TABLE I

TERTIARY PHOSPHINE AND AMINE BORANES

| Borane | M.P.[a] | B.P. | Mm. | Yield | $n_D^t$ | Formula | Boron Calcd. | Boron Found | B/P Ratio | Phosphorus Calcd. | Phosphorus Found |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Triethylphosphine | 47–48 | — | — | 93.5 | — | $C_6H_{18}BP$ | 8.20 | 8.24 | 1.03 | 23.47 | 22.9 |
| Tri-*n*-propylphosphine | 22.5–23[b] | 116–118 | 1.5 | 92.0 | $1.4672^{25}$ | $C_9H_{24}BP$ | 6.22 | 6.36 | 1.02 | 17.80 | 17.8 |
| Tri-*n*-butylphosphine | — | 115–117 | 0.8 | 79.0 | $1.4691^{25}$ | $C_{12}H_{30}BP$ | 5.00 | 5.03 | 1.03 | 14.33 | 14.2 |
| Phenyldimethylphosphine | — | 84–87 | 0.5 | 86.6 | $1.5504^{21}$ | $C_8H_{14}BP$ | 7.12 | 7.07 | 0.99 | 20.38 | 20.3 |
| *m*- and *p*-Ethylphenyldimethylphosphine[c] | — | 89–92 | 0.3 | 100 | $1.5388^{25}$ | $C_{10}H_{18}BP$ | 6.01 | 5.81 | 0.966 | 17.21 | 17.22 |
| 2,5-Dimethylphenyldi-*n*-butylphosphine | — | 140–141 | 0.5 | 83.3 | $1.5267^{20.5}$ | $C_{16}H_{30}BP$ | 4.10 | 4.08 | 0.99 | 11.72 | 11.7 |
| Triphenylphosphine | 182–184 | — | — | 83.4 | — | $C_{18}H_{18}BP$ | 3.92 | 3.67 | 0.94 | 11.22 | 11.22 |
| | | | | | | | Carbon | | | Hydrogen | |
| Triethylenediamine[d,e] (mono) | 164–165 | — | — | 80 | — | $C_6H_{15}BN_2$ | 57.18 | 57.30 | | 12.00 | 11.42 |
| Triethylenediamine[d,f] (bis) | 390 dec. | — | — | 100 | — | $C_6H_{18}B_2N_2$ | 51.52 | 51.53 | | 12.97 | 12.82 |

[a] All melting and boiling points are uncorrected. [b] Impure tri-*n*-propylphosphine borane reported to melt at about 10° (ref. 9a). [c] See Ref. 15. [d] First prepared in our laboratory by F. F. Caserio, Jr., and R. I. Wagner, unpublished results. [e] Recrystallized from benzene. [f] Insoluble in benzene.

exchange. Although triethylamine can be distilled from a mixture of pyridine and triethylamine borane, attempted distillation of the liquid residue at reduced pressures has resulted in sometimes violent decompositions.[11]

The necessary tertiary phosphine intermediates were prepared *via* the standard Friedel-Crafts and/or Grignard procedures.[12–15]

The phosphine boranes were found to be generally colorless, mobile liquids which were relatively stable to both water and air. In contrast to the amine boranes,[5] the phosphine boranes and the triethylenediamine boranes reacted very sluggishly with 2% alcoholic silver nitrate solution. All of the phosphine boranes gave strong infrared absorption near 4.2 μ with a weaker band at 4.35 μ.

## EXPERIMENTAL

*Phosphine boranes.* In a typical experiment, 23 g. (0.2 mole) of triethylamine borane was mixed under argon with 40.4 g. (0.2 mole) of tri-*n*-butylphosphine and the mixture distilled slowly through a Vigreux column to remove triethylamine, b.p. 88–90° $n_D^{21}$ 1.3990. When approximately two-thirds of the amine had been distilled, the mixture was attached to a water aspirator to remove the remaining amine. Distillation of the liquid residue yielded 34.1 g. of tri-*n*-butylphosphine borane (0.158 mole, 79%) as a clear liquid, b.p. 115–117° at 0.8 mm.

The analytical data for this and the other boranes are listed in Table I.

*Phosphines.* The necessary tertiary phosphines were prepared *via* standard Friedel-Crafts and/or Grignard techniques.[12–15]

*Acknowledgment.* We are indebted to Mr. Karl Sterner for the chemical analyses.

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[11] A decomposition has been observed during attempted vapor pressure measurements of pyridine borane. H. C. Brown and L. Domash, *J. Am. Chem. Soc.*, **78**, 5384 (1956).

[12] B. Buchner and L. B. Lockhart, Jr., *J. Am. Chem. Soc.*, **73**, 755 (1951); B. Buchner and L. B. Lockhart, Jr., *Org. Syn.*, **31**, 88 (1951).

[13] (a) W. J Jones, W. C. Davies, S. T. Bowden, C. E. Edwards, V. E. Davis, and L. H. Thomas, *J. Chem. Soc.*, 1446 (1947); (b) G. W. Fenton and C. K. Ingold, *J. Chem. Soc.*, 2342 (1929).

[14] G. M. Kosolapoff, *Organophosphorus Compounds*, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 45, 54.

[15] R. A. Baldwin and R. M. Washburn, *J. Org. Chem.*, in press.

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# Complexes of Diols with Cuprammonium Reagent

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Experimental work was previously reported[1] in which the method of continuous variation was applied to the reaction between cuprammonium and diol-containing compounds. From this work, it was concluded that the cuprammonium-diol complex has a copper-diol ratio of 2:1. The lack of symmetry in the curves obtained for certain carbohydrates was assumed to be caused by hydroxyl groups not associated with the diol structure. Formation of a 2:1 copper-diol complex seemed conclusive from experiments with *cis*- and *trans*-

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[1] E. J. McDonald, *J. Org. Chem.*, **25**, 111 (1960).

