STEROIDS

XXVI. Synthesis of steroido [17, 16-d] isoxazoles

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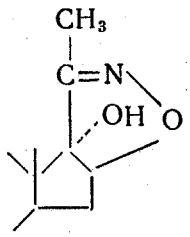
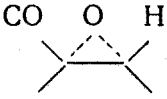
Compounds with interesting pharmacological properties are found among the heterocyclic derivatives of the steroids (steroidoisoxazoles, steroidopyrazoles, steroidopyrimidines, etc.) synthesized in recent years [1, 2]. The introduction of heterocyclic groupings into the steroid molecules leads both to an enhancement of the hormonal activity of the steroids [1] and also to a contraction in their activity spectra [2].

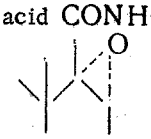
Continuing investigations of derivatives of steroids with oxygen and nitrogen functions in ring D [3], we have carried out the synthesis of a new class of steroidoisoxazoles [4], whose isoxazole ring is linked to ring D and not to rings A and B as has been described previously in the literature [5].

From our preliminary investigations with the oxime of 3β-hydroxy-16α, 17α-oxidopregn-5-en-20-one (Ia) it is known from the Beckmann rearrangement [6] that it has the anti configuration with respect to the steroid nucleus.* When the oxime (Ia) and the corresponding oxime of the allo series (Ib), obtained from 3β-hydroxy-16α, 17α-oxido-5α-pregnan-20-one (IVb), are boiled in nitrobenzene or heated above the melting point, compounds isomeric with them and having similar characteristic absorption frequencies in the IR spectrum arise. This makes it possible to assume the formation of the syn-oximes (IIa, b) or compounds with the isoxazoline structure



In view of the information given below, the isomeric compounds may be assigned the structure of syn-oximes (IIa, IIb). When the oximes (Ia) and (IIa) are acetylated with acetic anhydride in pyridine in the cold and also when they are heated, the diacetates (Ie) and (IIe) of similar elemental composition are obtained. If compounds with an isoxazoline structure were present, acetylation of the tertiary hydroxyl could take place only under more severe conditions with a catalyst or, which is more likely, dehydration would occur with the formation of a fully aromatized heterocycle.

Also in favor of the syn-oxime structure is the positive Widmann color reaction [7] with the oximes (Ia, Ib) and (IIa, IIb)—the liberation of free iodine when the acetic acid solutions are heated with potassium iodide. This reaction is characteristic for oximes containing an oxide ring in the α position. Moreover, the IR spectrum of the oxime (IIb), taken in dilute CCl_4 solution, has an absorption frequency at 3020 cm^{-1} which can be assigned to the absorption of an incompletely alkylated epoxide group  [8]. This frequency cannot be assigned to the absorption due to the formation of an intramolecular OH—O hydrogen bond, since the spectrum contains a frequency at 3590 cm^{-1} corresponding to the absorption of a hydroxy group not participating in a hydrogen bond.

