

1. CHEMISTRY

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

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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 graecum*. 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-spirostenol[7a,7-d]tetrazol-3 β -yl acetate, prepared from (25R)-7-oxo-5-spirostenol-3 β -yl acetate by the Schmidt reaction, gave on Marker degradation 20-oxo-7a-aza-B-homo-5,16-pregnadieno[7a,7-d]tetrazol-3 β -yl acetate. The latter on partial hydrogenation over Pd-BaSO₄, 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-3 β ,17 β -diol diacetate was prepared from 5-androstene-3 β ,17 β -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-17 β -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 17 α -alkylamino-methyl-17 β -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 antian-drogen character.

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

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Certain 7 α -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. 2 α - and 2 β -methyl substituents were introduced by alkylation of 7 α -methyltestosterone followed by rearrangement of the double bond to the 5-ene-position and reduction to the 3 α - and 3 β -alcohols. 2,7 α -dimethylestrane analogs were obtained by conjugate addition to 2-methylestra-4,6-dien-3-ones followed by reduction. Stereochemical assignments were made by n.m.r. studies of the various isomers. 2,7 α -dimethylandrostanes having a 4-ene-3-one moiety were potent androgenic compounds. Conversion to the 5-ene-3 β -ols essentially eliminated androgenic activity. The resulting compounds were potent post-coital antifertility agents. However, they exhibited somewhat surprising uterotrophic 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 11 β ,13 β - and 13 β ,16 β -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-13 β -(3'-phenoxypropyl)-1,3,5(10)-trien-17 β -ol (1) and 17 α -ethynyl-17 β -hydroxy-13 β -(3'-hydroxypropyl)gon-4-en (2). Several derivatives of