Mikhailov[7] and Garst, et al.,[32] showed that solvation takes place in several ketyls. However, as the present experiments do not shed light on the degree of solvation of the metal-o-dimesitoylbenzene ketyl complex the solvating molecules are not shown in Figure 5.

Conclusions

Chelate ring formation with alkali metals has been studied since the earlier work of Sidgwick, et al.,[33] with acetylacetonates and benzoylacetonates to the recent results of da Silva[30] with complexones. The character of the bond between anion and alkali metal cation has been a subject of much controversy but the evidence offered, usually based on stability constants of the complexes, could not give a definite answer; current views consider these complexes to be electrostatically bonded.[7] Direct evidence, however, can be obtained when one of the ions is paramagnetic. In this case it is possible to observe unpaired electron

(32) J. Garst, D. Walmsley, C. Hervitt, W. Richards, and E. Zabolotny, J. Am. Chem. Soc., 86, 421 (1964).
(33) N. V. Sidgwick and F. M. Brewer, J. Chem. Soc., 127, 2379 (1925).

density at the nucleus or nuclei of the other ion. Copper(II) chelates of diamagnetic ligands have been studied by Wiersema and Windle.[34] For alkali metal cations we have to rely upon radical ligands. Chelate formation with a radical anion has been previously postulated by Luckhurst and Orgel[10] to explain the ion association between sodium ion and benzyl ketyl.

Complexes of the type studied here in which the ligand has been reduced by the alkali metal have a certain percentage of covalent bonding.

(34) A. K. Wiersema and J. J. Windle, J. Phys. Chem., 68, 2316 (1964).

Diazirines. I. Some Observations on the Scope of the Ammonia–Hydroxylamine-O-sulfonic Acid Diaziridine Synthesis. The Preparation of Certain Steroid Diaziridines and Diazirines

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Several steroidal diaziridines were prepared from the corresponding ketones by reaction with ammonia and hydroxylamine-O-sulfonic acid. Sharp selectivity was observed; reaction occurred with nonconjugated C-2 and C-3 ketones, but not with C-11, C-17, C-20, or conjugated C-3 ketones. Diazirines were prepared from diaziridines by facile oxidation using silver oxide. Unlike the diaziridines, the diazirines were found to be very stable, relatively nonpolar compounds. The pyrolysis of 3,3-azo-5α-androstan-17β-ol acetate at 135–145° afforded primarily 5α-androst-2-en-17β-ol acetate. 3,3-Azo-17α-methyl-5α-androstan-17β-ol showed a high anabolic–androgenic ratio when assayed according to the oral levator ani assay.

Substances containing a diaziridine (A) or diazirine (B) function[1] have been reported in the literature[2-4]

only recently, and the incorporation of either of these groups into a complex molecule has not been noted. Accordingly, we thought it of interest to attempt the synthesis of representative steroidal diaziridines and diazirines in order to shed light on the scope of the reaction and to determine the effect of these groupings on the biological activity of the parent molecule.
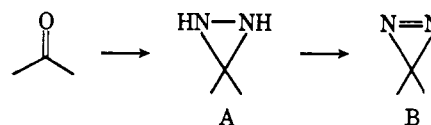
The synthetic procedures used in this work are modifications of those already reported[5] for the preparation of these systems and involve the treatment of a ketone successively with ammonia and hydroxylamine-O-sulfonic acid (or chloramine), affording the

(1) Since the terms "diaziridine" and "diazirine" refer to the three-membered rings, A and B, respectively, in their entirety, the nomenclature of the steroids having these groups as part of the skeleton becomes impossibly complex. For this reason, these terms will be used only when referring to the general class of three-membered rings containing two nitrogen atoms and the terms "hydrazi" and "azo" will refer only to the pair of singly or doubly bonded nitrogen atoms.

(2) (a) E. Schmitz, Angew. Chem., 71, 127 (1959); (b) H. J. Abendroth and G. Henrich, ibid., 71, 283 (1959); German Patent 1,082,889 (1960); (c) S. R. Paulsen, Belgian Patent 588,352 (1959).
(3) S. R. Paulsen, Angew. Chem., 72, 781 (1960); E. Schmitz and R. Ohme, ibid., 73, 115 (1961).
(4) E. Schmitz, "Advances in Heterocyclic Chemistry," Vol. 2, A. R. Katritzky, Ed., Academic Press Inc., New York, N. Y., 1963, p. 83.
(5) E. Schmitz and R. Ohme, Chem. Ber., 94, 2166 (1961).

