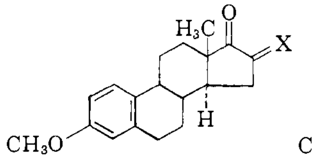
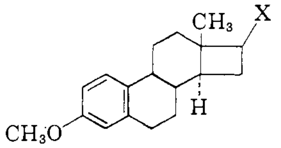
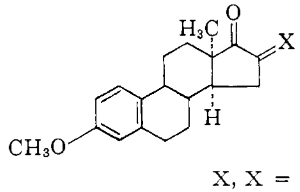
and one secondary methyl (doublet, $J = 5.7$) at 9.06τ.



I, X = H_2
II, X = NOH
III, X = N_2



IV, X = COOH
V, X = $COOCH_3$
VI, X = CH_2OH
VII, X = CH_2OMs
VIII, X = $CH_2SC_6H_5$
IX, X = CH_3



X, X = H_2
XI, X = NOH
XII, X = N_2

Lumiestrone methyl ether (X)[6] was nitrosated with *n*-butyl nitrite and potassium *t*-butoxide to give, in 91% yield, 16-oximinolumiestrone methyl ether (XI), m.p. 147–148°. Treatment of XI with chloramine gave, in 82% yield, 16-diazolumiestrone methyl ether (XII), m.p. 143–145°. Ultraviolet irradiation of diazoketone XII afforded an amorphous acid, m.p. 63–64°, which was shown by thin layer chromatography to contain none of the crystalline D-noracid IV. It follows, therefore, that diazoketone III has not been converted photolytically to the lumidiazoketone XII prior to ring contraction, and that the D-noracid IV almost certainly has retained the original *trans* C–D ring fusion of estrone.

Acknowledgments.—We are grateful to the National Institutes of Health for a grant in support of this work, and to the Schering Corporation for a generous gift of estrone.

[6] W. S. Johnson, D. K. Banerjee, W. P. Schneider, C. D. Gutsche, W. E. Shelberg and L. J. Chinn, *J. Am. Chem. Soc.*, **74**, 2832 (1952).

[7] Fellow of the Alfred P. Sloan Foundation.

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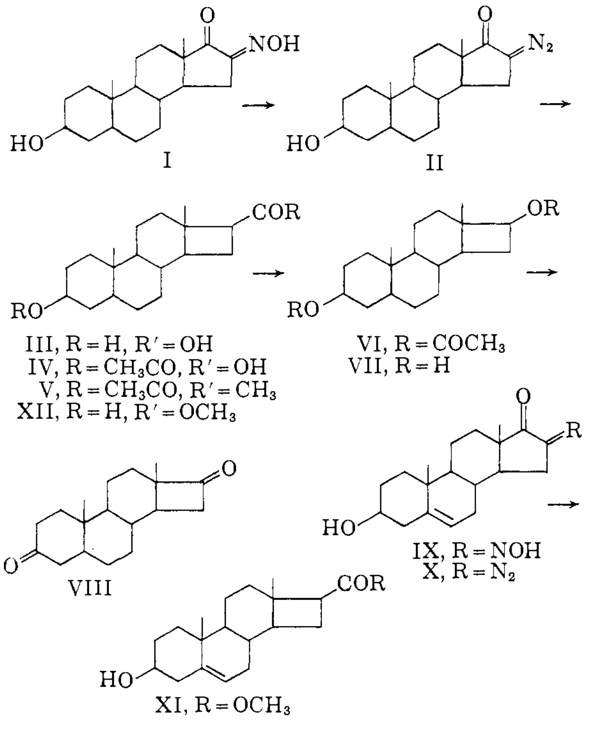
RECEIVED NOVEMBER 2, 1961

D-NORSTEROIDS

Sir:

The synthesis of variants of the naturally occurring steroid hormones has attracted considerable effort in the last decade.[1] The motivation behind this work has been largely the hope of discovering hormone analogs with modified and for one reason or another especially desirable biological activities. We wish to report the synthesis of a new family of compounds which we believe to be of unusual chemical as well as possible biological interest, the *D-norsteroids*.[2]

