A.V.Smolobochkin, A.S.Gazizov, A.R.Burilov, M.A.Pudovik, O.G.Sinyashin
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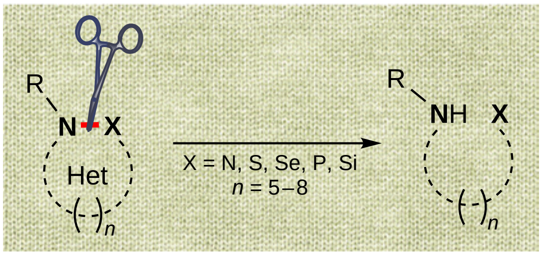
Ring-opening reactions of nitrogen-containing heterocyclic compounds at the nitrogen – heteroatom bond

Andrey V. Smolobochkin, Almir S. Gazizov, Alexander R. Burilov, Michail A. Pudovik, Oleg G. Sinyashin

Arbuzov Institute of Organic and Physical Chemistry, FRC Kazan Scientific Center
of the Russian Academy of Science, 420088 Kazan, Russian Federation

For the first time, published data on ring-opening reactions of heterocyclic compounds occurring *via* the nitrogen – heteroatom bond and resulting in acyclic nitrogen-containing polyfunctional compounds, have been systematized. The processes in which nitrogen, sulfur, selenium, phosphorus and silicon act as heteroatoms are considered. The transformations are analyzed, classified according to the type of reagent that promotes the cleavage of the specified bond, as well as the nature of the heteroatom. Examples of practical use of the resulting compounds are given.
The bibliography includes 154 references.

Keywords: ring opening, bond cleavage, nitrogen-containing heterocyclic compounds, polyfunctional compounds, amines.



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1. Introduction

Over the past decade, the number of studies devoted to the synthesis of polyfunctional acyclic compounds from heterocycles based on the cleavage of carbon – heteroatom (O, N, *etc.*) bonds has increased. In 2019, our research team published a review article[1] in the Russian Chemical Reviews on reactions of nitrogen-containing heterocyclic compounds involving ring opening at the carbon – nitrogen bond. This review noted that the bond-cleavage approach allows for the simple and minimal number of steps required to obtain acyclic bifunctional compounds otherwise difficult to access. Most bond-cleavage reactions are stereoselective, which is crucial for the synthesis of biologically active compounds.

Since 2019, a number of reviews have appeared describing synthetic approaches to new derivatives by cleaving the carbon – heteroatom bond in heterocyclic compounds. Most of these studies reported ring opening at the carbon – heteroatom bond in small (three- and four-membered) heterocycles,[2–7] which is likely due to the ease of opening such strained systems (Fig. 1 *a*). However, there are significantly fewer review articles describing similar processes in medium-sized (five- and six-membered) heterocycles (see Fig. 1 *b*).[8–10]

A.V.Smolobochkin. Doctor of Chemical Sciences, Senior Researcher at the Arbuzov Institute of Organic and Physical Chemistry, FRC Kazan Scientific Center of RAS.
E-mail: smolobochkin@iopc.ru
Current research interests: chemistry of heterocyclic and organophosphorus compounds, chemistry of acetals.
A.S.Gazizov. Doctor of Chemical Sciences, Lead Researcher at the same Institute.
E-mail: agazizov@iopc.ru
Current research interests: chemistry of nitrogen-containing acetals, chemistry of heterocyclic and organophosphorus compounds.
A.R.Burilov. Doctor of Chemical Sciences, Professor, Chief Researcher, Head of Laboratory of the same Institute.
E-mail: burilov@iopc.ru
Current research interests: chemistry of calix[4]resorcinol and acyclic polyphenols, chemistry of nitrogen-, phosphorus-containing acetals, supramolecular chemistry.
M.A.Pudovik. Doctor of Chemical Sciences, Professor, Chief Researcher at the same Institute. E-mail: pudovik@iopc.ru
Current research interests: chemistry of organophosphorus and organosilicon compounds, chemistry of calixarenes and pyridoxal.
O.G.Sinyashin. Academician of RAS, Doctor of Chemical Sciences, Professor, Scientific Director of the IOPC FRC KazSC RAS.
E-mail: oleg@iopc.ru
Current research interests: chemistry of organoelement compounds; synthesis, structure and properties of organophosphorus and organometallic compounds; electrochemical synthesis and catalysis.
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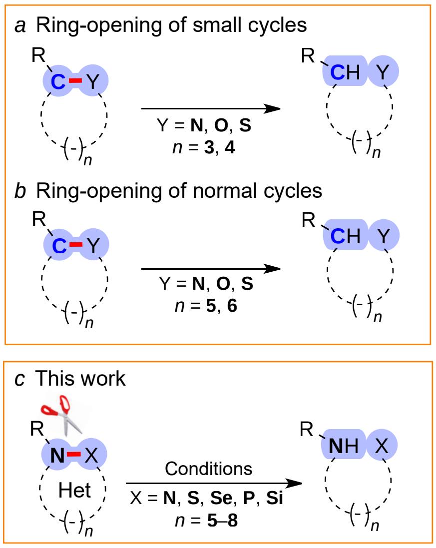


Figure 1. Synthesis of acyclic polyfunctional compounds based on ring opening of small (*a*) and medium-sized (*b*) rings at the carbon–heteroatom and nitrogen–heteroatom (*c*) bond.

There are virtually no reviews devoted to the ring-opening of nitrogen-containing heterocycles at the nitrogen–heteroatom bond, which can provide an access to various functionalized acyclic nitrogen-containing compounds. Such compounds play an important role in the pharmaceutical and chemical industries[11–15] and are often used as synthons for the production of a variety of biologically active substances. This review provides the first summary of methods for synthesizing acyclic nitrogen-containing polyfunctional compounds by ring opening of nitrogen-containing heterocycles at the nitrogen–heteroatom bond (see Fig. 1 *c*). The material is classified by the nature of the bond being cleaved and the type of reagent enabling the process. We hope this information will help synthetic chemists to gain a deeper insight into the state-of-the-art effective methods based on the ring opening of five-, six-, seven-, and eight-membered N-heterocycles at the nitrogen–heteroatom bond.

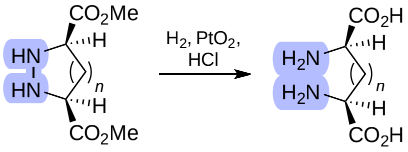
2. N–N bond cleavage

One of the most studied processes involving ring opening at the N–N bond is the reaction of heterocyclic compounds involving reducing agents. The widespread use of this method is due to its convenience and high selectivity. Hydrogen and samarium(II) iodide are most commonly used reducing agents.

2.1. N–N bond hydrogenolysis

This Section describes the types of the N–N bond cleavage that enable the synthesis of acyclic diamines, diamides, or aminoamides in which the functional groups are separated by spacers of different structures. Hydrogenolysis of the N–N bond in cyclic hydrazines **1a–c** with two ester functionalities was carried out over platinum oxide under a stream of hydrogen in dilute hydrochloric acid (Scheme 1). This gave diamines **2a–c** in good yields.[16]

Scheme 1

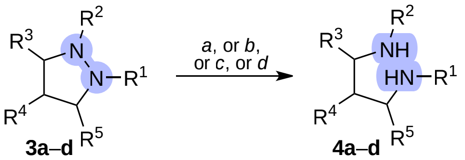


1a–c
2a–c (92–97%)

n = 1 (**a**), 2 (**b**), 3 (**c**)

Several reactions involving pyrazolidine derivatives have been described. For example, hydrogenation of pyrazolidine **3a** on palladium gives diamine **4a** with high stereoselectivity (conditions *a*).[17] Similar reaction of compound **3b** in the presence of platinum oxide also delivers diamine **4b** but in significantly lower yield (conditions *b*).[18] The use of boron hydride as a reducing agent delivered diamine **4c** as a racemate (conditions *c*).[19,20] And in the study,[21] 1,3-diphenylpropane-1,3-diamine (**4d**) with optical purity >99% was synthesized by reduction of 1-acetyl-3,5-diphenylpyrazolidine (**3d**) with Raney nickel (Ni-Ra) followed by treatment with (–)-dibenzoyl-L-tartaric acid (conditions *d*) (Scheme 2).

Scheme 2

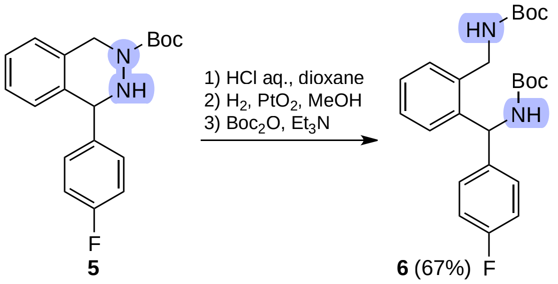


3a–d
4a–d

(*a*) 1) H_2, Pd/C, EtOH, 22°C; 2) Li, NH_3, THF, –78°C;
for $R^1 = R^2 = CO_2Et$, $R^3 = CH{=}CH_2$, $R^4 = H$
$R^5 = CH{=}CH–Ph$ (**a**, 74%, 98% *ee*);
(*b*) H_2, PtO_2/C, MeOH, rt; for $R^1 = Ac$, $R^2 = H$, $R^3 = CH{=}CH_2$,
$R^4 = Me$, $R^5 = CH_2OH$ (**b**, 79%);
(*c*) BH_3, THF, Δ, 8 h; for $R^1 = Ph$, $R^2 = Ac$, $R^3 = Me$, $R^4 = H$,
$R^5 = CH_2CH_2Ph$ (**c**, 93%);
(*d*) 1) CF_3CO_2H, CH_2Cl_2; 2) H_2, Ni-Ra, AcOH, CH_2Cl_2,
(–)-dibenzoyl-*L*-tartaric acid;
for $R^1 = R^4 = H$, $R^2 = Ac$, $R^3 = R^5 = Ph$ (**d**, 85%, >99% *ee*);
ee is enantiomeric excess

The reaction sequence involving removal of *tert*-butoxycarbonyl (Boc) protective group from the nitrogen atom of 3,4-dihydrophthalazine **5**, hydrogenolysis of the N–N bond, and subsequent protection of both nitrogen atoms to give the substituted 1,4-diamine **6** (Scheme 3).[22]

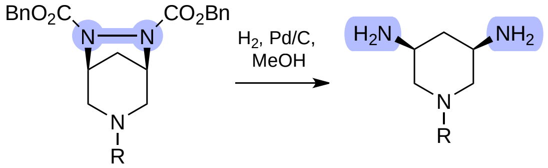
Scheme 3



5
6 (67%)

Based on the reduction of triazabicyclo[3.2.1]octanes **7a–d** in the presence of palladium on carbon, an effective method for

Scheme 4



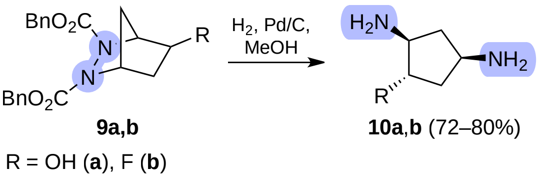
7a–d
8a–d (67–88%)

R = 3,4-$(MeO)_2C_6H_3CH_2CH_2$ (**a**, 62%),
4-$MeOC_6H_4CH_2$ (**b**, 82%), 3,4,5-$(MeO)_3C_6H_2$ (**c**, 38%),
Boc (**d**, 93%)

the synthesis of (3*S*,5*R*)-piperidine-3,5-diamine derivatives **8a–d** was developed (Scheme 4).[23–25] The target products are formed in moderate to high yields.

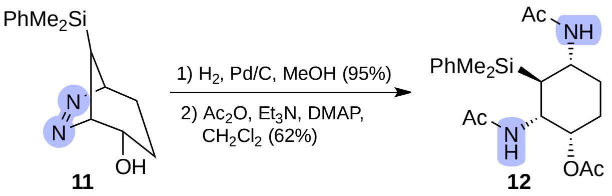
Reductive cleavage of the N–N bond in bicyclic hydrazides **9a,b** provided an access to cyclopentane diamines **10a**,**b** in good yields (Scheme 5).[26–29]

Scheme 5



It is worth noting the study,[30] which demonstrated the possibility of cleaving the N=N bond in compound **11**. The process was carried out in a stream of hydrogen over Pd/C, followed by acylation of the amino groups. In this case, the final product **12** retains the silyl functionality (Scheme 6).

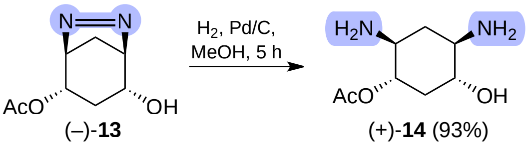
Scheme 6



DMAP is 4-dimethylaminopyridine

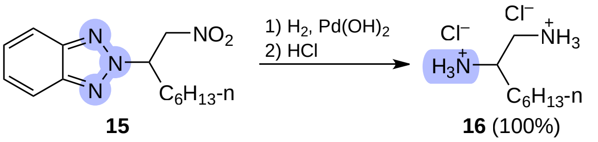
In addition, publication[31] should be mentioned, describing the hydrogenation of the bicycle (–)-**13** over Pd/C in methanol to afford dideoxystreptamine monoester (+)-**14**, which exhibits antibacterial activity (Scheme 7).