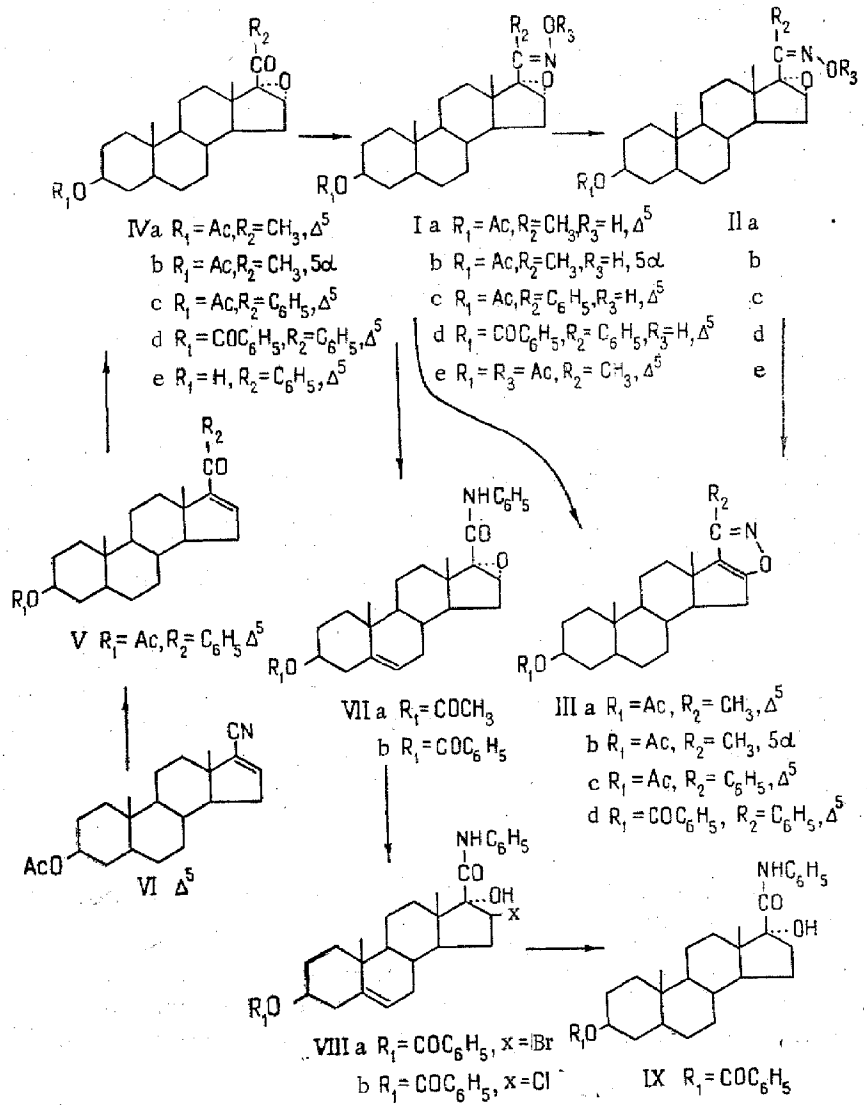
Under the conditions of the Beckmann rearrangement, i.e. under the action of phosphorus oxychloride in pyridine at room temperature, the syn-isomers (IIa, IIb), unlike the anti-isomers (Ia, Ib) described previously, do not form the normal products of the rearrangement, methylamides of 3β-acetoxy-16α,-17α-oxidoetianic acid  , but cyclize to form 3β-acetoxy-(5α)-androst-5-eno [17, 16-d]-3'-methylisoxazoles (IIIa, IIIb).

*The configuration of the ketoximes is called anti or syn according to whether the hydroxy group is in the trans or cis position, respectively, with respect to the steroid nucleus.

The steroido [17, 16-d]-3'-methylisoxazoles (IIIa, IIIb) are formed also by the action on the oximes (IIa, IIb) of other acidic agents, sulfosalicylic acid and hydrochloric acid in acetic acid solutions [9]. Cyclization of the syn-oximes (II) into the steroidoisoxazoles (III) (with the splitting out of a molecule of water) probably takes place through the preferred nature of this reaction to the normal Beckmann rearrangement, since the trans-exchange of the migration radicals is hindered by the low "electronegativity" of the methyl group.

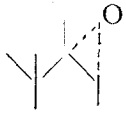
In order to extend to other series of steroids the features found for 16α,17α-epoxy-20-ketones of the pregnane series with respect to the inversion of the configuration of the anti-oximes and the cyclization of the syn-oximes to the steroidoisoxazoles, we have synthesized derivatives of the 17β-benzoylandrostane series, analogs of pregnane, in which the methyl group has been replaced by a phenyl group. 17β-Benzoyl-3β-hydroxyandrosta-5,16-diene acetate (V), the starting material for the synthesis of the oximes (Ic, Id) was obtained by a modification of Butenandt and Schmidt-Tome's method [10] by the action of phenylmagnesium bromide on 17-cyano-3β-hydroxyandrosta-5,16-diene (VI).

The epoxidation of substance (V) with hydrogen peroxide in an alkaline medium and its subsequent acylation gave the acyl derivatives of 3β-hydroxy-17β-benzoyl-16α,17α-oxidoandrost-5-ene (VIc, VId). The reaction of the latter with hydroxylamine hydrochloride in anhydrous pyridine led to the anti-oximes of the 3β-acyloxy-17β-benzoyl-16α,17α-oxidoandrost-5-enes (Ic, Id), which, like the oximes of the pregnane series (Ia, Ib), are converted into the syn-oximes (IIc, IId) on being heated above their melting points or on being boiled in nitrobenzene.



