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UNSATURATED 1,5-DIKETONES AND THEIR HALOGEN-SUBSTITUTED DERIVATIVES — PREPARATION AND USE IN THE SYNTHESIS OF HETEROCYCLES

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Published data and the results of the authors' own research on methods for the production of unsaturated 1,5-diketones and halogen-substituted 2-pentene-1,5-diones and their use in the synthesis of difficultly obtainable pyrylium, 3,5-dichloropyrylium, and 3-chlorothiopyrylium salts, aroylfurans, 4-chloroaroylfurans, isoxazolines, pyrazolines, 3,5-dichloropyridines, 1,4-tetramethylenebispyridines, and others are summarized. Aspects of the structure of 2-pentene-1,5-diones and their 2,4-dichloro-substituted analogs and features of their heterocyclization are discussed in comparison with pentane-1,5-diones and their 2,4-dichloro-substituted derivatives.

INTRODUCTION

One of the principal characteristics of unsaturated 1,5-diketones is their exceptionally easy heterocyclization, which makes it possible to use them as the starting materials for the synthesis of difficultly obtainable and new heterocyclic compounds. At the present time there have been no reviews on methods for the production of unsaturated 1,5-diketones and their halogen derivatives or their transformations. In the last twenty years experimental data have accumulated on the development of preparative methods for the production of unsaturated 1,5-diketones, investigation of their structure, and determination of the characteristics of their cyclization. Their prospects in organic synthesis are not subject to doubt.

1. Methods for the Production of Unsaturated 1,5-Diketones

1.1. Hydrolysis of Pyrylium Salts. One of the main methods for the production of unsaturated 1,5-diketones is the hydrolysis of pyrylium salts by the action of bases, which is of interest in connection not only with their synthesis but also with the chemistry of pyrylium salts.

The first representatives of this type of compound were obtained by Dilthey [1, 2]; the aryl-substituted compounds proved stable, while the alkyl-substituted derivatives could only be kept for a short time under normal conditions. Various products from the hydrolysis of the pyrylium salts were formed, depending on the operation of such factors as the pH of the medium, the temperature, and the number and position of substituents in the pyridine ring (and also the nature of the substituents) [1-10]. It is necessary to discuss in detail the conditions leading to the formation of the unsaturated 1,5-diketones. The following scheme for the hydrolysis of pyrylium salts is generally accepted [1-4]: The hydroxide ion adds at the α or γ position of the pyrylium ring with the formation of the γ- or α-pyranol, which undergoes decyclization and is converted into the unsaturated diketone.

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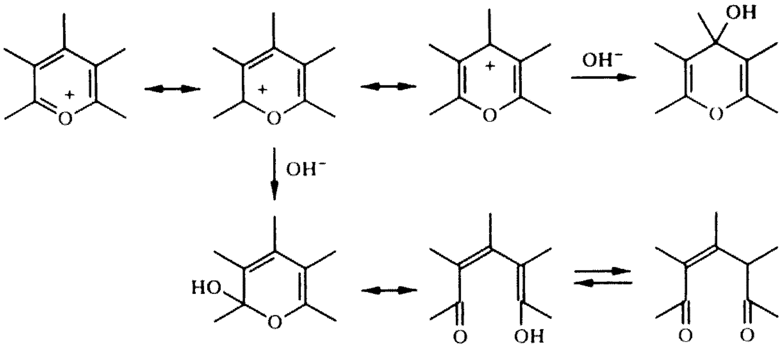
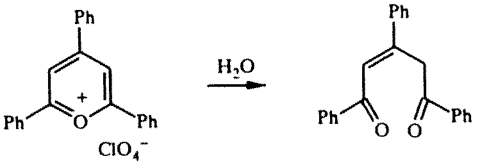
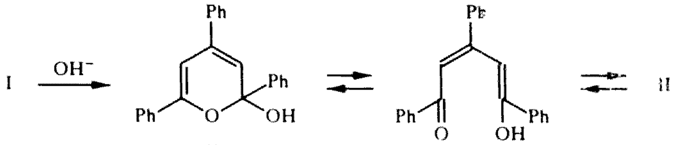


Depending on the above-mentioned factors, hydrolysis gave mixtures of the *cis* and *trans* isomers or only the *cis* isomers of 2-pentene-1,5-diones or mixtures of the unsaturated 1,5-diketones and the corresponding ketoenols etc. [1-10]. Under mild conditions the *cis* isomers of 2-pentene-1,5-diones are mostly formed from "symmetrically" substituted pyrylium salts [8-10]. Thus, 2-pentene-1,5-dione (II) was obtained with a quantitative yield during the hydrolysis of 2,4,6-triphenylpyrylium perchlorate (I) in water—acetone solution or dimethoxyethane [6].



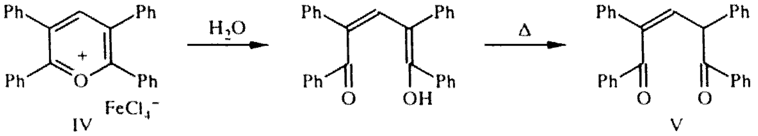
I II

At pH > 11 triphenylpyrylium perchlorate is hydrolyzed to a mixture of the pentenedione (II) and 2-hydroxy-2H-pyran (III). The mixture was separated, and the structure of the compounds was determined on the basis of NMR, IR, and UV spectroscopy [3, 4].



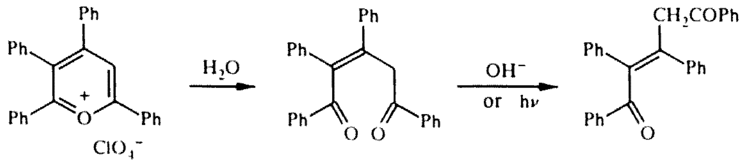
III

From 2,3,5,6-tetraphenylpyrylium tetrachloroferrate (IV) in an aqueous solution of sodium bicarbonate at a temperature no higher than room temperature, Basselier [6] obtained a ketoenol, which was converted into the crystalline unsaturated diketone (V) when heated:



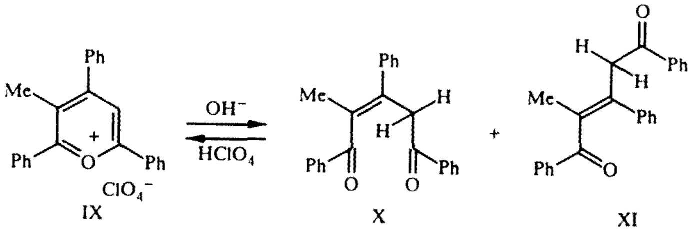
IV V

Hydrolysis of the unsymmetrically substituted 2,3,4,6-tetraphenylpyrylium perchlorate (VI) under mild conditions gave *cis*-1,2,3,5-tetraphenyl-2-pentene-1,5-dione (VII), which was converted into the *trans* isomer (VIII) by treatment with alkali or by the action of UV light [7]:

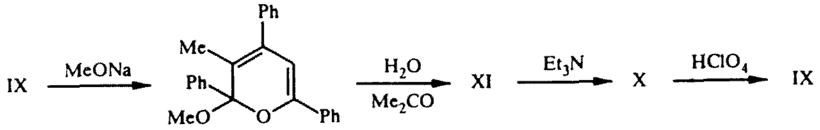


VI VII VIII

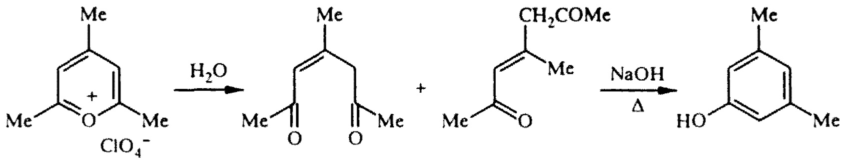
According to the authors of [7], the treatment of 3-methyl-2,4,6-triphenylpyrylium tetrachloroferrate with sodium bicarbonate at 0°C gave 2-methyl-1,3,5-triphenyl-2-pentene-1,5-dione, which exists in methanol solution in the form of the *cis* or *trans* isomer. Evidence for the structure of the isomers is presented in the papers by Fischer [8-10]. More recently it was established that the respective *cis* and *trans* isomers (X) and (XI), containing a methyl group at the double bond, are formed during the hydrolysis of the perchlorate (IX) [10]:



