

Cyclophosphamides from Aminosugars and Aminonucleosides (I)

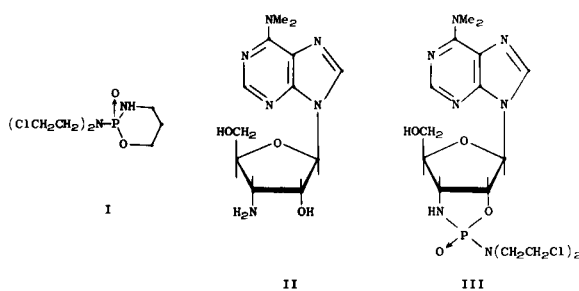
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Condensation of bis-(2-chloroethyl)phosphoramidic dichloride with 3'-amino-3'-deoxy-*N,N*-dimethyladenosine afforded the 2',3'-cyclicphosphorodiamidate (III). By an improved synthesis, methyl 3-amino-3-deoxy- β -D-ribofuranoside was obtained as a model compound for conversion to the analogous 2,3-cyclicphosphorodiamidate (XII). Existence of the latter as two diastereomers due to phosphorus asymmetry was shown by nmr analysis, using comparison with the 5-(*O*-*p*-nitrobenzoate) (XIII) as a basis for assignments.

Cyclophosphamide (I) has been widely studied for its properties as an anticancer drug (2,3). Numerous analogs have also been prepared and studied (2,4,5), but in none of these so far has the amino alcohol moiety been an amino sugar. In place of an amino alcohol which is simply a carrier group for the *N*-phosphoryl nitrogen mustard, the amino alcohol moiety of puromycin aminonucleoside (II) (6,7) has been combined with the mustard phosphoramidate group to give a compound (III) of two anticancer

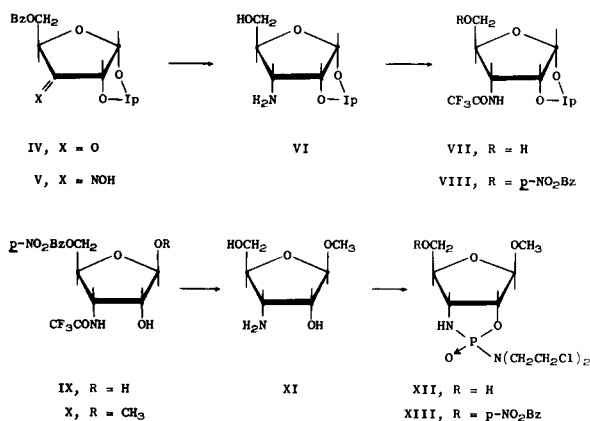
reduced stereoselectively to 3-amine, isolated as the acetamide. The protecting groups were all acid-labile, and acid deblocking led to the amine hydrochloride of the free sugar. On the other hand, for preparation of the methyl furanoside, it was essential to use acid-stable, base-sensitive covering groups at the 3-amine and 5-hydroxyl, so that the 1,2-(*O*-isopropylidene) group (abbreviated *Ip*) could be removed independently, and the risk of ring enlargement during methanolysis could be avoided.



components. Release of both components might be expected upon hydrolysis or enzymatic activation of the phosphorodiamidate *in vivo* (8).

Treatment of puromycin aminonucleoside (II) with bis-(2-chloroethyl)phosphoramidic dichloride, $(\text{ClCH}_2\text{CH}_2)_2\text{NPOCl}_2$ (9,10) was seen as a simple, straightforward synthesis of III. Phosphorylation of II at the 2'-hydroxyl and 3'-amine could be predicted, but attachment at the 5'-hydroxyl and 3'-amine could not be excluded as a possibility. To study this possibility, phosphorylation of methyl 3-amino-3-deoxy- β -D-ribofuranose (XI) with bis-(2-chloroethyl)phosphoramidic dichloride was undertaken as a model.

