the enzyme, in a rather specific manner, which has nothing to do with its hydrolytic function. On the other hand, the inhibition by glucose predicted from Scheme I results from its direct participation in the reaction sequence.

From equation 2 and the corresponding reaction pathway, certain kinetic and thermodynamic parameters of the system can be calculated. The average of the apparent Michaelis constants, K_s' for the solubilized enzyme system was calculated to be $0.8 \times 10^{-3} M$.[7] From equation 2, K_s' is seen to be identical with k_2/k_1, the dissociation constant of the enzyme–substrate complex. Thus, at *p*H 6.4 and 30° the standard free energy change of substrate binding is 4280 cal.

A second parameter of the system was calculated from a plot of v_0/v_0' *versus* (Glu) as shown in Fig. 1,[7] where v_0 is the velocity of the uninhibited reaction. The reciprocal of the slope of the plot, which is equal to k_5/k_4 from Scheme I, has an average value for the system from several normal rat liver homogenates of 0.12 *M*.

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[CONTRIBUTION FROM THE ORGANIC CHEMICAL RESEARCH SECTION, LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID CO.]

The Reaction of Periodate with Aminosugars. Anomalous Overoxidations of Aminofuranosides

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The reaction of sodium metaperiodate with various 3-aminoribofuranosyl derivatives and with one 3-aminoarabinofuranosyl derivative results in the consumption of two rather than the expected one molar equivalent of oxidant. Two 5-aminoribofuranosides reacted with four equivalents of periodate. Various 2- and 3-aminopyranosides reacted "normally." It is shown that the bis-aldehyde, which is obtained from the oxidation of the corresponding nonamino furanosides, is neither an intermediate nor the final product of the oxidation of the 3-aminofuranosides. The implications of this anomalous behavior for structure determinations are discussed.

Oxidative cleavage of 1,2-glycol and 1,2-aminoalcohol systems by periodate is a very convenient and useful tool for structure determinations, especially in the fields of carbohydrate and nucleoside chemistry.[1] In general, these systems react with one molar equivalent of periodate. However, we now wish to report that various 3-aminoribofuranosyl derivatives and one 3-aminoarabinofuranoside react with *two* molar equivalents of this oxidant. On the other hand, various 2- and 3-aminopentopyranosyl and hexopyranosyl derivatives have been found to react in the "normal" sense—that is, with the theoretically-required two equivalents of periodate.[2]

Overoxidation of aminofuranosides was first observed in this Laboratory with certain aminosugar derivatives, the furanoside configuration of which was likely but was not rigorously established at the time. Therefore, methyl 3-amino-3-deoxy-β-D-ribofuranoside (III) was prepared as a model aminofuranoside of unequivocal structure. This compound previously has been reported,[3] without physical data, as a low melting solid. For this study, it was obtained as a crystalline solid by a two-step synthesis in 43% over-all yield from 2,5-di-*O*-benzoyl-3-phthalimido-3-deoxy-β-D-ribofuranosyl chloride (I),[3] which is available from the antibiotic puromycin *via* the corresponding 1-*O*-acetyl derivative V. Methanol treatment of I gave a 65% yield of the blocked methyl glycoside (II), which on deblocking with methanolic butylamine[4] afforded a 67% yield of the desired methyl 3-aminoribofuranoside (III), m.p. 107–109°, $[\alpha]^{25}D$ −37° (1.1% H_2O). The assigned furanoside structure was unequivocally verified by N-phthaloylation in 58% yield to the previously reported[3] methyl 3-phthalimido-3-deoxy-β-D-ribofuranoside (IV) and also by conversion of IV to 1-*O*-acetyl-2,5-di-*O*-benzoyl-3-phthalimido-3-deoxy-β-D-ribofuranoside (V)[3] by benzoylation followed by acetolysis with acetic acid–acetic anhydride–sulfuric acid. This last sequence (III → IV → V) previously has been carried out starting with crude III.[3]

Periodate treatment of methyl 3-aminoribofuranoside (III) confirmed our original impression that 3-aminofuranosides would consume two, rather than the anticipated one, molar equivalents of oxidant. Thus, reaction of III with sodium metaperiodate in aqueous solution at room temperature resulted in an uptake of two molar equivalents of oxi-

