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Synthesis of novel 16-spiro steroids: Spiro-7′-(aryl)tetrahydro-1*H*-pyrrolo[1,2-*c*][1,3]thiazolo-*trans*-androsterone hybrid heterocycles

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ABSTRACT

The 1,3-dipolar cycloaddition of azomethine ylide derived *in situ* from the reaction of acenaphthylene-1,2-dione and 1,3-thiazolane-4-carboxylic acid to various exocyclic dipolarophiles synthesized from *trans*-androsterone and *trans*-dehydroandrosterone afforded a library of novel spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-(7′-aryl)-tetrahydro-1*H*-pyrrolo [1,2-*c*][1,3]thiazolo-*trans*-androsterone/dehydroandrosterone hybrid heterocycles respectively. These reactions proceeded stereo-specifically affording a single isomer of the 16-spiro steroids in excellent yields.

1. Introduction

Steroids are extensively available in nature and are well known for their profound biological activities and use in traditional medicines [1]. Syntheses of several modified steroids have received considerable attention in the recent years. In particular, the syntheses of new compounds comprising heterocyclic rings either fused or linked to the steroid framework have gained much importance [2]. Apart from being synthons for further modifications into more complex molecules, these steroidal heterocycles have been reported to possess a wide range of biological activities [2].

Spiro steroids are important class of compounds that are frequently found in nature, such as spirostanes, which include a spiroacetal moiety in the structure and show significant biological activities [3]. Generally, spiro compounds constitute a vital group of many naturally occurring compounds identified by their highly noticeable biological activities [4]. For example, coerulescine, horsfiline and elacomine exhibit anti tumor activity [5], whereas rynchophylline and corynoxeine are used in traditional Chinese medicine for the treatment of neurological and cardiovascular diseases, respectively [6]. The pentacyclic spirotryprostatin A and B compounds were shown to inhibit the growth of human chronic myelogenous leukemia K562 cells and human promyelocytic leukemia HL-60 cells [7].

The best studied spiro steroids are those which contain a spiro heterocyclic ring at C-17 [8], whereas the reports on the synthesis of C-16 spiro heterocyclic steroids are scarce [9]. The known C-16 spiro steroids are the cycloalkano derivatives [10], dioxaphosphorinanes [11], pyrazolines [12] and pyrrolidines [13]. In this context, we herein report the synthesis of novel C-16 spiro pyrrolo[1,2-*c*][1,3]thiazole containing *trans*-androsterone and *trans*-dehydroandrosterone hybrid heterocycles *via* 1,3-dipolar cycloaddition reactions. It is pertinent to note that the compounds with spiro pyrrolo[1,2-*c*][1,3]thiazole substructure are known to exhibit acetylcholinesterase (AChE) inhibition [14] and anti-tubercular activities [15]. Several methods have been devised to construct such bio-important spiro heterocycles of which 1,3-dipolar cycloaddition represents the widely investigated one [16]. In particular, the 1,3-dipolar cycloaddition of azomethine ylides to exocyclic olefins offers a versatile protocol for the synthesis of poly-functionalized spiro pyrrolo[1,2-*c*][1,3]thiazoles [14,15].

2. Experimental

The melting points were measured in open capillary tubes and are uncorrected. The ^{1}H, ^{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

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II Elemental CHNS analyzer. IR spectra were recorded in a Shimadzu FTIR-8400S using KBr pellet. The single crystal X-ray data set for **2k** and **3i** were collected on Bruker Kappa APPEXII diffractometer with Mo–K_α (λ = 0.71073 Å) 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 Aldrich and used without any further purification.

*2.1. General procedure for the synthesis of 16-(E)-arylidene-trans-androsterones **2** and 16-(E)-arylidene-trans-dehydroandrosterones **5***

A mixture of *trans*-androsterone **1** or *trans*-dehydroandrosterone **4** (1 mmol) and aromatic aldehyde (1 mmol) was dissolved in ethanol (5 mL) to which an alcoholic solution of potassium hydroxide (10%) was added drop wise. The mixture was allowed to stir for 60 min at ambient temperature and the progress of the reaction monitored by TLC intermittently. After completion of the reaction, the precipitated solid was filtered and washed with ethanol (10 mL) to afford the product **2** or **5** as colorless solid.

*2.1.1. (E)-16-(2-Methylphenyl)methylidene-trans-androsterone (**2h**)*

Obtained as white solid; Yield 97%; m.p. 180–182 °C; ^{1}H NMR 0.72–0.76 (m, 1H), 0.86 (s, 3H), 0.97 (s, 3H), 0.93–1.04 (m, 2H), 1.13–1.47 (m, 8H), 1.56–1.95 (m, 8H), 2.41 (s, 3H), 2.33–2.43 (m, 1H), 2.74 (dd, *J* = 15.9, 6.3 Hz, 1H), 3.58 (m, 1H), 7.22–7.24 (m, 3H), 7.44–7.46 (m, 1H), 7.65 (s, 1H). ^{13}C NMR 12.4, 14.5, 20.0, 20.6, 28.4, 29.2, 31.1, 31.4, 31.7, 34.7, 35.7, 36.9, 38.0, 44.9, 47.9, 49.7, 54.5, 71.1, 125.8, 128.6, 129.0, 130.6, 130.7, 134.4, 136.8, 138.7 and 209.8.

*2.1.2. (E)-16-(2-Methoxyphenyl)methylidene-trans-androsterone (**2i**)*

Obtained as white solid; Yield 98%; m.p. 142–144 °C; ^{1}H NMR 0.71–0.76 (m, 1H), 0.86 (s, 3H), 0.95 (s, 3H), 0.96–1.03 (m, 1H), 1.15–1.42 (m, 7H), 1.60–1.94 (m, 8H), 2.34–2.44 (m, 1H), 2.77 (dd, *J* = 15.2, 5.5 Hz, 1H), 3.52–3.61 (m, 1H), 3.86 (s, 3H), 5.08 (brs, 2H), 6.89–7.00 (m, 2H), 7.31–7.50 (m, 2H), 7.84 (s, 1H). ^{13}C NMR 12.4, 14.5, 20.6, 28.4, 29.4, 31.1, 31.4, 31.7, 34.7, 35.7, 36.9, 38.0, 44.9, 47.7, 49.6, 54.5, 55.5, 71.1, 110.8, 120.2, 124.7, 127.7, 129.6, 130.7, 136.0, 158.7 and 209.8.

*2.1.3. (E)-16-(3-Bromophenyl)methylidene-trans-androsterone (**2h**)*

Obtained as white solid; Yield 96%; m.p. 176–178 °C; ^{1}H NMR 0.72–0.78 (m, 1H), 0.87 (s, 3H), 0.95 (s, 3H), 0.95–1.03 (m, 1H), 1.15–1.43 (m, 7H), 1.57–1.95 (m, 9H), 2.35–2.46 (m, 1H), 2.83 (dd, *J* = 15.9, 6.3 Hz, 1H), 3.57–3.64 (m, 1H), 4.78 (brs, 1H), 7.25–7.33 (m, 2H), 7.43–7.49 (m, 2H), 7.65 (s, 1H). ^{13}C NMR 12.3, 14.5, 20.5, 28.4, 29.1, 31.1, 31.4, 31.6, 34.7, 35.7, 36.9, 38.0, 44.8, 47.7, 49.4, 54.5, 71.1, 122.8, 128.8, 130.2, 131.3, 132.0, 132.7, 137.5, 137.7 and 209.5.

*2.1.4. (E)-16-(Naphthyl)methylidene-trans-androsterone (**2k**)*

Obtained as white solid; Yield 96%; m.p. 172–174 °C; ^{1}H NMR 0.65–0.76 (m, 1H), 0.86 (s, 3H), 0.92–0.99 (m, 2H), 1.02 (s, 3H), 1.06–1.48 (m, 7H), 1.55–1.99 (m, 8H), 2.38–2.49 (m, 1H), 2.72 (dd, *J* = 15.9, 6.3 Hz, 1H), 3.52–3.61 (m, 1H), 5.09 (brs, 1H), 7.47–7.63 (m, 4H), 7.85–7.89 (m, 2H), 8.13–8.17 (m, 1H), 8.19 (s, 1H). ^{13}C NMR 12.3, 14.5, 20.6, 28.4, 29.4, 31.1, 31.4, 31.8, 34.7, 35.7, 36.9, 38.0, 44.8, 48.1, 49.5, 54.5, 71.1, 124.1, 125.1, 126.2, 126.6, 126.9, 128.7, 129.6, 129.9, 132.2, 132.5, 133.6, 138.4 and 209.5.

*2.1.5. (E)-16-(4-Bromophenyl)methylidene-trans-dehydroandrosterone (**5c**)*

Obtained as white solid; Yield 96%; m.p. 254–256 °C; ^{1}H NMR 0.98 (s, 3H), 1.08 (s, 3H), 1.04–1.15 (m, 2H), 1.24–1.67 (m, 6H), 1.72–2.00 (m, 5H), 2.17–2.46 (m, 4H), 2.84 (dd, *J* = 15.8, 6.5 Hz, 1H), 3.50–3.59 (m, 1H), 5.39–5.41 (m, 1H), 7.36–7.41 (m, 3H), 7.53–7.56 (m, 2H). ^{13}C NMR 14.2, 19.4, 20.4, 29.3, 31.0, 31.2, 31.6, 31.7, 36.7, 37.2, 42.2, 47.3, 49.8, 50.4, 71.6, 120.7, 123.4, 131.6, 131.7, 131.9, 134.6, 136.7, 141.2 and 209.6.