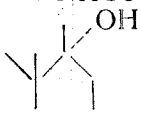
Under the conditions of the Beckmann rearrangement and under the action of acidic agents, the syn-oximes (IIc, IId), like the syn-oximes of the pregnane series, are converted into 3β-acyloxyandrost-5-eno[17, 16-d]-3'-phenyloxazoles (IIIc, IIId). The IR spectra of the steroidoisoxazoles (III) contain absorption frequencies belonging to an aromatic system of bonds (1600–1610 cm^{-1}), and ester groups (1724–1740 cm^{-1}) and contain no frequencies in the 3000–3600 cm^{-1} region. In the UV spectra of (IIIa, IIIb) there are absorption maxima at 230 mμ (log ε 3.72 ± 0.02), which are characteristic for steroidoisoxazoles having no additional conjugation in the steroid nucleus [11]. The isoxazole (IIIc) has λ_{max} 242 mμ (log ε 4.08).

Under the conditions of the Beckmann rearrangement, the anti-oximes (Ic, Id) are converted not into benzamides of the androstane series but into a mixture of the anilides (VIIa, VIIb) isomeric with them and steroido [17, 16-d]-3'-phenylisoxazoles identical with those described above. The structure of the anilides of the 3-acyloxy-16α,17α-oxidoeti-5-enoic acids (VIIa, VIIb) was established by their reactivity and by spectroscopic data. The amides formed by the rearrangement proved to be stable compounds and it may therefore be assumed that they were anilides. If the benzamides $NHCOC_6H_5$ had been formed from them, high reactivity would have been expected [6]. According to ideas



on the bimolecular mechanism of the saponification of the amide bond and the steric factors active in this process [12], the anilides (VII) should be stable to acid and alkaline hydrolysis while under the same conditions the benzamides should be more unstable. The stability of the anilides to hydrolysis is due to the fact that the quaternary carbon atom (C_{17}) with its substituents creates steric hindrance to the approach of the attacking particle to the carbonyl group. Conversely, in the benzamides there is no steric hindrance to hydrolysis, since the carbonyl group suffering attack is attached only to a phenyl radical.

In actual fact, in the anilide of 3-benzoyloxy-16α,17α-oxidoeti-5-enoic acid (VIIb) the amide link is stable to hydrolysis. When the anilide (VIIb) is boiled with an aqueous solution of hydrogen bromide or when it is subjected to the action of hydrochloric acid in acetone, the amide bond is not broken but the oxide ring opens with the formation of a bromohydrin or chlorohydrin (VIIa, VIIb) as takes place under similar conditions with compounds of the type of hydroxy-oxidopregnenone [13]. The debromination of compound (VIIIa) by boiling it with Raney nickel led to the anilide of 3β-benzoyloxy-17α-hydroxyeti-5-enoic acid (IX). When the latter was boiled with alkaline solutions of caustic potash in methanol and ethylene glycol, only the benzoyloxy group in position 3 was saponified. The isomeric benzamide $NHCOC_6H_5$ should be extremely unstable and be readily converted into hydroxyandrostenone.



The IR spectra of the anilides (VII)–(IX) give additional proof of their structure. The IR spectra of these anilides, taken in paraffin oil, have the following absorption frequencies: 3360 (>NH), 1720 (ester >CO), 1683–1690 cm^{-1} (amide >CO). When the IR spectra of dilute solutions of the anilides were recorded, the ester frequency rose to 1734 and the amide frequency to 1698 cm^{-1}. Literature data indicate [14] that amides of the type $AlkNHCOC_6H_5$ absorb in the 1655–1665 cm^{-1} region, and amides of the type ArNHCOAlk at 1680–1710 cm^{-1}.

The raising of the amide frequency for the anilides is connected with the fact that in the case of a phenyl group the interaction of the unshared pair of the nitrogen atom with the carbonyl group is considerably less (because of conjugation with the aromatic nucleus) than in the case of methyl, so that the amide frequency of the anilides approaches the frequency of a free carbonyl group.

