.2, 59.5, 59.8, 657, 108.5, 122.0, 125.4, 126.7, 127.0, 127.3, 127.5, 127.8, 128.1, 128.5, 131.3, 135.6, 137.4, 142.1, 178.7; HRMS (ESI) Calcd. for $\text{C}_{25}\text{H}_{25}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 369.1889; Found: 369.1896.

ethyl 1'-methyl-2-oxo-4'-phenylspiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4d). light orange oil; 7.1:1 dr, yield 81%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.44 (t, $J = 7.2$ Hz, 3H), 2.57 (s, 3H), 2.99 (d, $J = 9.6$ Hz, 1H), 3.21-3.30 (m, 2H), 3.41-3.47 (m, 1H), 4.05-4.10 (m, 1H), 4.42-4.49 (m, 2H), 6.93-6.97 (m, 6H), 7.00-7.16 (m, 2H), 7.65 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 14.1, 42.1, 55.1, 59.5, 59.7, 63.2, 66.4, 114.2, 124.0, 125.1, 126.8, 127.7, 127.8, 127.9, 130.0, 137.3, 138.4, 150.6, 178.0; HRMS (ESI) Calcd. for $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 351.1630; Found: 351.1638.

tert-butyl 4'-(4-methoxyphenyl)-1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4e). light orange oil; 10.0:1 dr, yield 79%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.63 (s, 9H), 2.57 (s, 3H), 2.99 (d, $J = 9.6$ Hz, 1H), 3.19-3.29 (m, 2H), 3.36-3.42 (m, 1H), 3.65 (s, 3H), 3.98-4.03 (m, 1H), 6.57 (d, $J = 8.7$ Hz, 2H), 6.88 (d, $J = 8.7$ Hz, 2H), 6.91-6.96 (m, 1H), 7.06-7.12 (m, 1H), 7.16 (d, $J = 7.5$ Hz, 1H), 7.59 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 28.0, 42.3, 54.5, 55.0, 59.6, 60.0, 66.2, 84.2, 113.2, 114.2, 123.8, 125.1, 127.7, 128.9, 129.3, 130.0, 138.8, 149.0, 158.3, 178.2; HRMS (ESI) Calcd. for $\text{C}_{24}\text{H}_{29}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$: 409.2049; Found: 409.2054.

tert-butyl 4'-(3-methoxyphenyl)-1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4f). light orange oil; 10.0:1 dr, yield 79%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.63 (s, 9H), 2.57 (s, 3H), 2.99 (d, $J = 9.6$ Hz, 1H), 3.19-3.29 (m, 2H), 3.36-3.42 (m, 1H), 3.65 (s, 3H), 3.98-4.03 (m, 1H), 6.57 (d, $J = 8.7$ Hz, 2H), 6.88 (d, $J = 8.7$ Hz, 2H), 6.91-6.96 (m, 1H), 7.06-7.12 (m, 1H), 7.16 (d, $J = 7.5$ Hz, 1H), 7.59 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 28.0, 42.3, 54.5, 55.0, 59.6, 60.0, 66.2, 84.2, 113.2, 114.2, 123.8, 125.1, 127.7, 128.9, 129.3, 130.0, 138.8, 149.0, 158.3, 178.2; HRMS (ESI) Calcd. for $\text{C}_{24}\text{H}_{29}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$: 409.2049; Found: 409.2054.

ylate (4f). light orange oil; 10.1:1 dr, yield 80%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.65 (s, 9H), 2.58 (s, 3H), 2.98 (d, $J = 9.6$ Hz, 1H), 3.22-3.32 (m, 2H), 3.40-3.46 (m, 1H), 3.63 (s, 3H), 4.04-4.09 (m, 1H), 6.52 (s, 1H), 6.58 (d, $J = 7.8$ Hz, 2H), 6.94-6.99 (m, 2H), 7.09-7.14 (m, 1H), 7.20 (d, $J = 7.5$ Hz, 1H), 7.62 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 28.0, 42.2, 54.9, 55.1, 59.4, 59.6, 66.4, 84.2, 112.6, 113.2, 114.1, 120.2, 123.8, 125.0, 127.7, 128.7, 130.0, 138.8, 138.9, 149.0, 159.1, 178.1; HRMS (ESI) Calcd. for $\text{C}_{24}\text{H}_{29}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$: 409.2049; Found: 409.2052.

