Supplementary Data

Stereoselective synthesis of novel dispiro oxindole-pyrrolothiazolo-androsterone hybrids

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Supplementary Data content

1. General experimental procedure for the synthesis **3**, **4**
2. NMR spectral data for all compounds
3. 1D and 2D NMR data for representative compounds **3b** and **4b**

1. Experimental

The melting points were measured in open capillary tubes and are uncorrected. The ^1H , ^{13}C and the 2D NMR spectra were recorded on a Bruker (Avance) 300 MHz NMR instrument using TMS as internal standard and CDCl_3 as solvent. Standard Bruker software was used throughout. Chemical shifts are given in parts per million (δ -scale) and the coupling constants are given in Hertz. Elemental analyses were performed on a Perkin Elmer 2400 Series II Elemental CHNS analyzer. The single crystal X-ray data set for **3e** was collected on Bruker Kappa APPEXII diffractometer with Mo-K_α ($\lambda = 0.71073 \text{ \AA}$) radiation. SHELXTL software was used for structure solution and refinement. Silica gel-G plates (Merck) were used for tlc analysis with a mixture of petroleum ether (60–80°C) and ethyl acetate as eluent. All the chemicals were purchased from Sigma–Aldrich and used without any further purification.

General procedure for the synthesis of spiro[5'.3'']oxindole-spiro[6'.16]-7'-aryl-tetrahydro-1H-pyrrolo[1',2'-c][1',3']thiazolo trans-dehydroandrosterones / androsterones 3 and 4 : A mixture of the appropriate steroidal exocyclic dipolarophile (**1** or **2**, 1 mmol), isatin (1 mmol) and 1,3-thiazolane-4-carboxylic acid (1.2 mmol) was refluxed in methanol (10 mL) for 4–5 h. The progress of the reaction was monitored by thin layer chromatography. After completion of the reaction as evident from TLC, the reaction mixture was cooled to room temperature and poured into crushed ice. The resultant precipitate was filtered, washed with 5% hexane-ethyl acetate (10 mL) and dried under vacuum to get the products **3** or **4** as pale yellow solid.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-phenyl-tetrahydro-1H-pyrrolo[1',2'-c][1',3']thiazolo-trans-dehydroandrosterone (3a): Obtained as pale yellow solid; Yield 92%; m.p. 196–198°C; Anal. Calcd. for $\text{C}_{37}\text{H}_{42}\text{N}_2\text{O}_3\text{S}$: C, 74.71; H, 7.12; N, 4.71. Found: C, 74.68; H, 7.18; N, 4.68. ^1H

NMR 0.27–0.34 (m, 1H), 0.38 (s, 3H), 0.54 (td, $J = 11.3, 5.2$ Hz, 1H), 0.75–0.83 (m, 1H), 0.86 (s, 3H), 0.93–0.98 (m, 2H), 1.20–1.44 (m, 5H), 1.49–1.56 (m, 2H), 1.71–1.98 (m, 3H), 2.10–2.26 (m, 2H), 2.38 (dd, $J = 13.2, 4.2$ Hz, 1H), 2.82 (dd, $J = 9.6, 7.2$ Hz, 1H), 2.91 (dd, $J = 9.5, 5.5$ Hz, 1H), 3.42–3.47 (m, 1H), 3.58 (s, 2H), 3.65 (d, $J = 9.3$ Hz, 1H), 4.66–4.74 (m, 1H), 5.24–5.26 (m, 1H), 6.80–7.63 (m, 10H). ^{13}C NMR 14.1, 19.1, 19.8, 30.2, 30.8, 31.0, 31.3, 31.4, 33.1, 36.5, 36.9, 42.0, 46.8, 47.4, 48.1, 50.5, 54.6, 71.5, 71.9, 72.5, 74.2, 109.8, 120.8, 122.4, 122.8, 125.7, 129.2, 129.8, 130.1, 130.6, 140.0, 140.8, 141.0, 178.6, 219.3.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(4-chlorophenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-dehydroandrosterone (3b): Obtained as pale yellow solid; Yield 93%; m.p. 194–195°C; Anal. Calcd. for $\text{C}_{37}\text{H}_{41}\text{ClN}_2\text{O}_3\text{S}$: C, 70.62; H, 6.57; N, 4.45. Found: C, 70.68; H, 6.50; N, 4.52. ^1H NMR 0.28–0.40 (m, 1H), 0.35 (s, 3H), 0.54 (td, $J = 11.3, 4.9$ Hz, 1H), 0.75–0.83 (m, 3H), 0.86 (s, 3H), 0.87–1.03 (m, 2H), 1.03–1.78 (m, 6H), 1.91–1.97 (m, 2H), 2.15–2.27 (m, 2H), 2.37 (dd, $J = 13.4, 4.1$ Hz, 1H), 2.81 (dd, $J = 9.6, 7.2$ Hz, 1H), 2.89 (dd, $J = 9.5, 5.6$ Hz, 1H), 3.42–3.49 (m, 1H), 3.59 (s, 2H), 3.67 (d, $J = 9.6$ Hz, 1H), 4.66–4.73 (m, 1H), 5.27–5.30 (m, 1H), 6.80–7.39 (m, 8H), 7.88 (brs, 1H). ^{13}C NMR 14.2, 19.9, 30.4, 30.9, 31.1, 31.5, 33.1, 36.5, 37.0, 42.2, 46.9, 47.3, 48.3, 50.4, 54.5, 71.6, 72.1, 72.5, 74.2, 109.6, 120.7, 122.5, 125.9, 128.8, 129.4, 129.8, 131.3, 133.4, 136.2, 140.8, 141.0, 178.3, 219.2.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(4-bromophenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-dehydroandrosterone (3c): Obtained as pale yellow solid; Yield 96%; m.p. 199–201°C; Anal. Calcd. for $\text{C}_{37}\text{H}_{41}\text{BrN}_2\text{O}_3\text{S}$: C, 65.96; H, 6.13; N, 4.16. Found: C, 65.94; H, 6.15; N, 4.19. ^1H NMR 0.27 (s, 3H), 0.28–0.34 (m, 1H), 0.46 (td, $J = 11.2, 4.8$ Hz, 1H), 0.69–0.80 (m, 1H), 0.78 (s, 3H), 0.85–0.91 (m, 1H), 1.11–1.63 (m, 6H), 1.69–1.89 (m, 4H), 2.04–2.20 (m, 3H), 2.31 (dd, $J = 13.4, 3.7$ Hz, 1H), 2.71–2.76 (m, 1H), 2.82 (dd, $J = 9.6, 5.7$ Hz, 1H), 3.35–3.42 (m,

