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1,3-DIOXENIUM CATIONS: SYNTHESIS AND PROPERTIES* (REVIEW)

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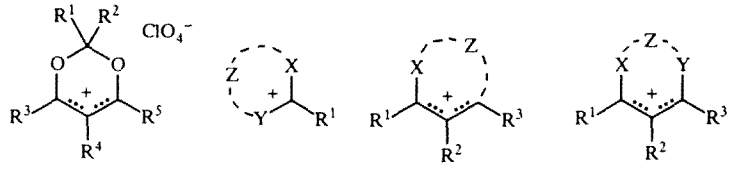
The features and prospects of the new reaction of 1,3-keto-enols, ketones, and acids yielding 1,3-dioxenium salts were investigated. The results of studies of the structure, topomerization, and transformations of 1,3-dioxenium cations — a new family of stable heterocyclic cations of the allyl type — were generalized.

1. INTRODUCTION

We reported on synthesis of previously unknown 1,3-dioxenium cations (I) for the first time in 1993 [1]. These cations belong to a relatively extensive group of heterocyclic cations of the nonaromatic type which includes 1,3-dioxanium, 1,3-dioxolanium, 4H-1,3-benzoxazinium, 1,3-dithinium, and other cations, for example. Cations of the carbenium type (II), in which the usual carbenium center in the ring is stabilized by conjugation with neighboring (O, S, N) heteroatoms, and cations of the allyl type (III and IV), in which the allyl (propenyl) cation, a three-carbon heterocycle fragment, is also stabilized by conjugation with neighboring heteroatoms in the ring in positions 1 and/or 3, can formally be distinguished in this group, basically represented by five- and six-member heterocycles.



I II III IV

X, Y = O, S, NR; Z = $(CR_2)_n$ or similar unconjugated chain

The new 1,3-dioxenium cations belong to the last subgroup of heterocations. This subgroup is represented by a comparatively small number of prepared and investigated compounds: 1,3,2-dioxaborines (V) (X = O) [2, 3], 1,3,2-oxazaborines (V) (X = NR) [4], their gallium and indium analogs [5], and furanium cations (VI) (X = O [6] and their analogs — thiophene cations [7] and pyrrole [8] (VI) (X = S, NR), detected by spectral methods only in solutions.

The basic transformations of the most studied 1,3,2-dioxaborines (V) and furanium salts (VI) are due to the high reactivity of the R^3 and/or R^5 alkyl substituents in them with respect to electrophilic reagents (aldehydes, ortho esters, etc.).

V
X = O, NR

VI
X = O, S, NR

*Dedicated to É. Ya. Lukevits on his 60th birthday.

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Many of the products formed in these reactions have valuable spectral characteristics. Reactions with phenols yielding 1-benzopyrylium salts are also known for 1,3,2-dioxaborines [9].

In studying 1,3-dioxenium salts (I), we focused attention on explaining the synthetic boundaries of their formation and reactions with electrophilic reagents. Some transformations with nucleophilic reagents were also investigated. Great attention was focused on further transformations of the 1,3-dioxenium cation derivatives obtained.

2. SYNTHESIS OF 1,3-DIOXENIUM SALTS

The first representatives of the new family of 1,3-dioxenium cations were obtained by the reaction of the simplest ketones (acetone, cyclohexanone) and 1,3-diketones (acetylacetone, benzoylacetone, dibenzoylmethane) in the presence of 16% perchloric acid solution in AcOH and acetic anhydride [1].

The hypothetical mechanism of this reaction (Scheme 1), with two alternative paths A and B, includes stages of activation by protonation of the ketone or 1,3-diketone in the keto-enol form, subsequent nucleophilic addition of the carbonyl oxygen of the keto-enol or ketone to the carbenium carbon center with formation of intermediate P_1 or P_1', which turns into intermediate P_2 or P_2' in conditions promoting dehydration and is then cyclized into the dioxenium cation.

Of the two proposed paths, path A is the most probable, since it implies activation by protonation of the keto-enol, which is more basic than ketone. Actually, the basicity of ketones and diketones has been repeatedly investigated by different methods, and it was shown in [10] that 1,3-diketones in the keto-enol form are usually stronger bases than ketones, although the effect of substituents and solvation can lead to levelling of the basicities and even higher basicity of the ketone (Scheme 1).

Different transformations take place to some degree with both components in acid medium: keto-enol conversions, isomerization, splitting. Several isomeric mono- and diprotonated forms can be formed in protonation of 1,3-keto-enol [11-13]

Scheme 1

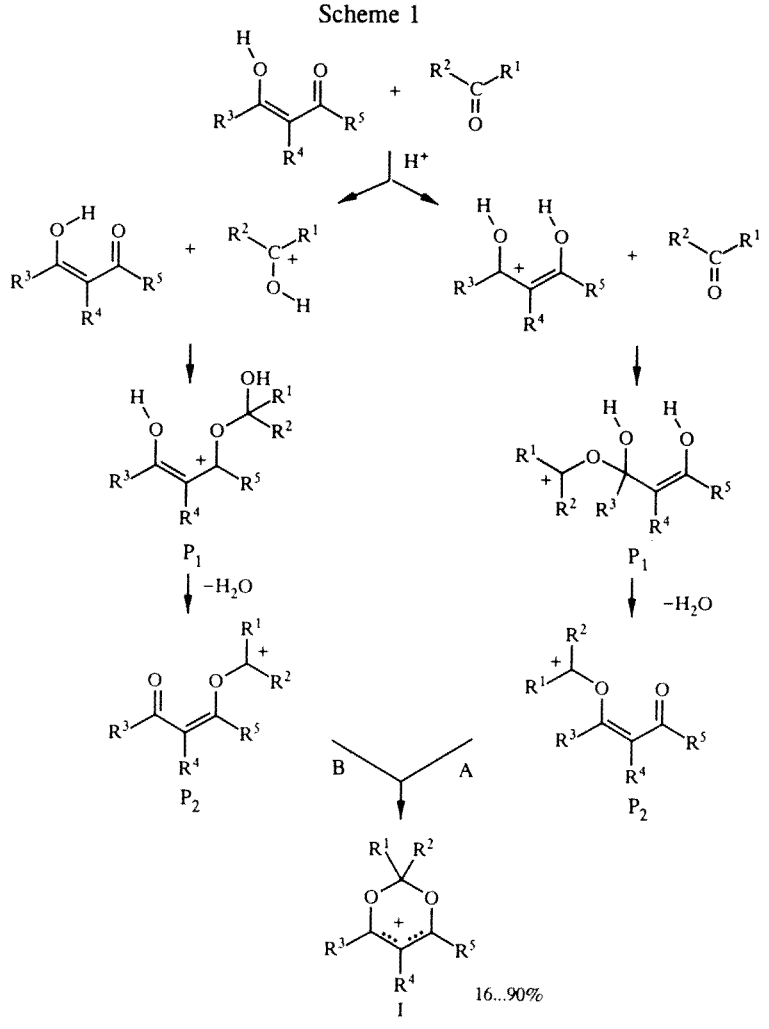


TABLE 1. 2-R^1-2-R^2-4-R^3-5-R^4-6-R^5-1,3-Dioxenium Perchlorates (I)

Compound	R^1	R^2	R^3	R^4	R^5
Ia	CH_3	CH_3	CH_3	H	CH_3
Ib	C_9H_{14}*		CH_3	H	CH_3
Ic	CH_3	CH_3	CH_3	$(CH_2)_4$	
Id	CH_3	CH_3	Ph	H	CH_3
Ie	$(CH_2)_5$		Ph	H	CH_3
If	C_9H_{14}*		Ph	H	Me
Ig	CH_3	CH_3	Ph	CH_3	CH_3
Ih	$(CH_2)_5$		Ph	Me	Me
Ii	CH_3	CH_3	Ph	$(CH_2)_4$	
Ij	CH_3	CH_3	Ph	$(CH_2)_3$	
Ik	$(CH_2)_5$		Ph	$(CH_2)_3$	
Il	$(CH_2)_5$		Me	$C_6H_4(CH_2)_2$†	
Im	CH_3	i-C_3H_7	Ph	$(CH_2)_3$	
In	CH_3	i-C_4H_9	Ph	$(CH_2)_3$	
Io	CH_3	CH_3	Ph	H	Ph
Ip	$(CH_2)_5$		Ph	H	Ph
Iq‡	CH_3	C_2H_5	Ph	H	CH_3
Ir‡	CH_3	C_3H_7	Ph	H	CH_3
Is‡	C_2H_5	C_2H_5	Ph	H	CH_3
It‡	CH_3	CH_2Ph	Ph	H	CH_3
Iu‡	C_6H_{12}**		Ph	H	CH_3
Iv‡	$(CH_2)_4$		Ph	H	CH_3
Iw‡	$(CH_2)_5$		Ph	$(CH_2)_3$	
Ix‡	$(CH_2)_5$		CH_3	H	CH_3

*Bicyclo[3.3.1]nonyl-3,7-ene.

†1,2,3,4-Tetrahydronaphtho[*h*].

‡Characterized as 6-(4-methoxystyryl)-1,3-dioxenium derivative.

**3-Methyl-1,5-pentamethylene.

with dynamic equilibrium established between them, and the position of the equilibrium is determined by many factors: the structure of the starting keto-enol, the nature of the solvent, the acid, the temperature, etc.

In general, in examining and selecting the most probable mechanism of formation of 1,3-dioxenium cations, the problem of the complex composition (multicomponent character) of the reaction mixture, and thus the indeterminancy of the structure of the reacting forms of the substrates, then arises.

We investigated the factors of the structure of the reagents that determine the boundaries of the reaction of formation of salts I and looked for the optimum conditions of this process [14].

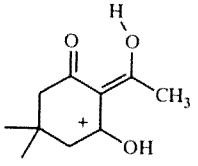
The starting keto-enol is hypothetically primarily protonated in synthesis of dioxenium salts, forming the enolium cation, which undergoes nucleophilic attack by the oxygen atom of the ketone carbonyl group. The requirements of, first, high basicity of the keto-enol required for its protonation, and second, the capacity for effective delocalization of the positive charge in the emergent cation of the allyl type due to the donor properties of the substituents and planarity of the system, follow from this; the last quality can play a decisive role in stabilization of the dioxenium I cations formed. With respect to the ketone, higher nucleophilicity is more important.

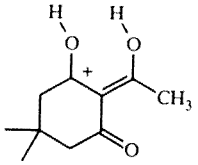
Since intramolecular cyclization of the 1,3-keto-enol O-carbenium ester P_2 is probably the concluding act in the path to I (Scheme 1), where the carbenium carbon of the ketone fragment is converted from the trigonal (sp^2) to the tetrahedral (sp^3) configuration, the requirement for the electronic characteristics of the substituent in this fragment will evidently be the opposite: they should not effectively delocalize the positive charge on the carbenium carbon of the ketone component. The validity of these arguments has been tested experimentally.