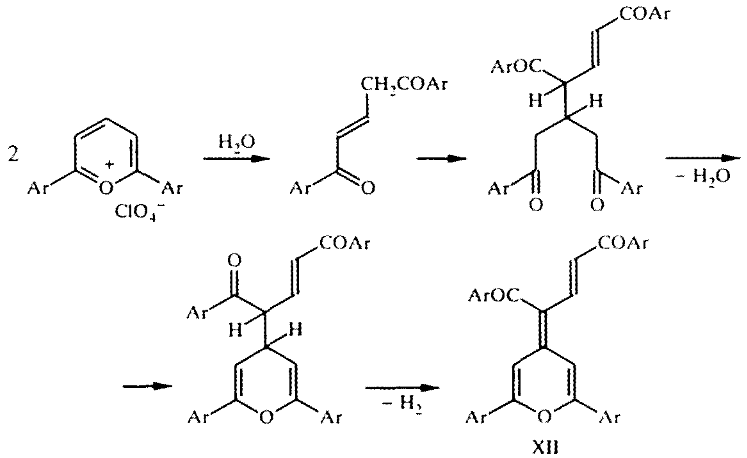
The pyrylium salt (IX) is converted by the action of sodium methoxide into 3-methyl-2-methoxy-2,4,6-triphenyl-2H-pyran, which gives the *trans* isomer (XI) in water—acetone solution; when heated with triethylamine in acetone, (XI) isomerizes to the *cis* isomer (X) [10]:



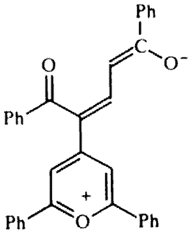
In spite of the instability of alkyl-substituted 2-pentene-1,5-diones, Williams [11] established by NMR and IR spectroscopy that the hydrolysis of 2,4,6-trimethylpyrylium perchlorate gave a difficultly separable mixture of the *cis* and *trans* isomers of 1,3,5-trimethyl-2-pentene-1,5-dione. The product undergoes extensive transformations during storage, and 3,5-dimethylphenol is formed when it is heated with alkali:



An unusual type of hydrolysis was discovered in the case of pyrylium salts unsubstituted at the γ position [5]. It was found that the treatment of 2,6-diarylpyrylium salts with a water—acetone solution of alkali gave the *trans* isomers of 2-pentene-1,5-diones [5], while the dimers (XII) of the respective 2-pentene-1,5-diones were formed with yields of 66-80% during the action of aqueous solutions of bases or when an equimolar mixture of the 2,6-diarylpyrylium perchlorates was boiled briefly with water and pyridine in acetonitrile [5, 12, 13]:

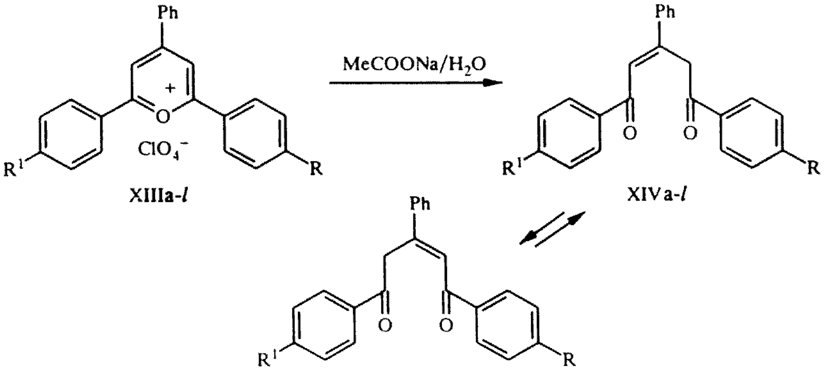


A similar dimer was isolated with a yield of 32% when 2,6-diphenylpyrylium salts were boiled in dimethylformamide [14]. The data from x-ray crystallographic analysis of the obtained dimers (XII) indicated a significant contribution from the betaine form [13], e.g., (XIIa) with Ar = Ph:



XIIa

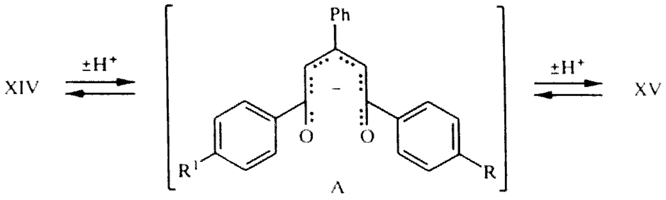
Fischer studied the structure and tautomerism of unsymmetrically substituted unsaturated 1,5-diketones, produced during the hydrolysis of pyrylium salts, in detail by means of the data from the NMR and IR spectra [8-10, 15]. Thus, hydrolysis of the pyrylium perchlorates (XIIIa-*l*) with an aqueous solution of sodium acetate gave a mixture of the respective isomers (XIV, XV) with the double bond in various positions [8, 9]:



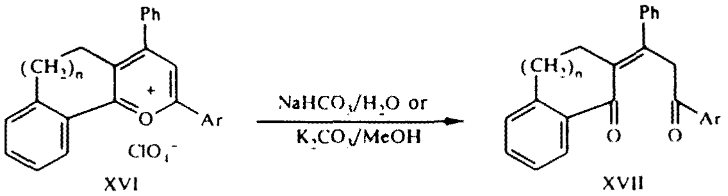
XVa-*l*

XIII—XV a R = Me, R^1 = OMe; b R = H, R^1 = OMe; c R = Cl, R^1 = OMe; d R = Br, R^1 = OMe; e R = NO_2, R^1 = OMe; f R = H, R^1 = Me; g R = I, R^1 = Me; h R = NO_2, R^1 = Me; i R = Cl, R^1 = H; j R = Br, R^1 = H; k R = I, R^1 = H; l R = NO_2, R^1 = H

As a result of kinetic investigations it was established that the substituents R and R^1 have little effect on the state of the equilibrium. In solution the contents of the above-mentioned isomers are equal, indicating that they are very close in energy. The ratio of the isomers and the rate of their mutual transformation are affected by the basicity of the medium. For example, the rate of the mutual transformation is increased if triethylamine or dicyclohexylmethylamine is added. This can be explained by the intermediate formation of the anion (A) having delocalized charge, stabilized by the aryl groups [9]:

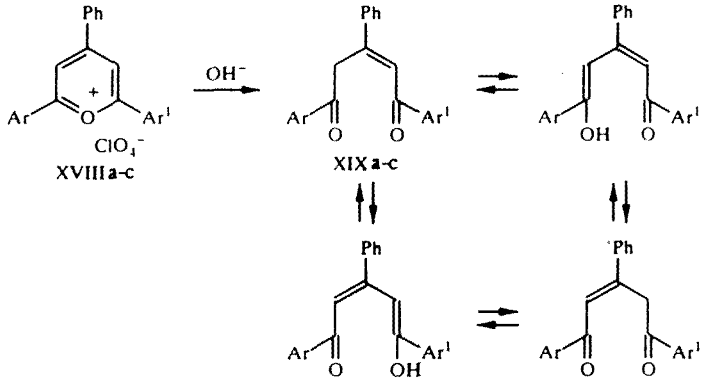


Such tautomerism with change in the position of the double bond is not observed in the case of 1-[4-tolyl]-2-methyl-3,5-diphenyl-2-pentene-1,5-dione [9]. Only unsaturated 1,5-diketones with the structure (XVII) are formed during the hydrolysis of condensed pyrylium salts of the (XVI) type under mild conditions [9, 15]:



Ar = Ph, C_6H_4-Me-4; n = 1, 2, 3

During the alkaline hydrolysis of symmetrically and unsymmetrically substituted pyrylium perchlorates (XVIIIa-c) the corresponding 1,3,5-triaryl-2-pentene-1,5-diones (XIXa-c) were obtained. The state of the keto—enol equilibrium in various solvents was studied by PMR spectroscopy for systems in which the existence of two keto and two enol forms is possible [16].

