SYNTHESIS OF MONO- AND DILACTONES FROM 2,7-DISUBSTITUTED 4-OCTENE-1,8-DIOIC ACIDS

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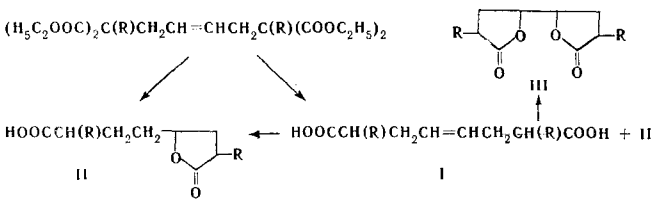
2,7-Disubstituted 4-octene-1,8-dioic acids are formed by heating the γ-lactones of 2,7-disubstituted 4-hydroxyoctane-1,8-dioic acids to 250°C. The bromination of these unsaturated dicarboxylic acids gives γ,γ'-dilactones of 2,7-disubstituted 4,5-dihydroxyoctane-1,8-dioic acids.

This paper is devoted to the synthesis of new mono- and dilactones on the basis of 2,7-disubstituted 4-octene-1,8-dioic acids (I). Lactones with this sort of structure have received very meager study [1, 2]. Starting acids I (Table 1) were obtained as in [3, 4] by the alkaline hydrolysis of the tetraethyl esters of 1,6-disubstituted 3-hexene-1,1,6,6-tetracarboxylic acids with subsequent decarboxylation of the free acids. The γ,δ-unsaturated acids are already partially cyclized during their preparation to form the γ-lactones of 2,7-disubstituted 4-hydroxyoctane-1,8-dioic acids (II). These lactones were synthesized in higher yields by the decarboxylation of I at 250-260°C and also by heating them in the presence of catalytic amounts of sulfuric acid (Table 2). The structures of the lactones (R = C_4H_9 in the case of II) were confirmed by the IR spectra, in which bands were observed at 1710 and 1760 cm^{-1} (vibrations of the carbonyl groups in the acids and γ-lactones) and at 3100-3300 cm^{-1} (OH in acids).



Unsaturated acids I are brominated in CCl_4 to give γ,γ'-dilactones of 2,7-disubstituted 4,5-dihydroxyoctane-1,8-dioic acids (III) (Table 3). There is a band at 1760 cm^{-1} in the IR spectrum of dilactone III (R = iso-C_5H_{11}), which confirms its lactone structure.

EXPERIMENTAL

2,7-Disubstituted 4-Octene-1,8-dioic Acids (Ia-h). With continuous stirring, 0.2 mole of the tetraethyl ester of the 1,6-disubstituted 3-hexene-1,1,6,6-tetracarboxylic acid was added to a hot solution of 50 g of sodium hydroxide in 50 ml of water, and the reaction mixture was heated on a water bath for 6 h. The resulting viscous mass was dissolved in the smallest possible amount of water, and the solution was extracted with ether and acidified with hydrochloric acid. The oily layer was separated from the aqueous layer, and the latter was extracted with ether. The ether extracts were added to the bulk of the product, and the mixture was dried with anhydrous magnesium sulfate. The ether was removed by distillation, and the residue was heated at 170-200° and ~100 mm. The resulting viscous mass was fractionated in vacuo. In most cases, the distillate began to crystallize immediately. The solid acids were recrystallized from

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TABLE 1. 2,7-Disubstituted 4-Octene-1,8-dioic Acids

Compound	R	bp, °C (mm)	mp, °C (from hexane)	d_4^{20}	n_D^{20}	Empirical formula	Found				Calc.,				Yield, %
							C, %	H, %	equiv. wt.	MR_D	C, %	H, %	equiv. wt.	MR_D	
Ia	CH_3	205—208 (5)	76	—	—	$C_{10}H_{16}O_4$	60,2	7,9	101	—	60,0	8,0	100	—	81
Ib	C_2H_5	205—210 (3)	78	—	—	$C_{12}H_{20}O_4$	63,2	9,1	115	—	63,2	8,8	114	—	70
Ic	C_3H_7	217—222 (3)	—	1,0343	1,4719	$C_{14}H_{24}O_4$	64,9	9,9	129	69,29	65,6	9,4	128	69,47	64
Id	n-C_4H_9	210—212 (1)	68	1,0048	1,4690	$C_{16}H_{28}O_4$	67,5	10,2	140	78,71	67,6	9,9	142	78,71	87
Ie	i-C_4H_9	210—212 (3)	78	1,0098	1,4670	$C_{16}H_{28}O_4$	67,5	9,9	143	78,04	67,6	9,9	142	78,71	69
If	n-C_5H_{11}	228—230 (3)	78	0,9813	1,4670	$C_{18}H_{32}O_4$	68,9	10,1	157	87,95	69,2	10,2	156	88,21	80
Ig	i-C_5H_{11}	223—225 (3)	74	—	—	$C_{18}H_{32}O_4$	69,3	10,3	157	—	69,2	10,2	156	—	61
Ih	$C_6H_5CH_2$	—	153*	—	—	$C_{22}H_{24}O_4$	75,2	7,3	174	—	75,0	6,8	176	—	78

*After decarboxylation, the reaction product began to crystallize and was recrystallized from alcohol.