There are several syntheses described for 3-amino-3-deoxy-D-ribose. The most direct and convenient is the one of Sowa (11) whereby the oxime of 1,2-(*O*-isopropylidene)-5-(*O*-trityl)- α -D-erythropentofuranos-3-ulose was



3-Amino-3-deoxy-1,2-(*O*-*Ip*)- α -D-ribofuranose (VI) (12) was obtained by lithium aluminum hydride reduction of the oxime (V) of 5-(*O*-benzoyl)-1,2-(*O*-*Ip*)- α -D-erythropentofuranos-3-ulose (IV) (13,14). About 9% of the xylo epimer of VI was also formed, and could be removed by recrystallization of VI, or, more conveniently, after *N*-acylation into VII. The trifluoroacetamide group of VII combined the ideal properties of acid-stability and base sensitivity, properties retained in the 5-(*O*-*p*-nitrobenzoyl) group of the ester derivative (VIII). The *Ip* group was then selectively hydrolyzed with 90% trifluoroacetic acid (15) in nearly quantitative yield. Mild methanolysis of IX favored formation of the β -anomer (X)—the β/α ratio

of the crude product was 9:1--and X was freed of the α -anomer by recrystallization. In contrast, methanolysis of the analog of IX bearing a 3-phthalimido group, previously recommended (16) for acid-stability, was accompanied by ring opening to the *N*-substituted methyl phthalamate. Deblocking of X with methanolic butylamine afforded crystalline methyl 3-amino-3-deoxy- β -D-ribofuranoside (XI). The cyclic phosphorodiamidate mustard (XII) was obtained by treating XI with bis-(2-chloroethyl)phosphoramidic dichloride in the presence of triethylamine, in molar equivalent quantities. Inspection of nmr spectra revealed that the product (XII) consisted of two isomers, in unequal amounts. Two singlets appeared for C.1-H in deuteriochloroform, indicating that both were β -anomers. In dimethylsulfoxide- d_6 there was only one singlet for C.1-H, but the *O*-methyl appeared as two slightly resolved singlets. A broad multiplet near 4.4 δ in deuteriochloroform, 4.1 in dimethylsulfoxide, was identified as C.3-H by its partial collapse on deuterium oxide exchange of the N-H. A sharp multiplet near 4.8 δ appeared to consist of a stronger quartet superposed on a weaker one, and was assigned to C.2-H, as the partly resolved isomers; the splitting into a quartet was attributed to coupling with phosphorus ($J = 2.2$ Hz in both isomers) (17) in addition to the observed coupling with C.3-H ($J_{2,3} = 3.5$ Hz for the major isomer). A one-proton multiplet just upfield from C.3-H was reasonably assigned to C.4-H. The protons on C.5 could then be designated as the two protons obscured by the *N,N*-bis(2-chloroethyl) group in the 3.0-3.9 δ region (in deuteriochloroform). This was reasonable in comparison to the location of C.5-H₂ at 3.7-3.8 δ in VI, VII, and other sugars containing the HOCH₂ group. The occurrence of two isomers of XII was explained as the formation of two diastereoisomers, owing to phosphorus asymmetry--not as a mixture of 2,3- and 3,5-cyclic phosphoramides.

That this was so, and that there was no cyclization between the 3-NH and 5-OH, was confirmed by *p*-nitrobenzoylation at C.5. The expected downfield shift of C.5-H₂ was then clearly observed, by the appearance of C.5-H₂ as a strong, rough singlet in the C.3-H region. The shift, $\Delta \delta$, was about 1.0 p.p.m., estimated most accurately in dimethylsulfoxide solutions, and involved two full protons. This shift compared well with $\Delta \delta$ of 0.97 and 0.94 p.p.m. previously observed (in deuteriochloroform) (18) on 5-(*O-p*-nitrobenzoylation) of furanoses. Acetylation of XII caused a similar but smaller downfield shift (about 0.6 p.p.m. in deuteriochloroform) of the C.5-H₂; $\Delta \delta$ of 0.45 p.p.m. were previously observed on 5-(*O*-acetylations) (18). Partial purification of the major diastereomer of XII was accomplished in low yield by crystallization; the nmr spectrum of this sample (isomeric ratio 82:18) facilitated interpretation of the spectrum of XII.

