Reactions of fused pyrrole-2,3-diones with dinucleophiles

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DOI: http://dx.doi.org/10.3998/ark.5550190.p008.889

Abstract

This review summarizes a series of studies on the reactions of 1*H*-pyrrole-2,3-diones, fused at the C^5-N^1 bond to nitrogen-containing heterocycles, with nucleophiles, leading to the formation of C–C bonds. Reactions of pyrrolobenzoxazinetrione and pyrroloquinoxalinetrione with CH,OH-, CH,NH-binucleophiles, and dienophiles are discussed.

Keywords: 1*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-trione, 1*H*-pyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-trione, binucleophiles, heterocyclization

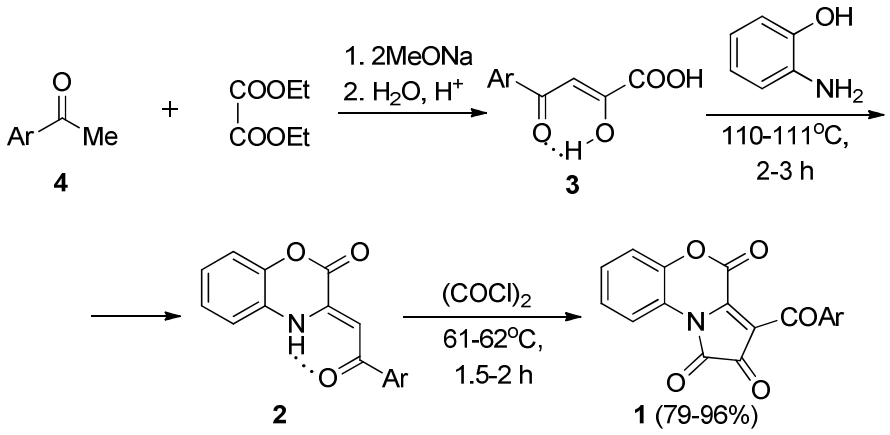
Table of Contents

1. Introduction

The chemistry of 1*H*-pyrrole-2,3-diones annulated with azaheterocycles on the [e] side first evolved in the seventies, when the application of pyrrole-2,3-dione derivatives as synthetic blocks for the construction of alkaloid molecules was first demonstrated.[1-5] Until the early nineties these annulated pyrrolediones were studied almost exclusively as subjects for photo-reduction and photocyclisation, or as dienophiles in Diels-Alder reactions (for the production of intermediate compounds in the synthesis of alkaloids). A large number of these studies were performed by a certain groups of investigators.[1-3] Individual reports on reactions with nucleophilic reagents, allylboronation, reduction, and thermal transformations of 1*H*-pyrrole-2,3-diones annulated with azaheterocycles on the [e] side have only begun to be published recently. In the present review we consider publications on the interaction of 4-acyl-1*H*-pyrrole-2,3-diones fused to 1,4-benzoxazine and quinoxalin-2-one fragments with nucleophiles, leading to the initial formation of a C–C bond.

2. Synthesis of 3-Aroyl-1*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-triones

Synthesis of 3-aroyl-1*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-triones **1**, which was first described in 1992,[6-8] involves the interaction of substituted 1,4-benzoxazine-2-ones **2** with oxalyl chloride (Scheme 1). Benzoxazinones[9] **2** were synthesised by reaction of *o*-aminophenol with aroylpyruvic acids **3**, which were obtained by Claisen condensation between acetophenones **4** and diethyl oxalate.



1, **2**: Ar = Ph, C_6H_4Me-4, C_6H_4OMe-4, C_6H_4Cl-4, C_6H_4Br-4, α-naphthyl, 5-methyl-2-furyl, 2-thienyl, C_6H_4OEt-4, $C_6H_4NO_2$-4

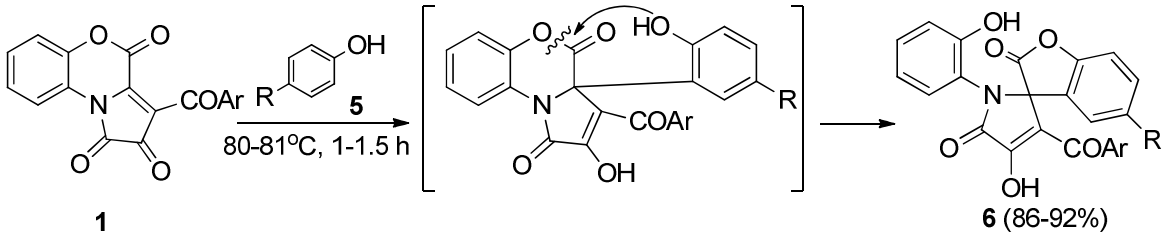
Scheme 1. Synthesis of 3-aroyl-1*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-triones (**1**).

3. Formation of a C–C Bond by Reactions of 3-Aroyl-1*H*-pyrrolo[2,1-*c*]-[1,4]benzoxazine-1,2,4-triones with Nucleophiles

Nucleophilic transformations of 3-aroyl-1*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-triones by the action of OH- and NH-mono-, and NH,NH-, NH,OH-, NH,SH-, and CH,NH-binucleophiles are convenient methods for the synthesis of carbonyl derivatives of five- and six-membered nitrogen-containing heterocycles, ensembles of such heterocycles, and fused heterocyclic systems.[8,10-13] In most studies on the interaction of pyrrolobenzoxazinetriones with binucleophiles, the initial C–N[10-23], C–O[6,8,24], and C–S[8,25] bonds formation occurs, and there are few studies on the formation of a C–C bond, an important structural unit of organic chemistry.

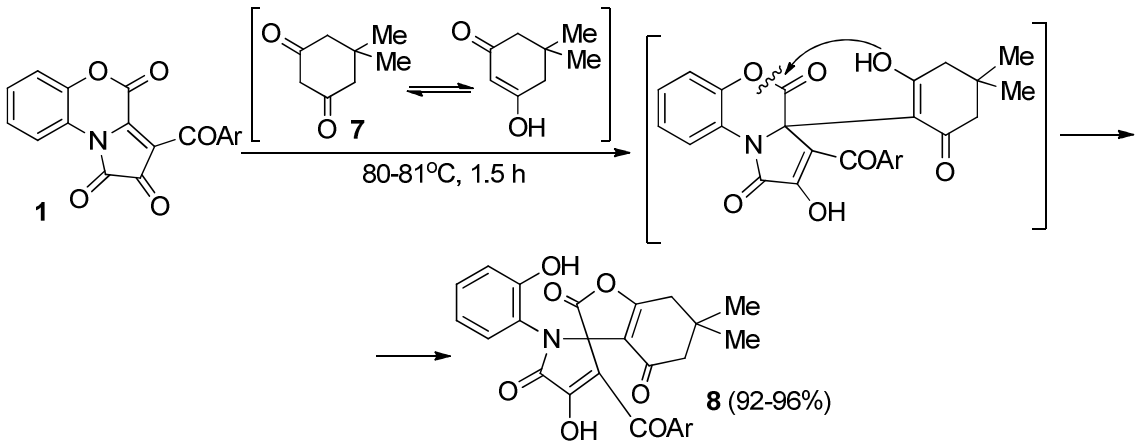
3.1. Reactions with CH,OH-binucleophiles

The reaction of pyrrolobenzoxazinetriones **1** with phenols **5** that have free *ortho* positions leads to the formation of spiro products – substituted 2-oxo-2,3-dihydrobenzofurans **6** (Scheme 2).[8]



Scheme 2. Reaction of pyrrolobenzoxazinetriones (**1**) with phenols (**5**).

