SYNTHESIS AND HETEROCYCLIZATIONS OF *ortho*-AMINO(ALKYNYL)NAPHTHALENES

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Abstract. *This review covers the synthetic methods for ortho-amino(alkynyl)naphthalenes and their heterocyclizations into polynuclear N–, O–, S–, P– and B–heterocycles, reported from 1983 to 2023.*

Contents

1. Introduction

Among a variety of synthetic methodologies for the preparation of heterocyclic derivatives, cyclization reactions of alkynes are one of the most attractive ways to directly construct diverse heterocycles under mild conditions (for selected reviews on this topic see ref.[1-11]). Alkynes are abundant and readily accessible raw materials. In addition, alkyne reactions are highly favorable thermodynamically and tolerant to most functional groups. There are many very useful reactions of alkynes that lead to heterocycles and carbocycles, *e.g.* electrophilic, nucleophilic and free radical additions, intramolecular Diels-Alder reactions and other cycloadditions, transition metal-catalyzed alkyne and enyne metathesis, transition metal carbene-promoted annulations of alkynes, Bergman and related diyne cyclizations, the Pauson-Khand reaction and so on.

For the last decade, our laboratory has been conducting research aimed at developing synthetic methods, studying the physicochemical properties and reactivity of alkynyl derivatives of 1,8-bis(dimethylamino)naphthalene. The latter is also known as the "proton sponge" due to reduced kinetic basicity (low rate of proton addition/elimination). The structure of 1,8-bis(dimethylamino)naphthalene (DMAN) features several characteristics, *e.g.* lone pair/lone pair repulsions of the *peri* dimethylamino groups, favorable lone pair/π overlap and lone pair/methyl nonbonded interactions. In the corresponding monoprotonated cation $DMAN{\cdot}H^+$, the lone pairs swing round into the molecular plane to form the nonlinear N–H···N hydrogen bond, the nitrogen atoms can approach closer, and the naphthalene ring can become more planar. Thus, the high basicity of DMAN is due to steric inhibition of conjugation in the free base, relief of nonbonded repulsions and stabilization of the cation by the hydrogen bond. Numerous studies have revealed many other remarkable properties of DMAN, in particular, its low *N*-nucleophilicity combined with the high *C*-nucleophilicity and diverse reactivity of the NMe_2 groups (for reviews, see [12-15]). While studying 2-alkynyl and 2,7-dialkynyl derivatives of the proton sponge, we noticed their increased tendency to heterocyclization resulting in the pyrrole ring closure. This fact prompted us to analyze available data on the synthesis and heterocyclization reactions of *ortho*-amino(alkynyl)naphthalenes and to reveal the specificity of the proton sponge derivatives.

The review contains two sections: the first one is devoted to the synthesis, and the second one, to the heterocyclizations of *ortho*-amino(alkynyl)naphthalenes. Within each of them, 2-alkynylnaphthalen-1-amines, isomeric 2-alkynylnaphthalen-1-amines, and, finally, 3-alkynyl-2-aminonaphthalenes are sequentially

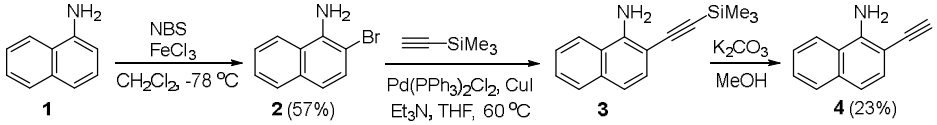
considered. The literature from the 1983 to the 2022 is covered, approximately 60% of references are from the last ten years.

2. Synthesis of *ortho*-amino(alkynyl)naphthalenes

In most cases, the synthesis of *ortho*-amino(alkynyl)naphthalenes has been based on the Sonogashira coupling[16,17] of *ortho*-amino(halo)naphthalenes with terminal alkynes, but other specific approaches have also been described.