1H), 3.51 (s, 2H), 3.58 (d, $J = 9.6$ Hz, 1H), 4.58–4.66 (m, 1H), 5.17–5.18 (m, 1H), 6.73–7.39 (m, 8H), 8.10 (brs, 1H). ^{13}C NMR 14.3, 19.2, 19.8, 29.6, 30.3, 30.8, 31.1, 31.4, 33.1, 36.5, 36.9, 42.1, 46.8, 47.5, 48.2, 50.2, 54.5, 71.5, 72.0, 72.2, 74.3, 109.7, 115.4, 120.7, 121.5, 122.4, 125.7, 129.3, 129.5, 129.8, 131.7, 136.6, 140.9, 178.6, 219.3.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(4-fluorophenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-dehydroandrosterone (3d): Obtained as pale yellow solid; Yield 89%; m.p. 190–192°C; Anal. Calcd. for $\text{C}_{37}\text{H}_{41}\text{BrN}_2\text{O}_3\text{S}$: C, 65.96; H, 6.13; N, 4.16. Found: C, 65.90; H, 6.18; N, 4.24. ^1H NMR 0.32 (s, 3H), 0.33–0.41 (m, 1H), 0.52–0.58 (m, 1H), 0.81–1.00 (m, 3H), 0.85 (s, 3H), 1.29–1.71 (m, 6H), 1.75–1.97 (m, 4H), 2.15–2.28 (m, 3H), 2.40 (dd, $J = 13.5, 4.2$ Hz, 1H), 2.79–2.93 (m, 1H), 3.46–3.50 (m, 1H), 3.60 (s, 2H), 3.69 (d, $J = 9.6$ Hz, 1H), 4.67–4.70 (m, 1H), 5.25–5.26 (m, 1H), 6.80–7.43 (m, 8H), 7.91 (brs, 1H). ^{13}C NMR 14.2, 19.9, 22.6, 29.5, 30.4, 30.8, 31.2, 31.3, 33.2, 36.5, 37.0, 42.2, 46.9, 47.5, 48.3, 50.4, 54.4, 65.7, 71.6, 72.2, 72.5, 74.5, 109.5, 115.3, 115.6, 120.6, 120.7, 122.5, 125.9, 129.5, 129.6, 129.7, 131.5, 133.3, 140.7, 141.0, 160.6, 163.8, 178.3, 219.2.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(4-methylphenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-dehydroandrosterone (3e): Obtained as pale yellow solid; Yield 95%; m.p. 215–217°C; Anal. Calcd. for $\text{C}_{38}\text{H}_{44}\text{N}_2\text{O}_3\text{S}$: C, 74.96; H, 7.28; N, 4.60. Found: C, 74.90; H, 7.21; N, 4.66. ^1H NMR 0.28 (s, 3H), 0.38 (td, $J = 12.9, 4.5$ Hz, 1H), 0.57 (td, $J = 11.3, 4.8$ Hz, 1H), 0.78–0.96 (m, 2H), 0.85 (s, 3H), 0.87–0.96 (m, 1H), 1.28–1.53 (m, 7H), 1.71–1.99 (m, 3H), 2.15–2.27 (m, 2H), 2.33 (s, 3H), 2.45 (dd, $J = 13.4, 4.4$ Hz, 1H), 2.82 (dd, $J = 9.7, 6.7$ Hz, 1H), 2.93 (dd, $J = 9.7, 5.9$ Hz, 1H), 3.42–3.46 (m, 1H), 3.59 (d, $J = 6.6$ Hz, 1H), 3.65 (d, $J = 6.9$ Hz, 1H), 3.69 (d, $J = 9.9$ Hz, 1H), 4.70–4.73 (m, 1H), 5.27–5.28 (m, 1H), 6.77–7.49 (m, 8H), 7.59 (brs, 1H). ^{13}C NMR 14.0, 19.1, 19.9, 21.0, 29.6, 30.3, 30.8, 31.3, 31.5, 33.4, 36.5, 37.0, 42.1, 46.8, 48.0, 48.4,