Racheva and co-workers reported the interaction of pyrrolobenzoxazinetriones with cyclic enols (dimedone and indanedione). These enols are known to exist in solution as an enol tautomer with the hydroxy group and hydrogen atom at the double bond in a fixed *cis* orientation and they are capable of acting as 1,3-CH,OH-binucleophiles. The reaction of 3-aroyl-1*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-triones **1** with 5,5-dimethyl-1,3-cyclohexanedione **7** (dimedone) produced substituted 1*H*-pyrrole-2-spiro-3'-(2',4'-dioxo-2',3',4',5',6',7'-hexahydro-1'-benzofurans) **8** (Scheme 3).[26,27]



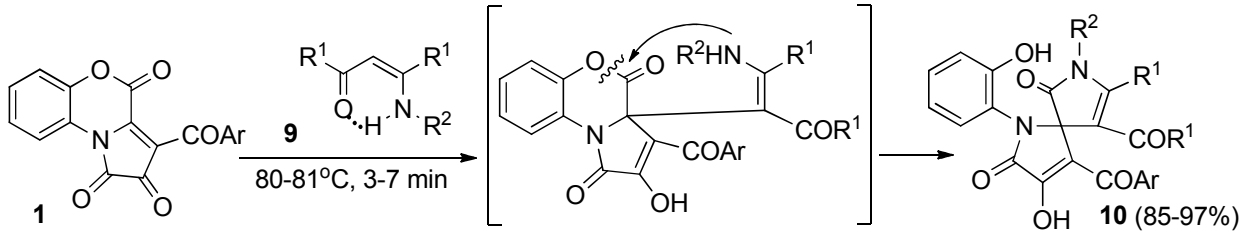
Scheme 3. Reaction of pyrrolobenzoxazinetriones (**1**) with dimedone (**7**).

Racheva and co-workers hypothesised that the described reaction (Scheme 3) involves the initial addition of an activated C^2H group in the enol form of **7** to the C^{3a} in molecule **1**. This is followed by furan ring closure via intramolecular attack by the enolic OH group on the lactone carbonyl carbon atom C^4 in the oxazine ring and opening of the latter at C^4–O^5. This interaction may be regarded as an example of regioselective construction of the difficult to access spiro[1-benzofuran-3,2′-pyrrole] system with various substituents in several positions on both heterocycles.

3.2. Reactions with CH,NH-binucleophiles

3.2.1. Reactions with acyclic CH,NH-binucleophiles

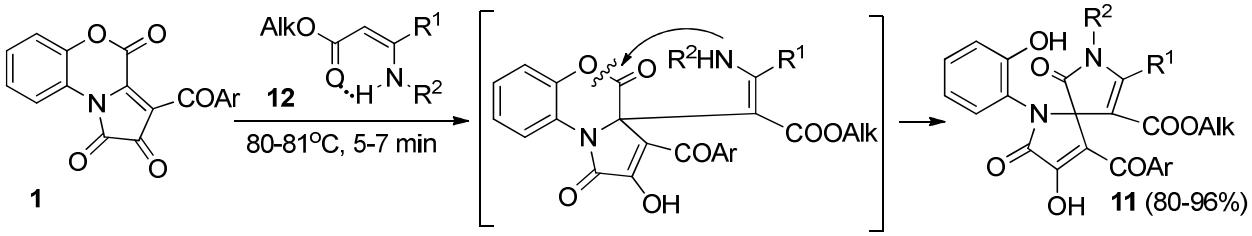
A series of reports described the interactions of 3-aroyl-1*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-triones with acyclic CH,NH-binucleophiles (enamino ketones **9**), which exist as Z isomers with an intramolecular hydrogen bond formed by the NH proton and ketone carbonyl oxygen atom. Additionally, the *β*-CH and NH groups are oriented on different sides with respect to the C=C double bond, which makes compounds **9** difficult to react as binucleophiles. Racheva and co-workers[28] described the reaction of pyrrolobenzoxazinetriones **1** with acyclic enamino ketones **9**, produced substituted 1,7-diazaspiro[4.4]nona-3,8-diene-2,6-diones **10** (Scheme 4).



Scheme 4. Interaction of pyrrolobenzoxazinetriones (**1**) with acyclic enamino ketones (**9**).

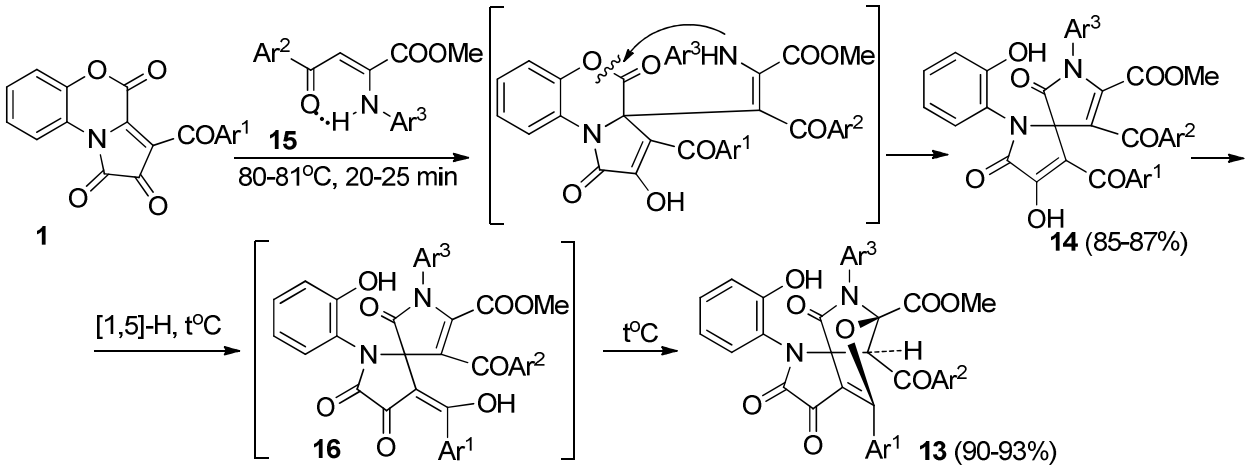
Presumably, in the first step, the activated *β*-CH group in acyclic enamino ketone **9** is added at the carbon atom in the 3a-position of pyrrolobenzoxazinetrione **1**. Next, isomerisation of the enamino fragment from the *Z* to the *E* configuration and pyrrole ring closure occurs. This results from the intramolecular attack by the amino group on the lactone carbonyl carbon atom C^4 in the oxazine ring of **1**, which is accompanied by cleavage of the C^4–O^5 bond.