Table I. Diaziridines and Diazirines

Product[a]	Yield, %[b]	M.p., °C.[c]	[α]D, deg.	Molecular formula	Anal., %					
					C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found
Diaziridines										
3,3-Hydrazi-5α-androstan-17β-ol acetate (I)[d]	68 (37) A	154–156	+14.4	$C_{21}H_{34}N_2O_2$	72.78	72.90	9.89	10.21	8.08	7.98
3,3-Hydrazi-5α-androstan-17β-ol (II)[d]	54 (20) B	149–151	+12.7	$C_{19}H_{32}N_2O$	74.95	74.67	10.60	10.63		
3,3-Hydrazi-17α-methyl-5α-androstan-17β-ol (V)[d]	56 (20) C	175–178	+1.0	$C_{20}H_{34}N_2O$	75.42	75.13	10.77	10.73		
3,3-Hydrazi-5β-androstan-17-one (X)[d]	53 (35) C	150–152	+112.6	$C_{19}H_{30}N_2O$	75.45	74.88	10.00	10.12	9.26	9.13
3,3-Hydrazi-17α-methyl-5α-androst-9(11)-en-17β-ol (XIII)[e]	f (32) D	192–196	−20.8	$C_{20}H_{32}N_2O$	75.89	75.40	10.20	10.31	8.85	8.79
Diazirines										
3,3-Azo-5α-androstan-17β-ol acetate (III)[d]	78 (42)[g,h] E	133.5–134.5	+16:4	$C_{21}H_{32}N_2O_2$	73.21	73.31	9.37	9:47	8.13	8 60
3,3-Azo-1α-methyl-5α-androstan-17β-ol acetate (IV)[i]	49 (23) F	120–121	−8.0	$C_{22}H_{34}N_2O_2$	73.43	72.73	9.82	9.83	7.81	7.25
3,3-Azo-17α-methyl-5α-androstan-17β-ol (VI)[d]	76 (61)[j] C	153–154	+1.4	$C_{20}H_{32}N_2O$	75.87	75.53	10.20	10.14	8.85	8.91
3,3-Azo-2α,17α-dimethyl-5α-androstan-17β-ol (VII)[k,l]	55 (39)[m] A	117–118	+3.9	$C_{21}H_{34}N_2O$	76.31	76.03	10.37	10.42	8.47	8.29
3,3-Azo-4α,17α-dimethyl-5α-androstan-17β-ol (VIII)[e,n]	68 (28) F	139.5–141	−28.2	$C_{21}H_{34}N_2O \cdot 0.5CH_3OH$	74.51	74.56	10.47	10.50	8.09	8.22
3,3-Azo-17α-methyl-5β-androstan-17β-ol (IX)[e]	25 (20) E	118–120	+2.0	$C_{20}H_{32}N_2O$	75.89	75.61	10.20	10.20	8.85	8.64
3,3-Azo-17α-ethyl-5α-estran-17β-ol (XI)[e]	47 (33) A	106–108	+24.6	$C_{20}H_{32}N_2O \cdot 0.5H_2O$[o]	73.79	73.54	10.22	10.42	8.61	8.44
2,2-Azo-5α-androstan-17β-ol acetate (XII)[p]	22 (10) A	153–155	+30.0	$C_{21}H_{32}N_2O_2$	73.21	72.50	9.37	9.63	8.13	8.24
3,3-Azo-17α-methyl-5α-androst-9(11)-en-17β-ol (XIV)[e]	72 (59) E	142–144	+6.5	$C_{20}H_{30}N_2O$	q		9.62	9.58	8.91	8.63
3,3-Azo-9α,11β-dichloro-17α-methyl-5α-androstan-17β-ol (XV)	f (65)[r] G	171–174	+36.2	$C_{20}H_{30}N_2Cl_2O \cdot 0.5H_2O$[o,s]	60.97	60.68	7.92	8.22		
3,3-Azoestr-5(10)-en-17-one (XVII)	31 (22)[t] A	117.5–119.5	+243.0	$C_{18}H_{24}N_2O$	76.01	75.53	8.51	8.15	9.85	9.93
3,3-Azo-5α-pregnan-20-one (XVIII)[d]	23 (12) C	142–143.5	+101.0	$C_{21}H_{32}N_2O$	76.77	76.82	9.82	10.06	8.53	8.55
3,3-Azoestr-5(10)-en-17β-ol (XIX)[u]	23 (17) H	94–97	+135.0	$C_{18}H_{26}N_2O$	75.48	76.10	9.16	9.45		
3,3-Azoestr-5(10)-en-17β-ol acetate (XX)	f (82)[v] J	114–115	+72.0	$C_{20}H_{28}N_2O_2$	73.13	73.09	8.59	8.74	8.53	8.82

[a] Footnotes in this column refer to the origin of the parent ketone. [b] Yields are calculated on the parent ketones, and are for good quality material obtained directly upon chromatographic separation. Yields in parentheses refer to material of analytical quality. Solvents of recrystallization are indicated by capital letters: A, methylene chloride–hexane; B, ethyl acetate–hexane; C, acetone–hexane; D, ethanol; E, hexane; F, methanol; G, acetone–petroleum ether; H, ether–petroleum ether; J, petroleum ether. [c] All melting points are with decomposition. [d] Article of commerce. [e] See Experimental. [f] Recrystallized directly without chromatography. [g] A series of experiments was carried out in which the times of reaction are compared to resulting yield of product as follows: contact time with methanolic ammonia (min.), reaction time with hydroxylamine-O-sulfonic acid (min.), yield chromatographed product (%): 20, 150, 36; 40, 270, 67; and 90, 240, 78. [h] In one run the oxime of 5α-dihydrotestosterone acetate was isolated and characterized as a by-product (m.p. 195–197°, mixture melting point with authentic oxime 195–197°). [i] German Patent 1,122,944 (1962). [j] Two experiments as in footnote g gave: 15, 210, 58; 120, 60, 76. [k] H. J. Ringold, E. Batres, O. Halpern, and E. Necoechea, J. Am. Chem. Soc., 81, 427 (1959). [l] N.m.r. 0.16 p.p.m. (doublet, J = 7 c.p.s., 2-CH₃). For the parent ketone, n.m.r. 0.98 p.p.m. (doublet, J = 7 c.p.s., 2-CH₃). [m] Two experiments as in footnote g gave: 15, 150, 37; 210, 60, 55. [n] N.m.r. 0.08 p.p.m. (doublet, J = 7 c.p.s., 4-CH₃). For the parent ketone, n.m.r. 0.98 p.p.m. (doublet, J = 7 c.p.s., 4-CH₃). [o] Evidence for hydrate is found in a weak to medium broad band at about 6 μ in the infrared spectrum. [p] R. L. Clark, J. Org. Chem., 28, 2626 (1963). [q] Satisfactory analysis for carbon could not be obtained. [r] Yield of product based on precursor, XIV. [s] Anal. Calcd. for Cl: 17.93. Found, 18.35. [t] Compound prepared from 17α-ethynyl-5α-estr-5(10)-en-17β-ol-3-one (see text). For an alternate unambiguous synthesis, see the Experimental section. [u] (a) H. L. Dryden, Jr., Gayle M. Webber, R. R. Burtner, and J. A. Cella, J. Org. Chem., 26, 3237 (1961); (b) N. A. Nelson and R. B. Garland, J. Am. Chem. Soc., 79, 6313 (1957). [v] Yield based on precursor XIX.

