and distilled. After removing the solvent and a small forerun, 1.5 g. liquid was obtained, b.p. 96° (12 mm.). The infrared spectrum showed major bands at 3065, 3040, 1585, 1575, 1485, 1230, 1185, 1046, 1015, 1010, 800, and 700 cm.$^{-1}$.

Anal. Calcd. for C_8H_9NO: C, 71.09; H, 6.71; N, 10.36; O, 11.84. Found: C, 70.77; H, 6.80; N, 10.05; O, 12.74.[7]

Picrate.—This was prepared from 3-allyloxypyridine with ethanolic picric acid, and the solution was diluted with water. It was recrystallized from absolute ethanol giving yellow crystals, m.p. 56–58°.

Anal. Calcd. for $C_{14}H_{12}N_4O_8$: C, 46.16; H, 3.32; N, 15.38. Found: C, 46.31; H, 3.29; N, 15.20.

Steroidal Heterocycles. VIII.[1] Metal–Ammonia Reduction of Δ^4-Steroidal [3,2-*c*] Pyrazoles

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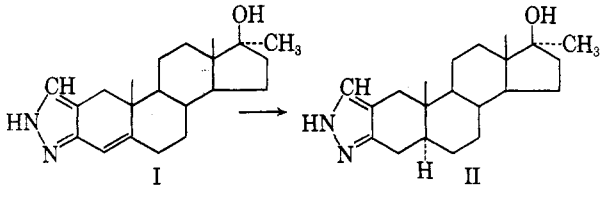
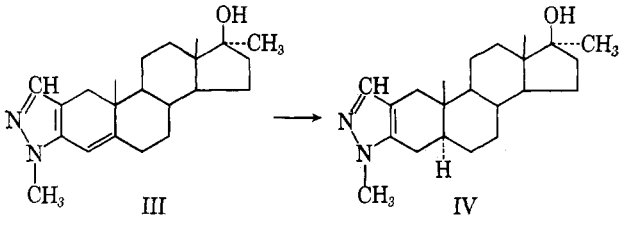
In our investigations of steroidal pyrazoles an alternate route to 5α-steroidal [3,2-*c*]pyrazoles[2] was desired. Since Δ^4-steroidal [3,2-*c*]pyrazoles were readily available,[2] reduction of these compounds to the corresponding 5α-derivatives appeared attractive. Catalytic hydrogenation has been shown to afford primarily the 5β-isomers.[3] Metal–ammonia reduction was then considered, since the product, if the pyrazole ring remained intact, might be expected to be the 5α-isomer by analogy with the reduction of steroidal Δ^4-3-ones[4] and other conjugated systems.[5]

Treatment of 17β-hydroxy-17α-methylandrost-4-eno-[3,2-*c*]pyrazole (I)[2a] with sodium or lithium in liquid ammonia–tetrahydrofuran–ethanol afforded 17β-hydroxy-17α-methylandrostano[3,2-*c*]pyrazole (II),[2a] the saturated A/B-*trans* compound, in 62 to 76% yield.



No reduction of the pyrazole ring or formation of the 5β isomer was detected; apparently only unchanged pyrazole I contaminated the crude product. Pyrazole II was recovered unchanged when treated under the same conditions.

Two factors may be responsible for the nonreduction of the pyrazole ring: (1) the "aromatic" pyrazole ring, which is more electronegative than the aryl ring (reduced under the conditions used[6]), is more resistant to electron addition, considered to be the initial step of the reductive process[7]; (2) metal salt formation may prevent reduction of the ring. The second possibility can not be the major factor since the N-methyl derivative of I, 17β-hydroxy-17α-methylandrost-4-eno[3,2-*c*]-2′-methylpyrazole (III),[2b] which has no acidic hydrogen, is reduced in 75% yield to the N-methyl derivative of II, 17β-hydroxy-17α-methylandrostano[3,2-*c*]-2′-methylpyrazole (IV)[2b] with lithium–ammonia–*t*-butyl alcohol (see Experimental). Pyrazole IV can be recovered in 75% yield when treated under the same conditions (thin layer chromatographic examination of the mother liquors show some decomposition products along with additional quantities of pyrazole IV).[8] Similar results have been obtained with pyrrole and 1-methylpyrrole.[9]



The 4,5-double bonds in pyrazoles I and III are probably reduced in a manner similar to the reduction of styrene-type double bonds.[10]

Experimental[11]

