transverse structural periods are 200 to 325 as compared to approximately 115 Å. (II).

System II is also distinctive in that the apparent calculated spacings change with the cosine of the angle of departure of the muscle axis from perpendicularity to the X-ray beam, indicating that the diffracting elements are two-dimensional. Type I elements are also believed to have a thin dimension,[2] but apparently this is not fine enough to result in the corresponding diffraction phenomenon.

DEPARTMENT OF BIOLOGY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE, MASSACHUSETTS RICHARD S. BEAR

RECEIVED AUGUST 9, 1945

ADDITION OF DERIVATIVES OF CHLORINATED ACETIC ACIDS TO OLEFINS

Sir:

The chain reaction whereby the elements of carbon tetrachloride and of chloroform may be added to the double bonds of olefins[1] has been reported.[2] Furthermore, it has been found that (among other substances) derivatives of chlorinated acetic acids will add to olefins to give excellent yields of the following type of compounds

$$RCH{=}CH_2 + CHCl_2COOCH_3 \longrightarrow RCH_2CH_2CCl_2COOCH_3 \quad (1)$$

$$RCH{=}CH_2 + CCl_3COCl \longrightarrow RCHClCH_2CCl_2COCl \quad (2)$$

Octene-1 (32 g.) and methyl dichloroacetate (177 g.) were heated in a flask for four hours at 100° in the presence of diacetyl peroxide (2 g.). About 57 g. remained in the flask after removal of the starting materials at reduced pressure. This material upon distillation gave 29 g. of a fraction which boiled at 74–75° (0.3 mm.) ($n^{20}D$ 1.4561) and a residue (28 g.). It is presumed that the former is methyl α,α-dichlorocaprate (40% yield).

Anal. Calcd. for $C_{11}H_{20}O_2Cl_2$: Cl, 27.85; mol. wt., 255. Found: Cl, 28.17; mol. wt., 255.

The residue was distilled in a molecular still. From the chlorine content (23.45%) and the molecular weight (357) of the middle fraction, it appears likely that this fraction is a mixture of dimethyl tetrachlorosuccinate (13%), and the condensation product made up of two molecules of octene-1 and one molecule of methyl dichloroacetate (87% = 46% yield on the basis of octene-1 used).

A better yield of the mono addition product and a smaller amount of the higher condensation products (two or more molecules of octene-1 to one molecule of chlorinated acetic acid derivative) were obtained when octene-1 (25 g.) and trichloroacetyl chloride (180 g.) were heated in a flask in the presence of diacetyl peroxide (2 g.) and the reaction mixture was worked up as described above. The yield of α,α,γ-trichlorocapryl chloride (b. p. 123–126°/, 0.3 mm., $n^{20}D$ 1.4830) was 81%, based on the octene-1 used.

Anal. Calcd. for $C_{10}H_{16}OCl_4$: Cl, 48.2; mol. wt., 294. Found: Cl, 48.1; mol. wt., 294.

The condensation of methyl monochloroacetate and octene-1 gave only about a 10% yield of a condensate, based on the octene-1 used.

The reactions cited are assumed to proceed via a free radical chain reaction initiated by the free radicals formed by the decomposition of the diacyl peroxide.

$$(CH_3COO)_2 \longrightarrow CH_3\cdot + CO_2 + CH_3COO\cdot \quad (1)$$

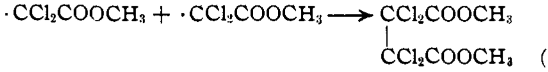
$$CHCl_2COOCH_3 + CH_3\cdot \longrightarrow CH_4 + \cdot CCl_2COOCH_3 \quad (2)$$

$$RCH{=}CH_2 + \cdot CCl_2COOCH_3 \longrightarrow R\dot{C}HCH_2CCl_2COOCH_3 \quad (3)$$

$$R\dot{C}HCH_2CCl_2COOCH_3 + CHCl_2COOCH_3 \longrightarrow RCH_2CH_2CCl_2COOCH_3 + \cdot CCl_2COOCH_3 \quad (4)$$

$$R\dot{C}HCH_2CCl_2COOCH_3 + RCH{=}CH_2 \longrightarrow R\dot{C}HCH_2CHRCH_2CCl_2COOCH_3 \quad (5)$$

$$R\dot{C}HCH_2CHRCH_2CCl_2COOCH_3 + CHCl_2COOCH_3 \longrightarrow RCH_2CH_2CHRCH_2CCl_2COOCH_3 + \cdot CCl_2COOCH_3 \quad (6)$$



$$\cdot CCl_2COOCH_3 + \cdot CCl_2COOCH_3 \longrightarrow \begin{array}{c} CCl_2COOCH_3 \\ | \\ CCl_2COOCH_3 \end{array} \quad (7)$$