The authors of manuscripts[29,30] reported the synthesis of substituted alkyl 2,5-dihydro-1*H*-pyrrole-2-spiro-3'-(2-oxo-2,3-dihydro-1*H*-pyrrole-4-carboxylates) **11** from pyrrolobenzoxazinetriones **1** and acyclic *β*-enamino esters **12** (Scheme 5). The reaction follows a scheme analogous to the one shown above.



Scheme 5. Interaction of pyrrolobenzoxazinetriones (**1**) with acyclic *β*-enamino esters (**12**).

Racheva and coworkers[31,32] reported the synthesis of a structurally unique bridged heterocyclic system (7-oxa-2,9-diazatricyclo[6.2.1.0^{1,5}]undecane **13**) through intermolecular cyclisation of 1,7-diazaspiro[4.4]nona-3,8-diene-8-carboxylates **14** (Scheme 6). Compounds **14** were obtained from the reaction of 3-aroyl-1*H*-pyrrolo[2,1-c][1,4]benzoxazine-1,2,4-triones **1** with α-enamino esters **15**.



Scheme 6. Interaction of pyrrolobenzoxazinetriones (**1**) with α-enamino esters (**15**)

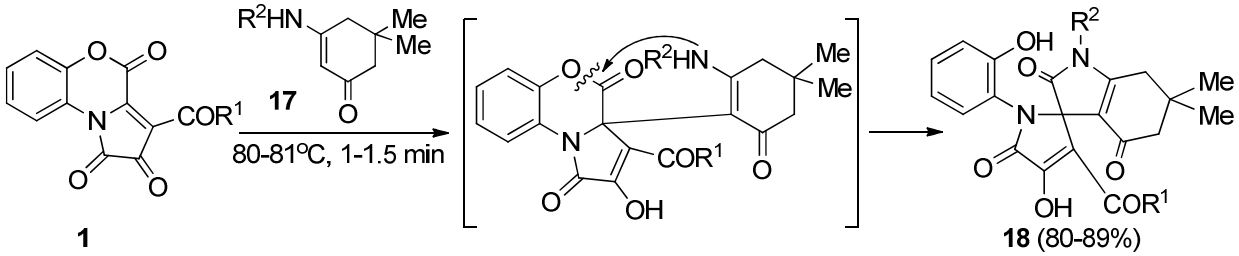
Formation of compounds **14** occurred in a similar manner as described above. Intramolecular cyclization of compounds **14** to bridged structures **13** during the attempted recrystallisation from ethyl acetate involves the addition of the enolic hydroxy group in the hydroxymethylidene tautomer **16** at the C^5 atom of the neighbouring pyrrole ring.

3.2.2. Reactions with cyclic CH,NH-binucleophiles

3-Amino-5,5-dimethyl-2-cyclohexenones **17** are regarded as dimedone imines, and they exist as the corresponding enamino tautomers. The authors[33-37] selected these compounds to be used as 1,3-CH,NH-binucleophiles due to their simplicity of preparation[38] and the ease with which the substituent on the nitrogen atom can be varied. It should be noted that cyclic enamino ketones **17** exist as (*E*)-isomers with a fixed *cis* orientation of the NH group and hydrogen atom at the double bond. They are capable of acting as 1,3-CH,NH-binucleophile.

To estimate the effect of substituents in the substrate and reagent on the reaction course, the authors[35] used pyrrolobenzoxazinetriones **1**, which have an electron-acceptor (bromine atom) and electrondonor (methoxy group) substituents in the *para* position of the 3-benzoyl group, and enamines **17**, which have various substituents on the nitrogen atom.

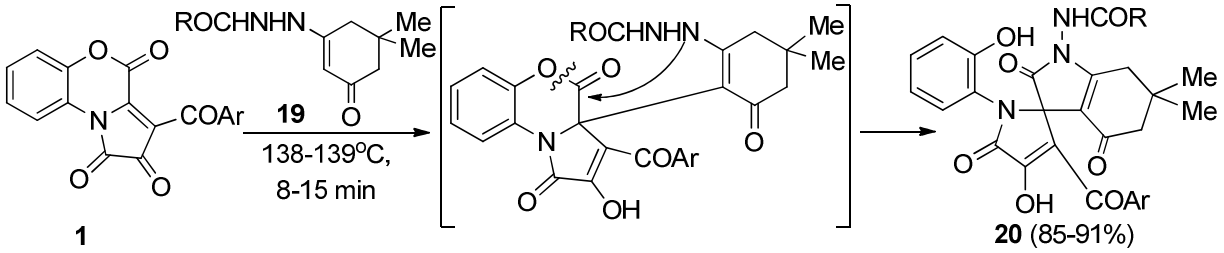
3-Aroyl-1*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-triones **1** interacted with 3-amino-5,5-dimethyl-2-cyclohexenones **17**, and resulted in the formation of a substituted spiro-bis-heterocyclic system **18** (Scheme 7).



Scheme 7. Interaction of pyrrolobenzoxazinetriones (**1**) with 3-amino-5,5-dimethyl-2-cyclohexenones (**17**)

The authors[35] reported that alkyl or aryl substitution of the nitrogen atom in enamines **17** almost does not affect the course of the reaction. They noted only an appreciable reduction in the reaction rate with N-aryl-substituted compounds **17**. An analogous effect was produced by introducing a methoxy group to the *para* position of the benzoyl substituent in pyrrolobenzoxazinetrione **1**, but the reaction direction did not change.

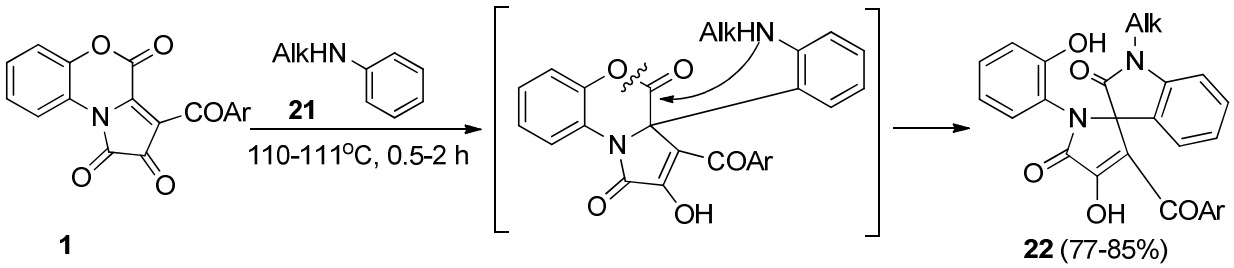
3-Aroyl-1*H*-pyrrolo[2,1-c][1,4]benzoxazine-1,2,4-triones **1** react with cyclic enehydrazino ketones **19** in a similar way to produce compounds **20** (Scheme 8).[39,40]



Scheme 8. Interaction of pyrrolobenzoxazinetriones (**1**) with cyclic enehydrazino ketones (**19**).