*2.1.6. (E)-16-(4-Fluorophenyl)methylidene-trans-dehydroandrosterone (**5d**)*

Obtained as white solid; Yield 98%; m.p. 248–250 °C; ^{1}H NMR 0.98 (s, 3H), 1.10 (s, 3H), 1.02–1.16 (m, 2H), 1.31–1.66 (m, 4H), 1.71–2.01 (m, 7H), 2.17–2.47 (m, 4H), 2.85 (dd, *J* = 15.7, 5.3 Hz, 1H), 3.50–3.59 (m, 1H), 5.3–3.41 (m, 1H), 7.08–7.13 (m, 2H), 7.40 (s, 1H), 7.51–7.55 (m, 2H). ^{13}C NMR 14.2, 19.5, 20.4, 29.2, 30.9, 31.2, 31.5, 31.6, 36.7, 37.1, 42.2, 47.3, 49.9, 50.3, 71.6, 115.7, 116.0, 120.8, 131.9, 132.1, 132.2, 135.5, 135.6, 141.2, 161.4, 164.7 and 209.5.

*2.1.7. (E)-16-(4-Methylphenyl)methylidene-trans-dehydroandrosterone (**5e**)*

Obtained as white solid; Yield 97%; m.p. 272–274 °C; ^{1}H NMR 0.98 (s, 3H), 1.01–1.14 (m, 2H), 1.07 (s, 3H), 1.31–1.66 (m, 4H), 1.71–2.00 (m, 7H), 2.17–2.48 (m, 3H), 2.38 (s, 3H), 2.88 (dd, *J* = 15.8, 6.1 Hz, 1H), 3.52–3.55 (m, 1H), 4.82 (brs, 1H), 5.39–5.41 (m, 1H), 7.21–7.27 (m, 2H), 7.43–7.46 (m, 3H). ^{13}C NMR 14.3, 19.5, 20.4, 21.5, 29.4, 30.9, 31.2, 31.6, 36.7, 37.1, 42.2, 47.3, 49.9, 50.4, 71.6, 120.8, 129.5, 130.4, 132.8, 133.2, 135.0, 139.6, 141.2 and 209.9.

*2.1.8. (E)-16-(2-Chlorophenyl)methylidene-trans-dehydroandrosterone (**5g**)*

Obtained as white solid; Yield 97%; m.p. 250–252 °C; ^{1}H NMR 1.00 (s, 3H), 1.07 (s, 3H), 1.06–1.15 (m, 2H), 1.29–1.65 (m, 5H), 1.70–1.90 (m, 5H), 1.97–2.21 (m, 2H), 2.26–2.48 (m, 3H), 2.75 (dd, *J* = 15.9, 6.3 Hz, 1H), 3.49–3.58 (m, 1H), 5.37–5.38 (m, 1H), 7.27–7.33 (m, 2H), 7.41–7.55 (m, 2H), 7.78 (s, 1H). ^{13}C NMR 14.2, 19.5, 20.4, 29.2, 30.9, 31.2, 31.6, 36.7, 37.1, 49.2, 47.5, 49.8, 50.3, 71.6, 120.8, 126.6, 129.2, 129.9, 130.0, 133.8, 135.7, 138.2, 141.2 and 208.9.

*2.1.9. (E)-16-(2-Methylphenyl)methylidene-trans-dehydroandrosterone (**5h**)*

Obtained as white solid; Yield 98%; m.p. 215–217 °C; ^{1}H NMR 1.00 (s, 3H), 1.07 (s, 3H), 1.06–1.14 (m, 2H), 1.26–1.89 (m, 10H), 1.97–2.17 (m, 2H), 2.26–2.36 (m, 3H), 2.41 (s, 3H), 2.76 (dd, *J* = 16.1, 5.9 Hz, 1H), 3.52–3.56 (m, 1H), 5.37–5.38 (m, 1H), 7.24–7.25 (m, 3H), 7.46–7.47 (m, 1H), 7.67 (s, 1H). ^{13}C NMR 14.2, 19.5, 19.9, 20.4, 29.3, 30.9, 31.2, 31.6, 36.7, 37.2, 42.2, 47.6, 50.0, 50.4, 71.6, 120.8, 125.8, 126.4, 128.6, 129.0, 130.6, 130.8, 134.4, 136.6, 138.7, 141.2 and 209.4.

*2.1.10. (E)-16-(2-Methoxyphenyl)methylidene-trans-dehydroandrosterone (**5i**)*

Obtained as white solid; Yield 96%; m.p. 128–130 °C; ^{1}H NMR 0.99 (s, 3H), 1.07 (s, 3H), 1.08–1.14 (m, 2H), 1.28–1.90 (m, 10H), 1.96–2.20 (m, 2H), 2.26–2.48 (m, 3H), 2.80 (dd, *J* = 15.6, 6.3 Hz, 1H), 3.50–3.57 (m, 1H), 3.86 (s, 3H), 5.37–5.39 (m, 1H), 6.90–7.01 (m, 2H), 7.32–7.51 (m, 2H), 7.86 (s, 1H). ^{13}C NMR 14.2, 19.5, 20.4, 29.4, 30.9, 31.2, 31.6, 36.7, 37.1, 42.2, 47.4, 50.0, 50.3, 55.5, 71.6, 110.8, 120.2, 120.9, 124.7, 127.9, 129.6, 130.7, 135.9, 141.1, 158.7 and 209.6.

*2.1.11. (E)-16-(3-Bromophenyl)methylidene-trans-dehydroandrosterone (**5j**)*

Obtained as white solid; Yield 97%; m.p. 222–224 °C; ^{1}H NMR 0.98 (s, 3H), 1.08 (s, 3H), 1.02–1.15 (m, 2H), 1.31–1.67 (m, 8H), 1.72–2.01 (m, 3H), 2.18–2.50 (m, 4H), 2.86 (dd, *J* = 16.2, 6.3 Hz,

1H), 3.49–3.58 (m, 1H), 5.39–5.41 (m, 1H), 7.26–7.35 (m, 2H), 7.44–7.50 (m, 2H), 7.66 (s, 1H). ^{13}C NMR 14.2, 19.5, 20.4, 29.2, 30.9, 31.2, 31.5, 31.6, 36.7, 37.1, 42.2, 47.4, 49.8, 50.3, 71.6, 120.8, 122.8, 128.8, 130.2, 131.4, 132.0, 132.8, 137.3, 137.7, 141.2 and 209.3.

*2.1.12. (E)-16-(Naphthyl)methylidene-trans-dehydroandrosterone (**5k**)*

Obtained as white solid; Yield 97%; m.p. 134–136 °C; ^{1}H NMR 1.05 (s, 3H), 1.07 (m, 3H), 1.08–1.13 (m, 2H), 1.22–1.62 (m, 6H), 1.72–2.52 (m, 6H), 2.75 (dd, *J* = 15.6, 6.0 Hz, 1H), 3.49–3.55 (m, 1H), 4.85 (brs, 1H), 5.14 (m, 2H), 5.33–5.34 (m, 1H), 7.49–7.64 (m, 4H), 7.86–8.16 (m, 3H), 8.21 (s, 1H). ^{13}C NMR 14.3, 19.5, 20.4, 29.5, 30.9, 31.2, 31.5, 31.6, 36.7, 37.1, 42.2, 47.8, 50.1, 50.3, 71.6, 120.9, 124.0, 125.1, 126.2, 126.7, 126.9, 128.7, 129.6, 130.0, 132.2, 132.4, 133.6, 138.2, 141.0 and 209.3.

*2.2. General procedure for the synthesis of spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-(7′-aryl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo trans-androsterones/dehydroandrosterones **3** and **6***

A mixture of the appropriate steroid arylidine (**2** or **5**, 1 mmol), acenaphthylene-1,2-dione (1 mmol) and 1,3-thiazolane-4-carboxylic acid (1.2 mmol) was taken in methanol (10 mL) and refluxed for 3–5 h. The progress of the reaction was monitored by TLC. After completion of the reaction as evident from TLC, the reaction mixture was cooled and poured into ice cooled water. The resultant precipitate was filtered, dried and purified by filtration column using petroleum ether: ethyl acetate (9:1) as eluting solvent to get the product **3** or **6** as pale yellow solid.

*2.2.1. (16R,5′R,7′R,7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-phenyl-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-androsterone (**3a**)*

Obtained as pale yellow solid; Yield 87%; m.p. 181–183 °C; Anal. Calcd. for $C_{41}H_{45}NO_3S$: C, 77.93; H, 7.18; N, 2.22. Found: C, 77.89; H, 7.22; N, 2.19. ^{1}H NMR −0.28–(−0.21) (m, 1H), −0.06 (s, 3H), 0.53–0.54 (m, 2H), 0.57 (s, 3H), 0.71–0.78 (m, 1H), 0.85–0.88 (m, 2H), 1.02–1.06 (m, 1H), 1.11–1.26 (m, 6H), 1.47–1.60 (m, 4H), 1.68–1.71 (m, 2H), 2.56 (dd, *J* = 13.2, 4.5 Hz, 1H), 2.94 (dd, *J* = 10.8, 4.5 Hz, 1H), 3.12 (dd, *J* = 10.7, 6.4 Hz, 1H), 3.47–3.55 (m, 1H), 3.64 (d, *J* = 8.7 Hz, 1H), 3.86 (d, *J* = 5.1 Hz, 1H), 3.89 (d, *J* = 6.9 Hz, 1H), 4.77–4.83 (m, 2H), 7.31–8.15 (m, 11H). ^{13}C NMR 12.1, 13.7, 20.0, 28.1, 28.3, 30.6, 31.3, 31.4, 33.9, 35.0, 35.4, 36.6, 38.0, 44.7, 47.1, 49.1, 51.2, 54.6, 56.3, 71.0, 71.7, 72.0, 80.8, 120.8, 125.4, 126.3, 127.6, 127.8, 128.3, 128.5, 130.1, 130.5, 131.7, 132.2, 134.4, 136.7, 141.0, 205.8 and 218.6.

