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THERMOLYSIS OF DERIVATIVES OF AMINO SUGARS

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ABSTRACT

Amino groups influence the course of the pyrolysis of carbohydrate derivatives and result in substantial dehydration and charring *N*-Phenylglycosylamines and their acetates rearrange with almost quantitative loss of water or acetic acid and retention of the arylamino groups The sharp dehydration reaction contrasts with the behaviour of the corresponding phenyl glycosides on thermolysis, which results in cleavage of the phenolic groups and subsequent breakdown of the glycosyl moiety Thermal analysis and chemical data indicate that charring of other derivatives of amino sugars is due to intermediate formation of glycosylamines from thermal reaction of the amino group with glycosidic centres

INTRODUCTION

A variety of phenyl glycosides has been investigated in this laboratory as model compounds for understanding the mechanism of the cleavage of the glycosidic bond[1–4] and decomposition of the sugar units during the pyrolysis and combustion of cellulosic materials[5–7] These investigations have shown that the cleavage of the glycosidic bond takes place through a transglycosylation reaction involving nucleophilic displacement of the aglycon by free hydroxyl, amino, or acetamido groups[3] After the transglycosylation reaction, the resulting free aglycon evaporates and the new inter- or intra-molecular transglycosylation product is decomposed on further heating However, there is a substantial difference between the decomposition of the normal sugar units and those containing amino and acetamido groups Pyrolytic decomposition of 2-deoxy and normal glycosides leaves[1 2] ~3 2–14% of residue at 400°, whereas the corresponding amino- and acetamido-glycosides leave[3] substantial amounts of carbonaceous residue, reaching up to 41% at 400°. Since the process of dehydration and charring is of special interest in the flame-proofing of cellulosic materials, the nature and mechanism of the reactions involved have been investigated with a variety of amino sugars, including free 2-amino-2-deoxy sugars, *O*-glycosides having an amino group either in the aglycon or glycosyl moiety, and *N*-glycosylamines, which are the expected transglycosylation or condensation products of the amino-sugar derivatives.

RESULTS

O-*Glycosides* — Fig 1 shows the thermogram of *p*-aminophenyl β-D-glucopyranoside which dehydrates by losing 7% of water at ~93° (t g a), melts sharply at 158° (d t a) without weight loss, and decomposes within the narrow range of 275–325°. The decomposition reaches a maximum rate at 305° (d.t g) and leaves 46% of carbonaceous residue at 400° As seen from Table I, the thermal decomposition of this compound is very similar to that of phenyl 2-amino-2-deoxy-β-D-glucopyranoside[3], but differs sharply from that of phenyl β-D-glucopyranoside which gives only 11% of char under identical conditions. The thermogram of the latter compound