The conversion of the anti-oximes (Ic, Id) by the Beckmann rearrangement into the anilides (VII) and the steroido-[17, 16-d]-3'-phenylisoxazoles (IIIc, IIId), whose formation is possible only from the syn-oximes (IIc, IId) shows that the inversion of the configuration of the oximes from the anti forms to the syn forms takes place during the rearrangement, a phenomenon frequently occurring in the Beckmann rearrangement of oximes of alkyl aryl ketones [15].

Preliminary biological tests (carried out in the Scientific Research Institute for Natural and Medicinal Substances, Prague) have shown that the steroidoisoxazoles have no androgenic, anabolic, or gestagenic activity.

Experimental

Anti-oximes of the 3-acetates of 3β-hydroxy-16α,17α-oxidopregn-5-en-20-one and the corresponding 5α-saturated compound (Ia, b) and the 3β-acyloxy-17β-benzoyl-16α,17α-oxidoandrost-5-enes (Ic, Id).

0.016 mole of one of the ketones (IVa–d) in 120 ml of pyridine was treated with 0.09 mole of hydroxylamine hydrochloride and the mixture was left for 4 days at room temperature. The solution was poured into 1200 ml of ice water, and the precipitate was filtered off, washed with water, dried, and recrystallized from ethyl and methyl alcohols. The anti-oximes had a double melting point: after melting for the first time, they solidified and then melted again at about 50°–100° C with decomposition (corresponding to syn-oximes). Table 1 gives the first melting points for the anti-oximes.

Syn-oximes of the 3-acetates of 3β-hydroxy-16α-oxidopregn-5-en-20-ones and of the corresponding 5α-saturated compound (IIa, IIb) and the 3β-acyloxy-17β-benzoyl-16α,17α-oxidoandrost-5-enes (IIc, IId).

A mixture of 0.03 mole of one of the anti-oximes (Ia–d) and 100 ml of nitrobenzene was boiled for 2 min. The

cooled solution was treated with ether, and the precipitate was filtered off, carefully washed with ether, and recrystallized from ethyl and methyl alcohols (see Table 1).

Diacetate of the anti-oxime of 3β-hydroxy-16α,17α-oxidopregn-5-en-20-one (Ie).

One gram of the oxime (Ia) was heated in 30 ml of a mixture of acetic anhydride and dry pyridine (1:1) for 1 hr at 75°–80° C. The cooled solution was poured into 300 ml of ice water, and the precipitate was filtered off and washed with water. Weight 0.8 g, mp 202°–203° C (from methanol). IR spectrum: 1743 cm^{-1} (ester >CO), 1788 (>C=N–OAc), 1642 cm^{-1} (>C=N–).

Found, %: C 69.90; H 8.37; N 3.35. Calculated for $C_{25}H_{35}NO_5$, %: C 69.91; H 8.21; N 3.26.

Diacetate of the syn-oxime of 3β-hydroxy-16α,17α-oxidopregn-5-en-20-one (IId).

A mixture of 0.25 g of the oxime (IIa), 6 ml of acetic anhydride, and 11 ml of dry pyridine was heated for 1 hr at 75°–80° C. This gave 0.15 g of a substance with mp 171°–171.5° C (from 60% aqueous methanol). IR spectrum: 1755 cm^{-1} (ester >CO, >C=N–OAc).

Found, %: C 70.15; H 8.30; N 3.39. Calculated for $C_{25}H_{35}NO_5$, %: C 69.91; H 8.21; N 3.26.

Table 1

Substance	Configuration	Yield, %	Mp, °C	ν_{max}, cm^{-1}	Found, %			Formula	Calculated, %		
					C	H	N		C	H	N
(Ia)	Anti	55	188	3334, 1725	71.19	8.64	3.63	$C_{23}H_{33}NO_4$	71.27	8.58	3.64
(IIa)	Syn	65	263–265 decomp.	3190, 1724	71.14	8.61	3.70				
(Ib)	Anti	66	150–153	3340, 1735	70.66	9.04	3.59	$C_{23}H_{35}NO_4$	70.89	9.05	3.59
(IIb)	Syn	65	274–276 decomp.	3240, 1730*	71.01	8.91	3.87				
(Ic)	Anti	37	216	3360, 1705	74.88	7.88	3.05	$C_{28}H_{35}NO_4$	74.80	7.84	3.11
(IIc)	Syn	61	246–248 decomp.	3240, 1730	74.86	7.66	3.23				
(Id)	Anti	40	210	3450, 1710	77.70	7.39	2.62	$C_{33}H_{37}NO_4$	77.47	7.29	2.74
(IId)	Syn	36	278–279 decomp.	3250, 1715	77.66	7.25	2.80				

*3590, 3020 cm^{-1} (0.2% solution in CCl_4).