*2.2.2. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(4-chlorophenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-androsterone (**3b**)*

Obtained as pale yellow solid; Yield 79%; m.p. 158–160 °C; FT-IR: 3427, 2924, 2852, 1724, 783, 729. Anal. Calcd. for $C_{41}H_{44}ClNO_3S$: C, 73.91; H, 6.66; N, 2.10. Found: C, 73.98; H, 6.70; N, 2.16. ^{1}H NMR –0.27–(–0.06) (m, 2H), 0.05 (m, 3H), 0.39–0.51 (m, 2H), 0.58 (s, 3H), 0.67–0.78 (m, 1H), 0.83–0.88 (m, 3H), 1.01–1.25 (m, 6H), 1.41–1.54 (m, 4H), 1.67–1.69 (m, 2H), 2.47 (dd, *J* = 13.4, 4.7 Hz, 1H), 2.91 (dd, *J* = 10.5, 5.1 Hz, 1H), 3.07 (dd, *J* = 10.5, 6.3 Hz, 1H), 3.46–3.53 (m, 1H), 3.64 (d, *J* = 8.1 Hz, 1H), 3.79 (d, *J* = 8.1 Hz, 1H), 3.83 (d, *J* = 10.2 Hz, 1H), 4.71–4.78 (m, 1H), 7.30–8.16 (m, 10H). ^{13}C NMR 12.0, 14.1, 20.0, 28.1, 29.1, 30.6, 31.3, 33.8, 34.5, 35.4, 36.6, 38.0, 44.7, 44.9, 47.1, 48.8, 50.0, 54.6, 55.5, 71.0, 72.0, 72.3, 79.8, 120.8, 125.5, 126.1, 127.9, 128.3, 128.8, 131.4, 131.8, 132.2, 133.5, 134.6, 135.7, 141.3, 205.8 and 218.9.

*2.2.3. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(4-bromophenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-androsterone (**3c**)*

Obtained as pale yellow solid; Yield 81%; m.p.186–188 °C; Anal. Calcd. for $C_{41}H_{44}BrNO_3S$: C, 69.28; H, 6.24; N, 1.97; Found: C, 69.17; H, 6.26; N, 1.86. ^{1}H NMR −0.25–(−0.07) (m, 2H), –0.05 (s, 3H), 0.40–0.48 (m, 2H), 0.58 (s, 3H), 0.68–0.73 (m, 1H), 0.83–0.90 (m, 3H), 1.02–1.26 (m, 6H), 1.42–1.54 (m, 4H), 1.68–1.71 (m, 2H), 2.46 (dd, *J* = 13.1, 4.3 Hz, 1H), 2.90 (dd, *J* = 10.5, 4.8 Hz, 1H), 3.07 (dd, *J* = 10.2, 6.0 Hz, 1H), 3.44–3.54 (m, 1H), 3.64 (d, *J* = 8.1 Hz, 1H), 3.77–3.83 (m, 2H), 4.71–4.78 (m, 1H), 7.21–8.15 (m, 10H). ^{13}C NMR 12.1, 14.1, 20.0, 22.6, 28.1, 29.0, 30.6, 31.2, 31.3, 31.6, 33.8, 34.6, 35.4, 36.6, 37.9, 44.6, 47.1, 48.8, 50.2, 54.6, 55.5, 71.0, 71.9, 72.1, 80.0, 120.9, 121.6, 125.5, 126.1, 127.9, 128.3, 130.5, 131.7, 132.3, 134.5, 136.1, 141.3, 205.9 and 219.0.

*2.2.4. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(4-fluorophenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-androsterone (**3d**)*

Obtained as pale yellow solid; Yield 75%; m.p. 172–174 °C; Anal. Calcd. for $C_{41}H_{44}FNO_3S$: C, 75.78; H, 6.82; N, 2.16. Found: C, 75.73; H, 6.86; N, 2.19. ^{1}H NMR −0.26–(−0.15) (m, 1H), −0.04–(−0.05) (m, 1H), −0.01 (s, 3H), 0.46–0.53 (m, 2H), 0.58 (s, 3H), 0.70–0.79 (m, 1H), 0.83–0.91 (m, 3H), 0.95–1.07 (m, 2H), 1.12–1.29 (m, 6H), 1.47–1.68 (m, 4H), 2.52 (dd, *J* = 13.1, 4.3 Hz, 1H), 2.92 (dd, *J* = 10.7, 4.4 Hz, 1H), 3.10 (dd, *J* = 10.5, 6.3 Hz, 1H), 3.47–3.54 (m, 1H), 3.64 (d, *J* = 8.4 Hz, 1H), 3.82–3.87 (m, 2H), 4.70–4.76 (m, 1H), 7.00–8.16 (m, 10H). ^{13}C NMR 12.0, 14.0, 20.0, 28.1, 28.8, 30.6, 31.3, 31.4, 33.9, 34.7, 35.4, 36.6, 38.0, 44.7, 47.1, 48.9, 50.4, 54.6, 55.5, 71.0, 72.0, 72.1, 80.2, 115.3, 115.6, 120.8, 125.5, 126.2, 127.8, 128.3, 130.6, 131.6, 131.8, 132.2, 132.8, 134.6, 141.2, 160.6, 163.9, 205.8 and 220.0.

*2.2.5. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(4-methylphenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-androsterone (**3e**)*

Obtained as pale yellow solid; Yield 83%; m.p. 191–193 °C; Anal. Calcd. for $C_{42}H_{47}NO_3S$: C, 78.10; H, 7.33; N, 2.17. Found: C, 78.15; H, 7.39; N, 2.21. ^{1}H NMR −0.29–(−0.19) (m, 1H), −0.05 (s, 3H), 0.58 (s, 3H), 0.50–0.64 (m, 2H), 0.71–0.79 (m, 1H), 0.83–0.90 (m, 3H), 1.06–1.26 (m, 7H), 1.47–1.67 (m, 6H), 2.32 (s, 3H), 2.56 (dd, *J* = 13.4, 4.3 Hz, 1H), 2.93 (dd, *J* = 11.0,4.0 Hz, 1H), 3.11 (dd, *J* = 10.8, 6.3 Hz, 1H), 3.46–3.55 (m, 1H), 3.63 (d, *J* = 8.4 Hz, 1H), 3.85 (d, *J* = 6.3 Hz, 1H), 3.88 (d, *J* = 5.4 Hz, 1H), 4.73–4.80 (m, 1H), 7.14–8.14 (m, 10H). ^{13}C NMR 12.1, 13.8, 20.0, 21.0, 28.2, 28.4, 30.6, 31.3, 31.5, 33.9, 35.0, 35.4, 36.7, 38.0, 44.7, 47.1, 49.1, 51.0, 54.7, 56.0, 71.0, 71.8, 72.1, 80.8, 120.8, 125.4, 126.3, 127.7, 128.3, 129.2, 130.0, 130.5, 131.9, 132.1, 133.6, 134.7, 137.3, 141.1, 205.7 and 218.6.

*2.2.6. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(4-methoxyphenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-androsterone (**3f**)*

Obtained as pale yellow solid; Yield 87%; m.p. 170–172 °C; Anal. Calcd. for $C_{42}H_{47}NO_4S$: C, 76.21; H, 7.16; N, 2.12. Found: C, 76.17; H, 7.19; N, 2.21. ^{1}H NMR −0.28–(−0.17) (m, 1H), −0.05 (s, 3H), 0.50–0.65 (m, 2H), 0.58 (s, 3H), 0.71–0.79 (m, 1H), 0.83–0.95 (m, 4H), 1.04–1.12 (m, 2H), 1.12–1.28 (m, 3H), 1.47–1.57 (m, 3H), 1.63–1.75 (m, 4H), 2.56 (dd, *J* = 13.2, 4.5 Hz, 1H), 2.94 (dd, *J* = 10.8, 4.2 Hz, 1H), 3.12 (dd, *J* = 11.0, 6.4 Hz, 1H), 3.46–3.55 (m, 1H), 3.63 (d, *J* = 8.7 Hz, 1H), 3.79 (s, 3H), 3.77–3.86 (m, 2H), 4.70–4.75 (m, 1H), 6.84–8.14 (m, 10H). ^{13}C NMR 12.0, 13.8, 20.0, 28.2, 30.6, 31.3, 31.5, 33.9, 35.0, 35.4, 36.6, 38.0, 44.7, 47.1, 49.1, 51.1, 54.6, 55.2, 55.7, 71.0, 71.8, 72.0, 80.7, 113.9, 120.7, 125.4, 126.2, 127.7, 128.2, 128.7, 130.5, 131.1, 131.8, 132.1, 134.6, 141.0, 159.0, 205.8 and 218.6.

*2.2.7. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(2-chlorophenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-androsterone (**3g**)*

Obtained as pale yellow solid; Yield 89%; m.p. 179–181 °C; FT–IR: 3446, 2926, 2854, 1712, 783. Anal. Calcd. for $C_{41}H_{44}ClNO_3S$: C, 73.91; H, 6.66; N, 2.10. Found: C, 73.95; H, 6.76; N, 2.18. ^{1}H NMR −0.51 (td, *J* = 13.1, 5.5 Hz, 1H), −0.17–(−0.05) (m, 2H), 0.45 (s, 3H), 0.53 (s, 3H), 0.53–0.66 (m, 2H), 0.81–0.97 (m, 6H), 1.07–1.15 (m, 3H), 1.21–1.31 (m, 3H), 1.38–1.42 (m, 3 H), 2.06 (dd, *J* = 13.5, 4.2 Hz, 1H), 2.90–3.02 (m, 2H), 3.38–3.46 (m, 1H), 3.54 (d, *J* = 6.0 Hz, 1H), 3.69 (d, *J* = 5.7 Hz, 1H), 4.54 (d, *J* = 8.4 Hz, 1H), 4.74–4.81 (m, 1H), 7.19–8.18 (m, 10H). ^{13}C NMR 12.0, 15.2, 19.8, 27.9, 30.6, 31.2, 32.4, 33.1, 33.4, 35.2, 36.5, 37.8, 44.5, 46.7, 47.3, 48.0, 50.2, 54.4, 70.9, 72.8, 74.3, 77.4, 120.8, 125.5, 126.2, 127.2, 128.0, 128.2, 128.6, 129.4, 130.4, 131.9, 132.2, 135.2, 135.4, 136.4, 142.4, 207.1 and 220.0.

