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Chemistry of Dioxacycloalkanes: VII.* Synthesis and Properties of Substituted 1,3-Dioxolanes Derived from Carbocyclic Aldehydes

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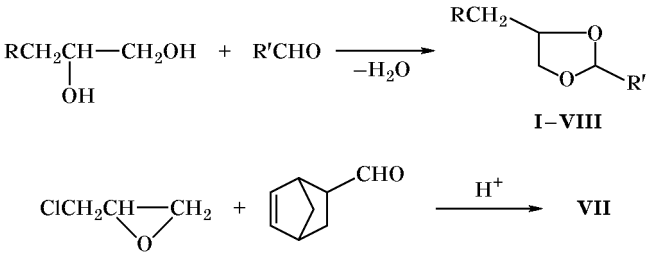
Abstract—Reactions of 3-cyclohexenecarbaldehyde, 6-methyl-3-cyclohexenecarbaldehyde, bicyclo[2.2.1]-hept-5-ene-*endo*-2-carbaldehyde, and benzaldehyde with 1,2-propanediol and 3-chloro-1,2-propanediol gave the corresponding 2,4-substituted 1,3-dioxolanes. Their reactions with peroxyacetic acid, bromine, dichlorocarbene, and nucleophiles were studied. The effect of the substituents in the diol and aldehyde on their relative reactivity is discussed.

In the preceding communications we reported on the results of studying reactions of 3-(2-chloroethoxy)-1,2-epoxypropane with various alcohols [2] and of α,β-unsaturated aldehydes [3] and trichloroacetaldehyde [4] with 3-chloro-, 3-(2-chloroethoxy)-, and 3-(2-chloro-1-chloromethylethoxy)-1,2-propanediols. 1,3-Dioxolane derivatives are used as tranquilizers [5] and plasticizers [6] and are also promising as monomers for polymerization and polycondensation [7]. However, there are very limited published data on the synthesis and properties of 1,3-dioxolanes derived from aldehydes with a carbocyclic radical.

The present article describes the synthesis of 2,4-disubstituted 1,3-dioxolanes by reactions of 3-cyclohexenecarbaldehyde, 6-methyl-3-cyclohexenecarbaldehyde, bicyclo[2.2.1]hept-5-ene-*endo*-2-carbaldehyde, and benzaldehyde with 1,2-propanediol and 3-chloro-1,2-propanediol in toluene in the presence of KU-2 cation exchanger (Scheme 1). The progress of the reactions was monitored by GLC. The products were quantitated by the internal standard technique [8] using dimethyl or diethyl phthalate (the peak areas were corrected on the basis of artificial calibration mixtures). GLC analysis of compounds **I**–**VIII** showed the presence of two isomers at a ratio of 55:45. We failed to isolate pure isomers from the reaction mixtures, but the ^{1}H NMR spectra of isomeric mixtures also indicated formation of *cis* and *trans* structures (see Experimental).

The initial rates ($W_0 \times 10^4$) of formation of 1,3-dioxolanes **I** and **V** from 3-cyclohexenecarbaldehyde were 2.76 and 5.60 mol l^{-1} s^{-1}, respectively. These reactions were considerably faster than those with bicyclo[2.2.1]hept-5-ene-*endo*-2-carbaldehyde to form dioxolanes **III** and **VII** (1.75 and 2.40 mol l^{-1} s^{-1}) and with benzaldehyde to form dioxolanes **IV** and **VIII** (1.80 and 2.46 mol l^{-1} s^{-1}, respectively). The same conclusion follows from the yields of the target products; according to the GLC data, no other products were formed in the above reactions.

Scheme 1.



I–**IV**, R = H; **V**–**VIII**, R = Cl; **I**, **V**, R′ = 3-cyclohexenyl; **II**, **VI**, R′ = 6-methyl-3-cyclohexenyl; **III**, **VII**, R′ = bicyclo[2.2.1]hept-5-en-*endo*-2-yl; **IV**, **VIII**, R′ = Ph.