3β-Acyloxy-(5α)-androst-5-enone[17,16-d]-3'-(methyl, phenyl)isoxazoles (IIIa)–(IIId).

Method 1. At a temperature of −10° to 5° C, a solution of 0.06 mole of phosphorus oxychloride in 7 ml of pyridine was added to a solution of 0.012 mole of one of the syn-oximes (IIa)–(IId) in 30 ml of dry pyridine. Then the mixture was stirred at room temperature for 5 hr. The solution was poured into 370 ml of ice water, and the precipitate which deposited was filtered off, washed with water, and recrystallized (Table 2).

Method 2. A mixture of 0.027 mole of one of the syn-oximes (IIa)–(IId) and 0.043 mole of sulfosalicylic acid in 600 ml of glacial acetic acid was heated for 3.5 hr at 60°–70° C. After cooling, the solution was diluted with water, and the precipitate was filtered off, washed with water, dried, and recrystallized.

Acetate of 17-benzoyl-3β-hydroxyandrosta-5,16-diene (V).

Over 20 min, at room temperature, a solution of 6.7 g of 17-cyano-3β-hydroxyandrosta-5,16-diene (VI) [10] in 80 ml of dry anisole was added to an ethereal solution of phenylmagnesium bromide prepared from 8.04 g of magnesium turnings, 47 ml of bromobenzene, and 150 ml of dry ether. The mixture was stirred at the same temperature for 10 hr and was left overnight. Then the solution was cooled to 0° C, and 400 ml of 50% aqueous acetic acid was added in such a way that the temperature did not rise above +5° C. The ether was distilled off in vacuum and the other solvents with steam. The oily residue was extracted with ether and the extract was dried with anhydrous sodium sulfate. The solvent was distilled off to dryness and the residue was crystallized from methanol. 2.8 g of the yellowish substance was acetylated with 5 ml of acetic anhydride in 50 ml of pyridine at room temperature for 20 hr. The solution was poured into water, the oily substance was extracted with ethylene chloride, the extract was washed with water, the solvent was distilled off to dryness, and the residue was recrystallized from methanol. Weight 2.32 g (27%), mp 152°–154° C (from ethyl alcohol), λ_{max} 254 mμ (log ε 4.08); IR spectrum: 1720 (ester >CO), 1643 cm^{-1} (conj. >CO).

Found, %: C 80.19; H 8.04. Calculated for $C_{28}H_{34}O_3$, %: C 80.34; H 8.19.

17β-Benzoyl-3β-hydroxy-16α,17α-oxidoandrost-5-ene (IVe).

A solution of 5.8 g of the acetate of 17-benzoyl-3β-hydroxyandrosta-5,16-diene (V) in 700 ml of methanol and 1 ml of 1N caustic soda was treated at +10° C with 1 ml of a 27.4% solution of hydrogen peroxide. The solution was stirred for 5 hr and left for 20 hr at room temperature, and then 700 ml of water was added. The precipitate which deposited was filtered off, washed with water, and recrystallized from ethyl alcohol. Weight 4.46 g (82%), mp 149°–152.5° C (from ethyl acetate). A mixture with the starting material had mp 125°–128° C; IR spectrum: 3200 (–OH), 1662 cm^{-1} (conj. >CO).

Found, %: C 79.41; H 8.31. Calculated for $C_{26}H_{32}O_3$, %: C 79.56; H 8.22.

The acetate of IVe (IVc) had mp 156°–158° C (from methyl and ethyl alcohols); IR spectrum: 1730 (ester >CO), 1672 cm^{-1} (conj. >CO).

Found, %: C 77.46; H 7.85. Calculated for $C_{28}H_{34}O_4$, %: C 77.39; H 7.88.

The benzoate of IVe (IVd) had mp 181°–183° C (from ethyl acetate and ethyl alcohol); IR spectrum: 1707 (ester >CO), 1660 cm^{-1} (conj. >CO).

