

Figure 1—Benesi-Hildebrand plot for salicylic acid-adenosine complexation in 0.05 M phosphate buffer at pH 7 after storage for 19 hr at 27°.

possessed greater surface activity. These factors are believed to contribute to the reduction of platelet aggregation, thus aggravating and prolonging the local effect.

Spectrophotometric techniques were used to evaluate complex formation between salicylic acid and adenosine or adenosine triphosphate. The absorbance decrease at 296 nm was measured in the presence of various concentrations of adenosine or adenosine triphosphate in 0.05 M phosphate buffer at pH 7. The Benesi-Hildebrand equation (7) was applied to the data obtained to form the plots shown in Figs. 1

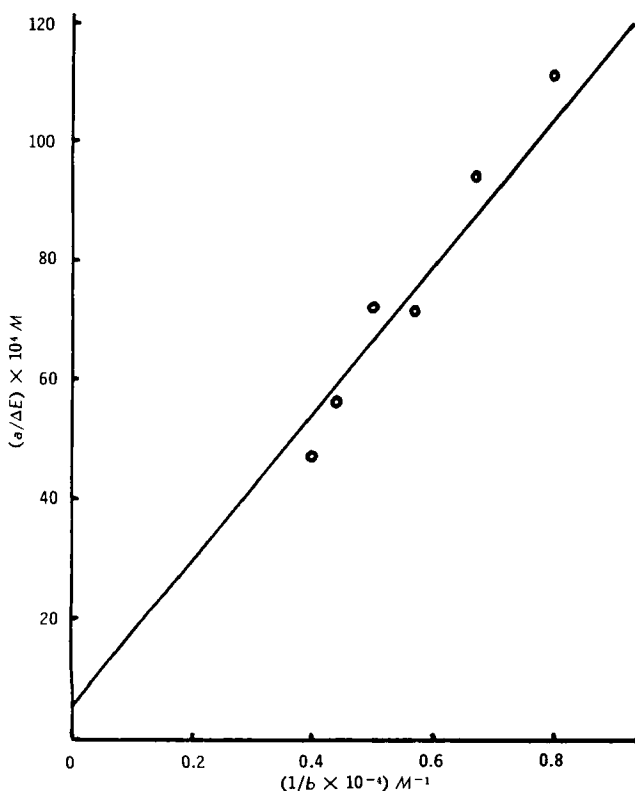


Figure 2—Benesi-Hildebrand plots for salicylic acid-adenosine triphosphate complexation in 0.05 M phosphate buffer at pH 7 after storage for 24 hr at 27°.

and 2, from which the complexation constants could be determined.

This work is continuing for verification of these findings and further investigation on complexation with other adenine nucleotides.

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O-Alkyloxime Derivatives: A New Group of Compounds with Antibacterial Activity

Keyphrases □ O-Alkyloxime derivatives—synthesized and screened as potential antibacterial agents □ Antibacterial agents, potential—synthesis and screening of O-alkyloxime derivatives

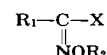
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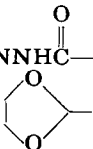

Medicinal agents with various types of activity incorporate the pharmacophoric grouping Am-C-C-X, where Am is amino, alkylamino, or dialkylamino and X is C, N, O, or S. Interest in the alkoxyimino grouping as a potential pharmacophore led to the preparation of some new polyfunctional compounds in which Am is alkoxyimino rather than amino or substituted amino.

The new compounds that were prepared and tested as antimicrobials are listed in Table I. The one aldehyde, 2-methoxyiminophenylacetaldehyde (VIII), was inactive, but its bisulfite (XI), dioxolane (X), and semicarbazone (IX) derivatives showed some activity. Of the two sulfides, one was active and one was not. The one sulfonic acid derivative was active, as were all of the S-acetyl-2-alkoxyiminoalkylmercaptans.

Preparation of the aldehyde was through the selenium dioxide oxidation of acetophenone oxime O-methyl ether (1). The aldehyde was converted to its biologically active derivatives by standard methods (2, 3).