1,3-Diketone. The 1,3-diketones selected for investigation of the structure can arbitrarily be divided into four types: 1) alkyl- and/or aryl(styryl)-substituted diketones, where the alkyl (aryl, styryl) substituent is electroneutral or a donor (i.e., compounds such as acetylacetone, α-alkylbenzoylacetone, 2-alkylcyclanones and their analogs); 2) diketones with acceptor substituents (CF_3, CF_2H, COR, CH_2OEt groups); 3) 2-acylphenols; 4) acetoacetic ester and its analogs.

Of the diketones listed, only the first ones form 1,3-dioxenium cations (Table 1) [1, 14, 15]. Most of the 1,3-dioxenium salts obtained are highly hygroscopic. It is important to note that the resistance to hydrolysis is a function of the presence and number of phenyl substituents in positions 4(6) of the ring. Although the salts obtained from acetylacetone or acetyl-cyclohexanone are very rapidly (5-10 min) hydrolyzed by atmospheric moisture, the salts obtained from dibenzoylmethane can be stored for months without noticeable hydrolysis.

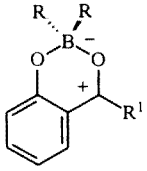
The fact that we were unable to obtain salts I from 1,1,1,5,5,5-hexafluoroacetylacetone, 1,1,1-trifluoroacetylacetone, 1,1-difluoroacetylacetone, thenoyltrifluoroacetone, and oxalyldiacetophenone, that is, diketones with strong acceptor groups, indicates the very important role of substituents in positions 1 and/or 3 of the keto-enol that delocalize the positive charge. However, the type I target product could also not be obtained from 2-acetyldimedone. In this case, the acceptor substituent would be in position 5 of the dioxenium ring and would destabilize cation I only inductively. Here the lack of success is probably because the carbonyl group, which does not participate in the formation of a hydrogen bond with the enol of the 2-acetyl group, is protonated in 2-acetyldimethone. For this reason, a cation of the 1,3-dioxypropenium type (VI) with a *cis-trans* configuration is formed instead of the required cation (VII) with a *cis-cis* configuration.

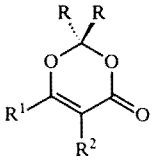

VI

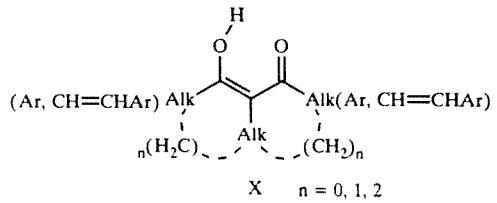

VII

Considering 2-acylphenols as analogs of 1,3-keto-enols with a fixed enol group and since they easily form the corresponding benzodioxaborines (VIII) with BF_3 and its complexes [4], it was natural to assume that they will also form benzodioxenium salts. However, in ordinary conditions (0-20°C), the type I products sought could not be obtained from 2-acetylphenol or 2-butyrylphenol, and the external signs of the reaction indicated the occurrence of other condensation processes. We actually know that 2-acylphenols in acid medium enter into autocondensation, forming 2-(2-hydroxyphenyl)-1-benzopyrylium salts [16]. This condensation perhaps takes place more rapidly than formation of the dioxenium ring; the causes of the lack of success could also be sought in the features of the thermodynamically disadvantageous intermediate states of this reaction, which reduce the aromaticity of the benzene ring.

Finally, acetoacetic ester was used as the diketone component. The initial premise was the research by Japanese and German colleagues on synthesis of 1,3-dioxen-4-ones (IX) from acetoacetic ester derivatives [17, 18], where sulfuric acid and a large excess of acetic anhydride were used for condensation with the ketone.


VIII


IX


X n = 0, 1, 2

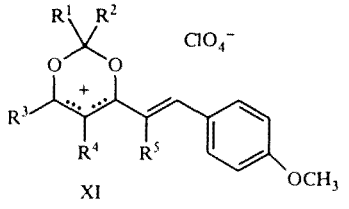
This process probably passes through intermediate formation of 4-hydroxy- or 4-alkoxydioxenium salt, so that an attempt was made to obtain this salt with the usual method. However, it was not possible to separate salt-like products. Due to the lower basicity of acetoacetic ester in comparison to diketones from the first group, formation of the 1,3-dioxenium cation is probably strongly slowed. This is also indicated by the studies on synthesis of dioxenones IX, where condensation was conducted for several hours at a low temperature.

Diketones of the first type and their type X homologs with alkyl, aryl, and styryl donor groups which contain bridge structures with CH_2 units are thus suitable for synthesis of 1,3-dioxenium salts.

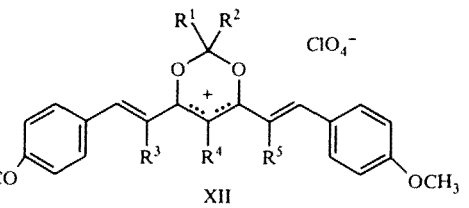
The possibilities of synthesizing salts I from synthons of 1,3-keto-enols of the acylacetylene, β-chlorovinyl ketone, and other types are still beyond the limits of examination.

Ketone. The ketones selected for investigation can arbitrarily be divided into four groups: 1) aliphatic ketones; 2) cycloalkanones and 2-adamantanone; 3) aliphatic-aromatic ketones and benzophenone; 4) other compounds containing a C=O group, including polyfunctional compounds.

1,3-Dioxenium perchlorates I could only be obtained from ketones of the first and second group (Table 1) [1, 14, 15]. Many ketones (cyclopentanone, methyl ethyl ketone, diethyl ketone, etc) forming cations I according to Scheme 1 cannot be separated in the crystalline state in ordinary conditions, but it is easy to obtain well-crystallized styryl derivatives (XI, XII) with high yields when 4-methoxybenzaldehyde is added to the reaction mixtures.



XI

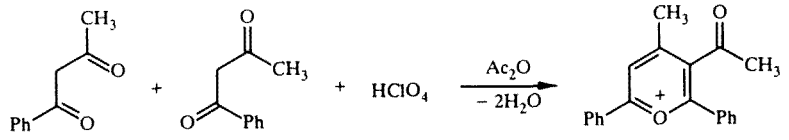


XII

Salts I could not be obtained with alkylaryl ketones (acetophenone, *p*-methylacetophenone, propiophenone, etc.) and benzophenone. This can be attributed to the well-known [19] lower tendency of these ketones to form cyclic acetals. In the case of acetophenones, competitive condensation reactions probably take place much more rapidly: autocondensation of acetophenone to dypnone with subsequent acylation to 2,6-diaryl-6-methylpyrylium salts [20] and to a lesser degree, condensation of diketone with acetophenone, which also yields pyrylium salts [21]. Protonation of the carbonyl oxygen takes place in the case of highly basic benzophenone, and the diphenyloxycarbenium cation, which is not very active for steric and electronic reasons, is formed.

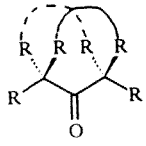
In studying the possibilities of varying the structure of the ketone component introduced in the reaction, the suitability of some other reagents containing a C=O group, functionalized acetones (acetoacetic ester and acetonedicarboxylic acid diethyl ester) in particular, for synthesis of salts I was also examined. This approach is totally logical, since the corresponding cyclic acetals (dioxanes and dioxolanes) obtained from these compounds are known [19, pp. 328-329]. However, it was not possible to separate any salt product. The same result was obtained when acetylacetone, benzoylacetone, and 1,1,3-trichloroacetone were tested in the role of the ketone. When the duration of the reaction was increased to 5-6 h, 3-acetyl-2,6-diphenyl-4-methylpyrylium perchlorate (XIII) (Scheme 2) was separated as a result of autocondensation of benzoylacetone [14]

Scheme 2



XIII

In all cases reported, the acceptor substituent in the α-position to the acetone C=O group probably significantly changes the ability of acetone to form the 1,3-dioxenium cation. We will hypothesize that this effect is manifested by facilitation of enolization of this group. Enolization of ketones is such a process in acid-catalyzed synthesis of salts I, also formed with a high yield in the case of totally nonenolized 2-adamantanone due to the rigidity of the carbon backbone (see compounds Ib and If in Table 1). Facilitation of enolization accelerates crotonic condensation to α,β-unsaturated ketones and results in the fact that such (for simple dialkylketones) a process becomes basic in the case of strongly enolized ketones. Subsequent acid-catalyzed acetylation of the α,β-unsaturated ketone obtained by acetic anhydride yields the pyrylium salt when the reaction lasts long enough.



XIV R = H, Alk, Ar

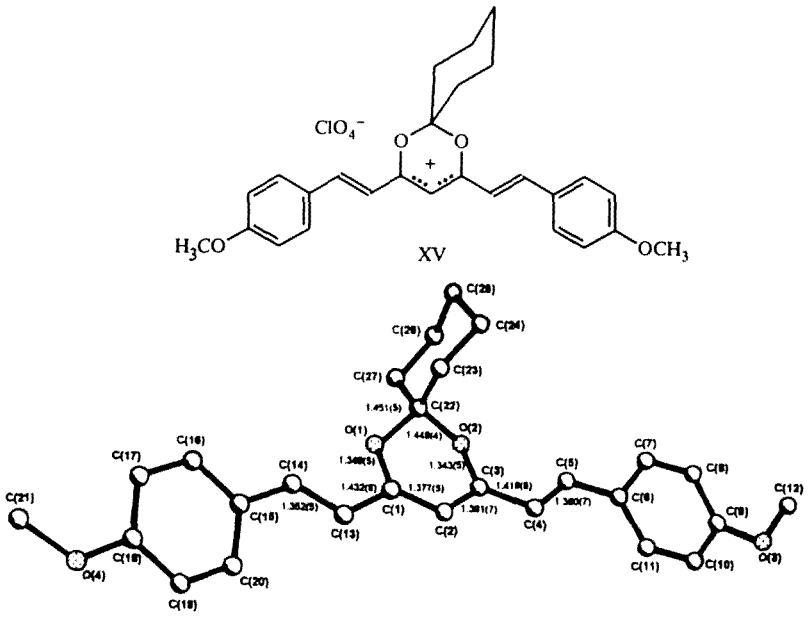


Fig. 1. Structure of 4,6-bis(4-methoxystyryl)-2,2-pentamethylene-spiro-1,3-dioxenium perchlorate (XV).

A low tendency toward (as in the simplest dialkylketones) or impossibility of enolization (as in 2-adamantanone) with simultaneous low basicity is thus the basic requirement for the ketone for successful synthesis of salts I. As a consequence, only homologs of acetone and cycloalkanones of type XIV are suitable for this reaction.

