SYNTHESIS AND PROPERTIES OF FURANYL 1,3-DIOXOLANES. 2.* SYNTHESIS OF NEW DERIVATIVES OF FURANYL 1,3-DIOXOLANES

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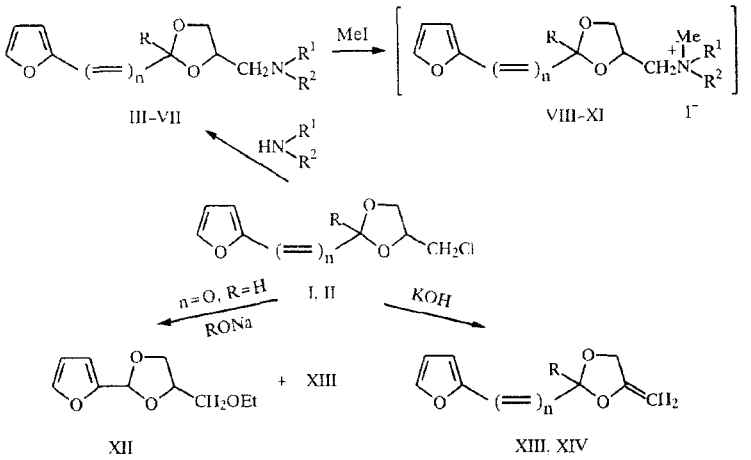
New derivatives of furnayl 1,3-dioxolanes containing amino, ammonium, alkoxy, and vinyl groups in the dioxolane fragment were synthesized.

In the previous communication [1] we described the synthesis of a series of furanyl dioxolanes with a chloroalkyl fragment on the dioxolane ring. The present communication indicates the feasibility of transforming these compounds into new derivatives of dioxolane. It is known that the introduction of amino, ammonium, vinyl, and ether fragments into molecules often significantly enhances their biological activity. With the aim of expanding the series of physiologically active dioxolanes and their activity spectra, and also of obtaining new intermediates and monomers based upon the chloroalkyl derivatives I and II for organic synthesis, we obtained the earlier unknown substituted furanyl 1,3-dioxolanes III-XI and XIV.



I n = 0, R = H; II n = 1, R = Me; III n = 0, R = H, (R^1—R^2) = $(CH_2)_5$; IV n = 0, R = H, NR^1R^2 = morpholino; V n = 1, R = Me, (R^1—R^2) = $(CH_2)_5$; VI n = 1, R = Me, NR^1R^2 = morpholino; VII n = 1, R = Me, $R^1 = R^2$ = n-Bu; VIII n = 0, R = H, $R^1 = R^2$ = n-Bu; IX n = 0, R = H, NR^1R^2 = morpholino; X n = 1, R = Me, (R^1—R^2) = $(CH_2)_5$; XI n = 1, R = Me, $R^1 = R^2$ = n-Bu; XII R = OEt; XIII n = 0, R = H; XIV n = 1, R = Me

Methods for the obtaining some analogs of our synthesized compounds are described in the earlier literature [2-4]. However, experiments using these methods without modification for the synthesis of compounds III-XIV did not lead to the expected results. The chemical lability of the furanyl fragment in the raw materials and final products was responsible for pronounced tarring, low yields of the desired materials, and extended processing times. Thus, upon reproducing the method of [2] for the preparation of the new aminosubstituted dioxolanes III-VII by boiling with excess amine over a reaction time of 8-12 h, the yield of product did not exceed 34%. We worked up a means of obtaining aminodioxolanes by the interaction of

*For Communication 1, see [1].

