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Chemistry of Dioxacyclanes: VII.[1] Synthesis of 1,3-Dioxolane Derivatives from 3-(2-Propenyloxy)propane-1,2-diol and Their Properties

A. Kh. Kerimov

Institute of Polymeric Materials, Academy of Sciences of Azerbaijan, Sumgait, Azerbaijan

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Abstract — 2,4-Disubstituted 1,3-dioxolanes were synthesized by reactions of benzaldehyde and its *para*-chloro derivatives, as well as 3-cyclohexenecarboxaldehyde with 3-(2-propenyloxy)-1,2-propanediol. The products were brought into bromination, dichlorocarbene addition, and epoxidation reactions. It is found that when both components of the heterogeneous reaction of dioxolane ring formation have a double bond, the acid catalyst in strongly deactivated.

Dioxolane derivatives deserve attention as prospective pharmaceuticals. They have found applications as anesthetics [2] and sedatives [3], as well as perfumes [4] and monomers for practically important polymers, including those used in contact lenses [5]. However, there is scarce information in the patent and periodical literature concerning synthesis of 1,3-dioxolanes from unsaturated diols and properties of such compounds, while the available data are not infrequently contradictory [6, 7].

The present work reports the synthesis of 2-phenyl-, 2-*p*-chlorophenyl-, and 4-(2-propenyloxymethyl)- 2-(3-cyclohexenyl)-1,3-dioxolanes from benzaldehyde, its *p*-chloro derivative, 3-cyclohexenecarbaldahyde, and 3-(2-propenyloxy)-1,2-propanediol in the presence of KU-2 cation exchanger (H^+ form) or TsOH, as well as some transformations of the products.

$$CH_2{=}CHCH_2OCH_2\underset{\displaystyle CH_2OH}{\underset{|}{C}}HOH + R{-}CH{=}O$$

I **II–V**

$$\xrightarrow[-H_2O]{} \underset{\displaystyle CH_2}{\underset{\|}{C}}HCH_2OCH_2{-}\text{(dioxolane ring)}{-}R$$

VI–IX

$$CH_2{=}CHCH_2OCH_2\underset{O}{CH}{-}CH_2 + p\text{-}ClC_6H_4CHO \xrightarrow{H^+} \textbf{VII},$$

R = C_6H_5 (**II, VI**), *p*-ClC_6H_4 (**III, VII**), 3-cyclohexenyl (**IV, VIII**), 3,4-dibromocyclohexyl (**V, IX**).

By GLC we studied the effect of steric and electronic factors on the rate of reaction of compounds **I** and **II**–**V**, and also the effect on the yield of the target products **VI**–**IX** of temperature, reactant ratio, catalyst nature, and reaction time. The consumption of substituted dioxolanes **VI**–**IX** was estimated by the internal calibration technique [8] using as standards diethyl and dipropyl phthalates. The retention-time order of the components of the reaction mixture (on an example of the synthesis of compound **VIII**) is as follows: toluene (solvent) < 3-cyclohexenecarboxaldehyde (**IV**) < 3-(2-propenyloxy)-1,2-propanediol < dipropyl phthalate (standard) < 4-(2-propenyloxymethyl)-2-(3-cyclohexenyl)-1,3-dioxolane (**VIII**).

The example of the synthesis of compound **VII** was used to find that the optimal reaction temperature is 130°C. Raising the temperature has almost no yield effect, while its lowering slows down the reaction. The reaction is performed in toluene (or other inert solvents) at an aldehyde–diol molar ratio of 1 : 1.2. The catalyst (KU-2) is added in a 0.3% proportion to aldehyde **II**–**V**. The reaction time is 5 h. The yield of compound **VII** is 82%.

To assess the effect of the substituent in the carbonyl component on the reactivity of the latter we reacted benzaldehyde (**II**), *para*-chlorobenzaldehyde (**III**), and an aldehyde with a nonaromatic substituent with the same number of carbon atoms in the ring, 3-cyclohexehecarboxaldehyde (**IV**).

