

pyridine-water (4:1) as solvent) as the sulfur-containing fragment in LBF hydrolysates.

Methyl pantothenate (1.5 moles), β -mercaptoethylamine (1.5 moles) and acetamide (0.0025 mole) were refluxed in two liters of methanol for eleven hours. Assay^{2,4} showed 2400 LBF units per mg. of product. Excess methyl pantothenate was hydrolyzed by treatment for one hour at room temperature with *N* methanolic KOH. After neutralization with methanolic HCl and removal of the solvent, the residue was partitioned between *n*-butanol and water. The butanol contained 18,000 LBF units per mg. of solids. After drying, the butanol solution was poured onto a Superfiltrol column (20 g. adsorbent per g. of solids), the latter washed thoroughly with butanol, then developed with water-saturated butanol. The most active fractions contained 29,000 to 30,000 LBF units per mg. of solids.

Though non-crystalline, this product appears essentially pure, and is indistinguishable from LBF prepared from natural sources in (a) R_F values on paper from water-saturated butanol (0.93) or *n*-amyl alcohol (0.76) and (b) activity for *Lactobacillus helveticus*, *Saccharomyces carlsbergensis*, and *Lactobacillus arabinosus*.² Both products give an immediate nitroprusside test only after reduction with NaCN; activity for *L. helveticus* was unchanged by such reduction. Both products are destroyed by digestion with a liver enzyme with release of 0.03 μ g. of calcium pantothenate per LBF unit. Thus LBF may exist as N-(pantothenyl)- β -aminoethanethiol or as the corresponding disulfide.

Anal. Calcd. for $C_{11}H_{22}O_4N_2S$: N, 10.07; S, 11.52; Found: N, 10.2; S, 12.0. *Pantetheine* and *pantethine* are suggested as names for the thiol and disulfide forms, respectively, of the growth factor. Its relation to coenzyme A was indicated previously.²

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AN EFFICIENT SEPARATION OF DYSPROSIUM AND YTTRIUM¹

Sir:

A rapid and efficient separation of the difficultly separable rare earth pair, dysprosium and yttrium, has been accomplished by elution with 5% ammonium citrate solution at room temperatures on Nalcite H.C.R. resin. This is achieved because of a shift in the order of elution of yttrium relative to the other rare earths. With 0.1% citrate

(1) This work was performed in the Ames Laboratory of the Atomic Energy Commission.

solution, the order of elution is Dy-Y-Tb,² while the order observed with 5% citrate is Dy-Tb-Y. Previously, it had been reported³ that elution at 100° of tracer amounts of rare earths with 5% citrate showed yttrium eluting ahead of dysprosium.

When eluting with 5% citrate at pH values greater than 2.8, the rare earth band immediately precedes the hydrogen band on the column, and results in a square-type band front. At lower pH values, the ammonium ions pass the rare earth ions and consequently the rare earths are on an ammonium bed. The resultant band front at these lower pH values is sloping and the elution curves resemble those previously obtained with other rare earths using similar conditions.⁴ At all pH values when 5% ammonium citrate is used as eluant, the observed order of elution is Dy-Tb-Y.

A load of 7.6 g. of oxides was placed on a column containing 450 g. of resin and eluted with 5% citrate. The resin bed length was 60 cm. and the diameter was 4 cm. These oxides, obtained by column fractionation of R_2O_3 from gadolinite ore, had the composition 10% Dy_2O_3 , 89% Y_2O_3 , 0.5% Ho_2O_3 , 0.5% Tb_4O_7 . Analyses were made by spectrophotometric and spectrographic methods. At a pH value of 2.80, 85% of the available Y_2O_3 was obtained spectrophotometrically pure (>99%). Previous work using 0.1% citrate at pH values of 5.5-6.0, eluted less than 10% of the available Y_2O_3 with comparable purity. The total time of a run using 5% citrate at a pH of 2.80 is only one-third that required with 0.1% citrate. The concentration of rare earths in the eluate using 5% citrate is correspondingly higher.

It appears that the most efficient way to obtain pure Y_2O_3 and pure Dy_2O_3 from an ore concentrate involves two ion exchange procedures: (1) first a preliminary elution using 0.1% citrate with pH values between 5.8 and 6.1, which separates dysprosium and yttrium from the other rare earths; (2) elute the yttrium-dysprosium fractions so obtained with 5% citrate using a pH value of 2.8, to obtain the pure salts.

(2) F. H. Spedding, E. I. Fulmer, J. E. Powell, T. A. Butler, and I. S. Yaffe, paper presented before the Sept. 1950 meeting of the American Chemical Society in Chicago.

(3) B. H. Ketelle and G. E. Boyd, *THIS JOURNAL*, **69**, 2800 (1947).

(4) F. H. Spedding, A. F. Voigt, E. M. Gladrow and N. R. Sleight, *ibid.*, **69**, 2777 (1947).

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RECEIVED OCTOBER 26, 1950

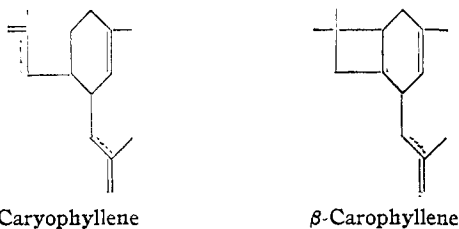
THE STRUCTURE OF THE CARYOPHYLLENES

Sir:

An optically inactive α -caryophyllene (humulene), n_D^{20} 1.5035, was prepared from hop oil by fractionation in an efficient column with sub-

sequent chromatography on alumina employing *n*-heptane as developer and tetranitromethane as a streak indicator. Similar methods yielded a pure β -caryophyllene, $[\alpha]_D^{20} -8.8^\circ$, n_D^{20} 1.4994, from clove oil. Application of these chromatographic procedures to the dehydrogenation (with benzene and a palladium catalyst¹) products of α - and β -caryophyllene yielded naphthalenic and benzenic fractions identical in their ultraviolet and infrared spectra. Oxidation of the naphthalenic fraction from β -caryophyllene with alkaline permanganate produced 1,2,4-benzenetricarboxylic acid anhydride, identified by melting point (158°), mixed melting point and X-ray diffraction pattern. Similar dehydrogenation of an impure β -caryophyllene, n_D^{20} 1.4980, from clove oil, led to the isolation of a blue and a purple azulenic fraction.

