

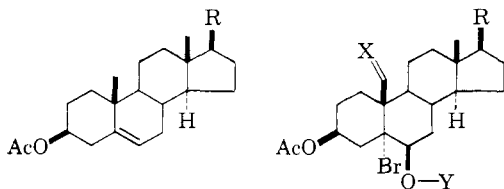
A CONVENIENT SYNTHESIS OF 19-NORSTEROIDS

Sir:

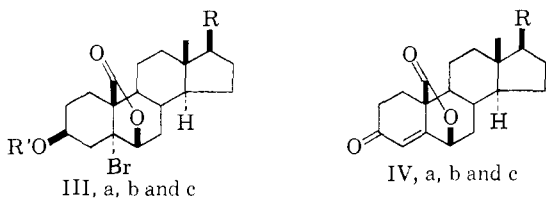
The medical importance of 19-norsteroids is well known.¹ We wish to report a general conversion of readily available 3 β -acetoxy- $\Delta^{5,6}$ -steroids of the type (I) into the corresponding 19-nor compounds of the type (V) by the application of nitrite photolysis.²

Treatment of (Ia, Ib and Ic) with hypobromous acid³ gave the bromohydrins (IIa³, Y = H, X = H₂), m.p. 172–174°; (IIb, Y = H, X = H₂) m.p. 171–172°, [α]^{26D} +1.9° (all rotations in 1% CHCl₃ solutions); (IIc, Y = H, X = H₂), m.p. 171–174°, [α]^{25.5} +7°. These bromohydrins were nitrosated using nitrosyl chloride and pyridine. Photolysis of the resulting nitrites (IIa, IIb and IIc, Y = NO, X = H₂) in toluene at 0° with a 500-watt Hanovia lamp gave the nitroso dimers which were rearranged to the oximes (IIa, X = NOH, Y = H), m.p. 176–180°, [α]^{21D} -35°; (IIb, X = NOH, Y = H) m.p. 178.5–180°, [α]^{26D} -11°; and (IIc, X = NOH, Y = H) m.p. 173–178°, [α]^{26D} -5.4°, respectively.

The 19-oximes with nitrous acid² gave the corresponding aldehydes (in hemiacetal form) which,

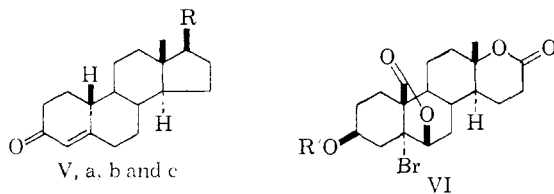


I, a, b, and c
II, a, b and c
a, R = cholesterol sidechain
b, R = 17-ketone
c, R = CH₃-CO



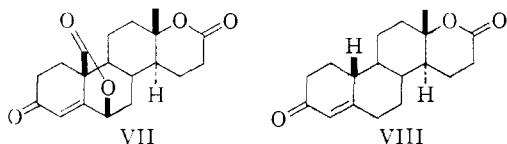
III, a, b and c

IV, a, b and c



V, a, b and c

VI



VII

VIII

(1) G. Pincus, "Vitamins and Hormones," Academic Press, New York, N. Y., 1959, Vol. 17, p. 307; J. H. Fried, T. S. Bry, A. E. Oberster, R. E. Beyler, T. B. Windholtz, J. Hannah, L. H. Sarett and S. L. Steelman, *J. Am. Chem. Soc.*, **83**, 4663 (1961).

(2) D. H. R. Barton, J. M. Beaton, L. E. Geller and M. M. Pechet, *ibid.*, **83**, 4076 (1961).

(3) Y. Ueno, *J. Pharm. Soc. Japan*, **72**, 1622 (1952).

without purification were oxidized with chromic acid in acetone to the lactones (IIIa, R' = Ac), m.p. 170–172°, [α]^{22D} -16.2°; (IIIb, R' = Ac), m.p. 221–229°, [α]^{27D} -13° and (IIIc, R' = Ac) m.p. 153–157° and 161–164°, [α]^{22.5D} +13°. The lactone (IIIb, R' = Ac) with peracetic acid enlarged the ring D to furnish the D-homodilactone (VI, R' = Ac) m.p. 268–272°, [α]^{25.5D} -58.4°. The 3 β -acetate in these lactones was removed with HCl in dioxane and water to yield the lactone alcohols (IIIa, R' = H), m.p. 173.5–178.5°, [α]^{25.5D} -17.9°; (IIIb, R' = H), m.p. 221–232°, [α]^{25.5D} +10°; (IIIc, R' = H), m.p. 210–214°, [α]^{23D} +18° and (VI, R' = H), m.p. 244–247°, [α]^{26D} -66.1°. Oxidation with chromic acid in acetone and treatment with hot pyridine or HCl/CHCl₃ yielded the conjugated ketones (IVa), m.p. 179–184°, [α]^{26D} -102°, $\lambda_{\text{max}}^{\text{MeOH}}$ 238 m μ (ϵ = 12,500); (IVb) m.p. 291–293°, [α]^{23.5D} -86°, $\lambda_{\text{max}}^{\text{MeOH}}$ 235 m μ (ϵ = 12,000); (IVc) m.p. 236–239°, [α]^{23.5D} -246°; $\lambda_{\text{max}}^{\text{MeOH}}$ 237 m μ (ϵ = 12,700); and (VII) m.p. 293.5–298.5°, [α]^{21.5D} -191°, $\lambda_{\text{max}}^{\text{MeOH}}$ 233 m μ (ϵ = 16,200). The conjugated ketones (IVa, IVb, IVc, and VII) with zinc and acetic acid for fifteen minutes at reflux temperature, followed by mild acid treatment, gave 19-norcholestenone (Va) as a low-melting solid, [α]^{26D} +44.2°, $\lambda_{\text{max}}^{\text{MeOH}}$ 240 m μ (ϵ = 14,000); 19-norandrostendione (Vb), m.p. 164–169°, [α]^{27D} +136°, $\lambda_{\text{max}}^{\text{MeOH}}$ 241 m μ (ϵ = 17,000); 19-norprogesterone (Vc), m.p. 143–146°, [α]^{25D} +142°, $\lambda_{\text{max}}^{\text{MeOH}}$ 240 m μ (ϵ = 17,000) 19-nortestolactone (VIII), m.p. 195–199°, [α]^{26D} -16.9°, $\lambda_{\text{max}}^{\text{MeOH}}$ 238 m μ (ϵ = 17,000). The constants for (Vb, Vc and VIII) are in good agreement with the literature.^{4,5,6}

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(4) H. Hagiwara, S. Noguchi and M. Nishikawa, *Chem. and Pharm. Bull. Japan*, **8**, 84 (1960).

(5) J. S. Mills, H. J. Ringold, and C. Djerassi, *J. Am. Chem. Soc.*, **80**, 6118 (1958).

(6) *Chem. Abs.*, **53**, 8215a (1959).

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CONFIGURATIONAL STABILITY OF SULFONYL CARBANIONS GENERATED BY DECARBOXYLATION REACTION¹

Sir:

Through a comparison of the rates of base-catalyzed racemization and isotopic exchange of I, it was concluded in a former study² that the sulfonyl carbanion was capable of maintaining configurational stability to a degree that varied widely with solvent. Thus $k_{\text{exchange}}/k_{\text{racemization}}$ ranged between 10 and about 2000. Another study revealed that sulfoxide and phosphine oxide groups in II and III

(1) This work was supported by a grant from the National Science Foundation.

(2) D. J. Cram, D. A. Scott and W. D. Nielsen, *J. Am. Chem. Soc.*, **83**, 3696 (1961).