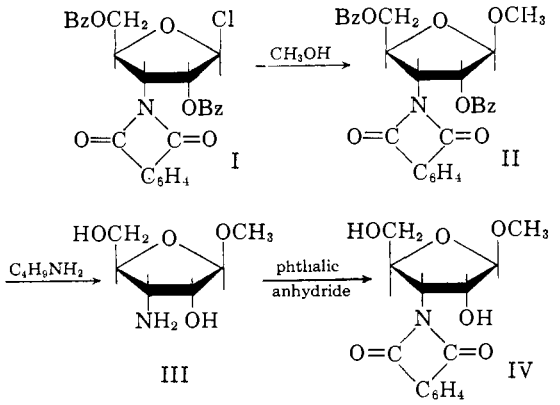
(1) See E. L. Jackson, ["Organic Reactions," Vol. II, 1944, p. 341] for a general review of periodic acid oxidation. This subject is also reviewed with especial reference to its application in carbohydrate chemistry by J. M. Bobbitt, [*Advances in Carbohydrate Chemistry*, **11**, 1 (1956)] and J. R. Dyer ["Methods of Biochemical Analysis," Vol. III, 1956, p. 111]. The use of periodate oxidation for the determination of nucleoside anomeric configuration was first described by J. Davoll, B. Lythgoe and A. R. Todd, [*J. Chem. Soc.*, 833 (1946)].

(2) G. E. McCasland and D. A. Smith [THIS JOURNAL, **73**, 5164 (1951)] studied the reaction of the *cis*- and *trans*-2-aminocyclohexanols and 2-aminocyclopentanols with lead tetraacetate and also with sodium periodate. They observed over-oxidation of the aminohexanols and of the aminopentanols on treatment with lead tetraacetate. Their periodate studies were carried out with equivalent amounts of oxidant and aminoalcohol and, therefore, over-oxidation could not be observed.

The periodate oxidation of inosamines proceeds as expected with the uptake of 6 molar equivalents of oxidant [T. Posternak, *Helv. Chim. Acta*, **33**, 1597 (1950); H. Straube-Rieke, H. A. Lardy and L. Anderson, THIS JOURNAL, **75**, 694 (1953); G. R. Allen, Jr., of this Laboratory, unpublished results]. The only reported exception is D,L-*epi*inosamine-2 which consumes approximately 8 molar equivalents after 50 hours (H. Straube-Rieke, *et al.*, above).

(3) B. R. Baker, J. P. Joseph and R. E. Schaub, *ibid.*, **77**, 5905 (1955).

(4) L. Goldman, J. W. Marsico and R. B. Angier, *ibid.*, **78**, 4173 (1956).



dant within one hour, and essentially no further uptake of oxidant after an additional 47 hours. In sodium bicarbonate solution, III consumed two molar equivalents of periodate within seven minutes. After 45 minutes, this value had not changed appreciably. When III was treated with aqueous periodic acid, an uptake of about two molar equivalents was observed within seven minutes. Oxidation then continued more slowly and, after 25 hours, almost three molar equivalents of oxidant had been consumed. At this time the *p*H of the solution was 1.7. This further oxidation (beyond two equivalents) with the unbuffered periodic acid solution can be explained by assuming a slow hydrolysis of the initial oxidation product followed by oxidation of the resulting fragments.

Similar results were observed on sodium metaperiodate treatment of the 3-aminoribofuranosyl-containing nucleosides, 9-(3-amino-3-deoxy-β-D-ribofuranosyl)-6-dimethylaminopurine (VI),[5] 6-amino-9-(3-amino 3-deoxy-β-D-ribofuranosyl) purine (3′-amino-3′-deoxyadenosine, VII)[6] and 1-(3-amino-3-deoxy-β-D-ribofuranosyl)-4-amino-2[1H]pyrimidinone (3′-amino-3′-deoxycytidine, VIII).[7] Each of these aminonucleosides consumed essentially two equivalents of oxidant within approximately 24 hours. However, the rate of periodate consumption was considerably slower than the rate observed with methyl 3-aminoribofuranoside (III). Thus, III reacted with two molar equivalents of periodate within one hour, whereas the purine nucleosides (VI and VII) consumed 1.6 equivalents after six hours, and the pyrimidine nucleoside (VIII) consumed only 1.2 equivalents after three hours.

Overoxidation also was observed with methyl 3-amino-3-deoxy-β-D-arabinofuranoside[8] which took up 1.96 molar equivalents of periodate within 46 minutes. Again the reaction stopped at this level, so that after 18 hours essentially no additional oxidant had been consumed.[9]

(5) B. R. Baker, J. P. Joseph and J. H. Williams, THIS JOURNAL, **77**, 1 (1955).

(6) B. R. Baker, R. E. Schaub and H. M. Kissman, *ibid.*, **77**, 5911 (1955).