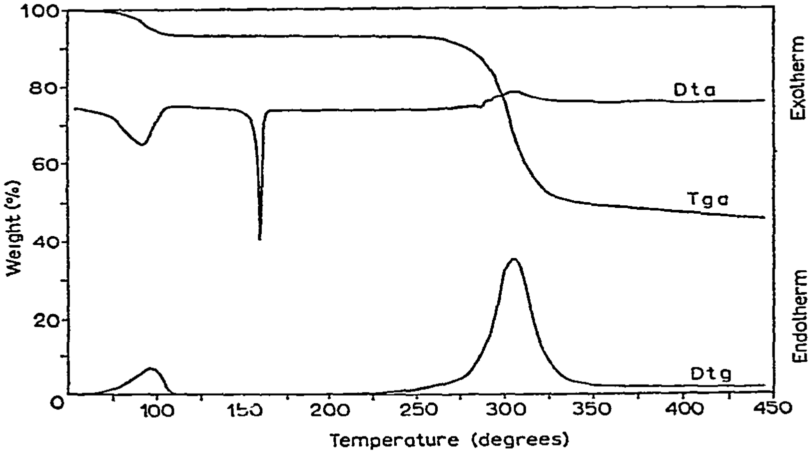


Fig 1 Thermogram of *p*-aminophenyl β-D-glucopyranoside

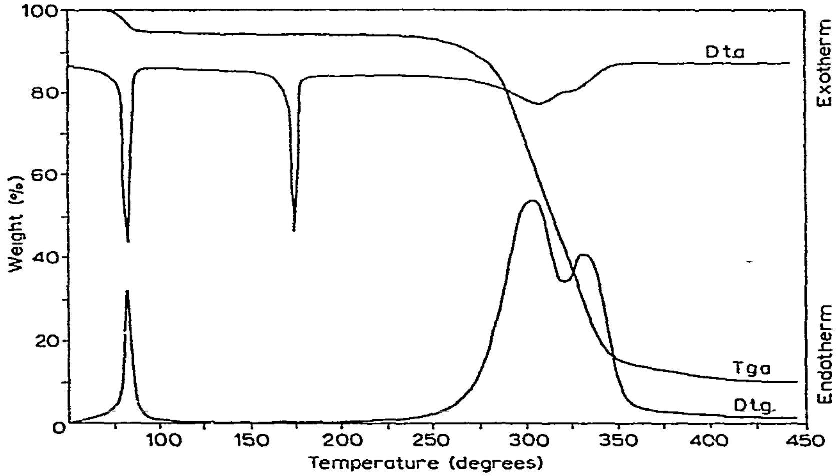


Fig 2 Thermogram of phenyl β-D-glucopyranoside

TABLE I

THERMAL ANALYSIS FEATURES OF PHENYL GLYCOSIDES

Glycoside	*D t a peaks*			*D t g peaks*		*T g a. residue at 400° (%)*	*Literature*	
	Dehydration (degrees)	*M p*	*Dec*	*Dehydration (degrees)*	*Dec*		*M p (degrees)*	*Ref.*
p-Aminophenyl β-D-glucopyranoside	93	158	305	93	306	46	156–158	20
Phenyl 2-amino-2-deoxy-β D-glucopyranoside	80	178	264	80	284	41	172	21
Phenyl β-D-glucopyranoside	85	176	305	—	311	11	176	22
			330		336			23
Phenyl 2-deoxy-β-D-glucopyranoside	—	165	296	—	299	7	163–165	24
p-Aminophenyl β-D xylopyranoside	—	192	277	—	275	58	192–193	25
Phenyl β-D-xylopyranoside	—	181	288	—	297	12	178–180	23
								26

was selected as a standard for comparison and is reproduced in Fig 2 Table I also provides a similar comparison between *p*-aminophenyl β-D-xylopyranoside and phenyl β-D-xylopyranoside

N-*Glycosylamines* – Fig 3 shows the thermogram of *N*-phenyl-D-glucosylamine which may be compared with that of the corresponding *O*-glycoside, phenyl β-D-glucopyranoside^2 (Fig 2) The *N*-glycoside gives a melting endotherm at 153°

