PYROLYSIS OF SUBSTITUTED PHENYL β-D-GLUCOPYRANOSIDES AND 2-DEOXY-α-D-*arabino*-HEXOPYRANOSIDES*

F. SHAFIZADEH, R. A. SUSOTT, AND G. D. MCGINNIS
*Wood Chemistry Laboratory**, Department of Chemistry and School of Forestry, University of Montana, Missoula, Montana 59801 (U. S. A.)*

(Received July 29th, 1971; accepted for publication, September 6th, 1971)

ABSTRACT

Thermal analysis and parallel chemical and physical investigations of substituted phenyl β-D-glucopyranosides and the corresponding 2-deoxy-α-D compounds have shown that the pyrolytic reactions, leading to decomposition of the sugar molecule, are initiated by the cleavage of the glycosidic group. Furthermore, the thermal stability of the glycosides and kinetics of the pyrolysis process are related to the electron density of the glycosidic bond.

INTRODUCTION

The glycosidic bond in various carbohydrate compounds can be cleaved with acids[1,2], alkali[3,4], specific enzymes[5,6], ultraviolet radiation[7,8], γ-radiation[9,10], and heat[11–13]. Cleavage of the glycosides under acid conditions has been most extensively investigated and shown to proceed through a heterolytic mechanism which is influenced by the nature of the glycosidic group and the glycosyl moiety. At the other extreme, thermal cleavage remains relatively unexplored and obscure, mainly because it is complicated by other concurrent and consecutive pyrolytic reactions. The thermal transformations of carbohydrates start with physical changes, such as dehydration noted in this report, "plastic crystal" transitions of the 1,6-anhydro sugars[14–16], melting, and distillation[17]. These events are followed or accompanied by chemical reactions in which the glycosyl moiety remains intact, such as thermal anomerization of a free sugar[13], cleavage of the glycosidic group, formation of anhydro sugars, and polymerization[12,17–20]. Ultimately, the sugar moiety is decomposed to a variety of pyrolytic products through competing pathways[11,17,21,22].

In this study, several aryl β-D-glucopyranosides and the corresponding 2-deoxy-α-D-glycopyranosides were investigated as model compounds to find the effects of various groups on the cleavage of the glycosidic bond and to determine the sequence and nature of the accompaning pyrolytic reactions. These investigations were carried out by combining the techniques of thermal-analysis methods with parallel physical and chemical experiments, which provided a powerful tool for unravelling the sequence of the thermal effects.

*Dedicated to Professor M. Stacey, C.B.E., F.R.S., in honour of his 65th birthday.
**Established through a grant from the Hoerner–Waldorf Corporation of Montana.

RESULTS AND DISCUSSION

Thermal analysis of phenyl β-D-glucopyranoside provided the pattern shown in Fig. 1. In this thermogram, differential thermal analysis (d.t.a.), thermogravimetric analysis (t.g.a.), and derivative thermogravimetry (d.t.g.) curves reflect the sequence of physical transformations and chemical reactions as the sugar is heated at a con-

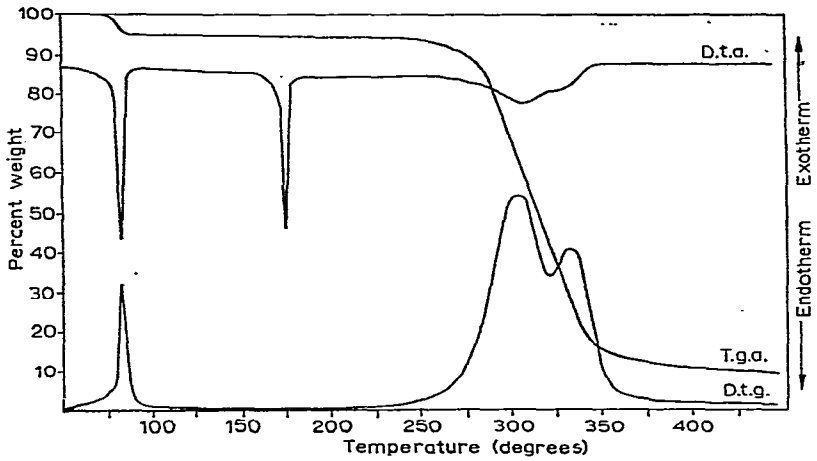


Fig. 1. Thermogram of phenyl β-D-glucopyranoside.

