ISSN 1070-4280, Russian Journal of Organic Chemistry, 2017, Vol. 53, No. 12, pp. 1769–1787. © Pleiades Publishing, Ltd., 2017.
Original Russian Text © I.V. Dyachenko, V.D. Dyachenko, 2017, published in Zhurnal Organicheskoi Khimii, 2017, Vol. 53, No. 12, pp. 1735–1754.

REVIEW

Cycloalka[*c*]pyridine Derivatives. Methods of Synthesis and Chemical Properties

I. V. Dyachenko[a]* and V. D. Dyachenko[a, b]

[a] *Taras Shevchenko Lugansk National University, ul. Oboronnaya 2, Lugansk, 91011 Ukraine*
**e-mail: ivladya87@mail.ru*

[b] *Kostroma State University, ul. Dzerzhinskogo 17, Kostroma, 156005 Russia*

Received May 29, 2017

Abstract—The review generalizes and systemizes data published over the past 15 years on the synthesis and chemical properties of cycloalka[*c*]pyridine derivatives that are important intermediate products used in the synthesis of alkaloids, enzyme inhibitors, and drugs for the treatment of cardiovascular diseases and bronchial asthma.

DOI: 10.1134/S1070428017120016

1. INTRODUCTION

Cycloalka[*c*]pyridine ring system is a structural fragment of many alkaloids [1–6] that are next to indole alkaloids in their abundance [7]. Compounds containing a cycloalka[*c*]pyridine fragment are used as intermediate products in the synthesis of alkaloids [8–10], optical materials for Langmuir–Blodgett films [11–13], precursors to CNS agents [14], chromophores [15–17], enzyme inhibitors [18–21], fungicides [22, 23], potassium receptor antagonists [24], and drugs for the treatment of cardiovascular diseases [25], bronchial asthma, tumors [26], and viral infections [26, 27]. Cycloalka[*c*]pyridine derivatives were shown to exhibit

Ivan Vladimirovich Dyachenko was born in 1987 in Lugansk. In 2009, he graduated from the Taras Shevchenko Lugansk National University and in 2012 finished post-graduate courses therein. Candidate of chemical sciences. Since 2014, he works as assistant professor at the Department of Chemistry and Biochemistry of the Taras Shevchenko Lugansk National University.

Fields of scientific interest: enamino ketones, nitrogen heterocycles, nucleophilic vinylic substitution reactions.

Vladimir Danilovich Dyachenko was born in 1961 in Brusovka village, Lugansk oblast, Ukraine. In 1983, he graduated from the Shevchenko Voroshilovgrad (now Lugansk) State Pedagogical Institute and in 1985–1988 studied at post-graduate courses at the same institute. Candidate of Chemical Sciences since 1990, Doctor of Chemical Sciences since 1998, head of the Laboratory of Organic Synthesis since 1990, associate professor of the Department of Chemistry since 1995. Since 1994, he heads the Department of Chemistry and Biochemistry of the Taras Shevchenko Lugansk National University, in 2008–2014, dean of the Faculty of Natural Sciences, professor since 2001. Since 2016, chief researcher of the Kostroma State University. V.D. Dyachenko has trained 8 candidates of sciences.

Fields of scientific interest: CH acids, activated alkenes, chalcogen- and nitrogen-containing heterocyclic compounds.

anticonvulsant [28–31], antibacterial [32, 33], neurotropic [34], and antimicrobial activities [35–37].

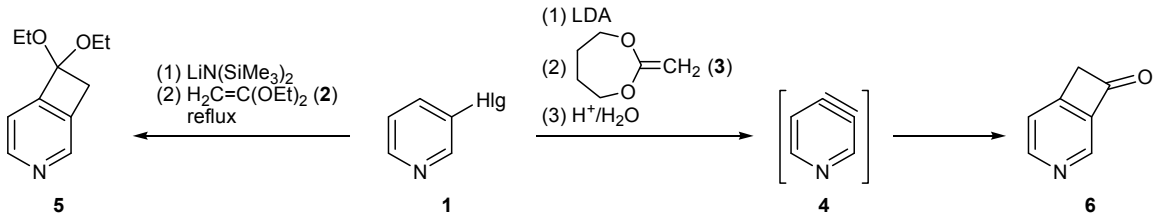
Despite significant advances in the chemistry of cycloalka[*c*]pyridines, neither methods of their synthesis nor chemical properties have been systemized so far. The present review analyzes relevant data published since 2000 until now.

2. FUSION OF A CARBOCYCLE TO PYRIDINE

The synthesis of cycloalka[*c*]pyridine derivatives via intermolecular annulation of a carbocycle on a preexisting pyridine ring has been poorly explored. Two versions of such syntheses have been reported: (1) the reaction of 3-halopyridines **1** with 5 equiv of ketene acetal **2** and 2 equiv of lithium hexamethyldisilylazide (LiHDMS) [38] and (2) [2+2]-cycloaddition of cyclic ketene acetal **3** to 3-halopyridine **1** in the presence of lithium diisopropylamide (LDA) [39]. Both reactions involve intermediate formation of 3,4-didehydropyridine **4**. Compounds **5** and **6** were thus obtained in 25 and 28% yield, respectively (Scheme 1).

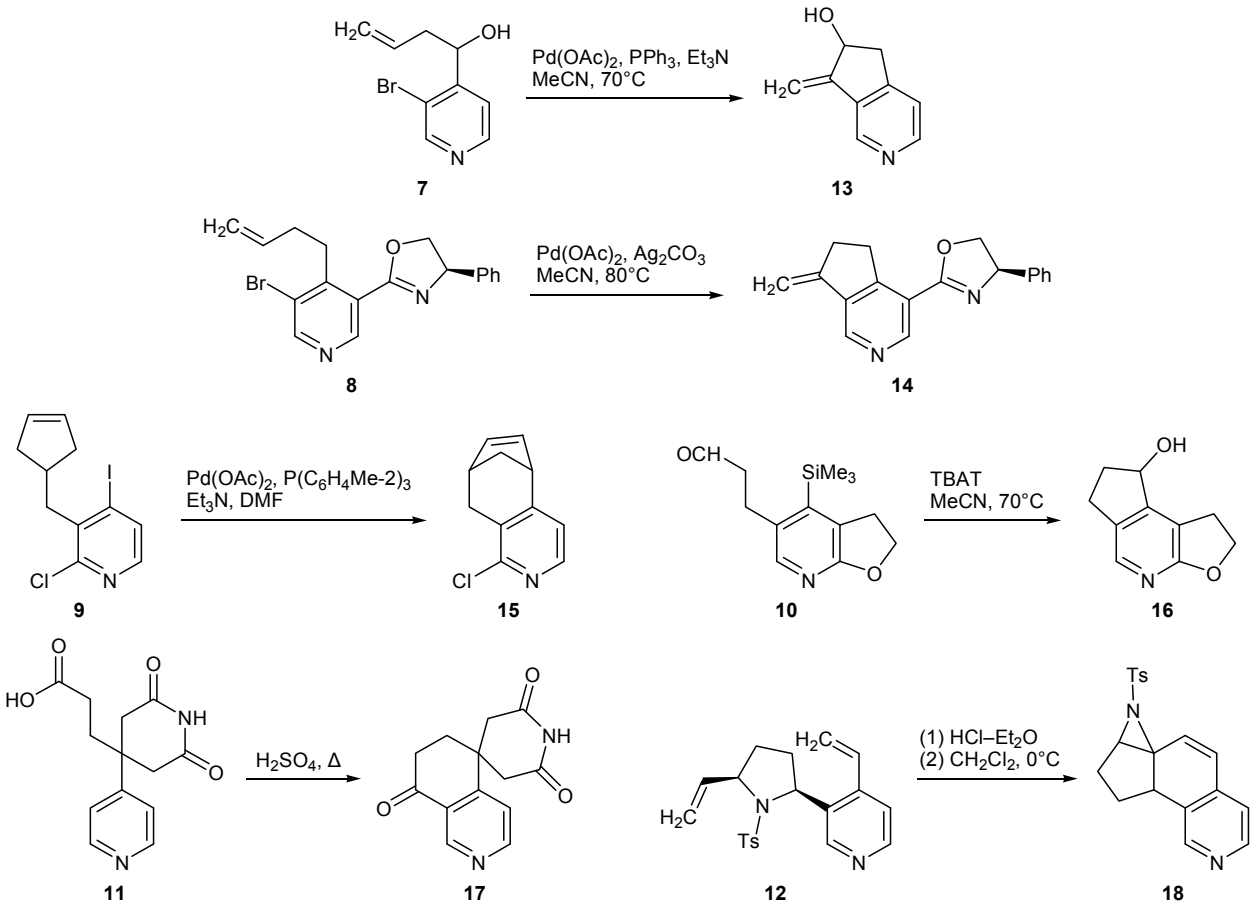
Intramolecular annulation on a pyridine ring has also been described in a few publications. This method implies preferentially intramolecular nucleophilic substitution of a halogen atom in position *2* or *3* of

Scheme 1.



Hlg = Cl, Br.

Scheme 2.



pyridines **7**–**9** or of trimethylsilyl group in the 4-position of **10**, intramolecular acylation of pyridine **11** at position *3* with carboxylic acid, or intramolecular cycloaddition in **12** in the presence of a ruthenium catalyst. As a result, cycloalka[*c*]pyridines **13**–**18** were obtained in 13–80% [40], 14–83% [41], 15–76% [42], 16–39% [43], 17–71% [44], and 18–64% yields [45] (Scheme 2).

3. FUSION OF A PYRIDINE RING TO CARBOCYCLE

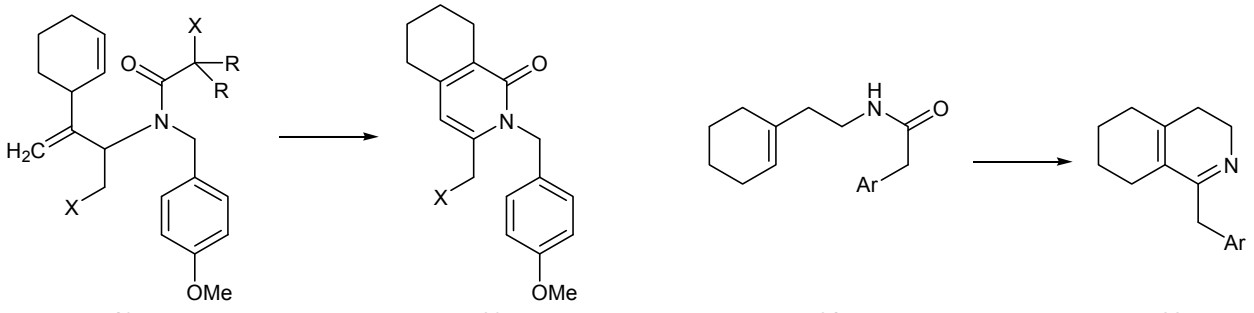
Methods for the synthesis of cycloalka[*c*]pyridines based on the closure of pyridine ring on already existing carbocycle have been studied in sufficient detail due to accessibility of the initial reactants and experimental simplicity. Several examples of such intramolecular transformations have been reported. Intramolecular acylation of dienamide **19** in toluene in the presence of [CuCl] in a nitrogen atmosphere in 16 h afforded 2,3-substituted 5,6,7,8-tetrahydroisoquinolin-1(2*H*)-ones **20** in 12–29% yield [46] (Scheme 3). 1-Substituted 3,4,5,6,7,8-hexahydroisoquinoline **22** was synthesized in 90–96% yield by intramolecular cyclodehydration of cyclohexene **21** in acetonitrile at 25°C in the presence of $AlCl_3$ and KI [47] (Scheme 3).

Substituted 1,3-dithiane **23** was reported to undergo intramolecular cyclization to 1-(thiophen-2-yl)-5,6,7,8-tetrahydroisoquinoline **24** in 75% yield on heating in THF (100°C) in the presence of $HgO–BF_3 \cdot Et_2O–HCl$ [48]. Smiles rearrangement of substituted cycloalkenes **25** on heating in dioxane in the presence of *t*-BuOK gave cycloalka[*d*]furo[2,3-*b*]pyridines **26**. The reaction direction did not change when the solvent was replaced by DMFA, and *t*-BuOK, by NaH or EtONa [49] (Scheme 4).

Numerous intermolecular reactions leading to the formation of a pyridine ring fused to a carbocycle have been reported. The carbocycle is usually represented by cyclopentane and cyclohexane derivatives such as ketones, cycloalkenes, enamines, and enamino ketones. Enamines **27** derived from 2-acylcycloalkanones reacted with CH acids **28** in anhydrous ethanol in the presence of sodium ethoxide at room temperature according to the nucleophilic vinylic substitution path (S_NVin) to give 3-thioxo- [50–52], 3-selenoxo- [53], or 3-(dicyanomethylidene)cycloalka[*c*]pyridine derivatives **29** [54–56]. Likewise, the reactions of enamino ketones **27** with cyclic CH acids **30** and **31** under analogous conditions produced fused cycloalka[*c*]pyridines **32** [57] and **33** [58]. Morpholinium thiolate **34** was obtained in 57% yield by S_NVin reaction of enamine **35** with 2-cyanoethanethioamide (**28**) in ethanol at 20°C [59] (Scheme 5).

