Steroidal Heterocycles: Synthesis and Structure of Imidazo[2,1-*b*]-thiazolo-, Thiazolo[3,2-*a*]benzimidazolo-, and Thiazolo[3,2-*b*]-*s*-triazolo-derivatives

By **Joginder S. Bajwa** and **Peter J. Sykes,*** Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ

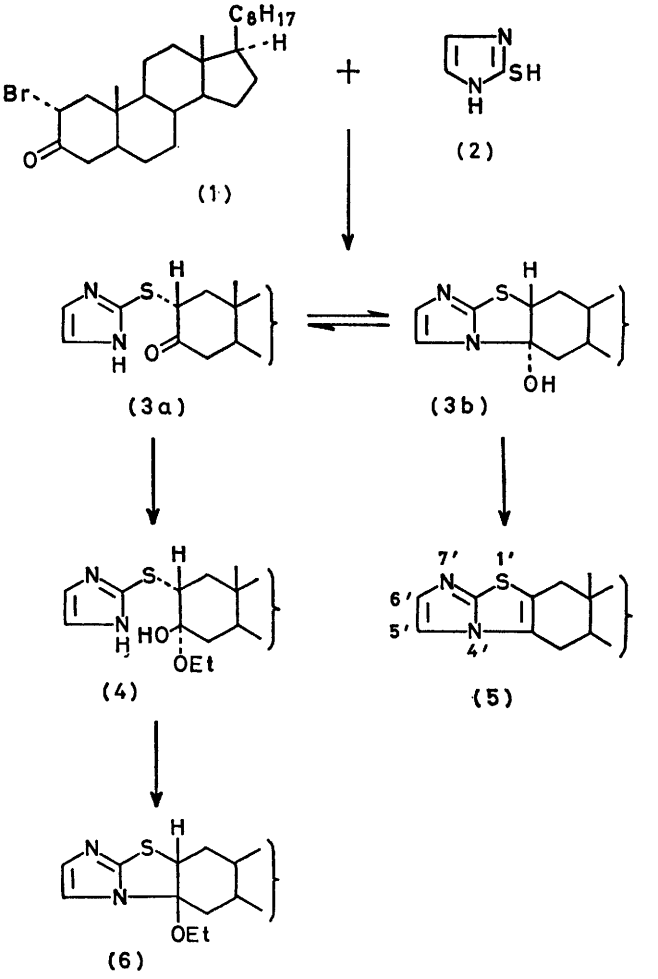
The condensation of 2α-bromo-5α-cholestan-3-one (1) with 2-mercaptoimidazole (2) in refluxing ethanol gave 5α-cholest-2-eno[2,3-*b*]-(imidazo[2,1-*b*]thiazole) (5) and 3β-ethoxy-2'β,3'-dihydro-5α-cholestano[2,3-*b*]-(imidazo[2,1-*b*]thiazole) (6), whereas the reaction of 2-mercaptoimidazole (2) with 16α-bromo-3-methoxyestra-1,3,5(10)-trien-17-one (7) gave the uncyclised product 16α-(imidazol-2-ylthio)-3-methoxyestra-1,3,5(10)-trien-17-one (8). Under analogous reaction conditions, the condensation of 2-mercaptoimidazole (2), 2-mercaptobenzimidazole (12), 3-mercapto-1,2,4-triazole (35), and their derivatives with 2α-bromo-3-oxo-steroids gave the expected cyclised products. However, from the condensation reactions between 3-mercapto-1,2,4-triazoles (35) and (36) with the 16α-bromo-17-oxo steroid (7) only 17β-ethoxy-3-methoxy-5',6'-dihydro[16,17-*e*]-(thiazolo-[3,2-*b*]-(*s*-triazole) (44) and its 2'-methyl derivative (45) were isolated. The structures of all the condensation products were determined with the help of i.r., ^{1}H n.m.r., and ^{13}C n.m.r. spectroscopy.

As a part of our studies directed towards the development of new aza-steroids [1] of biological interest containing a bridgehead nitrogen atom, we report the results of the condensation reactions taking place between some mercapto-azoles and various steroidal α-bromo-ketones.

The reaction of 2α-bromo-5α-cholestan-3-one (1) with 2-mercaptoimidazole (2) in refluxing ethanol gave two products (5) and (6) in 26% and 35% yields respectively. The structures of these products are assigned from the evidence below.

