sorption spectra, and by bioassay and paper chromatography with an authentic sample of tetracycline.

The active principles excreted by *Curvularia lunata* were non-dialyzable and were completely inactivated by heating in aqueous solution at 100° for 5 minutes. These observations suggest that the catalysts are enzymes. The *p*H optimum for tetracycline production and for 12a-deoxytetracycline utilization was about 4.6. Warburg studies revealed that oxygen was required and that it was the only gas involved in the reaction. Approximately 1 atom of oxygen was utilized per mole 12a-deoxytetracycline consumed. Since *Curvularia lunata*, preparations have no marked effect on tetracycline it is concluded that the products of the reaction are derived from 12a-deoxytetracycline and are not tetracycline degradation products. To account for the stoichiometry observed, the other reaction products must average 1 atom of additional oxygen per molecule.

Efforts to obtain crystalline material from fractions 1 and 2 have been unsuccessful. Additional column chromatography of fractions 1 and 2 yielded more cleanly resolved preparations, each of which by paper chromatography still contained more than one substance. The best preparation from fraction 1 showed ultraviolet absorption maxima in 0.1 *N* HCl characteristic of anhydro derivatives. Fraction 2 is believed to contain an 11a-hydroxylated product based on a consideration of the spectra obtained in 0.1*N* HCl and 0.1*M* sodium borate, and the fact that refluxing with methanolic HCl failed to yield an anhydro product.

While other cultures, *e.g.*, *Curvularia pallescens* and *Botrytis cinerea*, were also able to 12a-hydroxylate 12a-deoxytetracycline, several strains of *Streptomyces aureofaciens* were not.

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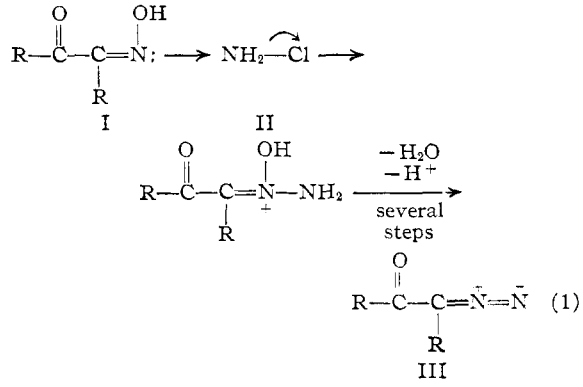
THE FORSTER REACTION AND DIAZOALKANE SYNTHESIS

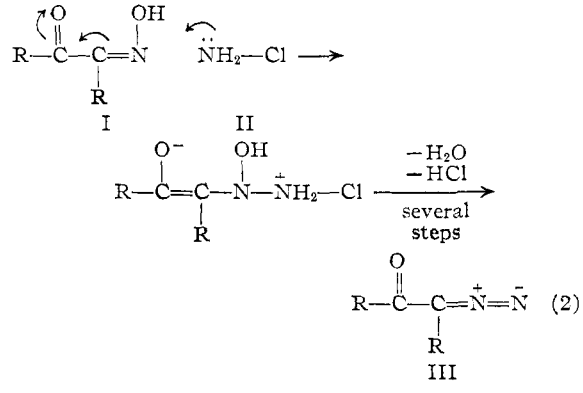
Sir:

The reaction of α-oximinoketones (I) with chloramine (II) to give diazoketones (III) was first reported by Forster in 1915.[1] As a technique for the preparation of cyclic diazoketones, this reaction has found several recent applications.[2,3,4] We have speculated about the mechanism of this transformation, and consider a sequence of steps initiated by a nucleophilic displacement at the chloramine nitrogen, as shown in equation (1), to be most plausible. The first step finds close analogy in the well-known Raschig



synthesis of hydrazine from chloramine and ammonia,[5] and more distant analogy in the Kocheshkov amine synthesis.[6] *A key feature of the process represented in (1) is the irrelevance of the carbonyl function.*

Alternate mechanisms, whose first step would be reminiscent of a Michael addition, also may be imagined for the Forster reaction. This type of process, outlined in equation (2), assigns a vital role to the carbonyl function.[7]



We have sought an experimental distinction between these two mechanisms, and wish to report results which support the nucleophilic displacement process (1) and provide a new route to diazoalkanes which may be of general interest.

