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REVIEW

Catalysis in the Synthesis of S,N-Heterocycles and O,N-, S,N-, and O,S,N-Macroheterocycles

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Abstract—The review systemizes and generalizes published data on the catalytic syntheses of six-, seven-, and eight-membered S,N-heterocycles and O,N-, S,N-, and O,S,N-macroheterocycles.

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1. INTRODUCTION

Heterocyclic compounds of various natures constitute base fragments of many biologically active compounds and are used as models for studying structure–property relationships. Up to now, vast data have been accumulated in world scientific literature on methods of synthesis of heterocyclic compounds. In this review we consider catalytic methods of synthesis of six-, seven-, and eight-membered S,N-heterocycles and

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Fields of scientific interest: catalysis, chemistry of O,S,N-heterocyclic compounds, including polycyclic ones and macrocycles.

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Fields of scientific interest: synthesis and properties of saturated O,S,N-heterocyclic compounds.

macroheterocycles via intramolecular cyclization of aromatic substrates and condensation of amino thiols with halogen derivatives, as well as the synthesis of N-substituted six-, seven-, and eight-membered heterocycles by catalytic cyclothiomethylation of aromatic amines with two-component CH_2O–H_2S and CH_2O–dithiol systems. Particular attention has been given to catalytic transamination of *N*-alkyl S,N-heterocycles and catalytic recyclization of oxathiacycloalkanes by the action of primary aromatic amines. The possibility of one-pot syntheses of various macrocycles from *N*,*N*-bis(methoxymethyl)arenamines and α,ω-dithiols in the presence of *d*- and *f*-metal catalysts has been demonstrated. Efficient synthetic approaches to partially hydrogenated 1,4-benzothiazines, phenothiazines, 1,4(5)-benzothiazepines, and benzothiazocin-(on)es, N-substituted 1,3,5-dithiazinanes, 1,5,3-dithiazepanes, 1,5,3-dithiazocanes, and O,N-, S,N-, and O,S,N-macroheterocycles have been systemized. Data on biological activity and complexing properties of some compounds are also given.

2. CATALYSIS IN THE SYNTHESIS OF SIX-MEMBERED S,N- HETEROCYCLES

2.1. Synthesis of Partially Hydrogenated 1,4-Benzothiazines and Phenothiazines

1,4-Benzothiazines exhibit antimicrobial [1], antimalarial [2], ant-inflammatory [3], antitumor [4], and fungicidal properties [5]. 3,4-Dihydro-2*H*-1,4-benzothiazines **1a**–**1g** were synthesized by reaction of 2-bromobenzenethiol with amino acid derivatives [6], followed by deprotection of the amino group in intermediate 2-(2-bromophenylsulfanyl)ethanamines with trifluoroacetic acid and intramolecular cyclization of the resulting primary amine in the presence of copper(I) iodide and potassium carbonate. The yield of **1a**–**1g** was 61–72% (Scheme 1). The synthesis of 3,4-dihydro-2*H*-1,4-benzothiazines was also catalyzed by $MoO_2Cl_2(dmf)_2$ [7]. 2-Nitrobenezenethiol reacted with 1-bromo-3-methylbut-2-ene to give intermediate sulfide which underwent cyclization in the presence of 5 mol % of $MoO_2Cl_2(dmf)_2$ in toluene at 185°C (15 h) to produce 3-(prop-1-en-2-yl)-3,4-dihydro-2*H*-1,4-benzothiazine (**2**) in 63% yield (Scheme 2). The yield of **2** increased to 89% when 10 mol % of the catalyst was used. Another synthesis of 3,4-dihydro-2*H*-1,4-benzothiazines is based on the reaction of 2-bromobenzenethiols with 2-bromoethanamine with the formation of 2-(2-bromophenylsulfanyl)ethanamine [8] and cyclization of the latter in the presence of a strong base, lithium diisopropylamide (LDA); 3,4-dihydro-2*H*-1,4-benzothiazines **3a**–**3c** were thus obtained in 87–93% yield (Scheme 2).

2*H*-1,4-Benzothiazine-3(4*H*)-one (**4**) was synthesized in 83% yield by condensation of 2-aminobenzenethiol with chloroacetic acid [9] on heating in ethanol in the presence of sodium acetate. 2-(Alkylsulfanyl)anilines [10] reacted with bromoacetyl bromide in the presence of aluminum oxide or under microwave irradiation to afford compound **4** and its 7-methyl derivative **5** (yield 72–80%; Scheme 3). Analogous cyclization of 2,2′-(alkane-α,ω-diyldisulfanediyl)dianiline with bromoacetyl bromide gave no macrocyclic compound **6** but 2*H*-1,4-benzothiazin-3(4*H*)-one (**4**, 74%) [10]. Intramolecular cyclization of enamines [11] in boiling 1,4-dioxane catalyzed by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) quantitatively produced 3,4-dihydro-2*H*-1,4-benzothiazine 1,1-dioxides **7** (Scheme 4).

Phenothiazines constitute another group of fused six-membered S,N-heterocycles that are used as insecticides, polymerization inhibitors, optoelectronic materials, antioxidants, paints [12, 13], and various medicinal agents [14–16]. Phenothiazines are commonly synthesized by heating diphenylamines with elemental sulfur at a high temperature [17]. Successful catalytic synthesis of phenothiazines was also reported [18]. Ring closure in diphenylamine in the presence of elemental sulfur (S_8) and I_2 gave 89% of 10*H*-phenothiazine (**8**). The same compound was obtained in quantitative yield under catalysis by Al_2O_3 in combination with microwave radiation [19] (Scheme 5). The reaction of 2-bromo-*N*-(2-iodophenyl)aniline with thioacetamide in the presence of copper(I) iodide also led to the formation of **8** (Scheme 5) [20]. A complex of copper(I) iodide with L-proline has been proposed [15] to catalyze the synthesis of phenothiazines. The reaction of 2-iodoaniline with 2-bromobenzenethiol

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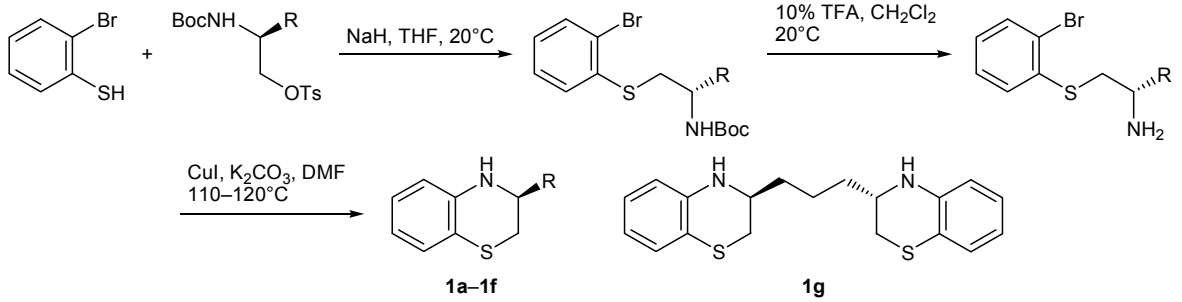
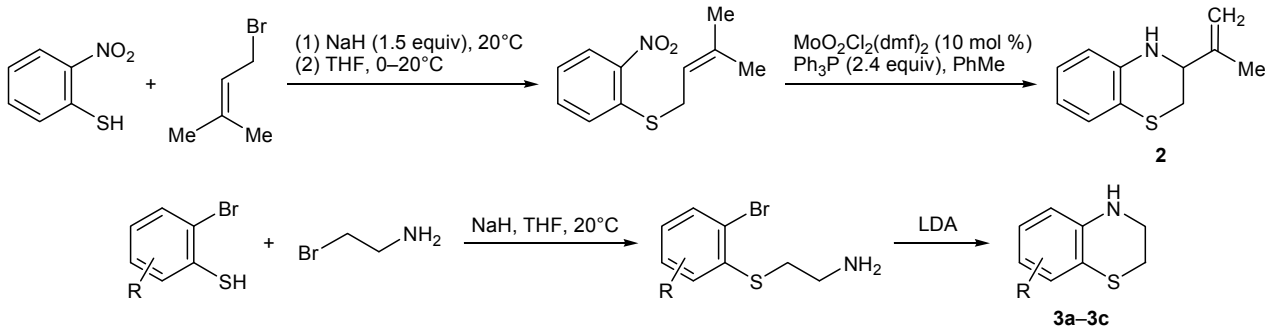
Fields of scientific interest: metal complex catalysis, chemistry of organoaluminum and organomagnesium compounds and O,S,N-heterocycles.

Scheme 1.



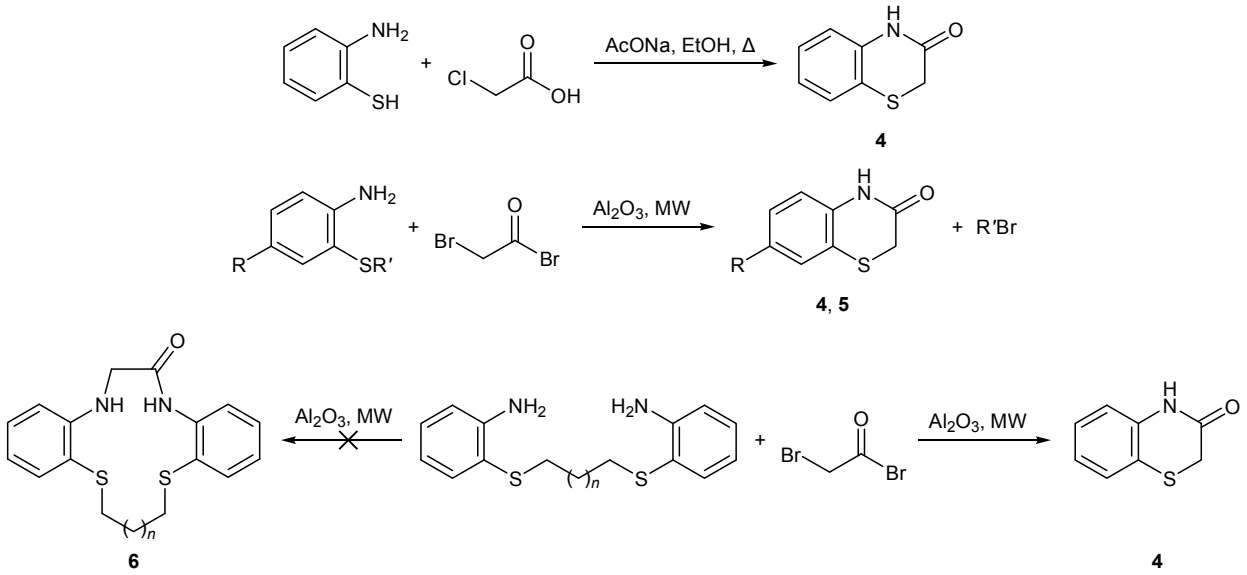
R = Me (**a**), *i*-Pr (**b**), *i*-Bu (**c**), EtCH(Me) (**d**), $PhCH_2$ (**e**), 4-$(PhCH_2O)C_6H_4CH_2$ (**f**).

Scheme 2.



R = H (**a**), 4-Me (**b**), 5-MeO (**c**).

Scheme 3.



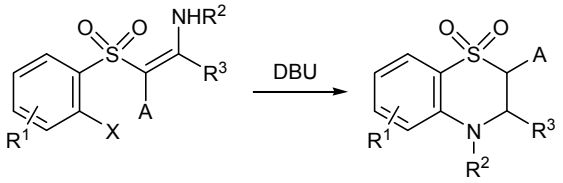
R = H, Me; R′ = Me, Et, Pr, $PhCH_2$; *n* = 0, 1, CH_2OCH_2.

in the presence of CuI/L-proline afforded 90% of 10*H*-phenothiazine (**8**) (Scheme 5).

N-Substituted phenothiazines **9** were synthesized in up to 92% yield by three-component condensation of 1-bromo-2-iodobenzene with primary amines and 2-bromobenzenethiol in the presence of tris(dibenzylideneacetone)dipalladium $Pd_2(dba)_3$ [16] (Scheme 6). The condensation of 2-aminobenzenethiol [21] with *o*-dihalobenzenes catalyzed by CuI and K_2CO_3 gave substituted phenothiazines **10a**–**10e** in 64–91% yield

(Scheme 6). High yields of S,N-heterocycles **10** were obtained in the CuI-catalyzed reaction with all dihalobenzenes, except for 1,2-dichlorobenzene. Electron-donating groups in the dihalobenzene molecule reduced the yield of **10**, whereas electron-withdrawing groups increased it. A probable mechanism of formation of phenothiazines in this reaction is illustrated by Scheme 7. Due to higher acidity of the SH group than NH_2, 2-aminobenzenethiol reacts with potassium carbonate to give potassium 2-aminobenzenethiolate which is converted to more stable copper 2-aminobenzenethiolate **A** by the action of copper(I) iodide. Oxidative addition of **A** to dihalobenzene leads to complex **B**, and reductive elimination of CuBr yields complex **C**. Activation of the NH_2 group with K_2CO_3 promotes oxidative addition of copper ion with the formation of complex **D**, and the latter is reduced with KI to form phenothiazine (**8**) with regeneration of CuI.

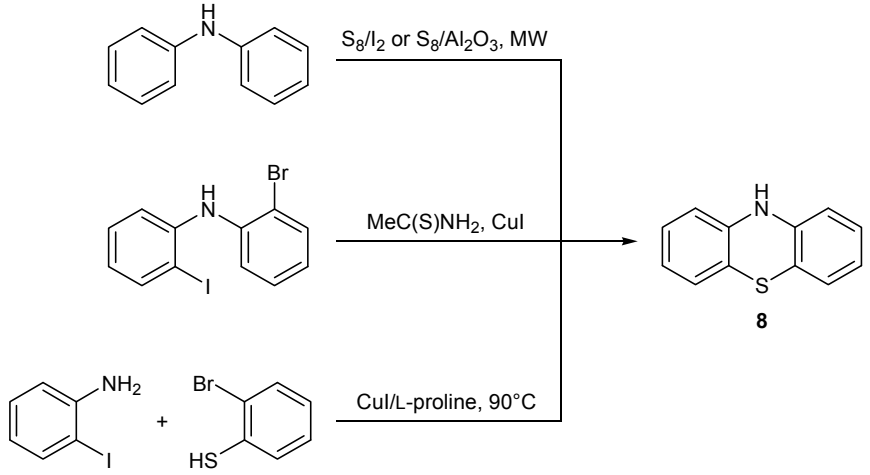
Scheme 4.