tert-butyl 4'-(2-methoxyphenyl)-1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4g). light orange oil; 7.1:1 dr, yield 75%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.67 (s, 9H), 2.48 (s, 3H), 2.66 (d, $J = 9.6$ Hz, 1H), 3.18-3.28 (m, 3H), 3.31 (s, 3H), 4.18-4.23 (m, 3H), 6.35 (d, $J = 7.8$ Hz, 1H), 6.62-6.68 (m, 2H), 6.81-6.85 (m, 1H), 6.97-7.03 (m, 2H), 7.32 (d, $J = 7.5$ Hz, 1H), 7.67 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 28.0, 42.1, 48.3, 53.9, 57.4, 60.2, 68.9, 83.6, 108.8, 113.4, 119.7, 123.1, 124.4, 126.6, 127.0, 127.3, 127.5, 130.6, 139.1, 149.6, 156.7, 179.1; HRMS (ESI) Calcd. for $\text{C}_{24}\text{H}_{29}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$: 409.2049; Found: 409.2056.

tert-butyl 4'-(3,4-dimethoxyphenyl)-1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4h). light orange oil; 6.9:1 dr, yield 85%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.60 (s, 9H), 2.54 (s, 3H), 2.93 (d, $J = 9.6$ Hz, 1H), 3.17-3.38 (m, 3H), 3.60 (s, 3H), 3.71 (s, 3H), 3.97-4.02 (m, 1H), 6.36 (s, 1H), 6.53 (s, 2H), 6.92-6.97 (m, 1H), 7.06-7.11 (m, 1H), 7.20-7.23 (m, 1H), 7.55 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 27.9, 42.2, 55.1, 55.5, 55.6, 59.5, 59.6, 66.0, 84.1, 110.3, 111.0, 114.1, 119.8, 123.7, 125.0, 127.7, 129.6, 130.1, 138.8, 147.7, 148.1, 148.9, 178.0; HRMS (ESI) Calcd. for $\text{C}_{25}\text{H}_{31}\text{N}_2\text{O}_5$ $[\text{M}+\text{H}]^+$: 439.2155; Found: 439.2160.

tert-butyl 4'-(benzo[d][1,3]dioxol-5-yl)-1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4i). light orange oil; 8.2:1 dr, yield 80%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.63 (s, 9H), 2.53 (s, 3H), 2.95 (d, $J = 9.3$ Hz, 1H), 3.15-3.29 (m, 2H), 3.32-3.35 (m, 1H), 3.92-3.97 (m, 1H), 5.78-5.79 (m, 1H), 6.43-6.52 (m, 3H), 6.95-6.98 (m, 1H), 7.09-7.17 (m, 2H), 7.62 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 28.1, 42.2, 55.0, 59.6, 60.2, 66.4, 84.3, 100.7, 107.6, 108.4, 114.3, 121.3, 123.9, 125.2, 127.8, 130.1, 131.5, 138.9, 146.2, 147.2, 149.1, 178.3;

HRMS (ESI) Calcd. for $C_{24}H_{27}N_2O_5$ $[M+H]^+$: 423.1842; Found: 423.1851.

tert-butyl 1'-methyl-2-oxo-4'-m-tolylspiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4j). light orange oil; 10.2:1 dr, yield 78%; 1H NMR ($CDCl_3$, 300 MHz) δ (major): 1.64 (s, 9H), 2.13 (s, 3H), 2.56 (s, 3H), 2.95 (d, $J = 9.6$ Hz, 1H), 3.19-3.24 (m, 1H), 3.29 (d, $J = 9.6$ Hz, 1H), 3.38-3.44 (m, 1H), 4.01-4.06 (m, 1H), 6.73-6.82 (m, 3H), 6.88-6.95 (m, 2H), 7.05-7.08 (m, 1H), 7.16-7.18 (m, 1H), 7.59 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (major): 21.1, 28.0, 42.2, 55.2, 59.5, 59.6, 66.3, 84.0, 114.0, 123.6, 124.7, 125.0, 127.4, 127.6, 127.7, 128.6, 130.0, 137.2, 138.7, 149.0, 178.1; HRMS (ESI) Calcd. for $C_{24}H_{29}N_2O_3$ $[M+H]^+$: 393.2100; Found: 393.2106.