diaziridine A, which on oxidation (silver oxide) gives the diazirine B. Although the oxidation step appears to be a consistently smooth, high-yield reaction, formation of the steroid diaziridine in our experience often proceeds, if at all, in only moderate yields, and in addition is apparently subject to severe electronic and steric restrictions. Under the conditions used in this work, the only ketones found to be reactive were the nonconjugated 2(5α)- and 3(5α and 5β)-ketones. In contrast, Δ⁴-3-ketones (17α-ethylestr-4-en-17β-ol-3-one, testosterone, progesterone, and 1-dehydrotestosterone) as well as 17-ketones (estrone and androsterone), 20-ketones (progesterone, 5α-dihydroprogesterone, and cortisone-3-ketal), and 11-ketones (cortisone-3-ketal) were unreactive. These results are consistent with the order of steroid ketonic reactivity normally observed.[6] Further in this paper examples are given wherein molecules containing keto groups at C-3 (nonconjugated) as well as C-17 or C-20 undergo selective reaction at the former site. Although the presence of one adjacent methyl group at either C-2 or C-4 did not hinder formation of the diaziridine, an adjacent gem-dimethyl group (4,4-dimethylandrost-5-en-17β-ol-3-one acetate) prevented reaction. We have also found that diaziridine yields apparently are dependent on the reaction time of the ketone with ammonia (see footnotes g, j, and l in Table I), an observation which supports the hypothesis of a reaction pathway proceeding via a ketimine intermediate.[2a,7,8]

Diaziridines are basic and form salts, but they are also rather readily hydrolyzed in acid solution.[9] The diaziridines prepared in the course of this investigation were usually difficult to isolate in pure form. For this reason, extensive efforts were not expended toward this end. If after one or two attempts at isolation pure material could not be obtained, the crude diaziridine was oxidized directly to the corresponding diazirine, which was isolated readily in every case. The various diazirines and those diaziridines which could be characterized are presented in the table.

On the other hand, the diazirine function is surprisingly inert and stable[4]; acid[5] and alkali[10] have no effect on the group at room temperature. The polarity of the diazirine grouping as judged by the chromatographic behavior of steroids containing the group is quite low. Thus, on silica gel or alumina chromatography the parent ketone is eluted after the corresponding diazirine.

The ultraviolet absorption of these diazirines in methanol was characteristic, appearing at 350-352 and 366-370 mμ, both maxima having extinction coefficients

of 70-100. This contrasts with the reported ultraviolet absorption for diazirine itself of 321 mμ in methanol[4] and of a multiplet at 295-360 mμ (ε ~180), presumably determined in the gas phase.[11] An interesting observation concerning the effect of the diazirine grouping on the chemical shift of neighboring protons is discussed toward the conclusion of this paper.

The initial compounds prepared in this study were the diaziridine I and diazirine III derived from 5α-dihydrotestosterone acetate. These compounds exhibited interesting biological activity, the diaziridine showing potent androgenic properties combined with a low anabolic–androgenic ratio, whereas the diazirine reversed this effect and showed a high anabolic-androgenic ratio when assayed by the levator ani procedure[12] (subcutaneous route of administration). As anticipated, the corresponding 17α-methyl derivatives V and VI showed similar properties on oral administration. This observation concerning the effect of the diazirine group was of sufficient importance to warrant the preparation of a variety of related compounds. Accordingly, we prepared the 1α-, 2α-, and 4α-methyl diazirines IV, VII, and VIII, respectively, the 5β-derivative IX,[13] the 17α-ethyl-5α-estrane diazirine XI, and the 2-diazirine XII. The starting ketone in each case was either a literature compound or was synthesized by an established route.

For the preparation of ring-C-substituted analogs the Δ⁹(¹¹)-diazirine XIV was obtained via the diaziridine XIII. Reaction of the former with chlorine gave the 9,11-dichloro derivative XV; however, treatment of XIV with hypobromous acid failed to afford the 9α-bromo-11β-hydroxy compound.