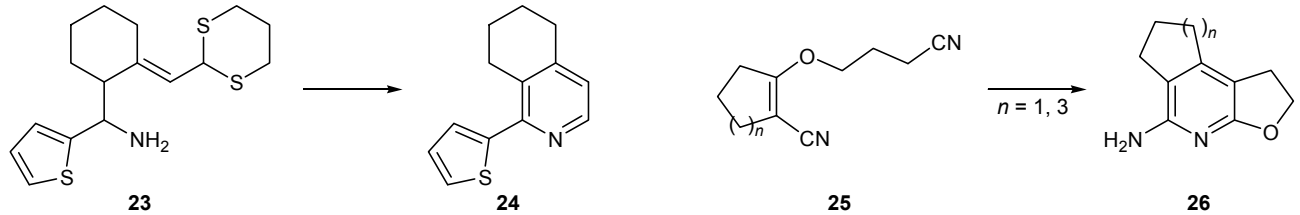
Perhydrocycloalka[*c*]pyridines **36** were synthesized by Michael addition of ethyl cycloalkenecarboxylates **37** to *N*-benzyl-2-tosylacetamide **38** in THF in the

Scheme 3.

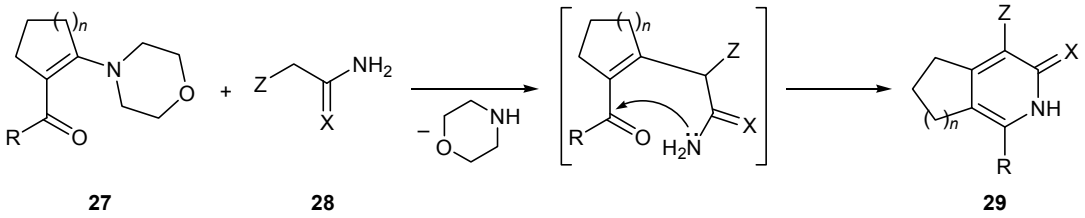


X = H, Cl; R = Me, Cl; Ar = 3-$MeOC_6H_4$, 3-HOC_6H_4, 4-$O_2NC_6H_4$, Ph, 4-$MeOC_6H_4$, 2-HOC_6H_4, 2,4-$Cl_2C_6H_3$.

Scheme 4.

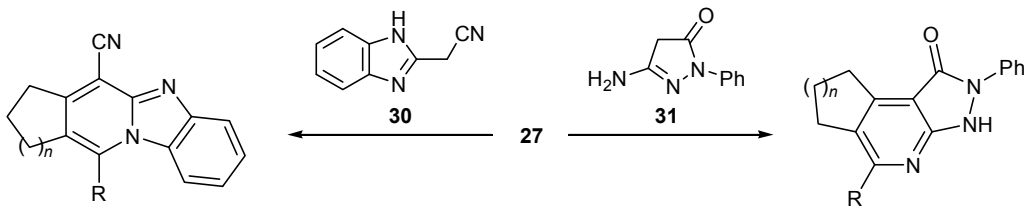


Scheme 5.



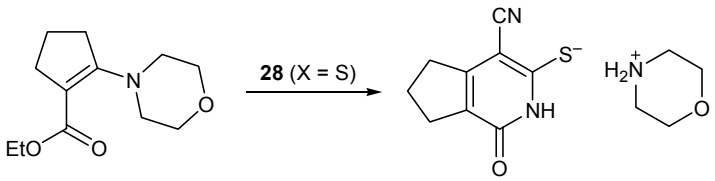
27 **28** **29**

R = Me, Ph, 2-ClC_6H_4; X = S, Se, $C(CN)_2$; *n* = 1–4; Z = CN, COOEt, CONHR′ (R′ = Ar, Alk, H).



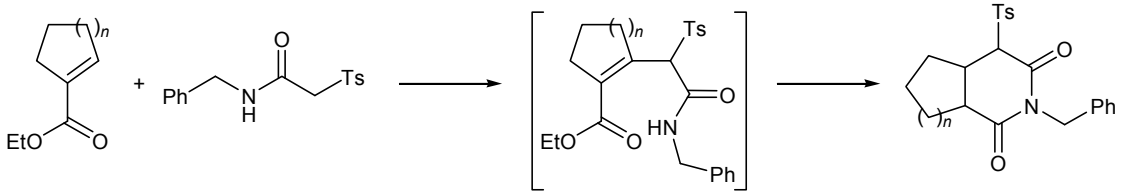
32 **30** **27** **31** **33**

n = 1–4; R = Ar, Alk, Ht.



35 **34**

Scheme 6.



37 **38** **39** **36**

n = 1, 2.

presence of triethylamine, followed by intramolecular cyclization of adducts **39** [60] (Scheme 6).

The condensation of 2-acylcyclohexanones **40** with 2-cyanoethanethioamide (**28**) in methanol at 60°C in the presence of triethylamine gave 5,6,7,8-tetrahydroisoquinoline-3(2*H*)-thiones **41** [61]. In the reaction of 2-acetylcyclohexanone with **28** in ethanol in the presence of morpholine or piperidine a mixture of 1-methyl-3-sulfanylidene-2,3,5,6,7,8-hexatetrahydroisoquinoline-4-carbonitrile (**41**) and 4-methyl-2-sulfanylidene-1,2,5,6,7,8-hexahydroquinoline-3-carbonitrile (**42**) was formed, compound **41** being the major product [62]. 2-Cyanoacetamide **28** (X = O) reacted with diketones **40** in a similar way. The reaction in DMSO in the presence of triethylamine at 80°C afforded a mixture of isoquinoline **41** and quinoline **42**, the former prevailing [63] (Scheme 7).

Substituted 2,4-diacetylcyclohexanones **43** regioselectively reacted with CH acids **28** to give 5,6,7,8-tetrahydroisoquinoline-3(2*H*)-chalcogenones **44** (X = S [64–66], Se [67]). The condensations were carried out on heating in anhydrous ethanol in the presence of morpholine (X = S) or triethylamine (X = Se). The reaction of **43** with malononitrile (**45**) as CH acid on heating in ethanol in the presence of piperidine lead to the formation of 81–89% of 5,6,7,8-tetrahydroisoquinoline-3(2*H*)-ones **46** [68] (Scheme 8).

Pyrazole-fused cycloalka[*c*]pyridines **47** were synthesized by reaction of **43** with 3-amino-1-phenyl-

1*H*-pyrazol-5(4*H*)-one (**31**) in boiling ethanol in the presence of sodium ethoxide (yield 78–88%) [69]. The condensation of methyl 4,4-dimethyl-2-oxo-cyclohexane-1-carboxylate (**48**) with 2-cyanoethanethioamide (**28**) in boiling methanol in the presence of KOH gave 1,3-dihydroxy-6,6-dimethyl-5,6,7,8-tetrahydroisoquinoline-4-carbonitrile (**49**) [70] (Scheme 9).

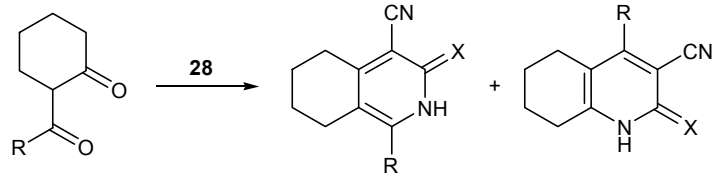
Cycloalka[*c*]pyridine-3(2*H*)-thiones **50** were obtained by the Michael reaction involving exchange of methylene components. The addition of 2-cyano-2-cycloalkylideneethanethioamides **51** to 2-ylidenemalononitriles **52** in boiling ethanol in the presence of piperidine gave intermediates **53** which lost malononitrile molecule to form alkenes **54**, and intramolecular cyclization of the latter via aza-Michael reaction and subsequent dehydrogenation led to final products **50**. Compounds **50** were also synthesized by reaction of cycloalkylidenemalononitriles **55** with 2-[aryl(hetaryl)-methylidene]-2-cyanoethanethioamides **56** under analogous conditions [71, 72] (Scheme 10).

Cyclohexylidenemalononitrile **55** reacted with phenyl isothiocyanate in boiling benzene in the presence of tetrabutylammonium bromide to give a mixture of products, among which isothiochromene, 5,6,7,8-tetrahydroisoquinoline-1(2*H*)-thione, and 5,6,7,8-tetrahydroisoquinolin-1(2*H*)-one derivatives **57**–**59** were identified [73]. If piperidine was used as catalyst and the reaction was carried out in boiling ethanol, the only product was cycloalka[*c*]pyridine-1(2*H*)-thione derivative **60**; it was likely to be formed through intermediate adduct **61** [74] (Scheme 11).

Cycloalka[*c*]pyridines **62** were synthesized in 71–96% yield by reaction of substituted acetylenes **63** with Schiff bases **64** in DMF at 100°C under catalysis by $Pd(OAc)_2$ [75, 76]. Ketone oximes **65** reacted with alkynes **63** in boiling toluene [77] or THF [78] in the presence of $RhCl(PPh_3)_3$ or $(i\text{-}PrO)_3P$ to give cycloalka[*c*]pyridines **66** in 79–89% yield (Scheme 12).

2-[4-Cyano-5,6,7,8-tetrahydroisoquinolin-3(2*H*)-ylidene]propanedinitrile (**69**) was obtained by condensation of Mannich ketones **67** with malononitrile dimer **68** in the presence of piperidine at 50°C [79]. Dialdehyde **70** reacted with hydroxylamine hydrochloride in boiling glacial acetic acid to produce 26% of

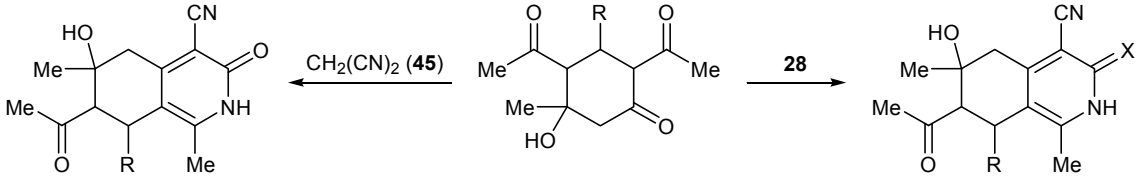
Scheme 7.



40 **41** **42**

R = thiophen-2-yl, Me, Ar; X = O, S.

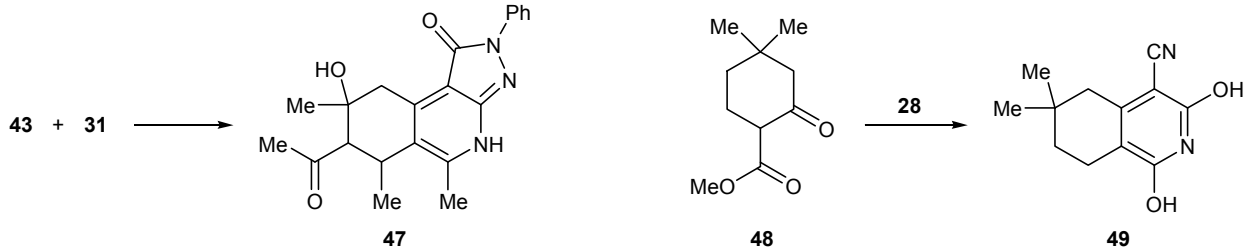
Scheme 8.



46 **43** **44**

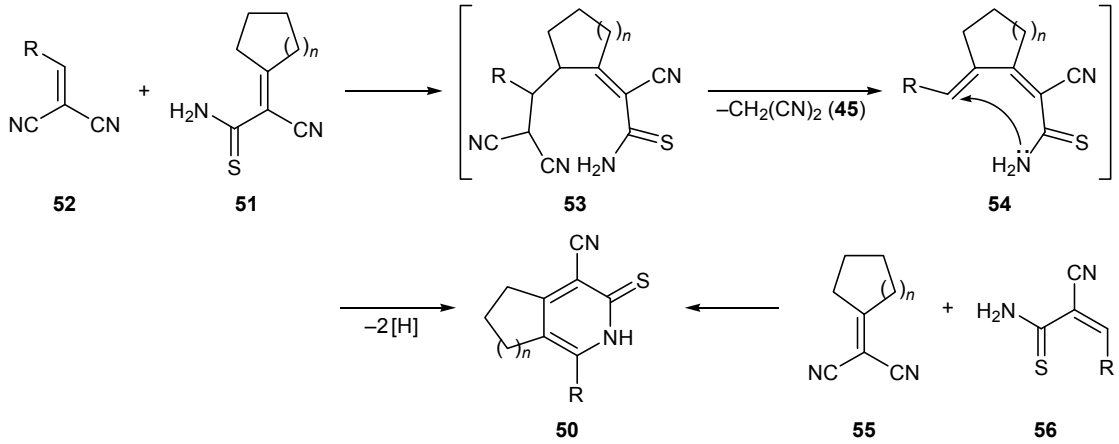
R = Alk, Ht, Ar; X = S, Se.

