Synthesis and Structure of Some Aryl-substituted Thiiranes

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Abstract—A number of aryl-substituted 1,2-chlorohydrins was prepared by treating 1,2-epoxy-3-chloropropane with arylmagnesium bromide. The reaction of the aryl-substituted 1,2-chlorohydrins with sodium hydroxide solution furnished the corresponding oxiranes, the key compounds in the synthesis of a number of previously unknown thiiranes.

We report here on the studies concerning preparation of thiiranes and their amino derivatives [1-12].

To this end as initial products aryl-substituted 1,2-chlorohydrins **I–IV** were synthesized from 1,2-epoxy-3-chloropropane and arylmagnesium bromides.

$$ArMgBr + CH_2-CH-CH_2Cl \longrightarrow ArCH_2CHCH_2Cl$$

$$OH$$

$$I-IV$$

$$Ar = 4-CH_3C_6H_4(I); 4-(CH_3)_2CHC_6H_4(II); C_6H_5CH_2(III);$$

$$(IV).$$

The studies showed that the best yields of 1,2-chlrohydrins **I-IV** were obtained at the ratio of arylmagnesium bromide to 1,2-epoxy-3-chloropropane of 1:2. At equimolar reagents ratio the yield of the target product strongly decreased. We succeeded in raising the yield of 1,2-chlorohydrins **I-IV** by 20–30%, and also refined the data on certain physicochemical constants that had been previously not enough precisely determined as was indicated in [13].

We established that in all cases alongside 1.2-chlorohydrins **I–IV** arose a small amount of a side products, 1-chloro-3-bromo-2-propanol and chlorocyclopropanol [14].

The synthesis of aryl-substituted oxiranes **V-VIII** was accomplished by reaction of an appropriate

$$\begin{array}{c} \text{ArCH}_2\text{CHCH}_2\text{Cl} + \text{NaOH} & \\ \stackrel{|}{\text{OH}} & \text{NaCl} + \text{H}_2\text{O} \end{array} \begin{array}{c} \text{ArCH}_2\text{CH-CH}_2 \\ \text{V-VIII} \end{array}$$

1,2-chlorohydrin **I-IV** with 28% solution of sodium hydroxide.

Aryl-substituted thiiranes **VIII–XII** were prepared by thioepoxidation of the corresponding oxiranes **V–VIII** with thiourea in the presence of sulfuric acid.

We demonstrated that the acid catalysis (here with sulfuric acid) plays an essential part in the anionotropic conversion of oxiranes into thiiranes and it ensures high yields of the target products (70–85%).

The structure of compounds **I-XII** obtained was confirmed by IR, ¹H and ¹³C NMR spectra. The physical constants of compounds **I-XII** are listed in Table 1.

In the IR spectra of all 1,2-chlorohydrins **I-IV** synthesized is observed a broad absorption band in the 3380-3400 cm⁻¹ region that is conserved at dilution with CCl₄ to the concentration of 0.005 M. This fact is incompatible with an intermolecular association, and the band is characteristic of an intramolecular hydrogen bond O···Cl [15].

The stretching vibrations of the C-Cl bond appear in all IR spectra in the region 765-785 cm⁻¹. In the IR spectra were also revealed weak absorption bands in 2000-1720 cm⁻¹ region characterizing the substitution types in the aromatic ring [16]. In the IR spectra of the obtained oxiranes **V-VIII** in contrast to the 1,2-chlorohydrins are observed strong bands in the region 830-840, 1015-1020, and 1240-1250 cm⁻¹

