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.

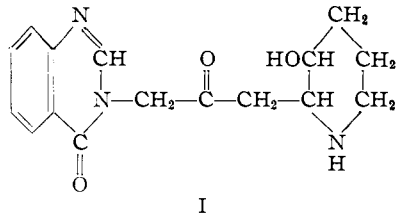
UNIVERSITY OF SOUTHERN CALIFORNIA
LOS ANGELES 7, CALIFORNIA NORMAN KHARASCH

RECEIVED JUNE 19, 1950

THE STRUCTURE OF FEBRIFUGINE AND ISOFEBRIFUGINE[1]

Sir:

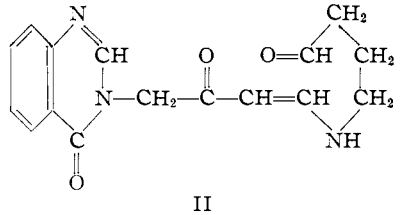
We wish to propose for febrifugine and isofebrifugine, two of the alkaloids from *Dichroa febrifuga*,[2] structures based on I.



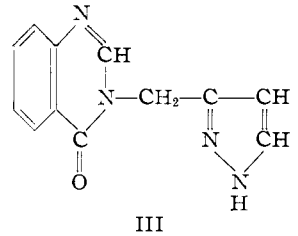
I

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.).



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*.

GATES AND CRELLIN LABORATORIES J. B. KOEPFLI
CALIFORNIA INSTITUTE OF TECHNOLOGY
JOHN A. BROCKMAN, JR.
PASADENA 4, CALIFORNIA JAMES MOFFAT

RECEIVED MAY 27, 1950

(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

development of their citrate complexes at *p*H 2.1 on an anion exchange column. No column runs have yet been made using macro quantities of these elements, though batch equilibrations indicate that the resin capacity is satisfactory for this purpose.

A solution of the tracers Pm^{147} and Eu^{154} in 0.25 ml. of 0.0125 *M* citric acid, adjusted to *p*H 2.1 with hydrochloric acid (final chloride concentration about 0.003*M*), was put on a column of 250–500 mesh Dowex A-1 resin 14.9 cm. long and 0.08 sq. cm. cross section. This column had been prepared by treating the original chloride form of the resin with citrate solution of the same concentration and *p*H. Elution at the rate of 1.5 ml. per hour with the same citrate solution gave the results shown in Fig. 1. The solid curve shows the tracer count without absorber. The broken line extension of the europium section represents the count taken with an absorber of 39.3 mg. per sq. cm., which cuts out the Pm^{147} radiation. The count with absorber is multiplied by 3.7 to correct for the partial absorption of the Eu^{154} activity. The extension of the promethium section was obtained by difference. The order of elution of these two elements is the reverse of that obtained by cation exchange.[1]

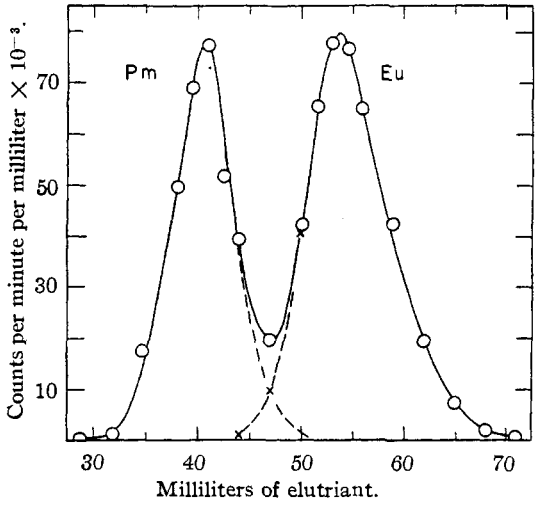


Fig. 1.

These investigations are being extended to find the optimum conditions for such separations, to apply them to macro quantities and to the other rare earth elements, and to study the mechanism of the exchange.

This work was done under the auspices of the U. S. Atomic Energy Commission.

RADIATION LABORATORY
UNIVERSITY OF CALIFORNIA E. H. HUFFMAN
BERKELEY, CALIFORNIA R. L. OSWALT

RECEIVED MAY 15, 1950

(1) B. H. Ketelle and G. E. Boyd, THIS JOURNAL, 69, 2800 (1947); E. R. Tompkins and S. W. Mayer, *ibid.*, 69, 2859 (1947); Mayer and Tompkins, *ibid.*, 69, 2866 (1947).