1,2-cyclohexanediols. In the latter instance, a constant total molar concentration of copper plus hydroxyl groups rather than of copper plus diol groups was maintained. The maximum optical density, therefore, *did not reflect the composition of the copper-diol complex.* Repetition of this work, using reaction mixtures containing various copper-diol proportions, gave results that are in keeping with the formation of a cuprammonium-diol complex in which the copper-diol ratio is 1:1. This is in agreement with the findings of Reeves.[2]

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(2) R. E. Reeves and P. Bragg, *J. Org. Chem.*, *in press*.

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# Potential Anticancer Agents.[1] LVIII. Analogs of Chlorambucil. VIII. Monofunctional Alkylating Agents Derived from ω-(*p*-Aminophenyl)alkanoic Acids

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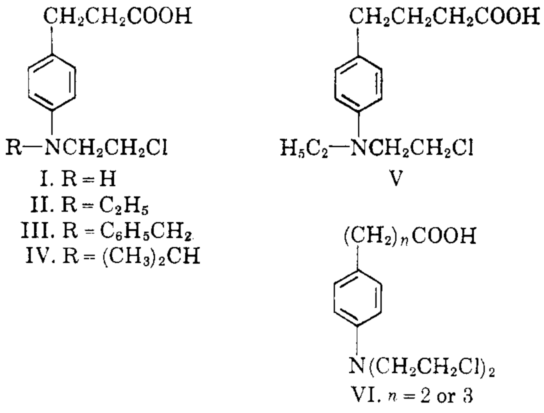
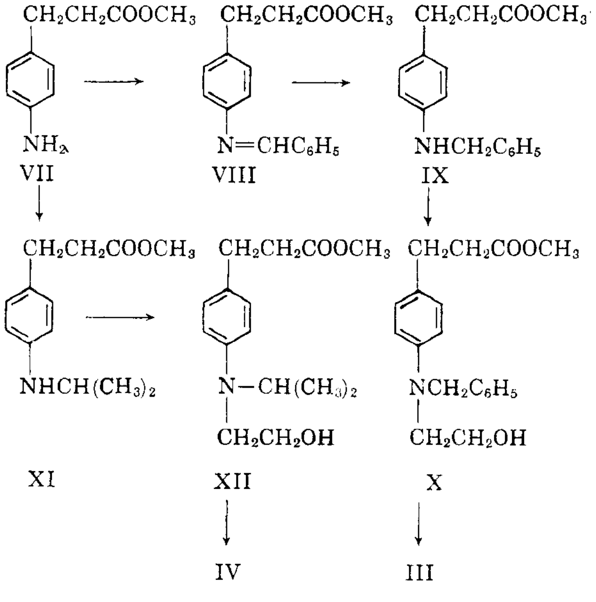
A previous paper[2] described the preparation of the monofunctional alkylating agents (I and II) derived from 3-(*p*-aminophenyl)propionic acid. The "one-armed" mustard (II) was an especially interesting compound for comparison with the difunctional alkylating agent (VI, $n = 2$) as a test of the hypothesis that a monofunctional alkylating group might be as effective as a difunctional agent in effecting irreversible enzyme inhibition.[3] In order to study the effect of the *N*-alkyl group, two other "one-armed" mustards (III and IV) have been prepared, as well as an *N*-ethyl "one-armed" homolog (V) which can be directly compared with chlorambucil[4] (VI, $n = 3$).



I. R = H
II. R = $C_2H_5$
III. R = $C_6H_5CH_2$
IV. R = $(CH_3)_2CH$
V
VI. $n = 2$ or 3

Methyl 3-(*p*-aminophenyl)propionate[2] (VII) was used as the starting material for the preparation of both III and IV. The reaction of benzaldehyde with VII[2] gave a 92% yield of the crystalline anil (VIII), which was hydrogenated over Raney nickel to afford the benzylamine (IX) as a low-melting solid in 89% yield. Hydrogenation at low pressure (20 p.s.i.) was essential; at 50 p.s.i. hydrogenolysis occurred, regenerating the primary amine (VII). The absence of VII in the low-pressure product could be demonstrated by paper chromatography. Treatment of IX with ethylene oxide in aqueous acetic acid gave a good yield of the chromatographically homogeneous sirup (X) which, without purification, was allowed to react with phosphoryl chloride at reflux. The crystalline acid (III) was formed in 82% yield, hydrolysis of the ester group occurring during the decomposition of the chlorination reaction mixture with water.



The conversion of VII to the *N*-isopropyl ester (XI) was accomplished by treatment with 2-bromopropane in the presence of potassium carbonate until paper chromatography of the product showed the absence of VII. Analysis of the crude product suggested that it was contaminated with some dialkylated product although this inference was not obvious from the paper chromatographic data. The crude product, which contained XI, was treated with ethylene oxide in aqueous acetic acid and the hydroxyethylation product was subjected

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(2) W. A. Skinner, H. F. Gram, and B. R. Baker, *J. Org. Chem.*, **25**, 777 (1960).

(3) H. F. Gram, C. W. Mosher, and B. R. Baker, *J. Am. Chem. Soc.*, **81**, 3103 (1959).

(4) J. L. Everett, J. J. Roberts, and W. C. J. Ross, *J. Chem. Soc.*, 2386 (1953).