The relatively high yields of dioxolanes **I** and **V** may be due to better accessibility of the equatorial aldehyde group in 3-cyclohexenecarbaldehyde for nucleophilic attack, as compared with the *endo*-aldehyde group in the norbornene derivative [9]. Benzene

* For communication VI, see [1].

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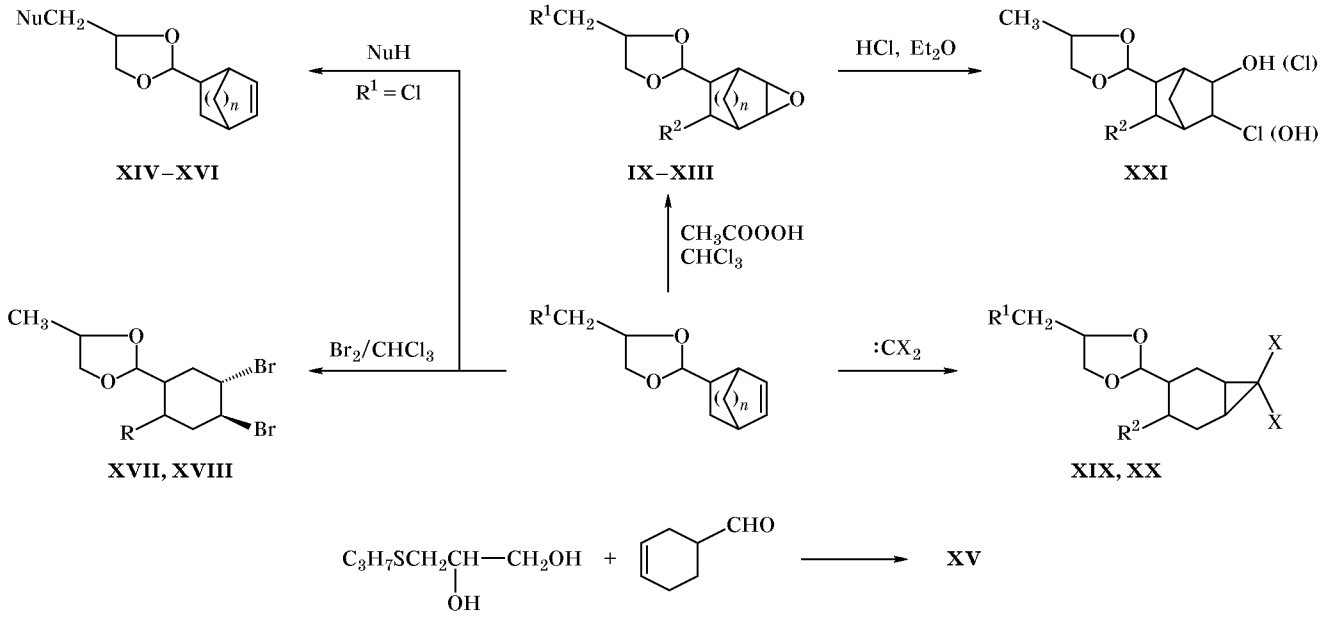
Scheme 2.



IX, n = 0, $R^1 = R^2$ = H; **X**, n = 0, R^1 = H, $R^2 = CH_3$; **XI**, n = 0, R^1 = Cl, R^2 = H; **XII**, n = 1, $R^1 = R^2$ = H; **XIII**, n = 1, R^1 = Cl, R^2 = H; **XIV**, n = 0, Nu = CH_3O; **XV**, n = 0, Nu = C_3H_7S; **XVI**, n = 1, Nu = $(C_2H_5)_2N$; **XVII**, R = H; **XVIII**, R = CH_3; **XIX**, R^1 = H, $R^2 = CH_3$, X = Cl; **XX**, R^1 = Cl, R^2 = H, X = Br.

ring is also known to reduce electrophilic properties of the carbonyl group attached thereto [10].