Treatment of the amino nucleoside (II) with bis-(2-chloroethyl)phosphoramidic dichloride in dimethylformamide solution containing triethylamine afforded the cyclic phosphorodiamidate (III) cleanly and in good yield, so long as the volume of solvent was limited so that nearly quantitative crystallization of triethylamine hydrochloride occurred. As with XII, the nmr spectrum of III showed the presence of two isomers, and these could even be slightly resolved by thin-layer chromatography. By analogy with XII, these were explained as diastereomers, owing to phosphorus asymmetry, and it was assumed that there was no phosphorylation of the 5-OH.

EXPERIMENTAL

Methods.

Melting points were determined on a Fisher-Johns hot stage and are uncorrected. Ir spectra were determined as liquid film or, for solids, in Nujol mull; data are recorded only where useful for structural assignment. Nmr spectra were determined in chloroform- d solutions at 60 MHz, except where noted in dimethylsulfoxide- d_6 (DMSO), or in deuterium oxide, or at 100 MHz; tetramethylsilane was always the internal reference, except in deuterium oxide. Signals are described as singlet (s), doublet (d), triplet (t), quartet (q) or multiplet (m). Integrated signal ratios were determined routinely and were as expected from the structural assignments. Thin-layer chromatography (tlc) of the sugar derivatives was done on silica gel, in benzene-methanol (4:1) as developer, the spots detected with iodine or with uv light. In processing reaction products, solutions were dried with magnesium sulfate, which was removed by filtration. The Celite filter-aid, used where noted, is a diatomaceous earth. Solvents were removed *in vacuo* on a spin evaporator.

5-(*O*-Benzoyl)-1,2-(*O*-isopropylidene)- α -D-erythropentofuranos-3-ulose (IV).

Crude, syrupy 5-(*O*-benzoyl)-1,2-(*O*-isopropylidene)- α -D-xylofuranose (13) (containing 5-10% of 3,5-dibenzoate) was best oxidized with ruthenium tetroxide (14) by a modified procedure (19), which required vigorous stirring for 8 hours, with repeated addition of reagents after 2 hours and after 5 hours. The ketone was crystallized from ether-pentane in 66% yield, m.p. 86-89° (lit. 97-98.5°, 98-99°) (13,14). Purity was completely sufficient for conversion to the oxime.

5-(*O*-Benzoyl)-1,2-(*O*-isopropylidene)- α -D-erythropentofuranos-3-ulose Oxime (V).

A solution of 11.7 g. (40.0 mmoles) of the ketone (IV) and 9.7 g. (140 mmoles) of hydroxylamine hydrochloride in 120 ml. of pyridine-95% ethanol (1:1) was refluxed for 2 hours and concentrated. The syrupy residue was dissolved in 300 ml. of dichloromethane and washed with 1 *M* hydrochloric acid and with water. Drying and removal of solvent then afforded a solid residue (12.2 g.), m.p. 128-131°. Recrystallization from 30 ml. of carbon tetrachloride and 10 ml. of chloroform afforded 11.4 g. (92%), m.p. 130-132°; ν_{μ} 2.99 (N-OH), 5.76 (C=O). A 1:1 mixture of *syn* and *anti* isomers in solution was revealed by nmr of C.1-H and C.2-H as pairs of doublets ($J_{1,2} = 4.2$ Hz); δ 8.85 s (N-OH), 6.02-6.17 (1-H), 5.3-5.5 m (4-H), 5.07-5.2 (2-H), 4.48-4.9 m (5-H₂), 1.52 s and 1.46 s (1p).

Anal. Calcd. for C₁₅H₁₇NO₆: C, 58.6; H, 5.58; N, 4.56. Found: C, 58.8; H, 5.58; N, 4.67.

3-Amino-3-deoxy-1,2-(*O*-isopropylidene)- α -D-ribofuranose (VI).

