C. From V.—To a solution of 5 g. (0.025 mole) of 2,4-dinitrophenylhydrazine in 25 ml. of concentrated sulfuric acid, 36 ml. of water, and 125 ml. of ethanol, 3 g. (0.01 mole) of V was added. The reaction mixture was stirred at room temperature for 16 hr. The crystalline reaction product, formed in almost quantitative yield, was separated by filtration. After recrystallization from dimethylformamide, yellow needles of XIII were obtained.

Anal. Calcd. for $C_{21}H_{13}ClN_6O_4$: C, 56.20; H, 2.92; N, 18.72; Cl, 7.90. Found: C, 55.84; H, 3.12; N, 18.34; Cl, 7.77.

Acknowledgment.—We are indebted to Dr. Al Steyermark and his staff for the microanalyses and to Mr. S. Traiman and his co-workers for the infrared spectra.

Heterocyclic Studies. X. A Steroidal 1,2-Diazepin-4-one[1]

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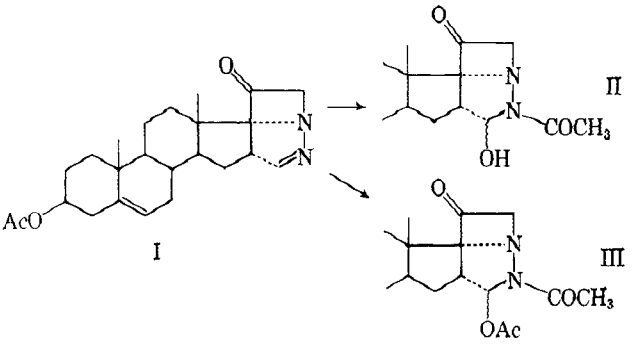
Acylation of the diazabicyclic ketone system (I) results in addition of acid or anhydride to the C=N bond. I is isomerized to the diazepinone (IV) by heating in acetic acid with sodium acetate. The steroidal diazepinone differs greatly in reactivity from the methylphenyldiazepinone (VI) and fails to undergo the characteristic ring contractions and transannular reaction of the latter.

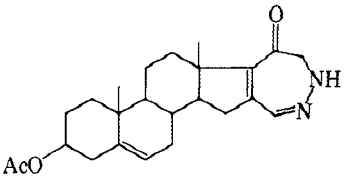
In a previous article we recorded the preparation of a series of nitrogenous steroid derivatives in which the 1,2-diazabicyclo[3.2.0]heptene ring system is fused to the pregnane D-ring.[2] The compounds in this series are of interest, *per se*, as an addition to the growing catalog of nitrogen-containing steroids, some of which have proven to be of pharmacological importance.[3] From a chemical standpoint, however, the steroid nucleus represents a convenient framework to which the heterocyclic rings can be attached in a sterically restricted way, providing an opportunity to expand our knowledge of the 1,2-diazabicyclo[3.2.0]heptane and 1,2-diazepine systems.

A number of nuclear transformations of the bicyclic ketone (I) have been described in which the heterocyclic system remained intact, and it was observed that the compound displays the high carbonyl reactivity characteristic of four-membered cyclic ketones.[2] We now report the results of further study on the heterocyclic chemistry of I.

The diazabicycloheptenone system in I is resistant to mild hydrolysis or oxidation, but reaction occurs with acetyl chloride or, under forcing conditions, with acetic anhydride. With both reagents two products can be isolated which involve the addition of the elements of acetic acid in one case and of acetic anhydride in the other. The infrared spectra of these derivatives contain three and four carbonyl bands, respectively; in both cases the characteristic low wave-length band at 5.56–5.57 μ indicates retention of the four-membered cyclic ketone group. A band at 6.01–6.06 μ in both spectra must be due to an amide carbonyl, and the structures of these products can be assigned as II and III, resulting from addition to the azomethine bond in the pyrazoline ring of I. Similar additions have been observed in the indolenine series[4]; benzoyl chloride in aqueous alkali leads to the 1-benzoyl-2-indolinol, and acetic anhydride to the N-acetylcarbinolamine acetate. The formation of III with acetyl chloride is rather surprising, however, and this reaction, as well as the transformations of the adducts, is being studied further.