It was found that the initial rate of dioxolane ring formation for aldehydes **II** and **III** ($V_0 \times 10^{-4}$) is 1.35 and 1.74 mol l^{-1} s^{-1}, which is much higher than the corresponding value for compound **IV** (0.285 mol l^{-1} s^{-1}). Thus, in the optimal conditions, the yields of the target products with aldehydes **II** and **III** are 76 and 82%, respectively, while with aldehyde

[1] For communication VII, see [1].

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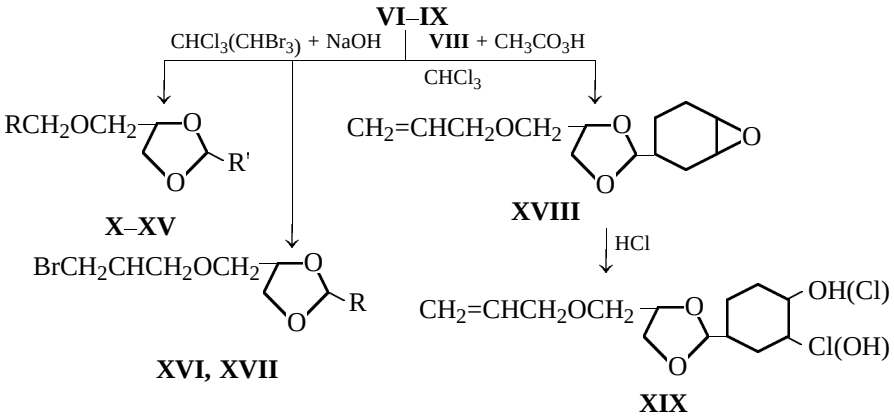
IV the yield is no higher than 16%. These results are inconsistent with the experimental data for the reactions of the latter with 1,2-propanediol or 3-chloro-1,2-propandiol [9, 10], where the yield of the corresponding dioxolane is as high as 78%. Moreover, the yield of compound **VIII** in the reaction in a homogeneous system with TsOH instead of KU-2 is sharply increased (85%). Intermittent addition of fresh portions of KU-2 to the system, too, slightly increases the yield of compound **VII**. The above findings suggest that the difficult reaction between **IV** with **I** is more likely associated with a change in the catalyst activity (as the result of increased unsaturation of the system) than in the reactivity of compound **IV**. Apparently, when the reagents each contain a double bond and, consequently, the target product contains two double bonds, adsorption saturation of the cation-exchanger surface takes place, thus blocking sulfo groups of the catalyst [11] and much reducing its activity.

It was found that dioxolanes containing a double bond are convenient objects for synthesis of their *gem*-dichloro(dibromo)cyclopropane derivatives. From dioxolanes with two double bonds, polyhalogenated polycyclic compounds [12] are formed, which can find diverse industrial applications. Thus, reactions of dichlorocarbene generated from $CHCl_3$ and 50% aqueous NaOH [13] with compounds **VI, VII**, and **IX** and of dibromocarbene with compound **VII** provide 2-substituted 4-[2,2-dichloro(dibromo)cyclopropylmethoxymethyl]-1,3-dioxolanes **X**–**XII** and **XIII**, respectively. With compound **VIII**, depending on conditions, dichlorocarbene selectively adds either to one or two double bonds of the ring to give monoadduct **XIV** or diadduct **XV** (see table). Compounds **VI, VII** were shown to be brominated by the double bond, affording *trans*-dibromo derivatives **XVI, XVII** in high yields (see table). However, compound **VIII** which contains two double bonds could not be selectively brominated by one of them. Therefore, compound **IX** was prepared indirectly by reacting compound **I** with aldehyde **V**; the latter was obtained by bromination of compound **IV** and used *in situ*.