stant rate. The first endothermic peak at 82° in the d.t.a. curve, which corresponds to a rapid weight-loss of 6% in the t.g.a. and a sharp peak in d.t.g., reflects the loss of water of crystallization. The second endotherm, at 175°, corresponds to the melting point of the glucoside. These physical transformations are followed by a broad, endothermic peak centered at 305°, and a shoulder at 330° originating from the pyrolytic reactions. As discussed later, the t.g.a. and d.t.g. data show that the bulk of the glycoside is pyrolyzed and lost in this region. The decomposition leaves a small but stable residue which amounts to ~11% at 400°. The sequence of reactions in this region, which lead to the final decomposition of the sugar and the factors that govern the rate of decomposition, were studied by several other methods.

In order to determine the primary reaction products, the decomposition process was investigated by isothermal heating of phenyl β-D-glucopyranoside at 280° to different levels of weight loss which was controlled and recorded by the t.g.a. instrument. The remaining materials were analyzed by g.l.c., u.v., and t.l.c. methods. The u.v. and g.l.c. analyses gave the amounts of phenyl β-D-glucopyranoside, free phenol, and 1,6-anhydro-β-D-glucopyranose present at different stages of heating (see Table I). These data showed that the phenyl glycoside is consumed much faster than could be accounted for by the weight loss (due to volatilization) plus accumulation of phenol and 1,6-anhydro-β-D-glucopyranose in the heated mixture, suggesting the formation

TABLE I

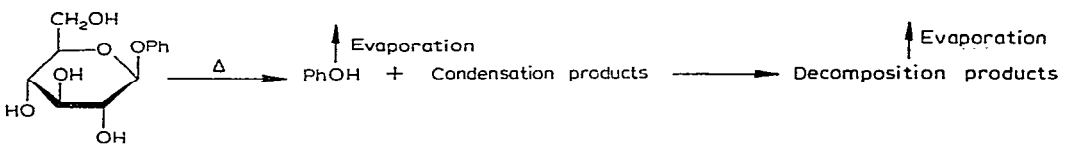
ANALYSIS OF PHENYL β-D-GLUCOPYRANOSIDE PYROLYZED AT 280°

Weight loss (%)	*Remaining glycoside* (%)	*Free phenol* (%)	*1,6-Anhydro-β-D-glucopyranose* (%)
15.6[a]	64.6[a]	3.9[a]	1.0[a]
32.9	25.0	6.7	1.5
50.1	2.0		1.7

[a]Based on the original weight.

of another non-volatile product. At 50% weight-loss, this product formed the main bulk of the residue which contained only small amounts of phenyl glycoside and 1,6-anhydro sugar and no free phenol or D-glucose. However, when the partially decomposed material was hydrolyzed in an acid solution, 70% of the original glycosyl units were recovered as D-glucose, indicating that the residue consisted mainly of non-volatile condensation or polymerization products of D-glucose. The fate of the aglycone was determined by g.l.c. analysis of the pyrolysis products at temperatures above 320°. Under these conditions, free phenol, resulting from the cleavage of the glycoside, readily evaporated and was quantitatively recovered.

The above experiments indicated that the sequence of pyrolytic reactions is initiated with cleavage of the glycosidic bond followed by condensation of the glycosyl moiety, as reported before for free sugars[18–20]. The thermal cleavage and condensation is similar to the acid-reversion process observed on hydrolysis of the polysaccharides[23]. Scheme 1 represents the sequence of reactions involved in the decomposition of the glycoside and evaporation of the products. The t.g.a. and d.t.g. data (see Fig. 1) show the level and the rate of weight loss produced by these reactions at different temperatures.



Scheme 1

Some of the factors that influence the cleavage of the glucosidic groups were investigated by comparing a series of phenyl β-D-glucopyranosides and phenyl 2-deoxy-α-D-*arabino*-hexopyranosides having different *para*-substituents. A similar pattern of thermal behavior and sequence of chemical reactions was observed for these compounds (see Figs. 2 and 3, and Table II), but there were minor differences in the pyrolysis region. The *p*-nitrophenyl glycosides gave a decomposition exotherm, instead of an endotherm, and a considerably greater residue. The comparative data listed in Table II also showed that the decomposition temperatures, recorded by d.t.a.