Several attempts were made to synthesize the 3,3-azo derivative of the Δ⁵(¹⁰)-17α-ethynyl ketone XVI. The only diazirine-containing product isolated was the 17-ketone XVII. De-ethynylation is presumably base catalyzed[14] (cf. XVI, arrows) and therefore could occur during diaziridine formation (ammonia) or during the subsequent silver oxide treatment (excess sodium hydroxide present after in situ generation of silver oxide). Since infrared and chromatographic (very low R_f on silica gel t.l.c.) evidence obtained from the crude diaziridine preparation indicated that the ethynyl group was still intact, it was reasonably assumed that de-ethynylation occurred during silver oxide treatment. Although no other oxidants were investigated, several attempts were made to alter conditions (e.g., elimination of excess sodium hydroxide) in order to preserve the 17-ethynyl group, but none were successful and only varying yields (0-45%) of the 17-keto diazirine XVII were obtained.
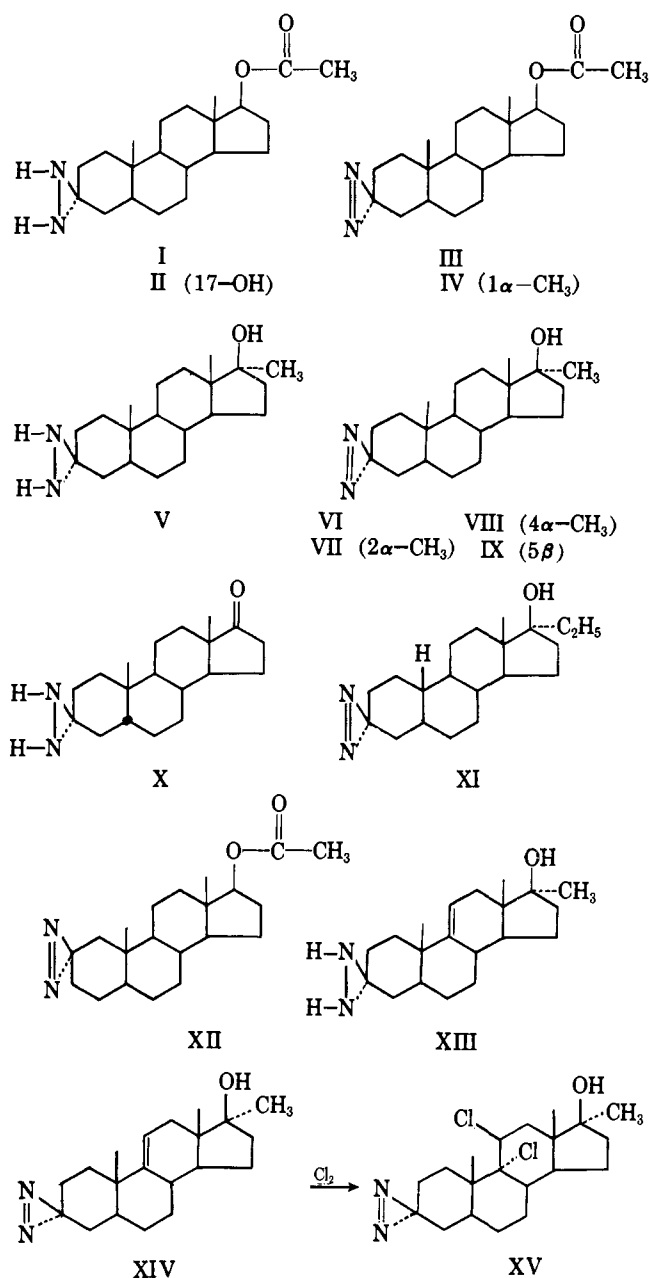
In order to establish unequivocally structure XVII for the de-ethynylated diazirine, estr-5(10)-en-17β-ol-3-one was converted to the corresponding diazirine XIX in 17% yield. Oxidation of the 17-alcohol to

(6) See H. J. E. Loewenthal, Tetrahedron, 6, 269 (1959), for leading references.

(7) In this connection note that diaziridines can be formed by reaction of Schiff bases with chloramine or hydroxylamine-O-sulfonic acid: E. Schmitz and R. Ohme, Chem. Ber., 95, 2012 (1962).

(8) An attempt was made to isolate the postulated unstable ketimine intermediate. Although from a methanolic ammonia solution of 17α-methyl-5α-androstan-17β-ol-3-one a crystalline substance was isolated which showed infrared absorption corresponding to a C=N linkage (6.08 μ) and an N—H function (3.05 μ), the 3-keto 5.83-μ band could never be completely eliminated. It is estimated that the material isolated was approximately 50% ketimine, the remainder being 3-ketone. This product lost ammonia rapidly on standing and after a few hours the infrared spectrum indicated the presence of 90% parent ketone.

(9) E. Schmitz and D. Habisch, Chem. Ber., 95, 680 (1962). Also see references cited in ref. 4.

(10) E. Schmitz and R. Ohme, Chem. Ber., 95, 795 (1962), and reference cited in ref. 4.

(11) H. M. Frey and I. D. R. Stevens, J. Chem. Soc., 3514 (1963).

(12) This assay is a modification of that reported by L. G. Hershberger, E. G. Shipley, and R. K. Meyer, Proc. Soc. Exptl. Biol. Med., 83, 175 (1953).

(13) An initial attempt to prepare IX via treatment of the 17-keto diaziridine X with methylmagnesium bromide failed (intractable tars). Diazirines are known to react with Grignard reagents to afford N-substituted diaziridines.[4,5,10]

(14) H. Langecker, Naturwiss., 46, 601 (1959). We thank Dr. J. P. Dusza for calling this reference to our attention.

I
II (17–OH)

III
IV (1α–CH₃)

V

VI   VIII (4α–CH₃)
VII (2α–CH₃) IX (5β)

X

XI

XII

XIII

XIV   XV

XVI   →   XVII

XVIII

XIX
XX (17–acetate)

the ketone afforded a product identical with that obtained from 17α-ethynylestr-5(10)-en-17β-ol-3-one (XVI). In addition, acetylation of the alcohol XIX gave the 17-acetoxy derivative XX.

The preparation of diaziridines from the $\Delta^{5(10)}$-3-ones is complicated by a competing rearrangement of the $\Delta^{5(10)}$-3-one system in the mildly basic medium to the conjugated Δ^4-3-ketone, which function is unreactive.

