DIMERIZATION REACTIONS OF 2-BENZOPYRYLIUM SALTS (REVIEW)

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Data on asymmetric dimerization reactions of 2-benzopyrylium salts and conversions of the resulting dimers are summarized.

Ten years ago [1], Korobka and Kuznetsov observed the ability of 2-benzopyrylium salts to undergo asymmetric dimerization. Investigations of subsequent years revealed the wide possibilities of such reactions, significantly exceeding the scope of traditional concepts of the chemistry of 2-benzopyrylium salts.

The exceptional facileness of occurrence of dimerization reactions, the diversity of the types of resulting dimers, and their high reactivity, which has made it possible to develop new approaches to the synthesis of some polycondensed aromatic compounds (substituted naphthalenes, chrysenes, and benz[*a*]anthracenes) and benzofurans and also to detect new types of disproportionation reactions, have provided a unique set of properties of 2-benzopyrylium salts, and, as published data have shown, no other heteroaromatic cation has such a set of properties.

1. FORMATION OF ASYMMETRIC DIMERS OF 2-BENZOPYRYLIUM SALTS

1.1. Formation of Dimers from 2-Benzopyrylium Salts

For the first time, dimerization of 2-benzopyrylium salts and subsequent processes related to it were observed during heating of 1-methyl-2-benzopyrylium perchlorates Ia-c with a free β-position of the heterocation in water-alcohol solutions of alkalies, where acylchrysenes IIa-c were obtained in 40-65% yields [1, 2].

As shown by model experiments, 1,5-diketones III, the usual intermediates in reactions of pyrylium salts with alkalies, do not participate in the described conversion, undergoing complete conversion to α-naphthols IV.

Anhydro bases V, which are formed in deprotonation of the methyl group in the 1 position of salts Ia-c and are able to react in two different ways, have been found to be the key intermediate in the formation of chrysenes. The first direction (α-1′ dimerization) was determined after the recovery of compound VI, which formed during the treatment of perchlorate Ia with an aqueous solution of CH_3COONa or a "proton sponge" in THF [3]. It probably occurs as a result of addition of anhydro base V, unscreened by substituents of the α-methine carbon atom, at the 1 position of the unreacted cation; the dimeric salt VII that is formed in this case is converted to its own pseudobase VI.

Such participation of methylene anhydro bases in dimerization reactions is known in the series of monocyclic pyrylium salts [4], 1-benzopyrylium salts [5], and their nitrogen-containing analogs [6].

Subsequently, it was shown that a second direction of reaction with starting cations is more characteristic of anhydro bases V, namely, a [4+2]-cycloaddition reaction [7], i.e., similarly to the previously observed reaction of 2-benzopyrylium salts with vinyl ethyl ether [8], which is probably similar to the reacting fragment of the anhydro base.

The cyclic oxonium intermediates VIII, which appear initially in this case, are converted after cleavage of the heterocycle and deprotonation of the methyl group to spirocyclic dimers IX. Their structure has been proven on the basis of IR, PMR, and mass spectroscopy and, in the case of dimer IXa (R = Me), also by x-ray diffraction analysis [7].

This conversion occurs during the reaction of salt I with various weak bases, especially during their dissolution in dimethylformamide (DMFA) with subsequent precipitation by water (yield 85-95%).

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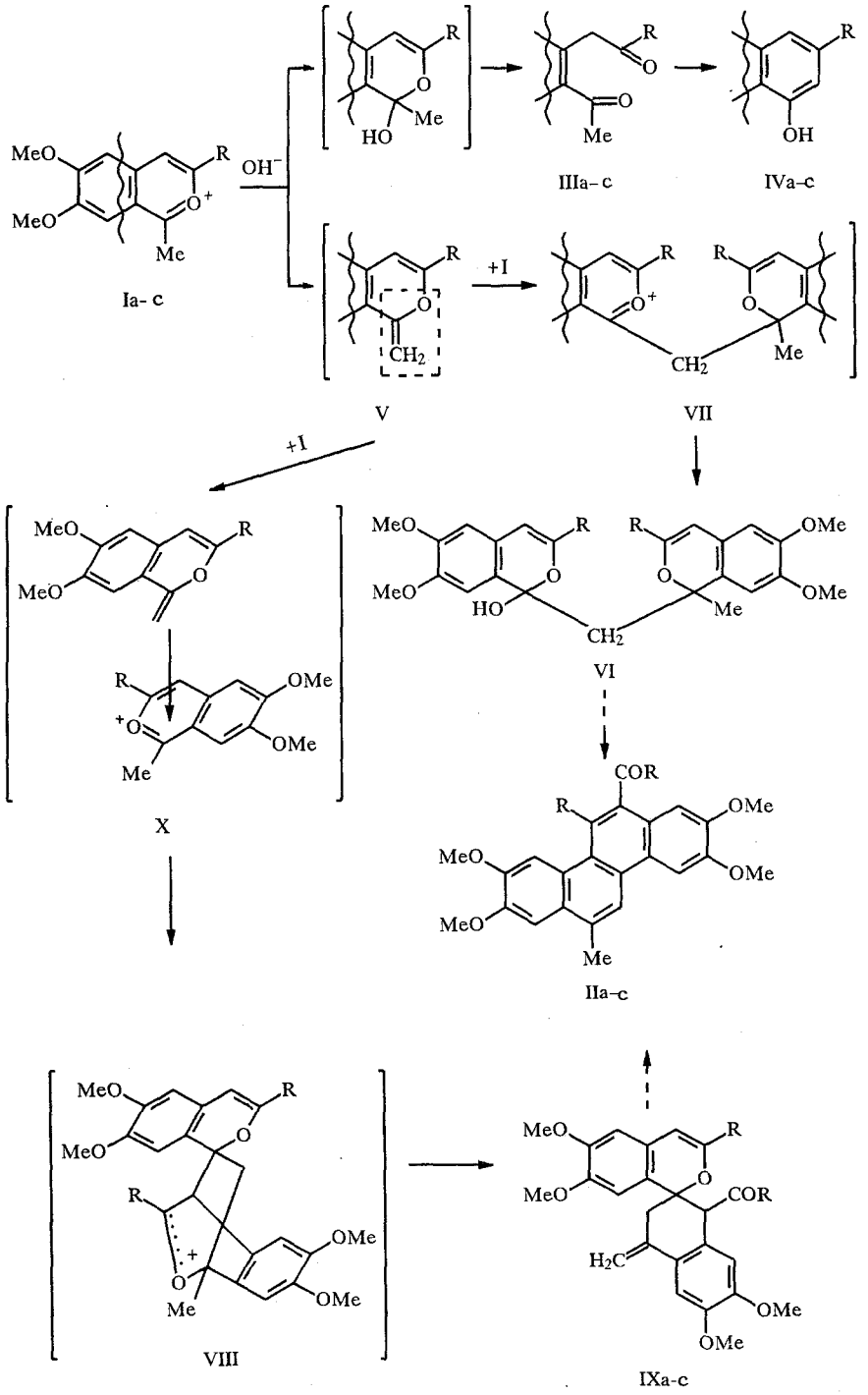
Unlike in the case of dimeric pseudobase VI, the formation of spirocycles IX is preceded by the appearance of a deep, rapidly disappearing color. It is due to a wide absorption band at 570 nm (for salt Ia) and suggests that charge-transfer complexes of type X are formed initially. Analogous intermediates participate in reactions of addition to isoquinolinium salts, also occurring by a Diels–Alder reaction with reversed electronic demands [9]. Previously, the only case of formation of spiro dimers, which was observed in the series of 2-alkyl-4H-1,3-thiazin-4-one, was described in [10] and [11].

During heating with alkalies, both dimeric pseudobase VI and spiro dimers IX are quantitatively converted to the corresponding chrysenes II (see Section 2).

Scheme 1

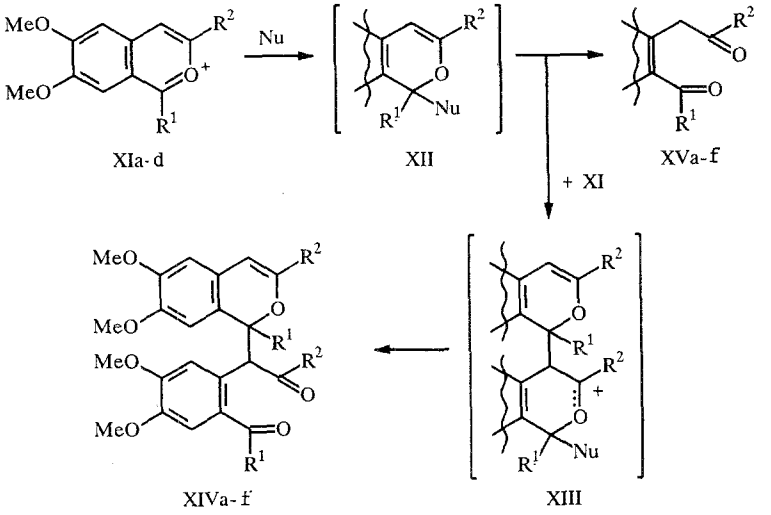


I–IV, IX a R=Me, b R=Ph, c R=3,4-$(OMe)_2C_6H_3$

The 1-H and 1-Ar-substituted 2-benzopyrylium salts XI, which are unable to form anhydro bases, undergo dimerization no less facilely than their 1-methyl analogs, but by a different route [12, 13].