(7) H. M. Kissman and M. J. Weiss, *ibid.*, **80**, 2575 (1958).

(8) B. R. Baker, R. E. Schaub and J. H. Williams, *ibid.*, **77**, 7 (1955).

(9) Periodate oxidation of the α- and β-anomers of methyl 3-amino-3-deoxy-D-ribofuranoside has been reported to result in the consumption of up to 2 and 3 molar equivalents of oxidant.[10]

(10) C. D. Anderson, L. Goodman and B. R. Baker, THIS JOURNAL, **80**, 5247 (1958).

It was also of interest to investigate the reaction of sodium metaperiodate with 5-aminopentofuranosides. In such structures the amino group is not adjacent to an hydroxyl group and, therefore, *a priori*, would not be expected to participate in a periodate oxidation. Surprisingly, two such examples, 9-(5-amino-5-deoxy-β-D-ribofuranosyl)-6-dimethylaminopurine[11] and 1-(5-amino-5-deoxy-β-D-ribofuranosyl)-5,6-dichlorobenzimidazole,[11] consumed four molar equivalents of periodate within 23 and 48 hours, respectively, indicating a complete oxidation of the sugar moiety. The corresponding non-amino ribosides, 6-dimethylamino-9-β-D-ribofuranosylpurine[12] and 5,6-dichloro-1-β-D-ribofuranosylbenzimidazole,[13] reacted normally and consumed one molar equivalent of periodate.

In contrast to this consistent pattern of overoxidation with the aminofuranosides, those aminopyranosides which were investigated reacted with periodate in the "normal" manner and consumed the expected two molar equivalents with no evidence of appreciable overoxidation. Thus, methyl 3-amino-3-deoxy-β-L-xylopyranoside[14] reacted with two molar equivalents of sodium metaperiodate within five minutes. After 24 hours, essentially no additional uptake of oxidant was observed. Similar results were obtained with the α- and β-anomers of methyl 3-amino-3-deoxy-D-xylopyranoside,[15a] and with 9-(2-amino-2-deoxy-β-D-allopyranosyl)-6-dimethylaminopurine.[15b]

A consideration of certain aspects of this overoxidation phenomenon is of interest. *A priori*, one would expect a 2- or 3-aminopentofuranoside (IX) to react with one equivalent of periodate to produce a bis-aldehyde (X). The second equivalent of oxidant then could be accounted for by a further oxidation of this bis-aldehyde. However, this interpretation is not valid since it is known that the very bis-aldehydes (X), which would have to be postulated as intermediates in the oxidation of the various aminofuranosides (IX) are actually obtained from the corresponding non-aminofuranosides (XI)[16] and have been shown to be resistant to further attack by periodate under comparable conditions.

Futhermore, it would appear that the final product—that is, the product obtained after the consumption of two molar equivalents of periodate—is also not the bis-aldehyde X. This was indicated by

(11) H. M. Kissman and B. R. Baker, Abstracts of Papers 130th Meeting of the A.C.S. Atlantic City, N. J., September, 1956, p. 190, paper in preparation.

(12) H. M. Kissman, C. Pidacks and B. R. Baker, THIS JOURNAL, **77**, 18 (1955).

(13) H. M. Kissman, R. G. Child and M. J. Weiss, *ibid.*, **79**, 1185 (1957).

(14) B. R. Baker and R. E. Schaub, *J. Org. Chem.*, **19**, 646 (1954).

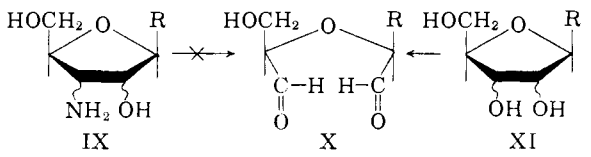
(15) (a) R. E. Schaub and M. J. Weiss, THIS JOURNAL, **80**, 4683 (1958); (b) F. J. McEvoy, B. R. Baker and M. J. Weiss, to be published.

(16) The formation of a bis-aldehyde on periodate oxidation of adenosine and of cytidine has been fully established.[17] The formation of bis-aldehydes from other non-amino pentofuranosides, such as 6-dimethylamino-9-β-D-ribofuranosylpurine,[12] methyl α-D-arabinofuranoside[18] and benzyl β-D-ribofuranoside,[19] is a reasonable assumption.[18]

(17) J. Davoll, B. Lythgoe and A. R. Todd, *J. Chem. Soc.*, 833 (1946).