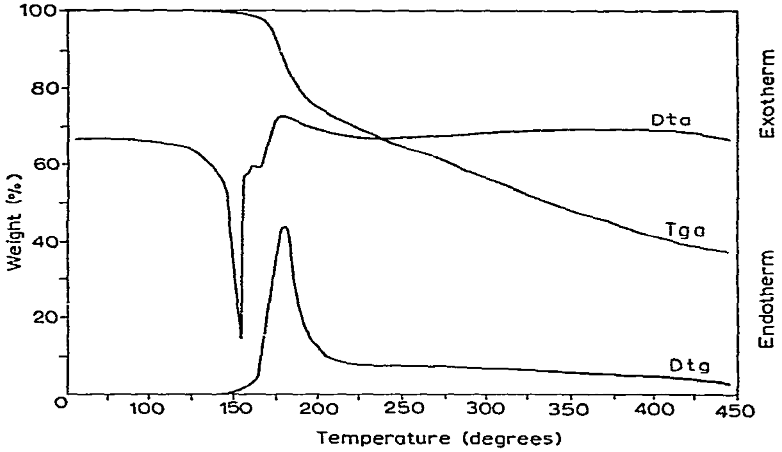


Fig 3 Thermogram of *N*-phenyl-D-glucosylamine

which is wider than that of the *O*-glycosides and, as discussed later, like the broad melting-point endotherm of the reducing sugars, indicates anomerization or rearrangement of the molecule The melting is closely followed by a very rapid, initial decomposition which ends at ~200° with 28% weight loss, leaving a residue that shows gradual loss of weight on further heating up to 400°

The thermal-analysis features of analogous *p*-substituted derivatives presented in Table II show that this behavior is typical for *N*-glycosides Comparison of these data with those reported for the corresponding *O*-glycosides^2 indicates that the latter compounds decompose at higher temperatures and leave far less residue Therefore, they must be pyrolyzed by a different mechanism In both series, the thermal stability of the molecule is related to the Hammett acidity factor^8 (σ) of the phenyl group However, the thermal stability increases with the acidity for *N*-glycosides and decreases for *O*-glycosides

Thermal-analysis data obtained for the corresponding 2-deoxy and fully *O*-acetylated glycosylamines are listed in Table II. Fig 4 shows the thermogram of 2-deoxy-*N*-phenyl-D-*arabino*-hexosylamine, representing the former class of compound The 2-deoxy group slightly increases the thermal stability of these compounds, but the melting and decomposition are still simultaneous or very close. However, for the latter compounds, represented by *N*-phenyl-D-glucosylamine tetra-acetate (Fig 5), acetylation clearly increases the thermal stability of the molecule, and

TABLE II

THERMAL ANALYSIS FEATURES OF *N*-ARYLGLYCOSYLAMINES

Compound	σ	*D t a peak*		*D t g peak (deg)*	*T g a residue at 400° (%)*	*Literature*	
		M p (deg)	*Dec (deg)*			*M p (deg)*	*Ref*
Unacetylated normal compounds							
N-*p*-Tolyl-D glucosylamine	−0 17	149	175^a	176	43	140–141	27
						140	28
N-Phenyl-D glucosylamine	0 00	153	179^a	179	41	149–150	27
						139–140	28
N-*p*-Bromophenyl-D-glucosylamine	+0 23	164	195^a	190	46	163–164	28
			319^a	320			
N-*p*-Nitrophenyl-D-glucosylamine	+0 78					193–194	27
	+1 27	196	225^a	223	56	184	28
N-Phenyl-D-xylosylamine	0 00	159	176^a	172	39	148	15
						140–141	29
N-Phenyl-lactosylamine	0 00	205	215^a	218	47	199–201	30
2-Deoxy compounds							
2-Deoxy-*N*-*p*-tolyl-D-*arabino*-hexosylamine	−0 17	196	205^a	205	38	192	31
2-Deoxy-*N*-phenyl-D-*arabino*-hexosylamine	0 00	199	210^a	209	36	193–194	32
N-*p*-Bromophenyl-2-deoxy D *arabino*-hexosylamine	+0 23	195	212^a	205	40	184–185	new
			305^a	307			
2-Deoxy-*N*-*p*-nitrophenyl-D *arabino* hexosylamine	+0 78	213	223	230	45	205–206	new
	+1 27		234^a				

TABLE II (*Continued*)