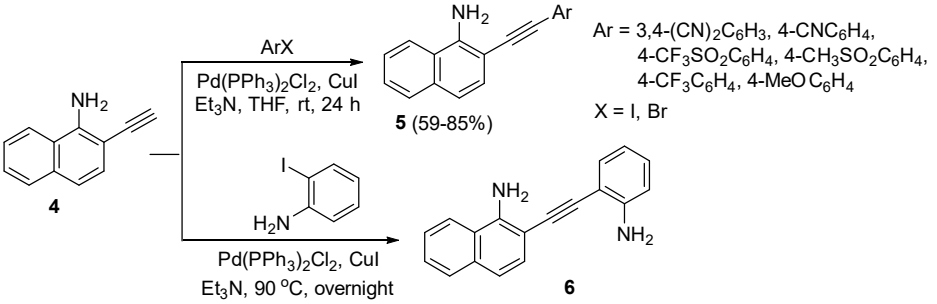
2.1. Synthesis 2-alkynylnaphthalen-1-amines

Typically, 1-aminonaphthalene **1** has been used as a starting material for the synthesis of title compounds. For example, treatment of 1-aminonaphthalene **1** with *N*-bromosuccinimide (NBS) in the presence of $FeCl_3$ in methylene chloride at -78 °C afforded 1-amino-2-bromonaphthalene **2** (Scheme 1).[18] *ortho*-Halogenation of compound **1** has also been performed with other electrophilic halogenating reagents. Pd/Cu-Catalyzed reaction of **2** with trimethylsilylacetylene and subsequent desilylation of the resulting product **3** gave 2-ethynylnaphthalen-1-amine **4** in moderate yield. The coupling of 1-amino-2-iodonaphthalene with trimethylsilylacetylene, even under milder conditions ($Pd(PPh_3)_2Cl_2$, CuI, *i*-Pr_2NH, toluene, rt, 12 h), proceeded more efficiently, leading to the formation of compound **3** in near quantitative yield.[19]



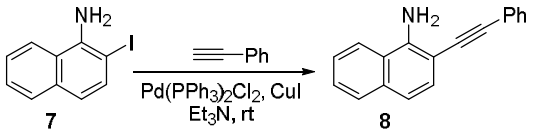
Scheme 1. Synthesis of 2-ethynylnaphthalen-1-amine **4**.

2-(Arylethynyl) derivatives of α-naphthylamine **5**, containing *para*-substituents of different electronic nature in the aryl fragment, were synthesized by Pd-catalyzed cross-coupling of 2-ethynylnaphthalene-1-amine **4** with aryl halides (Scheme 2).[19] 2-((2-Aminophenyl)ethynyl)naphthalen-1-amine **6** was prepared in a similar way.[20]



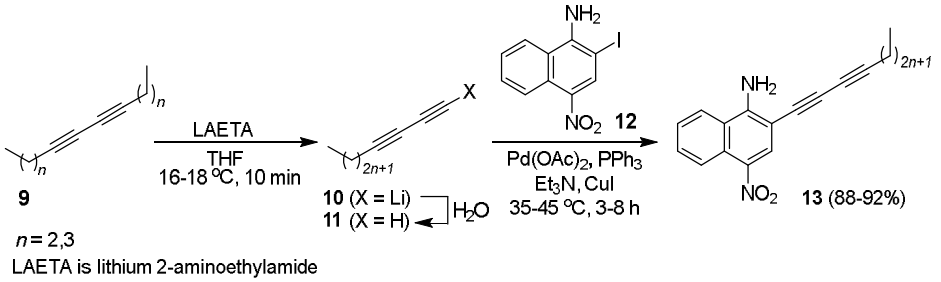
Scheme 2. Synthesis of 2-(arylethynyl)naphthalen-1-amines.

The 2-(phenylethynyl)naphthalen-1-amine **8** was also obtained directly by the coupling of iodide **7** with phenylacetylene (Scheme 3).[21]



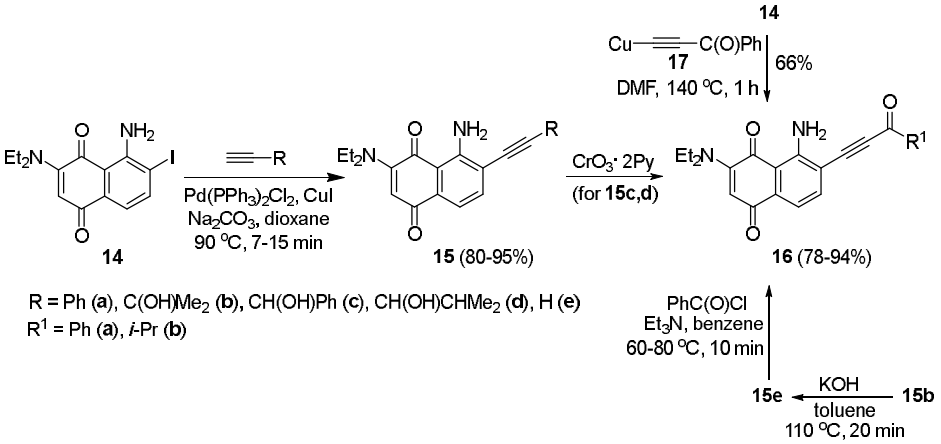
Scheme 3. Synthesis of 2-(phenylethynyl)naphthalen-1-amine **8**.