Submission of 5α-pregnane-3,20-dione to the usual sequence gave the 3,3-azo-20-one XVIII. The selective reaction of the keto group at C-3 over that at C-20 in the presence of excess reagents is noteworthy.

The effect of the diazirine grouping on the chemical shift of certain nearby protons is of interest. A recent report[15] describes the striking difference in chemical shift between the geminal axial and equatorial protons (H_a and H_e) adjacent to the diazirine ring in 1,1-azo-4-methylcyclohexane (C) (1.32 p.p.m. at $-50°$) and in 3,3-azo-8-thiabicyclo[3.2.1]octane (D) (1.57

(15) J. J. Uebel and J. C. Martin, *J. Am. Chem. Soc.*, **86**, 4618 (1964).
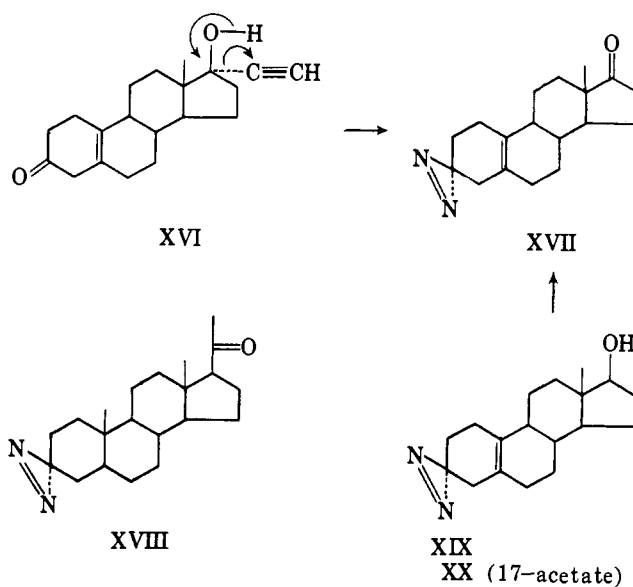
p.p.m.). This phenomenon is attributed to the shielding effect on the equatorial proton by the large magnetic anisotropy associated with the diazirine grouping.

C   D
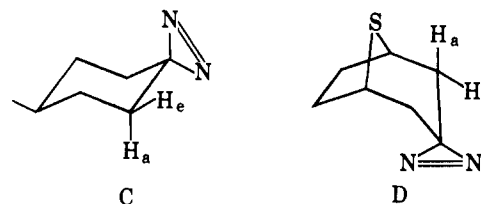
We have observed a similar effect on the ring-A equatorial methyl protons (β to the diazirine ring, as opposed to the α-proton examples, C and D) in 3,3-azo-2α,17α-dimethyl-5α-androstan-17β-ol (VII) and 3,3-azo-4α,17α-dimethyl-5α-androstan-17β-ol (VIII), relative to the methyl protons in the parent 2- and 4-methyl-3-ketones. The protons signals for these methyl groups are centered at 0.16 and 0.08 p.p.m., respectively (doublets, $J = 7$ c.p.s.), representing an unusually large upfield shift of 0.82 and 0.90 p.p.m.[16]


VII   VIII
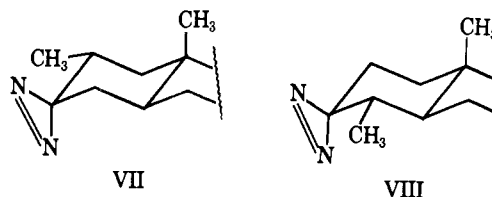
An important property of diazirines is their ability on pyrolysis to liberate nitrogen and what is apparently a singlet-state carbene.[18] We have investigated this reaction with several of the diazirines reported herein and have found, for example, that pyrolysis of III affords a good yield of 5α-androst-2-en-17β-ol acetate (XXI), a not unexpected course of reaction for a steroid A-ring carbene.[11,19]

(16) When VII is compared to the corresponding 3-deoxy compound, 2α,17α-dimethyl-5α-androstan-17β-ol,[17] the upfield shift of the methyl resonance is about 0.70 p.p.m.

(17) A. D. Cross, J. A. Edwards, J. C. Orr, B. Berköz, L. Cervantes, M. C. Calzada, and A. Bowers, *J. Med. Chem.*, **6**, 162 (1963).

(18) See H. M. Frey and I. D. R. Stevens, *Proc. Chem. Soc.*, 79 (1962), for pyrolysis of diazirine and the stereospecific insertion of the resulting methylene into *trans*-2-butene; also H. M. Frey and I. D. R. Stevens, *J. Chem. Soc.*, 3865 (1962), for pyrolysis of dimethyldiazirine to propene.

III → [structure] → XXI
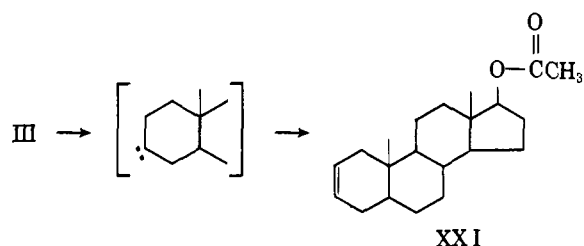
Further information concerning the reactions of steroid carbenes formed on pyrolysis of the corresponding diazirines will be the subject of a future report.

Biological Evaluation. Of the diazirines prepared in this study, the most interesting, according to the oral levator ani assay (rat),[12] remained the original 17-methyl derivative VI. This diazirine had an anabolic potency approximately three times that of 17-methyltestosterone and an androgenic potency (ventral prostrate) about one-fifth that of the same standard. Further evaluation of this interesting compound is in progress.