3.2.3. Reactions with N-alkylanilines

The interaction of 3-aroyl-1*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-triones **1** with N-alkylanilines **21** proceeds in a similar manner as the above reactions, thus giving rise to compounds **22** (Scheme 9).[41]

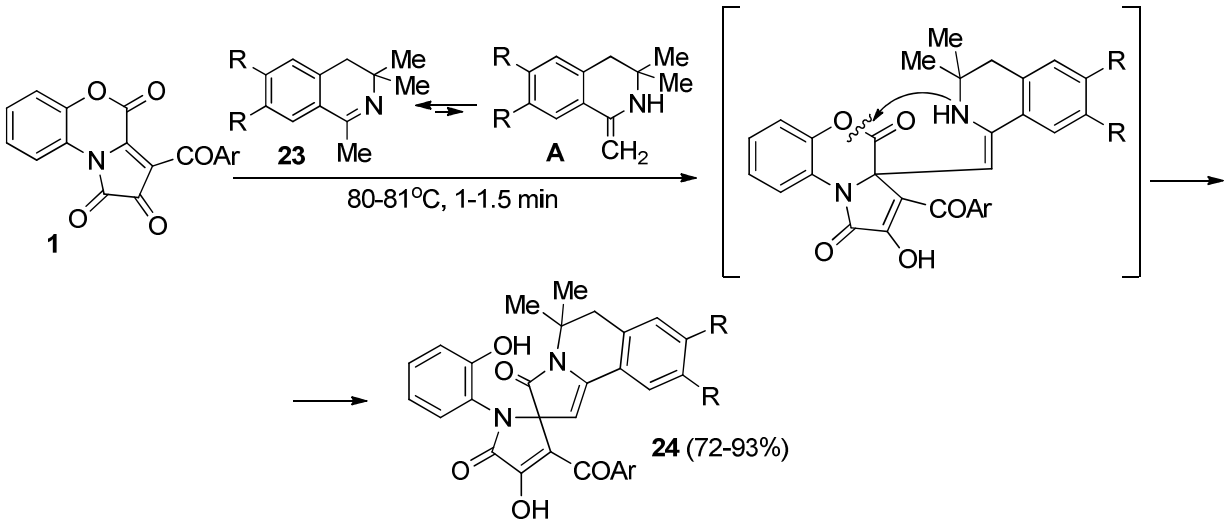


Scheme 9. Interaction of pyrrolobenzoxazinetriones (**1**) with N-alkylanilines (**21**).

3.2.4. Reactions with heterocyclic CH,NH-binucleophiles

One of the representatives of the heterocyclic enamines is substituted 1-methyl-3,4-dihydroisoquinoline, which can exist not only in imine form, but also in the tautomeric enamine form.[42] In its tautomeric form, 1-methylen-1,2,3,4-tetrahydroisoquinoline contains an enamino fragment with two nucleophilic groups, and is promising targets for research.

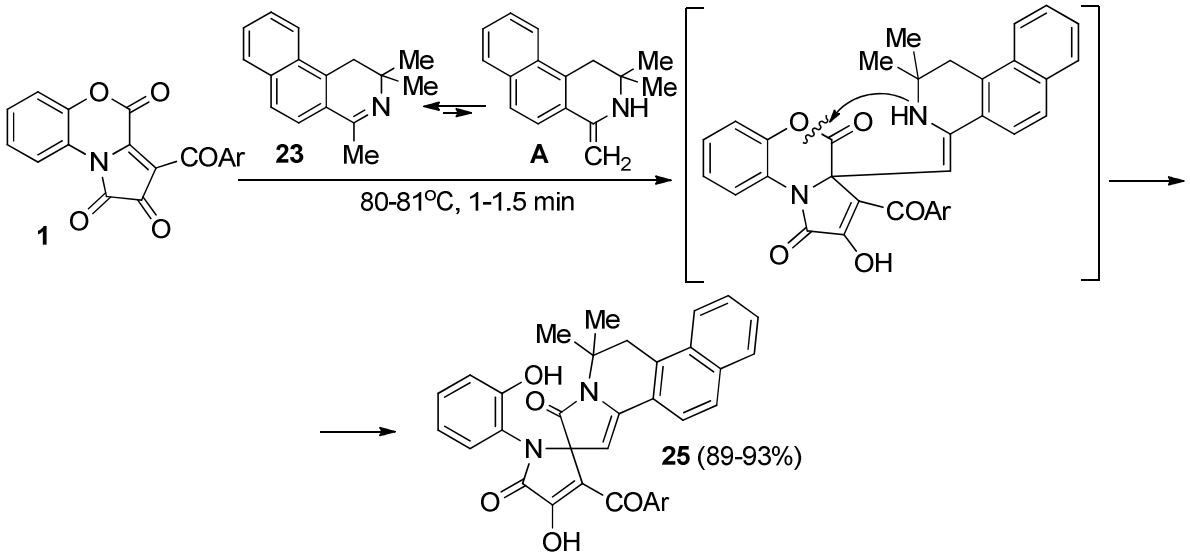
Pyrrolobenzoxazinetriones **1** interacted with 1-methyl-3,4-dihydroisoquinolines **23**, with sequential nucleophilic addition of *β*-CH and NH groups of the tautomeric enamine form **A** of isoquinolines **23** on the C^{3a} and C^{4} atoms of pyrrolobenzoxazinetriones **1** and pyrrole ring closure occurs. This results from the intramolecular attack by the NH group on the lactone carbonyl carbon atom C^{4} in the oxazine ring of **1**, which is accompanied by cleavage of the C^{4}–O^{5} bond. This resulted in the formation of the substituted 5',6'-dihydro-1*H*-spiro[pyrrole-2,2'-pyrrolo[2,1-*a*]isoquinoline]-3',5-diones **24** (Scheme 10).[43,44]



Scheme 10. Interaction of pyrrolobenzoxazinetriones (**1**) with isoquinolines (**23**).

