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Cyclization reactions of Kröhnke–Mukaiyama salts

Eugene V. Babaev[1]*

[1] *Moscow M. V. Lomonosov State University,*
1 Leninskie Gory, Moscow 119991, Russia; e-mail: babaev@org.chem.msu.ru

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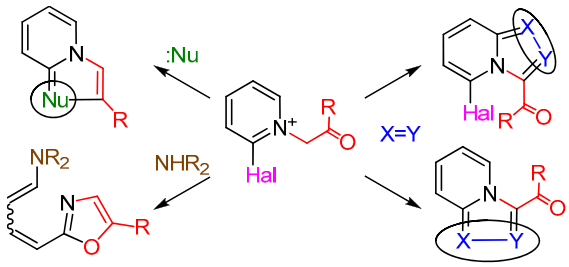


This review provides a systematic overview of original articles reporting cyclization reactions of 2-halo-*N*-phenacylpyridinium salts (Kröhnke–Mukaiyama salts) and their analogs. References published from the middle of 1950's until the present time are included.

Keywords: 2-halo-*N*-phenacylpyridinium salts, Kröhnke–Mukaiyama salts, cyclization–ring opening reactions, cycloaddition reactions, reactions with (bis)nucleophiles, reactions with electro/nucleophiles.

This review has been dedicated to cyclization reactions of 2-halo-*N*-phenacylpyridinium salts (Fig. 1). 2-Halopyridinium salts **I**, also known as Mukaiyama salts, are unusual in their ability to loose their halogen atom very easily,[1] while *N*-phenacylpyridinium salts **II** that readily form ylides are known as Kröhnke salts.[2] Both types of reactivity are present in Kröhnke–Mukaiyama salts **1**[3] by combining the ketomethylene motif of Kröhnke salts and the α-halo substituent of Mukaiyama salts.

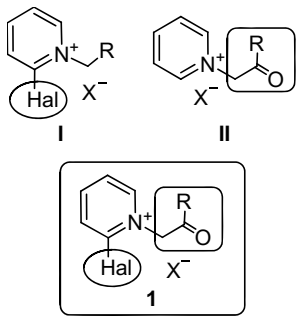


Figure 1. The general structures of pyridinium and 2-halopyridinium salts.

Due to the presence of Hal–C=N$^+$–CH$_2$–C=O moiety acting as 1,4-bielectrophilic atom chain in Kröhnke–Mukaiyama salts **1**, their cyclization to 5- and 6-membered rings can be accomplished with the help of 1,1- and 1,2-bisnucleophiles. In addition, the methylene group in salts **1** is strongly CH-acidic and tended to deprotonate, resulting in oxazole ring formation. At the same time, electro/nucleophilic species (1,2-ambiphiles[4]) are capable of reactions both with the nucleophilic CH$_2$ group and with the electrophilic α-position of pyridinium ring, giving rise to various azole structures. Finally, the substitution pattern at the nitrogen atom in Kröhnke–Mukaiyama salts is not symmetrical (in contrast to the Kröhnke salts **II**), thus the formed ylides can react with dipolarophiles by two routes at the two α-positions. The considerable diversity of these reactions is the topic of the present review.

It should be noted that the reactivity of Kröhnke–Mukaiyama salts has never been thoroughly reviewed in the literature. At the same time, our research group has obtained results of major importance in this area over the previous decade. It should be mentioned that our previous review[5] was devoted to the synthesis of cycloiminium salts with leaving group at the α-position, followed by their conversion to betaine ylides and oxazolium salts. The present review aims to fill this gap by covering publications from the middle of 1950's until the present time.

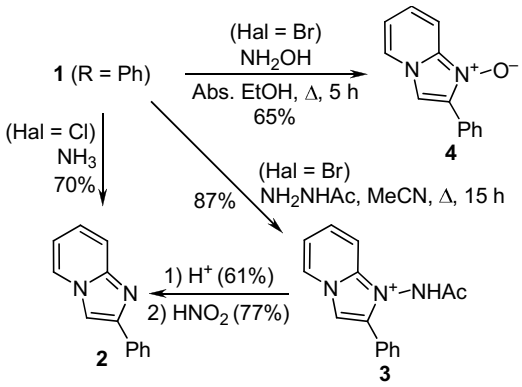
Reactions with 1,1-binucleophiles

The reactions of Kröhnke–Mukaiyama salts with binucleophilic species start, as a rule, at the electrophilic α-carbon atom of pyridine ring, subsequently involving the carbonyl group. Salt **1** was converted to the imidazo[1,2-*a*]-pyridine **2** by treatment with gaseous NH$_3$ (Scheme 1).[6] Lower yield (23%) was obtained by using ammonia

solution in DMF[7] (here and further the counterion in salts **1** is bromide).

The salt **1** was converted by treatment with NH_2NHAc to 1-acetylamino-2-phenylimidazo[1,2-*a*]pyridin-1-ium salt **3**,

Scheme 1

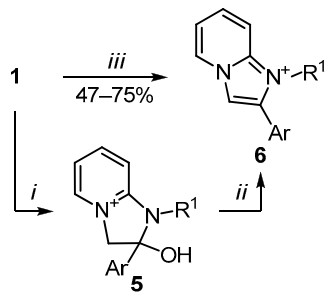


which underwent deacylation reaction followed by diazotation, forming the imidazopyridine **2**.[8] Reaction with NH_2OH led to imidazo[1,2-*a*]pyridine *N*-oxide **4**, provided that the reaction was performed under anhydrous conditions.[9]

The interaction of Kröhnke–Mukaiyama salts with aliphatic or aromatic primary amines[8,10–13] occurred analogously, with the only difference that the initially formed bicyclic hemiaminals **5** (Scheme 2) were capable of further dehydration to imidazo[1,2-*a*]pyridinium salts **6**.

The salts **1** also reacted with α-amino ketones, forming imidazo[1,2-*a*]pyridinium salts **7**, which underwent aroma-

Scheme 2



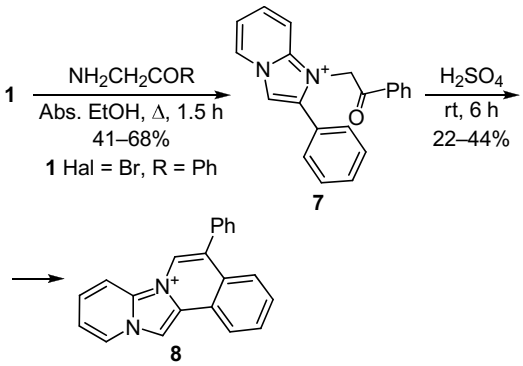
Hal = Cl, Br; R = Ar; R^1 = Alk, Ar
i: MeCN, rt, 1 h or PrOH, rt, 24 h;
ii: PPA, 100°C, 1 h; *iii*: NH_2R^1, Δ, 14 h

tization in the presence of acids, giving pyrido[2',1':2,3]-imidazo[5,1-*a*]isoquinolin-7-ium salts **8**[12] (Scheme 3).

