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THE FORMATION OF INTERMEDIATE LACTONES
DURING AMINOLYSIS OF DIETHYL XYLARATE

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ABSTRACT

The aminolysis of diethyl xylarate was found to proceed through intermediate lactones. In dimethyl sulfoxide at 30 °C in the presence of ethanolamine, the 1,5-diester is rapidly converted into ethyl D,L-xylaro-1,4-lactone, which reacts with the primary amine to give ethyl N-(2-hydroxyethyl)-D,L-xylaramide. This compound then forms N-(2-hydroxyethyl)-D,L-xylaramide-2,5-lactone, which in turn reacts with ethanolamine to produce the final product, N,N'-bis-(2-hydroxyethyl)-D,L-xylaramide. This sequence of reactions was established by ¹³C NMR spectroscopy.

INTRODUCTION

The aminolysis of diethyl galactarate has recently been shown to proceed through lactone intermediates.² These lactones account for the observed reactivity at room temperature of this diester towards primary amines. Xylarate diesters also exhibit reactivity towards amines³ and might therefore be expected to undergo lactonization during aminolysis. Accordingly, we followed the aminolysis of diethyl xylarate by ¹³C NMR spectroscopy to obtain evidence for the formation of intermediate lactones.

RESULTS AND DISCUSSION

Diethyl xylarate (1) dissolved in dimethyl sulfoxide in the presence of triethylamine formed a new compound that by ¹³C NMR spectroscopy could be assigned the structure for ethyl D,L-xylaro-1,4-lactone (2) in Table 1. This result suggests that lactonization of diethyl xylarate (1) is promoted by base

in a manner earlier observed for diethyl galactarate.² Diethyl xylarate was next allowed to react with two equivalents of ethanolamine in d_6 -dimethylsulfoxide at 30°C. High-field ^{13}C NMR spectra were acquired as the reaction proceeded. After 4 h the reaction was complete as shown by the transformation of the complex spectra of intermediates into the simple spectrum for the expected products, N,N' -bis-(2-hydroxyethyl)- D,L -xylaramide (5) and ethanol (Table 1). Since resonances could be assigned to carbons of the reaction species (1), (2), and (5), only the task of assigning resonances to the carbons of intermediates (3) and (4) remained.

In order to examine more closely the complex spectrum of a mixture of reaction species (1) through (5), the following stratagem was devised. Diethyl xylarate was allowed to react with just one equivalent of ethanolamine. The reactions stopped at a point determined by the consumption of all the base. A highly resolved spectrum (200 scans) of the resulting solution displayed resonances for all species. The group of low intensity resonances contained known resonances for the diester (1). The remaining low intensity resonances were assigned to the ethyl N -(2-hydroxyethyl)- D,L -xylaramide (3). The group of greater intensity resonances contained known resonances for ester-lactone (2) and for diamide (5). The remaining resonances, similar to those for (2), were assigned to N -(2-hydroxyethyl)- D,L -xylaramide-2,5-lactone (4). These assignments were consistent with the order of appearance and disappearance of resonances in spectra acquired during the course of the earlier, complete reaction. The assignments, intensities, and chemical shift values for all resonances are listed in Table 1. Data from the complete reaction indicate that lactonization of diester (1) is nearly complete (90%) within 20 min. The appearance of ester-lactone (2) and its disappearance through reaction with ethanolamine extended over a shorter period of about 10 min. The ester-amide (3) appears within 7 min from start of reaction and persists for about 20 min. Disappearance of (3) is caused by lactonization to produce the amide-lactone which appears within about 7 min from start of reaction and which persists at near steady state for over 50 min. Appearance of the final product, diamide (5), also occurs within about 7 min from start of reaction; its concentration reaches the level of completion within 4 h.

The aminolysis of diethyl xylarate differs from that of diethyl galactarate in two notable ways. One, the reactions are complete for DEX within 4 h, whereas aminolysis of DEG requires 18 h for completion under the same conditions.² Two, the intermediate ester-amide (3) observed during aminolysis of DEX was not seen during aminolysis of DEG.² The data in Table 1 indicate that lactonization of diethyl xylarate proceeds at a rate comparable to that for diethyl galactarate since in each instance the diester disappears within 20 min.² We are therefore led to conclude that the overall greater rate of aminolysis of DEX derives from a much greater rate of base attack on the lactone intermediates. Preliminary kinetic analysis even suggests that amine

