sium chloride, 0.01 base molar in poly-(4-vinylpyridine)[5] or 0.0157 M in 4-picoline, and 1–4 × 10^{-4} M in substrate. They were followed with a Cary spectrophotometer by the change in absorbance at 360 mμ. The products, 2,4-dinitrophenol and potassium 3-nitro-4-hydroxybenzenesulfonate, were characterized by their ultraviolet spectra. Good first order kinetics were obtained with DPNA in all cases and with NABS in the more acidic solutions. Some curvature was noted in the first order plots for reactions of NABS catalyzed by poly-(4-vinylpyridine) at pH values greater than 4; in these cases the reported rate constants correspond to the first 50% of reaction.[6] The spontaneous solvolyses were very slow relative to those catalyzed by the nitrogen bases (k_{obs} in absence of nitrogen base equalled 0.0004 min.$^{-1}$ for NABS at pH 4.5 and 0.004 min.$^{-1}$ for DNPA at pH 6.5), and in the range tested (0.002–0.02 base molar poly-(4-vinylpyridine), pH 3.6, 2 × 10^{-4} M NABS) the solvolytic rate constants were proportional to the polymer concentration. To assist in interpreting the data, both poly-(4-vinylpyridine) and 4-picoline were titrated with hydrochloric acid, the change in protonation of the bases being followed spectrophotometrically at 254 mμ. A plot of α, the fraction of nitrogen present as the free base, *versus* pH is shown in Fig. 1.

Data for solvolysis of DNPA are presented in Fig. 2. With the 4-picoline buffers, the observed rate constants increased linearly with increasing α, in accordance with data on the hydrolysis of substituted nitrophenyl esters conducted in aqueous solutions.[4] A concave k_{obs}–α plot was obtained for the reaction catalyzed by poly-(4-vinylpyridine). This result may be attributed to a reduction in the nucleophilicity of the nitrogens in the polymer as positive charges accumulate along the polymer chain.

A striking change was observed in the reactions of NABS (Fig. 3). As in the previous case the rate increased linearly with α for the picoline catalyzed reaction; however, for the solutions which contained poly-(4-vinylpyridine) the solvolytic rates *increased* as the pH was lowered and a maximum in the k_{obs}–α plot was attained near α = 0.6 (pH 3.6). The enhancement in the rates of the polymer catalyzed reaction may be rationalized on the basis that protonated nitrogen sites serve to attract or bind a negatively charged substrate (NABS) to the polymer coil where basic nitrogen sites are available to catalyze the solvolysis. Solvolyses of electrically neutral molecules such as DNPA are not subject to this binding. An estimate of the contribution of binding to the catalytic rate may be obtained from k_{obs} for α = 1 (pH 6.5, curve 2, Fig. 3), where essentially only conventional nucleophilic catalysis should operate, and curve 2, Fig. 2. On the assumption that curve 2 for the DNPA solvolysis provides a measure of the nucleophilicity of poly-(4-vinylpyridine) in acid solution, one may derive curve 3, Fig. 3, which represents the values of k_{obs} that would be expected if poly-(4-vinylpyridine) functioned only in the conventional sense. The difference between curves 1 and 3, Fig. 3, accordingly indicates the extent of reaction associated with ionic interaction between substrate and catalyst.

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(5) The polyvinylpyridine was prepared by the method of E. G. Fitzgerald and R. M. Fuoss, *Ind. Eng. Chem.*, **42**, 1603 (1950); the molecular weight was 60,000 (from viscosity).

(6) The values corresponding to higher conversions would be less.

(7) Hercules Powder Company Fellow, 1958; Public Health Service Research Fellow, 1960.

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A SYNTHESIS OF D-NORSTEROIDS

Sir:

Modified steroids are known in which the A, B, or C-ring of the normal steroid skeleton either has been contracted or reconstituted from a cleavage product into a cyclopentane ring.[1] A procedure is now described for the conversion of 17-ketosteroids to norsteroids containing a four-membered D-ring. No examples of such D-norsteroids have been reported previously.[2]

Base-catalyzed nitrosation of estrone methyl ether (I) gave 16-oximinoestrone methyl ether (II),[3] converted by chloramine in aqueous tetrahydrofuran, in 81% yield, to 16-diazoestrone methyl ether (III), m.p. 145–146°.[4] Irradiation of III with ultraviolet light (low pressure argon source) in aqueous tetrahydrofuran containing sodium bicarbonate gave, after acidification, the noracid IV, m.p. 188–189°, in 63% yield. The carboxyl group of acid IV, assigned the β-configuration on mechanistic grounds,[5] was converted by diazomethane to the methyl ester V, m.p. 103–104°. Since the hydrogen alpha to the carbomethoxy group in V was neither epimerizable by base nor unambiguously detectable by nuclear magnetic resonance, its presence was confirmed indirectly.