Scheme 9.



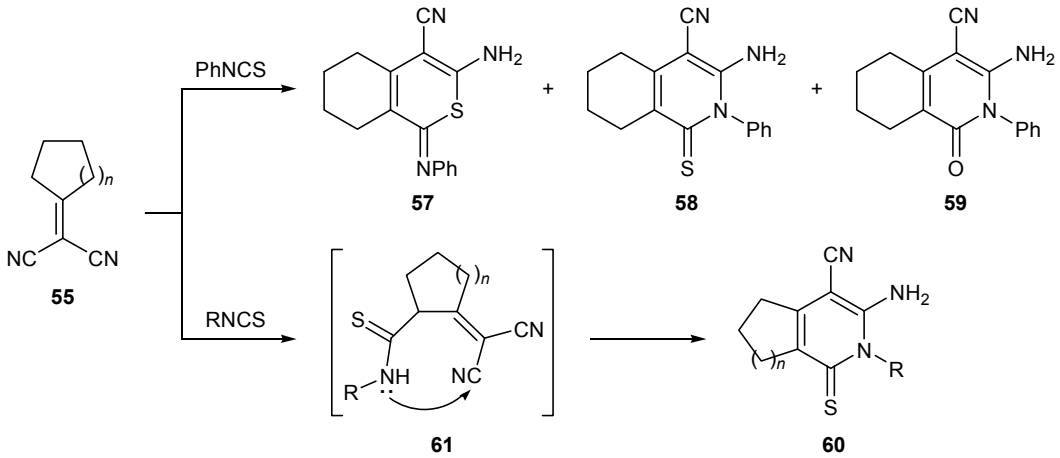
47 **48** **49**

Scheme 10.



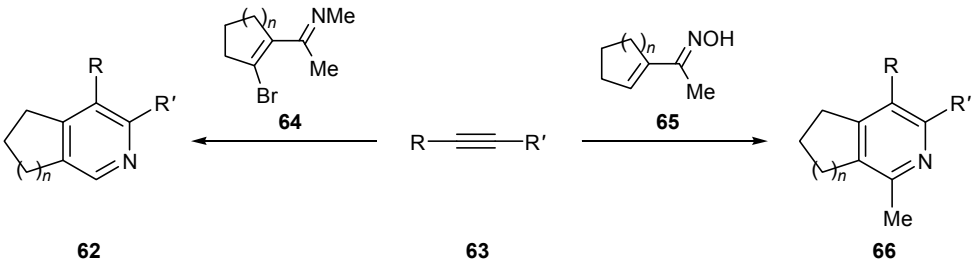
n = 1, 2.

Scheme 11.



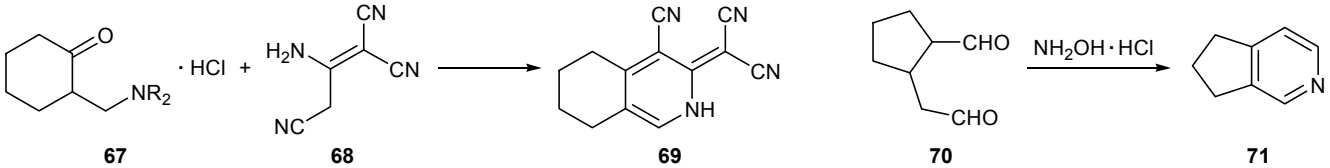
n = 1, 2; R = Ph, PhCO.

Scheme 12.



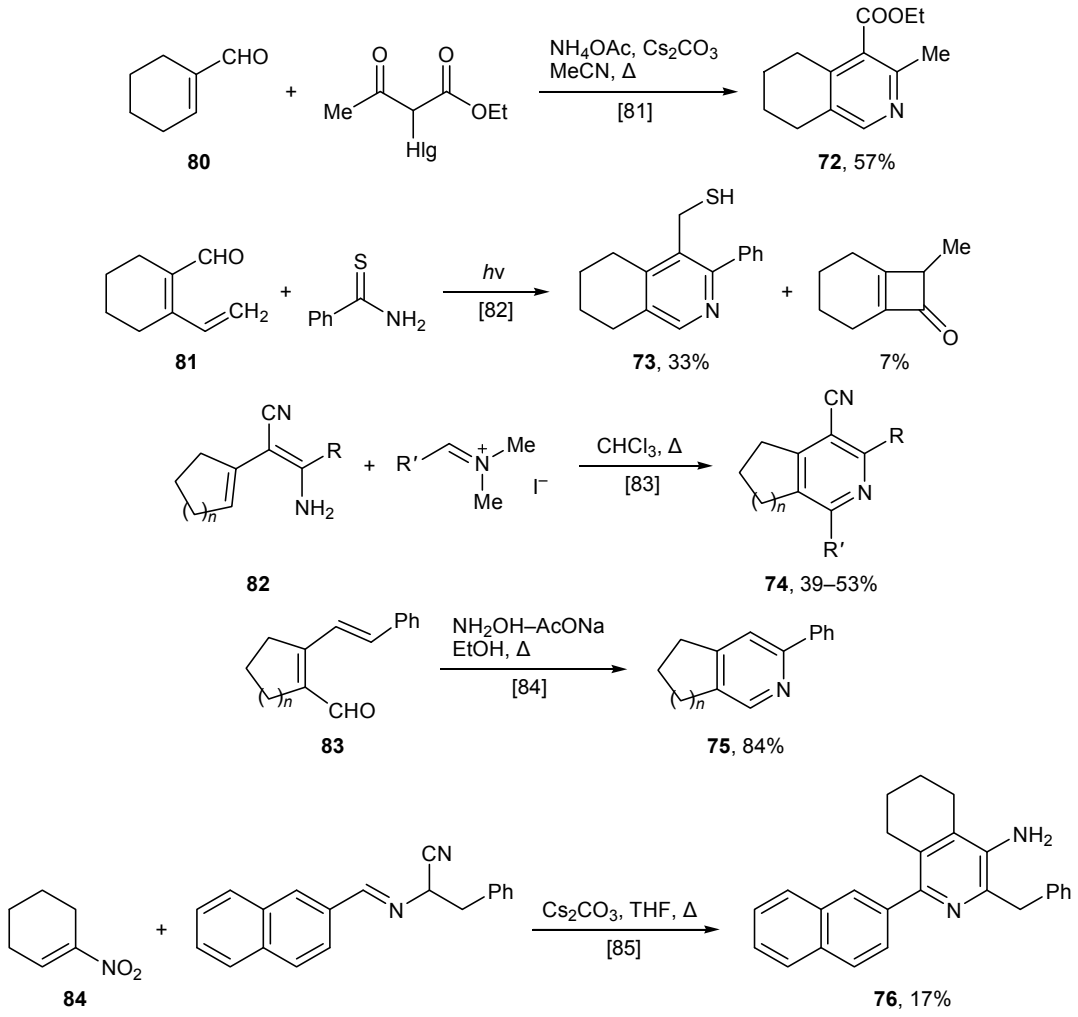
n = 1, 2; R, R′ = H, Ph, Me, $HOCH_2$, thiophen-2-yl.

Scheme 13.



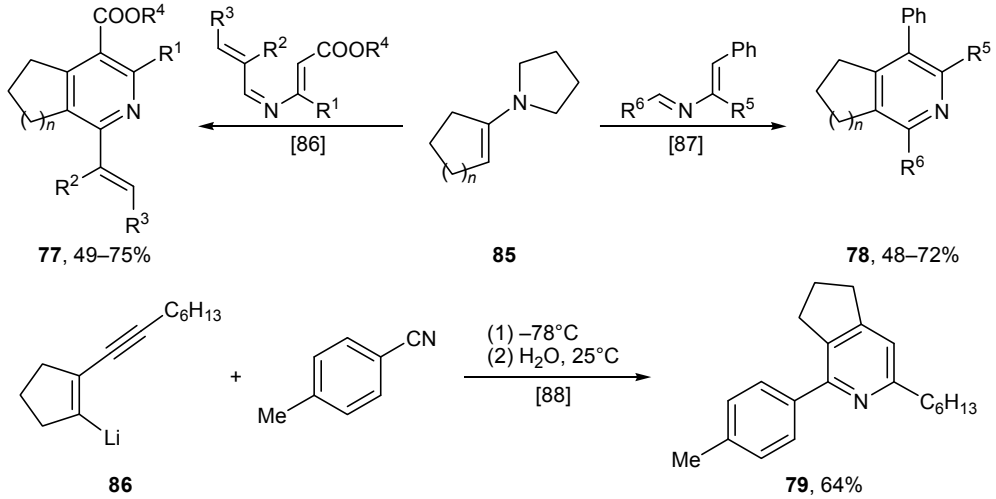
R_2N = piperidin-1-yl, Me_2N.

Scheme 14.



Hlg = F, Cl, Br; R = Me, Ph; R′ = H, Me, Ph, pyridin-2-yl; *n* = 1, 2.

Scheme 15.



n = 1, 2; R^1 = H, COOMe; R^2 = H, Me; R^3 = H, Me, Ph; R^4 = Me, Et; R^5 = pyridin-3-yl, furan-2-yl, thiophen-2-yl, Ph; R^6 = pyridin-3-yl, pyrrol-2-yl, thiophen-2-yl, Ph.

6,7-dihydro-5*H*-cyclopenta[*c*]pyridine (**71**) [80] (Scheme 13). Reactions of cycloalkene derivatives **80**–**86** with compounds containing an amino group necessary for the construction of pyridine ring were reported as convenient methods for the synthesis of cycloalka[*c*]pyridines **72**–**79** [81–88] (Schemes 14, 15).

4. SYNTHESIS FROM ACYCLIC PRECURSORS

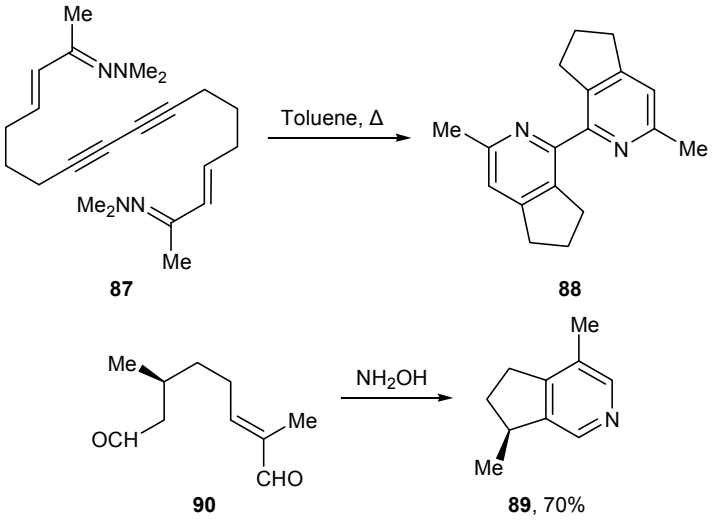
The strategy of synthesis of cycloalka[*c*]pyridines from acyclic starting compounds is represented in the literature by four types of reactions, namely intramolecular cyclization of a single precursor, cyclocondensation of dialdehydes with hydroxylamine, and cyclocondensations of diynes with isocyanates and nitriles. Only the latter version have been studied in sufficient detail, whereas examples of the first three are very few in number.

Double intramolecular hetero-Diels–Alder reaction of diyne **87** in boiling toluene led to the formation of 76% of 1,1′-bi(3-methyl-6,7-dihydro-5*H*-cyclopenta[*c*]pyridine) **88** [89]. The alkaloid actinidine **89** was synthesized by condensation of 2,6-dimethyloct-2-ene-1,8-dicarbaldehyde **90** with hydroxylamine in tetrahydrofuran in the presence of *p*-toluenesulfonic acid [90] (Scheme 16).

