treatment with piperidine, yielded a second new stereoisomer, m. p. 155–157°, $[\alpha]_D$ +84° (chloroform), it must have the same configuration around C_3 as podophyllotoxin and the second new stereoisomer must have the same configuration around C_3 as picropodophyllin. The stereoisomer melting at 159–161° is therefore the C_1-epimer of podophyllotoxin and is named epipodophyllotoxin, while the diastereoisomer melting at 155–157° is the C_1-epimer of picropodophyllin and is named epipicropodophyllin. The conversion of podophyllotoxin to epipodophyllotoxin through the halide represents a Walden inversion, an impossibility with the Borsche–Späth formula, II. Furthermore, production of the chloride by means of acetyl chloride is unexpected of a primary alcohol, II, and its ready hydrolysis by water is not typical of primary chlorides. Finally, the existence of four diastereoisomers differing only in configuration around the carbon atom bearing the hydroxyl group and the carbon atom α to the carbonyl group is compatible only with III.

Detailed experimental results and discussion will be presented in a later paper.

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THE ACID-CATALYZED REACTION OF STYRENE OXIDE AND ALLYL ALCOHOL

Sir:

The concern of Guss over "the present difficulties in the interpretation of the ring opening reactions of olefin oxides"[1] is shared by many investigators in this field.

These reactions may be interpreted as concerted displacements from such evidence as stereochemical inversion of the reacting carbon atom,[2] the kinetic order dependence on oxide and attacking reagent,[3] and the necessity for solvolysis.[4] Unsymmetrical 1,2-epoxides provide the added complication of a competition reaction wherein the efficiency of the solvolysis of the oxygen atom and the electronic and steric disposition of the displacing group and of the reacting carbon atoms assume dominant roles.

Two publications[5,6] provide experimental evidence which contradicts the generality of this theory. The specific cases involve acid-catalyzed reactions of styrene oxide with alcohols, which are claimed to produce 2-allyloxy-1-phenylethanols. The earlier work of Emerson[5] has been corrected by Reeve and Christoffel[7] for the case, methanol. We have evidence which contradicts the conclusion of Swern, Billen and Knight[6] that styrene oxide reacts with allyl alcohol in the presence of sulfuric acid to give 2-allyloxy-1-phenylethanol.

The alleged "2-allyloxy-1-phenylethanol" was synthesized by the prescribed method[6] and then treated with *p*-toluenesulfonyl chloride in pyridine. The product was heated with dry pyridine for twenty hours to give an ether-insoluble oil, which was converted to a crystalline iodide salt with sodium iodide in acetone. Analysis showed it to be a phenylallyloxyethylpyridinium iodide, m. p. 155–156°; *Anal.* Calcd. for $C_{16}H_{18}ONI$: C, 52.33; H, 4.94; N, 3.81. Found: C, 52.22; H, 5.20; N, 4.03. The exact identity of the salt was determined by heating it for three minutes in boiling 47% hydriodic acid. This gave allyl iodide and the known 1-(2-phenyl-2-hydroxyethyl)-pyridinium iodide,[8] m. p. 256–258°. An over-all yield of 70% was realized.

It is extremely improbable that any rearrangement has occurred. Bartlett and Lewis[9] have emphasized the non-participation of ether groups in replacement reactions. If the reaction with pyridine had involved the participation of the allyloxy group to form the intermediate styrene allyloxonium ion, then a large yield of 1-(1-phenyl-2-allyloxyethyl)-pyridinium *p*-toluenesulfonate should have been formed. This argument is strictly in agreement with the results of the pyridine reaction with styrene oxonium ion.[8] To supply additional evidence on this point, a sample of the major product of the base-catalyzed reaction of styrene oxide and allyl alcohol[5] was put through the same first three reactions as above. A different phenylallyloxyethylpyridinium iodide was obtained. This removes the possibility that both *p*-toluenesulfonate esters react by way of the same styrene allyloxonium ion intermediate.

From these considerations we conclude that the product of the acid-catalyzed reaction of styrene oxide with allyl alcohol is actually *2-allyloxy-2-phenylethanol.* The evidence then fits the theory that displacement reactions involving the styrene oxonium ion should be favored at the benzyl carbon, due to resonance stabilization of the transition state.

(1) Guss, THIS JOURNAL, **71**, 3460 (1949).
(2) Grigsby, Hind, Chanley and Westheimer, *ibid.*, **64**, 2606 (1942).
(3) Brönsted, Kilpatrick and Kilpatrick, *ibid.*, **51**, 446 (1929).
(4) Kusner, *Ukrain. Khem. Zhur.*, **7**, Wiss. Abt. 179 (1932).
(5) Emerson, THIS JOURNAL, **67**, 516 (1945).
(6) Swern, Billen and Knight, *ibid.*, **71**, 1152 (1949).
(7) Reeve and Christoffel, *ibid.*, **72**, 1480 (1950).
(8) King, Berst and Hayes, *ibid.*, **71**, 3498 (1949).
(9) Bartlett and Lewis, *ibid.*, **72**, 406 (1950).

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ELECTRON MICROSCOPE OBSERVATIONS OF CERTAIN FIBROUS STRUCTURES OBTAINED FROM CONNECTIVE TISSUE EXTRACTS

Sir:

Orekhovich, *et al.*,[1] have described a protein which they obtained from macerated, phosphate

(1) V. N. Orekhovich, A. A. Tustanovskii, K. D. Orekhovich and N. E. Plotnikova, *Biokhimiya*, **13**, 55 (1948).

extracted animal skins by extraction with citrate buffer at *p*H 4. The protein, to which they gave the somewhat dubious name "procollagen," separates out from the extract after dialysis, neutralization or salting out. In an examination of this substance with the electron microscope certain new structures were observed, as briefly described herein.