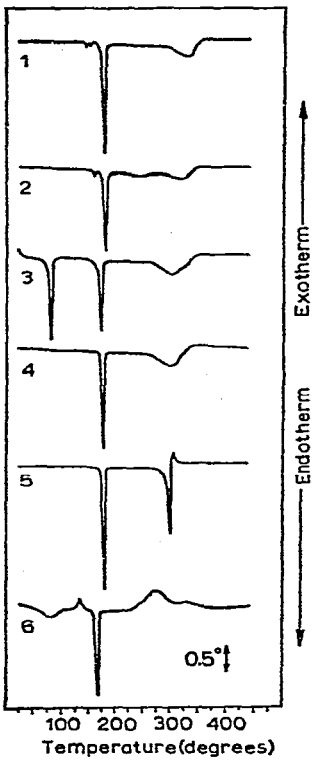


Fig. 2. D.t.a. signals of aryl β-D-glucopyranosides: 1, *p*-methoxyphenyl; 2, *p*-methylphenyl; 3, phenyl; 4, *p*-chlorophenyl; 5, *p*-bromophenyl; 6, *p*-nitrophenyl.

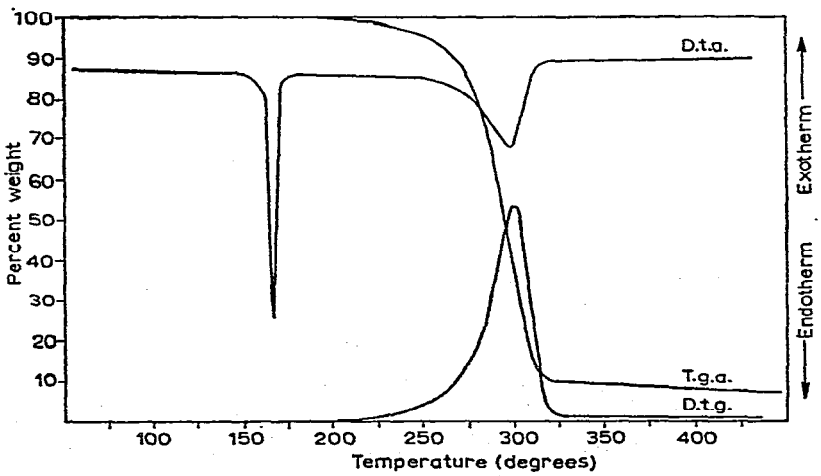


Fig. 3. Thermogram of phenyl 2-deoxy-α-D-*arabino*-hexopyranoside.

TABLE II

THERMAL ANALYSIS FEATURES OF ARYL GLYCOPYRANOSIDES

Aglycone	*σ*	*M.p. (degrees)*	*D.t.a. peaks*		*D.t.g. peak*	*T.g.a. data*
			M.p (degrees)	*Dec, (degrees)*	*Dec. (degrees)*	*Residue at 400° (%)*
	β-D-Glucopyranosides					
p-Methoxyphenyl	−0.27	175–177	178	336	336	8
p-Methylphenyl	−0.17	179–180	182	320	327	11
Phenyl (anhydrous)	0.00	171–172	175	305, 330	311, 336	11
p-Chlorophenyl	+0.23	173–175	178	300	309	12
p-Bromophenyl	+0.23	173	181	300	304	14
p-Nitrophenyl	+1.27 (0.78)	164–165	167	270[a], 325[a]	273, 326	39
	2-Deoxy-α-D-*arabino*-hexopyranoside					
p-Methylphenyl	−0.17	170	174	305	305	3.2
Phenyl	0.00	163.5	165	296	299	6.9
p-Chlorophenyl	+0.23	204–205	205	277	278	4.3
p-Nitrophenyl	+1.2 (0.78)	173–174	181	212, 267[a]	218, 249	28.5

[a]Exothermic

and d.t.g., are dependent on the electron density of the glycosidic bond. The glycosides containing better leaving-groups are decomposed at lower temperatures. Furthermore, the 2-deoxyglycosides, which are more susceptible to acid hydrolysis than normal glycosides[1,2], are also pyrolyzed at lower temperatures. It is interesting to note that the thermal cleavage of the glycosidic group and polymerization of the glycosyl moiety was first observed with methyl 2-deoxy-α,β-D-hexofuranosides[12] which are even more labile than the corresponding 2-deoxypyranosides.

