# SYNTHESIS AND TRANSFORMATIONS OF 4(5H)-OXAZOLONES AND THEIR SALTS (REVIEW)

**Yu. I. Ryabukhin, L. N. Faleeva, T. P. Kosulina, and V. G. Kul'nevich**

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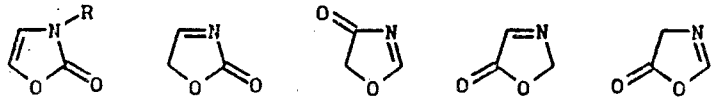
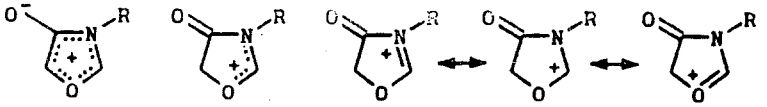
*The literature data on the synthesis and transformations of 4(5H)-oxazolones and their salts are correlated. An evaluation of the possibilities of the preparative utilization of the examined reactions is given.*

The chemistry of oxazolones, the group of which includes 2(3H)-oxazolone **1**, 2(5H)-oxazolone **2**, 4(5H)-oxazolone **3**, 5(2H)-oxazolone **4**, and 5(4H)-oxazolone (azlactone) **5**, has undergone appreciable development since the publication of earlier studies [1, 2].



1 2 3 4 5

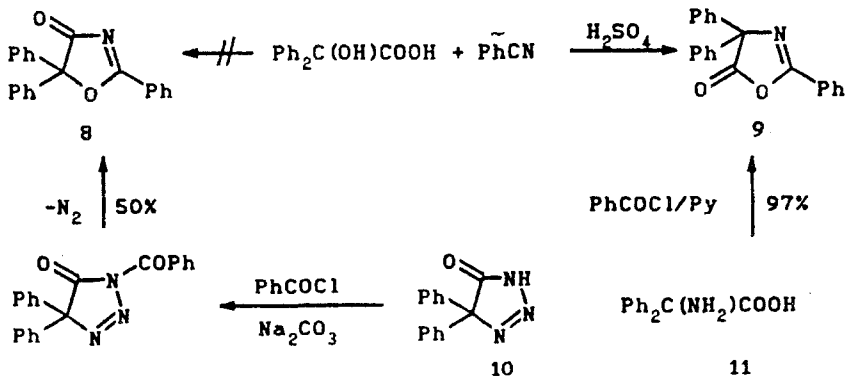
Subsequent reviews [3-5] do not contain complete information regarding the chemistry of 4(5H)-oxazolones **3** and 1,3-oxazolium 4-olates **6**. The aim of the present review was to bridge this gap and to correlate the accumulated material regarding the synthesis and transformations of 4(5H)-oxazolonium salts **7** and the mesomerically stabilized immonium, carbonium, and oxonium forms **A-C**:



6 7 A B C

4(5H)-Oxazolones **3**, the first representative of which was obtained in 1949 [6], have remained virtually uninvestigated for a long time because they are hard to obtain. The general preparative methods for the synthesis of their simplest derivatives — stable 4(5H)-oxazolonium perchlorates **7** — that were developed in the last decade have also made it possible to obtain oxazolones, derivatives of which have tranquilizing, antihypoxic [11], and cardiotropic activity and also display growth-regulating, insecticidal, tuberculostatic, and fungistatic activity [12]. Antidepressants, tranquilizers, analgesics, and memory and appetite stimulators [5, 13-16] have been found among 2-aminooxazolones. Oxazolone enters as a structural fragment into the composition of the antibiotic indolmycin, which is obtained via a biochemical pathway from tryptophan [17-19].

$\beta$-Hydroxy acid N-acylamides that are active coordinating agents have been obtained from oxazolonium salts [20]: $\alpha$-hydroxyalkyl-1H-1,2,4-triazoles [21, 22] and 1,3,5-triazines [22] are potential ligands for the synthesis of metal complexes [23] and as additives that improve the antifriction properties of lubricants [22].

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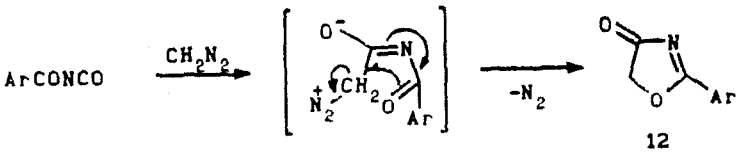
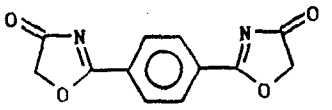
In 1899 [24] 4(5H)-oxazolone structure **8** was erroneously assigned to the product of the reaction of benzilic acid and benzonitrile. In 1957 in was assumed [25] and later experimentally confirmed [26, 27] that the properties of this product correspond to the structure of the isomeric 5(4H)-oxazolone **9**. And, in fact, in 1958, oxazolones **8** and **9** were obtained in the benzoylation of triazolone **10** [28] and diphenylglycine **11** [29] (see scheme above).

**Synthesis of 4(5)-Oxazolones and 1,3-Oxazolium 4-Olates**

Aroyl isocyanates [6, 30] react with diazomethane to give oxazolones **12**. Bis(oxazolone) **13** was similarly obtained from terephthalyl isocyanate in THF [31].



**12**

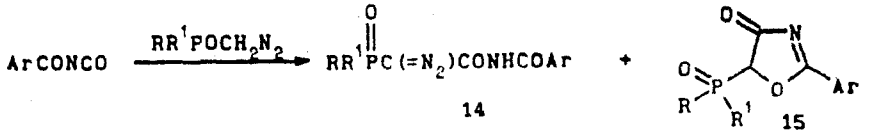


**13**

Ar = Ph, 2-$EtOC_6H_4$, 4-$ClC_6H_4$

Oxazolones **12** were also obtained by the action of diazomethane on N-aroylcarbamic acid azides ($N_3CONHCOAr$) [5, 32].

Phenyldiazomethane and diphenyldiazomethane have also been subjected to reaction with benzoyl isocyanate [30]. However, an oxazolone was obtained in low yield only in the case of phenyldiazomethane. Aroyl diisocyanates react with diazo phosphorus compounds to give diazo imides **14** and oxazolones **15** [33].



**14** **15**

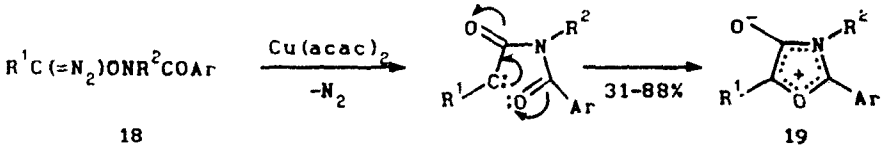
R, $R^1$ = OMe, OEt, Ph

The tautomeric (with respect to oxazolones) 4-hydroxyoxazoles **17** are obtained in low yields in a similar reaction with diazoacetic ester [30, 33-35] and diazoacetophenone [36]. Diazo compounds **17**, which are obtained as the principal products, undergo smooth cyclization to oxazoles **17** on heating.

**16** **17**

R = OEt, Ph; Ar = Ph, 4-$ClC_6H_4$, 4-$O_2NC_6H_4$

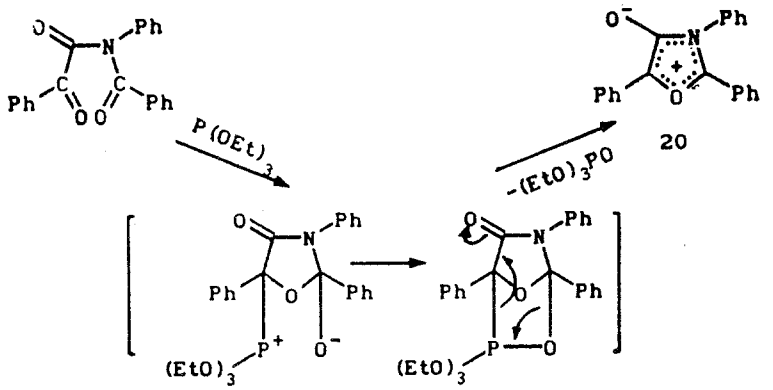
N-Substituted diazo compounds **18**, which are not capable of forming oxazolones, give mesoionic 1,3-oxazolium 4-olates **19** in the case of catalytic thermolysis in a nitrogen atmosphere [37-40].