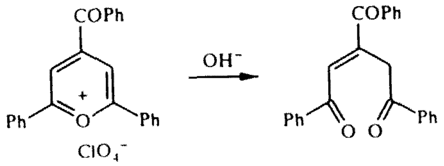


XVIII, XIX a Ar = Ar¹ = C_6H_4Me-4; b Ar = Ph, Ar¹ = C_6H_4Me-4;
c Ar = Ph, Ar¹ = C_6H_4OMe-4

The results of the investigations showed that not only the solvent but also the nature of the aryl substituents at positions 1 and 5 of 1,5-diketones have an effect. Thus, the state of the keto—enol equilibrium for the diketones (XIXa, b) differs greatly in tetrachloromethane and benzene. The content of the enolic form of compound (XIXa) amounts to 6% in tetrachloromethane and 25% in benzene; the corresponding values for (XIXb) are 25 and 4.6%. The diketone (XIXc) does not have such a large content of the enol in these solvents (10.5 and 4.6%).

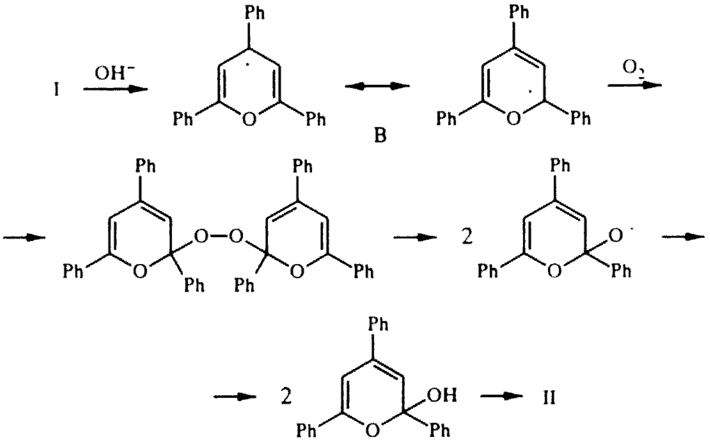
According to the data from the IR-spectroscopic investigations in [3, 17, 18], the (*s*)-*cis* conformation is preferred for 1,3,5-triaryl-2-pentene-1,5-diones.

It should be noted that the alkaline hydrolysis of 2,6-diphenyl-4-benzoylpyrylium perchlorate [19] gave the so-called "Kostanetskii compound" — an unsaturated triketone (XX) which has in due course attracted the attention of a series of chemists [20, 21].



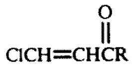
XX

In connection with the fact that the hydrolysis of pyrylium salts is one of the principal methods for the production of unsaturated 1,5-diketones, the results from the study of its mechanism are of considerable interest [22, 23]. The authors attribute a special role to the participation of atmospheric oxygen in the reaction. Thus, it was established that 2,4,6-triphenylpyrylium perchlorate (I) is converted quantitatively by the action of sodium hydroxide in acetone or dimethoxyethane in the absence of oxygen into the very stable free radical (B), which was identified by ESR. If the reaction mixture is in contact with atmospheric oxygen, 1,3,5-triphenyl-2-pentene-1,5-dione (II) is formed. The same diketone is formed during the oxidation of the free radical B by atmospheric oxygen. On the basis of the obtained data the authors [22, 23] proposed the following scheme of transformations I → II:



1.2. Ketovinylation of Carbonyl Compounds. The ketovinylation of carbonyl compounds by the action of β-chlorovinyl ketones is of interest for the synthesis of alkyl- and alkylaryl-substituted unsaturated 1,5-diketones.

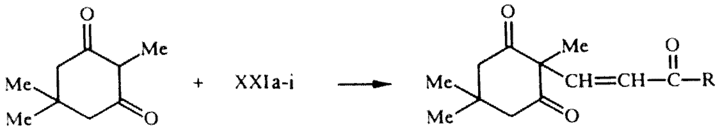
Kochetkov and coworkers [24-27] studied the ketovinylation of mono- and diketones with β-chlorovinyl ketones (XXIa-*l*); as a result they obtained a series of acyclic and semicyclic unsaturated di- and triketones. The success of ketovinylation depends to a considerable degree on the nature of the substituent R in the initial β-chlorovinyl ketone.


$$\mathrm{ClCH{=}CH\overset{\overset{\displaystyle O}{\|}}{C}R}$$

XXI a-*l*

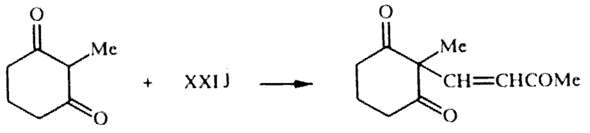
XXI a R = Ph, b R = C_6H_4Me-2, c R = C_6H_4Me-4, d R = C_6H_4Cl-2, e R = C_6H_4Cl-3, f R = C_6H_4Cl-4, g R = C_6H_4Br-2, h R = C_6H_4Br-4, i R = $C_6H_4NO_2$-4, j R = Me, k R = Et, *l* R = Pr

Thus, the aryl chlorovinyl ketones (XXIa-i) react with 1,3-cyclohexanediones more smoothly and with higher yields than their alkyl analogs (XXIj-*l*) [25, 28]. This can be explained by the lower stability of the products, i.e., the 3-alkyl-substituted unsaturated semicyclic triketones (XXIIa-i). The reaction of 2-methyldimedone with 1-chloro-3-aryl-1-propen-3-ones (XXIa-i) under the influence of sodium ethoxide in ethanol gives 90% yields of the respective 2-(2-aroylvinyl)-2-methyldimedones (XXIIa-i) [25, 28]:



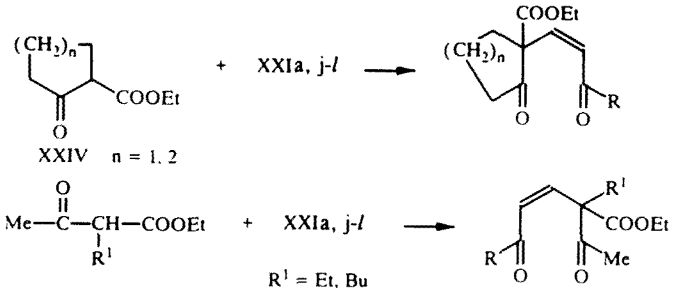
XXIIa-i

The best results were obtained with an equimolar ratio of sodium ethoxide and 2-methyldimedone. Under these conditions the latter is fully transformed into the corresponding sodium enolate, which reacts smoothly with β-chlorovinyl ketones with cooling in alcohol solution. With methyl β-chlorovinyl ketone under analogous conditions, 2-methyldihydroresorcinol reacts with difficulty, giving a low yield of the unsaturated triketone (XXIII) [26].

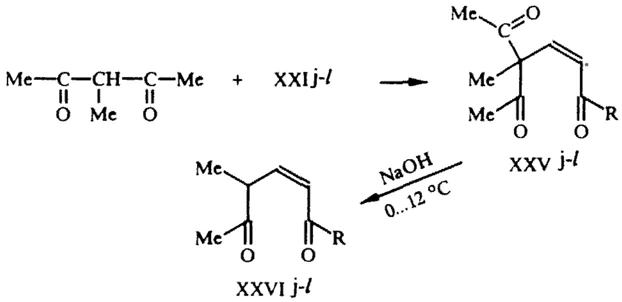


XXIII

The ketovinylation of α-ethoxycarbonylcyclanones (XXIV) and acetoacetic ester by alkyl (aryl) chlorovinyl ketones (XXIa, j-*l*) takes place successfully under the influence of metallic sodium, dispersed in dry benzene [24]:

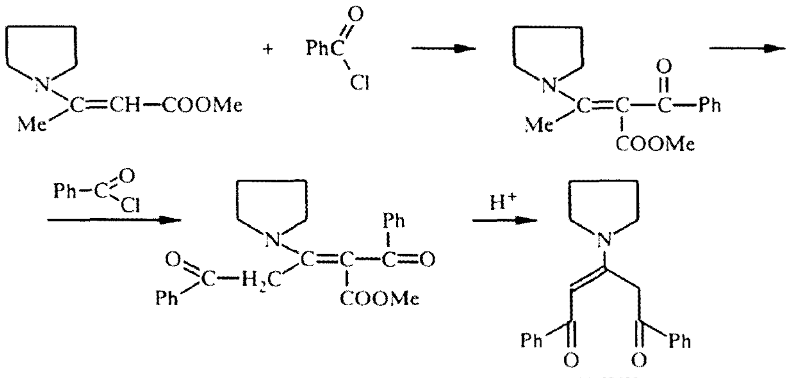


A significant benefit of ketovinylation is its use for the synthesis of alkyl-containing unsaturated 1,5-diketones [26]. Acetyl-substituted 2-pentene-1,5-diones (XXVj-*l*), which are stable when kept in the cold, were obtained when 3-methyl-1,3-pentanedione was used as substrate in reaction with the β-chlorovinyl ketones (XXIj-*l*) under the conditions described above [26].