In general form, this process can be represented as an attack of the endocyclic vinyl ether of adducts XII, which formed during addition of a nucleophile to one cation, at the 1 position of the other unreacted one. After cleavage of the charged heterocycle and deprotonation or hydrolysis (depending on the nature of the nucleophile), carboxonium intermediates XIII which appear in this case are converted to so-called 4-1′ dimers XIV.

Scheme 2



a R^1 = H, R^2 = Me; b R^1 = H, R^2 = Ph; c R^1 = H, R^2 = 3,4-$(OMe)_2C_6H_3$; d R^1 = Ph, R^2 = Me; e R^1 = R^2 = Ph; f R^1 = Ph, R^2 = 3,4-$(OMe)_2C_6H_3$; Nu = DMF, Et_3N, Py, OH

As does the formation of spirocyclic dimers IX, 4-1′ dimerization occurs in a wide range of conditions, but better in the presence of weak nucleophiles (see Section 3 for the reasons). As a rule, the yields of 4-1′ dimers are close to quantitative, but sometimes they decrease because of the concurrent formation of diketones XV.

1.2. Formation of Dimers from Adducts of 2-Benzopyrylium Salts and Their Cleaved Forms

Spirocyclic compounds IX and 4-1′ dimers XIV can be obtained not only directly from stable 2-benzopyrylium salts, but also during treatment of 1-methoxyisochromenes XVI with acetic or formic acid* with subsequent addition of water. In this case, dimers IX and XIV probably also formed via preliminary generation of 2-benzopyrylium cations, whose stability in solution depends on the strength of the acid used, the nature of the substituents in the cation, and the concentration. Thus, according to the data of UV spectroscopy, dissolution of isochromenes XIVd-f (R^1 = H) in acetic acid (10^{-1} mole/liter) results immediately in the formation of 4-1′ dimers XIV, and it is not possible to determine the formation of pyrylium acetates XI at such concentrations; after dilution of the obtained solutions by water, 4-1′ dimers XIVa-c were recovered in 90-95% yields.

At the same time, solutions of 2-benzopyrylium acetates XI, having the same absorption spectrum as the corresponding perchlorates, were obtained at a concentration of the order of 10^{-4} mole/liter. But treatment of isochromenes XVId-f with formic acid gives stable solutions of 2-benzopyrylium formates XI regardless of the concentration. However, dilution of these solutions by water also results in the formation of 4-1′ dimers XIVb and XIVc (R^2 = Ar) except for the case of isochromene XVId (R^2 = Me), when aldehyde ketone XVa (R^2 = Me) is recovered.

Even at concentrations of the order of 10^{-1} mole/liter, both in formic acid and in acetic acid, 1-aryl-substituted isochromenes XVIg-i generate stable 2-benzopyrylium cations. The addition of water results in the slow formation of a mixture of 4-1′ dimers XIVd-f and 1,5-diketones XVd-f in a ratio that depends complexly on the dilution rate and the solution concentration.

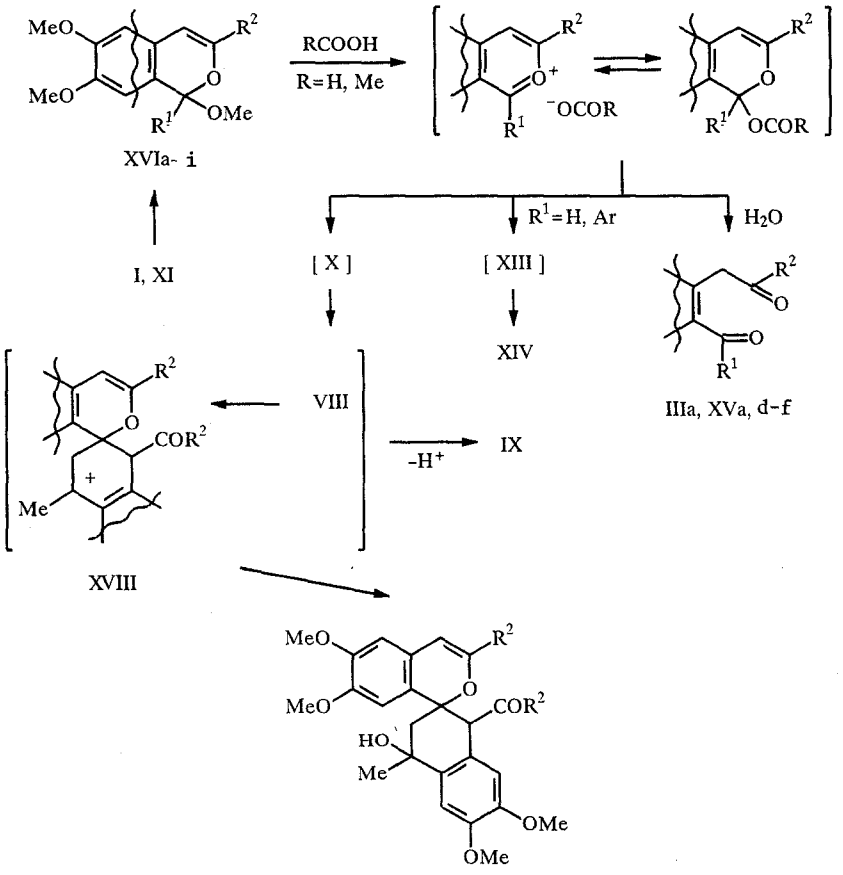
*Regeneration of the starting 2-benzopyrylium perchlorates occurred in the reaction of isochromenes XVI with perchloric acid.

Unlike in the case of 1-methyl-2-benzopyrylium perchlorates I, able to form two types of dimers VI and IX, the corresponding methoxyisochromenes XVIa-c are converted only to spirocyclic dimers during treatment with acetic acid and formic acid. Dimers IX were obtained in AcOH in almost quantitative yield, and their formation was also preceded by the appearance of a deep color, which we attributed to the intermediate formation of an X-type charge-transfer complex; however, it is not possible to ascertain the formation of a 2-benzopyrylium cation under these conditions. At the same time, 1-methyl-2-benzopyrylium formates Ia-c, obtained during dissolution of methoxyisochromenes XVIa-c in formic acid, are quite stable, and, like formates XIa-c (R^1 = H), after addition of water, they either dimerize quantitatively when R^2 = Ar or are converted to diketone IIIa (R^2 = Me). However, dimerization in this case gives a mixture of spirocyclic dimers IX, XVIIb, and XVIIc, with the latter as the main products; they are probably formed because of covalent hydration of intermediate cation XVIII.

2-Benzopyrylium formates (I, XI) that are generated during heating of solutions of 1,5-dicarbonyl compounds III and XV in formic acid dimerize without any differences from the same salts obtained from the corresponding methoxyisochromenes.

It is curious that in the paper that first described the preparation of 2-benzopyrylium salts with anions of organic acids for the case of 1-aryl-3,4-dialkyl-2-benzopyrylium formate obtained in the same way [14], no occurrence of any dimerization processes was noted. The presence of the substituent in the 4 position of the heterocycle of this salt hinders its dimerization.