Experimental

General. Melting points were taken on a Mel-Temp apparatus in open capillary tubes and are corrected. Optical rotations were determined at 25° in chloroform solution at 0.5–1.2% concentrations. Ultraviolet spectra were measured in methanol solution on a Cary recording spectrophotometer (Model 14), and infrared spectra were determined in pressed potassium bromide disks on a Perkin-Elmer spectrophotometer (Model 21). N.m.r. spectra were obtained on a Varian Model A-60 spectrometer in deuteriochloroform solution using tetramethylsilane as internal standard. Solutions were dried with anhydrous sodium sulfate and evaporations were carried out at reduced pressure. The petroleum ether used was that fraction boiling at 30–60°.

3,3-Hydrazi-17α-methyl-5α-androstan-17β-ol (V). General Procedure for Preparation of Steroid Diaziridines. The following procedure is illustrative. A solution of 502 mg. of 17α-methyl-5α-androstan-17β-ol-3-one in 50 ml. of methanol was treated at 0–2° with ammonia for 2 hr. (to saturation). The ammonia addition was stopped and 236 mg. of hydroxylamine-O-sulfonic acid was added in about ten small portions over a 10-min. period. The mixture was stirred for 1 hr. at 0–10° and diluted with 150 ml. of ice water. The solution was extracted with three 30-ml. portions of methylene chloride, the extracts were combined and dried, and the solvent was evaporated. The residue (536 mg.) was oxidized without further purification.

In several cases the product diaziridine was chromatographed on silica gel. After elution with ether-benzene solvent mixtures to remove the parent ketone and the by-products (oximes), the diaziridines were eluted using various concentrations of methanol in ether, and were usually obtained after solvent evaporation as a powdery solid. In the infrared these diaziridines exhibit a characteristic band at 3.09–3.11 μ.

The diaziridines which could be characterized are shown in Table 1.

3,3-Azo-17α-methyl-5α-androstan-17β-ol (VI). General Procedure for the Silver Oxide Oxidation of Diaziridines to Diazirines. The following procedure is illustrative. A solution of 506 mg. of crude 3,3-hydrazi-17α-methyl-5α-androstan-17β-ol (V) and 2.0 ml. (2.0 mmoles) of 1.0 N aqueous silver nitrate solution in 25 ml. of methanol was stirred rapidly while 0.8 ml. (2.0 mmoles) 2.5 N aqueous sodium hydroxide was added over a 10-min. period. The black mixture was stirred for 30 min. at room temperature and filtered through Celite[20] diatomaceous silica. The filtrate was diluted with 300 ml. of water and extracted with several 30-ml. portions of methylene chloride. The extracts were combined and dried, and the solvent was evaporated. The residue was chromatographed on 30 g. of silica gel and the product (398 mg.) was eluted using 2% ether in benzene. Recrystallization from hexane afforded 320 mg. of product.

Diazirines exhibit characteristic maxima in the ultraviolet spectra at 350–352 mμ (ε 70–90) and 366–370 mμ (ε 75–100) and characteristic infrared absorption at 6.32–6.35 μ.

The various diazirines obtained are listed in Table I.

4α,17α-Dimethyl-5α-androstan-17β-ol-3-one. To a solution of 480 mg. of lithium in 300 ml. of liquid ammonia was added a solution of 8.0 g. of 17-methyltestosterone in 70 ml. of tetrahydrofuran (distilled from lithium aluminum hydride).[21] The thick mixture slowly became white near the end of the addition. Methyl iodide (10 ml.) was added and the thick mixture rapidly became clear and colorless. Stirring was continued for 2 hr.; 50 ml. of ether was added and the ammonia was allowed to evaporate overnight at atmospheric pressure. To the residue was added 100 ml. of ether and 200 ml. of water; the mixture was shaken well and the layers were separated. The aqueous layer was extracted with ether; all organic portions were combined, washed with water and saturated aqueous sodium chloride, and dried. The solvent was evaporated and the residue (crystalline) was dissolved in acetone. The actone solution was concentrated to about 25 ml. and approximately 150 ml. of petroleum ether was added. The resulting crystalline precipitate (possibly a dimer) was filtered off and the filtrate was evaporated. The residue was recrystallized from acetone–water to yield 5.33 g. of pale yellow crystals, nearly homogeneous by t.l.c. One further recrystallization from acetone–water afforded a sample melting at 156–158° (mixture melting point with 2α,17α-dimethyl-5α-androstan-17β-ol-3-one 122–126°, and with 17α-methyl-5α-androstan-17β-ol-3-one 147–180°); [α]D −14.3°; λmax 2.92, 5.84, 8.58, and 10.60 μ (lit.[22] m.p. 154–156°).

17α-Methyl-5β-androstan-17β-ol-3-one. A solution of 2.86 g. (9.4 mmoles) of 17α-methyl-5β-androstane-3β,17β-diol[23] in 200 ml. of acetone was cooled to 0°

(19) The pyrolysis of diazocyclohexane gives a 100% yield of cyclohexene: L. Friedman and H. Shechter, *J. Am. Chem. Soc.*, **83**, 3159 (1961).

(20) Celite is the trademark of Johns-Manville Co. for diatomaceous earth silica products.

(21) R. E. Schaub and M. J. Weiss, *Chem. Ind.* (London), 2003, (1961); G. Stork, P. Rosen, and N. L. Goldman, *J. Am. Chem. Soc.*, **83**, 2965 (1961).

(22) British Patent 874,142 (1960).

