SYNTHESIS OF CYCLIC DIACETALS OF FUMARALDEHYDE, α,α'-DIBROMOSUCCINALDEHYDE, AND BUT-2-YNEDIAL

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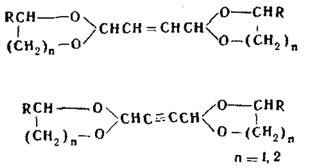
A number of cyclic diacetals of but-2-ynedial, fumaraldehyde, and α,α'-dibromosuccinaldehyde have been synthesized by the transacetalation of bis(dimethyl acetal)s of 1,2- and 1,3-glycols. The succinaldehyde derivatives have also been obtained by the bromination of the corresponding diacetals of fumaraldehyde.

We previously described the preparation of cyclic diacetals of succinaldehyde by the reaction of 2,5-dimethoxytetrahydrofuran with 1,2- and 1,3-glycols [1]. It has been established that these compounds possess the properties of myorelaxants [2].

It appeared of interest to study analogous derivatives containing double and triple bonds:



As has been shown previously, fumaraldehyde di(ethylene acetal) is formed from 2,5-dimethoxy-2,5-dihydrofuran and glycol with a 6% yield. In this work we performed the transacetalation of the bis(dimethyl acetal) of but-2-enedial with 1,2-and 1,3-glycols in the presence of p-toluenesulfonic acid in toluene. In this way it was possible to raise the yields of cyclic diacetals I–V (see Table 1) to 60–95%.

The bis(dimethyl acetal) of but-2-enedial formed by alkoxylation of furan under the action of bromine and methanol [3] possesses the trans configuration [4,5]. In its Raman spectrum we observed only one absorption band of the stretching vibrations of a trans-substituted C=C bond with a maximum in the range 1682–1690 cm^{-1}, and intense bands in the region of the nonplanar deformation vibrations of C—H at 918, 972, and 997 cm^{-1}. The Raman spectra of the cyclic diacetals I and II also have only one absorption band of the stretching vibrations of C=C, at 1691 cm^{-1}.

The transacetalation of but-2-ynedial bis(dimethyl acetal) with 1,2- and 1,3-glycols does not differ in principle from the transacetalation of fumaraldehyde bis(dimethyl acetal) and leads to the cyclic diacetals VI–IX with yields of 83–95% (see Table 1). The latter are less stable than I–V and polymerize on long storage.

The initial but-2-ynedial bis(dimethyl acetal) was obtained in good yield (83%) by a method somewhat modified by us [6] involving the dehydrobromination of dibromosuccinaldehyde diacetal with a suspension of powdered potassium hydroxide in tert-butyl alcohol. An attempt to use other alcohols (ethyl, isopropyl, and isoamyl) did not lead to the desired result.

In the bromination of fumaraldehyde bis(dimethyl acetal), it was found that in contrast to the information given previously (for example [6]), it is not a homogeneous product that is formed but the two isomeric dibromo derivatives X and XI. Similarly, the bromination of the cyclic diacetals I–IV in carbon tetrachloride gave in each case a mixture of two dibromo derivatives, one of which was crystalline and the other liquid, which did not yield to crystallization and vacuum distillation. With the exception of the isomeric dibromo derivatives of the cyclic diacetal II, the yields of which could not be determined accurately, mixture of almost equal amounts of the two isomers were formed. The crystalline isomers XII–XV obtained are shown in Table 2. We assume that the higher-melting isomer X and also the crystalline cyclic diacetals XII–XV are the meso forms and the low-melting isomer XI and the noncrystalline dibromo derivatives are the racemates. The IR spectra in carbon tetrachloride in the 500–650 cm^{-1} region showed that XI has intense absorption with maxima of 581 and 641 cm^{-1}, while X absorbs intensively at 567 cm^{-1} and only slightly at 581 cm^{-1}. All the crystalline isomers XII–XV also have intense bands with a maximum at 567 ± 2 cm^{-1} and a weak band at 580–585 cm^{-1}. After comparison of these data with the features of the IR spectra of the isomeric dibromostilbenes [7,8] the absorption bands of XI at 581 and 641 cm^{-1} must apparently be ascribed to the stretching vibrations of the C—Br bond of the racemic mixture of optically active forms in the skew conformation and in the trans conformation and the absorption bands of X and XII–XV at 567 cm^{-1} to the deformation vibrations of the C—H bond in the hindered conformation of the meso form. The weak band at 580–585 cm^{-1} shows the presence of only a small amount of the skew conformation, which in this case is energetically less favorable, in the meso form.