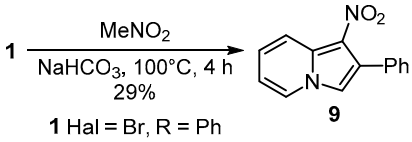
The reaction of nitromethane anion[14] with the salt **1** resulted in pyrrole ring closure and formation of 1-nitro-indolizine **9** (Scheme 4). While recyclization reactions involving nitromethane are quite common,[15] this is a relatively rare example where such reagent was used for cyclizations.

Phosphorus-centered 1,1-binucleophiles have also been used in heterocyclic synthesis, typically for recyclizations, but only rarely in two-component cyclizations. We identified a new, readily occurring heterocyclization reaction of 2-chloropyridinium salts by the action of $P(SiMe_3)_3$ in

Scheme 3

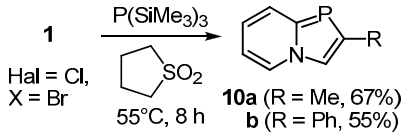


Scheme 4



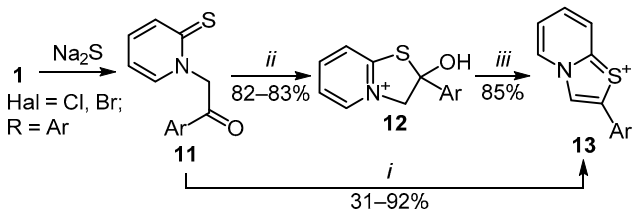
sulfolane under inert atmosphre,[6] giving [1,3]aza-phospholo[1,2-*a*]pyridines **10a**,**b** not only by a shorter route, but also in higher yields than described in the literature[16] (Scheme 5).

Scheme 5



The reaction of 2-bromopyridinium salts **1** with Na_2S providing pyridine-2-thiones **11** has been known for a long time.[17] As shown by Bradsher and Boliek,[18] the treatment of such thiones with strong acids leads to the formation of thiazolo[3,2-*a*]pyridinium salts **13** in 31–92% yields (Scheme 6). Later it was proved by Kröhnke[19] that the reaction proceeds *via* the formation of hydrates **12**. Compounds **12** were tested for hypoglycemic activity,[20] with 2-phenyl derivatives found to be the most active.

Scheme 6



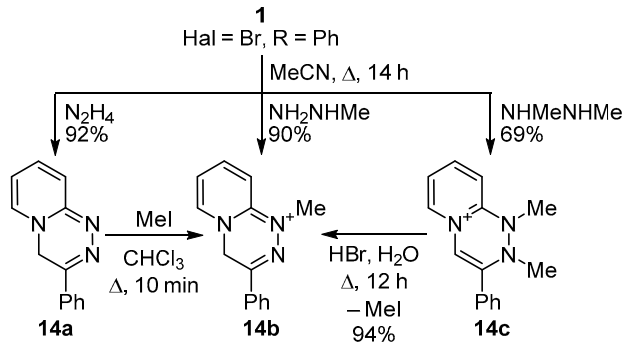
i: concd. H_2SO_4, rt, 8 h; *ii*: $HClO_4$, EtOH, 50°C, 2 min;
iii: H_2SO_4, HBr, 100°C, 2 h

Thus, the reaction of Kröhnke–Mukaiyama salts **1** with the simplest N-, S-, P-, and C-binucleophiles (1,1-type binucleophiles[4]) led to bridged azolopyridines. The reaction often proceeds *via* the formation of stable hydrates, which are aromatized in the presence of acids.

Reactions with 1,2-binucleophiles

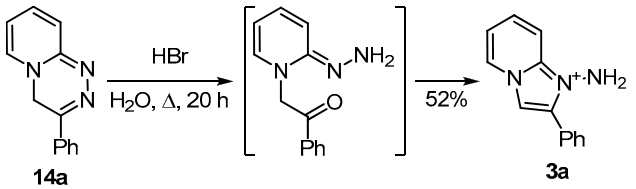
The reactions of Kröhnke–Mukaiyama salt **1** with hydrazines involve the formation of compounds **14** containing a triazine ring[8] (Scheme 7).

Scheme 7



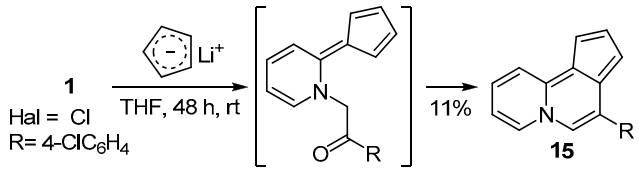
The triazinium salt **14b** can be obtained both by methylation of triazine **14a** (yield not reported) and by demethylation of salt **14c**. Triazine **14a** is converted by acidic hydrolysis to imidazo[1,2-*a*]pyridinium 1-amino derivative **3a** (Scheme 8)[8].

Scheme 8



Another example of 6-membered ring formation is the reaction of salt **1** with cyclopentadienyl lithium,[21] leading to cyclopenta[*a*]quinolizine **15** (Scheme 9). This process is virtually analogous to the synthesis of azulenes according to Hafner.[22]

Scheme 9



Thus, it is obvious that reactions between the 1,4-bielectrophilic moiety of Kröhnke–Mukaiyama salts and 1,2-binucleophiles of either NN- or CC-type result in the formation of 6-membered rings.

Reactions with 1,2-ambiphiles

We will first consider processes involving substitution of α-halogen atom and condensation at the CH_2 group. The first published example of this type was the reaction of 2-chloropyridinium salts with malononitriles in the presence of Hünig's base[23] (Scheme 10). The initially formed 1,2-dihydropyridines **16**, **17** smoothly cyclized to 2-aminoindolizines **18**, **19**. When excess base was used, formation of 2-ethoxyindolizines **20** was also detected (Table 1). Analogous reaction was performed in the series of 1-chloroisoquinolinium salts,[24] allowing to obtain pyrrolo[1,2-*a*]isoquinolines in a single step.

Scheme 10

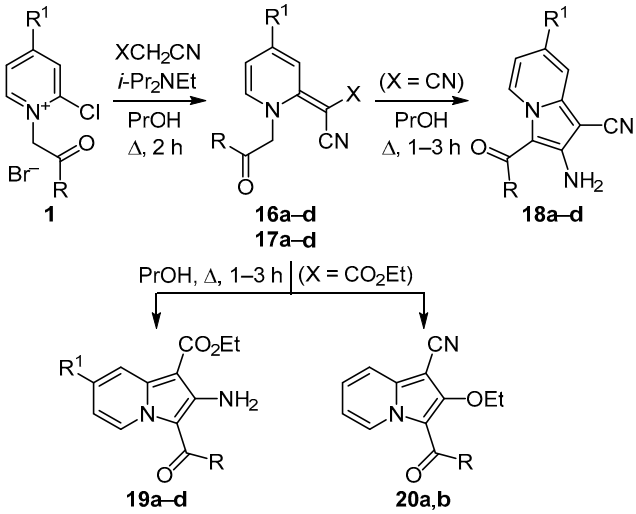
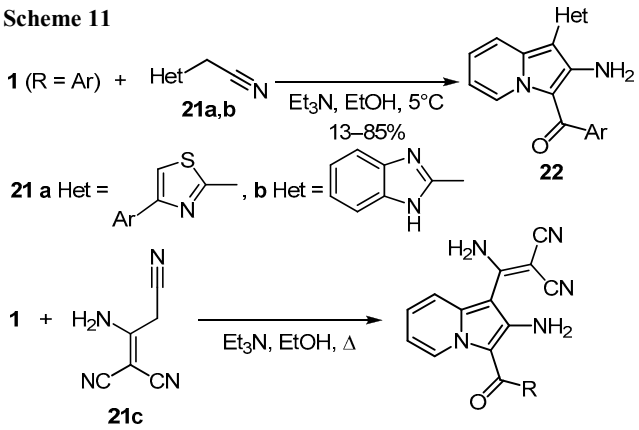


