of bromodifluoromethane, chlorodifluoromethane and difluoroiodimethane are concerted one-step reactions[2] but that the α-dehydrohalogenations of chloroform and most other haloforms are stepwise processes involving the formation of small concentrations of reactive intermediate carbanions.[1a,3] We wish now to report that ethyl orthothioformate and methyl orthothioformate, with potassium amide in liquid ammonia, undergo essentially complete transformation to tris-(alkylthio)· methyl anions, which, more slowly, lose thioalkoxy anions to give intermediate bis-(alkylthio)-methylenes, some of which are transformed to tetrakis-(alkylthio)-ethylenes.

Both methyl and ethyl orthothioformate react with potassium amide in ammonia to give green solutions, which are similar in color to those that may be prepared from potassium amide and bis-(methylthio)-methane,[4] but which acquire a brownish color on standing for several hours. Such a solution, prepared from 11.7 g. (76 mmoles) of methyl orthothioformate and 150 mmoles of potassium amide in about 150 ml. of ammonia, was allowed to reflux for an hour before the ammonia was allowed to evaporate. From the residue was isolated 1.8 g. (12 mmoles) of methyl orthothioformate and 2.7 g. (13 mmoles—40% based on unrecovered orthothioformate) of tetrakis-(methylthio)-ethylene, m.p. 59–60°, reported m.p. 61.5°;[6] sole n.m.r.[7] band at 7.63 τ (in carbon tetrachloride). Tetrakis-(ethylthio)-ethylene, prepared analogously from ethyl orthothioformate, melted at 50–53° and showed no melting-point depression when mixed with tetrakis-(ethylthio)-ethylene prepared from tetrachloroethylene and sodium thioethoxide.[8] In at least one previously reported α-elimination the concentration of intermediate carbanion was large enough to observe directly.[9] In the present case there are two observations that show that the reactant is transformed almost quantitatively to its conjugate base. After the addition of one equivalent of potassium amide to solutions of orthothioformates the green color is made no more intense by the addition of further amide. Treatment of a freshly prepared solution of the tris-(methylthio)-methyl anion with methyl iodide leads to the formation of 75% of methyl orthothioacetate, b.p. 98.5–100° (11 mm.), $n^{24.5}\text{D}$ 1.5680, $d^{24.5}_4$ 1.1197; molecular refractivity calcd. 49.21, found 49.22; sharp n.m.r.[7] absorption band at 8.20 τ and one with three times the integrated intensity at 7.92 τ (neat). *Anal.* Calcd. for $C_5H_{12}S_3$: C, 35.67; H, 7.19; S, 57.14. Found: C, 35.49; H, 7.42; S, 57.31.

The fact that tris-(alkylthio)-methyl anions may be generated in high concentrations is to be attributed to the relative ease of removal of a proton from orthothioformates[10,11] and to the difficulty of displacing thioalkoxy anions from saturated carbon atoms. The tetrakis-(alkylthio)-ethylenes formed in the reactions studied need not arise from the dimerization of bis-(alkylthio)-methylenes. They may just as plausibly be ascribed to the reaction of such a methylene with the much more abundant carbanions as shown below.

$$\begin{tikzcd}
(RS)_3CH + NH_2^- \arrow[r] & (RS)_3C^- \arrow[r] & RS\text{-}C\text{-}SR + RS^- \arrow[d, "(RS)_3C^-"] \\
 & (RS)_2C{=}C(SR)_2 + RS^- & (RS)_3C{-}C(SR)_2^- \arrow[l]
\end{tikzcd}$$

In view of the difficulty of displacing thioalkoxy anions from saturated carbon, an alternate mechanism involving the formation of the intermediate pentakis-(alkylthio)-ethane by the nucleophilic attack of tris-(alkylthio)-methyl anions on orthothioformate molecules seems improbable.

**Acknowledgment.**—We wish to acknowledge the support of this investigation by the U. S. Army Research Office (Durham).

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[2] J. Hine and P. B. Langford, *J. Am. Chem. Soc.*, **79**, 5497 (1957); J. Hine and D. C. Duffey, *ibid.*, **81**, 1131 (1959); J. Hine and A. D. Ketley, *J. Org. Chem.*, **25**, 606 (1960).

[3] J. Hine and S. J. Ehrenson, *J. Am. Chem. Soc.*, **80**, 824 (1958).

[4] We have alkylated such a solution of bis-(methylthio)-methane with propyl bromide and obtained the dimethyl mercaptal of butyraldehyde. The first report of such a reaction was by Arens, Fröhling and Fröhling,[5] who did not state what specific compounds they studied.

[5] J. F. Arens, M. Fröhling and A. Fröhling, *Rec. trav. chim.*, **78**, 663 (1959).

[6] B. Fetkenheuer, H. Fetkenheuer and H. Lecus, *Ber.*, **60**, 2535 (1927).

