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.

UNIVERSITY OF SOUTHERN CALIFORNIA
LOS ANGELES 7, CALIFORNIA NORMAN KHARASCH
RECEIVED JUNE 19, 1950

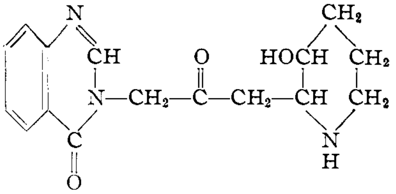
THE STRUCTURE OF FEBRIFUGINE AND ISOFEBRIFUGINE[1]

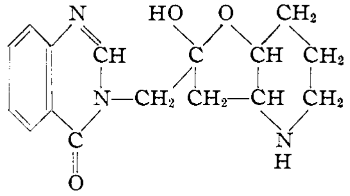
Sir:

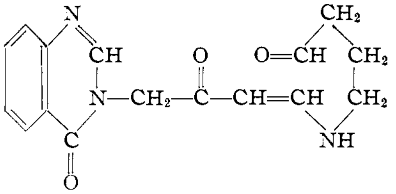
We wish to propose for febrifugine and isofebrifugine, two of the alkaloids from *Dichroa febrifuga*,[2] structures based on I.

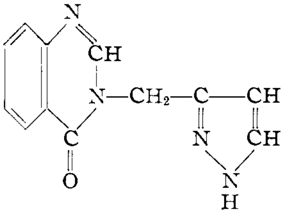
Both febrifugine and isofebrifugine give the same optically inactive periodate oxidation product[2b] for which we now propose structure II or a closely related isomer thereof. When II is heated in pyridine with semicarbazide hydrochloride, the pyrazole III, m. p. 187–188°,[3] is obtained. *Anal.*[4] 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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JOHN A. BROCKMAN, JR.
PASADENA 4, CALIFORNIA JAMES MOFFAT
RECEIVED MAY 27, 1950

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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).

A RARE EARTH SEPARATION BY ANION EXCHANGE

Sir:

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