The pyrolysis process, which results in the formation and volatilization of various degradation products, has often been treated as a single reaction for determining the rates and other related kinetic factors. This practice has been specially prevalent in mathamatical modelling of cellulosic fires which propagate with the formation of flammable pyrolysis products[2]. In view of the complexity of the consecutive and concurrent pyrolytic reactions, a similar approach was adapted for gaining further insight into the thermal decomposition of the glycosides. On this basis, a quantitative comparison of the reaction rates for each series was obtained by isothermal t.g.a., d.t.g., and e.s.r. studies. The isothermal t.g.a. records the weight loss following the cleavage of the glycoside which leads to evaporation of the aglycone and the decomposition and volatilization of the glycosyl moiety as shown in Scheme 1. The height of the d.t.g. curve gives the maximal rate of weight loss due to pyrolysis, and serves as another parameter for comparing the stability of the glycosides. The isothermal data obtained at 270° for the phenyl glycosides and the corresponding 2-deoxyglycosides (see Figs. 4 and 5) confirmed the results obtained by dynamic thermal-analysis methods. In other words, when the pyrolysis temperature was kept

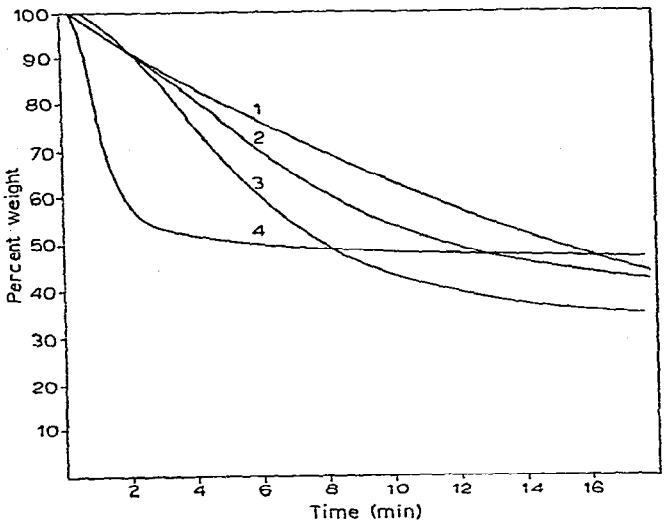


Fig. 4. The isothermal weight loss (and maximal rates in fraction per min) of aryl β-D-glucopyranosides at 270°: 1, *p*-methylphenyl (0.0419); 2, phenyl (0.0555); 3, *p*-chlorophenyl (0.0878); 4, *p*-nitrophenyl (0.363).

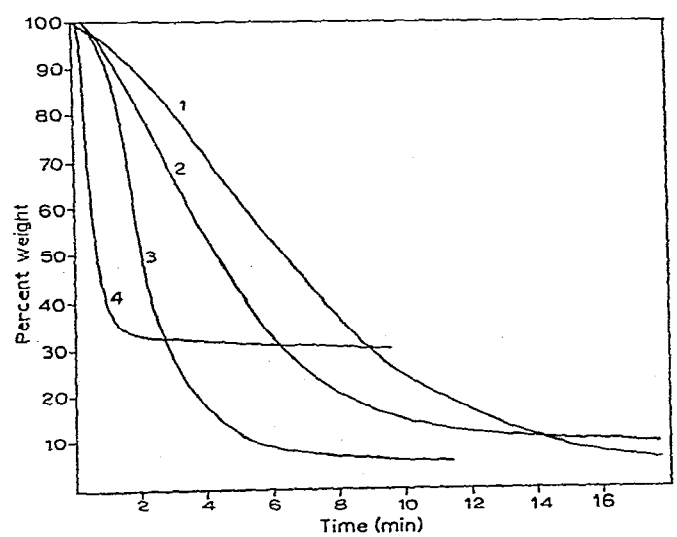


Fig. 5. The isothermal weight loss (and maximal rates in fraction per min) of aryl α-D-*arabino*-hexopyranosides at 270°: 1, *p*-methylphenyl (0.0924); 2, phenyl (0.132); 3, *p*-chlorophenyl (0.444); 4, *p*-nitrophenyl (0.884).

