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SYNTHESIS AND CHEMICAL TRANSFORMATIONS OF 2,3-DIHYDROPYRROLE-2,3-DIONES ANNELATED ON THE [*a*] SIDE BY AZAHETEROCYCLES. (REVIEW)

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Data on methods for the synthesis of 2,3-dihydro-2,3-pyrrolediones condensed with azaheterocycles on the [a] side are reviewed. Their reactions with nucleophilic reagents, allylboronation, reduction, and thermal transformations are discussed.

Keywords: pyrrole-2,3-diones [*a*]-annelated with azaheterocycles, allylboronation, nucleophilic reactions, recyclization, thermolysis.

The chemistry of 2,3-dihydro-2,3-pyrrolediones condensed with azaheterocycles on the [*a*] side first evolved in the seventies, when the application of 2,3-dihydro-2,3-pyrroledione derivatives as synthetic blocks for the construction of alkaloid molecules was first demonstrated [1-7].

It should be mentioned that up to the beginning of the nineties these annelated dihydropyrrolediones were studied almost exclusively as subjects for photoreduction and photocyclization or as dienophiles in Diels–Alder reactions (for the production of intermediate compounds in the synthesis of alkaloids). A large part of these papers belong to certain groups of investigators [1-5]. Single reports on reactions with nucleophilic reagents, allylboronation, reduction, and thermal transformations of 2,3-dihydro-2,3-pyrrolediones annelated with azaheterocycles on the [*a*] side have only begun to appear comparatively recently. This region of their chemical behavior has been studied little in spite of the fact that they exhibit high reactivity toward various nucleophiles (particularly with the presence of several electron-withdrawing substituents in the rings) and generate imidoylketenes during thermolysis.

In the present review we examine publications existing up to March, 2002, on methods for the production of dihydropyrrolediones condensed with azaheterocycles and their chemical transformations. The review does not include data on the chemistry of isatins and their aza analogs, which were described in [8], or data on the cycloaddition of these pyrrolediones, which have been discussed before [1-7, 9-11] and were reviewed in [11].

1. METHODS FOR THE SYNTHESIS OF 2,3-DIHYDRO-2,3-PYRROLEDIONES ANNELATED WITH AZAHETEROCYCLES ON THE [*a*] SIDE

1.1. Reaction of Enamines with Oxalyl Chloride

The most widely used method for the production of 2,3-dihydro-2,3-pyrrolediones and their derivatives annelated with azaheterocycles on the [*a*] side is the reaction of enamines with oxalyl dichloride. The latter

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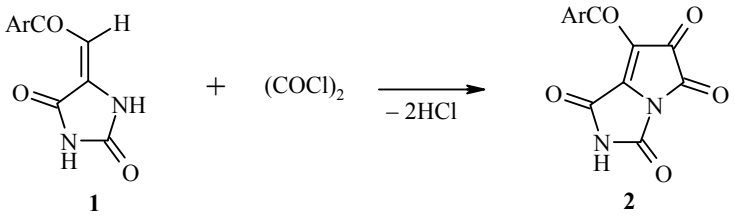
acylates both nucleophilic centers of the enamine (the primary or secondary amino group and the β-CH group) with the formation of a 2,3-dihydro-2,3-pyrroledione ring. The reaction is usually conducted in an inert aprotic solvent (ether [7, 9-11], chloroform [9, 12], dichloromethane [13], 1,2-dimethoxyethane [14], benzene [15, 16], dioxane [17]) or in pyridine in the range of 0-100°C for 1.5-3.5 h. The yields of the desired products are as a rule good particularly if the enamine contains at least one electron-withdrawing substituent (a COR or COOR group); there has been are no mention of the isolation of side products.

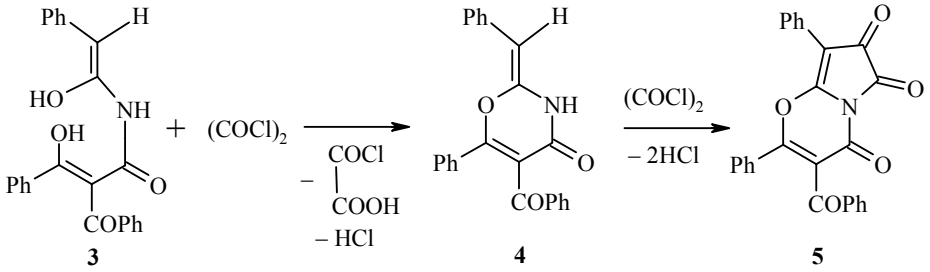
Thus, 4-phenacylideneimidazolidinediones **1** containing an enamine group form the respective substituted dihydropyrrolo[1,2-*c*]imidazolidinetetrones **2** when treated with oxalyl chloride [20].



1 **2**

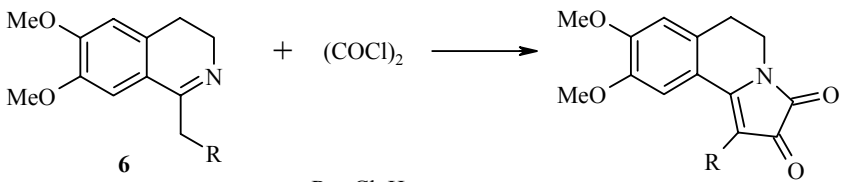
Ar = Ph, C_6H_4Me-4

The reaction of the N-substituted amide **3** with one mole of oxalyl chloride leads to the product from dehydration and closure of the 1,3-dioxazine ring, i.e., the enamine **4**, which is acylated by a second molecule of oxalyl chloride with the formation of a derivative of pyrrolo[2,1-*b*][1,3]oxazinetrione **5** [21].



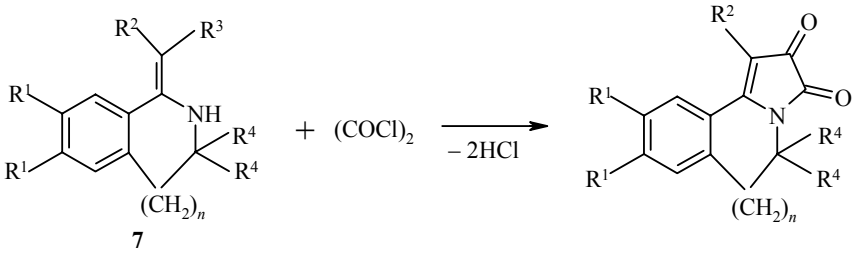
3 **4** **5**

During treatment with oxalyl chloride 1-chloromethyl- and 1-methyl-6,7-dimethoxy-3,4,6,7-tetrahydroisoquinolines **6** [14], the substituted tetrahydro derivatives **7** of isoquinolines (n = 1) [7, 9, 11, 17-19, 22, 23] and 5H-benzo[*c*]azepines (n = 2) [24-27], the cyclohexaannelated tetrahydroisoquinolines **8** [28] and the dihydroisoquinolines **9** [16], and tetrahydrofuro[3,2-*c*]pyridine [29] form the corresponding 2,3-dihydro-2,3-pyrrolediones annelated with the azaheterocycles on the [*a*] side with good yields (57-82%).



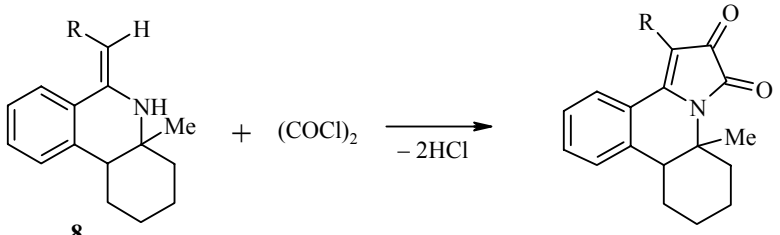
6

R = Cl, H



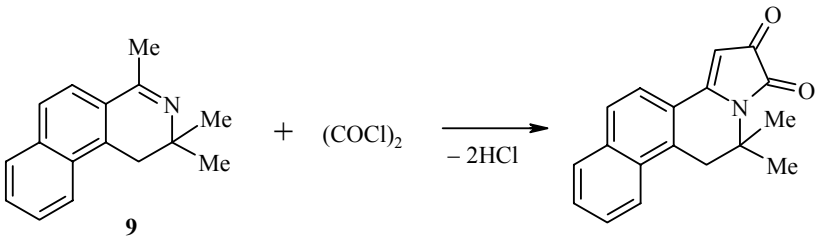
7

n =1, 2; R^1 = H, OAlk; R^2 = H, Ar, $COCCl_3$, COPh, $CONAlk_2$, COOAlk; R^3 = H, COOA1k; R^4 = H, Alk; R^4+R^4 = $(CH_2)_4$



8

R = H, COOEt



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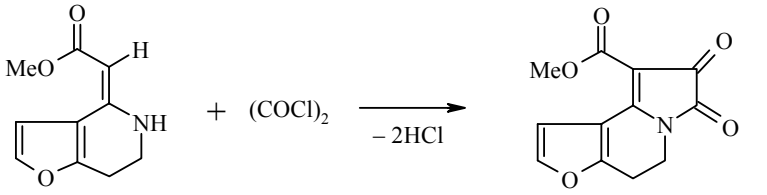

