Yields and conversions were calculated from the stoichiometric equations in the Discussion and checked for hydrogen balance. Tars were determined gravimetrically and analyzed from 93 to 95% C, 5 to 8% H, and less than 0.3 % N.

Specific reaction conditions are summarized in Table I.

Acknowledgments.—The author is indebted to K. Allen Pinkerton for the calibration and interpretations of the mass spectra and to Dr. Keith M. Taylor for his invaluable advice.

Reaction of Heterocyclic Polycarbonyl Compounds with Phosphite Esters. Alloxan and Parabanic Acid[1,2]

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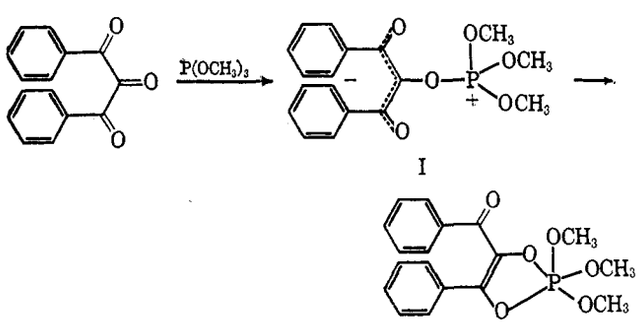
Received July 18, 1966

Trimethyl phosphite reacted with anhydrous alloxan at 22° and gave 5-hydroxy-6-methoxyuracil 5-dimethyl phosphate (XIII) in 92% yield. The reaction of the phosphite with alloxan monohydrate afforded the same enediol phosphate XIII in 30% yield, plus 5-hydroxybarbituric acid 5-dimethyl phosphate (XIX) in 40% yield. The two phosphates, XIII and XIX were converted into the same 5-hydroxy-2,4,6-trimethoxypyrimidine 5-dimethyl phosphate (XIV) by diazomethane. Alkylation of XIII with dimethyl sulfate gave the pyrimidine phosphate XIV in 20% yield, plus 1-methyl-2,4-dimethoxy-5-hydroxy-6(1)-pyrimidone 5-dimethyl phosphate (XXII) in 40% yield. Dimethyl phosphite converted alloxan or its monohydrate into 5-hydroxybarbituric acid 5-dimethyl phosphate (XIX) in 75% yield. Parabanic acid failed to react with trimethyl phosphite and with dimethyl phosphite. N,N'-Dimethylparabanic acid was converted into N-tetramethylbiparabanyl (XXV) in 91% yield by boiling triethyl phosphite. The biparabanyl XXV was hydrogenated to a mixture (80:20) of diastereomeric dihydrobiparabanyls (XXVI and XXVII).

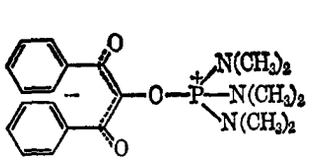
The reaction of trimethyl phosphite with 1,3-diphenylpropanetrione gave a 1,3,2-dioxaphospholene (II) with pentacovalent phosphorus.[3] The suspected dipolar intermediate I could not be detected.



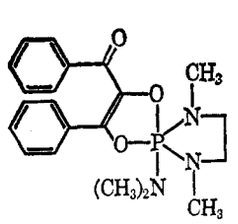
I

II, $\delta_{P^{31}} = +49.3$ ppm *vs.* H_3PO_4

The product of the reaction of trisdimethylaminophosphine with 1,3-diphenylpropanetrione was the crystalline dipolar adduct III, which showed no tendency to form a phosphorane.[4] However, when the carbon atoms of the aminophosphine were linked in the form of a five-membered ring, the resulting adduct had, again, a dioxaphospholene structure IV.[5]

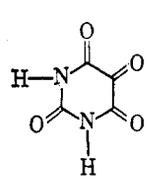


III, $\delta_{P^{31}} = -35.9$ ppm

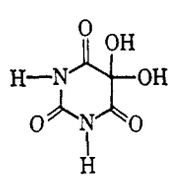


IV, $\delta_{P^{31}} = +31.9$ ppm

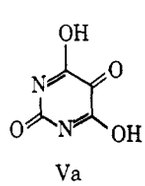
This paper is concerned with the reaction of heterocyclic polycarbonyl compounds with trialkyl phosphites. We have studied the behavior of alloxan (V) and of its monohydrate[6] (VI). This acidic ($pK = 6.6$) cyclic ureide can exist in several tautomeric forms like Va and Vb, which have quinonoid character.



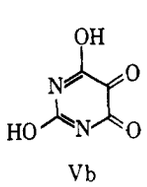
V



VI



Va



Vb

It is known[7] that trialkyl phosphites convert *p*-benzoquinone into an alkyl ether of a *p*-quinol phosphate (VIII); *i.e.*, the intermediate dipolar adduct VII underwent an alkyl group translocation. On the other hand, the reaction of the phosphite with an *o*-quinone[8] led to the dioxaphospholene IX as in the case of the triketone II.

(1) Organic Compounds with Pentavalent Phosphorus. Part XXIV Supported by Public Health Service Research Grant No. CA-04769-07 from the National Cancer Institute, and by the National Science Foundation GP-3341.

(2) Part XXIII: F. Ramirez, A. V. Patwardhan, and C. P. Smith, *J. Org. Chem.*, **31**, 3159 (1966).

(3) F. Ramirez, A. V. Patwardhan, and C. P. Smith, *ibid.*, **30**, 2575 (1965).

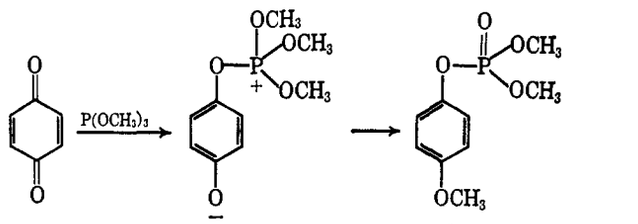
(4) F. Ramirez, A. V. Patwardhan, and C. P. Smith, *J. Am. Chem. Soc.* **87**, 4973 (1965).