constant, the glycosides with better leaving-groups pyrolyzed at faster rates. Direct relationship between the rates of pyrolysis and the corresponding σ values (see Table II) was observed for both normal glycosides and 2-deoxyglycosides. However, the rates of weight loss for 2-deoxyglycosides were about twice the rates for the

corresponding normal glycosides, except for the *p*-chlorophenyl derivatives in which the difference was much greater. A closer examination of the isothermal t.g.a. curves also indicated that with the normal compounds (Fig. 4), after ~50% weight loss, the remaining materials became more stable and pyrolyzed at a much slower rate. These data are consistent with the chemical analysis discussed above, which indicated the initial formation of D-glucose condensation products and subsequent decomposition of these products to volatile materials and char on further heating. The weight loss for the 2-deoxy compounds, however, as noted before, continued at a rapid rate until nearly all the compound was pyrolyzed. In both cases, the *p*-nitro derivatives again left a considerably larger residue than the other glycosides.

The maximal weight-loss rates at different constant temperatures obtained with t.g.a. (see Table III) were used to determine a procedural energy of activation for the pyrolysis process. This gave the values of 42.8 ±1.0 and 42.1 ±1.2 kcal. mole^{-1} for *p*-methoxyphenyl and *p*-bromophenyl β-D-glucopyranosides, respectively.

TABLE III

ISOTHERMAL WEIGHT-LOSS OF ARYL β-D-GLUCOPYRANOSIDES

Temp. (*degrees*)	*Rates* (*min*$^{-1}$)					
	p-*Methoxyphenyl*	p-*Methylphenyl*	*Phenyl*	p-*Chlorophenyl*	p-*Bromophenyl*	p-*Nitrophenyl*
260					0.0999	
270					0.229	0.265
280					0.429	
290					0.864	
300	0.0418	0.101	0.0893	0.211	1.66	
310	0.0856					
320	0.157					
330	0.270					
340	0.504					

The pyrolysis process was also investigated by e.s.r. spectroscopy which gave typical singlet signals, growing in intensity as the reactions continued. The free radicals associated with the charred residue were similar for all the glycosides studied and persisted at temperatures from ambient to 450° without significant change.

Isothermal growth of the e.s.r. signals plotted against time gave sigmoid curves from which the maximal rates of free-radical formation during the pyrolysis of the phenyl glycosides, given in Table IV, were calculated. Arrhenius plots of these data are shown in Fig. 6, and the calculated, procedural energies of activation are given in Table V. The data presented in Table IV and Fig. 6 again indicate the strong influence of the substituents and the straight relationship between the electron density of the glycosidic bonds and the rates of the pyrolysis process measured by free-radical formation. Furthermore, the values for activation energies derived from e.s.r. study of free-radical formation were nearly equivalent to those found for the weight loss