Scheme 7



Reduction of benzotriazole **15** gave diamine **16** in quantitative yield (Scheme 8).[32]

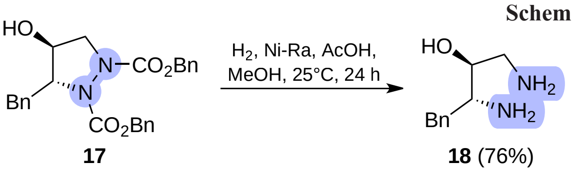
Scheme 8



Reactions involving benzotriazole derivatives are described in considerable detail in a review article by Katritzky *et al.*,[33] which also addresses issues related to the mechanism of triazole ring opening.

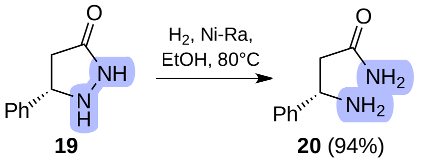
One-step transformation of compound **17** under catalytic hydrogenation conditions affords anti-1,2-aminoglycan **18**. This structural motif is found in phytospingosines and HIV protease inhibitors,[34] which is an important area of application for the presented methodology (Scheme 9).[35]

Scheme 9



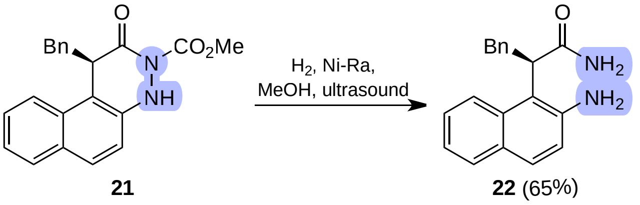
Hydrogenolysis of (*S*)-5-phenylpyrazolidin-3-one (**19**) over Raney nickel was proposed to obtain β-amino acid amide **20** in high yield (Scheme 10).[36–38]

Scheme 10



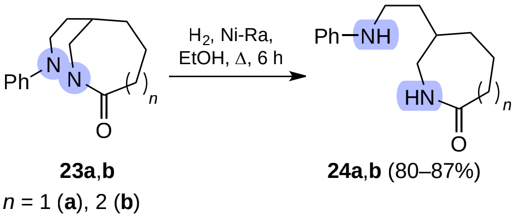
Ultrasonication-assisted catalytic hydrogenation of dihydrocinnolin-3-one **21** also afforded chiral amide **22** (Scheme 11).[39]

Scheme 11



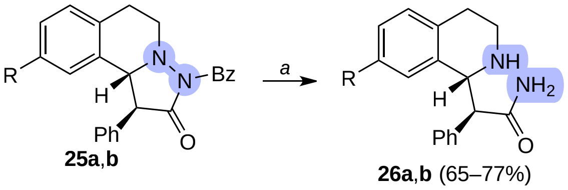
Shea and co-workers[40] developed a method for cleaving the N–N bond in bicycles **23a**,**b** based on Raney nickel-catalyzed hydrogenation of the substrates in boiling ethanol. This method provides a convenient approach to seven- and eight-membered nitrogen-containing heterocyclic compounds **24a**,**b** (Scheme 12).

Scheme 12



To carry out hydrogenolysis of the N–N bond in hexahydropyrazoloisoquinolines **25a**,**b**, the nitrogen atom was first deprotected with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and LiBr, which ultimately allowed the reduction of hydrazines to amines **26a**,**b** (Scheme 13).[41] Such amino derivatives can be useful for the preparation of peptides.

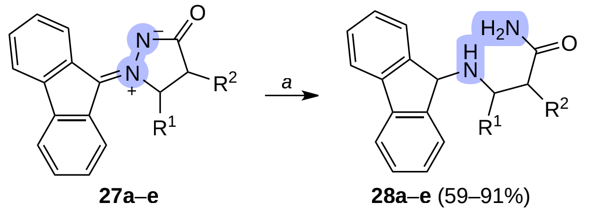
Scheme 13



(*a*) 1) DBU, LiBr, MeOH, 0°C, 1 h; 2) H_2, Ni-Ra, EtOH, 50°C, 16 h; R = H (**a**), MeO (**b**)

Azomethine imines **27a–e** were converted to β-aminoamides **28a–e** by reductive cleavage of the nitrogen–nitrogen bond (Scheme 14).[42–44] This reaction was carried out in the presence of Raney nickel and sodium borohydride upon heating in methanol. Remarkably, the process does not run under standard conditions using hydrogen and Raney nickel.

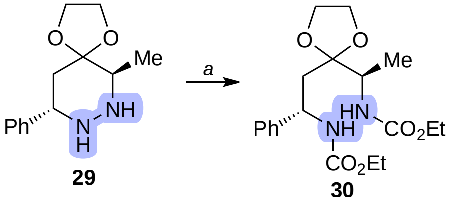
Scheme 14



(a) Ni-Ra, $NaBH_4$ or KBH_4, MeOH, 60°C;
R^1–R^2 = $(CH_2)_4$ (**a**), $(CH_2)_3$ (**b**); R^2 = H: R^1 = Bu^n (**c**), CH_2SiMe_3 (**d**), 4-$MeOC_6H_4$ (**e**)

Reductive cleavage of the N–N bond in cyclic hydrazine **29** can also be accomplished in a mixture of powdered zinc, acetic acid, and trifluoroacetic acid (Scheme 15).[45] Further protection of the free amino groups with ethyl chloroformate in the presence of Hünig's base gave dicarbamate **30**. The authors proposed that reductive cleavage is initiated by a single-electron transfer to the doubly protonated hydrazine dication.

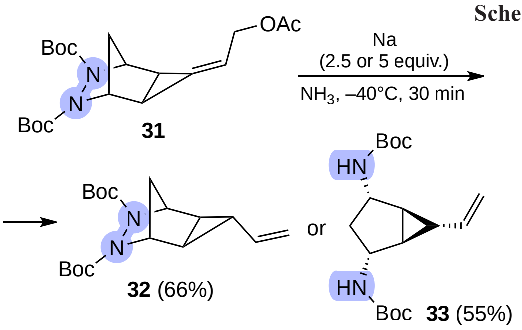
Scheme 15



(*a*) 1) Zn, AcOH, CF_3CO_2H, 90°C, 18 h;
2) ClCOOEt, Hunig's base, CH_2Cl_2

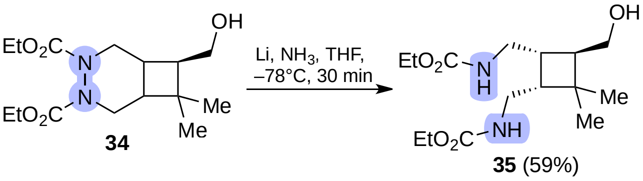
Clavier and co-workers[46] described an unusual method for reductive ring opening in polycyclic hydrazide **31** with a substituent containing an acetoxy group at the allyl position. Thus, upon treatment of the substrate with sodium metal in liquid ammonia (2.5 equiv.), terminal alkene **32** was isolated. The authors suggested that this is due to isomerization followed by removal of the acetoxy group. It should be noted that the vinyl group of product **32** is in the *trans* configuration of the three-membered ring. Increasing the amount of sodium to 5 equiv. delivered vinylcyclopropane **33** as a single diastereomer (Scheme 16).

Scheme 16



The reductive cleavage of the N–N bond in cyclic hydrazide **34** was snown[47] to be best accomplished using lithium metal in ammonia, leading to substituted cyclobutane **35** (Scheme 17).

Scheme 17



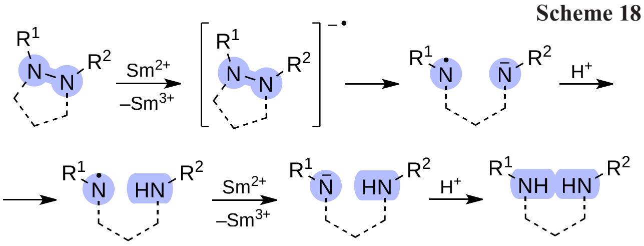
The method for synthesizing acyclic diamines, diamides, or aminoamides described in this Section involves cleavage of the N–N bond in cyclic hydrazines or hydrazides by reducing agents. This method affords products with high stereoselectivity and in good yields. Platinum oxide is used primarily for the selective synthesis of acyclic diamines or aminoamides from monocyclic five- or six-membered nitrogen-containing heterocyclic compounds. Palladium on carbon and Raney nickel are less selective, forming diamines from monocyclic and polycyclic hydrazides. It should be noted that only palladium on carbon is used for the hydrogenolysis of the N=N double bond.

2.2. N–N bond cleavage by samarium(II) iodide

A considerable number of studies have described the cleavage of the N–N bond by samarium(II) iodide, also known as Kagan's reagent. It is a highly reactive, mild, and selective single-electron reducing agent that has found increasing use in organic synthesis in recent years.[48–50]

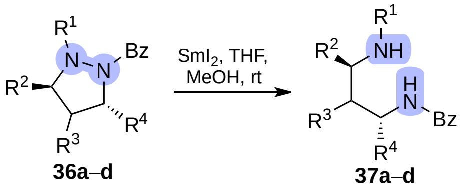
The mechanism of the SmI_2-mediated N–N bond reduction involves a single-electron transfer from the Sm^{2+} ion to the nitrogen atom of a cyclic hydrazine or hydrazide, resulting in an anion-radical, which splits into a radical and an anion (Scheme 18). In the next step, the proton plays a key role, the source of which is a protic solvent, most often an alcohol. Ultimately, an acyclic amine is formed from hydrazine, and an amide is formed from hydrazide.[51]

Scheme 18



Reduction of pyrazolidine derivatives **36a–d** with samarium(II) iodide yields a mixture of optically active diamines **37a–d** (Scheme 19), with an enantiomeric excess of >90%. Despite the high cost of the catalyst, this method provides an access to enantiomerically pure 1,3-diamines in high yields under mild conditions.[52–57]

Scheme 19



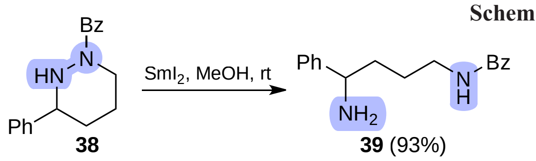
(83–98%, >90% *ee*)

R^3 = H: R^1 = Ac, R^2 = CH_2Bn, R^4 = All (**a**);
R^1 = Boc, R^2 = Bn, R^4 = Pr^n (**b**);
R^1 = Boc, R^2 = 4-$Bu^tC_6H_4CH_2$, R^4 = Pr^n (**c**);
R^1 = Bn, R^2 = R^3 = Ph, R^4 = H (**d**);
rt is room temperature, All is allyl

Under the same conditions, the hexahydropyridazine ring in compound **38** is opened to give substituted 1,4-diamine **39** (Scheme 20).[58,59]

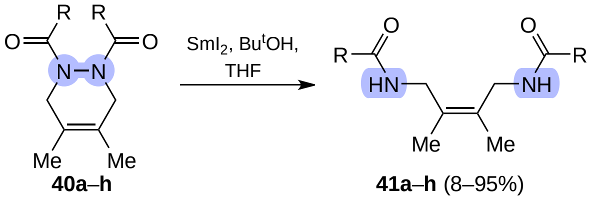
Reductive cleavage of the N–N bond in heterocycles **40a–h** occurs selectively in the presence of SmI_2 (Scheme 21).[60] Most diamides **41a–h** were isolated in yields exceeding 90%. The

Scheme 20



38 **39** (93%)

Scheme 21



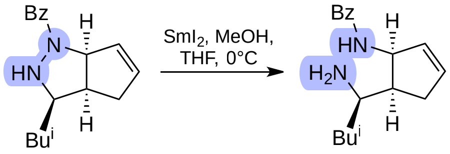
40a–h **41a–h** (8–95%)

R = 4-Bu^{n}C$_6$H$_4$ (**a**), 3,4-(F$_3$C)$_2$C$_6$H$_3$ (**b**), 4-F$_3$CC$_6$H$_4$ (**c**), 4-ClC$_6$H$_4$ (**d**), 3-MeOC$_6$H$_4$ (**e**), Me (**f**), Bu^{t}O (**g**), BnO (**h**)

lowest yields were observed for compounds containing electron-donating groups in the benzene rings.