*2.2.8. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(2-methylphenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-androsterone (**3h**)*

Obtained as pale yellow solid; Yield 91%; m.p. 171–173 °C; Anal. Calcd. for $C_{42}H_{47}NO_3S$: C, 78.10; H, 7.33; N, 2.17. Found: C, 78.21; H, 7.38; N, 2.27. ^{1}H NMR −0.31–(−0.153) (m, 2H) 0.14 (s, 3H), 0.22–0.29 (m, 2H), 0.55 (s, 3H), 0.62–0.73 (m, 2H), 0.83–0.87 (m, 3H), 0.95–1.15 (m, 5H), 1.42–1.69 (m, 6H), 2.27 (s, 3H), 2.40 (dd, *J* = 11.9, 5.8 Hz, 1H), 2.87 (dd, *J* = 9.7, 6.1 Hz, 1H), 3.00 (dd, *J* = 9.7, 6.1 Hz, 1H), 3.42–3.49 (m, 1H), 3.70 (s, 2H), 4.28 (d, *J* = 9.6 Hz, 1H), 4.76–4.83 (m, 1H), 7.14–8.16 (m, 10H). ^{13}C NMR 12.0, 14.1, 20.0, 28.1, 30.6, 30.9, 31.3, 33.8, 33.9, 35.3, 36.6, 37.9, 44.7, 47.2, 48.4, 48.8, 50.6, 54.5, 71.0, 72.5, 73.9, 79.1, 120.8, 125.4, 126.1, 126.2, 126.9, 127.9, 128.4, 130.2, 130.5, 130.6, 132.0, 132.1, 135.5, 135.8, 137.6, 141.8, 206.2 and 220.1.

*2.2.9. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(2-methoxyphenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-androsterone (**3i**)*

Obtained as pale yellow solid; Yield 78%; m.p. 190–192 °C; Anal. Calcd. for $C_{42}H_{47}NO_4S$: C, 76.21; H, 7.16; N, 2.12. Found: C, 76.12; H, 7.21; N, 2.19. ^{1}H NMR −0.44–(−0.41) (m, 1H), −0.20–(−0.15) (m, 1H), 0.01–0.07 (m, 1H), 0.33 (s, 3H), 0.54 (s, 3H), 0.64–0.67 (m, 2H), 0.82–0.95 (m, 5H), 1.04–1.12 (m, 4H), 1.22–1.39 (m, 3H), 1.42 (s, 2H), 1.53–1.68 (m, 2H), 2.91–2.96 (m, 2H), 3.43–3.45 (m, 1H), 3.62–3.69 (m, 5H), 4.45–4.48 (m, 1H), 4.82–4.85 (m, 1H), 6.81–8.15 (m, 10H). ^{13}C NMR 12.0, 14.4, 19.9, 22.5, 25.2, 29.0, 30.0, 30.5, 31.2, 31.3, 31.5, 33.6, 34.6, 35.3, 36.5, 37.9, 44.6, 47.1, 48.1, 54.5, 55.1, 70.8, 72.7, 110.2, 120.6, 120.7, 125.2, 126.2, 126.7, 127.8, 128.0, 128.3, 130.4, 131.9, 132.1, 135.7, 142.1, 157.9, 206.6 and 219.3.

*2.2.10. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(3-bromophenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-androsterone (**3j**)*

Obtained as pale yellow solid; Yield 80%; m.p. 180–182 °C; FT-IR: 3479, 2920, 2852, 1716, 783. Anal. Calcd. for $C_{41}H_{44}BrNO_3S$: C, 69.28; H, 6.24; N, 1.97; Found: C, 69.36; H, 6.32; N, 2.09. ^{1}H NMR −0.23 (td, *J* = 12.7, 4.0 Hz, 1H),−0.12–(−0.06) (m, 1H), 0.55 (s, 3H), 0.41–0.51 (m, 2H), 0.58 (s, 3H), 0.69–0.78 (m, 1H), 0.85–0.88 (m, 3H), 1.04–1.22 (m, 6H), 1.42–1.71 (m, 6H), 2.49 (dd, *J* = 13.2, 4.5 Hz, 1H), 2.92 (dd, *J* = 10.5, 4.8 Hz, 1H), 3.10 (dd, *J* = 10.5, 6.3 Hz, 1H), 3.45–3.55 (m, 1H), 3.63 (d, *J* = 8.1 Hz, 1H), 3.79–3.84 (m, 2H), 4.74–4.77 (m, 1H), 7.22–8.16 (m, 10H). ^{13}C NMR 12.1, 14.1, 20.0, 28.1, 29.1, 30.6, 31.2, 31.3, 33.8, 34.5, 35.4, 36.6, 38.0, 44.7, 47.1, 48.8, 50.1, 54.6, 55.6, 70.9, 71.8, 72.3, 79.8, 120.9, 122.7, 125.5, 126.1, 127.9, 128.3, 128.5, 130.1, 130.6, 130.7, 131.8, 132.2, 133.0, 134.6, 139.6, 141.3, 205.7 and 218.9.

*2.2.11. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-naphthyl-tetra-hydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-androsterone (**3k**)*

Obtained as pale yellow solid; Yield 89%, m.p. 174–176 °C; FT-IR: 3441, 2924, 2852, 1716, 783. Anal. Calcd. for $C_{45}H_{47}NO_3S$: C, 79.26; H, 6.95; N, 2.05. Found: C, 79.33; H, 7.02; N, 2.18. ^{1}H NMR −0.43–(−0.37) (m, 1H), −0.25–(−0.18) (m, 1H), −0.11 (s, 3H), 0.06–0.25 (m, 3H), 0.46 (s, 3H), 0.58–0.70 (m, 2H), 0.81–0.91 (m, 4H), 1.05–1.10 (m, 3H), 1.23–1.26 (m, 3H), 1.35–1.42 (m, 3H), 2.30 (dd, *J* = 13.7, 4.3 Hz, 1H), 2.89 (dd, *J* = 9.7, 6.8 Hz, 1H), 2.97 (dd, *J* = 9.7, 5.9 Hz, 1H), 3.39–3.47 (m, 1H), 3.70 (d, *J* = 6.6 Hz, 1H), 3.75 (d, *J* = 6.9 Hz, 1H), 4.82 (d, *J* = 9.3 Hz, 1H), 5.06–5.09 (m, 1H), 7.42–8.18 (m, 13H). ^{13}C NMR 11.9, 14.7, 19.8, 26.9, 27.9, 30.5, 31.2, 33.5, 33.8, 34.6, 35.2, 36.5, 37.8, 44.5, 47.4, 48.2, 48.6, 54.4, 70.9, 73.1, 73.6, 78.6, 120.9, 123.7, 125.5, 125.7, 126.1, 126.3, 127.5, 127.7, 128.0, 128.5, 128.7, 130.5, 132.0, 132.2, 132.9, 133.9, 134.0, 135.5, 142.0, 206.4 and 220.3.

*2.2.12. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-phenyl-tetra-hydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-dehydroandrosterone (**6a**)*

Obtained as pale yellow solid; Yield 88%; m.p. 191–193 °C; Anal. Calcd. for $C_{41}H_{43}NO_3S$: C, 78.18; H, 6.88; N, 2.22. Found: C, 78.25; H, 6.76; N, 2.29. ^{1}H NMR −0.22–(−0.15) (m, 1H), −0.04 (s, 3H), 0.31–0.39 (m, 1H), 0.61 (td, *J* = 13.8, 4.8 Hz, 1H), 0.78 (s, 3H), 0.83–0.90 (m, 2H) 1.03–1.39 (m, 6H), 1.50–1.71 (m, 3H), 1.86–1.93 (m, 1H), 2.11–2.24 (m, 2H), 2.60 (dd, *J* = 13.1, 4.7 Hz, 1H), 2.95 (dd, *J* = 11.0, 4.4 Hz, 1H), 3.13 (dd, *J* = 10.8, 6.6 Hz, 1H), 3.41–3.48 (m, 1H), 3.64 (d, *J* = 8.7 Hz, 1H), 3.86–3.93, (m, 2H), 4.76–4.83 (m, 1H), 5.26–5.27 (m, 1H), 7.31–8.14 (m, 11H). ^{13}C NMR 13.3, 19.1, 19.7, 30.3, 30.4, 31.3, 31.4, 31.5, 35.1, 36.4, 36.9, 42.1, 46.8, 49.2, 50.2, 51.3, 56.4, 71.4, 71.6, 71.7, 80.9, 120.9, 121.0, 125.4, 126.3, 127.6, 127.8, 128.2, 128.5, 130.1, 130.5, 131.6, 132.2, 134.3, 136.6, 140.5, 141.0, 205.6 and 218.2.