The starting point for the preparation of completely saturated D-norandrostanes was 16-oximinoandrostan-3β-ol-17-one (I),[3] which was converted in good yield by treatment with chloramine[4] into 16-diazoandrostan-3β-ol-17-one (II), m.p. 176.5–177.5° (dec.), $[\alpha]_D - 119°$ (*Anal.* Calcd. for $C_{19}H_{28}O_2N_2$: C, 72.11; H, 8.92; N, 8.85. Found: C, 71.93; H, 9.07; N, 8.86) showing characteristic intense infrared absorption in the 4.79 and 5.97 μ regions. Irradiation of II in aqueous dioxane[5] gave an excellent yield of acidic product, m.p. 185–200°, from which a single, homogeneous acid (III), m.p. 217–218°, $[\alpha]_D + 44°$ (*Anal.* Calcd. for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87; neut. eq., 306.4. Found: C, 74.30; H, 9.77; neut. eq., 298) could be isolated in *ca.* 30% yield. This acid was converted to the corresponding D-norpregnane by a three-step sequence. Acetylation of III with the use of acetic anhydride and pyridine gave the corresponding acetate (IV), m.p. 237–238°, $[\alpha]_D + 30°$ (*Anal.* Calcd. for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 72.31; H, 9.21). Treatment of IV with oxalyl chloride followed by dimethylcadmium gave about 60% of D-norpregnan-3β-ol-20-one acetate (V), m.p. 162.5–163.5°, $[\alpha]_D + 80°$ (*Anal.* Calcd. for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89. Found: C, 76.17; H, 9.73).



Evidence that the D-norsteroids described above are correctly formulated has been obtained by Baeyer–Villiger oxidation of V, using perbenzoic acid, to obtain the diacetate VI, m.p. 108.5–109.0°

[1] See, for example, L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959.

[2] An independent program aimed at the D-norsteroids has been carried out by Professor M. P. Cava at Ohio State University, *J. Am. Chem. Soc.*, **84**, 115 (1962).

[3] M. Huffman and M. H. Lott, *J. Biol. Chem.* **207**, 431 (1954).

[4] M. P. Cava, R. L. Litle and D. R. Napier, *J. Am. Chem. Soc.*, **80**, 2257 (1958).

[5] For other examples of photochemical ring-contractions, see ref. 4, W. Kirmse, *Angew. Chem.*, **69**, 106 (1957), and J. Meinwald and P. G. Gassman, *J. Am. Chem. Soc.*, **82**, 2857 (1960).

(*Anal.* Calcd. for $C_{22}H_{34}O_4$: C, 72.89; H, 9.45. Found: C, 72.90; H, 9.51), then ester hydrolysis to give the diol VII and finally Sarett oxidation to give D-norandrostane-3,16-dione (VIII), m.p. 148.5–149.5° (*Anal.* Calcd. for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.80; H, 9.55). The infrared spectrum of VIII gives unmistakable evidence for the presence of a cyclobutanone ring (intense infrared band at 5.64 μ, in addition to cyclohexanone absorption at 5.83 μ).

For elaboration of hormone analogs, it would be desirable to have D-norsteroids with a Δ^4-3-ketone system. With this requirement in view, a similar reaction sequence starting from 16-oximinoandrost-5-ene-3β-ol-17-one[6] (IX) has been carried out. In this series, the irradiation of the corresponding diazo ketone (X), m.p. 200–201° (dec.), $[\alpha]_D$ − 187° (*Anal.* Calcd. for $C_{19}H_{26}O_2N_2$: C, 72.58; H, 8.34; N, 8.91. Found: C, 72.57; H, 8.46; N, 9.06), gave a mixture of acids. Diazomethane esterification and chromatography gave the methyl ester XI, m.p. 164–165° (*Anal.* Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.44; H, 9.51). Proof that these Δ^5-compounds have structures analogous to those established in the saturated series is provided by the catalytic hydrogenation of XI which gave rise to the saturated ester XII identical in all respects (infrared, rotation, mixture m.p.) with an authentic sample of XII, m.p. 133–134°, $[\alpha]_D$ + 55° (*Anal.* Calcd. for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 74.95; H, 10.02), obtained by treatment of III with diazomethane.

The important problems of establishing the stereochemistry of these D-norsteroids and of elaborating hormone analogs are currently receiving our attention, and we hope to be able to report the full details of these studies in a subsequent publication.

Acknowledgments.—We wish to express our thanks to Professor D. H. R. Barton, who encouraged us in this work, and to the Schering Corporation for generous gifts of starting materials.

