

DEGRADATION REACTION OF  $\alpha$ -D-GALACTOPYRANURONIC ACID  
IN ACETIC ANHYDRIDE-BASE SYSTEM

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$\alpha$ -D-Galactopyranuronic acid was converted to 1,2,3-tri-*O*-acetyl-4-deoxy- $\beta$ -L-threo-4-hexenopyranuronic acid (3) and 3-acetoxy-6-(diacetoxymethyl)-2*H*-pyran-2-one respectively by treatment with acetic anhydride-4-(dimethylamino)pyridine or acetic anhydride-acetic acid-pyridine. Further degradation of 3 in acetic anhydride-triethylamine gave comanic acid.

Generally, carbohydrates can be defined as polyoxyaldehydes in which sometimes the terminal carbon or the internal carbon exists as carboxyl or ketone group. This special structure of carbohydrates promotes dehydration by  $\beta$ -elimination under mild reaction conditions in the presence of acid or base, and a variety of aromatic compounds, such as 2-furaldehyde, 2-furoic acid, 5-hydroxymethyl-2-furaldehyde, reductic acid, phenolic compounds, catechols, chromones, etc. have been identified as degradation products.<sup>1)</sup> But this peculiar reactivity of carbohydrates is difficult to be controlled and has seldom been used for synthetic reactions, except for preparation of 2-furaldehyde<sup>2)</sup> and 5-hydroxymethyl-2-furaldehyde.<sup>3)</sup> Consequently, if ruling factors become clear, it would be possible to control degradation reactions of carbohydrates and to use them as synthetic reactions.

Based on these considerations, we have investigated degradation reactions of uronic acids in the acetic anhydride-base system and previously reported about the selective degradation reactions of triacetates of D-glucurono-6,3-lactone and D-mannurono-6,3-lactone in the acetic anhydride-base system leading to 3-acetoxy-6-(diacetoxymethyl)-2*H*-pyran-2-one (4) or 2,5,6,6-tetraacetoxy-2,4-hexadienoic acid by changing kind of base catalysts.<sup>4)</sup>

In the present investigation, degradation reactions of  $\alpha$ -D-galactopyranuronic acid (1) in the acetic anhydride-base system have been studied.

First, the effect of kind of base catalysts on degradation reactions of 1 was investigated. When the degradation reaction with triethylamine was carried out at room temperature for 24 h (volume ratio of triethylamine to acetic anhydride=10:1), degradation of 1 proceeded nonselectively giving 1,2,3-tri-*O*-acetyl-4-deoxy- $\beta$ -L-threo-4-hexenopyranuronic acid (3)<sup>5)</sup> and 4 in only 11.1% and 7.0% yields along with dark brown humine-like compound. On the other hands, when 4-(dimethylamino)pyridine was used in place of triethylamine, the selective conversion of 1 to 3 was achieved by treatment with acetic anhydride at room temperature for 24 h, and 3 was obtained in 94.5% yield along with a trace of 4. Further, when 1 was treated in the acetic anhydride-acetic acid-pyridine (10:3.3:1 volume ratio) system at 100 °C for 25 h,

Table 1. Degradation of  $\alpha$ -D-Galactopyranuronic Acid in Acetic Anhydride-Base System