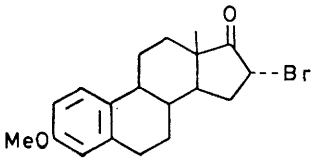
Since the i.r. spectrum of the first product (m.p. 205—207 °C) shows no carbonyl or hydroxy-absorption, the product was assigned the expected structure, 5α-cholest-2-eno[2,3-*b*]-(imidazo[2,1-*b*]thiazole) (5), consistent with the molecular formula $C_{30}H_{46}N_2S$ obtained by mass spectrometry and elemental analysis. In the ^{1}H n.m.r. spectrum, both the protons 5'-H and 6'-H were found to have the same chemical shift, δ 7.25. The infrared spectrum of the second product (m.p. 150—151 °C) also indicates the absence of any hydroxy or carbonyl group and, on the basis of the molecular formula $C_{32}H_{52}N_2OS$ and the i.r. spectra, this product was assigned structure (6). This structure is supported by the ^{1}H n.m.r. spectrum which exhibits a singlet at δ 7.05 (5'-H and 6'-H), a doublet of doublets at δ 4.02 (2H), and a quartet at δ 3.55 (3β-OCH_2CH$_3$). The triplet corresponding to the methyl protons of the ethoxy-group overlaps with the signals of the angular and side-chain methyl groups of the steroid.

It is known [2] from the general reactions of α-bromo-ketones with 2-mercaptoimidazoles that the initial product from the reaction of the steroid (1) with this reagent (2) will first be the *S*-alkylated product which may exist either in the acyclic (3a) or cyclic form (3b). Dehydration of the intermediate (3b) leads to the fully aromatic system (5). However, if the intermediate (3a) reacts first with ethanol present in the reaction mixture, then the hemi-acetal (4) results. Ring closure of the latter finally yields the cyclised product (6) where the probable stereochemistry of the ethoxy-group precludes its elimination.



The reaction of 2-mercaptoimidazole (2) with 16α-bromo-3-methoxyestra-1,3,5(10)-trien-17-one (7) under

similar conditions affords only 16α-(imidazolyl-2-thio)-3-methoxyestra-1,3,5(10)-trien-17-one (8). Structure (8) is confirmed by the i.r. spectrum which exhibits absorptions at 1 720 cm^{-1} (C=O) and 3 300 cm^{-1} (NH) and the



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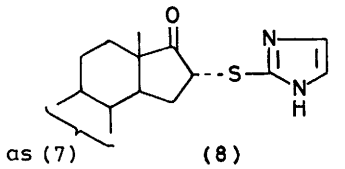


as (7) (8)

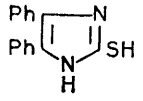
^1H n.m.r. spectrum which exhibits two signals at δ 7.0 (4′-H and 5′-H) and 7.70 (NH).

Under analogous reaction conditions, the condensation of 2α-bromo-5α-cholestan-3-one (1) with 2-mercapto-4,5-diphenylimidazole (9), 2-mercapto-4,5-dihydroimidazole (10), and 2-mercaptobenzimidazole (12) gave the fused compounds (16), (18), and (22) respectively.

Mohan and Pujari [3] have assigned structure (21), on the basis of ^1H n.m.r. spectroscopy, for the product obtained by the reaction of 2-mercapto-5-methoxybenzimidazole (14) and chloroacetone. Since the methyl group [in compound (13)] and the methoxy-group [in compound (14)] are both electron-donating groups, the product obtained by the condensation of the steroid (1) with 2-mercapto-5-methylbenzimidazole (13) is by analogy assigned structure (23).

Similarly, the condensation reactions between the α-bromo-ketone (15) and the various mercapto-azoles (9), (10), (12), and (13) furnished the cyclised products (17), (19), (24), and (25) respectively; likewise the reaction of the αβ-unsaturated bromo-ketone (26) with the mercaptoazoles (2), (10), (12), and (13) gave the expected condensation products (27—30) respectively.

The condensation of the steroid (1) with 2-mercapto-4-methyl-4,5-dihydroimidazole (11) in refluxing ethanol gave a product in 42% yield. To establish the structure of this product, the reaction of 2-mercapto-4-methyl-4,5-dihydroimidazole with chloroacetone, which can theoretically give two products (32) and (33), was reinvestigated.[4] ^{13}C N.m.r. spectroscopy shows that the product obtained by the above reaction has structure (32). The ^{13}C-chemical shifts of the various carbons in the compounds (31) and (32) are given in the Table. Compound (31) was prepared by the reaction of chloro-



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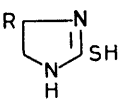
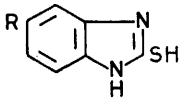
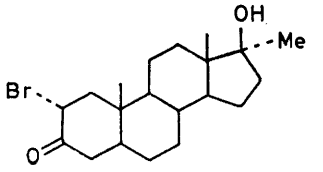


