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# HIGH TEMPERATURE ALKALINE DEGRADATION OF PHENYL β-D-GLUCOPYRANOSIDE[1]

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## ABSTRACT

The degradation of phenyl β-D-glucopyranoside in aqueous alkali under various conditions has been studied at 100°C and 150-170°C. The effects of a stronger nucleophile, variations in hydroxide ion concentration at constant ionic strength, and temperature were investigated. The level of $^{18}O$ incorporation into the product phenol from the solvent and the rate constant differences associated with methylating the C-2 hydroxyl group were also investigated. The results indicate that, at both 100 and 170°C, phenyl β-D-glucopyranoside degradation proceeded by an $S_NicB(2)$ reaction. At both temperatures the expected $S_NicB(2)$ product levoglucosan formed in less than quantitative yields because of competing reactions which occurred after the rate-determining step.

## INTRODUCTION

During alkaline pulping at 170°C, the polymeric carbohydrate components of wood experience random bond cleavages which cause pulp viscosities to drop. The reactivities of alkyl glycosides in alkali at 170°C have been extensively studied in order to understand the mechanisms of bond cleavages that occur with the wood carbohydrates. Phenyl glycosides have not been studied under pulping

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conditions, because these models are much more reactive that the alkyl glycosides, primarily because of the better leaving group ability of the phenoxide ion relative to that of an alkoxide ion.

In 1945, McCloskey and Coleman[3] studied the 100°C reaction of phenyl β-D-glucopyranoside (1) with potassium hydroxide and proposed an $S_N icB(2)$ mechanism[4] (Figure 1) to explain the observed results. Critical steps in the mechanism are ionization of C(2)-OH, a pyranose ring conformation change from the $^4C_1$ to $^1C_4$, and C(2)-oxyanion bridging to C(1). Displacement of the aglycon by C(2)-oxyanion yields phenolate ion (2) and 1,2-anhydro-α-D-glucopyranose (3). In
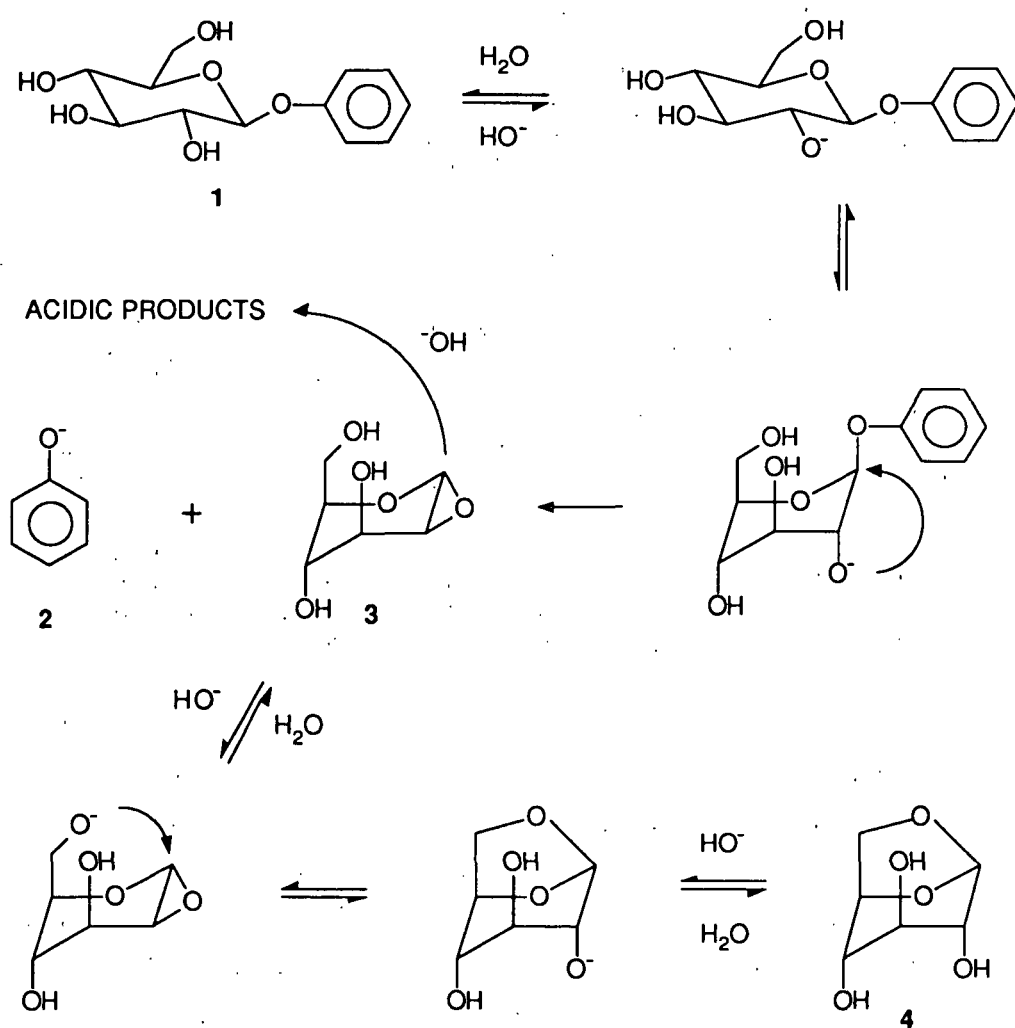


Figure 1. $S_N icB(2)$ mechanism for phenyl β-D-glucopyranoside.

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subsequent rapid reactions, the 1,2-anhydride reacts intramolecularly to form levoglucosan (4) or, by attack of hydroxide ion at the oxirane ring to form glycosyl products which degrade rapidly to acidic products.

Lindberg[5] was the first to propose that alkaline degradation of alkyl $\beta$-D-glucosides at 170°C may also occur by the $S_N icB(2)$ mechanism. This hypothesis was based on the observation that $\beta$-D-glucopyranosides were reactive and produced some levoglucosan while $\alpha$-D-linked models were less reactive and gave no levoglucosan. This observation by Lindberg was later used by Corbett and Richards[6] to possibly explain random glycosidic bond cleavage of cellulose.