One of the primary aims of this work has been the conversion of I to the diazepinone (IV) and a comparative study of the reactions of this compound with those of



IV

the counterpart (VI) in which methyl and phenyl substituents replace the ring D residues. The chemistry of the latter compound has been explored extensively,[5] and a number of ring-contraction and transannular reactions have been encountered. Some of these transformations that are of importance in connection with the present work are recapitulated in Scheme I. The reactions of the steroid series have revealed a much diminished tendency for rearrangement and interconversion of the bicyclic and seven-membered ring systems.

In the previous paper[2] it was noted that the conditions sufficient for the conversion V → VI (Scheme I), namely treatment with very mild acid or base, were without effect on the steroidal bicyclic ketone (I). A number of attempts to bring about a parallel isomerization by employing more vigorous acid or basic condi-

(1) Supported by Grant A-3629 from the National Institute of Arthritis and Metabolic Diseases.

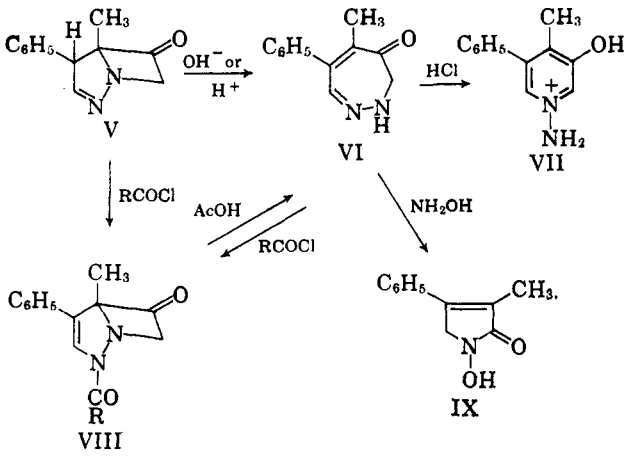
(2) J. A. Moore, W. F. Holton, and E. L. Wittle, *J. Am. Chem. Soc.*, **84**, 390 (1962).

(3) M. Alauddin and M. Martin-Smith, *J. Pharm. Pharmacol.*, **14**, 325, 469 (1962).

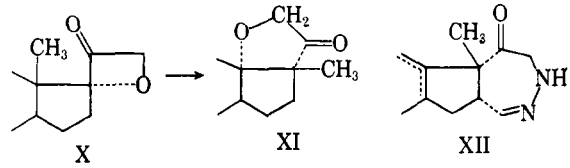
(4) H. Leuchs, A. Heller, and A. Hoffmann, *Ber.*, **62**, 871 (1929), and earlier references cited there.

(5) (a) J. A. Moore and R. W. Medeiros, *J. Am. Chem. Soc.*, **81**, 6026 (1959); (b) J. A. Moore and J. Binkert, *ibid.*, **81**, 6029 (1959); (c) J. A. Moore, F. J. Marascia, R. W. Medeiros, and E. Wyss, *ibid.*, **84**, 3022 (1962).

SCHEME I



tions were fruitless. Refluxing in dilute ethanolic sulfuric acid caused only hydrolysis of the 3-acetate group. These conditions bring about cleavage of the related 17,21-oxido 20-ketone (X) with attendant methyl migration to give the 17β-methyl 13α,21-oxide (XI),[6] and there is a possibility that acid-catalyzed rearrangement of I might lead to a corresponding 17β-methyldiazepine (XII) rather than IV. More drastic acid

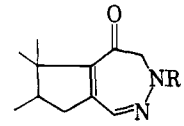


treatment of I gave dark amorphous resins in which the 5.6-μ infrared band characteristic of I was absent, but no crystalline products were obtained. Similarly, vigorous alkaline conditions caused destruction of the four-membered ring, but products could not be isolated.

Successful conditions were found when I was heated on the steam bath in acetic acid solution containing a large amount of sodium acetate. Dilution with water gave an olive precipitate which on chromatography furnished brilliant deep yellow needles of an isomeric compound in 16% yield based on the bicyclic ketone consumed. The ultraviolet spectrum was remarkably similar to that of the diazepinone (VI), with a long wavelength maximum at 405 mμ; a similar bathochromic shift occurred in alkaline solution. The infrared spectrum contained a sharp band at 2.89 and a carbonyl band at 6.04 μ. In the n.m.r. spectrum,[7] besides the typical skeletal proton resonances, peaks were present at 7.08 (—C*H*=N), 6.76 (broad, N*H*), and 3.58 p.p.m. (slightly split, COC*H*$_2$NH).