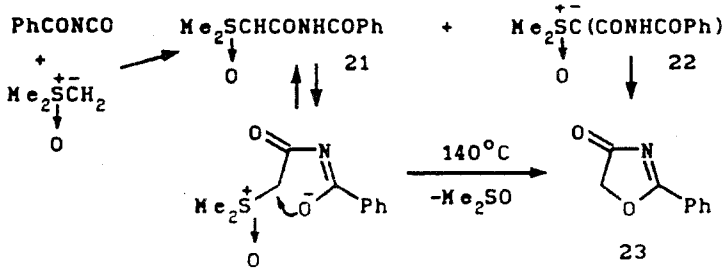
**18** **19**

$R^1$ = H, 4-$O_2NC_6H_4$; $R^2$ = Me, Ph; Ar = Ph, 4-$MeOC_6H_4$, 4-$BrC_6H_4$

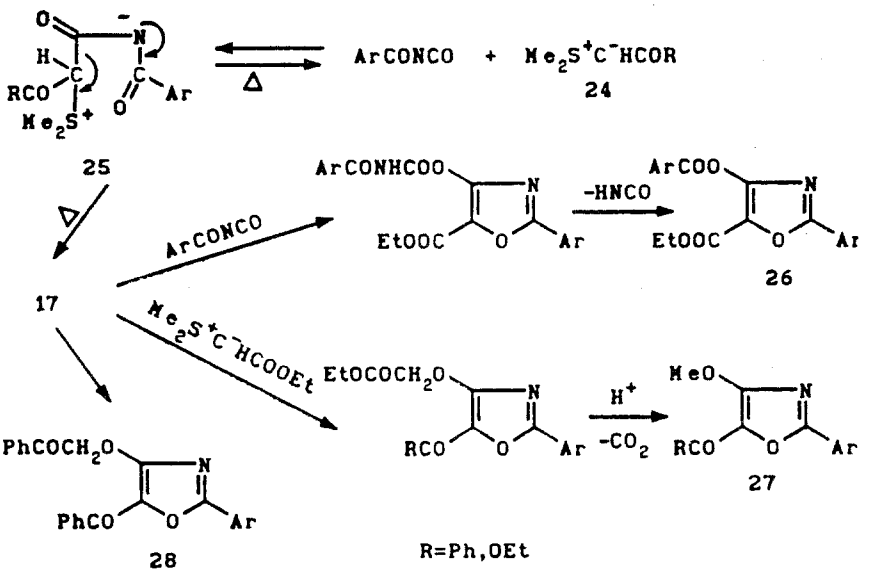
Oxazolium olates **20**, were obtained by treatment of phenylglyoxylic acid N-benzoylanilides with triethyl phosphite [4].



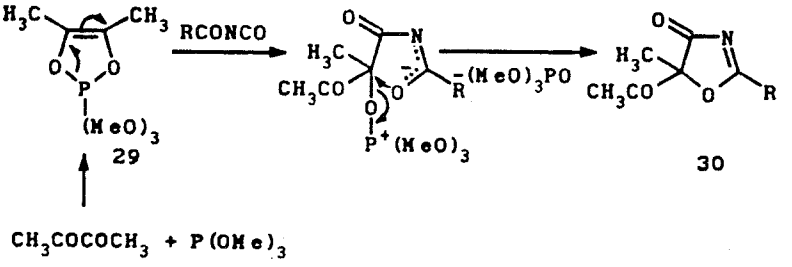
Benzoyl isocyanate reacts with methylenedimethyloxysulfurane to give mono- and dibenzoylcarbamoylmethylids **21** and **22**, which are converted smoothly to oxazolone **23** by hydrolysis [36].



Benzoyl- and carbethoxy-substituted sulfur ylids **24** react with aroyl isocyanates to give adducts **25** in good yields; the adducts are converted to 4-hydroxyisoxazoles **17** (50-60% yields) on heating (for 2 h) in decalin. The reaction is often complicated by the formation of dibenzoylurea and oxazoles **26-28** because of partial thermal cleavage of adducts **25** and reaction of the regenerated starting reactants with oxazoles **17** [36, 41].

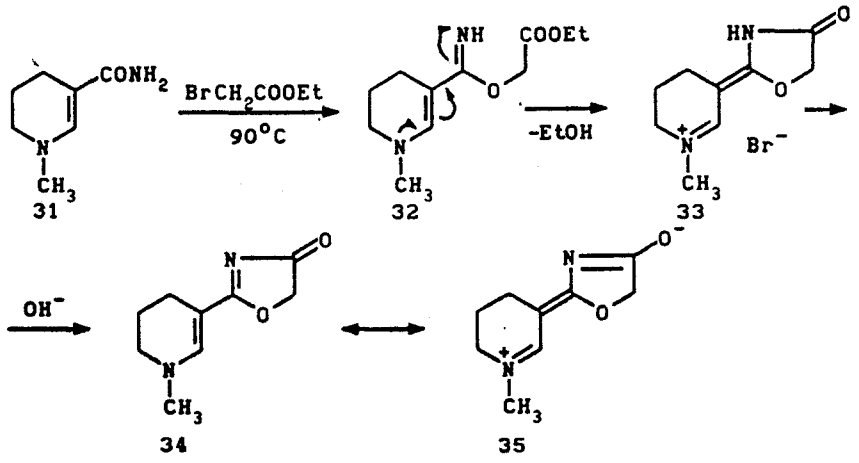


5-Acyloxazolones **30** can be obtained by the reaction of dioxaphosphalenes **29** with cyanates [42-45].

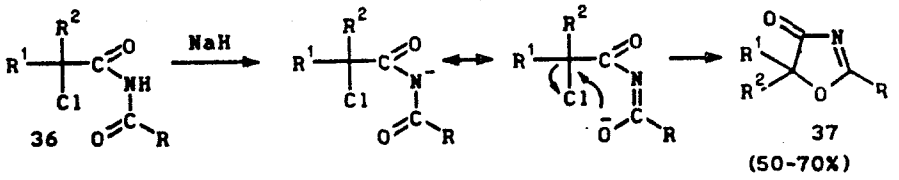


$R = C_6H_5$, 4-$FC_6H_4$, 4-$CH_3OC_6H_4$, $OCH_3$, $OC_2H_5$, $OC_6H_5$, $N(C_6H_5)_2$

Oxazolone **34**, which is mesomerically stabilized by betaine **35**, was obtained by the reaction of tetrahydronicotinamide **31** with ethyl bromoacetate with subsequent cyclization of the resulting imino ester **32** and deprotonation of salt **33** [46, 47].

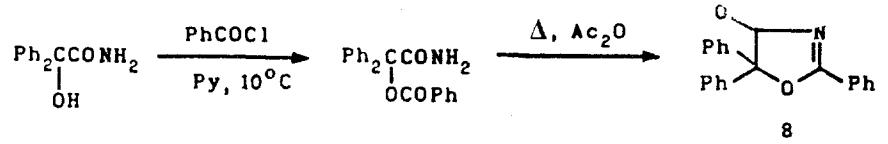


$\alpha$-Chloro imides **36**, which were obtained by acylation of arylamides or urethane with $\alpha$-chloro-substituted acid chlorides [48, 49], undergo cyclization to oxazolones **37** under the influence of NaH in benzene [2] or glyme [50-52].

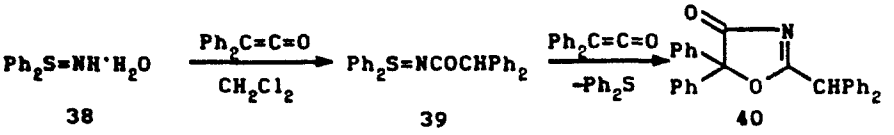


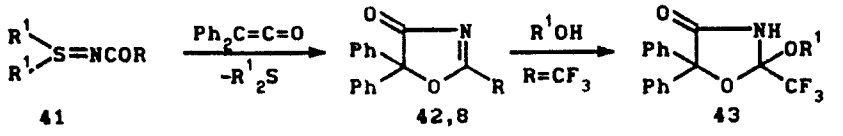
R=Ar, OEt; $R^1$ и $R^2$=H, Ph

Oxazolone **8** can be obtained from benzilic acid amide. However, this method is not preparative because of the difficulty involved in separating the $\alpha$-benzoyloxy amide from the competitively formed $\alpha$-benzoyloxy nitrile [48].



Oxazolone **40** was obtained in the reaction of sulfo imine **38** with a twofold excess of diphenylketene. Evidence that the intermediate is N-acyl sulfo imine **39** is provided by its formation when the reaction is carried out with equivalent amounts of the reagents, as well as by the synthesis from its analogs **41** of oxazolones **42** or **8** (when R = Ph) and 2-hydroxy(ethoxy) derivatives **43** [53].