Compound	σ	*D t a peak*		*D t g peak (deg)*	*T g a residue at 400° (%)*	*Literature*	
		M p. (deg)	*Dec. (deg)*			*M p (deg)*	*Ref.*
Acetates							
N-*p*-Tolyl-β-D-glucopyranosylamine tetra acetate	−0 17	148	259	261	29	150–151	27
						148	33
N-Phenyl-α-D-glucopyranosylamine tetra-acetate	0 00	147	270	269	27	149–150	15, 27
N-Phenyl-β-D-glucopyranosylamine tetra-acetate	0 00	97	276	267	27	95–96	15
						93–94	27
N-*p*-Bromophenyl-β D-glucopyranosylamine tetra-acetate	+0 23	162	287	290	27	160–162	15
			334[a]	339		162	33
N-*p*-Nitrophenyl-β D glucopyranosylamine tetra-acetate	+0 78	155	320	318	36	168–169	27
	+1 27					153	33
N-Phenyl-β-D-xylopyranosylamine triacetate	—	155	244	246	29	151	15

[a] Exothermic

decomposition takes place at ~100° above the melting point as an entirely separate event Here again, the initial decomposition proceeds very sharply and leaves a substantial amount of residue Both series show a direct relationship between the thermal stability and Hammett σ values.

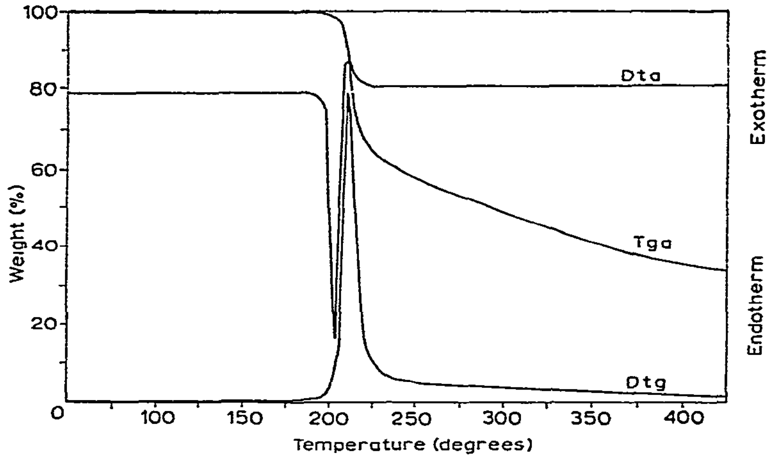


Fig 4 Thermogram of 2-deoxy-*N*-phenyl-D-*arabino*-hexosylamine.

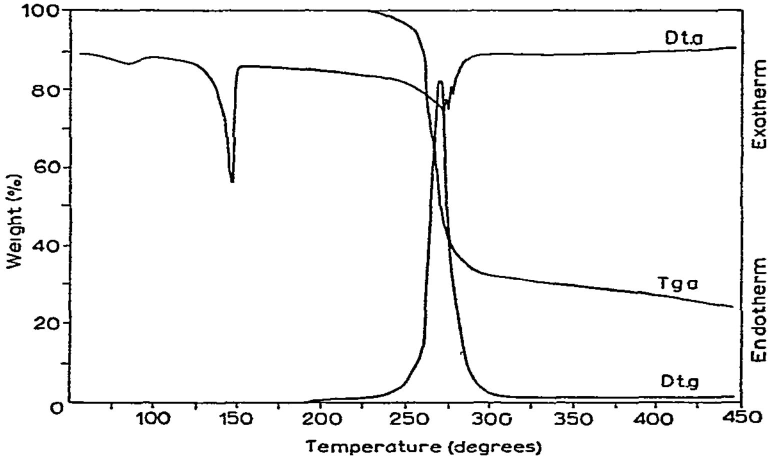


Fig 5 Thermogram of *N*-phenyl-D-glucosylamine tetra-acetate

Reducing sugars — As reported for α-D-xylopyranose, β-D-glucopyranose[9], and cellobiose[10], reducing sugars give a rather broad, melting endotherm due to simultaneous thermal anomerization The molten material condenses with the loss of water and formation of a heterogeneous polymer, which is decomposed on further heating Ultimately, a moderate quantity of carbonaceous residue is left because of the concurrent charring reactions Thermal-analysis data for 2-amino-2-deoxy-D-glucose hydrochloride and related amino-sugar derivatives, presented in Fig 6 and Table III, show that these compounds behave differently They melt and decompose almost simultaneously at ~200° and leave a residue of more than 40%