An example of the ring-opening in hexahydrocyclopentapyrazole **42** under similar conditions has been reported,[61] affording 1,3-diamine **43** (Scheme 22). Similar structural motif is found in the anti-influenza drug peramivir.[62, 63]

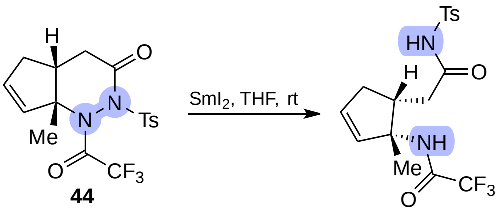
Scheme 22



42 **43** (93%)

The iodide samarium(II)-mediated ring opening of one of the rings of hexahydro-1*H*-cyclopenta[*c*]pyridazine **44** gave carbocycle **45**, containing two amide substituents (Scheme 23).[64]

Scheme 23

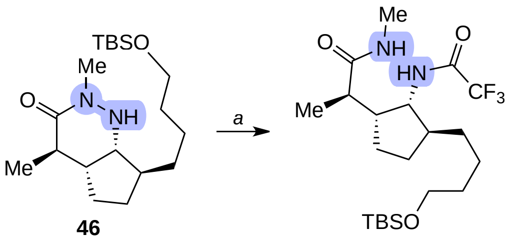


44 **45** (57%)

Ts is *p*-toluenesulfonyl (tosyl)

Acylation of the amine nitrogen atom of cyclic hydrazide **46** and reductive cleavage of the nitrogen–nitrogen bond gave trifluoroacetamide **47** (Scheme 24).[65]

Scheme 24

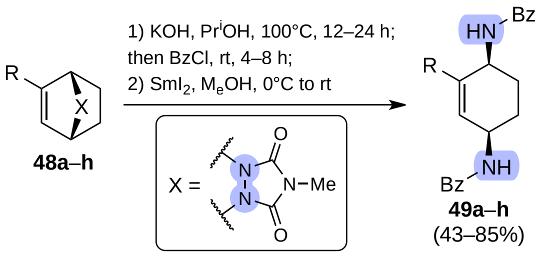


46 **47** (81%)

(*a*) 1) (CF$_3$CO)$_2$O, CH$_2$Cl$_2$, pyridine, 0°C;
2) SmI$_2$, HMPA, THF, 0°C;
TBS is *tert*-butyldimethylsilyl, HMPA is hexamethylphosphoric triamide

In 2016, Sarlah and co-workers[66,67] proposed an unusual method for the synthesis of 1,4-diaminocyclohex-2-ene derivatives (Scheme 25). The first step involves hydrolysis of the urazoline moiety of compounds **48a–h**, followed by benzoylation of the intermediate hydrazine. The second step involves SmI$_2$-mediated reduction of the nitrogen–nitrogen bond methanol to afford the target products **49a–h**.

Scheme 25

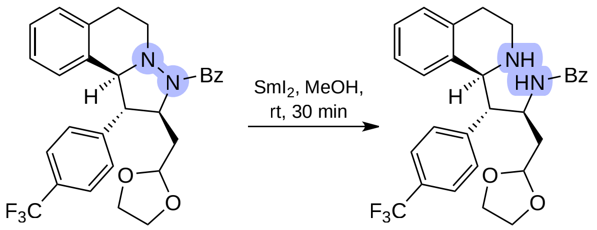


48a–h **49a–h** (43–85%)

R = H (**a**), Me (**b**), Bu^t (**c**), Cl (**d**), TMS (**e**), CH$_2$CH$_2$NHBz (**f**), CH$_2$CH$_2$CO$_2$H (**g**), CH$_2$OPr^i (**h**); TMS is trimethylsilyl

A number of studies[68–71] describe the cleavage of the N–N bond in hexahydropyrazoloisoquinoline **50**, resulting in the polyfunctional tetrahydroisoquinoline **51** (Scheme 26). The high selectivity of the process should be noted, allowing the preservation of chiral centres, acetal, and benzoyl groups in the product.

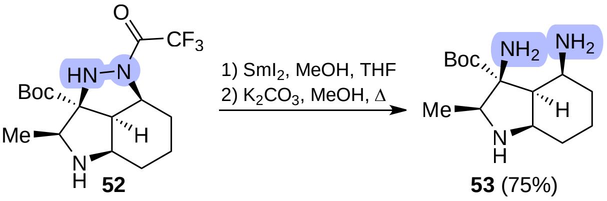
Scheme 26



50 **51** (82%)

The single-electron reduction of hydrazide **52** followed by removal of the trifluoroacetyl protective group furnishes hydrogenated inloline **53** with two amino substituents (Scheme 27).[72]

Scheme 27



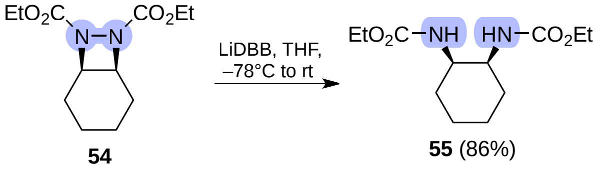
52 **53** (75%)

Consequently, cleavage of the N–N bond by samarium(II) iodide in mono- and polycyclic nitrogen-containing heterocyclic compounds leads to the target acyclic diamines, diamides, and aminoamides. Such reactions feature high product yields, selectivity, and tolerance to the presence of various functional groups in the substrate.

2.3. N–N bond cleavage by other reagents and catalysts

This Section discusses not only intramolecular processes but also intermolecular ones. The N–N bond cleavage was accomplished under the action of either reducing agents (in examples not included in the previous sections), metal catalysts,

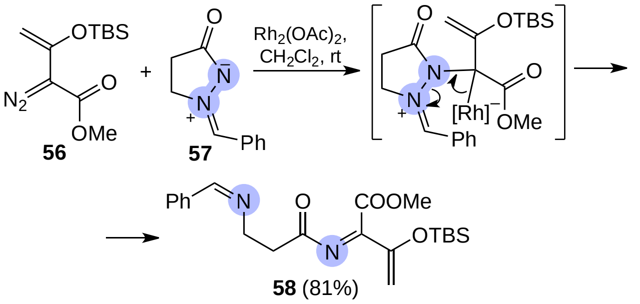
Scheme 28



or nucleophilic reagents. Thus, the 1,2-diazetidine ring opening in compound **54** by lithium di-*tert*-butylbiphenyl (DBB) as a reducing agent gave diamide **55** in high yield (Scheme 28).[73]

The reaction of ester **56** with azomethine imine **57** in the presence of a catalytic amount of rhodium acetate at room temperature in dichloromethane afforded acyclic diimine **58** rather than the expected cycloaddition product. The authors suggest that the reaction proceeds *via* an intermediate compound, which is formed from rhodium acetate, ester **56**, and azomethine imine **57** (Scheme 29).[74,75]

Scheme 29

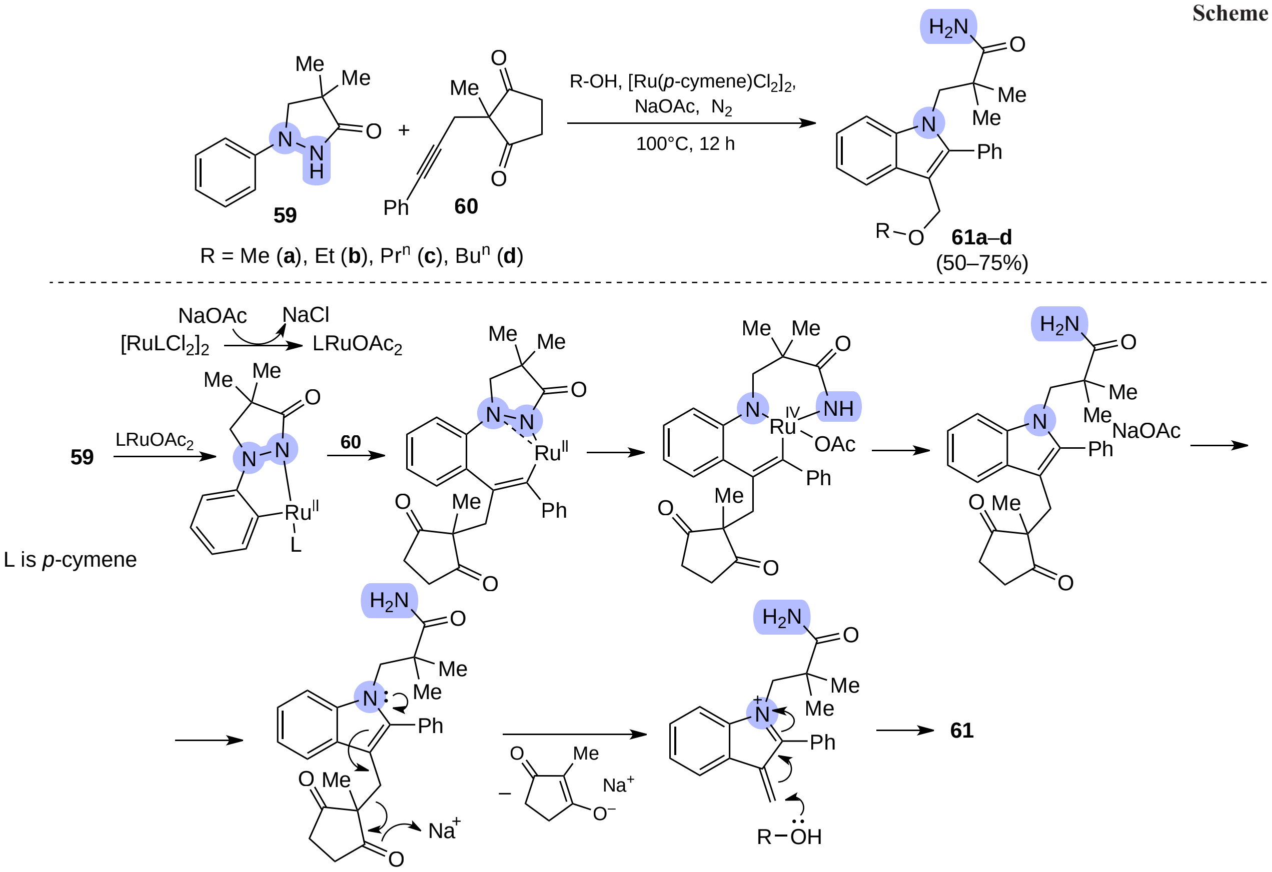


A method for the synthesis of various 3-(alkoxyalkyl)-1H-indoles based on the reaction of pyrazolidinone **59** with cyclic ketone **60** in the presence of dimeric (p-cymene)ruthenium dichloride has been reported (Scheme 30).[76–79] The advantages of the proposed method are a good product yield and high regioselectivity achieved by optimizing the reaction conditions. Various bases (NaOAc, KOAc, CsOAc, LiOAc, K_2CO_3, Na_2CO_3) were used and it was the use of NaOAc that allowed the product to be obtained in the highest yield. Based on mechanistic experiments, the authors proposed a plausible reaction pathway. The lower part of Scheme 30 shows only the main steps of the process. In the first step, ligand exchange delivers an active catalyst, which in turn reacts with pyrazolidin-3-one **59**. Subsequently, through a series of steps, the N–N and C–C bonds are cleaved, ultimately leading to indoles **61a–d**.

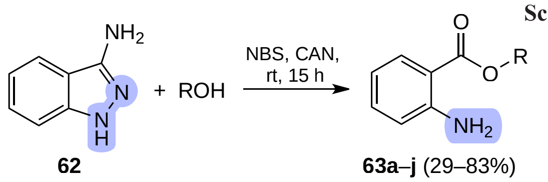
Mention should be made of the study,[80] which reports the oxidative ring opening of 3-aminoindazole **62** at the N–N bond to afford various 2-aminobenzoates **63a–j** (Scheme 31). When optimizing the reaction conditions, the authors focused on the choice of oxidizing agent. When using O_2, di-*tert*-butyl peroxide, benzoyl peroxide, *meta*-chloroperoxybenzoic acid, and (diacetoxyiodo)benzene, the reaction did not proceed. Trace amounts of the product were formed only under the action of $K_2S_3O_8$, $Na_2S_3O_8$, or *tert*-butyl peroxybenzoate.