(18) E. L. Jackson and C. S. Hudson, THIS JOURNAL, **59**, 994 (1937).

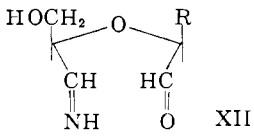
(19) R. K. Ness, H. W. Diehl and H. G. Fletcher, Jr., *ibid.*, **76**, 763 (1954).



IX X XI

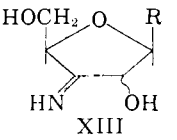
paper chromatographic comparison of the periodate oxidation products obtained from these nucleoside pairs: 3′-amino-3′-deoxycytidine[7] and cytidine, 3′-amino-3′-deoxyadenosine[6] and adenosine, 9-(3-amino-3-deoxy-β-D-ribofuranosyl)-6-dimethylaminopurine (VI)[5] and 6-dimethylamino-9-β-D-ribofuranosylpurine.[20] In each case, the product obtained on oxidation of the aminoribofuranosylnucleoside gave a chromatogram which was substantially different from the chromatogram of the product (bis-aldehyde X[16]) obtained after oxidation of the corresponding non-amino nucleoside.[22]

It also appears that the additional equivalent of periodate cannot be accounted for by a reaction involving a change in the oxidation state of the amino nitrogen.[23] This was indicated by the isolation of ammonium iodate in 30% yield from the reaction of periodate with 9-(3-amino-3-deoxy-β-D-ribofuranosyl)-6-dimethylaminopurine. The possibility was considered that the oxidation had proceeded *via* an intermediate aldehydoaldimine (XII) which then underwent further oxidation to an aldehydonitrile as suggested by McCasland and Smith.[2] However, the oily oxidation product from methyl 3-aminoribofuranoside (III) did not exhibit the characteristic nitrile band in the infrared. Also, the isolation of ammonium iodate described above contraindicates the possibility of nitrile for-



XII

mation since it is unlikely that under the mild conditions of this experiment hydrolysis of the nitrile would have taken place.[24]



XIII

Finally, we would point out that inasmuch as it now appears that the ultimate product of periodate oxidation of an aminopentofuranosyl nucleoside is probably not the bis-aldehyde obtained by oxidation of the corresponding non-amino nucleoside, the convenient periodate–molar rotation procedure[17] for the determination of α- or β-nucleoside configuration is inapplicable to these compounds.[20] These results also becloud the use of periodate data for the determination of the ring size of aminosugars. However, it is worth noting that the uptake of the second molar equivalent of periodate with the aminofuranosides was considerably slower than the uptake of the first equivalent. The only apparent exception to this was the bicarbonate-buffered periodate reaction with methyl 3-aminoribofuranoside (III) where the uptake was 1.98 molar equivalents within seven minutes. On the other hand, the three 3-aminopyranosyl glycosides of this investigation reacted with two molar equivalents almost immediately. Although the aminopyranosyl nucleoside, 9-(2-amino-2-deoxy-β-D-allopyranosyl)-6-dimethylaminopurine, reacted somewhat slower, its uptake of two molar equivalents was still considerably faster (one hour) than that of the aminofuranosyl nucleosides.

Further investigations in this field are not contemplated.

Acknowledgment.—We wish to thank Mr. L. Brancone and staff for microanalyses and Mr. W. Fulmor and staff for rotation and spectral determinations.

Experimental[25]

Methyl 2,5-Di-*O*-benzoyl-3-phthalimido-3-deoxy-β-D-ribofuranoside (II).—To 25 cc. of reagent methanol was added 1.0 g. of 2,5-di-*O*-benzoyl-3-phthalimido-3-deoxy-β-D-ribofuranosyl chloride (I). The solution was refluxed for 10 minutes in a flask protected from moisture and then was evaporated to dryness *in vacuo*. The resulting glass was dissolved in ether and the ether solution was evaporated to dryness. The residue was dissolved in 15 cc. of reagent methanol and allowed to cool slowly. The white needles which separated were collected by filtration and air-dried; yield 0.64 g. (65%), m.p. 84–86°, unchanged after recrystallization from absolute ethanol; $[\alpha]^{25}D$ −153° (1.2% in $CHCl_3$).

