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1. CHEMISTRY

1. Chemical and pharmacological studies on steroidal saponins isolated from *Trigonella foenum graceum*

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Five new steroidal saponins named as B, C, D, E and G have been isolated from an ethanolic extract of leaves of *Trigonella foenum graceum*. Three of these saponins have been found to possess diosgenin as aglycone and different sugars in different molar ratio. Some pharmacological activities of the saponins B, C, D and the mixture of all five saponins (named as A) were assessed. Substances A and D produced a marked increase in rat blood pressure at 1 mg dose while B and C did not produce any significant effect at this dose. However, all the compounds produced cardiotonic activity when tested using frog's heart perfusion *in situ*.

2. A novel approach for the total synthesis of 12-thiaequilenin and its 3-deoxy analogue

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This communication constitutes the very first report on a new approach towards the total synthesis of the hitherto unknown 12-thiasteroids mentioned above. The starting materials, 6-methoxy-1-mercaptomethylnaphthalene (**I**) and 1-mercaptomethylnaphthalene (**II**) are converted into the corresponding lead mercaptides (**III** & **IV**) in high yields. These lead salts (**III** & **IV**) on treatment with *N*-bromosuccinimide (NBS) afforded *N*-(6-methoxy-1-mercaptomethylnaphthyl) succinimide and *N*-(1-mercaptomethylnaphthyl) succinimide (**V** & **VI**) which on treatment with 2-methyl-1,3-cyclopentanedione gave the anticipated 3-methoxy-12-thia-8,14-seco-1,3,5(**10**),6,8-estrapentaene-14,17-dione (**VII**) and 12-thia-8,14-seco-1,3,5(**10**),6,8-estrapentaene-14,17-dione (**VIII**) in 70% yield. Cyclodehydration of **VII** & **VIII** to furnish the above mentioned 12-thiasteroids is in progress.

3. 7a-Aza-B-homo(7a,7-*d*)tetrazole analogues of progesterone and testosterone

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We have synthesised 7a-aza-B-homo[7a,7-*d*]tetrazole analogues of progesterone and testosterone, which are worthy of biological testing. (25R)-7a-Aza-B-homo-5-spirosteno[7a,7-*d*]tetrazol-3β-yl acetate, prepared from (25R)-7-oxo-5-spirosten-3β-yl acetate by the Schmidt reaction, gave on Marker degradation 20-oxo-7a-aza-B-homo-5,16-pregnadieno[7a,7-*d*]tetrazol-3β-yl acetate. The latter on partial hydrogenation over Pd-$BaSO_4$, followed by hydrolysis and Oppenauer oxidation gave 7a-aza-B-homo-4-pregneno-[7a,7-*d*]tetrazole-3,20-dione. 7a-Aza-B-homo-5-androsteno[7a,7-*d*]tetrazole-3β,17β-diol diacetate was prepared from 5-androstene-3β,17β-diol diacetate. The tetrazolosteroid was partially hydrolysed. The product on Oppenauer oxidation gave 3-oxo-7a-aza-B-homo-4-androsteno[7a,7-*d*]tetrazol-17β-yl acetate.

4. Synthesis and examination of new 17-spiro-steroids

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During the search for aldosterone-blocking steroids we examined the possibilities of synthesizing new types of steroid-spiro-heterocycles. Spiro-oxiranes, prepared from 17-keto-steroids were used as starting materials. These were transformed with aliphatic primary amines into 17α-alkylamino-methyl-17β-hydroxy-steroids, from which thiourea derivatives were prepared. Using the ring closure reactions of the latter, spiro-imino-oxazolidines and thiooxazolidines, as well as spiro-1,2,4-oxathiazines (representing a new heterocyclic ring system), were synthesized. All structures were confirmed by chemical and physical methods. Certain biological data and chemical transformations of these compounds turned our attention to the steroid-spiro-oxazolidinones. Several methods were developed for the synthesis of this earlier, scarcely investigated, class of compounds. The aldosterone-blocking effect of some of the new steroid-spiro-oxazolidinone derivatives equals that of Spironolactone, while others possess remarkable antiandrogen character.

5. Synthesis and activity (post-coital antifertility and hormonal) of 2,7α-dimethyl steroids

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Certain 7α-methyl steroids possess post-coital antifertility activity in the hamster when administered on days 3–8 of pregnancy. Detailed examination of the effect of further substitution on the activity of these compounds was therefore initiated. 2α- and 2β-methyl substituents were introduced by alkylation of 7α-methyltestosterone followed by rearrangement of the double bond to the 5ene-position and reduction to the 3α- and 3β-alcohols. 2,7α-dimethylestrane analogs were obtained by conjugate addition to 2-methylestra-4,6-dien-3-ones followed by reduction. Sterochemical assignments were made by n.m.r. studies of the various isomers. 2,7α-dimethylandrostanes having a 4-ene-3-one moiety were potent androgenic compounds. Conversion to the 5-ene-3β-ols essentially eliminated androgenic activity. The resulting compounds were potent post-coital antifertility agents. However, they exhibited somewhat surprising uterotropic activity and had significant affinity for uterine estrogen receptor. Since 2-substituents have such important influence on the modulation of hormonal activities, further substitution in this position is under study.

6. The synthesis of 11β,13β- and 13β,16β-propano steroids: probes of hormonal activity

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As a continuation of our studies directed towards the synthesis of modified steroids with improved antifertility activity, we have synthesized 3-methoxy-13β-(3'-phenoxypropyl)-1,3,5(10)-trien-17β-ol (**1**) and 17α-ethynyl-17β-hydroxy-13β-(3'-hydroxypropyl)gon-4-en (**2**). Several derivatives of