The reaction of substituted 4-anilino-1,2,3-benzotriazine **64** with cyclic secondary amines (pyrrolidine, piperidine, and morpholine) affords 2-amino-N-(2-aryl)-$N'N'$-disubstituted benzamidines **65a–c** in high yields (Scheme 32).[81,82] It should be noted that heating 1,2,3-benzotriazine derivatives typically promotes the cleavage of bonds in the triazine ring, releasing a nitrogen molecule. The remaining part of the molecule reacts with amines to give more stable compounds.[83]

Scheme 30



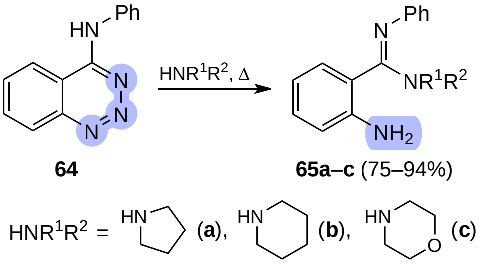
Scheme 31



62 **63a–j** (29–83%)

R = Me (**a**), Et (**b**), Pr^n (**c**), Bu^n (**d**), n-C_5H_{11} (**e**), Pr^i (**f**), Bu^i (**g**), CH_2CH_2OMe (**h**), CH_2CH_2OEt (**i**), CD_3 (**j**);
NBS is *N*-bromosuccinimide, CAN is cerium(IV)-ammonium nitrate

Scheme 32

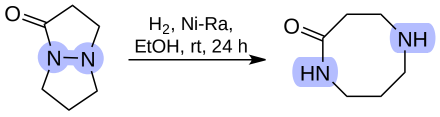


64 **65a–c** (75–94%)

2.4. Ring expansion *via* the N–N bond cleavage

This Section presents examples of the N–N bond cleavage leading to ring expansion. Unlike other Sections, in which the reaction products are acyclic nitrogen-containing compounds, this Section presents synthetic approaches to macrocyclic compounds. This is because cleavage of the N–N bridging bond in two-ring heterocycles does not result in the formation of new bonds, as demonstrated in previous Sections. It should be emphasized that the products of such reactions are polyfunctional macrocyclic compounds, which are extremely difficult to obtain using 'classical' methods. Such ring enlargement occurs primarily through hydrogenolysis of the N–N bond in tetrahydro-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole derivatives. For example, hydrogenation of tetrahydro-1*H*,5*H*-pyrazolo[1,2-*a*]-pyrazol-1-one **66** in the presence of Raney nickel at room temperature for 1 day afforded 1,5-diazacyclooctan-2-one **67** in a nearly quantitative yield (Scheme 33).[84]

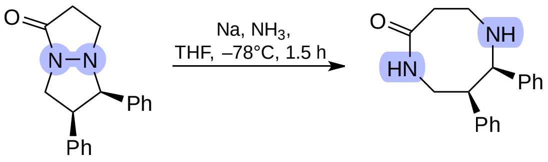
Scheme 33



66 **67** (96%)

Treatment of tetrahydropyrazolopyrazolone derivative **68** with sodium metal in liquid ammonia furnished macrocyclic amide **69** (Scheme 34).[85] However, the yield of the product in this case was only 30%.

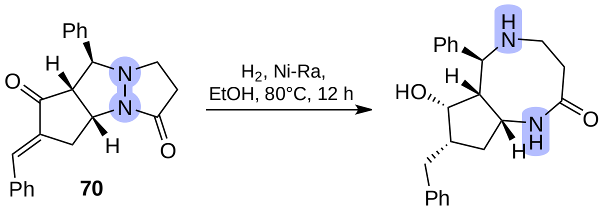
Scheme 34



68 **69** (30%)

It was observed that during high-pressure hydrogenation of heterocycle **70**, not only the valuable eight-membered macrocycle **71** was formed, but also the multiple bond and the keto group of the cyclopentane moiety were reduced.[86] Product **71** was isolated in good yield and with fairly high enantioselectivity (Scheme 35).

Scheme 35



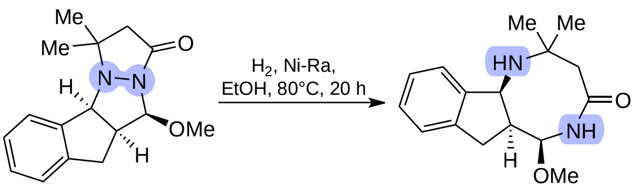
70

dr is diastereomeric ratio

71 (80%, 97% *ee*, *dr* > 19 : 1)

Using this approach, Lee *et al.*[87] obtained annulated macrocycle **73** from tetracycle **72** (Scheme 36). The product yield was 98% with a great predominance of one of the diastereomers (*dr* > 50 : 1).

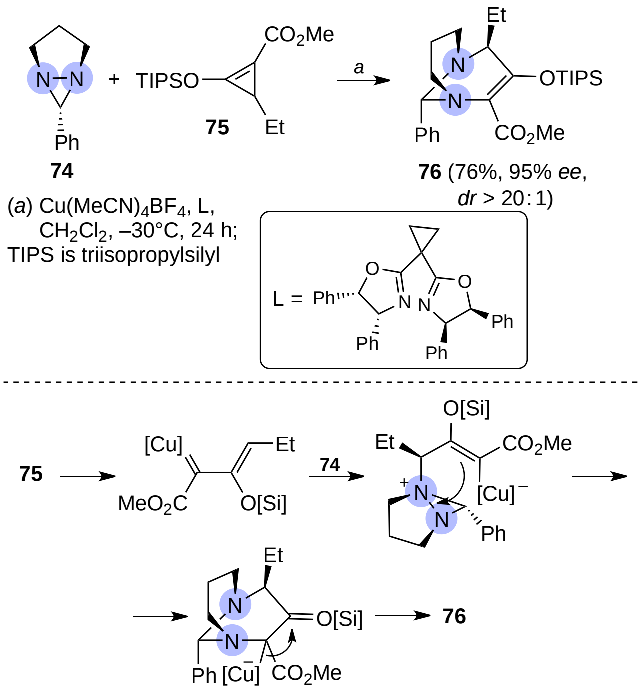
Scheme 36



72 **73** (98%)

It is important to mention studies,[88,89] in which a stereoselective method for the synthesis of macrocycle **76** was developed based on the reaction of 6-phenyl-1,5-diazabicyclo[3.1.0]hexane (**74**) with cyclopropene **75**. The cycloaddition product was isolated in good yield. Scheme 37 shows the plausible reaction pathway. In the first step, the cyclopropene unit undergoes ring-opening to form the *Z*-isomer of the alkene. Diaziridine **74** attacks the alkene to afford an intermediate ester. Then, nucleophilic substitution occurs involving the second nitrogen atom, accompanied by cleavage of the N–N bond and the formation of product **76**.

Scheme 37



74 **75** **76** (76%, 95% *ee*, *dr* > 20 : 1)

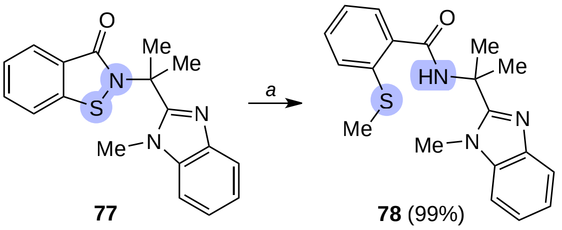
(*a*) $Cu(MeCN)_4BF_4$, L, CH_2Cl_2, –30°C, 24 h;
TIPS is triisopropylsilyl

The information presented in this Section on ring expansion by the N–N bond cleavage indicates the high potential of this approach. Its advantages primarily stem from the elimination of the need for preliminary multi-step modification of the starting compounds to introduce the desired functional groups, as well as the high yields of macrocyclic compounds.

3. N–S bond cleavage

The cleavage of the bond between the nitrogen and sulfur atoms in heterocyclic compounds leads to derivatives of amino(amido) sulfide and aminosulfonic acid, which are widely used in organic, bioorganic, and medicinal chemistry.[90,91] Such structural motifs are part of drugs such as diltiazem,[92] ectinaskidine-743,[93] taurine,[94] *etc.*, and therefore simple approaches to compounds of this class are needed. For example, Song and co-workers[95] used the treatment of substituted benzo[*d*]isothiazol-3(2*H*)-one **77** with sodium borohydride followed by methylation at the sulfur atom to obtain arylmethylthioether **78** in quantitative yield (Scheme 38).

Scheme 38

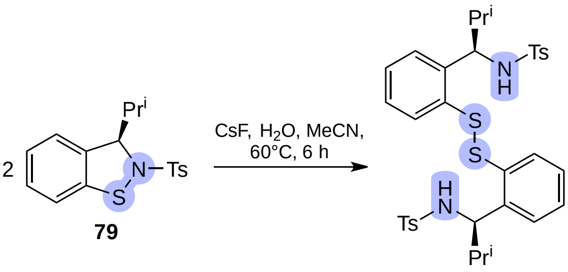


77 **78** (99%)

(*a*) 1) $NaBH_4$, EtOH, 0°C, 30 min; 2) Me_3I, EtOH, 0°C, 30 min

Reboul *et al.*[96] proposed a method for the preparation of benzo[*d*]isothiazole dimer **79** with the S–S bond in the presence of cesium fluoride and water. The reaction yields unstable sulfenyl fluoride, which, when treated with water, is converted to disulfide **80** (Scheme 39).

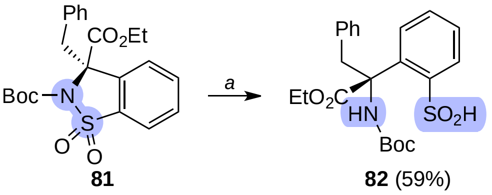
Scheme 39



79 **80** (20%)

Treatment of 2,3-dihydrobenzo[*d*]isothiazole-1,1-dioxide **81** with naphthalene sodium (NaphNa) in 1,2-dimethoxyethane with cooling for 2 min gave 2-(aminomethyl)benzenesulfinic acid derivative **82** in moderate yield (Scheme 40).[97–99]

Scheme 40



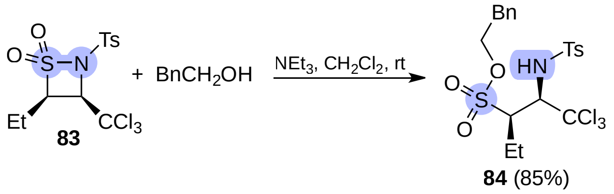
81 **82** (59%)

(*a*) 1) NaphNa, 1,2-dimethoxyethane, –78°C, 2 min;
2) H_2O

According to the authors, such optically pure amino acid derivatives can serve as building blocks for the synthesis of biologically active compounds.

The reaction of 1,2-thiazetidin-1,1-dioxide **83** with 2-phenylethan-1-ol in the presence of triethylamine in dichloromethane at room temperature afforded 2-aminoethane-1-sulfonic acid ester **84** in high yield (Scheme 41).[100,101]

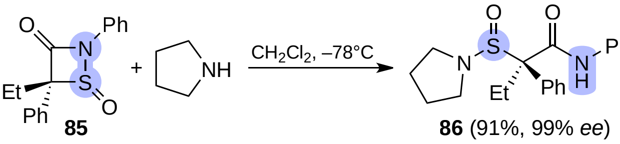
Scheme 41



83 **84** (85%)

The reaction between 1,2-thiazetidin-3-one 1-oxide **85** and pyrrolidine is of interest as it produces polyfunctional amide **86**, which was isolated in high yield and with high enantiomeric excess (Scheme 42).[102]

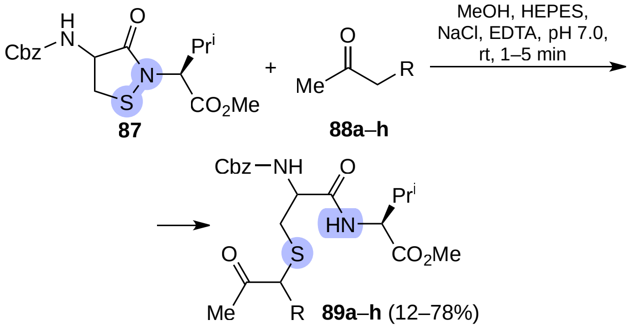
Scheme 42



85 **86** (91%, 99% *ee*)

A synthetic approach to polyfunctional thioesters is described in a number of papers.[103–106] It involves reactions of carboxylic acid ester **87** with various carbonyl compounds **88a–h** (Scheme 43). The resulting products **89a–h** are potential agents for the treatment of type 2 diabetes mellitus.

Scheme 43



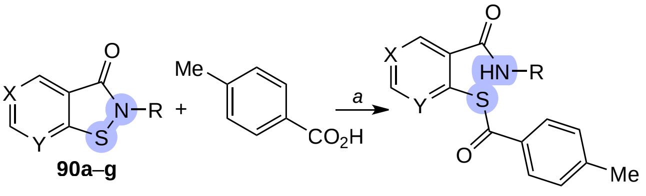
87 **88a–h** **89a–h** (12–78%)

R = Ac (**a**), Bz (**b**), $C(O)CF_3$ (**c**), $C(O)CO_2H$ (**d**), SO_2Me (**e**),
SO_2Ph (**f**), NO_2 (**g**), CN (**h**);
Cbz is benzyloxycarbonyl, HEPES is 4-(2-hydroxyethyl)-1-piperazinoethanesulfonic acid;
EDTA is ethylene diamine tetraacetic acid

In 2017, Morimoto *et al.*[107] studied the reactions of *N*-alkyl- and *N*-arylbenzoisothiazolones **90a–g** with *p*-toluic acid in the presence of triethyl phosphite in DMF. The products were *S*-toluoyl-substituted thioanalogs of salicylamides **91a–g** (Scheme 44).