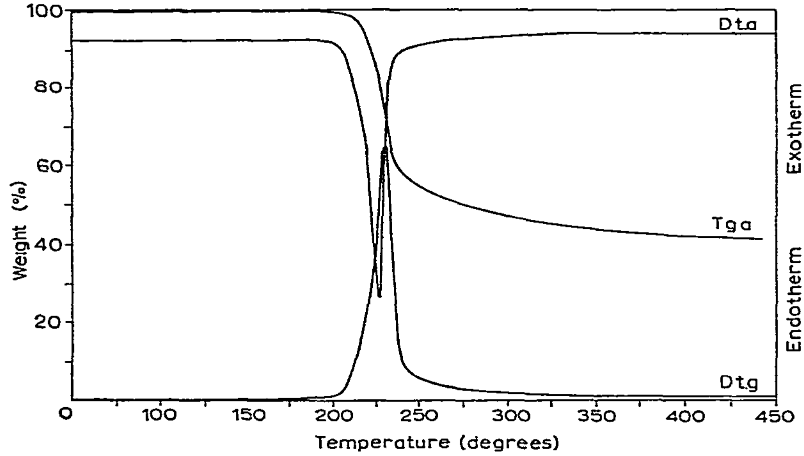


Fig 6 Thermogram of 2-amino-2-deoxy-D-glucose hydrochloride

TABLE III

THERMAL ANALYSIS FEATURES OF AMINO SUGARS

Monosaccharide	*D t a peaks*		*D t g peak (degrees)*	*T g a residue at 400° (%)*
	M p (degrees)	*Dec*		
2-Amino-2-deoxy-D-glucose, HCl	Dec	214	217	43 0
2-Amino-2-deoxy-D-galactose, HCl	Dec	200	203	42 8
2-Amino-2-deoxy-D-mannose, HCl	Dec	189	193	43 2
2-Acetamido-2-deoxy-D-glucose	218	231 (exo)	235	44 3
2-Acetamido-2-deoxy-D-galactose	172	200 (285–350)	210, 263	44 3

Chemical analysis — Thermal analysis of the glycosylamines showed a rapid, initial decomposition and weight-loss at relatively low temperatures, followed by a very slow pyrolysis of the residue on further heating More insight into the nature of the initial, sharp reaction was obtained by chemical analysis of the products and comparison with the products formed from the pyrolysis of the corresponding *O*-glycosides

Pyrolysis of the *O*-glycoside provides a nearly quantitative yield of the free aglycon and a variety of carbonyl compounds resulting from the fission of the glycosyl radicals[1,2,11–13] Pyrolysis of *N*-glycosides, however, gave mainly water from unacetylated compounds and acetic acid from acetylated compounds. As shown in Table IV, the amount of water or acetic acid produced in the pyrolytic reaction of the hexose derivatives was close to four moles. No measurable quantities of aniline or its substituted derivatives could be found in the volatile fraction. These data were corroborated by elemental analysis of the residues, which showed 80–90% of the original nitrogen content and a loss of hydrogen, oxygen, and carbon, corresponding to the dehydration and de-esterification reactions. These data indicate that, in contrast to the *O*-glycosides, pyrolysis of the *N*-glycosides does not involve the initial cleavage of the glycosyl radical from the aglycon.