The presence of chlorine atom in the initial diol favors its reaction with aldehydes and increases the yield of the product. Taking into account that the rate-determining stage is nucleophilic attack on the protonated aldehyde group by the hydroxy group which is remote from the chlorine atom, the latter is likely to exert through-space effect on the reaction center. Consideration of the Newman projections shows that among three possible conformations of 3-chloro-1,2-propanediol the most energetically favorable is transoid φ^3 [11] which gives rise to hydrogen bonding between the chlorine atom and the primary hydroxy group. Such a structure facilitates approach of the reagent and subsequent migration of proton to the leaving group ($-\overset{+}{O}H_2$).

Oxidation of compounds **I**–**III** and **V**–**VII** with 50% peroxyacetic acid afforded the corresponding *cis*-2-(1,2-epoxy-4-cyclohexyl)- and *cis*-2-(5,6-epoxybicyclo[2.2.1]hept-*endo*-2-yl)-1,3-dioxolanes **IX**–**XIII** in good yield. Treatment of compounds **I** and **II** with bromine resulted in formation of dibromo derivatives **XVII** and **XVIII**. The chlorine atom in the 4-chloromethyl group of **V** and **VII** is readily replaced by methoxy, propylthio, and diethylamino group to form products **XIV**–**XVI**. Dichloro- and dibromocarbenes add to compounds **II** and **V**, yielding products **XIX** and **XX** (Scheme 2). The structure of dioxolanes **I**–**VIII** and products of their transformations was proved by elemental analyses, determination of MR_D, and ^{1}H NMR and IR spectra. Compound **VII** was also synthesized in 19% yield by the procedure described in [12] from 3-chloro-1,2-epoxypropane in the presence of H_2SO_4 (d = 1.84). The IR spectra of **I**–**VIII** contained absorption bands at 1050, 1140, and 1240 cm^{-1} due to vibrations of the C–O–C fragments, a weak band in the region 1645–1650 cm^{-1} (C=C), a band at 945 cm^{-1} (*trans*-C=CH), and a strong band at 3030–3040 cm^{-1} (=C–H). Compounds **IV** and **VIII** also showed a strong IR band at 1590 cm^{-1} belonging to stretching vibrations of the aromatic ring. The band at 750 cm^{-1} in the spectra of **V**–**VIII** corresponds to the C–Cl bond. Epoxy derivatives **IX**–**XIII** are characterized by absorption at 850 and 920 cm^{-1}, typical of oxirane ring. The presence of epoxy group in **XII** was confirmed by reaction with hydrogen chloride in diethyl ether, which afforded the corresponding chlorohydrin **XXI**.

EXPERIMENTAL

The IR spectra were measured on a UR-20 instrument from samples prepared as thin films. The ^{1}H NMR spectra of solutions of 2,4-disubstituted 1,3-dioxolanes in CCl_4 were obtained on a Tesla BS-487B