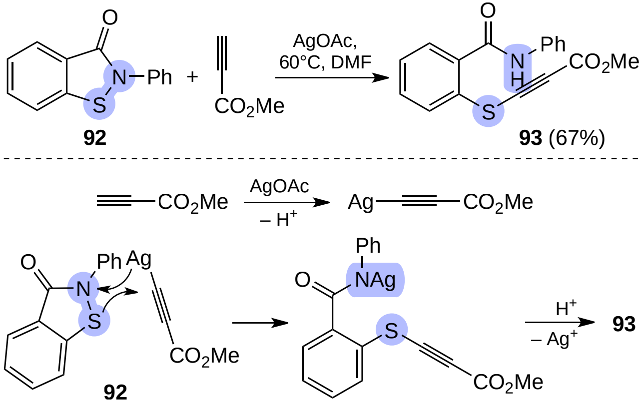
2-Phenylbenzo[*d*]isothiazol-3(2*H*)-one (**92**) can react with methyl propiolate in the presence of silver acetate. This method allows the 2-(ethynylthio)benzamide derivative **93** to be obtained in a good yield in a single step under mild conditions (Scheme 45).[108,109] The reaction is likely commenced with the formation of silver acetylide, which reacts with heterocycle **92**. The resulting cleavage of the N–S bond ultimately gives amide **93**.

Scheme 44



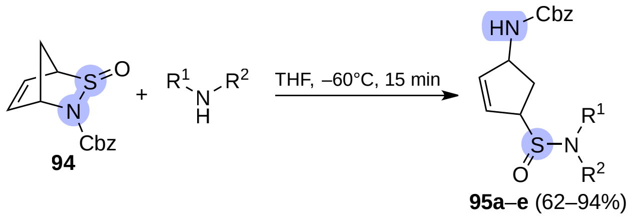
(*a*) $(EtO)_3P$, DMF, 25°C;
R = Pr^i: X = CNO_2, Y = CH (**a**); X = Y = CH (**b**);
X = CCF_3, Y = CH (**c**); X = Ac, Y = CH (**d**); X = N, Y = CH (**e**);
R = 2-pyridyl: X = CNO_2, Y = CH (**f**); X = Y = CH (**g**)

Scheme 45



Scheme 46 shows the reaction of amide **94** with amines, which occurs in THF upon cooling to –60°C for 15 min to give diamides **95a–e** in high yields (see Scheme 46).[110,111]

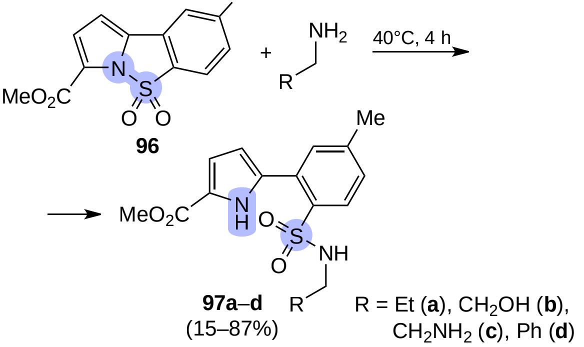
Scheme 46



R^1 = H: R^2 = Bn (**a**), Bu^i (**b**), NH_2Val-PheOMe (**c**);
R^1–R^2 = $(CH_2)_4$ (**d**), $(CH_2)_2O(CH_2)_2$ (**e**)

A method for synthesizing *ortho*-sulfonamide-substituted 2-arylpyrroles, which are extremely difficult to obtain otherwise, deserves attention.[112,113] It is based on the reaction of sultam **96** with aliphatic amines (Scheme 47). Benzylamine proved to be the least reactive — the yield of product **97d** was only 15%. The resulting 2-arylpyrroles **97a–d** may find application in organic light-emitting devices (OLEDs).

Scheme 47



R = Et (**a**), CH_2OH (**b**), CH_2NH_2 (**c**), Ph (**d**)

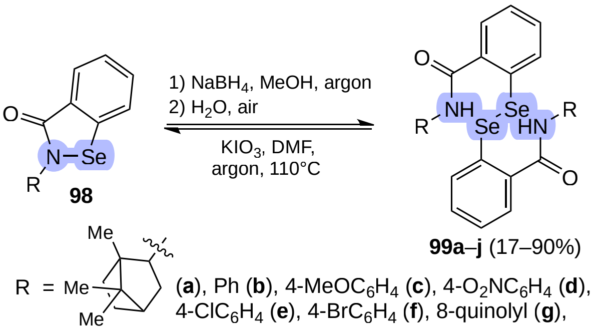
Thus, ring opening at the nitrogen–sulfur bond primarily occurs in 2,3-dihydrobenzo[*d*]isothiazole derivatives, which is likely due to the availability of this heterocyclic compound. Sodium borohydride or naphthalene are used as reducing agents. The N–S bond cleavage is primarily carried out by the action of nucleophilic reagents, such as alcohols, amines, and ketones. Most of the reactions described in this Section are intermolecular.

4. N–Se bond cleavage

Selenium-containing amino acids are a class of organic compounds that have been actively studied in recent decades. This is primarily due to the fact that such derivatives exhibit varying biological activity.[114–118] For example, selenocysteine, a selenium-containing analogue of cysteine, is the twenty-first proteinogenic amino acid. The chemistry of selenocysteine has attracted the attention of many specialists working in the fields of chemical biology, organic chemistry, and pharmacology.

One method for synthesizing diselenides involves the reduction of compounds **98** with sodium borohydride in an inert atmosphere. The N–Se bond can be reversibly reduced in the presence of potassium iodate (Scheme 48). Diselenides **99a–j** possess antioxidant and antitumour properties.[119–123]

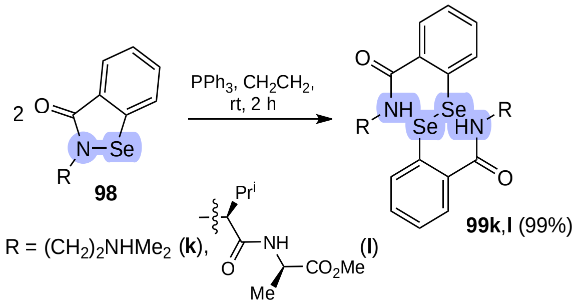
Scheme 48



(**a**), Ph (**b**), 4-$MeOC_6H_4$ (**c**), 4-$O_2NC_6H_4$ (**d**), 4-ClC_6H_4 (**e**), 4-BrC_6H_4 (**f**), 8-quinolyl (**g**), Me (**h**), Bu (**i**), Bn (**j**)

Diselenides **99k,l** can be obtained from benzo[*d*][1,2]-selenazole-3(2*H*)-ones **98** by treatment with triphenylphosphine in dichloromethane at room temperature for 2 h (Scheme 49), in practically quantitative yield.[124,125]

Scheme 49

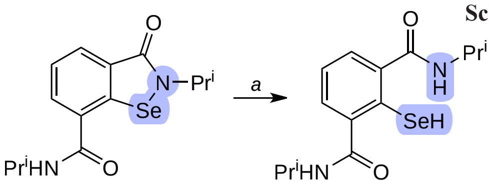


Opening of the selenazolidine ring in compound **100** with sodium in liquid ammonia followed by treatment with hydrochloric acid leads to selenol **101** (Scheme 50).[126]

When attempting to obtain selenoxide by treating benzo-[*d*][1,2]selenazol-3(2*H*)-ones **98** with hydrogen peroxide, hydroperoxy(aryl)selenium derivatives **102a–d** were unexpectedly isolated (Scheme 51).[127,128]

Alkylaryl and arylaryl selenides **104a–g** were obtained in good yields by reacting 2*H*-benzo[*d*][1,3,2]thiaselenazole-1,1-

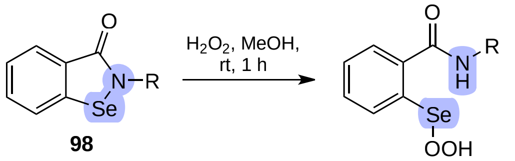
Scheme 50



100 **101** (77%)

(*a*) 1) Na, NH_3, THF, –60°C, 30 min; 2) HCl aq., rt, 30 min

Scheme 51

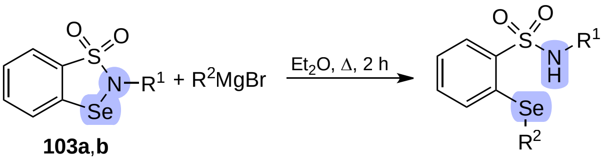


98 **102a–d** (38–60%)

R = Ph (**a**), Me (**b**), Et (**c**), Pr^i (**d**)

dioxides **103** with Grignard reagents. The lowest yield was observed for selenide **104b**, which contained two butyl groups (Scheme 52).[129]

Scheme 52



103a,**b** **104a–g** (54–84%)

R^1 = Bu^t (**103a**, **104a–d**), Pr^n (**103b**, **104e–g**);
104: R^2 = Pr^n (**a**, **e**), Bu^n (**b**), Ph (**c**, **f**), 3-MeOC_6H_4 (**d**, **g**)

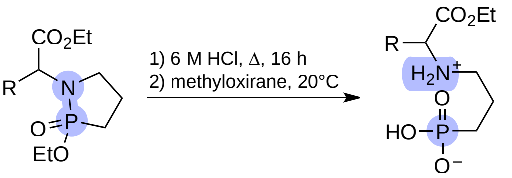
Ring opening reactions at the nitrogen–selenium bond primarily involve derivatives of benzo[*d*][1,2]selenazol-3(2*H*)-one, due to the availability of such heterocyclic compounds. When using reducing agents, the products are amide-substituted selenols. Treatment with hydrogen peroxide allows the isolation of individual hydroperoxy(aryl)selenium derivatives.

5. N–P bond cleavage

The N–P bond cleavage in heterocycles delivers acyclic aminophosphoryl derivatives. Such compounds are phosphorus analogs of natural proteinogenic amino acids and, as a consequence, exhibit a wide spectrum of biological activities.[130,131] Aminophosphoryl compounds are also of interest as ligands for coordination chemistry.[132–134]

Ring opening in 2-ethoxy-1,2-azaphospholidin-2-oxides **105a**,**b** as a result of their sequential treatment with hydrochloric acid and methyloxirane leads to amino acids **106a**,**b** (Scheme 53).[135]

Scheme 53

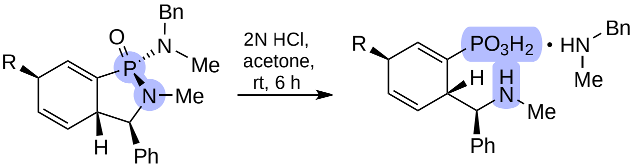


105a,**b** **106a**,**b** (43–59%)

R = H (**a**), Me (**b**)

Acidic hydrolysis of the N–P bond in heterocycles **107a**,**b** affords aminophosphonic acids **108a**,**b**. It should be noted that the target compounds can be obtained under mild conditions in virtually quantitative yields (Scheme 54).[136–138]

Scheme 54

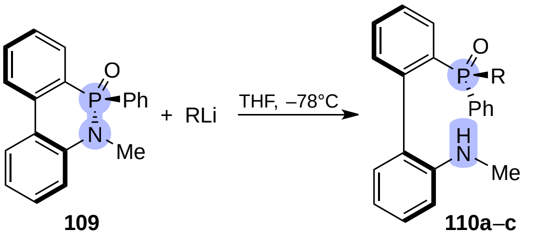


107a,**b** **108a**,**b** (>97%)

R = H (**a**), Bn (**b**)

A method for the synthesis of aminophosphoryl compounds based on the cleavage of their N–P bond by various nucleophiles has been reported.[139,140] Dibenzo[*c*,*e*][1,2]azaphosphinine-6-oxide **109** reacts with organolithium compounds to give phosphine oxides **110a–c** (Scheme 55). The authors note that Grignard reagents do not react with this substrate, which is possibly due to their low nucleophilicity.