(20) Originally,[12] the assignment of a β-configuration to the 9-ribofuranosyl derivative of 6-dimethylaminopurine was partially based on a favorable comparison of the molecular rotation value of its periodate oxidation product with the molecular rotation of the product obtained on periodate oxidation of the corresponding 3′-amino-3′-deoxynucleoside (VI), which has been unequivocally demonstrated to be a β-nucleoside [B. R. Baker and J. P. Joseph, THIS JOURNAL, **77**, 15 (1955)]. Since this procedure for the determination of anomeric configuration is now invalid, it was necessary to establish the β-configuration of this riboside of 6-dimethylaminopurine by another method. This was done by synthesizing it from 6-chloro-9-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-purine,[21] a compound which has been converted to adenosine.

(21) H. M. Kissman and M. J. Weiss, *J. Org. Chem.*, **21**, 1053 (1956).

(22) Recently D. R. Walters, J. D. Dutcher and O. Wintersteiner [THIS JOURNAL, **79**, 5077 (1957)] have reported that the 3-ethylamino-3,6-dideoxyhexopyranoside, methyl N-ethylmycosaminide, which is derived from the antibiotics nystatin and amphotericin B, consumes the expected 2 molar equivalents of periodate to give the known crystalline bis-aldehyde, D′-methoxy-D-methyldiglycolic aldehyde; see also R. Kuhn and W. Bister, *Ann.*, **617**, 92 (1958).

(23) Ammonia does not react with sodium periodate under the conditions of these experiments.

(24) The suggestion also has been made[24a] that the reaction with the first equivalent of periodate afforded an intermediate hydroxyketimine XIII which was hydrolyzed to ammonia and a hydroxyketone which then underwent cleavage with a second molar equivalent of periodate to an aldehydoacid. Possible confirmatory evidence for this hypothesis might be obtained by comparing the oxidation rates of aminofuranoside pairs which after reaction with the first equivalent of periodate would afford the same hydroxyketimine (XIII). Consumption of the second equivalent of periodate would then be expected to proceed at identical rates. On this basis, the periodate oxidation of 9-(3-amino-3-deoxy-β-D-xylofuranosyl)-6-dimethylaminopurine[24b] was compared with that of the corresponding 3-aminoribofuranoside (VI). The xyloside consumed 1.5 molar equivalents of periodate after 24 hours and this value did not appreciably change after six days. However, the first equivalent was consumed within 17 minutes. In contrast, the 3-aminoribofuranoside (VI) took up two molar equivalents of periodate within 24 hours. Since the xyloside failed to consume two molar equivalents of periodate it cannot be assumed that the oxidation of both nucleosides proceeds by the same mechanism and therefore these results, unfortunately, are not comparable. (a) We wish to thank Professor E. Wenkert for helpful discussion on this point. (b) R. E. Schaub, M. J. Weiss and B. R. Baker, THIS JOURNAL, **80**, 4692 (1958).

(25) Melting points are uncorrected.

Anal. Calcd. for $C_{28}H_{23}NO_8$: C, 67.2; H, 4.63; N, 2.80. Found: C, 67.4; H, 4.85; N, 2.76.

Methyl 3-Amino-3-deoxy-β-D-ribofuranoside (III).—In 30 cc. of reagent methanol, 1.47 g. of methyl 2,5-di-*O*-benzoyl-3-phthalimido-3-deoxy-β-D-ribofuranoside (II) was suspended and to this was added 1.75 cc. of *n*-butylamine.[4] The resulting solution was refluxed for 18 hours and was then evaporated to dryness *in vacuo*. To the residual solid and gum, 25 cc. of water was added. The solid was removed by filtration and washed with water. The aqueous solution was extracted with ether several times, and the ether solution was dried over magnesium sulfate and evaporated to dryness *in vacuo*. There remained 450 mg. of a gum which crystallized from ethyl acetate containing a trace of absolute ethanol. The yield of methyl 3-amino-3-deoxy-β-D-ribofuranoside was 0.32 g. (67%), m.p. 104–106°. Recrystallization from ethyl alcohol–petroleum ether (90–100°) afforded white crystals, m.p. 107–109°, $[\alpha]^{25}D$ −37° (1.1% in H_2O).

Anal. Calcd. for $C_6H_{13}NO_4$: C, 44.2; H, 8.03; N, 8.59. Found: C, 44.2; H, 7.96; N, 8.85.

Methyl 3-Phthalimido-3-deoxy-β-D-ribofuranoside (IV).—In 3 cc. of dimethylformamide, 140 mg. of methyl 3-amino-3-deoxy-β-D-ribofuranoside (III) was heated with 140 mg. of phthalic anhydride for 3.5 hours at reflux temperature. On evaporation to dryness *in vacuo*, there remained a solid and gum. This was triturated with absolute ether leaving 145 mg. (58%) of the phthalimido derivative IV as a white solid, m.p. 174–176°. Recrystallization from absolute ethanol raised the m.p. to 184–186°. This material was identical with an authentic sample[3] by infrared analysis.