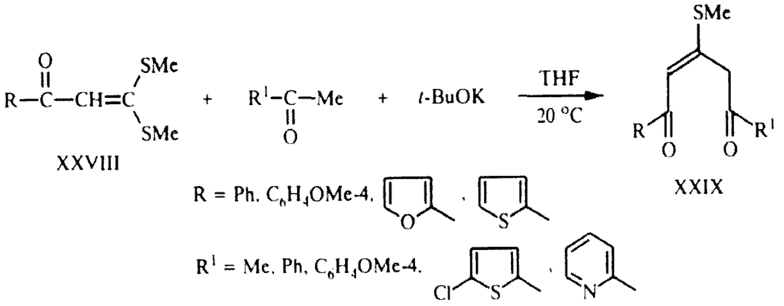
During the action of alkali (0 °C) the triketones (XXVj-*l*) eliminate the acetyl group and are converted into the difficultly obtainable alkyl-substituted 2-pentene-1,5-diones (XXVIj-*l*) with yields of 76-81%. During storage the latter gradually resinify, but this does not prevent their immediate use after preparation in nucleophilic and electrophilic reactions, including the synthesis of heterocyclic compounds.

1.3. Other Methods for the Production of Unsaturated 1,5-Diketones. The acylation of the enamine methyl β-pyrrolidinocrotonate by benzoyl chloride gave 1,5-diphenyl-3-pyrrolidino-2-pentene-1,5-dione (XXVII) [29]:



XXVII

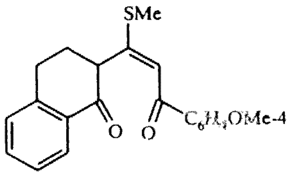
The use of the dithioacetals of α,β-unsaturated ketones (XXVIII) containing aryl and heteroaryl substituents in the Michael reaction is of undoubted interest [30, 31]. Their reaction with methyl aryl and heteroaryl ketones in the presence of two equivalents of potassium *tert*-butoxide gave a series of difficultly obtainable unsaturated 1,5-diketones (XXIX).



XXVIII

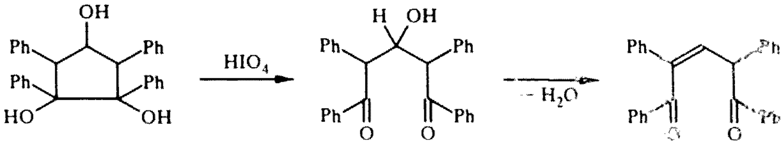
XXIX

The unsaturated semicyclic 1,5-diketone (XXX) was obtained from α-tetralone and 3,3-bis(methylthio)-1-(4-methoxyphenyl)-2-propen-1-ol under the described conditions [30]:



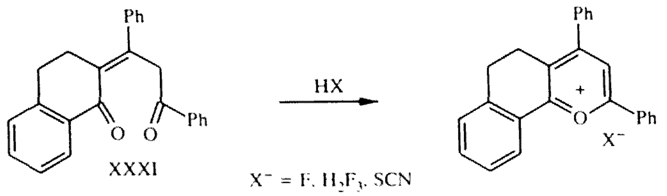
XXX

1,2,4,5-Tetraphenyl-2-pentene-1,5-dione was obtained during the oxidation of 1,2,4-trihydroxy-1,2,3,5-tetraphenylcyclopentane [33]:

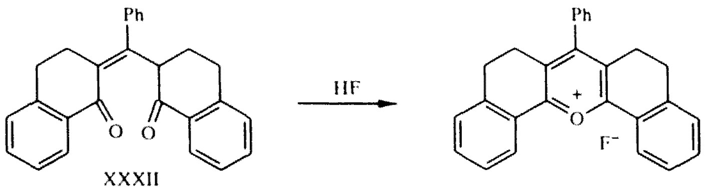


2. Unsaturated 1,5-Diketones in the Synthesis of Heterocyclic Compounds

Unsaturated 1,5-diketones undergo heterocyclization extremely readily with protic (organic and inorganic) and aprotic (HF, H_3PO_4, $FeCl_3$, BF_3, etc.) as catalysts. This was the reason for their use in the synthesis of difficultly obtainable pyrylium salts [6, 37-42]. From the diketone (XXXI), Katritzky [37-41] obtained 2,6-diphenyl-7,8-benzo-5,6-dihydrochromylium monofluoride, trifluoride, and thiocyanate, and from the diketone (XXXIIa) he obtained 5,6,8,9-tetrahydro-7-phenyldibenzo[*c*,*h*]xanthylium fluoride:

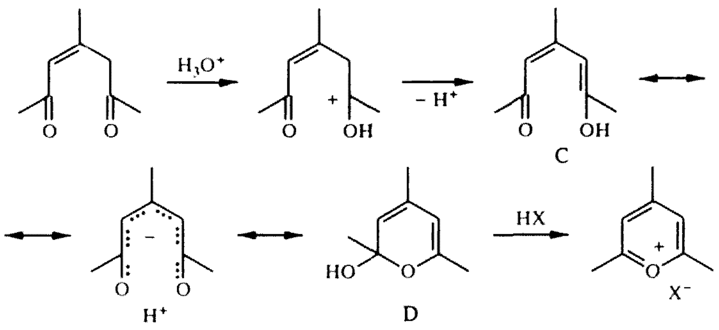


XXXI



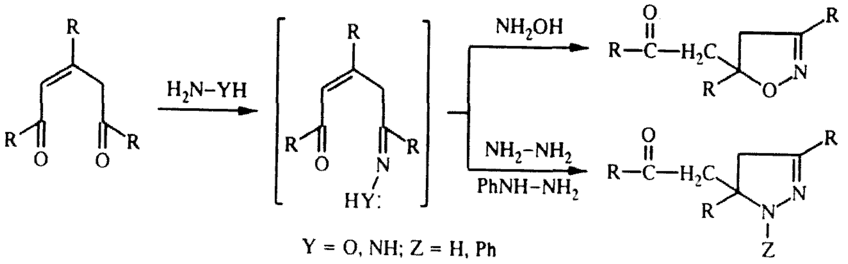
XXXII

Kinetic investigations [34-36, 40] made it possible to propose the following mechanism for the heterocyclization of unsaturated 1,5-diketones to pyrylium salts:



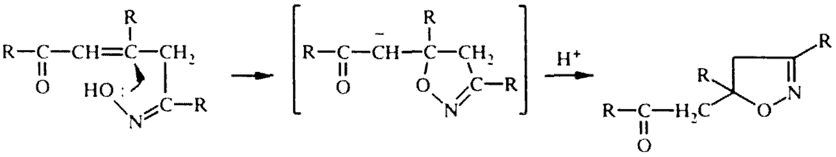
The determining stage in the transformation of 2-pentene-1,5-dione into the pyrylium salt is its enolization to the ketodienol C. The latter undergoes cyclization at a high rate to the unstable 2-hydroxy-2H-pyran D, which is dehydrated to the pyrylium cation.