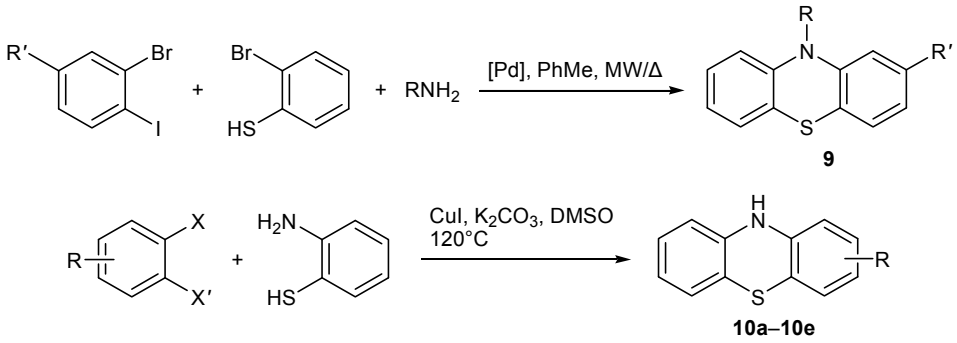
7

R^1 = H, Hlg; R^2 = Alk, Ar; R^3 = H, Alk, AlkS, AlkNH; A = CN, COOAlk, acyl; X = F, Cl.

Scheme 5.

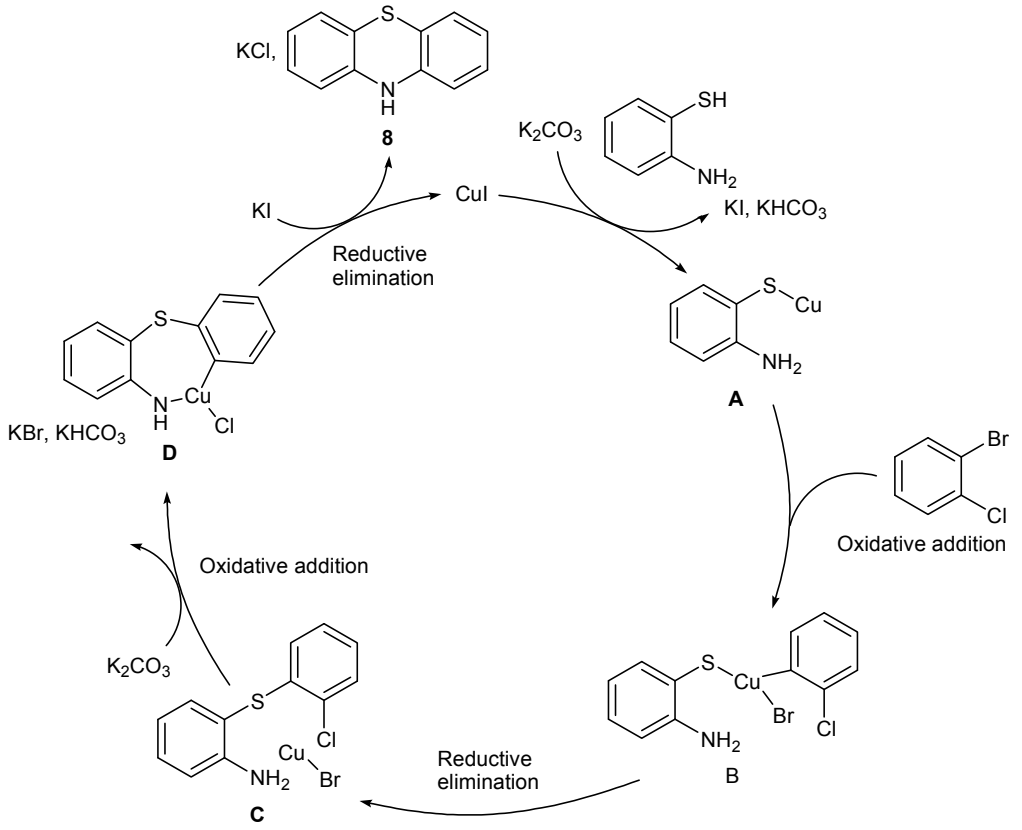


Scheme 6.



9, R = Ph, MeC_6H_4, FC_6H_4, ClC_6H_4; R′ = Cl, F, CF_3, Me; **10**, R = H (**a**), MeO (**b**), CF_3 (**c**), O_2N (**d**), COOH (**e**); X = Cl, Br; X′ = Cl, Br, I.

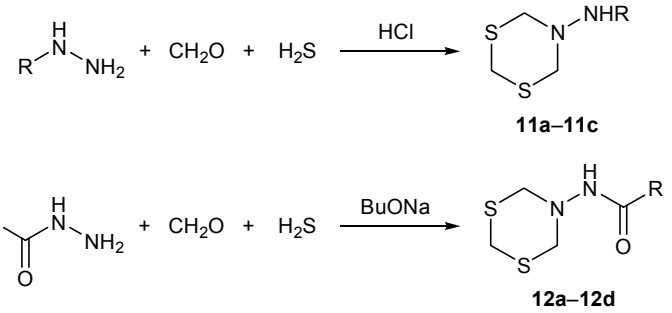
Scheme 7.



2.2. Synthesis of N-Substituted 1,3,5-Dithiazinanes

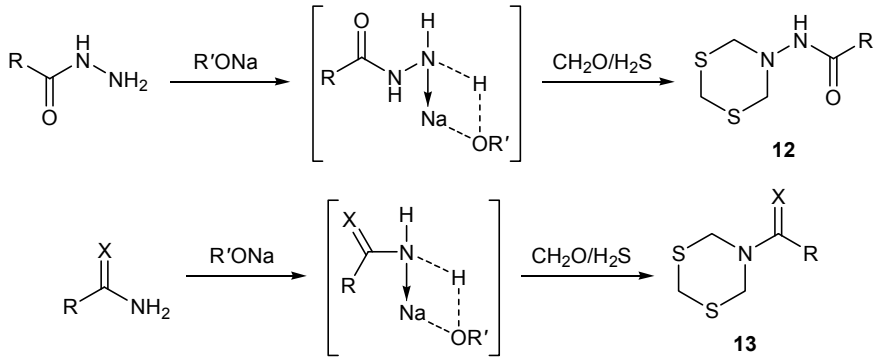
N-Substituted 1,3,5-dithiazinanes exhibit antibacterial, antimicrobial, diuretic, antitubercular [22–26], bactericidal, herbicidal, insecticidal, and acaricidal activities [27–30]. Catalytic methods of synthesis of these compounds have been described in a few publications. Three-component condensation of arylhydrazines with formaldehyde and H_2S at 0°C under acidic conditions gave thermodynamically stable six-membered 1,3,5-dithiazinan-5-amines **11a**–**11c** in low yields (19–26%) [31] (Scheme 8). Likewise, *N*-(1,3,5-dithiazinan-5-yl) carboxamides **12a**–**12d** were synthesized in 55–68% yield by cyclothiomethylation of aromatic (heteroaromatic) carboxylic acid hydrazides with formaldehyde and H_2S in the presence of sodium butoxide [32] (Scheme 8). Carboxylic acid hydrazides, amides, and thioamides undergo successful cyclothiomethylation at the primary amino group in the presence of alkali metal alkoxides to give 1,3,5-dithiazinanes **12** and **13** [32, 33]; the role of alkali metal alkoxide as promoter consists of enhancing the mobility of hydrogen atoms in the NH_2 group via formation of intermediate complex (Scheme 9).

Scheme 8.



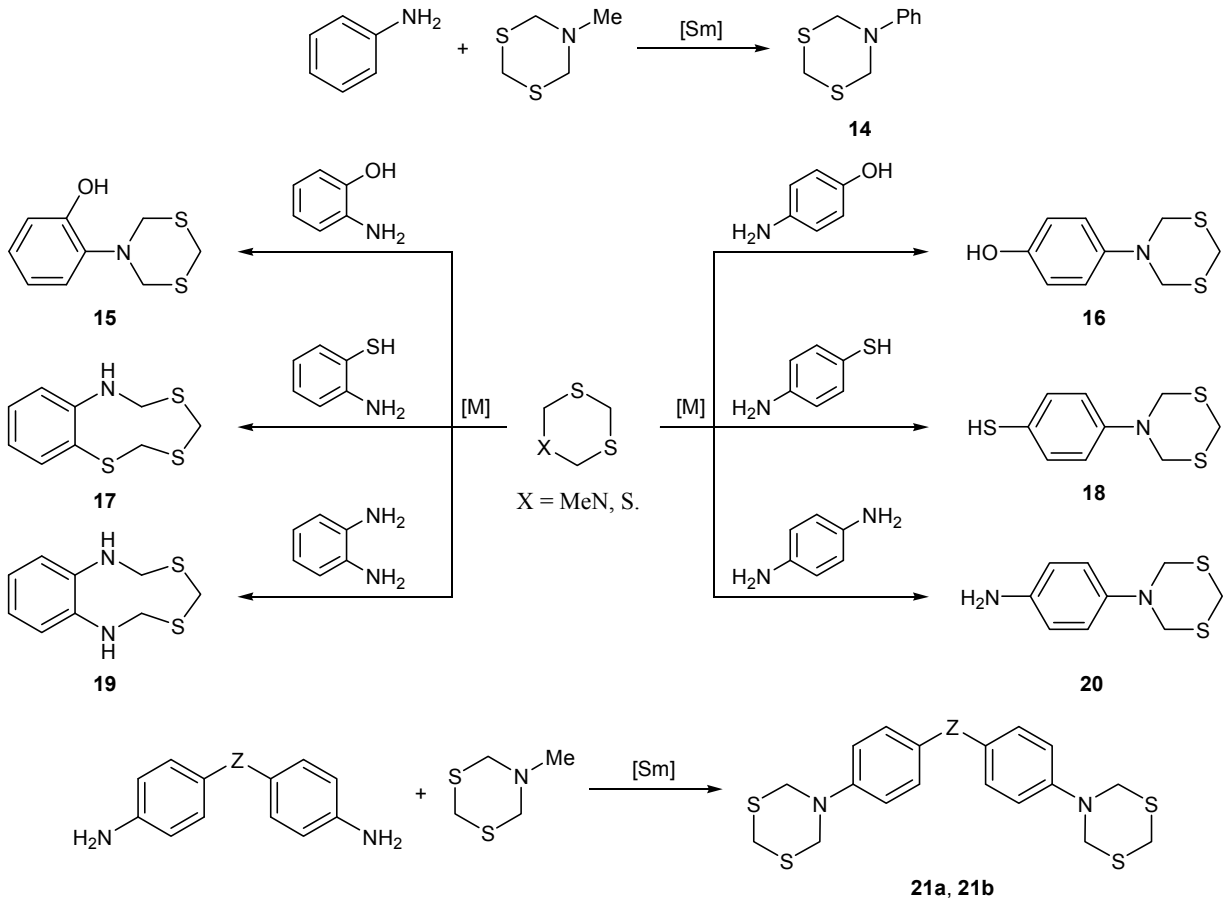
11, R = Ph (**a**), $PhCH_2$ (**b**), Ts (**c**); **12**, R = pyridin-4-yl (**a**), Ph (**b**), 2-$MeOC_6H_4$ (**c**), $HOC_6H_4CH_2$ (**d**).

Scheme 9.



R = Alk, Ar; R′ = Alk; X = O, S.

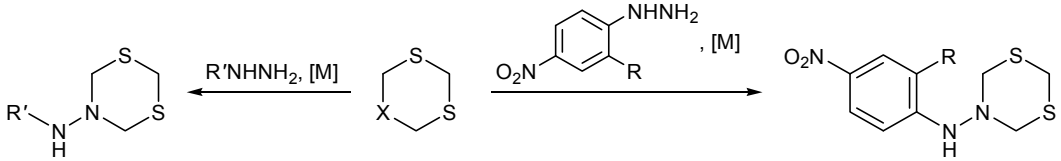
Scheme 10.



21, Z = CH_2 (**a**), O (**b**).

Apart from the classical three-component condensation, 1,3,5-dithiazinanes can be synthesized by catalytic transamination of *N*-methyl-1,3,5-dithiazinane or recyclization of 1,3,5-trithiane with primary amines. For example, aniline reacted with *N*-methyl-1,3,5-dithiazinane in the presence of a samarium catalyst to give 68% of *N*-phenyl-1,3,5-dithiazinane **14** [34] (Scheme 10). Other aromatic amines reacted with an equimolar amount of *N*-methyl-1,3,5-dithiazinane in the presence of 5 mol % of $Sm(NO_3)_3 \cdot 6H_2O$ in a similar way, yielding 51–91% of *N*-aryl-1,3,5-dithiazinanes **15**, **16**, **18**, and **20**, 6,7-dihydro-1,3,5,7-benzotrithiazonine (**17**), and 1,2,6,7-tetrahydro-3,5,1,7-benzodithiadiazonine (**19**) (Scheme 10). Recyclization

Scheme 11.



11, R′ = Ph (**a**), $PhCH_2$ (**b**); **22**, R = H (**a**), O_2N (**b**); X = NMe, S.

of 1,3,5-trithiane with aromatic amines [35, 36] catalyzed by 5 mol % of $FeCl_3 \cdot 6H_2O$ selectively produced 1,3,5-dithiazinanes **15**, **16**, **18**, and **20** in 60–86% yield. Transamination of *N*-methyl-1,3,5-dithiazinane with aromatic diamines in the presence of 5 mol % of $Sm(NO_3)_3 \cdot 6H_2O$ led to selective formation of bis-1,3,5-dithiazinanes **21a** and **21b** [37] (yield 50–58%; Scheme 10).

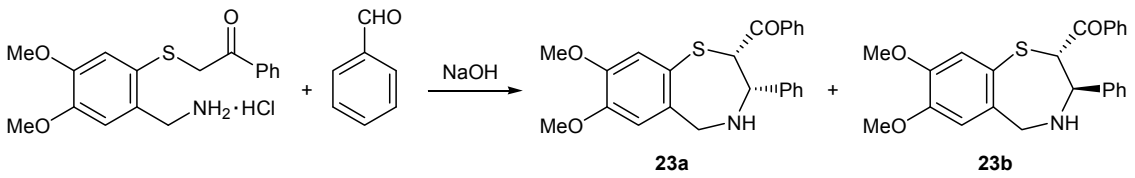
Mild (20°C) catalytic transamination of *N*-methyl-1,3,5-dithiazinane with arylhydrazines in the presence of $CoCl_2/\gamma$-Al_2O_3 [34] gave *N*-phenyl(benzyl)-1,3,5-dithiazinan-5-amines **11a** and **11b** and *N*-[nitro(dinitro)-phenyl]-1,3,5-dithiazinan-5-amines **22a** and **22b** in more than 80% yield. In the absence of a catalyst, the yield did not exceed 15% (Scheme 11). The titanium complex Cp_2TiCl_2 catalyzed recyclization of 1,3,5-trithiane with arylhydrazines to obtain compounds **11a**, **11b**, **22a**, and **22b** in 60–69% yield [35].