Table 1. Yields of dihydropyridines **16**, **17** and indolizines **18**–**20** in reactions of 2-chloropyridinium salts with malononitriles

Compound	X	R	R^1	Yield, %
16a	CN	Ph	H	95
16b	CN	Ph	Me	64
16c	CN	4-MeC_6H_4	H	93
16d	CN	Me	H	65
17a	CO_2Et	Ph	H	35
17b	CO_2Et	4-MeC_6H_4	H	86
17c	CO_2Et	Me	Me	37
17d	CO_2Et	4-BrC_6H_4	H	42
18a		Ph	H	61
18b		Ph	Me	95
18c		4-MeC_6H_4	H	91
18d		Me	H	92
19a		Ph	H	92
19b		4-MeC_6H_4	H	80
19c		Me	Me	40
19d		4-BrC_6H_4	H	80
20a		Ph		14
20b		4-BrC_6H_4		24

The reactions of salts **1** with α-hetarylacetonitriles **21a** (containing 4-arylthiazole as heterocycle, 13–68% yield)[25] and **21b** (containing benzimidazole as heterocycle, 30–85% yield)[26] proceeded analogously, leading to 3-substituted indolizines **22** (Scheme 11). The reaction of salt **1** with malononitrile dimer **21c** occurred similarly, with condensation at the CH_2CN group, giving 55–68% yield.[3]

Scheme 11



R = OEt (55%), Ph (53%), 4-ClC$_6$H$_4$ (68%), 4-MeOC$_6$H$_4$ (66%)

Indolizine derivatives **23** were also formed in the reactions of 2-bromopyridinium salts **1** with β-keto acids, β-dicarbonyl compounds, or diethylmalonate[27] (Scheme 12, Table 2). During the study it was found that keto acids reacted by forming derivatives of indolizyl-1-carboxylic acids, while malonic ester gave 2-hydroxyindolizines. At the same time, unsymmetrical β-diketones produced product mixtures.

Scheme 12

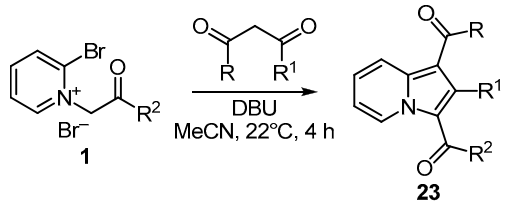


Table 2. Yields of indolizines **23** in reactions of 2-bromopyridinium salts **1** with β-dicarbonyl compounds

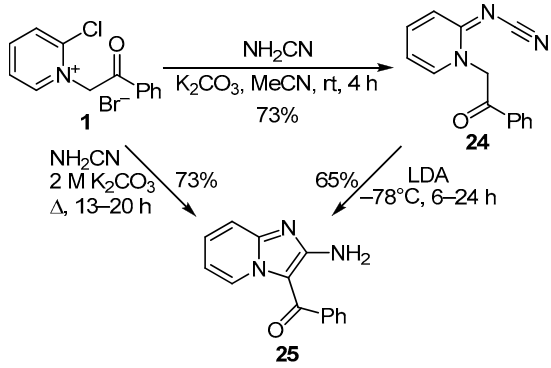
R in **23**	R^1	R^2	Yield, %
OEt	Me	Me	44
OEt	Ph	Me	63
OEt	3-MeOC$_6$H$_4$	Me	44
OEt	3,4-Me$_2$C$_6$H$_3$	Me	46
OEt	Me$_2$CH	Me	23
OEt	Me	Me$_2$CH	36
OEt	Ph	Me$_2$CH	33
OEt	3-MeOC$_6$H$_4$	Me$_2$CH	30
OEt	3,4-Me$_2$C$_6$H$_3$	Me$_2$CH	30
OEt	Me	Ph	53
OEt	Ph	Ph	47
Me	Me	OEt	13
Me	Me	Me$_2$CH	24
Me$_2$CH	Me$_2$CH	Me	36
Me$_2$CH	Me$_2$CH	Me$_2$CH	35
Me/Ph	Ph/Me	Ph	41*
CH$_2$CMe$_2$CH$_2$		OEt	11
OEt	OH	Me	40
OEt	OH	Me$_2$CH	41
OEt	OH	Ph	49

* ~4:3 mixture.

As reported by chemists from Spain in 1999, the reaction of 2-chloropyridinium salt **1** with cyanamide was used for the synthesis of 2-aminoimidazo[1,2-*a*]pyridine **25**, and the stable intermediate **24** was successfully isolated[28] (Scheme 13).

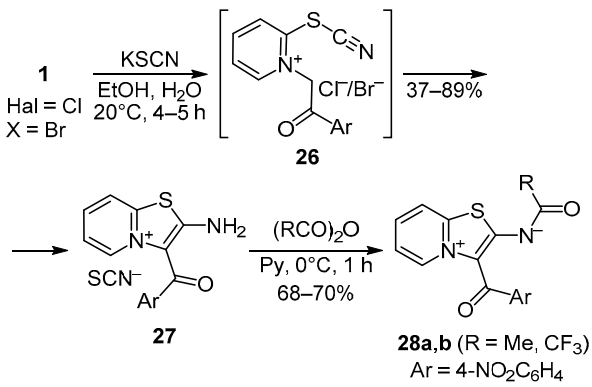
Biologically active analogs of imidazopyridine having 2-(*N*-methylcarbamoyl)-1-phenylvinyl group at position 6 were formed in 30–50% yields.[29] The analogous reaction with KCNO in the case of the same salt[30] led to a mixture of imidazo[1,2-*a*]pyridine and *N*-phenacylpyridin-2-one.

Scheme 13



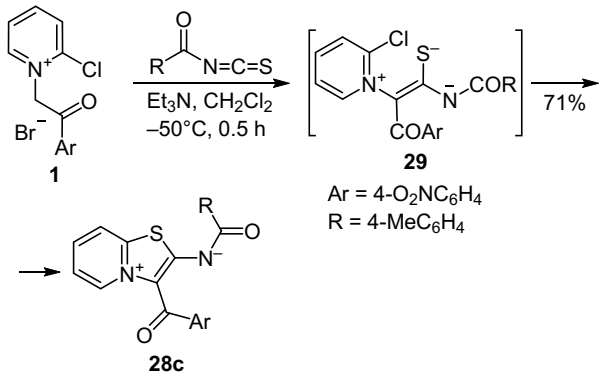
The reaction of KSCN with salts **1** resulted in thiazolo[3,2-*a*]pyridinium 2-amino derivatives **27**[31,32] (Scheme 14). It should be noted that this represented a new approach to the synthesis of thiazoles from CNC+CS building blocks. A remarkable feature of this reaction was the substitution of two halide ions (Cl^- and Br^-) by SCN^-, forming salts **27**, the composition of which was determined by anion chromatography. One of the salts **27** was converted by treatment with acid anhydrides to the mesoionic derivatives **28a**,**b**. A range of salts **27** was tested for pesticide activity,[32] and it was determined that the salts **27** exhibited moderate herbicidal activity by suppressing the germination of seeds.