1,3-Diynes **11**, formed *in situ* as a result of the so-called "acetylene zipper" reaction (**9→10→11**), reacted with 2-iodo-4-nitronaphthalen-1-amine **12** under mild conditions giving rise to 1-arylalka-1,3-diynes **13** (Scheme 4).[22-24] The transformations were carried out in a one-pot mode.



Scheme 4. Synthesis of 1-(1-amino-4-nitronaphthalen-2-yl)alka-1,3-diynes **13**.

It is known that electron-deficient 1-alkynes, in particular, conjugated ynones, do not undergo the Sonogashira reaction. 2-(Acylethynyl) derivatives of 8-aminonaphthoquinone **16** were obtained in two steps by coupling iodide **14** with Favorskii alcohols and subsequent oxidation of alkynes **15** (Scheme 5).[25] Compound **16b** was also synthesized *via* the Stephens-Castro reaction of iodide **14** with a copper(I) acetylide **17** or by acylation of 8-amino-7-ethynylnaphthalene **15e** with benzoyl chloride under basic conditions.[25]



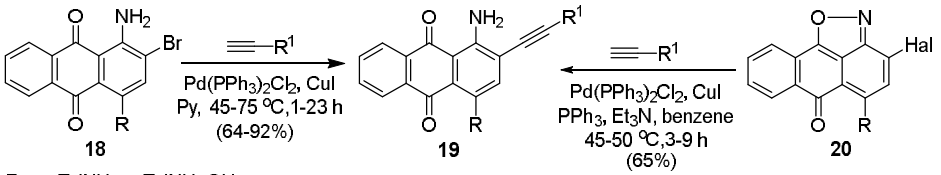
Scheme 5. Three synthetic methods for compounds **16**.

Two synthetic methods for 1-amino-2-alkynylanthraquinones **19** have been reported.[26-28] The first of them was based on the coupling of 1-amino-2-bromoanthraquinones **18** with terminal arylacetylenes, leading to the formation of the desired products **19** in 64-92% yields (Scheme 6). It was also shown that the reaction of 3-haloisoxazolanthrones **20** (R=*m*-Tol, *p*-Tol) with phenylacetylene is accompanied by the opening of the isoxazole ring to give compounds **19** in 65% yields.

2-Ethynyl-*N*-methylnaphthalen-1-amine **23** was synthesized similarly to compound **4** (Scheme 7).[29] Three-step synthesis included *N*-methylation of 1-amino-2-bromonaphthalene **2** by successive treatment with methyl lithium and dimethyl sulfate, coupling of the resulting 2-bromo-*N*-methylnaphthalen-1-amine **21** with trimethylsilylacetylene and desilylation of product **22**.

The coupling of bromide **21** with phenylacetylene in the same catalytic system, but using dimethylformamide as a solvent and at a higher temperature, afforded

N-methyl-2-(phenylethynyl)naphthalen-1-amine **24** (Scheme 8).[30] The reaction of ethyl (2-bromonaphthalen-1-yl)carbamate **25** with various 1-alkynes gave 2-alkynyl derivatives **26**.[31]

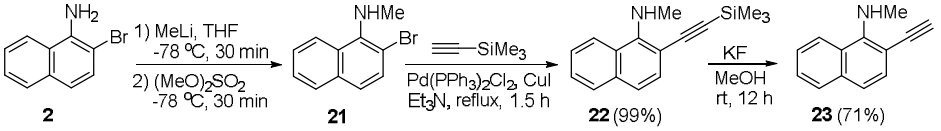


R = *p*-TolNH, *m*-TolNH, OH

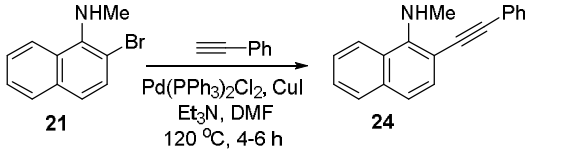
R^1 = Ph, $C(OH)Me_2$, 4-MeO-C_6H_4, 4-NO_2-C_6H_4, 4-Br-C_6H_4, 1,5-dimethyl-1*H*-pyrazol-4-yl, *etc.*

Hal = Br, I

Scheme 6. Alternative approaches to the synthesis of 1-amino-2-alkynylanthraquinones **19**.