50.4, 54.9, 71.5, 71.8, 72.4, 74.5, 109.3, 120.8, 122.2, 126.0, 129.2, 129.5, 129.6, 129.8, 134.2, 137.0, 140.5, 140.9, 178.2, 219.0.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(4-methoxyphenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-dehydroandrosterone (3f): Obtained as pale yellow solid; Yield 89%; m.p. 211–213°C; Anal. Calcd. for C₃₈H₄₄N₂O₄S: C, 73.04; H, 7.10; N, 4.48. Found: C, 73.12; H, 7.16; N, 4.52. ¹H NMR 0.27 (s, 3H), 0.41 (td, *J* = 12.6, 4.2 Hz, 1H), 0.57 (td, *J* = 11.1, 4.8 Hz, 1H), 0.83–0.85 (m, 2H), 0.85 (s, 3H), 0.88–0.97 (m, 2H), 1.18–1.70 (m, 6H), 1.76–1.98 (m, 4H), 2.10–2.28 (m, 3H), 2.46 (dd, *J* = 13.5, 4.2 Hz, 1H), 2.83 (dd, *J* = 9.9, 6.3 Hz, 1H), 2.93 (dd, *J* = 9.7, 5.9 Hz, 1H), 3.45–3.50 (m, 1H), 3.59 (d, *J* = 6.9 Hz, 1H), 3.64–3.69 (m, 2H), 3.79 (s, 2H), 4.67–4.70 (m, 1H), 6.79–7.51 (m, 8H), 8.00 (brs, 1H). ¹³C NMR 13.9, 19.1, 19.9, 29.6, 30.4, 30.5, 30.8, 31.3, 31.4, 33.5, 36.5, 37.0, 42.1, 46.9, 48.4, 50.4, 54.6, 55.2, 71.6, 71.9, 72.2, 74.8, 109.5, 113.9, 115.3, 120.9, 122.2, 125.8, 129.1, 129.5, 129.6, 140.6, 140.8, 158.9, 178.7, 219.2.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(2-chlorophenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-dehydroandrosterone (3g): Obtained as pale yellow solid; Yield 87%; m.p. 189–191°C; Anal. Calcd. for C₃₇H₄₁ClN₂O₃S: C, 70.62; H, 6.57; N, 4.45. Found: C, 70.66; H, 6.52; N, 4.48. ¹H NMR 0.21 (td, *J* = 12.8, 5.1 Hz, 1H) 0.44 (td, *J* = 10.8, 6.0 Hz, 1H), 0.58 (s, 3H), 0.71 (td, *J* = 12.2, 4.2 Hz, 1H), 0.78–0.83 (m, 1H), 0.84 (s, 3H), 0.90–0.95 (m, 2H), 1.21–1.58 (m, 6H), 1.75–1.92 (m, 2H), 2.13–2.25 (m, 2H), 2.19 (dd, *J* = 13.8, 4.2 Hz, 1H), 2.82 (dd, *J* = 8.8, 5.6 Hz, 1H), 2.87–2.83 (m, 1H), 3.41–3.44 (m, 1H), 3.47 (d, *J* = 5.1 Hz, 1H), 3.61 (d, *J* = 5.1 Hz, 1H), 4.45 (d, *J* = 8.7 Hz, 1H), 4.66–4.70 (m, 1H), 5.22–5.23 (m, 1H), 6.80–7.89 (m, 10H). ¹³C NMR 15.1, 19.1, 19.8, 30.3, 30.9, 31.0, 31.5, 32.4, 33.5, 36.5, 36.9, 42.1, 45.6, 47.1, 47.9, 49.3, 50.3, 71.5, 72.3, 73.4, 73.5, 109.6, 120.5, 122.7, 126.2, 127.1, 128.2, 129.3, 129.7, 131.9, 135.1, 136.2, 141.1, 141.3, 178.2, 219.1.