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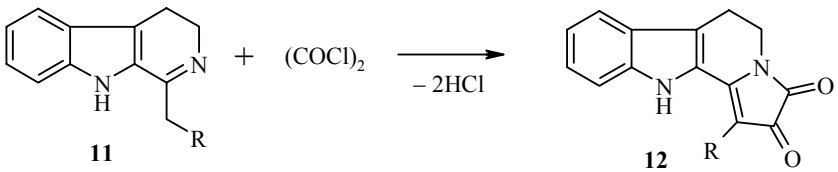
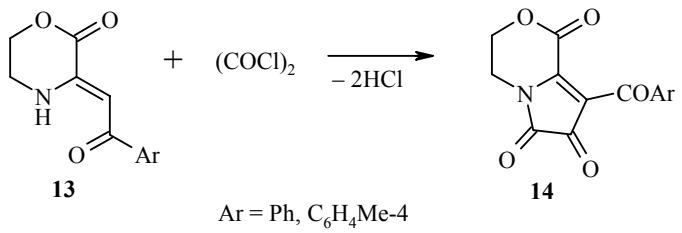
In the analogous reaction of substituted 1-methyl- and 1-chloromethyldihydropyridoindoles **11** with oxalyl chloride the corresponding tetrahydroindolizinoindole-2,3-diones **12** are formed [14].



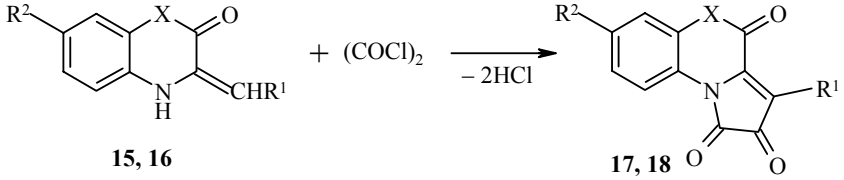
11 **12**

R = H, Cl

The 8-aroyltetrahydro-1H-pyrrolo[2,1-*c*][1,4]oxazinetriones **14** are formed with almost quantitative yields when (*Z*)-3-phenacylidene perhydrooxazinones **13** are boiled with oxalyl chloride in absolute chloroform or dichloroethane (2-3 h) [30].

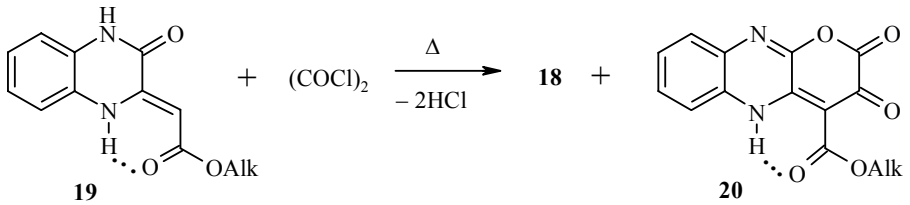


The corresponding pyrrole-2,3-diones **17** (X = O) and **18** (X = NH, NPh) [*a*]-annelated with azaheterocycles were obtained with quantitative yields from 3-methylene-3,4-dihydro-2H-1,4-benzoxazin-2-ones [31], 3-alkoxycarbonylmethylene-3,4-dihydro-1H-1,4-benzoxazin-2-ones [32], and (*Z*)-3-phenacylidene-3,4-dihydro-2H-1,4-benzoxazin-2-ones [33] **15** and also 1-H- and 1-phenyl-(*Z*)-3-phenacylidene-2-quinoxalone [33] and 3-alkoxycarbonylmethylene- and 1-phenyltetrahydro-2-quinoxalones **16** [34] with oxalyl chloride under analogous conditions [32-34].

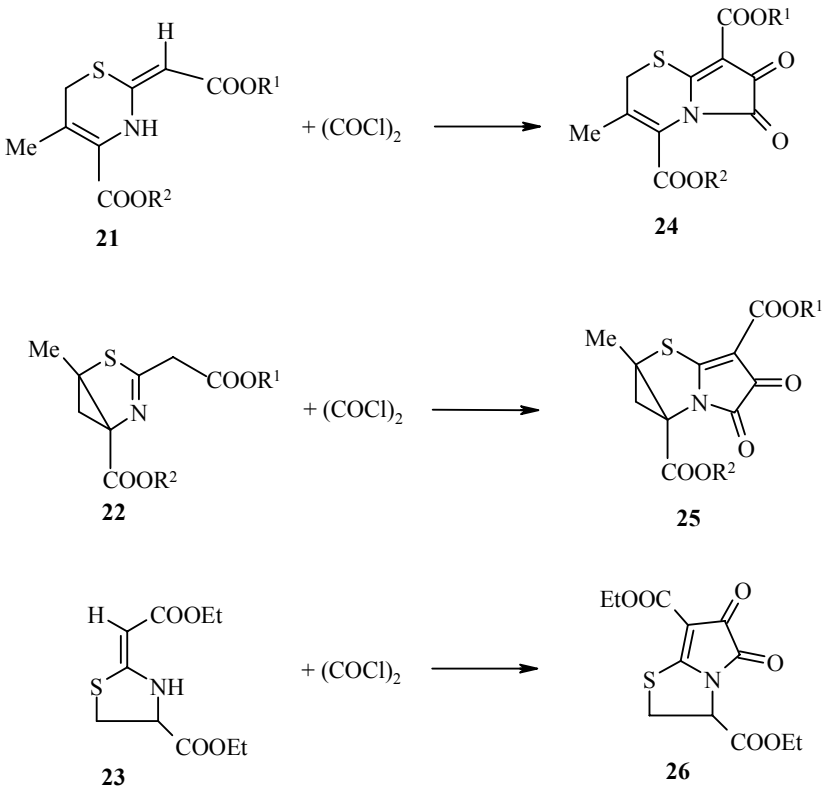


15-**18** R^1 = H, COOMe, COOEt, COAr, where Ar = Ph, C_6H_4Me-4, C_6H_4Cl-4, C_6H_4Br-4, C_6H_4OMe-4, C_6H_4OEt-4, $C_6H_4NO_2$-4; R^2 = H, Me;
15, **17** X = O, **16**, **18** X = NH, NPh

Dihydro-2H-pyrano[2,3-*b*]quinoxalinediones **20** are formed with yields of 5-15% together with products of type **18** (X = NH, R^1 = COOAlk, where Alk = Me, Et, R^2 = H) when equimolar amounts of tetrahydroquinoxalones **19** and oxalyl chloride are boiled in chloroform [35, 36].



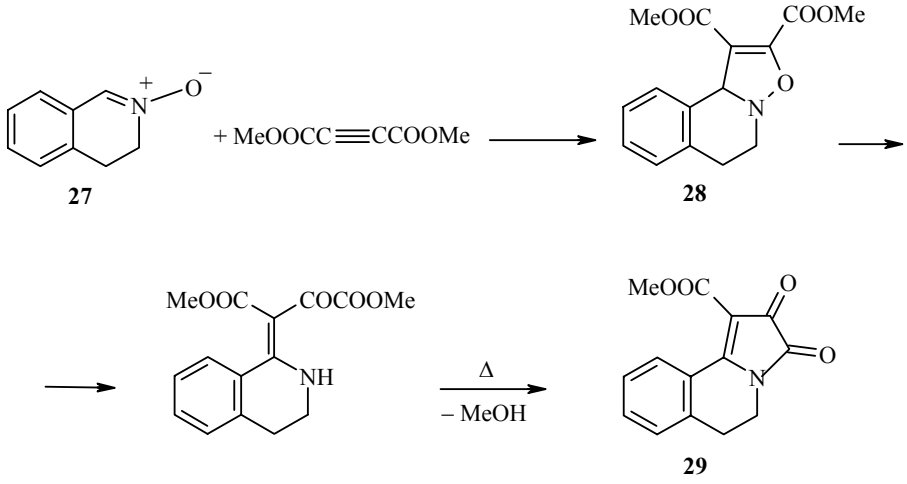
The reaction of substituted dihydrothiazines **21**, their bicyclo analogs **22**, and thiazolidines **23** with oxalyl chloride in dry dichloromethane with the addition of triethylamine leads to the corresponding annelated pyrrolediones **24**-**26** [37].



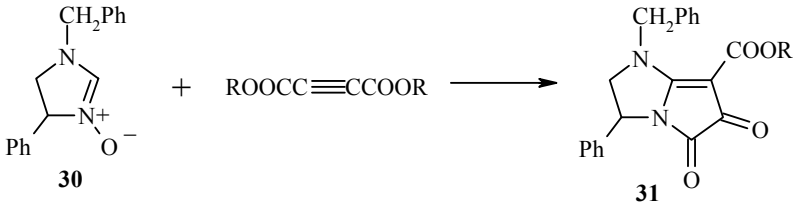
R^1 = Me, Et; R^2 = Me, $CH_2CH{=}CH_2$

1.2. Cycloaddition of Acetylenecarboxylic Esters to N-Oxides

Tetrahydropyrrolo[2,1-*a*]isoquinoline-2,3-dione (**29**) was obtained from acetylenedicarboxylic ester and 3,4-dihydroisoquinoline N-oxide **27** through the 1,3-dipolar cycloaddition product **28**, opening of the last dihydrooxazole ring, and subsequent thermal cyclization [38, 39].