In reaction with hydroxylamine, hydrazine, and phenylhydrazine substituted 2-pentene-1,5-diones form five-membered heterocyclic compounds (isoxazolines, pyrazolines, or N-phenylpyrazolines) [43, 44]:

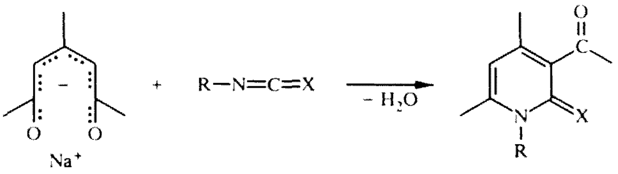


Y = O, NH; Z = H, Ph

Attack by the nucleophile clearly takes place initially at the more active carbonyl. The isoxazolines or pyrazolines are then formed as a result of intramolecular heterocyclization (according to the scheme presented below):

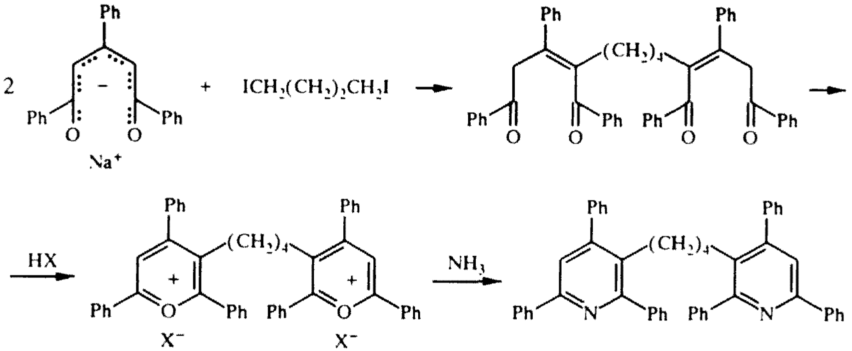


The action of sodium methoxide on unsaturated 1,5-diketones leads to the formation of sodium enolates, which are converted with isocyanates or their thio and seleno analogs into the corresponding R—N-pyridin-2-ones (or thiones or selenones):



X = O, S, Se

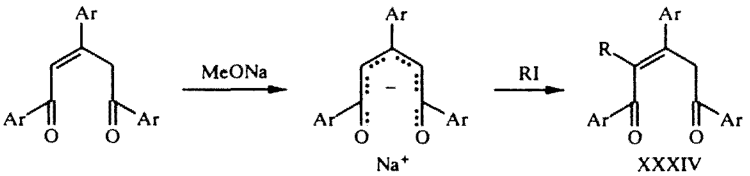
With 1,4-diiodobutane as alkylating agent it is possible to obtain the bispyrylium salts (XXXIII), in which the pyrylium groups are attached at positions 3, unlike the previously known salts with 2,2'-, 3,4'-, and 4,4'-bonds [46]:



XXXIII

ortho-Xylylene diiodide also reacts like 1,4-diiodobutane with sodium enolates [46].

It should be noted that the reaction of sodium enolates with alkyl-, alkenyl-, and aryl-substituted RI in DMSO or DMFA gives new representatives of unsaturated 1,5-diketones (XXXIV) [45]:



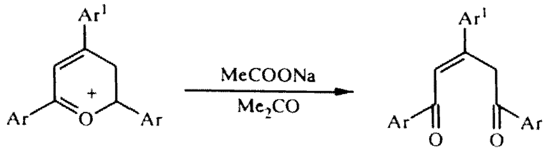
XXXIV

R = alkyl, $CH_2=CH-CH_2-$, $Me-CH=CH-CH_2-$, $PhCH_2-$, $4-BrC_6H_4CH_2-$

3. Halogen-Substituted Unsaturated 1,5-Diketones and Their Heterocyclization

3.1. Chlorination of 2-Pentene-1,5-diones. Until recently there have been no data on the chlorination of unsaturated 1,5-diketones.

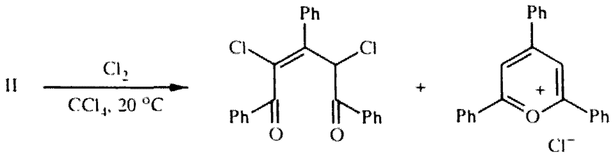
An investigation has now been carried into the chlorination of 1,3,5-triaryl-substituted 2-pentene-1,5-diones (II) (XXXVa-c) [47-49], produced as a result of the alkaline hydrolysis of the respective pyrylium salts:



II; XXXVa-c

XXXV a Ar = Ph, Ar^1 = C_6H_4OMe-4; b Ar = Ph, Ar^1 = C_6H_4Cl-4; c Ar = C_6H_4Cl-4, Ar^1 = Ph

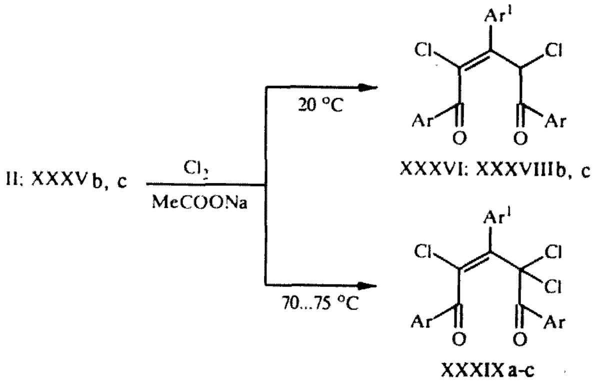
The first attempt at chlorination in the case of 1,3,5-triphenyl-2-pentene-1,5-dione (II) in tetrachloromethane under mild conditions at 20°C led to a low yield (37%) of its 2,4-dichlorine-substituted derivative (XXXVI) and to a 50% yield of 2,4,6-triphenylpyrylium chloride (XXXVII) [47, 48]:



XXXVI

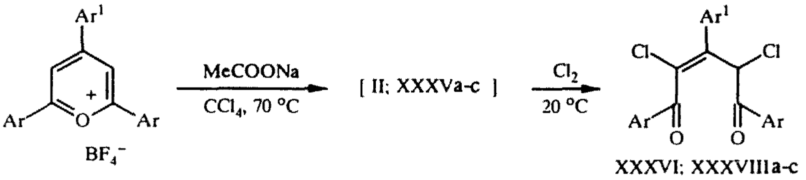
XXXVII

In order to suppress the formation of pyrylium salts of the (XXXVII) type during the chlorination of the pentenediones (II) (XXXVa-c), the action of such additives as sodium acetate, sodium carbonate, barium carbonate, etc., that combine with hydrogen chloride was investigated. The best results were obtained when sodium acetate was used [47, 48]. In this case the yields of the dichlorine-substituted pentenediones (XXXVI, XXXVIIIb, c) during the chlorination of the pentenediones (II) (XXXVb, c) at 20°C amounted to 80-88%, while at 70-75°C the trichlorine-substituted pentenediones (XXXIXa-c) were isolated [48]:



XXXIX a Ar = Ar^1 = Ph; XXXVIII, XXXIX b Ar = Ph, Ar^1 = C_6H_4Cl-4; c Ar = C_6H_4Cl-4, Ar^1 = Ph

In view of the fact that pyrylium salts are converted into the corresponding 2-pentene-1,5-diones with high yields by the action of aqueous sodium acetate in acetone, the chlorination of these salts was also studied in the presence of sodium acetate [49]. The treatment of pyrylium tetrafluoroborates with the latter, followed by chlorination of the reaction mixture cooled to 20°C, gave 2,4-dichloro-1,3,5-triaryl-2-pentene-1,5-diones (XXXVI, XXXVIIIa-c) with yields of 84-88% [47, 49]:

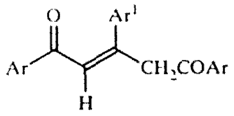


XXXVIII a Ar = Ph, Ar^1 = C_6H_4OMe-4

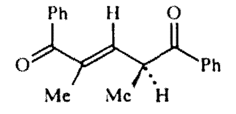
The structure of the dichloropentenediones (XXXVI, XXXVIIIb, c) was confirmed quite convincingly by the use of physical methods of investigation. By IR and ^1H and ^{13}C NMR spectroscopy and calculation of the structure of the molecule of (XXXVI) by molecular mechanics, it was possible to establish that the dichlorine-substituted compounds mentioned above exist predominantly in the *trans-s-trans* form with an eclipsed conformation of the $C_{(4)}$—Cl and $C_{(5)}$=O bonds. In the IR spectra of the dichloropentenediones (XXXVI, XXXVIIIb, c) there are two bands in the regions of 1660-1680 and 1708-1720 cm^{-1}, corresponding to the vibrations of the conjugated and unconjugated C=O group. The presented dichloropentenedione structure is confirmed by the presence of a band for the stretching vibrations of the C=C bond in the region of 1616-1630 cm^{-1}, by the intensity ratio of the C=C and C=O bands (in the range of 3.0-3.9), and also by the difference in the values of these bands (40-47 cm^{-1}) [50].

The initial diones (II) (XXXVb, c), for which the intensity of the C=C and C=O vibrations and the difference in the values of these bands are 0.6-0.8 and 76-78 cm^{-1} respectively, exist preferentially in the form of the *s-cis* conformers.

