Reactions of Phosphodiester Anions with Phosgene

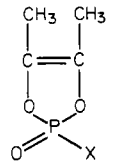
Fausto Ramirez* and James F. Marecek

Department of Chemistry, State University of New York at Stony Brook, Stony Brook, New York 11794

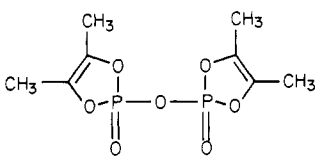
Received August 26, 1982

The mechanisms of reactions of phosgene with the *N*-methylpyridinium salts of diphenyl phosphate and 1,2-dimethylethenylene phosphate (or 4,5-dimethyl-2-oxido-2-oxo-1,3,2-dioxaphosphole) have been studied by ^{31}P NMR spectrometry in dichloromethane at various temperatures and molar ratios of reactants. The products are mixtures of pyrophosphates and phosphorochloridates in proportions that vary with the structure of the phosphodiester and the experimental conditions. The reactions have also been carried out in benzene suspension. The conditions can be adjusted to give exclusively and in high yields (over 85%) either bis(1,2-dimethylethenylene) pyrophosphate or 1,2-dimethylethenylene phosphorochloridate (or 2-chloro-4,5-dimethyl-2-oxo-1,3,2-dioxaphosphole). These cyclic enediol phosphoryl derivatives are excellent reagents for the synthesis of complex biological phosphodiesters.

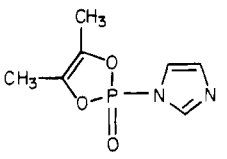
In a review[1] published in 1973, it was stated that the reaction of acyclic dialkyl phosphate anions, $(RO)_2P(O)O^-$ with phosgene yields as a final product the corresponding phosphorochloridate, $(RO)_2P(O)Cl$. An examination of the papers[2-4] quoted in that review to support this statement reveals that those investigations dealt only with reactions of dialkyl monothio- and dithiophosphates, $(RO)_2PSO^-$ and $(RO_2)P(S)S^-$. To our knowledge the literature does not contain detailed investigations of the reactions of acyclic dialkyl or diaryl phosphates with phosgene. The present paper reports such a study with two types of phosphodiesters, diphenyl hydrogen phosphate, $(C_6H_5O)_2P(O)(OH)$ (**1**), and 1,2-dimethylethenylene hydrogen phosphate (**2**; or 4,5-dimethyl-2-hydroxy-2-oxo-1,3,2-dioxaphosphole).[5] We have included the cyclic enediol phosphate **2** (abbreviated CEP-OH) in order to clarify the pathways by which it is converted into the useful phosphorylating reagents, namely bis(1,2-dimethylethenylene) pyrophosphate[6,7] (**3**, CEP-OCEP) and 1,2-dimethylethenylene phosphorochloridate (**4**, or 2-chloro-4,5-dimethyl-2-oxo-1,3,2-dioxaphosphole, CEP-Cl).[8-10] These reagents, CEP-OCEP and CEP-Cl, as well as *N*-[(1,2-dimethylethenylenedioxy)-phosphoryl]imidazole[8,11] (**5**) derived from them, have been widely applied to the synthesis of complex biological phosphodiesters.[12-15]