tert-butyl 1'-methyl-2-oxo-4'-p-tolylspiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4k). light orange oil; 12.9:1 dr, yield 79%; 1H NMR ($CDCl_3$, 300 MHz) δ (major): 1.64 (s, 9H), 2.16 (s, 3H), 2.56 (s, 3H), 2.96 (d, $J = 9.6$ Hz, 1H), 3.19-3.30 (m, 2H), 3.38-3.43 (m, 1H), 4.02-4.07 (m, 1H), 6.85 (s, 4H), 6.91-6.96 (m, 1H), 7.07-7.12 (m, 1H), 7.17 (d, $J = 7.5$ Hz, 1H), 7.61 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (major): 20.9, 28.1, 42.3, 54.8, 59.5, 60.0, 66.6, 84.1, 114.2, 123.8, 125.2, 127.7, 127.8, 128.5, 130.2, 134.3, 136.3, 138.9, 149.1, 178.2; HRMS (ESI) Calcd. for $C_{24}H_{29}N_2O_3$ $[M+H]^+$: 393.2100; Found: 393.2102.

tert-butyl 4'-(2-fluorophenyl)-1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4l). light orange oil; 8.3:1 dr, yield 81%; 1H NMR ($CDCl_3$, 300 MHz) δ (major): 1.67 (s, 9H), 2.54 (s, 3H), 2.89 (d, $J = 9.6$ Hz, 1H), 3.18-3.26 (m, 2H), 3.33-3.38 (m, 1H), 4.23-4.27 (m, 1H), 6.63-6.68 (m, 1H), 6.78-6.79 (m, 2H), 6.99-7.08 (m, 3H), 7.40-7.42 (m, 1H), 7.71 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (major): 28.0, 41.9, 47.6, 58.0, 60.0, 67.8, 83.9, 114.2, 114.5 (d, $J_{CF} = 22.1$ Hz), 123.4, 123.5 (d, $J_{CF} = 3.5$ Hz), 124.6, 126.1 (d, $J_{CF} = 15.2$ Hz), 127.6, 128.2, 128.3 (d, $J_{CF} = 2.6$ Hz), 129.8, 139.3, 149.3, 160.8 (d, $J_{CF} = 244.0$ Hz), 178.6; HRMS (ESI) Calcd. for $C_{23}H_{26}FN_2O_3$ $[M+H]^+$: 397.1849; Found: 397.1854.

tert-butyl 4'-(2-bromophenyl)-1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4m). light orange oil; 12.8:1 dr, yield 75%; 1H NMR ($CDCl_3$, 300 MHz) δ (major): 1.64 (s, 9H), 2.51 (s, 3H), 2.96 (d, $J = 9.0$ Hz, 1H), 3.03-3.13 (m, 2H), 3.35-3.39 (m, 1H), 4.25-4.28 (m, 1H),

6.67-6.72 (m, 2H), 6.88-6.90 (m, 1H), 7.05-7.07 (m, 1H), 7.17-7.22 (m, 2H), 7.67 (d, $J = 8.1$ Hz, 1H), 7.73-7.76 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 28.1, 41.8, 53.6, 58.1, 62.2, 67.9, 83.9, 114.2, 123.3, 124.8, 126.0, 126.9, 127.6, 128.0, 129.7, 129.8, 132.2, 139.6, 139.7, 149.2, 178.9; HRMS (ESI) Calcd. for $\text{C}_{23}\text{H}_{26}\text{BrN}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 457.1049; Found: 457.1049. ^1H NMR (CDCl_3 , 400 MHz) δ (minor): 1.46 (s, 9H), 2.64 (s, 3H), 3.18-3.12 (m, 3H), 3.42 (d, $J = 10.2$ Hz, 1H), 4.45-4.49 (m, 1H), 6.99-7.03 (m, 1H), 7.19-7.28 (m, 3H), 7.36 (d, $J = 9.0$ Hz, 1H), 7.53-7.55 (m, 1H), 7.62-7.64 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (minor): 27.9, 41.9, 55.6, 59.4, 60.7, 65.1, 83.6, 114.4, 123.7, 124.8, 125.5, 126.9, 128.4, 128.7, 128.8, 130.1, 130.9, 132.8, 139.2, 148.6, 176.5; HRMS (ESI) Calcd. for $\text{C}_{23}\text{H}_{26}\text{BrN}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 457.1049; Found: 457.1047.