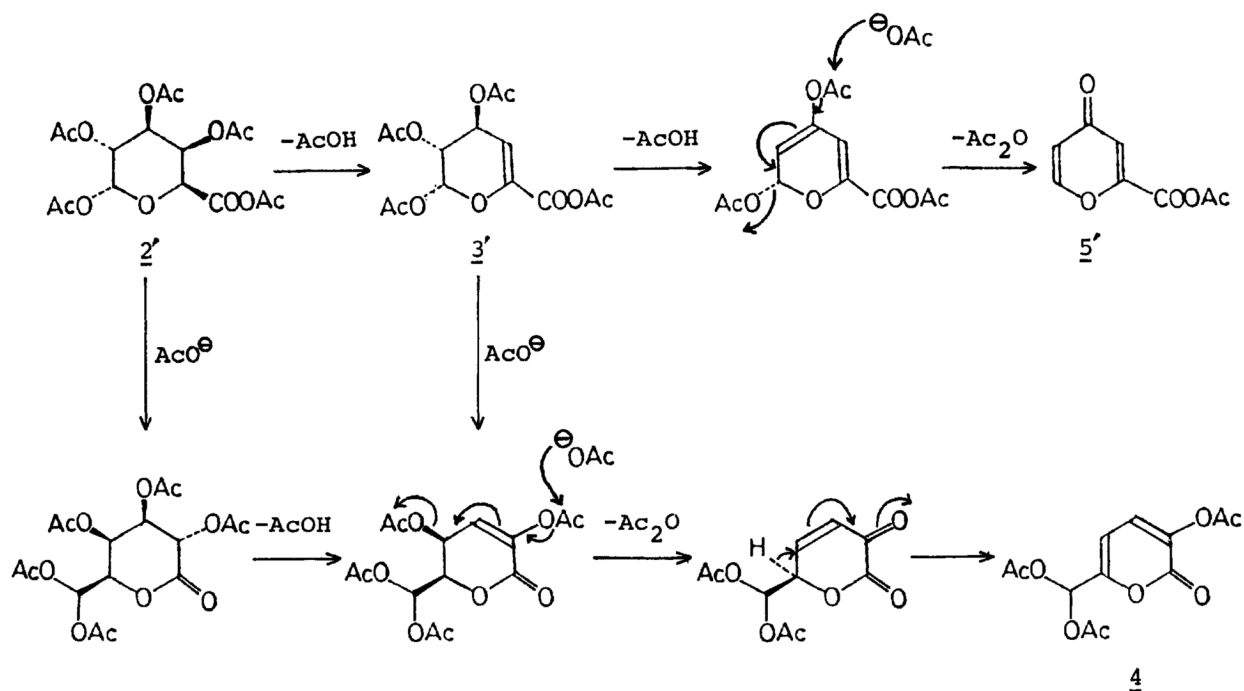
Base	Starting material	Reaction temp/°C	Reaction time/h	Yield/% <u>3</u>	Yield/% <u>4</u>	Yield/% <u>5</u>
Et <sub>3</sub> N	<u>1</u>	r.t.	24	11.1	7.0	-
	<u>1</u>	r.t.	24	94.5	trace	-
	<u>1</u>	100	25	trace	37.0	trace
Et <sub>3</sub> N	<u>2</u>	r.t.	24	82.0	5.7	-
*	<u>2</u>	55	42.5	38.5	18.7	12.5
*	<u>2</u>	70	22	26.2	24.5	24.3
*	<u>3</u>	70	30	-	4.5	65.3

4 was obtained as the main product in 37.0% yield along with a trace of 3 and 5.<sup>6)</sup> From these results, it was made clear that kind of base catalysts was one of the ruling factors in the degradation reaction of 1 in the acetic anhydride-base system. A typical example of the degradation reactions of 1 was carried out as follows. A solution of 0.5 g (2.57 mmol) of 1 and 1.0 g (8.20 mmol) of 4-(dimethylamino)-pyridine in 10 ml of acetic anhydride was stirred at room temperature for 24 h and then the reagent was evaporated under reduced pressure. The dark brown residual oil was extracted with water. The aqueous solution was treated with ion exchange resin (DOWEX 50W-X2), and 3 was obtained in 94.5% yield. From the water insoluble part, a trace of 4 was separated.

Next, to control the degradation reaction of 1 in the acetic anhydride-triethylamine system, 1 was acetylated prior to the degradation reaction. Acetylation of 1 proceeded selectively by the use of acetic anhydride as acetylating agent in the presence of trifluoroacetic acid or pyridine as a catalyst to give 1,2,3,4-tetra-*O*-acetyl- $\alpha$ -D-galactopyranuronic acid (2). 2 was degraded by treatment with acetic anhydride-triethylamine (10:1 volume ratio) at room temperature for 24 h to afford 3 in 82.0% yield along with 4 in 5.7% yield. At elevated temperatures, by the degradation reaction of 2 in acetic anhydride-triethylamine, 3 was obtained in lower yield, and 4 and 5 were also afforded as shown in Table 1. These degradation reactions of 2 in acetic anhydride-triethylamine were carried out in the similar way as shown above for the degradation reaction of 1 in acetic anhydride-base.

Although the mechanism of the conversion of 2 to 4 or 5 has not been investigated, it seems reasonable to assume that the first two steps of the degradation reaction of 2 to 5 in acetic anhydride-triethylamine were  $\beta$ -eliminations of the

the mixed anhydride (2'), and the final step was elimination of acetic anhydride catalyzed by acetoxy anion, as shown below. On the other hands, another direction



of the degradation reaction of 2 in acetic anhydride-triethylamine leading to 4 was assumed to proceed by combination of recyclization of 2' or 3' catalyzed by acetoxy anion,<sup>7)</sup> and eliminations of acetic acid and acetic anhydride. Thus, the concentration of acetoxy anion in the reaction system was assumed as a ruling factor to determine the directions of the degradation reaction of 2 to 4 or 5. And if 3 is used as a starting material in place of 2, the selectivity of  $\beta$ -elimination of 3' would be higher than that in the case of the degradation of 2, and 5 would be obtained selectively, because of the lower concentration of acetoxy anion existing with 3'.