(10) R = H
(11) R = Me



(12) R = H
(13) R = Me
(14) R = OMe



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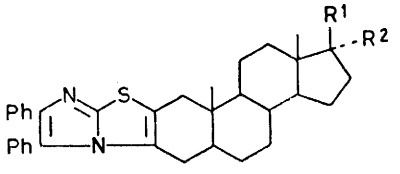
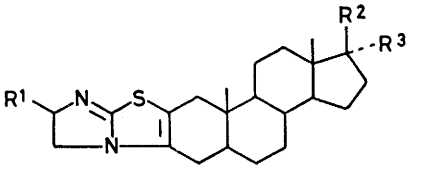
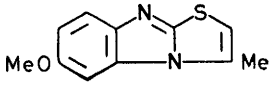


(16) R^1 = C_8H_{17}, R^2 = H
(17) R^1 = OH, R^2 = Me



(18) R^1 = H, R^2 = C_8H_{17}, R^3 = H
(19) R^1 = H, R^2 = OH, R^3 = Me
(20) R^1 = Me, R^2 = OH, R^3 = Me



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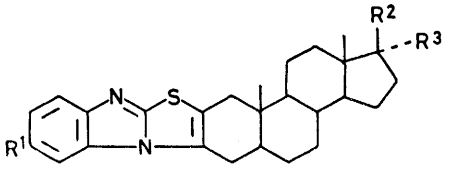


(22) R^1 = H, R^2 = C_8H_{17}, R^3 = H
(23) R^1 = Me, R^2 = C_8H_{17}, R^3 = H
(24) R^1 = H, R^2 = OH, R^3 = Me
(25) R^1 = Me, R^2 = OH, R^3 = Me

acetone with 2-mercapto-4,5-dihydroimidazole (10) with chloroacetone.

In the ^{13}C n.m.r. spin-coupled spectrum of the compound (31), carbons 3 and 7a are easily distinguished from the other carbons as they remain singlets. Since the bridgehead carbon is expected to have the largest relaxation time (lowest intensity peak), the downfield signal at 168.06 p.p.m. was assigned to 7a-C, the other downfield signal, at 130.76 p.p.m., being therefore assigned to 3-C. The signal at 92.79 p.p.m. was attributed to 2-C without ambiguity as 2-C appears as a doublet in the spin-coupled spectrum in contrast to 5-C and 6-C which appear as triplets. Out of the remaining three resonances, the low-field signal (58.84 p.p.m.) was assigned to 6-C whilst that at high field (44.07 p.p.m.) was assigned to 5-C by analogy with the observation [5,6] that in nitrogen heterocyclic compounds, the carbon atoms bonded to ring nitrogen atoms are deshielded and occur further downfield compared with those bonded to bridgehead nitrogen atoms.

^{13}C Chemical shifts (p.p.m.) of 5,6-dihydroimidazo[2,1-b]thiazoles

Compound	2-C	3-C	5-C	6-C	7a-C	3-CH_3	5-CH_3
(31)	92.79	130.76	44.07	58.84	168.06	12.25	
(32)	94.13	132.06	52.33	68.22	168.31	13.78	22.44

In the ^{13}C n.m.r. spectrum of the compound (32) the chemical shifts of 2-C, 3-C, and 7a-C are easily assigned by comparison with compound (31). It is known [7] that replacement of a proton by a methyl group on an sp^3 carbon causes the latter to become more deshielded by 6—10 p.p.m. Consequently the shift from 58.84 p.p.m. in compound (31) to 68.22 p.p.m. in its 6-methyl derivative (32) identifies this signal as arising from 6-C. However, it is noted that the chemical shift of 5-C is also shifted downfield by 8.26 p.p.m. If this compound, however, had possessed structure (33), carbons 5-C and 6-C would have had chemical shifts of 68.22 and 52.33 p.p.m. respectively. This possibility is ruled out since by substituting a hydrogen at 5-C in structure (31) by a methyl group, the chemical shift of 5-C could not be expected to increase by 24.15 p.p.m. nor could the chemical shift of 6-C decrease by 6.51 p.p.m.

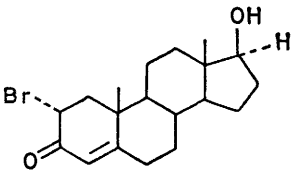
Further confirmation of structure (32) is based upon an analogy with the work of Kochergin and Krasovskii [8] on the synthesis of 3-methyl-6-phenylimidazo[2,1-*b*]-thiazole (34) in which the phenyl group at position 6 was established by an unambiguous synthesis.

By analogy with structure (32), the product obtained by the condensation of compounds (11) and (15) is assigned structure (20). In the ^1H n.m.r. spectrum, the multiplet at δ 4.05 was assigned to 6′-H, the two multiplets at δ 3.18 and 3.80 were assigned to two protons at 5′-C, and the doublet at δ 1.35 was attributed to 6′-methyl protons.