Yields, constants, and elemental analyses of compounds **I**–**XXI**

Comp. no.	Yield, %	bp, °C (*p*, mm)	d_4^{20}	n_D^{20}	MR_D		Found, %		Formula	Calculated, %	
					found	calcd.	C	H		C	H
I	78	58–59 (2)	1.0092	1.4690	46.42	46.79	71.08	9.50	$C_{10}H_{16}O_2$	71.39	9.58
II	59	95–97 (5)	0.9942	1.4680	50.96	51.41	72.14	9.86	$C_{11}H_{18}O_2$	72.48	9.95
III	63	69–71 (1)	1.0437	1.4780	49.02	49.21	73.04	8.87	$C_{11}H_{16}O_2$	73.30	8.94
IV	68	53–54 (2)	1.0948	1.5060	44.28	44.76	73.38	6.62	$C_{10}H_{11}O_2$	73.60	6.79
V	88	110–112 (2)	1.1272	1.4910	52.07	51.66	58.95	7.60	$C_{10}H_{15}ClO_2$ [a]	59.26	7.46
VI	70	96–98 (2)	1.1158	1.4915	56.28	56.24	60.72	7.81	$C_{11}H_{17}ClO_2$ [b]	60.97	7.91
VII	76	85–87 (2)	1.1717	1.5010	53.97	54.08	61.25	7.16	$C_{11}H_{15}ClO_2$ [c]	61.53	7.03
VIII	80	105–106 (2)	1.2139	1.5280	50.39	50.73	60.15	5.48	$C_{10}H_{11}ClO_2$ [d]	60.46	5.57
IX	80	89–90 (3)	1.1044	1.4710	46.62	46.70	65.32	8.66	$C_{10}H_{16}O_3$	65.19	8.74
X	82	145–147 (25)	1.0858	1.4700	50.94	51.32	66.18	8.97	$C_{11}H_{18}O_3$	66.64	9.15
XI	81	125–126 (1)	1.2437	1.4940	51.18	51.56	54.75	6.80	$C_{10}H_{15}ClO_3$ [e]	54.92	6.91
XII	68	104–106 (2)	1.1399	1.4850	49.33	49.12	67.11	8.09	$C_{11}H_{16}O_2$	67.32	8.21
XIII	70	140–142 (5)	1.2610	1.5070	54.44	53.94	57.09	6.38	$C_{11}H_{15}ClO_3$ [f]	57.27	6.54
XIV	37	89–90 (3)	1.5042	1.4720	53.06	52.66	66.49	8.98	$C_{11}H_{18}O_3$	66.63	9.14
XV	36	142–146 (2)	1.0497	1.5022	69.13	68.14	64.12	9.26	$C_{13}H_{22}O_2S$ [g]	66.41	9.14
XVI	70	107–108 (2)	1.0211	1.4950	71.78	71.62	71.59	9.88	$C_{15}H_{25}NO_2$ [h]	71.67	10.02
XVII	69	127–128 (2)	1.6610	1.5420	62.15	62.79	36.32	4.87	$C_{10}H_{16}Br_2O_2$ [i]	36.61	4.91
XVIII	63	160–162 (3)	1.5869	1.5330	66.90	67.41	38.36	5.49	$C_{11}H_{18}Br_2O_2$ [j]	38.62	5.30
XIX	75	140–142 (3)	1.2114	1.4980	61.25	61.61	52.04	6.94	$C_{11}H_{18}Cl_2O_3$ [k]	52.18	7.16
XX	40	180–185 (2)	1.6789	1.5470	70.73	69.71	35.04	3.98	$C_{11}H_{15}Br_2ClO_2$ [l]	35.27	4.03
XXI	70	140–142 (2)	1.5090	1.2483	55.66	56.07	56.59	7.28	$C_{11}H_{17}ClO_3$ [m]	56.77	7.36

[a] Found, %: Cl 17.35; calculated, %: Cl 17.49. [b] Found, %: Cl 16.15; calculated, %: Cl 16.36. [c] Found, %: Cl 16.04; calculated, %: Cl 16.51. [d] Found, %: Cl 17.07; calculated, %: Cl 17.84. [e] Found, %: Cl 16.05; calculated, %: Cl 16.21. [f] Found, %: Cl 14.94; calculated, %: Cl 15.36. [g] Found, %: S 12.75; calculated, %: S 13.22. [h] Found, %: N 5.14; calculated, %: N 5.57. [i] Found, %: Br 48.28; calculated, %: Br 48.72. [j] Found, %: Br 45.64; calculated, %: Br 46.42. [k] Found, %: Cl 28.82; calculated, %: Cl 28.00. [l] Found, %: Cl + Br 51.87; calculated, %: Cl + Br 52.13. [m] Found, %: Cl 14.88; calculated, %: Cl 15.23.

spectrometer at 80 MHz using HMDS as internal reference. Gas–liquid chromatography was performed on a Chrom-4 instrument equipped with a thermal-conductivity detector (2400 × 4-mm stainless steel column packed with 5% of XE-60 on Chromaton N-AW-DMCS; oven temperature 190°C; carrier gas helium, flow rate 30 ml/min; detector current 80 mA).

