REACTION OF DIHALOCARBENES WITH CHROMENES UNDER INTERPHASE-CATALYSIS CONDITIONS

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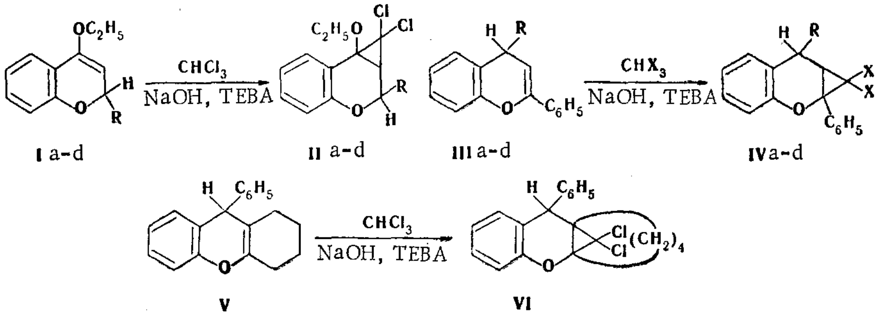
Reactions involving the interphase dichloro- and dibromocyclopropanation of 2H- and 4H-chromenes that contain ethoxy, aryl, alkyl, and hetaryl substituents in the pyran ring were studied. It is shown that products of addition of dihalocarbenes to the double bond of the chromenes are formed in high yields in all cases.

Dihalocyclopropane derivatives of chromenes are attracting attention as intermediates for the synthesis of compounds of the benzoxepine series [1] that have a broad spectrum of biological activity [2]. However, little study has been devoted to the reactions of dihalocarbenes with chromenes, and these reactions have not been investigated at all under interphase-catalysis conditions. Only the addition of dichloro- and dibromocarbenes generated from esters of trihaloacetic acids has been described [1, 3, 4]. Chromenes that contain various substituents in the pyran ring have not been previously subjected to such transformations.

We used interphase catalysis [5] to generate dihalocarbenes. We observed that brief (10-15 min) stirring of chloroform solutions of chromates I, III, and V with 40-50% aqueous NaOH in the presence of catalytic amounts of triethylbenzylammonium chloride leads to the formation of the corresponding gem-dichlorocyclcopropane derivatives II, IV, and VI. Dibromocyclopropane adduct IVd was obtained from chromene IIIa when bromoform was used.



I a R=Ph; b R=o-$CH_3C_6H_4$; c R=CH_3; d R=2-thienyl; II a R=Ph; b R=o-$CH_3C_6H_4$; c R=CH_3; d R=2-thienyl; III a R=Ph; b R=CH_2Ph; c R=p-$CH_3C_6H_4$; d R=2-thienyl; IV a R=Ph, X=Cl; b R=CH_2Ph, X=Cl; c R=p-$CH_3C_6H_4$, X=Cl; d R=Ph, X=Br; e R=2-thienyl; X=Cl

Only products of addition to the double bond are formed in high yields, regardless of the substituents in the pyran ring and the position of the double bond. We did not observe incorporation of the dihalocarbenes at the C—H bond in a single case, although the formation of products of simultaneous addition and incorporation of dichlorocarbene in the interphase dichlorocyclopropanation of 1-methyl-1,2-dihydroquinoline [6] and products of incorporation at the C—H bond in the case of 2H-thiochromene [6] has been described.

The thiophene ring remains unaffected in the reaction of chromenes Id and IIId, which contain an α-thienyl substituent, with dichlorocarbene. The absence in the IR spectra of the reaction products of an absorption band at 1650-1700 cm^{-1}, which is characteristic for the double bond of vinyl ethers as compared with the starting substances, serves as evidence for the formation of products of addition to the C=C bond. The IR spectra of all of the dihalo-

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TABLE 1. Characteristics of the Compounds Obtained