Scheme 3



XVI a $R^1 = R^2 = Me$; b $R^1 = Me$, $R^2 = Ph$; c $R^1 = Me$, $R^2 = 3,4\text{-}(OMe)_2C_6H_3$; d $R^1 = H$, $R^2 = Me$; e $R^1 = H$, $R^2 = Ph$; f $R^1 = H$, $R^2 = 3,4\text{-}(OMe)_2C_6H_3$; g $R^1 = Ph$, $R^2 = Me$; h $R^1 = H$, $R^2 = Ph$; i $R^1 = Ph$, $R^2 = 3,4\text{-}(OMe)_2C_6H_3$

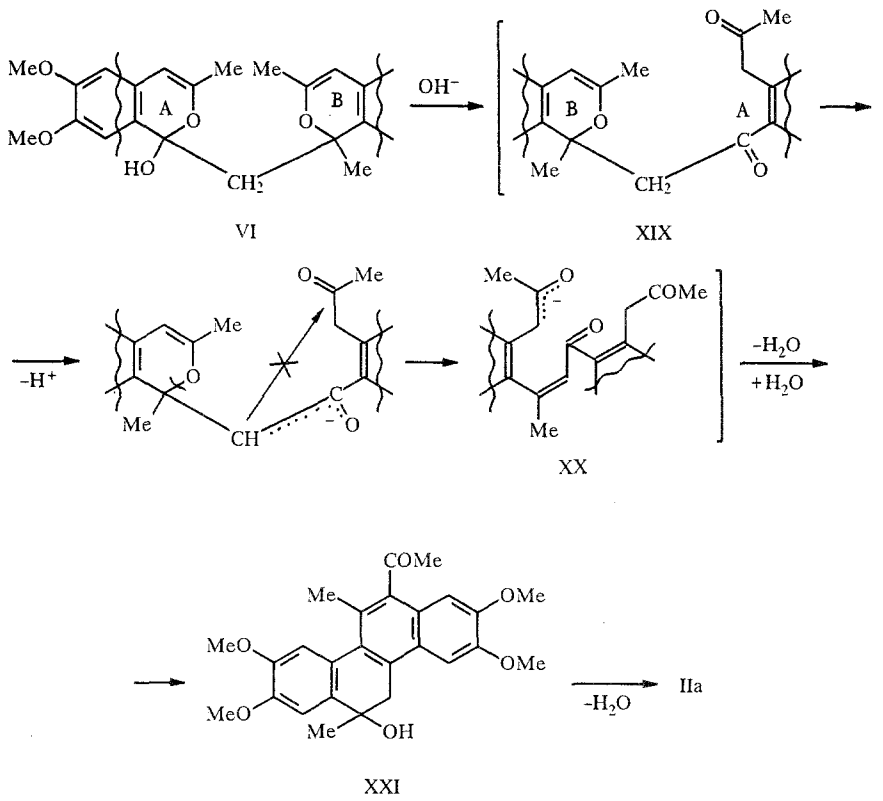
2. REACTIONS OF DIMERS

2.1. Formation of Final Products of α-1′ Dimerization and Spirodimerization from Dimers, 2-Benzopyrylium Salts, and Their Cleaved Forms

Unlike their analogs in the series of quinolinium [6], 1-benzopyrylium [5], and thiazinium salts [10, 11], dimers VI and IX, obtained from 1-methyl-substituted 2-benzopyrylium salts, tend very much to undergo various conversions, especially aldol-crotonic-type reactions.

As was already mentioned, the conversion of dimers of both types to the corresponding acylchrysenes II in the presence of water-alcohol alkalies occurs with quantitative yield. For α-1′ dimer VI, this conversion is now* described by the following scheme:

Scheme 4

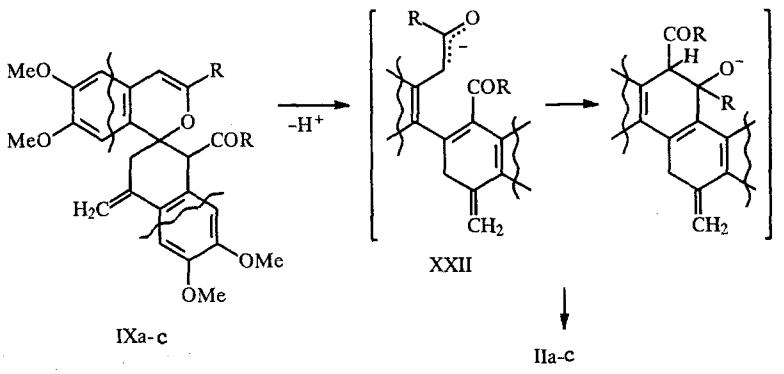


After cleavage of the heterocycle in fragment A of dimeric pseudobase VI, intermediate XIX, which can be considered as an adduct of a monomeric 2-benzopyrylium salt (fragment B) and an unusual methylene-active compound, is formed. We studied the characteristics of conversions of such adducts specially in a separate paper [8], which subsequently helped in interpretation of the transformations of various types of dimers. After deprotonation of the methylene group in adduct XIX, cleavage of the isochromene ring occurs (intrafragment cyclization with formation of substituted naphthol does not occur); hydration of the double bond and aldol condensations occur in the resulting triketone XX. Dihydro compound XXI can be recovered after brief heating of dimeric pseudobase VI; its conversion to aromatic acetylchrysene IIa occurs during subsequent heating or during recrystallization from acetic acid.

For spiro dimers IX, in the presence of alkalies, this conversion can be represented as follows:

*Previously, in [3] Korobka et al. proposed a somewhat different mechanism.

Scheme 5

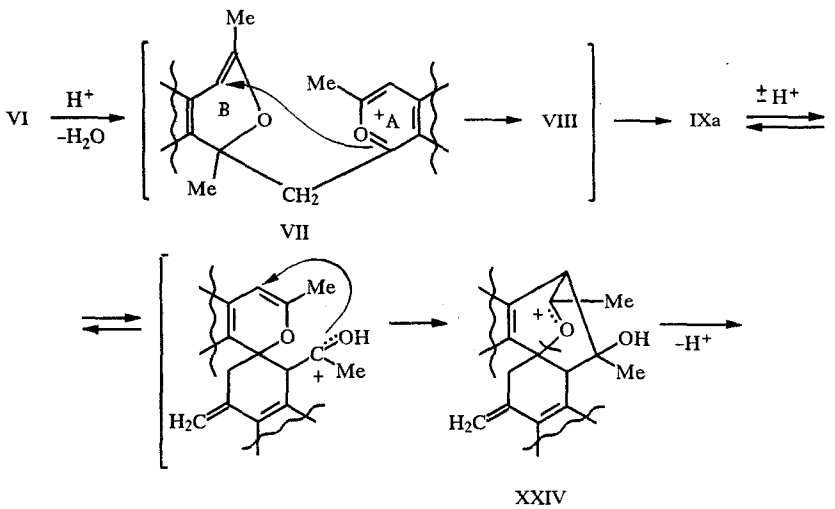


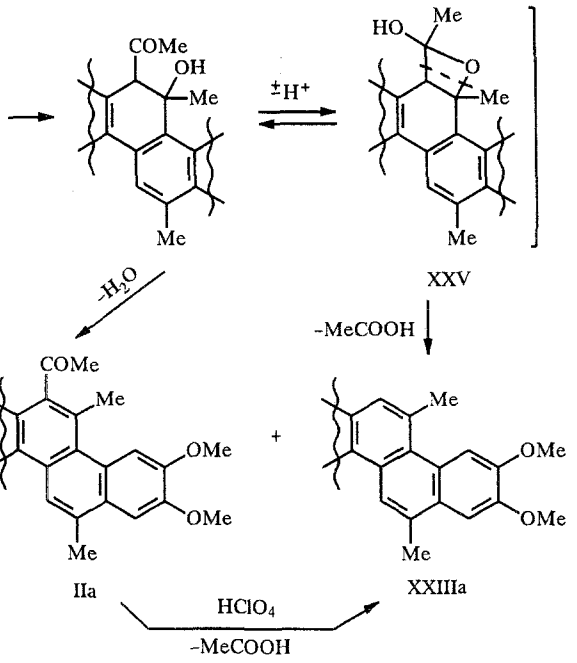
Also in this case, the reaction probably begins with deprotonation, causing cleavage of the heterocycle; as a result of aldol condensation, abstraction of water, and prototrophic rearrangement, the resulting enolate anion XXII is converted to corresponding acylchrysene II. Acylchrysenes are also definitely formed similarly from hydrated spiro dimers XVII.

In a strongly nonnucleophilic medium (e.g., 70% $HClO_4$ in an acetic acid solution at 20°C), dimers of any type undergo complete retrodecomposition into the starting salts or their cleaved forms. However, when the conditions are specially selected, some intramolecular conversions of dimers can be carried out even in an acid medium. Thus, during heating of dimeric pseudobase VI in acetic acid, a mixture of chrysene IIa and its deacetylated analog XXIIIa is formed in high yield. The first step of this process is probably the formation of dimeric salt VII. Subsequently, as a result of intramolecular interfragment interaction, the formation of a $C_{(4B)}-C_{(1A)}$ bond occurs, resulting in already known cyclic oxonium intermediate VIII. The fact of recovery of spiro dimer IXa under these conditions (after brief heating) makes this mechanism more probable than the previously proposed one [3], which assumed the occurrence, directly in dimeric salt VII, of an intramolecular retro Diels–Alder reaction. Subsequently, in accordance with the mechanism of recyclization of adducts of 2-benzopyrylium salts with CH_2-active compounds in an acid medium [8], spiro dimer IXa probably is converted to bridging intermediate XXIV (a para bonding mechanism [15]), forming, as a result, chrysene IIa or its deacetylated analog XXIIIa.