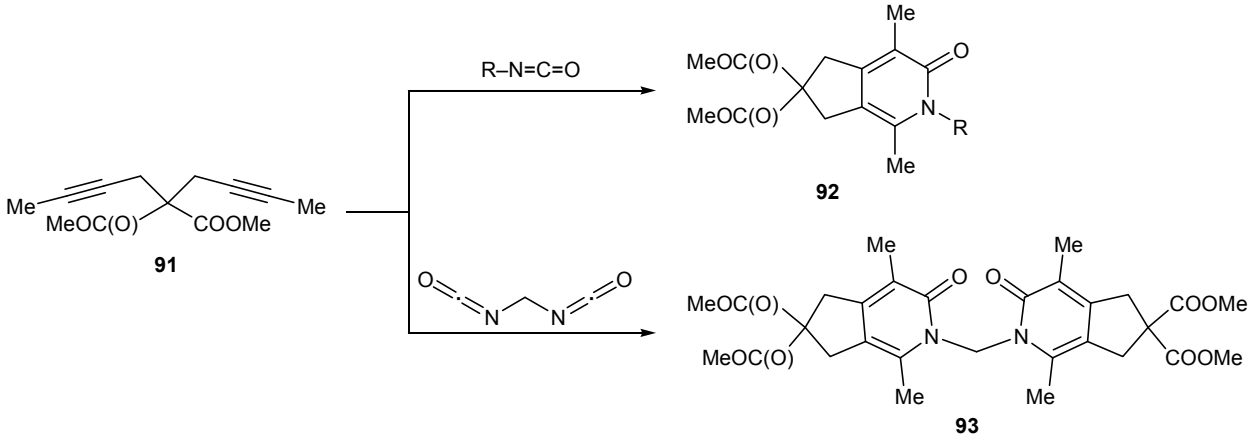
Iridium-catalyzed [2+2+2]-cycloaddition of diyne **91** with isocyanates in boiling 1,2-dichloropropane afforded cyclopenta[*c*]pyridin-3-one derivatives **92** in high yields (80–99%). Analogous reaction with methylene diisocyanate gave functionalized 2,2′-methylenedi(cyclopenta[*c*]pyridine) **93** in 99% yield [91] (Scheme 17).

[2+2+2]-Cyclotrimerization of diyne **94** with ethyl isocyanate in the presence of Ru(III) salts in boiling

Scheme 16.

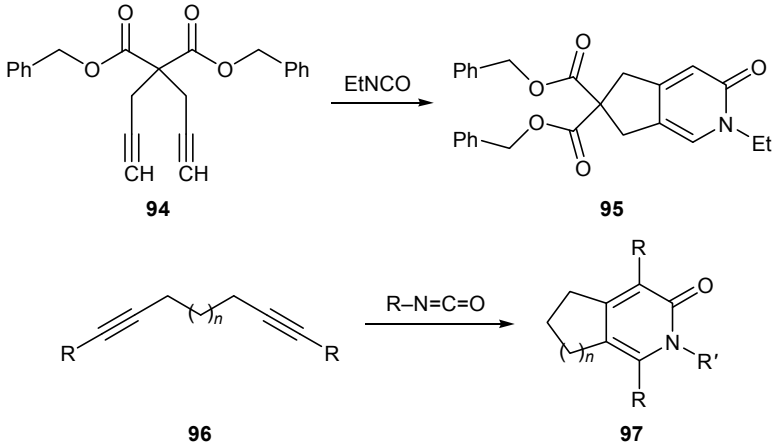


Scheme 17.



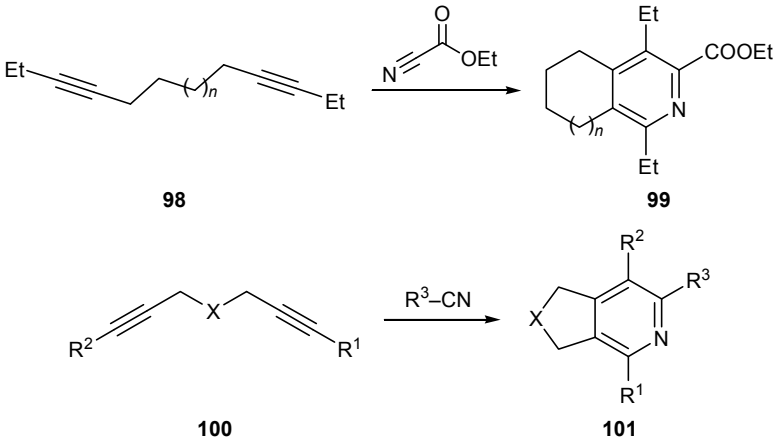
R = Alk, Ar, Ht.

Scheme 18.



R = H, Me, Et; R′ = Ph, Bu, $PhCH_2$; *n* = 1–3.

Scheme 19.



R^1, R^2 = H, Me, Et, naphthalen-1-yl, pyridin-1-yl; R^3 = NMe_2, pyrrolidin-1-yl, Ph, Ht, Alk, CH_2CN; X = $C(COOMe)_2$, $(CH_2)_n$; *n* = 1–3.

acetone, toluene, or dioxane produced substituted 2-ethylcyclopenta[*c*]pyridin-3-one **95** in 93% yield [92]. Rhodium complexes catalyzed [2+2+2]-cycloaddition of diynes **96** to isocyanates in chloroform on heating; as a result, cycloalka[*c*]pyridin-3(1*H*)-ones **97** were formed in 48–98% yield [93] (Scheme 18).

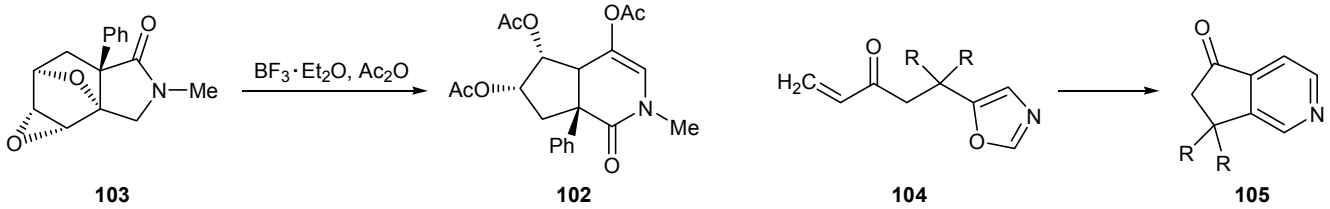
Rhodium-catalyzed [2+2+2]-cycloaddition of alkynes **98** to nitriles in methylene chloride at room temperature under argon afforded 63–84% of fused pyridines **99** [94]. Diynes **100** were quantitatively converted to cycloalka[*c*]pyridines **101** by reaction with nitriles in the presence of different catalysts such as iron(II) salts in THF at 20°C [95–97], Ir(II) on heating in benzene [98], Co(II) in THF, toluene, or ethanol [99–107], Ni(II) in benzene or toluene on heating [108–111], and Ru(II) on heating in 1,2-dichloroethane [112] (Scheme 19).

5. RECYCLIZATIONS AND CROSS-RECYCLIZATIONS

Recyclizations and cross-recyclizations were rarely reported as methods for the synthesis of cycloalka[*c*]-pyridine derivatives due to poor yields and low selectivity. Substituted cyclopenta[*c*]pyridine **102** was obtained in 29% yield by Wagner–Meerwein-type recyclization of 2,6a-epoxyoxireno[*e*]isoindole **103** on heating in benzene [113]. Substituted oxazoles **104** in boiling 1,2-dichlorobenzene in the presence of $Cu(OTf)_2$ underwent intramolecular Diels–Alder reaction leading to cyclopenta[*c*]pyridin-5-ones **105** in 24–55% yield [114, 115] (Scheme 20).

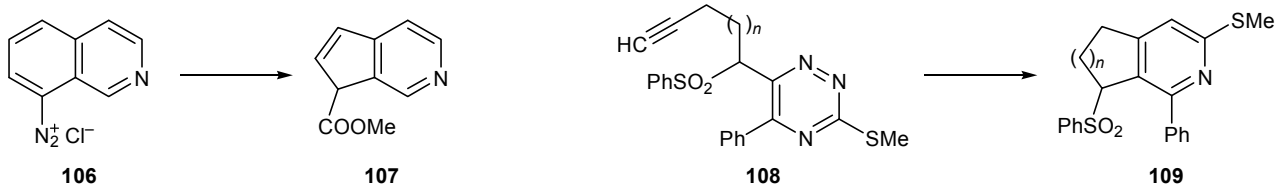
Methyl 7*H*-cyclopenta[*c*]pyridine-7-carboxylate (**107**) was formed as a result of isomerization of isoquinoline-8-diazonium chloride (**106**) in methanolic

Scheme 20.



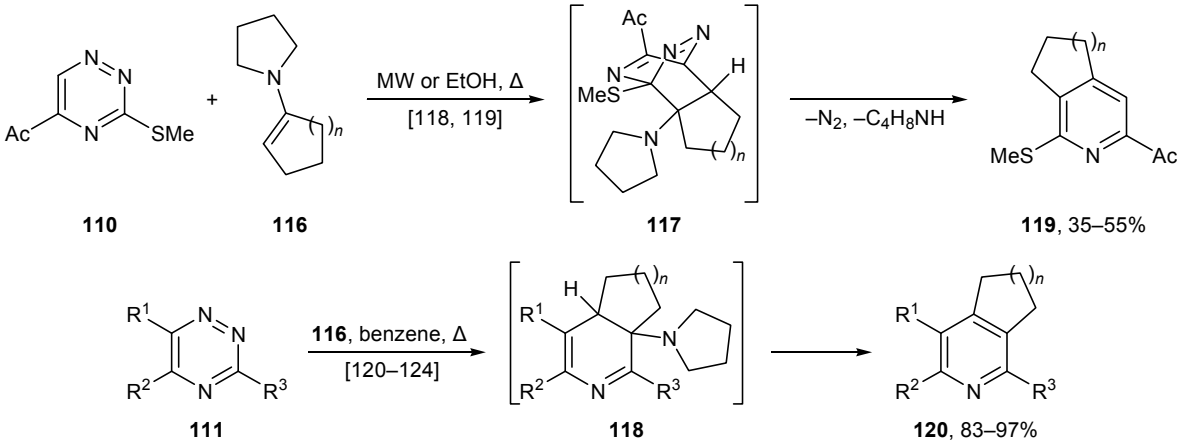
R = H, Me.

Scheme 21.



n = 1, 2.

Scheme 22.



R^1 = Ph, $PhS(CH_2)_3$, 4-FC_6H_4, 4-$MeOC_6H_4$; R^2 = H, CN, MeC=NOMe, quinolin-2-yl, Ac; R^3 = pyridin-2-yl, COOEt, $MeSO_2$, MeS; *n* = 1–3.

$NaHCO_3$ at 0°C in 3 h [116]. Intramolecular Diels–Alder reaction of 1,2,4-triazines **108** on heating for a short time (3–7 min) in bromobenzene under nitrogen gave cyclopenta[*c*]pyridine derivatives **109** in 27–29% yield [117] (Scheme 21).

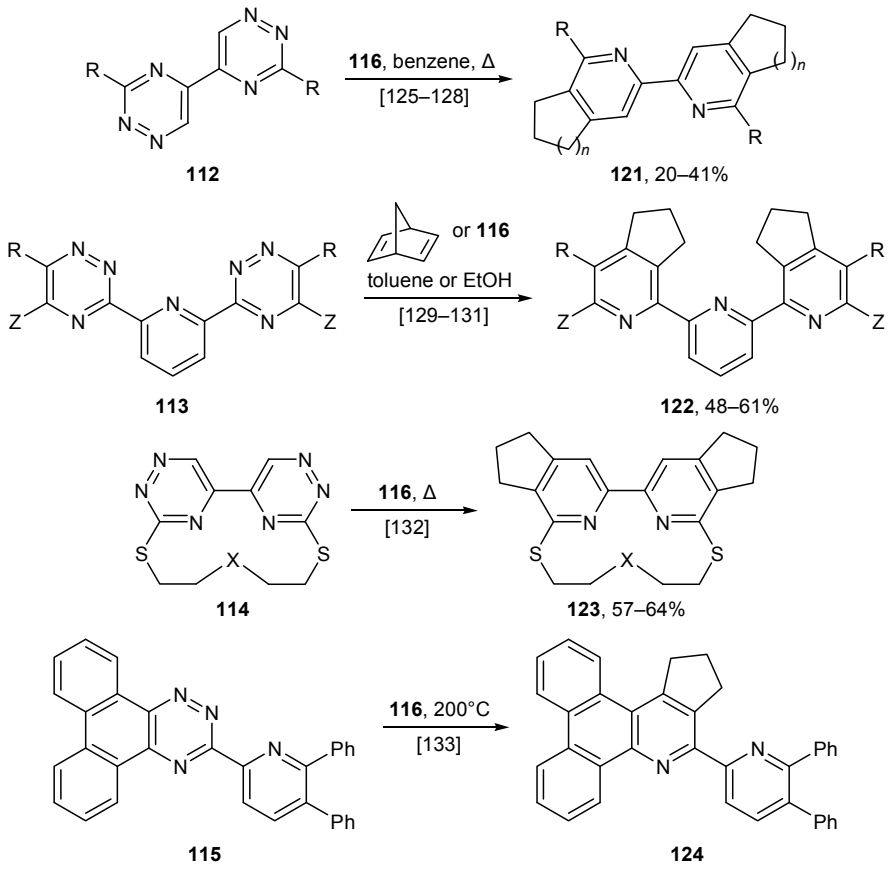
Cross-recyclization of substituted 1,2,4-triazines **110**–**115** with enamines **116** involved intermediate formation of cycloadducts **117** and **118**, and the subsequent elimination of pyrrolidine and nitrogen molecules afforded cycloalka[*c*]pyridines **119**–**124** [118–133] (Schemes 22, 23).