*2.2.13. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(4-chlorophenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-dehydroandrosterone (**6b**)*

Obtained as pale yellow solid; Yield 86%; m.p. 190–192 °C; FT-IR: 3443, 2926, 2854, 1724, 783. Anal. Calcd. for $C_{41}H_{42}ClNO_3S$: C, 74.13; H, 6.37; N, 2.11. Found: C, 74.21; H, 6.39; N, 2.21. ^{1}H NMR −0.17 (td, *J* = 12.4, 4.7 Hz, 1H), 0.05 (s, 3H), 0.25–0.32 (m, 1H), 0.47–0.55 (m, 1H), 0.78 (s, 3H), 0.88–0.93 (m, 2H), 1.01–1.29 (m, 4H), 1.34–1.39 (m, 1H), 1.49–1.54 (m, 2H), 1.71–1.75 (m, 1H), 1.83–1.88 (m, 2H), 2.10–2.25 (m, 2H), 2.50 (dd, *J* = 13.4, 4.7 Hz, 1H), 2.91 (dd, *J* = 10.7, 4.7 Hz, 1H), 3.08 (dd, *J* = 10.7, 6.1 Hz, 1H), 3.40–3.47 (m, 1H), 3.63 (d, *J* = 8.1 Hz, 1H), 3.80 (d, *J* = 8.1 Hz, 1H), 3.85 (d, *J* = 9.9 Hz, 1H), 4.71–4.78 (m, 1H), 5.22–5.24 (m, 1H), 7.30–8.14 (m, 10H). ^{13}C NMR 13.8, 14.0, 19.1, 19.8, 29.1, 29.7, 30.4, 31.2, 31.4, 34.6, 36.5, 36.9, 42.1, 46.8, 49.1, 50.3, 50.4, 55.7, 71.4, 72.0, 80.0, 120.9, 121.0, 125.5, 126.2, 127.9, 128.3, 128.8, 130.6, 131.4, 131.7, 132.3, 133.6, 134.5, 135.6, 140.6, 141.3, 205.7 and 218.6.

*2.2.14. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(4-bromophenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-dehydroandrosterone (**6c**)*

Obtained as pale yellow solid; Yield 89%; m.p. 187–189 °C; Anal. Calcd. for $C_{41}H_{42}BrNO_3S$: C, 69.48; H, 5.97; N, 1.98. Found: C, 69.35; H, 5.89; N, 1.87. ^{1}H NMR −0.16 (td, *J* = 13.2, 5.4 Hz, 1H), 0.06 (s, 3H), 0.24–0.32 (m, 1H), 0.47–0.53 (m, 1H), 0.79 (s, 3H), 0.83–0.90 (m, 3H), 1.07–1.43 (m, 5H), 1.57–1.61 (m, 2H), 1.81–1.86 (m, 2H), 2.11–2.24 (m, 2H), 2.50 (dd, *J* = 13.3, 4.6 Hz, 1H), 2.91 (dd, *J* = 10.7, 4.7 Hz, 1H), 3.08 (dd, *J* = 10.5, 6.0 Hz, 1H), 3.40–3.48 (m, 1H), 3.63 (d, *J* = 8.1 Hz, 1H), 3.80 (d, *J* = 8.1 Hz, 1H), 3.84 (d, *J* = 10.2 Hz, 1H), 4.71–4.78 (m, 1H), 5.22–5.24 (m, 1H), 7.22–8.15

(m, 10H). ^{13}C NMR 14.1, 19.1, 19.7, 22.6, 28.9, 30.3, 31.2, 31.3, 31.5, 34.6, 36.4, 36.8, 42.0, 46.8, 49.0, 50.1, 50.5, 55.6, 71.4, 71.8, 80.1, 120.8, 121.0, 121.7, 125.5, 126.1, 127.9, 128.2, 128.8, 130.5, 131.6, 131.7, 132.3, 134.3, 136.0, 140.5, 141.2, 205.7 and 218.6.

*2.2.15. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(4-fluorophenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-dehydroandrosterone (**6d**)*

Obtained as pale yellow solid; Yield 80%; m.p. 179–181 °C; Anal. Calcd. for $C_{41}H_{42}FNO_3S$: C, 76.01; H, 6.53; N, 2.16. Found: C, 76.08; H, 6.48; N, 2.30. ^{1}H NMR −0.21–(0.13) (m, 1H), 0.01 (s, 3H), 0.31–0.35 (m, 1H), 0.51–0.58 (m, 1H), 0.79 (s, 3H), 0.83–0.90 (m, 2H), 1.08–1.30 (m, 5H), 1.35–1.40 (m, 1H), 1.58–1.62 (m, 1H), 1.72–1.85 (m, 3H), 2.07–2.25 (m, 2H), 2.55 (dd, *J* = 13.4, 4.7 Hz, 1H), 2.93 (dd, *J* = 10.8, 4.5 Hz, 1H), 3.10 (dd, *J* = 10.7, 6.4 Hz, 1H), 3.40–3.48 (m, 1H), 3.63 (d, *J* = 8.4 Hz, 1H), 3.84 (d, *J* = 8.4 Hz, 1H), 3.88 (d, *J* = 10.2 Hz, 1H), 4.70–4.77 (m, 1H), 5.24–5.26 (m, 1H), 7.00–8.15 (m, 10H). ^{13}C NMR 13.6, 19.1, 19.8, 22.6, 28.8, 30.4, 30.5, 31.3, 31.4, 34.8, 36.4, 36.9, 42.1, 46.8, 49.1, 50.3, 50.6, 55.6, 71.4, 71.9, 72.0, 80.3, 115.3, 115.6, 120.9, 125.5, 126.2, 127.9, 128.3, 130.6, 131.7, 132.2, 132.7, 134.5, 140.6, 141.2, 160.6, 163.9, 205.6 and 218.5.

*2.2.16. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(4-methylphenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-dehydroandrosterone (**6e**)*

Obtained as pale yellow solid; Yield 85%; m.p. 184–186 °C; Anal. Calcd. for $C_{42}H_{45}NO_3S$: C, 78.35; H, 7.04; N, 2.18. Found: C, 78.32; H, 7.09; N, 2.24. ^{1}H NMR −0.23–(−0.166) (m, 1H), −0.03 (m, 3H), 0.36–0.38 (m, 1H), 0.54–0.63 (m, 1H), 0.78 (s, 3H), 0.72–0.90 (m, 3H), 1.07–1.42 (m, 6H), 1.71–1.73 (m, 2H), 1.88–1.93 (m, 1H), 2.05–2.16 (m, 1H), 2.22–2.25 (m, 1H), 2.32 (s, 3H), 2.58 (dd, *J* = 13.2, 4.5 Hz, 1H), 2.94 (dd, *J* = 10.8, 4.2 Hz, 1H), 3.12 (dd, *J* = 10.7, 6.5 Hz, 1H), 3.41–3.49 (m, 1H), 3.63 (d, *J* = 8.7 Hz, 1H), 3.88 (d, *J* = 8.7 Hz, 2H), 4.73–4.80 (m, 1H), 5.28–5.30 (m, 1H), 7.11–8.13 (m, 10H). ^{13}C NMR 13.3, 19.1, 19.7, 21.0, 28.2, 30.3, 30.4, 31.3, 31.4, 35.1, 36.4, 36.9, 42.1, 46.8, 49.2, 50.2, 51.4, 56.1, 71.4, 71.7, 80.9, 120.8, 121.0, 125.4, 126.3, 127.8, 128.2, 129.2, 129.4, 129.9, 130.5, 131.6, 132.2, 133.4, 134.4, 137.3, 140.5, 140.9, 205.6 and 218.3.

*2.2.17. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(4-methoxy-phenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-dehydroandrosterone (**6f**)*

Obtained as pale yellow solid; Yield 87%; m.p. 199–201 °C; Anal. Calcd. for $C_{42}H_{45}NO_4S$: C, 76.45; H, 6.87; N, 2.12. Found: C, 76.51; H, 6.93; N, 2.18. ^{1}H NMR −0.22–(−0.16) (m, 1H), −0.03 (s, 3H), 0.31–0.40 (m, 1H), 0.57–0.64 (m, 1H), 0.79 (s, 3H), 0.80–0.90 (m, 1H), 1.16–1.24 (m, 4H), 1.28–1.40 (m, 3H), 1.62–1.73 (m, 2H), 1.89–1.94 (m, 2H), 2.12–2.26 (m, 2H), 2.59 (dd, *J* = 13.2, 4.5 Hz, 1H), 2.94 (dd, *J* = 10.8, 4.2 Hz, 1H), 3.13 (dd, *J* = 10.8, 6.6 Hz, 1H), 3.41–3.54 (m, 1H), 3.63 (d, *J* = 8.7 Hz, 1H), 3.79 (s, 3H), 3.85–3.90 (m, 2H), 4.69–4.76 (m, 1H), 5.27–5.28 (m, 1H), 6.84–8.13 (m, 10H). ^{13}C NMR 13.3, 19.1, 19.7, 28.0, 30.3, 30.5, 31.4, 35.2, 36.4, 36.9, 42.1, 46.8, 49.3, 50.2, 51.5, 55.2, 55.7, 71.4, 71.6, 71.7, 81.0, 113.9, 120.8, 121.0, 125.4, 126.2, 127.8, 128.2, 128.4, 130.5, 131.1, 131.6, 132.0, 132.2, 134.3, 140.5, 140.9, 159.0, 205.6 and 218.3.