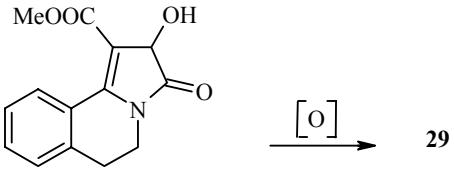
With acetylenedicarboxylic esters the dihydroimidazole N-oxide **30** forms tetrahydro-1H-pyrrolo[1,2-*a*]-imidazole-5,6-diones **31** [40].



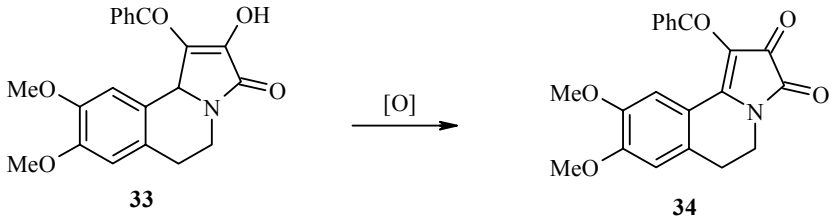
R = Me, Et

1.3. Oxidation of Substituted Dihydropyrrolones Annelated on the [*a*] Side

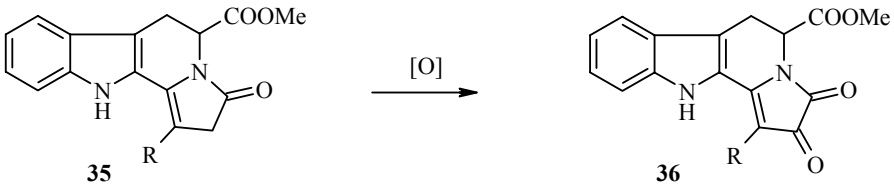
During the oxidation of 2-hydroxytetrahydropyrrolo[2,1-*a*]isoquinolin-3-one **32** in air the corresponding dione **29** is formed [39].



From another substituted tetrahydropyrrolo[2,1-*a*]isoquinolin-3-one **33** under the same conditions the analog of product **29**, i.e., compound **34**, was obtained [41]. Its structure was confirmed by X-ray crystallographic analysis [42].



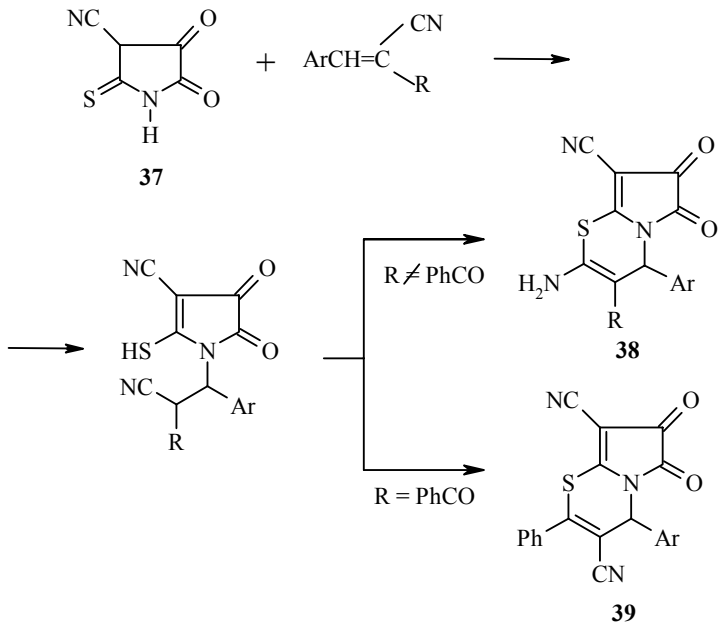
The oxidation of 3-oxotetrahydroindolizinoindoles **35** in butanol (95-100°C, 70 h) led to the 2,3-dioxo derivatives **36** [43].



R = Me, COOEt

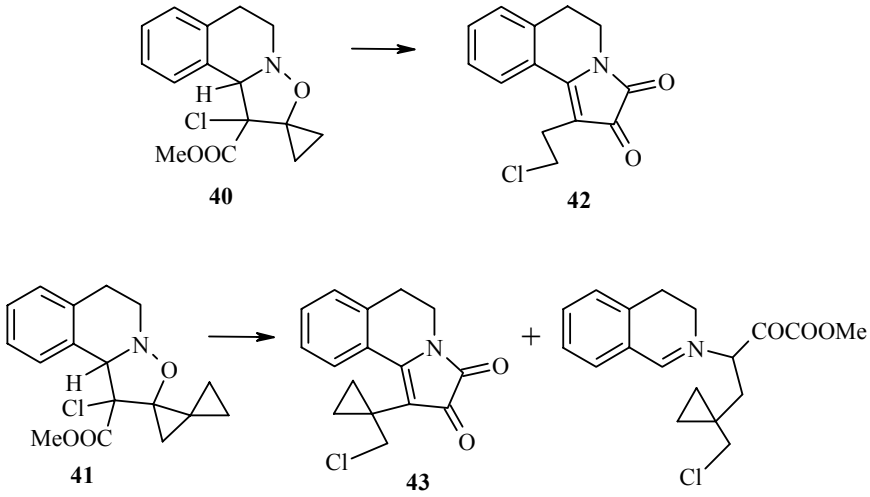
1.4. Other Methods

3-Cyano-2-thioxotetrahydropyrrole-4,5-dione **37** reacts with acrylonitrile derivatives with the formation of the corresponding Michael adducts, which readily undergo cyclization to the substituted 6,7-dihydro-4H-pyrrolo[2,1-*b*][1,3]thiazine-6,7-diones **38** or **39**, depending on R [44].



R = CN, PhCO, COOEt, $CSNH_2$; Ar = Ph, C_6H_4Cl-4, C_6H_4OMe-4

Thermolysis of the spiro compounds **40** or **41** in xylene in a sealed tube at 150°C (3-3.5 h) leads to 1-substituted 2,3-dioxo-5,6-dihydropyrrolo[1,2-*a*]isoquinolines **42** or **43** [45].

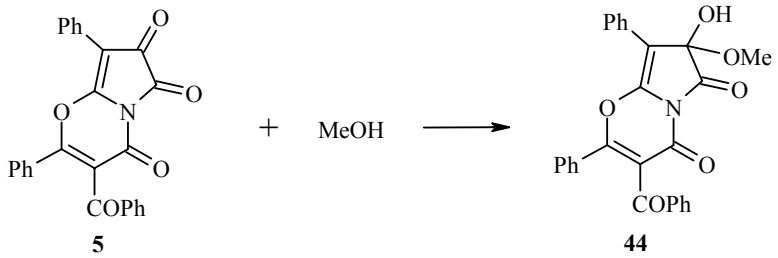


2. REACTIONS OF 2,3-DIHYDRO-2,3-PYRROLEDIONES CONDENSED WITH AZAHETEROCYCLES ON THE [*a*] SIDE WITH NUCLEOPHILES

2.1. Reactions with Water and Alcohols

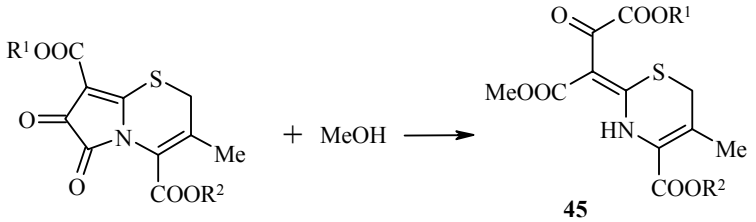
2,3-Dihydro-2,3-pyrrolediones annelated with azaheterocycles on the [*a*] side and not containing a C=O group at position 4 of the pyrroledione ring are apparently resistant to the action of OH nucleophiles; in a number of the described cases their isolation involves pouring the reaction mass into water; some of their

transformations are carried out with boiling in alcohol. However, it is known that 5-phenyl-substituted 4H-dihydropyrrolo[2,1-*b*][1,3]oxazinetrione **5** boiled in methanol forms the corresponding semiacetal **44**, the structure of which was confirmed by the mass spectrum [21].

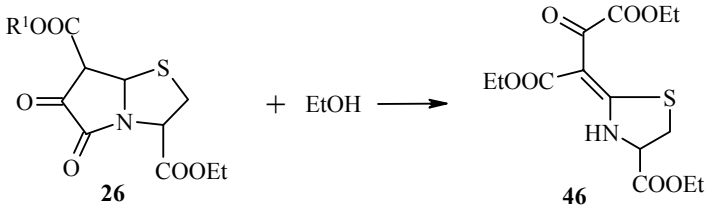


5 **44**

Compounds with a C=O group (in an ester, acyl, or aroyl substituent) at position 4 of the pyrroledione ring react vigorously with OH nucleophiles. Thus, in the case of the diesters **24** and **26** the products from opening of the dihydropyrroledione ring **45** and **46** are formed as a result of nucleophilic addition of methanol or ethanol to the lactam carbonyl [37].