A solution of 3.07 g. (10.0 mmoles) of the oxime (V) in 15 ml. of anhydrous tetrahydrofuran was added dropwise to a suspension of 2.2 g. (58 mmoles) of lithium aluminum hydride in 15 ml. of tetrahydrofuran. The temperature rose, and the mixture was refluxed for 3 hours, then cooled and treated with 20 ml. of tetrahydrofuran-water (1:1). The white, gelatinous solid was collected on a filter, washed with tetrahydrofuran, and the combined filtrate was concentrated. The residual solid was triturated with two 25-ml. portions of water, more alumina was removed by filtration, and the filtrate concentrated. The residual amine was dissolved by trituration with three 25-ml. portions of dichloromethane, which were filtered through Celite, combined, and concentrated. The chromatographically homogeneous (R_f 0.3) residue (1.50 g., 79%) crystallized, m.p. 58-61° (lit., 63-67°) (12); nmr δ 5.83 d (1-H; $J_{1,2} = 3.8$ Hz), 4.52 t (2-H; $J_{1,2} \cong J_{2,3} = 4$ Hz), 3.5-4.0 m (4-H), 3.8 rough s (5-H₂), 3.0-3.35 m (3-H), 1.52 s and 1.33 s (1p). Presence of a weak doublet at δ 5.98 ($J = 3.5$ Hz) indicated the presence of 5-7% of the D-xylo epimer. This could be removed by recrystallization from 40 ml. of ether to give 0.77 g. (43%), m.p. 66-67°.

3-Deoxy-1,2-(*O*-isopropylidene)-3-trifluoroacetamido- α -D-ribofuranose (VII).

A solution of 1.9 g. (10 mmoles) of amino sugar (VI) in 40 ml. of dichloromethane and 4 ml. of pyridine was cooled to 0° and treated dropwise with 3.8 ml. of trifluoroacetic anhydride. The solution was stirred for 1.5 hours at room temperature, washed with two 35-ml. portions of cold water, dried, and evaporated. The residual syrup was stirred with methanol (30 ml.) for 5 minutes to decompose any *O*-trifluoroacetate, and evaporated. After a second treatment, evaporation afforded 2.5 g. of VII, m.p. 135-148°. Recrystallization from 10 ml. of 2-propanol and 6 ml. of petroleum ether (b.p. 30-60°) afforded 2.1 g. (75%), m.p. 156-158°, R_f 0.7 on tlc; ir μ 2.93, 3.15, 3.31 (NH, OH), 5.82 (C=O); nmr δ 6.8s broad (exchangeable, NH), 5.95 d (1-H, $J_{1,2} = 3.9$ Hz), 4.71 q (2-H, $J_{1,2} = 3.9$ Hz, $J_{2,3} = 4.9$ Hz), 4.5-4.1 m (3-H), 4.1-3.7 m (4-H), 3.83 rough s (5-Hz), 1.59 s and 1.39 s (1p).

Anal. Calcd. for C₁₀H₁₄F₃NO₅: C, 42.1; H, 4.95; N, 4.91. Found: C, 42.0; H, 4.90; N, 4.89.

3-Deoxy-1,2-(*O*-isopropylidene)-5-(*O*-*p*-nitrobenzoyl)-3-trifluoroacetamido- α -D-ribofuranose (VIII).

A solution of 9.60 g. (33.7 mmoles) of the amide (VII) in 100 ml. of dry pyridine was treated at 0° with 7.60 g. (41.0 mmoles) of *p*-nitrobenzoyl chloride, and stored at 5° for 18 hours. Excess chloride was decomposed with 1 ml. of water, and the mixture was poured into 300 ml. of cold water. Two 125-ml. dichloromethane extracts, which were combined and washed with aqueous sodium bicarbonate, afforded 14.7 g. of residue which crystallized. Recrystallization from 35 ml. of methanol and 7 ml. of water yielded 13.6 g. (93%), m.p. 127-129°; ir μ 5.78-5.81 (C=O), 8.33 (CF₃); nmr δ (DMSO-*d*₆) 9.45 (NH), 8.33 d and 8.20 d (*p*-C₆H₄, $J_{AB} = 9$ Hz), 5.89 d (1-H, $J_{1,2} = 3.9$ Hz), 4.79 t (2-H, $J_{1,2} \cong J_{2,3} = 4$ Hz), 4.5 (5-H₂), 1.53 s and 1.36 s (1p).