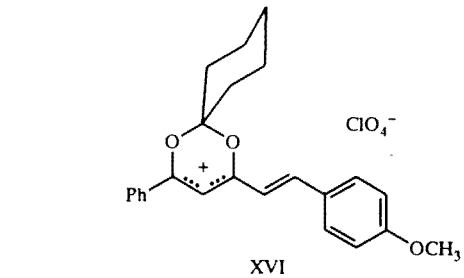
Acid. Solutions of $HClO_4$, H_2SO_4, HBF_4, $HSbCl_6$, CF_3COOH, HCl, HBr, and CF_3SO_3H in acetic acid were used to determine the effect of a protic acid on the reaction of synthesis of salts I, and they were tested for obtaining the corresponding 2,2-pentamethylene-spiro-4-methyl-6-phenyl-1,3-dioxenium salt. The effect of the concentration of acid on the yield of product was determined for perchloric acid. A 16% concentration was optimum. The use of solutions of higher concentration accelerates side reactions of condensation, oxidation, and splitting. The reaction time increases and the yield of product decreases with solutions of lower concentration. In the case of HBF_4, 1,3,2-dioxaborine was formed similar to [2]. With respect to the other acids, it was only possible to obtain hexachloroantimonate and triflate (as the styryl derivative). Solutions of strong protic acids in AcOH with weak oxidizing power and with a weakly polarized anion are thus suitable for synthesis of dioxenium salts.

Dehydrating Agent. The possibilities of substitution of acetic anhydride by other dehydrating agents were also investigated: P_2O_5, $Mg(ClO_4)_2$, $(RCO)_2O$, and RCOCl (where R = Alk) were also investigated. Phosphoric anhydride and anhydrone were ineffective in this reaction. On the contrary, 1,3-dioxenium salts formed as easily with acetyl chloride, anhydride, and propionic acid chloride as with Ac_2O. The role of these substances in the reaction is perhaps not limited to binding of the water formed alone, but is completed by acylation of the OH groups in the reagents or intermediates.

Optimization of the Conditions. The best yields of products I were observed when equimolar amounts of diketone, ketone, acid, and a two-fold amount of dehydrating agent were used in synthesis. To exclude overheating (the reaction takes place exothermically) and to successfully separate the product, dry Et_2O was added to the reaction mixture. Synthesis was conducted at temperatures from 0 to 10°C.

It was found as a result that the structure of the 1,3-keto-enol, which favors stabilization of its protonated form, and the low basicity and enolizability of the ketone are the factors that determine the boundary conditions of synthesis of 1,3-dioxenium salts I. Acetic acid solutions of strong protic acids and lower aliphatic acid (chloro)anhydrides are most effective as the acid and dehydrating agents. As a function of the degree of correspondence of the structure of the keto-enol and ketone with the requirements listed above, the yields of salts I are within the limits of 16 to 90%.

The IR spectra of salts I contain absorption bands of a phenyl substituent in the 1606-1573 cm^{-1} region, an allyl fragment in the 1566-1540 cm^{-1} and 1526-1500 cm^{-1} region, and bands of C—O and C—O—C bonds in the 1266-1240 cm^{-1} and 1226-1180 cm^{-1} region.



XVI

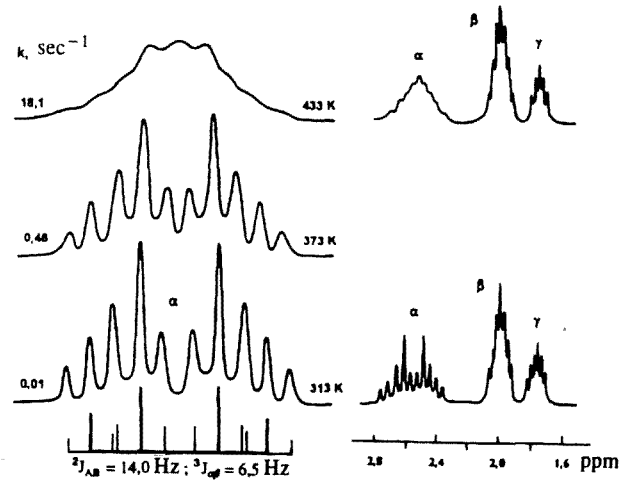


Fig. 2. Part of the PMR spectrum of 4-phenyl-6-(4-methoxystyryl)-2,2-pentamethylenespiro-1,3-dioxenium perchlorate (XVI) illustrating the resonance signals of α,γ-methylene protons and the temperature-dependent spectrum of α-methylene protons (300 MHz, $C_6D_5NO_2$).

The following signals (δ, $CDCl_3$, 300 MHz) are easily identified in the PMR spectra of cations I of similar structure: CH_3 protons from position 2 in the ring in the form of a singlet in the 1.90-2.19 ppm region; CH_3 protons from ring position 4 as a singlet in the 2.50-2.79 ppm region; a proton from ring position 5 as a singlet in the 6.67-8.18 ppm region; protons of the phenyl substituent from ring position 6: a two-proton triplet of *meta*-protons at 7.52-7.71 ppm, a one-proton triplet of a *para*-proton at 7.72-7.96 ppm, and a two-proton doublet of *ortho*-protons at 7.83-8.22 ppm.

3. STRUCTURE OF THE 1,3-DIOXENIUM CATION

We conducted an x-ray structural analysis of a stable styryl derivative — 4,6-bis(*p*-methoxystyryl)-2,2-pentamethylene-spiro-1,3-dioxenium perchlorate (XV) ($C_{27}H_{29}O_4 \cdot ClO_4 \cdot ½H_2O$) — to confirm the structure of the 1,3-dioxenium cations and reveal their structural characteristics [15]. The molecular structure of the cation is shown in Fig. 1.

As shown, the dioxenium ring is in the envelope conformation (the dihedral angle along the $O_1—O_2$ line is equal to 40.3°), while the 2,2-spiro-annelated cyclohexane ring has a chair conformation. The bond lengths, $C_1—C_2$ = 1.377(5) Å and $C_2—C_3$ = 1.391(7) Å, are almost equal within the limits of the experimental error, just as $C_1—O_1$ = 1.348(5) Å and $C_3—O_2$ = 1.343(5) Å. The values of the $C_1—C_2$ and $C_2—C_3$ bond lengths are close to the calculated values of the C—C bond lengths in the allyl cation: 1.385 Å (STO-3G) [22] and 1.372 Å [6-311++G(D_1)] [23]; 1.387 Å [6-31G(d)] [23] in the tetramethylallyl cation.

This comparison clearly demonstrates the character of the distribution of the electron density in the ring of XV and perhaps in 1,3-dioxenium cations in general, and also indicates their similarity to allyl cations. The pronounced alteration of the bonds in the vinyl fragments of styryl substituents also support consideration of molecule XV as a distyryl-substituted allyl cation and not a substituted heptamethinecyanine cation.

TABLE 2. Activation Parameters of Enantiotopomerization of the Spiro Carbon Center in 2-R^1-2-R^2-4-Phenyl-6-R^3-1,3-dioxenium (I) Perchlorates*

R^1	R^2	R^3	k_{25}, sec^{-1}	$\Delta G^{\neq}_{25}$, kcal/mole	$\Delta H^{\neq}$, kcal/mole	$\Delta S^{\neq}$, e.u.
$(CH_2)_5$		CH_3	$<6\cdot10^{-2}$	>19,1 †	—	—
$(CH_2)_5$		$(CH)_2C_6H_4OCH_3$-*p*	$1,3\cdot10^{-3}$	21,4	17,4 ± 0,1	-13,4 ± 0,2
$(CH_2)_2CH(CH_3)(CH_2)_2$		$(CH)_2C_6H_4OCH_3$-*p*	$1,0\cdot10^{-4}$	22,9	16,7 ± 0,1	-16,6 ± 0,4
$(CH_2)_4$		$(CH)_2C_6H_4OCH_3$-*p*	$0,9\cdot10^{-2}$	20,2	17,1 ± 0,1	-13,8 ± 0,3

*The activation parameters were calculated with the rate constants determined in the 40-160°C range; the thermostating step was 10°C.

†Decomposed above 70°C.

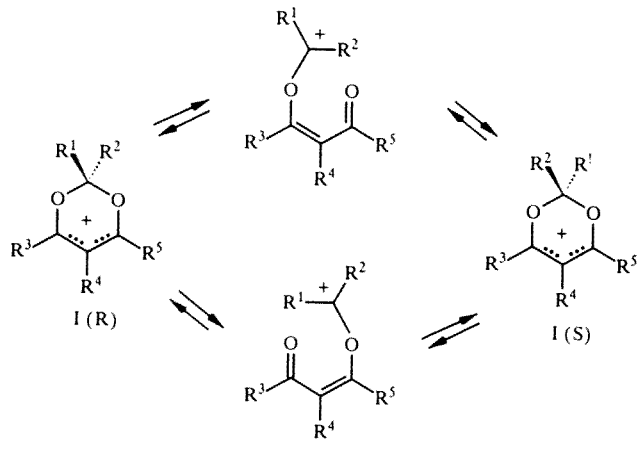
4. STEREODYNAMICS

The PMR spectrum of cation XV and other symmetric 2,2-pentamethylene spiro-annelated 1,3-dioxenium cations I ($R^3 = R^5$) contains multiplet signals of α-, β-, and γ-methylene protons with an intensity ratio of 4:4:2. On the contrary, the spectra of asymmetric cations I ($R^3 \neq R^5$, i.e., R^3 = Ph, R^5 = Me or $CH{=}CHC_6H_4OCH_3$-4, for example) present a more complex picture at room temperature due to the paired chemical nonequivalence of the methylene group protons.

The temperature evolution of the AB-quartet signal of α-methylene protons in 2,2-pentamethylenespiro-4-phenyl-6-(4-methoxystyryl)-1,3-dioxenium perchlorate (XVI) is shown in Fig. 2. The peaks forming the quartet are additionally split due to the spin–spin interaction of the α-methylene protons with the vicinal protons of the β-methylene group. The dynamic ^1H NMR spectrum of the α-methylene protons exhibits a distinct tendency toward simplification to an ordinary triplet signal, but complete averaging was impossible due to decomposition of the investigated compound at high temperature. Such spectral behavior is due to inversion of the tetrahedral configuration of the prochiral spiro carbon center. The energy barriers of enantiotopomerization in nitrobenzene-D_3 solution were calculated by complete computer analysis of the line shape and are given in Table 2.

The values of the energy barriers obtained are much higher than expected for ring inversion in 1,1-disubstituted cyclohexanes (9-12 kcal·mole^{-1} [24]). They can apparently be assigned to a dissociative-recombination mechanism of inversion (see Scheme 3). It was previously shown that this type of intramolecular dissociative mechanism, which includes opening of B—N bonds, rotation around B—O bonds, and subsequent ring closure, controls inversion of the configuration of the stereogenic boron centers in 1,3,2-oxazaborines [25].