Mesoionic compounds **127** were obtained in 15–44% yield by cross-cyclization of substituted 1,2,4-triazin-5(4*H*)-ones **125** with 2 equiv of cycloalkanones **126** in the presence of TsOH [134]. The reaction of equimolar amounts of **126** and **128** in the presence of an amine (B) under reflux or microwave irradiation gave 25–91% of cycloalka[*c*]pyridines **129** [135] (Scheme 24).

The natural alkaloid gardenamide A (**131**) was synthesized in 71% yield by heating cyclopenta[*c*]-pyran derivative **130** in boiling benzene in the presence of Ag_2CO_3 and NH_3 [136] (Scheme 25).

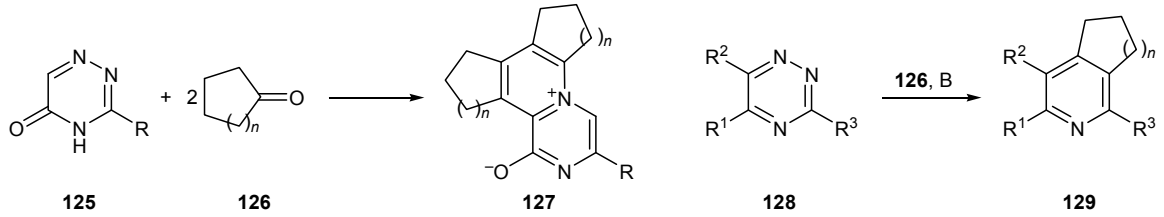
Cross-recyclization of substituted furo[3,4-*c*]pyridine **132** with activated alkenes **133** in methylene chloride at room temperature involved intermediate formation of Diels–Alder adducts **134** which were converted in 2–3 h *in situ* to tetrahydroisoquinolines **135** in 63–92% yield [137] (Scheme 26). A three-step synthesis of 1-methyl-5,6,7,8-tetrahydroisoquinoline

Scheme 23.



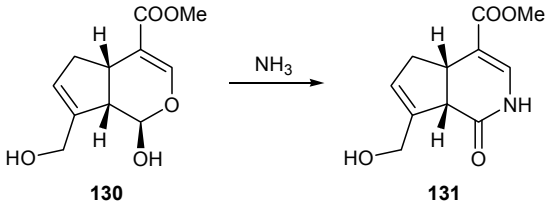
112, **121**, *n* = 1–4; R = MeS, Me, $(Me)_2CHS$; **113**, **122**, R = Pr, *i*-Bu, Ph, 4-MeC_6H_4, thiophen-2-yl, naphthalen-2-yl; Z = CN, COOEt; **114**, **123**, X = CH_2, O.

Scheme 24.



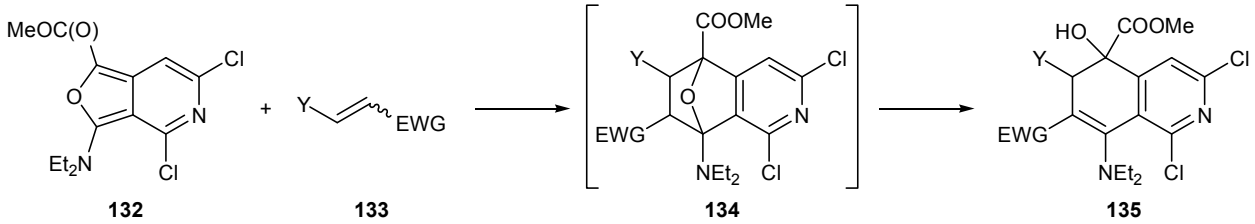
127, R = Ph, MeS, 4-MeC_6H_4, 4-ClC_6H_4; *n* = 1, 2; **129**, *n* = 1–8; B = morpholine, pyrrolidine, piperidine, $MeNH_2$, Et_2NH, $BuNH_2$; R^1 = furan-2-yl, Ph, H, Me; R^2 = H, Me, furan-2-yl; R^3 = pyridin-3-yl, COOEt.

Scheme 25.



(**136**) in 44% yield was reported in [138]. For this purpose, ketone **137** was treated with 3-trimethylsilyl-2-methylprop-1-ene in the presence of $TiCl_4$ in methylene chloride at 23°C; alkene **138** thus formed was subjected to ozonation in CH_2Cl_2 at 78°C in the presence of PPh_3, and the resulting aldehyde **139** was

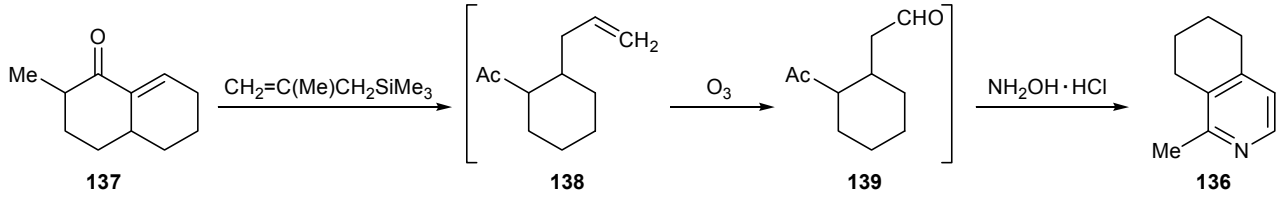
Scheme 26.



132 **133** **134** **135**

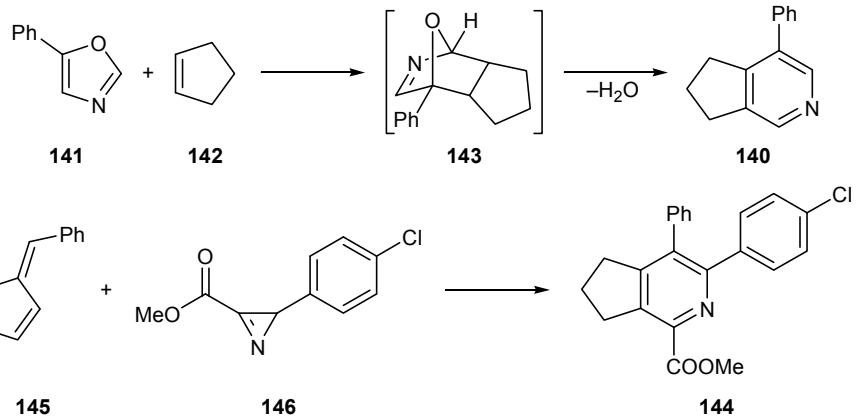
Y = H, COOMe, Ph; EWG = CN, COOMe, NO_2.

Scheme 27.



137 **138** **139** **136**

Scheme 28.



141 **142** **143** **140**

145 **146** **144**

treated with hydroxylamine in acetonitrile at 80°C (Scheme 27).

3-Phenylcyclopenta[*c*]pyridine **140** was synthesized in 11% yield by the reaction of 5-phenyloxazole **141** with cyclopentene **142** under microwave irradiation at 180°C. Presumably, the primary product was Diels–Alder adduct **143** [139] (Scheme 28). Substituted cyclopenta[*c*]pyridine **144** was synthesized in 93% yield by cross-recyclization of fulvene **145** with 2*H*-azirine **146** in THF at 25°C [140].

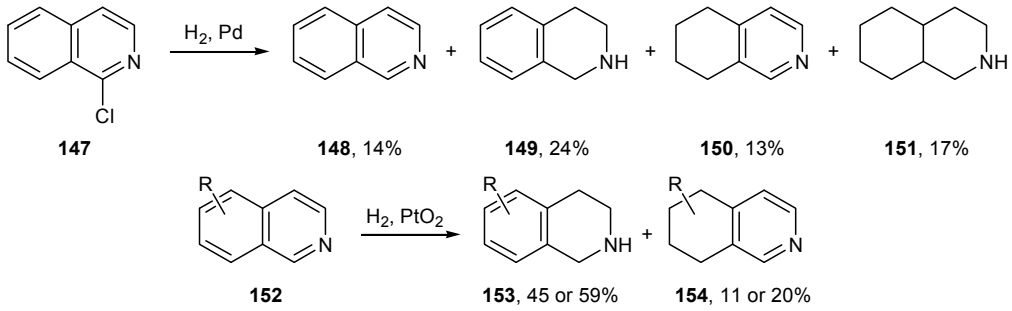
6. SELECTIVE REDUCTION OF THE CARBOCYCLE IN ISOQUINOLINE

The reduction of 1-chloroisoquinoline (**147**) with hydrogen over palladium catalyst in benzene at 100°C usually gives a mixture of isoquinoline (**148**) and partially and completely hydrogenated isoquinolines **149**–**151** [141]. The hydrogenation of *N*-(isoquinolin-1-yl)- and *N*-(isoquinolin-5-yl)acetamides **152** over PtO_2 in CF_3COOH at 60°C afforded a mixture of partially hydrogenated derivatives **153** and **154** [142, 143] (Scheme 29).

5,6,7,8-Tetrahydroisoquinoline (**150**) was obtained by treatment of compound **155** with SbF_5 in cyclohexane or CF_3SO_3H at 25°C (yield 94 and 85%, respectively) [144, 145]. The reduction of **155** with hydrogen in the presence of RuH_2 in *p*-xylene at 80°C under pressure (3 atm) gave 44% of **150** [146, 147] (Scheme 30).

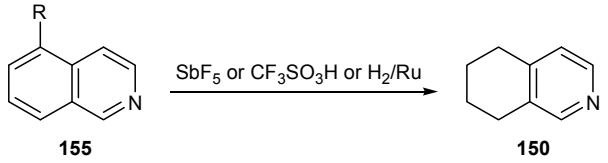
Selective reduction of the carbocycle in methyl isoquinoline-5-carboxylate **156** hydrogen was achieved in trifluoroacetic acid using platinum(IV) oxide as catalyst; methyl 5,6,7,8-tetrahydroisoquinoline-5-carboxylate **157** was obtained in 58% yield [148]. 1-Substituted isoquinoline **158** was selectively and quantitatively hydrogenated to 5,6,7,8-tetrahydroiso-

Scheme 29.



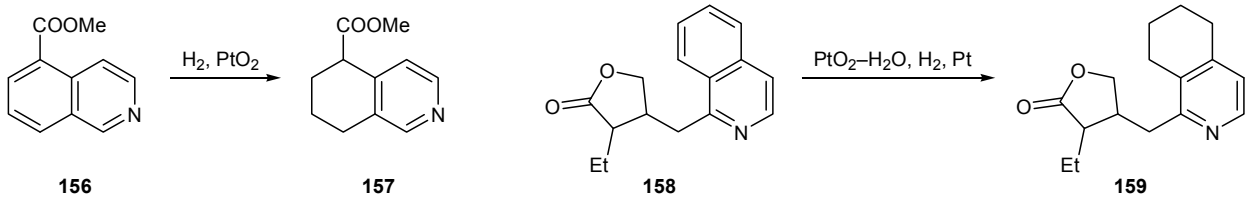
R = 1-NHAc, 5-NHAc.

Scheme 30.

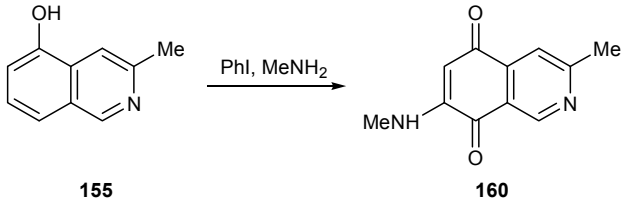


R = H, OH.

Scheme 31.



Scheme 32.



quinoline **159** with in the presence of Adams' catalyst under a pressure of 20 Pa [149] (Scheme 31).

Preliminary treatment of 5-hydroxy-3-methylisoquinoline **155** with iodobenzene and methylamine in acetonitrile in the presence of $CeCl_3 \cdot 7H_2O$ at 0°C afforded 94% of 3-methyl-7-(methylamino)isoquinoline-5,8-dione (**160**) [150] (Scheme 32).

7. CHEMICAL PROPERTIES

Transformations of functionalized cycloalka[*c*]pyridine derivatives can involve both functional substituents and some positions in the pyridine ring and carbocycle. In this review we consider only the first steps of these transformations.

The alkylation of cycloalka[*c*]pyridines **161** with alkyl halides **162** was regioselective, and the products were corresponding sulfides **163**. The reactions were carried out in DMF in the presence of KOH or Na_2CO_3 [151–154] (Scheme 33).

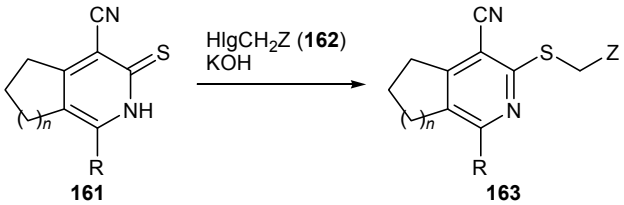
3-Methylcycloalka[*c*]pyridine-4-carbonitriles **164** reacted with sodium azide in acetic acid to produce 58–61% of 4-(2*H*-tetrazol-5-yl)-substituted derivatives **165** [155]. Treatment of the same substrates with 50% aqueous hydroxylamine as nucleophile in boiling ethanol led to the formation of *N*-hydroxy amides **166** in 5–57% yield [156]. Thioamides **167** were synthesized in 73–94% yield by reaction of **164** with *O*,*O*-diethyl hydrogen dithiophosphate in concentrated aqueous HCl at 80°C [156]. The oxidation of tetrahydro-

isoquinoline **164** (n = 2) with hydrogen peroxide in acetic acid at 70°C afforded 3-methyl-5,6,7,8-tetrahydroisoquinoline-4-carbonitrile 2-oxide (**168**, yield 94%) [157] (Scheme 34).