2-(3-Cyclohexenyl)-4-methyl-1,3-dioxolane (I). *a*. A mixture of 55.1 g (0.5 mol) of 3-cyclohexene-carbaldehyde, 45.6 g (0.6 mol) of 1,2-propanediol, 70 ml of toluene, and 0.17 g (0.3% relative to the aldehyde) of KU-2 cation exchanger was stirred for 5 h at 130°C with azeotropic distillation of water. The mixture was filtered, the filtrate was evaporated under reduced pressure, and the residue was purified by vacuum distillation. Yield 63.8 g (76%) (see table). The progress of the reaction was monitored by GLC. ^{1}H NMR spectrum (CCl_4), δ, ppm: 0.9–1.20 m (5H, CH_3CHCH_2), 1.45–2.25 m (7H, $CH_2CH_2CHCH_2$), 3.15–4.25 m (3H, CH_2O, CHO), 4.55 d (1/2H, OCHO-*trans*), 4.63 d (1/2H, OCHO-*cis*), 5.48 s (2H, CH=CH). Compounds **II**–**VIII** were synthesized in a similar way.

b. A mixture of 36.6 g (0.3 mol) of bicyclo[2.2.1]-hept-5-ene-*endo*-2-carbaldehyde, 29.6 g (0.32 mol) of 3-chloro-1,2-epoxypropane, 50 ml of toluene, and 3.3 g (9 wt % with respect to the aldehyde) of H_2SO_4 (d = 1.84) was refluxed for 5 h. The mixture was then cooled to 18–20°C and washed with a 5% solution of alkali and with water. The aqueous phase was extracted with toluene, the combined extracts were dried over $MgSO_4$ and evaporated, and the residue was distilled under reduced pressure. Yield of **VII** 12.3 g (19%), bp 84–85°C (2 mm), d_4^{20} = 1.1683, n_D^{20} = 1.4940.

2-(3,4-Epoxycyclohexyl)-4-methyl-1,3-dioxolane (IX). To a mixture of 25.2 g (0.15 mol) of compound **I** and 70 ml of chloroform we added with stirring

at 18–20°C 30.4 g of 50% peroxyacetic acid over a period of 60 min. The mixture was stirred for an additional 1.5 h and treated with a 5% solution of sodium carbonate. The organic phase was washed with water, dried over $MgSO_4$, and evaporated, and the residue was distilled under reduced pressure to isolate compound **IX** (see table). ^{1}H NMR spectrum (CCl_4), δ, ppm: 1.25–2.25 m (7H, $CH_2CH_2CHCH_2$), 2.95 d (2H, 2CH, oxirane), 3.25–4.30 m (3H, CH_2O, CHO), 4.55 d (1/2H, OCHO-*trans*), 4.65 d (1/2H, OCHO-*cis*). Compounds **X**–**XIII** were obtained in a similar way (see table).

2-(3-Cyclohexenyl)-4-methoxymethyl-1,3-dioxolane (XIV). A mixture of 9.6 g (0.3 mol) of methanol and 4 g of powdered sodium hydroxide was stirred for 60 min at 65–70°C, 20.3 g (0.1 mol) of compound **V** was added, and the mixture was heated to 75–80°C and stirred for 4 h at that temperature. It was then cooled, diluted with ether, neutralized with acetic acid, washed with water, dried over $MgSO_4$, and evaporated. Vacuum distillation of the residue gave product **XIV** (see table).