2, X = OH
4, X = Cl



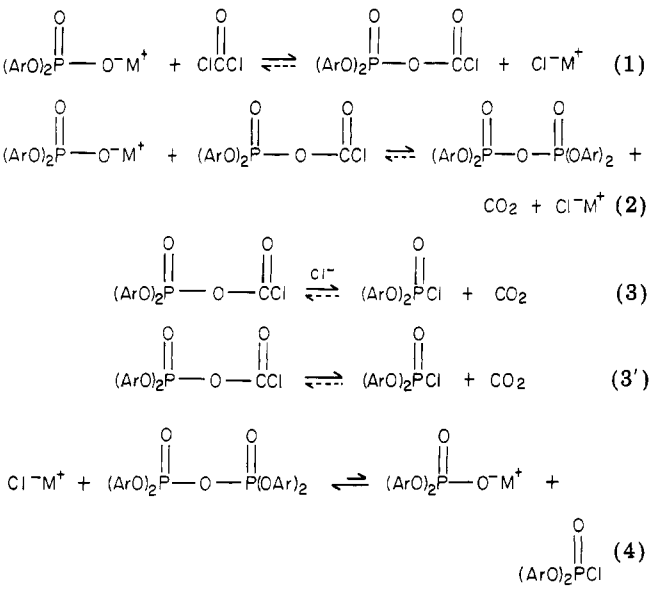
3



5

Results and Discussion

Reactions of the Acyclic Phosphodiester. The free acid diphenyl hydrogen phosphate does not react appreciably with phosgene at 20 °C in dichloromethane solution within ca. 24 h. However, salts of this acid, e.g., the *N*-methylpyridinium salt, are quite reactive toward phosgene under comparable conditions and even at 0 and −80 °C. Some of the results are summarized in Table I. These reactions give two products, tetraphenyl pyrophosphate (**6**) and diphenyl phosphorochloridate (**7**) in proportions that vary with the temperature of the reaction (expts 1 and 2) and the molar ratio of the reagents. These and other experiments suggest that the products are formed as a result of several consecutive and competing steps as shown in eq 1-4.



Equation 1 describes the formation of a hypothetical chlorocarbonyl phosphate intermediate presumably by an

(1) Babad, H.; Zeiler, A. G. *Chem. Rev.* **1973**, *73*, 75; cf. p 85.
(2) Cadogan, J. *J. Chem. Soc.* **1961**, 3067.
(3) Aaron, H. S.; Uyeda, R. T.; Frack, H. F.; Miller, J. I. *J. Am. Chem. Soc.* **1962**, *84*, 617.
(4) Green, M.; Hudson, R. F. *J. Chem. Soc.* **1963**, 1004.
(5) Ramirez, F.; Marecek, J. F.; Tsuboi, H.; Chaw, Y. F. *Phosphorus Sulfur* **1978**, *4*, 325.
(6) Ramirez, F.; Marecek, J. F.; Ugi, I. *Synthesis* **1975**, 99.
(7) Ramirez, F.; Marecek, J. F.; Ugi, I. *J. Am. Chem. Soc.* **1975**, *97*, 3809.
(8) Ramirez, F.; Okazaki, H.; Marecek, J. F. *Synthesis* **1975**, 637.
(9) Ramirez, F.; Okazaki, H.; Marecek, J. F. *Synthesis* **1976**, 819.
(10) For a previous preparation of the phosphorochloridate by a different reaction see: Gozman, I. P. *Izv. Akad. Nauk SSSR* **1968**, 2362.
(11) Ramirez, F.; Ricci, J. S.; Okazaki, H.; Tasaka, K.; Marecek, J. F. *J. Org. Chem.* **1978**, *43*, 3635.
(12) Ramirez, F.; Marecek, J. F. *Acc. Chem. Res.* **1978**, *11*, 239.
(13) Rainier, S.; Jain, M. K.; Ramirez, F.; Ioannou, P. V.; Marecek, J. F.; Wagner, R. *Biochim. Biophys. Acta* **1979**, *558*, 187.
(14) Jain, M. K.; Ramirez, F.; McCaffrey, T. M.; Ioannou, P. V.; Marecek, J. F.; Leunissen-Bijvelt, J. *Biochim. Biophys. Acta* **1980**, *600*, 678.
(15) Ramirez, F.; Mandal, S. B.; Marecek, J. F. *Synthesis* **1982**, 402.

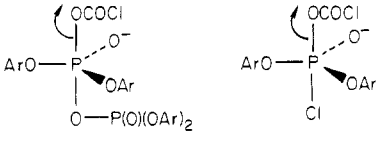
0022-3263/83/1948-0847$01.50/0

Table I. Reactions of Phosphodiesters with Phosgene: N-Methylpyridinium Phosphodiester Salt + ClCOCl in CH_2Cl_2 Solution[a]