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(2-methylphenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-dehydroandrosterone (3h): Obtained as pale yellow solid; Yield 92%; m.p. 170–172°C; Anal. Calcd. for C₃₈H₄₄N₂O₃S: C, 74.96; H, 7.28; N, 4.60. Found: C, 74.90; H, 7.21; N, 4.66. ¹H NMR 0.24 (td, *J* = 12.6, 4.7 Hz, 1H), 0.47 (s, 3H), 0.47–0.54 (m, 1H), 0.73–0.85 (m, 2H), 0.84 (s, 3H), 0.88–0.95 (m, 1H), 1.19–1.54 (m, 5H), 1.65–1.98 (m, 4H), 2.11–2.30 (m, 2H), 2.24 (s, 3H), 2.38 (dd, *J* = 13.8, 4.5 Hz, 1H), 2.76–2.88 (m, 2H), 3.42–3.50 (m, 2H), 3.53 (d, *J* = 5.4 Hz, 1H), 3.63 (d, *J* = 5.7 Hz, 1H), 4.14 (d, *J* = 9.6 Hz, 1H), 4.70–4.75 (m, 1H), 5.24–5.25 (m, 1H), 6.80–7.63 (m, 8H), 8.0 (brs, 1H). ¹³C NMR 14.3, 19.2, 19.8, 20.0, 29.6, 30.1, 30.9, 31.4, 32.7, 36.5, 36.9, 42.1, 46.6, 46.9, 48.0, 49.3, 50.3, 71.5, 72.5, 73.5, 73.8, 109.6, 120.8, 122.5, 126.2, 126.3, 126.8, 129.4, 129.7, 130.2, 130.4, 135.9, 137.2, 140.9, 141.1, 178.3, 219.8.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(2-methoxyphenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-dehydroandrosterone (3i): Obtained as pale yellow solid; Yield 86%; m.p. 197–199 °C; Anal. Calcd. for C₃₈H₄₄N₂O₄S: C, 73.04; H, 7.10; N, 4.48. Found: C, 73.02; H, 7.21; N, 4.55. ¹H NMR 0.13 (td, *J* = 12.6, 4.8 Hz, 1H), 0.32–0.38 (m, 1H), 0.45 (s, 3H), 0.59–0.66 (m, 1H), 0.77 (s, 3H), 0.81–0.92 (m, 3H), 1.14–1.48 (m, 6H), 1.67–1.84 (m, 4H), 1.98–2.18 (m, 3H), 2.78 (d, *J* = 6.9 Hz, 2H), 3.34–3.40 (m, 1H), 3.43 (d, *J* = 4.8 Hz, 1H), 3.53 (d, *J* = 5.4 Hz, 1H), 3.62 (s, 2H), 4.27 (d, *J* = 9.3 Hz, 1H), 4.69–4.72 (m, 1H), 5.13–5.14 (m, 1H), 6.71–7.67 (m, 8H), 7.67 (brs, 1H). ¹³C NMR 14.5, 19.1, 19.8, 22.6, 29.6, 30.3, 31.0, 31.4, 32.7, 36.5, 36.9, 42.0, 44.9, 46.0, 46.9, 47.9, 50.3, 55.0, 71.5, 72.0, 72.5, 73.6, 109.4, 110.1, 115.3, 120.8, 122.5, 126.5, 126.6, 127.9, 129.4, 129.5, 130.4, 140.9, 141.2, 157.7, 178.3, 219.4.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(3-bromophenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-dehydroandrosterone (3j): Obtained as pale yellow solid; Yield 88%; m.p. 189–191°C; Anal. Calcd. for C₃₇H₄₁BrN₂O₃S: C, 65.96; H, 6.13; N, 4.16. Found: C, 65.90; H, 6.18;