The structural assignment IV for this product rests on these physical properties and analogy to the isomerization V → VI (Scheme I). The alternative diazepine structure XII can be dismissed on the basis of the infrared and particularly the ultraviolet spectra. The reactions that have been observed are consistent, with structure IV, but a number of the important transformations of VI so far have failed when applied to the steroidal diazepinone.

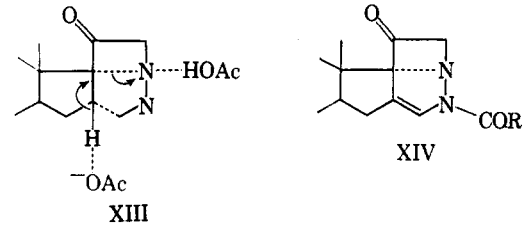
Treatment of IV with methyl sulfate in alkali followed by reacetylation gave a single yellow monomethyl derivative which must be IVb. The infrared spectrum contained the same carbonyl bands as that of IV but no NH band. The n.m.r. spectrum contained a sharp peak at 3.39 p.p.m. (NC*H*$_3$) superimposed on a symmetrical pair of doublets with midpoint 3.48 p.p.m. ($\delta_B - \delta_A$ = 13.9 c.p.s., J_{AB} = 13 c.p.s.) due to the COC*H*$_2$N group. This splitting of the methylene protons, which is not seen in the n.m.r. spectrum of the corresponding 2-methyl derivative of the nonsteroidal diazepinone (VI), indicates nonequivalence of these protons due to a fairly rigid nonplanar heterocyclic ring in IVb. Acetylation of IV with acetic anhydride or acetyl chloride gave a yellow monoacetyl derivative, assigned structure IVc. These simple substitutions have been observed with the methylphenyldiazepinone (VI),[5b] but in the latter case a major product also results from attack at the N-1 position (—N=), *e.g.*, the formation of VIII in the reaction with acid chlorides.[5c]



IVb, R = CH$_3$
c, R = COCH$_3$

Although a conjugated carbonyl group in IV is clearly indicated by the infrared spectrum, no reaction was observed with either semicarbazide or hydroxylamine, both of which react readily with VI, the latter in a transannular manner to give IX.[5b] Attempts to bring about a ring contraction of IV to an aminopyridine with acid, parallel to the transformation VI → VII so far have been unsuccessful; partially deacetylated IV was recovered at room temperature, and on heating only resinous material was produced.

The pronounced differences in reactivity of both the diazabicycloheptenone and diazepinone systems in the two series must arise from a combination of steric and electronic factors. The ease with which V is converted to VI, especially in base, is presumably due to the lability conferred on the C-4 proton in V by the phenyl substituent. The resistance of I to isomerization in acid or base alone can be attributed to the absence of a similar mobilization of the 16β proton, since there must be some relief of strain in passing from I to IV. The role of acetate ion in the isomerization of I is quite clear-cut, and it appears that we are dealing here with simultaneous catalysis by acid and base in the debridging reaction as indicated in XIII.



(6) W. S. Allen, S. Bernstein, M. Heller, and R. Littell, *J. Am. Chem. Soc.* **77**, 4784 (1955); J. Herz, J. Fried, P. Grabowich, and E. F. Sabo, *ibid.*, **78**, 4813 (1956); R. Hirschmann, G. A. Bailey, G. I. Poos, R. Walker, and J. M. Chemerda, *ibid.*, **78**, 4814 (1956).

(7) N.m.r. spectra were measured at 60 Mc. in deuteriochloroform solution; peak positions are expressed in parts per million relative to internal tetramethylsilane.