[7] A Varian A-60 instrument was used.

[8] P. Claesson, *J. prakt. Chem.*, [2] **15**, 193 (1877).

[9] C. G. Swain and E. G. Thornton, *J. Am. Chem. Soc.*, **83**, 4033 (1961).

[10] *Cf.* L. H. Slaugh and E. Bergman, *J. Org. Chem.*, **26**, 3158 (1961); S. Oae, W. Tagaki and A. Ohno, *J. Am. Chem. Soc.*, **83**, 5036 (1961).

[11] When triphenylmethane is added to a green solution containing two equivalents of bis-(methylthio)-methane per equivalent of potassium amide the solution becomes red. The red color is not discharged by the addition of excess triethyl orthothioformate. We therefore conclude that both of the sulfur compounds are weaker acids than triphenylmethane.

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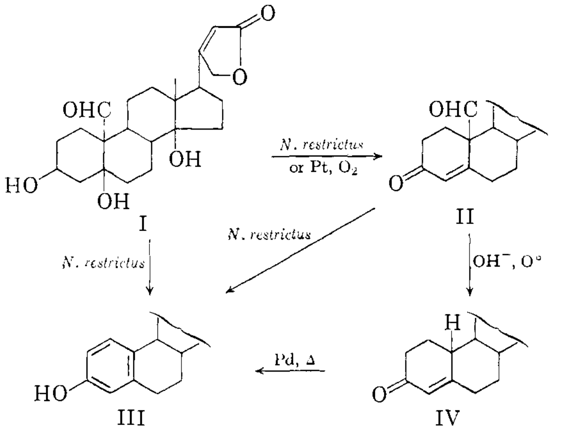
## MICROBIOLOGICAL TRANSFORMATIONS. II. THE AROMATIZATION OF RING A OF STROPHANTHIDIN

*Sir:*

A recent paper described the conversion of strophanthidin (I) to the anhydrostrophanthidone II by *Chaetomium globosum*.[1] We report herewith the transformation of I to II and thence to the new phenol III by *Nocardia restrictus*.



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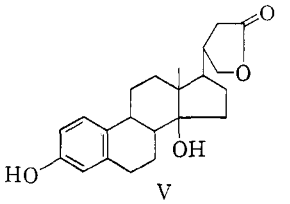
[1] C. J. Sih, S. M. Kupchan, O. El Tayeb and A. Afonso, *J. Med. Pharm. Chem.*, in press.

Fermentation of strophanthidin by the general procedure previously described,[1] with *Nocardia restrictus*, produced two principal transformation products. Paper chromatography[2] revealed that both were less polar than strophanthidin. Separation was effected by chromatography upon silica gel and fractional crystallization. The product with higher $R_f$ was characterized as the anhydrostrophanthidone II.[1,3] The second product was a new phenolic compound (III), m.p. 263–265° dec., $[\alpha]^{27}\mathrm{D}$ +78° ($c$ 0.76, pyr.); $\lambda_{\max}^{\text{alc}}$ 217 m$\mu$ ($\epsilon$ 25,600), 280 m$\mu$ ($\epsilon$ 2,200); $\lambda_{\max}^{\text{Nujol}}$ 2.88 $\mu$, 3.03 $\mu$, 5.77 $\mu$, 6.22 $\mu$, 6.30 $\mu$, 6.68 $\mu$.[4] Acetylation of III yielded a monoacetate, m.p. 206–208°, $[\alpha]^{25}\mathrm{D}$ +66° ($c$ 0.70, chf.); $\lambda_{\max}^{\text{MeOH}}$ 215 m$\mu$ ($\epsilon$ 22,100), 267 m$\mu$ ($\epsilon$ 680), 275 m$\mu$ ($\epsilon$ 640); $\lambda_{\max}^{\text{chf}}$ 2.88 $\mu$; 5.60 $\mu$, 5.72 $\mu$, 6.15 $\mu$, 6.30 $\mu$, 6.70 $\mu$. Catalytic hydrogenation of III with platinum (hydrogen consumption: 1 mole equivalent) yielded the dihydro derivative V, characterized by direct comparison with a sample prepared from dihydrostrophanthidin by the procedure of Turner and Meschino.[5] Catalytic oxidation of I in the presence of platinum and oxygen, followed directly by treatment with alkali at 0°, yielded the 19-noranhydrostrophanthidone IV, m.p. 240–241°, $[\alpha]^{27}\mathrm{D}$ +33° ($c$ 2.67, chf.); $\lambda_{\max}^{\text{chf}}$ 2.85 $\mu$, 5.60 $\mu$, 5.72 $\mu$ 6.01 $\mu$, 6.15 $\mu$; $\lambda_{\max}^{\text{EtOH}}$ 230 m$\mu$ ($\epsilon$ 24,700). Dehydrogenation of IV over palladium black in refluxing ethanol gave phenol III.