Scheme 55

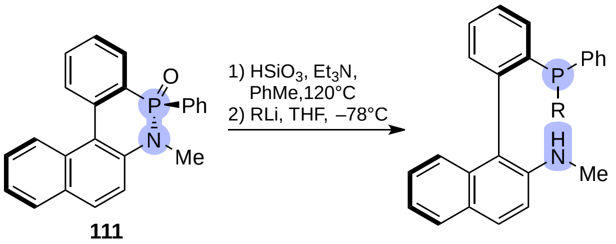


109 **110a–c**

R = Me (**a**), Pr^i (**b**), Bu^t (**c**) (59–73%, *dr* > 50%)

The preparation of aminophosphines by reduction of the similar phosphamide **111** to phosphine followed by cleavage of the N–P bond with lithium reagents is described. It should be noted that when using phenyllithium, the enantiomeric excess of products **112a**,**b** was 96% (Scheme 56).[141]

Scheme 56



111 **112a**,**b** (73–78%, >70% *ee*)

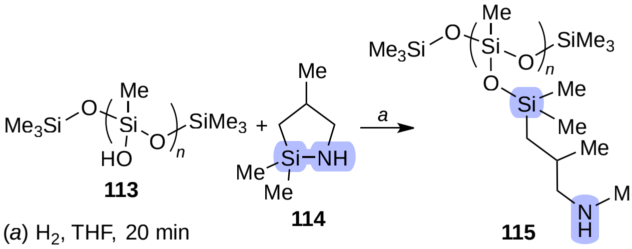
R = Ph (**a**), Bu^n (**b**)

Examples of the N–P bond cleavage in heterocycles are represented primarily by reactions of 1,2-azaphospholidine-2-oxide and 5*H*-dibenzo[*c*,*e*][1,2]azaphosphinine-6-oxide derivatives under the action of acids and electrophilic agents, respectively. Processes involving organolithium compounds, accompanied by ring opening, allow the functionalization of aminophosphine and aminophosphine oxide in a single step.

6. N–Si bond cleavage

Currently, organosilicon compounds find various applications. For example, silyl protection is often used in organic chemistry, which is associated with the easy cleavage of the silicon–heteroatom bond.[142–144] The importance of organosilicon polymers for humans is difficult to overestimate, with polymers containing aminoxyloxane monomers being of particular interest due to their widespread use in industry and everyday life.[145,146] Aminosiloxanes impart new properties to materials or improve existing ones, for example, adhesion, flexibility, *etc*.[147–150] One method for synthesizing such polymers involves the reaction of oligomer **113** with 2,2,4-trimethyl-1,2-azasilolidine (**114**) in a stream of hydrogen, leading to product **115** (Scheme 57).[151]

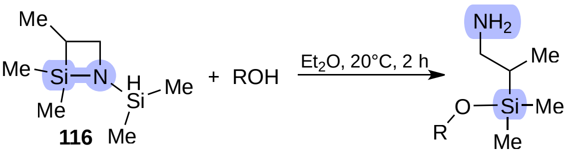
Scheme 57



(*a*) H_2, THF, 20 min

The reaction of 1-aza-2-silacyclobutane **116** with methyl, isopropyl, and *tert*-butyl alcohols in diethyl ether under mild conditions gave aminosilanes **117a–c** (Scheme 58).[152]

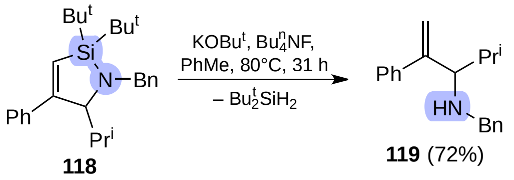
Scheme 58



R = Me (**a**), Pr^i (**b**), Bu^n (**c**) **117a–c** (76–88%)

As a result of the initial cleavage of the N–Si bond in azasilacyclopentene **118**, the prop-2-ene-1-amine derivative **119** is formed. Di-*tert*-butylsilane was isolated as a by-product in this reaction (Scheme 59).[153]

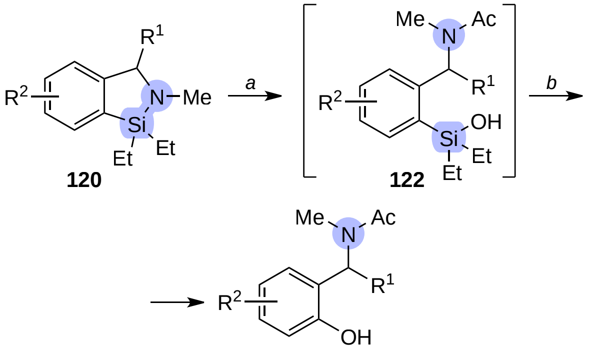
Scheme 59



119 (72%)

Direct oxidation of azasilolanes **120** under various conditions afforded phenols **121** in low yields (<20%) due to competitive oxidation of the amino group, which required the authors to protect it before the silane oxidation. Thus, exposure of azasilolanes **120a–e** to air for 2 h promoted the formation of amides **122a–e**. Subsequent oxidation of amides **122** afforded amidophenols **121a–e** (Scheme 60).[154]

Scheme 60



121a–e (62–80%)

(*a*) 1) THF, air, rt, 2 h; 2) Ac_2O, Et_3N, DMAP, CH_2Cl_2, rt, 2 h;
(*b*) H_2O_2, KHF_2, KF, $KHCO_3$, THF, MeOH, rt, 16 h;
R^1 = H: R^2 = H (**a**), 3-ClC_6H_4 (**b**), 3-BrC_6H_4 (**c**), 2-$MeOC_6H_4$ (**d**);
R^1 = Me, R^2 = H (**e**)

7. Conclusion

Analyzing the literature data presented above, we can conclude that methods for synthesizing acyclic polyfunctional compounds from nitrogen-containing heterocycles by cleaving the nitrogen–heteroatom bond are finding increasing application in organic chemistry. Simple reactions give rise to complex compounds that are difficult to obtain using labor-intensive ‘classical’ methods based on the creation of new bonds. When the initial cyclic compound molecule contains several chiral centres, bond cleavage prevents racemization, which is crucial for the synthesis of both biologically active compounds and catalysts.

Among all the methods presented in this review, the synthesis of macrocyclic compounds by cleavage of the N–N bond in bicyclic nitrogen-containing heterocycles may also be noted. This approach allows for the single-step synthesis of high-yield macrocycles containing multiple functional groups, which are extremely difficult to obtain from linear molecules. In our opinion, this particular approach will see rapid development in the coming years, leading to the emergence of new compounds and materials with practically useful properties.

Samarium(II) iodide is considered the most promising reducing agent for cleaving the N–N bond. This is primarily due to its selectivity, which provides the synthesis of polyfunctional amines and amides in a single step. However, the high cost of samarium(II) iodide is a serious obstacle to its widespread use in the chemical industry.

One effective method for synthesizing a wide range of aminosulfonic acid derivatives involves cleavage of the N–S bond in heterocyclic compounds. The proposed approach allows for the production of products under mild conditions with high stereoselectivity, which is crucial for identifying potential biologically active compounds.

Despite the advances made in the synthesis of polyfunctional nitrogen-containing acyclic compounds based on the cleavage of the nitrogen–heteroatom bond in cyclic precursors, further work is needed in this area, particularly in the area of stereoselective heterocycle opening. Addressing this problem will open up new possibilities for obtaining structurally diverse polyfunctional amines, which will be of great importance for the development of new drugs and catalysts, and will also provide convenient starting materials for the creation of modern materials.

8. List of abbreviations

The following abbreviations are used in this review:
All — allyl,
Boc — *tert*-butoxycarbonyl,
CAN —cerium(IV)-ammonium nitrate,
Cbz — carboxybenzyl,
DBB — di-*tert*-butykbiphenyl,
DBU — 1,8-diazabicyclo[5.4.0]undec-7-ene,
DMAP — 4-dimethylaminopyridine,
dr — diastereomeric ratio,
EDTA — ethylene diamine tetraacetic acid,
ee — enantiomeric excess,
HEPES — 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid,

HMPA — hexamethylphosphoric triamide,
NaphNa — sodium naphthalene,
NBS — *N*-bromosuccinimide,
Ni-Ra — Raney nickel,
rt — room temperature,
TBS — *tert*-butyldimethylsilyl,
TIPS — triisopropylsilyl,
TMS — trimethylsilyl,
Ts — *p*-toluenesulfonyl (tosyl).

9. References

1. A.V.Smolobochkin, A.S.Gazizov, A.R.Burilov, M.A.Pudovik, O.G.Sinyashin. *Russ. Chem. Rev.*, **88** (11), 1104 (2019); https://doi.org/10.1070/RCR4891
2. Y.Takeda, W.M.C.Sameera, S.Minakata. *Acc. Chem. Res.*, **53** (8), 1686 (2020); https://doi.org/10.1021/acs.accounts.0c00395
3. S.Meninno, A.Lattanzi. *ACS Org. Inorg. Au*, **2** (4), 289 (2022); https://doi.org/10.1021/acsorginorgau.2c00009
4. A.J.Plajer, C.K.Williams. *Angew. Chem., Int. Ed.*, **61** (1), e202104495 (2022); https://doi.org/10.1002/anie.202104495
5. J.Xuan, X.-K.He, W.-J.Xiao. *Chem. Soc. Rev.*, **49** (9), 2546 (2020); https://doi.org/10.1039/C9CS00523D
6. M.Pineschi. *Eur. J. Org. Chem.*, (18), 2643 (2020); https://doi.org/10.1002/ejoc.201901853
7. A.Ghosh, R.Dey, P.Banerjee. *Chem. Commun.*, **57** (44), 5359 (2021); https://doi.org/10.1039/D1CC00998B
8. E.Ota, J.Yamaguchi. *Eur. J. Org. Chem.*, **28** (20), e202401322 (2025); https://doi.org/10.1002/ejoc.202401322
9. K.Leškovskis, J.M.Zaķis, I.Novosjolova, M.Turks. *Eur. J. Org. Chem.*, (36), 5027 (2021); https://doi.org/10.1002/ejoc.202100755
10. F.Sun, E.V.Van der Eycken, H.Feng. *Adv. Synth. Catal.*, **363** (23), 5168 (2021); https://doi.org/10.1002/adsc.202100746
11. E.L.Lieu, T.Nguyen, S.Rhyne, J.Kim. *Exp. Mol. Med.*, **52** (1), 15 (2020); https://doi.org/10.1038/s12276-020-0375-3
12. S.Thakral, V.Singh. *Curr. Bioact. Compd.*, **15** (3), 316 (2019); https://doi.org/10.2174/1573407214666180614121140
13. P.B.Tsafack, A.Tsopmo. *Heliyon*, **8** (9), e10456 (2022); https://doi.org/10.1016/j.heliyon.2022.e10456
14. B.ten Brink, C.Damink, H.M.L.J.Joosten, J.H.J.Huis in't Veld. *Int. J. Food Microbiol.*, **11** (1), 73 (1990); https://doi.org/10.1016/0168-1605(90)90040-C
15. J.Chen, L.Cui, S.Lu, S.Xu. *Cell Death Dis.*, **15** (1), 42 (2024); https://doi.org/10.1038/s41419-024-06435-w
16. Y.Arakawa, T.Goto, K.Kawase, S.Yoshifuji. *Chem. Pharm. Bull.*, **43** (3), 535 (1995); https://doi.org/10.1248/cpb.43.535
17. J.J.Van Veldhuizen, D.G.Gillingham, S.B.Garber, O.Kataoka, A.H.Hoveyda. *J. Am. Chem. Soc.*, **125** (41), 12502 (2003); https://doi.org/10.1021/ja0302228
18. F.M.Guerra, M.R.Mish, E.M.Carreira. *Org. Lett.*, **2** (26), 4265 (2000); https://doi.org/10.1021/ol006873f
19. K.A.Kochetkov, A.N.Tavtorkin, N.I.Vorozhtsov, L.A.Sviridova, A.M.Moroz, I.R.Dorozhkova. *Russ. Chem. Bull.*, **60** (4), 702 (2011); https://doi.org/10.1007/s11172-011-0109-8
20. L.A.Sviridova, G.A.Golubeva, A.N.Tavtorkin, K.A.Kochetkov. *Amino Acids*, **43** (3), 1225 (2012); https://doi.org/10.1007/s00726-011-1187-5
21. J.Li, L.Xu. *Tetrahedron*, **71** (19), 2858 (2015); https://doi.org/10.1016/j.tet.2015.03.067
22. W.Zhang, J.Y.Mo, W.He, P.Kennepohl, G.M.Sammis. *Chem. – Eur. J.*, **25** (4), 976 (2019); https://doi.org/10.1002/chem.201805249
23. A.Blond, P.Dockerty, R.Álvarez, S.Turcaud, T.Lecourt, L.Micouin. *J. Org. Chem.*, **78** (23), 12236 (2013); https://doi.org/10.1021/jo401994y
24. G.-S.Jiao, L.Cregar, J.Wang, S.Z.Millis, C.Tang, S.O'Malley, A.T.Johnson, S.Sareth, J.Larson, G.Thomas. *Proc. Natl. Acad. Sci. USA*, **103** (52), 19707 (2006); https://doi.org/10.1073/pnas.0606555104
25. G.-S.Jiao, L.Cregar, M.E.Goldman, S.Z.Millis, C.Tang. *Bioorg. Med. Chem. Lett.*, **16** (6), 1527 (2006); https://doi.org/10.1016/j.bmcl.2005.12.038
26. M.Pasco, R.Moumné, T.Lecourt, L.Micouin. *J. Org. Chem.*, **76** (12), 5137 (2011); https://doi.org/10.1021/jo2001512
27. A.Blond, R.Moumné, G.Bégis, M.Pasco, T.Lecourt, L.Micouin. *Tetrahedron Lett.*, **52** (25), 3201 (2011); https://doi.org/10.1016/j.tetlet.2011.04.034
28. R.Moumné, M.Pasco, E.Prost, T.Lecourt, L.Micouin, C.Tisné. *J. Am. Chem. Soc.*, **132** (38), 13111 (2010); https://doi.org/10.1021/ja1037885
29. C.Bournaud, M.Bonin, L.Micouin. *Org. Lett.*, **8** (14), 3041 (2006); https://doi.org/10.1021/ol060972x
30. R.T.Dey, T.K.Sarkar. *J. Org. Chem.*, **75** (13), 4521 (2010); https://doi.org/10.1021/jo100724w
31. R.Chênevert, F.Jacques. *Tetrahedron: Asymmetry*, **17** (6), 1017 (2006); https://doi.org/10.1016/j.tetasy.2006.03.014
32. R.Robiette, T.-V.Tran, A.Cordi, B.Tinant, J.Marchand-Brynaert. *Synthesis*, (18), 3138 (2010); https://doi.org/10.1055/s-0030-1258176
33. A.R.Katritzky, X.Lan, J.Z.Yang, O.V.Denisko. *Chem. Rev.*, **98** (2), 409 (1998); https://doi.org/10.1021/cr941170v
34. J.Erickson, D.J.Neidhart, J.Van Drie, D.J.Kempf, X.C.Wang, D.W.Norbeck, J.J.Plattner, J.W.Rittenhouse, M.Turon, N.Wideburg, W.E.Kohlbrenner, R.Simmer, R.Helfrich, D.A.Paul, M.Knigge. *Science*, **249** (4968), 527 (1990); https://doi.org/10.1126/science.2200122
35. B.S.Kumar, V.Venkataramasubramanian, A.Sudalai. *Org. Lett.*, **14** (10), 2468 (2012); https://doi.org/10.1021/ol300739b
36. X.Wu, B.Liu, Y.Zhang, M.Jeret, H.Wang, P.Zheng, S.Yang, B.Song, Y.R.Chi. *Angew. Chem., Int. Ed.*, **55** (40), 12280 (2016); https://doi.org/10.1002/anie.201606571
37. A.Chan, K.A.Scheidt. *J. Am. Chem. Soc.*, **130** (9), 2740 (2008); https://doi.org/10.1021/ja711130p
38. H.Kawai, A.Kusuda, S.Nakamura, M.Shiro, N.Shibata. *Angew. Chem., Int. Ed.*, **48** (34), 6324 (2009); https://doi.org/10.1002/anie.200902457
39. Z.Wu, J.Wang. *Chem. Sci.*, **10** (8), 2501 (2019); https://doi.org/10.1039/C8SC04601H
40. C.L.Molina, C.P.Chow, K.J.Shea. *J. Org. Chem.*, **72** (18), 6816 (2007); https://doi.org/10.1021/jo070978f
41. L.Hesping, A.Biswas, C.G.Daniliuc, C.Mück-Lichtenfeld, A.Studer. *Chem. Sci.*, **6** (2), 1252 (2015); https://doi.org/10.1039/C4SC02612H
42. A.Bongers, C.Clavette, W.Gan, S.I.Gorelsky, L.Betit, K.Lavergne, T.Markiewicz, P.J.Moon, N.Das Neves, N.K.Obhi, A.B.Toderian, A.M.Beauchemin. *J. Org. Chem.*, **82** (2), 1175 (2017); https://doi.org/10.1021/acs.joc.6b02713
43. A.Bongers, P.J.Moon, A.M.Beauchemin. *Angew. Chem., Int. Ed.*, **54** (51), 15516 (2015); https://doi.org/10.1002/anie.201507548
44. C.Clavette, W.Gan, A.Bongers, T.Markiewicz, A.B.Toderian, S.I.Gorelsky, A.M.Beauchemin. *J. Am. Chem. Soc.*, **134** (39), 16111 (2012); https://doi.org/10.1021/ja305491t
45. B.M.Trost, J.S.Tracy. *Org. Lett.*, **19** (10), 2630 (2017); https://doi.org/10.1021/acs.orglett.7b00961
46. K.Le Jeune, S.Chevallier-Michaud, D.Gatineau, L.Giordano, A.Tenaglia, H.Clavier. *J. Org. Chem.*, **80** (17), 8821 (2015); https://doi.org/10.1021/acs.joc.5b01205
47. J.Deng, R.P.Hsung, C.Ko. *Org. Lett.*, **14** (21), 5562 (2012); https://doi.org/10.1021/ol3026796
48. M.M.Heravi, A.Nazari. *RSC Adv.*, **12** (16), 9944 (2022); https://doi.org/10.1039/D1RA08163B
49. Y.Gao, D.Ma. *Nat. Synth.*, **1** (4), 275 (2022); https://doi.org/10.1038/s44160-022-00046-z
50. D.J.Edmonds, D.Johnston, D.J.Procter. *Chem. Rev.*, **104** (7), 3371 (2004); https://doi.org/10.1021/cr030017a