(23) German Patent 875,516 (1953).

in ice–salt and Jones reagent[24] (chromic acid in sulfuric acid) was added dropwise. When approximately 2.5 ml. (2.0 equiv.) had been added, the characteristic yellow color of the oxidant persisted. Isopropyl alcohol (1 ml.) was added to discharge the color; the mixture was diluted with 900 ml. of water and then extracted with several portions of ether. The extracts were combined, washed with saturated aqueous sodium chloride, and dried. The solvent was evaporated and the residue was chromatographed on 120 g. of alumina. The product (2.29 g.) was eluted in 25% ether in benzene and was recrystallized from acetone–hexane to yield 1.99 g. of colorless platelets, m.p. 82–85°; $[\alpha]_D$ +6.2°; λ_{max} 2.92, 5.85, 7.28, and 8.75 μ.

Anal. Calcd. for $C_{20}H_{32}O_2$: C, 78.89; H, 10.60. Found: C, 78.72; H, 11.09 (lit.[25] $[\alpha]^{25}D$ +3° (CHCl₃), and a double m.p., 74–76° and 119–121°, from petroleum ether on a Köfler stage).

17α-Ethyl-5α-estran-17β-ol-3-one. To a solution of 210 mg. of lithium in 200 ml. of liquid ammonia was added 2.820 g. of 17α-ethylestr-4-en-17β-ol-3-one in 30 ml. of tetrahydrofuran. The blue solution was stirred for 0.5 hr. and 5 g. of ammonium chloride was added. The ammonia was evaporated and 100 ml. of water was added. The layers were separated and the aqueous phase was extracted with ether. The organic phases were combined, washed with water and saturated aqueous sodium chloride, and dried. The solvent was evaporated and the residue was recrystallized from methanol to give 1.848 g. of product, m.p. 206–209°. Recrystallization from methanol afforded an analytical sample, m.p. 209–211°; $[\alpha]_D$ +34.6°; λ_{max} 2.94, 5.87, 7.73, and 10.25 μ.

Anal. Calcd. for $C_{20}H_{32}O_2 \cdot 0.25CH_3OH$: C, 77.83; H, 10.64. Found: C, 77.81; H, 10.73.

17α-Methyl-5α-androst-9(11)-en-17β-ol-3-one. To a solution of 431 mg. of lithium in 125 ml. of liquid ammonia was added a solution of 1.921 g. of 17α-methylandrosta-4,9(11)-dien-17β-ol-3-one in 200 ml. of ether. The mixture was stirred for 1.5 hr. and 10 g. of ammonium chloride was added to discharge the color. The mixture was allowed to warm to room temperature to evaporate the ammonia and 300 ml. of water was added. The mixture was stirred well, the layers were separated, the aqueous layer was extracted with ether, and all organic portions were combined. The solution was dried and the solvent was evaporated. The residue (exhibiting only slight absorption at 5.83 μ) was dissolved in 100 ml. of acetone, cooled to 0°, and 2.0 ml. of Jones reagent[24] was added over a 20-min. period. The yellow-green mixture was stirred for 15 min. and diluted with 700 ml. of water. The mixture was saturated with salt and extracted with ether. The extracts were combined, washed with saturated aqueous sodium chloride, and dried, and the solvent was evaporated. The residue was recrystallized from acetone to give 1.140 g. of product. The analytical sample, recrystallized from methylene chloride–petroleum ether, had m.p. 192–194°; $[\alpha]_D$ 0°; λ_{max} 2.93, 5.90, 6.03 (shoulder), 10.55, and 10.67 μ.

Anal. Calcd. for $C_{20}H_{30}O_2 \cdot 0.5H_2O$: C, 77.11; H,

10.03; H₂O, 2.98. Found: C, 77.18; H, 10.10; H₂O, 3.22 (Karl Fischer).

3,3-Azo-9α,11β-dichloro-17α-methyl-5α-androstan-17β-ol (XV). Chlorine was bubbled through a solution of 96 mg. of 3,3-azo-17α-methyl-5α-androst-9(11)-en-17β-ol (XIV) and 0.5 ml. of pyridine in 5 ml. of chloroform for 45 sec. and the solution was allowed to stand for 30 min. at room temperature. The yellow solution was diluted with 50 ml. of methylene chloride, the resulting precipitate was filtered, and the filtrate was washed with 10% aqueous sodium thiosulfate, 8% aqueous sulfuric acid, 10% aqueous sodium bicarbonate, and saturated aqueous sodium chloride, and dried. The solvent was evaporated and the residue was recrystallized from acetone–petroleum ether to afford 78 mg. of product: m.p. 171–174° dec.; λ_{max} 2.96, 6.15 (broad), 6.33, 10.30, and 10.68 μ; 282 (ϵ 410), 350 (ϵ 170), and 365 mμ (ϵ 150); for further characterization see Table I.

3,3-Azoestr-5(10)-en-17-one (XVII). A solution of 18 mg. of 3,3-azoestr-5(10)-en-17β-ol (XIX) in 1 ml. of acetone was cooled to 0° (ice–salt) and 0.01 ml. of Jones reagent[24] was added. The solution was stirred for 3 min. at 0° and diluted with 15 ml. of ice water, and the aqueous mixture was extracted with methylene chloride and ether. The extracts were combined and dried, and the solvent was evaporated. The oily residue was chromatographed on 2.5 g. of alumina. The product (crystalline, nearly homogeneous by t.l.c.) was eluted in 200 ml. of 25% benzene in petroleum ether. Recrystallization from hexane afforded a product, m.p. 116–118°; mixture melting point with the material obtained by treatment of the 17α-ethynyl derivative in the usual manner (XVI → XVII) was 116–118°. The infrared spectra and the R_f on t.l.c. of the two samples were identical.