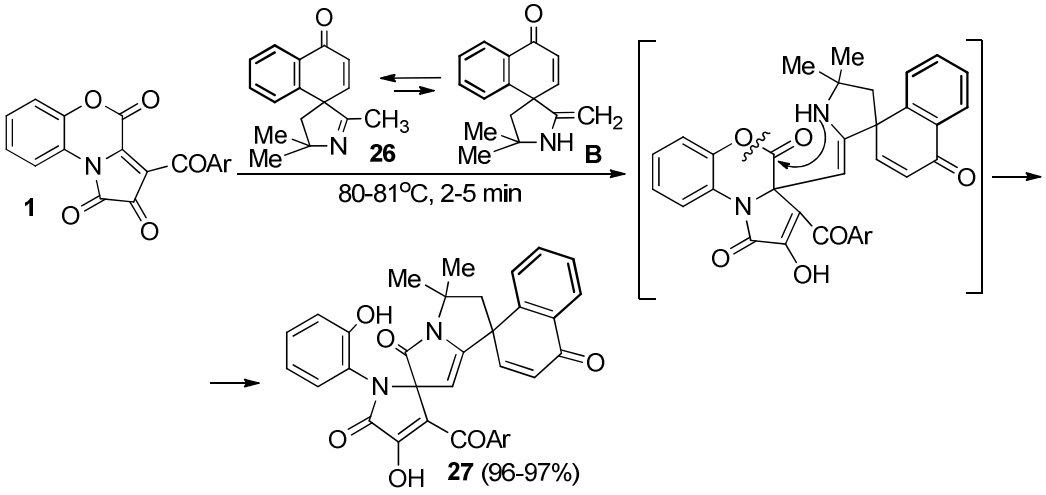
The described interaction (Scheme 10) may be an example of a regioselective synthetic pathway to a previously inaccessible spiro-bis-heterocyclic pyrrolo[2,1-a]isoquinoline-2-spiro-2-pyrrole system.

A previous report[44] described a novel approach to access the 13-azagonanes – heterocyclic analogs of steroids, which have a spiro-fused pyrrole ring at C^{16} of the steroid skeleton.[45] This approach consisted of an interaction of pyrrolobenzoxazinetriones **1** with 2,2,4-trimethyl-1,2-dihydrobenzo[*f*]isoquinoline **23**, and resulted in the formation of substituted benzo[*f*]pyrrolo[2,1-a]isoquinoline-9-spiro-2-pyrroles **25** (Scheme 11).



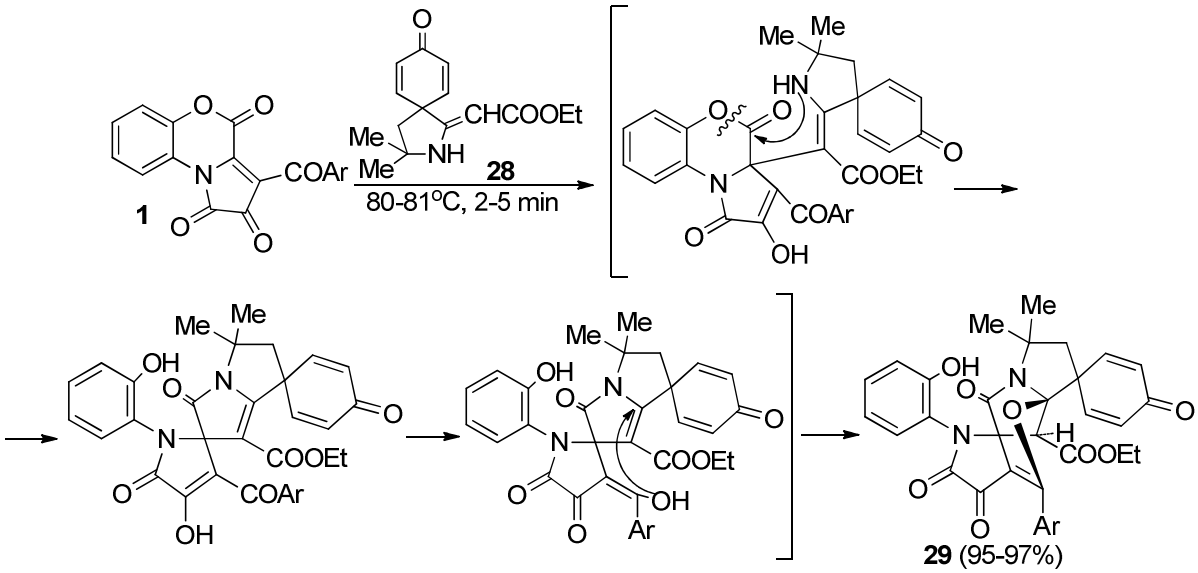
Scheme 11. Interaction of pyrrolobenzoxazinetriones (**1**) with 1,2-dihydrobenzo[*f*]isoquinoline (**23**).

Another example of spiro-heterocyclization is the reaction of 3-aroyl-1*H*-pyrrolo-[2,1-*c*][1,4]benzoxazine-1,2,4-triones with spiro heterocyclic enamines. Konovalova *et al.*[46] described the interaction of 3-aroyl-1*H*-pyrrolo-[2,1-*c*][1,4]benzoxazine-1,2,4-triones **1** with 2′,5′,5′-trimethyl-4′,5′-dihydro-4*H*-spiro[naphthalene-1,3′-pyrrol]-4-one **26**, which may be regarded as potential 1,3-CH,NH-binucleophile, to give substituted 2′,3′-dihydrodispiro[naphthalene-1,1′-pyrrolizine-6′,2″-pyrrole]-4,5′,5″(1″*H*)-triones **27** (Scheme 12). This reaction is an example of regioselective synthesis of a previously inaccessible dispiro heterocyclic system with various substituents at several positions of both heterocyclic fragments.



Scheme 12. Interaction of pyrrolobenzoxazinetriones (**1**) with spiranes (**26**).

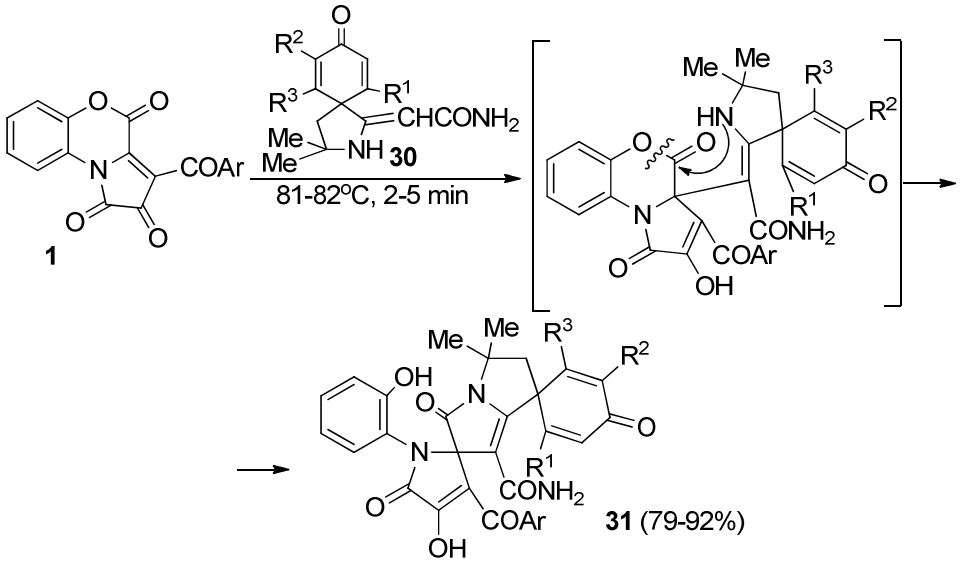
While continuing studies on analogous transformations, Konovalova and coworkers[47,48] examined the reaction of the same pyrrolobenzoxazinetriones with a spiro heterocyclic enamine containing an additional functional group (ester moiety). The reactions of 3-aroyl-1*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-triones **1** with ethyl (2*Z*)-2-(3,3-dimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)-acetate **28** were carried out by heating equimolar amounts of the reactants in boiling anhydrous benzene for 2–5 min. As a result, they isolated high yields of substituted ethyl 3′,4,4′,13′-tetraoxospiro[2,5-cyclohexadiene-1,9'-(7′-oxa-2′,12′-diazatetracyclo[6.5.1.0^{1,5}.0^{8,12}]tetradec-5′-ene)]-14′-carboxylates **29** (Scheme 13), whose structure was confirmed by the X-ray diffraction data.[48]