(5) F. Ramirez, A. V. Patwardhan, H. J. Kugler, and C. P. Smith, *Tetrahedron Letters*, **No. 26**, 3053 (1966).

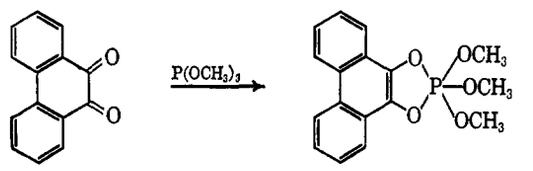
(6) H. Biltz, *Ber.*, **45**, 3659 (1912).

(7) (a) F. Ramirez and S. Dershowitz, *J. Org. Chem.*, **22**, 856 (1957); (b) *ibid.*, **23**, 778 (1958); (c) *J. Am. Chem. Soc.*, **81**, 587 (1959); (d) F. Ramirez, C. H. Chen, and S. Dershowitz, *ibid.*, **81**, 4338 (1959).

(8) For documentation see: (a) F. Ramirez, *Pure Appl. Chem.*, **9**, 337 (1964); (b) F. Ramirez, C. P. Smith, A. S. Gulati, and A. V. Patwardhan, *Tetrahedron Letters*, **No. 19**, 2151 (1966).

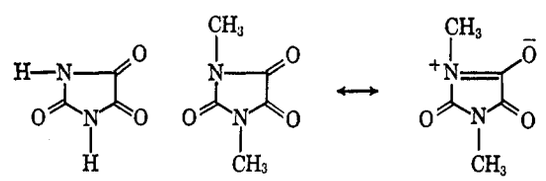


VII VIII, $\delta_{P^{31}} = +3.7$ ppm



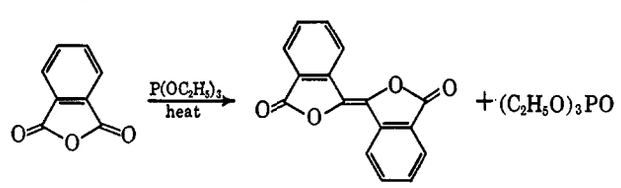
IX, $\delta_{P^{31}} = +45.1$ ppm

Another heterocyclic studied was parabanic acid (X) and its N,N'-dimethyl derivative XI.[9] These imidazoletriones are not related to α-diketones or to quinones, but could be regarded as analogous to maleimide (*cf.* resonance structure XIa).



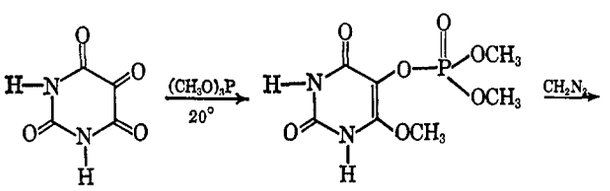
X XI XIa

Trialkyl phosphites converted phthalic anhydride into biphthalyl (XII) at elevated temperatures.[10] It was of interest to determine if this type of reductive coupling could be effected in the parabanic acid series.

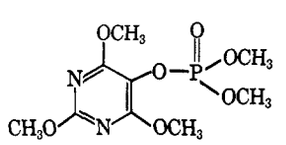


XII

Reaction of Alloxan and of Its Monohydrate with Trimethyl Phosphite.—Anhydrous alloxan (V) reacted with trimethyl phosphite in methylene chloride solution at about 22°. The reaction was vigorous and afforded 5-hydroxy-6-methoxyuracil 5-dimethyl phosphate (XIII) in 92% yield.

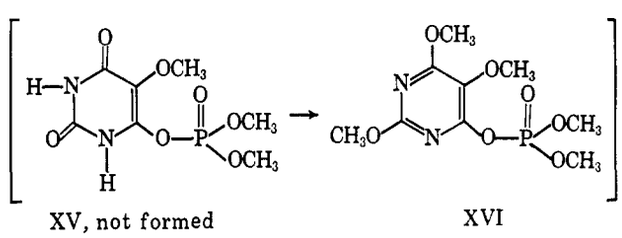


V XIII, $\delta_{P^{31}} = +1.2$ ppm



XIV, $\delta_{P^{31}} = +2.2$ ppm

The enediol ether phosphate structure XIII was based on the following evidence. (1) The colorless, high-melting (195–197°) material had formula $C_7H_{11}O_7N_2P$. (2) It was a phosphate, since the P^{31} nmr shift was +1.2 ppm *vs.* H_3PO_4.[11] The signal was a septet, showing that the P nucleus was coupled only to the six protons of the two equivalent methoxy groups of the phosphate. (3) The H^1 nmr spectrum disclosed these methoxy protons as a doublet at τ 6.15, $J_{HP} = 11.4$ cps. The methyl ether appeared as a singlet at τ 5.97. The acidic ureide protons gave a broad signal at *ca.* τ 4.6. (4) The infrared spectrum had bands at 5.83, 5.95, and 6.02 μ, as expected of structure XIII. (5) When a suspension of the uracil phosphate XIII in methanol was treated with triethylamine, a clear, orange solution was formed. Treatment of this solution with diazomethane afforded products of oxygen alkylation and of nitrogen alkylation; the main product was 5-hydroxy-2,4,6-trimethoxypyrimidine 5-dimethyl phosphate (XIV). This low-melting phosphate had a 6 H^1 doublet, $J_{HP} = 11.7$ cps, at τ 6.08, a 6 H^1 singlet at 5.98, and a 3 H^1 singlet at 6.05. The spectrum was similar in benzene and in $CDCl_3$ solutions, *i.e.*, the aspect of the 6 H^1 singlet was independent of the nature of the solvent. This showed that the molecule had a symmetrical distribution of the four substituents on the pyrimidine ring, as in XIV. Therefore, the methylation product can not be 6-hydroxy-2,4,5-trimethoxypyrimidine 6-dimethyl phosphate (XVI), and its precursor was not 6-hydroxy-5-methoxyuracil 6-dimethyl phosphate (XV). Other isomers of hydroxymethoxyuracil phosphate XIII were excluded on the basis of these data.