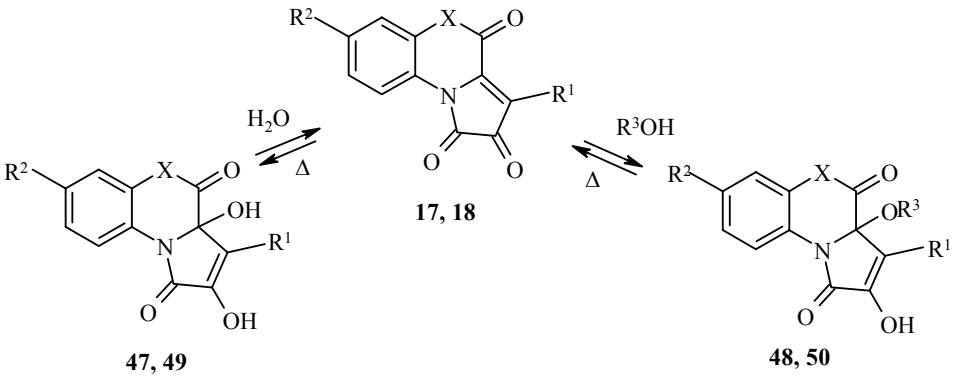
24 **45**



26 **46**

R^1 = Me, Et, R^2 = Me

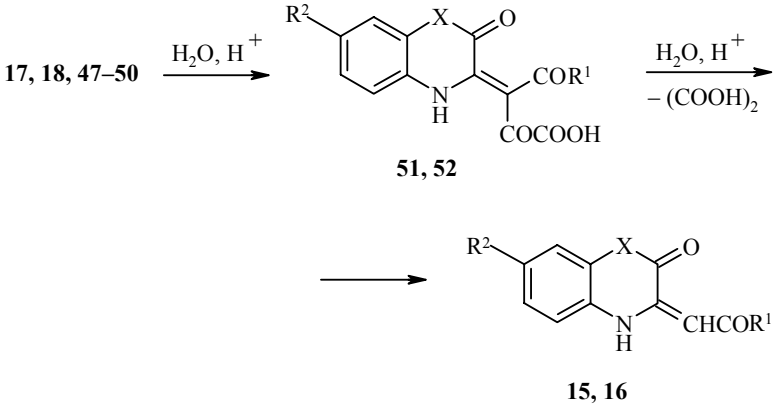
The compounds **17** and **18** mentioned in section 1, which are derivatives of 4H-dihydropyrrolo[2,1-*c*]-[1,4]benzoxazine-1,2,4-triones **17** and tetrahydropyrrolo[1,2-*a*]quinoxaline-1,2,4-triones **18** with substituents R^1 = COOAlk or COAr, react with water or alcohol almost instantaneously at room temperature when solutions of the reagents (in an equimolar ratio) are cautiously mixed. Quantitative yields of the products **47**, **48** and **49**, **50** respectively from addition to the $C_{(3a)}$ atom are obtained. The reaction is reversible, and when the adducts **47** and **49** are boiled in toluene with a Dean–Stark tube or the adducts **48** and **50** are kept under vacuum (100-150°C) the water or alcohol is eliminated and the initial compounds are formed [32, 33, 46, 47].



47, 49 **17, 18** **48, 50**

47-50 R^1 = COOAlk, COAr, where Alk = Me, Et,
Ar = Ph, C_6H_4Me-4, C_6H_4OMe-4, C_6H_4Cl-4, $C_6H_2Me_3$-2,4,6;
R^2 = H, Me; R^3 = Me, Et, Pr; **17**, **47**, **48** X = O; **18**, **49**, **50** X = NH, NPh

When the 3-aroyl-substituted compounds **17** [47] and **18** [33, 34] or their hydrate and alcohol adducts **47-50** [33, 34] are boiled in a mixture (10:1) of dioxane and 10% HCl (0.5-1 min) or in water (5-10 min) the pyrrole ring is opened, and the keto acids **51** and **52** are formed. Oxalic acid is eliminated from the latter, and the products **15** [47] and **16** [31, 33] are formed. The last products were identified by comparison with authentic samples, obtained by the reaction of methyl 4-aryl-2-hydroxy-4-oxo-2-butenoates with *o*-aminophenol, *o*-amino-*p*-cresol, and *o*-phenylenediamine.



51, 52 **15, 16**

15, **16**, **51**, **52** R^1 = Ar = Ph, C_6H_4Me-4, C_6H_4OMe-4, C_6H_4Cl-4, $C_6H_2Me_3$-2,4,6;
R^2 = H, Me; **15**, **51** X = O; **16**, **52** X = NH

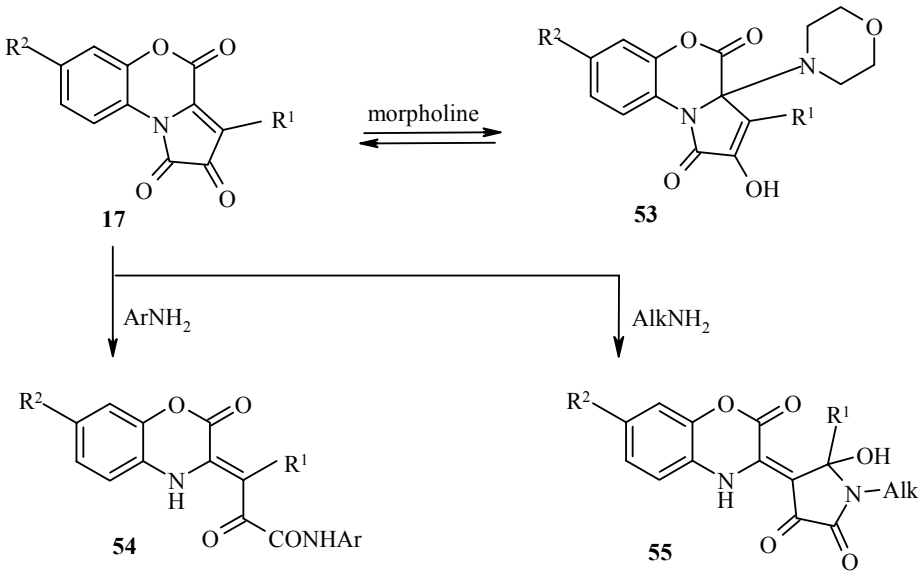
The reaction of tetrahydropyrrolo[1,2-*a*]quinoxalinetriones of type **18** (R^1 = COAr, where Ar = C_6H_4R-4, R = H, Me, Cl, Br; R^2 = H) [33, 34] with methanol (with brief boiling of equimolar amounts of the reagents in dioxane) takes place both at the $C_{(1)}$ atom with the formation of the methyl esters of keto acids of type **52** and at the $C_{(3a)}$ atom with the formation of adducts of type **50** (X = NH) [33].

The realization of two directions for the initial addition of mono-OH-nucleophiles to the $C_{(1)}$ and $C_{(3a)}$ atoms is typical of monocyclic 4-acyl-2,3-dihydro-2,3-pyrrolediones [31] and also of pyrrolediones annelated with azaheterocycles on the [*a*] side [47, 48] and is probably the result of the strain in the nonaromatic pyrroledione ring and also the presence of the two electron-withdrawing substituents, which increase its electrophilicity. In the products from the addition of water and methanol [47] the strain in this ring is reduced on account of transition of the carbon atom at position 3a from a state of sp^2-hybridization to a state of

sp^3-hybridization. In the case of dihydropyrrolo[2,1-*c*][1,4]benzoxazinetriones and tetrahydropyrrolo[1,2-*a*]-quinoxalinetriones **17** and **18** the addition of water and alcohols is the only method for the construction of systems of type **47**-**50** containing hydroxy and alkoxy groups at the bridgehead position 3a.

2.2. Reactions with Amines

3-Aroyl-4H-dihydropyrrolo[2,1-*c*]benzoxazine-1,2,4-triones **17** (R^1 = COAr) [33, 47] react readily and almost instantaneously with an equimolar amount of an amine (at room temperature with alkyl- and dialkylamines and after briefly heating with arylamines) and form three types of products, i.e., the adducts **53** (analogs of **47** and **48**) [33, 47], the substituted 2H-dihydro-1,4-benzodioxazin-2-ones **54** (analogs of **51**) [49], and the products **55** from intramolecular cyclization of the latter [32, 49].