Table 1. Yields, melting points, and MR_D values of compounds I-XII

Comnd	Yield, %	bp, °C	$n_{ m D}^{20}$	d_4^{20}	MR_D		Found, %			Formula	Calculated, %			D
no.		(mm Hg)			found	calcu- lated	С	Н	Cl or S	Formula	С	Н	Cl or S	$R_{ m f}$
I	65	106 (1.3)	1.5410	1.1272	51.48	51.17	65.27	6.90	19.34	$C_{10}H_{13}OCl$	65.04	7.10	19.20	0.43
II	61	140 (2.8)	1.5285	1.0791	60.72	60.41	67.94	7.87	16.38				16.66	0.51
III	71	134–135 (4)	1.5398	1.1271	51.39	51.17	64.91	6.83	19.07	$C_{10}H_{13}OCl$	65.04	7.10	19.20	0.53
IV	56	145–146 (1.1)	1.6230	1.2532	61.89	61.89	70.67	5.82	16.35	C ₁₃ H ₁₃ OCl	70.35	5.94	16.07	0.62
${f V}$	68	70 (1.3)	1.5192	1.0155	44.31	44.20	80.81	8.29	-	$C_{10}H_{12}O$	81.04	8.16	_	0.68
VI	63	98 (3)	1.5135	0.9854	53.84	54.16	81.52	9.36	_	$C_{12}H_{16}O$	81.77	9.15	=	0.86
VII	74	90-91	1.5220	1.0266	44.03	44.20	81.17	8.03	_	$C_{10}H_{12}O$	81.04	8.16	_	0.77
		(0.4)												
VIII	85	154-155	1.6131	1.1430	56.07	56.04	84.42	6.29	-	$C_{13}H_{12}O$	84.75	6.57	_	0.41
		(4)												
IX	83	98 (1.3)	1.5642	1.0518	50.81	50.68	73.43	7.18	19.31	$C_{10}H_{12}S$	73.12	7.36	19.52	0.71
X	70	110 (2)	1.5430	1.0037	60.36	60.53	74.67	8.52	16.58	$C_{12}H_{16}S$	74.94	8.39	16.67	0.82
XI	71	129	1.5625	1.0469	50.92	50.68	73.31	7.12	19.16	$C_{10}H_{12}S$	73.12	7.36	19.52	0.75
		(2.5)												
XII	80	134-135	1.6508	1.1427	62.21	62.56	77.69	6.23	16.37	$C_{13}H_{12}S$	77.95	6.04	16.07	0.74
	<u> </u>	(1)	<u> </u>	<u> </u>	<u> </u>	<u> </u>	<u> </u>	<u> </u>	<u> </u>	L	<u> </u>	<u> </u>	<u> </u>	<u> </u>

Table 2. Parameters of 1H NMR and IR spectra of compounds I–XII

Compd.	¹ H NMR spectrum (CCl ₄), δ, ppm						IR spectrum, cm ⁻¹						
	CH ₃ , s	ArCH ₂ , d	CH ₂ X, d	CH, m	Ar, s	ОН	CH ₂ Cl	oxirane	thiirane	frequencies of substitution type			
I II	2.15 1.30	2.65 2.60	3.30 3.25	3.65 1.85 3.70	6.70 6.75	3400 3380	770 765	-	_ _	840, 1790, 1960 1790, 1910			
Ш		2.65 3.30 t		3.50	6.95	3390	765	_	_	840, 1790, 1960			
IV		2.45	3.15	4.15	6.65 7.10	3390	785	_	_	830, 1720, 1930			
\mathbf{V}	2.20	2.65	2.35 2.70	2.80	6.60	_	_	830, 1020, 1250	_	805, 1785, 1900			
VI	1.30	2.60	2.25 2.60	2.75	6.70	_	_	840, 1020, 1240	=	810, 1780, 1820			
VII	_	2.65	2.20 2.45	2.85	6.95	_	_	830, 1015, 1240	_	700, 730, 1810			
VIII	_	3.20	2.35 2.65	3.30	7.2- 8.2	_	_	830, 1015, 1245	_	815, 1720, 1925			
IX	2.20	2.70	2.08 2.25	2.70	6.60	_	_	_	635	820, 1700, 1910			
X	1.20	2.60	2.10 2.30	2.75	6.75	_	_	_	625	820, 1710, 1910			
XI	_	2.75	1.85 2.25	2.85	6.85	_	_	_	625	690, 750, 1930			
XII	_ 	3.20	2.10 2.30	3.20	7-8	_ 	_	_ L	625	805, 1780, 1910			

corresponding to asymmetrical, symmetrical, and pulse vibrations of the oxirane ring. Unlike the IR spectra of oxiranes, in the spectra of thiiranes **IX–XII** are present absorption bands at 625–635 cm⁻¹ from the stretching vibrations of the C–S bond in the three-membered thiirane ring.