XV, not formed XVI

A possible explanation of the course of the reaction of trimethyl phosphite with alloxan is shown in Scheme I.

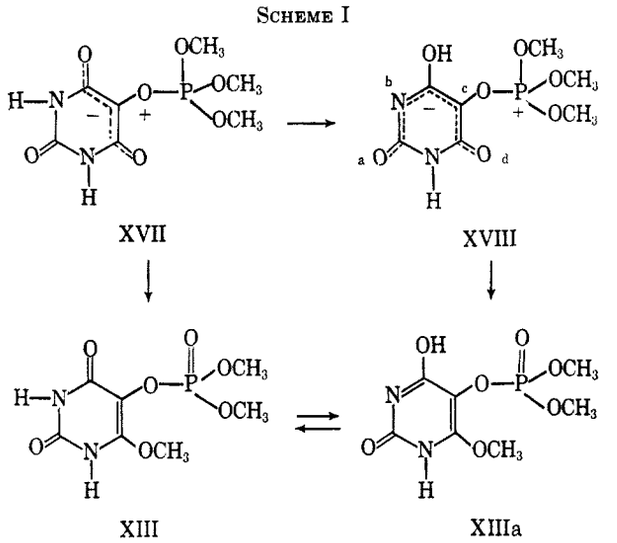
The phosphorus attacked the oxygen atom of the middle carbonyl group of the trioxo system of alloxan. The dipolar adduct XVII resembled adduct I derived from 1,3-diphenylpropanetrione. However, the former can undergo a rapid proton shift from N to O, to give adduct XVIII, with a highly delocalized negative charge. Adduct XVIII is a polydent anion that can undergo self-alkylation at one of four positions a–d; evidently position d is favored. In this scheme, the rearranged adduct XVIII is much more stable than the initial adduct XVII; therefore, cyclization of the alloxan phosphite adduct to a phosphorane is prevented, and the rearranged adduct XVIII has an opportunity to undergo the alkyl group translocation. In this sense, alloxan behaved more like a *p*-quinone than like an *o*-quinone or like a vicinal triketone toward trialkyl phosphites.

(9) H. Biltz and E. Topp, *Ber.*, **46**, 1387 (1913).

(10) (a) F. Ramirez, H. Yamanaka, and O. H. Basedow, *J. Org. Chem.*, **24**, 1838 (1959); (b) *J. Am. Chem. Soc.*, **83**, 173 (1961).

(11) For documentation see F. Ramirez, A. V. Patwardhan, N. Ramanathan, N. B. Desai, C. V. Greco, and S. R. Heller, *ibid.*, **87**, 543 (1965).

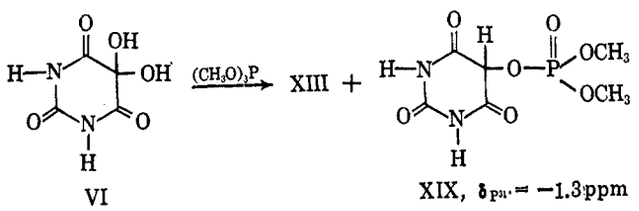
SCHEME I



XVII XVIII

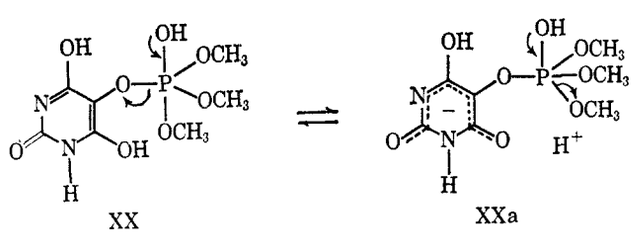
XIII XIIIa

The reaction of alloxan monohydrate (VI) with trimethyl phosphite gave two products: the uracil phosphate XIII in 30% yield, and 5-hydroxybarbituric acid 5-dimethyl phosphate (XIX) in 40% yield.



VI XIX, $\delta_{P^{31}} = -1.3$ ppm

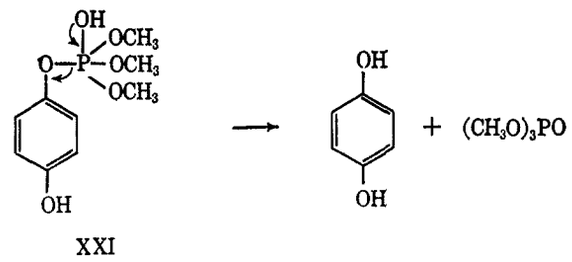
This result can be explained with the aid of Scheme I. Addition of water to the dipolar adduct XVIII could give the transient intermediate XX with pentacovalent phosphorus.[12] The latter should exist mostly as the conjugate base XXa, because of the high acidity of barbituric acid (pK = 4.0). Intermediate XXa should collapse to give the observed products, the barbituric acid phosphate XIX plus methanol, since the high electron density in the conjugate base prevents it from acting as a leaving group. The alternate hydrolysis path to trimethyl phosphate plus 5-hydroxybarbituric acid (*cf.* XX) is thus avoided.



XX XXa

A hydrolysis to trimethyl phosphate would be expected from intermediate XX, since the reaction of trimethyl phosphite with *p*-benzoquinone in the presence of water gave mostly trimethyl phosphate plus hydroquinone,[7] presumably *via* intermediate XXI.

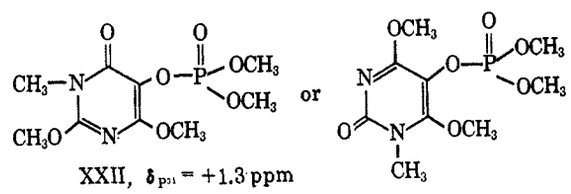
(12) (a) F. Ramirez, O. P. Madan, N. B. Desai, S. Meyerson, and E. M. Banas, *J. Am. Chem. Soc.*, **85**, 2681 (1963); (b) F. Ramirez, A. V. Patwardhan, N. B. Desai, and S. R. Heller, *ibid.*, **87**, 549 (1965); (c) F. Ramirez, O. P. Madan, and C. P. Smith, *ibid.*, **87**, 690 (1965).