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TABLE 1. Constants for Compounds III-XIV

Compound	Empirical formula	bp, °C/press., Pa (mp, °C)	d_4^{20}	n_D^{20}	Yield, %
III	$C_{13}H_{19}NO_3$	148 / 931	1,2034	1,5009	65
IV	$C_{12}H_{17}NO_4$	157,5 / 931	1,1813	1,5045	40
V	$C_{16}H_{23}NO_3$	(71,5)	—	—	53
VI	$C_{15}H_{21}NO_4$	172 / 931	1,0717	1,5221	60
VII	$C_{19}H_{31}NO_3$	177 / 798	1,1510	1,4825	45
VIII	$C_{17}H_{30}INO_3$	(128)	—	—	86
IX	$C_{13}H_{20}INO_4$	(152)	—	—	81
X	$C_{17}H_{26}INO_3$	(186)	—	—	60
XI	$C_{20}H_{34}INO_3$	(133)	—	—	42
XII	$C_{10}H_{14}O_4$	138 / 1330	1,3257	1,4074	64
XIII	$C_8H_8O_3$	98 / 798	1,2115	1,980	87
XIV	$C_9H_{10}O_3$	120 / 798	1,2936	1,5250	82

chlorides I and II with secondary amines under phase transfer catalysis in the amine/potassium carbonate system in the presence of TEBAC as catalyst. The processes were complete in 3-4 h, and the yields of amino derivatives III-VII fell in the range of 40-65% (Table 1). The aminodioxolanes obtained were transformed into the corresponding ammonium salts VIII-XI, which were soluble in water and therefore convenient for use in producing the preparative form of the corresponding biologically active material.

Sodium ethylate in ethanol was used to obtain the alkoxylated product XII from the chloride I. Along with the ethoxydioxolane XII, the yield of which was 64%, the 4-methylenedioxolane XIII was obtained in 18% yield. Evidently the increasing basicity of the reagent in passing from the amine to the alcoholate is accompanied by the formation of the dehydrochlorination product along with the substitution product. In this regard, potassium hydroxide was used for the synthesis of the 4-methylenedioxolanes XIII and XIV. However, when the reaction was carried out according to the method of [3] without solvent using finely-divided KOH at 160°C, the process was accompanied by heavy tarring and the formation of side products, and the process required 8-12 h. The separation of these mixtures was extremely complicated, and the yields of the desired products after purification did not exceed 10-22%. In order to establish optimum conditions for the dehydrochlorination of the starting dioxolane I and II, the process was conducted in sterically relatively voluminous and therefore noncompetitive protic solvents such as glycerine, or isopropyl or tetrahydrofurfuryl alcohols. In solution of the two latter solvents, tarring was not observed, by-products were not formed, the reaction time contracted to 2-4 h, and the yields of 4-methylene-1,3-dioxolanes XIII and XIV were appreciably increased.

The IR spectra of all synthesized compounds retained the absorption bands for the furan ring in the 720, 930, 1000, 1250, and 1500 cm^{-1} regions, for the dioxolane ring in the 1150, 1120, 1110, 1010, and 1000 cm^{-1} regions, and in the spectra of compounds V-VII, X, XI, XIII, and XIV in the 1600 cm^{-1} region indicating the presence of the double bond. The ^1H NMR spectra (Table 2) showed signals for the furan ring in the 6.2-7.35 ppm region and for the dioxolane ring in the 4.0-5.9 ppm region.

EXPERIMENTAL

The IR spectra were recorded with a Specord IR-71 instrument, and the ^1H NMR with a Tesla BS-467 spectrometer, using TMS as internal standard, in CCl_4 or acetone-d_6. The course of the reactions and the purity of the materials was monitored by TLC on Silufol-254 plates in toluene–ethanol, 20:3 or hexane–ethyl acetate, 6:1, with visualization by iodine vapor.

Elemental analytical data corresponded with the calculated values.

2-(2-Furyl)-4-aminomethyl-1,3-dioxolanes (III-VII). To 0.02 mole of chloride I or II was added 0.06 ml of the corresponding amine, 2.76 g (0.02 mole) of finely-powdered K_2CO_3, and 0.3 g of TEBAC and the mixture was stirred vigorously for 4 h at 70°C. After cooling, water was added and the aqueous infusion was extracted with ether, dried with calcined magnesium sulfate, the ether was evaporated under low vacuum and the residue was fractionated under vacuum (see Table 1).