3. CATALYSIS IN THE SYNTHESIS OF SEVEN-MEMBERED S,N-HETEROCYCLES

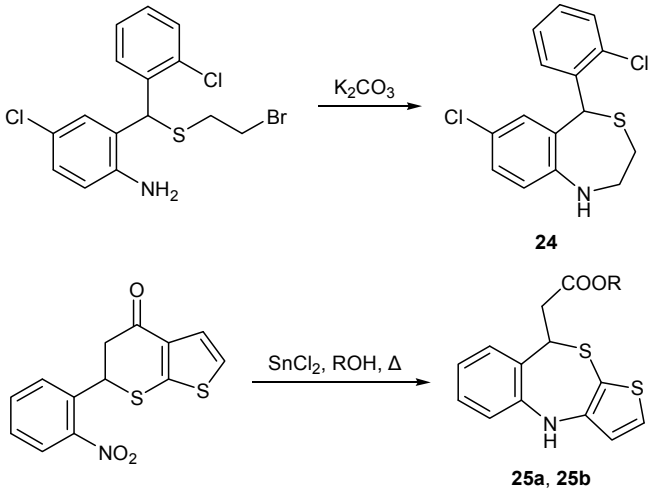
3.1. Synthesis of 2,3,4,5-Tetrahydro-1,4- and 1,2,3,5-Tetrahydro-4,1-benzothiazepines

Stereoisomeric 2,3,4,5-tetrahydro-1,4-benzothiazepines **23a** and **23b** were isolated in an overall yield of 75% in the reaction of 2-[(benzoylmethyl)sulfanyl]-4,5-dimethoxybenzylaminium hydrochloride with benzaldehyde in the presence of sodium hydroxide [38] (Scheme 12). Intramolecular cyclization of 2-[(2-bromoethylsulfanyl)(2-chlorophenyl)methyl]-4-chloroaniline in dimethylformamide with potassium carbonate as a base gave 7-chloro-5-(2-chlorophenyl)-1,2,3,5-tetrahydro-4,1-benzothiazepine (**24**) in 89% yield [39] (Scheme 13); compound **24** attracts interest as potential drug for the treatment of type II diabetes. Intramolecular heterocyclization of 6-(2-nitrophenyl)-

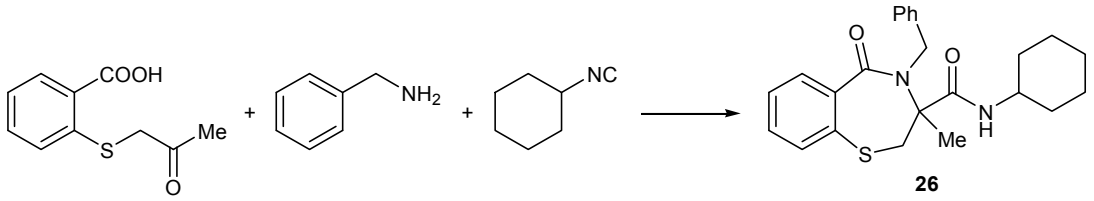
Scheme 12.



Scheme 13.



Scheme 14.



5,6-dihydro-4*H*-thieno[2,3-*b*]thiopyran-4-one in boiling alcohol catalyzed by $SnCl_2$ [40] was reported as a convenient method of synthesis of methyl and ethyl 4,9-dihydrothieno[3,2-*b*][4,1]benzothiazepine-9-carboxylates **25a** and **25b** (yield ~99%; Scheme 13). Intermolecular heterocyclization of 2-[(2-oxopropyl)-sulfanyl]benzoic acid with benzylamine in the presence of cyclohexyl isocyanide in boiling methanol afforded 87% of substituted 3,4-dihydro-1,4-benzothiazepin-5(2*H*)-one **26** [41] (Scheme 14).

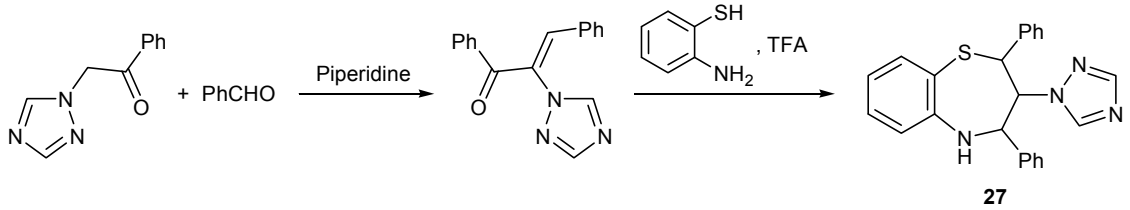
3.2. Synthesis of 2,3,4,5-Tetrahydro-1,5-benzothiazepines

The condensation of 1-phenyl-2-(1*H*-1,2,4-triazol-1-yl)ethanone with benzaldehyde in the presence of a catalytic amount of piperidine [42] provided an efficient method of synthesis of 2,3,4,5-tetrahydro-1,5-benzothiazepines. Initially formed substituted enone reacted with 2-aminobenzenethiol in the presence of CF_3COOH to give 2,3,4-substituted 2,3,4,5-tetrahydro-1,5-benzothiazepine **27** in 72% yield (Scheme 15).

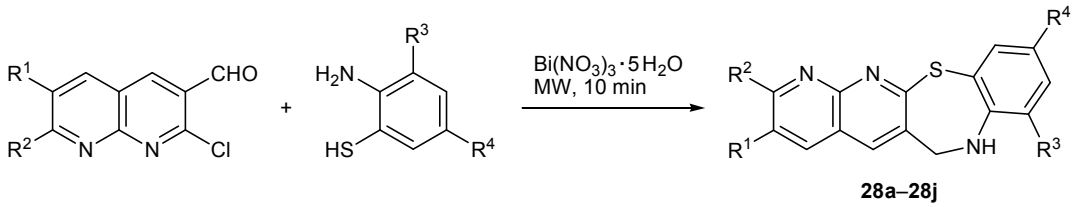
2,3,4,5-Tetrahydro-1,5-benzothiazepines can also be synthesized according to another approach. The microwave-assisted reaction of halogen-substituted aldehydes of the 1,8-naphthyridine series with 2-aminobenzenethiol derivatives catalyzed by crystalline $Bi(NO_3)_3 \cdot 5H_2O$ in 10 min afforded up to 80% of 5,6-dihydro[1,8]naphthyridino[2,3-*b*][1,5]benzothiazepines **28a**–**28j** (Scheme 16) [43]. Substituted 2-bromobenzenethiols smoothly reacted with 3-bromopropan-1-amine to produce 3-[(2-bromophenyl)sulfanyl]propan-1-amine which underwent LDA-promoted intramolecular cyclization to 2,3,4,5-tetrahydro-1,5-benzothiazepines **29a**–**29c** in 87–93% yield [8] (Scheme 17). Likewise, the reaction of 2-(bromomethyl)aziridines with 2-aminobenzenethiol gave intermediate 3-bromopropylsulfanyl derivatives, and intramolecular cyclization of the latter in the presence of potassium carbonate led to the formation of *N*-(2,3,4,5-tetrahydro-1,5-benzothiazepin-3-yl)sulfonamides **30a**–**30c** in up to 80% yield (Scheme 17) [44].

2,3-Dihydro-1,5-benzothiazepin-4(5*H*)-ones can be synthesized via heterocyclization involving oxirane ring opening. Diastereoselective reaction of 2-aminobenzenethiol with methyl oxirane-2-carboxylate under microwave irradiation resulted in the formation of *cis*- and *trans*-3-hydroxy-2-(4-methoxyphenyl)-2,3-dihy-

Scheme 15.

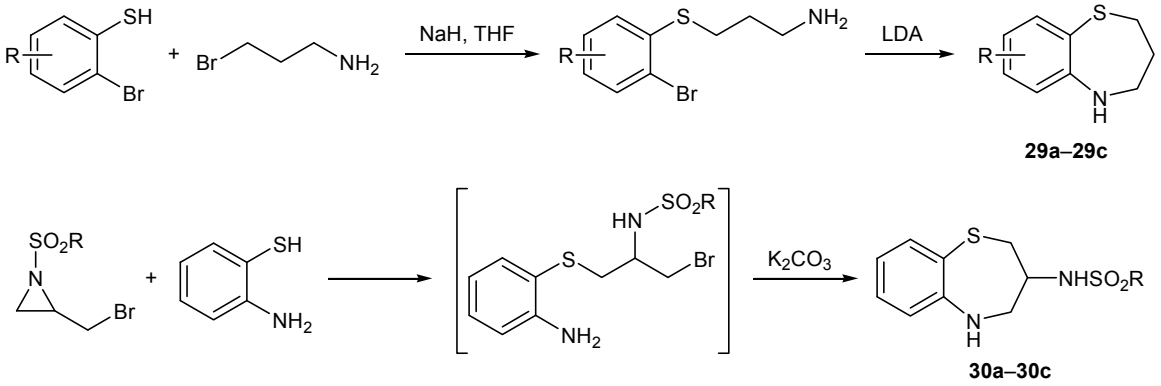


Scheme 16.



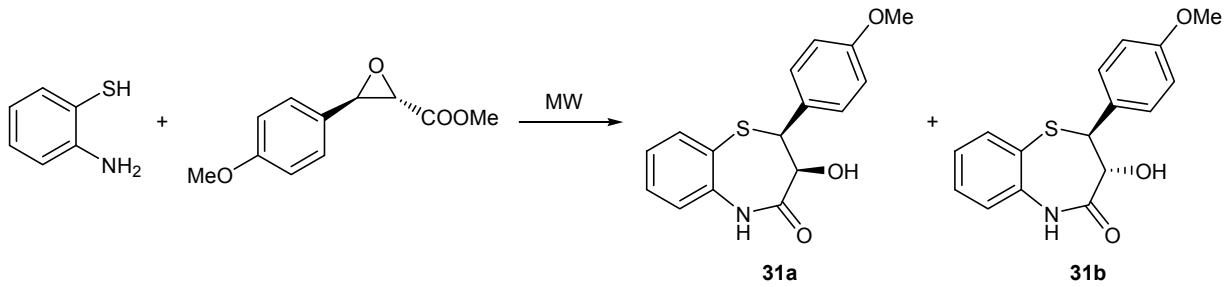
$R^1 = R^2 = R^3 = R^4 = H$ (**a**); $R^1 = Me$, $R^2 = R^3 = R^4 = H$ (**b**); $R^1 = MeO$, $R^2 = R^3 = R^4 = H$ (**c**); $R^1 = R^3 = R^4 = H$, $R^2 = Me$ (**d**); $R^1 = Cl$, $R^2 = R^3 = R^4 = H$ (**e**); $R^1 = R^2 = R^4 = H$, $R^3 = Me$ (**f**); $R^1 = R^2 = R^3 = H$, $R^4 = Me$ (**g**); $R^1 = R^3 = Me$, $R^2 = R^4 = H$ (**h**); $R^1 = R^2 = R^4 = H$, $R^3 = Cl$ (**i**); $R^1 = R^2 = R^3 = H$, $R^4 = Cl$ (**j**).

Scheme 17.

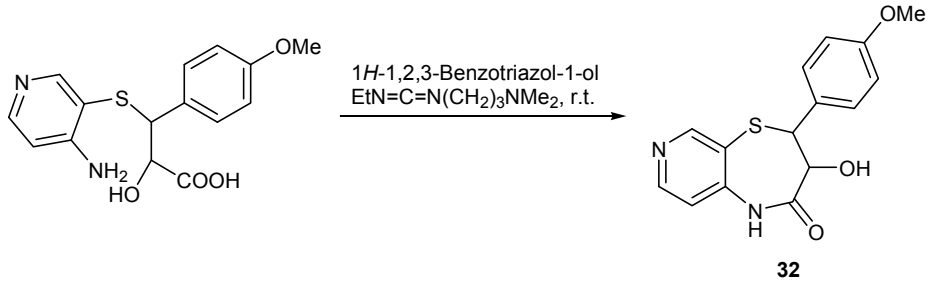


29, R = H (**a**), 4-Me (**b**), 5-MeO (**c**); **30**, R = Ph (**a**), 4-MeC_6H_4 (**b**), Me (**c**).

Scheme 18.



Scheme 19.

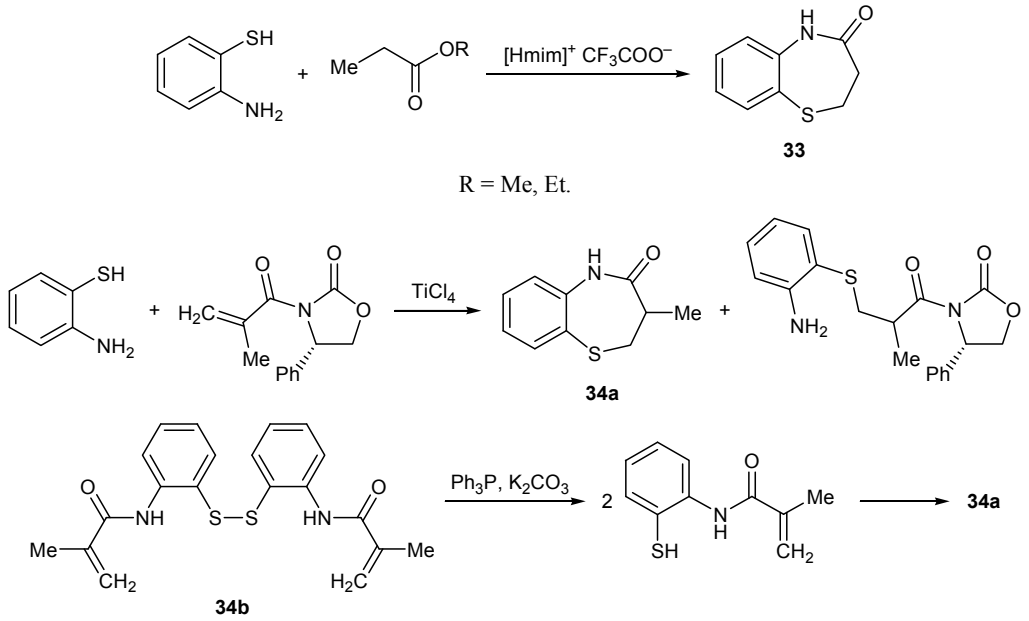


dro-1,5-benzothiazepin-4(5*H*)-ones **31a** and **31b**. The isomer ratio depended on the reaction time, solvent nature, and irradiation power. After 20 min at a power of 390 W, the *cis*/*trans* isomer ratio was 9:1 (overall yield 75%). Increase of the microwave irradiation power to 490 W for 10 min favored formation of the *trans* isomer [45, 46] (Scheme 18).

