phere; the refractive indices of the compounds do not change over 50 days. Contrary to this, trimethylsiloxytriethyltin (b.p. 99° (20 mm.)) synthesized by the same method seemed to absorb carbon dioxide easily from air to form a crystalline solid during the distillation or on standing. By bubbling carbon dioxide into trimethylsiloxytriethyltin in acetone, a white precipitate of bis-(triethyltin) carbonate is formed immediately. Thus it is clear that the stability of a trimethylsiloxytrialkyltin compound depends upon the nature of the alkyl groups attached to the tin atom.

It is also worth noting that the two compounds shown in the table are monomeric in benzene solution, while the tetraalkyl-1,3-bis-(trimethylsiloxy)-distannoxanes, $(Me_3SiOSnR_2)_2O$ (R = Me, Et, *n*-Pr, *n*-Bu), are dimeric, as has been reported.[4]

The infrared spectra of the two compounds show a strong absorption associated with the stretching vibration of the Si-O-Sn group near 980 cm.$^{-1}$; that of tetraalkyl-1,3-bis-(trimethylsiloxy)-distannoxanes has been reported[3] to have two strong absorptions near 980 and 910 cm.$^{-1}$.

(4) R. Okawara, *Proc. Chem. Soc.*, in press.

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PROCESS FOR BIOSYNTHESIS OF 7-CHLORO-6-DEMETHYLTETRACYCLINE

Sir:

The biosynthesis of 7-chloro-6-demethyltetracycline and the related 6-demethyltetracycline by mutant strains of *Streptomyces aureofaciens* has been described by McCormick, *et al.*[1,2] These mutants apparently lack the enzyme system which inserts the methyl group derived from methionine (as shown by Miller, *et al.*[3]) into the molecule. We have found that "normal" strains of *S. aureofaciens* form 6-demethyltetracyclines when grown in sulfonamide containing media. Among the organisms used in our experiments were these strains of *S. aureofaciens:* NRRL B-2209, NRRL B-1286, NRRL B-1287, NRRL B-1288, ATCC 12416a, ATCC 12416b, and ATCC 12416c.

These strains were grown in shaken Erlenmeyer flasks and in aerated fermenters in a medium containing extraction process soybean meal, glucose, sodium chloride and powdered calcium carbonate. Sulfaguanidine was added to the autoclaved medium to give a final concentration of 1 g. per l. Both the powdered form and a hydrochloric acid solution of the sulfonamide were used. After 5 days incubation at 25°, samples were removed from the fermentations and prepared for chromatographic analysis by acidification to pH 2.5 with sulfuric acid. The cell-free liquid obtained after acidification and centrifuging was analyzed for the presence of members of the tetracycline group of antibiotics by the paper chromatographic systems mentioned earlier.[4] The samples taken from the sulfaguanidine-supplemented fermentations contained substantial amounts of 7-chloro-6-demethyltetracycline and 7-chlorotetracycline, as well as traces of tetracycline and 6-demethyltetracycline. The crystalline 7-chloro-6-demethyltetracycline hydrochloride isolated from a 30-l. fermentation was compared with the material prepared by the McCormick processes.[1,2] There were no significant differences in infrared and ultraviolet spectra, rotation, and melting point, and a Kuhn–Roth degradation showed the absence of the C-methyl moiety. Chemical stability studies using 2 *N* HCl and 0.2 *N* NaOH showed that the material from the sulfaguanidine supplemented fermentations had the same stability in these reagents as 7-chloro-6-demethyltetracycline.[1,2] Other sulfonamides found effective in shifting these fermentations from the production of 7-chlorotetracycline to the formation of 7-chloro-6-demethyltetracycline included sulfanilamide, sulfadiazine, sulfathiazole, sulfapyridine, sulfasuxidine, sulfamerizine, and sulfisoxazole. Further experiments which showed that this diversionary effect was reversed in part by addition to the fermentation of methionine provide additional support to the hypothesis that the sulfonamides interfere with methionine metabolism of *S. aureofaciens.*

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(2) J. R. D. McCormick, N. O. Sjolander, U. Hirsch, and E. R. Jensen, U. S. Patent 2,878,289 (1959).

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(4) D. Perlman, L. J. Heuser, J. M. Barrett, and J. A. Boska, *J. Bacteriol.*, **80**, 419 (1960).

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A NOVEL REARRANGEMENT OF THE STEROID NUCLEUS. SYNTHESIS OF 18-NOR-D-HOMOSTEROIDS[1]

Sir:

Recent work on the photolysis of steroid nitrite esters[2] has demonstrated the utility of this reaction in the synthesis of structures only difficultly obtainable by other methods.

We now wish to report the photolytic conversion of steroid 11β-hydroxy-17-keto nitrite esters to 18-nor-D-homo-$\Delta^{13(17a)}$-11β-hydroxy-17-keto steroids.