But if α-1′ or spiro dimers IXa and XVII are treated with a strong acid during heating in alcohol, water, or other solvents having basicity, the formation of a mixture of chrysenes IIa and XXIIIa is also accompanied by their retrodecomposition. However, during heat, the resulting salt Ia is gradually converted to the same mixture of chrysenes containing insignificant amounts of α-naphthol IVa (scheme 6).

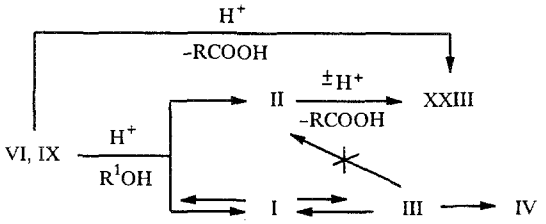
Scheme 6





Under these conditions, other 1-Me-2-benzopyrylium salts Ib and Ic and also, unlike in the case of an alkaline medium (see Section 1), their cleaved forms IIIa-c behave similarly (scheme 7).

Scheme 7



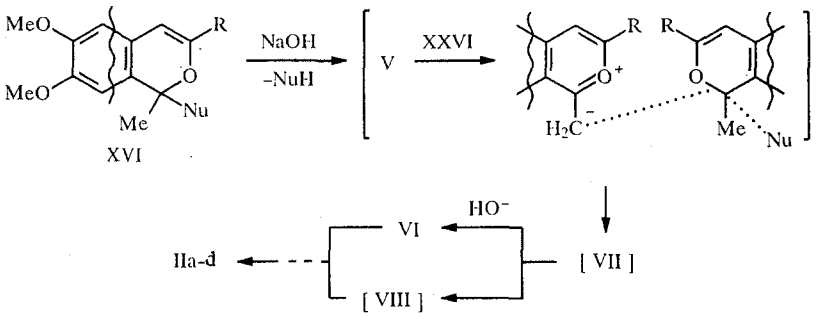
R^1=H, Alk

The insignificant degree of conversion of 1,5-diketones III to α-naphthols IV is probably due to the high rates of their cyclization to 2-benzopyrylium cations and subsequent dimerization processes. Such an explanation also essentially eliminates the assumption of the possibility of formation of chrysenes under these conditions directly from two molecules of 1,5-diketone III [3], i.e., under these conditions the dimerization of 2-benzopyrylium salts and their cleaved forms occurs via intermediate formation of anhydro bases of type V. But the selection of the further route (the α-1′ variant, [4+2]-cycloaddition, or their simultaneous occurrence) is probably governed, as in an alkaline medium, by the experimental conditions (the temperature, the solvent, and the nature of the base).

As concerns the formation of deacetylated chrysene XXIIIa under the above-described conditions, it has been shown that acetylchrysene IIa is facilely deacetylated in the presence of strong acids, but does not change during heating in acetic acid [2]. Therefore, its formation from dimers VI and IX in acetic acid occurs in earlier steps, possibly in the intermediate oxetane XXV (scheme 6). In the presence of strong acids, this process is also accompanied by deacetylation of the already formed acetylchrysene II. The ability of acylchrysenes IIa-c to lose an acyl group depends on the nature of the substituent in it. Thus, similarly to acetylchrysene IIa, veratroylchrysene IIc was deacetylated during heating in the presence of strong acids, but the benzoyl group in compound IIb was retained under these conditions.

Acylchrysenes II can also be formed from some adducts of 2-benzopyrylium salts during their reaction with concentrated solutions of alkalies [16]. In this case, direct participation of the starting 2-benzopyrylium cation in the dimerization process is unlikely. Rather, the formation of dimeric salt VII, able to react subsequently in two directions, occurs by an S_N2 mechanism where the reagent is anhydro base V, which appears during abstraction of NuH, and the starting adduct is the substrate.

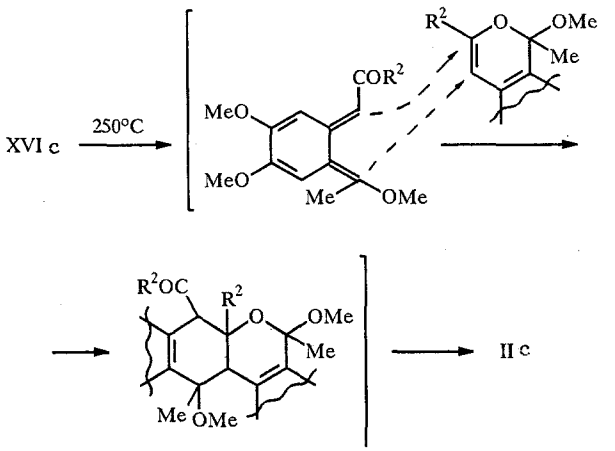
Scheme 8



The yield of the thus-obtained acylchrysenes II is higher than during their formation directly from 2-benzopyrylium salts. Furthermore, unlike in the case of salt Id (R^1 = Me, R^2 = H), which forms a complex mixture of products in the presence of alkalies, the corresponding cyanoisochromene XXVI (R = H, Nu = CN) is converted to formylchrysene IId in 60% yield.

Acylchrysene IIc was also obtained in 50% yield during thermolysis of methoxyisochromene XVIc. In this case, it is conceivable that electrocyclic cleavage of the heterocycle in the adduct is possible together with a mechanism proposed in the preceding scheme. The resulting o-quinoid acts as a diene, and the vinyl fragment of the unreacted adduct acts as an external dienophile.

Scheme 9

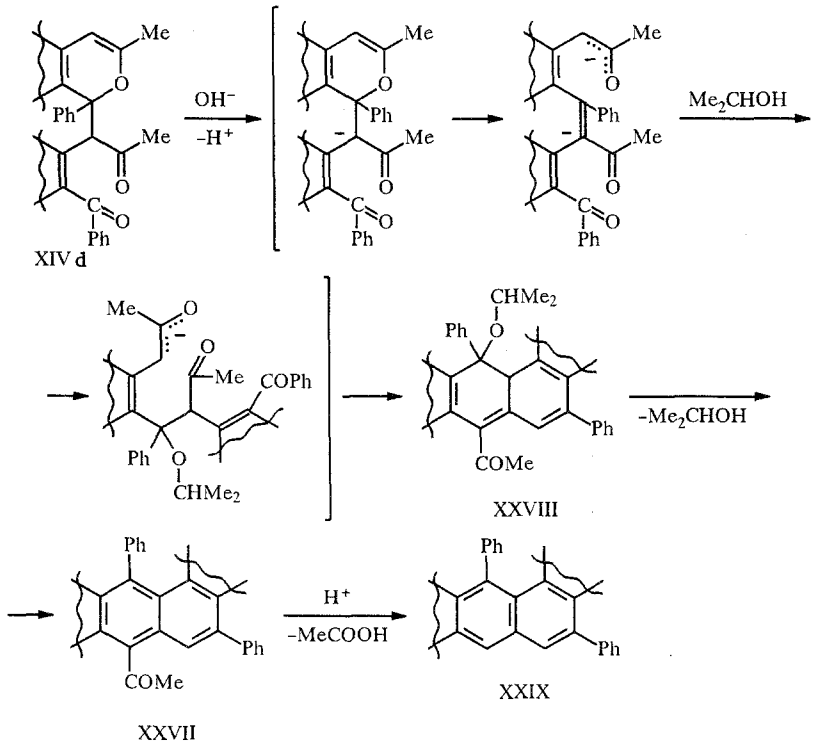


2.2. Conversions of 4-1′ Dimers

The possibilities of 4-1′ dimerization are significantly less limited by structural demands imposed on 2-benzopyrylium salts in comparison with α-1′ and spiro processes, where a 1-methyl group must be present; therefore, the range of 4-1′ dimers and the range of their conversions are significantly broader.

2.2.1. Conversions of 4-1′ Dimers Occurring by an Aldol-Type Reaction. Just as α-1′ and spiro dimers, 4-1′ dimers can be considered as adducts of a monomeric 2-benzopyrylium salt and a methylene-active compound; therefore, their transformations are significantly similar.

