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]

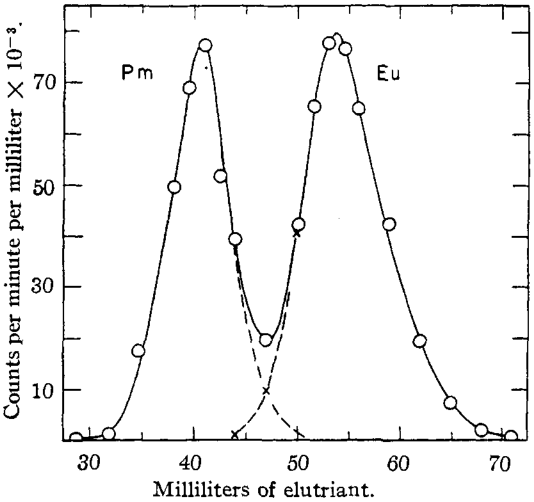

Fig. 1.

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.

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(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.

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(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).

Found: C, 66.5; H, 6.1; N, 4.0) of the ketone was reduced to the *dl-amine,* characterized through its *hydrochloride* (m. p. 258–259°; *Anal.* Calcd. for $C_{19}H_{24}NClO_4$: C, 62.4; H, 6.6; Cl, 9.7. Found: C, 62.1; H, 6.6; Cl, 9.6) and N-*acetyl derivative* (m. p. 178–179°; *Anal.* Calcd. for $C_{21}H_{25}NO_5$: C, 67.9; H, 6.8. Found: C, 67.7; H, 6.6)

Colchinol methyl ether [*hydrochloride,* m. p. 258–259°, $[\alpha]^{20}D$ − 88.7° (*c* 0.76, ethanol); N-*acetyl derivative,* m. p. 201–202°, $[\alpha]^{20}D$ − 86.6° (*c* 0.67, methanol)] was racemized by heating its N-*benzylidene derivative* [m. p. 145–146°; *Anal.* Calcd. for $C_{26}H_{27}NO_4$: C, 74.8; H, 6.5. Found: C, 75.0; H, 6.3; $[\alpha]^{25}D$ + 23.3° (*c* 0.73, dioxane)] with methanolic benzyltrimethylammonium hydroxide. The *dl*-colchinol methyl ether then isolated by acid hydrolysis formed a *hydrochloride* (m. p. 258–259°; *Anal.* Calcd. for $C_{19}H_{24}NClO_4$: OCH_3, 33.9. Found: OCH_3, 33.4) and N-*acetyl derivative* (m. p. 180–181°) both of which had zero rotation and gave no depression in mixed melting point determinations with the corresponding synthetic compounds. In addition, the ultraviolet and infrared absorption spectra of natural *l*-colchinol methyl ether hydrochloride and N-acetyl derivative were identical with those of the synthetic *dl*-counterparts.

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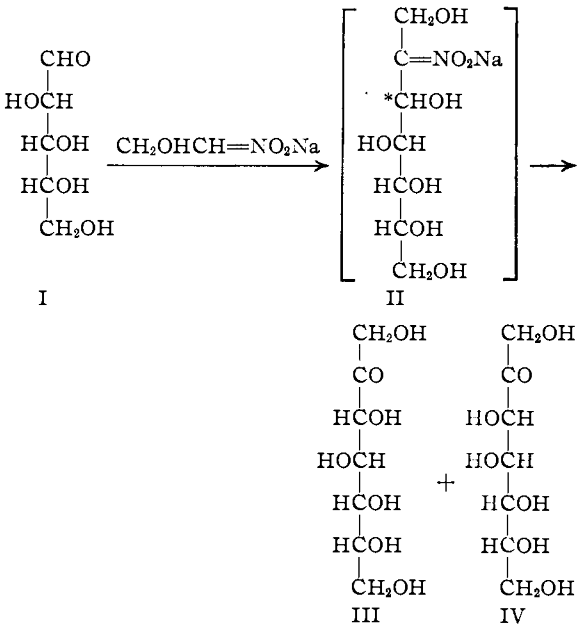
A NEW KETOSE SYNTHESIS

Sir:

Heretofore, only a single general method has existed for the synthesis of ketose sugars from aldose sugars of lower carbon content. The key reaction of this synthesis is the condensation of diazomethane with a substituted aldonyl chloride to produce a substituted diazodesoxyketose.[1] Hydrolysis of the latter then produces a ketose sugar containing one more carbon atom than the aldose precursor of the substituted aldonyl chloride. The synthesis is generally applicable to the acetylated aldonyl chlorides.[2] The yields afforded by the individual reactions of this synthesis are satisfactory. However, the number of consecutive reactions involved is relatively large and, consequently, the over-all yield of higher-carbon ketose from aldose is low.

It has now been observed that an aldose sugar may be converted to a mixture of two ketose sugars containing two additional carbon atoms by a sequence of only two reactions: The addition of sodium *aci*-2-nitroethanol to D-arabinose (I) produced the amorphous seven-carbon sodium *aci*-nitroalcohols (II). Decomposition of the mixed salts with aqueous sulfuric acid then gave a mixture of D-glucoheptulose (III), and D-mannoheptulose (IV). From 5 g. of D-arabinose there was obtained 1.6 g. (23%) of the mixed, crystalline heptuloses. Fractional crystallization produced the pure ketose sugars showing the following constants: D-glucoheptulose,[3] m. p. 170–172°, $[\alpha]^{25}D$ 67.4°, in water, *c* 2; D-mannoheptulose,[4] m. p. 151–152°, $[\alpha]^{25}D$ 29.4°, in water, *c* 2.3.



The method should be generally applicable for the synthesis of higher-carbon ketose sugars from aldose sugars.

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[1] Gätzi and Reichstein, *Helv. Chim. Acta*, **21**, 186 (1938).

[2] Wolfrom, Waisbrot and Brown, THIS JOURNAL, **64**, 2329 (1942).

[3] Austin, *ibid.*, **52**, 2106 (1930).

[4] LaForge, *J. Biol. Chem.*, **28**, 511 (1917).