REACTION OF 2,4-DISUBSTITUTED 1,3-DIOXOLANES WITH DIHALOCARBENES

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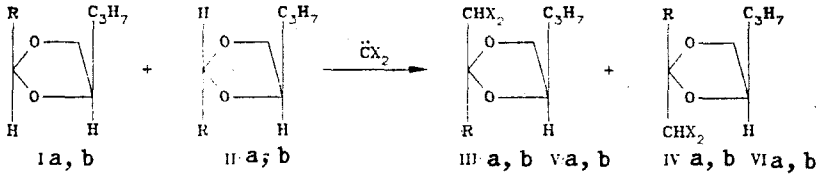
The insertion of dihalocarbenes into the $C_{(2)}$—H bond of cis- and trans-2-alkyl-4-propyl-1,3-dioxolanes leads to mixtures of stereoisomers.

It is known that dihalocarbenes (CCl_2 and CBr_2) are inserted into cyclic acetals at the $C_{(2)}$—H bond to give 2-dihalomethyl-1,3-dioxolanes [1, 2].

We have investigated the reaction of equimolar mixtures of cis- and trans-2,4-dialkyl-1,3-dioxolanes I and II with dihalocarbenes:



I, II a R=CH_3, b R=C_4H_9; III, IV X=Cl; V, VI X=Br

The reaction products are the corresponding 2-(dihalomethyl) derivatives IIIa, b-VIa, b. Because of the close boiling points we were unable to isolate the individual isomers in pure form. However, the structures of the isomers were proved unequivocally on the basis of GLC and PMR spectral data. For example, in the spectra of mixtures of the isomers the presence of CX_2H groups is responsible for the existence of two singlet signals at 5.40 and 5.48 ppm (X = Cl), 5.29 and 5.36 ppm (X = Br). The singlet at weak field at (5.48 and 5.36 ppm) is related to the hydrogen atoms of the dihalomethyl groups of isomers IIIa, b and Va, lb, while the singlet at stronger field (45.40 and 5.29 ppm) is related to the protons of the same groups of isomers IVa, b and VIa, b. The yields of the product dibromomethyl derivatives (40-60%) are higher than those of the dichloromethyl derivatives (20-30%). In all cases, IVa, b and VIa, b, which are derivatives of the cis forms Ia, b, are formed with greater selectivity (IIIa:IVa = 35:65, IIIb:IVb =30:70, Va:VIa = 40:60, Vb:VIb = 35:65). For completely understandable reasons, an increase in the bulk of the substituent in the 2 position of the ring increases the relative activities of cis forms Ia, b. The selectivity of the insertion of the dihalocarbene changes very little when chlorine is replaced by bromine. A study of the reaction of the reaction of the mixture of Ia + IIa isomers with dichlorocarbene showed that, when the temperature is increased from 10°C to 60°C, the overall yields of the products of the reaction of IIIa and IVa increases from 20% to 60%, while the selectivity of the formation of isomer IVa decreases. Thus at 10°C, 40°C, and 60°C, the IIIa:IVa isomer ratios are 35:65, 42:58, and 48:52.

EXPERIMENTAL

The reaction products were analyzed with LKhM-8MD (thermal-conductivity detector, a 3-m long column packed with 5% SE-30 silicone oil on N-AW as the support, and helium as the carrier gas) and Carlo Erba (a 50-m long glass capillary column packed with the same phase) chromatographs. The PMR spectra of solutions of the compounds in $CDCl_3$ were recorded with a Tesla BS-567 (100 MHz) spectrometer relative to tetramethylsilane (TMS). The mass spectra were obtained with an MKh-1306 spectrometer with an ionizing-electron energy of 70 eV and an ionization-chamber temperature of 150°C.