Epoxidation of the synthesized 1,3-dioxolanes with 55% peracetic acid in chloroform revealed a considerable difference in the reactivity of the ring and 2-propenyl double bonds: With any amount of peracetic acid, the reaction occurs highly selectively by the ring double bond and yields (with compound **VIII**) 4-(2-propenyloxymethyl)-*cis*-2-(3,4-epoxycyclohexyl)-1,3-dioxolane (**XVIII**). Under these conditions, as would be expected, compounds **VI** and **VII** undergo no oxidation.

The composition of compounds **VI**–**IX** and their transformation products was proved by the elemental analyses, and their structures, by the molecular weights and ^{1}H NMR and IR spectra. Analysis of compounds **VI**–**IX** by GLC shows that they are mixtures of two isomers which give well-resolved peaks with a 55:45 ratio. However, we failed to separate these isomers. The ^{1}H NMR spectra of compounds **VI**–**XVII**, too, reveal the presence of *cis* and *trans* isomers (see Experimental). Compound **VII** was also synthesized from 3-(2-propenyloxy)-1,2-epoxypropane in the presence of H_2SO_4 (ρ 1.84 g/cm^3) by the procedure in [14] (yield 19%).

The IR spectrum of epoxide **XVIII** contains absorption bands at 800 and 920 cm^{-1}, assignable to the epoxy group. The presence of the latter was also proved by the conversion of compound **XVIII** into chlorohydrin **XIX** (a mixture of regioisomers). The IR spectrum of compounds **XIX** lacks bands at 800 and 920 cm^{-1} and contains a broad band at 3450–3500 cm^{-1} characteristic of associated OH group.



R = 2,2-dichlorocyclopropyl, R' = C_6H_5 (**X**), *p*-ClC_6H_4 (**XI**), 3,4-dibromocyclohexyl (**XII**); R = 2,2-dibromocyclopropyl, R' = *p*-ClC_6H_4 (**XIII**); R = CH_2=CH, R' = 7,7-dichlorobicyclo[4.1.0]heptyl (**XIV**); R = 2,2-dichlorocyclopropyl, R' = 7,7-dichlorobicyclo[4.1.0]heptyl (**XV**); R = C_6H_5 (**XVI**), *p*-ClC_6H_4 (**XVII**).

Constants, yields, and elemental analyses of substituted 1,3-dioxolanes **VI**–**XIX**

Comp. no.	Yield, %	bp, °C (*p*, mm)	d_4^{20}	n_D^{20}	MR_D		Found, %			Formula	Calculated, %		
					found	calculated	C	H	Hlg		C	H	Hlg
VI	76	125–128(1)	1.0891	1.5110	60.59	60.89	70.62	7.14	–	$C_{13}H_{16}O_3$	70.88	7.32	–
VII	82	130–132(2)	1.1719	1.5210	66.18	65.76	61.14	5.85	12.33	$C_{13}H_{15}ClO_3$	61.30	5.93	13.92
VIII	85[a]	112–115(2)	1.0354	1.4800	61.54	61.83	69.32	8.90	–	$C_{13}H_{20}O_3$	69.61	8.98	–
IX	68	150–152(1)	1.5463	1.5360	77.45	77.83	40.32	4.98	41.17	$C_{13}H_{20}Br_2O_3$	40.64	5.24	41.60
X	53	122–124(2)	1.1570	1.4820	74.71	74.22	53.28	5.44	23.88	$C_{14}H_{16}Cl_2O_3$	55.46	5.32	23.38
XI	48	193–194(2)	1.3302	1.5380	79.39	79.09	49.73	4.36	31.70	$C_{14}H_{15}Cl_3O_3$	49.80	4.47	31.49
XII	60	179–181(1)	1.6037	1.5360	90.80	91.16	35.73	4.25	48.67	$C_{14}H_{20}Br_2Cl_2O_3$	36.00	4.31	49.40
XIII	75	200–202(1)	1.6764	1.5770	84.32	84.89	39.12	3.48	45.28	$C_{14}H_{15}Br_2ClO_3$	39.42	3.54	45.77
XIV	78	160–162(2)	1.2161	1.5030	74.68	75.16	54.36	6.27	22.65	$C_{14}H_{20}Cl_2O_3$	54.73	6.55	23.07
XV	80	200–204(1)	1.3210	1.5140	88.93	88.49	45.94	5.03	36.74	$C_{15}H_{20}Cl_4O_3$	46.18	5.16	36.35
XVI	66	179–180(2)	1.5979	1.5550	76.35	76.89	40.84	4.16	41.58	$C_{13}H_{16}Br_2O_3$	41.08	4.24	42.04
XVII	64	196–198(1)	1.6574	1.5640	81.33	81.76	37.43	3.52	46.84	$C_{13}H_{15}Br_2ClO_3$	37.66	3.64	47.10
XVIII	70	138–140(5)	1.1105	1.4860	62.13	62.45	64.83	8.14	–	$C_{13}H_{20}O_4$	64.98	8.39	–
XIX	70	166–169(1)	1.1780	1.5010	69.20	68.69	56.04	7.85	12.29	$C_{13}H_{21}ClO_4$	56.42	7.65	12.81