XXI

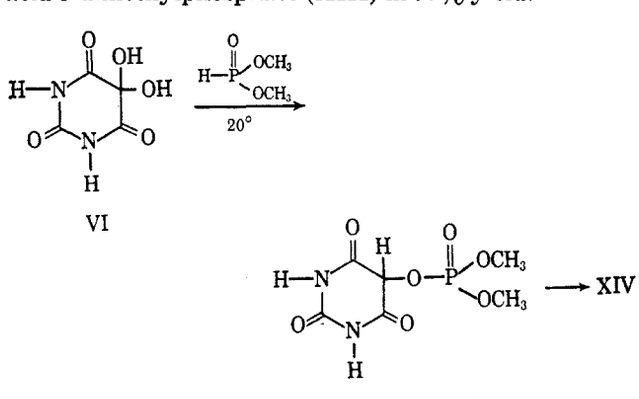
The methylation of the uracilphosphate XIII was carried out with dimethyl sulfate in acetone, in the presence of potassium carbonate. Under these conditions, the minor product (*ca.* 20%) was the *sym*-trimethoxypyrimidine 5-phosphate (XIV) and the major product (*ca.* 50%) was an N-methylated isomer. This substance (mp 90°) could be either the 6(1)-pyrimidone 5-phosphate XXII, or the 2(1)-pyrimidone isomer XXIII. The former is in better agreement with the presence of a band at 5.92 μ in the infrared spectrum. The H^1 nmr spectrum is given in the Experimental Section.

XIII ⟶ XIV +



XXII, $\delta_{P^{31}} = +1.3$ ppm XXIII

Reaction of Alloxan and of Its Monohydrate with Dimethyl Phosphite.—Alloxan hydrate reacted with dimethyl phosphite at 25° and gave 5-hydroxybarbituric acid 5-dimethylphosphate (XIX) in 77% yield.



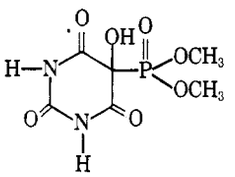
VI XIV

XIX, $\delta_{P^{31}} = -1.3$ ppm

The structure of the phosphate XIX was based on the P^{31} nmr shift (−1.3 ppm) which corresponded to a phosphate and not to an α-hydroxy phosphonate. The signal was a doublet of septets indicating a coupling of the P nucleus with the lone methine proton and with the six methoxy protons. The proton nmr spectrum is described in the Experimental Section. Diazomethane converted the phosphate XIX into the same 5-hydroxy-2,4,6-trimethoxypyrimidine 5-dimethyl phosphate (XIV) described above.

The reaction of anhydrous alloxan with dimethyl phosphite gave also the hydroxybarbituric acid phosphate XIX. It is quite possible that the initial product of the reaction of dimethylphosphite with alloxan or with its hydrate is the α-hydroxy phosphonate

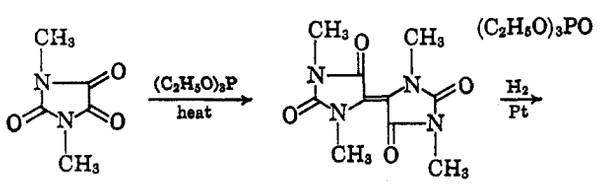
(XXIV) which then underwent isomerization to the phosphate XIX. However, the observations reported here do not shed light on this question.



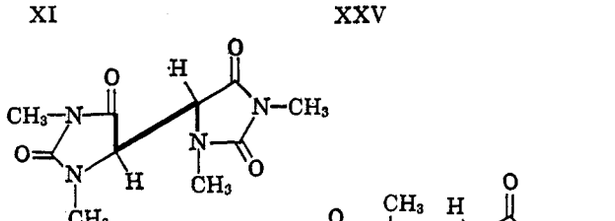
XXIV, not observed

Attempted Reaction of Parabanic Acid with Trimethyl Phosphite and with Dimethyl Phosphite.—No reaction could be induced in these systems, under the conditions given in the Experimental Section.

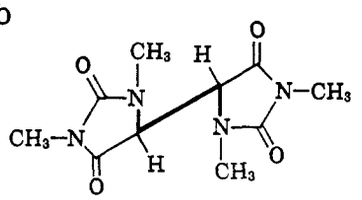
Reaction of N,N′-Dimethylparabanic Acid with Triethyl Phosphite at Elevated Temperatures.—No reaction was observed between the N,N′-dimethylparabanic acid (XI) and trimethyl or triethyl phosphite at 25°. However, when the methylparabanic acid and triethyl phosphite were kept for 4 hr at reflux temperature, a reductive dimerization to N-tetramethylbiparabanyl (XXV) and triethyl phosphate was observed. The high-melting (217°), deep yellow biparabanyl XXV was isolated in 91% yield. The H^1 nmr spectrum had two signals of equal intensities at τ 6.66 and 6.90. The infrared spectrum had two strong carbonyl bands at 5.73 and 5.88 μ, respectively.