By the procedure of Baker, Joseph and Schaub,[3] this product (IV) was converted, *via* benzoylation and acetolysis, to 1-*O*-acetyl-2,5-di-*O*-benzoyl-3-phthalimido-3-deoxy-β-D-ribofuranoside (V). The product so obtained was identical by infrared and mixed melting point comparison with authentic V.[3]

Procedures for Periodate Oxidation Experiments.—A. Approximately 0.3 millimole of sample was accurately weighed. To this was added 10.00 ml. of water, and then 5.00 ml. of approximately 0.5 *N* sodium metaperiodate or periodic acid. When the oxidation was carried out in a bicarbonate-buffered solution, 250 mg. of sodium bicarbonate was added after the addition of the water. The time was noted and 3.00-ml. aliquots were taken at specific times. Blank experiments were made routinely.

To each aliquot was added in turn, 10 ml. of saturated sodium bicarbonate, 1 ml. of 1 *N* acetic acid and 10.00 ml. of approximately 0.1 *N* sodium arsenate. The sample was allowed to remain at room temperature (21–32°) for 10 minutes, and then 2 ml. of 30% potassium iodide solution and 2–3 drops of starch indicator solution were added. The sample was titrated with standardized 0.1 *N* iodine solution.

With methyl 3-amino-3-deoxy-β-D-ribofuranoside (III)

Time	8 min.	17	33	1 hr.	4	24	48
$NaIO_4$	1.60	1.77	1.80	1.96	1.96	1.99	2.06

Time	7 min.	15	30	45
$NaIO_4$ (HCO_3^-)	1.98	1.98	2.07	2.13

Time	7 min.	15	34	25.5 hr.
HIO_4	1.96	2.11	2.20	2.85

With 9-(3-amino-3-deoxy-β-D-ribofuranosyl)-6-dimethylaminopurine (VI)[5]

Time	20 min.	6 hr.	12	24	48
$NaIO_4$	0.88	1.58	1.84	1.92	1.96

With 6-amino-9-(3-amino-3-deoxy-β-D-ribofuranosyl)-purine (3′-amino-3′-deoxyadenosine, VII)[6]

Time	10 min.	5 hr.	24	48
$NaIO_4$	1.19	1.56	1.83	2.07

With 1-(3-amino-3-deoxy-β-D-ribofuranosyl)-4-amino-2-[1-H]pyrimidinone (3′-amino-3′-deoxycytidine, VIII)[7]

Time	5 min.	30	2 hr.	3	21	27.5
$NaIO_4$	1.14	1.16	1.22	1.22	2.13	2.13

With methyl 3-amino-3-deoxy-α-D-arabinofuranoside[8]

Time	13 min.	46	48.5 hr.
$NaIO_4$	1.44	1.96	2.06

Time	5 min.	29	50	84
$NaIO_4$ (HCO_3^-)	0.96	1.70	1.85	1.98

With 9-(3-amino-3-deoxy-β-D-xylofuranosyl)-6-dimethylaminopurine[24b]

Time	6 min.	17	40	60	23 hr.	144
$NaIO_4$	0.90	1.00	1.02	1.07	1.50	1.60

With 9-(5-amino-5-deoxy-β-D-ribofuranosyl)-6-dimethylpurine[11]

Time	10 min.	4 hr.	23	47
$NaIO_4$	1.29	2.98	4.03	4.15

With 1-(5-amino-5-deoxy-β-D-ribofuranosyl)-5,6-dichlorobenzimidazole[11]

Time	2 hr.	6	12	24	48
$NaIO_4$	1.70	1.85	2.41	2.97	3.98

With 6-dimethylamino-9-β-D-ribofuranosylpurine[12]

Time	20 min.	6 hr.	12	24	48
$NaIO_4$	0.89	1.07	1.09	1.05	1.16

With 5,6-dichloro-1-β-D-ribofuranosylbenzimidazole[13]

Time	0.5 hr.	6	48
$NaIO_4$	1.09	0.95	1.13

With methyl 3-amino-3-deoxy-β-L-xylopyranoside[14]

Time	5 min.	15	1 hr.	24
$NaIO_4$	2.08	2.10	2.10	2.22

With methyl 3-amino-3-deoxy-α-D-xylopyranoside[14a]