Scheme 7. Synthesis of 2-ethynyl-*N*-methylnaphthalen-1-amine **23**.



R = $SiMe_3$, *n*-Bu, Ph

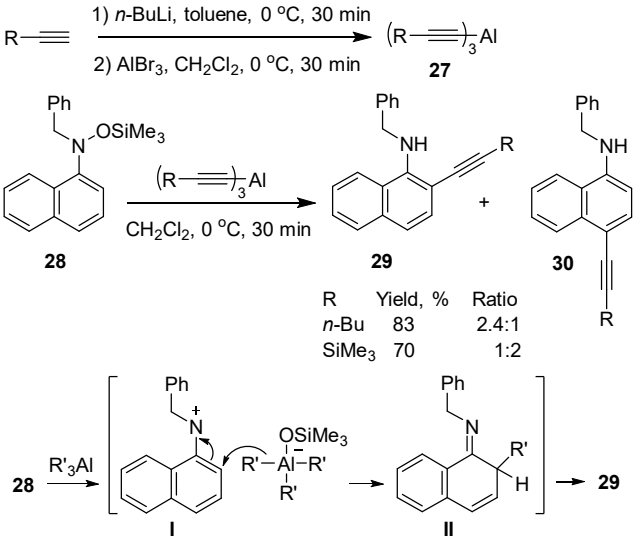
Scheme 8. Synthesis of *N*-alkyl(acyl)-2-alkynylnaphthalen-1-amines *via* the Sonogashira coupling.

One of the first reports on the synthesis of 2-alkynylnaphthalen-1-amines dates back to 1983.[32] In particular, it was shown that the treatment of *N*-benzyl-*N*-(naphthalen-1-yl)-*O*-(trimethylsilyl)hydroxylamine **28** with a 4-fold excess of trialkynylaluminum **27** in dichloromethane leads to the formation of a mixture of 2- and 4-alkynylnaphthylamines **29** and **30** in the ratio shown in the Scheme 9. According to the authors, oxophilic trialkynylaluminum **27** is able to heterolytically cleave the N–O bond in the starting hydroxylamine **28**, giving rise to intermediate cation **I**. Nucleophilic attack of the trialkynylaluminate ion at the *ortho* (or *para*) position of **I** results in imine **II** formation. Amino-imine tautomerization completes the process.

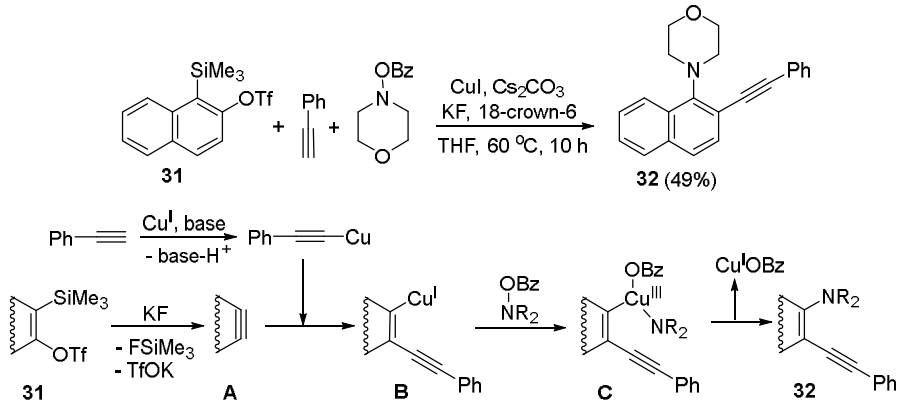
Cu(I)-Catalyzed three-component reaction of triflate **31** with phenylacetylene and morpholinobenzoate in the presence of potassium fluoride and cesium carbonate led to the formation of 1-morpholino-2-(phenylethynyl)naphthalene **32** (Scheme 10).[33] Presumably, in the course of the reaction, under the action of KF, the initial triflate **31** is converted into aryne **A**. Its interaction with formed *in situ* (phenylethynyl)copper gives copper complex **B**. The latter, reacting with morpholinobenzoate, is transformed into intermediate **C**. Reductive elimination of the copper(I) benzoate provides the final product **32**.