The reaction of 3-mercapto-1,2,4-triazole (35) with the α-bromo-ketone (15) can theoretically lead to either of the two products (37) and (38) or both. However, when this reaction was carried out in refluxing ethanol, only one product was isolated, which is shown to have structure (38) on the basis of the following evidence.

The reaction of 3-mercapto-1,2,4-triazole (35) with chloroacetone has been shown [9] to give 5-methylthiazolo[3,2-*b*]-*s*-triazole (41), and the structure of this compound was assigned without ambiguity by Tamura and his co-workers,[10] who prepared it in 90% yield by dehydrocyclisation of 3-amino-2-formamido-4-methylthiazolium mesitylene-sulphonate with polyphosphoric acid. The analogous isomer, 5-methylthiazolo[2,3-*c*]-*s*-triazole (42), has been obtained by the reaction of 2-hydrazino-4-methylthiazole with formic acid.[9] Further, the two isomeric compounds are distinguished by ^1H n.m.r. spectroscopy. The triazole 3-H in (42) is deshielded and occurs at a lower field (δ 8.60) [9] than the triazole 2-H in (41) which occurs at δ 8.13.[10]

Thus, by analogy with the formation of the thiazalotriazole (41) from the reaction of chloroacetone with the thiol (35), the product obtained by the condensation of the 2α-bromo-3-oxo-steroid (15) with 3-mercapto-1,2,4-triazole (35) is assigned structure (38). This



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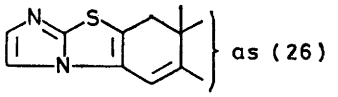

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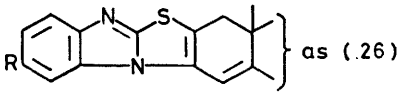
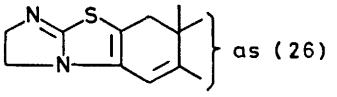


(29) R = H
(30) R = Me



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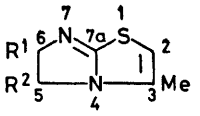
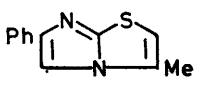


(31) $R^1 = R^2 = H$
(32) R^1 = Me, R^2 = H
(33) R^1 = H, R^2 = Me

structure is supported by the ^1H n.m.r. spectrum in which the chemical shift (δ 8.07) of the triazole proton correlates well with the chemical shift of 2-H (δ 8.13) in (41).

Similarly, the condensation of 2α-bromo-5α-cholestan-



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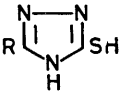
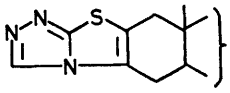
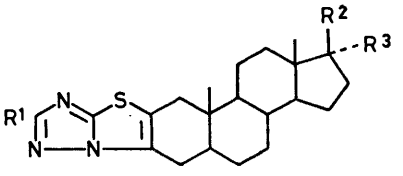


(35) R = H
(36) R = Me



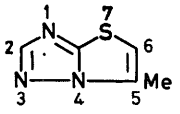
as (38)

(37)



(38) R^1 = H, R^2 = OH, R^3 = Me
(39) R^1 = H, R^2 = C_8H_{17}, R^3 = H
(40) R^1 = Me, R^2 = C_8H_{17}, R^3 = H

3-one (1) with 3-mercapto-1,2,4-triazole (35) and 3-mercapto-5-methyl-1,2,4-triazole (36) gave the ring A fused compounds (39) and (40) respectively. However, under analogous conditions, the reaction of the estratrienone (7) with the thiols (35) and (36) gave only the ring D fused products (43) and (44) respectively. The



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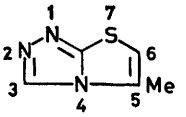

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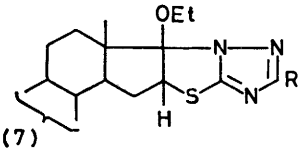

as (7)

(43) R = H
(44) R = Me

structure of the products were identified by ^1H n.m.r. spectroscopy.

EXPERIMENTAL

M.p.s were determined on a Gallenkamp apparatus. I.r. spectra were recorded in bromoform on a Perkin-Elmer 157G spectrometer. ^1H N.m.r. spectra were recorded in deuteriated chloroform using tetramethylsilane as an internal standard on a Nuclear Magnetic Resonance Ltd. EM 360 (60 MHz) or a Varian HA 100 (100 MHz) spectrometer. Mass spectrometry was carried out on an A.E.I. MS 902 instrument. ^{13}C N.m.r. spectra were obtained in deuteriated chloroform solutions on a Varian CFT-20 n.m.r. spectrometer operating at 20—80 MHz in the Fourier Transform mode at a probe temperature of 30 °C.