Recent cellulose model studies[7-10] have shown that the $S_N icB(2)$ mechanism may be the most predominant reaction pathway present for those model systems; however alternative reaction pathways, such as an $S_N 1$ reaction mechanism, appear to occur simultaneously.[7,8] An $S_N 2$ mechanism has generally been discounted as a possible reaction pathway.[9] Henderson[11] has suggested that an $S_N icB(2)$-ro mechanism[12] could be important in the case of $\beta$-D linked cellulose models. Also in model systems, oxygen-aglycon cleavage can account for up to 20% of the observed products.[8-10]

One of the main pieces of evidence for the presence of an $S_N icB(2)$ mechanism was the production of levoglucosan. However, the levoglucosan yield varied with the model compound,[8,10] reaction conditions,[10] and nucleophiles present.[9] Because of these yield variations, it is difficult to determine the extent of the $S_N icB(2)$ mechanism in the model systems. The behavior of phenyl $\beta$-D-glucopyranoside under the more drastic conditions associated with alkaline pulping has been studied here in order to provide information on the significance of levoglucosan formation and the $S_N icB(2)$ reaction mechanism in the case of alkyl glycoside models and, ultimately, in the case of wood carbohydrates.

## RESULTS AND DISCUSSION

### Kinetic Studies

Phenyl $\beta$-D-glucopyranoside degradation has been followed by

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measurement of phenolate ion production with ultraviolet (UV) spectroscopy.[13,14] Gas chromatographic (GC) analysis was chosen to monitor the reaction in this study. The GC technique allows direct measure of all neutral reaction species and circumvents the possible interference of UV chromophores formed in the degradation of glucosyl products.[15] During the course of our studies, Kiryushina *et al.*[16,17] compared UV and GC techniques in connection with degradation of phenyl β-D-glucopyranoside in caustic at 170°C and concluded that the UV technique grossly underestimated the amount of reaction that occurred.

A low temperature alkaline degradation of phenyl β-D-glucopyranoside was run to determine the applicability of the analytical procedure. A large ratio of sodium hydroxide to substrate was used to achieve pseudo-first-order reaction kinetics and facilitate determination of rate constants. The final kinetic equation was:[18]

$$\ln R = \ln R_o - k_r t$$

where    $R$ = the phenyl β-D-glucopyranoside concentration,

$R_o$ = R at time zero, and

$k_r$ = the pseudo-first-order reaction rate constant for degradation.

All products ($P_i$) proved to be stable over the reaction periods used, and rate constants for product formation were obtained from parallel pseudo-first-order kinetics:[18]

$$P_i - P_{i,o} = k_i \left( \frac{R_o}{k_r} \right) [1 - \exp(-k_r t)]$$

where    $P_i$ = the concentration of product i.

$P_{i,o}$ = $P_i$ at time zero, and

$k_i$ = the pseudo-first-order reaction rate constant for formation of product i.

Fast-Flow Reactor

The projected half life for phenyl β-D-glucopyranoside at 170°C

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in caustic was calculated to be approximately 30 seconds. To study the reaction, we used a modification of the fast-flow reactor developed by Green, et al.[19] (Figure 2).

For a reaction run, solutions were drawn into the syringes from their respective reservoirs by movement of the syringe pistons. Pre-determined amounts of caustic and carbohydrate liquors were forced into their warm-up coils by movement of a piston and allowed to warm to reaction temperature. In a preliminary experiment, phenyl β-D-glucopyranoside was shown to be stable in the aqueous medium at 170°C for times longer than the warm-up period. These solutions were then forced through the mixer by a second piston movement and reacted for a set time period. The reaction was stopped by forcing water, by movement of the quench water piston, to carry the reacted liquor into the sample holder where the liquors were thermally quenched with iced water.

## Degradation Studies

Phenyl β-D-glucopyranoside was initially degraded with 1 M sodium hydroxide at 100.6°C. The reaction had a $k_r$ of $5.02 \pm 0.04 \times 10^{-5}$ sec$^{-1}$ and $k_{levo}$ of $4.43 \pm 0.03 \times 10^{-5}$ sec$^{-1}$. The phenyl β-D-glucopyranoside rate constant is comparable to the 100°C degradation rate constant of $5.3 \times 10^{-5}$ sec$^{-1}$ calculated from the graphical data presented by Lai, et al.[13] Conversion of phenyl β-D-glucopyranoside to levoglucosan, as defined by the ratio of $k_{levo}$ to $k_r$, was 0.88. This amount is consistent with the 88% yield reported by McCloskey and Coleman.[5]

The high temperature degradation of phenyl β-D-glucopyranoside was examined by mechanistic probes. Five possible reaction mechanisms were considered: $S_N icB(2)$, $S_N icB(2)$-ro, $S_N1$, $S_N2$, and $S_N2Ar$.[20] Table 1 presents the expected response of each type of mechanism to the reaction probes. Although some mechanisms give the same response to certain probes, there is a unique set for each mechanism. For selected probe experiments, NaCl was added to maintain constant ionic strength. [The nucleophilicity of NaCl was examined against the $S_N2$ model methyl α-D-glucopyranoside at 182°C

Figure 2. Fast flow reactor.