[a] Obtained in the presence of TsOH.

EXPERIMENTAL

The IR spectra were measured on a UR-20 instrument in thin films. The ^{1}H NMR spectra were obtained on a Tesla BS-487V spetrometer (80 MHz) in CCl_4, internal standard HMDS. Gas chromatography was performed on a Chrom-4 chromatograph, detector katharometer, stainless-steel column (3600 × 4 mm), packing 5% XE-60 on Chromaton N-AW-DMCS, oven temperature 170 to 210°C, carrier gas helium at a rate of 30 ml/min, detector current 75 mA.

4-(2-Propenyloxymethyl)-2-(*p*-chlorophenyl)-1,3-dioxolane (VII). *a*. A mixture of 46.39 g of benzaldehyde (**III**), 46.26 g of diol **I**, 0.14 g of KU-2 cation exchanger (H^+ form), and 60 ml of toluene was heated at 130°C with azeotropic distillation of the water formed. The reaction progress was followed by GLC with sampling at 30-min intervals. The reaction was complete within 5 h. After cooling to room temperature, the reaction mixture was filtered to separate KU-2, the solvent was distilled off, and the residue was vacuum-distilled to obtain compound **VII**. ^{1}H NMR spectrum, δ, ppm: 3.20–4.20 m (7H, $CH_2O \cdot CH_2CHCH_2$), 4.80–5.20 m (2H, CH_2=C), 5.45 m (1H, C=CH), 5.55 d (1H, *trans*-OC^2HO, *J* 7 Hz), 5.75 d (1H, *cis*-OC^2HO, *J* 7 Hz), 7.15 s (4H, C_6H_4).

Compound **VI** was prepared in a similar way.

b. A mixture of 28 g of benzaldehyde (**III**), 24 g of 3-(2-propenyloxy)-1,2-epoxypropane, 50 ml of toluene, and 2.52 g (9% per aldehyde, by weight) H_2SO_4 (ρ 1.84 g/cm^3) was heated under reflux for 5 h; after cooling to 18–20°C, the reaction mixture was washed with 5% aqueous NaOH and water. The aqueous layer was treated with toluene, the extracts were combined with the organic layer, dried with $MgSO_4$, the solvent was removed, and the residue was vacuum-distilled to obtain 8.4 g (19%) of compound **VII**, bp 128–130°C (2 mm), d_4^{20} 1.1689, n_D^{20} 1.5790.