2-Ethynyl-*N,N*-dimethylnaphthalen-1-amine **33** was synthesized similarly to 2-ethynyl-*N,N*-dimethylaniline *via* the Sonogashira coupling of *N,N*-dimethyl-2-iodnaphthalene with trimethylsilylacetylene and subsequent desilylation.[34,35] The yield and characteristics of **33** were not given. The reaction of alkyne **33** with *ortho*-diiodobenzene in the $Pd(PPh_3)_2Cl_2$/CuI/*n*-$BuNH_2$/Et_2O catalytic system

afforded 2-((2-iodophenyl)ethynyl)-*N,N*-dimethylnaphthalen-1-amine **34** in the only 27% yield (Scheme 11).[34] 2-((1-Aminonaphthalen-2-yl)ethynyl)-*N,N*-dimethylnaphthalen-1-amine **35** was obtained similarly using 1-amino-2-bromonaphthalene as a coupling partner.[35]



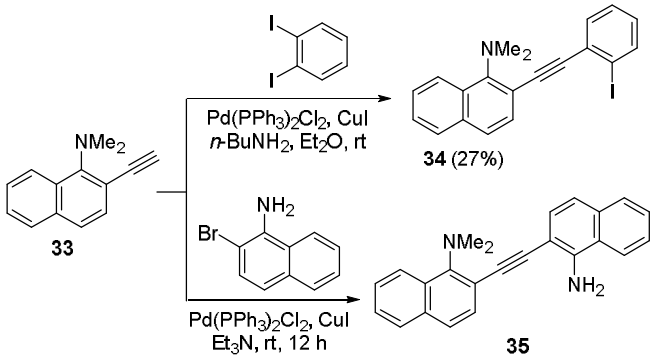
Scheme 9. Synthesis of *N*-alkyl-2-alkynylnaphthalen-1-amines using trialkynylaluminum reagents.



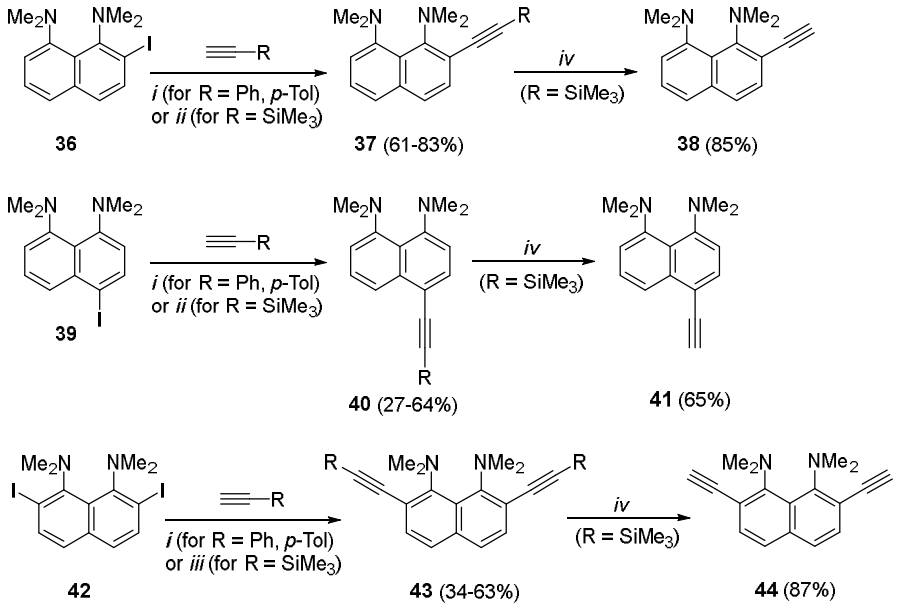
Scheme 10. Synthesis of *N*-alkyl-2-alkynylnaphthalen-1-amines *via* an aryne intermediate.