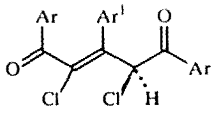
In the ^1H NMR spectra of the dichloropentenediones (XXXVI, XXXVIIIb, c) there is a multiplet for the aromatic protons in the region of δ 7.30-8.12 and a one-proton singlet for the 4-H of the α-chloromethylene fragment. The latter is shifted downfield compared with the singlet of 4-H in the pentenediones (II) (XXXVb, c) as a result of the effect of the chlorine atom and appears at δ 6.46-6.77 ppm, which corresponds to the data for 3-methyl-1,5-diphenyl-2,4-dichloro-1,5-pentenedione [51].



cis-s-cis-1,3,5-Triaryl-2-pentene-1,5-diones (II) (XXXVb, c)



trans-s-trans-2,4-Dimethyl-1,5-diphenyl-2-pentene-1,5-dione (XL)

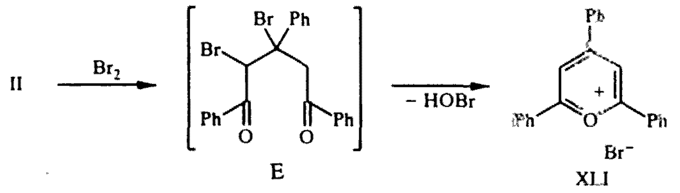


trans-s-trans-1,3,5-Triaryl-2,4-dichloro-2-pentene-1,5-diones (XXXVI, XXXVIIIb, c)

During investigation of the stereochemistry of dichloropentenediones, compound (XL) was used as a model having a proton at the double bond in light of the fact that the methyl groups and the chlorine atoms have similar effective van der Waals radii and occupy identical stereochemical positions in the molecule. The experimental results were confirmed by theoretical MNDO calculations [50].

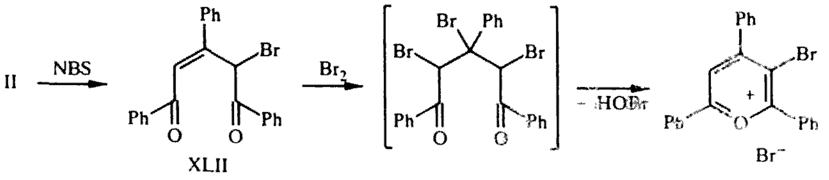
The structural difference between the initial pentenediones (II) (XXXVb, c) and the dichloropentenediones (XXXVI, XXXVIIIb, c) obtained from them can be explained by the type of chlorination. The most likely is *cis*-addition of the chlorine at the double bond and *trans*-elimination of hydrogen chloride with the formation of a $C_{(3)}{=}C_{(4)}$ π bond; a similar type of process at the second stage leads to the *trans-s-trans* isomers of the dichloropentenediones.

3.2. Bromination of 2-Pentene-1,5-diones. During an attempt at the synthesis of bromine-substituted 1,3,5-triphenylpyrylium bromide [it was assumed that the addition of bromine at the double bond of 1,3,5-triphenyl-2-pentene-1,5-dione (II) would lead to spontaneous heterocyclization of the dibromide] the pyrylium bromide (XLI) was unexpectedly obtained [52]:



The cyclization of the intermediately formed dibromo diketone E clearly takes place as a result not of dehydration but of the elimination of HOBr.

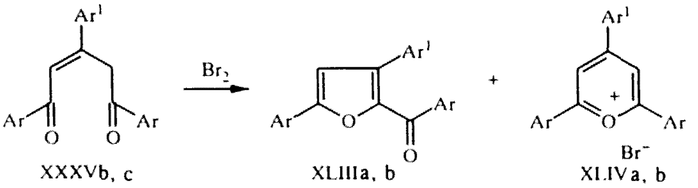
It was not possible to obtain 3-bromo-2,4,6-triphenylpyrylium bromide by the successive treatment of compound (II) first with bromosuccinimide and then with bromine [52]:



By the action of bromine on the dione (II) in tetrachloromethane under mild conditions at 20°C in the presence of sodium acetate it was possible to obtain a mixture of 4-bromo-2-pentene-1,5-dione (XLII) and 2,4,6-triphenylpyrylium bromide (XLI) with yields of 43 and 50% respectively [47].

$$\text{II} \xrightarrow[\substack{\text{CCl}_4,\ 20\ ^\circ\text{C},\\ \text{MeCOONa}}]{\text{Br}_2} \text{XLII} + \text{XLI}$$

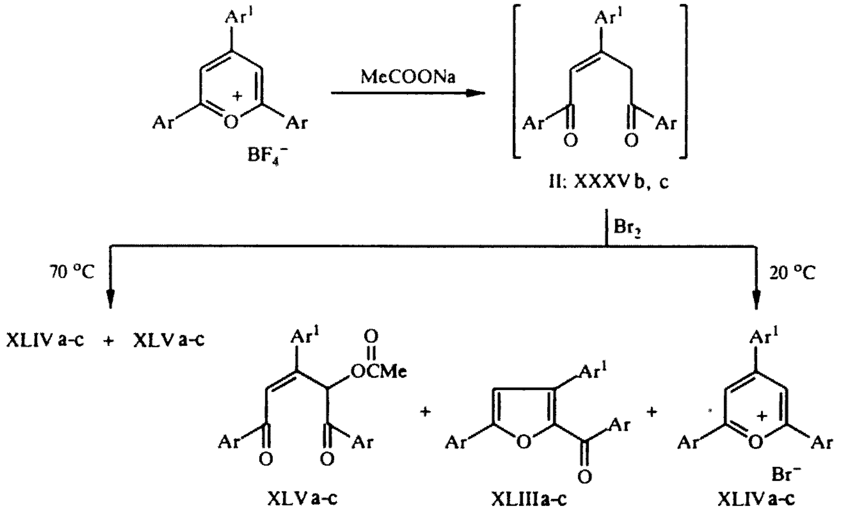
It should be noted that only the triphenyl-substituted pentenedione (II) forms the monobromo derivative (XLII) under the described conditions, whereas the diketones (XXXVb, c) containing various substituents are converted into the corresponding aroylfurans (XLIIIa, b) and pyrylium bromides (XLIVa, b) with yields of 23-25% and 41-46% respectively.



XLIII, XLIV a Ar = Ph, Ar^1 = C_6H_4Cl-4; b Ar = C_6H_4Cl-4, Ar^1 = Ph

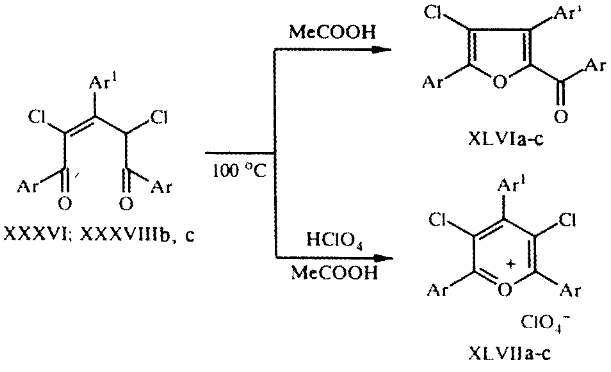
During the successive action of sodium acetate and then of bromine on the pyrylium salt (i.e., bromination of the pentenediones *in situ*) it was found that temperature had a significant effect on the nature of the obtained products; at 20°C a mixture of the corresponding pyrylium bromide (XLIV) (12-15%), the aroylfuran (XLIII) (30-35%), and acetoxypentenedione (XLV) (28-30%) was obtained, whereas at 70°C the main reaction product was acetoxypentenedione (49-71%), and salt formation was almost completely suppressed [47]. [The yields of the salts (XLIV) amounted to only 2-5%].

The difference in the nature of the transformations of the pentenediones (II) (XXXVb, c) (selective during chlorination and uncertain during bromination) is explained by the high mobility of the bromine atom in the molecule, due not only to the lower energy of the C—Br bond but also to the position of the bromine atom.



