

## COMMUNICATIONS TO THE EDITOR

## THE SYNTHESIS OF 19-NORALDOSTERONE ACETATE

Sir:

We recently reported a new photochemical reaction<sup>1</sup> which could be applied<sup>2</sup> to a simple synthesis of aldosterone acetate. We now describe how this reaction can be used for the synthesis of 19-substituted corticosterones, for 19-norcorticosterone acetate and finally for the preparation of 19-noraldosterone acetate.

Corticosterone 3,20-bisethylene ketal<sup>3</sup> was acetylated and nitrosated to furnish the 21-acetate 11 $\beta$ -nitrite (I, R = NO, X = Y = H<sub>2</sub>), m.p. (from methylene chloride-hexane) 134-137°, [ $\alpha$ ]<sub>D</sub> +4° (all rotations in 1% CHCl<sub>3</sub> solutions), photolysis of which in toluene solution<sup>1</sup> gave the 18-oxime (I, R = H, X = H<sub>2</sub>, Y = NOH) (16%), m.p. (from acetone) 246-252°, [ $\alpha$ ]<sub>D</sub> -44°, and a non-crystalline 19-oxime (I, R = H, X = NOH, Y = H<sub>2</sub>). Treatment of the 18-oxime with nitrous acid<sup>2</sup> afforded the 18-aldehyde (in hemi-acetal form I, R = H, X = H<sub>2</sub>, Y = O), m.p. (from acetone) 189-194°, [ $\alpha$ ]<sub>D</sub> +3°, which on digestion with 90% aqueous acetic acid<sup>4</sup> gave aldosterone acetate (II, R = Me).

Treatment of the crude 19-oxime (see above) with nitrous acid<sup>2</sup> gave the 19-aldehyde (III, R = Ac) (34% from starting nitrite), m.p. 269-275°, [ $\alpha$ ]<sub>D</sub> +47°, characterized by mild alkaline hydroly-

sis to (III, R = H), m.p. 259-260°, [ $\alpha$ ]<sub>D</sub> +61°. Treatment of the latter with dioxane containing *N* HCl (133:15) at room temperature overnight afforded the 19-oxygenated isomer (IV, R = H) of aldosterone, m.p. 195-199°, [ $\alpha$ ]<sub>D</sub> +218°. Reduction of (III, R = Ac) with excess of lithium aluminum hydride in refluxing tetrahydrofuran gave the corresponding 11,19,21-triol, m.p. (from acetone-hexane) 156-162°, [ $\alpha$ ]<sub>D</sub> +4°, which with dioxane-HCl at room temperature as above furnished 19-hydroxycorticosterone with constants in good agreement with those recently recorded.<sup>5</sup>

Treatment of (IV, R = H) (3.08 g.) in methanol (300 ml.) with 0.5 *N* NaOH in methanol (60 ml.) at room temperature gave (after 15 min.) 19-norcorticosterone (V, R = R' = H) with constants in good agreement with those given in the literature.<sup>6</sup> After acetylation, the derived 19-norcorticosterone acetate (2.93 g.) was nitrosated in the usual way<sup>1</sup> and the product in benzene (120 ml.) was irradiated as before.<sup>1,2</sup> The total product was treated with nitrous acid<sup>2</sup> and chromatographed over alumina to give 19-noraldosterone acetate (II, R = H) (585 mg.), m.p. (from ethyl acetate-hexane) 155-163°, [ $\alpha$ ]<sub>D</sub> +79°,  $\lambda_{\max}$  239  $\mu$  ( $\epsilon$  = 17,350 in methanol).<sup>7</sup>

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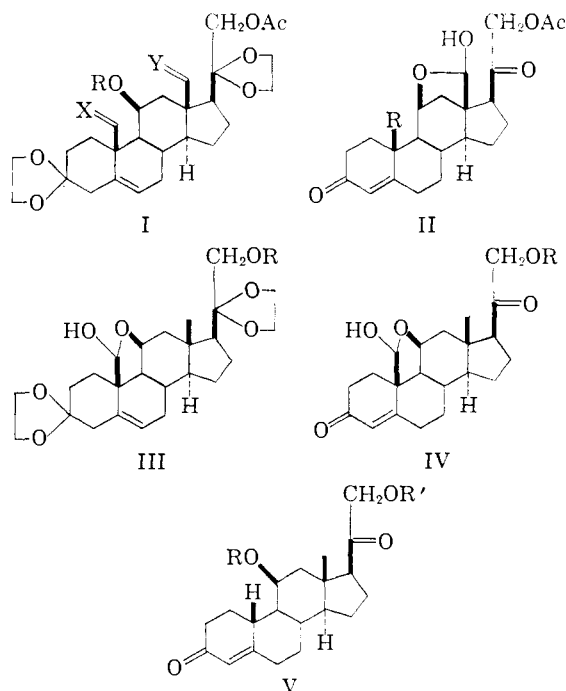
(7) All compounds showed ultraviolet and infrared spectra in accordance with their assigned constitutions and gave satisfactory analytical data.

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METHYLENE RADICALS AND THERMAL GAS PHASE DECOMPOSITION OF DIAZOMETHANE<sup>1</sup>

Sir:

The thermal decomposition of diazomethane (DM) above 350° has long been known to yield methylene radicals,<sup>2,3</sup> while the low temperature decomposition seems to be a molecular process.<sup>3,4</sup> Despite many inconsistencies noted in this earlier work regarding the reactions of the radicals, Pearson, *et al.*,<sup>3</sup> concluded from their studies, using DM decomposition and other sources, that the methylene was in a singlet electronic state. Study of the uncatalyzed thermal decomposition

(1) Supported in part by the Office of Naval Research.

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