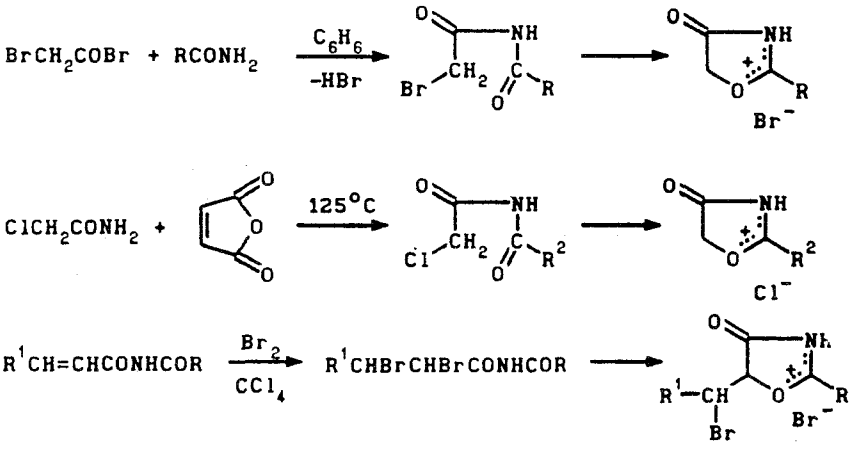




R=Ph,$CH_3$,$CF_3$; $R^1$=H,Et

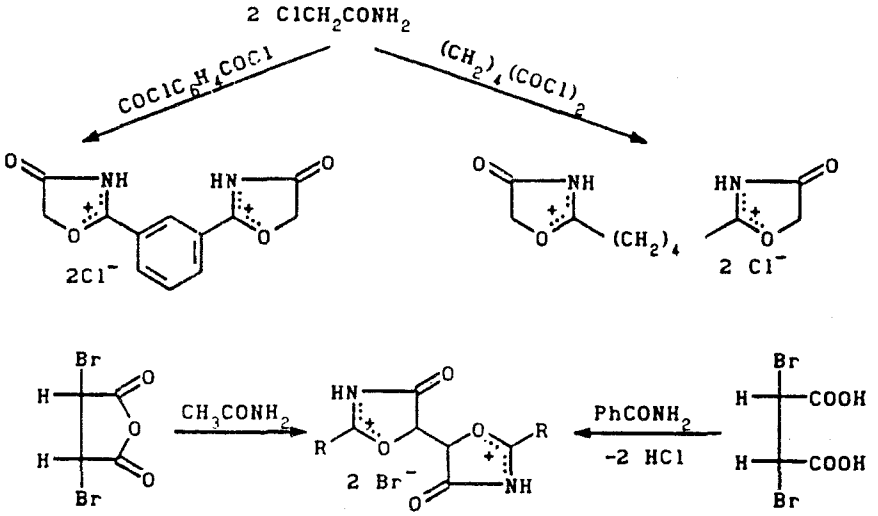
**Synthesis of 4(5)-Oxazolonium Salts**

The methods for the synthesis of oxazolonium salts that were proposed in 1964 were based on the reaction of bromoacetic acid halides with amides [54, 55] or the reaction of $\alpha$-chloroacetamide with maleic anhydride [54], as well as the bromocyclization of cinnamic and maleic acid N-acylamides [56, 57].



R=Me,Ph; $R^1$=Ph,COOH; $R^2$= CH=CHCOOH

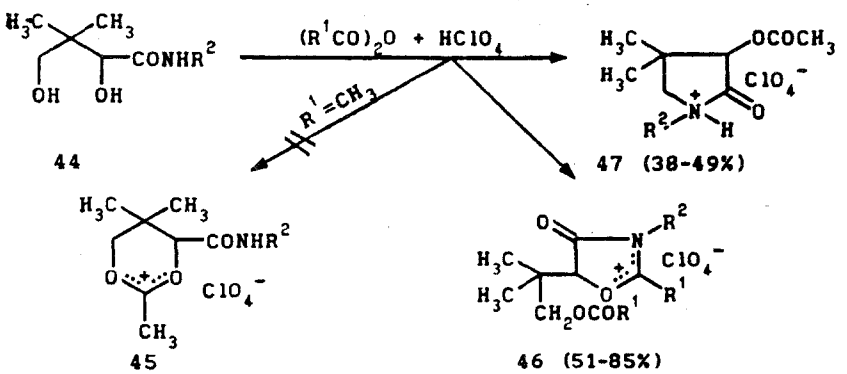
These methods have also been used to obtain bis(oxazolonium) salts [58, 59].



R=Me,Ph

The described [54-59] methods for the synthesis and purification of oxazolonium salts attest to their stability in water and alcohol, which contradicts the results obtained in studies of the reactivities of oxazolones and their salts [6-8, 42, 60, 61] and raises doubts as to the reliability of the proof of the structures of the substances described in these studies.

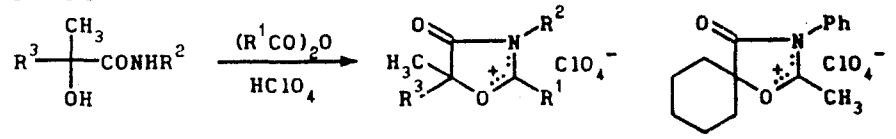
The reliable production of oxazolonium salts **46** was first reported in [7, 62], in which the researchers planned to accomplish the synthesis of 1,3-dioxanium perchlorates **45** by the reaction of pantoic acid amide **44** ($R^2$ = H) with



**45**, **46** $R^2$=H, $CH_3$; **46** $R^1$=$CH_3$, $C_2H_5$, $C_3H_7$; **47** $R^2$=$CH_3$, $C_4H_9$

aliphatic acid anhydrides and $HClO_4$ [63, 64]. N-Substituted amides **44**, retaining the tendency to undergo heterocyclization that is peculiar to γ-hydroxy amides, give pyrrolidonium perchlorates **47** instead of oxazolonium salts [10, 65].

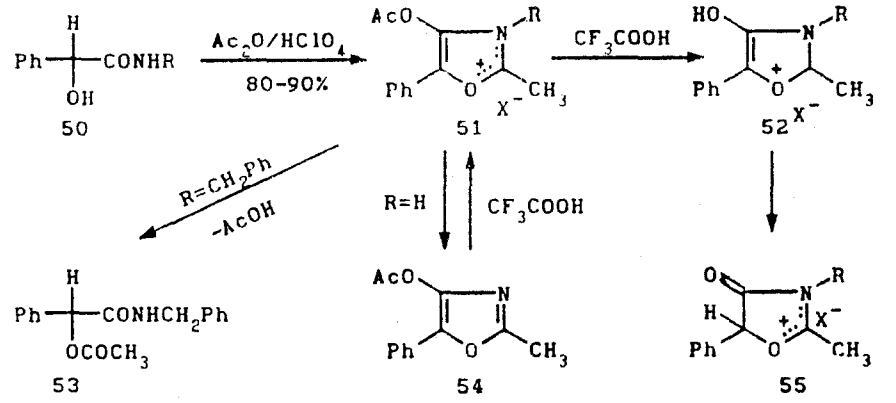
A general preparative method for the synthesis of salts **48** and their spirocyclic analogs **49** by the reaction of α-hydroxy acid amides or cyclohexanol-1-carboxylic acid anilide with alkanecarboxylic acid anhydrides and $HClO_4$ was subsequently developed [8].



**48** (50-90%) **49** (75%)

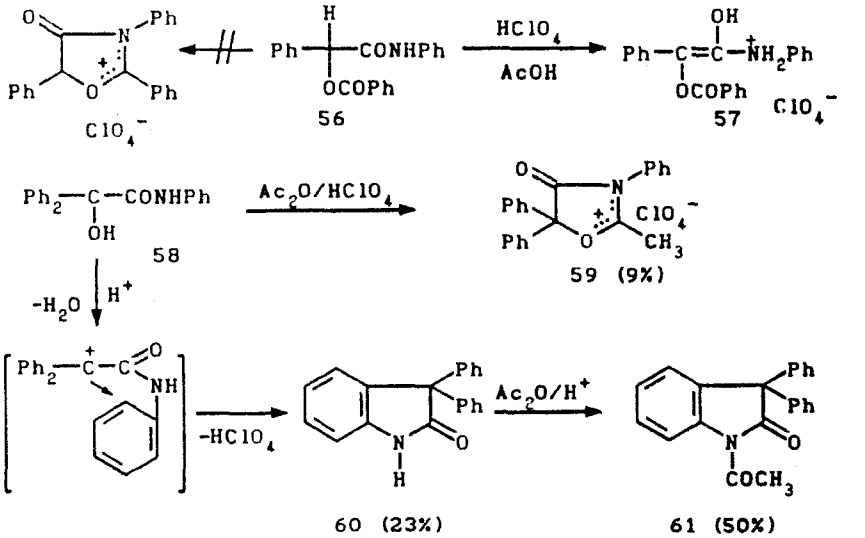
$R^1$=Alk; $R^2$=H,$CH_2Ph$,Ph; $R^3$=H,Me

Instead of the expected salts **45**, the reaction of mandelic acid amides **50** with acetic anhydride and $HClO_4$ gives, due to prototropic rearrangement of their enol acetates, 4-acetoxyoxazolium salts **51** [66], which in water are deprotonated quantitatively to give oxazole **54** or undergo rearrangement to N-benzylamide **53**. In trifluoroacetic acid salts **51** undergo deacetylation with rapid prototropic rearrangement of the resulting hydroxyoxazolium salts **52** to oxazolonium salts **55**.