Scheme 3



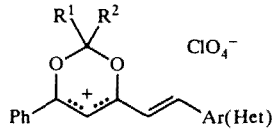
A similar ionization mechanism with breaking of C—O bonds and subsequent intramolecular recombination of ion pairs was proposed for topomerization of dioxolane carboxylates [26]. This process and I(R) ⇌ I(S) conversion, shown in Scheme 3, are a characteristic tendency of many organic reactions when a covalent compound dissociates with formation of ion pairs.

5. PROPERTIES OF 1,3-DIOXENIUM CATIONS

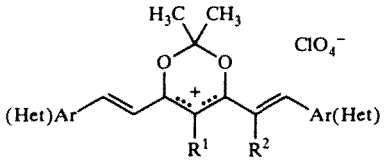
5.1. Reactions of 4(6)-Methyl(ene)-substituted 1,3-Dioxenium Cations with Electrophilic Reagents

At the sites of localization of the positive charge of 1,3-dioxenium cations, as in the case of other heterocyclic cations, alkyl substituents (methyl and methylene) have high C—H acidity and exhibit high activity in reactions with different electrophilic compounds. All of the reactions probably have a similar mechanism. It includes (see, e.g., Scheme 4 for the reaction with aldehydes) initial deprotonation of a methyl(ene)-substituted salt by an electrophilic reagent (aldehyde, formamide, etc.) to an anhydro base. The anhydro base, which has high nucleophilicity, reacts with the electrophile, activated by protonation. Splitting of the low-molecular-weight compound (water, alcohol) and formation of the final conjugated product subsequently follow.

Reactions with Aromatic Aldehydes [27]. It was found that in the softest conditions (solution of reagents — salt I and aldehyde — in acetic acid with an equimolar amount of acetic anhydride at 20-30°C), the reaction takes place with electron-enriched aromatic aldehydes having OH, OR, NR_2 donor substituents in position 4 or 3, 4 of the phenyl ring, yielding styryl derivatives XVII and XVIII.



XVII



XVIII

XVII a $R^1 = R^2 = CH_3$, Ar = phenyl; b $R^1 = R^2 = CH_3$, Ar = 1-naphthyl; c $R^1 + R^2 = (CH_2)_5$, Ar = 9-anthryl; d $R^1 = R^2 = CH_3$, Ar = 1-bromo-2-phenylvinyl; e $R^1 + R^2 = (CH_2)_5$, Ar = 3, 4-dimethoxyphenyl; f $R^1 = R^2 = CH_3$, Ar = 3,4-dihydroxyphenyl; g $R^1 + R^2 = (CH)_5$, Ar = 4-hydroxyphenyl; h $R^1 = R^2 = CH_3$, Ar = 4-dimethylaminophenyl; i $R^1 = R^2 = CH_3$, Het = 1-phenyl-2-chloro-4-methylpyrrol-3-yl; j $R^1 = R^2 = CH_3$, Het = 2-phenylindolizin-1-yl; k $R^1 + R^2 = (CH_2)_5$, Het = indol-3-yl.

XVIII a $R^1 = R^2 = H$, Ar = phenyl; b $R^1 = R^2 = H$, Ar = 4-acetylhydroxyphenyl; c $R^1 + R^2 = (CH_2)_3$, Ar = 3,4-methylenedihydroxyphenyl; d $R^1 = R^2 = H$, Het = indol-3-yl

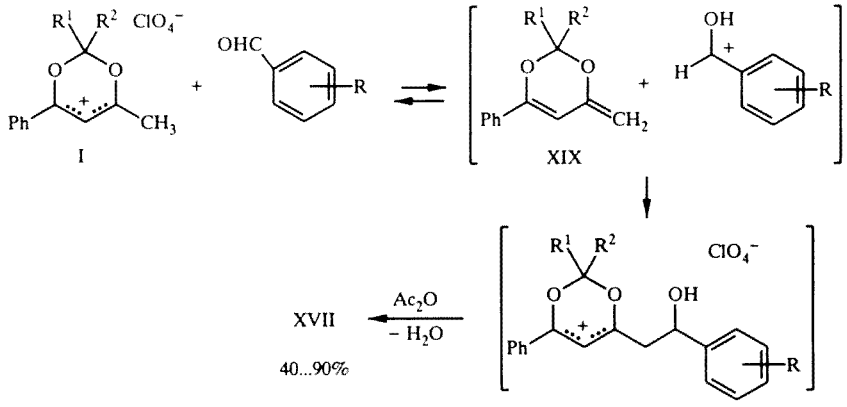
Electron-enriched heterocyclic aldehydes, for example, indole-3-aldehyde, 1-phenyl-2-chloro-4-methylpyrrole-3-aldehyde, 2-phenylindolizin-1-aldehyde, behave similarly in this reaction. At the same time, the reaction is successfully completed with benzaldehyde, α-bromocinnamaldehyde, naphthalene-1-aldehyde, and anthracene-9-aldehyde only on heating to 60-70°C. All of this can easily be explained based on the generally accepted mechanism for such processes (Scheme 4). Deprotonation with subsequent formation of a styryl derivative stabilized by donor groups takes place in the case of aldehydes with electron-donor substituents, while the equilibrium of the first stage is shifted to the left in the case of electron-neutral aldehydes (benzaldehyde and the others listed above), and significant stabilization of the cation in the last stage does not take place.

On the whole, dioxenium cations exhibit much higher reactivity in the described condensation than pyrylium [28], pyridinium [29], 1,3,2-dioxaborine cations [4], and other heterocyclic cations. The yields of XVII and XVIII are within the limits of 40-90%.

TABLE 3. Characteristics of the Long-wave Absorption Maxima of 1,3-Dioxenium Styryl Derivatives (XVII and XVIII) (CH_3CN)

Compound	λ_{max}, nm	$\varepsilon \cdot 10^{-4}$	Compound	λ_{max}, nm	$\varepsilon \cdot 10^{-4}$
XVIIa	462	6,3	XVIIi	493	7,8
XVIIb	514	4,2	XVIIj	574	5,6
XVIIc	633	2,7	XVIIk	546	5,7
XVIId	490	5,0	XVIIIa	501	8,2
XVIIe	535	6,7	XVIIIb	512	8,0
XVIIf	526	7,4	XVIIIc	595	9,6
XVIIg	513	7,3	XVIIId	630	13,7
XVIIh	616	8,6			

Scheme 4



Salts XVII and XVIII are intensely colored, stable, crystalline substances. The IR spectra of these compounds contain characteristic absorption bands of aryl substituents at 1613-1580 cm^{-1} and C=C bonds at 1553-1526 cm^{-1}.

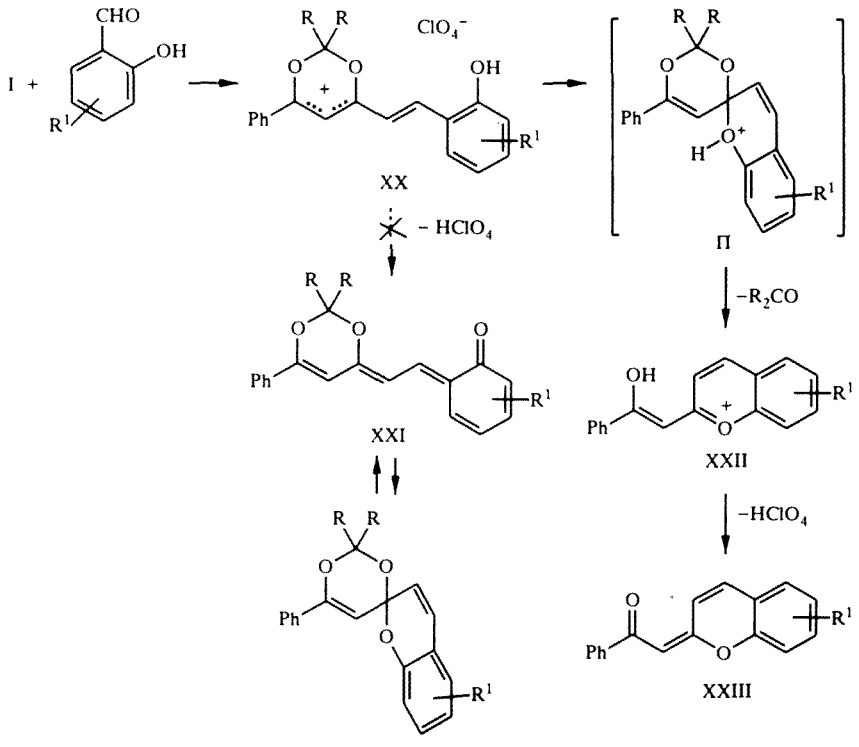
The electronic absorption spectra of 1,3-dioxenium monostyryl derivatives XVII are characterized by long-wave absorption with a maximum in the 462-633 nm region (Table 3). The extent of the π-system and the presence of electron-donor groups in the (het)aryl substituent affect the position of the maximum. A bathochromic shift of the absorption band maximum from 462 to 514 and 633 nm, respectively, is observed in the series of compounds XVIIa-c with aryl substituents — phenyl, 1-naphthyl, 9-anthryl. The molar extinction coefficient decreases from $6.3 \cdot 10^4$ $cm^{-1} \cdot mole^{-1} \cdot liter$ for compound XVIIa to $4.2 \cdot 10^4$ $cm^{-1} \cdot mole^{-1} \cdot liter$ and $2.7 \cdot 10^4$ $cm^{-1} \cdot mole^{-1} \cdot liter$ for compound XVIIb and XVIIc, probably due to an increase in the noncoplanarity of the π system.

Going to π-excess, nitrogen-containing, hetaryl substituents results in a long-wave shift of the absorption band maximum (compare compounds XVIIa and XVIIi-k). Intensification of the electron-donor properties of the groups in the phenyl substituent is accompanied by a bathochromic shift in the absorption band maximum and an increase in the molar extinction coefficient [see compounds XVIIa, XVIIf, XVIIh].

Longer wave absorption with a maximum in the 501-630 nm region (Table 3) and higher intensity of absorption (molar extinction coefficient) (see compounds XVIIa and XVIIIa, XVIIk and XVIIId) are characteristic of bis-styryl derivatives XVIIIa-d, which have a more extensive π system than the monostyryl derivatives. The effect of the structure on the spectral characteristics of compounds XVIII is similar to compounds XVII, and in the XVIIIa-d series, it is also accompanied by a long-wave shift of the absorption maximum and an increase in the molar extinction coefficient.