Citrate extracts of rat, calf and steer skins and of rat tail tendon, after filtration or centrifugation, show no clearly defined structures but only a deposit of extremely fine filaments (50 Å. or less) as viewed in chromium-shadowed preparations. After dialysis against water the preparations are densely populated with fibrous structures of varying widths, lengths and shapes.

Under certain conditions fibrils having a banded structure with an axial periodicity (*ca.* 650 Å.) similar to collagen fibrils, native or reconstituted from acetic acid solution[2,3] were observed. However, in addition to, and sometimes to the exclusion of, such collagen-like fibrils there appeared structures which are always very thin, sometimes fibrous (Fig. 1, A), sometimes broad, flat segments (Fig. 1, B), but which have the distinctive characteristic of an axial repeating pattern several times that of normal collagen. These differ distinctly from the stretched collagen fibrils previously described.[2] Axial "periods" averaged about 2000 Å. in one type of preparation and about 2600 Å. in another type. In phosphotungstic acid stained preparations detailed banded structure was frequently observed between the main bands, but in other cases no such fine structure was observed. In all shadowed preparations the main bands stand out sharply in contrast to the thin interband regions.

Experiments designed to determine the composition, properties and origin of these structures are in progress.

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RECEIVED MAY 19, 1950

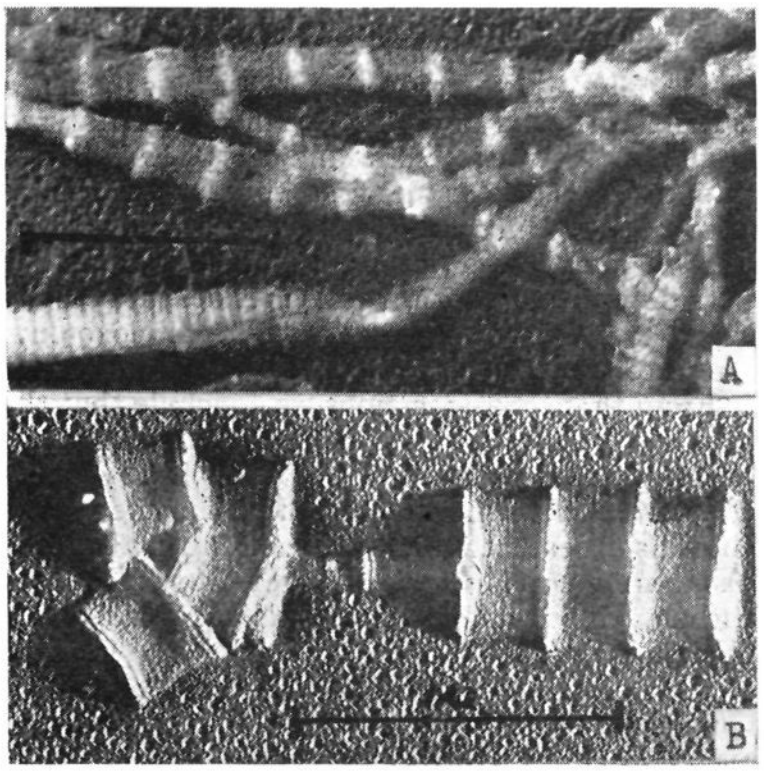

Fig. 1.—Electron micrographs of fibrils precipitated from citrate buffer extract. Shadowed with chromium. A. From calf skin. Note collagen-type fibril (at bottom of figure) together with long-spacing-type fibrils. Magnification 25,000. B. From skin of two day rat. Note flat segmented fibril of long-spacing type. Magnification 32,000.

(2) C. E. Hall, M. A. Jakus and F. O. Schmitt, *J. Cell. Comp. Physiol.*, **20**, 11 (1942).

(3) F. O. Schmitt and J. Gross, *J. Am. Leather Chem. Assoc.*, **43**, 658 (1948).

EXPLOSION HAZARD IN THE PREPARATION AND USE OF 2,4-DINITROBENZENESULFENYL CHLORIDE

Sir:

I was recently informed that a worker in one of the large commercial laboratories had incurred a violent explosion during an attempt to prepare 2,4-dinitrobenzenesulfenyl chloride. The detonation occurred when the solvent, *sym*-tetrachloroethane, had been nearly removed from a reaction mixture in which the chlorinolysis of fifteen grams of 2,4-dinitrophenyl disulfide had been effected.[1] The apparent cause of this explosion was overheating of the sulfenyl chloride, above the temperatures recommended in the references cited, occasioned by the failure to regulate an electrical mantle employed as the source of heat for the distillation of the solvent.

Subsequent to the above incident, samples of 2,4-dinitrobenzenesulfenyl chloride have been supplied to reliable testing agencies for the purpose of studying the explosive characteristics of this reagent. The preliminary results from one of these series of tests show that the hazards involved in the explosion of 2,4-dinitrobenzenesulfenyl chloride are considerable, and that particular caution must always be exercised in the preparation, handling and storage of this sulfenyl chloride. The complete results of the explosive tests will be published as soon as all of the data have been accumulated and verified.

The major warning which we wish to stress at this time is that indiscriminate heating of 2,4-dinitrobenzenesulfenyl chloride above temperatures of 90–100° must be avoided. In addition, the following suggestions may be helpful. (1) All samples of the reagent should be labelled "Explosive," and stored in a part of the labora-

(1) The method of preparation was the one described by Kharasch, Wehrmeister and Tigerman, THIS JOURNAL, **69**, 1612 (1947). *Cf.*, also, *ibid.*, **71**, 2726 (1949); **72**, 1796 (1950); "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 456. These methods have been used scores of times, in the laboratory of the writer, without untoward incidents.