Scheme 14



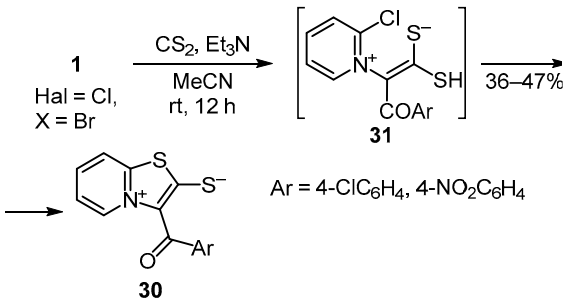
Compounds **16**, **17**, **24** (Schemes 10, 13) served as dihydropyridine intermediates in reactions involving α-halide substitution, which were isolated from reaction mixtures. Although the intermediate **26** could not be isolated, there was no doubt about its formation due to the strong nucleophilicity of rhodanide ion. However, in the case of the closely related reaction of salt **1** with 4-methylbenzoyl isothiocyanate (Scheme 15), leading to the product **28c** belonging to the same mesoionic compound class, the intermediate **29** appeared to be more preferrable,[6,33] because the nucleophilicity of isothiocyanato group was strongly suppressed and electrophilicity of the *sp*-hybridized carbon atom was dominant instead.

Scheme 15



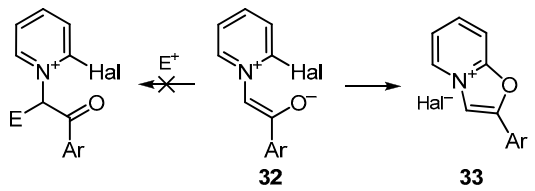
The ylides obtained from salts **1** reacted with carbon disulfide analogously,[34] forming the somewhat different mesoionic compounds **30** (Scheme 16). The reaction between CS_2 and methylene group likely proceeded *via* the adduct **31**. We should note that the usual Kröhnke salts also reacted with carbon disulfide in this particular way.[35]

Scheme 16



During the synthesis of compounds **30** by using triethylamine, the temperature had to be maintained below –45°C (Scheme 15), because the ylide intermediate **32** readily underwent intramolecular cyclization at higher temperatures, giving the oxazolo[3,2-*a*]pyridinium salt **33**[5] (Scheme 17). However, 2-halopyridinium ylides did not react with electrophiles (E^+) in reactions typical for Kröhnke ylides (alkylation, acylation, picrylation[2]) at temperatures below –45°C.

Scheme 17



With more reactive aryldiazonium salts, azo coupling could be accomplished at the CH_2 group, with the obtained hydrazones **34** giving smooth closure of triazolium ring, forming [1,2,4]triazolo[4,3-*a*]pyridin-1-ium salts **35a**–**h**[36] (Scheme 18, Table 3).

The reactions of salts **1** with pyridine homologs should be mentioned in particular. During such reactions, nucleophilic substitution of halide anion by pyridine

Scheme 18

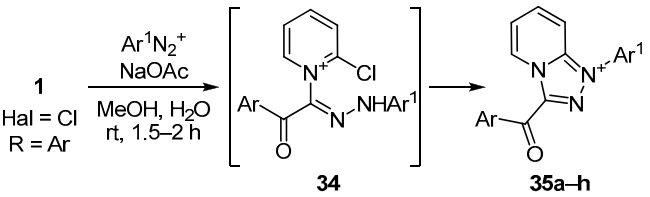
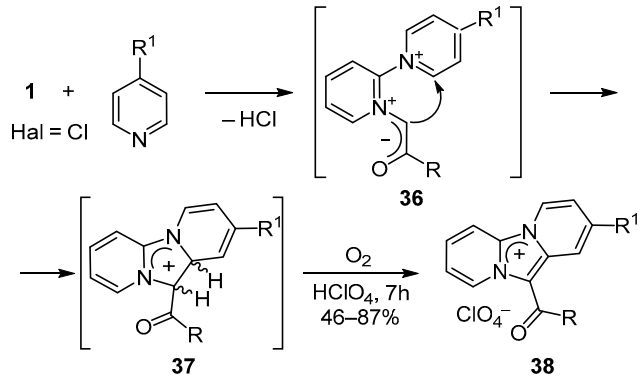


Table 3. Yields of [1,2,4]triazolo[4,3-*a*]pyridin-1-ium salts **35a**–**h**

Compound	Ar	Ar^1	Yield, %
35a	4-ClC_6H_4	Ph	63
35b	4-ClC_6H_4	4-BrC_6H_4	92
35c	4-$NO_2C_6H_4$	4-MeC_6H_4	62
35d	4-$NO_2C_6H_4$	4-MeC_6H_4CO	86
35e	4-$CH_3C_6H_4$	4-BrC_6H_4	70
35f	4-ClC_6H_4	4-MeC_6H_4	95
35g	4-ClC_6H_4	4-MeC_6H_4CO	74
35h	4-$NO_2C_6H_4$	4-BrC_6H_4	77

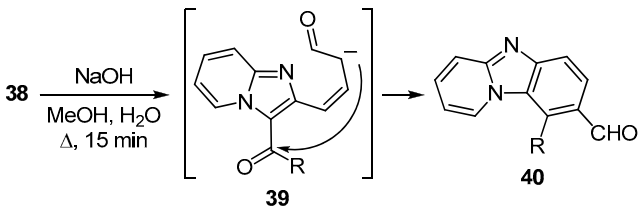
heteroatom was accompanied by nucleophilic attack of ylide carbon atom at the α-position of the coupled heterocyclic intermediate **36** with the formation of dihydro species **37** (Scheme 19). After oxidation with air oxygen, a tricyclic aromatic compound **38** was formed.[37]

Scheme 19



As demonstrated by us,[38] the obtained salts **38** represented useful intermediates for preparing benzimidazo[1,2-*a*]pyridine formyl derivatives **40**. The reaction proceeded through the open form **39** (Scheme 20).