Scheme 10

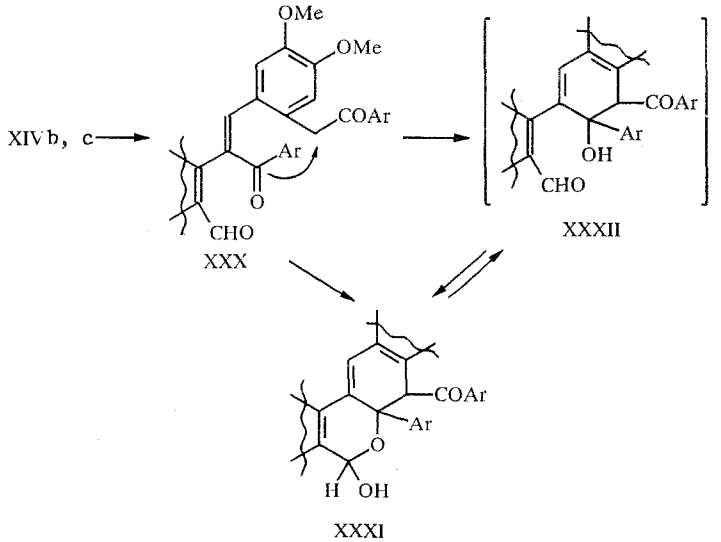


Thus, during heating in a mixture of aqueous alkali and isopropyl alcohol, dimer XIVd (R^1 = Ph, R^2 = Me) is quantitatively converted to benz[*a*]anthracene XXVII, and, during brief heating, dihydro derivative XXVIII, whose formation and behavior are similar to those of dihydrochrysene XXI, can be recovered [12].

Also, by analogy with the formation of chrysenes in the treatment of acetylanthracene XXVIII with strong acids, ipso substitution of the acetyl group occurs, leading to deacetylated anthracene XXIX.

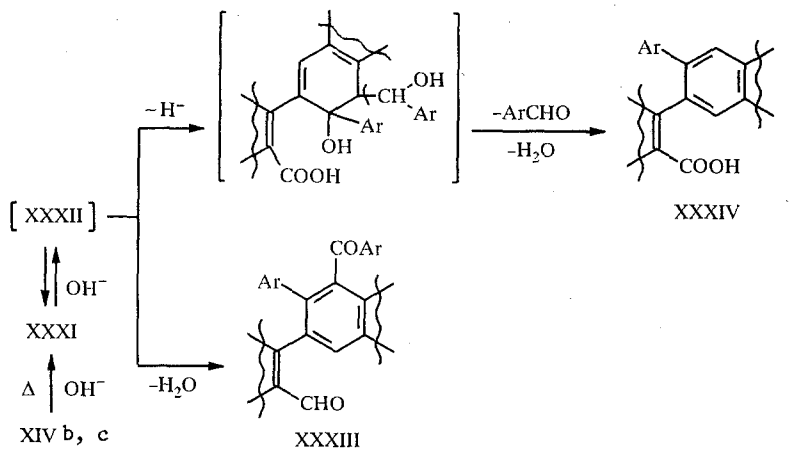
The formyl group introduces specifics into the conversions of 4-1′ dimers XIV (R^1 = H) [17]. Thus, during heating of dimers XIVb and XIVc (R^1 = H, R^2 = Ar) in isopropyl alcohol with sodium acetate, chalcones XXX, products of deprotonation of the methylene group and subsequent cleavage of the heterocycle, can be recovered.

Scheme 11



But if these dimers are treated with a mixture of aqueous alkali in dioxane (~20°C), cyclic hemiacetals XXXI are formed, probably obtained because of intramolecular interaction of formyl and hydroxyl groups in aldols XXXII. Under these conditions, products XXXI can also be obtained from chalcones XXX.

Scheme 12



But heating of dimers XIVb and XIVc in a strongly alkaline medium results in the formation of naphthalenes XXXIII, which can also be obtained under similar conditions from hemiacetals XXXI.

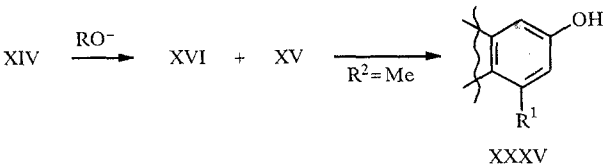
It has been observed that acids XXXIV are also formed together with naphthalenes XXXIII. Their formation is probably preceded by an intramolecular hydride shift between aldehyde and ketone groups in the intermediately formed hydroxy aldehyde XXXII with subsequent abstraction of an aromatic aldehyde.

The observed intramolecular disproportionation is a new type of Cannizzaro rearrangement, known previously only for α-keto aldehydes [18].

The occurrence of such a 1,7 hydride shift is probably due to conformational flexibility of the molecule of XXXII, enabling approach of the reaction centers, which was confirmed by analysis of molecular models. In the rather rigid molecules of aromatic naphthalenes XXXIII, the approach of the aldehyde and ketone groups is impossible, and they therefore withstand heating with alkalies without any changes.

All the described transformations of 4-1′ dimers in the presence of alkalies depend significantly on the nature of the solvent. The most suitable ones were found to be 2-propanol and dioxane, but with the use of ethanol and methanol partial dissociation of the dimers was observed because of nucleophilic substitution of the residue of the diketone fragment in the 1 position of the isochromene ring. As a result, ethers of pseudobases XVI and monomeric diketones XV or products of their intramolecular conversions, β-naphthols XXXV, were formed.

Scheme 13



The presented data indicate that 4-1′ dimers react more facilely in the S_N2 substitution reaction than do α-1′ dimers.

These are also probably the reasons why direct conversion of 2-benzopyrylium salts, able to undergo 4-1′-type dimerization, to final naphthalenes XXXIII and XXXIV or anthracene XXVIII occurs significantly worse than in the case of 1-Me-2-benzopyrylium salts [12]. Thus, direct conversion of 2-benzopyrylium salt XId to anthracene XXVIII occurs in low

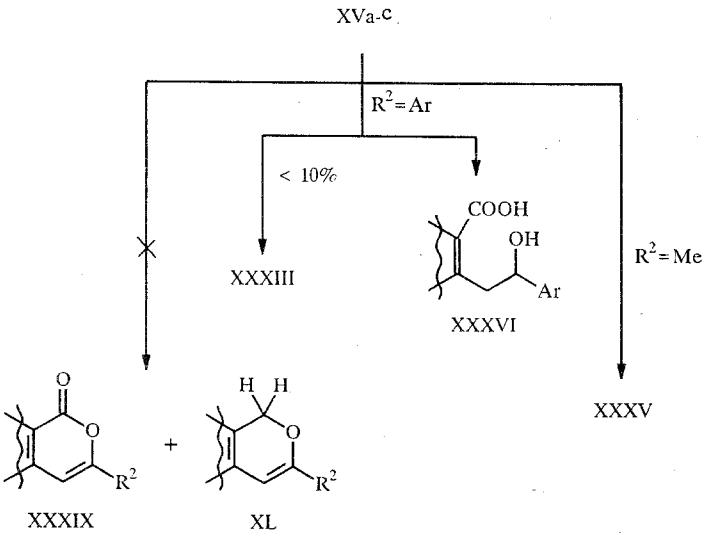
yield, with the final result depending not only on the nature of the alcohol, but also on the concentration of the alkali. For example, only β-naphthol is formed during treatment of this salt with a 2% aqueous alkali solution, but anthracene XXVIII is still formed in the presence of 50% aqueous alkali, albeit in < 20% yield. A better yield (40%) of anthracene XXVIII from salt XId could be obtained when the reaction was carried out in isopropyl alcohol with sodium isopropylate.

Complete conversion of diketone XVd to β-naphthol XXXV (R^1 = Ph) in an alkaline medium indicates that it does not participate in the formation of anthracene XXVIII from salt XId.

The situation is somewhat different in the case of keto aldehydes XVb and XVc (R^2 = Ar), for which no intramolecular aldol condensations are possible. During their treatment with alkalies, intermolecular condensations still occur, albeit with low yields (8-10%). Hydroxy acids XXXVI become the main products of such reaction, i.e., another type of Cannizzaro rearrangement occurs. The occurrence of precisely the rearrangement and not the reaction of the same name is explained, as in the case of 1,7 rearrangement, by favorable steric factors, ensuring facileness of hydride transfer to the δ position even in the presence of donor substituents in the aromatic ring bonded to the keto group [19].

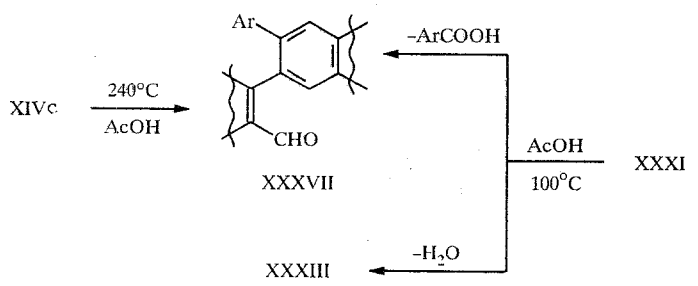
Under these conditions, aldehyde ketone XVa (R^2 = Me) is completely converted to β-naphthol XXXV (R^1 = H), a product of intramolecular aldol condensation.

