SYNTHESIS OF 2, 6-DERIVATIVES OF 1, 4-DIOXANE

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Stereoisomers of 6-halomethyl-2-hydroxymethyl-1, 4-dioxanes have been obtained via the cyclization of the monoallyl ether of glycerol. The stereoisomeric bromides differ considerably in their physical properties. The bromine atoms of the stereoisomers differ in their reactivity towards thiourea.

In 1943, A. N. Nesmeyanov and I. F. Lutsenko [1] described a method for obtaining 2, 6-bis(iodomethyl)-1, 4-dioxane from diallyl ether. Considerably later, Summerbell et al. [2, 3] isolated the cis (mp 92° C) and the trans (mp 71°—72° C) isomers of this compound and demonstrated their structures, and in the case of the cis isomer observed the considerable passivity of the iodine atoms in substitution reactions. Assuming a molecular model of 1, 4-dioxane with the ring in the chair conformation, the authors came to the conclusion that in the case of the cis isomer of 2, 6-bis (iodomethyl)-1, 4-dioxane the substituents occupied the more symmetrical, either diequatorial or diaxial positions, while the trans isomer corresponded to the less symmetrical equatorial-axial configuration. They stated that the IR spectra of the stereoisomers recorded in chloroform solution had differences in the 10.3–11.6-μ region.

It appeared of interest to obtain liquid stereoisomers of 2, 6-derivatives of 1, 4-dioxane and to compare their physical properties and make a more accurate assignment of the frequencies in the IR spectra.

We have synthesized 2-hydroxymethyl-6-iodomethyl-1, 4-dioxane (I) in the form of a mixture of stereoisomers by a method given in a US patent [4]. We found that in this method of synthesis the higher-boiling isomer Ib was obtained in extremely small amount and underwent decomposition when an attempt was made to distil it in vacuum.

In order to obtain more stable and comparatively low-boiling stereoisomers, we decided to synthesize 6-bromomethyl-2-hydroxymethyl-1, 4-dioxane (II) and study, even if only qualitatively, the activity of the bromine atom in the two stereoisomers in substitution reactions, particularly those with thiourea. As was expected, the considerable difference in the boiling points of the stereoisomers enabled them to be separated fairly completely.

It was found from a study of the reactions with thiourea that the high-boiling isomer IIb reacts considerably more slowly, with only 3% reaction taking place in 12 hr (Volhard titration), while with the low-boiling isomer IIa it was complete in 2.5 hr.

By alkylating the isothiouronium salts IIa and IIb, we obtained the corresponding sulfides IIIa and IIIb. The properties and analyses of the compounds synthesized are given in the table, and their IR spectra will be discussed in a subsequent communication.

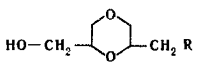
EXPERIMENTAL

2-Hydroxymethyl-6-iodomethyl-1, 4-dioxane (I) was obtained by Werner and Sholz's method [4].

6-Bromomethyl-2-hydroxymethyl-1, 4-dioxane (II). A 2-liter conical flask was charged with 216 g (1 mole) of mercuric oxide, 1 l of water, and 88.5 ml of 56% nitric acid and, with stirring 120 ml (1 mole) of glycerol monoallyl ether was added in portions. Then the reaction mixture was treated with a saturated aqueous solution of potassium bromide. The resinous precipitate that deposited was transferred to a reactor and treated with a mixture of 600 ml of chloroform and 150 ml of water. To the boiling solution was rapidly added 50 ml (1 mole) of bromine, the precipitate of mercuric bromide was separated off, and the chloroform layer was dried with magnesium sulfate. After the chloroform had been distilled off, the residue was fractionated in vacuum. The yield of a mixture of stereoisomers was 120 g (57% of theoretical). Redistillation in vacuum through an efficient column gave 70 g of IIa and 50 g of IIb.

6-Ethylthiomethyl-2-hydroxymethyl-1, 4-dioxane (III). By a published method [5], starting from 11.8 g (0.056 mole) of IIa, 4.2 g (0.056 mole) of thiourea, 7.25 ml (0.09 mole) of ethyl iodide, and 12 g (0.3 mole) of sodium hydroxide in 150 ml of 50% ethanol we obtained 5.5 g of IIIa.

Characteristics of 2,6-Derivatives of 1, 4-Dioxane



Compound	R	Bp, °C (press., mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Empirical formula	Found, % C	Found, % H	Found, % halogen	Found, % S	Calculated, % C	Calculated, % H	Calculated, % halogen	Calculated, % S	Yield, %
Ia	I	128 (9) decomp.	1.7995	1.5452	45.3	45.3	$C_6H_{11}IO_3$	27.8	4.3	50.1	—	27.9	4.27	49.2	—	50
Ib	I	150 (1)	—	—	—	—	"	—	—	—	—	—	—	—	—	6
IIa	Br	110 (0.5)	1.5866	1.5094	39.8	40.3	$C_6H_{11}BrO_3$	34.68	5.67	37.57	—	34.1	5.21	37.9	—	33
IIb	Br	173 (0.5)	1.6652	1.5261	39.0	40.3	"	34.38	5.87	38.18	—	34.1	5.21	37.9	—	25
IIIa	SC_2H_5	131 (1)	1.1442	1.5032	49.7	49.6	$C_8H_{16}SO_3$	50.35	8.60	—	16.6	50.0	8.32	—	16.9	55—60
IIIb	SC_2H_5	—	—	1.5065	—	—	"	50.8	8.35	—	16.58	50.0	8.32	—	16.9	15

Compound **IIIa**, with the same constants, was obtained similarly from **Ia**. With the same ratios and the same conditions, **IIb** gave **IIIb** (the time of the reaction with thiourea was increased to 30 hr). When an attempt was made to distil it in vacuum the **IIIb** decomposed. It was analyzed in the crude state.

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