Synthesis of styryl derivatives XX from 2-hydroxyaldehydes is of special interest. Deprotonation of the products could result in spirane derivatives of type XXI (Scheme 5).

Scheme 5



XXII a R^1 = 6-OCH_3, b R^1 = 5,6-HC=CH–HC=CH, c R^1 = 6-Br

Similar derivatives (benzopyrylium, for example) exhibit photochromism [30], but instead of the predicted compounds XX, 1-benzopyrylium phenacyl derivatives (XXIIa, b) were obtained as a result of the reaction. Cations XX are probably unstable and easily undergo intramolecular nucleophilic attack of the phenol hydroxy group in position 4 of the heterocycle. Structure II formed (intermediate or transition state) is probably subsequently transformed into stable 1-benzopyrylium salt (XXII) with opening of the dioxenium ring and elimination of the ketone substituent. Compounds XXII are easily deprotonated to 1-benzopyranylidene derivatives (XXIII).

Reactions with Formamides [27]. The reaction of methyl(ene)-substituted heterocyclic cations with formamides (similar reactions of pyrylium [28], quinaldinium [31], and other salts were investigated) is similar to condensation reactions with aromatic aldehydes. Similar to aldehydes, the electrophilic formyl group participates in condensation of formamide, and the donor group bound with it causes delocalization of the positive charge in the compound formed. As noted above, the mechanisms of the reactions are probably the same. However, due to the high donor properties of the amine fragment of the formamide, the electrophilicity of the formyl group of this fragment is reduced. For this reason, activators — acetic anhydride or $POCl_3$ in an inert solvent — are usually used in the reaction. Both activators were used in studying the reactions of 1,3-dioxenium cations with formamides.

The corresponding aminovinyl derivative could not be obtained by reaction of starting salt I and DMF in acetic anhydride: a resinous product of unestablished structure was separated. However, the aminovinyl salts (XXIVa, b) sought were obtained in the same conditions from N-methylformanilide and N,N-diphenylfluoramide with low yields (17 and 10%, respectively). The lack of success with the reaction with DMF is probably due to the high basicity and low electrophilicity of the amide, as in the case of 3-azapyrylium salts [32]. Deprotonation of salt I to anhydro base XIX, and then polymerization of the latter initially take place during the reaction (Scheme 6). Polymerization of vinyl ether XIX in this case is probably a faster process than its reaction with protonated or acylated formamides (XXV and XXVI) ($R^6 = R^7 = CH_3$) due to the low electrophilicity of the latter. Going to N-methylformanilide and N,N-diphenylformamide increases the electrophilicity of the corresponding hydroxy- or acetylhydroxycarbenium ions of type XXV, XXVI and the formation of the products sought, XXIVa, b.

The IR spectrum of salt XXIVb contains a band of C=N bond vibrations at 1640 cm^{-1}. The PMR spectrum of XXIVb has two times the number of signals grouped in two sets with respect to the chemical shifts, multiplicity, integral intensities, and spin–spin interaction constants. These sets can be assigned to *E,Z*-isomers of XXIVb (Fig. 3, $R^1 = R^2 = R^3$ = Ph)

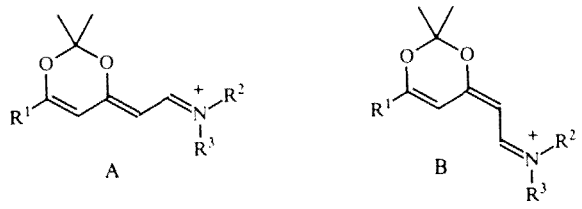
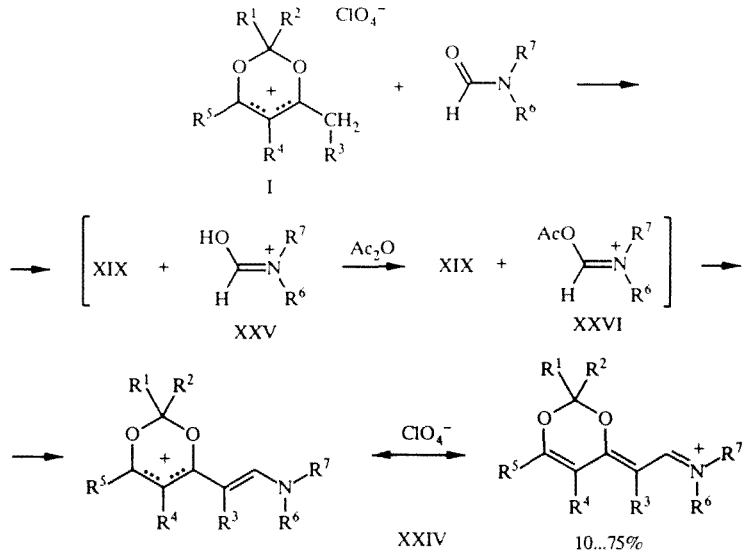


Fig. 3. *E,Z*-Isomers of cations of XXIV.

Scheme 6



XXIV a $R^1-R^2-R^6-CH_3$; R^3-R^4-H; R^5-R^7-Ph; b $R^1-R^2-CH_3$; R^3-R^4-H; $R^5-R^6-R^7-Ph$; e $R^1+R^2-(CH_2)_5$; R^3-R^6-H; R^4-CH_3; R^5-Ph; $R^7-C_6H_4OCH_3$-*p*; d $R^1+R^2-(CH_2)_5$; $R^3-R^4-R^6-H$; R^5-Ph; $R^7-C_6H_4Br$-*p*; e $R^1+R^2-(CH_2)_5$; $R^3+R^4-(CH_2)_2$; R^5-Ph; R^6-H; $R^7-C_6H_4CO_2E$· *p*, f $R^1-R^2-CH_3$; $R^3-R^4-R^6-H$; R^5-Ph; $R^7-C_6H_4COCH_3$-*p*; g $R^1-R^2-R^5-CH_3$; $R^3-R^4-R^6-H$; $R^7-C_6H_4COCH_3$-*p*; h $R^1+R^2-(CH_2)_5$; R^3-R^4-H; R^5-Ph; $R^6-R^7-CH_3$; i $R^1-R^2-R^5-R^6-R^7-CH_3$; R^3-R^4-H

present in the ratio of 3:1. The basic isomer has characteristic signals of vinyl group protons at 5.61 (1H, d, CH—C) and 8.85 ppm (1H, d, CH=N) and a dioxenium ring proton at 6.53 ppm (1H, s, H-5). It is important to note that the existence of isomers is only possible with significant localization of the positive charge on the nitrogen atom (see below).

The use of more electrophilic formanilides increases the yields of the products sought to 20-75% (compounds XXIVc-g). The reaction takes place very easily even at 30-40°C when the aromatic ring of the formanilide has a donor substituent (Alk, AlkO). In the case of acceptor substituents (CO_2Et, $COCH_3$), the reaction mixture was heated to 70-80°C to obtain acceptable yields. This characteristic is similar to the features of synthesis of 1,3-dioxenium styryl derivatives XVII and XVIII described above.

The IR spectra of XXIVc-g contain absorption bands at 3140 (N—H) and 1640 cm^{-1} (C=N), and the PMR spectra of XXIVd, f, g contain signals of two *E,Z*-isomers, probably A and B (Fig. 3, R^1 = Ph or Me; R^2 = Ar; R^3 = H). The signals of vinyl protons in the region of 6.12-6.40 (1H, d, CH—C) and 8.75-9.34 ppm (1H, d, CH=N), the ring proton at 6.35-7.20 (1H, s, H-5), and the amine at 10.70-12.00 ppm (1H, m, N—H) are characteristic.

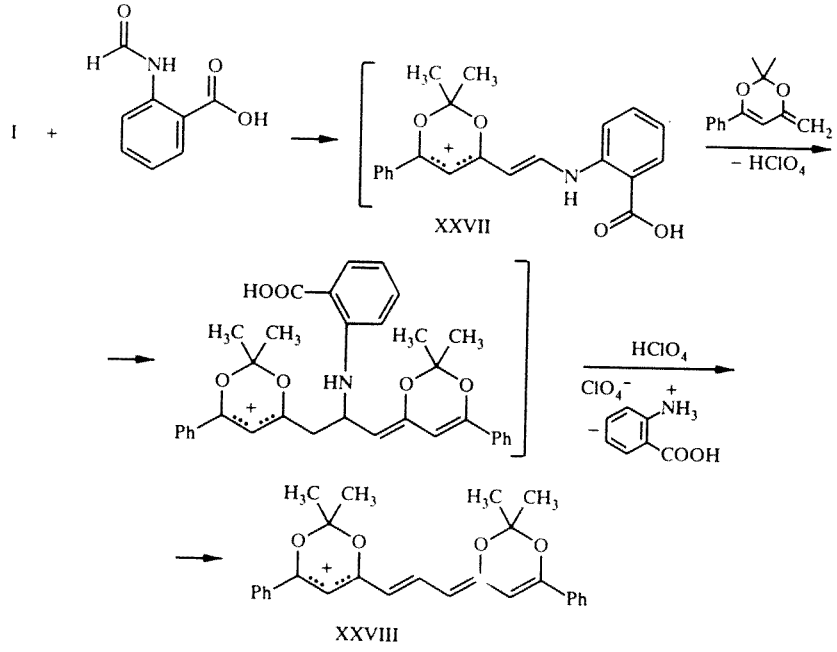
Trimethinecyanine (XXVIII) was obtained with a yield of 39% in the reaction of starting salt I and N-(2-carboxyphenyl)formamide in the same conditions. The possible scheme of the reaction (Scheme 7) includes intermediate formation of aminovinyl derivative (XXVII) in which the carboxyl substituent probably significantly decreases the π-electron density on the nitrogen atom, thus increasing the electrophilicity of position 2 of the vinyl group. Nucleophilic addition of

TABLE 4. Characteristics of the Long-wave Absorption Maxima of 1,3-Dioxenium Immonium Derivatives (XIV) (CH_3CN)

Compound	λ_{max}, nm	$\varepsilon \cdot 10^{-4}$	Compound	λ_{max}, nm	$\varepsilon \cdot 10^{-4}$
XXIVa	422	5,5	XXIVf	459	5,3
XXIVb	452	6,4	XXIVg	421	5,2
XXIVc	446	4,1	XXIVh	401	4,9
XXIVd	449	4,2	XXIVi	363	4,2
XXIVe	487	5,6			

anhydro base XIX (which is present in the reaction mixture), subsequent protonation of the amine fragment, splitting of 2-aminobenzoic acid ammonium salt, and formation of cyanine XXVIII take place according to this hypothesis.