The failure of I to furnish product XIV, analogous to VIII, on acylation has been rationalized previously on steric grounds[2]; the establishment of a double bond exocyclic to ring D in the bicyclic system would introduce severe additional strain. This consideration also would apply to the nonformation of XIV from the diazepinone (IV), but very probably an additional factor in this case is the greater rigidity of IV compared to the monocyclic diazepinone (VI), which is revealed by the n.m.r. spectrum of IVb and would preclude a 1,4-transannular interaction. This situation also may be responsible for the failure of IV to undergo ring contraction to a pyridine; the reaction VI → VII is considered to involve transannular formation of a diazabicyclo[4.1.0] system rather than a ring opening and reclosure sequence,[5b] requiring conformational mobility which is absent in IV.

Experimental[8]

Starting Material.—The ketone (I) was prepared as previously described.[2] The required 3β-hydroxy-5,16-etiadienic acid was prepared by the alkaline hydrolysis of 21-pyridinium-5,16-pregnadien-3β-ol-20-one iodide by an improved procedure in which the sparingly soluble sodium salt of the acid was crystallized and then acidified to give the crystalline acid directly, avoiding a rather troublesome extraction. The hypobromite degradation described[9] for the preparation of 3β-hydroxy-5-etienic acid gave only traces of the etiadienic acid when applied to dehydropregnenolone.

3β,3′-Diacetoxy-2′-acetyl-16α,17α,21-(3′,1′,1′-pyrazolidino)-5-pregnen-20-one (III).[10] **A.**—To a solution of 100 mg. of the bicyclic ketone (I) in 3 ml. of pyridine was added, with stirring at 5°, 0.55 ml. of acetyl chloride. A white precipitate of pyridinium chloride separated immediately, and, after adding an additional 2 ml. of pyridine, the reaction mixture was allowed to warm to 25°. The solid dissolved and the color of the solution became yellow and finally dark amber. After 6 hr. the solution was washed, dried, and evaporated, and the brown residue was chromatographed on 4 g. of neutral alumina. The first fraction, eluted with benzene, was crystallized from acetone–hexane to give 24 mg. of white needles of the diacetyl compound (III); m.p. 183–185°; λ^{KBr} 5.56, 5.70, 5.83, 6.01 μ; O.R.D. (*c* 0.116, dioxane), $[\alpha]_{589}$ −86°, $[\alpha]_{370}$ −207°, $[\alpha]_{325}$ +638, $[\alpha]_{300}$ −1230, $[\alpha]_{270}$ −1720, $[\alpha]_{242}$ −518.[11]

Anal. Calcd. for $C_{28}H_{38}N_2O_6$ (498.6): C, 67.44; H, 7.68; N, 5.62. Found: C, 67.27; H, 7.69; N, 5.72.

After elution of some oily material, later fractions eluted with chloroform–2% methanol crystallized from acetone–hexane as colorless leaflets, 15 mg., m.p. 191–194°, of the monoacetyl derivative (II), identical with material described in the following experiment.

B. 3β-Acetoxy-2′-acetyl-3′-hydroxy-16α,17α,21-(3′,1′,1′-pyrazolidino)-5-pregnen-20-one (II).—A solution of 500 mg. of I in 20 ml. of pyridine containing 0.36 ml. of acetyl chloride was stirred at 0° for 2 hr. and the pale yellow solution then was poured into ice–water and extracted with ether. The residue after evaporation, 524 mg. of white solid, was crystallized from ether to give 200 mg. of colorless prism, m.p. 193–195°, and 75 mg., m.p. 189–192°. Chromatography of the mother liquor on alumina gave an additional 80 mg. of the same product, m.p. 193–194° (total yield, 62%); none of the diacetyl derivatives was isolated. Recrystallization from ether–hexane gave colorless cubes; m.p. 194°; λ^{KBr} 5.57, 5.79, 6.06 μ; O.R.D. (*c* 0.094, dioxane), $[\alpha]_{589}$ −106°, $[\alpha]_{380}$ −234°, $[\alpha]_{323}$ +447°, $[\alpha]_{280}$ −1920, $[\alpha]_{250}$ −530.

Anal. Calcd. for $C_{26}H_{36}N_2O_5$ (456.6): C, 68.39; H, 7.95. Found: C, 67.87; H, 7.83.

For further acetylation of this compound to the diacetyl derivative, a solution of 50 mg. in 2 ml. of pyridine and 0.1 ml. of acetic anhydride was heated for 6 hr. on the steam bath. After pouring into water and extracting with ether, 57 mg. of brown solid was obtained and was chromatographed on 2 g. of alumina. The main fraction, 37 mg. after treatment with charcoal, was crystallized from ether–hexane to give 19 mg. of colorless crystals, m.p. 179–181°, infrared spectrum identical with that of III.