Scheme 13. Interaction of pyrrolobenzoxazinetriones (**1**) with spirane (**28**).

Analogous intramolecular cyclization was previously observed in the reaction of pyrrolobenzoxazinetriones with α-enamino esters.[31,32]

In 2014, the same group of authors[49] showed that 3-aroyl-1*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-triones **1** interacted with substituted 2-(3,3-dimethyl-8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)acetamides **30**, resulting in the formation of substituted dispiro pyrrolizidines **31** (Scheme 14).



Scheme 14. Interaction of pyrrolobenzoxazinetriones (**1**) with substituted 2-(8-oxo-2-azaspiro[4.5]deca-6,9-dien-1-ylidene)acetamides (**30**).

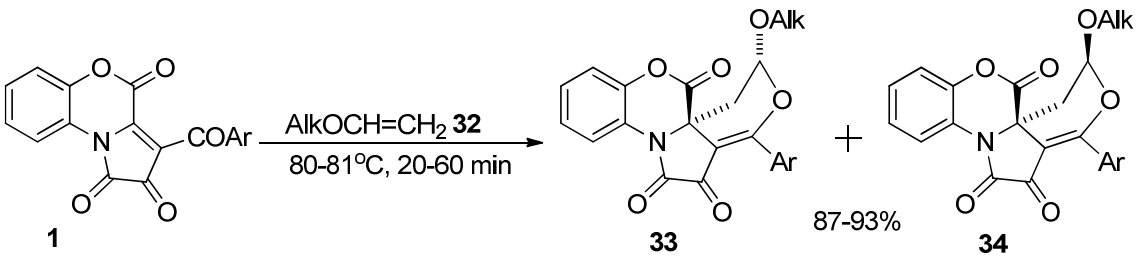
Konovalova *et al*. hypothesised that the described reaction involved the initial addition of an activated *β*-CH group of **30** to the C^{3a} in molecule **1**. This was then followed by closure of the pyrrole ring via an intramolecular attack by the NH group on the lactone carbonyl carbon atom C^4 in the oxazine ring and opening of the latter at C^4–O^5. It should be noted that the most favourable nucleophilic reaction centre is the acetamide group NH_2, according to semiempirical AM1 quantum-chemical calculations (Hyperchem 8.0 software package), but not the *β*-CH or NH groups of the enamine fragment. However, the NH_2 group does not participate during this interaction.

Products **27** and **31** may be regarded as dispiro heterocyclic, while products **29** are bridged analogs of the pyrrolizidine alkaloids. The examined reactions are examples of regioselective construction of difficult to access functionalised systems. Derivatives of pyrrolizidine alkaloids exhibit important pharmacological properties.[50] Among these compounds, the most significant are indicine *N*-oxide, platiphillin, and sarracine, which are important as antitumor and spasmolytic drugs.

3.2.5. Reactions with dienophiles

4-Acyl substituted pyrrolobenzoxazinetriones are able to participate as heterocyclic dienes fragment of the C^{3a}=C^3-C=O in thermally initiated [4+2]-cycloaddition reactions, and a fragment of the C^{3a}=C^3 in photochemically initiated [2+2]-cycloaddition reactions with polar dienophiles. The wide number of potential polar dienophiles leads to the possibility of the synthesis of inaccessible condensed heterocyclic systems. For example, the interaction of 3-aroylpyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-triones **1** with alkyl vinyl ethers **32** gives rise to the stereoisomers

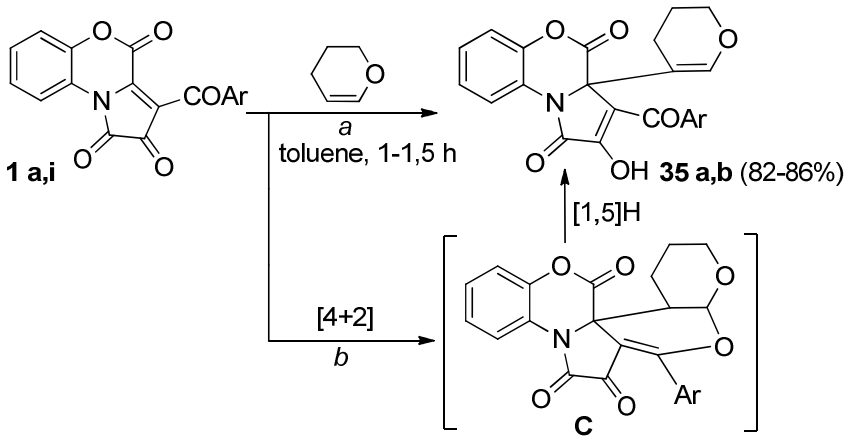
(1*R**,16*R**)- **33** and (1*S**,16*R**)-16-alkoxy-14-aryl-3,15-dioxa-10-azatetracyclo[8.7.0.0^{1,13}.0^{4,9}]heptadeca-4,6,8,13-tetraene-2,11,12-triones **34** (Scheme 15).[51-54]



Scheme 15. Interaction of pyrrolobenzoxazinetriones (**1**) with alkyl vinyl ethers (**32**).

Compounds **33** and **34** are formed via thermally initiated [4+2]-cycloaddition of 3-aroyl-1*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-1,2,4-triones **1** (O=C–C^{3}=C^{3a} conjugated diene system) to the polarised C=C bond of the alkyl vinyl ethers **32**. They may be regarded as heterocyclic analogs of 13(14→8)-abeo-steroids, dankasterone[55], and abeohyousterone[56], which possess a rarely occurring fused carbocyclic skeleton and exhibit pronounced antitumor activity.