Scheme 14



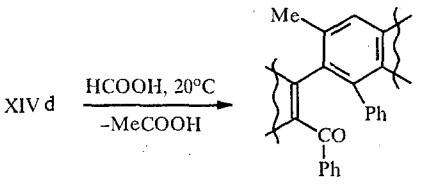
When special conditions are selected, transformations of 4-1′ dimers can be carried out even in an acid medium [17]. Thus, thermolysis of dimer XIVc with catalytic amounts of acetic acid is completed with the formation of naphthalenes XXXVII, which, together with other substituted naphthalenes XXXIII, is also formed during heating of cyclic hemiacetal XXXI in acetic acid.

Scheme 15



Aromatization with abstraction of a carboxylic acid molecule also occurs during holding of dimer XIVd in formic acid at 20°C.

Scheme 16



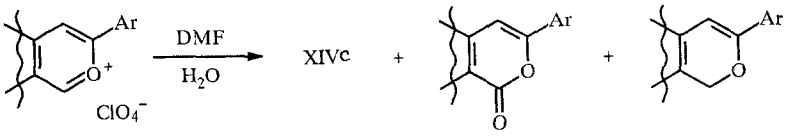
XXXVIII

Just as in the case of spiro dimers IX (see scheme 6), the recyclization of 4-1′ dimers XIV in an acid medium probably occurs by a para-bonding mechanism, and abstraction of carboxylic acid, resulting in the formation of naphthalenes XXXVII and XXXVIII, occurs in an intermediate oxetane analogous to XXV.

Unlike their 1-methyl-substituted analogs, during heating in aqueous or alcoholic solutions of strong acids, 1H- or 1-Ar-2-benzopyrylium salts do not form dimerization products, being converted only to the corresponding 1,5-diketones or, if possible, to products of their intramolecular condensation, i.e., β-naphthols XXXV. Also under these conditions, adduct XVI is probably formed in the first step of the reaction, but here the reacting electrophile is not the starting salt, but a proton, i.e., similarly to the previously described conversion of 1-CH_2R-2-benzopyrylium salts (R = H) to α-naphthols [20].

2.2.2. Disproportionation of 2-Benzopyrylium Salts via Preliminary Dimerization. A type of disproportionation, new for heteroaromatic cations, has been observed in reactions of 1-unsubstituted 3-Ar-2-benzopyrylium salts with some nucleophiles [13]. Its characteristic in comparison with known conversions of such cations [29] is preliminary dimerization of the 2-benzopyrylium salt with subsequent disproportionation in the dimer. The starting point of this investigation was the detection of insignificant amounts of isocoumarin XXXIX and isochromene XL, which are products of disproportionation of salt XIc during its dimerization in the presence of DMFA.

Scheme 17



XI c XXXIX XL

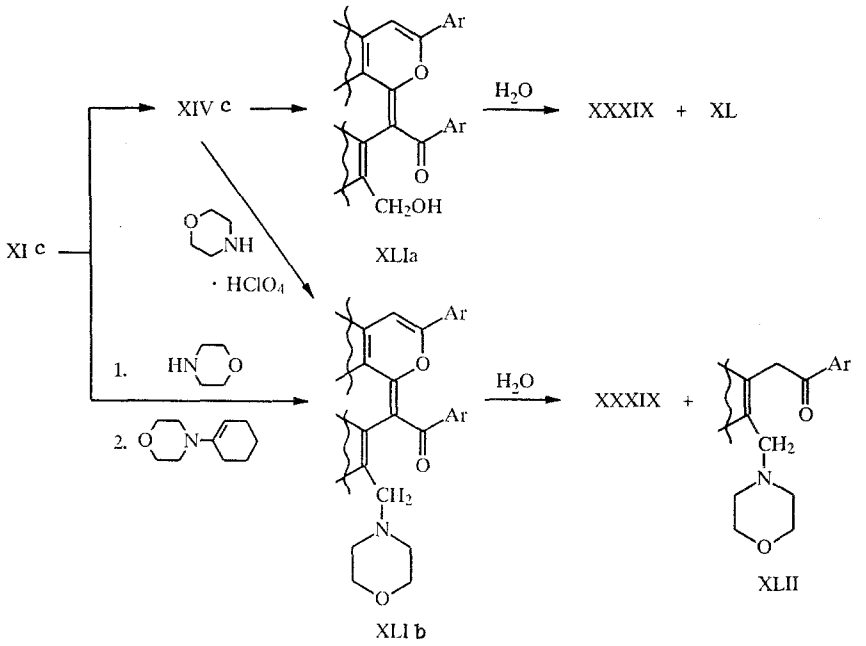
Ar=3,4-$(MeO)_2C_6H_3$

The yield of the products of disproportionation of XXXIX and XL increase sharply if dimer XIVc is heated directly with catalytic amounts of triethylamine perchlorate,* in which case it is possible to ascertain the formation of unstable orange compound XLIa.

But if this dimer is heated with morpholine perchlorate, another more stable compound, XLIb, is formed, and it, in its turn, decomposes into isocoumarin XXXIX and nitrogen-containing compound XLII, related to isochromene XL. But this colored "unsaturated" dimer XLIb can also be obtained directly from salt XIc during its heating in the presence of morpholine (7%), and it can be obtained in 40% yield in the presence of its enamine, acting in this case as a tertiary amine.

*Free perchloric acid cannot be used because, as was already noted, it immediately causes retrodecomposition of the dimer.

Scheme 18



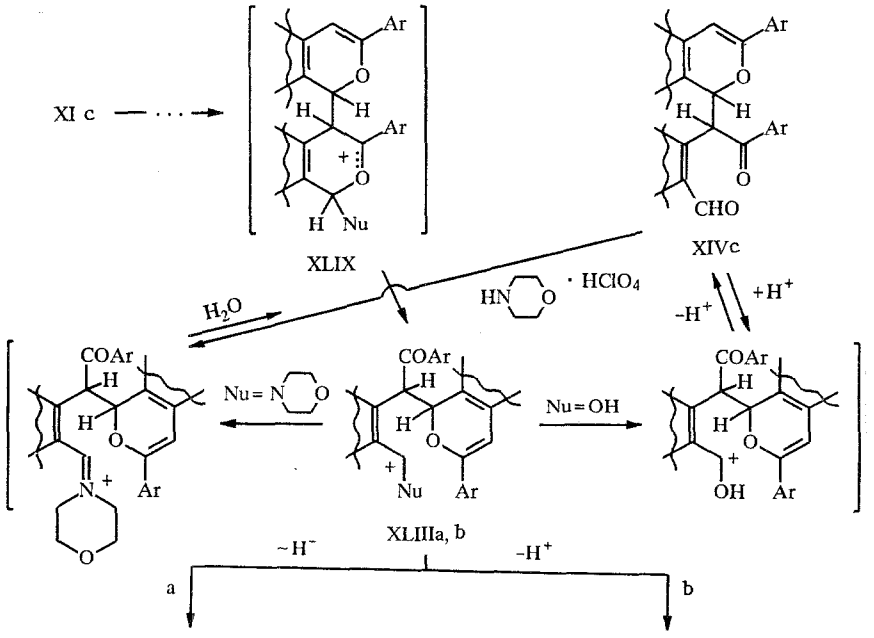
The reasons for the different yields of "unsaturated" dimer XLIb are probably the different effects of secondary and tertiary amines in the dimerization step, and they will be presented in more detail in Section 3.

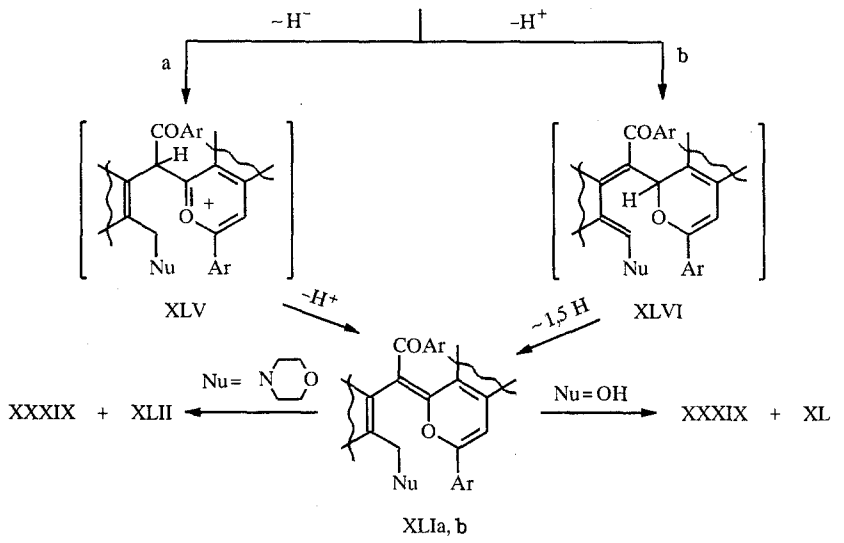
The nature of the added nucleophile also plays a significant role directly in the disproportionation step, when it determines the stability of intermediate XLIII, which forms after cleavage of the "lower" ring in dimeric carboxonium ion XLIV. When the nucleophile is a stabilizing positive charge, i.e., the morpholine group, intermediate XLIII immediately undergoes intramolecular transformation (direct preparation of "unsaturated" dimer XLI from salt XIc); but if Nu = OH, cation XLIII is mainly deprotonated to dimer XIVc, and only in insignificant amounts is it able to be converted to "unsaturated" dimer XLIa, decomposing subsequently into isocoumarin XXXIX and isochromene XL.