All the starting steroidal α-bromo-ketones were prepared by the known literature routes.

General Procedure for the Condensation Reactions.—A solution of the steroidal α-bromo ketone (1×10^{-5} mol) and mercaptoazole (1.5×10^{-5} mol) in absolute alcohol (40 ml) was refluxed for 24 h. The reaction mixture was concentrated under *vacuo*, diluted with water and neutralised with 28% ammonium hydroxide. The solid formed was filtered off, washed with water, and dried. The crude product was either directly recrystallised from a suitable solvent or chromatographed over alumina (40 g, activity II) before recrystallisation.

5α-Cholest-2-eno[2,3-b]-(*imidazo*[2,1-b]*thiazole*) (5) *and* 3β-*Ethoxy-2'β,3'-dihydro-5α-cholestano*[2,3-b]-(*imidazo*[2,1-b]*thiazole*) (6).—Chromatography on alumina (eluant ethyl acetate) of the crude product followed by recrystallisation of the eluate from ethanol gave (6) as white shining *plates* (35%), m.p. 150—151 °C; $\nu_{max.}$ 1 495, 1 455, 1 365, and 1 065 cm^{-1}; δ 0.62, 0.80 and 0.90 (methyl groups), 3.55 (q, 2 H, 3β-OC$H_2$$CH_3$), 4.02 (dd, 1 H, 2'β-H), and 7.05 (s, 2 H, 5'-H and 6'-H) (Found: C, 74.75; H, 10.25; N, 5.3%; M^+ — S, 480.406 916. $C_{32}H_{52}N_2OS$ requires C, 74.95; H, 10.25; N, 5.45%; M — S, 480.407 944).

Further elution of the column with chloroform followed by recrystallisation of the eluate from ethanol gave (5) as white *crystals* (26%), m.p. 205—207 °C; $\nu_{max.}$ 1 465, 1 440, and 1 380 cm^{-1}; δ 0.70, 0.80, 0.87 and 0.92 (methyl groups), and 7.25 (s, 2 H, 5'-H and 6'-H) (Found: C, 76.8; H, 10.0; N, 5.8%; M^+, 466.338 027. $C_{30}H_{46}N_2S$ requires C, 77.2; H, 9.95; N, 6.0%; M^+, 466.338 155).

16α-(Imidazol-2-ylthio)-3-methoxyestra-1,3,5(10)-trien-17-one (8).—The crude product was recrystallised from ethanol to give white *crystals* (47%), m.p. 150—153 °C; $\nu_{max.}$ 3 300 (NH), 1 720 (C=O), 1 605, 1 575, 1 520, 1 500, 1 460, and 1 380 cm^{-1}; δ 0.87 (s, 3 H, 18-CH_3), 3.75 (s, 3 H, 3-OCH_3), 6.60—7.20 (m, 3 H, 1-H, 2-H, and 4-H), 7.05 (s, 2 H, 4'-H and 5'-H), and 7.70 (br s, 1 H, N*H*) (Found: M^+, 382.172 352. $C_{22}H_{26}N_2O_2S$ requires M^+, 382.171 490).

5',6'-Diphenyl-5α-cholest-2-eno[2,3-b]-(*imidazo*[2,1-b]-*thiazole*) (16).—Chromatography of the crude product on alumina followed by recrystallisation of the eluate from acetone gave white *crystals* (45%), m.p. 237—239 °C; $\nu_{max.}$ 1 600, 1 500, 1 465, 1 440, and 1 380 cm^{-1}, δ 0.64, 0.79, 0.82, and 0.88 (methyl groups), and 7.06—7.64 (benzene ring protons) (Found: C, 81.45; H, 8.6; N, 4.45%; M^+, 618.399 477. $C_{42}H_{54}N_2S$ requires C, 81.5; H, 8.8; N, 4.55%; M^+, 618.400 752).

17β-Hydroxy-17α-methyl-5',6'-diphenyl-5α-androst-2-eno[2,3-b]-(*imidazo*[2,1-b]*thiazole*) (17) was recrystallised from benzene to give white *crystals* (62%), m.p. 255—257 °C, $\nu_{max.}$ 3 590 (OH), 1 590, 1 495, 1 465, 1 455, 1 435, and 1 375 cm^{-1}, δ 0.85 (s, 6 H, 18-CH_3 and 19-CH_3), 1.20 (s, 3 H, 17-CH_3), and 7.05—7.45 (m, 10 H, benzene ring protons) (Found: C, 78.55; H, 7.4; N, 5.15%; M^+, 536.284 862. $C_{35}H_{40}N_2OS$ requires C, 78.35; H, 7.5; N, 5.2%; M^+, 536.286 121).