3-Azidomethyl-5,6,7,8-tetrahydroisoquinoline-4-carbonitrile (**169**) was obtained in 96% yield by reaction of 2-(chloromethyl)-5,6,7,8-tetrahydroisoquinoline-4-carbonitrile (**170**) with sodium azide in DMSO [158] (Scheme 35). 3-(Indol-3-yl)-1-(methylsulfanyl)cycloalka[*c*]pyridines **171** were formed in 26–53% yield in the Fischer reaction of 3-acetyl derivatives **172** with phenylhydrazine and zinc chloride at 190°C under microwave irradiation [159] (Scheme 35).

The alkylation of 3-methoxy-1-methyl-5,6,7,8-tetrahydroisoquinoline (**173**) with *p*-bromophenacyl

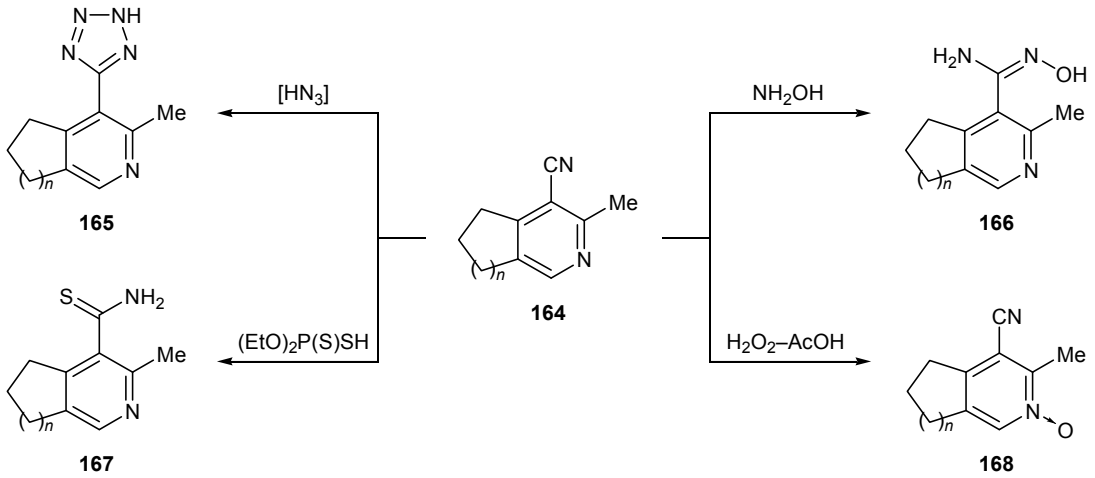
Scheme 33.



161 **163**

n = 1, 2; R = H, morpholin-4-yl, Me, piperidin-1-yl, pyrrolidin-1-yl, Ph, Pr; Hlg = Cl, Br; Z = H, Alk, ArCO, Ht, $CONH_2$.

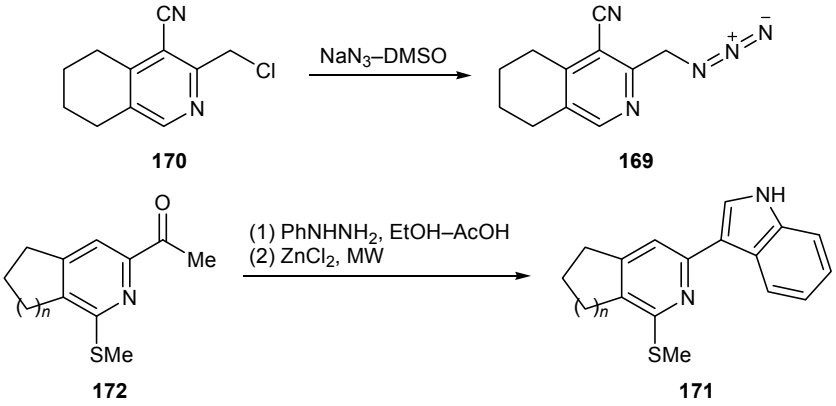
Scheme 34.



165 **166** **164** **167** **168**

n = 1–3.

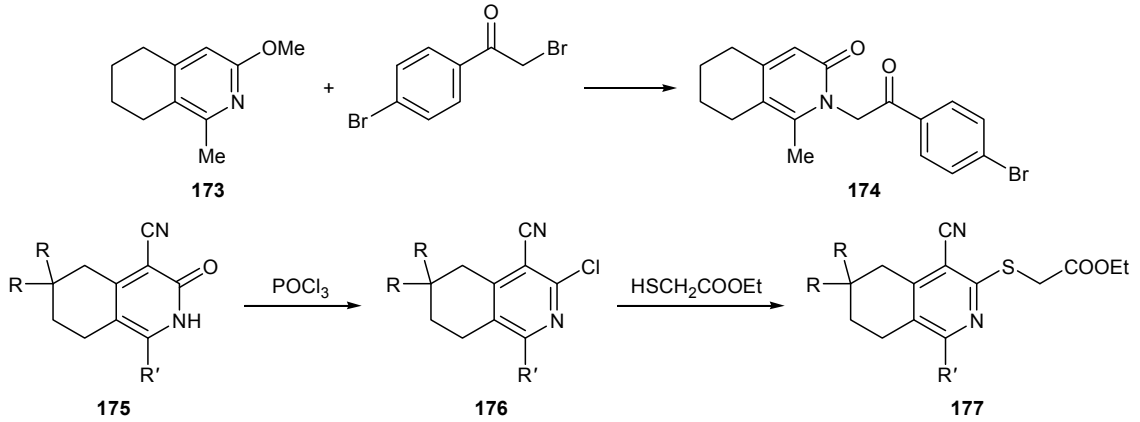
Scheme 35.



170 **169** **172** **171**

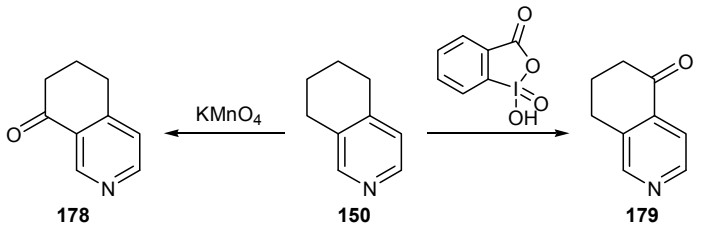
n = 1–4.

Scheme 36.

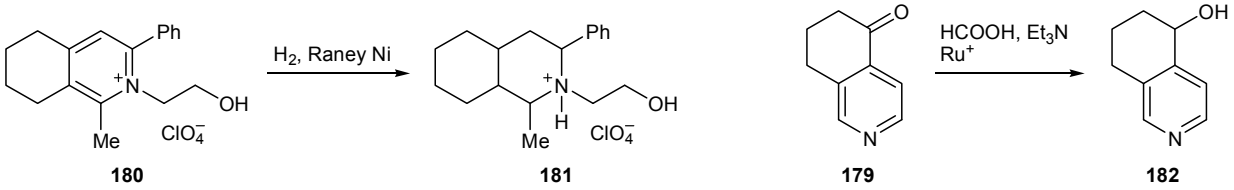


R = H, Me; R′ = Me, Pr, *i*-Pr, $PhCH_2$, *i*-Bu, Ph, furan-2-yl.

Scheme 37.



Scheme 38.



bromide in boiling acetonitrile gave 38% of *N*-substituted 5,6,7,8-tetrahydroisoquinolin-3(2*H*)-one **174** [160]. Treatment of 5,6,7,8-tetrahydroisoquinolin-3(2*H*)-ones **175** with $POCl_3$ afforded the corresponding 3-chloro derivatives **176** [161] capable of reacting with ethyl 2-sulfanylacetate via replacement of the chlorine atom with formation of sulfides **177** [162] (Scheme 36).

Regioselective oxidation of 5,6,7,8-tetrahydroisoquinoline (**150**) to 6,7-dihydroisoquinolin-8(5*H*)-one (**178**) was achieved using potassium permanganate [163]. In the reaction of **150** with 2-iodylbenzoic acid in THF, 70% of isomeric 7,8-dihydroisoquinolin-5(6*H*)-one (**179**) was obtained [164, 165] (Scheme 37).

Tetrahydroisoquinolinium perchlorate **180** was selectively hydrogenated over Raney nickel at 140°C (10 MPa) to 2-(2-hydroxyethyl)-1-methyl-3-phenyldecahydroisoquinolinium perchlorate (**181**) [166] (Scheme 38). The reduction of 7,8-dihydroisoquinolin-5(6*H*)-one (**189**) with a mixture of formic acid and triethylamine in the presence of ruthenium complexes involved only the oxo group to give the corresponding alcohol **182** in 96% yield [167] (Scheme 38).

8. CONCLUSION

Cycloalka[*c*]pyridine derivatives are extensively and thoroughly studied due to their potential utility in the design of materials for medical, agricultural, and engineering purposes. At present, the synthesis of alkaloids and their analogs containing a cycloalka[*c*]-pyridine moiety as a structural unit is more advantageous than their isolation from natural sources.

These reasons stimulate interest of researchers in cycloalka[*c*]pyridine derivatives, as follows from the increasing number of experimental studies in relevant fields.