OXYGEN FREE WATER RESERVOIR

SAMPLE HOLDER

QUENCH WATER SYRINGE 3

REACTION COILS

OIL BATH

= VALVE

MIXER

WARM-UP COILS

WASTE

CARBOHYDRATE SOLUTION RESERVOIR

CARBOHYDRATE SOLUTION SYRINGE 1

CAUSTIC SOLUTION SYRINGE 2

CAUSTIC SOLUTION RESERVOIR
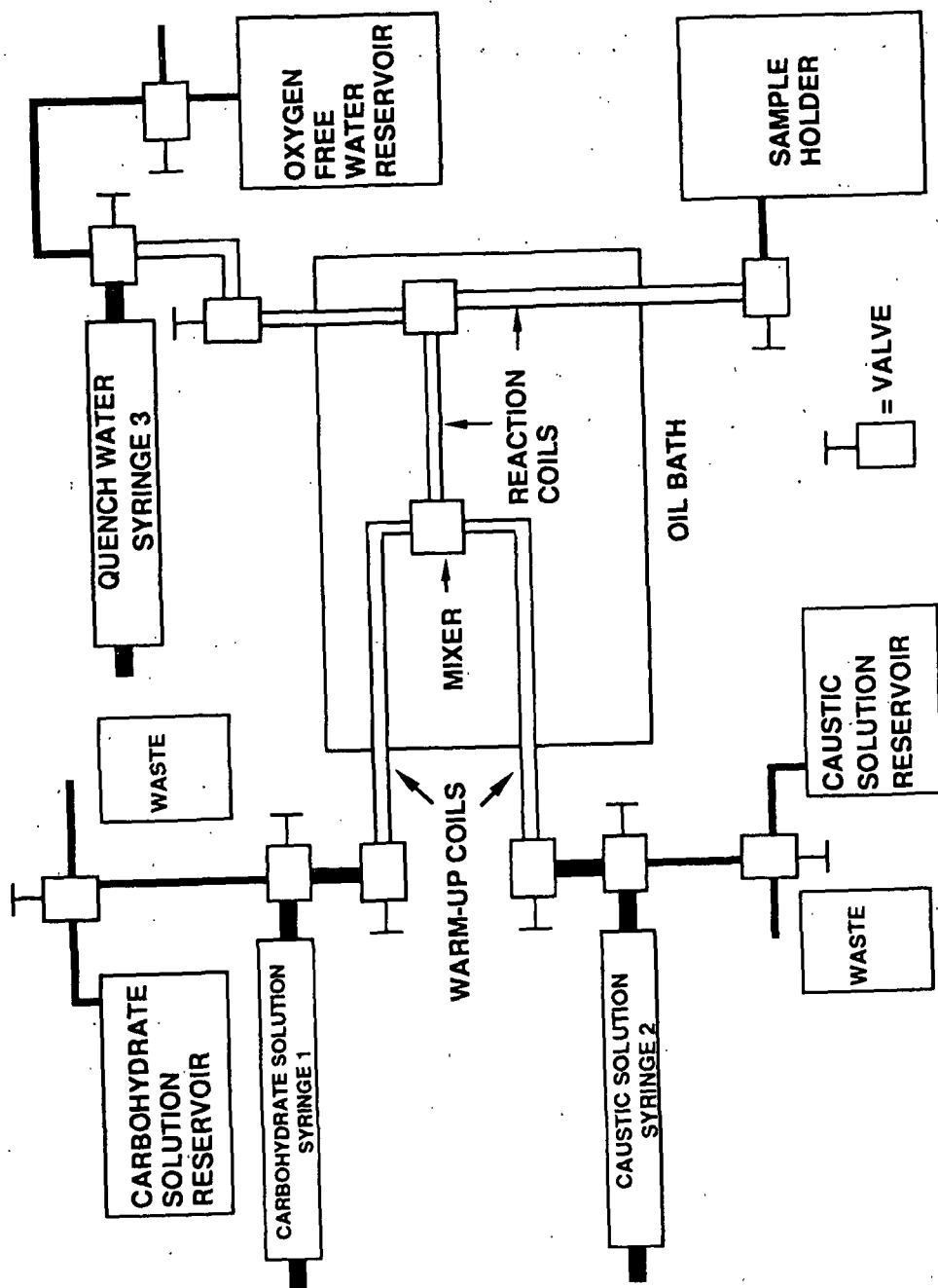
WASTE

Table 1.    Summary of reaction mechanisms and expected responses to mechanistic probes.

| Reaction Mechanism | Bond Cleavage[a] | Nucleophilic Effect | C(2)-OH Blocking | $\Delta S^{\ddagger}$ [b,c] | Levo Yield |
|---|---|---|---|---|---|
| $S_N1$ | G-O | none | none | ++ | ? |
| $S_N2$ | G-O | increase | none | -- | none |
| $S_N2Ar$ | O-A | increase | none | -- | none |
| $S_N icB(2)$ | G-O | none | decrease | - | high |
| $S_N icB(2)$-ro | $C_1$-$O_5$ | none | decrease | - | none |

[a]  G-O is the glucosyl-oxygen bond; O-A is the oxygen-aglycon bond; and $C_1$-$O_5$ is the anomeric carbon-pyranose ring oxygen bond.
[b]  Expected order.[21]  [c]  The symbols + for positive values, - for negative values, ++ for a more positive value, and -- for more negative values.

in 0.5 M NaOH and 2.0 M NaCl; no effect was found on the reaction rate *vs.* the 0.5 M NaOH case.[9]] Prior to using these probes, we established that the rate of loss of starting material and the rates of formation of products were reproducible in a simple 170°C, alkali reaction. Therefore, single degradations were used in subsequent experiments.

**Point of Bond Cleavage**

Phenyl β-D-glucopyranoside was degraded at 171.6°C in 2.5 M NaOH containing 8.6% $^{18}O$ labeled water and the liberated phenol was analyzed for its $^{18}O$ content. A modified data analysis program developed by Henderson[11] was used to calculate that 0.2% oxygen-aglycon cleavage took place. Thus, basically all cleavage occurred at the glucosyl-oxygen bond and the $S_N2Ar$ mechanism was not significant.

**Effect of a Stronger Nucleophile**

Phenyl β-D-glucopyranoside degradation rate constants of 0.0345 sec⁻¹ with just sodium hydroxide and 0.0349 sec⁻¹ with 0.1 M sodium sulfide added were observed (Table 2, Exp. 1 and 2). Under the alkaline conditions used, sodium sulfide hydrolyzes to sodium hydrosulfide and sodium hydroxide;[9] the hydrosulfide anion is a stronger nucleo-

Table 2.  Experimental data for high temperature phenyl β-D-glucopyranoside degradations.

| Exp. # | Temp.,°C | Reagent Molarities (M) | | | Observed Reaction Rate Constants x $10^{-2}$ (sec$^{-1}$)[a] | | |
|---|---|---|---|---|---|---|---|
| | | NaOH | Na$_2$S | NaCl | $k_r$ | $k_{levo}$ | $k_p$ |
| 1 | 171.6 | 1.39 | 0.102 | 1.00 | 3.49 ± 0.18 | 2.50 ± 0.12 | 3.24 ± 0.14 |
| 2 | 171.6 | 1.50 | - | 1.00 | 3.45 ± 0.19 | 2.92 ± 0.05 | 3.49 ± 0.11 |
| 3 | 171.6 | 2.50 | - | - | 5.99 ± 0.39 | 4.71 ± 0.21 | - |
| 4 | 159.6 | 2.50 | - | - | 2.48 ± 0.01 | 2.02 ± 0.02 | 2.39 ± 0.06 |
| 5 | 149.6 | 2.50 | - | - | 1.07 ± 0.04 | 0.88 ± 0.02 | 1.07 ± 0.04 |
| 6 | 171.6 | 0.50 | - | 2.00 | 1.22 ± 0.04 | 1.03 ± 0.02 | - |
| 7 | 171.6 | 1.00 | - | 1.50 | 2.37 ± 0.11 | 1.93 ± 0.05 | 2.32 ± 0.19 |

[a] Values represent best fit of linear regression of the raw data and the associated 95% confidence limit.

phile than hydroxide anion. The rate constant difference with and without sodium hydrosulfide is comparable to that of 1,5-anhydro-cellobiitol, a model compound which is not considered to react by an $S_N2$ mechanism.[9] Therefore, the $S_N2$ pathway is an unlikely mechanism for phenyl β-D-glucopyranoside degradation.