Time	5 min.	10	25	40
$NaIO_4$ (HCO_3^-)	2.09	2.14	2.16	2.15

With methyl 3-amino-3-deoxy-β-D-xylopyranoside[14a]

Time	5 min.	20	50	3 hr.	6	9
$NaIO_4$		2.16		2.15	2.23	2.27
$NaIO_4$ (HCO_3^-)	2.04		2.10			

With 9-(2-amino-2-deoxy-β-D-allopyranosyl)-6-dimethylaminopurine[15]

Time	1 hr.	12	24	48
$NaIO_4$	1.80	1.97	2.03	2.16

With adenosine[17]

Time	8 min.	13	17	32	48	1 hr.	24
$NaIO_4$	1.01		1.01		1.01		1.01
$NaIO_4$ (HCO_3^-)	1.00		1.00	1.00	1.01		
HIO_4		1.02				1.02	1.05

With cytidine[17]

Time	20 min.	6 hr.	12	24	48
$NaIO_4$	0.98	1.10	1.03	1.01	1.03

With ammonia

Time	5 min.	15	30	6 hr.	12	24
$NaIO_4$		0		0	0.02	0.14
$NaIO_4$ (HCO_3^-)	0	0	0			

B.[26] The above procedure was modified in order that smaller samples could be used. In this modification, 5.00 ml. of approximately 0.01 *N* sodium metaperiodate was added to an accurately weighed 5-mg. sample, and the time noted. At specific intervals a 1.00-ml. aliquot was withdrawn. To this was added 1.0 ml. of saturated sodium bicarbonate solution, 0.2 ml. of 1 *N* acetic acid and 1.00 ml. of approximately 0.05 *N* sodium arsenite solution, and the mixture allowed to stand at room temperature for 10 minutes. Then 0.6 ml. of 30% potassium iodide solution and 2–

(26) We wish to thank Mr. W. E. Meyer and Dr. J. B. Patrick for assistance in developing this procedure.

3 drops of 1% starch solution were added, and the mixture titrated with standardized 0.01 *N* iodine solution.

In the following results, periodate uptake is expressed in terms of molar equivalents. Although most of the experiments were repeated at least once, only a representative set of values is reported.

Comparison of the Periodate Oxidation Products from 3'-Amino-3'-deoxycytidine, 3'-Amino-3'-deoxyadenosine and 9-(3-Amino-3-deoxy-β-D-ribofuranosyl)-6-dimethylaminopurine (VI) with those from the Corresponding Non-amino Nucleosides.—The periodate oxidation products of the aminonucleosides and the corresponding non-amino nucleosides were compared by means of circular paper chromatography in the apparatus described[27] by Kawerau. At specific reaction times, 40–50 γ of the periodate reaction mixture were spotted on Whatman #1 circular chromatography paper (KCT-26, specially slotted for use in the Kawerau apparatus), and the paper was developed with the solvent system indicated. The butanol–water system was 1-butanol saturated with water. Spots were located by inspection under ultraviolet light. The R_f values of the limits of the spots were

Compound	Solvent	*Rf*	*Rf*(mean)
3'-Amino-3'-deoxy-adenosine	BuOH–H_2O	0.57–0.63	0.60
Adenosine	BuOH–H_2O	.55– .82	.69
VI	BuOH–H_2O	.75– .82	.79
6-Dimethylamino-9-β-D-ribofuranosyl purine	BuOH–H_2O	.77– .95	.86
3'-Amino-3'-deoxy-cytidine	Isopropyl alc.–1 *N* NH_4OH (7:2)	.52– .57	.55
Cytidine		.26– .46	.37

(27) E. Kawerau, "Chromatographic Methods," Vol. 1, H. Reeve Angel and Co., New York 7, N. Y., 1956, part 2, p. 7.

Isolation of Ammonium Iodate from Periodate Reaction with 9-(3-Amino-3-deoxy-β-D-ribofuranosyl)-6-dimethylaminopurine (VI).—To a mixture of 588 mg. of the aminonucleoside VI and 7.5 cc. of water was added 908 mg. of periodic acid (4 mmole). All the components dissolved and a white solid precipitated on standing at room temperature for 36 hours. This solid was collected and dried; 118 mg. (30%).

Anal. Calcd. for NH_4IO_3: N, 7.41; H, 2.29; I, 65.8. Found: N, 7.26; H, 2.09; I, 65.9.

To the filtrate was added 20 cc. of a saturated, aqueous picric acid solution, and the solid which precipitated was collected and washed with the minimum of cold water to afford 157 mg. (20%), m.p. 248° (some dec.). Admixture of 6-dimethylaminopurine picrate[28] did not change the m.p.