Reduction of acid IV with lithium aluminum hydride gave, in 78% yield, alcohol VI, m.p. 141–142°. Reaction of VI with methanesulfonyl chloride gave, in 72% yield, mesylate VII, m.p. 154–155°. Reaction of mesylate VII with sodium thiophenolate in warm dimethylsulfoxide gave, in 75% yield, the sulfide VIII, m.p. 111–112°. Desulfurization of VIII with Raney nickel in ethanol afforded, in 68% yield, substance IX, m.p. 50–51°. Kuhn–Roth oxidation of IX gave 1.56 equivalents of acetic acid, ruling out the possibility that both C-methyls in the molecule might be attached to the same carbon atom. The nuclear magnetic resonance spectrum of IX confirmed this conclusion, and showed one unsplit tertiary methyl at 9.11τ

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(1) For examples involving rings A, B, and C, respectively, see: (a) F. L. Weisenborn and H. E. Applegate, *J. Am. Chem. Soc.*, **81**, 1960 (1959); (b) F. Sorm and H. Dykova, *Coll. Czech.*, **13**, 407 (1948); (c) N. L. Wendler, R. F. Hirschmann, H. R. Slates, and R. W. Walker, *J. Am. Chem. Soc.*, **77**, 1632 (1955).

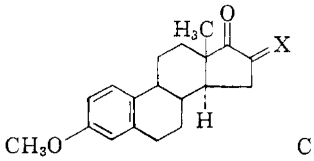
(2) Further examples of this class, obtained independently by the same general method as that outlined here, are described in the accompanying communication: J. Meinwald, G. G. Curtis and P. G. Gassman, *J. Am. Chem. Soc.*, **84**, 116 (1962).

(3) F. Litvan and R. Robinson, *J. Chem. Soc.*, 1997 (1938).

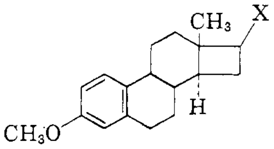
(4) Melting points are uncorrected. Satisfactory analyses were obtained for all compounds whose melting points are reported.

(5) J. Meinwald and P. G. Gassman, *J. Am. Chem. Soc.*, **82**, 5445 (1960).

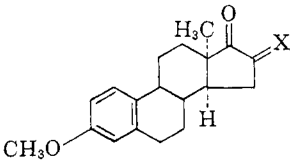
and one secondary methyl (doublet, $J = 5.7$) at 9.06τ.



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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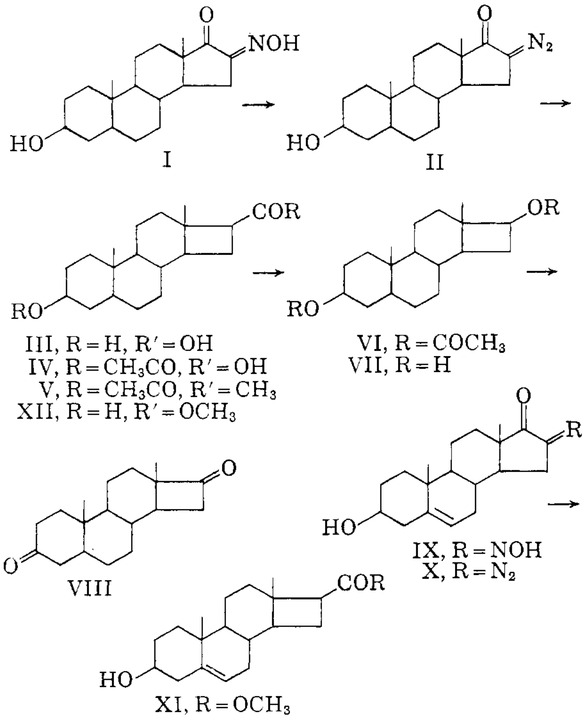
D-NORSTEROIDS

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).



I
II
III, R = H, R′ = OH
IV, R = CH_3CO, R′ = OH
V, R = CH_3CO, R′ = CH_3
XII, R = H, R′ = OCH_3
VI, R = $COCH_3$
VII, R = H
VIII
IX, R = NOH
X, R = N_2
XI, R = OCH_3

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°

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[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).