**Effect of Methylating C(2)-OH**

Blocking the C(2)-OH with a nonionizable group provides a simple method to determine whether $S_Ni$ type mechanisms occur and the relative importance of underlying reaction pathways. 2-O-Methyl phenyl β-D-glucopyranoside (5) in 2.5 M NaOH at 171.6°C exhibited a degradation reaction rate constant of $4.67 \pm 0.89 \times 10^{-5}$ sec$^{-1}$. The reduction in the rate constant by a factor of 1300 times observed for the blocked and unblocked (Table 2, Exp. 3) models is comparable to the factor of 2400 reported in a similar study with p-nitrophenyl β-D-galactopyranoside at 55°C.[22] Thus, an $S_Ni$ type mechanism is the dominant reaction pathway.

The large decrease in the rate constant by blocking OH-2 also indicates the absence of any appreciable underlying reaction mechanisms. A much smaller effect on the rate constant decrease, such as a factor of four seen with methyl β-D-glucopyranoside,[8] would have been expected for a mixed $S_N1$ and $S_NicB(2)$ mechanism. Therefore, the only viable mechanisms for phenyl β-D-glucopyranoside alkaline degradation appear to be $S_NicB(2)$ and $S_NicB(2)$-ro.

**Apparent Thermodynamic Functions of Activation**

The apparent thermodynamic functions of activation for phenyl β-D-glucopyranoside degradations at 150-170°C in 2.5 M NaOH (Table 2, Exp. 3,4,5) were $\Delta H\ddagger$ of 28.3 kcal mol$^{-1}$ and $\Delta S\ddagger$ of -1.3 cal mol$^{-1}$ °K$^{-1}$. The $\Delta H\ddagger$ and $\Delta S\ddagger$ values for phenyl β-D-glucopyranoside are compared to those of other glycosides degraded at 170°C in 2.5 M NaOH in Table 3.

The $\Delta S\ddagger$ value for phenyl β-D-glucopyranoside (-1.3 cal mol$^{-1}$ °K$^{-1}$) is similar to those of glycosides believed to react by $S_NicB(2)$ mechanisms[10,23] and similar to the value for the $S_NicB(2)$-ro reaction associated with the glucosyl-oxygen bond cleavage in 1,5-anhydro-

Table 3. Thermodynamic data for phenyl $\beta$-D-glucopyranoside and other glycosides.

| Glycoside | Proposed Mechanism | $\Delta H\ddagger$, kcal/mol | $\Delta S\ddagger$, cal/mol L | Ref |
|---|---|---|---|---|
| Phenyl $\beta$-D-glucopyranoside[a] | $S_NicB(2)$ | 28.3 | -1.3 | * |
| 1,5-Anhydromannobiitol[b] | $S_NicB(2)$-ro | 35.3 | -4.3 | 11 |
| Levoglucosan[c] | $S_NicB(2)$ | 32.8 | -3.8 | 23 |
| 1,5-Anhydro-2,3,5-tri-O-methyl-cellobiitol[a] | $S_NicB(2)$ | 35.5 | -3.2 | 10 |
| 1,5-Anhydrocellobiitol[d] | $S_N1$ | 41.7 | 6.9 | 7 |
| Methyl $\alpha$-D-glucopyranoside[a] | $S_N2$ | 32.4 | -13.6 | 23 |
| 1,5-Anhydrocellobiitol[a] | mixed $S_NicB(2)$ & $S_N1$ | 37.1 | 1.0 | 7 |

* This study. [a] Glucosyl-oxygen bond cleavage. [b] $C_1$-$O_5$ ring opening. [c] $C_1$-$O_6$ ring opening. [d] Oxygen-aglycon bond cleavage.

mannobiitol.[11] The small difference between $\Delta S\ddagger$ values for compounds reacting by the $S_N1cB(2)$ and $S_N1cB(2)$-ro pathways does not allow a distinction to be made as to which mechanism is operative. However, it is apparent that an $S_N1$ mechanism, which would be expected to have a much more positive $\Delta S\ddagger$ value (Table 3), can be ruled out.

The 28.3 kcal mol$^{-1}$ $\Delta H\ddagger$ value for phenyl $\beta$-D-glucopyranoside is much lower than the $\Delta H\ddagger$ values for other compounds in Table 3 reacting by the $S_Ni$ mechanisms.[10,11,23] The difference in the $\Delta H\ddagger$ values is attributed to the fact that the phenoxy anion is a much better leaving group than the alkyloxy anions in the other compounds. For the $S_NicB(2)$-ro reaction mechanism, the ring oxygen is the leaving group. Both 1,5-anhydromannobiitol and phenyl $\beta$-D-glucopyranoside contain similar substituents [i.e., ring oxygen oxyanion and C(5) groups] and would be expected to exhibit similar $\Delta H\ddagger$ values for an $S_NicB(2)$-ro mechanism. The $\Delta H\ddagger$ value for the phenyl $\beta$-D-glucopyranoside degradation was much lower than that for 1,5-anhydromannobiitol, thus, indicating that an $S_NicB(2)$ rather than an $S_N1cB(2)$-ro pathway is

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operative. The low $\Delta H^{\ddagger}$ value also ruled out the presence of an $S_N1$ mechanism.

### Effect of Varying the Hydroxide Concentration at Constant Ionic Strength

An analytical method suggested by Lai, *et al.*[13] and modified by later researchers[7,8,10,11] was used to further probe the presence of the $S_N icB(2)$ mechanism; the method examined the effect of hydroxide concentration at constant ionic strength.