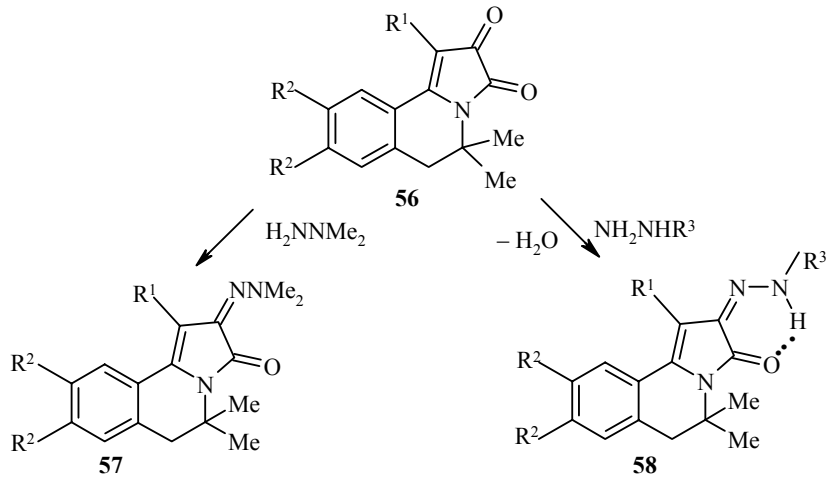


R^1 = COC_6H_4R-4 (R = H, Me); R^2 = H, Me; Alk = CH_2Ph, Bu; Ar = $C_6H_2Me_3$-2,4,6, C_6H_4OEt-4, $C_6H_4NO_2$-4, $C_6H_3NO_2$-3-Me-4, Ph, C_6H_4OMe-4, $C_6H_3Cl_2$-2,3, 2-pyridyl, 2-quinolyl, C_6H_4NHPh-2

From the trione **18** (R = Me, R^2 = H) and aniline the product of type **54** from attack by the amine at the $C_{(1)}$ atom and opening of the pyrroledione ring and also the substituted tetrahydroquinoxalinone of type **16** formed from it as a result of elimination of PhNHCO (by the action of the aniline) were obtained [31, 33].

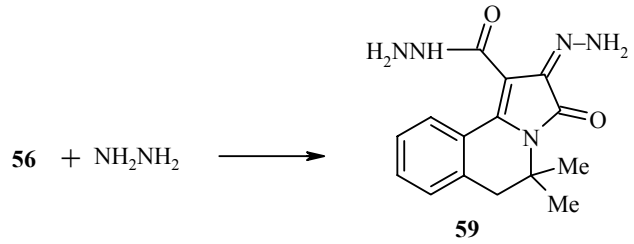
2.3. Reactions with Hydrazines and Hydroxylamine

The reaction of substituted 5,5-dimethyltetrahydropyrrolo[1,2-*a*]isoquinolinediones **56** [16, 50, 52] with hydrazine hydrate, N,N-dimethylhydrazine, phenylhydrazine, semicarbazide, and thiosemicarbazide boiled in ethanol takes place at the $C_{(2)}$=O group with the formation of the corresponding derivatives **57** or (with favorable structural factors) **58** with an intramolecular hydrogen bond [50, 51].

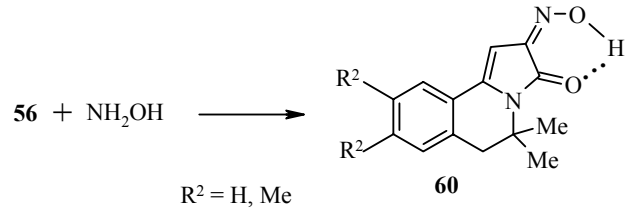


R^1 = H, Ph, COOEt, morpholinocarbonyl, R^2 = H, OMe; R^3 = H, Ph, $CONH_2$, $CSNH_2$

In a compound of the **56** type with a 1-ethoxycarbonyl group (R^1 = COOEt, R^2 = H) under analogous conditions the latter takes part, together with the $C_{(2)}$=O group [16, 50, 52], in reaction with hydrazine hydrate, and the product **59** is formed [51].

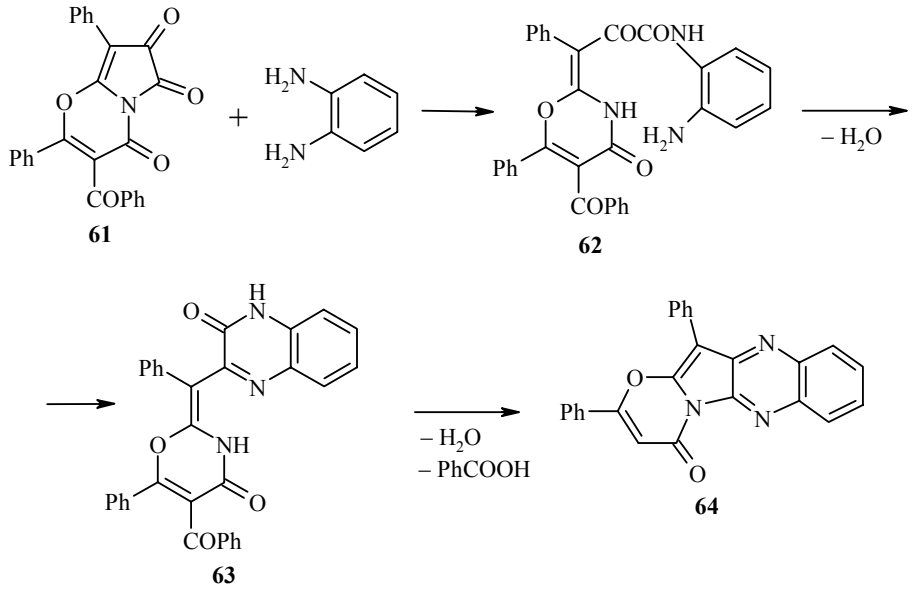


When diones of the **56** type (R^1 = H, R^2 = H, Me) are boiled with hydroxylamine in ethanol (10 min) the corresponding oximes **60**, which exist as *Z*-isomers with an intramolecular hydrogen bond, are formed [51].

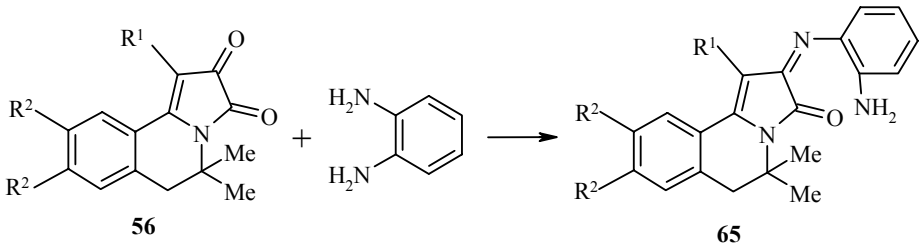


2.4. Reactions with *o*-Phenylenediamine

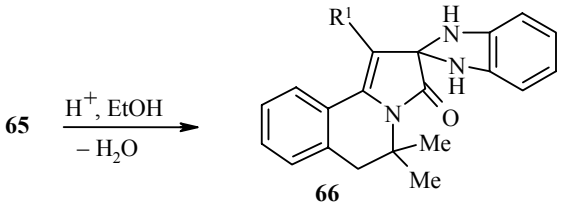
Substituted 4H-dihydropyrrolo[2,1-*b*][1,3]oxazinetrione **61** reacts with *o*-phenylenediamine at the $C_{(3)}$=O group with aminolysis of the $C_{(3)}$–N bond followed by cyclization of the obtained oxazinone **62** to the substituted 2-quinoxalone **63**. When treated with polyphosphoric acid the latter undergoes cyclization with simultaneous removal of the benzoyl group to a derivative of 1,3-oxazino[3,2-*a*]pyrrolo[4,5-*b*]quinoxaline **64** [21].



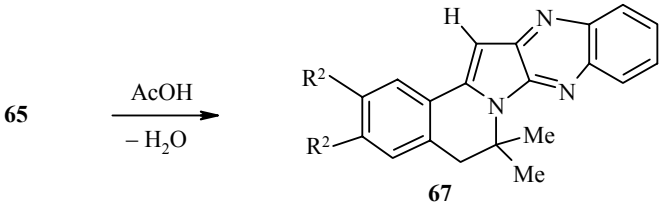
5,5-Dimethyl-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinolinediones **56** react with *o*-phenylenediamine at the $C_{(2)}$=O group with the formation of the corresponding derivatives **65**. Depending on the conditions and on the nature of substitution, the latter undergo cyclization to the spiro derivatives of benzimidazoline **66** (in ethanol) or the annelated benzopyrazines **67** and **68** (in acetic acid, see the scheme), and in the latter case hydrolytic elimination of the piperidinocarbonyl and morpholinocarbonyl groups occurs [17, 50].