expt	reactant	molar equiv of phosgene	temp, °C	addn time, min.	reaction time, h	products (molar ratios)
1	$(ArO)_2P(O)O^-$	10	−80	20	3	$(ArO)_2P(O)OP(O)(OAr)_2$ + $(ArO)_2P(O)Cl$ (2.5:1)
2	$(ArO)_2P(O)O^-$	10	0	20	3	$(ArO)_2P(O)OP(O)(OAr)_2$ + $(ArO)_2P(O)Cl$ (1:2.5)
3	$(ArO)_2P(O)O^-$	10	0	120	3	$(ArO)_2P(O)OP(O)(OAr)_2$ + $(ArO)_2P(O)Cl$ (1:2)[b]
4	CEPO⁻[c]	10	−80	20	3	CEP-OCEP
5	CEPO⁻	10	0	20	0.5	CEP-OCEP + CEP-Cl (1.5:1)
6	CEPO⁻	30	−80	20	0.1	CEP-OCEP + CEP-Cl (2.5:1)[d]
7[e,j]	$(ArO)_2P(O)OP(O)(OAr)_2$	2	20	*f*	365	no reaction
8[g,j]	$(ArO)_2P(O)OP(O)(OAr)_2$	2	20	*f*	365	some $(ArO)_2P(O)Cl$
9[h,j]	$(ArO)_2P(O)OP(O)(OAr)_2$	2	20	*f*	200	$(ArO)_2P(O)OP(O)(OAr)_2$ + $(ArO)_2P(O)Cl$ (1:1)
10[e,j]	CEP-OCEP	2	20	*f*	0.25	traces of CEP-Cl
11[g,j]	CEP-OCEP	2	20	*f*	0.25	CEP-Cl[i]

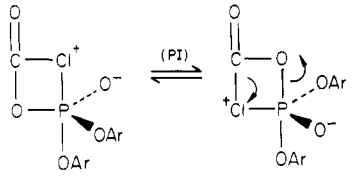
[a] For the general procedure see the Experimental Section. [b] At 50% higher dilution than in expt 2. [c] CEP = cyclic enediol phosphoryl or (1,2-dimethylethenylenedioxy)phosphoryl. [d] No ^{31}P NMR signal attributable to CEP-OCOCl was detected in this or other experiments. [e] 1 M solution in benzene. [f] Mixed at once. [g] 1 M solution in benzene containing 10 mol % of $(n\text{-}C_4H_9)_4N^+Cl^-$. [h] 1 M solution in CH_2Cl_2 containing 50 mol % of $(n\text{-}C_4H_9)_4N^+Cl^-$. [i] The presence of 10 mol % of $(n\text{-}C_4H_9)_4N^+Cl^-$ increased the rate of formation of CEP-Cl by approximately a factor of 90. [j] Experiments 7–11 are control experiments.

addition–elimination mechanism involving the phosphate anion and carbonyl chloride. This type of intermediate has been postulated in similar reactions of mono- and dithiophosphates.[2-4] Owing to the enhanced electrophilicity of the chlorocarbonyl phosphate vs. phosgene, the diphenyl phosphate anion preferentially reacts with the intermediate to yield tetraphenyl pyrophosphate as depicted in eq 2. All attempts to detect the chlorocarbonyl phosphate by means of ^{31}P NMR spectrometry failed (e.g., in expt 3). This suggests that the reaction of eq 2 is faster than that of eq 1, otherwise the chlorocarbonyl phosphate intermediate would accumulate. Alternatively, if the reaction of eq 3 or 3′ were fast in the time scale of our measurements, the phosphorochloridate would be the sole observed product. The two reactions of the chlorocarbonyl phosphate can generate the observed phosphorochloridate; both the bimolecular reaction with chloride ion (eq 3) and the unimolecular rearrangement accompanied by elimination of CO_2 (eq 3′) are regarded as addition–eliminations via oxyphosphorane intermediates.[16] Formulas 8 and 9



8

9



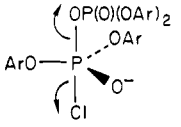
10

11

depict the oxyphosphoranes in the formation of the pyrophosphate and the phosphorochloridate, respectively, by bimolecular reactions. No permutational isomerization[17,18] (PI) is needed to achieve reaction according to the apical entrance–departure rule.[16d] One PI, however, is needed for the formation of phosphorochloridate by the unimolecular process as shown in formulas 10 and 11. The available data do not allow a choice between the bimolecular and the unimolecular process as the source of the phosphorochloridate.