The governing equation[7,8,10,11,13] for the analysis of an $S_N icB(2)$ reaction is:

$$\frac{1}{k_{obs}} = \frac{1}{k} + \frac{1}{k\,K\,[OH^-]}$$

where $k_{obs}$ = the observed rate constant,

$K$ = the equilibrium constant for formation of the conjugate base of the glucoside, and

$k$ = the rate constant for conversion of the ionized glycoside to product

A plot of $k_{obs}$ versus the reciprocal of the hydroxide ion concentration was linear (Figure 3), giving supporting evidence for the presence of an $S_N icB(2)$ mechanism.

### Formation of 1,6-Anhydro-β-D-glucopyranose and Phenol

The levoglucosan yield (Table 4), except for the addition of sodium sulfide, averaged ca. 83% and appeared independent of temperature, ionic strength, and hydroxide concentration at constant ionic strength. This behavior is different from that seen by earlier researchers[7,10] because their models exhibited several different reaction pathways, while phenyl β-D-glucopyranoside degrades in caustic by only the $S_N icB(2)$ mechanism.

Hydrosulfide ion addition to the reaction system caused a 10% decrease in levoglucosan yield. This data and the less than 100% yield of levoglucosan in the other cases indicates that the oxirane ring of the 1,2-anhydride (3) is susceptible to opening by a variety of nucleophiles, as seen in Figure 1. This effect of hydrosulfide ion was reported pre-
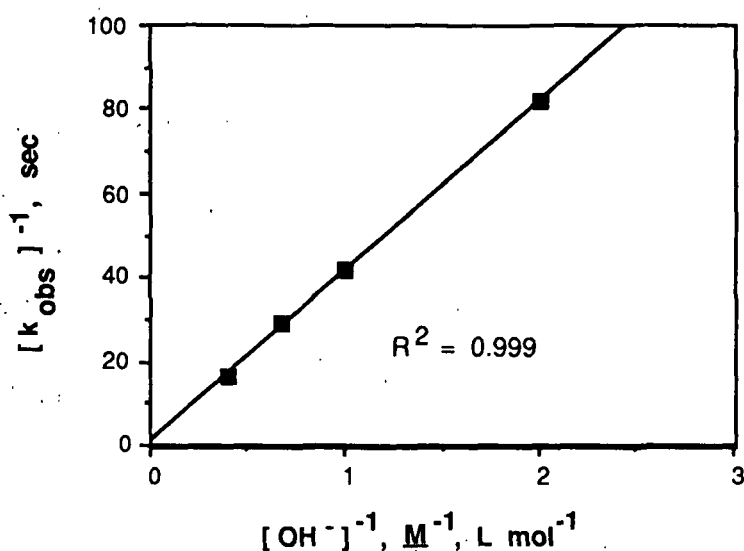
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Figure 3. Relationship between the reciprocals of hydroxide ion concentration and observed rate constant for phenyl β-D-glucopyranoside at constant ionic strength of 2.5 M at 171.6°C (Table 2, experiments 2,3,6,7).

Table 4. Levoglucosan and phenol formation from phenyl β-D-glucopyranoside degradations.

| | Reagent Molarities (M) | | | | |
|---|---|---|---|---|---|
| Temp., °C | NaOH | NaCl | $Na_2S$ | $X_{levo}$[a] | $X_p$[b] |
| 149.6 | 2.5 | - | - | 0.82 | 1.00 |
| 159.6 | 2.5 | - | - | 0.82 | 0.96 |
| 171.6 | 2.5 | - | - | 0.79 | - |
| 171.6 | 0.5 | - | - | 0.86 | - |
| 171.6 | 0.5 | 2.0 | - | 0.84 | - |
| 171.6 | 1.0 | 1.5 | - | 0.82 | 1.00 |
| 171.6 | 1.5 | 1.0 | - | 0.85 | 1.00 |
| 171.6 | 1.4 | 1.0 | 0.10 | 0.72 | 0.93 |

[a] $X_{levo}$ is the ratio of $k_{levo}$ to $k_r$.
[b] $X_p$ is the ratio of $k_p$ to $k_r$.

viously by Blythe and Schroeder.[9]

In earlier studies, the observed yield of levoglucosan was equated with the extent of $S_N icB(2)$ mechanism. It is now clear from
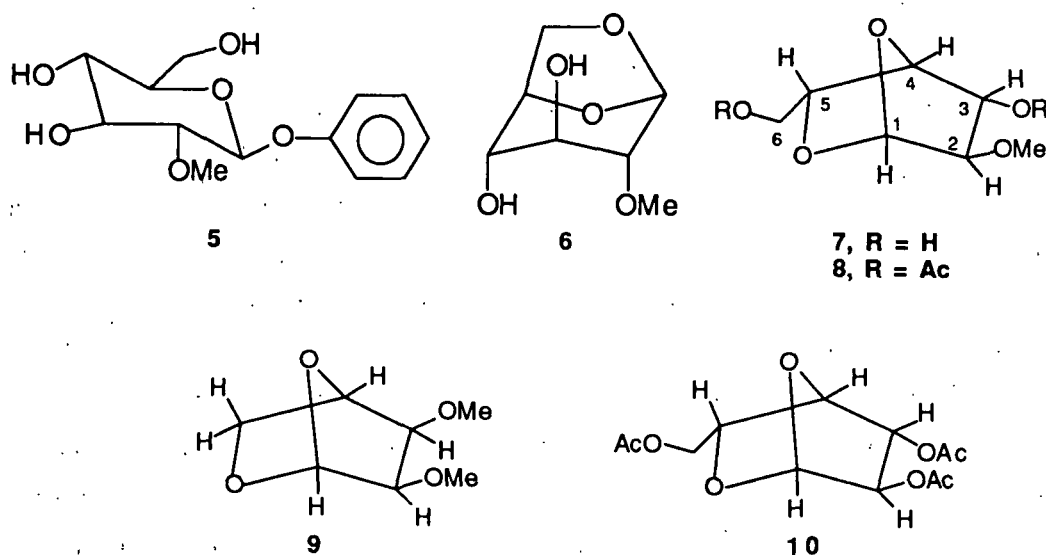
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our data that the amount of that pathway was underestimated. For degradations in NaOH alone, a 1.20 multiplying factor, which is the reciprocal of the levoglucosan yield noted in this study, could be applied to the amount of $S_N icB(2)$ mechanism originally determined. For 1,5-anhydro-2,3,6-tri-O-methyl-cellobiitol, the original 0.5 M NaOH data suggested a 67% $S_N icB(2)$ level,[10] but the adjusted value would be 80%. The multiplying factor was not extended to sodium sulfide studies[9] because the reaction conditions were quite different.

