2,8-Dihydro-6H-dibenzo[*a*][3,6]phenanthroline (II).—A solution of 2,2′-diaminobenzophenone (2.1 g.) and 1,3-cyclohexanedione (1.1 g.) in acetic acid (20 ml.) was heated under reflux for 30 min. A crystalline solid separated which possessed the properties of a ketone but not those of an aromatic primary amine.[5]

The acetic acid mother liquors were diluted with water (100 ml.), boiled, and cooled to yield II (2.2 g., 81%). It recrystallized from aqueous ethanol as colorless needles: m.p. 180–181°; $\lambda_{max}^{C_2H_5OH}$ 269, 336, 354, 372 mμ (ε 41,509, 35,810, 4819, 5808).

Anal. Calcd. for $C_{19}H_{14}N_2$: C, 84.4; H, 5.2; N, 10.4. Found: C, 84.2; H, 5.0; N, 10.6.

The **picrate** was prepared in ethanol solution and recrystallized as green needles from aqueous acetic acid; m.p. 205–207°.

Anal. Calcd. for $C_{25}H_{17}N_5O_7$: N, 14.0. Found: N, 13.8.

5,6-Dihydro-5-methyl-6-oxobenzo[*a*][3,6]phenanthroline (III).—A mixture of benzo[*a*][3,6]phenanthroline methiodide[1] (0.8 g.), potassium ferricyanide (5.0 g.), and NaOH (2 *N*, 50 ml.) was heated under reflux for 5 hr. The suspended solid was collected, dried, and crystallized from ethanol as yellow needles; yield of III, 0.39 g. (71%); m.p. 217–218°; $\lambda_{max}^{CHCl_3}$ 259, 316, 329, 372 mμ (ε 41,210, 5129, 5395, 8222).

Anal. Calcd. for $C_{17}H_{12}N_2O$: C, 78.4; H, 4.65; N, 10.8. Found: C, 78.3; H, 4.7; N, 10.9.

(5) A possible structure for this compound is 2,2′-di(3-oxocyclohexylimino)benzophenone (0.38 g., 9%). It recrystallized from aqueous formic acid as pale green plates, m.p. 336–340°. *Anal.* Calcd. for $C_{25}H_{24}N_2O_3$: N, 7.0. Found: N, 6.9. The di(hydrogen sulfate) separated from a solution of base in 1:1 ethanol and 2 *N* H_2SO_4 as green prisms, m.p. above 400°. *Anal.* Calcd. for $C_{25}H_{28}N_2O_{11}S_2$: N, 4.7. Found: N, 4.9.

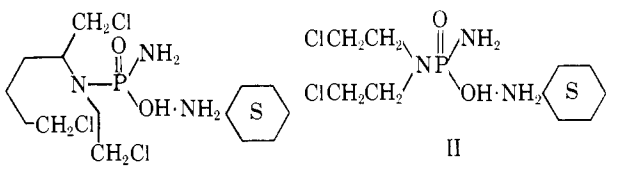
Cyclohexylammonium Hydrogen N-2-Chloroethyl-N-5-chloro(1-chloromethyl)pentyl Phosphorodiamidate[1]

GERT OLSEN AND ORRIE M. FRIEDMAN[2]

Department of Chemistry, Brandeis University, Waltham, Massachusetts 02154

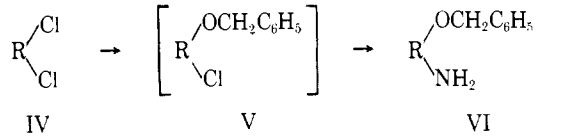
Received June 23, 1965

We report here the synthesis of a new phosphorodiamidic acid mustard (I) structurally analogous to the known potent antitumor agent, N,N-bis(2-chloroethyl)phosphorodiamidic acid cyclohexylamine[3] (II), in which the bis(2-chloroethyl)amine mustard moiety in II is replaced by the more cytoactive nitrogen-mustard, N-2-chloroethyl-N-5-chloro(1-chloromethyl)pentylamine (III).[4]

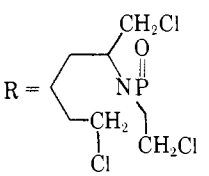


I

II



IV V VI



(1) Supported by a research grant (CA-02130) from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service.

(2) To whom inquiries should be addressed.

(3) O. M. Friedman, E. Boger, H. Sommer, and V. Grublianskas, *J. Med. Chem.*, **6**, 50 (1963).