It is assumed that reactions (5) and (6) are responsible for the formation of the high boiling materials.

Insofar as we know, the propagation of the chain reaction, as indicated in steps (3) and (4), will take place if the radical R in the unsaturated compound is aliphatic and if it is attached to a carbon atom which has a hydrogen atom attached to it. The basis for this statement and the basis for the structures assigned to the compounds formed in this interesting reaction will be presented in the near future in a comprehensive paper now in preparation.

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[1] The reaction has also been extended to compounds containing triple bonds; the double or triple bond does not necessarily need to be terminal.

[2] Kharasch, Jensen and Urry, *Science*, **102**, 128 (1945).

PRODUCTION OF GLIOTOXIN AND A SECOND ACTIVE ISOLATE BY *PENICILLIUM OBSCURUM* BIOURGE

Sir:

Recently we have been able to isolate gliotoxin, as well as a second heretofore unreported antibiotic, from a culture of *Penicillium obscurum* Biourge. Removal of the two substances from the broth was effected by extraction at *p*H 2 with benzene. Addition of approximately equal parts of petroleum ether to the concentrated extract resulted in the separation of the crude Isolate 1. Purification was accomplished by repeated crystallizations. The material melted at 192–193°[1]

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[1] All melting points are corrected.

and the analysis of our Isolate 1 conforms to the formula for gliotoxin proposed by Dutcher,[2] *et al.*

Anal. Calcd. for $C_{13}H_{14}N_2O_4S_2$: C, 47.85; H, 4.32; N, 8.59; S, 19.65. Found: C, 47.89; H 4.44; N, 8.76; S, 19.76.

Isolate 2 was obtained from the mother liquor, available after the removal of gliotoxin, by chromatography on a column of alumina and elution with benzene containing 4% methanol. Large, pale yellow, rhombic crystals separated from the eluate. In general, Isolate 2 was found to be more soluble than gliotoxin. The material melted at 159–160° and showed a specific rotation of $[\alpha]^{19}\text{D}$ $-197°$ (*c*, 0.600 in chloroform). The analysis and molecular weight indicated a formula corresponding to one-half of that proposed by Weindling[3] for gliotoxin, which probably will have to be doubled because of the degradation products obtained. A methoxyl determination failed to demonstrate the presence of any such group in the molecule.

Anal. Calcd. for $C_7H_8NO_2S$: C, 49.41; H, 4.71; N, 8.24; S, 18.82; mol. wt., 170. Found: C, 49.43; H, 4.68; N, 8.14; S, 18.84; mol. wt., 184, 194 (Rast).

The ultraviolet absorption spectra of gliotoxin and Isolate 2 showed almost identical maxima and minima.

Both reduction with hydriodic acid and alkaline hydrolysis with barium hydroxide of Isolate 2 gave products which on the basis of analysis, melting points and mixed melting point, were identical with those obtained from gliotoxin.[4,5]

An attempt to form crystalline acylation products of both gliotoxin and the second isolate resulted in the formation of the dibenzoate (m. p. 198–199°)[4] of gliotoxin, but thus far no crystalline benzoate of Isolate 2 has been secured. The quantitative acetylation procedure of Freed and Wynne,[6] however, indicated the consumption of identical amounts of acetic acid for both compounds.

The comparative antibacterial values of gliotoxin and Isolate 2, as determined by a broth dilution method, indicated the former to possess approximately ten times the bacteriostatic properties of the latter. The assay values were based on tests against a limited number of pathogenic bacteria, representing both gram-positive and gram-negative types.