Phenol formation (Table 4), which provided another means to monitor phenyl β-D-glucopyranoside degradation, was close to stoichiometric for all cases, except in the sodium sulfide experiment. Further experimental work did not reveal the cause of phenol loss in the latter case.

**Products from Phenyl 2-O-methyl-β-D-glucopyranoside Degradation**

Two neutral products were found in the phenyl 2-O-methyl-β-D-glucopyranoside (5) (Figure 4) degradation at 171.6°C in 2.5 M NaOH. One product, 1,6-anhydro-2-O-methyl-β-D-glucopyranose (6), was identified against an authentic standard. The other product is believed to be 1,4-anhydro-2-O-methyl-α-D-glucopyranose (7).

^{1}H and ^{13}C NMR analyses of 8 (acetylated 7) indicated the absence of a phenyl ring, presence of one methoxyl and two acetate groups, and the presence of a low field ^{1}H signal (5.52 *ppm*). The two acetyl groups suggested the formation of an anhydro ring, along with the presence of the pyranose ring. The low field signal is indicative of an anhydro ring at C(1), an acetal carbon;[24] the singlet at C(1) suggested a rigid structure in which C(1) and C(2) protons 90° are to each other.[25] The C(1)-proton postulated for 8 and the C(1)-proton of 1,4-anhydro-2,3-di-O-methyl-α-D-ribopyranose (9)[26] are in very similar environments and would be expected to have similar ^{1}H NMR resonances. Indeed, the C(1)-H signals for both 8 and 9 appear as singlets at 5.52 *ppm*. Also, 8 and 2,3,6-tri-O-acetyl-1,4-anhydro-α-D-glucopyranose[27] (10) have nearly identical C(5)-C(6) environments and show a great deal of similarities in the 3.9 to 4.8 *ppm* region of their ^{1}H NMR spectra. These data

5        6        7, R = H
                     8, R = Ac

9              10

help support the spectral assignments made for **8**.

Figure 4 presents a possible scheme for the formation of the 1,6-
and 1,4-anhydrides, **6** and **7**, from treatment of phenyl 2-O-methyl-β-D-
glucopyranoside (**5**) with alkali. Capon[28] has postulated a similar
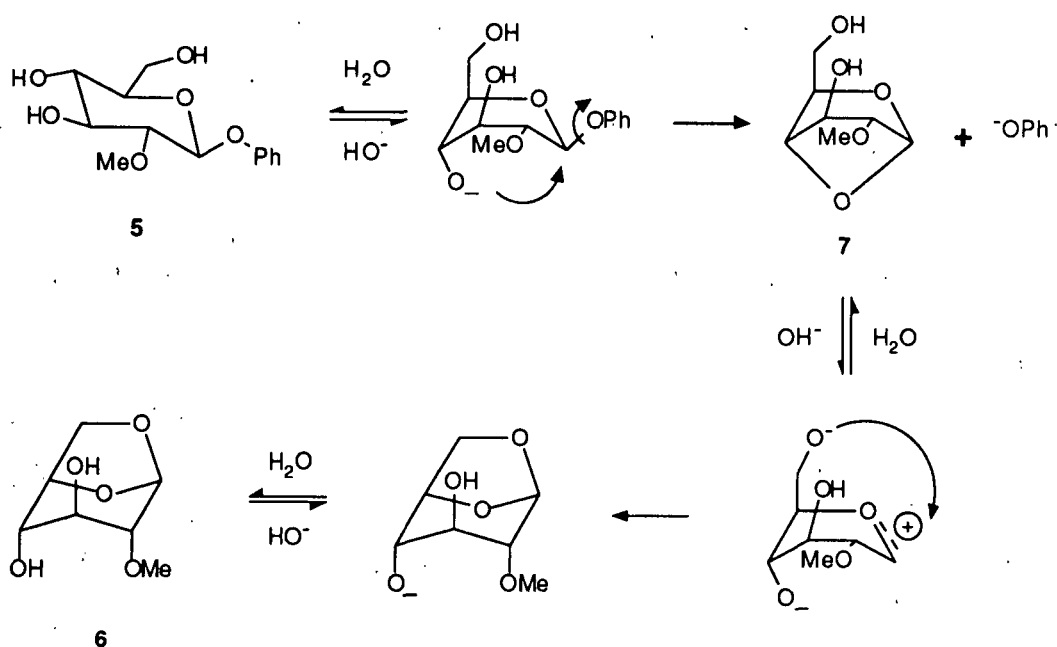


Figure 4.      Proposed mechanism for alkaline degradation of phenyl
                 2-O-methyl-β-D-glucopyranoside (**5**).

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scheme for the formation of 1,6-anhydro-β-D-mannopyranose during the alkaline degradation of phenyl β-D-mannopyranoside. In this scheme, the C(4)-oxyanion displaces the phenoxide ion at C(1), an intramolecular $S_N2$ displacement, to give the 1,4-anhydride 7. Analogous chemistry has been observed upon treating 2,3,6-tri-O-benzyl-1-fluoro-β-D-glucopyranose in alkali to give 1,4-anhydro-2,3,6-tri-O-benzyl-α-D-glucopyranose.[29] The 1,6-anhydride (6) is postulated to form via an $S_N1$ mechanism involving a C(6)-oxyanion and a C(1)-cation. In support of this sequence of steps, a time-product profile showed that the ratio of 1,4-anhydride to 1,6-anhydride was high initially, but decreased with time.

## CONCLUSIONS

The 100°C alkaline degradation of phenyl β-D-glucopyranoside exhibited a reaction rate constant similar to that obtained by Lai, *et al.*[13] and an 88% levoglucosan yield consistent with McCloskey and Coleman.[3] The 170°C-degradation of phenyl β-D-glucopyranoside appears to go by an $S_NicB(2)$ reaction pathway. The lower conversion to levoglucosan with $Na_2S$ present (72%) and the less than quantitative yield observed with NaOH alone (82%) suggested that 1,2-anhydro-α-D-glucopyranose, a key intermediate in the $S_NicB(2)$ reaction, was being partially diverted to acidic products by the nucleophiles ($HO^-$ and $HS^-$).