2-(3-Cyclohexenyl)-4-(2-propenyloxymethyl)-1,3-dioxolane (VIII). A mixture of 27.54 g of aldehyde **IV**, 39.65 g of diol **I**, 0.083 g of *p*-toluenesulfonic acid (0.3% per aldehyde, by weight), and 60 ml of toluene was heated for 130°C for 5 h with azeotropic distillation of the water formed. After cooling to room temperature, the reaction mixture was washed with 5% aqueous potassium carbonate and water. The aqueous layer was treated with toluene (2 × 30 ml), the extracts were combined with the organic layer, dried with $MgSO_4$, the solvent was removed, and the residue was vacuum-distilled to obtain compound **VIII**. ^{1}H NMR spectrum, δ, ppm: 1.50–2.50 m (7H, $CH_2 \cdot CH_2CHCH_2$), 3.00–4.25 m (7H, $CH_2OCH_2CHCH_2$), 4.64 d (1H, *trans*-OC^2HO, *J* 7 Hz), 4.76 d (1H, *cis*-OC^2HO, *J* 7 Hz), 4.50–4.80 m (2H, CH_2=C), 5.60 s (2H, CH=CH), 5.65–6.10 m (1H, C=CH).

2-(3,4-Dibromocyclohexyl)-4-(2-propenyloxymethyl)-1,3-dioxolane (IX). Bromine, 47.9 g, was added with stirring at –10 to –5°C to a solution of 33 g of aldehyde **IV** in 80 ml of carbon tetrachloride, after which the reaction mixture was stirred for an additional 1.5–2 h at that temperature. Toluene, 70 ml,

was then added, and CCl_4 was distilled off with a Dean–Stark trap. *p*-Toluenesulfonic acid, 0.1 g (0.3% per aldehyde, by weight) and 42.3 g diol **I** were added to the residue (3,4-dibromocyclohexanecarboxaldehyde and toluene). The water formed was azeotropically distilled at 130°C for 5 h. Further workup was performed as described for compound **VII**.

2-(*p*-Chlorophenyl)-4-(2,2-dichlorocyclohexylpropylmethoxymethyl)-1,3-dioxolane (XI). Chloroform, 22.3 g, was added dropwise with stirring to a mixture of 50 ml of 50% aqueous NaOH, 10 ml of benzene, 0.4 g of triethylbenzylammonium chloride, and 25.5 g of dioxolane **VII**. The reaction mixture warmed up to 30°C. After all chloroform had been added, the mixture was stirred for an additional 3 h, diluted with diethyl ether, washed with 1% aqueous acetic acid and water, dried with $MgSO_4$. Removal of the solvent by distillation followed by vacuum distillation gave 16.3 g (48%) of compound **XI**. ^{1}H NMR spectrum, δ, ppm: 0.88–1.20 m (1H, CH), 1.40–1.90 m (2H, CH_2), 3.20–4.40 m (7H, $CH_2OCH_2 \cdot CHCH_2$), 5.45 s (1H, *trans*-OC^2HO, *J* 6 Hz), 5.57 s (1H, *cis*-OC^2HO, *J* 6 Hz), 7.25 s (4H, C_6H_4).

Compounds **X, XII**–**XV** were prepared in a similar way.

4-(2,3-Dibromopropoxymethyl)-2-(*p*-chlorophenyl)-1,3-dioxolane (XVII). Bromine, 17.6 g, was added dropwise with stiriing to a mixture of 25.5 of dioxolane **VII** and 80 ml of chloroform at –10 to –5°C. The resulting mixture was stirred for an additional 1.5–2 h at that temperature and then washed with 5% aqueous NaOH and water. The aqueous layer was treated with chloroform, the extract was combined with the organic layer, and dried with $MgSO_4$. Removal of the solvent by distillation followed by vacuum distillation gave compound **XVII**. IR spectrum, ν, cm^{-1}: 650, 670 (C–Br), 780, 810 (C–Cl), 1010, 1200 (C–O–C), 1590 (aromatic ring). Other absorption bands in the spectrum belong to stretching (2820–2880 cm^{-1}) and bending (1340–1460 sm^{-1}) vibrations of C–H bonds in CH and CH_2 groups [15].

Compound **XVI** was prepared in a similar way.