N, 4.24. ¹H NMR 0.28 (s, 3H), 0.35–0.43 (m, 1H), 0.56 (td, *J* = 11.4, 5.0 Hz, 1H), 0.78–0.83 (m, 1H), 0.84 (s, 3H), 0.86–0.95 (m, 2H), 1.21–1.53 (m, 5H), 1.75–1.98 (m, 4H), 2.10–2.25 (m, 3H), 2.45 (dd, *J* = 13.5, 4.5 Hz, 1H), 2.84 (dd, *J* = 9.9, 6.9 Hz, 1H), 2.93 (dd, *J* = 9.8, 5.8 Hz, 1H), 3.41–3.48 (m, 1H), 3.60 (d, *J* = 6.6 Hz, 1H), 3.65 (d, *J* = 6.6 Hz, 1H), 3.72 (d, *J* = 9.9 Hz, 1H), 4.71–4.78 (m, 1H), 5.25–5.26 (m, 1H), 6.78–7.49 (m, 8H), 7.63 (brs, 1H). ¹³C NMR 14.0, 19.1, 19.9, 30.4, 30.8, 31.2, 31.4, 33.4, 36.5, 37.0, 42.1, 46.8, 48.0, 48.3, 50.3, 55.3, 71.5, 71.8, 72.3, 74.7, 109.6, 120.8, 122.2, 125.9, 127.4, 128.5, 129.5, 129.6, 130.0, 137.3, 140.9, 178.6, 219.2.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-naphthyl-tetrahydro-1H-pyrrolo[1',2'-c][1',3']thiazolo-trans-dehydroandrosterone (3k): Obtained as pale yellow solid; Yield 85%; m.p. 195–197°C; Anal. Calcd. for C₄₁H₄₄N₂O₃S: C, 76.36; H, 6.88; N, 4.34. Found: C, 76.28; H, 6.91; N, 4.28. ¹H NMR 0.15 (s, 3H), 0.15–0.21 (m, 1H), 0.43 (td, *J* = 11.1, 5.0 Hz, 1H), 0.67–0.78 (m, 4H), 0.80–0.87 (m, 2H), 1.04–1.18 (m, 2H), 1.25–1.40 (m, 4H), 1.47–1.51 (m, 2H), 1.66–1.88 (m, 2H), 2.01–2.21 (m, 3H), 2.29 (d, *J* = 9.3 Hz, 1H), 2.82 (d, *J* = 6.6 Hz, 1H), 3.38–3.42 (m, 1H), 3.56 (d, *J* = 5.4 Hz, 1H), 3.66 (d, *J* = 5.4 Hz, 1H), 4.69 (d, *J* = 9.3 Hz, 1H), 4.97–5.03 (m, 1H), 5.19–5.20 (m, 1H), 6.81–7.96 (m, 12H). ¹³C NMR 15.1, 19.0, 19.7, 30.1, 30.9, 31.3, 32.7, 32.8, 36.4, 36.8, 42.0, 46.3, 47.2, 47.4, 47.8, 50.2, 71.4, 73.0, 73.2, 73.7, 109.8, 120.7, 122.6, 123.5, 125.6, 126.3, 127.4, 127.5, 128.7, 129.2, 129.7, 132.8, 133.8, 134.8, 140.9, 141.4, 178.3, 220.3.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-phenyl-tetrahydro-1H-pyrrolo[1',2'-c][1',3']thiazolo-trans-androsterone (4a): Obtained as white solid; Yield 86%, m.p. 189–191°C; Anal. Calcd. for C₃₇H₄₄N₂O₃S: C, 74.46; H, 7.43; N, 4.69. Found: C, 74.51; H, 7.44; N, 4.67. ¹H NMR 0.15–0.28 (m, 1H), 0.21 (s, 3H), 0.34–0.42 (m, 1H), 0.64 (s, 3H), 0.70–0.87 (m, 3H), 0.92–1.26 (m, 7H), 1.31–1.34 (m, 2H), 1.49–1.56 (m, 3H), 1.62–1.68 (m, 3H), 2.49 (dd, *J* = 13.4, 4.4 Hz, 1H), 2.84 (dd, *J* = 9.9, 6.6 Hz, 1H), 2.94 (dd, *J* = 9.9, 6.0 Hz, 1H), 3.49–3.54 (m, 1H), 3.60 (d, *J* = 6.9 Hz,