Reduction of 17β-Hydroxy-17α-methylandrost-4-eno[3,2-*c*]-pyrazole (I).—To a solution of 10.00 g. of 17β-hydroxy-17α-methylandrost-4-eno[3,2-*c*]pyrazole [m.p. 248.4–257.4°; $[\alpha]_D$ +134° (pyridine); λ_{max} 261 mμ (ϵ 10,600)[2a]] in 300 ml. of tetrahydrofuran (distilled from calcium hydride) and 300 ml. of liquid ammonia, was added 20 g. of sodium in portions during 5 min. with stirring at reflux. Two layers formed: a bronze colored upper layer and a gray opaque lower layer. The mixture was stirred at reflux for 1 hr. Ethanol (100 ml.) was added in 15 min. The mixture was stirred at reflux for an additional 6 hr. (upper bronze layer still present), then allowed to warm to room temperature overnight. The colorless mixture was concentrated under reduced pressure to about 200 ml. and then poured with stirring into 1500 ml. of ice–water. The mixture was filtered to yield light yellow crystals, m.p. 157–165°; partially resolidified, m.p. <215°; λ_{max} 223 mμ (ϵ 4600), 260 mμ (ϵ 130). Two recrystallizations from ethanol afforded 6.38 g. (63%) of fine colorless prisms (dried *in vacuo* at 120° for 20 hr.); m.p. 232–241°; $[\alpha]_D$ +34.9° (chloroform); λ_{max} 223 mμ (ϵ 4710).[2a]

(1) Paper VII: A. J. Manson, F. W. Stonner, H. C. Neumann, R. G. Christiansen, R. L. Clarke, J. H. Ackerman, D. F. Page, J. W. Dean, D. K. Phillips, G. O. Potts, A. Arnold, A. L. Beyler, and R. O. Clinton, *J. Med. Chem.*, **6**, 1 (1963).

(2) (a) R. O. Clinton, A. J. Manson, F. W. Stonner, A. L. Beyler, G. O. Potts, and A. Arnold, *J. Am. Chem. Soc.*, **81**, 1513 (1959); (b) R. O. Clinton, A. J. Manson, F. W. Stonner, H. C. Neumann, R. G. Christiansen, R. L. Clarke, J. H. Ackerman, D. F. Page, J. W. Dean, W. B. Dickinson, and C. Carabateas, *ibid.*, **83**, 1478 (1961).

(3) (a) R. O. Clinton, R. L. Clarke, F. W. Stonner, D. K. Phillips, K. F. Jennings, and A. J. Manson, *Chem. Ind.*, 2099 (1961); (b) R. O. Clinton, R. L. Clarke, F. W. Stonner, A. J. Manson, K. F. Jennings, and D. K. Phillips, *J. Org. Chem.*, **27**, 2800 (1962).

(4) D. H. R. Barton, D. A. J. Ives, and B. R. Thomas, *J. Chem. Soc.*, 903 (1954).

(5) D. H. R. Barton and C. H. Robinson, *ibid.*, 3045 (1954).

(6) H. L. Dryden, Jr., G. M. Webber, R. B. Burtner, and J. A. Cella, *J. Org. Chem.*, **26**, 3237 (1961).

(7) A. J. Birch, *Quart. Rev.* (London), **4**, 69 (1950).

(8) 1-Arylpyrazoles are reduced with sodium and alcohol to 1-arylpyrazolines or ring-opened products [T. L. Jacobs, "Heterocyclic Compounds," Vol. 5, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1957, pp. 104–105]. In this case the aryl ring apparently increases the electrophilic character of the pyrazole enough to make it susceptible to electron attack.

(9) S. O'Brien and D. C. C. Smith, *J. Chem. Soc.*, 4609 (1960).

(10) Isolated double bonds are not reduced with metals and amines, except under forcing conditions. For a discussion of the factors influencing metal–amine reductions, see ref. 7 and A. J. Birch and H. Smith, *Quart. Rev.* (London), **12**, 17 (1958).

(11) All melting points are corrected. Optical rotations were determined as 1% solutions at 25°. Ultraviolet spectra were determined on a Cary spectrophotometer. Nuclear magnetic resonance spectra were determined on a Varian A-60 spectrometer using tetramethylsilane as external standard.

From the mother liquors the following additional crops were obtained after treatment with activated carbon and several recrystallizations from ethanol: 1.18 g., m.p. 152–155°; resolidified, m.p. 224–245°, λ_{max} 223 mμ (ε 4650), 260 mμ (ε 96); 0.37 g., m.p. 153–157°; resolidified, m.p. 227–243°; 0.47 g., m.p. 207–242°.