*2.2.18. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(2-chlorophenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-dehydroandrosterone (**6g**)*

Obtained as pale yellow solid; Yield 91%; m.p. 182–184 °C; FT-IR: 3429, 2931, 2860, 1708, 785. Anal. Calcd. for $C_{41}H_{42}ClNO_3S$: C, 74.13; H, 6.37; N, 2.11. Found: C, 74.18; H, 6.35; N, 2.19. ^{1}H NMR −0.12–(−0.02) (m, 1H), 0.03–0.08 (m, 1H), 0.48 (s, 3H), 0.48–0.56 (m, 1H), 0.68–0.72 (m, 1H), 0.75 (s, 3H), 0.99–1.18 (m, 4H), 1.27–1.34 (m, 2H), 1.46–1.58 (m, 5H), 2.05–2.14 (m, 3H), 2.93 (dd, *J* = 9.5, 5.9 Hz, 1H), 2.98 (dd, *J* = 13.5, 5.5 Hz, 1H), 3.32–3.39 (m, 1H), 3.53 (d, *J* = 5.7 Hz, 1H), 3.69 (d, *J* = 6.0 Hz, 1H), 4.57 (d, *J* = 8.7 Hz, 1H), 4.79 (m, 1H), 5.06–5.07 (m, 1H), 7.19–8.17 (m, 10H). ^{13}C NMR 14.9, 19.0, 19.6, 30.1, 30.5, 31.0, 31.3, 32.5, 33.1, 36.4, 36.8, 42.0, 46.8, 47.1, 48.3, 50.0, 50.4, 72.6, 74.2, 77.3, 120.4, 120.9, 125.5, 126.3, 127.2, 128.0, 128.2, 128.6, 129.5, 130.5, 131.9, 132.0, 132.3, 132.4, 135.2, 135.4, 136.4, 140.6, 142.4, 206.9 and 219.8.

*2.2.19. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(2-methylphenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-dehydroandrosterone (**6h**)*

Obtained as pale yellow solid; Yield 89%; m.p. 181–182 °C; Anal. Calcd. for $C_{42}H_{45}NO_3S$: C, 78.35; H, 7.04; N, 2.18. Found: C, 78.23; H, 7.11; N, 2.32. ^{1}H NMR −0.13 (td, *J* = 12.3, 4.8 Hz, 1H), 0.10–0.21 (m, 1H), 0.15 (s, 3H), 0.27–0.37 (m, 1H), 0.76 (s, 3H), 0.78–0.90 (m, 3H), 1.08–1.19 (m, 4H), 1.37–1.43 (m, 1H), 1.54–1.59 (m, 2H), 1.68–1.72 (m, 2H), 2.08–2.22 (m, 2H), 2.29 (s, 3H), 2.44 (dd, *J* = 13.8, 4.5 Hz, 1H), 2.88 (dd, *J* = 10.1, 5.1 Hz, 1H), 3.01 (dd, *J* = 10.2, 6.0 Hz, 1H), 3.36–3.44 (m, 1H), 3.70 (s, 2H), 4.31 (d, *J* = 9.9 Hz, 1H), 4.76–4.83 (m, 1H), 5.17–5.19 (m, 1H), 7.12–8.15 (m, 10H). ^{13}C NMR 13.6, 19.0, 19.7, 19.9, 30.3, 30.4, 30.7, 31.1, 31.3, 34.0, 36.4, 36.8, 42.0, 46.9, 48.6, 49.0, 50.1, 50.7, 71.3, 72.1, 73.8, 79.2, 120.7, 120.8, 125.3, 126.0, 126.2, 126.9, 127.9, 128.3, 130.1, 130.5, 130.6, 131.8, 132.1, 135.3, 135.6, 137.6, 140.5, 141.7, 205.9 and 219.8.

*2.2.20. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(2-methoxy-phenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-dehydroandrosterone (**6i**)*

Obtained as pale yellow solid; Yield 80%; m.p.177–179 °C; Anal. Calcd. for $C_{42}H_{45}NO_4S$: C, 76.45; H, 6.87; N, 2.12. Found: C, 76.32; H, 6.76; N, 2.01. ^{1}H NMR (−0.13)–0.18 (m, 2H), 0.35 (s, 3H), 0.52–0.74 (m, 1H), 0.75 (s, 3H), 0.83–0.87 (m, 1H), 0.95–1.14 (m, 4H), 1.26–1.67 (m, 6H), 2.01–2.12 (m, 3H), 2.90–2.96 (m, 2H), 3.36–3.38 (m, 1H), 3.62–3.70 (m, 5H), 4.47–4.50 (m, 1H), 4.82–4.83 (m, 1H), 5.09–5.10 (m, 1H), 6.82–8.14 (m, 10H). ^{13}C NMR 14.1, 19.1, 19.7, 30.2, 30.5, 31.2, 31.4, 33.7, 36.4, 36.8, 42.0, 46.1, 46.9, 47.7, 48.5, 50.1, 55.1, 71.4, 72.5, 72.8, 78.0, 110.3, 120.7, 120.8, 125.3, 126.3, 127.9, 128.1, 128.4, 130.4, 130.6, 132.0, 132.1, 135.6, 140.6, 142.1, 158.0, 206.6 and 219.5.

*2.2.21. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-(3-bromophenyl)-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-dehydroandrosterone (**6j**)*

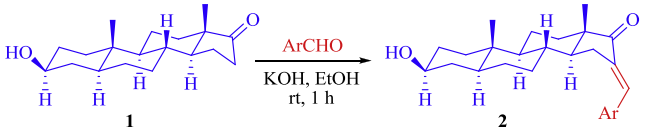
Obtained as pale yellow solid; Yield 82%; m.p. 201–203 °C; FT-IR: 3479, 2920, 2854, 1714, 781. Anal. Calcd. for $C_{41}H_{42}BrNO_3S$: C, 69.48; H, 5.97; N, 1.98. Found: C, 69.32; H, 5.89; N, 1.92. ^{1}H NMR −0.17 (td, *J* = 12.0, 4.5 Hz, 1H), 0.07 (s, 3H), 0.29–0.34 (m, 1H), 0.49–0.55 (m, 1H), 0.79 (s, 3H), 0.85–0.88 (m, 1H), 1.11–1.26 (m, 5H), 1.35–1.39 (m, 1H), 1.57–1.71 (m, 4H), 1.86–1.90 (m, 1H), 2.11–2.24 (m, 2H), 2.53 (dd, *J* = 13.2, 4.5 Hz, 1H), 2.93 (dd, *J* = 10.7, 4.6 Hz, 1H), 3.11 (dd, *J* = 10.7, 6.1 Hz, 1H), 3.44–3.48 (m, 1H), 3.63 (d, *J* = 8.1 Hz, 1H), 3.80–3.86 (m, 2H), 4.72–4.78 (m, 1H), 5.24–5.25 (m, 1H), 7.22–8.15 (m, 10H). ^{13}C NMR 13.6, 19.1, 19.7, 28.7, 30.4, 31.2, 31.3, 34.8, 36.4, 36.8, 42.0, 46.8, 49.1, 50.2, 50.7, 55.7, 71.4, 71.6, 71.8, 80.2, 120.9, 121.0, 122.7, 125.6, 126.2, 127.9, 128.2, 130.1, 130.5, 130.8, 131.5, 132.3, 133.0, 134.3, 139.3, 140.6, 141.1, 205.5 and 218.4.

*2.2.22. (16R, 5′R, 7′R, 7a′R)-Spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-7′-naphthyl-tetrahydro-1H-pyrrolo[1,2-c][1,3]thiazolo-trans-dehydroandrosterone (**6k**)*

Obtained as pale yellow solid; Yield 92%; m.p. 187–189 °C; FT-IR: 3431, 2929, 2858, 1712, 783. Anal. Calcd. for $C_{45}H_{45}NO_3S$: C, 79.49; H, 6.67; N, 2.06. Found: C, 79.52; H, 6.71; N, 2.18. ^{1}H NMR −0.19–(−0.15) (m, 1H), −0.09 (s, 3H), 0.04–0.07 (m, 1H), 0.25 (td, *J* = 13.8, 4.5 Hz 1H), 0.67 (s, 3H), 0.73–0.84 (m, 2H) 0.94–1.09 (m, 4H), 1.28–1.36 (m, 2H), 1.49–1.53 (m, 4H), 2.00–2.16 (m, 2H), 2.33 (dd, *J* = 13.8, 4.5 Hz, 1H), 2.89 (dd, *J* = 9.6, 6.0 Hz, 1H), 2.99 (dd, *J* = 9.6, 6.0 Hz, 1H), 3.33–3.40 (m, 1H), 3.69 (d, 6.9 Hz, 1H), 3.75, (d, 6.9 Hz, 1H), 4.85, (d, *J* = 9.6 Hz, 1H), 5.04–5.11 (m, 2H), 7.42–8.16 (m, 13H). ^{13}C NMR 14.2, 19.0, 19.6, 30.1, 30.4, 31.0, 31.2, 31.3, 33.9, 36.3, 36.7, 41.9, 47.1, 48.4, 48.8, 50.0, 71.3, 72.8, 73.6, 78.7, 120.6, 120.9, 123.6, 125.5, 125.6, 125.7, 126.3, 126.4, 127.5, 127.7, 128.0, 128.5, 128.7, 130.5, 131.8, 132.3, 132.9, 133.9, 134.0, 135.4, 140.5, 141.9, 206.2 and 218.4.