3,3-Azoestr-5(10)-en-17β-ol Acetate (XX). A solution of 100 mg. of 3,3-azoestr-5(10)-en-17β-ol (XIX) and 0.1 ml. of acetic anhydride in 1 ml. of pyridine was allowed to stand at room temperature for 18 hr. The solution was diluted with 10 ml. of water and extracted with four small portions of ether. The extracts were combined, washed with 30 ml. of 4% sulfuric acid in two portions and saturated aqueous sodium bicarbonate, and dried. The solvent was evaporated and the residue was recrystallized from petroleum ether to m.p. 114–115° dec.; λ_{max} 5.75, 6.32, 8.00, 9.55, and 9.76 μ; for further characterization see Table I.

Pyrolysis of 3,3-Azo-5α-androstan-17β-ol Acetate (III). Formation of 5α-Androst-2-en-17β-ol Acetate (XXI). A sample of 3,3-azo-5α-androstan-17β-ol acetate (III) (224 mg.) was heated under nitrogen at 140° for 5 min. Upon cooling, the liquid crystallized readily. (In a pilot experiment 72 mg. of III gave 65 mg., m.p. 85–89°, at this stage.) Recrystallization from methanol afforded 69 mg. of fine white needles, m.p. 96.5–97.5°; $[\alpha]_D$ +48°; λ_{max} 5.76, 6.06, 8.15, 9.65, 9.84, and 14.85 μ; λ_{max} 202 mμ (ϵ 730); n.m.r. 5.64 (doublet, J = 2 c.p.s., 2 protons, H—C₂=C₃—H), 4.60 (triplet, J = 7 c.p.s., 1 proton, C₁₇-H), 2.03 (singlet,

$$\overset{O}{\underset{\|}{}}$$

3 protons, O—C—CH₃), and 0.81 and 0.79 p.p.m. (both singlets, 6 protons, C₁₈—H₃, C₁₉—H₃).

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Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.69; H, 10.13. Found: C, 79.40; H, 10.33.

Reported for the Δ^2-derivative[26] m.p. 95–96°; $[\alpha]_D$ 49°; λ_{max} 5.75, 6.03, and 14.81 μ. The Δ^3-derivative[27] had m.p. 117–118°; $[\alpha]_D$ 42°; $\lambda_{max}^{CHCl_3}$ 6.07 μ; $\lambda_{max}^{CS_2}$ 12.94, 13.60, and 14.90 μ; the Δ^4-derivative[28] showed

m.p. 111–113°, $[\alpha]_D$ +71°; $\lambda_{max}^{mineral\ oil}$ 5.70, 8.01, 9.53, and 9.74 μ.

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Organic Polymers. Correlation between Their Structure and Catalytic Activity in Heterogeneous Systems. I. Pyrolyzed Polyacrylonitrile and Polycyanoacetylene

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Contribution from the Plastics Research Laboratory, Polymer Department, The Weizmann Institute of Science, Rehovoth, Israel. Received November 4, 1964

Polyacrylonitrile which is pyrolyzed in the presence of oxygen, and is assumed to contain systems of condensed pyridine rings,[2] is shown to be a strong hydrogen acceptor, being capable of dehydrogenating olefinic compounds in the vapor phase at elevated temperatures. The polymer becomes hydrogenated in the course of the process, and its activity decreases, but it can be restored by air oxidation at 140°. If the process is carried out in the presence of air, the polymer acts as an active dehydrogenation catalyst. It also causes double bond shifts and cis–trans isomerizations in olefinic systems. With the help of model compounds, the mechanism of the hydrogen transfer from substrate to catalyst surface is studied and is shown to occur partly in the form of a hydrogen atom and partly in the form of a hydride ion. The ability of pyrolyzed polymer to be reduced and to be reoxidized under mild conditions is shown to be a function of its proposed chemical structure. Comparison with other carbonaceous materials shows that pyrolyzed polyacrylonitrile and the structurally similar polycyanoacetylene behave in a specific way toward olefinic hydrocarbons. It is also shown, by using model compounds, that the transfer of an allylic hydrogen to several commercial dehydrogenation catalysts occurs exclusively in the form of a hydrogen atom.

Introduction

In recent years many polymers have been synthesized, stable at high temperatures,[3a] which show interesting physical properties such as semiconductivity and give significant signals in electron spin resonance spec-troscopy.[3b] Their catalytic activity in a heterogeneous system has been studied for the decomposition of hydrogen peroxide[4] and formic acid,[5,6] autoxidations,[6,7] dehydrogenations and dehydrations,[6,8,9] and the de[9] composition of hydrazine and nitrogen oxide.[6,8] The purpose of most of these studies has been to find a correlation between physical properties and catalytic activity, which has also been widely attempted for inorganic catalysts.[10]

In the present paper the first results are described of a study, whose purpose can be said to be threefold: (1) to find a correlation between catalytic activity and the *chemical* structure of the polymer, which might throw more light on the phenomenon of heterogeneous catalysis in general; (2) to obtain information about the structure of the polymer from its behavior with respect to chemical reactions; (3) to find ways of synthesizing specific organic catalysts which might resemble those used in industrial, high-temperature applications as well as those encountered in biochemical systems.

Pyrolyzed polyacrylonitrile has been chosen as the first polymer because its structure has been studied to some extent.[2]

As the structure proposed for pyrolyzed polyacrylonitrile can be synthesized in principle by the polymerization and heat treatment of cyanoacetylene in the absence of air, this monomer has been polymerized

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