TABLE 2. γ-Lactones of 2,7-Disubstituted 4-Hydroxyoctane-1,8-dioic Acids

Compound	R	bp, °C (mm)	d_4^{20}	n_D^{20}	Empirical formula	Found					Calc.					Yield, %	
						C, %	H, %	equiv. wt.		MR_D	C, %	H, %	equiv. wt.		MR_D	A	B
								in the cold	on heating				in the cold	on heating			
IIb	C_2H_5	201—203 (1)	1,0839	1,4703	$C_{12}H_{20}O_4$	63,2	8,8	228	115	58,70	63,2	8,8	228	114	58,62	12	86
IIc	C_3H_7	215—220 (3)	1,0471	1,4690	$C_{14}H_{24}O_4$	65,2	9,3	254	127	68,08	65,6	9,4	256	128	67,86	10	—
IId	n-C_4H_9	222—226 (3)	1,0162	1,4695	$C_{16}H_{28}O_4$	66,8	10,0	284	143	77,90	67,6	9,9	284	142	77,10	12	93
IIe	i-C_4H_9	245—246 (4)	1,0199	1,4670	$C_{16}H_{28}O_4$	67,1	10,0	286	140	77,25	67,6	9,9	284	142	77,10	11	91
IIg	i-C_5H_{11}	245—250 (3)	0,9980	1,4700	$C_{18}H_{32}O_4$	69,8	10,3	314	157	87,22	69,2	10,2	312	156	86,34	11	—

TABLE 3. γ,γ'-Dilactones of 2,7-Dialkyl-4,5-dihydroxyoctane-1,8-dioic Acids

Compound	R	bp, °C (mm)	mp, °C	Empirical formula	Found			Calc.			Yield, %
					C, %	H, %	equiv. wt.*	C, %	H, %	equiv. wt.*	
IIIb	C_2H_5	201—203 (3)	124	$C_{12}H_{18}O_4$	63,5	8,3	111	63,7	8,0	113	69
IIId	n-C_4H_9	226—227 (1)	107	$C_{16}H_{26}O_4$	68,6	9,9	138	68,1	9,2	141	87
IIIe	i-C_4H_9	229—230 (1)	134	$C_{16}H_{26}O_4$	68,3	9,3	143	68,1	9,2	141	73
IIIg	i-C_5H_{11}	236—240 (2)	135	$C_{18}H_{30}O_4$	69,9	10,3	156	69,7	9,7	156	75

*On heating.

hexane (Table 1). They were chromatographed in a benzene–carbon tetrachloride–ethanol–acetic acid system (4 : 4 : 2 : 1.5). The liquid (10-12%) remaining after separation of the crystals was fractionated repeatedly to give γ-lactones IIb-e, g (Table 2).

γ-Lactones of 2,7-Disubstituted 4-Hydroxyoctane-1,8-dioic Acids (II). A) The hydrolysis of the tetraethyl ester of the 1,6-disubstituted 3-hexene-1,1,6,6-tetracarboxylic acid and the workup of the hydrolysis product were similar to the methods described above. The acid remaining after removal of the ether was decarboxylated in vacuo (~100 mm) at 250-260°. Vacuum fractionation gave lactones II, the physical constants of which were in agreement with those of the compounds obtained above.

B) A mixture of 0.02 mole of acids Ib, d, e and 5 ml of 70% sulfuric acid was heated with vigorous stirring for 1 h at a temperature that was 5-10° above the melting point of the starting acid. The mixture was cooled and neutralized with potassium carbonate solution to give a slightly acidic mixture. The cyclization product was extracted with ether, and the ether extract was dried with anhydrous magnesium sulfate. The ether was removed by distillation, and the residue was fractionated in vacuo. The purity of the lactones was verified by chromatography on a thin layer of activity II aluminum oxide in a benzene–methanol–acetic acid system (3 : 1 : 0.5).

γ,γ'-Dilactones of 2,7-Disubstituted 4,5-Dihydroxyoctane-1,8-dioic Acids (III) (Table 3). A solution of 0.035 mole of bromine in 25 ml of carbon tetrachloride was added dropwise at −10 to −5° to a solution of 0.02 mole of acid I in 25 ml of carbon tetrachloride, and the mixture was allowed to stand overnight. The excess bromine was back-titrated with sodium thiosulfate solution, the oily layer was separated from the aqueous layer, and the latter was extracted with ether. The other extracts were added to the organic layer, and the mixture was dried with anhydrous sodium sulfate. The solvents were removed, and the residue was distilled at reduced pressure. The purity of the dilactones was verified on a thin, loose layer of activity II aluminum oxide in a benzene–acetone–ethanol system (50 : 17 : 1) with development of the chromatograms with iodine.

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