Fluorenone oxime (0.50 g.) was suspended in 15 *N* ammonium hydroxide (25 ml.) and a 5.25% solution of sodium hypochlorite (100 ml.) was added at 0° over a one-hour period. The mixture was extracted with petroleum ether several times over a four-hour period. These extracts yielded diazofluorene (0.19 g.), identified by infrared comparison with an authentic sample. Unreacted oxime (0.25 g.) was recovered from the aqueous layer.

Similar experiments were carried out with the oximes of benzophenone, acetophenone and

(1) M. O. Forster, *J. Chem. Soc.*, **107**, 260 (1915).

(2) M. P. Cava and R. L. Litle, *Chemistry and Industry*, 367 (1957); M. P. Cava, R. L. Litle and D. R. Napier, THIS JOURNAL, **80**, 2257 (1958).

(3) W. Kirmse, *Angew. Chem.*, **69**, 106 (1957).

(4) J. Meinwald and P. G. Gassman, Abstracts of Papers Presented before the Division of Organic Chemistry at the April 5–10, 1959, meeting of the American Chemical Society, p. 14-O.

(5) For an interesting review of chloramine chemistry see E. Colton and M. M. Jones, *J. Chem. Ed.*, **32**, 485 (1955).

(6) For a leading reference see P. L. Pauson, *Quart. Rev.*, **9**, 413 (1955).

(7) The authors are grateful to Professors Gilbert Stork and Ronald Breslow for a stimulating discussion during which this possibility came to light.

benzaldehyde. In each case, the diazoalkane was formed, although the conversions were not as good as that observed in the fluorenone case.[8,9]

In an attempt to develop this finding into a more useful synthetic technique, some preliminary experiments were carried out in which hydroxylamine-O-sulfonic acid (IV), a crystalline solid,[10] was substituted for chloramine. Fluorenone oxime was found to react with IV in aqueous base to give diazofluorene in *ca.* 60% yield. Similarly, benzophenone oxime gave diphenyldiazomethane (30%), while oximes of acetophenone and benzaldehyde gave small amounts of diazoalkanes.[9]

These results clearly indicate that a carbonyl group is not essential for the >C=NOH → >C=N_2 conversion, and therefore support a mechanism of type (1) for the Forster diazoketone synthesis.

Acknowledgment.—This work was supported in part by a grant from the National Science Foundation.

(8) It has been reported recently by L. A. Carpino, C. A. Giza and B. A. Carpino, THIS JOURNAL, **81**, 955 (1959), that "attempts to apply the Forster reaction to the synthesis of simple diazo compounds such as diazofluorene were unsuccessful." This failure to observe the desired reactions may possibly be a consequence of an unfortunate choice of experimental conditions.

(9) It is interesting to note that as by-products, benzhydrol was found to accompany the diphenyldiazomethane, and benzonitrile was formed along with phenyldiazomethane.

(10) F. Sommer, O. F. Schulz and M. Nassau, *Z. anorg. u. allgem. Chem.*, **147**, 142 (1925); G. Gever and K. Hayes, *J. Org. Chem.*, **14**, 813 (1949).

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SYNTHESIS OF THE TWO ANOMERIC 9-(2-DEOXY-D-RIBOFURANOSYL)-ADENIVEU*

Sir:

The several methods[1,2,3] for the synthesis of 2′-deoxynucleosides all involve rather complicated alterations of the functional groups of pentofuranosyl moieties already bound to purines or pyrimidines. The relative accessibility of 2-deoxy-D-ribose[4] makes a direct approach to the synthesis of 2′-deoxynucleosides from this sugar potentially more attractive. This Communication reports such an approach, the immediate objective being the synthesis of natural 2′-deoxyadenosine [9-(2-deoxy-β-D-ribofuranosyl)-adenine] (I) and its unnatural anomer (II).