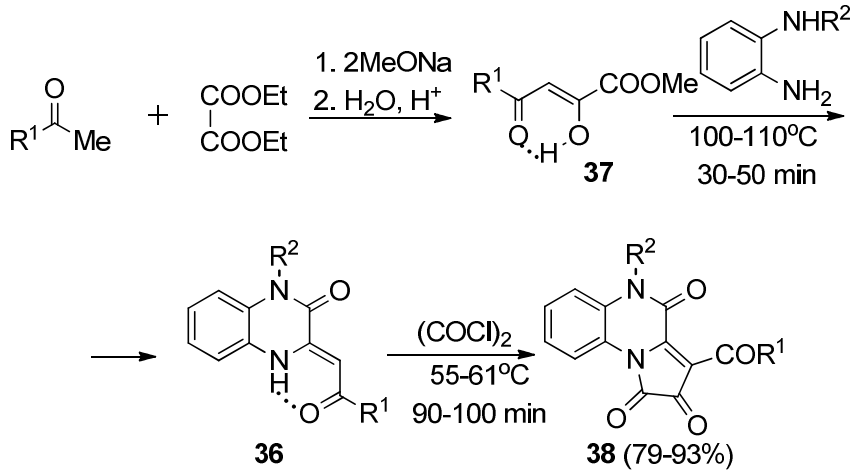
Babenysheva and coworkers[57] described the simple and effective synthesis of compounds **35**. They described the formation of compound **35** as an extremely easy nucleophilic addition (route *a*) of a polarised olefin to the most electrophilic site of compounds **1** (Scheme 16). A probable alternative mechanism (route *b*) involves the [4+2]-cycloaddition of olefin at the system of conjugated O=C–C^{3}=C^{4} bonds to form compound **C**, with a subsequent [1,5]-prototropic shift in the latter.



Scheme 16. Interaction of pyrrolobenzoxazinetriones (**1**) with olefin.

4. Synthesis of Pyrrolo[1,2-a]quinoxalin-1,2,4(5*H*)-triones

Initial 3,4-dihydroquinoxalin-2(1*H*)-ones **36** were formed by reacting the methyl esters of aroylpyruvic acids **37** with *o*-phenylenediamine.[58,59] Pyrrolo[1,2-a]quinoxalin-1,2,4(5*H*)-triones **38** were obtained by reacting the corresponding 3,4-dihydroquinoxalin-2(1*H*)-ones **36** with oxalyl chloride (Scheme 17).[60]



36, **38**: R^2 = H, R^1 = Ph, C_6H_4Me-4, C_6H_4OMe-4, C_6H_4Cl-4, C_6H_4Br-4, α-thienyl, R^2 = Ph, R^1 = Ph, C_6H_4OMe-4, C_6H_4Br-4, α-naphthyl, Bu-t

Scheme 17. Synthesis of pyrrolo[1,2-a]quinoxalin-1,2,4(5*H*)-triones (**38**).

5. Formation of a C-C Bond by Reactions Pyrrolo[1,2-a]quinoxalin-1,2,4(5*H*)-triones with Nucleophiles

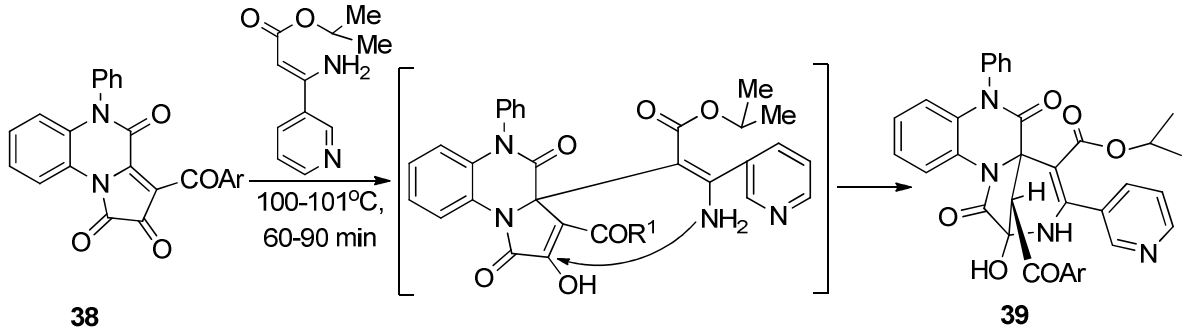
Interest in studies of the heterocyclic system of pyrrolo[1,2-a]quinoxaline-1,2,4(5*H*)-trione increased because this system is particularly resistant to "destruction". It is not split by the action of the nucleophilic reagents, thus allowing of this system is basis for the nucleophilic "superstructure" of new heterocycles.

In most studies on the interactions of pyrroloquinoxalintriones with binucleophiles, the initial C–N[8,58,61-65], C–O[8], C–S[8,25,66,67] bonds formation occurs, and there are few studies on the formation the C–C bond, which is described in this chapter.

5.1. Reactions with CH,NH-binucleophiles

5.1.2. Reactions with acyclic CH,NH-binucleophiles

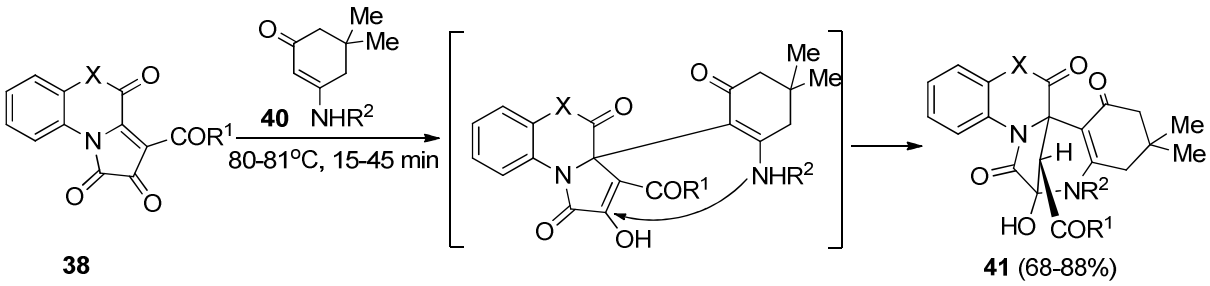
3-Aroyl-5-phenylpyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones **38** interacted with isopropyl 3-amino-3-(pyridin-3-yl)acrylate with sequential nucleophilic addition of β-CH and NH_2 groups of the enamine on the C^{3a} and C^{2} atoms of pyrroloquinoxalinetriones **38**. This resulted in the formation of the bridged compounds **39** (Scheme 18).[68]



Scheme 18. Interaction of pyrroloquinoxalinetriones (**38**) with isopropyl 3-amino-3-(pyridin-3-yl)acrylate.