When 4-androstene-11β-ol-3,17-dione[3] was converted to the 11β-nitrite (partial structure A; m.p. 157–159°; $[\alpha]$ +249° $\lambda\lambda^{Nujol}$ 5.76, 5.96, 6.07, 6.18, 12.90, 13.25 μ)[4] and the latter irradiated in toluene,[5] a compound was isolated by crystallization which was shown to be 18-nor-D-homo-4,13-(17a)-androstadiene-11β-ol-3,17-dione (I; partial

(1) Part IV in the series "Photolysis of Organic Nitrites"; part III, A. L. Nussbaum, C. H. Robinson, E. P. Oliveto and D. H. R. Barton, *J. Am. Chem. Soc.*, **83**, 2400 (1961).

(2) D. H. R. Barton, J. M. Beaton, L. E. Geller and M. M. Pechet, *ibid.*, **82**, 2640 (1960); D. H. R. Barton and J. M. Beaton, *ibid.*, **82**, 2641 (1960); A. L. Nussbaum, F. E. Carlon, E. P. Oliveto, E. Townley, P. Kabasakalian and D. H. R. Barton, *ibid.*, **82**, 2973 (1960); C. H. Robinson, O. Gnoj, A. Mitchell, R. Wayne, E. Townley, P. Kabasakalian, E. P. Oliveto and D. H. R. Barton, *ibid.*, **83**, 1771 (1961).

(3) T. Reichstein, *Helv. Chim. Acta*, **20**, 978 (1937).

(4) Rotations are in chloroform unless otherwise noted. Satisfactory analyses have been obtained for all new compounds.

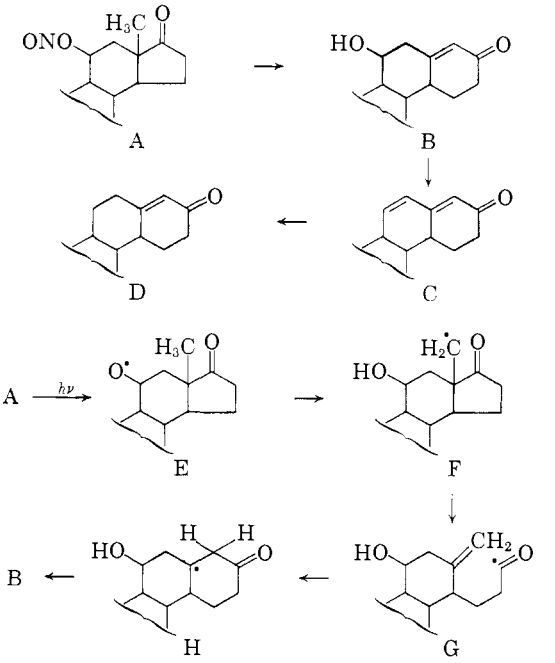
(5) We thank Mr. R. Armswood for technical assistance.

structure B; m.p. 269–273°; $[\alpha]_D$ +134° (pyr.); λ_{max}^{MeOH} 241 mμ, ε 33,500; $\lambda\lambda^{Nujol}$ 3.00, 6.00, 6.10, 6.20 μ) by its infrared and ultraviolet spectra and by chemical transformations. Compound I was acetylated readily with acetic anhydride in pyridine at room temperature to give the 11-acetate (m.p. 161–165°; $[\alpha]_D$ +148°; λ_{max}^{MeOH} 239 mμ, ε 34,200; $\lambda\lambda^{Nujol}$ 5.78, 6.00, 6.16, 8.00 μ). Dehydration of I with perchloric acid in methanol gave 18-nor-D-homo-4,11,13(17a)-androstatriene-3,17-dione (partial structure C; m.p. 189–192°; $[\alpha]_D$ −88°; $\lambda\lambda_{max}^{MeOH}$ 238 mμ, ε 15,200 and 280 mμ, ε 29,000; $\lambda\lambda^{Nujol}$ 6.00, 6.06, 6.20, 6.32 μ) which was hydrogenated to the known[6] 18-nor-D-homo-4,13(17a)-androstadiene-3,17-dione (partial structure D; m.p. 196–199°; $[\alpha]_D$ +49; λ_{max}^{MeOH} 242 mμ, ε 33,600; $\lambda\lambda^{Nujol}$ 6.01, 6.18 μ; reported[6] m.p. 196°; $[\alpha]$ +47°; $\lambda_{max}^{alc.}$ 243 mμ, ε 33,000) using palladium on calcium carbonate catalyst in benzene.[7]