Reduction using lithium instead of sodium afforded 76% of the pure pyrazole II.

17β-Hydroxy-17α-methylandrost-4-eno[3,2-*c*]-2′-methylpyrazole (III).[2b]—To a solution of 4.00 g. of 2-hydroxymethylene-17α-methylandrost-4-en-17β-ol-3-one, m.p. 179–180°,[12] in 350 ml. of ethanol was added a solution of 7.36 g. of sodium acetate trihydrate and 3.50 g. of methylhydrazine sulfate in 50 ml. of water. After the mixture was stirred and refluxed for 3.5 hr., it was concentrated under reduced pressure to a small volume and poured into 300 ml. of cold water. The mixture was filtered and the collected white solid was recrystallized from acetonitrile to yield 2.65 g. of light yellow crystals, m.p. 202–205°. Three additional recrystallizations from benzene–acetonitrile afforded 1.40 g. of fine cream colored plates, m.p. 203.6–205.8°; $[\alpha]_D$ +123.4° (chloroform); λ_{max} 219 (ε 11,100), 250 sh (ε 6300), 278 mμ (ε 10,500); δ p.p.m. (20%, $CDCl_3$), 1.45 ($C_{18}CH_3$), 1.50 ($C_{19}CH_3$), 1.77 (CH_3 at C-17), 4.30 (N–CH_3), 6.55 (–C–CH=), 7.72 (–N–CH=).

Anal. Calcd. for $C_{22}H_{30}N_2O$: C, 77.60; H, 9.47; N, 8.23. Found: C, 77.45; H, 9.33; N, 8.49.

Thin layer chromatography (2% methanol in chloroform) showed only one spot as detected by iodine, sulfuric acid, followed by heat. The previously reported sample [m.p. 175.2–193.2°; $[\alpha]_D$ +103.6° (chloroform); λ_{max} 272 mμ (ε 10,400)[2b]] was apparently a mixture of the 1′-methyl- and 2′-methylpyrazoles. The compound, whose preparation is described here, is now believed to be the 2′-methyl isomer rather than the 1′-methyl isomer because of its reduction to the known 5α-2′-methylpyrazole IV[2b] (see next paragraph). Its ultraviolet spectrum compared favorably with the spectrum [λ_{max}^{MeOH} 277.5 mμ (ε 10,200)] of 17α,20;20,21-bismethylenedioxy-11β-hydroxy-2′,16α-dimethyl-4-pregneno[3,2-*c*]pyrazole.[13]

Reduction of 17β-Hydroxy-17α-methylandrost-4-eno[3,2-*c*]-2′-methylpyrazole (III).—To a solution of 100 mg. of 17β-hydroxy-17α-methylandrost-4-eno[3,2-*c*]-2′-methylpyrazole (III), m.p. 203.6–205.8°, in 25 ml. of dry tetrahydrofuran and 35 ml. of dry *t*-butyl alcohol and 50 ml. of liquid ammonia was added 150 mg. of lithium wire. The dark blue mixture with bronze liquid floating on top was stirred and refluxed for two hours. The mixture turned colorless in 1.5 hr. Methanol (10 ml.) was added and the ammonia was allowed to evaporate. The mixture was concentrated to dryness under reduced pressure and the residue was taken up in ethyl acetate–water. The organic layer was washed with water and saturated sodium chloride solution and filtered through anhydrous sodium sulfate. Concentration of the solution under reduced pressure afforded colorless crystals, m.p. 217–222°. Recrystallization from acetone afforded 75 mg. of colorless flakes, m.p. 221.4–222.2°; $[\alpha]_D$ +37.6° (ethanol); λ_{max} 229 mμ (ε 4800); δ p.p.m. (10%, $CDCl_3$), 1.25 ($C_{18}CH_3$), 1.40 ($C_{19}CH_3$), 1.75 (CH_3 at C-17), 4.25 (–N–CH_3), 7.79 (–N=CH–).

Anal. Calcd. for $C_{22}H_{34}N_2O$: C, 77.14; H, 10.01. Found: C, 77.13; H, 10.08.