Intramolecular cyclization of 3-[(4-aminopyridin-3-yl)sulfanyl]-2-hydroxy-3-(4-methyoxyphenyl)propanoic acid in DMF at room temperature in the presence of *N*-ethyl-*N*′-(3-dimethylaminopropyl)carbodiimide and 1-hydroxybenzotriazole gave 26% of 3-hydroxy-4-(4-methoxyphenyl)-3,4-dihydropyrido-[3,4-*b*][1,4]thiazepin-2(1*H*)-one **32** which showed antihypertensive activity [47] (Scheme 19). In this reaction, carbodiimide activates the carboxy group which binds to the primary amino group, while 1-hydroxybenzotriazole acts as promoter accelerating the process.

2,3-Dihydro-1,5-benzothiazepin-4(5*H*)-one (**33**) was synthesized in up to 90% yield by reaction of 2-aminobenzenethiol with propanoic acid esters in the ionic liquid methylimidazolium trifluoroacetate [Hmim]-TFA [48, 49] (Scheme 20). Compound **33** was found to act as a potent NPY5 antagonist. Heterocyclization of 2-aminobenzenethiol with 3-metacryloyl-4-phenyloxazolidin-2-one catalyzed by $TiCl_4$ gave 56% of 3-methyl-2,3-dihydro-1,5-benzothiazepin-4(5*H*)-one (**34a**) as a potential vasodilator [50]. The same compound was also obtained in 40% yield by intramolecular cyclization of disulfide **34b** [51, 52] (Scheme 20).

Scheme 20.

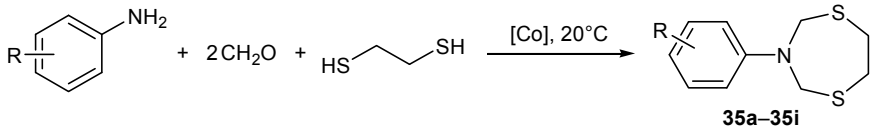


3.3. Synthesis of N-Substituted 1,5,3-Dithiazepanes

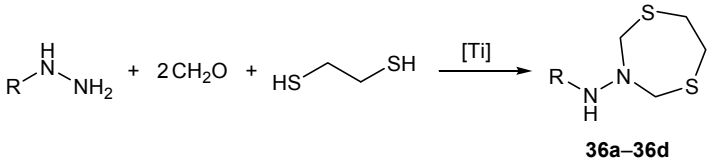
Three-component condensation of primary amines with formaldehyde and ethane-1,2-dithiol provides an efficient method of synthesis of N-substituted 1,5,3-dithiazepanes. Substituted anilines reacted with formaldehyde and ethane-1,2-dithiol at a molar ratio of 1:2:1 in the presence of cobalt catalyst at 20°C to give *N*-aryl-1,5,3-dithiazepanes **35a**–**35i** in 59–88% yield [53] (Scheme 21). Cyclocondensation of aryl(or benzyl)hydrazines with formaldehyde and ethane-1,2-dithiol catalyzed by Cp_2TiCl_2 afforded 60–77% of *N*-aryl(benzyl)-1,5,3-dithiazepan-3-amines **36a**–**36d** [54]. *N*-(1,5,3-Dithiazepan-3-yl) carboxamides **37a**–**37d** were obtained in up to 75% yield by $CuCl_2$-catalyzed reaction of carbohydrazides with formaldehyde and ethane-1,2-dithiol [55] (Scheme 21).

In this condensation, formaldehyde can be replaced by another methylating agent, e.g., *N*,*N*,*N*′,*N*′-tetramethylmethanediamine. 3-Hetaryl-1,5,3-dithiazepanes

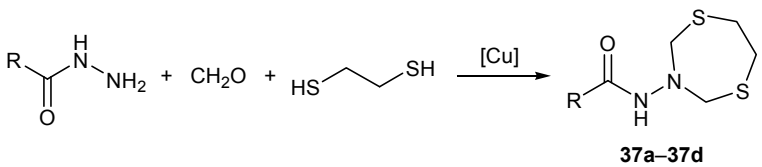
Scheme 21.



R = H (**a**), 3-Me (**b**), 4-Me (**c**), 2-Me (**d**), 3-OCH (**e**), 4-MeO (**f**), 2-O_2N (**g**), 3-O_2N (**h**), 4-ON (**i**).

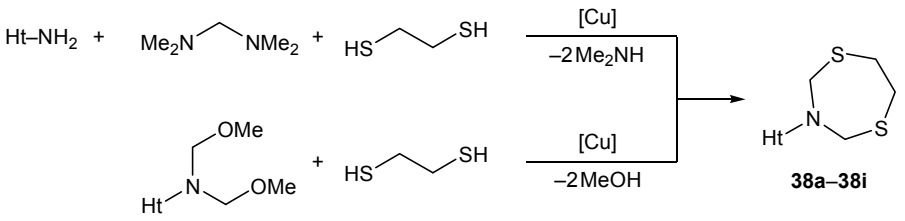


R = 4-$O_2NC_6H_4$ (**a**), 2,4-$(O_2N)_2C_6H_3$ (**b**), 4-MeC_6H_4 (**c**), $PhCH_2$ (**d**).



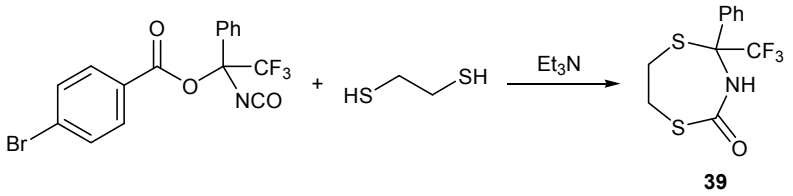
R = pyridin-4-yl (**a**), pyridin-3-yl (**b**), 2-$MeOC_6H_4$ (**c**), 4-$MeOC_6H_4$ (**d**).

Scheme 22.

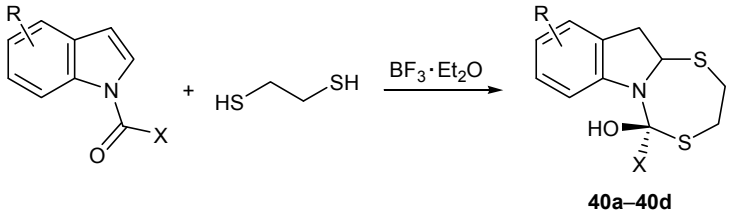


Ht = 5-methyl-1,2-oxazol-3-yl (**a**), 5-nitro-1,3-thiazol-2-yl (**b**), pyridin-3-yl (**c**), pyridin-2-yl (**d**), 5-bromopyridin-2-yl (**e**), 5-methylpyridin-2-yl (**f**), (pyridin-4-yl)methyl (**g**), 5-nitro-1,3-benzothiazol-2-yl (**h**), 2-(1*H*-indol-3-yl)ethyl (**i**).

Scheme 23.

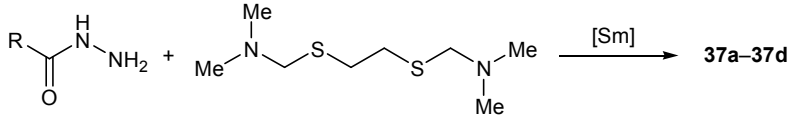


Scheme 24.



40, R = H (**a**), 9-O_2N (**b**), 9-MeO (**c**), 10-F (**d**); X = H, Me, $AcNHCH_2$, Ph.

Scheme 25.



R = pyridin-4-yl (**a**), pyridin-3-yl (**b**), 2-$MeOC_6H_4$ (**c**), 4-$MeOC_6H_4$ (**d**).

38a–**38i** were synthesized with high selectivity (yield 64–87%) by heterocyclization of primary heteroaromatic amines with *N*,*N*,*N*′,*N*′-tetramethylmethanediamine and ethane-1,2-dithiol in the presence of copper-based catalyst (Scheme 22) [56]. Alternatively, *N*-substituted 1,5,3-dithiazepanes **38a**–**38i** were obtained in 68–89% yield by $CuCl_2$-catalyzed two-component reaction of *N*,*N*-bis(methoxymethyl)hetarenamines with ethane-1,2-dithiol. No compounds **38** were formed in the absence of a catalyst [56].

2,2,2-Trifluoro-1-isocyanato-1-phenylethyl 4-bromobenzoate reacted with ethane-1,2-dithiol in the presence of triethylamine [57] to give 72% of 1,5,3-dithiazepan-4-one **39** (Scheme 23). The reaction involves two reaction centers of the initial isocyanate (nucleophilic substitution of the benzoate fragment on the quaternary carbon atom by one thiol group and addition of the second SH group to the N=C bond of the isocyanato group).

The reaction of *N*-acylindoles with ethane-1,2-dithiol in the presence of $BF_3 \cdot Et_2O$ as catalyst produced substituted 3,5,11,11a-tetrahydro-2*H*-1,5,3-dithiazepino[3,2-*a*]indol-5-ols **40a**–**40d** (yield 45–50%; Scheme 24) [58]. *N*-(1,5,3-Dithiazepan-3-yl) amides **37a**–**37d** were also synthesized in 73–78% yield by $SmCl_3 \cdot 6H_2O$-catalyzed thiomethylation of carboxylic acid hydrazides with *N*,*N*,*N*′,*N*′-tetramethyl-2,5-dithiahexane-1,6-diamine [55] (Scheme 25).

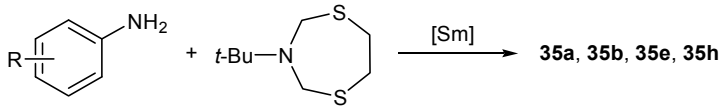
The possibility of efficient transamination of *N*-*tert*-butyl-1,5,3-dithiazepane with aniline and its *meta*-substituted derivatives in the presence of a lanthanide catalyst with selective formation of *N*-aryl-1,5,3-di-

thiazepanes **35a**, **35b**, **35e**, and **35h** (yield 64–78%) was shown in [53] (Scheme 26). Primary aromatic amines reacted with an equimolar amount of *N*-*tert*-butyl-1,5,3-dithiazepane or 1,3,6-oxadithiepane [59] under catalysis by 5 mol % of $Sm(NO_3)_3 \cdot 6H_2O$ to give 57–76% of *N*-aryl-1,5,3-dithiazepanes **41a**–**41f**. Compounds **41a**–**41f** showed fungicidal activity against some microscopic phytopathogenic fungi (*Bipolaris sorokiniana* and *Rhizoctonia solani*) [37].

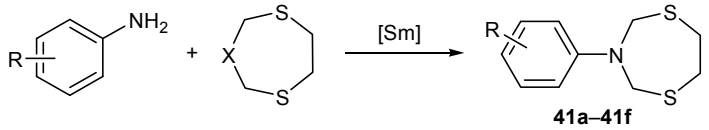
Transamination of *N*-*tert*-butyl-1,5,3-dithiazepane or recyclization of 1,3,6-oxadithiepane with carboxylic acid hydrazides in the presence of lanthanide catalysts (YbF_3, $SmCl_3 \cdot 6H_2O$) is an efficient method of synthesis of *N*-substituted 1,5,3-dithiazepanes **37a**–**37d** (yield 70–80%) [60] (Scheme 27). Samarium-catalyzed recyclization of 1,3,6-oxadithiepane with quinolinamines [61] afforded 80–95% of 1,5,3-dithiazepan-3-ylquinolines **42a**–**42e**. 5-(1,5,3-Dithiazepan-3-yl)-quinoline showed fungicidal activity against *Rhizoctonia solani*. Likewise, bis-1,5,3-dithiazepanes **43a**–**43c** were selectively obtained by recyclization of 1,3,6-oxadithiepane with aromatic diamines (*o*- and *p*-phenylenediamines and 3,4-diaminobenzoic acid) at a ratio of 2 : 1 in the presence of 5 mol % of $Sm(NO_3)_3 \cdot 6H_2O$ [59, 62] (Scheme 27).

Samarium-catalyzed recyclization of 1,3,6-oxadithiepane with biphenyldiamines led to selective formation of bis-1,5,3-dithiazepanes **44a**–**44c** and **45** in 60–67% yield [62]. Tetrakis-1,5,3-dithiazepane **46** was synthesized by the reaction of 1,1′-biphenyl-3,3′,4,4′-tetramine with 1,3,6-oxadithiepane catalyzed by 10 wt % of amorphous micro/mesoporous alumino-

Scheme 26.

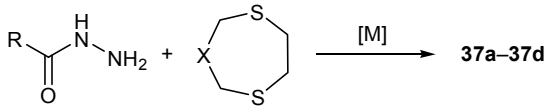


R = H (**a**), 3-Me (**b**), 3-OCH (**e**), 3-O_2N (**h**).

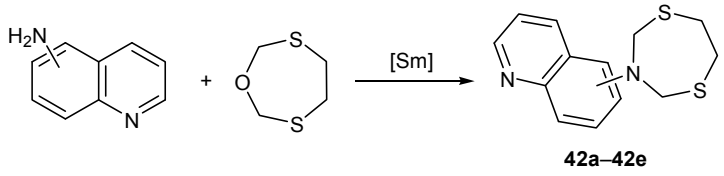


R = 2-OH (**a**), 4-OH (**b**), 3-HOC(O) (**c**), 4-HOC(O) (**d**), 4-SH (**e**); R = 4-HO-5-HOC(O) (**f**); X = *t*-BuN, O.

