EXPERIMENTAL[1]

***n*-Propyl-α-aminobenzylphosphonate**—A solution of 6.4 g (20 mmoles) of I (9), 4.21 g (20 mmoles) of dicyclohexylcarbodiimide, and 2.5 g (25 mmoles) of triethylamine in 100 ml of *n*-propanol was stirred for 16 hr at 25° and the dicyclohexylurea was removed by filtration. Evaporation of the *n*-propanol, partitioning of the residue between methylene chloride and 1 *N* HCl, and evaporation of the dried methylene chloride gave 7.9 g of a solid. Recrystallization of this solid from acetone afforded 5.5 g (76%) of the propyl ester, mp 181–182°; IR (KBr): 3300 (N—H), 1725 (C=O), and 1250 (P—O) cm^{-1}; NMR (d_6-dimethyl sulfoxide): δ 0.89 (t, 3, CH_3), 1.50 (m, 2, CH_3CH_2), 3.82 (m, 2, $CH_3CH_2CH_2O$), 5.12 (s, 2, $CH_2C_6H_5$), and 7.65 (s, 10, aromatic).

Anal.—Calc. for $C_{18}H_{22}NO_5P$: C, 59.50; H, 6.10; N, 3.86; P, 8.52. Found: C, 59.46; H, 6.17; N, 3.83; P, 8.12.

The ethyl ester, mp 188–190° [lit. (3) mp 183–189°], was obtained in a similar manner.

Anal.—Calc. for $C_{17}H_{20}NO_5P$: C, 58.45; H, 5.77; N, 4.01; P, 8.86. Found: C, 58.70; H, 5.81; N, 3.93; P, 8.69.

Propyl-α-aminobenzylphosphonate Hydrobromide—To a suspension of 3.6 g (10 mmoles) of the propyl ester II in 30 ml of acetic acid was added 10 g (5.5 mmoles/g) of 45% HBr in acetic acid. The suspension was stirred for 40 min, after which all of the ester had dissolved. The solution was diluted with dry ether to precipitate the hydrobromide, which was collected by filtration and recrystallized three times from methanol–ether to yield 2.5 g (81%) of the hydrobromide, mp 156–158°; IR (KBr): 1210 (P—O) cm^{-1}, no carbonyl absorption; NMR (D_2O): δ 0.85 (t, 3, CH_3), 1.60 (m, 2, CH_3CH_2), 3.83 (m, 2, $CH_3CH_2CH_2O$), 4.65 (d, 1, J = 16 Hz, CH—P), and 7.62 (s, 5, phenyl); mass spectrum (70 ev): *m/e* (relative intensity) 124(6), 122(10), 81(9), 79(10), 43(100), and 41(30).

Anal.—Calc. for $C_{10}H_{17}BrNO_3P$: C, 38.73; H, 5.53; N, 4.52; P, 9.99. Found: C, 39.20; H, 4.94; N, 4.55; P, 9.96.

[1] Melting points were determined with a Thomas-Hoover Unimelt melting-point apparatus and are corrected. NMR spectra were taken on a Jeolco model C-60-HL spectrometer using tetramethylsilane or sodium 2,2-dimethyl-2-silapentane-5-sulfonate as the internal standard. IR spectra were taken on either a Perkin-Elmer model 137 or 256 spectrophotometer. Mass spectra were taken by Dr. John K. Baker using a DuPont CEC model 21-492 spectrometer. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn.