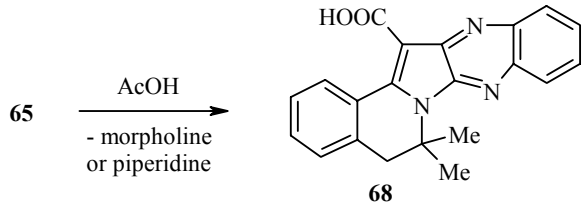
56, **65** R^1 = H, morpholinocarbonyl, piperidinocarbonyl, R^2 = H, OMe



65, **66** R^1 = morpholinocarbonyl, R^2 = H

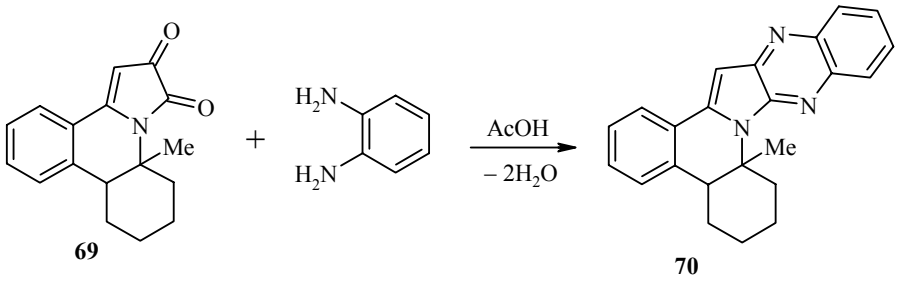


65, **67** R^1 = H, R^2 = H, OMe

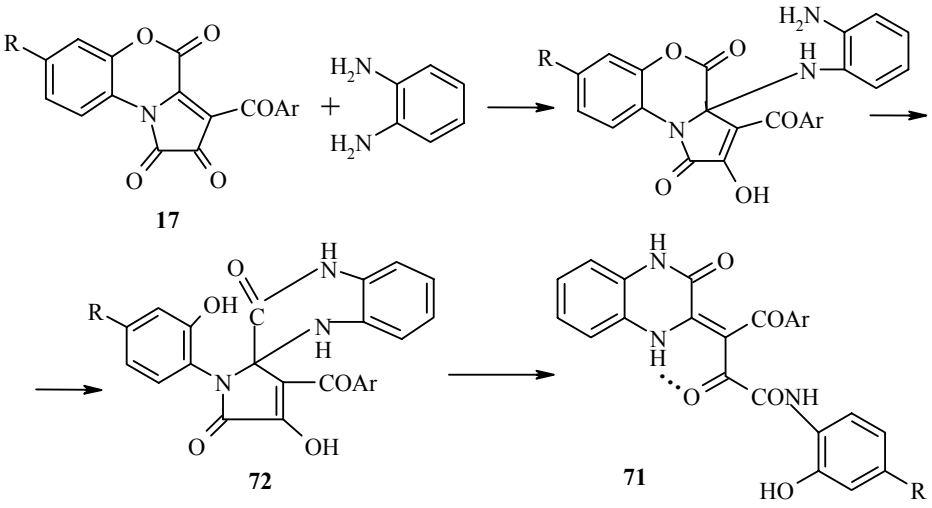


65 R^1 = morpholinocarbonyl, piperidinocarbonyl, R^2 = H

The annelated benzopyran **70** was likewise obtained from *o*-phenylenediamine and 4a-methyloctahydropyrrolo[1,2-*f*]phenanthridinedione (**69**) in acetic acid [53].



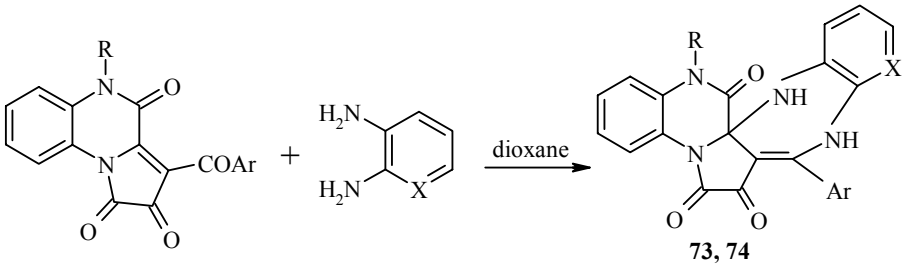
With an equimolar amount of *o*-phenylenediamine in an inert solvent (dioxane, chloroform, toluene) at room temperature 3-aroyldihydropyrrolobenzoxazinetriones of type **17** [33, 47] give almost quantitative yields of the benzopyrazinone derivatives **71** with an intramolecular hydrogen bond [33, 46, 54].



R = H, Me, Ar = Ph, C_6H_4Me-4

Initially the amino group adds to the $C_{(3a)}$ atom of compound **17**, a second amino group then attacks the lactone $C_{(4)}$=O group, and the oxazine ring opens at the $C_{(4)}$–$O_{(5)}$ bond. In the spiro compound **72** formed here the pyrrolone ring opens as a result of the strain in the spiro system and the ease of cleavage of the C–N bond in the NH–C–N fragment.

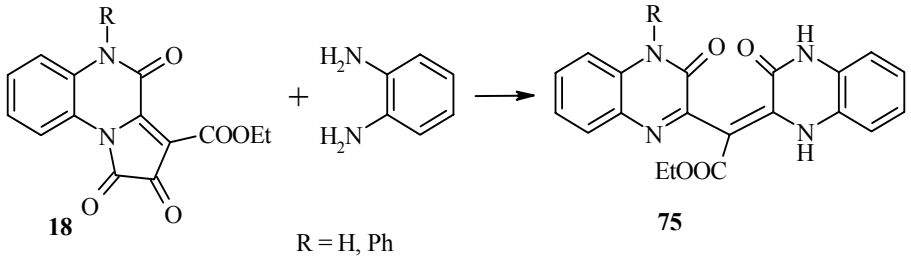
In the case of 3-aroyltetrahydropyrroloquinoxalinetriones of type **18** [33, 34] the $C_{(3a)}$ atom and the carbonyl group of the COAr fragment take part in reaction with the *o*-phenylenediamine, and as a result the products **73**, containing a benzodiazepine fragment, are formed with yields of ~100% when the reagents are briefly heated in dioxane [33, 46, 55].



73 X = CH, R = H, Ph, Ar = Ph, C_6H_4Me-4, C_6H_4OMe-4, C_6H_4OEt-4, C_6H_4Cl-4, C_6H_4Br-4, $C_6H_4NO_2$-4;
74 X = N, R = H, Ar = C_6H_4Me-4

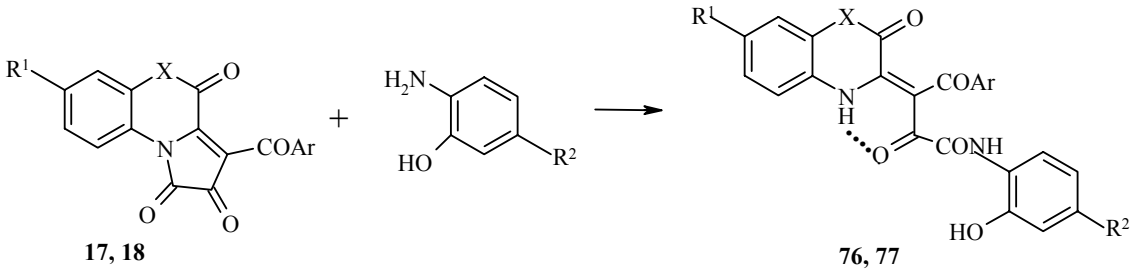
Similarly, the trione of type **18** (R = H, Ar = C_6H_4Me-4) [34] reacts with 2,3-diaminopyridine, leading to an almost quantitative yield of the product **74** with a pyridodiazepine fragment [56].

The products **75** were obtained with good yields from 3-ethoxycarbonyltetrahydropyrrolo[1,2-*a*]-quinoxalinetriones of type **18** [32] when warm solutions of equimolar amounts of the reagents were cautiously mixed [57, 58, 32].



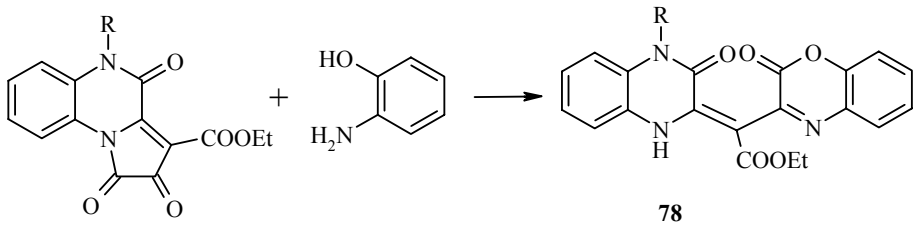
2.5. Reactions with *o*-Aminophenol and *o*-Amino-*m*-cresol

With *o*-aminophenol and *o*-amino-*m*-cresol in an inert aprotic solvent (dioxane, acetonitrile) at room temperature triones of types **17** and **18** give good yields of the products from attack by the amino group on the $C_{(1)}$ atom followed by opening of the five-membered ring **76** and **77** respectively [33].