However, cationic intermediate XLIIIa can be regenerated during heating of dimer XIVc with catalytic amounts of triethylamine perchlorate, and cation XLIIIb is formed during its reaction with protonated morpholine.

The formation of "unsaturated" dimers XLIa and XLIb can occur not only by a route of hydride shift with subsequent disproportionation of dimeric salt XLV (route "a"), but also by 1,5 hydrogen shift (equivalent to it in its result) in o-quinoid intermediate XLVI, which is formed after deprotonation of the acid methine group in intermediate XLIII (route "b") (scheme 19).

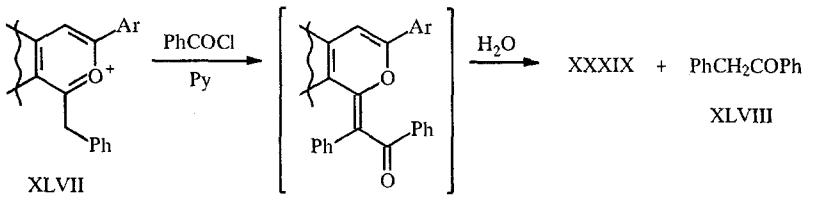
Scheme 19





But cleavage of "unsaturated" dimers XLI is probably due to hydration of the double bond with subsequent cleavage of the C−C bond similarly to the known decomposition of β-diketones [21]. Model experiments, where isocoumarin XXXIX and deoxybenzoin XLVIII were obtained during acylation of the active methylene group of salt XLVII after hydrolysis of the reaction mixture, confirmed this assumption.

Scheme 20



Ar=3,4-$(OMe)_2C_6H_3$

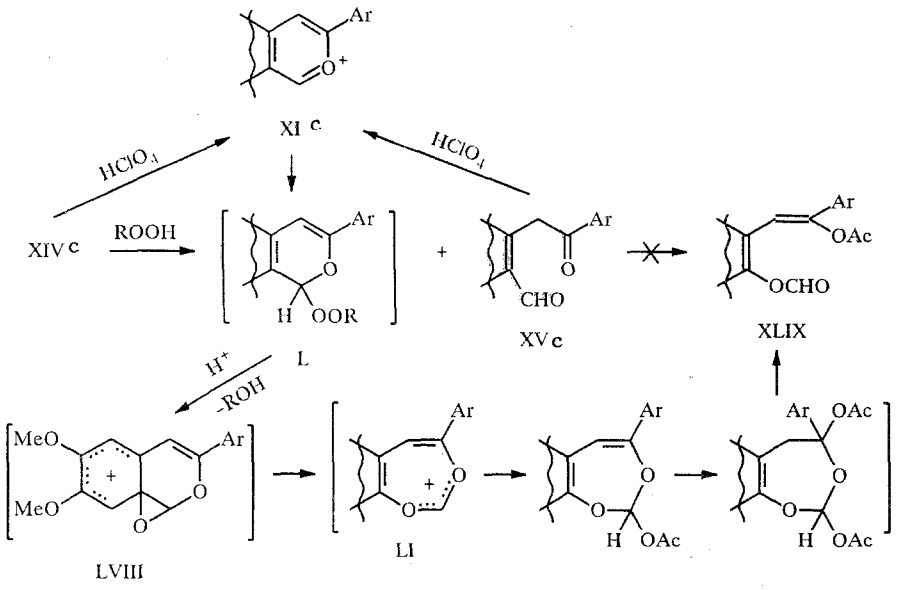
Comparing the results of the disproportionation reactions directly of 1H-2-benzopyrylium salts XIb and XIc and their cleaved forms XVb and XVc, we can conclude that they differ not only in their mechanism, but also in their final result.

2.2.3. Oxidation of 4-1′ Dimers. As was described above, during heating in acetic acid, dimers of 2-benzopyrylium salts undergo various intramolecular conversions. But when the dimers react with perchloric acid, they undergo retrodecomposition.

It has been observed that cleavage of the interphase C−C bond of dimer XIVc also occurs during holding of its acetic acid solution in air for 24 h [22]. However, here both aldehyde ketone XVc and diether XLIX are formed in 30% yield.

The observed conversion is probably substitution of a fragment of the aldehyde ketone in the 1 position of the isochromene ring of the dimer by peracetic acid (analogy with cleavage of 4-1′ dimers by alcoholic alkali, scheme 13), formed by oxidation of acetic acid by oxygen of air. Subsequently, in adduct L, a Baeyer−Villiger-type rearrangement, successive addition of 2 moles of acetic acid to seven-membered cationic intermediate LI, and ring cleavage with loss of 1 mole of acetic acid probably occur.

Scheme 21



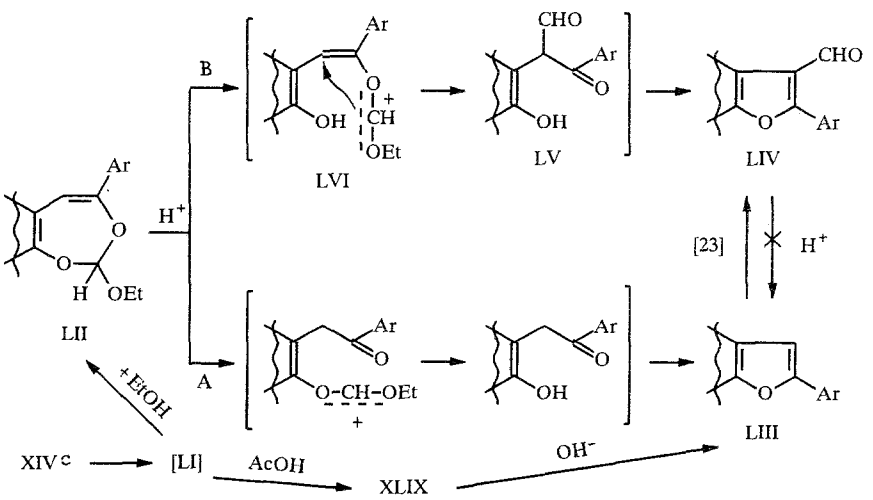
Ar=3,4-$(MeO)_2C_6H_3$

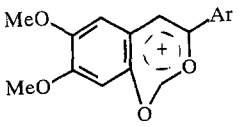
During oxidation of the dimer by a specially obtained acetic acid solution of peracetic acid, the time of formation of diether XLIX is decreased (after 1 h, its yield reaches 35%); in the presence of catalytic amounts of perchloric acid, its yield also increases significantly (up to 55%).

In the latter case, together with the above-described process of substitution in the dimer, its direct cleavage probably occurs by protonation of the interfragment C−C bond of perchloric acid. By two routes (as a result of cleavage of the C−C bond and cyclization of the abstracted aldehyde ketone XVc in the presence of $HClO_4$), this process results in the formation of 2-benzopyrylium salt XIc. And whereas, as shown by model experiments, the aldehyde ketone does not react with peracetic acid under the described conditions, 2-benzopyrylium salt XIc is, in fact, able to undergo oxidation. At the same time, the molar amount of perchloric acid that is evolved in the direct oxidation of perchlorate XIc initiates side conversions, unidentified by us, decreasing the yield of diester XLIX.

But if the $HClO_4$-catalyzed oxidation of dimer XIVc is carried out by hydrogen peroxide in ethanol, cyclic orthoester LII is formed in 60% yield and is probably the product of addition of a molecule of the solvent to cationic intermediate LI.

Scheme 22





LVII

In a acid medium, orthoether LII, stable with respect to bases, forms a mixture of furan LIII and its formyl derivative LIV, in which, depending on the conditions, either compound predominates. Furan LIII was also obtained during heating of diester XLIX in water-alcohol alkali. Furan LIII was facilely formulated according to Rieche [23], but, unlike the above-described processes of deacylation of chrysenes and anthracenes, the reverse transition LIV → LIII did not occur, even in the presence of perchloric acid. Therefore, such a route of formation of furan LIII is excluded during the treatment of orthoether LII with acids.