R=H,$CH_2Ph$; X=$ClO_4$,$CF_3COO$

Perchlorate **57** was obtained in an attempt to cyclize O-benzoylmandelic acid anilide **56**, while in the reaction of benzilic acid anilide **58** with acetic anhydride and $HClO_4$ oxindole **60** and its N-acetyl derivative **61** were isolated along with perchlorate **59** [67].

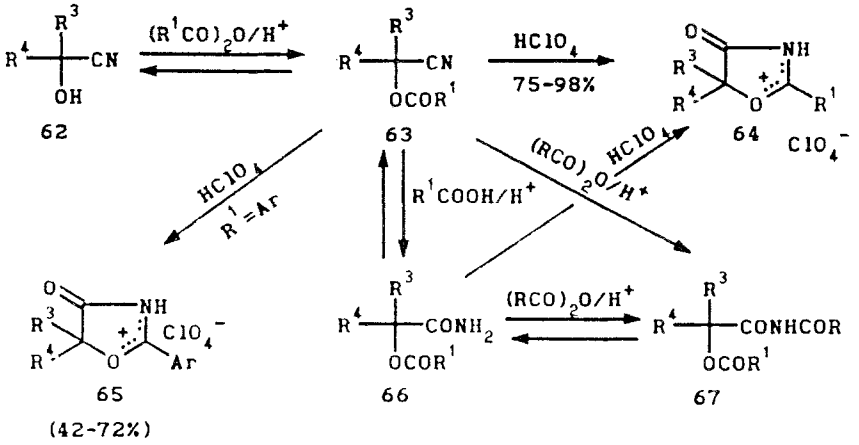


**60** (23%) **61** (50%)

A preparative method for the synthesis of salts **64** consists in the reaction of α-hydroxy nitriles **62** (acetaldehyde, acetone, and cyclohexanone cyanohydrins) with aliphatic acid anhydrides and $HClO_4$ [9, 60]. This

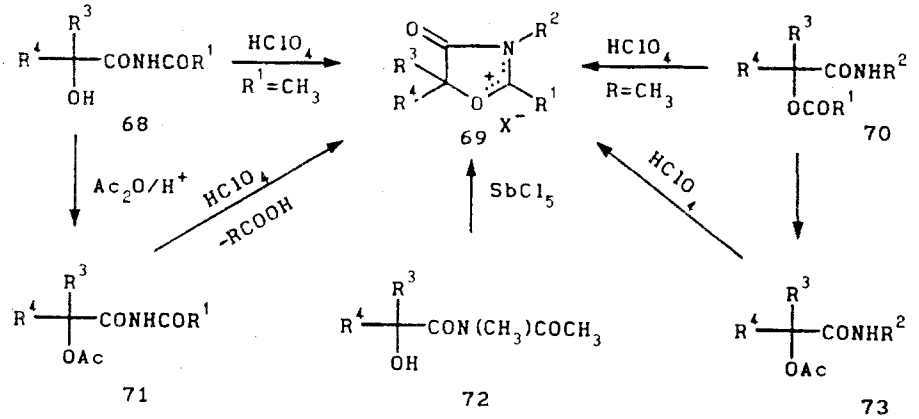
reaction evidently proceeds through the formation of α-acyloxy nitriles **63**. The latter are converted to oxazolonium salts by the action of $HClO_4$; this was used for the preparative synthesis of several 2-aryloxazolonium salts **65**. The formation of perchlorates **64** may proceed both via the direct cyclization of α-acyloxy nitriles **63**, as in the Ritter reaction, and through the formation of α-acyloxy amides **66** [8].

The possible formation of α-acyloxy acid N-acylamides **67** from α-hydroxy(acyloxy) acid nitriles and amides and their subsequent cyclization, accompanied by N-deacylation, does not exclude the possibility of realization of the **63, 66 → 67 → 64** pathway [9]. However, oxazolonium salts (previously described [54, 55] in the form of the hydrobromides) could not be obtained via this pathway from hydroxyacetonitrile and its benzoate. The formation of α-acetoxy- and α-benzoyloxyacetic acid N-acetylamides is not accompanied by cyclization in this case [9].



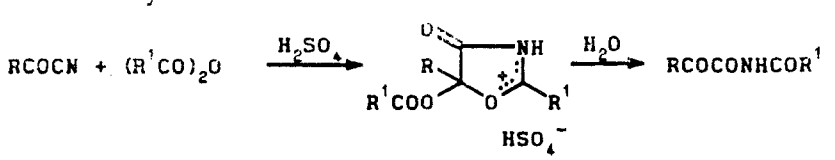

R R¹=Alk; R³=H, $CH_3$, R⁴=$CH_3$; R³+R⁴=$-(CH_2)_5-$

α-Hydroxy(acyloxy) acid N-acylamides **68**, **71**, and **72** are capable of undergoing cyclization to oxazolonium salts not only by the action of $HClO_4$ but also by the action of $SbCl_5$ [7]. Acetic anhydride, which is used as an agent that ties up water, is capable of participating in the reaction and in excess amounts leads to the formation of 2-methyl-substituted salts **69** by causing successive O-acetylation and N-deacylation (the **68 → 71 → 69** pathway) or transacylation (the **70 → 73 → 69** pathway).



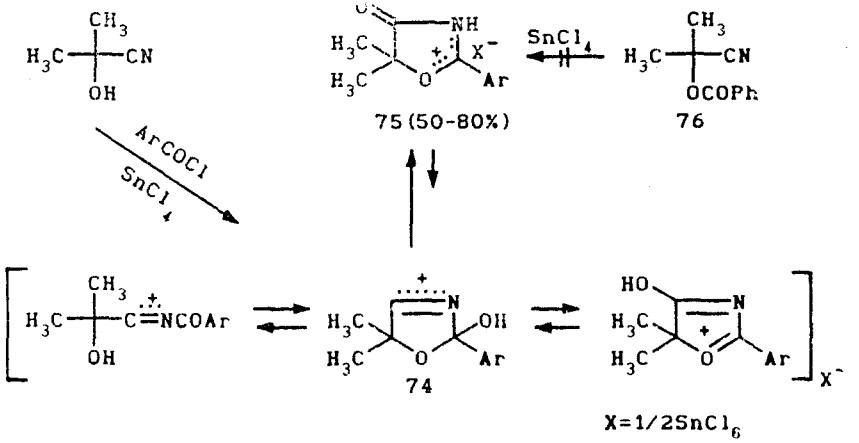

R¹=Me, Ph, CH=CHPh; R²=H, Me, Ph; R³=H, Me; R⁴=Me, $C(CH_3)_2CH_2OAc$; X=$ClO_4$, $SbCl_6$

5-Acyloxyoxazolium salts are formed in high yields in the reaction of α-keto nitriles with aliphatic acid anhydrides and $H_2SO_4$ [68]. Because of their low stabilities, they cannot be isolated from the reaction mixtures; they are hydrolyzed to α-keto acid N-acylamides.