In the ¹H NMR spectra of 1,2-chlorohydrins **I-IV** in the strong field at 1.30–2.15 ppm appear signals of protons from methyl groups attached to aromatic rings, and doublet signals in the region 2.60–2.65 ppm correspond to the methylene protons linked to the benzene ring. The proton signals of the methylene group in compound **III** bonded to benzyl group and the neighboring methine group appear at 1.5–1.9 ppm as a quartet due to spin-spin coupling. The protons signals from the methylene groups linked to chlorine in the molecules of 1,2-chlorohydrins give rise to doublet in the 3.15–3.30 ppm region, and the signal of methine proton appears as a multiplet at 3.50–4.15 ppm.

A strong signal in the downfield part of the $^1\mathrm{H}$ NMR spectra (6.70–6.95 ppm) originates from aromatic protons, and naphthyl protons of compound \mathbf{IV} give rise to a multiplet at 7.80–8.10 ppm. The proton signal of the hydroxy group in all studied 1,2-chlorohydrins overlapped with the resonance of $\mathrm{CH_2Cl}$ group as was proved by recording the spectrum in the presence of $\mathrm{D_2O}$.

In the ¹H NMR spectra of oxiranes **V-VIII** the protons of CH₂ group in the oxirane ring give rise to two doublets at 2.20–2.35 ppm and 2.45–2.70 ppm which correspond to hydrogens located in *cis*- and *trans*-positions. The methine proton signals in the oxirane ring of compounds **V-VIII** are shifted upfield as compared with 1,2-chlorohydrins and appear at 2.70–3.30 ppm. The ¹H NMR spectra of thiiranes **IX-XII** are similar in appearance to the oxirane spectra, but the proton signals of the CH₂ group in the thiirane ring are shifted upfield and give two doublets in the region 1.85–2.10 and 2.70–3.20 ppm.

EXPERIMENTAL

¹H NMR spectra were recorded on spectrometer Varian T-60 at operating frequency 60 MHz from solutions in CCl₄ with TMS as internal reference. ¹³C NMR spectra were registered on Varian VXR-400 instrument at operating frequency 100 MHz. IR spectra were measured on spectrophotometer Specord-75 IR from liquid films in the region 400-4000 cm⁻¹ (with prisms of KBr, NaCl, LiF). The progress of reactions was monitored and the purity of

compounds synthesized was checked by GLC using chromatograph Tsvet-126 equipped with a flame-ionization detector, glass column 1500×3 mm, stationary phase 5% SE-30 on Chromaton N-AW, carrier gas nitrogen. TLC of compounds **I–XII** was performed on Silufol UV-254 plates using as eluent ethanol–hexane mixture, 1:5.

4-Phenyl-1-chloro-2-butanol (III). To an ethereal solution of benzylmagnesium bromide obtained by a common procedure from 0.5 mol (93 g) of benzyl bromide, 0.5 g-atom (12 g) of magnesium in 200 ml of dry ether in the presence of 2-3 iodine crystals under external cooling with an ice bath was added dropwise at stirring a solution of 1 mol (92.5 g) of 1,2-epoxy-3-chloropropane in 100 ml of dry ether. Then the reaction mixture was heated to 35°C for 2 h more at constant stirring. Then at cooling the flask with an ice bath the reaction mixture was quenched with 10% solution of hydrochloric acid till two transparent layers formed. The upper organic layer was separated, the water layer was thrice extracted with ether. The combined organic solutions were washed with water and dried with anhydrous sodium sulfate. After removing the solvent the residue was subjected to a vacuum distillation. We obtained 65.5 g of 4-phenyl-1-chloro-2-butanol (III). Yield of compound **III** 71%, bp – 134–135°C (4 mm Hg), $n_{\rm D}^{20}$ 1.5398, d_4^{20} 1.1271. Published data [13]: bp 158–160°C (23 mm Hg), $n_{\rm D}^{20}$ 1.5371.

