

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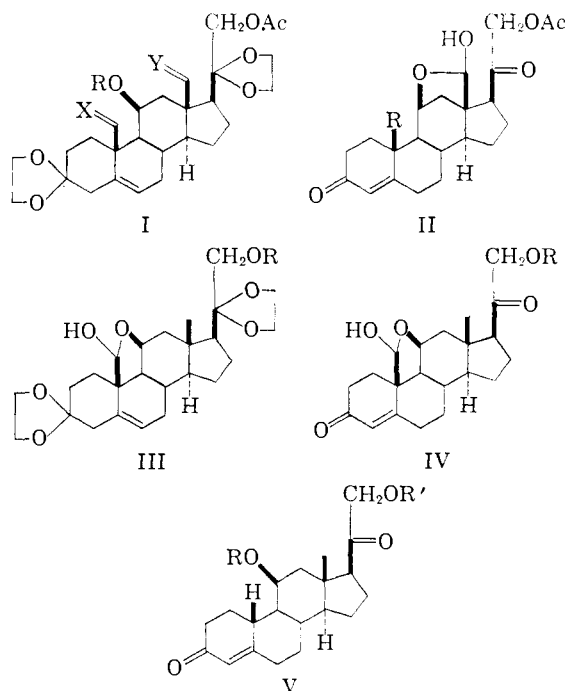
(7) All compounds showed ultraviolet and infrared spectra in accordance with their assigned constitutions and gave satisfactory analytical data.

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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.

(2) F. O. Rice and A. L. Glasebrook, *J. Am. Chem. Soc.*, **55**, 4329 (1933); **56**, 2381 (1934).

(3) T. G. Pearson, R. H. Purcell and G. S. Saigh, *J. Chem. Soc.*, 409 (1938), give a survey of earlier work.

(4) E. W. R. Steacie, *J. Phys. Chem.*, **35**, 1493 (1931).

of DM has been almost<sup>5</sup> neglected in the intervening interval.

Recent evidence supports the triplet state as the ground electronic level of methylene.<sup>6,7</sup> The question arises whether thermal decomposition of DM proceeds with conservation of spin angular momentum to give the singlet radical, or non-adiabatically to give triplet methylene. The latter possibility is analogous to the decomposition of isoelectronic N<sub>2</sub>O which yields O(<sup>3</sup>P) atoms, with a rate characterized by a lowered frequency factor.<sup>8</sup> Shantarovich<sup>5</sup> has reported the frequency factor for DM decomposition (studied below the high pressure limit at < 500°) as  $8 \times 10^{10}$  sec.<sup>-1</sup>, a little less than the value for N<sub>2</sub>O.

Our results on the thermal gas phase decomposition of DM support the singlet nature of the radical product. They show that the characteristic gas phase reactions of methylene with olefins, made familiar by photolysis studies of Kistiakowsky and co-workers<sup>9</sup> and others,<sup>10,11</sup> may also be observed with the thermally produced radicals; DM pyrolysis is a convenient source of these radicals at intermediate temperatures, in much higher yield than is obtained by photolysis of DM at 25°. <sup>7a</sup>

Decomposition of 1:10 mixtures of DM and olefins in a seasoned Pyrex bulb gave yields which were very low at 180°, improved substantially at 250°, and increased to 35% at 380°. Results at 300° (Fig. 1) with *cis*-butene-2 indicate that activated *cis*-dimethylcyclopropane undergoes the characteristic *cis-trans* geometric isomerization<sup>12</sup> in competition with collisional deactivation. Added oxygen, up to 10% of the total pressure, was without effect. Extrapolation to high pressures shows that addition to the double bond is essentially stereospecific. This is indicative of singlet radicals,<sup>9b,11</sup> and the correctness of the conclusion of Pearson, *et al.* The characteristic structural isomerization<sup>9c</sup> to pentenes of the excited cyclopropanes, and variation with pressure, is also seen. Extrapolation to high pressures indicates ~55% of *cis*-pentene-2 from addition to the C-H bond.<sup>10</sup> *trans*-Pentene-2 production is <2% above 20 cm., which is also indicative of the absence, or negligible production, of triplet methylene.<sup>7b</sup>