51. N.E.Brandukova, Y.S.Vygodskii, S.V.Vinogradova. *Russ. Chem. Rev.*, **63** (4), 345 (1994); https://doi.org/10.1070/RC1994v063n04ABEH000088
52. T.Hashimoto, Y.Takiguchi, K.Maruoka. *J. Am. Chem. Soc.*, **135** (31), 11473 (2013); https://doi.org/10.1021/ja405444c
53. L.Lykke, B.D.Carlsen, R.S.Rambo, K.A.Jørgensen. *J. Am. Chem. Soc.*, **136** (32), 11296 (2014); https://doi.org/10.1021/ja506694v
54. S.Shirakawa, P.J.Lombardi, J.L.Leighton. *J. Am. Chem. Soc.*, **127** (28), 9974 (2005); https://doi.org/10.1021/ja052307+
55. Y.Wang, Q.Wang, J.Zhu. *Chem. – Eur. J.*, **22** (24), 8084 (2016); https://doi.org/10.1002/chem.201601548
56. N.C.Giampietro, J.P.Wolfe. *J. Am. Chem. Soc.*, **130** (39), 12907 (2008); https://doi.org/10.1021/ja8050487
57. C.-J.Yang, C.Zhang, Q.-S.Gu, J.-H.Fang, X.-L.Su, L.Ye, Y.Sun, Y.Tian, Z.-L.Li, X.-Y.Liu. *Nat. Catal.*, **3** (7), 539 (2020); https://doi.org/10.1038/s41929-020-0460-y
58. X.Zhong, J.Lv, S.Luo. *Org. Lett.*, **17** (6), 1561 (2015); https://doi.org/10.1021/acs.orglett.5b00445
59. M.Kawasaki, H.Yamamoto. *J. Am. Chem. Soc.*, **128** (51), 16482 (2006); https://doi.org/10.1021/ja066726y
60. M.Sakurai, N.Kihara, N.Watanabe, Y.Ikari, T.Takata. *Chem. Lett.*, **47** (2), 144 (2018); https://doi.org/10.1246/cl.170970
61. M.Rueping, M.S.Maji, H.B.Küçük, I.Atodiresei. *Angew. Chem., Int. Ed.*, **51** (51), 12864 (2012); https://doi.org/10.1002/anie.201205813
62. D.F.Smee, R.W.Sidwell. *Exp. Opin. Investig. Drugs*, **11** (6), 859 (2002); https://doi.org/10.1517/13543784.11.6.859
63. L.J.Scott. *Drugs*, **78** (13), 1363 (2018); https://doi.org/10.1007/s40265-018-0981-8
64. K.Namba, Y.Shobo, K.Fujimoto, I.Shoji, M.Yoshida, K.Tanino. *Eur. J. Org. Chem.*, (24), 5196 (2014); https://doi.org/10.1002/ejoc.201402650
65. G.E.Keck, S.A.Heumann. *Org. Lett.*, **10** (21), 4783 (2008); https://doi.org/10.1021/ol801849u
66. M.Okumura, S.M.N.Huynh, J.Pospech, D.Sarlah. *Angew. Chem*., *Int. Ed*., **55** (51), 15910 (2016); https://doi.org/10.1002/ange.201609686
67. E.H.Southgate, J.Pospech, J.Fu, D.R.Holycross, D.Sarlah. *Nature Chem.*, **8** (10), 922 (2016); https://doi.org/10.1038/nchem.2594
68. C.Izquierdo, F.Esteban, A.Parra, R.Alfaro, J.Alemán, A.Fraile, J.L.G.Ruano. *J. Org. Chem.*, **79** (21), 10417 (2014); https://doi.org/10.1021/jo5018519
69. W.Li, J.Wei, Q.Jia, Z.Du, K.Zhang, J.Wang. *Chem. – Eur. J.*, **20** (22), 6592 (2014); https://doi.org/10.1002/chem.201402089
70. T.Hashimoto, Y.Maeda, M.Omote, H.Nakatsu, K.Maruoka. *J. Am. Chem. Soc.*, **132** (12), 4076 (2010); https://doi.org/10.1021/ja100787a
71. T.P.Lebold, M.A.Kerr. *Org. Lett.*, **11** (19), 4354 (2009); https://doi.org/10.1021/ol901744e
72. D.Just, D.Hernandez-Guerra, S.Kritsch, R.Pohl, I.Císařová, P.G.Jones, R.Mackman, G.Bahador, U.Jahn. *Eur. J. Org. Chem.*, (37), 5213 (2018); https://doi.org/10.1002/ejoc.201800585
73. M.J.Brown, G.J.Clarkson, G.G.Inglis, M.Shipman. *Org. Lett.*, **13** (7), 1686 (2011); https://doi.org/10.1021/ol200193n
74. Y.Qian, P.J.Zavalij, W.Hu, M.P.Doyle. *Org. Lett.*, **15** (7), 1564 (2013); https://doi.org/10.1021/ol400339c
75. L.Pezdirc, U.Grošelj, A.Meden, B.Stanovnik, J.Svete. *Tetrahedron Lett.*, **48** (30), 5205 (2007); https://doi.org/10.1016/j.tetlet.2007.05.142
76. Z.Yang, Q.Yue, M.Yang, H.Zhang, X.Cui. *J. Org. Chem.*, **85** (20), 12960 (2020); https://doi.org/10.1021/acs.joc.0c01614
77. Y.Xu, M.Shen, X.Zhang, X.Fan. *Org. Lett.*, **22** (12), 4697 (2020); https://doi.org/10.1021/acs.orglett.0c01475
78. Z.Fan, H.Lu, W.Li, K.Geng, A.Zhang. *Org. Biomol. Chem.*, **15** (27), 5701 (2017); https://doi.org/10.1039/C7OB01271C
79. Z.Zhang, H.Jiang, Y.Huang. *Org. Lett.*, **16** (22), 5976 (2014); https://doi.org/10.1021/ol502998n
80. Y.Zhou, Q.Song. *Org. Chem. Front.*, **5** (22), 3245 (2018); https://doi.org/10.1039/C8QO00872H
81. G.U.Baig, M.F.G.Stevens. *J. Chem. Soc., Perkin Trans. 1*, 2765 (1984); https://doi.org/10.1039/p19840002765
82. G.U.Baig, M.F.G.Stevens, K.Vaughan. *J. Chem. Soc., Perkin Trans. 1*, 999 (1984); https://doi.org/10.1039/p19840000999
83. Y.L.Prapurna, C.R.Reddy. In *Comprehensive Heterocyclic Chemistry IV*. (Elsevier, 2022). P. 1; https://doi.org/10.1016/B978-0-12-818655-8.00101-3
84. R.G.Sherrill. *Tetrahedron Lett.*, **48** (39), 7053 (2007); https://doi.org/10.1016/j.tetlet.2007.07.083
85. J.Gujral, T.P.Reddy, B.Gorachand, D.B.Ramachary. *ChemistrySelect*, **3** (27), 7900 (2018); https://doi.org/10.1002/slct.201801328
86. Q.-Q.Yang, X.Yin, X.-L.He, W.Du, Y.-C.Chen. *ACS Catal.*, **9** (2), 1258 (2019); https://doi.org/10.1021/acscatal.8b04942
87. H.Lee, D.Kang, S.H.Han, R.Chun, A.K.Pandey, N.K.Mishra, S.Hong, I.S.Kim. *Angew. Chem., Int. Ed.*, **58** (28), 9470 (2019); https://doi.org/10.1002/anie.201903983
88. K.Dong, K.O.Marichev, M.P.Doyle. *Organometallics*, **38** (20), 4043 (2019); https://doi.org/10.1021/acs.organomet.9b00427
89. H.Zheng, M.P.Doyle. *Angew. Chem., Int. Ed.*, **58** (36), 12502 (2019); https://doi.org/10.1002/anie.201906754
90. M.De Paolis, J.Blankenstein, M.Bois-Choussy, J.Zhu. *Org. Lett.*, **4** (7), 1235 (2002); https://doi.org/10.1021/ol025743z
91. O.O.Grygorenko, A.V.Biitseva, S.Zhersh. *Tetrahedron*, **74** (13), 1355 (2018); https://doi.org/10.1016/j.tet.2018.01.033
92. M.Chaffman, R.N.Brogden. *Drugs*, **29** (5), 387 (1985); https://doi.org/10.2165/00003495-198529050-00001
93. J.Held-Warmkessel. *Clin. J. Oncol. Nurs.*, **7** (3), 313 (2003); https://doi.org/10.1188/03.CJON.313-319
94. J.A.Sturman. *Physiol. Rev.*, **73** (1), 119 (1993); https://doi.org/10.1152/physrev.1993.73.1.119
95. J.-R.Guo, J.-F.Gong, M.-P.Song. *Org. Biomol. Chem.*, **17** (20), 5029 (2019); https://doi.org/10.1039/C9OB00449A
96. C.Spitz, J.-F.Lohier, J.S.O.Santos, V.Reboul, P.Metzner. *J. Org. Chem.*, **74** (10), 3936 (2009); https://doi.org/10.1021/jo900449a
97. Y.Li, M.Lei, L.Gong. *Nat. Catal.*, **2** (11), 1016 (2019); https://doi.org/10.1038/s41929-019-0357-9
98. Y.Li, M.Lei, W.Yuan, E.Meggers, L.Gong. *Chem. Commun.*, **53** (57), 8089 (2017); https://doi.org/10.1039/C7CC04691J
99. L.Wu, R.Liu, G.Zhang, D.Wang, H.Wu, J.Gao, Y.Jia. *Adv. Synth. Catal.*, **357** (4), 709 (2015); https://doi.org/10.1002/adsc.201400987
100. M.Zajac, R.Peters. *Chem. – Eur. J.*, **15** (33), 8204 (2009); https://doi.org/10.1002/chem.200900496
101. M.Zajac, R.Peters. *Org. Lett.*, **9** (10), 2007 (2007); https://doi.org/10.1021/ol070644c
102. T.Jian, L.He, C.Tang, S.Ye. *Angew. Chem., Int. Ed.*, **50** (39), 9104 (2011); https://doi.org/10.1002/anie.201102488
103. V.Gupta, H.Paritala, K.S.Carroll. *Bioconjugate Chem.*, **27** (5), 1411 (2016); https://doi.org/10.1021/acs.bioconjchem.6b00181
104. Z.D.Parsons, K.V.Ruddraraju, N.Santo, K.S.Gates. *Bioorg. Med. Chem.*, **24** (12), 2631 (2016); https://doi.org/10.1016/j.bmc.2016.03.054
105. V.Gupta, K.S.Carroll. *Chem. Commun.*, **52** (16), 3414 (2016); https://doi.org/10.1039/C6CC00228E
106. K.V.Ruddraraju, Z.D.Parsons, E.M.Llufrio, N.L.Frost, K.S.Gates. *J. Org. Chem.*, **80** (24), 12015 (2015); https://doi.org/10.1021/acs.joc.5b01949
107. P.Gangireddy, V.Patro, L.Lam, M.Morimoto, L.S.Liebeskind. *J. Org. Chem.*, **82** (7), 3513 (2017); https://doi.org/10.1021/acs.joc.7b00020
108. T.-Q.Yu, Y.-S.Hou, Y.Jiang, W.-X.Xu, T.Shi, X.Wu, J.-C.Zhang, D.He, Z.Wang. *Tetrahedron Lett.*, **58** (22), 2084 (2017); https://doi.org/10.1016/j.tetlet.2017.03.065
109. A.Henke, J.Srogl. *Chem. Commun.*, **46** (36), 6819 (2010); https://doi.org/10.1039/c0cc00885k
110. G.Papandrea, F.Ponticelli. *Synth. Commun.*, **38** (6), 858 (2008); https://doi.org/10.1080/00397910701845340