The new phosphordiamidic acid mustard I was prepared by a procedure paralleling that used for the synthesis of the simpler analog II. The known dichlorophosphoramidate[4] IV was condensed with sodium benzylate to give the benzyl chloro derivative V which, without isolation, was treated with ammonia, affording the benzyl amide VI as a solid crystalline product. Hydrogenolysis of the benzyl ester (VII) gave the phosphorodiamidic acid I isolated as a crystalline cyclohexylammonium salt.

When tested against the KB cell line in tissue culture, the cyclizable mustard phosphoramidic acid I interestingly showed about the same toxicity, ED_{50} = 30 μg./ml., as the simpler analog II, ED_{50} = 35 μg./ml.[5] The compound will be submitted for animal testing.

Experimental Section

Benzyl N-2-Chloroethyl-N-5-chloro-1-(chloromethyl)pentyl Phosphorodiamidate (V).—To a stirred suspension of 0.45 g. of sodium hydride in 10 ml. of sodium-dried benzene cooled in ice was added a solution of 1.03 ml. of benzyl alcohol, over a period of 10 min.; the mixture was stirred in the cold overnight. The resulting suspension of sodium benzylate was added over a period of 10 min. to a stirred solution of 3.55 g. of the dichlorophosphoramide III[4] in 25 ml. of dry benzene in the cold, and the stirring was continued for an additional 2 hr. in the cold. The resulting V, without isolation, was treated with ammonia by bubbling the gas through the cooled solution for 2 hr. until the precipitation of NH_4Cl was complete. After the suspended NaCl and NH_4Cl were filtered, the filtrate was treated with a mixture of 1 g. of Norit A and 1 g. of Nuchar $C_{190}N$. The resulting clear solution, on evaporation, left a residue of 3.1 g. (77%) of light yellow oil, $n^{26}D$ 1.5286.

Anal. Calcd. for $C_{15}H_{24}Cl_3N_2O_2P$: C, 44.85; H, 6.02; Cl, 26.48; P, 7.71. Found: C, 44.88; H, 6.10; Cl, 26.43; P, 7.57.

Cyclohexylammonium Hydrogen N-2-Chloroethyl-N-5-chloro-(1-chloromethyl)pentyl Phosphorodiamidate (I).—Hydrogenolysis of 1.5 g. of V over 0.4 g. of 10% palladium–charcoal in 50 ml. of absolute ethanol, cooled in ice, at a slight overpressure of hydrogen, was complete in 10 min. After filtration to remove the catalyst, 0.4 ml. of cyclohexylamine was added immediately, and the solution evaporated to dryness. The resulting clear oil was shaken with acetone and allowed to stand in the cold for 2 days when crystallization occurred. The product was filtered, washed with acetone, and thoroughly dried under vacuum to give 0.3 g. (20%) of crystalline product, m.p. 101–103°.

Anal. Calcd. for $C_{21}H_{31}Cl_3N_3O_2P$: C, 40.90; H, 7.62; Cl, 25.91; N, 10.22; P, 7.54. Found: C, 40.81; H, 7.48; Cl, 25.69; N, 10.05; P, 7.75.

(4) O. M. Friedman, H. Sommer, and E. Boger, *J. Am. Chem. Soc.*, **82**, 5202 (1960).

(5) By Dr. G. E. Foley, Children's Cancer Research Foundation, Inc., Boston, Mass. We are indebted to Dr. Sidney Farber, Director of the Foundation, for kind permission to report these preliminary results.

Synthesis of the Di-N-phenyl- and Di-N-(α-naphthyl)urethans of 1,1-Dimethylol-3-cyclopentene[1]

EDWARD J. GRUBBS

Department of Chemistry, San Diego State College, San Diego, California 92115

Received July 22, 1965

Recent interest in the biological activity of certain carbamates and urethans has sharply increased. Several pyridylurethan have been found to possess modest analgesic and sedative properties.[2] A variety of halogenated carbanilates have potent teriostatic activity.[3] The activity of these urethans w

(1) Supported by Research Corporation (Frederick Gardner Grant) and the National Science Foundation (Grant GP4417).

(2) N. P. Buu-Hoi, R. Rips, and C. Derappe, *J. Med. Chem.*,

(3) D. J. Beaver, D. P. Roman, and P. J. Stoffel, *J. Am. C* 1236 (1957); *J. Med. Chem.*, **6**, 501 (1963).