We have employed an interpretation, by Kistiakowsky, *et al.*,<sup>9</sup> that the variation of product proportions with pressure results from collisional deactivation of the hot cyclopropane molecules formed, rather than a recent proposal that the

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(7) (a) F. A. L. Anet, R. F. W. Bader and A. M. Van der Auwera, *J. Am. Chem. Soc.*, **82**, 3217 (1960); (b) H. M. Frey, *ibid.*, **82**, 5947 (1960).

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(9) (a) G. B. Kistiakowsky and A. L. Marshall, *J. Am. Chem. Soc.* **74**, 88 (1952); (b) G. B. Kistiakowsky and K. Sauer, *ibid.*, **78**, 5699 (1956); (c) H. M. Frey and G. B. Kistiakowsky, *ibid.*, **79**, 6373 (1957); (d) H. M. Frey, *Proc. Roy. Soc. (London)*, **A251**, 575 (1959); results of R. A. Holroyd and W. A. Noyes, Jr., *J. Am. Chem. Soc.*, **78**, 4831 (1956), should be compared.

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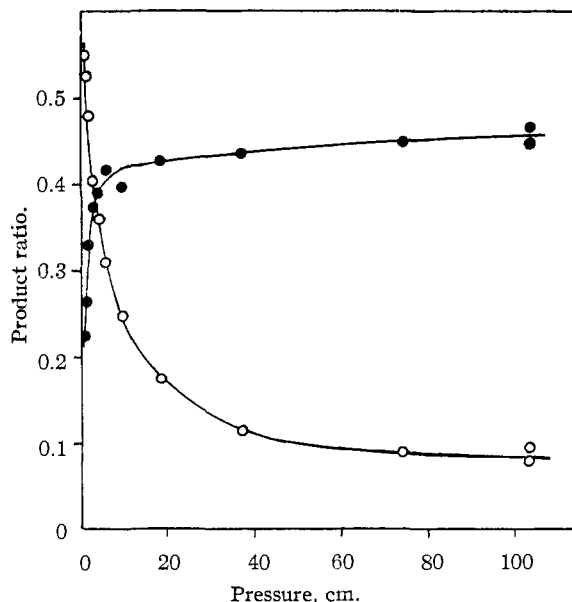


Fig. 1.—Variation of product ratios with total pressure (300°): O, dimethylcyclopropane (DMC) isomer ratios, *trans*/*(trans + cis)*; ●, DMC/(DMC + pentenes).

behavior arises from singlet-triplet transitions of methylene<sup>13</sup> at lower pressures: The apparent rate constants in these systems<sup>9,12</sup> are in some instances higher ( $\sim 10^8$  to  $10^{11}$  sec.<sup>-1</sup>) than are known magnitudes for singlet-triplet radiative processes, or for the intersystem crossing.<sup>7b</sup> In addition, different pressure dependence of the characteristic olefin formation, and of the *cis-trans* cyclopropane ratio, is observed for different substrate olefins, with the same radical source.<sup>9c,d,12</sup> The different pressure dependence between olefin formation and geometric isomerization, in one and the same system,<sup>9d,12</sup> also supports the present interpretation, at least at pressures above 1 cm.

The energies of dimethylcyclopropane produced in the present work, and *via* photolysis of DM,<sup>9d</sup> are quite similar, as judged by relative variation of products with pressure. Studies at different temperatures may assist in better estimates of the total energy of the product species, when coupled with accurate quantum statistical calculations of rate.

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#### DICHLOROFUOROMETHANESULFENYL CHLORIDE Sir:

Recently, Sheppard and Harris<sup>1</sup> concluded, on the basis of characteristic sulfenyl chloride reactions and fluorine magnetic resonance spectra, that the product of the fluorination of trichloromethanesulfenyl chloride, CCl<sub>3</sub>SCl, with mercuric fluoride is dichlorofluoromethanesulfenyl chloride,

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