111. L.Guideri, F.Ponticelli. *Tetrahedron Lett.*, **53** (41), 5507 (2012); https://doi.org/10.1016/j.tetlet.2012.07.139
112. J.K.Laha, R.A.Bhimpuria, A.M.Kumar. *Org. Chem. Front.*, **4** (11), 2170 (2017); https://doi.org/10.1039/C7QO00440K
113. J.K.Laha, N.Dayal, K.P.Jethava, D.V.Prajapati. *Org. Lett.*, **17** (5), 1296 (2015); https://doi.org/10.1021/acs.orglett.5b00290
114. R.Mousa, R.N.Dardashti, N.Metanis. *Angew. Chem., Int. Ed.*, **56** (50), 15818 (2017); https://doi.org/10.1002/anie.201706876
115. A.S.Rahmanto, M.J.Davies. *IUBMB Life*, **64** (11), 863 (2012); https://doi.org/10.1002/iub.1084
116. X.Zhang, H.He, J.Xiang, H.Yin, T.Hou. *J. Agric. Food Chem.*, **68** (51), 15061 (2020); https://doi.org/10.1021/acs.jafc.0c05594
117. Ö.Pehlivan, M.Waliczek, M.Kijewska, P.Stefanowicz. *Molecules*, **28** (7), 3198 (2023); https://doi.org/10.3390/molecules28073198
118. K.Ahmed, D.Ashraf, G.A.Chotana, A.Faisal, K.M.Khan, R.S.Z.Saleem. *Curr. Med. Chem.*, **29** (42), 6379 (2022); https://doi.org/10.2174/0929867329666220214104010
119. A.J.Pacuła, K.B.Kaczor, J.Antosiewicz, A.Janecka, A.Długosz, T.Janecki, A.Wojtczak, J.Ścianowski. *Molecules*, **22** (3), 492 (2017); https://doi.org/10.3390/molecules22030492
120. M.Iwasaki, N.Miki, Y.Tsuchiya, K.Nakajima, Y.Nishihara. *Org. Lett.*, **19** (5), 1092 (2017); https://doi.org/10.1021/acs.orglett.7b00116
121. S.Patel, M.Meenakshi, A.S.Hodage, A.Verma, S.Agrawal, A.Yadav, S.Kumar. *Dalton Trans.*, **45** (9), 4030 (2016); https://doi.org/10.1039/C5DT04356E
122. S.J.Balkrishna, B.S.Bhakuni, D.Chopra, S.Kumar. *Org. Lett.*, **12** (23), 5394 (2010); https://doi.org/10.1021/ol102027j
123. A.J.Pacuła, M.Obieziurska, J.Ścianowski, K.B.Kaczor, J.Antosiewicz. *ARKIVOC*, (iii), 153 (2018); https://doi.org/10.24820/ark.5550190.p010.311
124. D.Bhowmick, G.Mugesh. *Org. Biomol. Chem.*, **13** (34), 9072 (2015); https://doi.org/10.1039/C5OB01294E
125. K.Satheeshkumar, G.Mugesh. *Chem. – Eur. J.*, **17** (17), 4849 (2011); https://doi.org/10.1002/chem.201003417
126. G.Steinfeld, B.Kersting. *Z. Anorg. Allg. Chem*., **632** (12–13), 2010 (2006); https://doi.org/10.1002/zaac.200600107
127. K.P.Bhabak, G.Mugesh. *Chem. – Asian J.*, **4** (6), 974 (2009); https://doi.org/10.1002/asia.200800483
128. B.K.Sarma, G.Mugesh. *Chem. – Eur. J.*, **14** (34), 10603 (2008); https://doi.org/10.1002/chem.200801258
129. R.Lisiak, J.Młochowski. *Synth. Commun.*, **39** (17), 3141 (2009); https://doi.org/10.1080/00397910902730994
130. N.Makukhin, A.Ciulli. *RSC Med. Chem.*, **12** (1), 8 (2021); https://doi.org/10.1039/D0MD00272K
131. A.R.Garifzyanov, N.V.Shirshova, R.A.Cherkasov. *Russ. J. Gen. Chem.*, **75** (4), 537 (2005); https://doi.org/10.1007/s11176-005-0268-0
132. E.V.Goud, A.Sivaramakrishna, K.Vijayakrishna. *Top. Curr. Chem.*, **375** (1), 10 (2017); https://doi.org/10.1007/s41061-016-0090-7
133. V.A.Stepanova, I.P.Smoliakova. *Curr. Org. Chem.*, **16** (24), 2893 (2012); https://doi.org/10.2174/138527212804546723
134. M.C.B.Dolinsky, W.O.Lin, M.L.Dias. *J. Mol. Catal. A: Chem.*, **258** (1–2), 267 (2006); https://doi.org/10.1016/j.molcata.2006.05.040
135. I.M.Aladzheva, O.V.Bykhovskaya, P.V.Petrovskii, K.A.Lyssenko, M.Y.Antipin, T.A.Mastryukova. *Russ. Chem. Bull.*, **54** (11), 2635 (2005); https://doi.org/10.1007/s11172-006-0168-4
136. G.Ruiz-Gómez, A.Francesch, M.J.Iglesias, F.López-Ortiz, C.Cuevas, M.Serrano-Ruiz. *Org. Lett.*, **10** (18), 3981 (2008); https://doi.org/10.1021/ol801463g
137. G.Ruiz-Gómez, M.J.Iglesias, M.Serrano-Ruiz, F.López-Ortiz. *J. Org. Chem.*, **72** (25), 9704 (2007); https://doi.org/10.1021/jo701607s
138. I.Fernández, G.R.Gómez, I.Alfonso, M.J.Iglesias, F.L.Ortiz. *Chem. Commun.*, (43), 5408 (2005); https://doi.org/10.1039/b510685k
139. Y.Ma, X.Zhang, S.Yang. *Chem. – Eur. J.*, **23** (13), 3007 (2017); https://doi.org/10.1002/chem.201700218
140. Z.Lin, W.Wang, S.Yan, W.Duan. *Angew. Chem., Int. Ed.*, **54** (21), 6265 (2015); https://doi.org/10.1002/anie.201500201
141. Y.-N.Ma, M.-X.Cheng, S.-D.Yang. *Org. Lett.*, **19** (3), 600 (2017); https://doi.org/10.1021/acs.orglett.6b03625
142. M.Bols, C.M.Pedersen. *Beilstein J. Org. Chem.*, **13**, 93 (2017); https://doi.org/10.3762/bjoc.13.12
143. R.D.Crouch. *Synth. Commun.*, **43** (17), 2265 (2013); https://doi.org/10.1080/00397911.2012.717241
144. R.D.Crouch. *Tetrahedron*, **60** (28), 5833 (2004); https://doi.org/10.1016/j.tet.2004.04.042
145. B.E.Leland, J.Mondal, R.J.Trovitch. *Chem. Commun.*, **59** (25), 3665 (2023); https://doi.org/10.1039/D2CC07092H
146. D.Rother, T.Sen, D.East, I.J.Bruce. *Nanomedicine*, **6** (2), 281 (2011); https://doi.org/10.2217/nnm.10.159
147. D.M.Pacheco, J.R.Johnson, W.J.Koros. *Ind. Eng. Chem. Res.*, **51** (1), 503 (2012); https://doi.org/10.1021/ie2020685
148. B.Singh, J.Bouchet, Y.Leterrier, J.-A.E.Månson, G.Rochat, P.Fayet. *Surf. Coat. Technol.*, **202** (2), 208 (2007); https://doi.org/10.1016/j.surfcoat.2007.05.036
149. V.Sunkara, Y.-K.Cho. *ACS Appl. Mater. Interfaces*, **4** (12), 6537 (2012); https://doi.org/10.1021/am3015923
150. J.S.Andre, J.Grant, E.Greyson, X.Chen, C.Tucker, R.Drumright, C.Mohler, Z.Chen. *Langmuir*, **38** (19), 6180 (2022); https://doi.org/10.1021/acs.langmuir.2c00602
151. Z.Wang, E.V.Beletskiy, S.Lee, X.Hou, Y.Wu, T.Li, M.C.Kung, H.H.Kung. *J. Mater. Chem. A*, **3** (4), 1743 (2015); https://doi.org/10.1039/C4TA05954A
152. J.Ehbets, S.Lorenzen, C.Mahler, R.Bertermann, A.Berkefeld, J.Poater, E.Fritz-Langhals, R.Weidner, F.M.Bickelhaupt, R.Tacke. *Eur. J. Inorg. Chem.*, (11), 1641 (2016); https://doi.org/10.1002/ejic.201600077
153. Z.Nevárez, K.A.Woerpel. *Org. Lett.*, **9** (19), 3773 (2007); https://doi.org/10.1021/ol701424a
154. Q.Li, M.Driess, J.F.Hartwig. *Angew. Chem., Int. Ed.*, **53** (32), 8471 (2014); https://doi.org/10.1002/anie.201404620