Found, %: C 79.57; H 7.31. Calculated for $C_{33}H_{36}O_4$, %: C 79.80; H 7.30.

Table 2

Substance	Method of preparation	Yield, %	Mp, ° C (solvent for recrystallization)	ν_{max}, cm^{-1}	λ_{max} (log ε)	Found, %			Formula	Calculated, %		
						C	H	N			H	N
(IIIa)	1 2	58,5 85	184—186 (ethyl alcohol, methanol)	1724, 1610	230 (3.76)	74.64	8.38	3.88	$C_{23}H_{31}NO_3$*	74.74	8.46	3.76
(IIIb)	2	91	205—207 (ethyl alcohol, methanol)	1740, 1610	230 (3.70)	74.10	8.72	3.80	$C_{23}H_{33}NO_3$	73.88	8.72	3.77
(IIIc)	2	83	211.5—213.5 (acetone, methanol)	1735, 1600	242 (4.08)	77.89	7.93	3.28	$C_{28}H_{33}NO_3$	78.11	7.72	3.25
(IIId)	1	90	184.5—186 (ethyl alcohol)	1724, 1600	—**	80.40	6.97	2.82	$C_{33}H_{35}NO_3$	80.30	7.14	2.84

*Found, %: 11.5. Calculated for CH_3CO, %: 11.4.

**Very sparingly soluble in alcohol.

Beckmann rearrangement of the anti-oxime of the acetate of 17β-benzoyl-3β-hydroxy-16α,17α-oxidoandrost-5-ene (Ic).

At –13° to –10° C, a solution of 1 ml of phosphorus oxychloride in 5 ml of pyridine was added to a solution of 1 g of the anti-oxime (Ic) in 50 ml of dry pyridine, and the reaction mixture was stirred for 3 hr at +5° C. The solution was poured into 500 ml of ice water and the precipitate which deposited was filtered off. The weight of precipitate was 0.67 g. Successive recrystallization from ethanol and acetone gave 0.08 g of 3β-acetoxyandrost-5-eno[17,16d]-3'-phenylisoxazole (IIIc) with mp 211°–213° C. The IR and UV spectra of this substance coincided with the IR and UV spectra of (IIIc) obtained from the syn-oxime (IIc).

The mother liquors were combined, evaporated to dryness, and chromatographed on a column of 20 g of alumina. Benzene and a mixture of benzene and methylene chloride (3:2) eluted 0.22 g of the anilide of 3β-acetoxy-16α,17α-oxidoeti-5-enoic acid (VIIa). Yield 22%, mp 187.5°–190° C (from methyl and ethyl alcohols). IR spectrum: 3360 cm^{-1} (>NH), 1720 (ester >CO), 1683 cm^{-1} (>CONHC_6H_5).

Found, %: C 75.25; H 7.70; N 3.14. Calculated for $C_{28}H_{35}NO_4$, %: C 74.80; H 7.84; N 3.11.

Ethyl acetate eluted 0.2 g of an oily substance whose recrystallization from ethyl alcohol gave 0.11 g of the syn-oxime of the acetate of 17β-benzoyl-3β-hydroxy-16α,17α-androst-5-ene (IIc) with mp 244°–246° C (decomp.). A mixture with an authentic sample of (IIc) gave no depression of the melting point. Their IR spectra were identical.

Beckmann rearrangement of the anti-oxime of the benzoate of 17β-benzoyl-3β-hydroxy-16α,17α-oxidoandrost-5-ene (Id).

At –10° C, a solution of 3.5 ml of phosphorus oxychloride in 10 ml of pyridine was added to a solution of 1.8 g of the oxime (Id) in 90 ml of dry pyridine, and the reaction mixture was stirred at –10° to 0° C for 3 hr. The solution was poured into 1.1 *l* of ice water, and the oil that separated out was extracted with methylene chloride; the extract was washed with water and dried with anhydrous sodium sulfate, and the solvent was distilled off to dryness. The oily

residue was chromatographed on a column of 50 g of alumina. Methylene chloride eluted 1.3 g of substance. After recrystallization from acetone, 1.13 g of the anilide of 3β-benzoyloxy-16α,17α-oxidoeti-5-enoic acid (VIIb) was obtained. Yield 63%, mp 224°–227° C (decomp. from acetone). IR spectrum: 3360 cm^{-1}, 3400 (>NH), 1720 (ester >CO), 1690 cm^{-1} (>$CONHC_6H_5$).