The data indicate that phenyl β-D-glucopyranoside reacts similarly at 100°C and 170°C. From the observed levoglucosan yields for phenyl β-D-glucopyranoside and assuming a pure $S_NicB(2)$ mechanism in this case, it is now possible to estimate the amount of $S_NicB(2)$ mechanism occurring in other glucoside studies done at 170°C. This knowledge may be useful, because most of the glucosides exhibit multiple degradation pathways that produce nonunique degradation products.

## EXPERIMENTAL

### General Analytical Procedures

Melting points were determined on a Thomas Hoover capillary melting point apparatus calibrated against known compounds. Optical

rotations were performed on a Perkin-Elmer 141 recording polarimeter at room temperature. NMR spectra were recorded by Spectral Data Services (818 Pioneer, Champaign, IL 61820).

Gas liquid chromatography (GC) was performed on a Hewlett-Packard 5890 instrument utilizing a flame ionization detector and interfaced to a Hewlett-Packard 3392A integrator. Helium was used as the carrier gas at a flow rate of 30 mL min$^{-1}$. The column used was OV-1 on Supelcoport (100-120 mesh) in glass tubing (6 ft x 2 mm) rigged for on-column injection. Carbohydrate analyses were run using the conditions: injector, 275°C; detector, 300°C; and column, 130°C, for 1 minute, and 7°C min$^{-1}$ to 230°C. Phenol analyses were under the conditions: injector, 275°C; detector, 300°C; and column, 60°C, for 1 minute, and 7°C min$^{-1}$ to 110°C, and hold at 110°C for one minute.

Gas liquid chromatography/mass spectrometry was performed on a Hewlett-Packard 5895 system. The $^{18}$O phenol incorporation was determined using electron impact (EI) mass spectrometry and an OV-17 column. Operating conditions of the column were: start at 60°C and program at 7°C min$^{-1}$ to 300°C. The $^{18}$O enriched liquor was analyzed on Porapak Q by EI under isothermal conditions of 100°C. All other samples were analyzed on an OV-1 column by EI with column conditions starting at 130°C and programming at 7°C min$^{-1}$ to 300°C.

Materials Used

Samples of 1,6-anhydro-β-D-glucopyranose (levoglucosan),[9] phenyl β-D-glucopyranoside,[30] methyl α-D-glucopyranoside,[31] phenyl 2-O-methyl-β-D-glucopyranoside[32] were purified and crystallized prior to use; in each case the observed melting points and optical rotations agreed with literature values.[33-35]

Procedures for Kinetic Analysis

The high temperature kinetic samples were run in the modified fast flow reactor developed by Green et al.[19] Further description of the apparatus and procedures are provided by Molinarolo.[36]

All reaction solutions were made under oxygen-free nitrogen conditions. The carbohydrate reaction liquors contained model (0.01

16

M), methyl α-D-glucopyranoside internal standard (0.005 M), and oxygen-free water. All molarities shown in the parentheses are after mixing. The molarity of the reaction solution at room temperature accounts for thermal expansion of the liquids and mixing of equal volumes of reacting liquors. Sodium hydroxide reaction liquors were made from stock solution and diluted with oxygen-free water. Phenol internal standard, 4-isopropylphenol[37] (0.05 M), was added to all caustic reaction liquors prior to dilution. The sodium hydroxide molarity was measured by titration against potassium acid phthalate to a phenol-phthalein endpoint.

For salt effect experiments, sodium chloride was added with the sodium hydroxide stock solution prior to dilution. In the nucleophilic effect experiment, sodium sulfide stock was added with the stock sodium hydroxide prior to dilution. Sodium sulfide concentrations were measured by titration with 0.1 M mercuric chloride by an Orion silver/silver sulfide specific ion electrode and an Orion 901 ion-analyzer.[38] Samples were titrated to an endpoint of -450 to -400 mV. Liquor active alkali was determined by titration with 1.0 M HCl in the presence of formaldehyde to a phenolphthalein endpoint. The sodium hydroxide concentration was calculated by subtraction of the sodium sulfide concentration from the active alkali.[39]

Reaction Liquor Analysis

The carbohydrate reaction liquor sample (16 mL, ca. 0.01 mmol of glucoside) was neutralized to pH 7 with acetic acid (1 M). The solution was reduced *in vacuo* to a syrup. Isopropyl alcohol (reagent grade, 12 mL) was added to the syrup and the slurry was reduced *in vacuo* to dryness. The residue was acetylated overnight with pyridine/acetic anhydride (2:1, v/v, 2 mL) with gentle shaking. The reaction was quenched with cold water (10 mL), shaken for two minutes, and extracted with chloroform (2 x 5 mL). The chloroform layers were combined and washed with 1 M hydrochloric acid (2 x 75 mL) and water (3 x 10 mL). The chloroform layer was reduced *in vacuo* to dryness; the residue was transferred to a 4-mL vial with chloroform

(2 mL). The sample was reduced *in vacuo* to dryness to aid in the removal of any water that may have been carried over, and dissolved in ethyl acetate for GLC analysis.

The sample (16 mL, ca. 0.01 mmol phenolics) for phenol analysis was placed in a 50-mL Erlenmeyer flask and the NaOH concentration was adjusted to 0.5 M by addition of 5 M NaOH. Dimethyl sulfate (98%, 2 mL) was added and the flask was stoppered. The two phase solution was vigorously stirred for 15 minutes. Concentrated ammonium hydroxide (9 mL) was added to quench the excess dimethyl sulfate and the solution was stirred for another 15 minutes. The liquor was extracted with chloroform (2 mL) by stirring for two minutes. The chloroform layer was separated, placed in a 4-mL vial, and analyzed by GC.

### $^{18}$O Incorporation Experiment

Carbohydrate liquor (25 mL) was made as outlined above, but $^{18}$O water[40] was added prior to dilution to produce a final reaction liquor level of 8.6% $^{18}$O water. The sample was reacted in 2.5 M NaOH at 171.6°C for 20.62 seconds in the fast-flow reactor.