76 X = O, R^1 = H, Me; R^2 = H, Me, Ar = Ph, C_6H_4Me-4, C_6H_4OMe-4;
77 X = NH, R^1 = H; R^2 = H, Me, Ar = Ph, C_6H_4Me-4, C_6H_4OMe-4, C_6H_4OEt-4

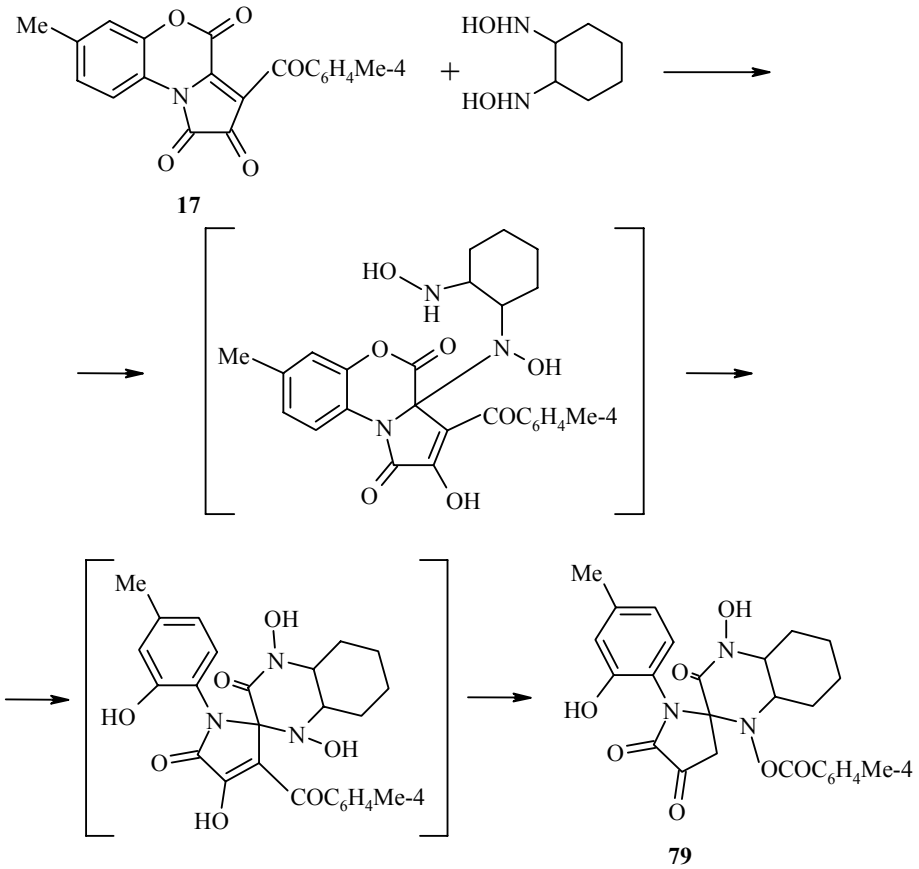
Compounds **78**, which are analogs of the products **75** obtained with *o*-phenylenediamine (see above), are formed from 3-ethoxycarbonyltetrahydropyrrolo[1,2-*a*]quinoxalinetriones of type **18** and *o*-aminophenol [57, 58].



18 R = H, Ph **78**

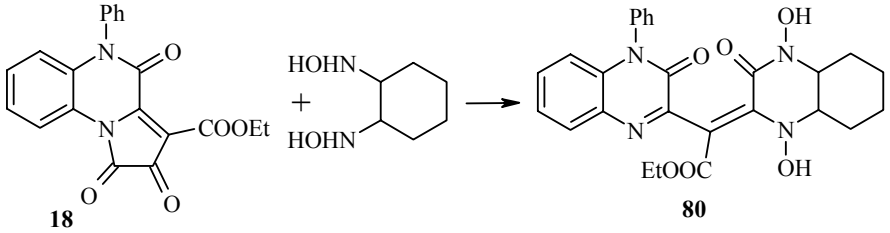
2.6. Reactions with 1,2-Di(hydroxylamino)cyclohexane

Short heating of dihydro-4H-pyrrolo[2,1-*c*]benzoxazinetrione of type **17** with 1,2-di(hydroxylamino)cyclohexane in dioxane leads to the product **79**, formed as a result of successive nucleophilic attack by the secondary amino groups on the $C_{(3a)}$ and $C_{(4)}$ atoms [33]. The reaction is accompanied by [1,4] acylotropic rearrangement of the aroyl group.



17 **79**

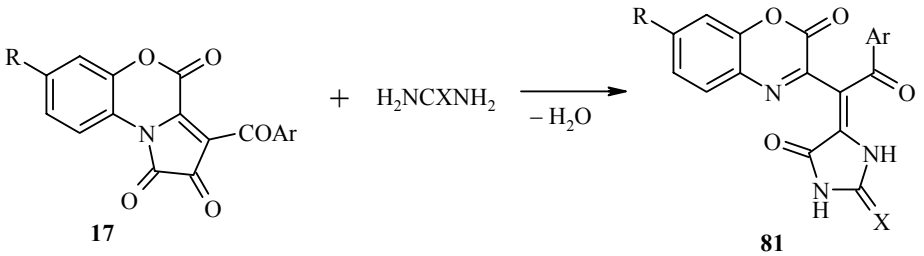
The reaction of 5-phenyl-3-ethoxycarbonyltetrahydropyrrolo[1,2-*a*]quinoxalinetrione of type **18** with the same binucleophile when solutions of the reagents are mixed and briefly heated leads to the product **80** [32] – the analog of the products **75** obtained from the triones and *o*-phenylenediamine (see p. 14).



18 **80**

2.7. Reactions with Urea and Thiourea

When the triones of type **17** [33, 47] are briefly boiled (3-5 min) with urea and thiourea in acetonitrile or dioxane, the products **81** are formed with good yields [59].



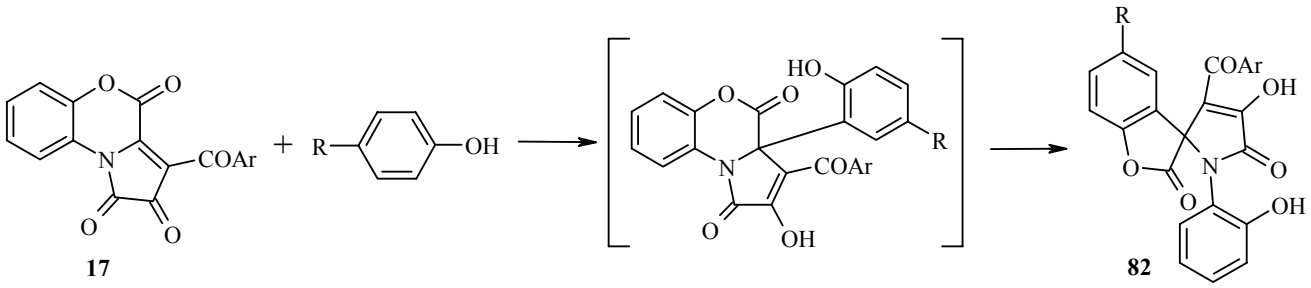
17 **81**

R = H, Me; Ar = Ph, C_6H_4Me-4; X = O, S

Compounds **81** are probably formed as a result of initial nucleophilic attack by the amino group at the $C_{(1)}$ atom of the initial triones, opening of the pyrroledione ring at the $N_{(10)}$–$C_{(1)}$ bond, attack by the second amino group at the $C_{(2)}$ atom of the side chain, and closure of the imidazolidinedione or imidazolidinonethione rings.

2.8. Reactions with Phenols

The reaction of triones of type **17** with phenols having free *ortho* positions leads to the formation of spiro products, i.e., substituted 2-oxo-2,3-dihydrobenzofurans **82** [58].

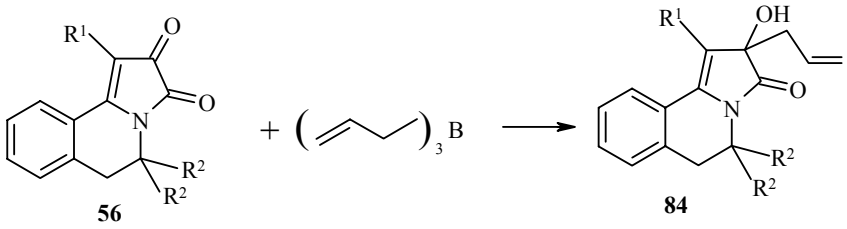


17 **82**

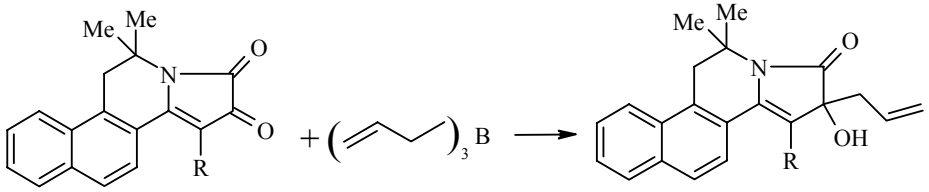
Ar = Ph, C_6H_4Me-4, R = H, Br

2.9. Allylboronation Reactions

Substituted tetrahydropyrrolo[1,2-*a*]isoquinoline-2,3-diones of type **56** [12, 17, 23, 52] and their benzannelated analogs **83** [16, 27, 60] react with triallylborane at the $C_{(2)}$=O group with the formation of the corresponding unsaturated alcohols **84** and **85** [60].