Anal. Calcd. for C₁₇H₁₇F₃N₂O₈: C, 46.9; H, 3.94; N, 6.44. Found: C, 47.1; H, 3.94; N, 6.44.

3-Deoxy-5-(*O*-*p*-nitrobenzoyl)-3-trifluoroacetamido- β -D-ribofuranose (IX).

A solution of 8.40 g. (19.3 mmoles) of VIII in 95 ml. of trifluoroacetic acid-water (9:1) was stirred at room temperature for

3.75 hours, and concentrated *in vacuo* to a solid residue, which was dried by addition and evaporation *in vacuo* of dichloromethane, then benzene. It weighed 7.4 g. (97%), m.p. 148-153°; nmr (DMSO-*d*₆) δ 8.37 d and 8.22 d (*p*-C₆H₄, $J_{AB} = 9$ Hz), 5.15 s (1-H, of β). Integration of these signals indicated IX was entirely β -anomer. Further purification was not attempted.

Methyl 3-Deoxy-5-(*O*-*p*-nitrobenzoyl)-3-trifluoroacetamido- β -D-ribofuranoside (X).

A solution of 13.0 g. (33.6 mmoles) of dihydroxy compound (IX) in 1% methanolic hydrogen chloride (prepared from 7.2 ml. of concentrated hydrochloric acid and 375 ml. of methanol) was kept at 25° for 7 hours, neutralized with solid sodium bicarbonate, filtered through Celite, and concentrated. The residual gum (β/α , 9:1) was dissolved in 350 ml. of ether, and the solution was clarified by filtration and concentrated to about 75 ml., whereupon white solid began to separate. Addition of 25 ml. of pentane and chilling at 5° afforded 8.3 g. (61%), m.p. 143-146°; ir μ 2.81, 3.09 (OH, NH), 5.78, 5.86 (C=O); nmr δ 8.27 s (*p*-C₆H₄), 7.1 d (NH, $J \cong 8$ Hz), 4.92 s (1-H), 3.33 s (OCH₃). Presence of 5% of the α -anomer was indicated by a weak singlet (OCH₃) at 3.57. The mother liquor afforded 3.4 g. containing 30-40% of the α -anomer (indicated by the singlet at 3.57 δ and a doublet at 5.12 for 1-H, $J = 3.8$ Hz). Further recrystallization afforded an analytical sample of X, m.p. 150-151.5°.

Anal. Calcd. for C₁₅H₁₅F₃N₂O₈: C, 44.1; H, 3.70; N, 6.86. Found: C, 44.2; H, 3.66; N, 6.82.

Methyl 3-Amino-3-deoxy- β -D-ribofuranoside (XI).

A solution of 9.40 g. (23.1 mmoles) of X in 250 ml. of methanol and 17 ml. of *n*-butylamine was refluxed for 18 hours, then concentrated. The solid residue was partitioned between 100 ml. of water (to dissolve the amine) and 50 ml. of dichloromethane (to dissolve the *n*-butyl-*p*-nitrobenzamide). The water layer was washed with 50 ml. of dichloromethane, and the combined organic layers were washed with 50 ml. of water. The water extracts were clarified by filtration and concentrated. The residual amine (3.9 g.) was dried by azeotropic removal of benzene and was recrystallized from 11 ml. of absolute ethanol and 10 ml. of petroleum ether (b.p. 90-100°) to yield 2.29 g. (60%), m.p. 108-110° (lit., 107-109°) (20); nmr (deuterium oxide external tetramethylsilane) δ 4.90 s (1-H), 3.40 s (OCH₃).