The phenol product with incorporated $^{18}$O was derivatized as outlined above. Analysis by GC/MS was used to measure the isotopic levels of $^{18}$O in the product and the water.[11]

### Degradation of 1 at 100°C and Methyl α-D-Glucopyranoside at 182°C

These degradations were performed in a bomb reactor as described earlier.[7-11] The low temperature degradation was performed at 100°C in 1.0 M NaOH with phenyl β-D-glucopyranoside as the reactant, while the salt experiment was performed at 181.6°C in 0.5 M NaOH and 2.0 M NaCl with methyl α-D-glucopyranoside. Reaction analyses were similar to those described above, but the internal standard was added after taking the sample.

### Phenyl 2-O-Methyl-β-D-Glucopyranoside Degradation

Phenyl 2-O-methyl-β-D-glucopyranoside (0.01 M) was reacted in 2.5 M NaOH for 24 hours at 171°C in a bomb reactor described earlier.[7-11] The solution was deionized with Amberlite MB-3 (H$^+$, OH$^-$) ion exchange resin (500 mL), and the resin was washed with water (1L). The

water fractions were combined and reduced *in vacuo* to a solid. The solid was acetylated with a mixture of pyridine and acetic anhydride (5 mL, 2:1, v/v) for two days with gentle agitation. The reaction was quenched with iced water (100 mL), stirred for 20 min, and extracted with chloroform (2 x 50 mL). The chloroform extracts were combined, washed with 1 M HCl (3 x 25 mL) and water (4 x 25 mL), and reduced *in vacuo* to a syrup.

The syrup was chromatographed on a silica gel column (Merck Kieselgel 60, 35 cm x 1.2 cm) by elution with ethyl acetate-chloroform (1:5, v/v). Fractions yielded the unknown believed to be the peracetate of 1,4-anhydro-2-O-methyl-α-D-glucopyranose and the peracetate of 1,6-anhydro-2-O-methyl-β-D-glucopyranose. The samples were analyzed by GC/MS and NMR.

An authentic sample of 1,6-anhydro-2-O-methyl-β-D-glucopyranose[23] (2 mg), acetylated by the procedure outlined for the reaction samples, had: $^{13}$C NMR data (CDCl$_3$) *ppm* 170.2, 169.3 (-C(=O)CH$_3$), 100.2 (C-1), 76.9, 73.5, 70.6, 68.9, 65.2 (C-2, C-3, C-4, C-5, C-6), 58.3 (-OCH$_3$), 21.1 (-C(=O)CH$_3$); $^1$H NMR data (CDCl$_3$) *ppm* 5.50 (1H, s, -C(1)H-), 4.88 (1H, t, J = 1.4 Hz), 4.67 (1H, s), 4.60 (1H, d, J = 5.2 Hz), 4.09 (1H, d, J = 7.6 Hz), 3.79 (1H, d of d, J = 7.6 Hz and 5.8 Hz), 3.52 (3H, s, -OCH$_3$), 3.07 (1H, s); 2.17 (3H, s), 2.12 (3H, s, -C(=O)CH$_3$); and EI mass spectrum in *m/z* (relative intensity) 158 (32), 129 (56), 126 (12), 116 (17), 113 (78), 112 (46), 97 (12), 87 (64), 85 (13), 81 (41), 74 (100), 71 (11), 70 (9), 43 (51).

The fraction identified as 1,6-anhydro-2-O-methyl-β-D-glucopyranose (6), as acetate derivative, had: $^{13}$C NMR data (CDCl$_3$) *ppm* 100.1 (C-1), 73.5, 70.6, 68.8, 65.2, 58.4 (-OCH$_3$), 21.1 (-C(=O)CH$_3$) [The NMR spectrum of the acetylated 1,6-anhydro-2-O-methyl-β-D-glucopyranose obtained in the reaction was virtually identical to that described above, but due to the extremely small sample size not all of the $^{13}$C-signals were visible above the noise level.]; $^1$H NMR data (CDCl$_3$) *ppm* 5.50 (1H, s, -C(1)H-); 4.88 (1H, t, J = 2.5 Hz), 4.67 (1H,s), 4.60 (1H, d, J = 5.3 Hz), 4.09 (1H, d, J = 7.6 Hz), 3.79 (1H, d of d, J = 7.5 Hz and 6.4 Hz), 3.52 (3H, s, -OCH$_3$), 3.07 (1H, s), 2.18 (3H, s), 2.12 (3H, s, -C(=O)CH$_3$); and EI mass spectrum in *m/z* (relative intensity) 158 (12),

129 (22), 126 (5), 116 (8), 113 (28), 112 (18), 97 (5), 87 (37), 85 (7), 81 (20), 74 (64), 71 (6), 70 (6), 43 (100). [The EI mass spectrum was similar to the known, with the signal intensities being similar, but not identical.]

The fractions believed to be 1,4-anhydro-2-O-methyl-α-D-gluco-pyranose (7), as acetate derivative (8), had: $^{13}$C NMR data (CDCl$_3$) *ppm* 102.7 (C-1), 97.0, 85.9, 79.1, 75.9, 63.0, 57.2, 55.4, 20.7 (-C(=O)CH$_3$ ); $^1$H NMR data (CDCl$_3$) *ppm* 5.52 (1H, s, -C(1)H-), 4.90 (2H, t of d, J = 3.0 Hz and 7.6 Hz, C(6)H$_2$-), 4.42 (1H, d of d, J = 8.6 Hz and 11.7 Hz), 4.27 (1H, d of d, J = 11.7 Hz and 4.5 Hz), 4.12 (1H, t of d, J = 3.0 Hz and 8.3 Hz), 3.63 (1H, d, J = 1.4 Hz), 3.39 (3H, s, -OCH$_3$ ), 2.12 (3H, s, -C(=O)CH$_3$ ), 2.08 (3H, s, -C(=O)CH$_3$ ) [The NMR spectrum showed some impurities, presumably giving rise to weak signals in the 2.0-2.2 and 3.4-3.6 *ppm* regions]; and EI mass spectrum in *m/z* (relative intensity) 177 (7), 141 (4), 140 (4), 129 (26), 115 (13), 113 (32), 112 (21), 87 (71), 85 (11), 81 (13), 74 (20), 71 (11), 69 (15), 43 (100).

## ACKNOWLEDGMENTS

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