5.1.2. Reactions with cyclic CH,NH-binucleophiles

An example of nucleophilic [3+3] addition of β-CH and NH groups of a cyclic enamine on the C^{3a} and C^{2} atoms of pyrrolo[1,2-a]quinoxaline-1,2,4(5*H*)-triones is the interaction of compounds **38** with 3-amino-5,5-dimethyl-2-cyclohexenones **40**, which gives rise to a bridged heterocyclic system of 3,10,13-triazapentacyclo[10.7.1.^{01,10}.0^{4,9}.0^{14,19}]icosa-4,6,8,14(19)tetraene-2,11,18-triones **41** (Scheme 19).[69,70]

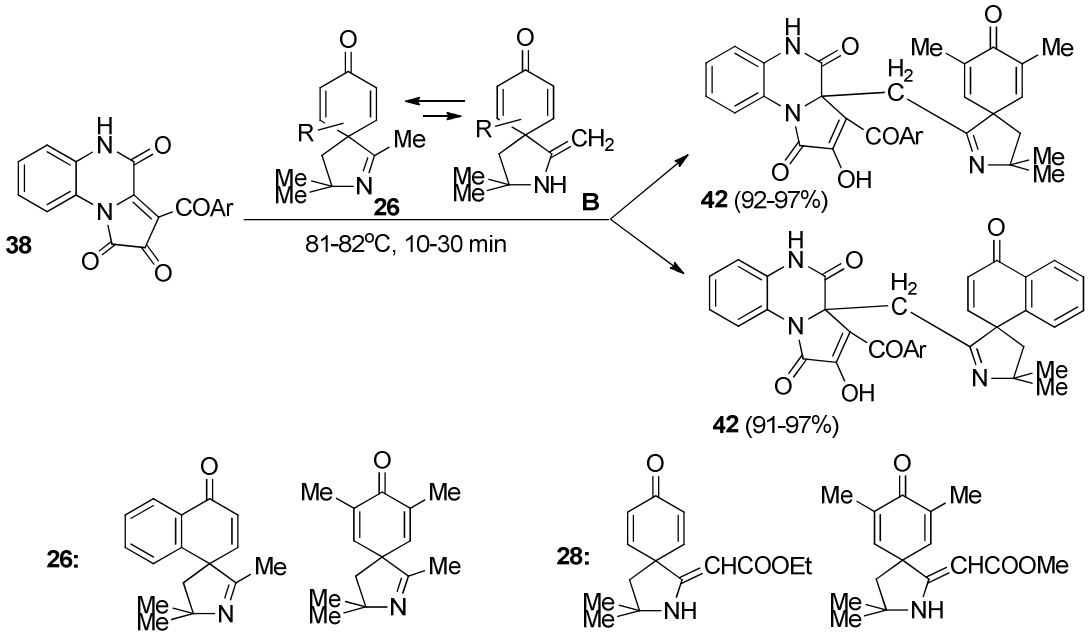


Scheme 19. Interaction of pyrroloquinoxalinetriones (**38**) with 3-amino-5,5-dimethyl-2-cyclohexenones (**40**).

5.1.3. Reactions with heterocyclic CH,NH-binucleophiles

A series of studies describe the interactions of pyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones with heterocyclic CH,NH-binucleophiles. Konovalova and coworkers[71] described the reaction of 3-

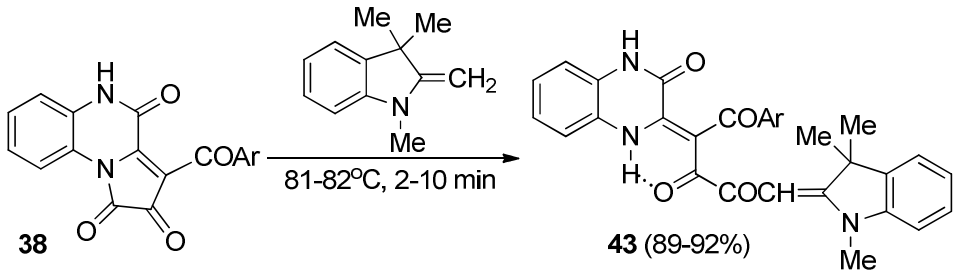
aroylpyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones **38** with substituted 1,3,3-trimethyl-2-azaspiro[4.5]dec-1-enes **26** resulting in the formation of products of addition **42** of the activated *β*-CH group of the tautomeric enamino form **B** of compounds **26** on the carbon atom in the position *3a* of pyrroloquinoxalinetriones **38** (Scheme 20).



Scheme 20. Interaction of pyrroloquinoxalinetriones (**38**) with spiranes (**26**).

The spiropyrroline fragment in the synthesised compounds **42** exists in the imine form, it was previously only observed in the enamine form.[72] This is because of the lack of intramolecular hydrogen bonds, which may stabilise the enamine form, in compounds **42**. The authors hypothesised that further intramolecular cyclisation of the substituted 3a-(pyrrolylmethyl)pyrroloquinoxalinediones **42**, which has been observed for 3a-(pyrrolylmethyl)pyrrolobenzoxazinediones[46], does not occur with the former compounds. This may be due to the decreased electrophilicity of the carbonyl carbon atom of the C^4=O group as compared to the electrophilicity of the ester carbon atom. Additionally, Konovalova *et al.*[71] attempted to modify the structure of the initial 1,3,3-trimethyl-2-azaspiro-[4.5]dec-1-enes in order to change the regioselectivity of their reaction with pyrroloquinoxalinetriones. It turned out that the reaction of 3-aroylpyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones **38** with 1,3,3-trimethyl-2-azaspiro[4.5]dec-1-enes **28** containing an additional ester group under analogous reaction conditions did not occur due to the increased steric hindrances at the reaction centre that were caused by the additional functional group.

In 2013, the first example of the interaction of 3-aroylpyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones **38** with a secondary enamine (1,3,3-trimethyl-2-methylidene-2,3-dihydro-1*H*-indole (Fischer's base)) was reported (Scheme 21).[73]



Scheme 21. Interaction of pyrroloquinoxalinetriones (**38**) with Fischer's base.

Presumably, in the described reaction, the attack by the $=CH_2$ group of Fischer's base on the C^1 atom of **38** is followed by the opening of the pyrrole ring via cleavage of the C^1–N^{10} bond, as described in[8] for the reactions of 3-aroylpyrrolo[1,2-*a*]quinoxaline-1,2,4(5*H*)-triones with mononucleophiles. No such pathway was observed previously in reactions of pyrroloquinoxalinetriones with enamines.

6. Conclusions

The described interactions may be regarded as an examples the initial formation of a C–C bond. The simple performance, mild conditions, good yields and easy purification of the products are among the advantages of these reactions.

The above examples show that recyclizations and heterocyclizations of 1*H*-pyrrole-2,3-diones annulated with azaheterocycles on the [e] side by the action of 1,3-CH,OH- and 1,3-CH,NH-binucleophiles are a convenient method of constructing inaccessible condensed and bridged azaheterocycles, bis-spiro-heterocyclic systems.

7. Acknowledgements

This work was supported by RFBR grants № 12-03-00146, 12-03-00696.

8. References

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