REFERENCES

1. Kartsev, V.G., *Azotistye geterotsikly i alkaloidy* (Nitrogen Heterocycles and Alkaloids), Kartsev, V.G. and Tolstikov, G.A., Eds., Moscow: IBS, 2001, vol. 1, p. 97.
2. Shi, J., *Baran Group Meeting*, 2006, vol. 10, p. 1.
3. Kisel', V.M., Kostyrko, E.O., and Kovtunenko, V.A., *Chem. Heterocycl. Compd*., 2002, vol. 38, no. 11, p. 1295.
4. Potikha, L.M. and Kovtunenko, V.A., *Russ. Chem. Rev*., 2009, vol. 78, p. 513.
5. Tolkunov, V. and Dulenko, V.I., *Izbrannye metody sinteza i modifikatsii geterotsiklov. Izoquinoliny: khimiya i biologicheskaya aktivnost'* (Selected Methods of Synthesis and Modification of Heterocycles. Isoquinolines: Chemistry and Biological Activity), Kartsev, V.G., Ed., Moscow: Nauchnoe Partnerstvo, 2008, p. 277.
6. Buske, A., Busemann, S., Muhlbacher, J., Schmidt, J., Porzel, A., Bringmann, G., and Adam, G., *Tetrahedron*, 1999, vol. 55, p. 1079.
7. Shklyaev, Yu.V., *Khim. Komp'yut. Model. Butlerov. Soobshch*., 2002, vol. 2, no. 7, p. 21.
8. Liou, J.-P. and Cheng, C.-Y., *Tetrahedron Lett*., 2000, vol. 41, p. 915.
9. Lipinska, T., *Tetrahedron Lett*., 2004, vol. 45, p. 8831.
10. Vernier, J.-M., Holsenback, H., Cosford, N.D.P., Whitten, J.P., Menzaghi, F., Reid, R., Rao, T.S., Sacaan, A.I., Lloyd, G.K., Suto, S.M., Chavez-Noriega, L.E., Washburn, M.S., Urrutia, A., and McDonald, I.A., *Bioorg. Med. Chem. Lett*., 1998, vol. 8, p. 2173.
11. Ashwell, G.J., Maxwell, A.A., and Green, A., *J. Mater. Chem*., 2002, vol. 12, p. 2192.
12. Ashwell, G.J. and Gandolfo, D.S., *J. Mater. Chem*., 2002, vol. 12, p. 411.
13. Ashwell, G.J., Ranjar, R., Whittam, A.J., and Gandolfo, D.S., *J. Mater. Chem*., 2000, vol. 10, p. 63.
14. Yoshizumi, T., Miyazoe, H., Sugimoto, Y., Takahashi, H., and Okamoto, O., *Synthesis*, 2005, p. 1593.
15. Ashwell, G.J., Robinson, B.J., Amiri, M.A., Locatelli, D., Quici, S., and Roberto, D., *J. Mater. Chem*., 2005, vol. 15, p. 4203.
16. Ashwell, G.J., Whittam, A.J., Amiri, M.A., Hamilton, R., Green, A., and Grummt, U.-W., *J. Mater. Chem*., 2001, vol. 11, p. 1345.
17. Ashwell, G.J., Tyrrell, W.D., and Whittam, A.J., *J. Am. Chem. Soc*., 2004, vol. 126, p. 7102.
18. Cavasotto, C.N., Ortiz, M.A., Abagyan, R.A., and Piedrafita, F.J., *Bioorg. Med. Chem. Lett*., 2006, vol. 16, p. 1969.
19. Ferlin, M.G., Gia, O., and Via, L.D., *ChemMedChem*, 2011, vol. 6, p. 1872.
20. Peukert, S., Schwahn, U., Gusstegen, S., Schreuder, H., and Hofmeister, A., *Synthesis*, 2005, p. 1550.
21. Wu, S.C., Yoon, D., Chin, J., van Kirk, K., Seethala, R., Golla, R., He, B., Harrity, T., Kunselman, L.K., Morgan, N.N., Ponticiello, R.P., Taylor, J.R., Zebo, R., Harper, T.W., Li, W., Wang, M., Zhang, L., Sleczka, B.G., Nayeem, A., Sheriff, S., Camac, D.M., Mozin, P.E., Everlof, J.G., Li, Y.-X., Ferraro, C.A., Kieltyka, K., Shon, W., Vath, M.B., Zvyaga, T.A., Gordon, D.A., and Robl, J.A., *Bioorg. Med. Chem. Lett*., 2011, vol. 21, p. 6693.
22. Al-Omran, F., Elassar, A.-Z.A., and El-Khair, A.A., *Tetrahedron*, 2001, vol. 57, p. 10163.
23. Hunt, J.C.A., Briggs, E., Clarke, E.D., and Whittingham, W.G., *Bioorg. Med. Chem. Lett*., 2007, vol. 17, p. 5222.
24. Hsin, L.-W., Chang, L.-T., Rothman, R.B., Dersch, C.M., Fishback, J.A., and Matsumoto, R.R., *J. Med. Chem*., 2010, vol. 53, p. 1392.
25. Hidaka, H., Ishikawa, T., and Inoue, D., JPN Patent Appl. no. 39-0059, 1991; *Ref. Zh., Khim*., 1993, no. 20O42P.
26. Reichelt, C., Schulze, A., Daghish, M., and Leistner, S., EP Patent Appl. no. 1623987, 2006; *Ref. Zh., Khim*., 2007, no. 07.10-19O.115P.
27. Chen, L., Stefanac, T., Turcotte, N., Hu, Z., Chen, Y., Bedard, J., May, S., and Jin, H., *Bioorg. Med. Chem. Lett*., 2000, vol. 10, p. 1477.
28. Sirakanyan, S.N., Ovakimyan, A.A., Noravyan, A.S., Dzhagatspanyan, I.A., Shakhatuni, A.A., Nazaryan, I.M., and Akopyan, A.G., *Pharm. Chem. J*., 2013, vol. 47, no. 3, p. 130.
29. Sirakanyan, S.N., Akopyan, E.K., Paronikyan, R.G., Akopyan, A.G., and Ovakimyan, A.A., *Pharm. Chem. J*., 2016, vol. 50, no. 5, p. 296.
30. Paronikyan, E.G., Noravyan, A.S., Akopyan, Sh.F., Dzhagatspanyan, I.A., Nazaryan, I.M., and Paronikyan, R.G., *Pharm. Chem. J*., 2007, vol. 41, no. 9, p. 466.
31. Paronikyan, E.G., Sirakanyan, S.N., Noravyan, A.S., Paronikyan, R.G., and Dzhagatspanyan, I.A., *Pharm. Chem. J*., 2001, vol. 35, no. 1, p. 8.
32. Paronikyan, E.G., Akopyan, Sh.F., Noravyan, A.S., Gaiosh, G., Dashyan, Sh.Sh., Paronikyan, R.V., and Stepanyan, G.M., *Pharm. Chem. J*., 2013, vol. 47, no. 5, p. 257.
33. Lebedyeva, I.O., Dotsenko, V.V., Turovtsev, V.V., Krivokolysko, S.G., Povstyanoy, V.M., and Povstyanoy, M.V., *Tetrahedron*, 2012, vol. 68, p. 9729.
34. Paronikyan, E.G., Noravyan, A.S., Dzhagatspanyan, I.A., and Arzanunts, E.M., *Khimiya i biologicheskaya aktivnost' kislorod- i serosoderzhashchikh geterotsiklov* (Chemistry and Biological Activity of Oxygen- and Sulfur-Containing Heterocycles), Kartsev, V.G., Ed., Moscow: IBS, 2003, vol. 1, p. 382.

35. Issac, Y.A., Ali, M.S., and Erian, A.W., *Sci. Pharm*., 2000, vol. 68, p. 389.
36. Elmegeed, G.A., Wardakhan, W.W., Younis, M., and Louca, N.A., *Arch. Pharm*., 2004, vol. 337, p. 140.
37. Kamal, A.M., Radwan, S.M., and Zaki, R.M., *Eur. J. Med. Chem*., 2011, vol. 46, p. 567.
38. Ibrahim-Ouali, M., Romero, E., and Bouleghlem, H., *Tetrahedron*, 2011, vol. 67, p. 3668.
39. Mariet, N., Ibrahim-Ouali, M., and Santelli, M., *Tetrahedron Lett*., 2002, vol. 43, p. 5789.
40. Zhao, J., Yang, X., Jia, X., Luo, S., and Zhai, H., *Tetrahedron*, 2003, vol. 59, p. 9379.
41. Robert, N., Hoaran, C., and Marsais, F., *Tetrahedron*, 2007, vol. 63, p. 3702.
42. Demers, S., Stevenson, H., Candler, J., Bashore, C.G., Arnold, E.P., O'Neill, B., and Coe, J.W., *Tetrahedron Lett*., 2008, vol. 49, p. 3368.
43. Koike, T., Hoachi, Y., Takai, T., and Uchikawa, O., *Tetrahedron Lett*., 2011, vol. 52, p. 3009.
44. Fadda, A.A. and Refat, H.M., *Synth. Commun*., 2000, vol. 30, p. 341.
45. Sang, Y., Zhao, J., Jia, X., and Zhai, H., *J. Org. Chem*., 2008, vol. 73, p. 3589.
46. Clark, A.J., Geden, J.V., Thom, S., and Wilson, P., *J. Org. Chem*., 2007, vol. 72, p. 5923.
47. Borthakur, S.K. and Goswami, B.N., *J. Indian Chem. Soc*., 2007, vol. 84, p. 1045.
48. Chen, M.Z. and Micalizio, G.C., *J. Am. Chem. Soc*., 2012, vol. 134, p. 1352.
49. Okuda, K., Watanabe, N., Hirota, T., and Sasaki, K., *Tetrahedron Lett*., 2010, vol. 51, p. 903.
50. Dyachenko, I.V. and Vovk, M.V., *Russ. J. Org. Chem*., 2013, vol. 49, p. 771.
51. Dyachenko, I.V. and Vovk, M.V., *Russ. J. Gen. Chem*., 2013, vol. 83, p. 1724.
52. Dyachenko, I.V. and Vovk, M.V., *Russ. J. Gen. Chem*., 2012, vol. 82, p. 251.
53. Dyachenko, I.V. and Dyachenko, V.D., *Russ. J. Gen. Chem*., 2015, vol. 85, p. 1668.
54. Dyachenko, I.V. and Vovk, M.V., *Ukr. Khim. Zh*., 2013, vol. 79, p. 114.
55. Dyachenko, I.V., Rusanov, E.B., Gutov, A.V., and Vovk, M.V., *Russ. J. Gen. Chem*., 2013, vol. 83, no. 7, p. 1383.
56. Dyachenko, I.V. and Vovk, M.V., *Chem. Heterocycl. Compd*., 2012, vol. 48, p. 1574.
57. Dyachenko, I.V. and Vovk, M.V., *Zh. Org. Farm. Khim*., 2013, vol. 11, no. 1, p. 49.
58. Dyachenko, I.V., Rusanov, E.B., and Vovk, M.V., *Russ. J. Org. Chem*., 2013, vol. 49, p. 1364.
59. Dotsenko, V.V., Krivokolysko, S.G., and Litvinov, V.P., *Monatsh. Chem*., 2008, vol. 139, p. 271.
60. Chen, H.-W., Hsu, R.-T., Chang, M.-Y., and Chang, N.-C., *Org. Lett*., 2006, vol. 8, p. 3033.
61. Lozinskii, M.O., Chernega, A.N., and Shelyakin, V.V., *Russ. J. Org. Chem*., 2002, vol. 38, no. 11, p. 1661.
62. Dotsenko, V.V., Krivokolysko, S.G., Polovinko, V.V., and Litvinov, V.P., *Chem. Heterocycl. Compd*., 2012, vol. 48, p. 309.
63. Van Linden, O.P.J., Wijtmans, M., Roumen, L., Rotteveel, L., Leuzs, R., and de Esch, I.J.P., *J. Org. Chem*., 2012, vol. 77, p. 7355.
64. Dyachenko, V.D., Sukach, S.M., Dyachenko, A.D., Zubatyuk, R.M., and Shishkin, O.V., *Russ. J. Gen. Chem*., 2010, vol. 80, p. 2037.
65. Sukach, S.M. and Dyachenko, V.D., *Russ. J. Org. Chem*., 2015, vol. 51, p. 1020.
66. Dyachenko, V.D. and Karpov, E.N., *Russ. J. Org. Chem*., 2014, vol. 50, p. 1787.
67. Dyachenko, V.D. and Sukach, S.M., *Chem. Heterocycl. Compd*., 2010, vol. 46, p. 1467.
68. Dyachenko, V.D., Sukach, S.M., and Dyachenko, A.D., *Chem. Heterocycl. Compd*., 2015, vol. 51, p. 51.
69. Dyachenko, V.D. and Sukach, S.M., *Russ. J. Gen. Chem*., 2012, vol. 82, p. 305.
70. Taltavull, J., Serrat, J., Gracia, J., Gavalda, A., Andres, M., Cordoba, M., Miralpeix, M., Vilella, D., Beleta, J., Ryder, H., and Pages, L., *J. Med. Chem*., 2010, vol. 53, p. 6912.
71. Elgemeie, G.H. and Ahmed, M.A., *Nucleosides, Nucleotides Nucleic Acids*, 2002, vol. 21, p. 837.
72. Elgemeie, G.H., El-Enany, M.M., Ismail, M.M., and Ahmed, E.K., *Nucleosides, Nucleotides Nucleic Acids*, 2002, vol. 21, p. 477.
73. El-Sayed, A.M. and Abdel-Ghany, H., *J. Heterocycl. Chem*., 2000, vol. 37, p. 1233.
74. Elassar, A.Z.A. and Elkholy, Y.M., *Chem. Heterocycl. Compd*., 2002, vol. 38, p. 1521.
75. Roesch, K.R., Zhang, H., and Larock, R.C., *J. Org. Chem*., 2001, vol. 66, p. 8042.
76. Roesch, K.R. and Larock, R.C., *J. Org. Chem*., 2002, vol. 67, p. 86.
77. Parthasarathy, K., Jeganmohan, M., and Cheng, C.-H., *Org. Lett*., 2008, vol. 10, p. 325.
78. Martin, R.M., Bergman, R.G., and Ellman, J.A., *J. Org. Chem*., 2012, vol. 77, p. 2501.
79. Hammouda, M., El-Ahl, A.S., El-Toukhee, Y.M., and Metwally, M.A., *J. Chem. Res., Synop*., 2002, p. 89.
80. Guandalini, L., Dei, S., Gualfieri, F., Romanelli, M.N., Scapecchi, S., Teodori, E., and Varani, K., *Helv. Chim. Acta*, 2002, vol. 85, p. 96.
81. Song, Z., Huang, X., Yi, W., and Zhang, W., *Org. Lett*., 2016, vol. 18, p. 5640.
82. Oda, K., Nakagami, R., Haneda, M., Nishizono, N., and Mashida, M., *Heterocycles*, 2003, vol. 60, p. 2019.