The Sonogashira coupling of mono- and diiodo derivatives of 1,8-bis(dimethylamino)naphthalene (proton sponge) **36**, **39**, **42** with phenyl-, *p*-tolyl- or (trimethylsilyl)acetylene yielded the corresponding 2- and 4-alkynyl- as well as 2,7-dialkynyl-1,8-bis(dimethylamino)naphthalenes **37**, **40**, **43** (Scheme 12).[36,37] Desilylation of the trimethylsilylethynyl derivatives provided alkynes **38**, **41**, **44**. It should be noted that in some cases during isolation and purification, compounds **37** and **43** underwent heterocyclization to benzo[*g*]indoles. These processes will be discussed in Section 3.1 (see Schemes 41 and 43).

2-Ethynyl-1,8-bis(dimethylamino)naphthalene **38** was then used as a starting compound to synthesize (naphthylethynyl) derivative **45** (Scheme 13).[38] The Glaser oxidative dimerization of compound **38** led to 1,4-diaryl-1,3-butadiyne **46**.[39]



Scheme 11. Synthesis of 2-(arylethynyl)-*N,N*-dimethylnaphthalen-1-amines.



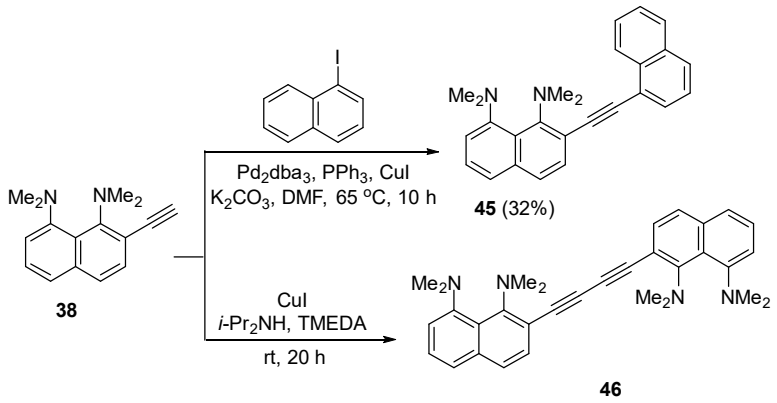
i - Pd_2dba_3, PPh_3, CuI, K_2CO_3, DMF, 50-60 °C, 8-10 h
ii - Pd_2dba_3, PPh_3, CuI, Et_3N, 50-60 °C, 8 h
iii - Pd_2dba_3, PPh_3, CuI, Et_3N, 70-75 °C, 2 h
iv - KF, MeOH, H_2O, rt, 12 h
Pd_2dba_3 is tris(dibenzylideneacetone)dipalladium(0)

Scheme 12. Synthesis of alkynyl derivatives of 1,8-bis(dimethylamino)naphthalene.

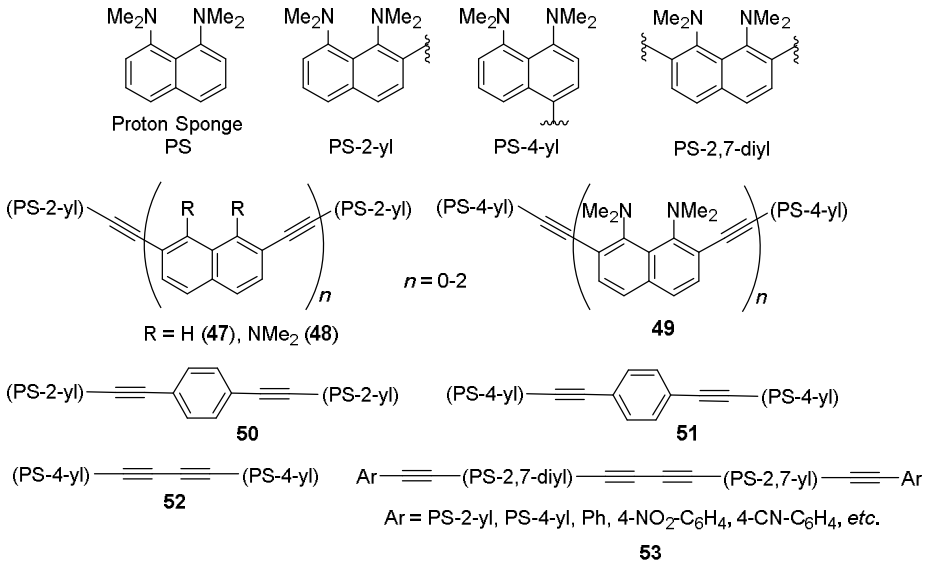
The Sonogashira couplings of iodides **36**, **39**, **42** with alkynes **38**, **41**, **44** and the Glaser reaction made it possible to obtain various proton sponge-based oligomers **47-53** (Scheme 14).[39-41]