2-(3,4-Epoxycyclohexyl)-4-(2-propenyloxymethyl)-1,3-dioxolane (XVIII). To a mixture of 22.4 g of compound **VIII** and 50 ml of chloroform, 30.4 g of 55% peracetic acid was added with stirring at 18–20°C over the course of 30 min. The mixture was stirred for an additional 1.5–2 h at that temperature and then treated with 5% aqueous sodium carbonate, washed with water, and dried with $MgSO_4$. Removal of the solvent by distillation followed by vacuum distillation gave compound **XVIII**. ^{1}H NMR spectrum, δ, ppm: 1.25–2.25 m (7H, $CH_2CH_2CHCH_2$), 2.95 d (2H, $\overset{O}{\diagup\diagdown}$CH–CH), 3.25–4.30 m (7H, $CH_2O \cdot CH_2CHCH_2$), 4.80–5.60 m (2H, CH_2=C), 4.65 d (1H, *trans*-OC^2HO, *J* 7 Hz), 5.70 d (1H, *cis*-OC^2HO, *J* 7 Hz), 5.80–6.10 m (1H, C=CH).

2-[4(3)-Chloro-3(4)-hydroxycyclohexyl]-4-(2-propenyloxymethyl)-1,3-dioxolane (XIX). Hydrogen chloride was barboted into a mixture of 24 g of dioxolane **XVIII** and 30 ml of diethyl ether at –7 to –5°C. Removal of the ether followed by vacuum distillation gave compound **XIX**. The IR spectrum of dioxolane **XIX** lacks bands at 800 and 920 cm^{-1} and contains a broad band at 3450–3500 cm^{-1} characteristic of associated OH group.

REFERENCES

1. Kerimov, A.Kh., *Zh. Org. Khim.*, 2001, vol. 37, no. 1, pp. 144–147.
2. Richard, S.P., *J. Label. Comp.*, 1974, vol. 10, no. 3, pp. 381–387.
3. Rohm, R., *Wiss. Z. Univ.*, 1980, vol. 29, no. 2, pp. 97–106.
4. Jpn. Patent 55-87 733, 1981, *Ref. Zh. Khim.*, 1981, 23H113p.
5. Jpn. Patent 56-139 196, 1984, *Ref. Zh. Khim.*, 1984, 4N27p.
6. Hibbert, H. and Timm, J.A., *J. Am. Chem. Soc.*, 1924, vol. 46, no. 5, pp. 1283–1290.
7. Burt, C.P. and Howlang, F., *J. Am. Chem. Soc.*, 1930, vol. 52, no. 1, pp. 217–219.
8. Ol'shanova, K.M., Potapova, M.A., and Morozova, N.M., *Praktikum po khromatograficheskomu analizu* (Manual on Chromatogaraphic Analysis), Moscow: Vysshaya Shkola, 1970, pp. 64–66.
9. Kerimov, A.Kh., Babaev, M.G., Alieva, E.S., and Mishiev, D.E., *Zh. Obshch. Khim.*, 1991, vol. 61, no. 10, pp. 2328–2332.
10. Kerimov, A.Kh., Babaev, M.G., and Mishiev, D.E., *Zh. Org. Khim.*, 1985, vol. 21, no. 3, pp. 645–648.
11. Polyanskii, N.G., Kozova, G.Ya., and Chernysheva, D.A., *Khim. Prom–st.*, 1970, no. 2, pp. 87–91.
12. Shostakovskii, S.M., Kolesnikov, R.V., Grigoreva, V.A., and Grigorev, A.A., Abstracts of Papers, *Vsesoyuznaya konferentsiya "Perspektivy razvitiya khimii karkasnykh soedinenii i ikh primenenie v otraslyakh promyshlennosti"* (All-Union Conf. "Prospects of Chemistry of Skeleton Compounds and Their Industrial Application," Kiev, 1986, p. 97.
13. Yanovskaya, L.A., Dombrovskii, V.A., and Khusid, A.Kh., *Tsiklopropany s funktsional'nymi gruppami* (Cyclopropanes with Functional Groups), Moscow: Nauka, 1980, pp. 79–95.
14. Rakhmankulov, D.L., Kantor, E.A., and Nurieva, R.Kh., Available from VINITI, 1979, Moscow, no. 4353-79.