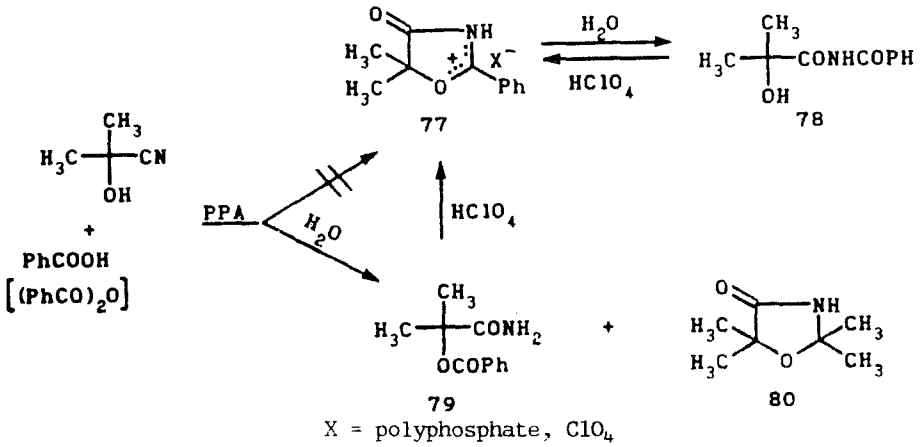

R = alkyl, cycloalkyl, phenyl, naphthyl, hetaryl; $R^1$ = H, alkyl, phenyl

An effective method for the synthesis of oxazolonium salts **75** consists in the direct (without a solvent) reaction of acetone cyanohydrin with aromatic acid halides in the presence of $SnCl_4$ [9]. This reaction evidently proceeds through the formation of acyl nitrilium salts **74** [69] rather than α-aroyloxy nitriles **76**, which do not give salts **75** under these conditions:

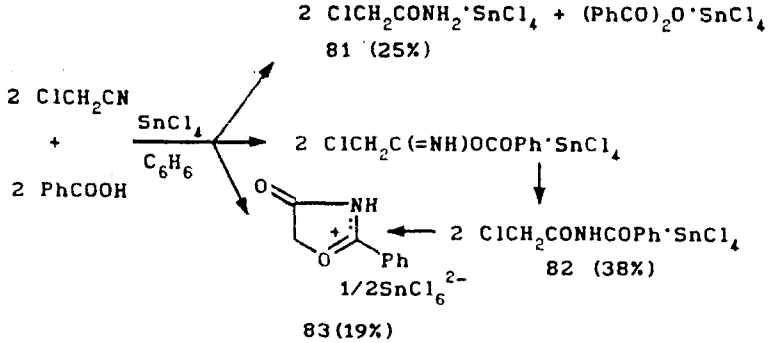



The possibility of the formation of acyl nitrilium salts is also not excluded in the reaction of α-hydroxy(acyloxy) nitriles **62** and **63** with acid anhydrides and $HClO_4$. This is confirmed indirectly by the ease of obtaining benzoic and phenylacetic acid N-acetylamides from the corresponding nitriles under similar conditions [70].

Amide **79** and oxazolidone **80** — the product of condensation of the α-hydroxyisobutyramide and acetone that are formed in the reaction — were isolated in attempts to obtain salt **77** or the product of its hydrolysis — N-benzoyl α-hydroxy amide **78** — from acetone cyanohydrin and benzoic acid or its anhydride in polyphosphoric acid (PPA).

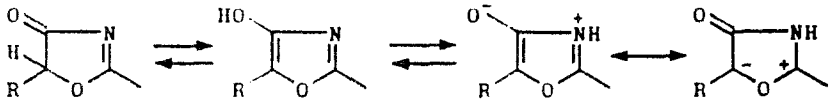



Oxazolonium hexachlorostannate **83** is formed in addition to molecular complexes **81** and **82** in the reaction of chloroacetonitrile, benzoic acid, and $SnCl_4$ [61]. This reaction does not occur when benzoic acid is replaced by its anhydride or chloride.



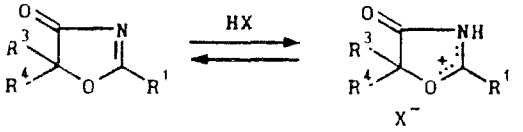
## Transformations of 4(5H)-Oxazolones and Their Salts and 1,3-Oxazolium 4-Olates

In the crystalline form and in solution oxazolones can exist in tautomeric forms **A** and **B**. In some cases their reactivities are due to mesoionic oxazoliumolate and ylid structures **C** and **D**.



The reality of the existence of the **A** ⇌ **B** equilibrium of the keto-enol type, which was repudiated in a previous review [4], is indicated by the existence in the **B** form of compounds that contain electron-acceptor substituents (R = Ph, COOPh, COOEt) in the 5 position of the ring. Evidence for the possibility of conversion of oxazolonium salts to the hydroxyoxazole form is provided by the results of their polarographic study [71] and the formation of 4-acetoxyoxazolium salts **51** — enol acetates of oxazolonium salts [66].

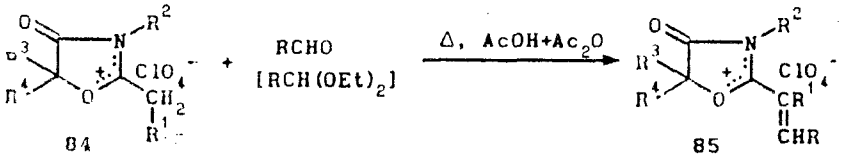
**Deprotonation.** Oxazolones have low activities; however, when they are treated with acids ($HClO_4$, HCl, HBr) in glacial acetic acid, ether, benzene, and other aprotic and low-basicity solvents, they are readily converted to the corresponding salts [9, 71, 72], of which the crystalline perchlorates display the greatest stability in the free state. The perchlorates are also formed from other salts (hexachlorostannates, hexachloroantimonates) by treatment of suspensions of them in glacial acetic acid with $HClO_4$ [7-9].



X = $ClO_4$, Cl, Br; $R^1$ = $CH_3$, Ar, CH=CHAr, CH=CHFur; $R^3$ = H, $CH_3$; $R^4$ = $CH_3$, $C(CH_3)_2CH_2OAc$

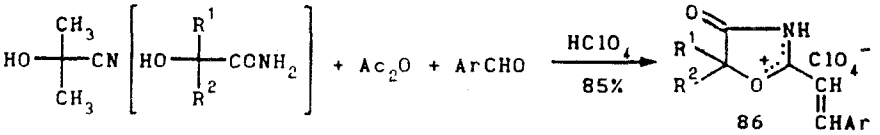
The ease of deprotonation of 2-aryl- and 2-styryl-substituted oxazolonium salts [9, 73, 74] with triethylamine, pyridine, aqueous alcohol, and ammonia, in addition to the accessibility of the synthesis, makes this method for obtaining oxazolones the most preparatively convenient pathway. However, the reactions of 2-alkyloxazolonium salts with triethylamine often proceed anomalously; this is associated with the α-CH acidity of the alkyl substituent [9]. 2-(o- and p-Hydroxystyryl)oxazolonium salts, for which competitive O-deprotonation to give spirochromene or quinoid structures is possible, also undergo N-deprotonation.

**Condensation with Carbonyl Compounds and Orthoformic Ester.** 2-Alkyl-substituted salts **84**, by manifesting the CH acidity of the methyl (methylene) group, readily condense with aromatic and cinnamic aldehydes, 5-substituted furfurals, 5-(p-nitrophenyl)-2-formylpyrrole, and the corresponding acetals to give salts **85** [8, 74-76].



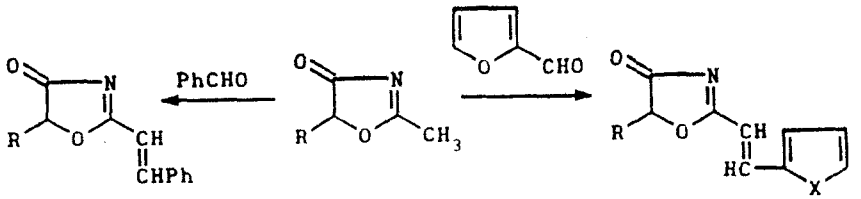
$R^{1-3}$ = H, $CH_3$; $R^4$ = $CH_3$, $C(CH_3)_2CH_2OAc$; R = Ar, Hetar, CH=CHPh

Perchlorates **86** were obtained by "one-reactor" synthesis by the reaction of α-hydroxy acid amides or nitriles with acetic anhydride, $HClO_4$, and aromatic aldehydes or acetals:



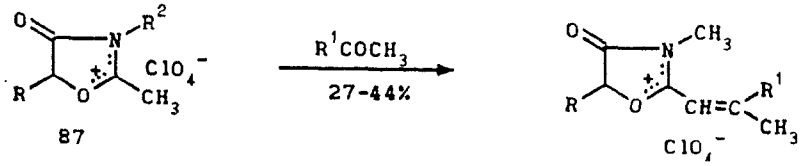
$R^1$ = H, $CH_3$; $R^2$ = $CH_3$, $C(CH_3)_2CH_2OAc$

2-Methyloxazolone is also capable of reacting with aldehydes in the case of catalysis by mineral acids; this sometimes makes it possible to accomplish the condensation more effectively, as, for example, with aldehydes of the furan series:



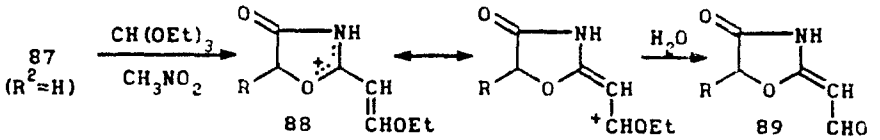
R=C(CH$_3$)$_2$CH$_2$OAc X=O,N-(4-NO$_2$C$_6$H$_4$)

The possibility of the condensation of oxazolonium salts with ketones has been demonstrated in the case of N-methyl-substituted salt **87** [74].