Equation 4 is an important reversible step in the sequence of reactions which lead to the observed products, pyrophosphate and phosphorochloridate. In dichloromethane solution, this equilibrium is overwhelmingly shifted in favor of the pyrophosphate and the chloride salt, as can be demonstrated by ^{31}P NMR measurements starting with preformed diphenyl phosphorochloridate and *N*-methylpyridinium diphenyl phosphate.[19] Once the equilibrium of eq 4 is set up, excess phosgene can react with diphenyl phosphate according to eq 1, followed by the reactions of eq 2 and 3 or 3′. Thus, the pyrophosphate initially formed can be slowly converted into phosphorochloridate. This sequence can be independently demonstrated as is shown in expts 7–9.[20]

The oxyphosphorane intermediate generated upon addition of chloride ion to the pyrophosphate (forward component of step 4) or of phosphate to phosphorochloridate (reverse reaction of step 4) is shown in formula 12. Al-



12

though the same oxyphosphorane intermediate is formed in the forward and reverse reactions, the transition states and, of course, the reactants, are different in the two re-

(16) (a) McEwen, W. E.; Berlin, K. D., Eds. "Organophosphorus Stereochemistry"; Dowden, Hutchinson, and Ross: Stroudburg, PA. 1975; Vol. I, II. (b) Ramirez, F.; Hansen, B.; Desai, N. B. *J. Am. Chem. Soc.* **1962**, *84* 4588. (c) Ramirez, F.; Madan, O. P.; Desai, N. B.; Meyerson, S.; Banas, E. M. *Ibid.* **1963**, *85*, 2681. (d) Westheimer, F. H. *Acc. Chem. Res.* **1968**, *1*, 70. (e) Gillespie, P.; Ramirez, F.; Ugi, I.; Marquarding, D. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 91. (f) Ramirez, F.; Nowakowski, M.; Marecek, J. F. *J. Am. Chem. Soc.* **1977**, *99*, 4515. (g) Sigal, I.; Westheimer, F. H. *Ibid.* **1979**, *101*, 752.

(17) For the *pseudorotation* mechanism to achieve permutational isomerization see: Berry, R. S. *J. Chem. Phys.* **1960**, *32*, 933.

(18) For the *turnstile rotation* mechanism to achieve permutational isomerization see: (a) Ugi, I.; Ramirez, F.; Marquarding, D.; Klusacek, H.; Gillespie, P. *Acc. Chem. Res.* **1971**, *4*, 288. (b) Ugi, I.; Ramirez, F. *Chem. Br.* **1972**, *8*, 198.

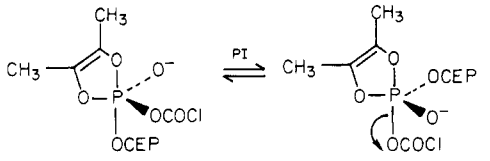
(19) For reasons of solubility, the forward step is studied by addition of tetra-*n*-butylammonium chloride to a dichloromethane solution of the pyrophosphate. The reverse step can also be studied by addition of the less soluble *N*-methylpyridinium salt of the phosphate to a dichloromethane solution of the phosphorochloridate. Both salts are sparingly soluble in benzene, and the admixture of phosphorochloridate and any salt of the phosphate yields a precipitate of the chloride salt plus the benzene-soluble pyrophosphate.

(20) Evidently, hydrolysis of phosgene generates chloride which introduces an important artifact in these mechanistic studies.

actions. Since equilibrium 4 favors the pyrophosphate, it follows that the activation energy for the reverse reaction is significantly lower than that for the forward reaction. This difference in rate constants may be due to a combination of higher ground-state and lower transition-state energies in the reverse reaction relative to the forward reaction.

It should be noted that the free acid diphenyl hydrogen phosphate, unlike its anion, does not react appreciably with diphenyl phosphorochloridate, which is the same behavior observed in the initial reaction with phosgene. Moreover, the rate of the reaction of the diphenyl phosphate anion with the phosphorochloridate (reverse reaction of eq 4) probably is not fast enough to explain the appearance of pyrophosphate in expts 1–3 (Table I).