5',6'-Dihydro-5α-cholest-2-eno[2,3-b]-(*imidazo*[2,1-b]*thi-*

azole) (18).—Chromatography on alumina (eluant chloroform) followed by recrystallisation of the eluate from ethanol gave fine brown *crystals* (41%), m.p. 211—213 °C, $\nu_{max.}$ 1 640, 1 560, 1 440—1 460, 1 400, and 1 380 cm^{-1}, δ 0.66, 0.80, and 0.87 (methyl groups), and 3.63 and 4.12 (each s, 4 H, 5′-H and 6′-H) (Found: C, 76.65; H, 10.35; N, 5.8%; M^+, 468.353 876 4. $C_{30}H_{48}N_2S$ requires C, 76.85; H, 10.3; N, 6.0%; M^+, 468.353 804).

17β-*Hydroxy*-17α-*methyl*-5′,6′-*dihydro*-5α-*androst*-2-*eno*[2,3-b]-(*imidazo*[2,1-b]*thiazole*) (19).—Recrystallisation from benzene gave white *crystals* (38%), m.p. 263—265 °C, $\nu_{max.}$ 3 590 (OH), 1 645, 1 565, 1 445, and 1 400 cm^{-1}, δ 0.90 (s, 6 H, 18-CH_3 and 19-CH_3), 1.25 (s, 3 H, 17-CH_3), and 3.65—4.25 (m, 4 H, 5′-H and 6′-H) (Found: C, 71.3; H, 8.8; N, 7.0%; M^+, 386.238 205. $C_{23}H_{34}N_2OS$ requires C, 71.5; H, 8.9; N, 7.25%; M^+, 386.239 173).

17β-*Hydroxy*-6′,17α-*dimethyl*-5′,6′-*dihydro*-5α-*androst*-2-*eno*[2,3-b]-(*imidazo*[2,1-b]*thiazole*) (20).—Recrystallisation from ethanol gave white *crystals* (42%), m.p. 220—222 °C (decomp.), $\nu_{max.}$ 3 570 (OH), 1 635, 1 555, 1 435, 1 395, and 1 365 cm^{-1}, δ 0.85 (s, 6 H, 18-CH_3 and 19-CH_3), 1.20 (s, 3 H, 17-CH_3), 1.35 (d, J 6 Hz, 3 H, 6′-CH_3), 3.18 and 3.80 (each m, 2 H, 5′-H), and 4.05 (m, 1 H, 6′-H) (Found: C, 71.85; H, 9.55; N, 7.1%; M^+, 400.252 081. $C_{24}H_{36}N_2OS$ requires C, 71.95; H, 9.55; N, 7.0%; M^+, 400.252 821).

5α-*Cholest*-2-*eno*[2,3-b]-(*thiazolo*[3,2-a]*benzimidazole*) (22).—Chromatography on alumina (eluant chloroform) followed by recrystallisation of the eluate from chloroform–ether gave a white *solid* (47%), m.p. 250—252 °C, $\nu_{max.}$ 1 480, 1 465, and 1 380 cm^{-1}, δ 0.58, 0.68, 0.82, and 0.90 (methyl groups) and 7.14—7.78 (benzene ring protons) (Found: C, 78.7; H, 9.3; N, 5.45%; M^+, 516.357 110. $C_{34}H_{48}N_2S$ requires C, 79.0; H, 9.35; N, 5.40%; M^+, 516.353 804).

6′-*Methyl*-5α-*cholest*-2-*eno*[2,3-b]-(*thiazolo*[3,2-a]*benzimidazole*) (23).—Chromatography on alumina (eluant ethyl acetate) followed by recrystallisation from ethanol gave white *crystals* (25%), m.p. 227—229 °C, $\nu_{max.}$ 1 480, 1 460, 1 380, and 1 270 cm^{-1}, δ 0.66, 0.82, and 0.90 (methyl groups), 2.45 (d, 3 H, 6′-CH_3), and 6.94 and 7.48 (m, 3 H, 5′-H, 7′-H and 8′-H) (Found: C, 79.05; H, 9.35; N, 5.2%; M^+, 530.370 136. $C_{35}H_{50}N_2S$ requires C, 79.2; H, 9.5; N, 5.3%; M^+, 530.369 453).

17β-*Hydroxy*-17α-*methyl*-5α-*androst*-2-*eno*[2,3-b]-(*thiazolo*[3,2-a]*benzimidiazole*) (24).—Recrystallisation from ethanol gave white *crystals* (52%), m.p. 224—226 °C, $\nu_{max.}$ 3 590 (OH), 1 595, 1 520, 1 480 and 740 cm^{-1}, δ 0.90 (s, 3 H, 18-CH_3), 0.94 (s, 3 H, 19-CH_3), 1.24 (s, 3 H, 17-CH_3), and 7.42—7.98 (m, 4 H, benzene ring protons) (Found: C, 74.45; H, 7.8; N, 6.25%; M^+, 434.238 916. $C_{27}H_{34}N_2OS$ requires C, 74.65; H, 7.9; N, 6.45%; M^+, 434.239 173).