1H), 3.67 (d, $J = 7.2$ Hz, 1H), 3.72 (d, $J = 9.9$ Hz, 1H), 4.70–4.77 (m, 1H), 6.79–7.89 (m, 9H), 7.89 (brs, 1H). ^{13}C NMR 12.1, 14.3, 20.1, 28.1, 30.6, 31.0, 31.3, 31.4, 33.5, 33.9, 35.5, 36.7, 38.0, 44.8, 47.1, 48.1, 48.2, 54.7, 55.3, 71.0, 71.8, 72.3, 74.8, 109.4, 122.1, 125.9, 127.4, 128.5, 129.5, 129.6, 130.1, 137.3, 140.8, 178.6, 219.2.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(4-chlorophenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-androsterone (4b): Obtained as white solid; Yield 88%, m.p. 204–206°C; Anal. Calcd. for $\text{C}_{37}\text{H}_{43}\text{ClN}_2\text{O}_3\text{S}$: C, 70.40; H, 6.87; N, 4.44. Found: C, 70.38; H, 6.82; N, 4.49. ^1H NMR 0.17–0.21 (m, 1H), 0.31 (s, 3H), 0.31–0.41 (m, 1H), 0.65 (s, 3H), 0.71–1.02 (m, 4H), 1.06–1.42 (m, 8H), 1.47–1.71 (m, 6H), 2.37 (dd, $J = 13.3, 4.3$ Hz, 1H), 2.81 (dd, $J = 9.6, 7.2$ Hz, 1H), 2.89 (dd, $J = 9.6, 5.7$ Hz, 1H), 3.43–3.58 (m, 1H), 3.59 (s, 2H), 3.65 (d, $J = 9.6$ Hz, 1H), 4.64–4.71 (m, 1H), 6.80–7.40 (m, 8H), 7.80 (brs, 1H). ^{13}C NMR 12.1, 14.6, 20.1, 28.2, 31.0, 31.3, 31.4, 33.2, 33.9, 35.6, 36.7, 38.1, 44.9, 47.2, 47.5, 47.9, 54.6, 54.7, 71.1, 72.1, 72.4, 74.4, 77.2, 109.5, 122.4, 125.9, 128.7, 129.4, 129.8, 131.3, 133.4, 136.2, 140.9, 178.5, 219.4.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(4-bromophenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-androsterone (4c): Obtained as white solid; Yield 85%, m.p. 199–201°C; Anal. Calcd. for $\text{C}_{37}\text{H}_{43}\text{BrN}_2\text{O}_3\text{S}$: C, 65.77; H, 6.41; N, 4.15. Found: C, 65.71; H, 6.46; N, 4.18. ^1H NMR 0.16–0.23 (m, 1H), 0.31 (s, 3H), 0.32–0.34 (m, 1H), 0.65 (s, 3H), 0.72–0.90 (m, 4H), 0.95–1.15 (m, 4H), 1.15–1.34 (m, 5H), 1.48–1.66 (m, 5H), 2.37 (dd, $J = 13.1, 4.1$ Hz, 1H), 2.78–2.83 (m, 1H), 2.89 (dd, $J = 9.4, 5.8$ Hz, 1H), 3.50–3.54 (m, 1H), 3.59 (s, 2H), 3.64 (d, $J = 9.3$ Hz, 1H), 4.64–4.72 (m, 1H), 6.80–7.78 (m, 8H), 7.78 (brs, 1H). ^{13}C NMR 12.1, 14.6, 20.0, 28.1, 31.0, 31.2, 33.1, 33.8, 35.5, 36.7, 38.0, 44.8, 47.1, 47.4, 47.9, 54.6, 71.0, 72.0, 72.3, 74.3, 109.5, 121.5, 122.3, 125.8, 129.3, 129.7, 131.7, 136.7, 141.0, 178.4, 219.4.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(4-fluorophenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-androsterone (4d): Obtained as white solid; Yield 89%, m.p. 193–195°C; Anal. Calcd. for C₃₇H₄₃FN₂O₃S: C, 72.28; H, 7.05; N, 4.56. Found: C, 72.32; H, 7.10; N, 4.66. ¹H NMR 0.18–0.24 (m, 1H), 0.28 (s, 3H), 0.31–0.37 (m, 1H), 0.65 (s, 3H), 0.73–0.86 (m, 4H), 0.92–1.27 (m, 6H), 1.30–1.34 (m, 2H), 1.48–1.52 (m, 4H), 1.65–1.71 (m, 2H), 2.82 (dd, *J* = 9.8, 7.0 Hz, 1H), 2.82 (dd, *J* = 9.8, 7.0 Hz, 1H), 2.90 (dd, *J* = 9.7, 5.9 Hz, 1H), 3.49–3.52 (m, 1H), 3.60 (m, 2H), 3.67 (d, *J* = 9.6 Hz, 1H), 4.66–4.69 (m, 1H), 6.78–7.44 (m, 8H), 7.85 (brs, 1H). ¹³C NMR 12.1, 14.4, 20.1, 28.1, 30.9, 31.3, 33.2, 33.9, 35.5, 36.7, 38.0, 44.8, 47.1, 47.7, 48.0, 54.5, 54.7, 71.0, 72.1, 72.3, 74.5, 109.5, 115.2, 115.5, 122.3, 125.8, 129.4, 129.7, 131.4, 131.5, 133.3, 140.8, 160.5, 163.8, 178.5, 219.4.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(4-methylphenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-androsterone (4e): Obtained as white solid; Yield 86%, m.p. 210–212°C; Anal. Calcd. for C₃₈H₄₆N₂O₃S: C, 74.72; H, 7.59; N, 4.59. Found: C, 74.65; H, 7.53; N, 4.64. ¹H NMR 0.14–0.22 (m, 1H), 0.21 (s, 3H), 0.33–0.41 (m, 1H), 0.64 (s, 3H), 0.78–0.87 (m, 4H), 0.95–1.35 (m, 8H), 1.47–1.55 (m, 4H), 1.63–1.71 (m, 2H), 2.33 (s, 3H), 2.48–2.51 (m, 1H), 2.79–2.85 (m, 1H), 2.91–2.98 (m, 1H), 3.48–3.52 (m, 1H), 3.60 (d, *J* = 6.9 Hz, 1H), 3.67–3.70 (m, 2H), 4.69–4.72 (m, 1H), 6.79–8.03 (m, 8H), 8.03 (brs, 1H). ¹³C NMR 12.1, 14.3, 20.2, 21.0, 28.3, 30.4, 31.0, 31.3, 31.5, 33.7, 33.9, 35.5, 36.8, 38.0, 44.9, 47.1, 48.2, 48.6, 54.8, 55.1, 71.1, 71.8, 72.2, 75.1, 109.6, 122.1, 125.2, 125.9, 129.2, 129.6, 129.9, 134.2, 137.1, 140.9, 178.9, 219.3.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(4-methoxyphenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-androsterone (4f): Obtained as white solid; Yield 95%, m.p. 211–213°C; Anal. Calcd. for C₃₈H₄₆N₂O₄S: C, 72.81; H, 7.40; N, 4.47. Found: C, 72.89; H, 7.44; N, 4.46. ¹H NMR 0.15–0.28 (m, 1H), 0.22 (s, 3H), 0.35–0.48 (m, 1H), 0.64 (s, 3H), 0.78–0.87 (m, 2H), 0.94–1.06