Anal. Calcd. for $C_{13}H_{12}N_8O_7$: C, 39.9; H, 3.09; N, 28.6. Found: C, 39.8; H, 3.56; N, 27.9.

6-Dimethylamino-9-β-D-ribofuranosylpurine.—A solution of 865 mg. (1.44 mmoles) of 6-chloro-9-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-purine (taken from a batch, a portion of which had been converted to adenosine in 61% yield)[21] in 25 cc. of absolute methanol containing 1.14 g. (25 mmole) of dimethylamine was heated in a stainless steel bomb at 100–110° for 5 hours. After cooling, the bomb was opened and the contents were evaporated under reduced pressure. The residual gum was redissolved in 20 cc. of methanol and 1 cc. of a 1 *N* methanolic sodium methoxide solution was added. The mixture was heated under reflux for 35 minutes and then was evaporated *in vacuo*. The residue was crystallized and recrystallized from acetone to afford 325 mg. (76%) with m.p. 183–184° undepressed by admixture of material prepared by the earlier method[12]; $[\alpha]^{27}D$ −57.8° (*c* 2.73 in water) (lit.[12] $[\alpha]^{25}D$ −62.6° in water).

Anal. Calcd. for $C_{12}H_{17}N_5O_4$: C, 48.80; H, 5.80; N, 23.72. Found: C, 48.80; H, 5.97; N, 23.79.

(28) B. R. Baker, J. P. Joseph and R. E. Schaub, *J. Org. Chem.*, **19**, 631 (1954).

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Addition Polymerization of Anhydrosugar Derivatives. I. A Polyanhydroglucose[1]

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Conditions for the polymerization of levoglucosan to high molecular weight branched polysaccharides are described. Periodate oxidations of the products can be interpreted by assuming a repeating sequence of twenty anhydroglucose units of which eleven are unsubstituted on C_2, C_3, and C_4, seven are unsubstituted on C_2 and C_3 or C_3 and C_4, and two are resistant to periodate oxidation. Molecular weights have been determined on fractionated and unfractionated samples by light scattering and are commonly from 20–50,000 and as much as 300,000 in the extreme. The monomer functionality and mechanism of polymerization are discussed and the products compared with other synthetic polysaccharides.

In 1918 Pictet[2] described the polymerization of levoglucosan, 1,6-anhydro-β-D-glucopyranose, a compound made by the simple pyrolysis *in vacuo* of cellulose or starch. Pictet heated levoglucosan to elevated temperatures in the presence of zinc chloride or platinum black and produced dimeric to octameric products which he described as dextrins. A small fraction of one of his products was also non-dialyzable.[2f] In the interim dextrans formed by bacterial action have been produced commercially as blood extenders and a condensation polymerization based on the dehydration of glucose to high molecular weight polymers in the presence of acids has been investigated in detail for its possible application for the same purpose,[3] yet this unique observation of addition polymerization in the carbohydrate series seems to have been ignored for thirty years.[4,5] In this Laboratory we have recently confirmed and improved Pictet's results and are now in the process of extending the reaction to other conditions and to related compounds.

The failure of previous workers to continue Pictet's work may have been due to the incompleteness of polymerization theory and the compara-

(1) Abstracted from a thesis submitted by J. daS. Carvalho in partial fulfillment of the requirements of the Master of Science degree.

(2) (a) A. Pictet and J. Sarasin, *Helv. Chim. Acta*, **1**, 87 (1918); (b) A. Pictet, *ibid.*, **1**, 226 (1918); (c) A. Pictet and J. Pictet, *ibid.*, **4**, 788 (1921); (d) *Compt. rend.*, **173**, 158 (1921); (e) A. Pictet and J. H. Ross, *ibid.*, **174**, 1113 (1922); (f) *Helv. Chim. Acta*, **5**, 876 (1922); (g) Hoffman-LaRoche and Co. A. G., German Patent 513,125 (Feb. 29, 1928).

(3) (a) P. T. Mora and E. Pacsu, THIS JOURNAL, **72**, 1045 (1950); (b) P. T. Mora and J. W. Wood, *ibid.*, **80**, 685 (1958); (c) P. T. Mora, J. W. Wood, P. Maury and B. G. Young, *ibid.*, **80**, 693 (1958).

(4) H. Pringsheim and K. Schmalz, *Ber.*, **55**, 3001 (1922).

(5) J. C. Irvine and J. W. H. Oldham, *J. Chem. Soc.*, 2903 (1925).