R=C(CH$_3$)$_2$CH$_2$OAc; R$^1$=CH$_3$, Ph, 2-methylfuryl; R$^2$ = CH$_3$

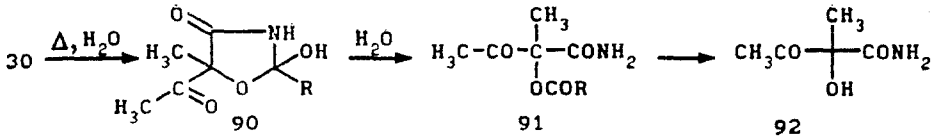
The reaction of salt **87** with ethyl orthoformate gives hard-to-crystallize perchlorate **88**, in which, as a consequence of mesomeric stabilization, the most electrophilic center is the $\beta$ position of the ethoxyvinyl substituent, as evidenced by its conversion to aldehyde **89** in water [12].



R=C(CH$_3$)$_2$CH$_2$OAc

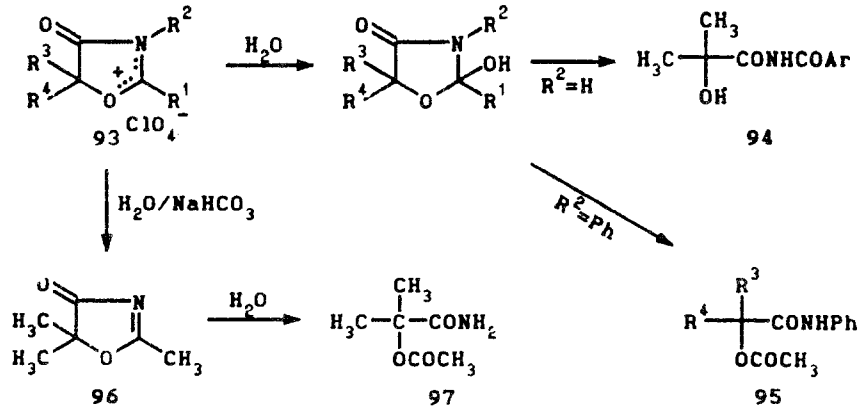
**Hydrolysis.** In water or under the influence of air moisture oxazolone **23** and its hygroscopic hexachlorostannate are converted to glycolic acid N-benzoylamide [6, 61]. In the alkaline alcoholysis of oxazolone **8** ring opening is accompanied by deacylation, and benzilic acid amide is formed [28].

5-Acetyloxazolones **30** (when R = OAlk) are hydrolyzed in water to 2-acetyllactic acid amide **92** or (when R = Ar) its O-aroyl derivatives **91**. Under more severe conditions 2-aryloxazolones **30** are cleaved to aromatic acids or their amides and acetone. Oxazolone **30** with a trichloromethyl group in the 2 position is extremely sensitive to air moisture and is readily converted initially to monohydrate **90** (R = $CCl_3$) and then to amide **92** [42].



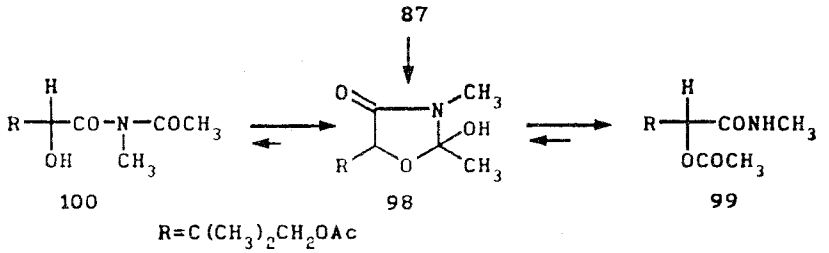
In water NH-oxazolonium salts **93** are converted exceptionally easily and quantitatively to $\alpha$-hydroxy acid N-aroylamides **94**, while their N-phenyl analogs are converted to $\alpha$-acyloxy acid anilides **95** [8, 20]. In addition to $\alpha$-acetoxyisobutyramide **97**, oxazolone **96**, which, because of the ease of hydrolysis, is obtained by deprotonation of the corresponding perchlorate **93** by pyridine [60], is formed in small amounts in $NaHCO_3$ solution (see scheme below).

In $NaHCO_3$ solution NH-oxazolonium perchlorate **87** is converted to pantoic acid O,O′-diacetylamide $CH_3COOCH_2C(CH_3)_2CH(OCOCH_3)CONH_2$. In water N-methyl-substituted salt **87** gives a mixture of O- and N-acetyl amides **99** and **100**. The amount of O-acetyl amide in solution increases with time; this is evidently associated

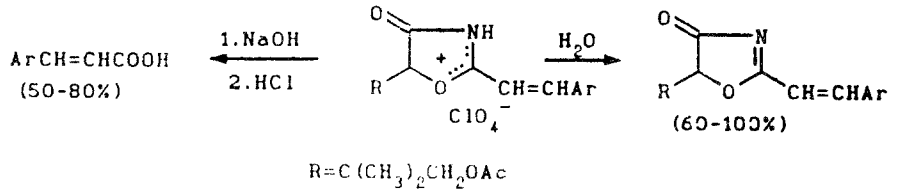


$R^1=CH_3$, Ar; $R^2=H$, Ph; $R^3=H$, $CH_3$; $R^4=CH_3$; $R^3+R^4=-(CH_2)_5-$

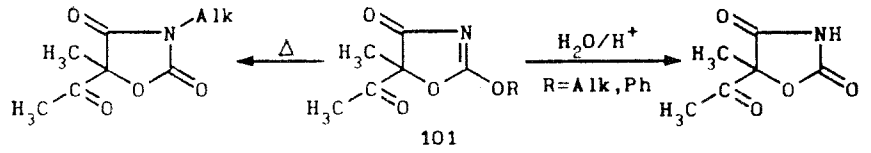
with the establishment of a dynamic equilibrium between these compounds and cyclic pseudobase **98** [7].



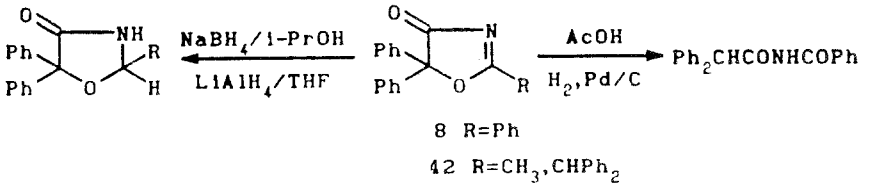
2-Styryl-substituted oxazolonium salts are deprotonated in water, while they are hydrolyzed by refluxing in alkalis to give (after acidification) cinnamic acids [8, 12].



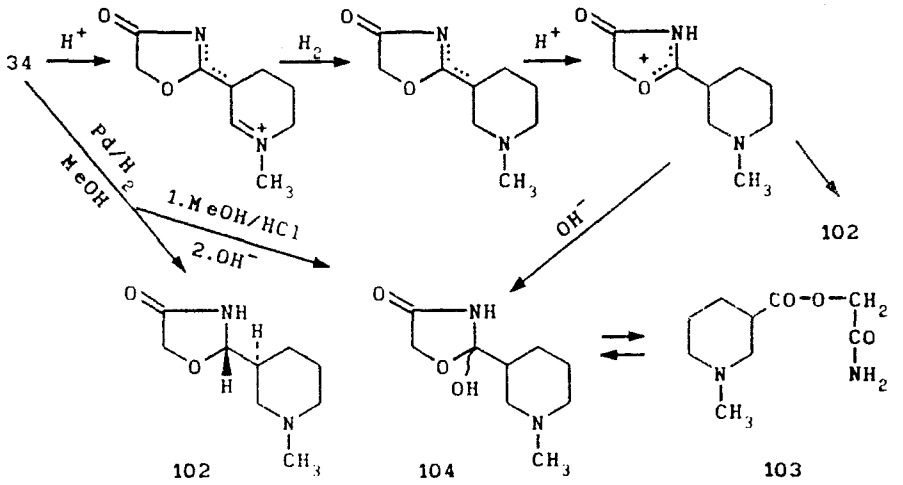
2-Alkoxy(phenoxy)oxazolones **101** in solutions of acids, as well as in the case of direct heating (without a solvent), retain the oxazolone ring, splitting out an alkoxy (phenoxy) group or undergoing the Chapman rearrangement to oxazolidinediones [44, 15].