17β-*Hydroxy*-6′,17α-*dimethyl*-5α-*androst*-2-*eno*[2,3-b]-(*thiazolo*[3,2-a]*benzimidazole*) (25).—Recrystallisation from benzene gave white *crystals* (49%), m.p. 158—160 °C, $\nu_{max.}$ 3 570 (OH), 1 625, 1 480, 1 460, 1 420, 1 375, and 1 365 cm^{-1}, δ 0.90 (s, 6 H, 18-CH_3 and 19-CH_3), 1.25 (s, 3 H, 17-CH_3), 2.45 (s, 3 H, 6′-CH_3), and 6.85—7.50 (m, 3 H, benzene ring protons) (Found: C, 74.8; H, 7.85; N, 5.95%; M^+, 448.254 856. $C_{28}H_{36}N_2OS$ requires C, 75.0; H, 8.1; N, 6.25%; M^+, 448.254 823).

17β-*Hydroxyandrosta*-2,4-*dieno*[2,3-b]-(*imidazo*[2,1-b]-*thiazole*) (27).—Recrystallisation from acetone gave yellow *crystals* (18%), m.p. 158—160 °C, δ 0.80 (s, 3 H, 18-CH_3), 1.10 (s, 3 H, 19-CH_3), 3.63 (t, 1 H, 17-H), 5.97 (s, 1 H, 4-H), and 7.20 and 7.30 (each s, 2 H, 5′-H and 6′-H) (Found: C, 71.55; H, 7.6; N, 7.8%; M^+, 368.189 773. $C_{22}H_{28}N_2OS$ requires C, 71.7; H, 7.65; N, 7.6%; M^+, 368.192 225).

17β-*Hydroxy*-5′,6′-*dihydroandrosta*-2,4-*dieno*[2,3-b]-(*imidazo*[2,1-b]*thiazole*) (28).—Recrystallisation from ethanol gave a yellow *solid* (15%), m.p. 255—257 °C, $\nu_{max.}$ 3 560 (OH), 1 620, 1 580, 1 550, 1 440, and 1 420 cm^{-1}, δ 0.80 (s, 3 H, 18-CH_3), 1.08 (s, 3 H, 19-CH_3), 3.70 (m, 3 H, 6′-H and 17-H), 4.15 (m, 2 H, 5′-H), and 5.55 (s, 1 H, 4-H) (Found: C, 71.6; H, 7.95; N, 7.45%; M^+ —S, 338.234 517. $C_{22}H_{30}N_2OS$ requires C, 71.3; H, 8.15; N, 7.55%; M^+ — S, 338.235 801).

17β-*Hydroxyandrosta*-2,4-*dieno*[2,3-b]-(*thiazolo*[3,2-a]-*benzimidazole*) (29).—Recrystallisation from ethanol gave a brown *solid* (27%), m.p. 275—279 °C; $\nu_{max.}$ 3 560 (OH), 1 615, 1 470, 1 460, and 1 450 cm^{-1}; δ 0.85 (s, 3 H, 18-CH_3), 1.15 (s, 3 H, 19-CH_3), 3.73 (t, 1 H, 17-H), 6.54 (s, 1 H, 4-H), and 7.20—7.90 (m, 4 H, benzene ring protons) (Found: C, 74.4; H, 7.2; N, 6.55%; M^+, 418 206 584, $C_{26}H_{30}N_2OS$ requires C, 74.6; H, 7.25; N, 6.7%; $M^{+\bullet}$ 418.207 154).

17β-*Hydroxy*-6′-*methylandrosta*-2,4-*dieno*[2,3-b]-(*thiazolo*-[3,2-a]*benzimidazole*) (30).—Recrystallisation from acetone gave a white *solid* (22%), m.p. 245—247 °C, $\nu_{max.}$ 3 560 (OH), 1 610, 1 455, and 1 360 cm^{-1}, δ 0.80 (s, 3 H, 18-CH_3), 1.10 (s, 3 H, 19-CH_3), 2.50 (s, 3 H, 6′-CH_3), 3.68 (t, 1 H, 17-H), 6.45 (s, 1 H, 4-H), and 6.98—7.75 (m, 3 H, benzene ring protons) (Found: C, 74.75; H, 7.4; N, 6.3%; M^+ —S, 400.247 712. $C_{27}H_{32}N_2OS$ requires C, 75.0; H, 7.45; N, 6.5%; M^+ — S, 400.251 451).