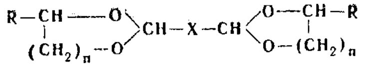
The dibromosuccinaldehyde bis(dimethyl acetal)s (X, XI) also undergo the transacetalation reaction in the presence of p-toluenesulfonic acid and glycols. Thus, by independent synthesis (method 2), X gave the cyclic diacetals XII–XV analogous to those obtained above by the bromination of the cyclic diacetals of fumaraldehyde (method 1).

The PMR spectra confirm the structure of the compounds obtained and show the low rate of inversion of the dioxane rings and the equatorial position of the bridge carbon atoms.

EXPERIMENTAL

The initial fumaraldehyde bis(dimethyl acetal), obtained as described by Makin and Telegina [3], was subjected to two vacuum distillations through a Widmer column 50 cm high. Fractions with the constants given

Table 1



Compound	X	n	R	Bp, °C (pressure, mm)	Mp, °C	n_D^{20}	d_4^{20}	MR_D		Empirical formula	Found, %		Calculated, %		Yield, %
								found	calculated		C	H	C	H	
I	CH=CH	1	H	—	90—91	—	—	—	—	$C_8H_{12}O_4$	56.08	7.08	55.80	7.03	60
II*	CH=CH	1	CH_3	97—103 (1)	—	1.4580	1.092	50.00	50.08	$C_{10}H_{16}O_4$	60.24	8.23	59.98	8.06	84
III	CH=CH	2	H	—	91—92	—	—	—	—	$C_{10}H_{16}O_4$	60.17	8.18	59.98	8.06	95
IV*	CH=CH	2	CH_3	—	75—85	—	—	—	—	$C_{12}H_{20}O_4$	63.10	8.92	63.12	8.83	95
V*	CH=CH	1	CH_2Cl	160—163 (0.5)	—	1.4930	1.313	59.52	59.82	$C_{10}H_{14}Cl_2O_4$**	44.19	5.34	44.51	5.24	82
VI	C≡C	1	H	115—117 (1.5)	51—52	—	—	—	—	$C_8H_{10}O_4$	56.61	6.16	56.47	5.92	83
VII*	C≡C	1	CH_3	115—120 (1.5)	—	1.4590	1.092	48.71	48.55	$C_{10}H_{14}O_4$	60.39	7.25	60.59	7.12	85
VIII	C≡C	2	H	—	102—103	—	—	—	—	$C_{10}H_{14}O_4$	60.42	7.19	60.59	7.12	95
IX*	C≡C	2	CH_3	—	75—80	—	—	—	—	$C_{12}H_{18}O_4$	63.58	8.06	63.69	8.02	94

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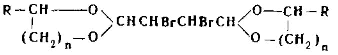
*Mixture of stereoisomers the existence of which is explained by the presence of two asymmetric carbon atoms in the acetal rings.

**Found, %: Cl 25.94. Calculated, %: Cl 26.35.

Table 2



Compound	n	R	Mp, °C	Empirical formula	Found, %			Calculated, %			Yield, %	
					C	H	Br	C	H	Br	method	method
XII	1	H	131—132	$C_8H_{12}Br_2O_4$	29.22	3.83	48.80	29.00	3.62	48.40	50	75
XIII*	1	CH_3	68—73	$C_{10}H_{16}Br_2O_4$	33.19	4.55	44.39	33.30	4.47	44.30	21	80
XIV	2	H	155—156	$C_{10}H_{16}Br_2O_4$	33.32	4.61	44.38	33.30	4.47	44.30	52	73
XV*	2	CH_3	123—130	$C_{12}H_{20}Br_2O_4$	37.18	5.32	40.98	37.10	5.19	41.18	45	87

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*Mixture of stereoisomers, the existence of which is due to the presence of two asymmetric carbon atoms in the acetal rings.

in the literature [9] were collected: bp 103–105° C (25 mm), n_D^{20} 1.424–1.426.