Scheme 7



To exclude irreversible deprotonation of the cation of 4-methyldioxenium I and increase the electrophilicity of the particles attacking anhydro base XIX, the Vilsmeier—Haack method was used with $POCl_3$ in CH_2Cl_2 in the reaction with DMF. The N,N-dimethylaminovinyl derivatives XXIVh, i sought were obtained. In the IR spectrum of XXIVi, the C=N bond absorbs at 1653 cm^{-1}. In the PMR spectrum of XXIVi, as in the case of salts XXIVb, d, f, g, there are signals of two *E,Z*-isomers of type A and B present in unequal quantities (75 and 25%). Heating of a solution of XXIVi in nitrobenzene-D_5 to 140°C does not cause coalescence of the signals of N—CH_3 groups; exchange broadening is also absent. This indicates the relatively high (>25 kcal/mole) barrier of *E,Z*-isomerization at the C=N bond and the immonium nature of compound XXIVi. The immonium structure is probably the most adequate in describing all salts XXIV. Charge localization is also supported by the fact that only products of the reaction for one of the active methyl groups — XXIVg and XXIVi — were obtained from 2,2,4,6-tetramethyl-1,3-dioxenium I with formamides; the second methyl group became inactive. Similar deactivation was not observed in reactions of salt I with aromatic aldehydes.

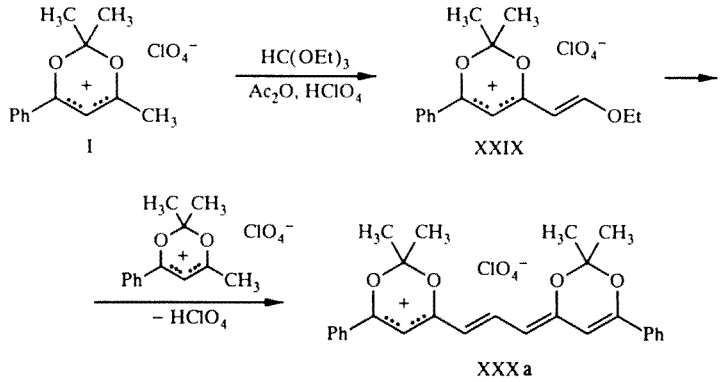
The long-wave absorption maxima in the electron spectra of dioxenium immonium derivatives XXIVa-i lie in the region of 363-487 nm (Table 4). Substituents R^5, R^6, and R^7 significantly affect their position. In going from $R^5 = R^6 = R^7 = CH_3$ to $R^5 = R^6 = R^7 = Ph$, which causes enlargement of the π system, a long-wave shift of the absorption band maximum is observed (see compounds XXIVf and XXIVg; XXIVh and XXIVi; XXIVa, XXIVb, and XXIVh). A change in the electron-

active properties of the substituents in phenyl nucleus R^7 is accompanied by a bathochromic shift of the absorption maximum in going from electron-donor to electron-acceptor groups (compounds XXIVc-f).

1,3-dioxenium methyl(ene)-substituted salts thus react with formamides in acetic anhydride and in CH_2Cl_2 in the presence of $POCl_3$ with formation of immonium derivatives, and the reaction with strongly basic and weakly electrophilic amides of the DMF type requires using a stronger activator, $POCl_3$.

Reactions with Triethyl Orthoformate. It was found in [33] that crystalline 2,2-dimethyl-4-(2-ethoxy)vinyl-1,3-dioxenium perchlorate (XXIX) is formed when a mixture of 2,2,4-trimethyl-6-phenyl-1,3-dioxenium perchlorate I, acetic anhydride, and 16% perchloric acid is heated in an excess of triethyl orthoformate to 60-70°C:

Scheme 8



XXXa

As shown, salt XXIX is formed with a good yield (84%) only if the reaction is conducted in a large (10-fold, mole) excess of the ortho ester in the presence of a 16% solution of $HClO_4$ in AcOH. Otherwise, a mixture of XXIX and trimethinecyanine (XXXa) is obtained. The latter is the basic product when the reaction is conducted in acetic acid with a two-fold amount of ortho ester and 0.5 mole of triethylamine. This observation is in good agreement with the decrease in the yields of trimethinecyanines found by Mizuno and Tanabe [34] in the reaction of tetrahydrobenzopyrylium salts with a large excess of the ortho ester. Actually, an excess of the ortho ester decreases the concentration of anhydro base XIX, preventing it from reacting with salt XXIX formed during the reaction. By suppressing dissociation of I into $HClO_4$ and the anhydro base, perchloric acid in turn reduces the concentration of the anhydro base even more. Perchlorate XXIX was more resistant to hydrolysis by atmospheric moisture than starting salt I and can be stored in air for weeks.

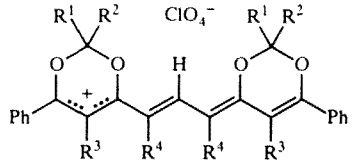
Ethoxyvinyl derivatives could also be separated from other methyl(ene)-substituted dioxenium salts, but in this case, the product was crystallized with difficulty or did not crystallize at all. For this reason, the oily mass obtained underwent further transformations to characterize the crystalline products (see transformations of ethoxyvinyldioxenium cations). Different trimethinecyanines were also obtained from methyl(ene)-substituted dioxenium salts with the method developed for synthesis of XXXa.

The electronic absorption spectra of cyanines XXXa-g (Table 5) are characterized by long-wave absorption with a maximum in the 611-696 nm region and high values of the molar extinction coefficient of $14.0 \cdot 10^4$-$21.0 \cdot 10^4$ $cm^{-1} \cdot mole^{-1} \cdot liter$. The position of the absorption band maxima is a function of substituents R^1-R^4, whose effect is primarily of a steric character. Substituents R^3 and R^4 in the series of compounds XXXb, d, f and XXXa, e g, which result in flattening of the molecular structure of the cyanines due to bridge bonds connecting cyclic fragments with an unsaturated methine chain, have a significant effect on their electronic absorption spectra. This is manifested by a long-wave shift of the absorption band maxima — 611, 633, 696 nm and 626, 653, 692 nm, respectively. At the same time, the effect of substituents R^1 and R^2, which have an insignificant effect on the coplanarity of the molar structure, is manifested to a much smaller degree (Table 5, compounds XXXa, b, c and XXXf, g). The high efficiency of annelation of the 5-member carbocycle is also probably due to the fact that the valence angle between the sp^2-hybridized carbon atoms in the π-conjugation chain decreases sharply (from ~120° to ~108°) in this ring.

Reactions with Alkoxy(vinyl)-Substituted Heterocyclic Cations. This reaction is similar to the XXIX → XXXa transition reported above. Monomethinecyanines XXXI are formed from methyl(ene)-substituted salt I and 4-ethoxyflavylium salts reported above.

TABLE 5. Characteristics of the Long-Wave Absorption Maxima of 1,3-Dioxenium Trimethinecyanines (XXX) (CH_3CN)

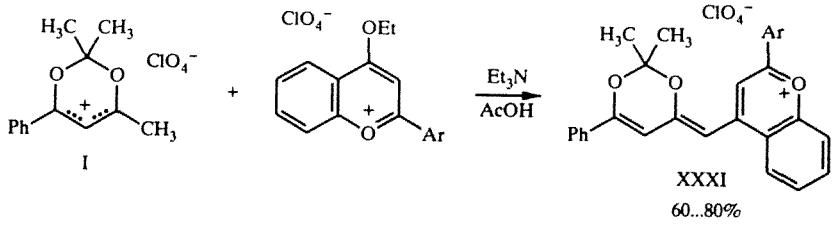
Compound	λ_{max}, nm	$\varepsilon \cdot 10^{-4}$	Compound	λ_{max}, nm	$\varepsilon \cdot 10^{-4}$
XXXa	626	15,7	XXXe	653	14,0
XXXb	633	16,8	XXXf	696	19,1
XXXc	639	21,0	XXXg	692	17,6
XXXd	611	14,4			



XXX

XXX	R^1	R^2	R^3	R^4
a	CH_3	CH_3	H	H
b	$(CH_2)_5$		H	H
c	C_9H_{14}		H	H
d	$(CH_2)_5$		CH_3	H
e	CH_3	CH_3	$(CH_2)_3$	
f	$(CH_2)_5$		$(CH_2)_2$	
g	CH_3	CH_3	$(CH_2)_2$	

Scheme 9

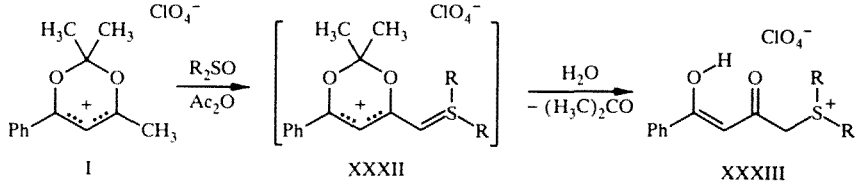


I XXXI 60...80%

A similar reaction course was observed for 2,6-diphenyl-4-methyl-3-azapyrylium salt; together with the azapyrylium bissulfonium salt, a noncyclic sulfonium salt — the product of hydrolysis of the corresponding azapyrylium salt — was separated [32].

Reactions with Nitroso Compounds. The reaction of methyl(ene)-substituted 1,3-dioxenium salts with *p*-nitrosodimethylaniline, *p*-nitrosodiphenylamine, and nitrosoresorcin consists of proton transfer from the methyl (methylene) group of the cation to the nitroso group. An anhydro base of type XIX and a protonated nitroso compound are formed; the first is polymerized in the reaction conditions due to the insufficient electrophilicity of the second, as in the previously cited example of the reaction of I with DMF in acetic anhydride.

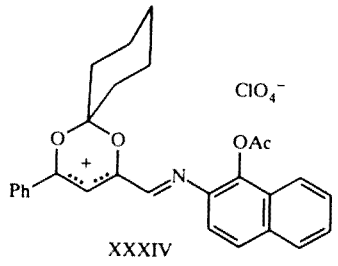
Scheme 10



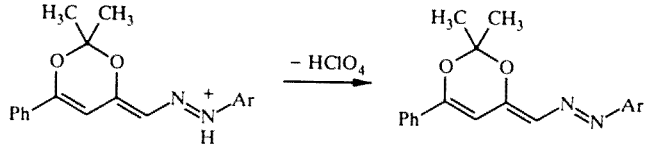
I XXXII XXXIII 60...90%

R = Me, Et, Ph

It was possible to obtain the corresponding product (XXXIV) with a 31% yield only by reaction of 2,2-pentamethylene-spiro-4-methyl-6-phenyl-1,3-dioxenium perchlorate with 2-nitroso-1-naphthol in acetic anhydride.



