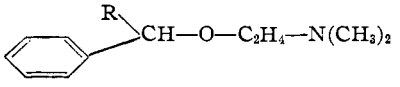
Multiplication of (13) by M giving the right-hand side of (14) retains only one parameter B for comparing various substances in the form of P. Although B is a proportionality constant, it possesses the dimensions of energy and not of volume. The term B can be expected to be constitutive since it depends upon the atomic and molecular configurations.

LAXMINARAYAN INSTITUTE OF TECHNOLOGY
NAGPUR UNIVERSITY
NAGPUR, INDIA RECEIVED JANUARY 12, 1949

Basically Substituted Pyrimidine and Imidazoline Derivatives as Histamine Antagonists

BY CHARLES H. TILFORD, M. G. VAN CAMPEN, JR., AND ROBERT S. SHELTON

A recent report[1] from this Laboratory showed the effectiveness of 2-[α-(2-dimethylaminoethoxy)-α-methylbenzyl]-pyridine (I) as an antihistaminic agent. The dimethylaminoethyl ethers of α-phenyl-4-methyl-6-methoxy-2-pyrimidinemethanol and α-phenyl-2-imidazolinemethanol have now been prepared and when tested *in vitro* were about 0.0025 as active as I.



R	Free base B. p. °C.	Mm.	Yield, %	Hydrochloride Formula	M. p., °C. (cor.)	% Halogen[a] (ionizable) Calcd.	Obs.	Activity,[b] γ/ml.
4-Methyl-6-methoxy-2-pyrimidyl	135–140	0.2	30	$C_{17}H_{23}O_2N_3 \cdot HCl$	149–151	10.49	10.40	20
				$C_{17}H_{23}O_2N_3 \cdot 2HCl$	176–178	18.95	18.90	20
2-Imidazolinyl	155–160	0.08	63	$C_{14}H_{21}ON_3 \cdot 2HCl$	246–247	22.14	22.0	20

[a] Determined by titration with silver nitrate using dichlorofluorescein indicator. [b] Minimal concentration of test compound necessary to antagonize 0.1 γ/ml. of histamine diphosphate on isolated guinea pig intestine.

Experimental

α-Phenyl-4-methyl-6-methoxy-2-pyrimidinemethanol.—To a stirred solution of 50 g. (0.23 mole) of α-phenyl-4-methyl-6-hydroxy-2-pyrimidinemethanol[2] in 300 ml. of 4% sodium hydroxide was added 34 g. (0.28 mole) of dimethyl sulfate over a period of thirty minutes at 50–60°. The reaction mixture was then stirred and heated on the steam-bath at 90–95° for two hours, made alkaline with 60 ml. of 10% sodium hydroxide, and extracted with 250 ml. of toluene. From the aqueous layer, 15 g. of unchanged starting pyrimidinemethanol was obtained by acidifying with glacial acetic acid and collecting the precipitate at the filter. The toluene extract was treated with a slight excess of alcoholic hydrochloric acid, cooled to −20°, and filtered. The yield of crude product melting at 153–156° (dec.) was 27 g. (63% based on unrecovered original pyrimidinemethanol). A sample was recrystallized from a butanone–ethanol mixture to give white crystals melting at 172–175° (dec.).

Anal. Calcd. for $C_{13}H_{14}O_2N_2 \cdot HCl$: Cl, 13.3. Found: Cl, 13.3.

α-Phenyl-2-imidazolinemethanol.—The procedure of Brockmuhl and Knoll[3] was followed using 71 g. (0.33 mole) of ethyl mandelimidate hydrochloride[4] and 20 g. (0.33 mole) of anhydrous ethylenediamine. The yield of crude base melting at 182–186° was 51 g. (88%). A sample was recrystallized from a butanone–ethanol mixture giving white crystals melting at 184–186°. The white crystalline hydrochloride was prepared and melted at 224–226°.

Anal. Calcd. for $C_{10}H_{12}ON_2 \cdot HCl$: Cl, 16.68. Found: Cl, 16.60

Aminoethers.—The general method of preparation is given in reference 1.

DEPARTMENT OF ORGANIC CHEMISTRY
RESEARCH LABORATORIES
THE WILLIAM S. MERRELL COMPANY
CINCINNATI, OHIO RECEIVED NOVEMBER 5, 1948

(1) Tilford, Shelton and Van Campen, THIS JOURNAL, **70**, 4001 (1948).

(2) Pinner, *Ber.*, **23**, 2948 (1890).

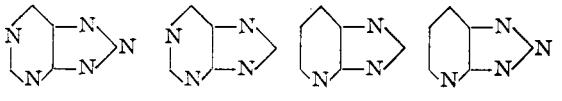
(3) Brockmuhl and Knoll, U. S. 1,999,989 (1931).

(4) Mackenzie, *J. Chem. Soc.*, **113**, 2 (1918).

Triazolo and Imidiazopyridines

BY J. R. VAUGHAN, JR., J. KRAPCHO[1] AND J. P. ENGLISH

The preparation and antibacterial properties of 1-ν-triazolo[d]pyrimidines (I) substituted analogously to the naturally-occurring purines (II) have been reported.[2] Since the *in vivo* activities of those compounds were not very striking, attention was turned to two other nuclei, both isoelectronic with the purine nucleus as is 1-ν-triazolo[d]-pyrimidine. This involved substituting a pyridine ring for the pyrimidine ring of the purines and the triazolo[d]pyrimidines, giving imidazo[b]pyridines (III) and pyrido[2,3-d]ν-triazoles (IV), respectively.



I II III IV

None of the compounds prepared (see Table I) showed antibacterial activity against strains of *Mycobacterium*, *Erssipelothrix*, pneumococcus streptococcus and *Pasteurela multocida*.[3]

The common starting material for these compounds is 2,3-diaminopyridine or some substituent thereof. The use of 5-chloro-2,3-diaminopyridine was much more satisfactory for a number of reasons. The development of an improved procedure for the preparation of 2-amino-5-chloro-

(1) Present address: Chemistry Department, University of Michigan, Ann Arbor, Michigan.

(2) Roblin, Lampen, English, Cole and Vaughan, THIS JOURNAL, **67**, 290 (1945).

(3) Tested under the direction of Dr. Harold J. White of these laboratories.