C. Using Acetic Anhydride.—A solution of 200 mg. of I in 0.5 ml. of acetic anhydride and 2.0 ml. of pyridine was heated on the steam bath for 17 hr. The solution then was poured into water, and the dark brown solid was collected and chromatographed on alumina. The fractions, eluted with benzene–chloroform, were crystallized from ether–hexane to give 30 mg. of colorless rosettes, m.p. 163–183°. Recrystallization gave rods, m.p. 166–176°, with infrared spectrum nearly identical with that of III prepared by procedure A. Later fractions gave 44 mg. of prisms, m.p. 180–185°, with infrared spectrum corresponding to the monoacetyl derivative (II).

3β-Acetoxy-1′,7′-dihydro-5,16-androstadieno[16,17:4,5′]-6′*H*-1′,2′-diazepin-6′-one (IV).—A solution of 3.0 g. of I and 15 g. of freshly fused sodium acetate in 300 ml. of glacial acetic acid was heated on the steam bath for 12 hr. The dark brown solution then was cooled and poured into 1.2 l. of water and the olive-brown solid was filtered, washed with water, and dried, giving 2.30 g. The filtrate was extracted with methylene chloride and the combined solids, 3.1 g., were chromatographed from benzene solution on 75 g. of neutral Grade I alumina. The first fractions, eluted with benzene and chloroform, contained 1.15 g. of brown solid which on several crystallizations from acetone–hexane gave 0.89 g. of unchanged I in several crops with melting points of 170–190°. The next fractions (0.83 g.) were partly oily and partly solid; after combining selected fractions with the mother liquor from I and rechromatographing, a total of 327 mg. of IV was obtained, m.p. 238–241. Recrystallization from benzene–hexane furnished glistening golden needles; m.p. 241–242°; λ_{max}^{EtOH} 220 (ε × 10^{-3}, 10.5), 253 (3.6), 321 (4.0), 405 mμ (2.8); $\lambda_{max}^{EtOH+NaOH}$ 283 (3.4), 323 (2.1), 410 mμ (4.8); λ^{KBr} 2.89, 5.78, 6.04 μ; O.R.D. (*c* 0.104, dioxane), $[\alpha]_{589}$ −120°, $[\alpha]_{455}$ +600°, $[\alpha]_{330}$ −3000°, $[\alpha]_{250}$ +5400°.

Anal. Calcd. for $C_{24}H_{32}N_2O_3$ (396.5): C, 72.69; H, 8.13; N, 7.07. Found: C, 72.48; H, 8.09; N, 6.84.

From later fractions in the chromatogram, eluted with chloroform–methanol, a very sparingly soluble colorless substance was isolated. Recrystallization from chloroform–hexane gave 60 mg. of white fluffy needles, m.p. 288–293°, λ_{max}^{EtOH} 250 mμ (ε 1600). Analysis suggested a dihydro composition; this compound has not been characterized further.

Anal. Calcd. for $C_{24}H_{34}N_2O_3$ (398.5): C, 72.33; H, 8.60; N, 7.03. Found: C, 72.23, 72.05; H, 8.63, 8.80; N, 6.80.

Acetylation of IV.—A solution of 50 mg. of IV in 5 ml. of pyridine was treated with 0.25 ml. of acetic anhydride and was allowed to stand overnight. After dilution with water and extraction with methylene chloride, the crude yellow product was crystallized from ether–hexane as needles, 34 mg., m.p. 204–209°. Further crystallizations from ether–hexane gave golden needles of IVc, m.p. 211–212°; λ^{KBr} 5.74, 5.94, 6.01, 6.33 μ.

Anal. Calcd. for $C_{26}H_{34}N_2O_4$ (438.5): C, 71.20; H, 7.82. Found: C, 71.31; H, 7.89.

Acetylation of 25 mg. of IV with acetyl chloride in pyridine gave mainly brown insoluble amorphous material; from the ether extracts was obtained 6 mg. of yellow crystals of IV with an infrared spectrum the same as that of the product from acetic anhydride.