The ambient behavior of orthoether LII in an acid medium is probably related to the possibility of its protonation at various positions of the heterocycle. Most probably, the addition of a proton at the vinyl fragment or at the oxygen atom in the 3 position of the dioxepin ring, resulting in cleavage of the $C_{(2)}-O_{(3)}$ bond (route A) results in formation of furan. At the same time, the initial protonation of the $O_{(1)}$ atom, initiating cleavage of the $O_{(1)}-C_{(2)}$ bond, is ultimately completed with formation of aldehyde LV (route B). In the latter case, before cyclization, intermediate LVI should undergo rearrangement similarly to vinyl esters [24].

Unfortunately, even in the cell of an NMR spectrometer at −70°C, the reaction of a solution of orthoether LII in SO_2 with trifluorosulfonic acid did not make it possible to detect a third possible direction of protonation, namely, at the exocyclic oxygen atom, i.e., to regenerate charged intermediate LI, probably able to exist as 2-benzohomopyrylium cation LVII.

The recovery of adduct LII, confirming the assumption of intermediate formation of cation LI, suggests that in the series of 2-benzopyrylium salts the oxidation by peroxides occurs not by the traditional ANRORC scheme [25], characteristic of analogous conversions of monocyclic pyrylium salts [26], but by the route of so-called ortho bonding [15], where the cleavage of the old ring is preceded by formation of a new one (intermediate LVIII). This mechanism and the mechanism of para bonding, which was proposed above for interpretation of the recyclization of dimers IX and XIV (and also adducts of 2-benzopyrylium salts with simple CH_2-active compounds [8]) in an acid medium, are essentially close.

3. PRINCIPLES OF THE DIMERIZATION OF 2-BENZOPYRYLIUM SALTS

Previously [27], we discussed the effect of the nature of the nucleophile added to the 2-benzopyrylium cation on the ability of the intermediate adduct to enter into subsequent intramolecular conversions. On the basis of experimental data, it was concluded that if there is a free electron pair at the α-atom of the nucleophile, the intermediate adducts are unstable, and ring cleavage occurs rather facilely. Such nucleophiles include ammonia and primary and, partially, secondary* amines.

But if there is no free electron pair at the α-atom of the nucleophile, the resulting adducts are stable and can be recovered (CH_2-active compounds, hydride-ion donors, Grignard reagents, and alkoxide anions).

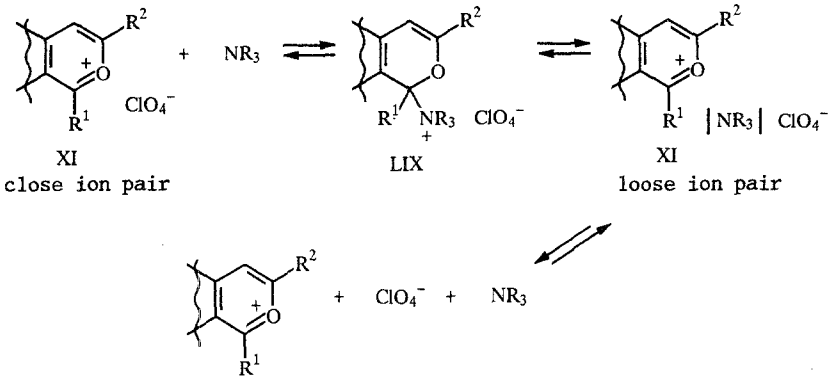
From the assumption that one of the participants in the 4-1′ dimerization process is an adduct, it follows that the nature of the nucleophile that formed it and, therefore, the above-considered principle also play a decisive role in the occurrence of the dimerization reactions. Indeed, 2-benzopyrylium salts do not react at all with the separately taken stable adduct, but dimerization products are not observed in their reactions with ammonia and primary amines (in the absence of acids as catalysts of the recyclization reaction).

Therefore, the previously proposed formal scheme of 4-1′ dimerization requires refinement: the intermediate adduct should not be both stable and prone to heterocycle-cleavage reactions. From these standpoints, the preferred occurrence of dimerization reactions of 2-benzopyrylium salts in the presence of so-called weak nucleophiles (DMFA, pyridine, triethylamine, and sodium acetate) becomes understandable.

*In this case, the stability of the adducts is significantly affected by the structure of the starting 2-benzopyrylium cation.

In the case of tertiary amines, adducts LIX are formed, which meet the above-enumerated requirements, and in which, in addition, because of the absence of bonding with the cation center, the 4 position of the heterocycle retains nucleophile properties. Therefore, it is conceivable that with increasing formation, they react here with the retained cation. However, in our opinion, a somewhat different, supplementary variant is more probable, according to which the weak nucleophile also changes the reactivity of the other cation in the dimerization step of the one acting as an electrophile. And this probably occurs as a result of dissociation of the resulting adduct LIX and establishment of equilibrium between the 2-benzopyrylium cation XI in the solution, although the cation is already in a dissociated state or in a loose ion pair with the starting adduct LIX.

Scheme 23



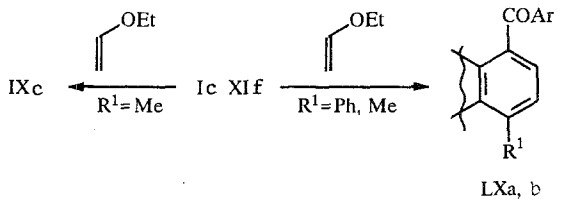
Degradation of the starting close ion pair, occurring in the presence of a tertiary amine, acting as a nucleophile in the first step but as a solvent in the second step, definitely increases the reactivity of the 2-benzopyrylium cation.

It can be assumed that an analogous equilibrium, whose existence was recently established for phosphorus-containing adducts of monocyclic pyrylium salts by electrochemical methods [28], is also possible for adducts of 2-benzopyrylium salts with Nu = $OCOCH_3$ because this nucleophile is also a good leaving group.

Degradation of the close ion pair also probably occurs for the part of 1-Me-2-benzopyrylium salts I whose cations act in the dimerization step (depending on its type) either as an electrophile or as a heterodiene. But in the formation of an anhydro base from the other part of the pyrylium salts, the weak nucleophile also acts as a base.

The described activating effect of weak nucleophile on the reactivity of 2-benzopyrylium salts is confirmed by the data of [8] on their reaction with vinyl ethyl ether, a reagent unable to change its properties under these conditions. Thus, salt XIf (R^1 = Ph) reacts with this ether only in DMFA solutions; but in the case of salt Ic (R^1 = Me), which does not react with vinyl ethyl ether in alcohol, compound LXb is formed in 60% yield during addition of small amounts of pyridine, and dimerization occurs with 30% yield.

Scheme 24



LX a R^1=Ph, b R^1=Me; Ar=3,4-$(OMe)_3C_6H_3$

Unfortunately, at present, there is not yet sufficient data to explain the 4-1′ dimerization of 2-benzopyrylium salts XI in the presence of alkalies, where this process depends complexly on the alkali concentration, the nature of the solvent, and other experimental conditions. It is very probable that the intermediate adduct in this case is not pseudobase XII (Nu = OH), and the nucleophile causing dimerization is not the hydroxide anion, as was assumed previously [12], but water or its association complexes [29]. A confirmation of the ability of water to cause dimerization is the fact of formation of dimers from 2-benzopyrylium formates (see Section 1.2).

In addition, 4-1′ dimerization in the presence of alkalies is not stereoselective, whereas, as a rule, in the presence of weak nucleophiles one diastereomer is formed.

In our opinion, one of the main factors governing the stereoselectivity of dimerization is the regular arrangement of the starting 2-benzopyrylium cations in crystals and sufficiently concentrated solutions, as occurs in the case of acridinium [30], N-phenylpyridinium [31], and some other cations [32]. Here the reaction of one or two salt molecules with the reagent, preceding dimerization, probably disrupts their mutual orientation only partially.

Proof of the significant role of the mutual orientation of the 2-benzopyrylium cations and their subsequent association is the absence of "cross dimerization" between 1-methyl-substituted salt Ic and its 1H analog XIc when only a mixture of spiro dimer IXc and 4-1′ dimer XIVc was obtained. Also unsuccessful were attempts to obtain an adduct instead of dimer IXc during treatment of the solution of salt Ia in DMFA by 3,6-diphenyl-1,2,4,5-tetrazine, which is considered [33] the best substrate for the reaction with anhydro bases of the various heteroaromatic cations.

Data on the stereoselectivity of dimerization of 2-benzopyrylium acetates and formates fit in this same series. Thus, methoxyisochromenes XVIa and XVIf, which dimerize in acetic acid, give an equimolecular mixture of diastereoisomers of the corresponding dimers IXa and XIVc. At the same time, dimerization of 2-benzopyrylium formates obtained from the same methoxyisochromenes, which occurs during dilution of the solutions by water, occurs stereoselectively. The observed results can be explained with a higher degree of probability by the fact that stable 2-benzopyrylium formates, unlike their acetates, can assume, in solution, a mutual orientation that is characteristic of these cations, and their appropriately structured aggregates then enter into a dimerization reaction.

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