2-Deoxy-D-ribose was converted to its amorphous diisobutyl mercaptal[5] and then mono-*p*-nitrobenzoylated to give crystalline 2-deoxy-5-*O*-*p*-nitrobenzoyl-D-ribose diisobutyl mercaptal (III) in 44% yield: m.p.[6] 74–75°, $[\alpha]^{20}D$ −10.2° (*c* 0.81, $CHCl_3$). *Anal.* Calcd. for $C_{20}H_{31}NO_6S_2$: C, 53.91; H, 7.01; N, 3.14. Found: C, 53.68; H, 6.91; N, 3.33. Demercaptalation of III yielded an amorphous product which then was fully acylated with *p*-nitrobenzoyl chloride in pyridine solution to give the two crystalline, anomeric 2-deoxy-1,3,5-tri-*O*-*p*-nitrobenzoyl-D-ribofuranoses (α-IV and β-IV) in a total yield of 82% based on III. One isomer, m.p. 164–165°, $[\alpha]^{20}D$ +69.9° ($CHCl_3$, *c* 0.66), is assigned structure α-IV. *Anal.* Calcd. for $C_{26}H_{19}N_3O_{13}$: C, 53.71; H, 3.29; N, 7.23. Found: C, 53.99; H, 3.56; N, 7.21. The second isomer, m.p. 172–173°, $[\alpha]^{20}D$ +17° ($CHCl_3$, *c* 0.36), is assigned structure β-IV. Found: C, 53.98; H, 3.57; N, 7.15.

Either α-IV or β-IV or a mixture of the two was found to serve equally well in the following steps. The ester, IV, was dissolved in methylene chloride and treated with a slight excess of hydrogen chloride, the precipitated *p*-nitrobenzoic acid (87%) filtered off and the solvent removed *in vacuo*. To the residue was added a solution of chloromercuri-6-benzamidopurine in anhydrous dimethyl sulfoxide. After two hours at room temperature, the product was precipitated with water and, after drying, treated with methanolic barium methoxide. The deacylated material was chromatographed on powdered cellulose using isopropyl ether–ethanol–water (16:4.5:1 v./v.). Adenine, I and II appeared in this order. Solvent was evaporated from I, the crystalline residue leached with methylene chloride and the remainder crystallized from water to give pure material which was dried *in vacuo* at 110° for 5 hr. (8.3% yield). After recrystallization from water it showed m.p. 191–194°, $[\alpha]^{25}_{589}$ − 25°; $[\alpha]^{25}_{450}$ −59°; $[\alpha]^{25}_{400}$ −72°; $[\alpha]^{25}_{360}$ −104°; $[\alpha]^{25}_{340}$ −127°; $[\alpha]^{25}_{330}$ −137° (H_2O, *c* 0.47). *Anal.* Calcd. for $C_{10}H_{13}N_5O_3$: C, 47.80; H, 5.21; N, 27.88. Found: C, 47.73; H, 5.28; N, 27.36 (sample dried 5 hr. at 100° *in vacuo*).

Authentic 9-(2-deoxy-β-D-ribofuranosyl)-adenine melts at 191–192° and does not depress the melting point of the synthetic product. A repurified commercial sample of I showed: $[\alpha]^{25}_{589}$ −26°; $[\alpha]^{25}_{400}$ − 71°; $[\alpha]^{25}_{360}$ −103°; $[\alpha]^{25}_{340}$ −128°; $[\alpha]^{25}_{330}$ −150°; $[\alpha]^{25}_{320}$ −173°; $[\alpha]^{25}_{310}$ −206° (H_2O, *c* 0.49). Both natural and synthetic I showed absorption peaks at 260 mμ, A_M for natural I being 15,900 and A_M for synthetic I being 16,600.

The infrared spectra of both were never found to be completely identical using the KBr-plate technique. However, we have observed that 2′-deoxyadenosine crystallizes with varying amounts of water and possibly in dimorphic forms, both natural and synthetic specimens even after rigorous drying often showing a m.p. of *ca.* 160–170° before finally melting at 191–192°.

The anomeric nucleoside (II), obtained in 18% yield, was recrystallized successively from ethanol–pentane, ethanol and methanol, m.p. 209–211°, $[\alpha]^{25}_{589}$ +71°; $[\alpha]^{25}_{450}$ +132°; $[\alpha]^{25}_{400}$ +173°;

* This Communication to the Editor was received prior to that of M. Hoffer, R. Duschinsky, J. J. Fox and N. Yung (THIS JOURNAL, **81**, 4112 (1959)) and was to have been published simultaneously; unfortunately the manuscript was filed pending acceptance of the later Communication, and then overlooked and not put in process of publication until after the other had appeared.—The Editors.

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(2) G. Shaw and R. N. Warrener, *ibid.*, 50 (1959).

(3) C. D. Anderson, L. Goodman and B. R. Baker, THIS JOURNAL, **80**, 6453 (1958).

(4) H. W. Diehl and H. G. Fletcher, Jr., *Arch. Biochem. Biophys.*, **78**, 386 (1958).

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(6) Melting points are corrected.