Likewise by reaction of p-tolyl-, p-isopropylphenyl-, α -naphthylmagnesium bromides with 1,2-epoxy-3-chloropropane in a dry ether solution were prepared the corresponding 1,2-chlorohydrins **I**, **II**, **IV**. Their physical constants are listed in Table 1. 1-Chloro-3-(4-methylphenyl)-2-propanol (**IV**) were prepared as described in [13]; as mentioned in [13], the data on the constants of compounds **I**, **IV** were incorrect.

1,2-epoxy-4-phenylbutane (**VII**). To a mixture of 18.5 g (0.1 mol) of 1-chloro-4-phenyl-2-butanol and 50 ml of hexane at vigorous stirring was added dropwise 20 g of 29% NaOH solution. Then the reaction mixture was heated for 2 h to 60°C. On cooling the reaction mixture was several times washed with water till neutral washings and dried with anhydrous sodium sulfate. On removing the solvent the reaction product was subjected to vacuum distillation to obtain 11 g (24%) of compound **VII**, bp 90–91°C (0.4 mm Hg), $n_{\rm D}^{20}$ 1.5220; ¹H NMR spectrum (CCl₄), δ , ppm: 2.20, 2.45 (2H, CH₂-oxirane), 2.85 (1H, CH), 2.65 t (2H, ArCH₂), 6.95 s (5H, C₆H₅); ¹³C NMR spectrum

(CDCl₃), δ , ppm: 52.57 (CH), 38.49 (CH₂-oxirane), 38.43 (CH₂CH), 147.42 (C_i), 134.30 (C_p), 129.31 (C_o), 127.54 (C_m). Found, %: C 81.17; H 8.03. C₁₀H₈O. Calculated, %: 81.04; H 8.16.

Likewise were obtained the other oxiranes **V**, **VI**, **VIII** whose constants are given in Table 1.

1,2-Epithio-4-phenylbutane (XI). Into a threeneck flask was charged 76 g (1 mol) of thiourea and 30 ml of sulfuric acid solution containing 1 g-equiv of the acid and 350 ml of water. At vigorous stirring the reaction mixture was cooled to 5-10°C and maintaining this temperature 148 g (1 mol) of 1,2-epoxy-4phenylbutane was added dropwise within 2 h. After completion of oxirane addition the reaction mixture was stirred for 1 h at room temperature and then hydrolyzed with a solution of 106 g (1 mol) of sodium carbonate in 450 ml of water. The organic layer was separated, the water layer was twice extracted with ether. The combined organic solutions were dried with anhydrous sodium sulfate. After removing ether the reaction product was subjected to vacuum distillation to obtain 116 g (71%) of compound **XI**, bp 129°C (2.5 mm Hg), $n_{\rm D}^{20}$ 1.5625; ¹H NMR spectrum (CCl₄), δ, ppm: 1.85, 2.25 (2H, CH₂-thiirane), 2.85 m (1H, CH), 2.75 t (2H, CH₂Ar), $6.8\overline{5}$ s (5H, C₆H₅); ¹³C NMR spectrum (CDCl₃), δ , ppm: 35.36 (CH), 25.94 (CH₂-thiirane), 141.08 (C_i), 128.41, 128.36 (C_°_m), 125.97 (C_n), 38.29 (CH₂ Ph), 35.60 (CH₂ CH). Found, %: C 73.31; H 7.12; S 19.16. C₁₀H₁₂S. Calculated, %: C 73.12; H 7.36; S 19.52.

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