tert-butyl 4'-(3-bromophenyl)-1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4n). light orange oil; 8.2:1 dr, yield 79%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.63 (s, 9H), 2.54 (s, 3H), 2.97 (d, $J = 9.3$ Hz, 1H), 3.16-3.25 (m, 2H), 3.33-3.39 (m, 1H), 3.94-3.99 (m, 1H), 6.81-6.90 (m, 2H), 6.91-6.96 (m, 1H), 7.07-7.14 (m, 3H), 7.18 (s, 1H), 7.61 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 28.0, 42.1, 54.7, 59.3, 59.6, 66.2, 84.3, 114.2, 122.0, 123.8, 125.0, 126.6, 127.9, 129.3, 129.6, 129.8, 130.8, 138.8, 140.1, 148.9, 177.9; HRMS (ESI) Calcd. for $\text{C}_{23}\text{H}_{26}\text{BrN}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 457.1049; Found: 457.1051.

tert-butyl 4'-(4-bromophenyl)-1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4o). light orange oil; 11.0:1 dr, yield 76%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.65 (s, 9H), 2.57 (s, 3H), 2.99 (d, $J = 9.3$ Hz, 1H), 3.20-3.27 (m, 2H), 3.38-3.42 (m, 1H), 3.98-4.03 (m, 1H), 6.87 (d, $J = 8.4$ Hz, 2H), 6.93-6.98 (m, 1H), 7.11-7.19 (m, 4H), 7.62-7.65 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 28.0, 42.1, 54.4, 59.3, 59.8, 66.4, 84.4, 114.3, 120.7, 123.9, 125.0, 128.0, 129.6, 130.9, 136.8, 138.8, 148.9, 177.9; HRMS (ESI) Calcd. for $\text{C}_{23}\text{H}_{26}\text{BrN}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 457.1049; Found: 457.1051.

tert-butyl 4'-(4-chlorophenyl)-1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4p). light orange oil; 13.1:1 dr, yield 81%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.62 (s, 9H), 2.53 (s, 3H), 2.96 (d, $J = 9.6$ Hz, 1H), 3.17-3.25 (m, 2H), 3.33-3.39 (m, 1H), 3.96-4.01 (m, 1H), 6.88-6.95 (m, 3H), 6.99 (d, $J = 8.4$ Hz, 2H), 7.06-7.12 (m, 2H), 7.60 (d, $J = 8.7$ Hz, 1H); ^{13}C NMR

(CDCl₃, 75 MHz) δ (major): 28.0, 42.1, 54.3, 59.3, 59.8, 66.4, 84.3, 114.2, 123.9, 125.0, 127.9, 128.0, 128.1, 129.2, 129.6, 132.4, 136.2, 138.7, 148.9, 177.9; HRMS (ESI) Calcd. for C₂₃H₂₆ClN₂O₃ [M+H]⁺: 413.1554; Found: 413.1562.

tert-butyl 4'-(2-chlorophenyl)-1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4q). light orange oil; 12.3:1 dr, yield 76%; ¹H NMR (CDCl₃, 300 MHz) δ (major): 1.65 (s, 9H), 2.52 (s, 3H), 3.01 (s, 2H), 3.12 (dd, *J* = 7.5, 9.6 Hz, 1H), 3.39 (dd, *J* = 3.3 Hz, 9.6 Hz, 1H), 4.32 (dd, *J* = 3.3 Hz, 7.5 Hz, 1H), 6.71-6.74 (m, 2H), 6.97-6.99 (m, 2H), 7.04-7.07 (m, 1H), 7.15-7.18 (m, 1H), 7.67-7.70 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ (major): 28.0, 41.8, 51.1, 58.0, 61.5, 68.0, 83.9, 114.1, 123.3, 124.7, 126.2, 127.5, 127.7, 128.8, 129.2, 129.8, 134.9, 137.6, 139.4, 149.2, 178.9; HRMS (ESI) Calcd. for C₂₃H₂₆ClN₂O₃ [M+H]⁺: 413.1554; Found: 413.1562.