**Reduction.** The hydrogenation of the C=N bond of oxazolones **8** and **42** with $NaBH_4$ or $LiAlH_4$ gives oxazolidines in high yields [53]. In acetic acid catalytic reduction is preceded by cleavage of the heteroring and the formation, in the case of oxazolone **8**, of diphenylacetic acid N-benzoylamide [28]. This hydrogenolysis pathway is evidently a special case and is explained by the ease of conversion of benzilic acid derivatives to diphenylacetic acid derivatives.

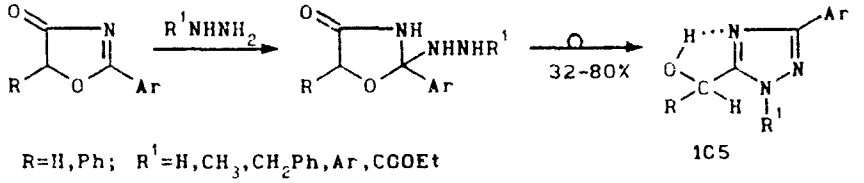


Oxazolidinone **102** and ester **103**, which exist in solution in ring-chain tautomerism with 2-hydroxyoxazolone **104**, are formed in the catalytic hydrogenation of oxazolone **34** in neutral and acidic media [47].

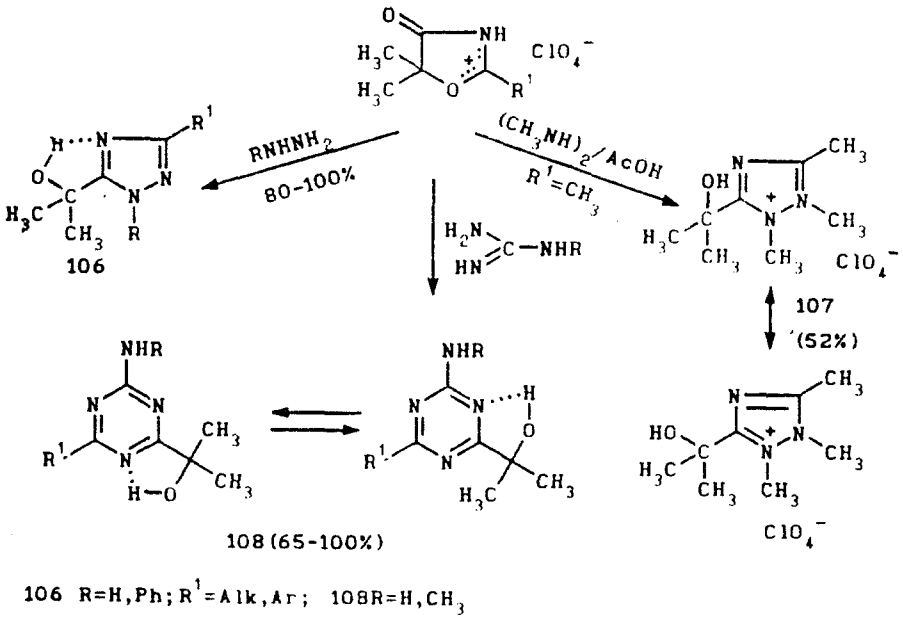


**Reactions with Binucleophiles.** Oxazolones and their salts are capable of undergoing recyclization reactions with 1,2- and 1,3-binucleophilic reagents to give α-hydroxyalkyl-substituted azoles and azines via an ANRORC mechanism.

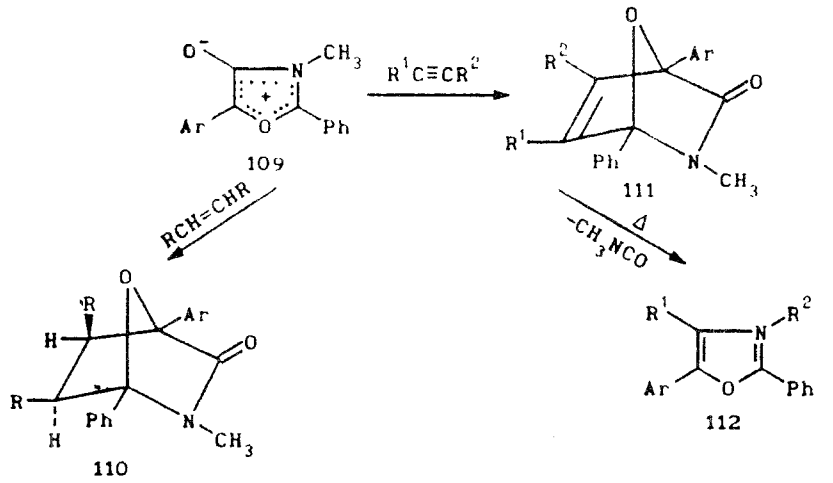
1H-1,2,4-Triazoles **105** were obtained in the reaction of oxazolones with hydrazines [30].



Triazoles **106** [21-23, 77], triazolium salt **107** [78], and 1,3,5-triazines **108** [22] were obtained in the reactions of oxazolonium salts with hydrazine, phenylhydrazine, *sym*-dimethylhydrazine, and guanidines.

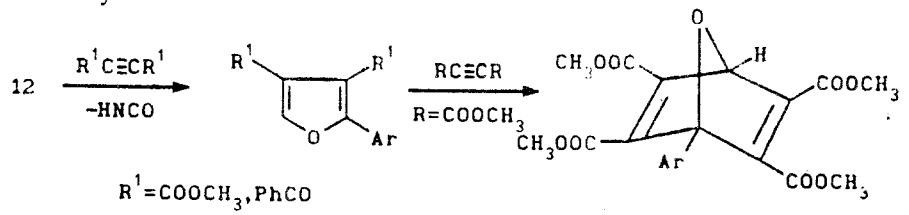


**Cycloaddition Reactions.** Oxazolium olates **109** react vigorously with ethylenic (fumaric and maleic acid nitriles and esters) [39, 79] and acetylenic [38, 80] dipolarophiles to give stable cycloadducts **110** and **111** or substituted furans **112** via a reaction of the retro Diels—Alder type.



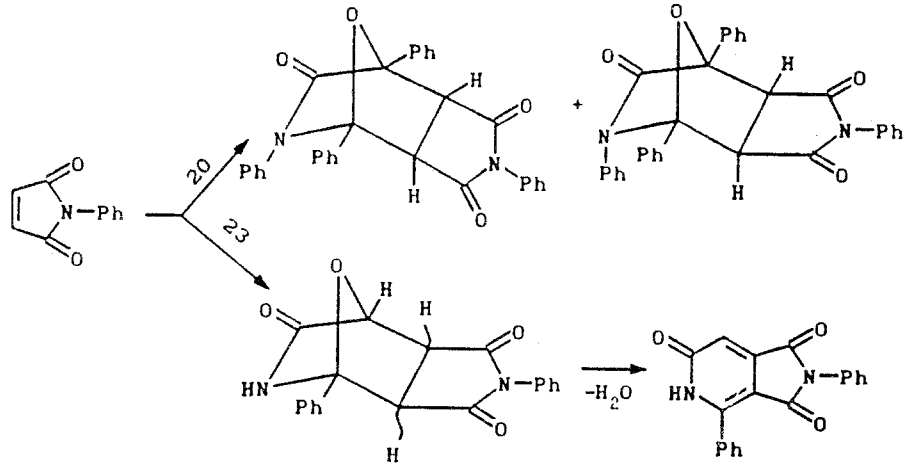
R=CN, $COOCH_3$; $R^1$ и $R^2$=$COOCH_3$, Ph or $R^1$=H, $CH_3$, Ph, a $R^2$=$COOCH_3$

Oxazolones **12** react similarly with activated acetylenes [80, 81]; the reaction may proceed with the addition of a second molecule of acetylene to the resulting furan, as occurs in the reaction of oxazolone (R = 4-$ClC_6H_4$) with dimethyl acetylenedicarboxylate.

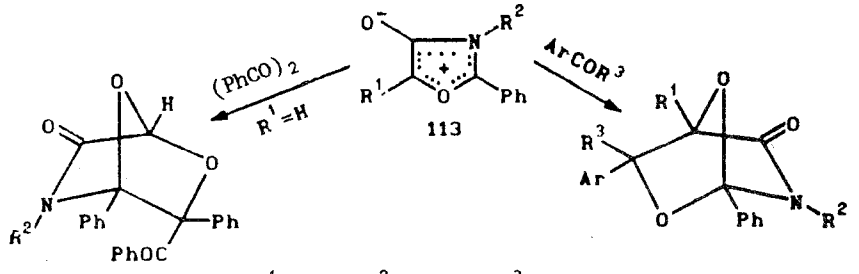


$R^1$=$COOCH_3$,PhCO

In addition to oxazolium olate **20**, oxazolone **23** hydrochloride also undergoes cycloaddition with N-phenylmaleinimide [39, 81].