Methyl 3-Amino-3-deoxy- β -D-ribofuranoside, 2,3-Cyclic-[*N'*,*N'*-bis-(2-chloroethyl)]phosphorodiamidate (XII).

To a finely divided suspension of 1.63 g. (10.0 mmoles) of amine (XI) in 16 ml. of dichloromethane at 0° containing 2.8 ml. (20.0 mmoles) of triethylamine was added dropwise over 15 minutes a solution at 0° of 2.59 g. (10.0 mmoles) of bis-(2-chloroethyl)phosphoramidic dichloride (10) in 17 ml. of dichloromethane. The suspension was warmed and stirred at room temperature. It became clear after 30 minutes, and after 3 hours was concentrated. The residual sticky solid was triturated with two 25-ml. portions of warm benzene. Insoluble triethylamine hydrochloride (2.42 g., 88% of theory) was collected on a filter. Evaporation of the filtrate afforded 3.42 g. (98% yield) of XII, contaminated with triethylamine hydrochloride (13% present) as the only impurity, according to nmr (δ 1.39 t, $J = 7$ Hz, CH₃), ir spectra, and tlc. Purification was accomplished by solution in 50 ml. of dichloromethane and washing with two 10-ml. portions of water. The organic layer was dried and concentrated to a homogeneous, pale, yellow-brown gum (3.04 g., 87% yield), R_f 0.3. Nmr spectra disclosed the presence of two stereoisomers, in a ratio of 37:63; δ (deuteriochloroform, 100 MHz) 5.10 s and

4.99 s (1-H, two kinds of β -anomers), 4.69-4.95 m (2-H, two superimposed quartets, $J = 2.2$ Hz and 3.5 Hz, $J = 2.2$ Hz and estimated 5.5 Hz), 4.65-3.90 (3-H, 4-H, and presumably NH), 3.9-3.0 (5-H₂, ClC₂H₄NC₂H₄Cl, and presumably OH), 3.38 s (OCH₃); δ (DMSO, 100 MHz), 5.68-5.35 (exchangeable, NH, JP-NH estimated 9 Hz), 4.92 s (1-H), 4.80-4.50 m (two quartets, one partly obscured, $J = 2.2$ Hz and 3.5 Hz, $J = 2.2$ Hz and undetermined), 4.13-3.98 m (3-H, on exchange collapses to doublet, $J_{2,3} = 3.5$ Hz), 3.98-3.77 m (4-H), 3.72-3.50 uneven t (2 x ClCH₂), 3.46-3.10 m (5-H₂, 2 x NCH₂), 3.21 s and 3.19 s (OCH₃, two kinds). No ionic Cl was found by elemental analysis.

Anal. Calcd. for C₁₀H₁₉Cl₂N₂O₅P: C, 34.4; H, 5.48; N, 8.02. Found: C, 34.3; H, 5.71; N, 7.77.

Values for C, H, and N from another sample were those for anhydrous XII. One sample was crystallized (8% recovery) from ether-ethyl acetate, m.p. 63-69°. The ratio of isomers was then 18:82; nmr (100 MHz) δ 5.16 weak s and 5.04 strong s (1-H, two kinds), 4.89 q (2-H, $J_{2,3} = 3.5$ Hz, JP-OCH 2.2 Hz), 4.43 rough t (3-H, on exchange collapses to doublet, $J_{2,3} = 3.5$ Hz), 4.33-4.17 m (4-H), 3.78-3.25 m (5-H₂), ClC₂H₄NC₂H₄Cl, 3.42 s (OCH₃), 2.3 (broad, NH and OH, exchangeable).

Methyl 3-Amino-3-deoxy-5-(*O*-*p*-nitrobenzoyl)- β -D-ribofuranoside, 2,3-Cyclic-[*N,N'*-bis(2-chloroethyl)]phosphorodiamidate (XIII).