tert-butyl 1'-methyl-2-oxo-4'-(3-(trifluoromethyl)phenyl)spiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4r). light orange oil; 8.9:1 dr, yield 70%; ¹H NMR (CDCl₃, 300 MHz) δ (major): 1.63 (s, 9H), 2.57 (s, 3H), 3.00 (d, *J* = 9.6 Hz, 1H), 3.21-3.29 (m, 2H), 3.39-3.45 (m, 1H), 4.05-4.10 (m, 1H), 6.91-6.93 (m, 1H), 7.05-7.14 (m, 4H), 7.24-7.28 (m, 2H), 7.57 (d, *J* = 8.1 Hz, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ (major): 28.0, 42.1, 55.0, 59.5, 59.6, 66.1, 84.4, 114.3, 123.6 (q, *J* = 3.9 Hz), 123.9, 124.6 (q, *J* = 3.8 Hz), 128.0, 128.3, 129.6, 131.2, 138.8, 138.9, 148.9, 177.9; HRMS (ESI) Calcd. for C₂₄H₂₆F₃N₂O₃ [M+H]⁺: 447.1817; Found: 447.1825.

tert-butyl 4'-(4-cyanophenyl)-1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4s). light orange oil; 8.4:1 dr, yield 77%; ¹H NMR (CDCl₃, 300 MHz) δ (major): 1.62 (s, 9H), 2.53 (s, 3H), 2.98 (d, *J* = 9.3 Hz, 1H), 3.17-3.22 (m, 2H), 3.36-3.42 (m, 1H), 4.00-4.04 (m, 1H), 6.85-6.90 (m, 1H), 7.00-7.11 (m, 4H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.59 (d, *J* = 8.1 Hz, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ (major): 28.0, 41.9, 54.7, 59.2, 59.6, 66.4, 84.5, 110.5, 114.3, 118.5, 123.9, 124.9, 128.1, 128.6, 129.2, 131.6, 138.7, 143.7, 148.8, 177.7; HRMS (ESI) Calcd. for C₂₄H₂₆N₃O₃ [M+H]⁺: 404.1896; Found: 404.1899.

tert-butyl 1'-methyl-4'-(4-nitrophenyl)-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4t). light orange oil; 6.9:1 dr, yield 82%; ¹H NMR (CDCl₃, 300 MHz) δ (major): 1.63 (s, 9H),

2.55 (s, 3H), 3.00 (d, $J = 9.6$ Hz, 1H), 3.20-3.25 (m, 2H), 3.39-3.45 (m, 1H), 4.06-4.10 (m, 1H), 6.86-6.91 (m, 1H), 7.03-7.11 (m, 2H), 7.15 (d, $J = 8.7$ Hz, 2H), 7.60 (d, $J = 8.1$ Hz, 1H), 7.88-7.90 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 28.0, 41.9, 54.5, 59.2, 59.8, 66.5, 84.6, 114.4, 123.0, 124.0, 124.9, 128.2, 128.8, 129.2, 138.7, 146.0, 146.6, 148.8, 177.7; HRMS (ESI) Calcd. for $\text{C}_{23}\text{H}_{26}\text{N}_3\text{O}_5$ $[\text{M}+\text{H}]^+$: 424.1794; Found: 424.1799.

tert-butyl 5-bromo-1'-methyl-2-oxo-4'-phenylspiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4u). light orange oil; 8.8:1 dr, yield 70%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.65 (s, 9H), 2.58 (s, 3H), 3.00 (d, $J = 9.3$ Hz, 1H), 3.15-3.23 (m, 2H), 3.44-3.50 (m, 1H), 4.05-4.10 (m, 1H), 7.00 (d, $J = 7.5$ Hz, 2H), 7.05-7.14 (m, 3H), 7.19-7.23 (m, 1H), 7.28-7.33 (m, 1H), 7.50 (d, $J = 8.7$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 28.0, 42.0, 55.3, 59.5, 66.2, 84.6, 115.7, 116.8, 127.1, 127.7, 128.0, 128.3, 130.5, 132.3, 137.4, 137.8, 148.8, 177.2; HRMS (ESI) Calcd. for $\text{C}_{23}\text{H}_{26}\text{BrN}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 457.1049; Found: 457.1058.