General procedure for obtaining the cyclic diacetals. A mixture of 0.1 mole of a bis(dimethyl acetal), 0.2 mole of the appropriate glycol, and 0.1 g of p-toluenesulfonic acid in 200 ml of toluene was heated in a Wood's metal bath in a flask fitted with a stirrer and a condenser for downward distillation. With vigorous stirring at a bath temperature of 100 to 120° C, 20–25 ml of a mixture of methanol and toluene was distilled off. After cooling, the main solution was washed with an aqueous solution of potassium carbonate and dried, and the toluene was distilled off under a gentle vacuum. The residue was crystallized from methanol or ethanol or distilled in vacuum.

Bromination of the methyl diacetal of fumaraldehyde. With stirring and cooling, 88.0 g (0.55 mole) of bromine in 50 ml of carbon tetrachloride was added over 2 hr to a solution of 88.0 g (0.5 mole) of fumaraldehyde bis(dimethyl acetal) in 100 ml of carbon tetrachloride, the temperature being kept at 0 to +10° C. The mixture was stirred at room temperature for a further 1 hr 30 min, and the solvent was distilled off in vacuum in a current of nitrogen. The residue was treated with 100 ml of petroleum ether, and the precipitate that deposited was filtered off and washed with 50 ml of cooled petroleum ether. This gave 45–50 g (27–30%) of X. Mp 94–95° C (from 50% methanol). Found, %: C 28.71; H 4.80; Br 47.49. Calculated for $C_8H_{16}Br_2O_4$, %: C 28.50; H 4.76; Br 47.60. Another 100 ml of petroleum ether was added to the filtrate, and the mixture was cooled to −50° C and filtered. The residue was washed with cooled petroleum ether. This gave 70–76 g (42–45%) of XI. Mp 42–43° C (from 50% methanol). Found, %: C 28.52; H 4.66; Br 47.18. Calculated for $C_8H_{16}Br_2O_4$, %: C 28.50; H 4.76; Br 47.60.

2-Butynedial bis(dimethyl acetal). A mixture of 33.6 g (0.1 mole) of X or XI, 28 g (0.5 mole) of powdered caustic potash, and 150 ml of tert-butyl alcohol was boiled with stirring for 6 hr. The cooled solution was decanted off, and this was followed by washing with water, extraction with ether, drying, and distillation. This yielded 14.5 g (83%) of 2-butynedial bis(dimethyl acetal), bp 96–98° C (11 mm), n_D^{20} 1.4345 [according to the literature [10]: bp 97.5° C (11 mm), n_D^{20} 1.43447].

Cyclic diacetals of dibromosuccinaldehyde (XII–XV). Method 1. At 0° C, 8.8 g (0.055 mole) of bromine in 10 ml of carbon tetrachloride was added to a solution of 0.05 mole of one of the diacetals I–IV in 20 ml of carbon tetrachloride, and the mixture was then kept at room temperature for 2 hr. The dibromo derivatives XII and XIV so formed crystallized out and were filtered off. The carbon tetrachloride was distilled off from the reaction mixture containing the XIII, and the residue was crystallized at about 0° C and was then filtered off. The carbon tetrachloride was also distilled off from the reaction mixture containing the dibromo derivative XV, and then 15–20 ml of petroleum ether was added to the residue to precipitate the XV, which was filtered off. All the dibromo derivatives were recrystallized from ethyl acetate with dry ice cooling.

Method 2. The diacetals XII–XV were obtained by the transacetalation of X by the general method. After the mixture of methanol and toluene had been driven off, activated carbon was added to the hot solution and it was filtered. On cooling, the dibromo derivatives XII and XIV crystallized out, and they were filtered off. The toluene was distilled off from the solutions containing the dibromo derivatives XIII and XV in vacuum. The residue was treated with petroleum ether and the mixture was cooled to −50° C and filtered. Recrystallization was carried out in the same way as before. Mixtures with the corresponding dibromo derivatives obtained by method 1 gave no depression of the melting point.

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