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(8) Infrared spectra were obtained in potassium bromide disks with a Perkin-Elmer Infracord. Melting points were determined on Fisher-Johns block with calibrated thermometer.

(9) C. Djerassi and J. Staunton, *J. Am. Chem. Soc.*, **83**, 741 (1961).

(10) The nomenclature of the compounds in this series has presented some difficulties since existing rules for steroid nomenclature do not provide for the naming or numbering of compounds with a heterocyclic ring fused to the steroid nucleus. In constructing a fusion name, it seems desirable to place the steroid name first and to use a genetic numbering system in which the usual steroid numbering is retained and the atoms of the heterocyclic rings are primed, as in the name which has been used for IV.

The nomenclature of compounds with the ring system of I–III presents an additional problem since a fusion name is not possible. In the name originally used[2] for the parent system of I, 16α,17α,21-[3,1,1-(2-pyrazolino)]-pregnane, the attachment of the heterocyclic rings is indicated by the bonds between atoms of the steroid and heterocyclic rings (16α-3, 17α-1, and 21-1). Until some systematic alternative is developed this name will be retained, with the modification of primed numbers for the three atoms comprising the pyrazoline or pyrazolidine ring.

We wish to thank Dr. Harriet Geer, Parke, Davis and Co., and Dr. Leonard Capell and Donald Walker of Chemical Abstracts Service for their contributions and helpful discussions on these questions.

(11) We wish to express our thanks to Professor Carl Djerassi, Stanford University, for obtaining the optical rotatory dispersion data.

Alkaline Hydrolysis of IV.—A solution of 50 mg. of IV in 6 ml. of ethanol (containing some undissolved solid) was treated with 0.5 ml. of 5% aqueous sodium hydroxide solution. After stirring for 30 min., a heavy yellow precipitate began to separate. The mixture was stirred for an additional 18 hr. and then was diluted with water and filtered. The bright yellow powder, 43 mg., m.p. 250–252°, was recrystallized from acetone–hexane to give tiny golden flakes of the 3-hydroxydiazepine, m.p. 252–254°.

Anal. Calcd. for $C_{22}H_{30}N_2O_2$ (354.5): C, 74.54; H, 8.53. Found: C, 74.13; H, 8.68.

Methylation of IV.—To a solution of 100 mg. of IV in 15 ml. of ethanol at 0° was added 0.6 ml. of 10% potassium hydroxide solution and 0.07 ml. of methyl sulfate. Solid began to separate after 10 min., and the mixture then was kept at room temperature for 2 hr., diluted with water, acidified, and extracted with chloroform. The yellow solid obtained from the chloroform solution was reacetylated with acetic anhydride and the crude acetate was chromatographed on alumina. Crystallization of the first three fractions (79 mg.) from ether–hexane gave 55 mg. of glistening yellow flakes of IVb, m.p. 219°.

Anal. Calcd. for $C_{25}H_{34}N_2O_3$ (410.5): C, 73.14; H, 8.35; N, 6.82. Found: C, 73.16; H, 8.07; N, 6.55.

Steroids with Functional Sulfur Groups. IV.[1] The Isomerization of Some 2′-Methoxythiazolino[4′,5′:11α,9α]-11β-hydroxy Steroids

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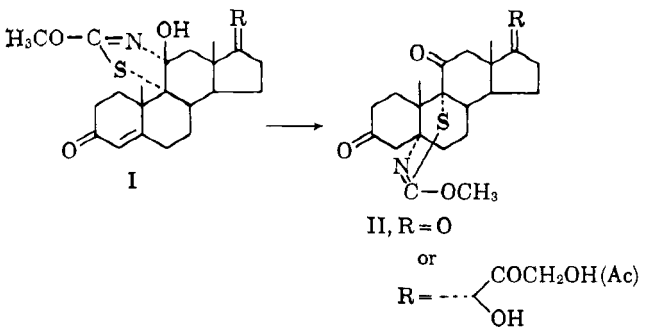
The effect of some modifications in ring A on the course of the rearrangement of 2′-methoxythiazolino[4′,5′:-11α,9α]-11β-hydroxy steroids to 2′-methoxydihydrothiazino steroids was studied. It was found that the α,β-unsaturated oxo system is the minimum requirement for such an isomerization. The Δ[1,4]-dien-3-one system led to the formation of a 2′-methoxydihydrothiazino[4′,5′,6′:1α,10,9α] steroid (X) and a 2′-methoxydihydrothiazino[4′,5′,6′:5α,10,9α] steroid (IX) in the ratio of 7:1.

