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.

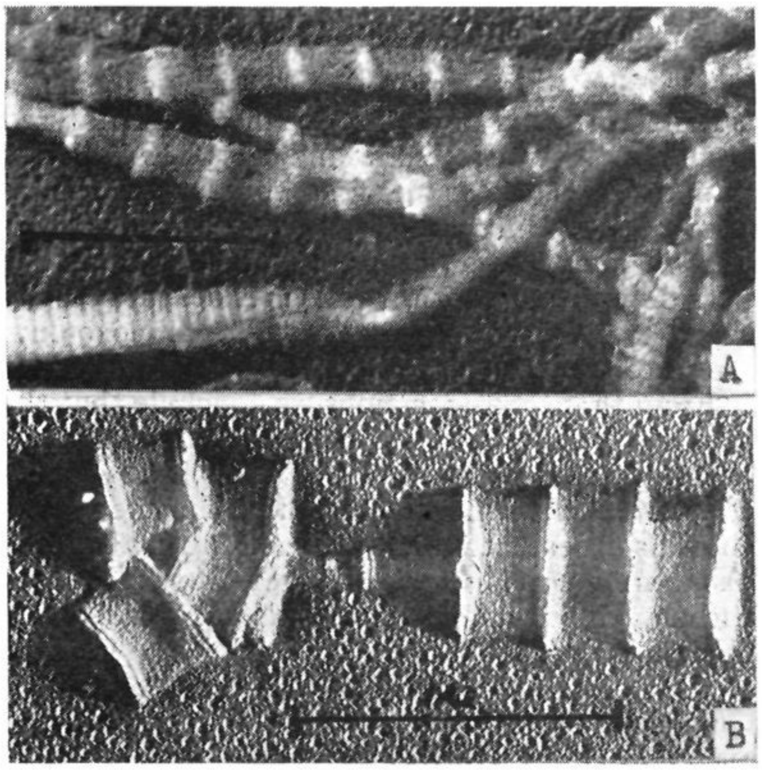

Fig. 1.—Electron micrographs of fibrils precipitated from citrate buffer extract. Shadowed with chromium. A. From calf skin. Note collagen-type fibril (at bottom of figure) together with long-spacing-type fibrils. Magnification 25,000. B. From skin of two day rat. Note flat segmented fibril of long-spacing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

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

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RECEIVED MAY 19, 1950

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-

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[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).

[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.

tory where fires or explosions are least likely. (2) When necessary, the reagent may be readily disposed of by stirring it into several volumes of 20% sodium hydroxide solution, and flushing the resulting brown solution away in a stream of water.

To ensure the safe development of 2,4-dinitrobenzenesulfenyl chloride as a very useful, routine laboratory chemical, it is sincerely hoped that chemists who work with it will observe all suitable precautions.

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RECEIVED JUNE 19, 1950

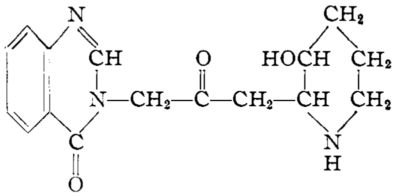
THE STRUCTURE OF FEBRIFUGINE AND ISOFEBRIFUGINE[1]

Sir:

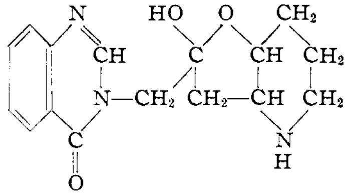
We wish to propose for febrifugine and isofebrifugine, two of the alkaloids from *Dichroa febrifuga*,[2] structures based on I.

Both febrifugine and isofebrifugine give the same optically inactive periodate oxidation product[2b] for which we now propose structure II or a closely related isomer thereof. When II is heated in pyridine with semicarbazide hydrochloride, the pyrazole III, m. p. 187–188°,[3] is obtained. *Anal.*[4] Calcd. for $C_{12}H_{10}ON_4$: C, 63.70; H, 4.46; N, 24.77. Found: C, 63.38; H, 4.44; N, 24.45. The pyrazole III was synthesized as follows: quinazolone-4 and propargyl bromide reacted to give 3-propargyl-4-quinazolone, m. p. 116–118°; calcd. for $C_{11}H_8ON_2$: C, 71.72; H, 4.38; N, 15.21; found: C, 71.66; H, 4.42; N, 15.25; which on treatment with diazomethane yielded III identical with III obtained from II. In order to establish the point of attachment in the pyrazole ring of III, it was hydrolyzed and the resulting crude aminomethylpyrazole (the picrate of which melted with decomposition at 199–200°) treated with nitrous acid. Without isolating the expected hydroxymethylpyrazole, the mixture was oxidized with alkaline permanganate to give 3(5)-pyrazolecarboxylic acid, m. p. 210–212°, identical with an authentic specimen.[5]

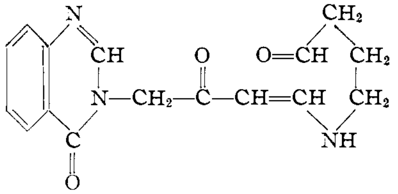
The four carbon atoms, one oxygen and one nitrogen of the original piperidine ring which remain to be accounted for should now be in the form of the semicarbazone of γ-aminobutyraldehyde. Although we have not attempted to isolate the latter itself we were able, after treating II with semicarbazide and removing III and heating the residue with cyclohexanone, to obtain a strong, volatile amine in the form of a picrolonate, m. p. 259–260° (dec.).



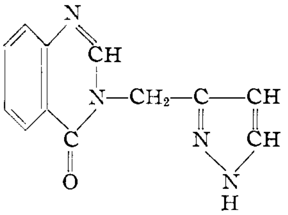
I



Ia



II



III

The alkaloids probably exist as diastereoisomers of the hemiketal Ia. Although it is impossible to be specific with respect to the configuration around any of the asymmetric centers, we have reason to believe that febrifugine and isofebrifugine differ only in configuration around the hemiketal carbon atom. This formulation accounts for the ready interconvertibility of the alkaloids and is in accord with their observed reactions.

We will submit a detailed account of this work in the near future and we expect to explore the preparation of new antimalarials based on the unique structure of these alkaloids.

We again gratefully acknowledge to Eli Lilly and Co., the gift of an additional supply of the crude bases from *D. febrifuga*.

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RECEIVED MAY 27, 1950

A RARE EARTH SEPARATION BY ANION EXCHANGE

Sir:

We have recently found a separation of promethium and europium in tracer quantities by

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(1) This investigation was supported by a research grant from the National Institutes of Health, Public Health Service.

(2) (a) Koepfli, Mead and Brockman, THIS JOURNAL, **69**, 1837 (1947); (b) **71**, 1048 (1949); (c) Kuehl, Spencer and Folkers, *ibid.*, **70**, 2091 (1948). Compare Chou, Fu and Kao, *ibid.*, **70**, 1765 (1948).

(3) All melting points are corrected.

(4) All analyses by Elek Micro Analytical Laboratory, Los Angeles.

(5) von Auwers and Cauer, *Ann.*, **470**, 297 (1929).