XLIII—XLV a Ar = Ph, Ar^1 = C_6H_4Cl-4; b Ar = C_6H_4Cl-4, Ar^1 = Ph; c Ar = Ar^1 = Ph

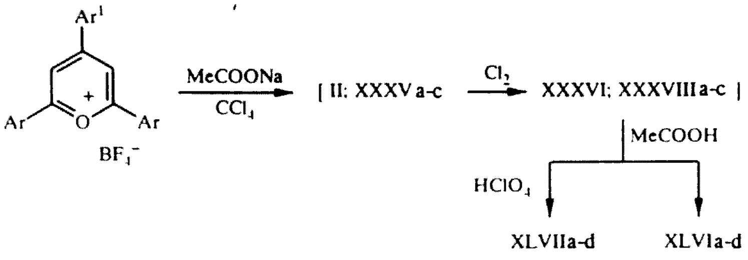
3.3. Heterocyclization of 2,4-Dichloro-2-pentene-1,5-diones. It is well known that a characteristic feature of pentenediones is the exceptionally easy heterocyclization by the action of acids under normal conditions with the formation of pyrylium salts [37-41]. However, the 2,4-dichloro-substituted pentenediones (XXXVI, XXXVIIIb, c), which exist predominantly in the form of the *trans-s-trans* isomers [50] with the eclipsed conformation of the $C_{(4)}$—Cl and $C_{(5)}$=O bonds, are significantly less susceptible to this transformation. Thus, their heterocyclization requires heating to 100°C, and the nature of the transformations depends on the acidity of the medium; with heating in acetic acid, the 4-chloroaroylfurans (XLVIa-c) are formed with yields of ~90%, and with perchloric acid 3,5-dichloro-2,4,6-triarylpyrylium perchlorates (XLVIIa-c) are formed with yields of 42-51% [53, 54].



XLVI, XLVII a Ar = Ar^1 = Ph; b Ar = Ph, Ar^1 = C_6H_4Cl-4; c Ar = C_6H_4Cl-4, Ar^1 = Ph

With acetic anhydride in a mixture of acetic and perchloric acids, the yields of the 3,5-dichloro-2,4,6-triarylpyrylium perchlorates are increased to ~75% [53].

The transformation of pyrylium salts into their 3,5-dichloro-substituted analogs is of considerable interest. The successive action of sodium acetate (65-70°C) on 2,4,6-triarylpyrylium fluoroborates, saturation of the reaction mixture with chlorine (20°C), and the addition of perchloric acid gave the 3,5-dichloro-2,4,6-triarylpyrylium perchlorates (XLVIIa-d) [53, 54]:

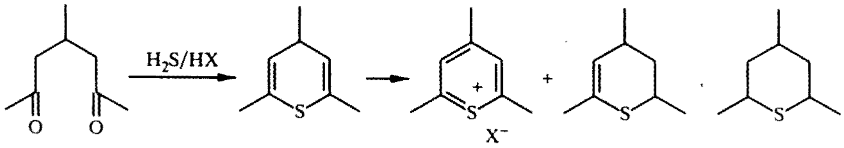


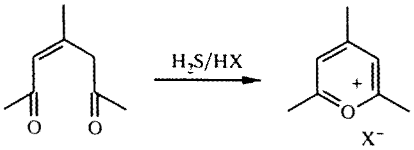
XLVI, XLVII d Ar = Ph, Ar^1 = C_6H_4OMe-4

The tetrafluoroborates of dichloro-substituted pyrylium salts were obtained similarly.

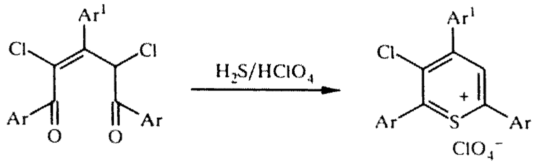
By monitoring the reaction by chromatography it is possible to detect the opening of the pyrylium ring clearly by the action of sodium acetate with the formation of the pentenediones (II) (XXXVa-c), their chlorination to the 2,4-dichloropentenediones (XXXVI, XXXVIIIa-c), and their subsequent heterocyclization by perchloric acid to the 3,5-dichloro-substituted pyrylium salts (XLVIIa-d). Change of the conditions at the last stage of the direct transition (boiling in acetic acid) leads to the 4-chloroaroylfurans (XLVIa-d).

The strong tendency of unsaturated 1,5-diketones and their derivatives to undergo heterocyclization shows up clearly during comparison of their behavior with the behavior of the saturated analogs in reactions with nucleophilic reagents. Thus, with hydrogen sulfide in the presence of acids, pentane-1,5-diones form pyrans or their disproportionation products, i.e., thiopyrylium salts and di- or tetrahydrothiopyrans [55, 56], whereas unsaturated 1,5-diketones do not enter into reaction with hydrogen sulfide under analogous conditions on account of the high rate of their heterocyclization with the formation of pyrylium salts [47, 53]:





For 2,4-dichloro-substituted pentane-1,5-diones it has not yet been possible to find conditions for cyclization to thiopyrans and thiopyrylium salts, whereas dichloropentenediones (XXXVI, XXXVIIIa-c) are converted into 3-chloro-2,4,6-triarylthiopyrylium perchlorates (XLVIIIa-d) with hydrogen sulfide and perchloric acid [47, 53]:



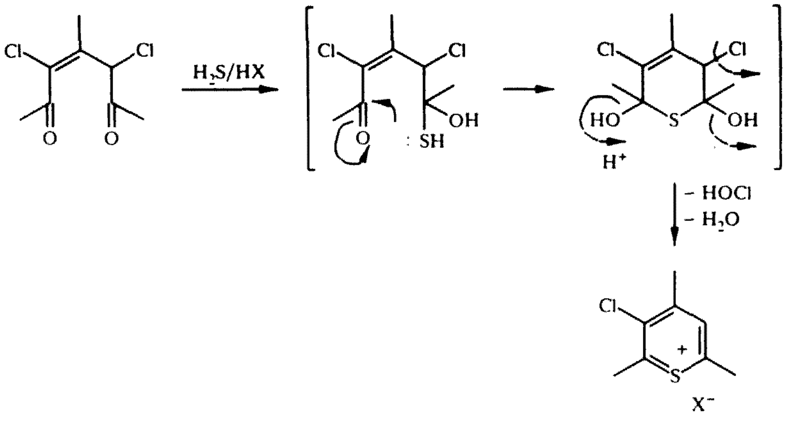
XXXVI; XXVIII a-c

XLVIII a-d

XLVIII a Ar = Ar^1 = Ph; b Ar = Ph, Ar^1 = C_6H_4OMe-4; c Ar = Ph, Ar^1 = C_6H_4Cl-4;
d Ar = C_6H_4Cl-4, Ar^1 = Ph

It should be mentioned that the degree of transformation is affected by the temperature. Whereas the yield of the thiopyrylium salt (XLVIII) in acetic acid and acetic anhydride at 20°C does not exceed 18%, the yield at 40°C amounts to 71-83% [47, 53].

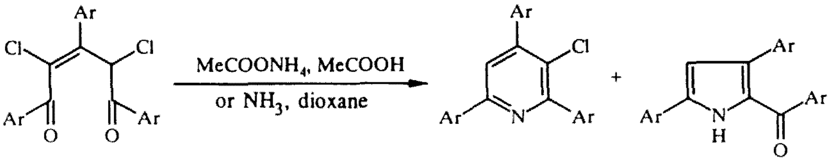
The transformation of the dichloropentenediones (XXXVI, XXXVIIIa-c) to 3-chloro-substituted thiopyrylium salts (XLVIII) can be represented by one of the following possible schemes:



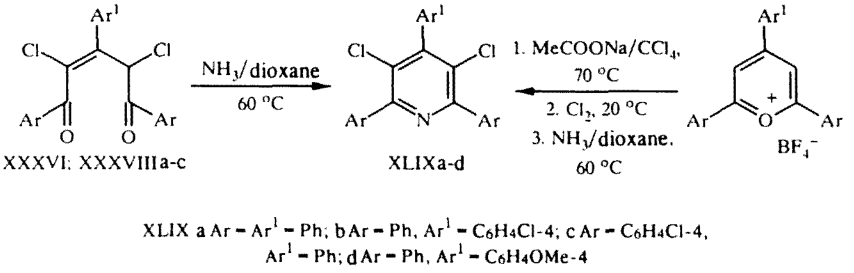
Thus, in spite of the fact that the presence of chlorine atoms in the molecules of unsaturated 1,5-diketones reduces their susceptibility to heterocyclization compared with pentenediones not containing chlorine, conditions were found for the synthesis of both 3,5-dichloro-2,4,6-triarylpyrylium and 3-chloro-2,4,6-triarylthiopyrylium salts. Saturated 2,4-dichloro-1,3,5-triarylpentane-1,5-diones do not undergo heterocyclization under such conditions [56].