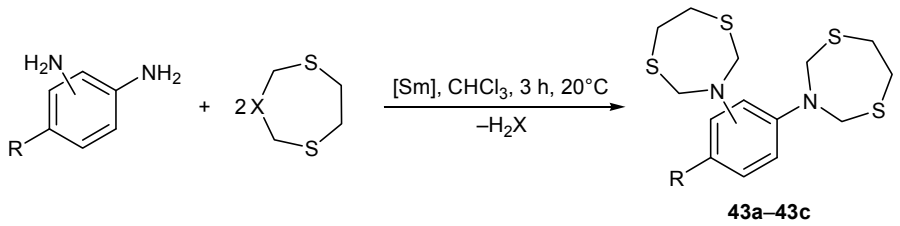
Scheme 27.



R = pyridin-4-yl (**a**), pyridin-3-yl (**b**), 2-$MeOC_6H_4$ (**c**), 4-$MeOC_6H_4$ (**d**); X = *t*-BuN, O; [M] = YbF_3, $SmCl_3 \cdot 6H_2O$.

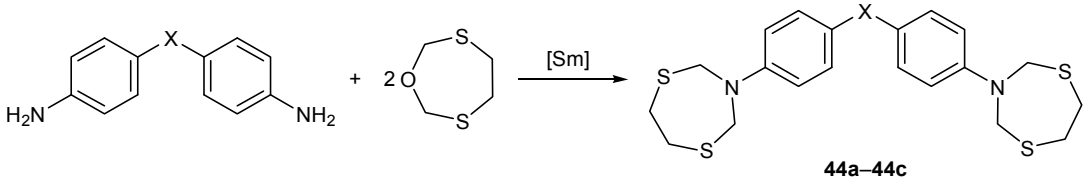


2-NH_2, 3-NH_2, 5-NH_2, 6-NH_2, 8-NH_2.

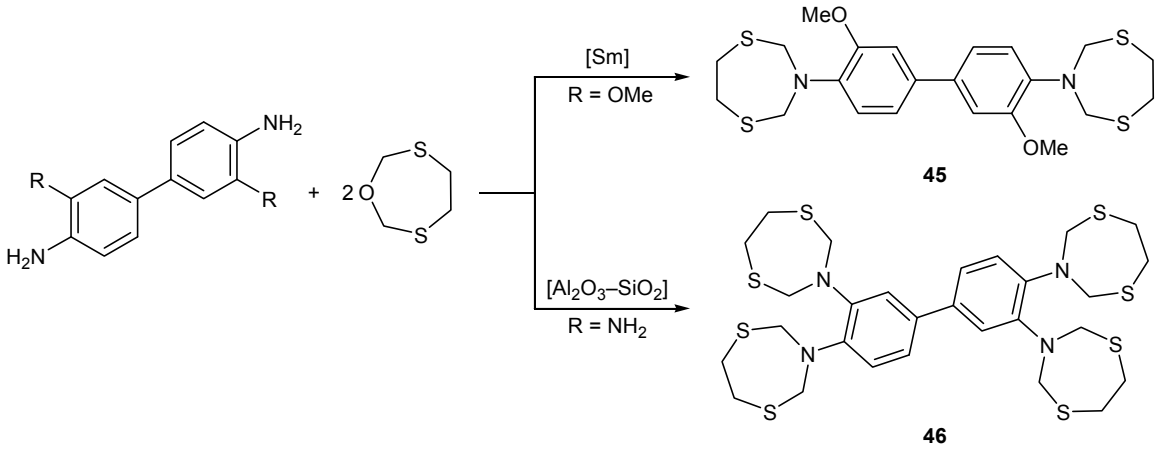


R = H, COOH; X = *t*-BuN, O.

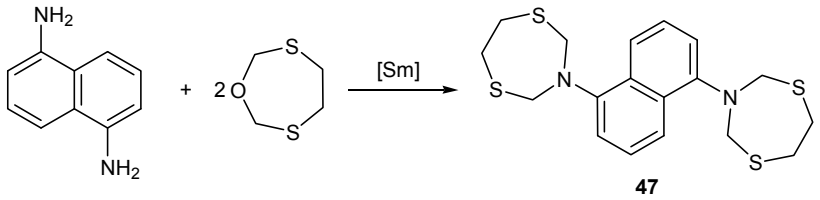
Scheme 28.



X = CH_2 (**a**), O (**b**), SO_2 (**c**).



Scheme 29.



silicate (Scheme 28). Catalytic recyclization of 1,3,6-oxadithiepane with naphthalene-1,5-diamine [62] selectively afforded *N*,*N*′-(naphthalene-1,5-diyl)di-(1,5,3-dithiazepane) (**47**) (Scheme 29).

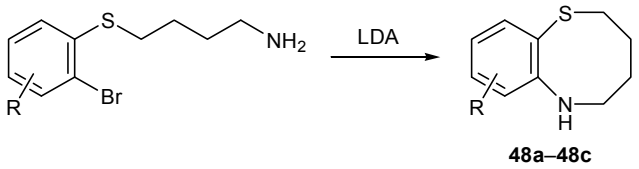
4. CATALYSIS IN THE SYNTHESIS OF EIGHT-MEMBERED S,N-HETEROCYCLES

4.1. Synthesis of Benzothiazocin(on)es

Benzothiazocines can be synthesized by LDA-catalyzed intramolecular cyclization of 4-(2-bromophenylsulfanyl)butan-1-amines prepared by reaction of substituted 2-bromobenzenethiols with 4-bromobutan-1-amine. 3,4,5,6-Tetrahydro-2*H*-1,6-benzothiazocines **48a**–**48c** were thus obtained in up to 90% yield [8] (Scheme 30). Intramolecular cyclization of 3-{[(2-amino-5-chlorophenyl)(2-chlorophenyl)methyl]sulfanyl}propanoic acid in the presence of ethyl(diisopropyl)amine, 4-dimethylaminopyridine, and *N*-ethyl-*N*′-(3-dimethylaminopropyl)carbodiimide afforded 98% of 8-chloro-6-(2-chlorophenyl)-1,3,4,6-tetrahydro-2*H*-5,1-benzothiazocin-2-one (**49**) [39]. Analogous transformation of methyl 2-{[2-(2-amino-5-chlorophenyl)-2-(2-halophenyl)ethyl]sulfanyl}acetates was catalyzed by hexa(methyllithium) in THF at –78°C to produce 8-chloro-6-(2-halophenyl)-5,6-dihydro-1*H*-4,1-benzothiazocin-2(3*H*)-ones **50** in 82–90% yield [39] (Scheme 31).

Palladium compounds in the presence of ethyl(diisopropyl)amine and carbon monoxide efficiently catalyzed heterocyclization/intramolecular carbonylation of 2-(2-iodobenzylsulfanyl)anilines with the formation of 5*H*-dibenzo[*b*,*g*][1,4]thiazocin-6(7*H*)-ones **51a**–**51c** (yield 92–97%) [63] (Scheme 32). *N*-Acetyl derivative of 8-bromonaphthalen-1-amine reacted with thiosalicylic acid in the presence of copper catalyst to give 2-(8-acetamidonaphthalen-1-ylsulfanyl)benzoic acid which underwent selective intramolecular cyclization

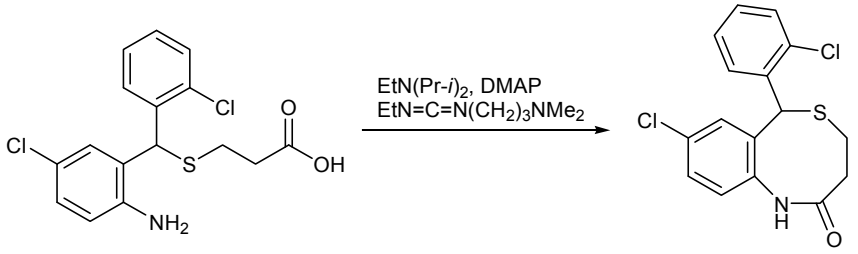
Scheme 30.



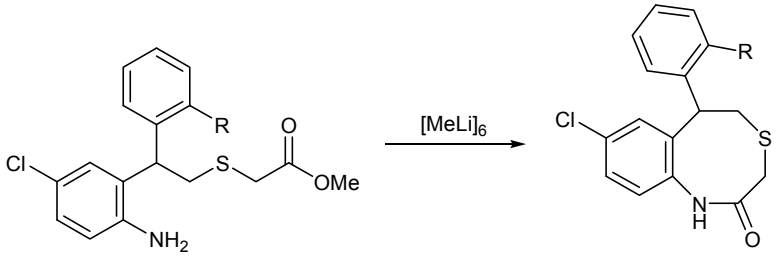
48a–48c

R = H (**a**), 2-Me (**b**), 2-MeO (**c**).

Scheme 31.



49



50

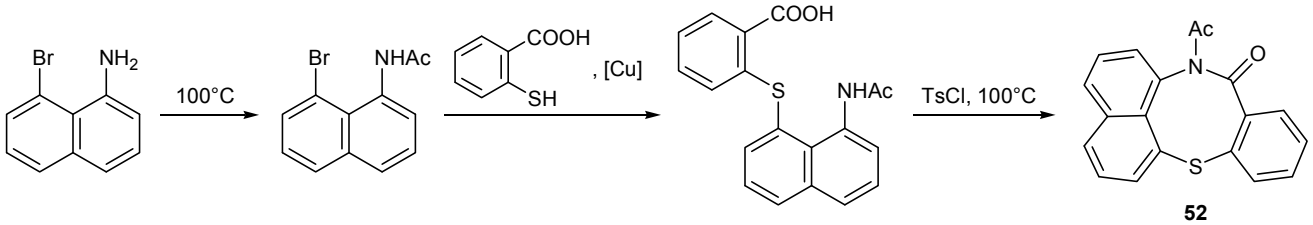
R = Cl, F.

Scheme 32.

51a–51c

R = H (**a**), Cl (**b**), CF_3 (**c**).

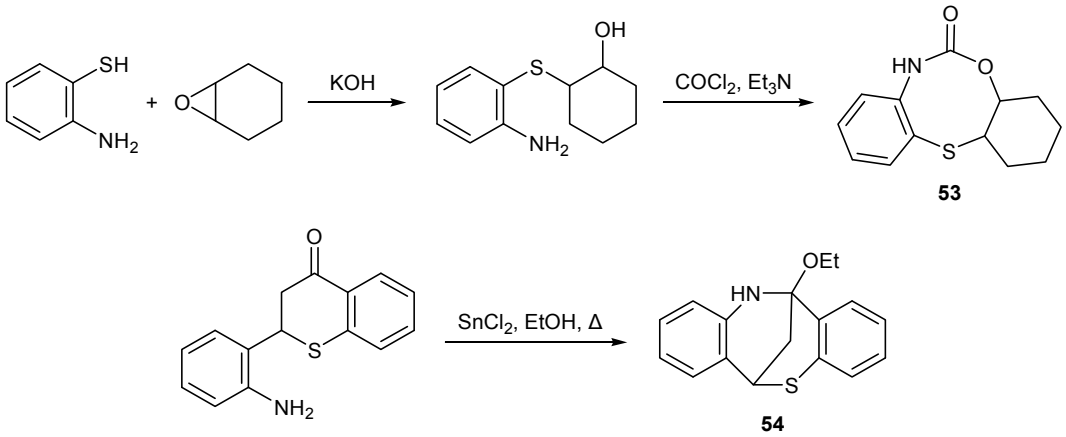
Scheme 33.



52

to fused tetracyclic 1,5-thiazocin-4-one derivative **52** in 98% yield [64] (Scheme 33). Opening of the oxirane ring in epoxycyclohexane by the action of 2-aminobenzenethiol led to the formation of 2-(2-aminophenylsulfanyl)cyclohexan-1-ol which was subjected to cyclization with phosgene in the presence of triethylamine to obtain 1,2,3,4,4a,12a-hexahydrodibenzo[*b*,*g*][1,6,3]oxathiazocin-6(7*H*)-one (**53**) [65] (Scheme 34).

Scheme 34.



The heterocyclization of 2-(2-aminophenyl)-2,3-dihydro-4*H*-1-benzothiopyran-4-one in boiling ethanol in the presence of $SnCl_2$ [66] provided a convenient method of synthesis of 6,12-methano-11,12-dihydro-6*H*-dibenzo[*b*,*f*][1,5]thiazocine derivative **54** in almost quantitative yield (99%; Scheme 34).

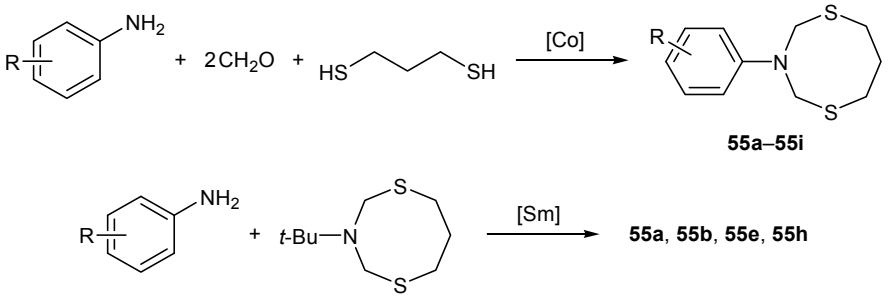
4.2. Synthesis of N-Substituted 1,5,3-Dithiazocanes

An efficient method for the synthesis of N-substituted 1,5,3-dithiazocanes is based on the three-component condensation of primary amines with a methylating agent (formaldehyde, *N*,*N*,*N*′,*N*′-tetramethylmethanediamine) and propane-1,3-dithiol. The cyclocondensation of aniline and its substituted derivatives with formaldehyde and propane-1,3-dithiol catalyzed by $Co(acac)_2$ resulted in the selective formation of *N*-aryl-1,5,3-dithiazocanes **55a**–**55i** in 69–95% yield [53]. *N*-Aryl-1,5,3-dithiazocanes **55a**, **55b**, **55e**, and **55h** were also synthesized by transamination of *N*-*tert*-butyl-1,5,3-dithiazocane with anilines in the presence of a samarium catalyst [53] (Scheme 35).