TABLE IV

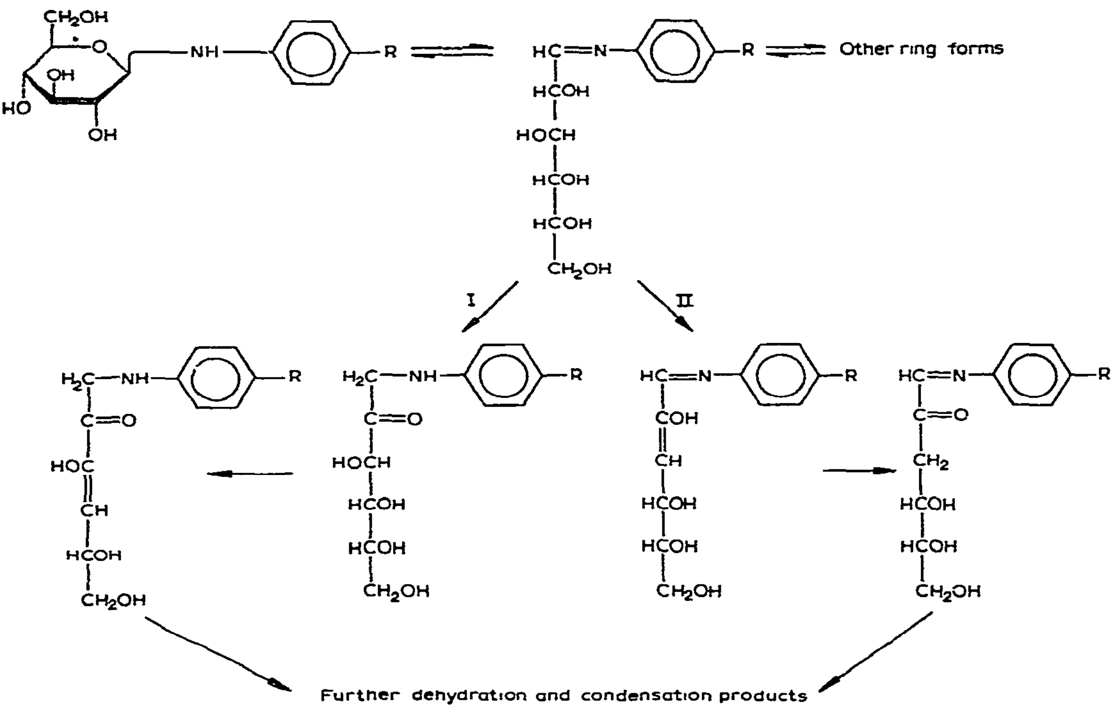
DEHYDRATION OR DE-ESTERIFICATION OF AMINO SUGAR COMPOUNDS

Compound	*Water*		*Acetic acid*	
	Found	*Calc*	*Found*	*Calc*
N-*p*-Bromophenyl-D-glucosylamine	20	21.5	—	—
N-*p*-Tolyl-β-D-glucopyranosylamine tetra-acetate	2.6	—	49	55
N-Phenyl-β-D-glucopyranosylamine tetra-acetate	3.1	—	46	57
N-*p*-Bromophenyl-β-D-glucopyranosylamine tetra-acetate	7	—	42	48
2-Amino-2-deoxy-D-glucose, HCl	31	33	—	—
2-Amino-2-deoxy-D-galactose, HCl	32	33	—	—
2-Acetamido-2-deoxy-D-glucose	43	41	9	(27)[a]

[a] *N*-Acetyl group

DISCUSSION

In a previous paper[3], it was shown that the thermolysis of phenyl 2-amino-2-deoxy-β-D-glucopyranoside, like the thermolysis of unsubstituted glycosides, involves a transglycosylation reaction. Participation of an amino group in this reaction should result in the formation of a glycosylamine. A similar thermal glycosylation involving condensation of 2-amino-2-deoxy-D-glucose hydrochloride and D-mannose to form 2-deoxy-2-D-mannosylamino-D-glucose has been already reported[14]. It has also been shown that the non-enzymic browning reactions which develop the color and flavor of food-stuffs on cooking and roasting are initiated by condensation of carbohydrates with amino groups of proteins. The resulting glycosylamines are then dehydrated and degraded into non-volatile and volatile products, which provide the color and flavor of heated food-stuffs[15–18]. The non-enzymic browning or Maillard reactions constitute one of the most extensively investigated and least understood aspects of carbohydrate chemistry. Scheme 1 shows two major pathways for decomposition of the molecule which involves anomerization, Amadori rearrangement (Path I) or formation of a 3-deoxy compound (Path II), followed by dehydration and fission of the molecule[16].