XI XXV



XXVI



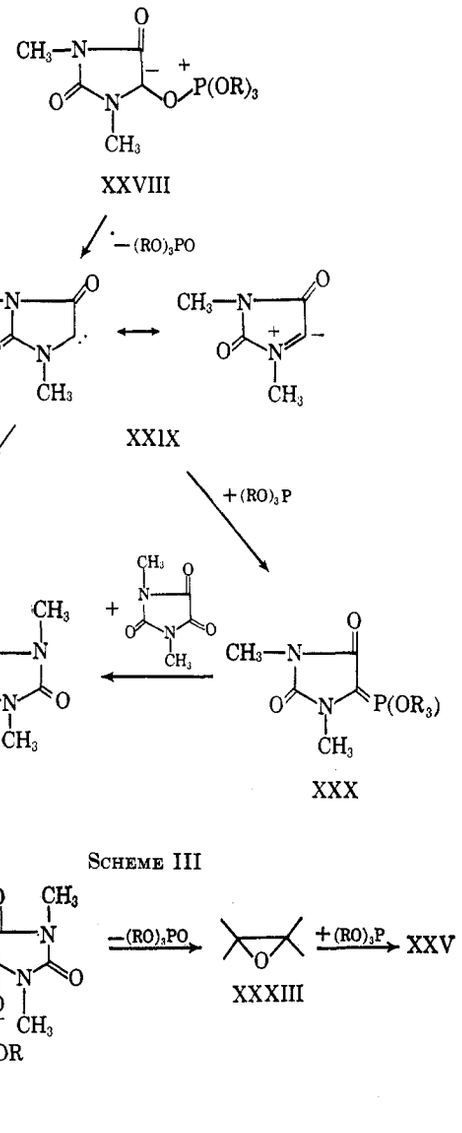
XXVII

The catalytic hydrogenation of biparabanyl XXV gave a mixture of the colorless diastereomeric dihydrobiparabanyls XXVI and XXVII, in the approximate proportion of 80:20. The H^1 nmr spectrum is described in the Experimental Section.

If the biparabanyl XXV had the *trans* configuration and if the hydrogenation is predominantly a *cis* addition, the major isomer should be racemic XXVI. However, since XXVI and XXVII might well be in equilibrium under the conditions of the hydrogenation, nothing can be said with certainty about these stereochemical questions.

The formation of the biparabanyl XXV can be explained by Scheme II. The 1:1 dipolar adduct (XXVIII) which was *formed only at elevated temperature*, can loose phosphate to give the resonance-stabilized

SCHEME II



SCHEME III

α-aminocarbene (XXIX). The latter can dimerize to biparabanyl XXV, or it can react with more phosphite to give the phosphitemethylene[13] XXX. The latter can react with more methylparabanic acid giving XXXI and then XXV in what amounts to a Wittig olefination reaction.[14]

A second reaction (Scheme III) proceeds *via* a 2:1 adduct XXXII which can loose phosphate to give the epoxide XXXIII, or react with more phosphite to give the previous intermediate XXXI. The epoxide can form biparabanyl XXV.

We have been unable to effect reductive dimerizations of this type starting with a variety of 2:1 adducts[15] analogous to XXXII, which were prepared at low temperatures. Therefore, we favor Scheme II for the production of the biparabanyl.

(13) F. Ramirez, O. P. Madan, and C. P. Smith, *J. Org. Chem.*, **30**, 2284 (1965).

(14) H. J. Bestman, *Angew. Chem. Intern. Ed. Engl.*, **4**, 645 (1965).

(15) (a) F. Ramirez and N. Ramanathan, *J. Org. Chem.*, **26**, 3041 (1961); (b) F. Ramirez, N. Ramanathan, and N. B. Desai, *J. Am. Chem. Soc.*, **84**, 1317 (1962); (c) F. Ramirez, N. B. Desai, and N. Ramanathan, *Tetrahedron Letters*, **No. 5**, 323 (1963); (d) F. Ramirez, N. Ramanathan, and N. B. Desai, *J. Am. Chem. Soc.*, **85**, 3465 (1963); (e) F. Ramirez, H. J. Kugler, and C. P. Smith, *Tetrahedron Letters*, **No. 4**, 261 (1965); (f) F. Ramirez, A. V. Patwardhan, and C. P. Smith, *J. Org. Chem.*, **31**, 474 (1966).

Experimental Section

P^{31} nmr shifts are given in parts per million *vs.* 85% H_3PO_4, taken at 40.5 Mc/sec. H^1 nmr shifts are given in parts per million from TMS = 10 (τ values), taken in a Varian A-60 instrument. Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

Conversion of Alloxan Monohydrate into Alloxan[6] [2,4,5,6-(1,3)-Pyrimidinetetrone].—The monohydrate (Eastman Kodak Co.) was colorless, turned red at 130°, and melted at 253–254° dec. The H^1 nmr spectrum (deuteriodimethyl sulfoxide, DMSO) had a singlet at τ −1.16 (NH) and a broad signal at about 2.5 (OH). The infrared spectrum (Nujol mull) had bands at 3.10 (shoulder at 3.05), 5.75, and 5.90 μ.

The monohydrate was kept for 12 hr at 200° (1 mm) in a sublimator. The yellow, anhydrous alloxan which sublimed, turned red at 230° and melted at 256° dec. The H^1 nmr spectrum (deuterio-DMSO) had a singlet at τ 1.50. The infrared spectrum (Nujol mull) had bands at 3.10 and at 5.75 μ, with shoulders at 5.68 and 5.90 μ.

Reaction of Anhydrous Alloxan with Trimethyl Phosphite in Methylene Chloride Solution. Formation of 5-Hydroxy-6-methoxyuracil 5-Dimethyl Phosphate [5-Hydroxy-6-methoxy-2,4-(1,3)-2-pyrimidinedione 5-Dimethyl Phosphate] (XIII).—Anhydrous alloxan (1.95 g) was added to a solution of trimethyl phosphite (10.2 g, 6 mole equiv) in methylene chloride (20 ml) at 0°, under N_2. No visible reaction was noted after 4 hr at 0°, and after 1 hr at 10°. After 5 min at 22°, the yellow color disappeared and an exothermic reaction was noted. The temperature was maintained at *ca.* 20° by external cooling. The crystals that separated after 15 hr at 20° were filtered and dried at 20° (1 mm); the yield of crude enol ether phosphate XIII, mp 190–195°, was 2.5 g (92%). Recrystallization from ethanol gave the phosphate XIII as colorless crystals, mp 195–197°.

Anal. Calcd for $C_7H_{11}N_2O_7P$: C, 31.6; H, 4.3; N, 10.5; P, 11.6. Found: C, 32.2; H, 4.1; N, 10.4; P, 11.1.

