evolved and the temperature of the reaction mixture fell. When all of the sulfuric acid had been added, the reaction mixture was distilled, and the white crystalline distillate which came over at 87–90° at 4 mm. pressure was analyzed by titration with 0.5 *N* sodium hydroxide. Sulfuric acid calculated for in a 0.5842 g. sample: 0.2360 g.; found: 0.2376 g. The freezing point of the material was measured and found to be 45–46° (uncor.). An attempt to distil di-(trimethylsilyl) sulfate at higher pressure and temperature resulted in violent auto-oxidation.

Lead Trimethylsilanolate.—About 1 g. of lead monoxide was shaken at room temperature in 25 cc. of $(CH_3)_3$-SiOH[2] for two days. The yellow color of the lead monoxide gradually changed to white. On filtration of the mixture and evaporation of the filtrate a white crystalline solid was obtained which was soluble in ether, toluene and absolute alcohol. For analysis, a sample was weighed into a centrifuge tube, dissolved in alcohol and diluted with dilute sulfuric acid. After standing overnight the precipitate was centrifuged, washed, dried at 110° and weighed as $PbSO_4$: calcd.: Pb, 53.7. Found: Pb, 59.1.

The authors acknowledge with thanks the analytical work carried out by E. W. Balis.

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RECEIVED JUNE 8, 1945

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COMMUNICATIONS TO THE EDITOR

THE ISOLATION OF A NEW LEUKOPOIETIC FACTOR FROM LIVER[1]

Sir:

A crystalline substance has been isolated by one of us (J. K. C.) which may be necessary for the production of leukocytes in man. When administered intravenously in doses ranging from 20 to 60 mg. to malnourished patients with leukopenia there was an increase within three to five and one-half hours of 45% to 174% above the initial white cell count in 12 of 14 patients. The neutrophiles increased from 37.4% to 257% above the initial levels during the same period.[2] Chemically the substance is not identical with folic acid,[3] adenylic acid[4] or the exudate factor,[5] although administration of these substances may produce a similar response. It is possible that the new substance is one of a group of substances whose lack in the diet is responsible for the nutritional macrocytic anemias described by Spies and Payne,[6] Moore, Vilter, Minnich and Spies,[7] and Wills[8] and it may be related similarly to the extrinsic factor of Castle.[9] Intramuscular injection of 30 mg. per day of an impure preparation elicited a positive hematological response in a patient with macrocytic anemia. Larger amounts of the substance are necessary before its antianemic properties can be correctly evaluated.

Isolation was accomplished by passing the portion of potent liver extract (Reticulogen, generously supplied by Dr. E. D. Campbell, The Lilly Research Laboratories) which was soluble in 66% acetone and insoluble in 90% acetone through acid activated Permutit. From a fraction of the filtrate a white neutral substance was obtained by fractional precipitation of a concentrated aqueous solution with acetone. By repeating this precipitation procedure and finally by slow evaporation of an aqueous solution, colorless crystals consisting of rosets of whetstone-shaped needles were obtained. Solutions of these crystals were also colorless. The crystals did not melt up to 360° and left considerable white ash on ignition. Tests for the primary aliphatic amino group were positive while tests for arginine and tyrosine were negative. The biuret reaction was negative and a test for the carbohydrate primary carbinol group showed only a faint trace of precipitate, in all probability due to a slight contamination of the substance with carbohydrate containing fractions. Elementary analysis revealed the presence of C, 28.25%; H, 4.70%; N, 5.42%; Na (as sulfate) 49.67%; sulfur and phosphorus were absent.

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RECEIVED OCTOBER 23, 1945

(1) The expenses of this special study were defrayed by grants from Eli Lilly and Company and the Research Corporation. General expense has been borne by many philanthropic persons, foundations and commercial concerns.

(2) Berry, Spies and Cline, *Southern Medical Journal*, **38**, 656 (1945).

(3) Berry, Spies and Doan, *ibid.*, **38**, 590 (1945).

(4) Berry, Doan and Spies, unpublished observations.

(5) Menkin, *Science*, **101**, 422 (1945).

(6) Spies and Payne, *The Journal of Clinical Investigation*, **12**, 229 (1933).

(7) Moore, Vilter, Minnich and Spies, *The Journal of Laboratory and Clinical Medicine*, **29**, 1226 (1944).

(8) Wills, *British Medical Journal*, **1**, 1059 (1931).

(9) Castle, *American Journal of Medical Science*, **178**, 748 (1929).

THE ABSOLUTE RATE CONSTANTS IN THE POLYMERIZATION OF LIQUID VINYL ACETATE

Sir:

We have determined the absolute rate constants for the elementary steps in the polymerization of pure liquid vinyl acetate, utilizing a technique applied by Melville [*Proc. Roy. Soc.* (London), **A163,** 511 (1937)] to polymerization in the vapor phase. The dependence of the rate of photopolymerization of vinyl acetate upon the frequency of a flashing light was determined, the polymerization being followed in a quartz dilatometer at 25°. Between the limiting rate for low frequencies of flashing and the higher limiting rate for high frequencies of flashing there occurs a region of transition, whose location reveals the average lifetime of the growing polymer chains. By combining this information with data obtained from the kinetic study of peroxide-induced polymerization we have calculated the rate constants for propagation and termination of chains and several related quantities.