(m, 3H), 1.06–1.18 (m, 5H), 1.26–1.30 (m, 3H), 1.45–1.66 (m, 6H), 2.47 (dd, $J = 13.5, 4.2$ Hz, 1H), 2.83 (dd, $J = 9.9, 6.3$ Hz, 1H), 2.94 (dd, $J = 9.9, 6.0$ Hz, 1H), 3.49–3.55 (m, 1H), 3.60 (d, $J = 6.9$ Hz, 1H), 3.65–3.68 (m, 1H), 3.80 (s, 3H), 4.64–4.69 (m, 1H), 6.79–7.53 (m, 8H), 7.91 (brs, 1H). ^{13}C NMR 12.1, 14.3, 20.1, 28.2, 30.4, 31.0, 31.3, 33.4, 33.6, 33.9, 35.5, 36.8, 38.0, 44.8, 47.2, 48.2, 48.5, 54.8, 55.2, 71.1, 72.0, 72.2, 75.0, 109.5, 114.0, 122.1, 125.9, 129.3, 129.6, 131.0, 140.8, 159.0, 178.8, 219.4.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(2-chlorophenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-androsterone (4g): Obtained as white solid; Yield 89%, m.p. 197–199°C; Anal. Calcd. for $\text{C}_{37}\text{H}_{43}\text{ClN}_2\text{O}_3\text{S}$: C, 70.40; H, 6.87; N, 4.44. Found: C, 70.38; H, 6.96; N, 4.51. ^1H NMR 0.06–0.08 (m, 1H), 0.16–0.23 (m, 1H), 0.54 (s, 3H), 0.64 (s, 3H), 0.65–0.76 (m, 2H), 0.80–0.96 (m, 3H), 1.07–1.21 (m, 5H), 1.25–1.32 (m, 3H), 1.50–1.55 (m, 5H), 2.18 (dd, $J = 13.5, 4.2$ Hz, 1H), 2.79–2.93 (m, 2H), 3.47 (d, $J = 5.1$ Hz, 1H), 3.48–0.53 (m, 1H), 3.61 (d, $J = 5.4$ Hz, 1H), 4.43 (d, $J = 8.7$ Hz, 1H), 4.65–4.73 (m, 1H), 6.81–7.88 (m, 8H), 7.88 (brs, 1H). ^{13}C NMR 12.2, 15.5, 20.0, 28.2, 31.1, 31.2, 31.4, 32.5, 33.5, 33.9, 35.6, 36.7, 38.1, 44.9, 45.7, 47.4, 47.6, 49.5, 54.8, 71.1, 72.4, 73.6, 109.5, 122.7, 123.1, 124.4, 126.3, 127.1, 128.2, 129.4, 129.8, 132.0, 135.2, 136.4, 141.6, 178.4, 219.4.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(2-methylphenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']