In a preceding paper,[1c] we reported a novel isomerization reaction involving the rupture of the C–N bond at C-11 of the thiazoline ring and reattachment of the nitrogen bearing function to C-5 with the resultant formation of a dihydrothiazine ring as shown (I → II).



It had appeared to us that this isomerization required the presence of an α,β-unsaturated oxo system in certain proximity to the thiazolino moiety. This study is a partial attempt to define more precisely the scope and limitations of this rearrangement, particularly with respect to ring A of the steroid molecule.

As expected, attempts to rearrange the 3-oxo saturated derivative, 2′-methoxythiazolino[4′,5′:11α,9α]-5α-androstan-11β-ol-3,17-dione (VIIa), to the dihydrothiazino compound did not materialize, thus attesting to the necessity for the presence of unsaturation. The starting material VIIa was prepared from 9β,11β-epoxy-5α-androstane-3,17-dione (IVa) by a similar reaction sequence described previously[1c] for the preparation of I (R = O). Compound IVa was obtained by catalytic hydrogenation of 9β,11β-epoxy-Δ⁴-androstene-3,17-dione (III) over palladium–charcoal in ethyl acetate. The hydrogenation furnished a mixture of isomers whose separation was achieved by chromatography on alumina. As expected from the presence of an 11β-substituent,[3] the 5α isomer was shown to be the predominant product. VIIa, thus prepared, when refluxed in methanol for a period of 24 hr., remained unchanged; however, prolonged refluxing (6 days) yielded a negligible amount of unidentified substance as revealed by thin layer chromatography. When compound VIIa was refluxed in aqueous ethanolic potassium carbonate, 9α-methylthio-5α-androstane-3,11,17-trione (VIII) was formed in accordance with our earlier observation.[1c] A singlet peak at τ 8.05 in the n.m.r. spectrum corroborated[1c] this structural assignment. Further elaboration of the methylthio function to obtain the sulfoxide or sulfone derivative by oxidation with monoperphthalic acid[4] or with the pyridine chromic acid complex[5] failed. An attempt to obtain the 9α-thiocyano compound (VIa) with cyanogen bromide[6] was also unsuccessful.

That the double bond alone is also insufficient for isomerization was shown by the refractoriness of 2′-methoxythiazolino[4′,5′:11α,9α]-Δ⁴-androstene-3ξ,11β,17β-triol (VIIc) toward prolonged refluxing (6 days) with methanol. VIIc was prepared by the methanolysis of VIc.[1c] The requirement of an α,β-unsaturated oxo system for isomerization to the dihydrothiazine derivative thus becomes apparent.

It became of some interest to study the effect of a 1,4-dienone system upon the isomerization of the thiazoline moiety. Accordingly, 9β,11β-epoxy-Δ[1,4]-andro-

(1) (a) In remembrance of the late Dr. Erich Mosettig of this Institute; (b) part II, Y. Ueda and E. Mosettig, *Steroids*, **1**, 361 (1963); (c) part III, I. Kitagawa, Y. Ueda, T. Kawasaki, and E. Mosettig, *J. Org. Chem.*, **28**, 2228 (1963).

(2) Visiting Scientist (1961–1963), National Institutes of Health, under the sponsorship of the Cancer Chemotherapy National Service Center, National Cancer Institute; Faculty of Pharmaceutical Sciences, University of Tokyo, Tokyo, Japan.

(3) J. Pataki, G. Rosenkranz and C. Djerassi, *J. Biol. Chem.*, **195**, 751 (1952).

(4) R. E. Shaub and M. J. Weiss, *J. Org. Chem.*, **27**, 2221 (1962).

(5) D. Edwards and J. B. Stenlake, *J. Chem. Soc.*, 3272 (1954).

(6) J. von Braun and R. Murjahn, *Ber.*, **59**, 1202 (1926); J. von Braun and P. Engelbertz, *ibid.*, **56**, 1573 (1923).