In our experiments the light was interrupted by a rotating slotted disk which gave dark periods three times as long as the light periods. The flashing frequency was varied from 6.3×10^{-4} to 380 cycles per second. The following quantities were measured within, it is believed, a factor of two or better:

Quantity and units	Limits of uncertainty Lower	Upper	Most probable value
Flashing frequency at midpoint of transition, sec.^{-1}	2.5×10^{-2}	1×10^{-1}	5×10^{-2}
Rate of photopolymerization at 25° with continuous illumination (moles/liter sec.)	6×10^{-5}	2.4×10^{-4}	1.2×10^{-4}
Rate of polymerization at 25° induced by 0.105 *M* benzoyl peroxide (moles/liter sec.)	5.6×10^{-5}	1.3×10^{-4}	8.4×10^{-5}
Rate constant for *spontaneous* decomposition of benzoyl peroxide in vinyl acetate at 25° (sec.^{-1})	2×10^{-8}	8×10^{-8}	4×10^{-8}

From these data the quantities listed below may all be calculated. The first two of these are rate constants common to photochemical, thermal and peroxide-induced polymerization of vinyl acetate. The remaining five quantities are related to the photopolymerization with continuous illumination under our specific conditions; similar quantities may be calculated for thermal or peroxide-induced polymerization by taking into account the specific conditions. The final quantity, extent of polymerization to establishment of the steady state, is computed by Equation 10 of Flory [THIS JOURNAL, **59**, 244 (1937)].

Quantity and units	Limits of uncertainty Lower	Upper	Most probable value
Rate constant for chain propagation, liters/mole sec.	2×10^{2}	5×10^{3}	1×10^{3}
Rate constant for chain termination, liters/mole sec.	1.6×10^{7}	4.0×10^{8}	8×10^{7}
Average lifetime of a growing chain, sec.	.63	2.5	1.3
Concentration of free radicals at the steady state, moles/liter	2×10^{-9}	5×10^{-8}	1×10^{-8}
Kinetic chain length	3×10^{3}	7.5×10^{4}	1.5×10^{4}
Time required for establishment of steady state, sec.	5	12	8
Extent of polymerization to establishment of steady state, %	0.0025	0.01	0.005

Details of this work will appear in a forthcoming publication.

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RECEIVED NOVEMBER 14, 1945

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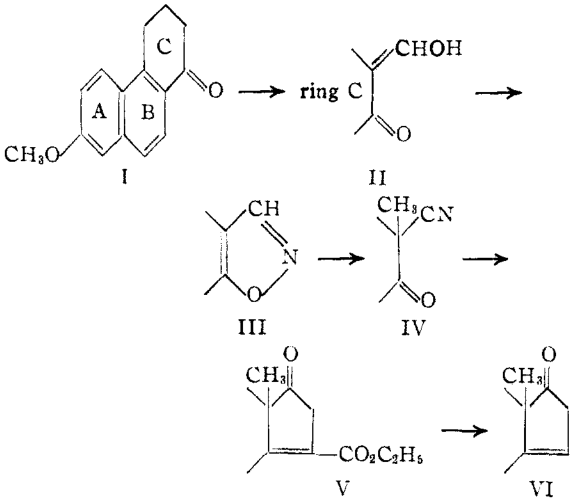
[*] Pittsburgh Plate Glass Fellow.

A NEW METHOD OF PRODUCING FUSED RING STRUCTURES RELATED TO THE STEROIDS. A SYNTHESIS OF EQUILENIN

Sir:

In connection with our studies on the Stobbe condensation of ketones with diethyl succinate,[1] we now wish to report on the behavior of an α-cyano ketone IV in this reaction. Instead of the expected half-ester, a neutral product was formed which proved to have the structure V. Thus in a single step there was produced the fused five-membered ring structure which is characteristic of ring D of the steroids. With this novel reaction we have been able to effect readily a total synthesis of equilenin, using the same starting material, namely, 1-keto-7-methoxy-1,2,3,4-tetrahydrophenanthrene (I),[2] that was employed by Bachmann, Cole and Wilds[3] in their classical synthesis of the hormone.



Condensation of I with ethyl formate[4] gave the 2-hydroxymethylene derivative II; m. p. 130–130.6° cor. *Anal.* Calcd. for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.37; H, 5.68. Reaction of II with hydroxylamine hydrochloride[5] afforded 10,11-dihydro-7-methoxyphenanthro[2,1-*d*]isoxazole, III; m. p. 139.5–140° cor. *Anal.* Calcd. for $C_{16}H_{13}O_2N$: C, 76.47; H, 5.21. Found·

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[1] *Cf.* Johnson, Goldman and Schneider, THIS JOURNAL, **67** 1357 (1945); Johnson, Johnson and Petersen, *ibid.*, **67**, 1360 (1945); Johnson and Petersen, *ibid.*, **67**, 1366 (1945).

[2] First prepared by Butenandt and Schramm, *Ber.*, **68**, 2083 (1935).

[3] Bachmann, Cole and Wilds, THIS JOURNAL, **62**, 824 (1940).

[4] *Cf.* Johnson, Anderson and Shelberg, *ibid.*, **66**, 218 (1944).

[5] *Cf.* Johnson and Shelberg, *ibid.*, **67**, 1745 (1945).