Ruzicka² has presented excellent evidence for the structure shown below for β -caryophyllene (from clove oil). Later³ a seven-membered ring structure was favored on the basis of the isolation, in low yield, of degradation products indicating the presence of such a ring system. Our demonstration of azulenic fractions as impurities in a dehydrogenation mixture from clove oil points to a probable similar origin for the seven-membered ring degradation products reported by Ruzicka and associates. Accepting then the original formulation of Ruzicka, shown below, for β -caryophyllene, and accepting the demonstration (verified in our laboratory) of Sörm and co-workers⁴ that α - and β -caryophyllene contain three and two double bonds, respectively, then our dehydrogenation results suggest the formula shown below for α -caryophyllene (from hop oil).



(1) H. Adkins and D. C. England, *THIS JOURNAL*, **71**, 2958 (1949); H. Adkins and G. F. Hager, *ibid.*, 2962.

(2) L. Ruzicka, *Chemistry & Industry*, **13**, 509 (1935).

(3) L. Ruzicka, K. Huber, P. A. Plattner, S. S. Deshpande and S. Studer, *Helv. Chim. Acta*, **32**, 716 (1939).

(4) F. Sörm, J. Mleziva, Z. Arnold and J. Pliva, *Collection Czechoslov. Chem. Commun.*, **14**, 699 (1949).

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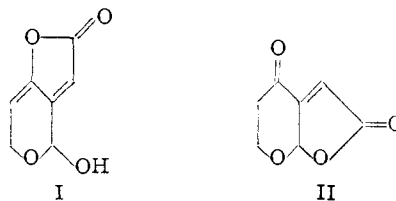
RECEIVED SEPTEMBER 1, 1950

AlloPATULIN

Sir:

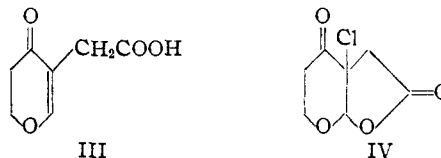
The structure (I) for patulin has now been established beyond question by degradative and

synthetic studies.^{1,2,3,4,5} None the less, much interest still attaches to the closely related structure (II), which has been suggested⁶ as an alternative to (I) for patulin, and whose reactions may be



expected to simulate those of the mold metabolite in many respects. We wish to record the synthesis of (II), which we designate here as *allop*patulin.

Desoxyapatulinic acid³ (III) was smoothly transformed by chlorine in dry chloroform to the chlorolactone (IV), m. p. 124.0 – 125.5° (calcd. for $C_7H_7O_4Cl$: C, 44.09; H, 3.67. Found: C, 43.99; H, 3.82). When the lactone was treated with an equivalent of potassium acetate



in anhydrous methanol, *allop*patulin (II), m. p. 116 – 117° (calcd. for $C_7H_6O_4$: C, 54.54; H, 3.90. Found: C, 54.56; H, 4.00) was formed. The lactone gave a normal **phenylhydrazone**, m. p. 195° (calcd. for $C_{13}H_{12}O_3N_2$: C, 63.93; H, 4.92; N, 11.48. Found: C, 63.75; H, 5.04; N, 11.32) and **semicarbazone**, m. p. $>270^\circ$ (calcd. for $C_8H_9O_4N_3$: C, 45.49; H, 4.26; N, 19.91. Found: C, 45.08; H, 4.47; N, 19.77).

Like patulin, *allop*patulin was converted to desoxyapatulinic acid (III) on hydrogenation. On the other hand, while patulin reacts with hydrogen chloride to give chlorodesoxyapatulinic acid (V, X = Cl),³ *allop*patulin reacted with that reagent to form **isochlorodesoxyapatulinic acid** (VI, X = Cl), m. p. 133 – 135° (*dec.*) (calcd. for $C_7H_7O_4Cl$: C, 44.09; H, 3.67. Found: C, 43.52; H, 3.71). Treatment of the chloro acid with diazomethane, followed by Brady's reagent (methanol) gave **methyl isomethoxydesoxyapatulinate dinitrophenylhydrazone**, m. p. 194 – 195° (*dec.*) (calcd. for $C_{15}H_{16}O_8N_4$: C, 47.37; H, 4.21; N, 14.73. Found: C, 47.53; H, 4.42; N, 14.77). With acetic acid, *allop*patulin gave **isoacetoxidesoxyapatulinic acid** (VI, X = OAc), m. p. 139 – 140° (calcd. for $C_9H_{10}O_6$: C, 50.47; H, 4.67. Found: C, 50.90; H, 5.04), which reverted to its progenitor when it was pyrolyzed.

(1) Woodward and Singh, *THIS JOURNAL*, **71**, 758 (1949).

(2) Woodward and Singh, *Experientia*, **6**, 238 (1950).

(3) Woodward and Singh, *Nature*, **165**, 928 (1950).

(4) Woodward and Singh, *THIS JOURNAL*, **72**, 1428 (1950).

(5) Dauben and Weisenborn, *ibid.*, **71**, 3853 (1949).

(6) Engel, Brzeski and Plattner, *Helv. Chim. Acta*, **32**, 1166 (1949); **32**, 1752 (1949).