TABLE 2. ^{1}H NMR Spectra for Compounds I-XIV

Compound	Furan			Ethylene	Dioxolane			4-CH_2-X
	5-H, s	3-H, s	4-H, s		2-R	4-R, q	5-H	
III	7,15	6,02	5,95	—	5,80 (2,5)*	4,00	3,70	3,5 m, 6H; 2,62 m, 6H
IV	7,20	6,25	6,01	—	5,80 (2,5)	4,08	3,75	3,65 m, 6H; 3,58 m, 4H
V	7,26	6,25	6,21	6,18 (17)	1,44 (3H, 17) *E*	4,10	3,80 (2)	3,48 m, 6H; 2,20 m, 6H
VI	7,31	6,28	6,18	6,15 (16)	1,46 d, *E*+*Z*	4,0	3,75	3,55 m, 6H; 3,40 m, 4H
VII	7,25	6,21	6,20	6,32 (12)	1,46 and 1,40 *E*	4,10	3,80 d (2)	3,46, 6H; 2,50 m, 8H; 1,1 t, $2CH_3$
VIII	7,16	6,12	6,05	—	5,80 (2,5)	4,01	3,80 d (3)	3,50, 6H; 2,44 m, 6H; 1,10 s, CH_3
IX	7,2	6,10	6,08	—	5,80 (2)	4,12	3,70 d (2)	3,60, 6H; 3,58, 4H; 1,20 s, CH_3
X	7,25	6,20	6,15	6,10 (14)	1,50 d, *E*+*Z*	4,14	3,96 d	3,46, 6H; 2,50, 6H; 1,10 s, CH_3
XI	7,20	6,21	6,16	6,40 (14)	1,46 d, *E*+*Z*	4,10	3,80 d	3,46, 6H; 2,20, 8H; 1,20 s, CH_3
XII	7,20	6,10	6,05	—	5,80 (2)	4,21	4,00	3,40, 4H; 1,10 t, CH_3
XIII	7,29	6,11	6,04	—	5,80 (2,5)	4,27	4,0 (4)	—
XIV	7,30	6,20	6,15	6,25 (16)	1,43 d, *E*+*Z*	4,30	4,11	—

*The spin–spin interactions, J in Hz, are given in parentheses.

2-(2-Furyl)-4-(1,3-dioxolanylmethyl)methylammonium Iodides (VII-XI). To 0.02 mole of the corresponding amine (III-VII) was added 0.04 mole of methyl iodide. The mixture was kept for 48 h at room temperature and the crystals were filtered off and recrystallized from alcohol.

2-(2-Furyl)-4-ethoxymethyl-1,3-dioxolane (XII). To 10.2 g (0.15 mole) of sodium ethylate in 50 ml of ethanol was added 15.65 g (0.1 mole) of compound I. The mixture was boiled for 4 h with vigorous stirring, the salt was filtered off, and the alcohol was distilled. The residue was fractionated under vacuum to give XII and XIII. The yield of the latter was 18%.

2-(2-Furyl)-4-methylene-1,3-dioxolane (XIII) and 2-Methyl-2-(2-furylethenyl)-4-methylene-1,3-dioxolane (XIV). Into a flask fitted with reflux condenser was placed 0.2 mole of potassium hydroxide, 30 ml of isopropyl or tetrahydrofurfuryl alcohol, and 0.1 mole of I or II, and the mixture was boiled for 6 h. Ice water was added, the aqueous solution was extracted with ether, and the ether extracts were combined and dried with magnesium sulfate. After removal of the drying agent, the residue after removal of the solvent was fractionated under vacuum.

REFERENCES

1. S. P. Gavrilova, T. G. Serkina, and L. A. Badovskaya, Khim. Geterotsikl. Soedin., No. 3, 322 (1993).
2. H. Orth, Angew. Chem., **64,** 544 (1952).
3. H. D. Scharf and E. Wolters, Ber., **111,** 639 (1978).
4. F. Fourneau and A. Chantalou, Bull. Soc. Chim. Fr., No. 2, 845 (1945).