Analogously, 1,4-androstadiene-11β-ol-3,17-dione,[8] 11β-hydroxyestrone 3-acetate[9] and androstane-3β,11β-diol-17-one 3-acetate[10] were converted to the corresponding 11-nitrites (respectively m.p. 109–111°; $[\alpha]_D$ +179°; λ_{max}^{MeOH} 239 mμ, ε 16,400; $\lambda\lambda^{Nujol}$ 5.72, 5.76, 6.00, 6.10, 6.22 μ; m.p. 176–178°; $[\alpha]_D$ +93; $\lambda\lambda_{max}^{MeOH}$ 268 mμ, ε 1,340 and 275 mμ, ε 1,200; $\lambda\lambda^{Nujol}$ 5.65, 5.72, 6.06, 6.20, 6.67, 8.3 μ and m.p. 134–136°; $[\alpha]_D$ +69°; $\lambda\lambda^{Nujol}$ 5.78, 6.08, 6.12, 8.12 μ) which were photolyzed to give, respectively, 18-nor-D-homo-1,4,13(17a)-androstatriene-11β-ol-3,17-dione (II; m.p. 254–257°; $[\alpha]_D$ +35° (pyr.); λ_{max}^{MeOH} 243 mμ, ε 32,600; $\lambda\lambda^{Nujol}$ 2.97, 6.02, 6.12, 6.18 μ), 18-nor-D-homo-1,3,5(10),-13(17a)-estratetraene-3,11β-diol-17-one 3-acetate (III; m.p. 181–183°; $[\alpha]_D$ +117° (pyr.); λ_{max}^{MeOH} 237 mμ, ε 19,500; $\lambda\lambda^{Nujol}$ 2.96, 5.70, 5.95, 6.15, 6.28, 6.68, 8.1 μ) and 18-nor-D-homo-13(17a)-androstene-3β,11β-diol-17-one 3-acetate[11] (IV; m.p. 165–168°; $[\alpha]_D$ −3° (pyr.); λ_{max}^{MeOH} 241 mμ, ε 15,200; $\lambda\lambda^{Nujol}$ 2.90, 5.75, 5.99, 6.12, 8.0 μ). Compound II was converted to the 11-acetate (m.p. 199–201°; $[\alpha]_D$ +80°; λ_{max}^{MeOH} 240 mμ, ε 32,000; $\lambda\lambda^{Nujol}$ 5.77, 6.00, 6.15, 6.24), and dehydrated to give 18-nor-D-homo-1,4,11,13(17a)-androstatetraene-3,17-dione (m.p. 200–202°; $[\alpha]_D$ −193°; $\lambda\lambda_{max}^{MeOH}$ 240 mμ, ε 15,700 (shoulder) and 278 mμ, ε 34,000; $\lambda\lambda^{Nujol}$ 5.99, 6.16, 6.21, 6.29 μ).

Further substantiation of partial structure B for the photolysis product is furnished by the following reactions. Treatment of compound IV with perchloric acid or potassium hydroxide in methanol gave 11,13(17a)-androstadiene-3β-ol-17-one (m.p. 255–258°; $[\alpha]_D$ −46°; λ_{max}^{MeOH} 284 mμ, ε 27,800; $\lambda\lambda^{Nujol}$ 2.98, 6.08, 6.18, 6.32 μ) which was converted to the 3-benzoate (m.p. 220–223°; $[\alpha]_D$ −22°; $\lambda\lambda_{max}^{MeOH}$ 238 mμ, ε 14,200 and 283 mμ, ε 23,800; reported[12] m.p. 223°; $[\alpha]_D$ −25°; λ_{max}^{MeOH} 283 mμ, ε 25,900), and hydrogenated to yield 18-nor-D-homo-13(17a)-androstene-3β-ol-17-one (m.p. 201–204°; $[\alpha]_D$ −36°; λ_{max}^{MeOH} 240 mμ, ε 16,200; $\lambda\lambda^{Nujol}$ 2.96, 6.05, 6.17 μ; reported[13] m.p. 194–196°.

Recently a free radical rearrangement which is formally of the Wagner–Meerwein type has been observed[14]; we believe that the rearrangement reported here is another instance of this reaction type. A plausible mechanism is indicated in partial structures E to H, the intermediate primary



radical F rearranging via the open chain intermediate G to the tertiary radical H, which then may lose a hydrogen atom to a radical species in the system to give the final product B.

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CORRECTION OF THE STRUCTURE OF A URINARY METABOLITE OF ALDOSTERONE[1]

Sir:

The major urinary metabolite of aldosterone, measured as the triacetoxy derivative, has been used to estimate the rate of secretion of the hormone in man.[2,3] The structure 3α,18,21-trihydroxy-11,20-diketopregnane, previously[4] assigned to the metabolite, however, was that of a contaminating

(1) This work was aided by Grant No. P-274 from the American Cancer Society, and by grants from the National Institutes of Health and the John and Mary R. Markle Foundation.

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