XXXIV



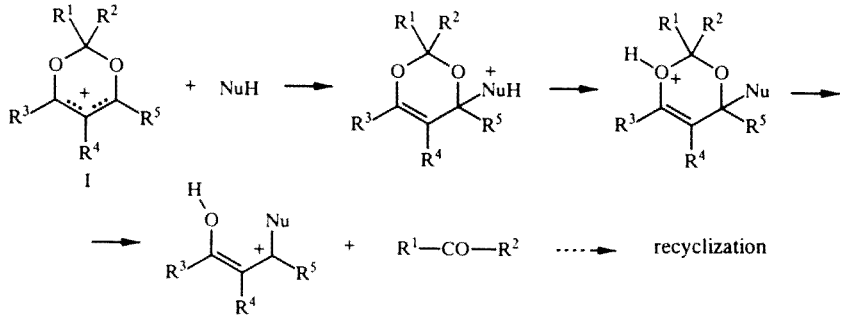
XXXV XXXVI

Reactions with Diazonium Salts. The reaction of methyl(ene)-substituted 1,3-dioxenium salts with diazonium cation tetrafluoroborates in acetic acid in the presence of triethylamine yields the corresponding hydrazo derivatives (XXXV) (15-40% yield), the aza analogs of dioxenium immonium salts XXIV. Similar to the latter, hydrazo derivatives XXXV are easily deprotonated, forming azo compounds XXXVI.

5.2. Reactions of 1,3-Dioxenium Cations with Nucleophilic Reagents

Dioxenium I cations easily react with nucleophiles, and a stage of irreversible opening of the dioxenium ring with elimination of the ketone fragment and formation of acyclic products, which can again be cyclized with inclusion of the diketone fragment of the starting ring in the new heterocycle, probably follows the first stage of addition of the nucleophile (Scheme 11). This type of reaction with nucleophiles was observed previously in the case of 1,2-dithiolium [35] and isothiazolium cations [36, 37] — heterocycles containing an allyl triad, like dioxenium, but aromatic in this case.

Scheme 11

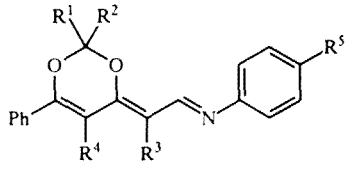


As indicated above, 1,3-dioxenium salts are subject to hydrolysis. Regeneration of the starting ketone, 1,3-keto enol, and perchloric acid used in synthesis of I actually takes place. The reaction of I with phenylhydrazine in AcOH yields the corresponding pyrazolium salt. This reaction is similar to transformation of isothiazolium or 1,2-dithiolium into pyrazole with an excess of phenylhydrazine [35, 37]. Similar to *o*-phenylenediamine, 1,5-benzodiazepinium salt is formed.

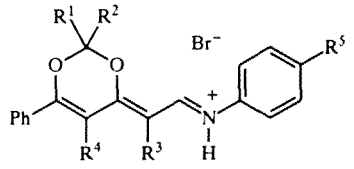
5.3. Condensations and Recyclizations of 1,3-Dioxenium Salt Derivatives

The further transformations of different derivatives obtained from alkyl-substituted dioxenium cations are perhaps of the greatest synthetic interest and novelty. We investigated some of these transformations. It was found that in hydrolysis of styryl-substituted dioxenium salts, the corresponding diketones are formed.

Immonium compounds XXIV were resistant to acid hydrolysis. Prolonged (5 h) boiling of a solution of XXIVd in a mixture of water, AcOH, and $HClO_4$ (5:4:1) did not result in hydrolysis — the starting salt was separated. Hydrolysis also did not occur in the reaction of bases and salts XXIVc-g (aqueous Me_3N, NaOH; K_2CO_3 in acetone). However, in the last case, 4H-dioxenylidenoaryliminoethanes (XXXVII) formed, which strikingly distinguishes salts XXIV from the styryl derivatives. This is probably caused by the noted immonium nature of compounds XXIV. The almost total charge localization on the N atom makes the O-heterocycle stable in reactions with bases. This charge localization simultaneously increases the acidity of the N—H bond so that rapid deprotonation and formation of imines (XXXVII) take place under the effect of a base. Compounds XXXVIIa-c are the first nonsalt derivatives of 1,3-dioxenium. They are promising for further transformations and are also interesting as potential physiologically active substances whose analogs — 1,3-dioxen-4-ones — have been widely studied [17, 18].



XXXVIIa-c

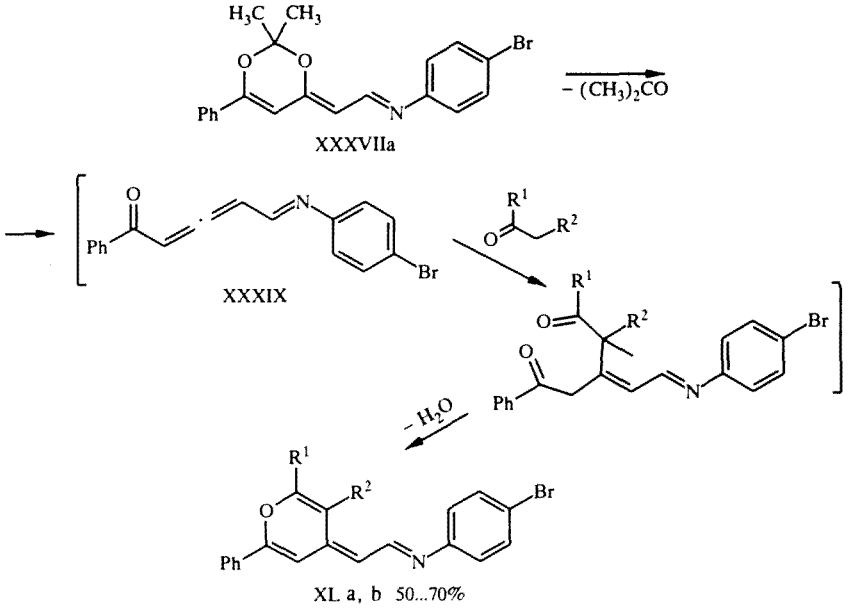


XXXVIIIa-c

XXXVII, XXXVIII: a $R^1 = R^2 = CH_3$; $R^3 = R^4 = H$; $R^5 = Br$; b $R^1 + R^2 = (CH_2)_5$; $R^3 + R^4 = (CH_2)_2$; $R^5 = Br$; c $R^1 = R^2 = CH_3$; $R^3 = R^4 = H$; $R^5 = COCH_3$

Azomethines XXXVII are easily converted into the starting immonium salts XXIV by different acids. Hydrobromides (XXXVIIIa-c) were thus obtained when solutions of compounds XXXVIIa-c in ethyl acetate were treated with an aqueous 40% solution of HBr.

Scheme 12



XXXVIIa

XXXIX

XL a, b 50...70%

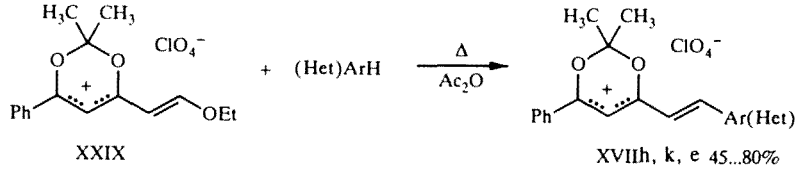
XL a $R^1 + R^2 = (CH_2)_4$, b $R^1 = CH_3$, $R^2 = COCH_3$

When solutions of XXXVIIa were boiled for 1 h in cyclohexanone or acetylacetone, 4H-pyranylidenoaryliminoethanes XLa, b were formed [27]. This transformation is probably similar to the transformation of the 1,3-dioxen-4-ones in similar conditions into 4H-pyran-4-ones (γ-pyrones) mentioned above [38, 39]. The reaction probably takes place via intermediate formation of keto allene (XXXIX) (Scheme 12), generated as a result of thermal elimination of a molecule of acetone. Michael addition of cyclohexanone or acetylacetone to the keto allene, cyclization, and dehydration subsequently take place. The described recyclization is very promising synthetically, since wide variations in the structure of substrates of XXXVII, the carbanion nucleophile, and use of nitrogenous nucleophiles for obtaining derivatives of benzodiazepines, quinolizines, pyrazolines, etc., are totally realistic.

We investigated the properties of ethoxyvinyldioxenium salts on the example of 2,2-dimethyl-6-phenyl-4-(2-ethoxyvinyl)-1,3-dioxenium perchlorate XXIX [33] and investigated the reactions with different nucleophiles, which can arbitrarily be divided into three groups based on the properties of the nucleophilic substrate.

Reactions with Electron-Enriched (hetero)Aromatic Compounds. It was found that salt XXIX reacts with some electron-excess (hetero)aromatic compounds — N,N-dimethylaniline, 1,3-dihydroxynaphthalene, 2-methylindole — with formation of the corresponding (het)arylvinyl derivatives of dioxenium XVIIh, k, *l*. Product XVIIh was obtained from 2,2,4-trimethyl-6-phenyl-1,3-dioxenium perchlorate and 4-dimethylaminobenzaldehyde, while XVIIk was obtained from indole-3-aldehyde (see above). Even when the reaction was conducted in rigorous conditions, it was not possible to conduct it with such traditionally active substrates in electrophilic substitution reactions as anisole, 1,3-dimethoxybenzene, 2-naphthol, and anthracene.

Scheme 13



XXIX XVIIh, k, e 45...80%

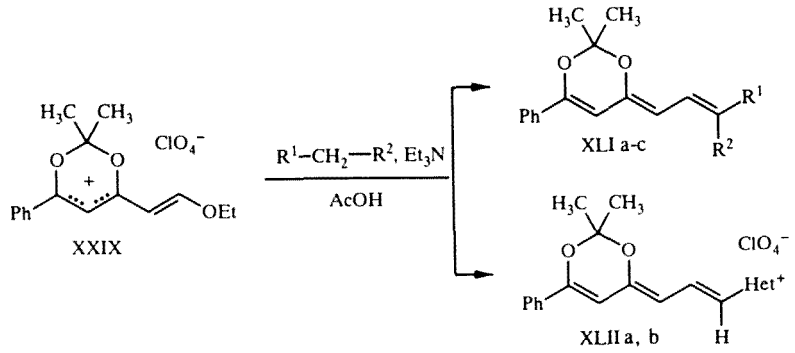
XVII h Ar = 4-dimethylaminophenyl k Het = indol-3-yl,
l Ar = 2,4- di(acetylhydroxy)naphthy-1-yl

As a consequence, the method is not very promising for obtaining (het)arylvinyl-substituted dioxenium salts due to the insufficient reactivity of the ethoxyvinyl cation, and the reaction of the methyl(ene)-substituted salt with the corresponding aldehyde should be used for obtaining these salts. However, when the aldehyde is difficult to obtain (for example, 2,4-dihydroxynaphthaldehyde or 2-methylindole-3-aldehyde) and the corresponding (het)arene is highly active, transformation of the XXIX → XVII type is preferable.