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[6] F. Stodola, E. C. Kendall and B. F. McKenzie, *J. Org. Chem.*, **6**' 841 (1941).

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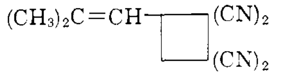
RECEIVED NOVEMBER 2, 1961

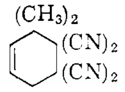
COMPETING CYCLOBUTANE FORMATION AND DIELS–ALDER REACTION

Sir:

We wish to report what appears to be the first observed instance of competitive formation of cyclobutane and cyclohexene adducts under mild conditions. The only previous instances of such competition are the condensation of tetrafluoroethylene with cyclopentadiene[1a] and the thermal dimerization of butadiene,[1b] both of which involve rather drastic conditions and are relatively unsuited for the determination of differences in reaction parameters. We have found that 4-methyl-1,3-pentadiene,[2] which will not undergo a normal Diels–Alder reaction with maleic anhydride, reacts overnight at room temperature with the more potent dienophile, tetracyanoethylene[3] to form in good yield a mixture of 3-(2-methylpropenyl)-1,1,2,2-tetracyanocyclobutane (I) and 3,3-dimethyl-4,4,5,5-tetracyanocyclohexene-1 (II). The cyclobutane (I) is isolated readily by ether extraction of the crude solid reaction product from tetracyanoethylene and excess methylpentadiene in tetrahydrofuran solution at room temperature,[3] to give a 69% yield of insoluble white crystals, m.p. 136–137° after recrystallization from benzene–cyclohexane (*Anal.* Calcd. for $C_{12}H_{10}N_4$: C, 68.5; H, 4.8; N, 26.6. Found: C, 68.8; H, 4.9; N, 26.1). The cyclohexene adduct (II) was obtained in 11% yield by passage of the ether extract through a short column of alumina, evaporation, recrystallization from benzene, cyclohexane and subsequent sublimation. The melting point of this compound appeared to lie in the range of 155–165°, but was obscured by sublimation and/or phase change even in a sealed tube (*Anal.* Calcd. for $C_{12}H_{10}N_4$: C, 68.5; H, 4.8; N, 26.6. Found: C, 68.8; H, 5.0; N, 26.2, by difference). Nuclear magnetic resonance and infrared spectra are in agreement with the assigned structures.[4]



I



II

In view of the possibility of these compounds arising from a common intermediate as postulated by Woodward[5] for the Diels–Alder reaction, a brief examination of the effect of synthesis conditions on the ratio of products was made. The crude product obtained in essentially quantitative yield at 2° (2400 min. time for color fading[3]) contained 12% II while at 57° (35 min.) 17% II was observed, as estimated by comparison of infrared spectra with known mixtures. The differences of enthalpy and entropy of activation are calculated to be 1.4 ± 0.5 kcal. (favoring I) and 1.4 ± 1.5 cal./°C. (favoring II), respectively. Reaction in cyclohexane (180 min. at 65°) gave a product containing more than 30% II in addition to a small amount of degradation products. Reaction in nitromethane[6] gave essentially pure I in 7 minutes at room temperature. The very small differences in activation parameters are to be expected if the two products are formed from a common high-energy intermediate or transition state, but are more likely fortuitous in view of the remarkable solvent effect. As can be seen above, the formation of I is more

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[1] (a) J. J. Drysdale, W. W. Gilbert, H. K. Sinclair and W. H. Sharkey, *J. Am. Chem. Soc.*, **80**, 245, 3672 (1958); (b) H. W. B. Reed, *J. Chem. Soc.*, 685 (1951).

[2] G. B. Bachman and C. G. Goebel, *J. Am. Chem. Soc.*, **64**, 787 (1942).

[3] W. J. Middleton, R. E. Heckert, G. L. Little and C. G. Krespan, *ibid.*, **80**, 2783 (1958).

[4] Elaboration of the spectra of these and related compounds will be reported in a forthcoming publication.

[5] R. B. Woodward and T. J. Katz, *Tetrahedron*, **5**, 70 (1959).

[6] D. W. Wiley, private communication, has found that the rates for cyclobutane formation from tetracyanoethylene and electron-rich olefins vary over a 10^{5-6} range depending on solvent, with nitromethane being one of the fastest and cyclohexane one of the slowest.