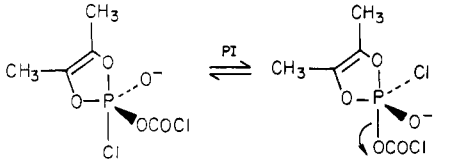
Reactions of the Cyclic Enediol Phosphodiester. These reactions follow the same general pathway shown in eq 1–4, but there are significant differences in the rates of some of the steps when the reactants are cyclic or acyclic. Under comparable conditions, less phosphorochloridate is formed in the cyclic case (expts 5 and 6), and in some experiments (cf. expt 4) no CEP-Cl is observed at all. These differences could result from the greater nucleophilicity of the $CEPO^-$ vs. that of the diphenyl phosphate anion in step 2 and the greater electrophilicity of CEPOCOCl vs. that of the acyclic chlorocarbonyl phosphate in steps 2 and 3 or 3′. The $CEPO^-$ anion is less hindered than the diphenyl phosphate anion, and this could, in part, account for the nucleophilicity difference. The electrophilicity difference is understandable in terms of the corresponding oxyphosphorane intermediates and the transition states leading to them. Formula **13** represents the oxyphosphorane that should result from attack by $CEPO^-$ on CEP-OCOCl (analogue of eq 2). For reasons previously given,[21] a five-membered ring should occupy the apical-equatorial position in the trigonal bipyramid. Oxyphosphorane **13** (and the transition state leading to it)



13 **14**

should be of lower energy than oxyphosphorane **8**, its analogue in the acyclic case, for steric and electronic reasons.[21] Note that the apical entrance–departure rule requires one PI to give oxyphosphorane **14** prior to the generation of CEP-OCEP, unlike in the acyclic case.

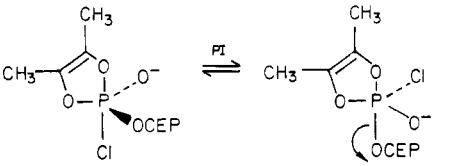
Formulas **15** and **16** represent the oxyphosphoranes involved in the formation of CEP-Cl from the reaction of chloride ion with CEP-OCOCl. The energetic advantage of **13** ⇌ **14** over **15** ⇌ **16**, when compared to the difference



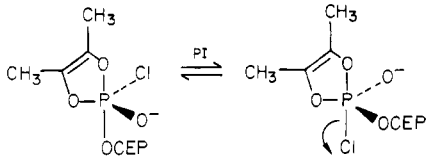
15 **16**

in energy between **8** and **9**, would account for the preference of CEPOCEP vs. CEP-Cl, when compared to the acyclic case. This argument involves also the expected higher energies of the ground state in the cyclic case, CEP-OCOCl relative to the acyclic chlorocarbonyl phosphate, both factors contributing to the lower activation energy in the reactions of the cyclic compounds.

In the cyclic case, the forward and reverse components of the equilibrium analogous to that shown in eq 4 proceed by way of pairs of oxyphosphoranes **17** ⇌ **18** (forward) and **19** ⇌ **20** (reverse). The constraint imposed by the five-



17 **18**

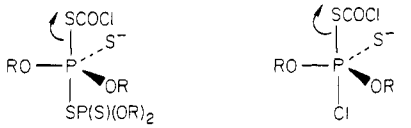


19 **20**

membered ring (apical–equatorial placement) requires the occurrence of one PI for the formation of $CEPO^-$ and CEP-Cl (forward) and the formation of CEP-OCEP and chloride ion (reverse). In the cyclic case, the initially formed oxyphosphoranes **17** and **19** are no longer energetically equivalent, although they become so as a result of PI (**17** ≡ **20**), **19** ≡ **18**).[22]

We had previously reported[6] that the reaction of 2 mol of *N*-$MePy^+$ (*N*-methylpyridinium) $CEPO^-$ with 1 mol of phosgene in benzene at 0 °C for 1.5 h gave the pyrophosphate CEP-OCEP in 85% yield. Subsequently,[9] we found that the reaction of the *N*-$MePy^+$ $CEPO^-$ with an *excess* of phosgene in benzene at 25 °C for 30 h gave the phosphorochloridate CEP-Cl in 88% yield. We assumed at that time that CEP-Cl originated from a reaction of the pyrophosphate CEP-OCEP with phosgene. The present study shows that this assumption is incorrect. The CEP-Cl is formed by a sequence of reactions analogous to those depicted in eq 1–4, in which the last reversible step is set up by the presence of chloride ion in the solution. The excess of phosgene simply shifts equilibrium 4 to the right, yielding CEP-Cl at the expense of reactions 1 and 3 or 3′ (when $CEPO^-$ is depleted).