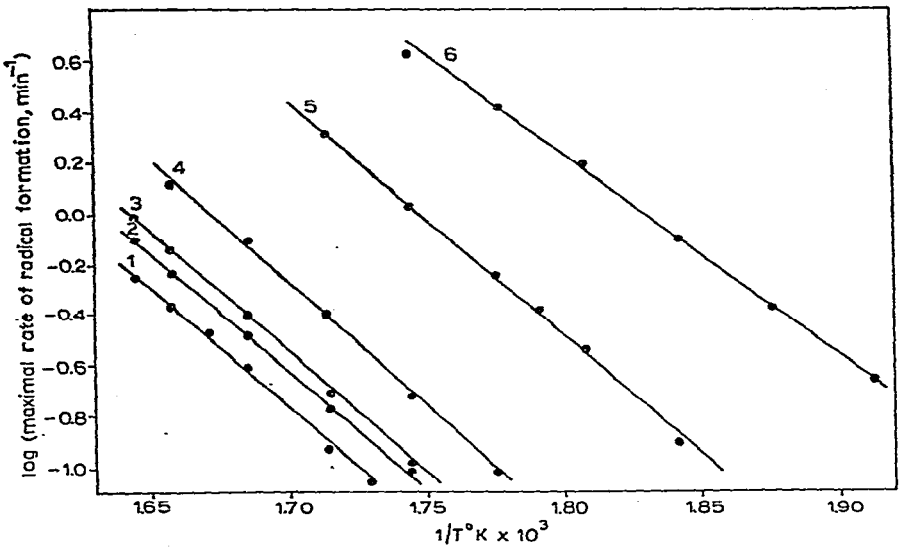


Fig. 6. Arrhenius plots of maximal rates of free-radical formation of aryl β-D-glucopyranosides: 1, *p*-methoxyphenyl; 2, *p*-methylphenyl; 3, phenyl; 4, *p*-chlorophenyl; 5, *p*-bromophenyl; 6, *p*-nitrophenyl.

by isothermal t.g.a. The e.s.r. data are specially significant because the stability, concentration, and physical characteristics (*g* values) of the free radicals indicated that they are mainly associated with the char as one of the end products of the pyrolytic reactions.

The close similarity of the energies of activation derived from free-radical formation and the pyrolytic weight-loss, and the general pattern showing close

TABLE IV

FREE-RADICAL FORMATION ON PYROLYSIS OF ARYL β-D-GLUCOPYRANOSIDES

Temp. (*degrees*)	*Rates* (min^{-1})					
	p-*Methoxyphenyl*	p-*Methylphenyl*	*Phenyl*	p-*Chlorophenyl*	p-*Bromophenyl*	p-*Nitrophenyl*
250						0.215
260						0.418
270					0.123	0.789
280					0.287	1.52
285					0.410	
290				0.0966	0.569	2.61
300		0.0982	0.105	0.189	1.09	4.21
305	0.0883					
310	0.119	0.170	0.193	0.396	2.07	
320	0.245	0.327	0.395	0.775		
325	0.336					
330	0.430	0.501	0.722	1.30		
335	0.558	0.796	0.976			

TABLE V

ACTIVATION ENERGIES FOR FREE-RADICAL FORMATION ON PYROLYSIS OF ARYL β-D-GLUCOPYRANOSIDES

Aglycone	*Ea* (*kcal.mole*$^{-1}$)
p-Methoxyphenyl	43.9 ±1.6[a]
p-Methylphenyl	41.7 ±0.6
Phenyl	44.7 ±0.9
p-Chlorophenyl	44.7 ±1.6
p-Bromophenyl	43.7 ±1.2
p-Nitrophenyl	35.7 ±0.9

[a]Least squares values

relationship between the nature of the glycosidic bond and the stability or the rates of pyrolysis determined by different methods show that the pyrolysis process is controlled by a rate-determining step involving the glycosidic group. In other words, under the pyrolytic conditions, cleavage of the glycosidic group is closely followed by other thermal reactions, including decomposition to volatile products and char formation which show the same overall energy of activation.

It is also interesting to find out whether thermal cleavage, as in acid hydrolysis[1,2], proceeds through a heterolytic mechanism, or conversely involves a homolytic process, as could be expected from the appearance of free radicals on heating. Since the free radicals are shown to be associated with char and thus could be formed by further degradation of the sugar moiety and the rates of reaction are directly related to the σ values, it seems most likely that the thermal cleavage of the glycosides proceeds through a heterolytic mechanism. Such a mechanism is also supported by the facts that the reaction could be catalyzed by addition of zinc chloride, and that the formation of phenolic free-radicals should lead to various condensation products rather than a quantitative recovery of the aglycone group as free phenol[13]. Further information about heterolytic thermal reactions has been obtained by investigating the effect of zinc chloride and sodium hydroxide on the thermal behavior of several β-D-xylopyranosides[13] and 1,6-anhydro-β-D-glucopyranose[17], and by analysis and isotopic tracing of the products formed from the latter compound[22].

EXPERIMENTAL

Preparation of aryl glycosides. — Phenyl β-D-glucopyranoside and its *para*-substituted derivatives were synthesized by the Helferich method[6,24,25], and the aryl 2-deoxy-α-D-*arabino*-hexopyranosides were prepared as described before[26]. These products and the corresponding Hammett σ values[27] are listed in Table II.