V

When anhydrostrophanthidone II was exposed to *N. restrictus*, a rapid and high-yield conversion to phenol III was observed. Fermentation of the 19-noranhydrostrophanthidone IV under the same conditions resulted in exceedingly slow conversion to phenol III. These findings are in good agreement with the recent studies of Morato, *et al.*,[6] on the biosynthesis of estrogens from androgens with human placental microsomes. The latter authors' observations support the sequence $\Delta^4$-androstenedione → 19-hydroxyandrostenedione → 19-oxo-androstenedione →····> estrone for the steps in biological estrogen formation. Furthermore, it was found that 19-norandrostenedione was a poor substrate for estrogen formation. The parallel findings in the respective studies that the 19-nor-steroids are less effective phenol-precursors than the corresponding 19-oxo-steroids suggest that the stepwise sequence may be similar for the microbiological and placental microsomal transformations. Work is currently under way to evaluate the hypothesis that biological conversion of II to III may proceed *via* $\Delta^1$-dehydrogenation to a 19-oxo-$\Delta^{1,4}$-dienone and then aromatization accompanied by liberation of a $C_1$ unit.[7]

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[2] H. R. Urscheler, Ch. Tamm and T. Reichstein, *Helv. Chim. Acta*, **38**, 897 (1955).

[3] A. Katz, *ibid.*, **40**, 831 (1957).

[4] Satisfactory analytical data were obtained for the new compounds reported herein.

[5] R. B. Turner and J. A. Meschino, *J. Am. Chem. Soc.*, **80**, 4862 (1958).

[6] T. Morato, M. Hayano, R. I. Dorfman and L. R. Axelrod, *Biochem. Biophys. Res. Comm.*, **6**, 334 (1961).

[7] Formaldehyde has recently been identified as appearing in stoichiometric ratio to estrone after placental microsomal aromatization of $\Delta^4$-androstenedione and 19-hydroxyandrostenedione (H. Breuer and P. Grill, *Z. physiol. Chem.*, **324**, 254 (1961)). However, in view of the facile biological interconversion of formaldehyde and formic acid (*cf.* F. M. Huennekens and M. J. Osborn, *Adv. in Enzymology*, **21**, 369 (1959)), it is possible that the formaldehyde may have arisen by reduction of a formic acid-equivalent.

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## SYNTHESIS OF BORON NITRIDE

*Sir:*

A broad resemblance of boron nitride to carbon in its various structural forms,[1,2] combined with certain physical characteristics, makes boron nitride a material of considerable theoretical interest and of growing importance in nuclear, refractory, electrical and lubrication technologies. While the synthesis of boron nitride has been studied fairly extensively,[3,4-8] current synthetic methods are beset with considerable technical difficulties. Accordingly, a straightforward synthesis adaptable to laboratory or large-scale production of boron nitride is of interest.

Orthoboric acid (1 mole) and urea (2 moles) are mixed and gradually heated. At about 60° the reactants melt with the evolution of water which is removed from the system in a stream of nitrogen or, preferably, under reduced pressure. As water is removed, the initially limpid liquid residue increases in viscosity and sets to a glass. Above about 165° (subsequent heating is most conveniently effected in a nitrogen stream) the glass undergoes decomposition, evolving a volatile sublimate and leaving a white, cinder-like residue (residue at 600° is 18.45 wt. % urea and boric acid reactants. *Anal.* B, 31.6; N, 20.5; remainder oxygen with only traces of carbon or hydrogen). Further heating of this BNO residue at temperatures up to 1300° does not yield a "boron nitride" of substantially improved purity. Thus, the very early claim of Darmstadt[9] to have prepared boron

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[1] R. S. Pease, *Acta. Cryst.*, **5**, 356 (1952).

[2] R. H. Wentorf, *J. Chem. Phys.*, **26**, 956 (1957); U. S. Patent 2,947,617 (Aug. 2, 1960).

[3] K. M. Taylor, *Ind. Eng. Chem.*, **47**, 2506 (1955); U. S. Patent 2,808,314 (Oct. 1, 1957).

[4] R. Taylor and C. A. Coulson, *Proc. Phys. Soc.*, **A65**, 834 (1952).

[5] A. A. Giardini, U. S. Bureau of Mines Information Circular 7664.

[6] G. H. Fetterley and G. R. Watson, U. S. Patent 2,801,903 (Aug. 6, 1957).

[7] L. A. Conant and E. F. Hittle, Canadian Patent 582,108 (Aug. 25, 1959).

[8] F. H. May and V. V. Levasheff, U. S. Patent 2,824,787 (Feb. 25, 1958).

[9] M. Darmstadt, *Lieb. Ann.*, **151**, 255 (1869).