1,5,3-Dithiazocan-3-amines **56a**–**56e** were obtained in 49–87% yield by Cp_2TiCl_2-catalyzed cyclocondensation of aryl(benzyl)hydrazines with formaldehyde and propane-1,3-dithiol [54]. 1,5,3-Dithiazocanes **57a**–**57d** with an acylamino group on the nitrogen were synthesized by three-component reaction of carboxylic acid hydrazides with formaldehyde and propane-1,3-dithiol in the presence of a catalytic amount of $CuCl_2$ [55] (Scheme 36). Apart from the three-component condensation, compounds **57a**–**57d** were formed in the reaction of arene(hetarene)carboxylic acid hydrazides with *N*,*N*,*N*′,*N*′-tetramethyl-2,6-dithiaheptane-1,7-diamine as thiomethylating agent under catalysis by samarium(III) chloride hexahydrate [55]. Likewise, the catalytic cyclothiomethylation of arylhydrazines with the same dithia diamine afforded 79–85% of *N*-aryl-1,5,3-dithiazocan-3-amines **56a**–**56e** [54] (Scheme 36).

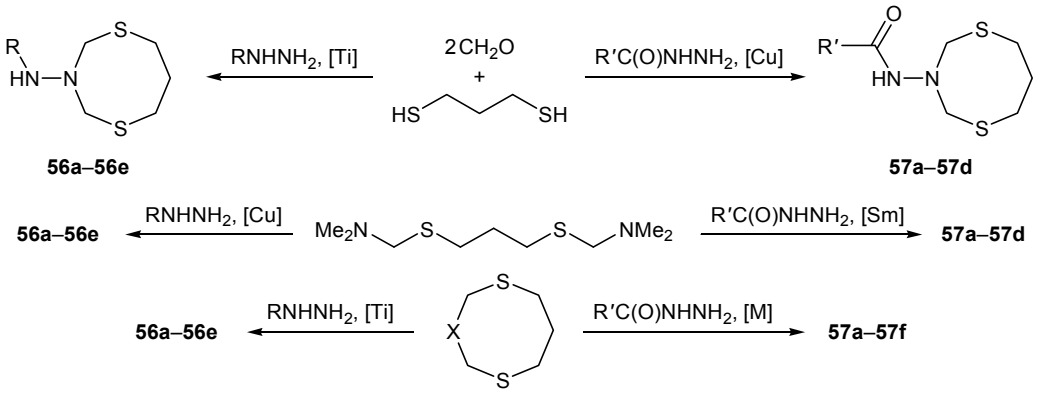
3-Hetaryl-1,5,3-dithiazocanes **58a**–**58i** were selectively synthesized under mild conditions by copper-catalyzed heterocyclization of hetarenamines with *N*,*N*,*N*′,*N*′-tetramethylmethanediamine and propane-1,3-dithiol [56]. *N*,*N*-Bis(methoxymethyl)hetarenamines are also capable of reacting with propane-1,3-dithiol in the presence of $CuCl_2$ to form compounds **58a**–**58i** with high selectivity (Scheme 37). Recycliza-

Scheme 35.



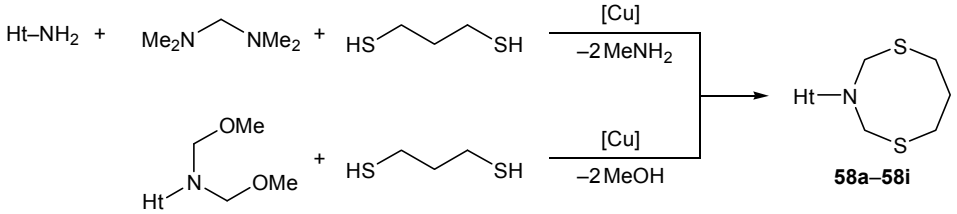
R = H (**a**), 3-Me (**b**), 4-Me (**c**), 2-Me (**d**), 3-MeO (**e**), 4-MeO (**f**), 2-O_2N (**g**), 3-O_2N (**h**), 4-ON (**i**).

Scheme 36.



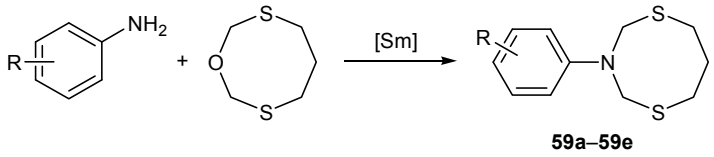
56, R = 4-$O_2NC_6H_4$ (**a**), 2,4-$(ON_2)_2C_6H_3$ (**b**), 4-MeC_6H_4 (**c**), $PhCH_2$ (**d**), Ph (**e**); **57**, R′ = pyridin-4-yl (**a**), pyridin-3-yl (**b**), 2-$MeOC_6H_4$ (**c**), 3-$MeOC_6H_4$ (**d**), MeO (**e**), *t*-BuO (**f**); X = *t*-BuN, O; [M] = YbF_3, $SmCl_3 \cdot 6H_2O$.

Scheme 37.

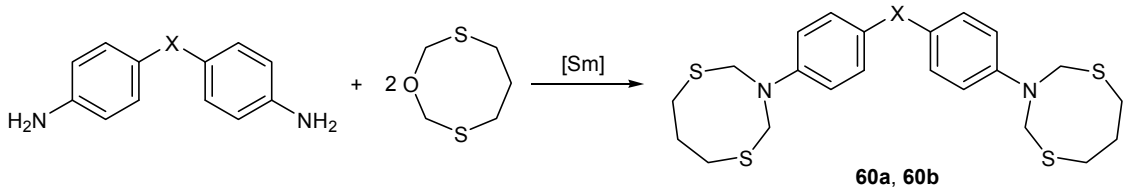


Ht = 5-methyl-1,2-oxazol-3-yl (**a**), 5-nitro-1,3-thiazol-2-yl (**b**), pyridin-3-yl (**c**), pyridin-2-yl (**d**), 5-bromopyridin-2-yl (**e**), 5-methylpyridin-2-yl (**f**), (pyridin-4-yl)methyl (**g**), 5-nitro-1,3-benzothiazol-2-yl (**h**), 2-(1*H*-indol-3-yl)ethyl (**i**).

Scheme 38.



R = 2-HO (**a**), 4-HO (**b**), 4-HS (**c**), 3-HOC(O) (**d**), 4-HOC(O) (**e**).



X = CH_2 (**a**), SO_2 (**b**).

tion of 1,3,7-oxadithiocane with aromatic amines in the presence of samarium catalyst gave 61–83% of *N*-aryl-substituted dithiazocanes **59a**–**59e** [59]. Samarium nitrate-catalyzed recyclization of 1,3,7-oxadithiocane with biphenyldiamines was reported [37, 59] as an efficient method of selective synthesis of bis-1,5,3-dithiazocanes **60a** and **60b** (Scheme 38). The potential of transamination and recyclization in the synthesis of dithiazocanes was demonstrated by reactions of aryl(benzyl)hydrazines with *N*-*tert*-butyl-1,5,3-dithiazocane catalyzed by Cp_2TiCl_2, which selectively produced 1,5,3-dithiazocan-3-amines **56a**–**56e** in 68–80% yield [67], as well as by lanthanide-catalyzed reactions of *N*-*tert*-butyl-1,5,3-dithiazocane and 1,3,7-oxadithiocane with carboxylic acid hydrazides, which quantitatively afforded N-substituted 1,5,3-dithiazocanes **57a**–**57f** [60] (Scheme 36).

5. CATALYSIS IN THE SYNTHESIS OF ARYL-SUBSTITUTED MACROHETEROCYCLES

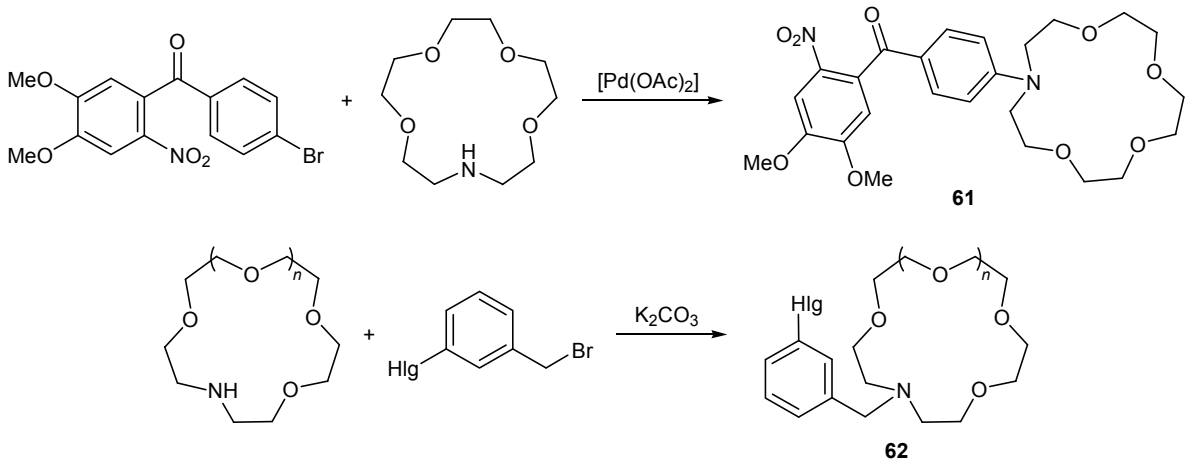
Macroheterocycles including benzene rings possess a rigid skeleton, which is important for the complexation with metal ions and organic molecules. Macroheterocycles are promising candidates as selective ligands for the extraction and separation of metal cations [68–70]; they are used to transport ions through membranes [71], in photosensitive systems [72], and as phase-transfer catalysts simulating enzymatic activity [73].

5.1. Synthesis of O,N-Macroheterocycles

As a rule, O,N-macroheterocycles are synthesized by reaction of a cyclic secondary amine with a halogen derivative in the presence of a catalyst. Aryl-substituted aza crown ether **61** was obtained by $Pd(OAc)_2$-catalyzed reaction of aryl bromide with aza-15-crown-5 [74]. Aza crowns **62** were synthesized in 92–96% yield in the presence of potassium carbonate [75] (Scheme 39).

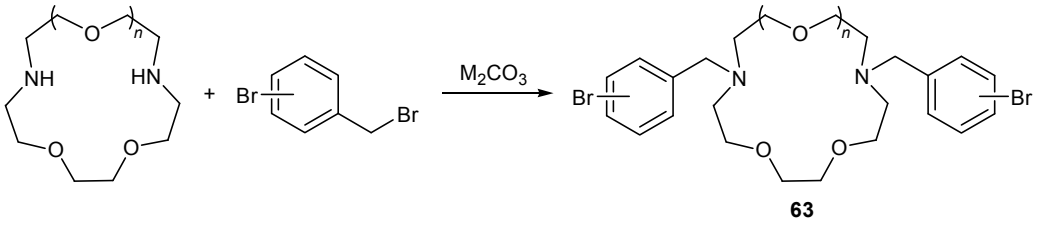
N,*N*′-Diaryl diaza crown ethers **63** were formed in 89–95% yield in the reactions of macrocyclic secon-

Scheme 39.

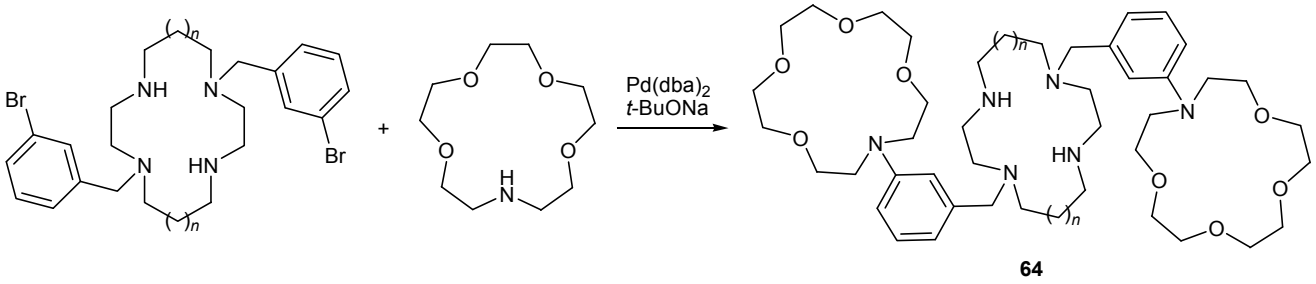


Hlg = Br, I; *n* = 1, 2.

Scheme 40.

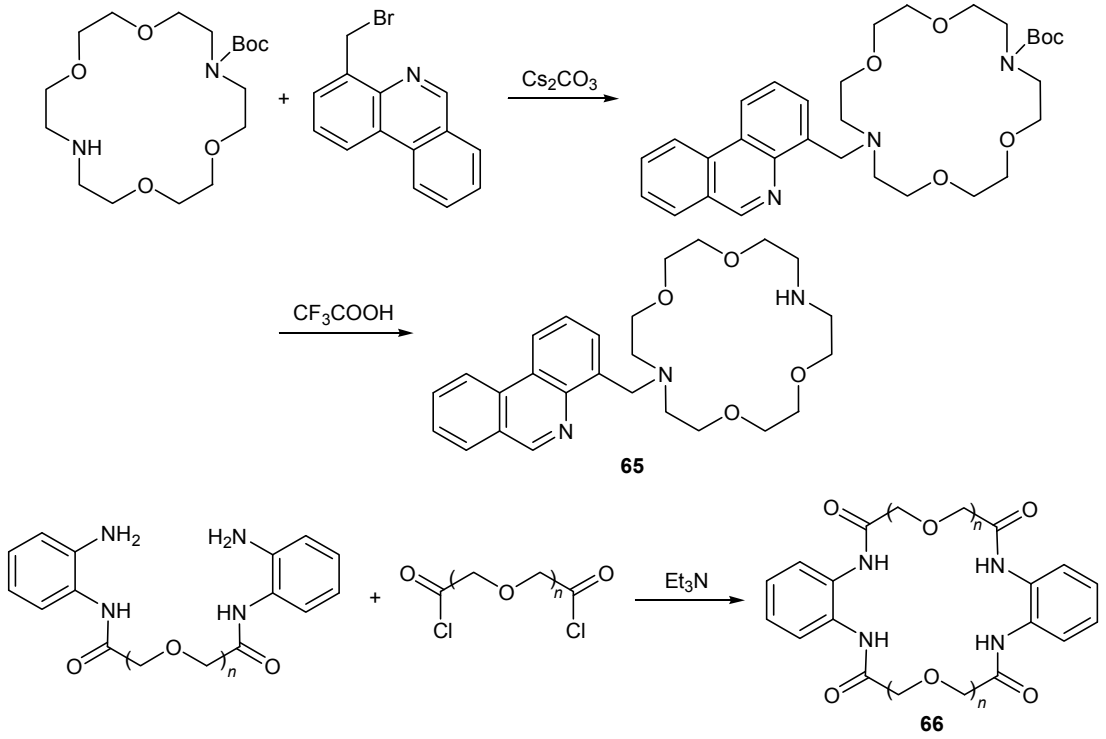


M = K, Na; *n* = 1, 2.



n = 0, 1.

