TABLE I

V	R	Yield,[a] %	Mp or bp (mm), °C	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
a	H	25	Waxen solid, 73	$C_6H_{11}NO$	63.6	9.75	12.37	63.5	9.89	12.19
b	CH_3	40	60 (17)	$C_7H_{13}NO$	66.0	10.2	11.05	65.9	10.34	10.95
c	*n*-Butyl	38	51 (0.5)	$C_{10}H_{19}NO$	71.0	11.23	8.80	70.8	11.10	8.84
d	Ethyl	34	34 (2.0)	$C_8H_{15}NO$						
e	Isopropyl	36	48 (0.5)	$C_9H_{17}NO$	69.7	11.03	9.03	69.35	11.07	9.19
f	*n*-Propyl	38	67 (1.5)	$C_9H_{17}NO$	69.7	11.03	9.03	69.32	11.10	9.29
g	Cyclopentyl	?	?	$C_{11}H_{19}NO$						
h	Cyclohexyl	60[b]	100 (0.1)	$C_{12}H_{21}NO$	74.0	10.75	7.20	73.8	11.01	6.95

[a] Based on crude IV. [b] Based on pure IV.

Table I lists appropriate yield and analysis data for V.

Biological Data.—Compounds III, IVh, Va, and Vc–e were tested for action against *Plasmodiasis berghei* in ICR/Ha Swiss mice and *P. gallinaceum* in chicks.[12] All were found to be inactive at dose levels of 1280 mg/kg for periods of 6–8 days.

Experimental Section[13]

Dihydropyran-2-methyl Tosylate (III).—The alcohol (II, Aldrich Chem. Co.) (34.5 g) was dissolved in 200 ml of pyridine. To this was added 75 g of *p*-toluenesulfonyl chloride. The mixture was warmed to 50° for 30 min, after which time cooling to room temperature produced a white precipitate of pyridine hydrochloride. Filtration and removal of the pyridine from the filtrate gave a solid which was recrystallized from EtOH. The yield of material melting at 47–48° was 48 g (79%). It was best preserved in a sealed vessel in the cold.

Dihydropyran-2-methylamine (IV).—For reaction of IV with NH_3, methyl-, ethyl-, propyl-, and isopropylamine, a threefold excess of the amine in absolute methanol and the tosylate were shaken and heated to 125° in a sealed steel vessel for 1 hr. Alternatively, the less volatile amines were placed in ethanol, along with the tosylate, and refluxed for 4 hr. After cooling, the contents were concentrated on a vacuum evaporator. After solvent removal the semisolid mass was made basic with 20% NaOH and continuously extracted with ether for 48 hr. The ether layer was dried with anhydrous K_2CO_3 and reduced in volume to yield the crude amine product (65–75% yield). Vacuum distillation produced pure, colorless oils (30–40%) which showed a correct analysis for the proposed structures. No definite boiling points were observed and spontaneous decomposition occurred at pot temperatures above 150°. After initial identification, no attempts were made to purity IV prior to conversion to V.

Pertinent infrared absorptions for all compounds of structure IV are: 3330–3400 (NH) (plus 1600 for IVa), 3060–3100 (HC=), 1650–1670 (C=C), 1245–1260 (C=CO), and 1070–1085 cm^{-1} (CO).

6-Aza-8-oxabicyclo[3.2.1]octane (V).—The crude amine IV (5 g) was added very slowly dropwise to stirred 2 *N* H_2SO_4 at 0°. Stirring was continued for 1 hr, after which time the pale orange solution was allowed to stand for 2 days at room temperature. The color usually changed to pink. The acid solution, cooled in ice, was then made basic with cold 50% NaOH. Continuous ether extraction for 48 hr, drying the ether layer with anhydrous K_2CO_3, and removal of ether yielded the crude amine product. Distillation under vacuum afforded 25–40% yields of almost pure V. In the case of Va, the distillation yielded a solid, easily sublimed from the crude below 50° (0.1 mm). Proper condenser cooling is required to ensure minimum loss. Purity assay was by gas chromatography and by thin layer chromatography on silica gel G with butanol–acetic acid–water eluent. The use of distilled IV in the above cyclization causes no coloration of the acid medium and gives higher yields of V.

Pertinent infrared absorptions for all compounds of structure V are: 3340 (NH of Va only), 1010–1050 (multiple) (CO), and 820–900 cm^{-1} (multiple) (NCO). The molecular weight for Va was found to be 114 (calcd 113).

(12) Antimalarial screening was carried out by Dr. L. Rane of the University of Miami Medical School.

(13) Gas chromatography separations utilized an Aerograph A-90-P2 instrument. Columns of silicone on Fluoropak (6 mm × 2 m) and Carbowax on Chromosorb (6 mm × 3 m and 9 mm × 4 m) were operated at a temperature range of 100–150°. Helium served as carrier gas. Elemental analyses and the molecular weight determination ($CHCl_3$) were obtained from Galbraith Laboratories, Inc., Knoxville, Tenn.

Book Reviews

Clinical Pathology. By C. H. GRAY. 4th ed. The Williams and Wilkins Co., Baltimore, Md. 1965. viii + 231 pp. 14.8 × 13 cm. $6.25.

This booklet is based on lectures in a British medical school and does not pretend to be a comprehensive treatise. It covers renal and liver functions, acid–base balance, edemas, hematology, fluid and salt balance, plasma proteins, inorganic ions, gastrointestinal tests, chemical tests for diabetes and other endocrine diseases, a short description of clinical factors in enzymology and genetics, remarks about the chemical pathology of the nervous system, nutritional deficiencies, and miscellaneous routine chemical pathology tests. There is a subject index but no Table of Contents; print and drawings are satisfactory. The book may serve as an orienting introduction to the background of clinical testing methods. It would be of greater value if there would be lists of literature references.

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Peptides and Amino Acids. By KENNETH D. KOPPLE. W. A. Benjamin, Inc., New York, N. Y. 1966. xi + 137 pp. 21 × 13.6 cm. Paperback.

This little booklet is designed to supplement standard college texts in organic chemistry which cannot offer an adequate chapter on amino acids and peptides. However, it does much more. The level of presentation is appropriate for graduate students or for organic chemists in general who do not specialize in peptide chemistry. It would serve well as a short introduction to this field and through its compact but meaningful reference lists points the way to reading in greater depth. The text is lucid, carefully prepared and proof-read, and beautifully illustrated. It should be useful as a brief survey of methodology and achievements, and of areas which urgently demand more research. Every medicinal chemist will ultimately face the question of what his compounds do at the biopolymeric level, and they should read this text to get oriented in this field.

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