In the reactions of the dithiophosphate anion with phosgene, the reactions analogous to those of steps 2 and 3 are assumed to proceed via oxyphosphoranes **21** and **22**,



21 **22**

respectively. For steric and electronic reasons[16e,21] oxyphosphoranes of type **21** with one or more P–S bonds are energetically unfavorable relative to analogues with P–O bonds. This analysis accounts for the predominance of thiophosphorochloridates instead of thiopyrophosphates in the corresponding reactions.[2–4]

(21) (a) Ramirez, F. *Acc. Chem. Res.* **1968**, *1*, 168. (b) Gillespie, P.; Hoffmann, P.; Klusacek, H.; Marquarding, D.; Pfohl, S.; Ramirez, F.; Tsolis, E. A.; Ugi, I. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 687. (c) Ramirez, F.; Ugi, I. *Bull. Soc. Chim. Fr.* **1974**, 453.

(22) A similar analysis can be made of the unimolecular mechanism to generate CEP-Cl from CEP-OCOCl (the analogue of step 3′). Now the required oxyphosphoranes (not shown) are spirobicyclic compounds with a five- and a four-membered ring attached to pentacovalent phosphorus.

Table II. ^{31}P NMR Chemical Shifts in Dichloromethane

compd	^{31}P shift,[a] ppm
$(C_6H_5O)_2P(O)OH$ (1)	−12.0
$(C_6H_5O)_2P(O)Cl$ (7)	−6.0
$(C_6H_5O)_2P(O)O(O)P(OC_6H_5)_2$ (6)	−24.8
CEP-OH[b] (2)	11.4[c]
CEP-Cl (4)	18.4
CEP-OCEP (3)	−1.6

[a] From 85% H_3PO_4 at 0 ppm. Positive values are downfield from the reference. [b] CEP = cyclic enediol phosphoryl. [c] 25% dimethyl sulfoxide added.

Experimental Section

Materials. Diphenyl hydrogen phosphate was prepared by a standard procedure. 1,2-Dimethylethenylene hydrogen phosphate (CEP-OH) was prepared as described.[5] *N*-Methylpyridinium diphenyl phosphate was prepared by reaction of pyridine with methyl diphenyl phosphate. *N*-Methylpyridinium 1,2-dimethylethenylene phosphate was prepared as described.[9] Phosgene gas was passed through anhydrous copper sulfate prior to its utilization in the reaction. The dichloromethane was strictly anhydrous.

General Procedure. A solution of the *N*-methylpyridinium salt of the phosphodiester (1.5 mmol) in anhydrous dichloromethane (10 mL) was added dropwise to a stirred solution of phosgene in dichloromethane (10 mL). The phosphate/phosgene molar ratios and the reaction temperatures are given in Table I. After the mixture was stirred for the time indicated, the solvent and excess phosgene were evaporated (30 torr, 15–20 °C). *N*-Methylpyridinium chloride precipitated as evaporation proceeded. The residue from the evaporation was shaken with dichloromethane (1 mL) and the solution separated from the chloride salt by careful decantation. The ^{31}P NMR spectrum of the solution was examined immediately, and the results are given in Table I. The pertinent chemical shifts are listed in Table II.

Care must be exercised to avoid water contamination during the above procedure. Hydrolysis during reaction introduces the following step as an artifact: $(C_6H_5O)_2P(O)Cl + H_2O \rightarrow (C_6H_5O)_2P(O)OH + HCl$ and CEP-Cl + $H_2O \rightarrow$ CEP-OH + HCl.

Acknowledgment. This research was supported by Grant CHE 81-10294 from the National Science Foundation.