Scheme 41.



n = 1, 2.

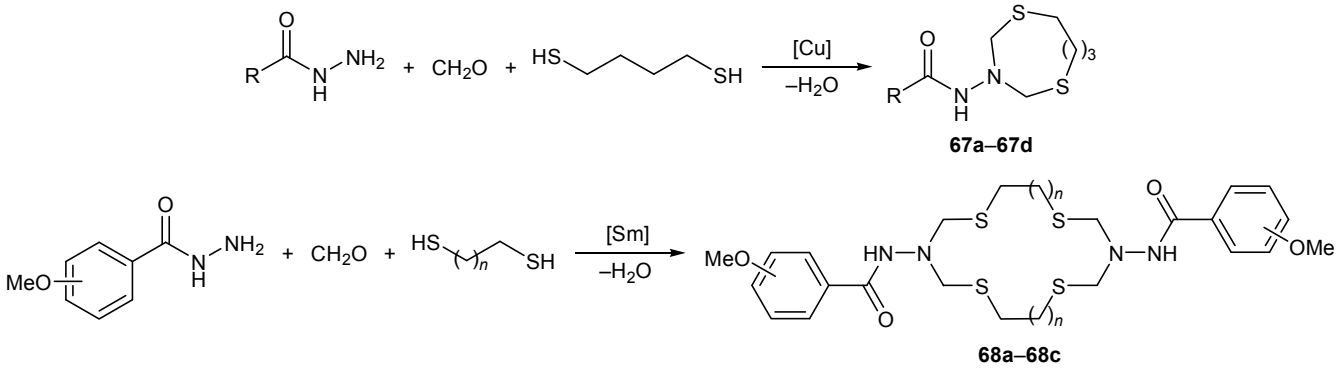
dary diamines with *m*- and *p*-bromobenzyl bromides using alkali metal carbonates as a base [76]. This approach proved to be efficient in the synthesis of macrotricyclic compounds **64** by $Pd(dba)_2$-catalyzed reaction of disubstituted cyclen and cyclam with aza crown ether [77] (Scheme 40).

4-(Bromomethyl)phenanthridine reacted with crown ether in the presence of Cs_2CO_3 to give a macrocyclic compound, and the subsequent removal of the protecting group from the nitrogen atom afforded 83% of tetraoxadiazacyclooctadecane **65** [78]. Macrocyclic dibenzotetraazalactams **66** were obtained in 63–72% yield by reaction of aromatic diamines with oxaalkanedioyl dichlorides in the presence of triethylamine (Scheme 41) [79].

5.2. Synthesis of S,N-Macroheterocycles

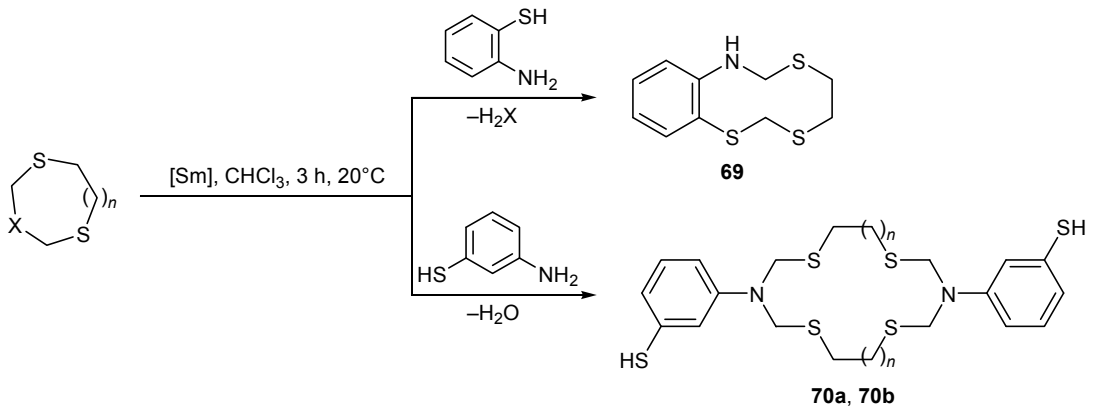
A classical method of synthesis of S,N-macrocycles is based on the three-component condensation of amines with formaldehyde and alkane-α,ω-dithiols. The reaction of carboxylic acid hydrazides with formaldehyde and butane-1,4-dithiol in the presence of

Scheme 42.



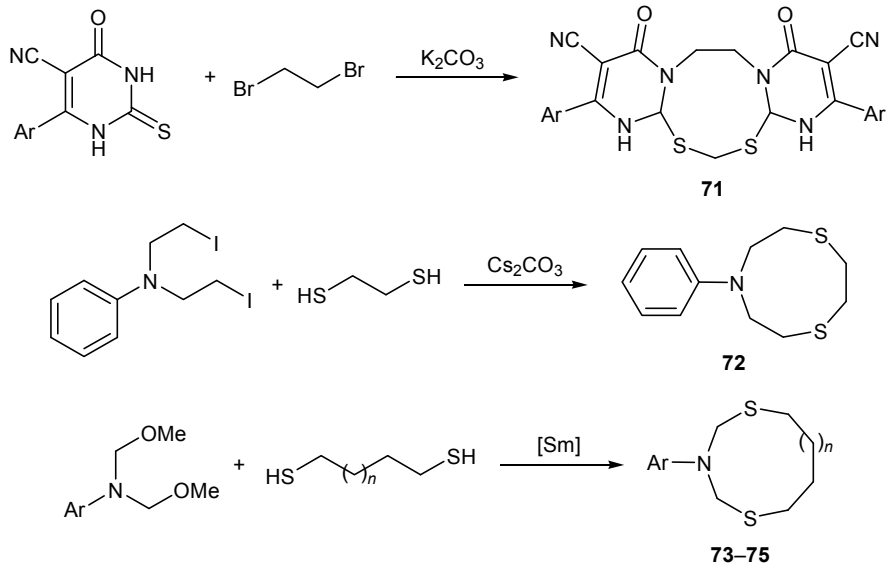
67, R = pyridin-4-yl (**a**), pyridin-3-yl (**b**), 2-$MeOC_6H_4$ (**c**), 3-$MeOC_6H_4$ (**d**); [Cu] = $CuCl_2 \cdot 2H_2O$; **68**, n = 3–5.

Scheme 43.



X = *t*-BuN, O; *n* = 1 (**a**), 2 (**b**).

Scheme 44.

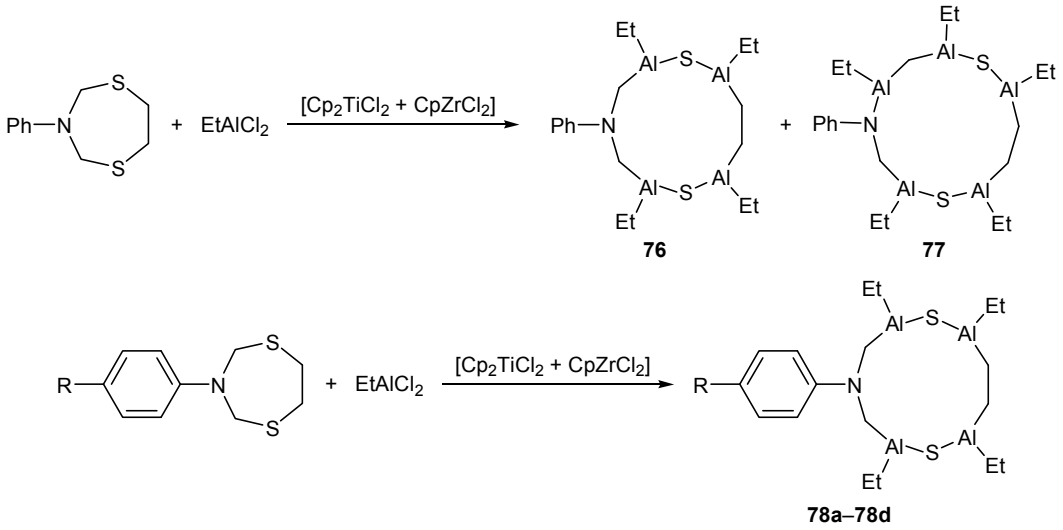


Ar = Ph (**a**), 3-MeC$_6$H$_4$ (**b**), 4-MeC$_6$H$_4$ (**c**), 2-MeOC$_6$H$_4$ (**d**), 3-MeOC$_6$H$_4$ (**e**), 2-ClC$_6$H$_4$ (**f**), 3-ClC$_6$H$_4$ (**g**), 4-ClC$_6$H$_4$ (**h**), 3-BrC$_6$H$_4$ (**i**), 4-BrC$_6$H$_4$ (**j**), 3-FC$_6$H$_4$ (**k**), 4-FC$_6$H$_4$ (**l**).

$CuCl_2 \cdot 2H_2O$ [80] gave the corresponding *N*-(1,5,3-dithiazonan-3-yl) amides **67a**–**67d**. Macroheterocycles **68a**–**68c** were synthesized by analogous samarium-catalyzed cyclothiomethylation of methoxybenzohydrazides with formaldehyde and pentane-1,5- and hexane-1,6-dithiols [80] (Scheme 42).

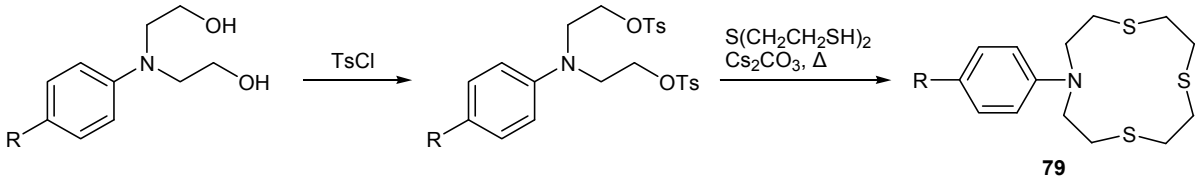
The two-component reaction of 2-aminobenzenethiol with *N*-*tert*-butyl-1,5,3-dithiazepane or 1,3,6-oxadithiepane [59] in the presence of 5 mol % of $Sm(NO_3)_3 \cdot 6H_2O$ led to the formation of 1,3,6,8-benzotrithiazecine **69**. Under analogous conditions, 3-aminobenzenethiol reacted with 1-oxa-3,6(7)-dithiacycloalkanes [81] to give 51–65% of 3,3′-[tetrathiadiazacyclotetra(hexa)decane-1,10-diyl]bis(benzenethiols) **70a** and **70b** (Scheme 43). Nine-membered S,N-pyrimidinaphanes **71** were synthesized by reaction of 6-aryl-4-oxo-2-sulfanyl-1,2,3,4-tetrahydropyrimidine-5-carbonitriles with 1,2-dibromoethane [82] in the presence of K_2CO_3. Heterocyclization of *N*,*N*-bis(2-iodoethyl)aniline with ethane-1,2-dithiol catalyzed by cesium carbonate gave 4-phenyl-1,4,7-dithiazonane (**72**) [83, 84] (Scheme 44). Pure 3-aryl-1,5-dithia-3-azacycloalkanes **73**–**75** were prepared by $Sm(NO_3)_3$/γ-Al_2O_3-catalyzed condensation of alkane-α,ω-dithiols with *N*,*N*-bis(methoxymethyl)anilines. Cycloaminomethylation of butane-1,4-dithiol afforded 84–92% of 3-aryl-1,5,3-dithiazonanes **73**, and 3-aryl-1,5,3-dithiazecanes **74** and 3-aryl-1,5,3-ditiazacycloundecanes **75**

Scheme 45.



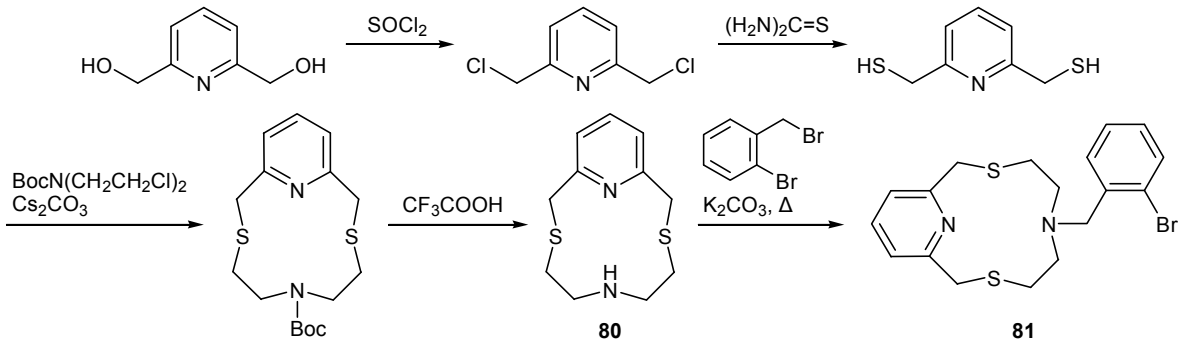
R = Me (**a**), MeO (**b**), Cl (**c**), Br (**d**).

Scheme 46.



R = O_2N, $H_2NC(O)$.

Scheme 47.



were obtained from pentane-1,5-dithiol and hexane-1,6-dithiol, respectively (yield 75–92%) [85].

Metallocene dichloride-based catalysts Cp_2MCl_2 made it possible to synthesize Al,S,N-macroheterocycles via reaction of $EtAlCl_2$ with 3-phenyl-1,5,3-dithiazepane. The reaction of 3-phenyl-1,5,3-dithiazepane with $EtAlCl_2$ in the presence of Mg–Cp_2TiCl_2–Cp_2ZrCl_2 (molar ratio 1:5:5:0.05:0.05) led to the formation of a mixture of tetraaluminadithiazacycloundecane **76** and pentaaluminadithiazacyclododecane **77** with an overall yield of ~80% [86]. *para*-Substituted 3-aryl-1,5,3-dithiazepanes reacted with $EtAlCl_2$ to give pure tetraaluminadithiazacycloundecanes **78a**–**78d** in 73–88% yield [86] (Scheme 45).