2-(3-Cyclohexenyl)-4-propylthiomethyl-1,3-dioxolane (XV). *a*. To 18.7 g (0.25 mol) of propanethiol we added dropwise 15 ml of a 40% solution of sodium hydroxide, and the mixture was stirred for 60 min at 85–90°C. The mixture was cooled to room temperature, 48.6 g (0.24 mol) of compound **V** was added in one portion, and the mixture was stirred for 3–4 h at 125°C. The product was isolated as described above for compound **XIV** and was purified by vacuum distillation (see table).

b. A mixture of 55.1 g (0.5 mol) of 3-cyclohexenecarbaldehyde, 76 g (0.5 mol) of 3-propylthio-1,2-propanediol, 70 ml of toluene, and 0.16 g (0.3 wt % with respect to the aldehyde) of KU-2 cation exchanger was stirred for 5 h at 130°C with azeotropic distillation of water. The mixture was filtered, and the solvent was distilled off. Vacuum distillation of the residue gave 79.5 g (66%) of compound **V** with bp 139–141°C (1 mm), d_4^{20} = 1.0486, n_D^{20} = 1.5016.

2-(Bicyclo[2.2.1]hept-5-en-*endo*-2-yl)-4-diethylaminomethyl-1,3-dioxolane (XVI). A mixture of 21.5 g (0.1 mol) of compound **VII**, 27.6 g of potassium carbonate, and 36.5 g (0.5 mol) of diethylamine was stirred for 3 h at 125–130°C. Excess diethylamine was distilled off, and the mixture was cooled, diluted with water, and stirred until dissolution of mineral salts. The organic phase was separated, and the aqueous phase was extracted with ether. The combined extracts were dried over $MgSO_4$ and evaporated, and the residue was subjected to vacuum distillation to isolate product **XVI** (see table).

2-(3,4-Dibromocyclohexyl)-4-methyl-1,3-dioxolane (XVII). Bromine, 25.6 g (0.16 mol), was added dropwise to a mixture of 25.2 g (0.15 mol) of compound **I** and 50 ml of chloroform, stirred at –5 to –10°C. The mixture was stirred for an additional 1.5–2 h and washed with a 5% solution of sodium hydroxide and water. The aqueous phase was extracted with chloroform, and the extract was combined with the organic phase, washed with water, dried over $CaCl_2$, and evaporated. The residue was distilled under reduced pressure to isolate 33.8 g (69%) of product **XVII** (see table). Compound **XVIII** was obtained in a similar way.

2-(7,7-Dichloro-4-methylbicyclo[4.1.0]hept-3-yl)-4-methyl-1,3-dioxolane (XIX). Chloroform, 15 ml, was added dropwise with stirring to a mixture of 25 ml of 50% aqueous sodium hydroxide, 10 ml of benzene, 0.2 g of benzyltriethylammonium chloride, and 9.2 g (0.05 mol) of compound **II**. The mixture spontaneously warmed up to 30°C. It was stirred for an additional 3 h, diluted with ether, washed with a 1% aqueous solution of acetic acid and with water, dried over $MgSO_4$, and evaporated. Vacuum distillation of the residue gave 21.5 g (63%) of product **XIX**. ^{1}H NMR spectrum (CCl_4), δ, ppm: 0.9–1.20 d (3H, CH_3), 1.45–2.25 m (7H, cyclohexane), 4.46 d (1/2H, OCHO-*trans*, J = 7 Hz), 4.59 d (1/2H, OCHO-*cis*, J = 7 Hz).

4-Chloromethyl-2-(7,7-dibromobicyclo[4.1.0]-hept-3-yl)-1,3-dioxolane (XX) was synthesized in a similar way (see table).

2-[2(3)-Chloro-3(2)-hydroxybicyclo[2.2.1]hept-5-yl]-4-methyl-1,3-dioxolane (XXI). Gaseous hydrogen chloride was passed at –10 to –15°C through a mixture of 11.8 g (0.06 mol) of compound **XII** and 50 ml of diethyl ether until a required amount was absorbed (by weight). The mixture was kept for 3–4 h, washed with a 2% solution of sodium carbonate and with water, dried over $MgSO_4$, and evaporated. Vacuum distillation of the residue gave 9.8 g (70%) of compound **XXI** (see table).

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