56 **84**

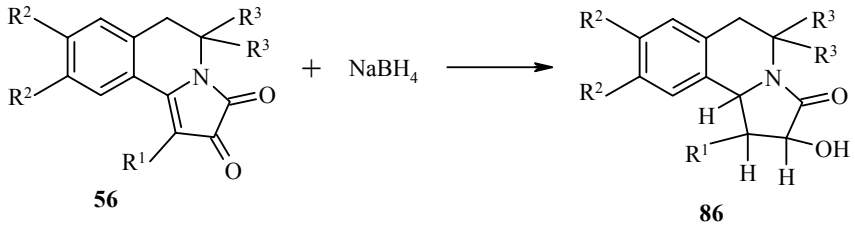


83 **85**

56, **84** R^1 = H, Me, pyrrolidinocarbonyl, piperidinocarbonyl, morpholinocarbonyl, R^2+R^2 = $(CH_2)_4$; **83**, **85** R = H, COOEt

2.10. Reduction of 2,3-Dihydrohetareno[*a*]pyrrole-2,3-diones

During the reduction of compounds of type **56** with sodium borohydride or with hydrogen over Raney nickel the $C_{(2)}$=O group is reduced to an alcohol group, and the double bond in the dihydropyrrole ring is hydrogenated, resulting in the formation of the keto alcohols **86** [12, 38, 39].

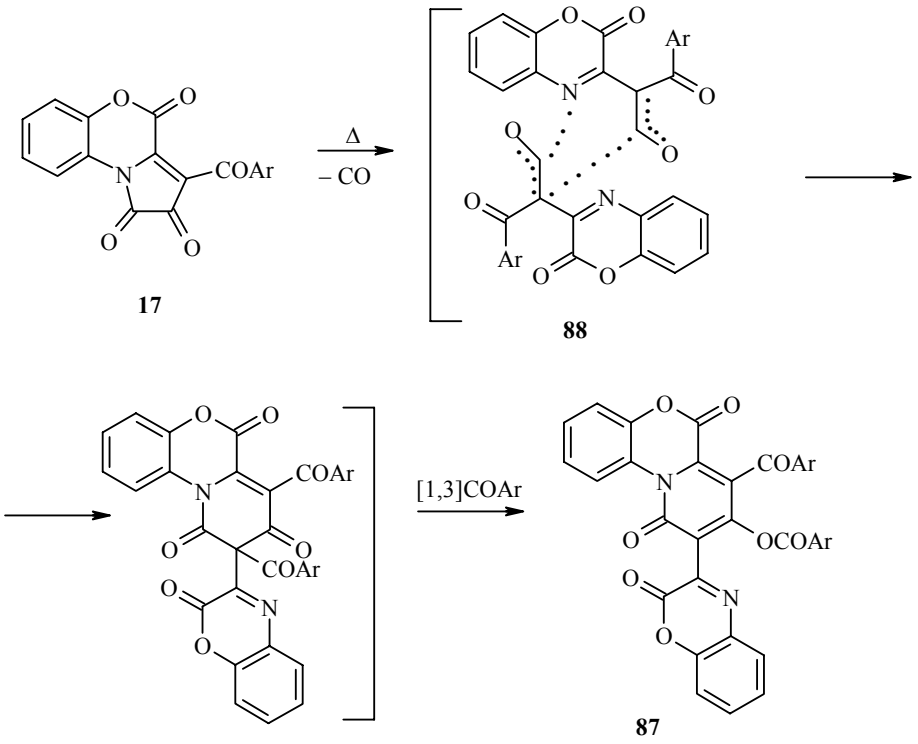


56 **86**

R^1 = H, COOMe, $C_6H_3(OEt)_2$-3,4; R^2 = H, OAlk, where Alk = Me, Et; R^3 = H, Me; R^3+R^3 = $(CH_2)_4$

2.11. Thermolysis of 2,3-Dihydropyrrole-2,3-diones Annelated with Azaheterocycles on the [*a*] Side

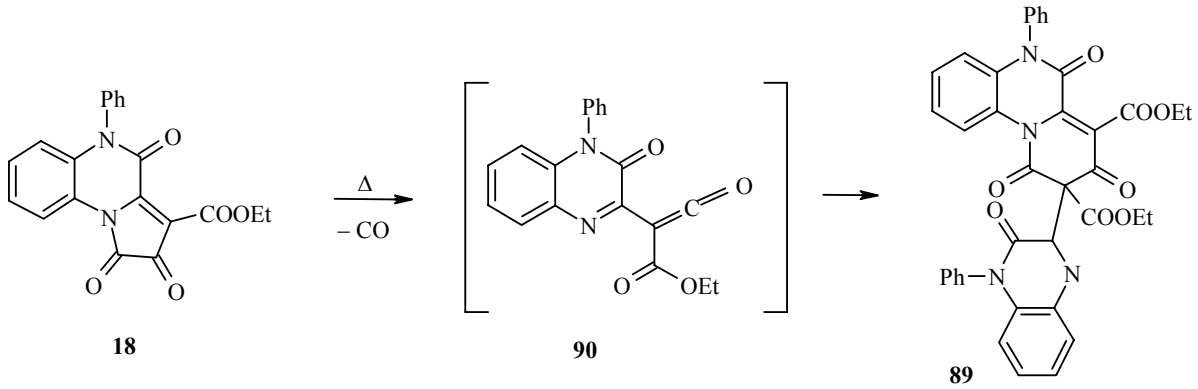
The treatment of 3-aroyldihydro-1H-pyrrolo[2,1-*c*]benzoxazinetriones of type **17** [47] in an inert aprotic solvent (Dowtherm A) at 160-190°C (20-30 min) leads to the products **87**, the structure of which was confirmed by X-ray crystallographic analysis [61].



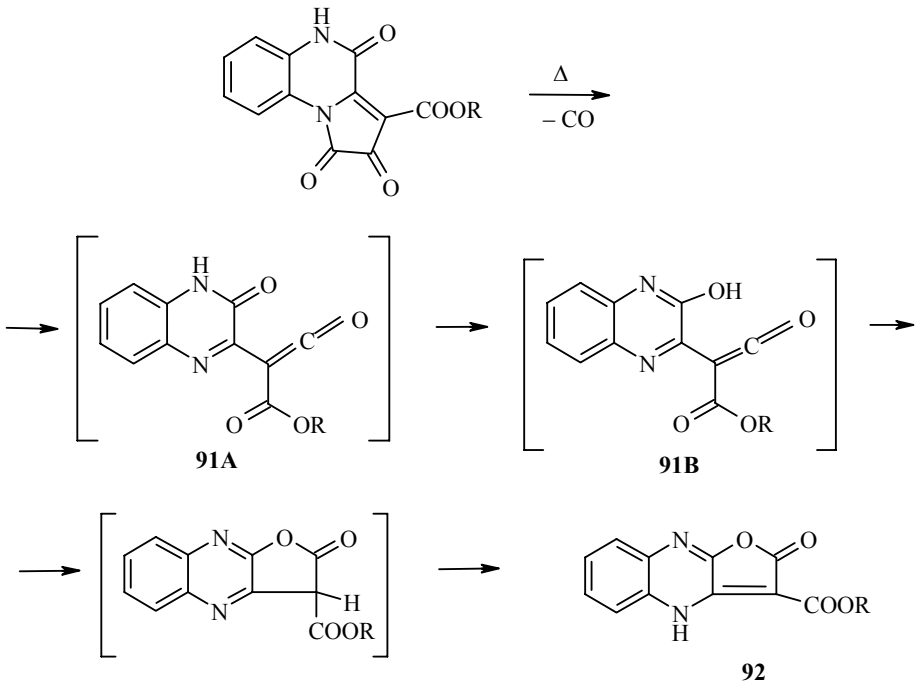
Ar = Ph, C_6H_4Me-4, C_6H_4OMe-4, C_6H_4Br-4, C_6H_4Cl-4

The products **87** are formed as a result of [4+2] cycloaddition, in which two molecules of **88** initially generated during thermolysis participate. One of them acts as diene (the N=C–C=C fragment) and the other as dienophile (the C=C bond of the ketene fragment) with subsequent acylotropic [1,3]-shift of the aroyl group.

Treatment of 5-phenyl-3-ethoxycarbonyltetrahydropyrrolo[1,2-*a*]quinoxalinetrione **18** in Dowtherm A at 185-187°C (20-30 min) led to the product **89**, the structure of which was confirmed by the data from X-ray crystallographic analysis [62]. In this case [4+2] cycloaddition also occurs with the participation of two molecules of the ketene **90**, but the above-mentioned acylotropic [1,3]-shift of the ester group does not occur.



Pyrolysis of the 5-unsubstituted esters **18** leads to the ketenes **91**, which readily change from the amide form A to the hydroxyimine form B. The latter then undergoes intramolecular cyclization (by acylation of the hydroxy group with the ketene fragment). This leads to the product **92**, which exists in the form where the proton is located at the nitrogen atom at position 4 [63].



R = Me, Et

In the time since the review was written a whole new series of interesting publications have appeared on 2,3-dihydro-2,3-pyrrolediones annelated with azaheterocycles on the [*a*] side. In our opinion the most important of these are the papers [64-68].

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