resulting from the very low activity of the ergosterol (7.5 dis./min./mg. $BaCO_3$).

It can be concluded that steroids derived from carboxyl-labeled acetate are labeled in the juxtapositions, C_{11} and C_{12}, as demanded by the squalene hypothesis and such a result strongly supports a concept of the intact utilization of the acyclic triterpene, squalene.

We wish to thank Professor D. J. Hanahan of the University of Washington for kindly supplying the C^{14}-ergosterol, Merck and Co., Inc., for a generous gift of ergosterol derivatives, and Dr. E. M. Baker of the Radiation Laboratory, University of California, for the C^{14} determinations.

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RECEIVED APRIL 9, 1956

INHIBITION OF REGENERATION IN HYDRA BY CERTAIN NEW 6-(PHENYLALKYL)-AMINOPURINES

Sir:

Methods have been developed for quantitatively studying the processes of regeneration in hydra, a primitive organism that may well serve as a model system of development and cell differentiation in higher animals.[1] Adenine and various adenine derivatives have been found to retard the formation of new tentacles in hydra whose hypostome and tentacles have been cut away. In an attempt to further characterize the nature of the effect, a variety of 6-(substituted)-purines have been synthesized and tested. Most of the compounds are considerably more active than adenine.

One series in particular, the 6-(ω-phenylalkyl)-aminopurines, is extremely active, especially certain higher homologs (Table I). In this animal system all members of the series are more effective than the recently reported cell division factor, for plants, kinetin (6-(2-furfuryl)-aminopurine),[2] which has an activity only 20 times that of adenine. The new compounds were prepared by condensing 3 to 5 parts of the appropriate amine[3] with one part of 6-methylmercaptopurine in a sealed micro Carius tube heated to 130 to 140° for 12 to 18 hours.[4] Excess solvent was removed under reduced pressure and the crystalline residue washed with cold alcohol and recrystallized from alcohol–water.

TABLE I

SYNTHESIS AND ACTIVITY OF 6-(ω-PHENYLALKYL)-AMINOPURINES

Compound 6-(R)-aminopurine	Yield, %	M.p., °C. (dec.)	Minimum concn. for full inhibition (μ mole/ml.)	Activity in terms of adenine
H-(Adenine)	..	...	5.0	1
1-Phenylmethyl-[a]	..	...	0.18	30
2-Phenylethyl-[b]	69	239–240	.04	130
3-Phenylpropyl-[c]	37	173–175	.02	250
4-Phenylbutyl-[d]	42	148–149	.003	1700
5-Phenylpentyl-[e]	40	145–147	.003	1700
7-Phenylheptyl-[f]	54	112–113	.001	5000

[a] C. G. Skinner and W. Shive, THIS JOURNAL, **77**, 6692 (1955). [b] *Anal.* Calcd. for $C_{13}H_{13}N_5$: C, 65.25; H, 5.47. Found: C, 65.14; H, 5.49. [c] *Anal.* Calcd. for $C_{14}H_{15}N_5$: C, 66.38; H, 5.97. Found: C, 66.19; H, 5.74. [d] *Anal.* Calcd. for $C_{15}H_{17}N_5$: C, 67.39; H, 6.41. Found: C, 67.13; H, 6.77. [e] *Anal.* Calcd. for $C_{16}H_{19}N_5$: C, 68.30; H, 6.81. Found: C, 68.19; H, 7.15. [f] *Anal.* Calcd. for $C_{18}H_{23}N_5$: C, 69.87; H, 7.49. Found: C, 69.99; H, 7.56.

Biological activity is expressed as the minimum concentration which will produce complete inhibition of visible tentacle formation after 18 hours at 27°. Relative activities are compared using adenine as a standard. All tests were conducted in a buffered (*p*H 7.4) solution containing all inorganic ions required for optimum rate of regeneration.

The strong inhibitions obtained at the very low concentrations of the higher analogs suggest that they block a fundamental controlling process rather than the gross metabolism of the organism. Current investigations are directed both at determining the structural specificity of the active compounds and at determining the system involved. A full report of the synthesis and testing of these and other 6-(substituted) purines is being submitted for publication.

BIOCHEMICAL INSTITUTE AND THE DEPARTMENT OF CHEMISTRY — RICHARD G. HAM[5]
THE UNIVERSITY OF TEXAS, AND THE CLAYTON FOUNDATION FOR RESEARCH — ROBERT E. EAKIN, CHARLES G. SKINNER
AUSTIN, TEXAS — WILLIAM SHIVE

RECEIVED APRIL 2, 1956

(1) R. G. Ham, D. C. Fitzgerald, Jr., and R. E. Eakin, *J. Exptl. Zool.*, manuscript submitted.

(2) C. O. Miller, F. Skoog, F. S. Okumura, M. H. Von Saltza and F. M. Skoog, THIS JOURNAL, **77**, 2662 (1955).

(3) 3-Phenylpropylamine, 4-phenylbutylamine and 5-phenylpentylamine were prepared by catalytic hydrogenation of the nitriles using Raney nickel. 5-Phenylvaleronitrile was prepared from 5-phenylvaleric acid kindly furnished by Dr. P. D. Gardner. 7-Phenylheptylamine also was furnished by Dr. Gardner, unpublished data.

(4) G. B. Elion, E. Burgi and G. H. Hitchings, THIS JOURNAL, **74**, 412 (1952).

(5) National Science Foundation Predoctoral Fellow.

A REARRANGEMENT INVOLVING A 1,5-PHENYL MIGRATION

Sir:

We have observed that 8-benzhydryl-1-naphthoic acid (Ia) isomerizes under Friedel–Crafts conditions to a cyclic hemiketal (IIa). This reaction involves a 1,5-phenyl migration, and is the first example of a rearrangement of this type.

Very few, if any, acid catalyzed reactions have been described in which an alkyl or aryl group is transferred directly between carbon atoms that are not adjacently bound. A case that can be formulated conveniently as a 1,3-methyl migration has been reported[1]; however, the possibility that the product resulted from a sequence of conventional 1,2-migrations cannot be excluded. Recently, Meinwald[2] conclusively demonstrated that the isomerization of α-cinenic acid, a reaction for which a 1,5-methyl migration had been proposed, did not actually involve a methyl shift.

Compound Ia[3] (1.00 g.) was converted to the acid chloride with thionyl chloride, then warmed with 1.2 ml. of stannic chloride in 20 ml. of carbon disulfide for ninety minutes. Upon hydrolysis and recrystallization, 0.90 g. of IIa was obtained; m.p.

(1) W. A. Mosher and J. C. Cox, THIS JOURNAL, **72**, 3701 (1950).

(2) J. Meinwald, *ibid.*, **77**, 1617 (1955).

(3) For the preparation of this compound see W. E. Bachmann and E. Chu *ibid.*, **58**, 1118 (1936).