Compound	mp, °C	IR spectrum, cm^{-1}	PMR spectrum		Found, %			Empirical formula	Calc., %			Yield, %
			solvent	δ, ppm (J, Hz)	C	H	Hal		C	H	Hal	
IIa	96—98	1610, 1580, 1220	CCl_4	1,0 (t, 3H, J=7,5); 2,1 (d, 1H, J=3,0); 3,2 (m, 2H); 5,3 (d, 1H, J=3,0); 6,5—7,5 (m, 9H)	64,6	4,9	21,1	$C_{18}H_{16}Cl_2O_2$	64,5	4,8	21,2	91
IIb	74—75	1610, 1585, 1230	CCl_4	1,05 (t, 3H, J=7,0); 1,95 (d, 1H, J=4,5); 2,3 (s, 3H); 3,3 (m, 2H); 5,4 (d, 1H, J=4,5); 6,4—8,3 (m, 8H)	65,3	5,1	20,2	$C_{19}H_{18}Cl_2O_2$	65,3	5,2	20,3	65
IIc[a]	94—96	1605, 1580, 1220	CCl_4	1,2 (t, 3H, J=6,0); 1,4 (d, 3H, J=7,0); 1,8 (d, 1H, J=3,0); 3,3 (m, 2H); 4,4 (dq, 1H J_d=3,0, J_q=7,0); 6,5—7,6 (m, 4H)	57,3	5,4	25,6	$C_{13}H_{14}Cl_2O_2$	57,2	5,2	26,0	72
IId	90—91	1610, 1585, 1210	CCl_4	1,05 (t, 3H, J=6,8); 2,25 (d, 1H, J=2,3); 3,3 (m, 2H); 5,55 (d, 1H, J=2,3); 6,4—7,6 (m, 7H)	56,5	4,3	20,8	$C_{16}H_{14}Cl_2O_2S$[b]	56,3	4,1	20,8	70
IVa	132—133	1590, 1230	CCl_4	2,5 (d, 1H, J=1,5); 4,25 (d, 1H, J=1,5); 6,5—7,5 (m, 14H)	71,7	4,3	19,3	$C_{22}H_{16}Cl_2O$	71,9	4,4	19,3	96
IVb	111—112	1580, 1230	CCl_4	2,1 (d, 1H, J=1,5); 2,7—3,5 (m, 3H); 6,3—7,2 (m, 14H)	72,6	4,6	18,9	$C_{23}H_{18}Cl_2O$	72,5	4,8	18,6	89
IVc	92—94	1585, 1225	—	—	72,6	4,8	18,6	$C_{23}H_{18}Cl_2O$	72,5	4,8	18,6	82
IVd	184—185	1585, 1220	C_6H_6	2,65 (d, 1H, J=1,5); 4,10 (d, 1H, J=1,5)	57,5	3,5	35,2	$C_{22}H_{16}Br_2O$	57,9	3,5	35,0	85
IVe	129—130	1580, 1220	CCl_4	2,50 (d, 1H, J=1,5); 4,50 (d, 1H, J=1,5; 6,35—7,55 (m, 12H)	64,3	3,9	19,0	$C_{20}H_{14}Cl_2OS$[c]	64,4	3,8	19,0	86
VI	230	1610, 1235	$CHBr_3$	4,15 (s, 1H); 1,0—2,5 (m, 8H)	69,8	5,1	20,6	$C_{20}H_{17}Cl_2O$	69,8	5,0	20,6	87

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[a] The PMR spectrum of IIc was recorded with a Tesla BS-487 spectrometer (80 MHz). [b] Found: S 9.6%. Calculated: S 9.4%. [c] Found: S 8.5%. Calculated: S 8.6%.

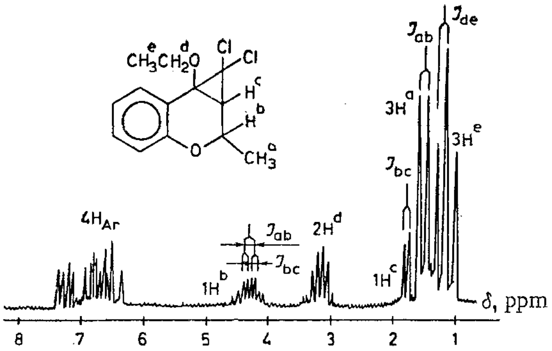

Fig. 1. PMR spectrum of 2-methyl-4-ethoxy(1,1-dichlorocyclopropa)[c]chroman.

cyclopropane derivatives obtained contain a strong absorption band at 1210-1235 cm^{-1} (pyran ring C—O—C), which indicates retention of the pyran ring.

As compared with starting chromenes I, III, and V, signals of vinyl protons at 4.35-4.49 ppm for Ia-d and at 5.25-5.40 ppm for IVa-d [sic] vanish in the PMR spectra of dichlorocyclopropanes II, IV, and VI, whereas signals at 1.8-2.65 ppm, which are characteristic for the protons of the gem-dihalocyclopropane ring [1, 4], appear in the spectra. A peculiarity of the PMR spectra of IIa-d is the appearance of signals of protons of the methylene fragment of the ethyl group in the form of a complex multiplet instead of a quartet with an integral intensity of 2H. The characteristic spectrum of IIa is presented in Fig. 1.

EXPERIMENTAL

The PMR spectra of the compounds were recorded with a Tesla BS-467 spectrometer (60 MHz) with hexamethyldisiloxane as the internal standard. The IR spectra of mineral oil suspensions of the compounds were recorded with a Specord IR-71 spectrometer with an NaCl prism. The physicochemical characteristics of the dihalocyclopropane derivatives are given in Table 1; the yields indicated in Table 1 are based on the recrystallized substances.

2-R-4-Ethoxy(1,1-dichlorocyclopropa)[c]chromans (IIa-d). A solution of 0.5 g of chromene Ia-d in 15 ml of chloroform was stirred for 1 min with 5 ml of 50% aqueous NaOH solution, after which 0.05 g of triethylbenzylammonium chloride was added, and stirring was continued for 10 min. The mixture was poured into 150-200 ml of water, the chloroform was separated, and the aqueous alkaline layer was extracted with ether. The combined ether—chloroform extract was washed with water until the wash water was neutral, dried with sodium sulfate, and evaporated *in vacuo* at 40°C. The solid residue was recrystallized from ethanol.