3. Results and discussion

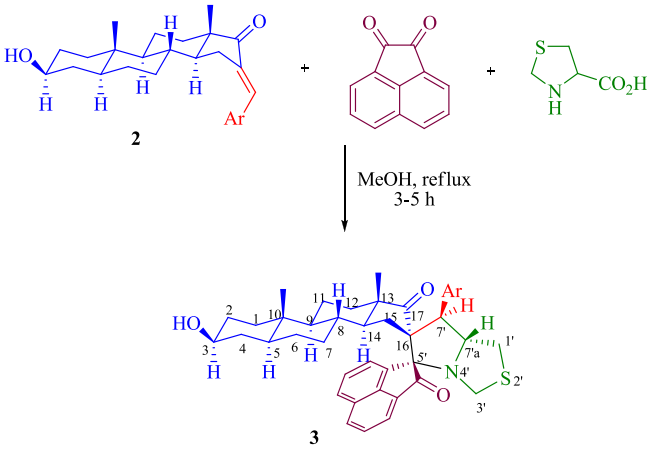
In the present study, the reaction of *trans*-androsterone **1** or *trans*-dehydroandrosterone **4** with various aromatic aldehydes in the presence of potassium hydroxide in ethanol at ambient temperature afforded (*E*)-16-arylmethylidene-*trans*-androsterones **2a–k** and (*E*)-16-arylmethylidene-*trans*-dehydroandrosterones **5a–k** respectively in quantitative yields (Schemes 1 and 3). A total of twenty-two of the above steroidal 16-exocyclic olefins were prepared, among which twelve (**2h–k**, **5c–e** and **5g–5k**) are new. The structure of all these dipolarophiles **2** and **5** was elucidated with the help of NMR spectroscopy and single crystal X-ray crystallographic studies. As a representative example, in the ^{1}H NMR spectrum of **2k**, a singlet at 8.19 ppm can be assigned to the methylidene proton whereas the naphthyl ring protons appear as multiplets at 7.47–8.17 ppm. A broad singlet at 5.09 ppm and a multiplet at 3.52–3.61 ppm are due to the OH and 3-CH protons respectively. The C-10 and C-13 angular methyl protons appear



Entry	Comp	Ar	Yield[a,b] (%)
1	**2a**	C_6H_5	97 (98)[18]
2	**2b**	*p*-ClC_6H_4	98 (91)[19]
3	**2c**	*p*-BrC_6H_4	96 (91)[19]
4	**2d**	*p*-FC_6H_4	98 (95)[19]
5	**2e**	*p*-$CH_3C_6H_4$	97 (91)[19]
6	**2f**	*p*-$CH_3OC_6H_4$	96 (94)[19]
7	**2g**	*o*-ClC_6H_4	98 (97)[18]
8	**2h**	*o*-$CH_3C_6H_4$	97
9	**2i**	*o*-$CH_3OC_6H_4$	98
10	**2j**	*m*-BrC_6H_4	96
11	**2k**	Naphthyl	96

[a]Yields were quantitative except for the loss during workup
[b]Yield given in the parenthesis are literature report

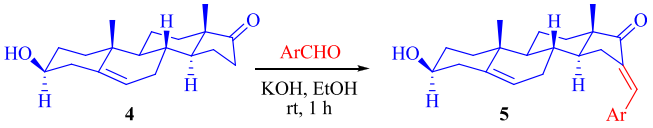
Scheme 1. Synthesis of 16-(*E*)-arylidene-*trans*-androsterones **2.** (See above-mentioned references for further information [18,19].)



Entry	Comp	Ar	Yield[a] (%)	mp (°C)
1	**3a**	C_6H_5	87	182–183
2	**3b**	*p*-ClC_6H_4	79	160–161
3	**3c**	*p*-BrC_6H_4	81	187–188
4	**3d**	*p*-FC_6H_4	75	173–174
5	**3e**	*p*-$CH_3C_6H_4$	83	192–193
6	**3f**	*p*-$CH_3OC_6H_4$	87	171–172
7	**3g**	*o*-ClC_6H_4	89	181–182
8	**3h**	*o*-$CH_3C_6H_4$	91	172–173
9	**3i**	*o*-$CH_3OC_6H_4$	78	191–192
10	**3j**	*m*-BrC_6H_4	80	182–183
11	**3k**	Naphthyl	89	176–177

[a]Isolated yields after flash filtration column

Scheme 2. Synthesis of dispiro-*trans*-androsterones **3.**



Entry	Comp	Ar	Yield[a,b] (%)
1	**5a**	C_6H_5	98 (94)[20]
2	**5b**	*p*-ClC_6H_4	97 (93)[20]
3	**5c**	*p*-BrC_6H_4	96
4	**5d**	*p*-FC_6H_4	98
5	**5e**	*p*-$CH_3C_6H_4$	97
6	**5f**	*p*-$CH_3OC_6H_4$	96 (91)[20]
7	**5g**	*o*-ClC_6H_4	97
8	**5h**	*o*-$CH_3C_6H_4$	98
9	**5i**	*o*-$CH_3OC_6H_4$	96
10	**5j**	*m*-BrC_6H_4	97
11	**5k**	Naphthyl	97

[a]Yields were quantitative except for the loss during workup
[b]Yield given in the parenthesis are literature report

Scheme 3. Synthesis of 16-(*E*)-arylidene-*trans*-dehydroandrosterones **5.** (See above-mentioned reference for further information [20].)

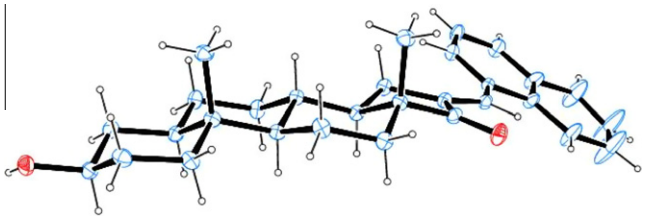


Fig. 1. ORTEP diagram of **2k.**

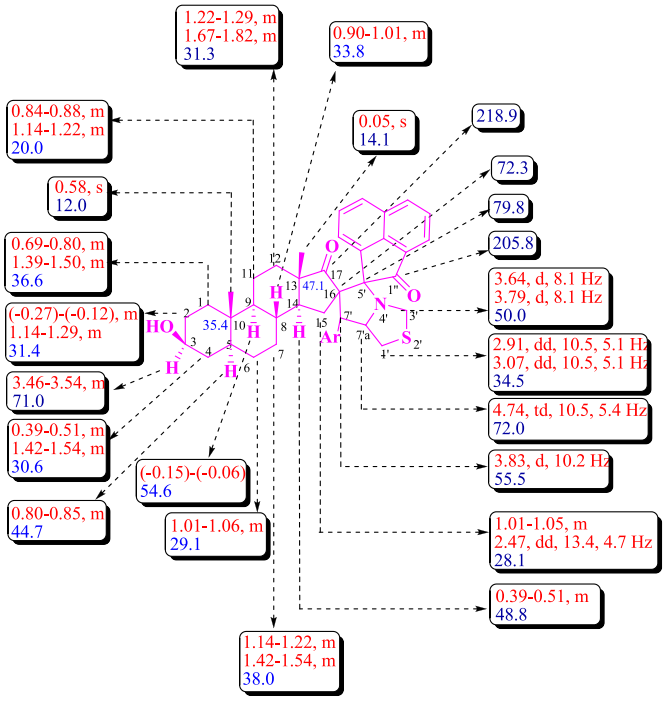


Fig. 2. ^{1}H and ^{13}C chemical shifts of **3b.**

as singlets at 1.02 and 0.86 ppm respectively whereas the steroidal ring protons appear as multiplets at 0.65–2.76 ppm. The structure of **2k** assigned from NMR spectroscopy was further confirmed from single crystal X-ray studies. The ORTEP diagram of **2k** [17] reveals (*E*)-configuration for the D-ring 16-exocyclic alkene (Fig. 1).

Initially, the 1,3-dipolar cycloaddition of azomethine ylides generated *in situ* from the reaction of 1,3-thiazolane-4-carboxylic acid and acenaphthylene-1,2-dione to (*E*)-16-arylmethylidene-*trans*-androsterones **2a–k** was investigated (Scheme 2). The reaction proceeded stereospecifically affording a single isomer of novel spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-(7′-aryl)-tetrahydro-1*H*-pyrrolo[1,2-*c*][1,3]thiazolo-*trans*-androsterones **3a–k** in excellent yields (75–91%). These cycloadditions were effected by refluxing an equimolar mixture of the reactants in methanol on a water-bath. After completion of the reaction as evident from the TLC, the mixture was poured into water to get the product as pale yellow solid. The excellent yield of **3** in conjunction with high atom economy (>91%) renders this protocol efficient and green (Scheme 2).

The structure of all the dispiro-*trans*-androsterones **3a–k** was elucidated with the help of ^{1}H, ^{13}C and two-dimensional NMR spectroscopy as illustrated for an example **3b**.

In the ^{1}H NMR spectrum of **3b**, a doublet at 3.83 ppm (J = 10.2 Hz) can be readily assigned to H-7′ on the basis of its multiplicity. The H-7′ shows a C,H-COSY correlation with a carbon signal at 55.5 ppm assigning it to 7′-C. Further, H-7′ has a H,H-COSY correlation with a triplet of doublets at 4.75 ppm (J = 10.5, 5.4 Hz), which can be assigned to H-7a′. The C,H-COSY correlation of H-7a′ assigns the carbon signal at 72.0 ppm to 7a′-C. It is evident from the H,H-COSY correlation of H-7a′ that the doublets of doublets at 2.91 and 3.07 ppm (J = 10.5, 5.1 Hz) accounting for 2 protons is due to 1′-CH_2 and from the C,H-COSY spectrum it is clear that 1′-CH_2 carbon appears at 34.5 ppm. The two doublets at 3.64 and 3.79 ppm with J = 8.1 Hz which can be assigned to 3′-CH_2 protons show (i) C,H-COSY correlation with a carbon signal at 50.0 ppm due to 3′-C and (ii) HMBC correlation with one of the spiro carbons 3′-C at 79.8 ppm thereby assigning the carbon signal at 72.3 to the other spiro carbon 6′-C. The H-7′ proton shows HMBC correlations with the C-17 carbonyl carbon at 218.9 ppm and methylene carbon at 28.1 ppm due to 15-C. The C,H-COSY correlation of the above carbon signal assigns the doublets of doublets at 2.47 ppm (J = 13.4, 4.7 Hz) and the multiplet at 1.01–1.05 ppm to the 15-CH_2 protons. The chemical shifts of the 15-CH_2 protons differ much by 1.44 ppm suggesting that one of the protons of 15-CH_2 may presumably lie in the shielding zone of the spiroacenaphthylen-1(2*H*)-one ring shifting it upfield and the other may be proximate to the carbonyl at C-17 shifting it downfield. The H,H-COSY correlation of 15-CH_2 protons disclose that the multiplet at 0.39–0.51 ppm is due to H-14 and from the C,H-COSY correlation of H-14, the signal at 48.8 ppm is assigned to 14-C. The protons of the two angular methyl groups at C-10 and C-13 appear as singlets at 0.58 and 0.05 ppm and the carbons appear at 12.0 and 14.1 ppm respectively. The distinct assignments of these two signals emerge from the fact that the singlet at 0.05 ppm shows a HMBC correlation with the carbonyl carbon at C-17, whereas the other singlet does not. Further, the C-13 angular methyl protons show HMBC correlations with a quaternary carbon at 47.1 ppm due to C-13 and a methylene carbon at 31.3 ppm which can be assigned to C-12. The C-10 angular methyl protons show HMBC correlations with a quaternary carbon at 35.4 ppm due to C-10 and a methylene carbon at 36.6 ppm due to C-1. The multiplet at 3.46–3.54 ppm is assigned to 3-CH proton on the basis of substitution. Further, the C,H-COSY correlation of this signal reveals that the carbon signal at 71.0 is due to C-3. Similarly, the ^{1}H and ^{13}C chemical shift of all the protons and carbons of **3b** were assigned unambiguously and are shown in Fig. 2. The selected H,H-COSY and HMBC correlations of **3b** are shown in Fig. 3. A more detailed discussion on the structural elucidation of **3b** is given in the supporting information.