Scheme 20



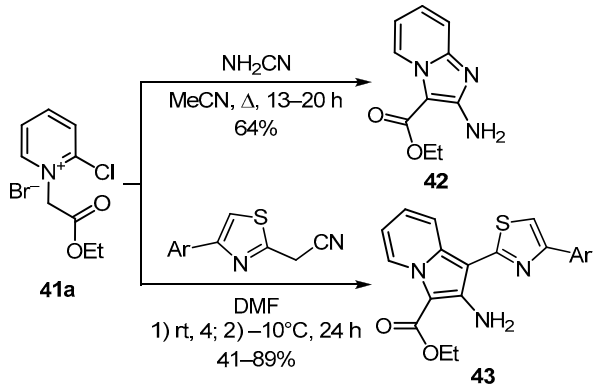
Thus, reactions of Kröhnke–Mukaiyama salts with reagents containing adjacent electrophilic and nucleophilic centers proceed with the formation of a five-membered ring having a cationoid, mesoionic, or covalent structure. The sequence of steps is determined by the nucleophilicity of the reagent (CH acid, rhodanide, cyanamide, pyridine)

attacking the α-position of the salt, or its electrophilicity (diazonium salt, carbon disulfide, aroyl isothiocyanate) reacting at the CH_2 group.

The reactivity of *N*-carboxymethylpyridinium salts

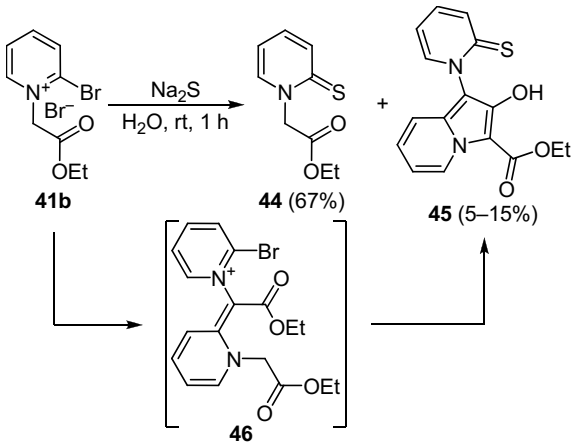
Kröhnke–Mukaiyama salts **41** containing acetic acid residue at the nitrogen atom also were capable of forming ylides, but there were some differences. For example, the salt **41a** readily reacted with cyanamide[28] and nitriles[39] (Scheme 21) forming the aminoheterocycles **42**, **43**, whereas its reaction with primary amines and KSCN resulted in resinous products.

Scheme 21



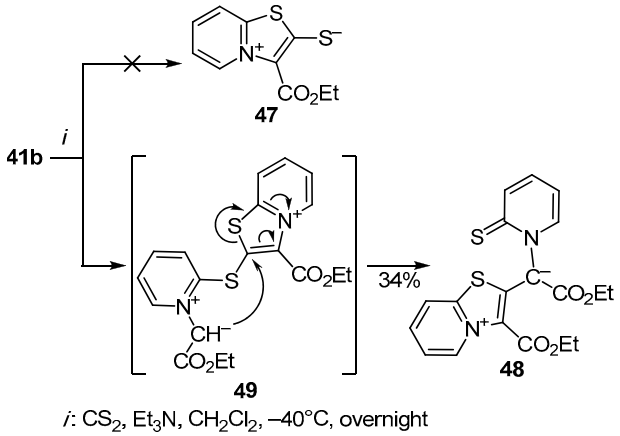
The reactions of salts **41** with sulfur-containing reagents gave different products. Thus, the reaction of salt **41b** with Na_2S gave not only the expected thione **44**, but also indolizine **45**,[40] probably *via* dimerization of the starting salt involving the generation of diester intermediate **46** (Scheme 22).

Scheme 22



A reaction of the same salt **41b** with CS_2 did not provide any traces of the expected mesoionic heterocycle **47** (see Scheme 16 for comparison), instead forming the mesoionic methide **48** (Scheme 23).[41] The reaction most likely proceeded through the stage of dimer **49** containing a CS_2 motif. Apparently, the high reactivity of 2-halo-substituted *N*-carbalkoxymethylpyridinium salts led to the peculiar results described above.

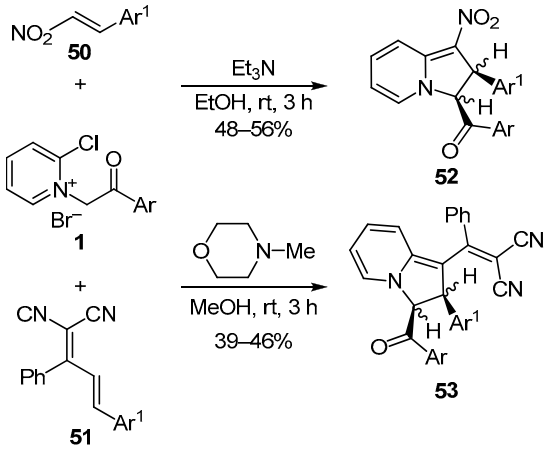
Scheme 23



Reactions with alkenes involving substitution of halogen anion

A range of processes have been described where Kröhnke–Mukaiyama salts participated in cycloaddition reactions in the expected manner, i.e., the electron-poor part of the alkene (diene) molecule added to the ylide moiety, while the electron-rich part substituted the halogen atom. The addition of nitroalkenes **50** to butadienes **51**[42,43] leading to dihydroindolizines **52**, **53** (Scheme 24) can serve as example.

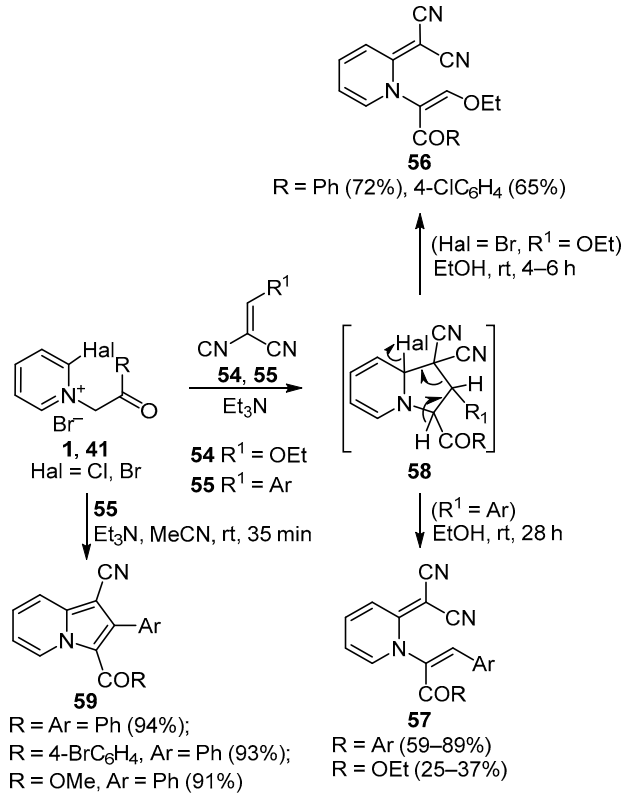
Scheme 24



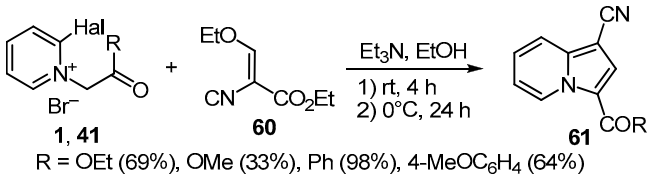
1,1-Dicyano-substituted alkenes, the ethoxy vinyl derivative **54**[44] and arylidene derivative **55**,[45] reacted with ylides of Kröhnke–Mukaiyama salts, followed by dissociation of double bond, forming the ambiphilic substitution products **56** and **57**, respectively (Scheme 25). The reason for such a course of this reaction, reminiscent of alkene metathesis, was the formation of intermediate **58**. At the same time, performing a reaction between arylidene derivatives of malonodinitrile and ylides derived from Kröhnke–Mukaiyama salts by using ultrasonication (100 kHz) allowed to obtain 1-cyanoindolizines **59**.[46]

It was recently shown that the interaction of Kröhnke–Mukaiyama salts **1**, **41** with (ethoxymethylidene)cyanoacetic ester **60** smoothly produced the 1-cyanoindolizines **61**[47] (Scheme 26), since one of the ethoxy groups was hydrolyzed during the reaction, followed by elimination.