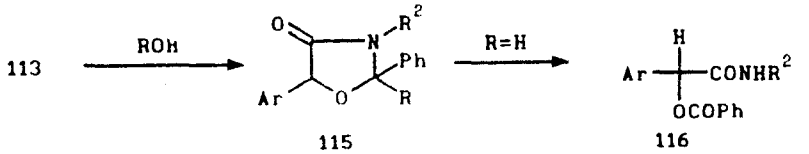
The reaction of carbonyl compounds with oxazolium olates **113** proceeds differently. Benzil, in contrast to aroylacetaldehydes, as well as aromatic aldehydes and ketones, gives adducts **114**, which correspond to reverse cycloaddition [40].



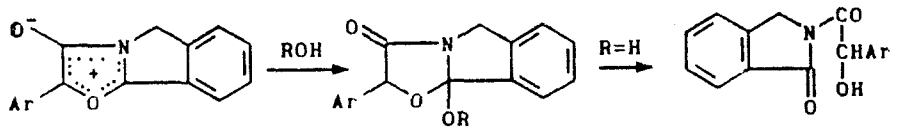
$R^1$=H,Ar; $R^2$=$CH_3$,Ar; $R^3$=H,$CH_3$,$CH_2CHO$,Ar

Oxazolium olates with no substituents in the 5 position of the ring display the highest activity in cycloaddition reactions [37, 79].

Oxazolium olates **113** ($R^1$ = Ar) and their analogs **117** also react with alcohols (with the exception of the sterically hindered tert-butyl alcohol) via a 1,3-dipolar cycloaddition mechanism to give oxazolidones **115** and **118**. In water [15] and acids [4, 5] the reaction is accompanied by hydrolytic opening of the heterorings to give α-benzoyloxy amides **116** and N-acylphthalimidines **119**.



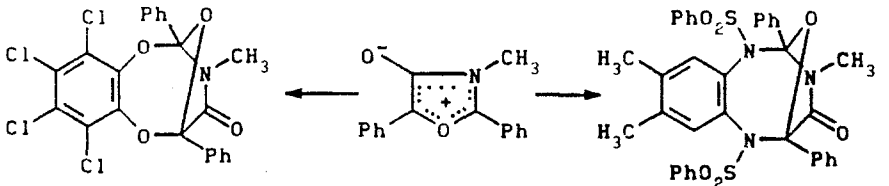

115 116




117 118 119

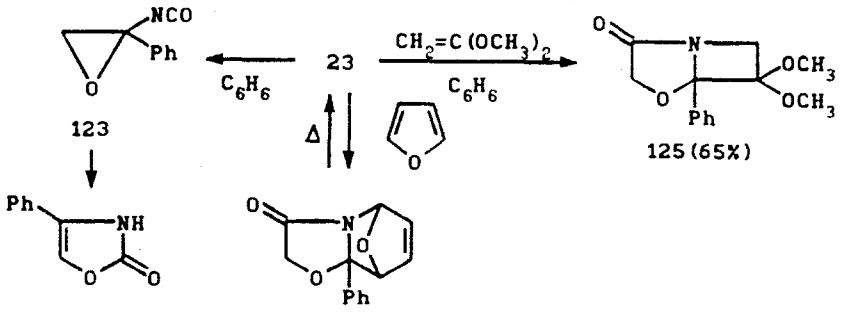
R=H,Alk; $R^2$=$CH_3$,Ph; Ar=4-$NO_2C_6H_4$

Oxazolium olate **120** reacts with chloranil and N,N'-diphenylsulfonylbenzoquinone diimine to give [4 + 4]-cycloaddition adducts **121** and **122** [82].




121 120 122

**Photoreactions.** 2(3H)-Oxazolone **124** was isolated in the UV irradiation of a benzene solution of oxazolone **23** with subsequent chromatography on silica gel [51]. The **123** → **124** skeletal rearrangement is a dark process and occurs in the action of catalytic amounts of dilute alkali or silica gel on isocyanate **123**. In the presence of dimethoxyethylene [51] and furan [50] the oxazolone, without undergoing rearrangement, gives [2 + 2]-photocycloadducts **125** and **126**.

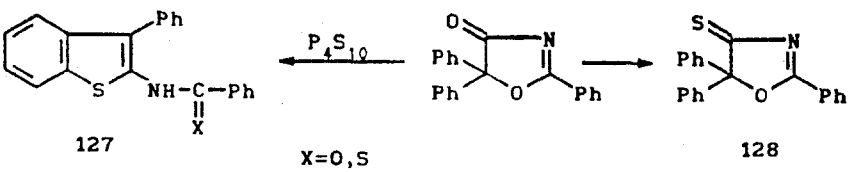



123 125 (65%)

124 (40%) 126

Oxazolone **23** does not undergo photoreaction with cyclohexene, methyl vinyl ether, styrene, and *cis*- and *trans*-2-butenes, which are rearrangement quenchers [50].

**Sulfuration.** 2-Thiobenzoylaminobenzothiophene **127** (X = S) with traces of the oxygen analog and, presumably, the expected 4-thioxooxazole **128** were obtained when oxazolone **8** was treated with phosphorus pentasulfide [15, 48].




127 X=O,S 128

It should be noted that the preparation of 4(5) oxazolones and oxazolonium salts and the syntheses based on them, as a rule, are distinguished in many cases by high yields of the desired compounds. In a theoretical and practical respect the possibilities of these compounds have not yet been exhausted, and research in this direction is a promising pursuit.

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# AMIDINE TAUTOMERISM IN THE 1,3-DIACYL-2-(5-SUBSTITUTED FURFURYL)THIOUREA SERIES. MOLECULAR STRUCTURE OF 1,3-DIACETYL-2-(5-ETHOXYCARBONYLFURFURYL)THIOUREA

**G. D. Krapivin, E. B. Usova, V. E. Zavodnik, A. I. Lutsenko, and V. G. Kul'nevich**

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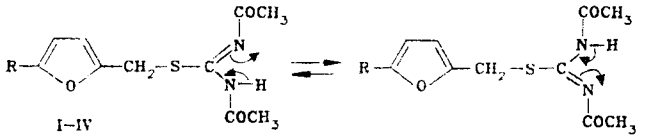
*The effect of substituents in the furan ring on the dynamics of amidine tautomerism in 1,3-diacetyl-2-(5-R-furfuryl)thioureas is demonstrated. The conformation of 1,3-diacetyl-2-(5-ethoxycarbonylfurfuryl)thiourea was established by x-ray diffraction analysis.*

It is known that the mechanism, rate, and thermodynamic parameters of amidine tautomerism depend on the concentration, the nature of the solvent, the character of the substituents attached to the nitrogen and carbon atoms of the N—C=N fragment, and a number of other factors such as, for example, the acid—base equilibrium in the case of prototropic tautomerism (for example, see [1-6]).

In the present paper we present the facts of the effect of substituents attached to the $C_{(2)}$ atom of the amidine fragment of the 1,3-diacetyl-2-furfurylthiourea I-IV molecules on amidine tautomerism.



I–IV

I R=$COOC_2H_5$; II R=$NO_2$; III R=CN; IV R=CHO

According to our data [7], only one set of signals corresponding to the protons of acyl groups is observed in the PMR spectra of II and its analogs (1,3-dipropionyl and 1,3-dibenzoyl derivatives) at room temperature; this is evidently the result of the rather fast (on the NMR time scale) exchange of a proton between the nitrogen atoms of the amido and imido groups. At −70°C the PMR spectra of dilute (≈0.05 mole/liter) solutions contain two distinctly resolved singlets of equal intensities of the protons of acetyl groups and a relatively narrow singlet of an NH proton at ≈12 ppm (Table 1); according to [3], this attests to slow exchange of the NH proton. The position of the signal of the NH proton indicates the possibility of the formation of an intramolecular hydrogen bond (IMHB). Raising the temperature leads to broadening and then to coalescence of the signals of the methyl groups. The coalescence temperature and, consequently, the energy barrier to exchange depend on the character of the substituent in the furan ring (see Table 1).

Transmission of the electronic properties of the substituents in I-IV should take place through the $CH_2$—S grouping, which is not a good conductor of these effects. The manifestation of a field effect and/or a dipole-dipole interaction between polar groups in the I-IV molecules should be associated with the realization of a certain

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