tert-butyl 1'-methyl-2-oxo-4'-(thiophen-2-yl)spiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4v). light orange oil; 9.1:1 dr, yield 81%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.47 (s, 9H), 2.56 (s, 3H), 3.08 (d, $J = 10.2$ Hz, 1H), 3.25-3.37 (m, 2H), 3.41 (d, $J = 10.2$ Hz, 1H), 3.92-3.98 (m, 1H), 6.58 (d, $J = 3.3$ Hz, 1H), 6.59-6.81 (m, 1H), 7.01 (d, $J = 5.1$ Hz, 1H), 7.20-7.32 (m, 2H), 7.49 (d, $J = 7.2$ Hz, 1H), 7.70 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 27.8, 41.9, 54.2, 59.5, 60.1, 64.3, 83.5, 114.6, 122.3, 124.0, 124.9, 126.4, 128.4, 131.2, 136.9, 139.6, 148.6, 176.6; HRMS (ESI) Calcd. for $\text{C}_{21}\text{H}_{25}\text{N}_2\text{O}_3\text{S}$ $[\text{M}+\text{H}]^+$: 385.1508; Found: 385.1517.

tert-butyl 1'-methyl-4'-(naphthalen-1-yl)-2-oxospiro[indoline-3,3'-pyrrolidine]-1-carboxylate (4w). light orange oil; >99:1 dr, yield 68%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 1.63 (s, 9H), 2.60 (s, 3H), 3.00 (d, $J = 9.3$ Hz, 1H), 3.25-3.33 (m, 2H), 3.55-3.60 (m, 1H), 4.81-4.85 (m, 1H), 6.65-6.70 (m, 1H), 6.81-6.87 (m, 1H), 6.95 (d, $J = 7.5$ Hz, 1H), 7.26-7.33 (m, 4H), 7.52 (d, $J = 8.1$ Hz, 1H), 7.62 (d, $J = 6.9$ Hz, 2H), 7.71-7.74 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 28.1, 42.1, 50.4, 58.8, 61.8, 67.7, 83.9, 113.7, 122.7, 123.2, 124.6, 125.0, 125.1, 125.2, 125.6, 127.3, 127.4, 128.5, 129.9, 132.1, 133.3, 134.7, 138.6, 148.8, 179.3; HRMS (ESI) Calcd. for $\text{C}_{27}\text{H}_{29}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 429.2100; Found: 429.2107.

1-tert-butyl 4'-ethyl 1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1,4'-dicarboxylate (4x).

light orange oil; >99:1 dr, yield 85%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 0.65 (t, $J = 7.2$ Hz, 3H), 1.63 (s, 9H), 2.42 (s, 3H), 2.78-2.85 (m, 2H), 2.97 (d, $J = 8.7$ Hz, 1H), 3.48-3.60 (m, 3H), 3.66-3.72 (m, 1H), 7.05-7.11 (m, 1H), 7.23-7.28 (m, 1H), 7.40-7.43 (m, 1H), 7.78 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 13.1, 27.9, 41.5, 53.3, 55.8, 56.4, 60.3, 66.9, 84.2, 114.3, 124.0, 124.3, 128.3, 130.2, 139.3, 149.0, 169.7, 176.6; HRMS (ESI) Calcd. for $\text{C}_{20}\text{H}_{27}\text{N}_2\text{O}_5$ $[\text{M}+\text{H}]^+$: 375.1842; Found: 375.1849.

1-tert-butyl 4'-ethyl 5-fluoro-1'-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1,4'-dicarboxylate (4y). light orange oil; >99:1 dr, yield 84%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 0.70 (t, $J = 7.2$ Hz, 3H), 1.62 (s, 9H), 2.41 (s, 3H), 2.70-2.81 (m, 2H), 2.89 (d, $J = 8.7$ Hz, 1H), 3.52-3.71 (m, 4H), 6.91-6.98 (m, 1H), 7.20-7.26 (m, 1H), 7.75-7.79 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 13.2, 28.0, 41.3, 53.2, 55.3, 56.6, 60.6, 66.7, 84.5, 111.8 (d, $J_{\text{CF}} = 25.1$ Hz), 114.7 (d, $J_{\text{CF}} = 22.7$ Hz), 115.5 (d, $J_{\text{CF}} = 7.8$ Hz), 132.2 (d, $J_{\text{CF}} = 8.7$ Hz), 135.2 (d, $J_{\text{CF}} = 2.4$ Hz), 149.0, 159.7 (d, $J_{\text{CF}} = 242.0$ Hz), 169.6, 175.9; HRMS (ESI) Calcd. for $\text{C}_{20}\text{H}_{26}\text{FN}_2\text{O}_5$ $[\text{M}+\text{H}]^+$: 393.1748; Found: 393.1757.