Scheme 1 Decomposition of glycosylamines

The thermal-analysis data of arylglycosylamines show a broad melting-point endotherm indicative of chemical rearrangement or anomerization[1,9,10] that has been extensively investigated[15,19] It should also be noted that these rearrangements must be responsible for the wide range of melting points reported for these compounds and reflected in Table II This process is followed by a rapid decomposition The decomposition reactions involve dehydration or de-esterification of the glycosylamines and their acetylated derivatives which produce nearly quantitative amounts of water or acetic acid and leave a non-volatile residue containing most of the original nitrogen After the initial dehydration reaction, the carbonaceous residue is further decomposed and slightly volatilized on continued heating The stability of the molecule is slightly increased by the introduction of a 2-deoxy group and substantially increased by acetylation of the hydroxyl groups The thermal stability of the molecule is also increased with the increased acidity of the aryl substituents, or the decreased basicity of the amino group

It is interesting to compare the above data with those for the pyrolysis of *O*-glycosides and the available information on Maillard reactions The glycosylamines are considerably less stable than the corresponding *O*-glycosides Furthermore, the retention of arylamino groups during pyrolysis of *N*-glycosides is in sharp contrast with the quantitative cleavage of aglycon groups on pyrolysis of the corresponding *O*-glycosides Also, the *O*-glycosides show a reverse order of stability with increase in the Hammett acidity of the aryl groups These data are in line with the mechanism of the initial browning reactions As shown in Scheme 1, the *N*-glycosides could undergo consecutive enolization, rearrangement, and dehydration without cleavage of the arylamino group The 2-deoxyglycosylamines, which could not give an Amadori product, could still react through Path II; acetylation hinders, but does not prevent, the reactions, and the initial enolization and rearrangements proceed faster as the amino group becomes more basic The subsequent browning reactions, however, involve hydrolysis and elimination of the amino group which are not favored under the pyrolytic conditions

The experimental data and theoretical considerations presented here also indicate that increased charring of other amino carbohydrate compounds must be due to the interaction of amino groups with glycosidic functions or with potentially available carbonyl groups produced during the pyrolysis process, followed by a series of dehydration reactions as postulated for the *N*-glycosylamines

EXPERIMENTAL

Preparation of derivatives of amino sugars — The samples of amino sugar used in the thermal analysis and pyrolysis experiments were synthesized by the standard methods or purchased from commercial sources The known compounds synthesized are listed in Tables I and II, and were characterized by the previously reported m p and literature references

The corresponding data could not be found for the following two compounds

N-*p*-Bromophenyl-2-deoxy-D-*arabino*-hexosylamine, m p 184–185°

Anal Calc for $C_{12}H_{16}BrNO_4$ C, 45 30, H, 5 07 Found C, 45 59, H, 5 13

2-Deoxy-*N*-*p*-nitrophenyl-D-*arabino*-hexosylamine, m p 205–206°

Anal Calc for $C_{12}H_{16}N_2O_6$ C, 50 70, H, 5 67 Found C, 50 63, H, 5 34

Analytical procedures — The thermal-analysis data were obtained by using the instruments and methods described in previous reports[1–3]

Pyrolysis experiments were carried out by two different methods In method (*a*), 2–3-g samples were placed in a micro-distillation unit and slowly heated at 10–20 mmHg until the pyrolysis was complete The volatile products were analyzed by g l c (Varian model 1800) and n m r spectroscopy (HA-60) Method (*b*) involved pyrolysis of 2-mg samples at 400° in a modified Perkin–Elmer pyrolysis unit connected directly to a Hewlett Packard F & M gas chromatograph as previously described[12]