The toxicity to mice of Isolate 2, however, was found to be almost identical with that reported for gliotoxin.[2]

Thanks are due to Dr. K. B. Raper, U. S. Department of Agriculture, Peoria, Ill., for the identification of the culture as *Penicillium obscurum* Biourge.

The isolation of the mold and broth filtrate preparation, as well as bacteriological and toxicological studies, were conducted by Dr. R. L. Mayer and Mr. W. S. Marsh of Ciba's Bacteriological Department.

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RECEIVED JULY 31, 1945

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[2] Johnson, Bruce and Dutcher, THIS JOURNAL, **65**, 2005 (1943).

[3] Weindling and Emerson, *Phytopathology*, **26**, 1068 (1936).

[4] Bruce, Dutcher, Johnson and Miller, *ibid.*, **66**, 614 (1944).

[5] Dutcher, Johnson and Bruce, *ibid.*, **66**, 617 (1944).

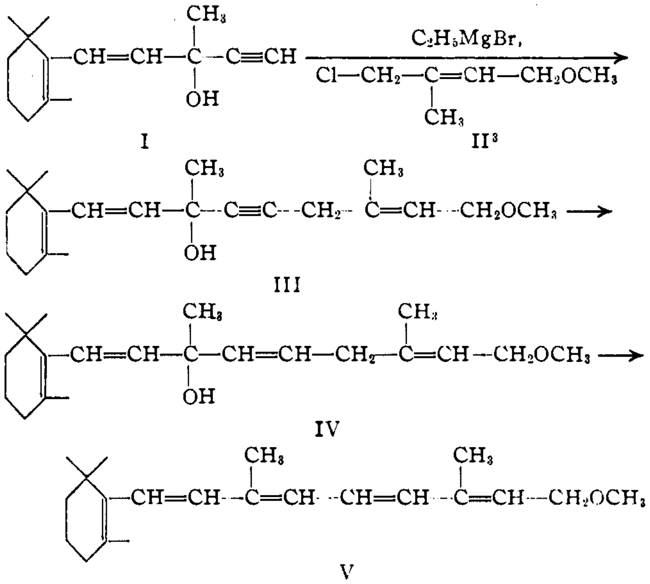
[6] Freed and Wynne, *Ind. Eng. Chem., Anal. Ed.*, **8**, 278 (1936).

A SYNTHESIS OF VITAMIN A METHYL ETHER—PRELIMINARY REPORT

Sir:

During the past decade there have been two reports in the literature describing the synthesis of Vitamin A or its derivatives. The first, by Kuhn and Morris,[1] yielded an impure mixture of unknown constitution which showed some biological activity. However, all attempted repetitions reported have been unsuccessful. The second, by Kipping and Wild in 1939,[2] concerned the methyl ether of Vitamin A but was devoid of any supporting physical, chemical or biological evidence.

The synthesis of the methyl ether of Vitamin A has been attempted in this Laboratory by the following scheme



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[1] Kuhn and Morris, *Ber.*, **70**, 853 (1937).

[2] Kipping and Wild, *Chemistry and Industry*, **58**, 802 (1939).

[3] Compound II and the analogous acetate were prepared by the reaction of isoprene with *t*-butyl hypochlorite in methanol and in glacial acetic acid, respectively. In both cases 1:2 and 1:4 addition products were isolated and their structures proven. Compound II, 1:2 product, b. p. 68–69° (55 mm.), $n^{24}\text{D}$ 1.4420. *Anal.* Calcd. for $C_6H_{11}OCl$: C, 53.53; H, 8.24; Cl, 26.34. Found: C, 53.46; H, 8.45; Cl, 26.27. Compound II, 1:4 product, b. p. 89–91° (55 mm.), $n^{23}\text{D}$ 1.4590. *Anal.* Found: C, 53.40; H, 8.20; Cl, 26.44

The acetate, 1:2 product, b. p. 61–63° (10 mm.), $n^{28}\text{D}$ 1.4445. *Anal.* Calcd. for $C_7H_{11}O_2Cl$: C, 51.70; H, 6.82; Cl, 21.81. Found: C, 51.90; H, 7.01; Cl, 21.96. The 1:4 product, b. p. 92–94° (10 mm.), $n^{28}\text{D}$ 1.4640. *Anal.* Found: C, 51.98; H, 6.83; Cl, 21.72.