Found, %: C 77.00; H 7.30; N 2.62. Calculated for $C_{33}H_{37}NO_4$, %: C 77.47; H 7.29; N 2.74.

Ethyl acetate eluted 0.3 g of a substance which, after recrystallization from alcohol, proved to be identical with 3β-benzoyloxyandrost-5-eno[17,16-d]-3'-phenylisoxazole (IIId).

Anilide of 3β-benzoyloxy-16β-bromo-17α-hydroxyeti-5-enoic acid (VIIIa).

A boiling solution of 1.33 g of the anilide of 3β-benzoyloxy-16α,17α-oxidoeti-5-enoic acid (VIIb) in 120 ml of acetone was treated with 27 ml of a 40% aqueous solution of hydrobromic acid, and the solution was boiled for another 40 min. The precipitate which deposited after cooling was filtered off and washed with water to neutrality. Weight 1.2 g (77%), mp 212.5°–213° C (decomp., from methanol). IR spectrum: 3500 cm^{-1}, 3380 (>NH, OH), 1690 (>$CONHC_6H_5$), 1608 cm^{-1} (arom.).

Found, %: C 66.95; H 6.55; Br 13.17; N 2.47. Calculated for $C_{33}H_{38}BrNO_4$, %: C 66.90; H 6.47; Br 13.49; N 2.34.

Anilide of 3β-benzoyloxy-16β-chloro-17α-hydroxyeti-5-enoic acid (VIIIb).

A boiling solution of 0.2 g of the anilide of 3β-benzoyloxy-16α,17α-oxidoeti-5-enoic acid (VIIb) in 35 ml of acetone was treated with 5 ml of concentrated hydrochloric acid. The solution was boiled for 10 min and was left for 2 hr at room temperature. Then it was poured into water and neutralized with sodium carbonate. The precipitate which deposited was filtered off and washed with water. Weight 0.13 g, mp 229°–230° C (decomp., from acetone). IR spectrum: 3500 cm^{-1}, 3385 (>NH, OH), 1685 (>$CONHC_6H_5$), and 1605 cm^{-1} (arom.).

Found, %: C 72.12; H 7.07; Cl 6.44; N 2.72. Calculated for $C_{33}H_{38}ClNO_4$, %: C 72.30; H 6.99; Cl 6.47; N 2.57.

Anilide of 3β-benzoyloxy-17α-hydroxyeti-5-enoic acid (IX).

A solution of 0.31 g of the anilide of 3β-benzoyloxy-16β-bromo-17α-hydroxyeti-5-enoic acid (VIIIa) in 150 ml of ethyl alcohol was boiled with 5 g of Raney nickel catalyst for 3 hr. The hot solution was filtered from the catalyst and the catalyst was washed with alcohol. The filtrate was cooled to 0° C and the precipitate which deposited was filtered off. Weight 0.13 g, mp 288.5°–290° C (decomp. from ethyl acetate and acetone). IR spectrum: 3500 cm^{-1}, 3415 (>NH, OH), 1715 (ester >CO), 1690 (>$CONHC_6H_5$), 1603 cm^{-1} (arom.).

Found, %: C 77.10; H 7.53; N 2.62. Calculated for $C_{33}H_{39}NO_4$, %: C 77.16; H 7.65; N 2.72.

Summary

1. A new type of steroido[17,16-d]-3'-(methyl, phenyl)isoxazoles has been synthesized by the cyclization of the syn-oximes of acylated 3β-hydroxy-16α,17α-oxidopregn-5-en-20-ones or their 5α-saturated derivatives and acylated 17β-benzoyl-3β-hydroxy-16α,17α-oxidoandrost-5-ones.

2. It has been established that the Beckmann rearrangement of the anti-oximes of acylated 17β-benzoyl-3β-hydroxy-16α,17α-androst-5-enes leads to a mixture of anilides and steroidoisoxazoles, which shows the inversion of the configuration of the oximes (from the anti to the syn form) during the rearrangement.

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