Acylmercaptans, sulfones, sulfonates, and sulfides were prepared by established procedures from the corresponding 2-alkoxyiminoalkyl bromides by displacing bromide with thiolacetate anion (4), sulfi-


Table I—Antimicrobial Activity of Oxime Derivatives

Compound	R ₁	R ₂	X	Melting Point	Boiling Point/torr (η/T°)	Yield, %	S. <i>aureus</i> Smith Strain	K. <i>pneumoniae</i> AD Strain
I	CH ₃	CH ₃	CH ₃ CH ₂ CH ₂ SCH ₂	—	97–98°/34 (1.4735/23)	67.2	+	—
II	C ₆ H ₅	CH ₃	CH ₃ CH ₂ CH ₂ SCH ₂	—	118–120°/0.10 (1.5539/23)	42.4	—	—
III	C ₆ H ₅	CH ₃ CH ₂	C ₆ H ₅ SO ₂ CH ₂	108–109°	—	80.0	+	—
IV	CH ₃	CH ₃	CH ₃ SO ₃ Na	— ^a	—	34.2	+	—
V	CH ₃	CH ₃	CH ₃ COSCH ₂	—	88–90°/28 (1.4879/23)	32.5	+	+
VI	CH ₃	CH ₃ CH ₂	CH ₃ COSCH ₂	—	97–98°/9 (1.4851/24)	61.7	+	+
VII	C ₆ H ₅	CH ₃ CH ₂	CH ₃ COSCH ₂	—	104°/0.02 (1.5598/24)	63.4	+	+
VIII	C ₆ H ₅	CH ₃	CHO	—	63–65°/0.035 (1.5455/20)	49	—	—
IX	C ₆ H ₅	CH ₃	$\text{CH}=\text{NNHC} \begin{array}{c} \text{O} \\ \parallel \\ \text{NH}_2 \end{array}$ 	195°	—	41	+	+
X	C ₆ H ₅	CH ₃		81–82°	—	52	+	+
XI	C ₆ H ₅	CH ₃	CH(OH)SO ₃ Na	— ^a	—	30	+	—

^a Decomposes.

Table II—Elemental Analysis of Oxime Derivatives

Compound	Molecular Formula	Analysis, %							
		Calculated				Found			
		C	H	N	S	C	H	N	S
I	C ₇ H ₁₅ NOS	52.17	9.32	8.70	19.88	52.24	9.26	8.57	20.20
II	C ₁₂ H ₁₇ NOS	64.58	7.62	6.28	14.35	64.78	7.77	6.40	14.17
III	C ₁₆ H ₁₇ NO ₃ S	63.37	5.61	4.62	10.56	63.36	5.89	4.73	10.50
IV	C ₈ H ₈ NNaO ₃ S	25.40	4.23	7.41	16.90	25.64	4.20	7.51	— ^a
V	C ₆ H ₁₁ NO ₂ S	44.72	6.83	8.70	19.88	43.27	6.29	8.83	19.80
VI	C ₇ H ₁₃ NO ₂ S	48.00	7.43	8.00	18.29	48.07	7.38	7.60	18.30
VII	C ₁₂ H ₁₃ NO ₂ S	60.76	6.33	5.91	13.50	59.84 ^b	6.09	5.93	13.55
VIII	C ₇ H ₉ NO ₂	— ^c	—	—	—	—	—	—	—
IX	C ₁₀ H ₁₂ N ₄ O ₂	54.09	5.41	24.54	—	54.32	5.33	24.92	—
X	C ₁₁ H ₁₃ NO ₃	63.77	6.28	6.76	—	63.63	6.45	6.56	—

^a Sulfur analysis unsatisfactory even after repeated crystallizations. ^b Could not be improved on recrystallization. ^c Analyzed as semicarbazone (Compound IX) after liberating the aldehyde from the bisulfite addition product with sodium carbonate.

nate anion (5), sulfate (6), and mercaptide (7), respectively. Preparation of the 2-alkoxyiminoalkyl bromides has been reported (8). Analytical data for new compounds reported are collected in Table II.

In the biological evaluation, with the exception of II and VIII (Table I), all compounds were active against *Staphylococcus aureus* and *Klebsiella pneumoniae* in an *in vivo* test. In this test, the compounds are added to agar medium and the test organisms are inoculated (about 3×10^5 cells) on the surface. The end-point (Table I) is the concentration of compound that prevents emergence of visible growth (200 ppm in all cases).

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