Based on these speculations, the degradation reaction of 3 was tried in acetic anhydride-triethylamine as follows. A solution of 0.5 g (1.66 mmol) of 3 in a mixture of 10 ml of acetic anhydride and 1 ml of triethylamine was heated at 70 °C for 30 h. Then the reagents were evaporated under reduced pressure. The dark brown residual oil was partitioned between water and benzene. The aqueous layer was treated with ion exchange resin (DOWEX 50W-X2) and after evaporation of water, crystals of 5 were obtained in 65.3% yield. From the benzene layer, 4 was separated in 4.5% yield by TLC on silica gel.

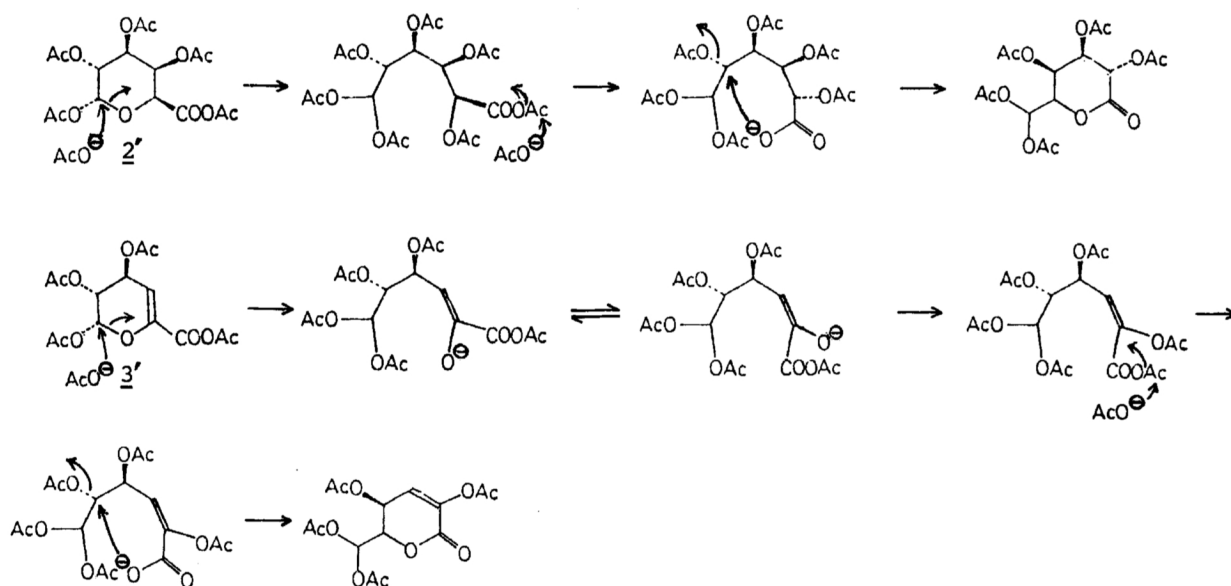
The results obtained by this investigation demonstrated the possibility of controlling degradation reactions of carbohydrates by suitable combinations of ruling factors. The scope of these degradation reactions and utilization of the degradation products such as 3, 4, and 5 are under investigation.

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#### References

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- 5) Physical constants of the product are as follows. IR(NaCl) 1740, 1654, 1420, 1370, 1220, 1070, 1010  $\text{cm}^{-1}$ ; NMR( $\text{CDCl}_3$ )  $\delta$  2.11(s, 3H,  $\text{CH}_3$ ), 2.15(s, 3H,  $\text{CH}_3$ ), 2.19(s, 3H,  $\text{CH}_3$ ), 5.27(dd, 1H, H-3,  $J=2.6$  and 7.0 Hz), 5.60(dd, 1H, H-2,  $J=3.6$  and 7.0 Hz), 6.20(d, 1H, H-1,  $J=3.6$  Hz), 6.42(d, 1H, H-4,  $J=2.6$  Hz), 7.96(s, carboxyl).
- 6) Mp 256-258  $^\circ\text{C}$  (decomp) (lit. 250  $^\circ\text{C}$ ), *Beilsteins Handbuch der Organischen Chemie*, **18**, 405(1934).
- 7) The mechanism of recyclization of **2'** and **3'** catalyzed by acetoxy anion was assumed as follows.



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