THE SYNTHESIS OF *dl*-COLCHINOL METHYL ETHER[1,2]

Sir:

Degradative evidence[3] strongly supports the formulation of colchinol methyl ether as 7-amino-1,2,3,9-tetramethoxydibenzo[a,c][1,3]cycloheptadiene (I). We wish to report the synthesis of I and its identity with *dl*-colchinol methyl ether, thus unequivocally establishing the 7-membered nature of ring B and the position of the amino group.

2,3,4,7-Tetramethoxy-10-phenanthroic acid was converted by Curtius degradation to the 10-phenanthrylamine (m. p. 153.5–154°; *Anal.* Calcd. for $C_{18}H_{19}NO_4$: C, 69.0; H, 6.1; N, 4.5. Found: C, 69.0; H, 6.2; N, 4.2) which was heated with sulfur dioxide to give the tetramethoxy-10-phenanthrol (m. p. 167–169°; *Anal.* Calcd. for $C_{18}H_{18}O_5$: C, 68.8; H, 5.8. Found: C, 68.7; H, 5.9). Treatment with nitrous acid led to 2,3,4,7-tetramethoxyphenanthrenequinone-9-oxime (m. p. 173–175°; *Anal.* Calcd. for $C_{18}H_{17}NO_6$: C, 63.0; H, 5.0; N, 4.1. Found: C, 63.0; H, 5.0; N, 4.1) and this was ring-opened with benzenesulfonyl chloride in pyridine to 2-(2′-cyano-4′-methoxyphenyl)-3,4,5-trimethoxybenzoic acid (m. p. 216.5–218°; *Anal.* Calcd. for $C_{18}H_{17}NO_6$: C, 63.0; H, 5.0; N, 4.1; eq. wt., 343. Found: C, 63.0; H, 5.1; N, 3.9; eq. wt., 341).

Using reactions parallel to those reported[4] in the non-methoxylated series, the synthesis proceeded from the cyano-acid to the cyano-aldehyde (m. p. 92–92.5°; *Anal.* Calcd. for $C_{18}H_{17}NO_5$: C, 66.1; H, 5.2. Found: C, 65.8; H, 5.2) to the cyano-cinnamic acid (m. p. 224–225°; *Anal.* Calcd. for $C_{20}H_{19}NO_6$: C, 65.0; H, 5.2; eq. wt., 369. Found: C, 65.0; H, 5.3; eq. wt., 371) and thence, by hydrogenation and hydrolysis to the carboxypropionic acid (m. p. 175–176.5°; *Anal.* Calcd. for $C_{20}H_{22}O_8$: C, 61.5; H, 5.7; eq. wt., 194. Found: C, 61.4; H, 5.9; eq. wt., 195). Hydrolysis of the intermediate β-keto ester formed by cyclization of the dimethyl ester gave 1,2,3,9-tetramethoxydibenzo[a,c][1,3]cycloheptadiene-7-one (m. p. 140.5–141°; *Anal.* Calcd. for $C_{19}H_{20}O_5$: C, 69.5; H, 6.1. Found: C, 69.3; H, 6.2). Wolff–Kishner reduction of the ketone gave material (m. p. 96–98°; *Anal.* Calcd. for $C_{19}H_{22}O_4$: C, 72.6; H, 7.1. Found: C, 72.6; H, 7.0) identical with dihydrodeaminocolchinol methyl ether (m. p. 96–98°) as shown by a mixed melting point determination. The *oxime* (m. p. 194–196°; *Anal.* Calcd. for $C_{19}H_{21}NO_5$: C, 66.5; H, 6.2; N, 4.1.

(1) This work was supported in part by a grant from the Cancer Research Coördinating Committee, University of California.

(2) Presented in part before the Division of Organic Chemistry at the Philadelphia Meeting of the American Chemical Society, April 11, 1950.

(3) Buchanan, Cook and Loudon, *J. Chem. Soc.*, 325 (1944); Barton, Cook and Loudon, *ibid.*, 176 (1945); Tarbell, Frank and Fanta, THIS JOURNAL, 68, 502 (1946).

(4) Rapoport and Williams, *ibid.*, 71, 1774 (1949).