2-Phenyl-4-R-(1,1-dichlorocyclopropa)[b]chromans (IVa-c, e) and 2,3-Tetramethylene-4-phenyl(1,1-dichlorocyclopropa)[b]chroman (VI). A 10-ml sample of 40% aqueous NaOH solution and 0.03 g of triethylbenzylammonium chloride were added to a solution of 1 g of chromene IIIa-d or V in 10 ml of chloroform, and the mixture was stirred vigorously for 10-15 min. The reaction product was isolated as described above. The colorless oil was dried *in vacuo* at 2-4 mm and recrystallized from n-butanol to give colorless crystals.

1,4-Diphenyl(1,1-dibromocyclopropa)[b]chroman (IVd). A 0.02-g sample of triethylbenzylammonium chloride and 15 ml of 50% NaOH were added to a solution of 2 g of 2,4-diphenyl-4H-chromene (IIIa) in 15 ml of bromoform, and the mixture was stirred vigorously for 5 min. The reaction product was separated from the alkaline solution as described above, and the ether—bromoform extract was evaporated *in vacuo* at room temperature. The solid residue was recrystallized from n-butanol to give a colorless crystalline substance.

LITERATURE CITED

1. W. E. Parham and L. P. Huestis, J. Am. Chem. Soc., 84, 813 (1962).
2. J. M. McCall, US Patent No. 4153612; Ref. Zh. Khim., 1, 0159P (1980).
3. C. Marcaillou, G. Fontaine, and P. Maitte, Compt. Rend., 267, 846 (1968).
4. B. Graffe, M. Sacquet, G. Fontaine, and P. Maitte, Compt. Rend., 269, 992 (1969).
5. M. Makosha, Usp. Khim., 46, 2174 (1977).

6. T. Greibrokk, Tetrahedron Lett., No. 17, 1663 (1972).
7. W. E. Parham and R. Koncos, J. Am. Chem. Soc., 83, 4034 (1961).

INVESTIGATION OF THE KINETICS OF THE NITRATION OF THIOPHENE DERIVATIVES

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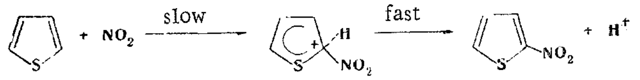
The kinetics of the nitration of thiophene derivatives with nitric acid in acetic anhydride were investigated. The nitration of 2-substituted thiophenes is a second-order reaction. The rate constants and activation parameters of the reaction were calculated. The possibility of the use of the Hammett and Yukawa–Tsuno equations for this reaction series is demonstrated. An isokinetic dependence is observed.

Some aspects of electrophilic substitution reactions in the thiophene series, including nitration, have been correlated in a monograph [1]. However, despite a detailed study of the mechanism of nitration, only one study has been devoted to the kinetics of this reaction [2]; Butler and Hendry investigated the kinetics of the nitration of thiophene with a mixture of nitric and sulfuric acids. Nitro groups enter the 4 and 5 positions in the nitration of thiophene and substituted thiophenes. 5-Nitrothiophenes are of greatest interest for the synthesis of monomers. Tirouflet and co-workers [3, 4] have shown that primarily 5-nitrothiophenes are formed in the nitration of some thiophene derivatives with a mixture of nitric acid with acetic anhydride. Having in view the subsequent use of nitro derivatives of thiophene for the synthesis of monomers, we investigated the kinetics of the nitration of thiophene and its derivatives with a mixture of nitric acid with acetic anhydride.

We investigated the yields of 5-nitro derivatives of thiophene as a function of the substrate concentration over the concentration range 0.03 to 0.85 mole/liter with nitrating mixture concentrations from 0.3 to 0.55 mole/liter at –20 to +65°C. According to the literature data [1, 5], the nitration of thiophene derivatives by the nitronium ion, in analogy with the benzene ring, proceeds through a slow step involving the formation of a σ complex with rapid splitting out of a proton:



The nitration is a second-order reaction, as determined graphically from the logarithmic dependence of the reaction rate on the concentration. It was determined experimentally that the reaction is first-order in the substrate and the nitrating agent. The overall second order of the reaction is also confirmed by the constancy of the reaction rate constants calculated from the equation for a second-order reaction for various degrees of conversion.

The rate constants calculated for a constant equimolar ratio of the reagents at various temperatures are presented in Table 1. The rate constants presented in Table 1 show that electron-donor substituents accelerate the reaction, whereas electron-acceptor substituents slow it down. The introduction of an iodine atom in the thiophene ring has little effect on the reaction rate, whereas the introduction of a bromine atom slows it down. The differences in the reaction rates for electron-acceptor substituents are due to both the activation energy and the pre-exponential multiplier. Electron-donor substituents are characterized by close values of the pre-exponential multiplier.

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