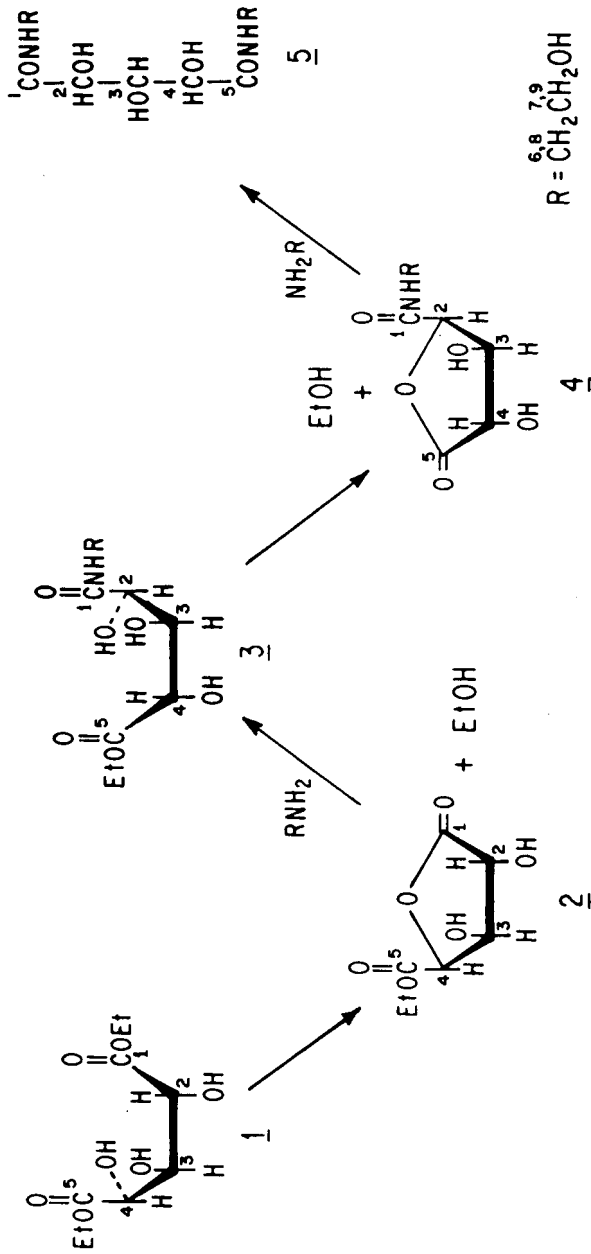


TABLE 1.
Relative ^{13}C -NMR Intensities During Ethanolaminolysis
of Diethyl Xylarate (1) in DMSO-d_6 ($\delta = 39.5$ ppm)

Species	Carbon-atom	Shift p.p.m.	Minutes at 30°														
			0	3	7	11	15	19	23	27	36	45	54	232			
<u>1</u>	C-1,5	172.29	20	14	6	3			1								
	C-2,4	71.10	28	22	8	4	3										
	C-3	73.18	15	12	4	3											
	C-6,8	60.23	25	19	8	5	3										
	C-7,9	14.20	13	*	5	3	3										
<u>2</u>	C-1	174.57			+		+										
	C-2	73.24			3	2											
	C-3	71.21			3	2	+										
	C-4	76.91			+		+										
	C-5	168.07			+		+										
	C-6	60.19					4	4	2	2							
	C-7	14.07		*	6	4	3	2	2								
<u>3</u>	C-1	172.44			3	3	3	2	2	2							
	C-2	71.74			5	4											
	C-3	72.59			4	4	3	3	3	2							
	C-4	71.40			4	4	4	3	3	2							
	C-5	172.32			5	3	3	3	2								
	C-6	41.13															
	C-7	59.80															
	C-8	60.23		*													
	C-9	14.20		*													
<u>4</u>	C-1	166.98					+						+				
	C-2	77.30			+		+	2		3	+						
	C-3	71.31			+		+		2	2	+						
	C-4	73.57					2		2	2							
	C-5	175.19					+										
	C-6	41.47			2	2	3		2	2							
	C-7	59.61				3	3	3	3	3	2	2	2				
<u>5</u>	C-1,5	172.56			3	6	8	10	12	13	15	17	17	22			
	C-2,4	71.82			4	6	8	9	12	12	13	15	16	20			
	C-3	72.27				3	5	5	6	7	7	9	8	11			
	C-6,8	41.53			6	8	11	11	13	14	15	17	19	23			
	C-7,9	59.68			5	8	10	10	13	14	15	16	18	23			
EtOH	C-1	56.07			7	9	11	11	13	13	13	14	14	15			
	C-2	18.50			4	5	7	7	7	8	7	8	8	9			
NH_2EtOH	C-1	63.32		31	17	14	12	10	9	8	6	5	4	3			
	C-2	44.09		19	13	12	10	10	9	8	6	5	5	3			

* Common resonances. + Resonance present but intensity below threshold level.

reaction with the xylaro-lactone intermediates (2) and (4) may be base catalyzed⁴ to a significantly greater extent than for the corresponding galactaro-lactone intermediates.

EXPERIMENTAL

Materials and Methods. Xylaric acid was prepared by nitric acid oxidation of xylose according to Chalov⁵ as modified by Wolfrom and Usdin.⁶ Ethanolamine was obtained from Aldrich.⁷

Proton decoupled ¹³C NMR spectra were determined at 90 MHz with a Bruker WH 360 pulse Fourier transform spectrophotometer. An initial spectrum of diethyl xylarate, 10% in d₆-dimethylsulfoxide, was obtained. 2.2 Equivalents of ethanolamine were added to the solution, and spectra in the constant intensity mode were recorded over 4 h to the completion of reaction.

Diethyl Xylarate. A solution of 2 g of crude xylaric acid in 100 mL of absolute ethanol plus 1 g of dry Amberlite 120-H⁺ resin⁸ was refluxed for 24 h. Resin was removed by filtration and the diester was recovered from the filtrate by rotatory evaporation. Recrystallization from diethyl ether (15 mL) gave 2.5 g (95% yield) of material. A portion of the diester was recrystallized (2X) to a constant mp of 69-70 °C. The ¹³C NMR spectrum (species 1 shifts in Table 1) supports the structure expected for the diethyl ester of a symmetrical trihydroxyglutaric acid (4).

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