1- tert-butyl 4'-ethyl 1',5-dimethyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1,4'-dicarboxylate

(4z). light orange oil; >99:1 dr, yield 85%; ^1H NMR (CDCl_3 , 300 MHz) δ (major): 0.63-0.68 (m, 3H), 1.62 (s, 9H), 2.29 (s, 3H), 2.42 (s, 3H), 2.77-2.82 (m, 2H), 2.92-2.96 (m, 1H), 3.48-3.70 (m, 4H), 7.05 (d, $J = 8.1$ Hz, 1H), 7.22 (s, 1H), 7.65 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ (major): 13.2, 21.0, 28.0, 41.6, 53.4, 55.9, 56.5, 60.4, 67.1, 84.1, 114.1, 124.6, 128.8, 130.3, 134.0, 136.9, 149.1, 169.9, 176.9; HRMS (ESI) Calcd. for $\text{C}_{21}\text{H}_{29}\text{N}_2\text{O}_5$ $[\text{M}+\text{H}]^+$: 389.1998; Found: 389.1998.

General Experimental Procedures for *in vitro* antibacterial activity

Using the literature precedent by Dhar et al.,¹³ the test compounds were dissolved in DMSO to obtain 1 mg/mL stock solutions. Seeds broth (broth containing microbial spores) was prepared in

NB from 24 h old bacterial cultures on nutrient agar (Hi-media, Mumbai) at 37 ± 1 °C. The colony forming units (cfu) of the seeded broth were determined by plate count technique and adjusted with the help of McFarland standards in the range of 10^4 - 10^5 cfu/mL. The final inoculum size was 10^5 cfu/mL for antibacterial assay. Testing was performed at pH 6.5 ± 0.2 for bacteria *Staphylococcus aureus*. Exactly 0.2 mL of the solution of test compound was added to 1.8 mL of seeded broth to form the first dilution. One mL of this was diluted with a further 1 mL of the seeded broth to give the second dilution and so on till six such dilutions were obtained. A set of assay tubes containing only seeded broth was kept as control and likewise solvent controls were also run simultaneously. The tubes were incubated in BOD incubators at 37 ± 1 °C for bacteria *Staphylococcus aureus*. The minimum inhibitory concentrations (MICs) were recorded by visual observations after 24 h (for bacteria *Staphylococcus aureus*) of incubation. Streptomycin was used as standards for bacterial *Staphylococcus aureus*.

The Copies of ^1H NMR and ^{13}C NMR Spectra for Compounds 4b-4z

^1H and ^{13}C NMR of 4b

¹H and ¹³C NMR of 4c

¹H and ¹³C NMR of 4d

¹H and ¹³C NMR of 4e

¹H and ¹³C NMR of 4f

¹H and ¹³C NMR of 4g

¹H and ¹³C NMR of 4h

¹H and ¹³C NMR of 4i

¹H and ¹³C NMR of 4j

¹H and ¹³C NMR of 4k

¹H and ¹³C NMR of 4I

¹H and ¹³C NMR of 4m

$^1\text{H} - ^1\text{H}$ COSY of 4m

NOESY of 4m

¹H and ¹³C NMR of 4m'

$^1\text{H} - ^1\text{H}$ COSY of 4m'

NOESY of 4m'

¹H and ¹³C NMR of 4n

¹H and ¹³C NMR of 4o

¹H and ¹³C NMR of 4p

¹H and ¹³C NMR of 4q

¹H and ¹³C NMR of 4r

¹H and ¹³C NMR of 4s

¹H and ¹³C NMR of 4t

¹H and ¹³C NMR of 4u

¹H and ¹³C NMR of 4v

¹H and ¹³C NMR of 4w

¹H and ¹³C NMR of 4x

¹H and ¹³C NMR of 4y

¹H and ¹³C NMR of 4z