17β-*Hydroxy*-17α-*methyl*-5α-*androst*-2-*eno*[2,3-e]-(*thiazolo*-[3,2-b]-s-*triazole*) (38).—Chromatography on alumina (eluant chloroform) followed by recrystallisation of the eluate from ethanol gave white *crystals* (23%), m.p. 115—118 °C, $\nu_{max.}$ 3 590 (OH), 1 465, 1 445, 1 420, 1 355, and 1 240 cm^{-1}, δ 0.90 (s, 3 H, 18-CH_3), 0.95 (s, 3 H, 19-CH_3), 1.24 (s, 3 H, 17-CH_3), and 8.07 (s, 1 H, 2′-H) (Found: C, 68.25; H, 7.95; N, 10.65%; M^+, 385.215 538. $C_{22}H_{31}N_3OS$ requires C, 68.55; H, 8.1; N, 11.0%; M^+, 385.218 773).

5α-*Cholest*-2-*eno*[2,3-e]-(*thiazolo*[3,2-b]-s-*triazole*) (39).—Chromatography on alumina (eluant chloroform) followed by recrystallisation of the eluate from ethanol gave white *needles* (32%), m.p. 188—190 °C, $\nu_{max.}$ 1 465, 1 440, 1 420, 1 380, and 1 355 cm^{-1}, δ 0.69, 0.83 and 0.89 (methyl groups), and 8.02 (s, 1 H, 2′-H) (Found: C, 74.3; H, 9.65; N, 8.7%; M^+, 467.333 948. $C_{29}H_{45}N_3S$ requires C, 74.45; H, 9.7; N, 9.0%; M^+, 467.333 404).

2′-*Methyl*-5α-*cholest*-2-*eno* [2,3-e]-(*thiazolo*[3,2-b]-s-*triazole*) (40).—Chromatography on alumina (eluant chloroform) followed by recrystallisation of the eluate from methanol gave a white *solid* (37%), m.p. 117—120 °C, $\nu_{max.}$ 1 470, 1 440, and 1 380 cm^{-1}, δ 0.67, 0.82, 0.84 and 0.90 (methyl groups), and 2.48 (s, 3 H, 2′-CH_3) (Found: C, 74.55; H, 9.8; N, 8.4%; M^+, 481.348 292. $C_{30}H_{47}N_3S$ requires C, 74.8; H, 9.85; N, 8.75%; M^+, 481.349 053).

17β-*Ethoxy*-3-*methoxy*-16β,17-*dihydroestra*-1,3,5(10)-*trieno*[16,17-e]-(*thiazolo*[3,2-b]-s-*triazole*) (43).—Chromatography on alumina (eluant ethyl acetate) followed by recrystallisation of the eluate from methanol gave white *crystals* (50%), m.p. 195—197 °C, $\nu_{max.}$ 1 605, 1 570, 1 495, 1 475, 1 450, 1 420, 1 380, and 1 365 cm^{-1}, δ 0.52 (s, 3 H, 18-CH_3), 1.40 (t, 3 H, 17β-OCH_2CH_3), 3.12 (q, 2 H, 17β-OCH_2CH_3), 3.72 (s, 3 H, 3-OCH_3), 4.50 (t, 1 H, 16β-H), 6.60—7.20 (m, 3 H, 1-H, 2-H and 4-H), and 7.90 (s, 1 H, 2′-H) (Found: C, 67.0; H, 7.05; N, 10.0%; M^+, 411.

$C_{23}H_{29}N_3O_2S$ requires C, 67.15; H, 7.1; N, 10.2%; *M*, 411).

17β-*Ethoxy*-3-*methoxy*-2′-*methyl*-16β,17-*dihydroestra*-1,3,5(10)-*trieno*[16,17-e]-(*thiazolo*[3,2-b]-s-*triazole*) (44).—Chromatography on alumina (eluant ethyl acetate) followed by recrystallisation of the eluate from methanol gave white *crystals* (49%), m.p. 193—195 °C, $\nu_{max.}$ 1 605, 1 570, 1 500, 1 430, 1 380, and 1 370 cm^{-1}, δ 0.60 (s, 3 H, 18-CH_3), 1.23 (t, 3 H, 17β-OCH_2CH_3), 2.40 (s, 3 H, 2′-CH_3), 3.30 (q, 2 H, 17β-OCH_2CH_3), 3.75 (s, 3 H, 3-OCH_3), 4.50 (t, 1 H, 16β-H), and 6.65—7.30 (m, 3 H, 1-H, 2-H, and 4-H) (Found: C, 67.55; H, 7.3; N, 7.8%; M^+, 425.214 102. $C_{24}H_{31}N_3O_2S$ requires C, 67.75; H, 7.35; N, 9.9%; M^+, 425.213 687).

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