A stirred solution at 0° of 416 mg. (1.10 mmoles) of (XIII) in 2 ml. of dry pyridine was treated with 254 mg. (1.32 mmoles) of *p*-nitrobenzoyl chloride and stored overnight at 0°. A few drops of water was added with stirring, then 10 ml. of water. Extraction with two 15-ml. portions of dichloromethane, drying, and evaporation afforded 0.60 g. of syrup. *p*-Nitrobenzoic acid was removed by re-solution in dichloromethane and washing with aqueous sodium bicarbonate. The final residue was a heavy syrup, 378 mg. (70%), homogeneous by tlc, R_f 0.6; μ 2.9-3.1 (NH), 5.78 (C=O), 6.5 and 7.4 (NO₂); nmr δ 5.1 broad s (1-H, two kinds, unresolved), 4.43 broad s (5-H₂), 3.37 s and 3.34 s (OCH₃, two kinds); δ (DMSO-*d*₆, 100 MHz) 5.69 uneven q (exchangeable, NH, J_{NH-CH} = 2 Hz, JP-NH = 9 Hz), 5.08 s (1-H), 4.95-4.73 m (2-H, quartet with $J = 2$ Hz and 3.5 Hz, second quartet obscured), 4.6-4.05 (3-H and 4-H), 4.34 rough s (5-H₂), 3.85-3.58 rough t (2 x ClCH₂), 3.55-3.15 m (2 x NCH₂), 3.24 s and 3.23 s (OCH₃, two kinds, barely resolved).

Anal. (22) Calcd. for C₁₇H₂₂Cl₂N₃O₈P: C, 41.0; H, 4.44; Cl, 14.2; N, 8.43. Found: C, 41.3; H, 4.61; Cl, 14.0; N, 8.02. 3'-Amino-3'-deoxy-*N,N'*-dimethyladenosine, 2',3'-Cyclic-[*N,N'*-bis(2-chloroethyl)]phosphorodiamidate (III).

A solution, prepared by warming of 1.47 g. (5.00 mmoles) of II (16,21) in 30 ml. of dry dimethylformamide was treated at room temperature with 1.40 ml. (10.0 mmoles) of triethylamine and chilled to 0°. The resultant fine suspension was stirred and treated with 1.30 g. (5.00 mmoles) of bis(2-chloroethyl)phosphoramidic dichloride (10). The mixture was stirred at 0° for 30 minutes, at room temperature for 6 hours, then was chilled again to complete crystallization of triethylamine hydrochloride, which was collected on a filter (71% recovery in one run). The filtrate was evaporated, and the residue was dissolved in 45 ml. of dichloromethane. The solution was washed with two 20-ml. portions of water (the water washes were re-extracted with a little dichloromethane), dried, and evaporated. The residual, white, foamed glass was freed of dimethylformamide by adding and removing dichloromethane *in vacuo*, to yield 1.23 g. (51%); λ max (ethanol), 275 μ (ϵ , 17,100). Presence of two spots on tlc, R_f 0.40, 0.45, was attributed to resolution of the two isomers (ratio, 1:1) discerned by nmr: δ 8.25 s (2-H), 7.90 s and 7.87 s (8-H, two kinds), 6.30 d and 6.02 d ($J = 5.2$ Hz and $J = 3.7$ Hz,

respectively, 1'-H, two kinds), 5.85-5.15 (NH, assumed), 5.0-4.0 (2-H, 3-H, 4-H, OH) 3.95-3.75 (5-H₂), 3.75-3.25 (ClC₂H₄NC₂H₄-Cl), 3.50 s (CH₃NCH₃).

Anal. (22) Calcd. for C₁₆H₂₄Cl₂N₇O₄P: C, 40.0; H, 5.04; Cl, 14.8. Found: C, 40.2; H, 5.02; Cl, 14.8.

Acknowledgment.

The authors are indebted to Mr. O. P. Crews and Mr. D. C. Meissner for large-scale preparation of the amine (VI).

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Received April 8, 1970

Menlo Park, California 94025