The structure of **3** elucidated from NMR spectroscopy was further confirmed by the single crystal X-ray crystallographic studies.

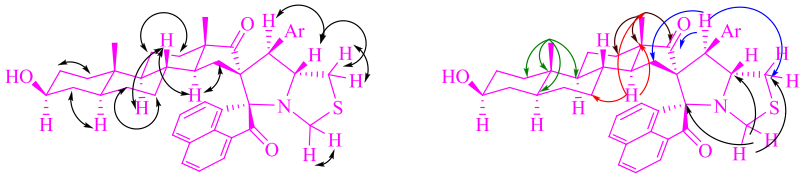


Fig. 3. Selected H,H-COSY and the HMBC correlations of **3b.**

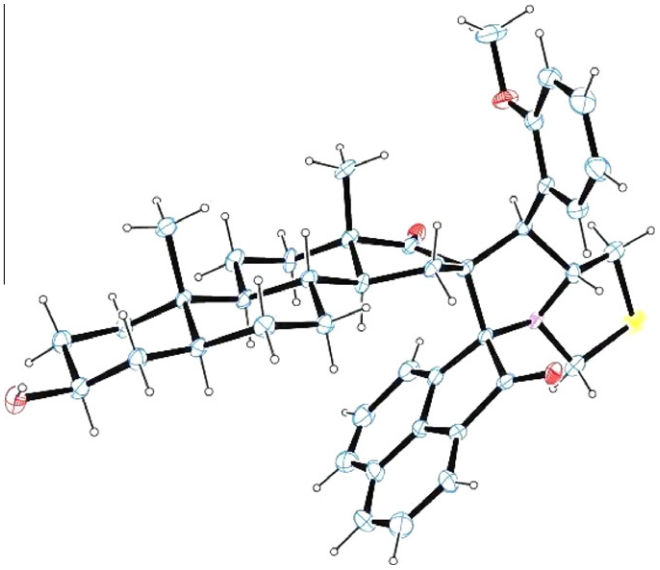


Fig. 4. ORTEP diagram of **3i.**

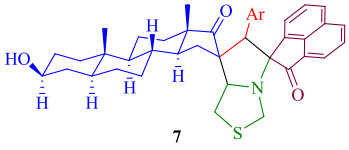
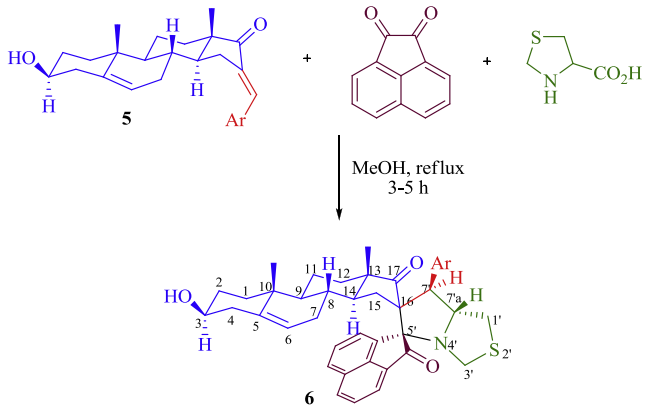


Fig. 5. The other regioisomer (not formed).

The ORTEP diagram of **3i** [17] shown in Fig. 4 discloses the absolute configuration of the newly formed chiral centers as 16-R, 5′-R, 7′-R, 7a′-R. Further, it is evident that H-7′ and H-7a′ are in *trans* relationship.

The cycloaddition of azomethine ylide to the dipolarophiles **2a–k** proceeds regioselectively as the electron rich carbon of the 1,3-dipole is added to the β-carbon, of the dipolarophiles **2** affording a single regioisomer **3**. These observations are in accord with the polarization of the C=C bond with a more electron-deficient β-carbon which could preferentially react with the electron-rich site of the approaching 1,3-dipole. The regiochemistry of the cycloadduct is also evident form ^{1}H NMR spectrum of the products. A doublet and a multiplet are observed in the range of 3.5–5.0 ppm, which are due to H-7′ and H-7a′ respectively. If the other regioisomer **7** was formed (Fig. 5), a singlet would have been expected for H-7′ instead of doublet.



Entry	Comp	Ar	Yield[a] (%)	mp (°C)
1	**6a**	C_6H_5	88	192–193
2	**6b**	*p*-ClC_6H_4	86	191–192
3	**6c**	*p*-BrC_6H_4	89	188–189
4	**6d**	*p*-FC_6H_4	80	180–181
5	**6e**	*p*-$CH_3C_6H_4$	85	185–186
6	**6f**	*p*-$CH_3OC_6H_4$	87	199–200
7	**6g**	*o*-ClC_6H_4	91	183–184
8	**6h**	*o*-$CH_3C_6H_4$	89	181–182
9	**6i**	*o*-$CH_3OC_6H_4$	80	178–179
10	**6j**	*m*-BrC_6H_4	82	203–204
11	**6k**	Naphthyl	92	188–189

[a]Isolated yields after flash filtration column

Scheme 4. Synthesis of dispiro-*trans*-dehydroandrosterones **6.**

Further, the facial selectivity involved in the above reaction leading to the formation of **3** is explicable from the fact that the azomethine ylide adds to the dipolarophile preferentially from the less hindered bottom side of the exocyclic C=C bond of **2**. The angular methyl group at 13th position of **2** presumably hinders the approach of the dipole from the top side (Fig. 6).

The 1,3-dipolar cycloaddition of azomethine ylide generated *in situ* from the reaction of acenaphthylene-1,2-dione and 1, 3-thiazolane-4-carboxylic acid to (*E*)-16-arylmethylidene-*trans*-dehydroandrosterones **5a–k** proceeds similar to (*E*)-16-arylmethylidene-*trans*-androsterones **2** affording novel *(16R, 5′R, 7′R,*

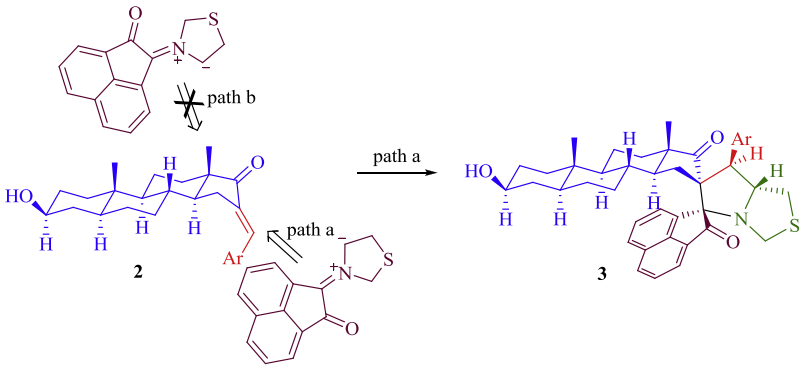


Fig. 6. Facial selectivity involved in the formation of **3.**

7a′R)-spiro[5′.2″]acenaphthylene-1″-one-spiro[16.6′]-(7′-aryl)-tetrahydro-1*H*-pyrrolo[1,2-*c*][1,3]thiazolo-*trans*-dehydroandrosterones **6a–k** in excellent yields (80–92%) stereospecifically (Scheme 4). The structure of **6** was elucidated with the help of one and 2D NMR spectroscopic data and the assignment of proton and carbon signals of **6** has also been done by straightforward considerations as done for **3**. As a representative case, the ^{1}H and ^{13}C chemical shifts of **6b** are shown in the supporting information. The absolute stereochemistry of the newly formed chiral centers of **6** was assigned in comparison with **3**.

In conclusion, a library of novel 16-spiro *trans*-androsterone/*trans*-dehydroandrosterone hybrid heterocycles **3a–k** and **6a–k** were synthesized in excellent yields stereospecifically through the 1,3-dipolar cycloaddition of azomethine ylides generated from the decarboxylative condensation of acenaphthylene-1,2-dione and 1,3-thiazolane-4-carboxylic acid to (*E*)-16-arylmethylidene-*trans*-androsterones **2a–k** and (*E*)-16-arylmethylidene-*trans*-dehydroandrosterones **5a–k** respectively. The cytotoxicity, AChE inhibition studies and anti-TB activity of these novel 16-spiro steroids **3** and **6** are currently underway.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.steroids.2012.12.017.

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[17] Crystallographic data (excluding structure factors) for compounds **2k** and **3i** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication numbers CCDC 907216 and 907215 respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223 762911 or e-mail: deposit@ccdc.cam.ac.uk].
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