Reactions with C—H-Active Compounds. It was found that ethoxyvinyldioxenium cation XXIX reacts with C—H-active compounds of the $R^1—CH_2—R^2$ type (where R^1 and/or R^2 are CN, COR, and other electron-acceptor groups), namely, malononitrile, 1,3-indanedione, barbituric acid, 2-methyl-4,6-di(4-tolyl)pyrylium perchlorate, and 1-ethylquinaldinium iodide. The reaction takes place while heating a mixture of XXIX, $R^1—CH_2—R^2$ and Et_3N in acetic acid to 80-90°C. Dioxenylidene derivatives of the nonsalt type — merocyanines (XLIa-c) (65-96% yield) and salt-like asymmetric trimethinecyanines (XLIIa, b) (40-85% yield) are formed.

Merocyanines XLIIa-c are red and brown crystalline substances. Their IR spectra contain absorption bands of aryl substituents at 1606-1580 cm^{-1}, a conjugated system of C=C bonds at 1553-1506 cm^{-1}, and absorption bands of CN, CO, and other functional groups, if any.

Scheme 14



XXIX XLI a-c XLII a, b

XLI a $R^1 = R^2 =$ CN, b $R^1 + R^2 =$, c $R^1 + R^2 =$;

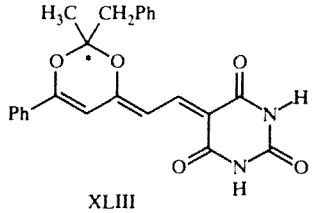
XLII a di(4-tolyl)pyridino-2-yl b 1- ethylquimolinio-2-yl

The PMR spectra of XLIa-c contain signals of heterocycle CH_3 groups at 1.83-1.86 ppm (6H, s), methine protons at 6.00-7.17 ppm (1H, d) and 7.99-8.12 ppm (1H, d), a heterocycle proton at 6.82-6.84 ppm (1H, s), and signals of a phenyl substituent in the region of 7.55-7.94 ppm.

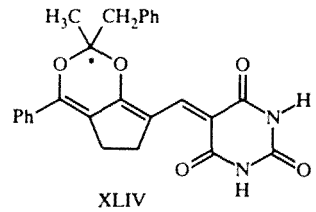
Trimethinecyanines XLIIa, b are intensely colored compounds. The IR spectrum of XLIIb contains the absorption band of a quinolinium ring at 1613 cm^{-1}, aryl groups at 1586 and 1553 cm^{-1}, and the powerful band of a conjugated C=C chain at 1493 cm^{-1}.

The transformation found is similar to the reactions of the ethoxyvinylpyrylium cation described by Wizinger in [40, 41]. However, it should be noted that the reactions of the ethoxyvinylpyrylium cation take place during prolonged boiling of the reaction mixtures, while the reaction with XXIX easily takes place at the temperature of dissolution of the reagents (60-80°C).

The investigated transformation of XXIX into merocyanines was used for synthesizing two other similar dioxenium salt derivatives — XLIII (46% yield) and XLIV (32% yield).



XLIII

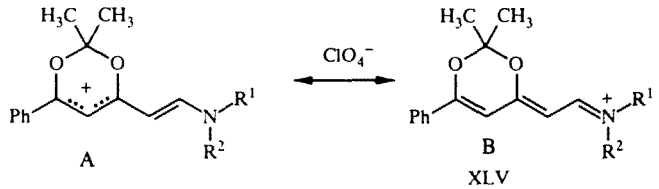


XLIV

Compounds XLIII and XLIV are the first derivatives of the dioxenium cation in which there is a chiral center — position 2 of the dioxenylidene ring. In addition, product XLIV is the first derivative of a methylene-substituted dioxenium salt of this type. Both merocyanines were synthesized from the corresponding ethoxyvinyl cations obtained in the form of an oil.

The approach tested in synthesis of XLIII and XLIV is a very promising method for preparation of a broad spectrum of different nonsalt dioxenylidene derivatives. They can be used as chiral synthons for subsequent transformations or can be of independent significance to the 4H-1,3-dioxen-4-ones of similar structure mentioned above [17, 18].

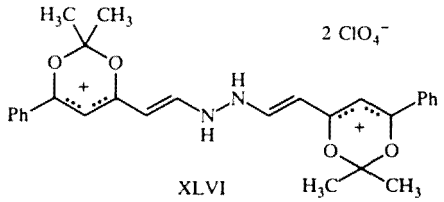
Reactions with N-nucleophiles. Reactions of the ethoxyvinyldioxenium cation with different N—H-active substrates are characterized by the greatest variety of products and thus the greatest synthetic attraction. Aliphatic and (hetero)aromatic primary and secondary amines, phenylhydrazine, hydrazine, amino acids, amides, acid hydrazides, and D-glucosamine were reacted with XXIX. Nucleophilic substitution of the ethoxyl group of cation XXIX by an amino group took place during the reaction, with formation of XLVa-k (29-97% yield), XLVI (87% yield), and XLVII (15% yield).



A B

XLV

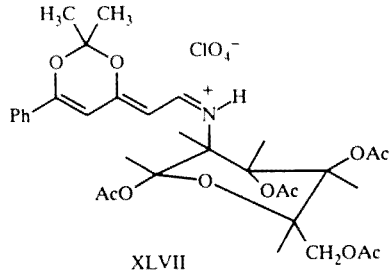
XLV R^1—NH—R^2: a *tert*-butylamine; b morpholine; c 4-aminoacetophenone; d 2-aminobenzoic acid; e 2-amino-4-nitro-6-chlorophenol; f 2-amino-5-bromopyridine; g N-acetyl-N-phenylhydrazine; h aminoacetic acid; i 4-tolueneamide; j 4-anisohydrazide; k carbamide.



XLVI

Products XLV are salts for which immonium structure B, in which the positive charge is localized on the nitrogen atom, is probably most probable, as for previously described salts XXIV. As a function of the nucleophilicity of the nitrogen atom of the substrate, the reaction was conducted in different solvents at different temperatures. With more active nucleophiles — aliphatic amines — the reaction took place at room temperature in dichloromethane with formation of XLVa, b. The reac-

tion was conducted with hydrazine in methanol; the product of bis-substitution at both NH_2 groups of XLVI was formed and easily deprotonated into azine.



XLVII

The reaction of XXIX with D-glucosamine, a representative of the class of amino sugars which are widely distributed in nature and play an important role in vital processes, was conducted similarly. The product of the reaction was transformed by acetylation into tetraacetate XLVII, which contains a 2-amino-2-deoxy-D-glucose fragment in the form of a mixture of α- and β-anomers, which was also characterized. The remaining compounds XLV were obtained by heating the reagents in acetic acid.

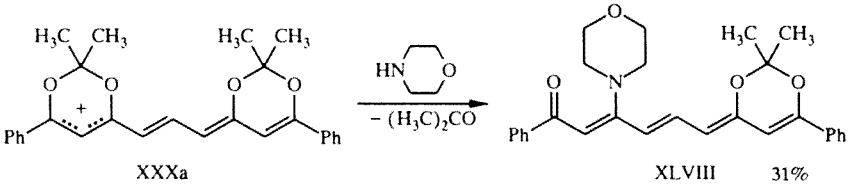
Compound XLVa is the first derivative of this type obtained from ethoxyvinyl cations and a highly basic primary aliphatic amine. The IR spectrum of XLVa contains a multiplet absorption band of the N—H bond at 3166 cm^{-1}, absorption bands of C=N bonds at 1640, C=C at 1580, and C—O—C bonds at 1246 cm^{-1}.

The PMR spectrum of XLVa contains the signals of two *E,Z*-isomers which can easily be assigned based on the values of the chemical shifts, multiplicity, spin–spin interaction constants, and integral intensity. Signals of a *tert*-butyl group at 1.48 ppm (9H, s), two methyl groups at 1.82 ppm (6H, s), vinyl protons at 6.10 (1H, d) and 8.23 ppm (1H, m, ring proton at 6.35 ppm (1H, s), and a phenyl substituent at 7.43-7.58 (3H, m) and 7.73 ppm (2H, d) are characteristic of basic isomer A (73%) (Fig. 3, R^1 = Ph, R^2 = *t*-Bu, R^3 = H).

The reactions of ethoxyvinyldioxenium salt XXIX with 2-hydroxyarylamines, hydrazine, hydrazides, and amides of aromatic acids are new transformations and were not described previously in studying the properties of similar pyrylium, dioxolanium, and other derivatives.

The new ethoxyvinyldioxenium cations are thus strong electrophiles with higher reactivity than ethoxyvinylpyrylium and ethoxyvinyldioxolanium cations in similar reactions. This situation widens the group of substrates capable of reacting with the cations investigated and thus the spectrum of products obtained. The investigated transformations demonstrate the relatively convenient method of incorporating a vinyldioxenylidene fragment, which can be both achiral and chiral, in different substrates, and this increases the practical importance of the compounds obtained.

Scheme 15



XXXa XLVIII 31%

Interesting products are formed in the reaction of dioxenium trimethinecyanines with nitrogenous nucleophiles. In the reaction of XXXa with morpholine, one of the two cyanine dioxene rings is opened and uncharged compound (XLVIII) is formed. It is probably possible to obtain other heterocycles in this reaction as a result of recyclization of products of type XLVIII using bifunctional nucleophiles.

A new reaction of keto enols in the cisoid configuration with ketones and strong acids, which results in the formation of 1,3-dioxenium salts, was thus found, and the conditions of conducting it were optimized. X-ray structural analysis showed that the dioxenium ring in 4,6-bis(4-methoxystyryl)-2,2-pentamethylylene-spiro-1,3-dioxenium perchlorate has an envelope conformation, while its carbon triad is related to allyl cations in structure.

The reactions of 1,3-dioxenium salts with different nucleophiles (water, alcohols, amines) are accompanied by ring opening and elimination of a ketone fragment. The reaction with cations that do not have stabilizing (aryl, styryl) substituents takes place especially easily.

Methyl(ene)-substituted 1,3-dioxenium cations react with different electrophilic reagents. Most of the transformations that take place are similar to the transformations of other methyl(ene)-substituted heterocyclic cations. However, the reactivity of the 1,3-dioxenium cation in similar reactions is higher than for other stable heterocyclic cations.

Ethyoxyvinyldioxenium salts were accessible, stable, and the most universal synthons in reactions with different C- and N-nucleophiles. 1,3-Dioxenylidene derivatives, including chiral derivatives of interest as synthons and potential physiologically active substances, were also obtained. Recyclization of dioxenylidene azomethines obtained from 1,3-dioxenium immonium derivatives into pyranylidene derivatives, which perhaps take place through the stage of thermal generation of a keto allene, was also found.

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