Scheme 25



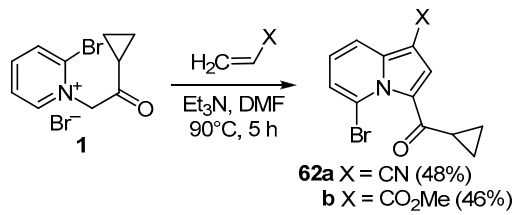
Scheme 26



Cycloaddition with conservation of halogen substituent

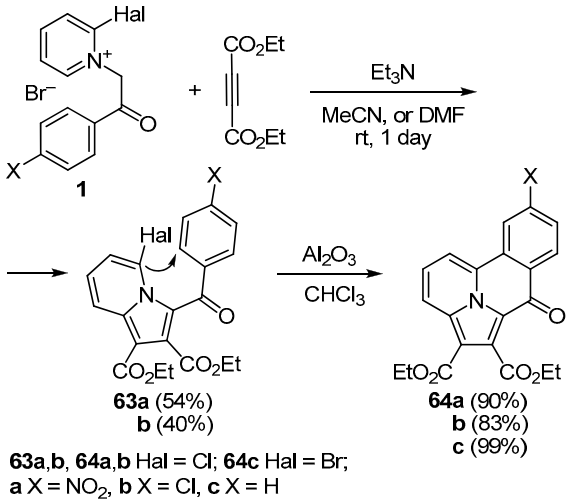
A range of reactions with dipolarophiles is known, in which the halogen atom in Kröhnke–Mukaiyama salts **1** is conserved. A notable example of such processes is the interaction of ylide obtained from 2-bromopyridinium salt **1**[48] with ethyl acrylate and acrylonitrile (Scheme 27), leading to 5-bromoindolizines **62a**,**b**.

Scheme 27



In addition, a similar reaction of 2-halopyridinium ylides **1** with acetylenedicarboxylic acid ester has been descrybed[49–51] (Scheme 28). This reaction allowed to isolate 5-haloindolizines **63a**,**b** that were characterized by X-ray structural analysis and were transformed during storage or in the presence of alumina to the tetracyclic compounds **64a**–**c**.

Scheme 28

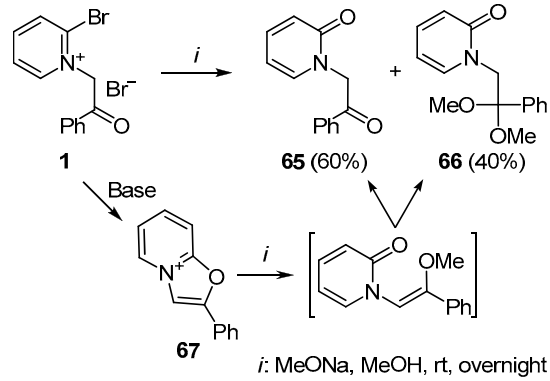


Thus, polar alkenes react regioselectively, albeit in a somewhat unexpected way, with ylides derived from Kröhnke–Mukaiyama salts. In the majority of cases, dihydroindolizine derivatives were formed, capable of aromatization when the alkene contained a cyano or alkoxy leaving group. However, in a series of cases the final indolizine molecule contained a halogen atom.

Cyclization and ring opening of salts

Treatment of 2-bromopyridinium salt **1** with MeONa provided not only *N*-phenacylpyridin-2-one **65**, but also the respective ketal **66**[52] (Scheme 29). A mixture of analogous composition was obtained by treating oxazolo[3,2-*a*]-pyridinium salt **67** with MeONa. Therefore, the Kröhnke–Mukaiyama salt underwent a tandem transformation in the presence of sodium methoxide.

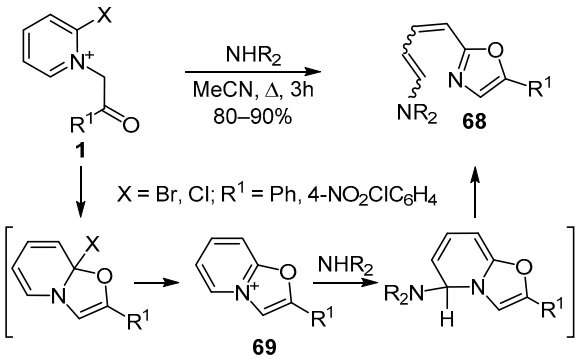
Scheme 29



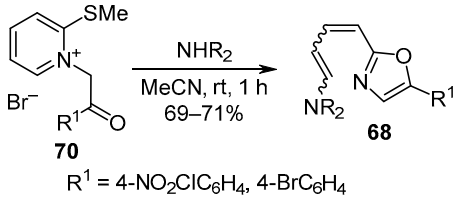
The reaction of Kröhnke–Mukaiyama salts **1** with secondary aliphatic amines produced the oxazolyl-2-butadienes **68**[53–55] (Scheme 30). Based on the observation that the analogous dienes **68** formed from bicyclic salts **69**, the mechanism was proposed for this unusual transformation.

The aforementioned reaction could be accomplished also with 2-MeS-substituted salts **70**, as well as on solid support (by substituting the CH_3 group by Merrifield resin fragment)[56,57] (Scheme 31).