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COMMUNICATIONS

Interaction of Salicylic Acid with Adenosine and Adenosine Triphosphate: Potential Mechanism of Intensifying Aspirin-Induced GI Blood Loss

Keyphrases □ Salicylic acid—interaction with adenosine and adenosine triphosphate, related to mechanism of intensifying aspirin-induced GI blood loss □ Adenosine and adenosine triphosphate—interaction with salicylic acid, mechanism of aspirin-induced GI blood loss □ Aspirin—salicylic acid-adenosine interaction, possible mechanism of intensifying aspirin-induced GI blood loss

To the Editor:

Several studies (1–4) indicated that aspirin-induced gastric or GI bleeding is usually a local effect resulting from contact of aspirin particles, or saturated solutions of aspirin surrounding these particles, with the mucosa. Maudlin (5) also stated that bleeding and ulceration are due to a local focal necrosis. However, Woznicki and Mrtek (6) expressed the opinion that the mechanism of aspirin-induced GI blood loss is due to a combination of both local and systemic effects. They explained the systemic effect by the role of aspirin in reducing platelet aggregation through elimination of the second wave of platelet aggregation induced by adenosine diphosphate. These authors defended their opinion by the fact that aspirin is being used experimentally to prevent formation of thromboemboli. However, no work has been published to support this theory.

Preliminary investigations in our laboratories have indicated interaction between salicylic acid and adenosine or adenosine triphosphate. The presence of the phosphate moiety does not appear to be critical for the complexation. The complexes formed also

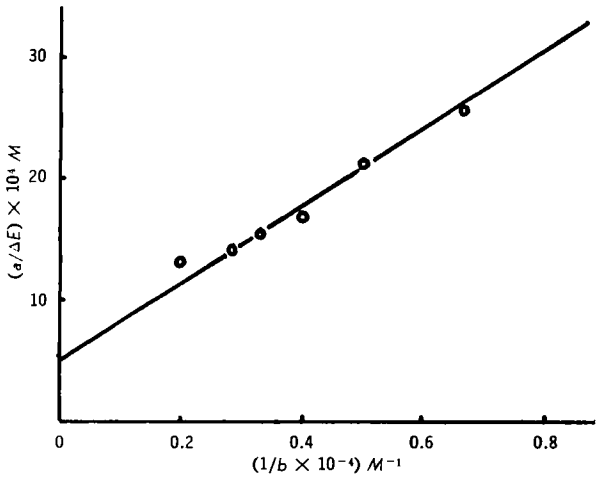

Figure 1—*Benesi–Hildebrand plot for salicylic acid–adenosine complexation in 0.05* M *phosphate buffer at pH 7 after storage for 19 hr at 27°.*

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

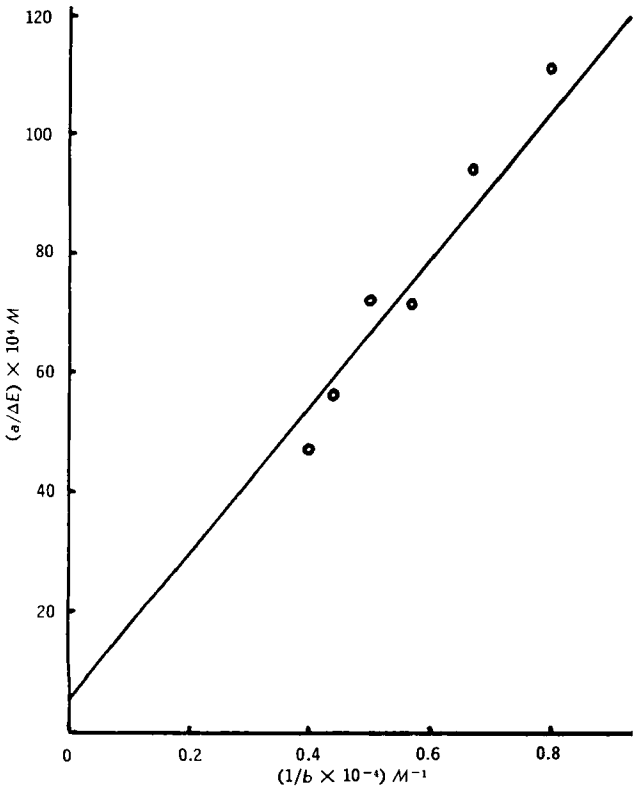

Figure 2—*Benesi–Hildebrand plots for salicylic acid–adenosine triphosphate complexation in 0.05* M *phosphate buffer at pH 7 after storage for 24 hr at 27°.*

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

To the Editor:

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-