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REFERENCES

1 F SHAFIZADEH, G D MCGINNIS, R A SUSOTT, AND H W TATTON, *J Org Chem*, 36 (1971) 2813
2 F SHAFIZADEH, R A SUSOTT, AND G D MCGINNIS, *Carbohyd Res*, 22 (1972) 63

3 F Shafizadeh, M H Meshreki, and R A Susott, *J Org Chem*, 38 (1973) 1190
4 F. Shafizadeh, Y Z Lai, and R A Susott, *Carbohyd Res*, 25 (1972) 387
5 F Shafizadeh, *Advan Carbohyd Chem*, 23 (1968) 419
6 F Shafizadeh, *J Polym Sci*, *Part C*, 36 (1971) 21
7 F Shafizadeh and Y L Fu, *Carbohyd Res*, 29 (1973) 113
8 K B Wiberg, *Physical Organic Chemistry*, Wiley, New York, 1964
9 F Shafizadeh and Y Z Lai, *Carbohyd Res*, 26 (1973) 83
10 F. Shafizadeh and Y Z Lai, *Carbohyd Res*, 31 (1973) 57
11 F Shafizadeh, G D McGinnis, and C W Philpot, *Carbohyd Res*, 25 (1972) 23
12 F Shafizadeh, C W. Philpot, and N Ostojic, *Carbohyd Res*, 16 (1971) 279
13 F Shafizadeh and Y Z Lai, *J Org Chem*, 37 (1972) 278
14 S A Barker, K Murray, and M Stacey, *Nature (London)*, 191 (1961) 142
15 G P. Ellis and J Honeyman, *Advan Carbohyd Chem*, 10 (1955) 95
16 J. E. Hodge, in H W Schultz, E A Day, and L M Libbey (Eds), *Chemistry and Physiology of Flavors*, Avi Publishing Co, Westport, Conn, 1967, p 465
17 J E Hodge, *Advan Carbohyd Chem*, 10 (1955) 169
18 G R Jurch, Jr, and J H Tatum, *Carbohyd Res*, 15 (1970) 233
19 K Smiataczowa, *Wiad Chem*, 25 (1971) 343, *Chem Abstr*, 75 (1971) 88848q
20 H G Latham, Jr, E L May, and E Mosettig, *J Org Chem*, 15 (1950) 884
21 C G Greig, D. H Leaback, and P G Walker, *J Chem Soc*, (1961) 879
22 A Robertson and R B Waters, *J Chem Soc*, (1930) 2729, R L Nath and H N Rydon, *Biochem J*, 57 (1954) 1
23 F Shafizadeh and R A Susott, *J Org Chem*, 38 (1973) 3710
24 F Shafizadeh and M Stacey, *J Chem Soc*, (1957) 4612
25 C K De Bruyne and F Van Wijnendaele, *Carbohyd Res*, 4 (1967) 102
26 E M Montgomery, N K Richtmyer, and C S Hudson, *J Amer. Chem Soc*, 64 (1942) 690, B Helferich and H Appel, *Z. Physiol Chem*, 205 (1932) 231, *Chem Abstr*, 26 (1932) 3268
27 B Capon and B E Connett, *J Chem Soc*, (1965) 4492
28 R Bognar and P Nanasi, *Magy Kem Foly*, 67 (1962) 32, *Chem Abstr*, 57 (1962) 3549d
29 F Weygand, *Ber*, 72 (1939) 1663
30 S Tsuiki, *Tohoku J Exp Med*, 61 (1955) 267, *Chem Abstr*, 50 (1956) 4043c
31 J L Barclay, A. B Foster, and W G Overend, *J Chem Soc*, (1955) 1541.
32 W. G Overend. M Stacey, and J Stanek, *J Chem Soc*, (1949) 2841; S Laland, W G Overend, and M Stacey, *ibid*, (1950) 1433
33 R. Bognar and P Nanasi, *J Chem Soc*, (1955) 185