thiazolo-trans-androsterone (4h): Obtained as white solid; Yield 90%, m.p. 195–196°C; Anal. Calcd. for $\text{C}_{38}\text{H}_{46}\text{N}_2\text{O}_3\text{S}$: C, 74.72; H, 7.59; N, 4.59. Found: C, 74.76; H, 7.64; N, 4.56. ^1H NMR 0.07–0.26 (m, 2H), 0.35 (s, 3H), 0.58–0.64 (m, 1H), 0.63 (s, 3H), 0.70–0.79 (m, 3H), 0.87–1.33 (m, 10H), 1.46–1.65 (m, 4H), 2.23 (s, 3H), 2.35–2.40 (m, 1H), 2.76–2.88 (m, 2H), 3.50–3.53 (m, 1H), 3.54 (d, $J = 5.7$ Hz, 1H), 3.63 (d, $J = 5.7$ Hz, 1H), 4.13 (d, $J = 9.3$ Hz, 1H), 4.69–4.76 (m, 1H), 6.81–8.10 (m, 8H), 8.09 (brs, 1H). ^{13}C NMR 12.1, 14.6, 19.8, 20.0, 28.1, 31.1, 31.4, 32.6,

32.8, 33.9, 35.5, 36.7, 38.0, 44.8, 46.7, 47.2, 47.7, 49.5, 54.7, 71.0, 72.6, 73.5, 74.0, 109.3, 122.4, 126.1, 126.4, 126.8, 129.4, 129.6, 130.2, 130.3, 136.0, 137.2, 141.2, 178.2, 220.2.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(2-methoxyphenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']thiazolo-trans-androsterone (4i): Obtained as white solid; Yield 96%, m.p. 197–199°C; Anal. Calcd. for C₃₈H₄₆N₂O₄S: C, 72.81; H, 7.40; N, 4.47. Found: C, 72.75; H, 7.46; N, 4.56. ¹H NMR 0.04–0.22 (m, 2H), 0.47 (s, 3H), 0.57–0.64 (m, 2H), 0.63 (s, 3H), 0.74–1.20 (m, 6H), 1.25–1.37 (m, 3H), 1.47–1.55 (m, 5H), 2.12 (dd, *J* = 13.4, 4.3 Hz, 1H), 2.83–2.85 (m, 2H), 3.50–3.56 (m, 2H), 3.61 (d, *J* = 5.7 Hz, 1H), 3.66–3.72 (m, 1H), 3.68 (s, 3H), 4.33 (d, *J* = 9.3 Hz, 1H), 4.74–4.80 (m, 1H), 6.70–7.84 (m, 9H), 7.84 (brs, 1H). ¹³C NMR 12.1, 14.9, 20.1, 28.2, 31.1, 31.4, 32.8, 33.9, 35.5, 36.7, 38.0, 44.8, 45.0, 46.2, 47.2, 47.6, 54.7, 55.1, 71.1, 72.2, 72.5, 73.8, 109.4, 110.2, 120.7, 122.4, 126.6, 126.8, 127.9, 129.4, 129.5, 130.6, 141.6, 157.9, 178.5, 219.6.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-(3-bromophenyl)-tetrahydro-1H-pyrrolo[1',2'-c][1',3']thiazolo-trans-androsterone (4j): Obtained as white solid; Yield 87%, m.p. 201–203°C; Anal. Calcd. for C₃₇H₄₃BrN₂O₃S: C, 65.77; H, 6.41; N, 4.15. Found: C, 65.71; H, 6.38; N, 4.19. ¹H NMR 0.16–0.24 (m, 1H), 0.33 (s, 3H), 0.32–0.39 (m, 1H), 0.66 (s, 3H), 0.73–1.02 (m, 4H), 1.07–1.24 (m, 4H), 1.23–1.36 (m, 2H), 1.49–1.62 (m, 5H), 1.73–1.77 (m, 1H), 2.39 (dd, *J* = 13.5, 4.2 Hz, 1H), 2.82 (dd, *J* = 9.6, 7.2 Hz, 1H), 2.91 (dd, *J* = 9.6, 5.7 Hz, 1H), 3.49–3.55 (m, 3H), 3.59 (s, 2H), 3.64 (d, *J* = 9.6 Hz, 1H), 4.66–4.73 (m, 1H), 6.81–7.42 (m, 8H), 7.86 (brs, 1H). ¹³C NMR 12.0, 14.6, 19.8, 28.0, 30.8, 30.9, 31.2, 31.7, 32.6, 33.6, 35.3, 36.6, 37.9, 44.6, 46.4, 46.9, 47.3, 49.7, 54.4, 70.2, 71.9, 72.4, 73.5, 109.7, 121.5, 122.4, 125.7, 128.5, 129.5, 130.0, 130.2, 132.6, 140.5, 142.3, 177.9, 219.7.

Spiro[5'.3'']oxindole-spiro[6'.16]-7'-naphthyl-tetrahydro-1H-pyrrolo[1',2'-c][1',3']thiazolo-trans-androsterone (4k): Obtained as pale yellow solid; Yield 91%; m.p. 196–198°C; Anal.

Calcd. for $C_{41}H_{46}N_2O_3S$: C, 76.13; H, 7.17; N, 4.33. Found: C, 76.15; H, 7.11; N, 4.39. ^1H NMR 0.07–0.09 (m, 1H), 0.10 (s, 3H), 0.11–0.21 (m, 1H), 0.47–0.68 (m, 2H), 0.54 (s, 3H), 0.73–0.82 (m, 3H), 0.87–1.03 (m, 4H), 1.09–1.33 (m, 5H), 1.43–1.53 (m, 5H), 2.30 (d, $J = 9.6$ Hz, 1H), 2.82 (d, $J = 6.9$ Hz, 1H), 3.47–3.51 (m, 1H), 3.57 (d, $J = 5.4$ Hz, 1H), 3.67 (d, $J = 5.4$ Hz, 1H), 4.67 (d, $J = 9.3$ Hz, 1H), 4.97–5.04 (m, 1H), 6.82–7.94 (m, 12H). ^{13}C NMR 12.0, 15.4, 20.0, 28.1, 31.1, 31.3, 32.7, 32.8, 33.7, 35.4, 36.6, 38.0, 44.8, 46.4, 47.5, 54.7, 71.0, 73.2, 73.3, 73.9, 109.5, 122.5, 123.6, 125.5, 125.6, 126.3, 126.5, 127.5, 128.7, 129.3, 129.7, 132.9, 133.9, 134.3, 141.5, 178.3, 220.3.

Figure 1. ^1H NMR spectrum of **3b**

Figure 2. ^{13}C NMR spectrum of **3b**

Figure 3. DEPT-135 spectrum of **3b**

Figure 4. H,H-COSY spectrum of **3b**

Figure 5. C,H-COSY spectrum of 3b

Figure 6. HMBC spectrum of 3b

Figure 9. DEPT-135 spectrum of 4b

Figure 10. H, H-COSY spectrum of 4b

Figure 11. C, H-COSY spectrum of 4b

Figure 12. HMBC spectrum of 4b