Thin layer chromatography (2% methanol in chloroform) showed only one spot as detected by iodine, sulfuric acid, followed by heat. The previously reported sample,[2b] prepared by the pyrolysis of the N-methylsemicarbazone of 2-hydroxymethylene-17α-methylandrostan-17β-ol-3-one [m.p. 186.6–198.0°, $[\alpha]_D$ +38.3° (EtOH), λ_{max} 229 mμ (ε 4900)] was apparently a mixture of mostly the 2′-methylpyrazole contaminated with the 1′-methylpyrazole. An examination of the n.m.r. spectrum of this sample (in chloroform, internal tetramethylsilane standard) shows two N-methyl peaks at 3.77 and 3.80 p.p.m. in a 3:2 ratio.

(12) H. J. Ringold, E. Batres, O. Halpern, and E. Necoechea, *J. Am. Chem. Soc.*, **81**, 427 (1959).

(13) R. Hirschmann, N. G. Steinberg, P. Buchschacher, J. H. Fried, G. J. Kent, M. Tishler, and S. L. Steelman, *ibid.*, **85**, 120 (1963). The 1′-methyl isomer had λ_{max}^{MeOH} 266.5 mμ (ε 13,100).

Pyrazolines. VIII. The Syntheses of 5,5-Diaryl-2-pyrazolines from the Reaction of Diazoalkanes with Methyl Acrylate[1]

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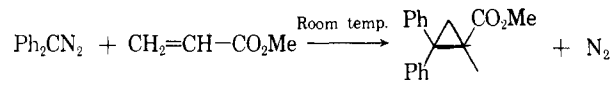
In the course of some kinetic studies on the thermal decomposition of selected 2-pyrazolines[2] we needed a sample of 5,5-diphenyl-3-carbomethoxy-2-pyrazoline I. However, a literature check showed that although the reaction of diphenyldiazomethane with methyl acrylate had been effected,[3] the actual isolation of the pyrazoline was not reported. This might not have been particularly surprising since this type of reaction has been often used for the synthesis of cyclopropanes[4] without concern for the presumed intermediate pyrazoline. However, the surprising feature of this observation was the fact that spontaneous nitrogen evolution is observed when diphenyldiazomethane is added to methyl acrylate.[3] This is in contrast to the fact that in most cases where the reaction of a diazoalkane with



an *alpha,beta*-unsaturated addend is used to effect the synthesis of a cyclopropane, the pyrazoline is first formed and then must be heated to varying temperatures to give the desired products.

A more careful perusal of the literature very quickly showed that although diphenyldiazomethane does lead to pyrazolines with some addends,[5–9] spontaneous cyclopropane formation has also been observed in several cases.[3,6,7,10,11] Furthermore, many cases of spontaneous cyclopropane formation in this type of reaction have been observed with the closely analogous diazofluorene.[12]

Spontaneous nitrogen evolution from reactions of diazoalkanes with *alpha,beta*-unsaturated addends has been recognized as being anomolous and has been discussed.[11–13] In general, the available evidence indicates that spontaneous formation of nitrogen-free products in this type of reaction involves initial formation of the 1-pyrazoline which then decomposes under

(1) For the previous paper in this series, see W. M. Jones and W. T. Tai, *J. Org. Chem.*, **27**, 1324 (1962).

(2) Unpublished work of D. G. Baarda.

(3) H. M. Walborsky and F. M. Hornyak, *J. Am. Chem. Soc.*, **77**, 6026 (1955).

(4) *Cf.* T. L. Jacobs in R. C. Elderfield, "Heterocyclic Compounds," Vol. 5, John Wiley and Sons, Inc., New York, New York, 1957, Chap. 2.

(5) H. Staudinger, E. Anthes, and F. Pfenninger, *Ber.*, **49**, 1928 (1916).

(6) J. van Alphen, *Rec. trav. chim.*, **62**, 210 (1943).

(7) J. van Alphen, *ibid.*, **62**, 334 (1943).

(8) W. M. Jones, *J. Am. Chem. Soc.*, **81**, 3776 (1959).

(9) L. F. Fieser and M. A. Peters, *ibid.*, **53**, 4080 (1931).

(10) F. J. Impasto, L. Barash, and H. M. Walborsky, *ibid.*, **81**, 1514 (1959).

(11) L. I. Smith and K. L. Howard, *ibid.*, **65**, 159 (1943).

(12) L. Horner and E. Lingnau, *Ann.*, **591**, 21 (1955).

(13) W. G. Young, L. J. Andrews, S. L. Lindenbaum, and S. J. Cristol, *J. Am. Chem. Soc.*, **66**, 810 (1944).