General Method for Carrying Out the Reaction of 2,4-Disubstituted 1,3-Dioxolanes with Dichlorocarbene. A 160-mg sample of 50% NaOH solution was added with stirring in the course of 2 h to a solution of 0.3 mole of substrates Ia+IIa [3] in 300 ml of $CHCl_3$ containing 1 g of triethylhexadecylammonium bromide, after which stirring was continued for 4 h. It was then washed with water until the wash waters were neutral and then dried with $MgSO_4$. The chloroform was removed by distillation, and vacuum rectification yielded a mixture of two isomers

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TABLE 1. PMR Spectra of IIIa, b-VIa, b

Compound	Chemical shifts, δ, ppm
IIIa	0,90 (3H, t, J=5,5 Hz, γ-CH_3); 1,17...1,37 (4H, m, α- and β-CH_2); 1,46 (3H, s, CH_3); 3,39...3,63 (1H, m, 4-H); 3,87...4,23 (2H, m, 5-H); 5,40 (1H, s, $CHCl_2$)
IVa	1,51 (3H, s, CH_3); 5,47 (1H, s, $CHCl_2$)
IIIb	0,99 (6H, t, J=7,5 Hz, CH_3); 1,06...1,81 (10H, m, CH_2); 3,15...3,68 (1H, m, 4-H); 3,84...4,22 (2H, m, 5-H); 5,44 (1H, s, $CHCl_2$)
IVb	5,48 (1H, s, $CHCl_2$)
Va	0,48 (3H, t, J=6,0 Hz, γ-CH_3); 0,71...1,13 (4H, m, α- and β-CH_2); 1,15 (3H, s, CH_3); 3,02...3,32 (1H, m, 4-H); 3,59...4,16 (2H, m, 5-H); 5,29 (1H, s, $CHBr_2$)
VIa	1,19 (3H, s, CH_3); 5,36 (1H, s, $CHBr_2$)
Vb	0,52 (6H, t, J=80 Hz, CH_3); 0,72...1,35 (10H, m, CH_2); 2,87...3,16 (1H, m, 4-H); 3,34...3,80 (2H, m, 5-H); 5,30 (1H, s, $CHBr_2$)
VIb	5,36 (1H, s, $CHBr_2$)

(see Table 1): 2-dichloromethyl-2-methyl-4-propyl-1,3-dioxanes IIIa and IVa ($C_8H_{14}Cl_2O_2$) with bp 68-70°C (10 mm) and M^+ 212; 2-butyl-2-dichloromethyl-4-propyl-1,3-dioxolanes IIIb and IVb ($C_{11}H_{20}Cl_2O_2$) with bp 73-75°C (10 mm) and M^+ 254; 2-dibromomethyl-2-methyl-4-propyl-1,3-dioxolanes Va and VIa ($C_8H_{14}Br_2O_2$) with bp 96-98°C (10 mm) and M^+ 300; 2-butyl-2-dibromomethyl-4-propyl-1,3-dioxolanes Vb and VIb ($C_{11}H_{20}Br_2O_2$) with bp 102-104°C (10 mm) and M^+ 342.

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HETEROCYCLIC BIOANTIOXIDANTS

1.* REACTION OF 3-NITRO-4-CHLOROCOUMARIN WITH THIOLATING AGENTS

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The reaction of 3-nitro-4-chlorocoumarin with thiolating agents in the presence of water leads to the formation of a mixture of 3-nitro-4-hydroxycoumarin, bis(3-nitro-4-coumarinyl) sulfide, and colored labile products of undetermined structure. The reaction path can be controlled by the choice of solvent, reagent ratio, and temperature regime and by the use of weakly basic additives.

Antioxidants (AO) are multipurpose products. The most fully studied are phenolic antioxidants, among which the sterically hindered phenols have the highest activity [2]. Natural heterocyclic compounds, including 3-hydroxypyridines, pyrones, coumarins, and related bicyclic systems, are a readily available raw materials. This makes it possible to conduct a synthetic investigation over a wide range of antioxidants (analogs of vitamins E and C, iron chelating agents, models of protective metalloenzymes) with retention of the biotic indications of the biological activity to a greater or lesser degree. This is particularly valuable in the development of pharmacologically active products [3], food additives, and medicinal stabilizers. Here it is necessary to take account of the special features of the natural antioxidants in the protective system of the organism, which are determined specifically in

*For the preliminary communication, see [1].

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