Scheme 30

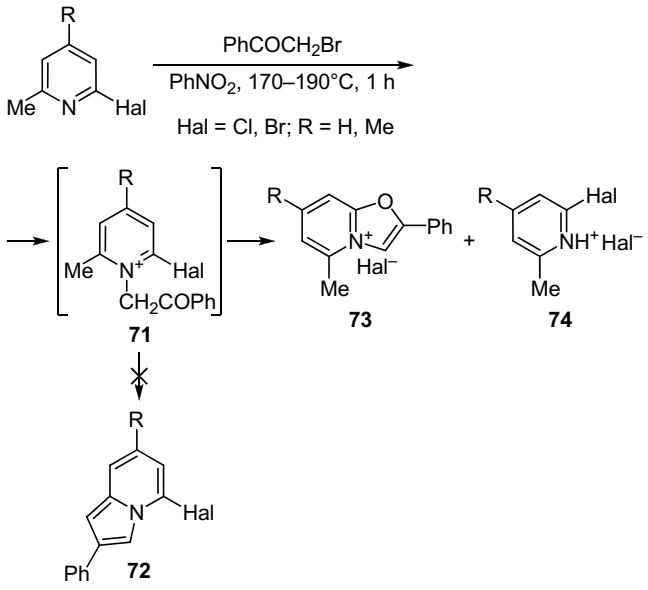


Scheme 31



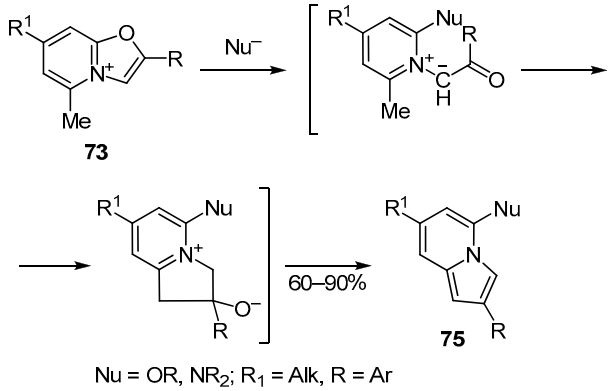
In conclusion, we will consider the reactivity of 6-CH_3 homologs **71** of Kröhnke–Mukaiyama salts. Already since the research by Chichibabin it has been assumed[58] (Scheme 32) that similar salts serve as precursors of 5-haloindolizines **72**. We showed[59] that salts **71** underwent cyclization at the moment of formation, giving oxazolopyridinium salts **73** in ~10% yields, while the HHal molecule remained a part of the halopyridine salts **74**. As a result, the salts **71** and indolizines **72** could not be isolated.

Scheme 32



Synthesis of 5-substituted indolizines **75** could be accomplished in good yields (60–90%) if homologous oxazolopyridines **73** were used in the reaction with nucleophiles (Scheme 33, see reviews[60,61]).

Scheme 33



Thus, the reactivity of Kröhnke–Mukaiyama salts is different from the related Kröhnke salts (due to the presence of reactive halogen substituent at α-position), and also different from Mukaiyama salts (due to the reactive *N*-phenacyl group). As a result, Kröhnke–Mukaiyama salts are capable of quite different transformations: annulation of various types (cationic, mesoionic, and neutral) of 5-membered rings, annulation of 6-membered rings, as well as pyridine ring conversion.

References

1. (a) Mukaiyama, T. *Angew. Chem.*, *Int. Ed.* **1979**, *18*, 707. (b) Mukaiyama, T. *Challenges in Synthetic Organic Chemistry*; Oxford University Press: Oxford, 1990, 226 p.
2. (a) Kröhnke, F. *Angew. Chem.*, *Int. Ed.* **1963**, *2*, 225. (b) Litvinov, V. P.; Shestopalov, A. M. *Russ. J. Org. Chem.* **1997**, *33*, 903. [*Zh. Org. Khim.* **1997**, *33*, 975.] (c) Zugravescu, I.; Petrovanu, M. *N-Ylid Chemistry*; Mc Graw-Hill, New York, 1976.
3. Tverdokhleb, N. M.; Khoroshilov, G. E.; Dotsenko V. V. *Tetrahedron Lett.* **2014**, *55*, 6593.
4. Babaev, E. V. *Chem. Heterocycl. Compd.* **1993**, *29*, 796. [*Khim. Geterotsikl. Soedin.* **1993**, 937.]
5. Babaev, E. V. *Review J. Chem.* **2011**, *1*, 161. [*Obzorn. Zh. Khim.* **2011**, *1*, 168.]
6. Babaev, E. V. Doct. Chem. Sci. Thesis; Moscow, 2007.
7. Kröhnke, F.; Kickhöfen, B.; Thoma C. *Chem. Ber.* **1955**, *88* (7), 1117.
8. Bradsher, C. K.; Brandau, R. D.; Boliek, J. E.; Hough, T. L. *J. Org. Chem.* **1969**, *34*, 2129.
9. Hand, E. S.; Paudler, W.W. *J. Org. Chem.* **1978**, *43*, 658.
10. Bellani, P.; Clavenna, G.; Sosio A. *Farmaco*, *Ed. Sci.* **1984**, *39*, 846.
11. Demchenko, A. M.; Chumakov, V. A.; Nazarenko, K. G.; Krasovskii, A. N.; Pirozhenko, V. V.; Lozinskii, M. O. *Chem. Heterocycl. Compd.* **1995**, *31*, 567. [*Khim. Geterotsikl. Soedin.* **1995**, 644.]
12. Bradsher, C. K.; Boliek, J. E.; Brandau, R. D. *J. Org. Chem.* **1970**, *35*, 2495.
13. Bradsher, C. K.; Frazer, M. G.; Burnham, W. S. *J. Heterocycl. Chem.* **1972**, *9*, 177.
14. Babaev, E. V.; Bozhenko, S. V.; Maiboroda, D. A. *Russ. Chem. Bull.* **1995**, *44*, 2203. [*Izv. Akad. Nauk*, *Ser. Khim.* **1995**, 2298.]
15. Babaev, E. V. *Chem. Heterocycl. Compd.* **1993**, *29*, 818. [*Khim. Geterotsikl. Soedin.* **1993**, *7*, 962.]
16. Märkl, G.; Pflaum S. *Tetrahedron Lett.* **1987**, *28*, 1511.