Thermal analysis. — The d.t.a. data were obtained with a DuPont Model 900 thermal analyzer equipped with a calorimeter cell accessory. All experiments were performed with 2-mg samples in covered 6-mm aluminum pans, with an empty pan as the reference. The cover was used to reduce vaporization of starting material and ensure temperature uniformity throughout the sample. Samples were heated at a

programmed rate of 15°/min in a 70 ml/min flow of nitrogen. Under these conditions, the recorded fusion temperatures of benzoic acid and lead standards were within 2° of the literature values.

For t.g.a., a Cahn RG Electro-balance was used and programmed heating of samples was carried out with a Research Incorporated Thermac 6000 temperature controller coupled with an elliptical radiant heater. Temperature was measured with a chromel–alumel thermocouple positioned 1 mm below the sample. For thermal scans, the sample size, configuration, atmosphere, and heating rate were the same as in d.t.a., so that the two methods would be comparable. The derivative of the t.g.a. signal (d.t.g.) was taken with a Cahn time derivative computer (Mark II). The results obtained are summarized in Figs. 1–3 and Table II. The same conditions were also used for isothermal t.g.a., except that the temperature was kept at 270 $\pm$0.5°. This gave the plots of weight against time and the maximal rates of weight loss as the peak of the d.t.g. curves, which are presented in Figs. 4 and 5.

The isothermal rates listed in Table III were obtained from 1 mg of ground samples containing 10% glycoside and 90% glass. These samples were pyrolyzed in 2.5-cm long, 2-mm capillary tubes for comparison with e.s.r. experiments. This method greatly reduced the vaporization of the sample prior to decomposition.

Chemical analysis. — T.l.c. was performed on silica gel 1 B-F (Bakerflex) with 1-butanol–acetone–water (4:5:1). The spots were detected by spraying with 10% sulfuric acid in methanol. A Varian Model 1800 instrument equipped with hydrogen flame detectors and connected to a Model 475 digital integrator was used for g.l.c. Carbohydrate compounds after trimethylsilylation were separated with a 6 ft $\times$ 0.25 inch steel tubing packed with Varaport 30 as the support and 3% SE-30 as the stationary phase. Phenols were analyzed with a column containing 10% Carbowax 20M supported on Fluropak 80. Concentrations of free phenol (λ_{max} 287, $\varepsilon = 2760$) and phenyl glucoside (λ_{max} 267, $\varepsilon = 833$) were also determined directly by the u.v. absorption in M sodium hydroxide.

Cleavage of the phenyl β-D-glucopyranoside. — Samples of the glycoside (10 mg) were heated isothermally at 280 $\pm$0.5° in the t.g.a. instrument. After reaching different levels of weight loss, they were removed and analyzed. Each experiment was repeated three times. The results obtained are given in Table I.

Other samples of the glycoside (3 mg) were weighed in small, aluminum boats and placed in the probe of a Varian Aerograph InDUCTOR Model 695 that was inserted in a small controlled heating unit, directly connected to the injection port of the g.l.c. instrument. From 320–410°, the initial pyrolysis products consisted almost entirely of free phenol. On heating at 410° for 1 min, 93 $\pm$9% of the aglycone was released and detected in this manner.

E.s.r. spectroscopy. — The e.s.r. experiments were carried out with a Varian E-3 spectrometer equipped with a specially designed, high-temperature accessory. The temperature was controlled with the Thermac 6000 as in t.g.a., but with a copper–constantan thermocouple positioned just outside the cavity.

The *g* values were all 2.0032 $\pm$0.0001, calculated relative to DPPH (2,2-

diphenyl-1-picrylhydrazyl free-radicals) in benzene ($g = 2.00354$)[28], and the peak-to-peak width of the absorption derivative was 21.5 gauss. Spin concentrations were estimated relative to DPPH diluted with potassium chloride by assuming[29] the concentration to be proportional to w^2h, where w is the peak-to-peak width of the absorption derivative in gauss, and h is the peak-to-peak amplitude. The resulting values were within the range of $1-2\times10^{19}$ spin/g. The e.s.r. signal intensity was plotted against time while holding the magnetic field constant. Formation rates of radicals were measured at the inflection points of the resulting sigmoid curves, which correspond to the maximal rates of increase in signal amplitude. This gave the data presented in Tables IV and V and Fig. 6.