The phosphate XIII was insoluble in benzene and methylene chloride, sparingly soluble in acetone and acetonitrile, and somewhat soluble in dimethylformamide (DMF) and DMSO. The P^{31} nmr spectrum in DMSO had a septet at +1.2 ppm. The H^1 nmr spectrum (deuterated DMSO) had a 2 H^1 broad signal at τ 4.6 (NH), a 3 H^1 singlet at 5.97 (CH_3OC), and a 6 H^1 doublet, J_{HP} = 11.2 cps, at 6.15 (CH_3OP). The infrared spectrum (Nujol mull) had a shoulder at *ca.* 3.24, and strong bands at 5.83, 5.95, and 6.03, and also bands at 7.8 (PO) and 9.50 μ ($POCH_3$).

Reaction of 5-Hydroxy-6-methoxyuracil 5-Dimethyl Phosphate (XIII) with Diazomethane. Isolation of 5-Hydroxy-2,4,6-trimethoxypyrimidine 5-Dimethyl Phosphate (XIV).—A suspension of XIII (2.2 g) in methanol was treated with triethylamine (0.7 ml). The clear, pink solution was mixed with an excess of ethereal diazomethane, and the mixture was kept for 12 hr at 10°. A few drops of acetic acid was introduced, and the solvent was evaporated. The colorless residue was kept for 24 hr at −20°, under hexane. The infrared and H^1 nmr spectra showed that this crude material was a mixture of O- and N-methylated derivatives. The mixture was extracted with three 25-ml portions of hexane. The hexane filtrate gave 0.9 g (36%) of **5-hydroxy-2,4,6-trimethoxypyrimidine 5-dimethyl phosphate (XIV)** (mp 60–65°) upon cooling and further work up of the mother liquid. The analytical sample had mp 69–71° (hexane).

Anal. Calcd for $C_9H_{15}N_2O_7P$: C, 36.7; H, 5.1; N, 9.5; P, 10.5. Found: C, 37.1; H, 5.7; N, 9.3; P, 9.9.

The H^1 nmr spectrum ($CDCl_3$) had a 6 H^1 singlet at τ 5.98 (2 equiv of CH_3OC), a 3 H^1 singlet at 6.05 (CH_3OC), and a 6 H^1 doublet, J_{HP} = 11.7 cps, at 6.08 [$(CH_3O)_2P$]. The infrared spectrum (in CCl_4) had bands at 6.25 (s), (shoulders at 6.10 and 6.18), 6.62 (w), 6.80 (s), 7.08 (s), 7.25 (s), 7.75 (s) (PO), 8.35 (s), 8.75 (s), 9.52 (s) ($POCH_3$), and 10.80 μ (when traces of N-methylated isomers were present, a weak band at 5.92 μ could be seen), $\delta_{P^{31}}$ = +2.2 ppm (in CH_2Cl_2).

Reaction of 5-Hydroxy-6-methoxyuracil 5-Dimethyl Phosphate (XIII) with Dimethyl Sulfate. Isolation of 5-Hydroxy-2,4,6-trimethoxypyrimidine 5-Dimethyl Phosphate (XIV) and of 1-Methyl-2,4-dimethoxy-5-hydroxy-6(1)-pyrimidone 5-Dimethyl Phosphate (XXII) or Its Isomer 1-Methyl-4,6-dimethoxy-5-hydroxy-2(1)-pyrimidone 5-Dimethyl Phosphate (XXIII).—To a suspension of XIII (1.2 g) in acetone (85 ml) was added potassium carbonate (20 g) and dimethyl sulfate (6 g, 10 mole equiv). The mixture was kept for 30 hr at reflux temperature and then filtered. The solid was washed with acetone (three 10-ml portions) the acetone fractions were combined and then evaporated; the residue was freed of excess dimethyl sulfate by distillation (0.1 mm, bath at 50°). The crude mixture of O- and N-methylated derivatives was extracted with hexane (three 35-ml portions). The hexane-soluble portion was **5-hydroxy-2,4,6-trimethoxypyrimidine 5-dimethyl phosphate** (XIV, 250 mg, 20%; see above).

The hexane-insoluble portion (760 mg, mp 65–85°) was one of the two possible N-methylpyrimidone phosphates (XXII or XXIII). One recrystallization from cyclohexane–benzene (80:20) gave the pure 6(1)- or 2(1)-pyrimidone (XXII or XXIII), mp 87–90° (530 mg, 40%).

Anal. Calcd for $C_9H_{15}N_2O_7P$: C, 36.7; H, 5.1; N, 9.5; P, 10.5. Found: C, 36.9; H, 5.3; N, 9.5; P, 10.6.

The H^1 nmr spectrum ($CDCl_3$) had a 3 H^1 singlet at τ 5.95 (CH_3OC), a 3 H^1 singlet at 6.00 (CH_3OC), a 6 H^1 doublet, J_{HP} = 11.6 cps, at 6.15 [$(CH_3O)_2P$], and a 3 H^1 singlet at 6.61 (CH_3N). The infrared spectrum (CH_2Cl_2) had bands at 5.95 (s) (C=O), 6.15 (s), 6.42 (s), 6.75 (m), 7.10 (w), 7.25 (s), 7.82 (s) (PO), 8.20 (s), 8.30 (s), 8.70 (w), 9.50 (s) ($POCH_3$), 9.82 (s), and 10.35 μ (ms); $\delta_{P^{31}}$ = +1.3 ppm (CH_2Cl_2).