17. Djerassi, C.; Pettit, G. R. *J. Am. Chem. Soc.* **1954**, *76*, 4470.
18. Bradsher, C. K.; Boliek, J. E. *J. Org. Chem.* **1967**, *32*, 2409.
19. Pauls, H.; Kröhnke, F. *Chem. Ber.* **1976**, *109*, 3653.
20. Blank B.; DiTullio N. W.; Krog A. J.; Saunders, H. L. *J. Med. Chem.* **1978**, *21*, 489.
21. (a) Gormay, P. V.; Rybakov, V. B.; Babaev, E. V. *Eur. J. Org. Chem.* **2010**, *28*, 5364. (b) Rybakov, V. B.; Gormay, P. V.; Babaev, E. V. *Acta Crystallogr.*, *Sect. E: Struct. Rep. Online* **2010**, *E66*, o2958. (c) Babaev, E. V.; Gormai P. V. *Pseudoazulenes* [in Russian]; Lambert Academic Publ.: Saarbrucken, 2016, p. 80.
22. (a) Ziegler, K.; Hafner, K. *Angew. Chem.* **1955**, *67*, 301. (b) Hafner, K.; Meinhardt, K.-P. *Org. Synth. Coll. Vol.* **1990**, *7*, 15.
23. Pauls, H.; Kröhnke, F. *Chem. Ber.* **1977**, *110*, 1294.
24. Fujita, R.; Watanabe, N.; Tomisawa, H. *Heterocycles* **2001**, *55*, 435.
25. Khoroshilov, G. E.; Demchak, I. V. *Visn. Kharkiv. Nats. Univ.*, *Khimiya*, **2007**, (770), 210.
26. Khoroshilov, G. E.; Saraeva, T. A.; Kuznetsov, K. Yu. *Chem. Heterocycl. Compd.* **2008**, *44*, 895. [*Khim. Geterotsikl. Soedin.* **2008**, 1109.]
27. Nugent, R. A.; Murphy, M. *J. Org. Chem.* **1987**, *52*, 2206.
28. Vega, J. A.; Vaquero, J. J.; Alvarez-Builla, J.; Ezquerra, J.; Hamdouchi, C. *Tetrahedron* **1999**, *55*, 2317.
29. Hamdouchi, C.; Ezquerra, J.; Vega, J. A.; Vaquero, J. J.; Alvarez-Builla, J.; Heinz, B. A. *Bioorg. Med. Chem. Lett.* **1999**, *9*(10), 1391.
30. Babaev, E. V.; Rybakov, V. B.; Zhukov, S. G.; Orlova, I. A. *Chem. Heterocycl. Compd.* **1999**, *35*, 479. [*Khim. Geterotsikl. Soedin.* **1999**, *4*, 542.]
31. Babaev, E. V.; Bush, A. A.; Orlova, I. A.; Rybakov, V. B.; Zhukov, S. G. *Tetrahedron Lett.* **1999**, *40*, 7553.
32. Babaev, E. V.; Bush, A. A.; Orlova, I. A.; Rybakov, V. B.; Iwataki, I. *Russ. Chem. Bull.* **2005**, *54*, 231. [*Izv. Akad. Nauk*, *Ser. Khim.* **2005**, 226.]
33. Babaev, E. V.; Bush, A. A. *Mesoionic Systems of Azolo[3,2-a]-pyridine Series* [in Russian]. Lambert Academic Publ.: Saarbrucken, 2016, p. 87.
34. Babaev, E. V.; Rybakov, V. B.; Orlova I. A.; Bush, A. A.; Maerle K. V.; Nasonov A. F. *Russ. Chem. Bull.* **2004**, *53*, 176. [*Izv. Akad. Nauk*, *Ser. Khim.* **2004**, 170.]
35. Kröhnke, F.; Gerlach, K. *Chem. Ber.* **1962**, *95*, 1108.
36. Topchiy, M. A.; Babaev, E. V. *Chem. Heterocycl. Compd.* **2016**, *52*, 727. [*Khim. Geterotsikl. Soedin.* **2016**, *52*, 727].
37. Pauls, H.; Kröhnke, F. *Chem. Ber.* **1976**, *109*, 3646.
38. Babaev, E. V.; Tikhomirov, G. A. *Chem. Heterocycl. Compd.* **2005**, *41*, 119. [*Khim. Geterotsikl. Soedin.* **2005**, 135.]
39. Khoroshilov, G. E.; Tverdokhleb, N. M.; Brovarets, V. S.; Babaev, E. V. *Tetrahedron* **2013**, *69*, 4353.
40. Babaev, E. V.; Smirnov, G. A.; Rybakov, V. B. *Chem. Heterocycl. Compd.* **2005**, *41*, 1071. [*Khim. Geterotsikl. Soedin.* **2005**, 1250.]
41. Rybakov, V. B.; Bush, A. A.; Troyanov, S. I.; Babaev, E. V.; Kemnitz, E. *Acta Crystallogr.*, *Sect. E: Struct. Rep. Online* **2006**, *E62*, o1673.
42. Khoroshilov, G. E.; Demchak, I. V. *Chem. Heterocycl. Compd.* **2008**, *44*, 109. [*Khim. Geterotsikl. Soedin.* **2008**, 130.]
43. Khoroshilov, G. E.; Demchak, I. V.; Brovarets, V. S.; Rusanov, E. B. *Zh. Org. Farm. Khim.* **2009**, *7*(1), 48.
44. Aitov, I. A.; Nesterov, V. N.; Sharanin, Yu. A.; Struchkov, Yu. T. *Russ. Chem. Bull.* **1996**, *45*, 417. [*Izv. Akad. Nauk*, *Ser. Khim.* **1996**, 434.]
45. Tverdokhleb, N. M.; Khoroshilov, G. E.; Zubatyuk, R. I.; Shishkin, O. V. *Chem. Heterocycl. Compd.* **2013**, *49*, 720. [*Khim. Geterotsikl. Soedin.* **2013**, 772.]
46. Abaszadeh, M.; Seifi, M. *Org. Biomol. Chem.* **2014**, *12*, 7859.
47. Ponomarenko, D. A.; Khoroshilov, G. E.; Krasnikov, D. A. *Chem. Heterocycl. Compd.* **2015**, *51*, 560. [*Khim. Geterotsikl. Soedin.* **2015**, *51*, 560.]
48. Shen, Y.-M.; Lv, P.-C.; Chen, W.; Liu, P.-G.; Zhang, M.-Z.; Zhu, H.-L. *Eur. J. Med. Chem.* **2010**, *45*, 3184.
49. Terent'ev, P. B.; Vinogradova, S. M.; Kost, A. N. *Chem. Heterocycl. Compd.* **1980**, *16*, 506. [*Khim. Geterotsikl. Soedin.* **1980**, 651.]
50. Babaev, E. V.; Pasichnichenko, K. Yu.; Rybakov, V. B.; Zhukov, S. G. *Chem. Heterocycl. Compd.* **2000**, *36*, 1192. [*Khim. Geterotsikl. Soedin.* **2000**, 1378.]
51. Rybakov, V. B.; Babaev, E. V.; Pasichnichenko, K. Yu. *Crystallogr. Repts.* **2002**, *47*, 622. [*Kristallografiya* **2002**, *47*, 678.]
52. Babaev, E. V.; Bozhenko, S. V.; Maiboroda, D. A.; Rybakov, V. B.; Zhukov, S. G. *Bull. Soc. Chim. Belg.* **1997**, *106*, 631.
53. Babaev, E. V.; Tsisevich, A. A. *Chem. Heterocycl. Compd.* **1998**, *34*, 254. [*Khim. Geterotsikl. Soedin.* **1998**, 278.]
54. Babaev, E. V.; Tsisevich, A. A. *J. Chem. Soc.*, *Perkin Trans. 1* **1999**, *4*, 399.
55. Rybakov, V. B.; Babaev, E. V.; Tsisevich, A. A.; Arakcheeva, A. V.; Schoenleber, A. *Crystallogr. Repts.* **2002**, *47*, 973. [*Kristallografiya* **2002**, *47*, 1042.]
56. Babaev, E. V.; Nasonov, A. F. *ARKIVOC* **2001**, (ii), 139.
57. Babaev, E. V. *Russ. J. Gen. Chem.* **2010**, *80*, 2655. [*Ross. Khim. Zh.* **2009**, *53*(5), 140.]
58. Tschitschibabin, A. DE Patent 464481.
59. Babaev, E. V.; Efimov, A. V.; Maiboroda, D. A. *Chem. Heterocycl. Compd.* **1995**, *31*, 962. [*Khim. Geterotsikl. Soedin.* **1995**, 1104.]
60. Babaev, E. V.; Alifanov, V. L.; Efimov, A. V. *Russ. Chem. Bull.* **2008**, *57*, 845. [*Izv. Akad. Nauk*, *Ser. Khim.* **2008**, 831.]
61. Babaev, E. V. *Chem. Heterocycl. Compd.* **2012**, *48*, 59. [*Khim. Geterotsikl. Soedin.* **2012**, 64.]