As in the case of the nucleophilic reactions with hydrogen sulfide, in the reaction with nitrogen-containing reagents there is a significant difference in the nature of the transformations of the 1,5-diketones containing and not containing chlorine atoms in the saturated and unsaturated chains.

With ammonium acetate in acetic acid at 60-80°C 2,4-dichloropentanediones are converted into 3-chloropyridines (72-92%) and a small amount of aroylpyrroles (~9%), whereas with ammonia in dioxane at 60°C aroylpyrroles are mainly formed (47-80%), and the 3-chloropyridines are minor products (9-16%) [57-59]:

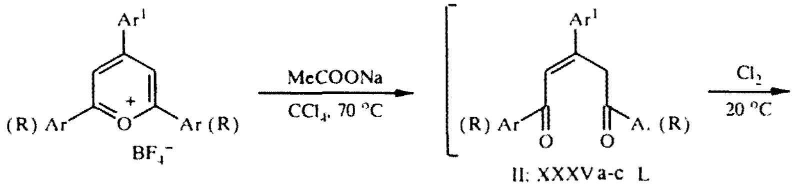


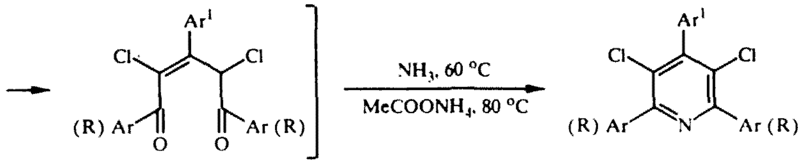
At 60°C under analogous conditions dichloropentenediones (XXXVI, XXXVIIIa-c) retain both chlorine atoms during heterocyclization [52, 53, 58], being converted into 3,5-dichloropyridines (XLIXa-d), while the yields of the latter with ammonium acetate amount to 76-94%, and the yields during the action of ammonia in dioxane amount to 52-61% [53]:



XLIX a Ar = Ar^1 = Ph; b Ar = Ph, Ar^1 = C$_6$H$_4$Cl-4; c Ar = C$_6$H$_4$Cl-4, Ar^1 = Ph; d Ar = Ph, Ar^1 = C$_6$H$_4$OMe-4

Particularly valuable in preparative respects is the direct transition from pyrylium salts to dichloropyridines, which is distinguished by its simplicity, selectivity, and fairly high yields of 56-62% [47, 53]:





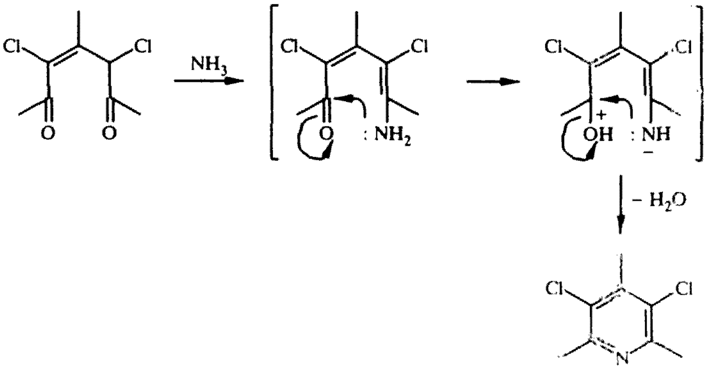
XXXVI; XXXVIIIa-c; LI

XLIX a-e

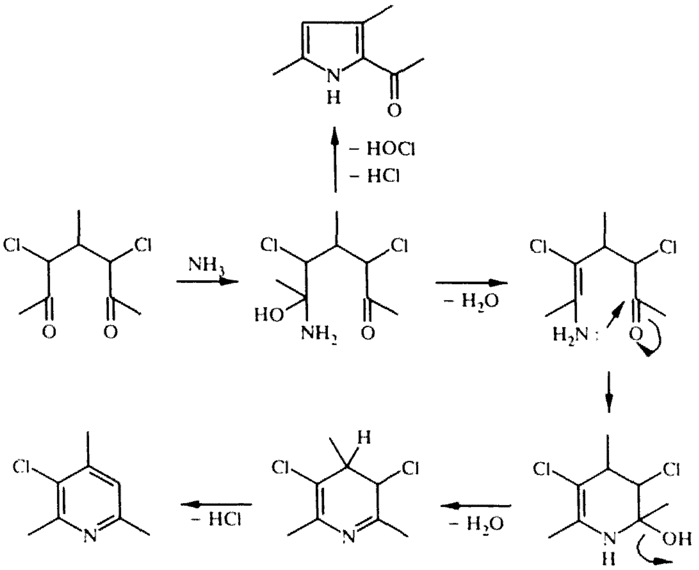
XLIXe, L, LI R = CMe_3, Ar^1 = Ph

It must be pointed out that the developed method with the successive action of sodium acetate, chlorine, and then ammonia or ammonium acetate makes it possible to realize the synthesis not only of aryl-substituted 3,5-dichloropyridines (XLIXa-d) but also of 2,6-di(*tert*-butyl)-4-phenyl-3,5-dichloropyridine (XLIXe), which could not be obtained from the respective difficultly obtainable 2-pentene-1,5-dione [47].

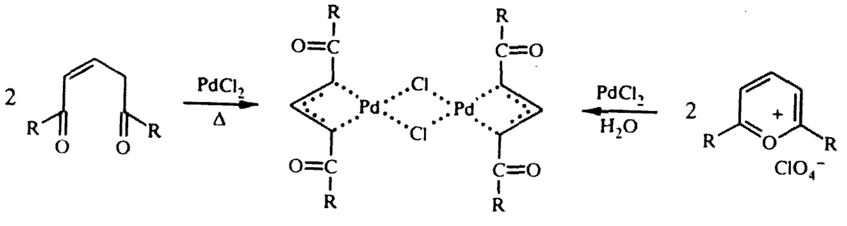
Under the described conditions there is no reaction between ammonia or ammonium acetate and the chlorine atoms of 2,4-dichloropentenediones. Initially, the more active carbonyl is attacked with the formation of an enamine. As a result, both chlorine atoms are at the double bonds of the conjugated system and are consequently unreactive. Heterocyclization therefore leads to 3,5-dichloropyridines [47]:



The presented probable mechanism agrees with the mechanism of the reaction of 2,4-dichloropentane-1,5-diones with ammonia, and this explains the formation of the 3-chloropyridines and aroylpyrroles [57, 58]:



3.4. 2-Pentene-1,5-diones as Ligands in the Synthesis of Complexes. 2-Pentene-1,5-diones unsubstituted at position 3 are of interest as ligands for the production of complexes with palladium chloride. This property was established during the study of the behavior of pyrylium perchlorates unsubstituted at position 4 toward palladium chloride when heated in an organic solvent with the addition of water. It was found that the pyrylium ring was opened under these conditions with the formation of the corresponding pentenediones, which behaved like compounds containing an allyl fragment and reacted readily with palladium chloride, forming binuclear π-allyl complexes [61, 62]:



R = Ph, CMe_3

As seen from the foregoing, 2-pentene-1,5-diones containing both a highly electrophilic double bond in the molecule and active carbonyl groups are extremely valuable synthons for the production of various heterocyclic compounds. The presence of the double bond gives rise to the exceptionally high susceptibility of 2-pentene-1,5-diones to heterocyclization with the formation of pyrylium salts, aroylfurans, isoxazolines, pyrazolines, etc. The introduction of halogen atoms into the structure of unsaturated 1,5-diketones retards the cyclization process, and this makes it possible to realize nucleophilic reactions by the reaction of hydrogen sulfide and acidic or nitrogen reagents with the formation of 3-chloro-substituted thiopyrylium salts, 3,5-dichloro-substituted pyrylium salts, 2-aroyl-4-chlorofurans, and 3,5-dichloropyridines. The presented data on the production and properties of 2-pentene-1,5-diones may provide the basis for the projected and controlled synthesis of new series of heterocyclic compounds.

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