Reaction of Alloxan Monohydrate (VI) with Trimethyl Phosphite in the Absence of Solvent. Formation of 5-Hydroxy-6-methoxyuracil 5-Dimethyl Phosphate (XIII), and of 5-Hydroxybarbituric Acid 5-Dimethylphosphate [5-Hydroxy-2,4,6(1H,3H,-5H)-pyrimidinetrione 5-Dimethyl Phosphate] (XIX).—The addition of alloxan hydrate to an excess of trimethyl phosphite, without solvent, resulted in a *violent reaction*, after an induction period of 2.5 min. However, the dropwise addition of 2 mole equiv of trimethyl phosphite (4.5 g) to alloxan hydrate (2.9 g), with stirring, under N_2, led to a vigorous, but controllable, reaction. A colorless, crystalline material was formed. After 2 hr, methylene chloride (20 ml) was added and the mixture was filtered. The insoluble crystals (3.3 g, *ca.* 80%), melted over a wide range (120–180°) and consisted of a mixture of **5-hydroxy-6-methoxyuracil 5-dimethyl phosphate** (XIII), and **5-hydroxybarbituric acid 5-dimethyl phosphate** (XIX), as indicated by the H^1 nmr spectrum in deuterated DMSO, and by the infrared spectrum in a Nujol mull. The H^1 nmr spectrum of the methylene chloride filtrate disclosed the presence of dimethyl methylphosphonate, $CH_3P(O)(OCH_3)_2$, [doublet, J_{HP} = 18 cps, at τ 8.50, and doublet, J_{HP} = 11.5 cps, at 6.10], and of dimethyl phosphite, $HP(O)(OCH_3)_2$, [doublet, J_{HP} = 705 cps, at τ 3.22, and doublet, J_{HP} = 12 cps, at 6.30].

The crystalline mixture (3.3 g) of phosphates XIII and XIX was dissolved in hot ethanol (50 ml), and the solution was kept for 2 days at 10°. The enol ether phosphate XIII (1.12 g, 30%) was collected and was identified by its characteristic H^1 nmr spectrum in deuterated DMSO. The ethanol filtrate was concentrated to a volume of about 20 ml, and the solution was kept for 4 days at 0°. The crystals of **5-hydroxybarbituric acid 5-dimethyl phosphate** (XIX, 1.53 g, 37%) were collected, and were identified by their characteristic H^1 nmr spectrum in deuterated DMSO. The same dioxophosphate was prepared from alloxan hydrate and dimethyl phosphite, as described below.

Reaction of Alloxan Hydrate with Dimethyl Phosphite in the Absence of Solvent. Formation of 5-Hydroxybarbituric Acid 5-Dimethyl Phosphate (XIX).—Dimethyl phosphite, $HP(O)(OCH_3)_2$, (11.5 g, 3 mole equiv) was added to alloxan hydrate (5.57 g) in the absence of solvent, at 25°. An exothermic reaction raised the temperature of the mixture to 85°, and resulted in a clear solution, which deposited colorless crystals. The crude **5-hydroxybarbituric acid 5-dimethyl phosphate** (XIX, 6.6 g, 77%) was collected after 12 hr at 20°. This material had a wide melting range (160–176°); its infrared spectrum (Nujol mull) showed sharp bands at 2.95 and 3.10 μ, which were not found in the recrystallized sample of the dioxophosphate XIX (*vide infra*); the spectrum differed also in the carbonyl region 5.8–6.0 and in the phosphate (PO) region 8.0–8.2 μ. Possibly, the crude material contained other tautomers of XIX and/or some α-hydroxy β-oxophosphonate.

The crude product (6.6 g) was recrystallized from ethanol (80 ml) to give XIX, of mp 170–178° (5.1 g, 60%); the infrared spectrum (Nujol mull) and the H^1 nmr spectrum were indistinguishable from those of the analytical sample. The latter, obtained after one additional crystallization from ethanol, had mp 180–183°.

Anal. Calcd for $C_6H_9N_2O_7P$: C, 28.6; H, 3.6; N, 11.2; P, 12.3. Found: C, 29.1; H, 3.7; N, 11.7; P, 12.4.

The dioxophosphate XIX was insoluble in benzene and methylene chloride, sparingly soluble in acetone and acetonitrile, and somewhat soluble in DMF and DMSO. The P^{31} nmr in DMSO had *two* septets centered at -1.3 ppm due to the coupling of the P nucleus with the six protons of the two CH_3O groups and with the single proton on the carbon. The H^1 nmr spectrum in deuterated DMSO had a 2 H^1 signal at τ -1.41 due to the acidic ureide NH protons, a 1 H^1 doublet, J_{HP} = 17 cps, at 4.18 due to the lone proton on carbon, coupled to phosphorus, and a 6 H^1 doublet, J_{HP} = 11.5 cps, at 6.20 due to the two equivalent methoxy groups on phosphorus. The infrared spectrum (Nujol mull) had broad absorption in the HX region at 3.7–4.0, a strong band at 5.78 (ureide CO), and strong bands at 6.00 and 6.18 μ, probably due to H-bonded lactam CO; there were bands at 8.00 and at 9.50 μ, attributed to the phosphate ester.

Formation of the Triethylammonium Salt of 5-Hydroxybarbituric Acid 5-Dimethyl Phosphate (XIX) and Reaction of the Salt with Diazomethane.—A suspension of the dioxophosphate XIX (2.2 g, 9 mm) in methylene chloride (30 ml) was treated, dropwise with triethylamine. A clear, red solution was obtained upon addition of *ca.* 1 mole equiv of the amine (1.4 ml). The solvent was removed at 20° (25 mm) and the red residue was dried at 90° (0.5 mm). This salt had $\delta_{P^{31}}$ = 0.0 ppm (*vs.* H_3PO_4). The H^1 nmr spectrum in $CDCl_3$ had a broad signal at τ -0.7, a 6 H^1 doublet, J_{HP} = 11.2 cps, at 6.15, and the quartet J_{HH} = 7 cps, at 6.80, and the triplet at 8.72, expected from the triethylamine. The infrared spectrum (CH_2Cl_2) had very strong bands at 6.00 and 6.20 μ.

A clear solution of the salt in methanol (15 ml) was treated with ethereal diazomethane. After 48 hr at 10°, the solution was treated with drops of acetic acid, and distilled. The residue (1.9 g) had an infrared spectrum (in CH_2Cl_2) which was identical with that of the crude product from the reaction of 5-hydroxy-6-methoxyuracil 5-dimethyl phosphate (XIII) with diazomethane.