83. Winter, A. and Risch, N., *Synlett*, 2003, p. 1959.
84. Trost, B.M. and Gutierrez, A.C., *Org. Lett*., 2007, vol. 9, p. 1473.
85. Bergner, I. and Opatz, T., *J. Org. Chem*., 2007, vol. 72, p. 7083.
86. Palacios, F., Herran, E., Alonso, C., and Rubiales, G., *Tetrahedron*, 2006, vol. 62, p. 7661.
87. Palacios, F., Alonso, C., Rubiales, G., and Ezpeleta, J.M., *Eur. J. Org. Chem*., 2001, p. 2115.
88. Dubbaka, S.R., Kienle, M., Mayr, H., and Knochel, P., *Angew. Chem., Int. Ed*., 2007, vol. 46, p. 9093.
89. Bushby, N., Moody, C.J., Riddick, D.A., and Waldron, I.R., *J. Chem. Soc., Perkin Trans. 1*, 2001, p. 2183.
90. Beckett, J.S., Beckett, J.D., and Hofferbrth, J.E., *Org. Lett*., 2010, vol. 12, p. 1408.
91. Onodera, G., Suto, M., and Takeuchi, R., *J. Org. Chem*., 2012, vol. 77, p. 908.
92. Alvarez, S., Medina, S., Domingues, G., and Perez-Gastells, J., *J. Org. Chem*., 2013, vol. 78, p. 9995.
93. Tanaka, K., Wada, A., and Noguchi, K., *Org. Lett*., 2005, vol. 7, p. 4737.
94. Tanaka, K., Suzuki, N., and Nishida, G., *Eur. J. Org. Chem*., 2006, p. 3917.
95. Wang, C., Wang, D., Xu, F., Pan, B., and Wan, B., *J. Org. Chem*., 2013, vol. 78, p. 3065.
96. Lane, T.K., D'Souza, B.R., and Louie, J., *J. Org. Chem*., 2012, vol. 77, p. 7555.
97. Wang, C., Li, X., Wu, F., and Wan, B., *Angew. Chem., Int. Ed*., 2011, vol. 50, p. 7162.
98. Onodera, G., Shimizu, Y., Kimura, J., Kobayashi, J., Ebihara, Y., Kondo, K., Sakata, K., and Takeuchi, R., *J. Am. Chem. Soc*., 2012, vol. 134, p. 10515.
99. Turek, P., Hocek, M., Pohl, R., Klepetazova, B., and Kotora, M., *Eur. J. Org. Chem*., 2008, p. 3335.
100. Hapke, M., Weding, N., and Spannenberg, A., *Organometallics*, 2010, vol. 29, p. 4298.
101. Hrdina, R., Kadlcikova, A., Valterova, I., Hodacova, J., and Kotora, M., *Tetrahedron: Asymmetry*, 2006, vol. 17, p. 3185.
102. Hapke, M., Kral, K., Fischer, C., Spannenberg, A., Gutnov, A., Redkin, D., and Heller, B., *J. Org. Chem*., 2010, vol. 75, p. 3993.
103. Gutnov, A., Heller, B., Fischer, C., Drexler, H.-J., Spannenberg, A., Sundermann, B., and Sundermann, C., *Angew. Chem., Int. Ed*., 2004, vol. 43, p. 3795.
104. Hrdina, R., Stara, I.G., Dufkova, L., Mitchel, S., Cisarova, I., and Kotora, M., *Tetrahedron*, 2006, vol. 62, p. 968.
105. Hoshi, T., Katano, M., Nozawa, E., Suzuki, T., and Hagiwara, H., *Tetrahedron Lett*., 2004, vol. 45, p. 3489.
106. Yong, L. and Butenschön, H., *Chem. Commun*., 2002, p. 2852.
107. Kase, K., Goswami, A., Ohtaki, K., Tanabe, E., Saino, N., and Okamoto, S., *Org. Lett*., 2007, vol. 9, p. 931.
108. Tekavec, T.N., Zuo, G., Simon, K., and Louie, J., *J. Org. Chem*., 2006, vol. 71, p. 5834.
109. Stolley, R.M., Duong, H.A., and Louie, J., *Organometallics*, 2013, vol. 32, p. 4952.
110. Kumar, P., Prescher, S., and Louie, J., *Angew. Chem., Int. Ed*., 2011, vol. 50, p. 10694.
111. Stolley, R.M., Maczka, M.T., and Louie, J., *Eur. J. Org. Chem*., 2011, p. 3815.
112. Yamamoto, Y., Ogawa, R., and Itoh, K., *J. Am. Chem. Soc*., 2001, vol. 123, p. 6189.
113. Zaitsev, V.P., Zubkov, F.I., Nadirova, M.A., Mertsalov, D.F., Nikitina, E.V., Novikov, R.A., and Varlamov, A.V., *Chem. Heterocycl. Compd*., 2016, vol. 52, no. 9, p. 736.
114. Ohba, M. and Izuta, R., *Heterocycles*, 2001, vol. 55, p. 823.
115. Ohba, M., Izuta, R., and Shimizu, E., *Tetrahedron Lett*., 2000, vol. 41, p. 10251.
116. Deprele, S., Kashemirov, B.A., Hogan, J.M., Ebetino, F.H., Barnett, B.L., Evdokimov, A., and McKenna, C.E., *Bioorg. Med. Chem. Lett*., 2008, vol. 18, p. 2878.
117. Branowska, D., Ostrowski, S., and Rykowski, A., *Chem. Pharm. Bull*., 2002, vol. 50, p. 463.
118. Lipinska, T., *Tetrahedron Lett*., 2002, vol. 43, p. 9565.
119. Lipinska, T.M., *Tetrahedron*, 2006, vol. 62, p. 5736.
120. Kozhevnikov, D.N., Kozhevnikov, V.N., Kozhevnikov, T.V., Nikitina, T.V., and Rusinov, V.I., *Mendeleev Commun*., 2002, vol. 12, p. 30.
121. Catozzi, N., Edwards, M.G., Raw, S.A., Wasnaire, P., and Taylor, R.J.K., *J. Org. Chem*., 2009, vol. 74, p. 8343.
122. Lipinska, T. and Iwanska, B., *Molbank*, 2006, vol. M469, p. 1.
123. Kopchuk, D.S., Khasanov, A.F., Kim, G.A., Nosova, E.V., Zyryanov, G.V., Kovalev, I.S., Rusinov, V.L., and Chupakhin, O.N., *Russ. Chem. Bull., Int. Ed*., 2015, vol. 64, p. 872.
124. Lipin'ska, T., *Chem. Heterocycl. Compd*., 2001, vol. 37, p. 231.
125. Branowska, D., *Molecules*, 2005, vol. 10, p. 265.
126. Branowska, D., *Tetrahedron*, 2004, vol. 60, p. 6021.
127. Branowska, D. and Rykowski, A., *Tetrahedron*, 2005, vol. 61, p. 10713.
128. Bronowska, D. and Kielak, J., *Pol. J. Chem*., 2003, vol. 77, p. 1149.
129. Kozhevnikov, V.N., Kozhevnikov, D.N., Rusinov, V.L., Chupakhin, O.N., and Konig, B., *Synthesis*, 2003, p. 2400.

130. Kozhevnikov, V.N., Kozhevnikov, D.N., Nikitina, T.V., Rusinov, V.L., Chupakhin, O.N., Zabel, M., and Konig, B., *J. Org. Chem*., 2003, vol. 68, p. 2882.
131. Gehre, A., Stanforth, S.P., and Tarbit, B., *Tetrahedron*, 2009, vol. 65, p. 1115.
132. Lawecka, J., Kazczmarzyk, Z., Wolinska, E., Olender, E., Branowska, D., and Rykowski, A., *Tetrahedron*, 2011, vol. 67, p. 3098.
133. Kopchuk, D.S., Chepchugov, N.V., Kim, G.A., Zyryanov, G.V., Kovalev, I.S., Rusinov, V.L., and Chupakhin, O.N., *Russ. Chem. Bull., Int. Ed*., 2015, vol. 64, p. 695.
134. Egorov, I.N., Tseitler, T.A., Kovalev, I.S., Slepukhin, P.A., Rusinov, V.L., and Chupakhin, O.N., *J. Org. Chem*., 2012, vol. 77, p. 6007.
135. Sainz, Y.F., Raw, S.A., and Taylor, R.J.K., *J. Org Chem*., 2005, vol. 70, p. 10086.
136. Bringmann, G., Hamm, A., Kraus, J., Ochse, M., Noureldeen, A., and Jumbam, D.N., *Eur. J. Org. Chem*., 2001, p. 1983.
137. Sarkar, T.K., Ghosh, S.K., and Chow, T.J., *J. Org. Chem*., 2000, vol. 65, p. 3111.
138. Hilf, J.A., Holzwarth, M.S., and Rychnovsky, S.D., *J. Org. Chem*., 2016, vol. 81, p. 10376.
139. Lehmann, J., Alzien, T., Martin, R.E., and Britton, R., *Org. Lett*., 2013, vol. 15, p. 3550.
140. Hong, B.-C., Gupta, A.K., Wu, M.-F., and Liao, J.-H., *Tetrahedron Lett*., 2004, vol. 45, p. 1663.
141. Omari-Qadry, K., Hamza, K., Sasson, Y., and Blum, J., *J. Mol. Catal. A: Chem*., 2009, vol. 308, p. 182.
142. Skupinska, K.A., McEachern, E.J., Skerlj, R.T., and Bridger, G.J., *J. Org. Chem*., 2002, vol. 67, p. 7890.
143. Skupinska, K.A., McEachern, E.J., Baird, I.R., Skerlj, R.T., and Bridger, G.J., *J. Org. Chem*., 2003, vol. 68, p. 3546.
144. Koltunov, K.Yu., Prakach, G.K.S., Rasul, G., and Olah, G.A., *J. Org. Chem*., 2007, vol. 72, p. 7394.
145. Koltunov, K.Yu., Prakash, G.K.S., Rasul, G., and Olah, G.A., *J. Org. Chem*., 2002, vol. 67, p. 4330.
146. Borowski, A.F., Sabo-Etienne, S., Donnadieu, B., and Chaudret, B., *Organometallics*, 2003, vol. 22, p. 1630.
147. Frediani, P., Pistolesi, V., Frediani, M., and Rosi, L., *Inorg. Chim. Acta*, 2006, vol. 359, p. 917.
148. Paivio, E., Berner, M., Tolvanen, A., and Jokela, R., *Heterocycles*, 2000, vol. 53, p. 2241.
149. Reimann, E., Renz, M., and Polborn, K., *Monatsh. Chem*., 2006, vol. 137, p. 1411.
150. Shi, X., Meng, T., Fan, Q., and Lu, Z., *Chin. J. Chem*., 2016, vol. 20, p. 1.
151. Paronikyan, E.G., *Khimiya i biologicheskaya aktivnost' kislorod- i serosoderzhashchikh geterotsiklov* (Chemistry and Biological Activity of Oxygen- and Sulfur-Containing Heterocycles), Kartsev, V.G., Ed., Moscow: IBS, 2003, vol. 2, p. 317.
152. Dotsenko, V.V., Sventukh, D.V., and Krivokolysko, S.G., *Chem. Heterocycl. Compd*., 2012, vol. 48, p. 1397.
153. Paronikyan, E.G., Noravyan, A.S., Dashyan, Sh.Sh., Tamazyan, R.A., Aivazyan, A.G., and Panosyan, G.A., *Chem. Heterocycl. Compd*., 2013, vol. 49, p. 1151.
154. Paronikyan, E.G., Akopyan, Sh.F., and Noravyan, A.S., *Chem. Heterocycl. Compd*., 2008, vol. 44, p. 1003.
155. Bliznets, I.V., Vasil'ev, A.A., Shorshnev, S.V., Stepanov, A.E., and Lukyanov, S.M., *Tetrahedron Lett*., 2004, vol. 45, p. 2571.
156. Lukyanov, S.M., Bliznets, I.V., and Shorshnev, S.V., *Arkivoc*, 2009, part (iv), p. 21.
157. Lukyanov, S.M., Bliznets, I.V., Shorshnev, S.V., Aleksandrov, G.G., Stepanov, A.E., and Vasil'ev, A.A., *Tetrahedron*, 2006, vol. 62, p. 1849.
158. Bliznets, I.V., Shorshnev, S.V., Aleksandrov, G.G., Stepanov, A.E., and Lukyanov, S.M., *Tetrahedron Lett*., 2004, vol. 45, p. 9127.
159. Lipinska, T.M. and Czarnocki, S.J., *Org. Lett*., 2006, vol. 8, p. 367.
160. Babaev, E.V., Efimov, A.V., Tsisevich, A.A., Nevskaya, A.A., and Rybakov, V.B., *Mendeleev Commun*., 2007, vol. 17, p. 130.
161. Paronikyan, E.G., Sirakanyan, S.N., and Noravyan, A.S., *Chem. Heterocycl. Compd*., 2003, vol. 39, p. 374.
162. Woller, J., Spindler, K., Sarodnick, G., and Kempter, G., *Pharmazie*, 1996, vol. 51, p. 937.
163. Dukat, M., Taroua, M., Dahdouh, A., Siripurapu, U., Damaj, M.I., Martin, B.R., and Glennon, R.A., *Bioorg. Med. Chem. Lett*., 2004, vol. 14, p. 3651.
164 Nicolaou, K.C., Baran, P.S., and Zhong, Y.-L., *J. Am. Chem. Soc*., 2001, vol. 123, p. 3183.
165. Nicolaou, K.C., Montagnon, T., Baran, P.S., and Zhong, Y.-L., *J. Am. Chem. Soc*., 2002, vol. 124, p. 2245.
166. Golikov, A.G., Kriven'ko, A.P., and Reshetov, P.V., *Izbrannye metody sinteza i modifikatsii geterotsiklov* (Selected Methods of Synthesis and Modification of Heterocycles), Kartsev, V.G., Ed., Moscow: IBS, 2003, vol. 1, p. 65.
167. Hsin, L.-W., Chang, L.-T., and Liou, H.-L., *Synlett*, 2008, p. 2299.