Registry No. 2, 20682-72-8; 3, 55894-94-5; 4, 21949-38-2; $(C_6H_5O)_2P(O)O(O)P(OC_6H_5)_2$, 10448-49-4; $(C_6H_5O)_2P(O)Cl$, 2524-64-3; $(C_6H_5O)_2P(O)O^-$, 48168-03-2; $(C_6H_5O)_2P(O)OH$, 838-85-7; $CEPO^-$, 50577-95-2; phosgene, 75-44-5.

Anion Formation and Ring Opening of 9-Substituted Purines in Liquid Ammonia Containing Potassium Amide[1]

Nico J. Kos, Henk C. van der Plas,* and Wouter J. F. Blees

Laboratory of Organic Chemistry, Agricultural University, Wageningen, The Netherlands

Received August 25, 1982

Reaction of 9-methylpurine, 6-chloro-9-methylpurine, and 2′,3′-*O*-isopropylidenenebularine with potassium amide in liquid ammonia leads to opening of the imidazole ring, yielding, after hydrolysis during the workup, 4-(substituted amino)-5-formamidopyrimidines. 6-Chloro-9-methylpurine gives, besides 6-chloro-4-(methylamino)-5-formamidopyrimidine as main product, small amounts of 9-methyladenine and 6-chloro-7,8-dihydro-8-oxo-9-methylpurine. The ring opening will involve adduct formation at position 8. Nebularine, adenosine, and 2′,3′-*O*-isopropylideneadenosine do not react. With a greater excess of potassium amide 2′,3′-*O*-isopropylideneadenosine loses the sugar moiety. The existence of an anion at position 8 can be proved in 9-methylpurine via scavenging with bromobenzene in liquid ammonia containing potassium amide, yielding the 8-phenyl derivative. With 6-chloro-9-(2-tetrahydropyranyl)purine this reaction gives 6-anilino-9-(2-tetrahydropyranyl)purine. Scavenging of 9-methyladenine with bromobenzene gives 6-anilino-9-methylpurine. ^1H and ^{13}C NMR spectroscopy confirm that in this strongly basic medium 7- and 9-methyladenine and 6-(methylamino)-9-methylpurine deprotonate at C-8 and lose a proton from the amino group. Both 8-(methylthio)- and 8-amino-9-methylpurine give with potassium amide in liquid ammonia opening of the imidazole ring, yielding 5-(cyanoamino)-4-(methylamino)pyrimidine, which can react further to give either 8-amino-9-methylpurine or 7,8-dihydro-8-oxo-9-methylpurine.

In an extension of our study of the reactivity of 2-, 6- and 8-substituted purines toward potassium amide in liquid ammonia[2–4] we became interested in the behavior of 9-substituted purines. In this strongly basic medium these compounds cannot be deprotonated at N-9, making them considerably more reactive toward nucleophilic agents than the purines, being unsubstituted at position 9. In anionic purines only position 6 is attacked by the amide ion, and in neutral purines positions 6 and 8 are approximately equally reactive.[5]

The reactivity of purines containing a leaving group is determined not only by its position but also by the position of the substituent on nitrogen.[6] Besides substitution, often ring opening occurs, leading to either an imidazole or a

(1) Part 96 on pyrimidines from this laboratory. For part 95 see: Kos, N. J.; van der Plas, H. C., submitted for publication in *J. Org. Chem.*
(2) Kos, N. J.; van der Plas, H. C.; van Veldhuizen, A. *J. Org. Chem.* **1979**, *44*, 3140.
(3) Kos, N. J.; van der Plas, H. C.; van Veldhuizen, A. *Recl. Trav. Chim. Pays-Bas* **1980**, *99*, 267.
(4) Kos, N. J.; van der Plas, H. C. *J. Org. Chem.* **1980**, *45*, 2942.
(5) Lister, J. H. In "The Chemistry of Heterocyclic Compounds. Fused Pyrimidines"; Brown, D. J., Ed.; Wiley: New York, 1971; Part II. Miller, J. In "Reaction Mechanisms in Organic Chemistry 8, Aromatic Nucleophilic Substitution"; Eaborn, C., Chapman, N. B., Eds.; Elsevier: Amsterdam, 1968.
(6) Badger, R. J.; Barlin, G. B. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1176.

0022-3263/83/1948-0850$01.50/0