The crude product (1.9 g) of the methylation was sublimed at 110° (0.1 mm), yielding 750 mg of colorless crystals mp 65–67°. Crystallization from hexane gave **5-hydroxy-2,4,6-trimethoxypyrimidine 5-dimethyl phosphate** (XIV, mp 67–71°) identified by its infrared and H^1 nmr spectra (see above).

Reaction of Anhydrous Alloxan with Dimethyl Phosphite in the Absence of Solvent.—Dimethyl phosphite (9.3 g, 3 mole equiv) was added to anhydrous alloxan (4.0 g) under N_2. The exothermic reaction led initially to a clear solution, which then deposited crystals. After 12 hr at 20°, the mixture was diluted with benzene (25 ml), stirred for 30 min, and filtered. The solid was washed with benzene (25 ml) and the benzene fractions were combined (*vide infra*).

The colorless solid obtained above (4.1 g, 58%) proved to be 5-hydroxybarbituric acid 5-dimethyl phosphate (XIX), $\delta_{P^{31}}$ = -1.3 ppm (in DMSO). The identification was confirmed by infrared and H^1 nmr spectra.

N,N′-Dimethylparabanic Acid.—It was prepared from N,N′-dimethylurea and oxalyl chloride, as described.[9] It was recrystallized from water and dried at 100° (0.1 mm, mp 154–155°; infrared bands were at 5.70 and 5.78 μ (CH_2Cl_2); a H^1 nmr singlet was at τ 6.80 ($CDCl_3$).

Reaction of N,N′-Dimethylparabanic Acid (XI) with Triethyl Phosphite. Formation of N-Tetramethylbiparabanyl (XXV).—A suspension of XI (4.42 g) in triethyl phosphite (20.6, 4 mole equiv) was kept for 2 hr at 20°, without any evidence of reaction. The mixture was then kept for 4 hr at reflux temperature, and the yellow solution was distilled to remove all liquids boiling below 45° (35 mm). The residue was treated with cold ethanol (140 ml) and filtered. The **N-tetramethylbiparabanyl** (XXV, 3.8 g, 91%, mp *ca.* 200°) was recrystallized twice from ethanol, affording yellow needles, mp 216–217°.

Anal. Calcd for $C_{10}H_{12}N_4O_4$: C, 47.6; H, 4.8; N, 22.2; mol wt, 252. Found: C, 47.4; H, 4.8; N, 22.0; mol wt, 246 (isothermal distillation in CH_2Br_2).

The H^1 nmr spectrum ($CDCl_3$) had two singlets of equal intensities at τ 6.66 and 6.90; these are attributed, respectively, to the six equivalent protons of the two methyl groups attached to the imide nitrogens, and to the six equivalent protons of the two methyl groups attached to the amide nitrogens. The infrared spectrum (in CH_2Cl_2) had two carbonyl bands of nearly equal intensities; at 5.73 (ureide CO) and at 5.88 μ (unsaturated lactam).

Catalytic Hydrogenation of N-Tetramethylbiparabanyl (XXV).—A suspension of the yellow biparabanyl (1.0 g) in ethanol (100 ml) was hydrogenated in the presence of PtO_2 catalyst (150 mg) at 40 psi, at 20°. The colorless product was filtered while hot. On cooling, the crude, colorless dihydrobiparabanyl XXVI or XXVII (0.82 g, mp 165–175°) separated. One recrystallization from ethanol gave the analytical sample, mp 185–186°.

Anal. Calcd for $C_{10}H_{14}N_4O_4$: C, 47.2; H, 5.5; N, 22.0. Found: C, 47.1; H, 5.7; N, 21.7.

The H^1 nmr spectrum ($CDCl_3$) had one strong and one weak set of three singlets each. The singlets of the major set were at τ 5.65 (methine H^1) and at 7.00 and 7.02 (CH_3N); the integrated ratio of the first signal to the other two was as 1:6. The methine H^1 of the weak set was shifted 4.5 cps to low field relative to that of the strong set. One CH_3N signal of the weak set was shifted 2 cps to low field, the other 11 cps to high field of the corresponding signals of the major set. The infrared spectrum (CH_2Cl_2) had one strong carbonyl band at 5.80 and a weak carbonyl band at 5.65 μ (proportion *ca.* 4:1). It was assumed that the crystalline material in solution consisted of a major and a minor diastereomer, possibly easily interconverted.

Attempted Reaction of Parabanic Acid with Trimethyl Phosphite.—No identifiable product could be isolated when the reagents were kept for 15 days at 20° or for 16 hr at 100° (1:3 mole ratio).

Attempted Reaction of Parabanic Acid with Dimethyl Phosphite.—The following conditions failed to cause a reaction between these substances: (1) 48 hr at 20°; (2) 24 hr in boiling xylene; (3) 1 hr at 20°; 10 hr at 125°, in the presence of a few drops of triethylamine.

Acid-Catalyzed Condensation of a Reissert Compound with Acrylonitrile

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The acid-catalyzed condensation of 2-benzoyl-1,2-dihydroisoquinaldonitrile (I) with acrylonitrile afforded a pale yellow solid product to which the structure 2-(1-isoquinolyl)-3-cyano-5-phenylpyrrole (III) has been assigned. This compound was hydrolyzed to the corresponding carboxylic acid, which, in turn, was decarboxylated to give 2-(1-isoquinolyl)-5-phenylpyrrole (VII). The latter compound, in turn, was synthesized independently in a completely unambiguous manner. Other reactions of the initial condensation product are described, and a mechanism for its formation is suggested.

In a previous communication,[1] a description was given of the acid-catalyzed condensation of 2-benzoyl-1,2-dihydroisoquinaldonitrile (I) with 1,1-diphenylethylene to produce 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine. A similar reaction has now been carried out between I and acrylonitrile, with hydrochloric acid as catalyst, and the hydrochloride (II) of 2-(1-isoquinolyl)-3-cyano-5-phenylpyrrole (III) was obtained. Treatment of II with sodium hydroxide solution afforded III, which showed the characteristic in-

(1) T. T. Yee, W. E. McEwen, and A. P. Wolf, *Tetrahedron Letters*, 3115 (1965).