ACKNOWLEDGMENTS

The authors are grateful to the U. S. Forest Service, Forest Products Laboratory, Madison, Wisconsin, and the National Science Foundation, for their financial support and interest in this work.

REFERENCES

1 F. SHAFIZADEH, *Advan. Carbohyd. Chem.*, 13 (1958) 9.
2 B. CAPON, *Chem. Rev.*, 69 (1969) 407.
3 A. DYFVERMAN AND B. LINDBERG, *Acta Chem. Scand.*, 4 (1950) 879.
4 C. E. BALLOU, *Advan. Carbohyd. Chem.*, 9 (1954) 59.
5 A. GOTTSCHALK, *Advan. Carbohyd. Chem.*, 5 (1950) 49.
6 R. L. NATH AND H. N. RYDON, *Biochem. J.*, 57 (1954) 1.
7 A. GUILLAUME AND G. TAURET, *Compt. Rend.*, 201 (1935) 1057.
8 L. J. HEIDT, *J. Amer. Chem. Soc.*, 61 (1939) 2981.
9 G. O. PHILLIPS, F. A. BLOUIN, AND J. C. ARTHUR, *Radiation Res.*, 23 (1964) 527.
10 J. S. MOORE AND G. O. PHILLIPS, *Carbohyd. Res.*, 16 (1971) 79.
11 F. SHAFIZADEH, *Advan. Carbohyd. Chem.*, 23 (1968) 419.
12 W. G. OVEREND, F. SHAFIZADEH, AND M. STACEY, *J. Chem. Soc.*, (1951) 994.
13 F. SHAFIZADEH, G. D. MCGINNIS, R. A. SUSOTT, AND H. W. TATTON, *J. Org. Chem.*, 36 (1971) 2813.
14 F. SHAFIZADEH, G. D. MCGINNIS, C. W. PHILPOT, AND R. A. SUSOTT, *Carbohyd. Res.*, 13 (1970) 184.
15 F. SHAFIZADEH, G. D. MCGINNIS, R. A. SUSOTT, AND C. W. PHILPOT, *Carbohyd. Res.*, 15 (1970) 165.
16 G. W. SMITH AND F. SHAFIZADEH, *J. Chem. Soc.*, (*B*), (1971) 908.
17 F. SHAFIZADEH, C. W. PHILPOT, AND N. OSTOJIC, *Carbohyd. Res.*, 16 (1971) 279.
18 I. J. GOLDSTEIN AND T. L. HULLAR, *Advan. Carbohyd. Chem.*, 21 (1966) 431.
19 J. W. LISKOWITZ AND B. CARROLL, *Carbohyd. Res.*, 5 (1967) 245.
20 H. SUGISAWA AND H. EDO, *J. Food Sci.*, 31 (1966) 561.
21 G. A. BYRNE, D. GARDINER, AND F. H. HOLMES, *J. Appl. Chem.* (*London*), 16 (1966) 81.
22 F. SHAFIZADEH AND Y. Z. LAI, *J. Org. Chem.*, in press.
23 W. G. OVEREND, C. W. REES, AND J. S. SEQUEIRA, *J. Chem. Soc.*, (1962) 3429.
24 J. CONCHIE AND G. A. LEVVY *Methods Carbohyd. Chem.*, 2 (1963) 345.
25 K. W. ROSEMUND AND E. GÜSSOW, *Arch. Pharm.* (*Weinheim*), 38 (1954) 287.
26 F. SHAFIZADEH AND M. STACEY, *J. Chem. Soc.*, (1957) 4612.
27 K. B. WIBERG, *Physical Organic Chemistry*, Wiley, New York, 1964.
28 M. BERSOHN AND J. C. BAIRD, *An Introduction to Electron Paramagnetic Resonance*, Benjamin, New York, 1966, p. 70; M. S. BLOIS, JR., H. W. BROWN, AND J. E. MALING, *Neuvième Colloque Ampère*, (Geneva: Librairie Payot, 1960), p. 243.
29 D. M. GARDNER AND G. K. FRAENKEL, *J. Amer. Chem. Soc.*, 78 (1956) 3279.