An efficient method of synthesis of S,N-macrocycles is heterocyclization of ditosyl derivatives with alkane-α,ω-dithiols. Trithiazacyclododecanes **79** were synthesized in quantitative yield by reaction of bis-*p*-toluenesulfonate with 2,2′-sulfanediyldiethanethiol catalyzed by Cs_2CO_3 [87] at 70°C (Scheme 46).

Heterocyclization of α,ω-dithiols with α,ω-dihaloalkanes provides an equally efficient synthetic route to

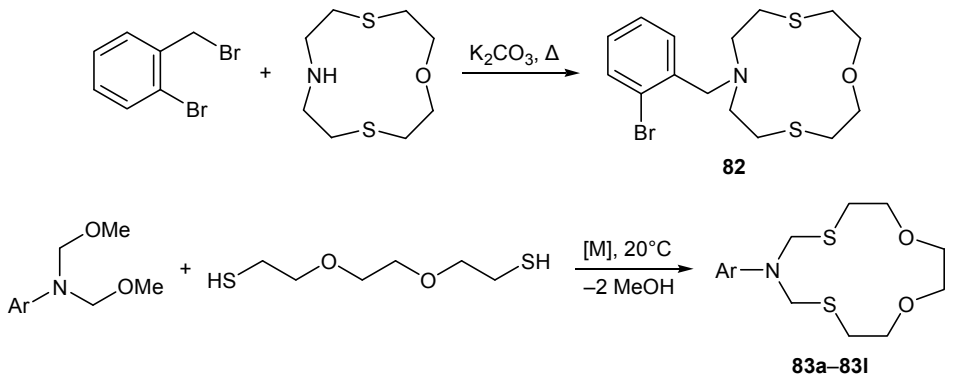
S,N-macroheterocycles. For instance, (pyridine-2,6-diyl)di(methanethiol) synthesized by successive treatment of pyridine-2,6-diyldimethanol with thionyl chloride and thiourea reacted with Boc-protected bis(2-chloroethyl)amine in the presence of cesium carbonate as catalyst to produce bicyclic dithiadiaza macrocycle **80** [88] (Scheme 47). The subsequent reaction of **80** with an equimolar amount of 2-bromobenzyl bromide in the presence of K_2CO_3 gave S,N-crown **81**.

5.3. Synthesis of O,S,N-Macroheterocycles

The reaction of oxadithiazacycloalkane with organic halogen derivatives underlies one of the simplest and most efficient methods of synthesis of *N*-substituted O,S,N-macrocycles. Heating of 1-oxa-4,10-dithia-7-azacyclododecane with 2-bromobenzyl bromide in the presence of potassium carbonate [88] gave aryl-substituted 12-membered O,S,N-crown ether **82**. Cycloaminomethylation of 3,6-dioxaoctane-1,8-dithiol with *N*,*N*-bis(methoxymethyl)anilines catalyzed by $Sm(NO_3)_3/\gamma$-Al_2O_3 was studied with the goal of developing an efficient synthetic approach to 13-membered O,S,N-macroheterocycles [85]; 6-aryl-1,11-dioxa-4,8-dithia-6-azacyclotridecanes **83a**–**83l** were thus synthesized in quantitative yield (Scheme 48).

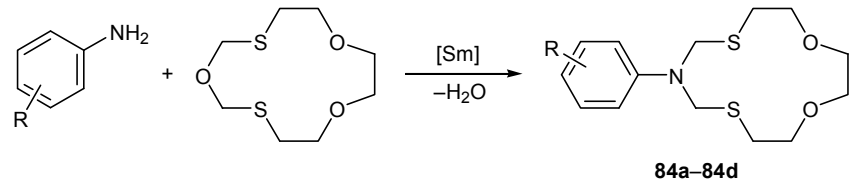
The selective synthesis of *N*-aryl-1,11-dioxa-4,8-dithia-6-azacyclotridecanes **84a**–**84d** by samarium-catalyzed recyclization of trioxadithiacyclotridecane with aromatic amines was discussed in [89]. Catalytic recyclization of 1,6,9-trioxa-3,12-dithiacyclotridecane with quinolinamines in the presence of 5 mol % of $Sm(NO_3)_3 \cdot 6H_2O$ afforded 80–88% of 1,11-dioxa-4,8-dithia-6-azacyclotridecan-6-ylquinolines **85a**–**85e** (Scheme 49). 2-Fluoronitrobenzene reacted with 1,4-dioxa-7,13-dithia-10-azacyclopentadecane in the presence of Cs_2CO_3 at 60°C under nitrogen (72 h),

Scheme 48.

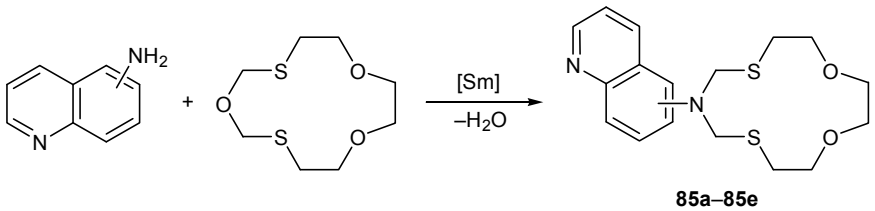


Ar = Ph (**a**), 3-MeC_6H_4 (**b**), 4-MeC_6H_4 (**c**), 2-$MeOC_6H_4$ (**d**), 3-$MeOC_6H_4$ (**e**), 2-ClC_6H_4 (**f**), 3-ClC_6H_4 (**g**), 4-ClC_6H_4 (**h**), 3-BrC_6H_4 (**i**), 4-BrC_6H_4 (**j**), 3-FC_6H_4 (**k**), 4-FC_6H_4 (**l**).

Scheme 49.

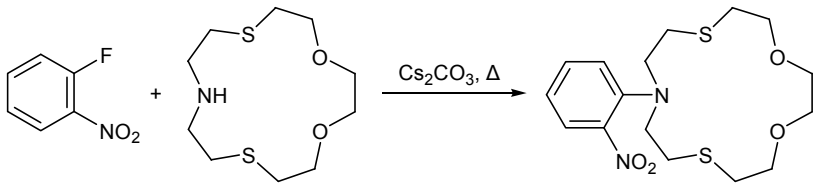


R = 4-HO (**a**), 4-HS (**b**), 4-HOC(O) (**c**), R = 4-HO-5-HOC(O) (**d**).



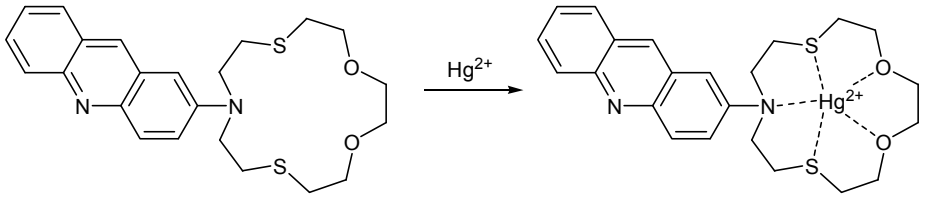
2-NH_2, 3-NH_2, 5-NH_2, 6-NH_2, 8-NH_2.

Scheme 49 (Contd.).



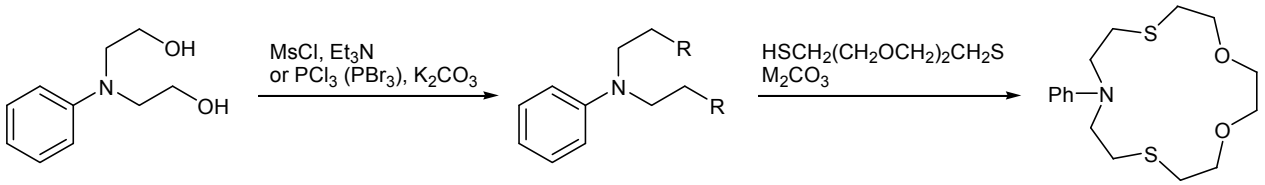
86

Scheme 50.



87

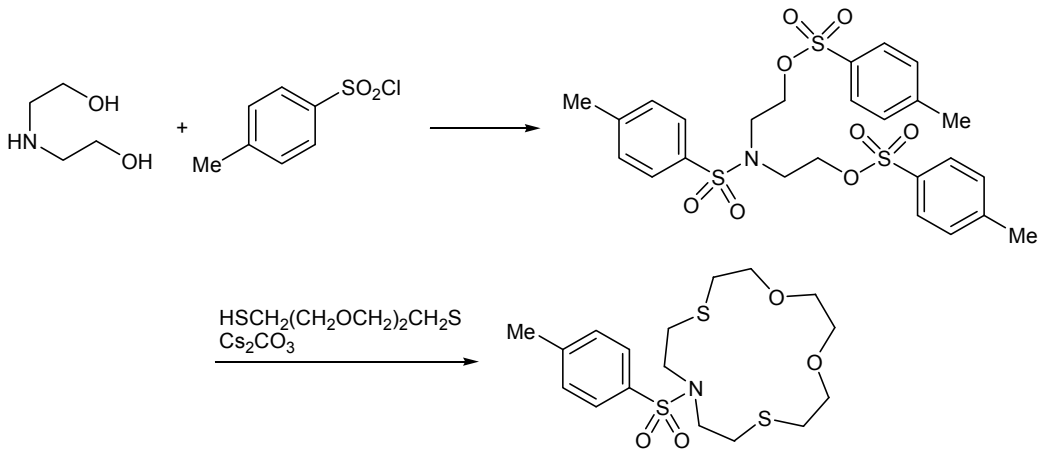
Scheme 51.



88

R = MsO, Hlg (Cl, Br); M = K, Cs.

Scheme 52.



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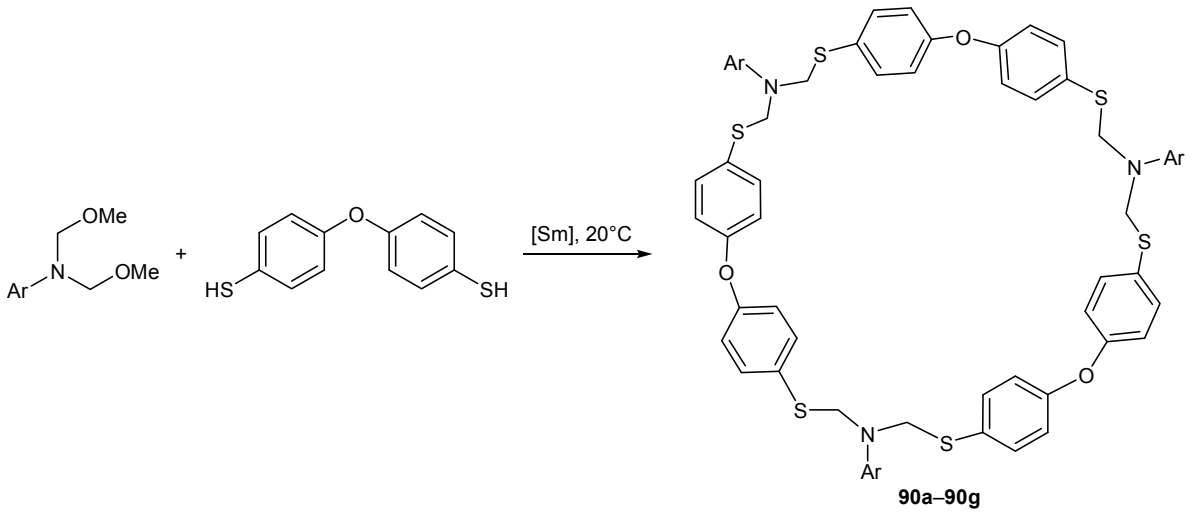
yielding 92% of *N*-(2-nitrophenyl)-1,4-dioxa-7,13-dithia-10-azacyclopentadecane (**86**) [90–92]. 1,4-Dioxa-7,13-dithia-10-azacyclopentadecane **87** was synthesized by heterocyclization of acridin-2-amine with the corresponding azadithia crown ether [93]. Compound **87** is an example of fluorescent probe ensuring selective radiometric detection of mercury ions in water (Scheme 50) [94].

O,S,N-Macroheterocycles were successfully synthesized by heterocyclization of bis-methanesulfonates (dihalides) with α,ω-dithiols. Bis-methanesulfonate derived from 2,2′-(phenylimino)diethanol efficiently reacted with 3,6-dioxaoctane-1,8-dithiol in the presence of potassium carbonate [95, 96] to produce 10-phenyl-1,4-dioxa-7,13-dithia-10-azacyclopentadecane (**88**) with high selectivity (Scheme 51). Like-

Scheme 53.



Ar = 3-ClC_6H_4 (**a**), 3-MeC_6H_4 (**b**), 4-MeC_6H_4 (**c**), 2-$MeOC_6H_4$ (**d**), 2-ClC_6H_4 (**e**), 2-BrC_6H_4 (**f**), 4-BrC_6H_4 (**g**).

wise, macrocycle **88** was obtained in 75% yield by the reaction of α,ω-dihalides with the same dithiol in the presence cesium carbonate [97, 98].

An original synthesis of 1,4-dioxa-7,13-dithia-10-azacyclopentadecane **89** was reported in [99]. Compound **89** was obtained in 97% yield by heterocyclization of 4-methyl-*N*,*N*-bis{2-[(4-methylbenzenesulfonyl)oxy]ethyl}benzenesulfonamide with 3,6-dioxaoctane-1,8-dithiol in the presence of cesium carbonate (Scheme 52). Unique 42-membered O,S,N-cyclophanes **90a**–**90g** were synthesized in 65–81% yield by $Sm(NO_3)_3 \cdot 6H_2O$-catalyzed 3 : 3 intermolecular cyclocondensation of *N*,*N*-bis(methoxymethyl)anilines with 4,4′-oxydibenzenethiol [100] (Scheme 53).

6. CONCLUSION

The data given in the present review illustrate successful development over the past 15 years of the synthesis of S,N-heterocycles, namely 1,4-benzothiazines, phenothiazines, 1,3,5-dithiazinanes, partly hydrogenated 1,4(5)-benzothiazepines, 1,5,3-dithiazepanes, partly hydrogenated benzothiazocin(on)es, 1,5,3-dithiazocanes, and O,N-, S,N-, and O,S,N-macroheterocycles, via catalytic hetrocyclizations. Catalytic heterocyclizations are characterized by broad synthetic potential, and they make it possible to synthesize heterocycles with a desired structure with high selectivity. Introduction of metal complex catalysis methods into practical organic synthesis not only improved the known methods but also gave rise to new ways of constructing heterocyclic compounds.

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