2,4-(Diphenylethynyl)naphthalen-1-amine derivative **56** was obtained as a by-product of the hydroamination of diphenylbutadiyne under the action of potassium isopropyl(phenyl)amide in tetrahydrofuran at elevated temperatures (Scheme 15).[42] Two molecules of diphenylbutadiyne are involved in the formation of the compound **56**. The product of the initial hydroamination, *e.g.* potassium salt **54**, enters

into the reaction of nucleophilic addition to the C≡C bond of another diphenylbutadiyne molecule giving rise to intermediate **55**. The mechanism of the final cycloaromatization step was not investigated by the authors.



Scheme 13. Synthesis of naphthylethynyl and diyne derivatives of the proton sponge.

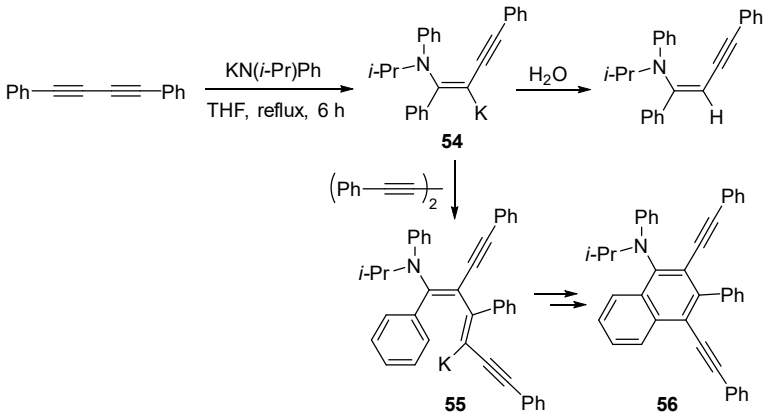


Scheme 14. Oligo(arylene-ethynylenes) and 1,4-diaryl-1,3-butadiynes based on the proton sponge.

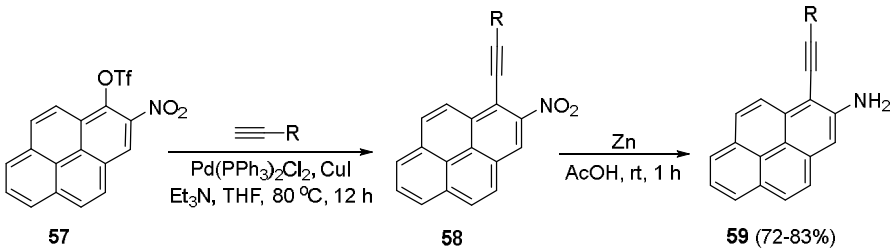
2.2. Synthesis of 1-alkynylnaphthalen-2-amines

Data on the synthesis of the title compounds is scarce. To the best of our knowledge, the only example of compounds containing 1-alkynyl-2-aminonaphthalene fragment with an unsubstituted amino group are pyrene derivatives **59** (Scheme 16).[43] The latter were synthesized starting from 2-nitropyren-1-yl trifluoromethanesulfonate **57** *via* the Sonogashira coupling with terminal alkynes followed by reduction of the nitro group product **58**.

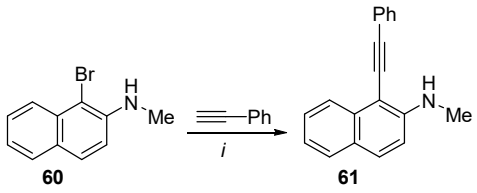
N-Methyl-1-(phenylethynyl)naphthalen-2-amine **61** was synthesized by coupling *N*-methyl-1-bromonaphthalen-2-amine **60** with phenylacetylene in the $Pd(PPh_3)_2Cl_2$/CuI/Et_3N/DMF catalytic system at high temperature (Scheme 17).[30]



Scheme 15. Synthesis of 2,4-(diphenylethynyl)naphthalen-1-amine derivative **56**.



Scheme 16. Synthesis of 1-alkynylpyren-2-amines.



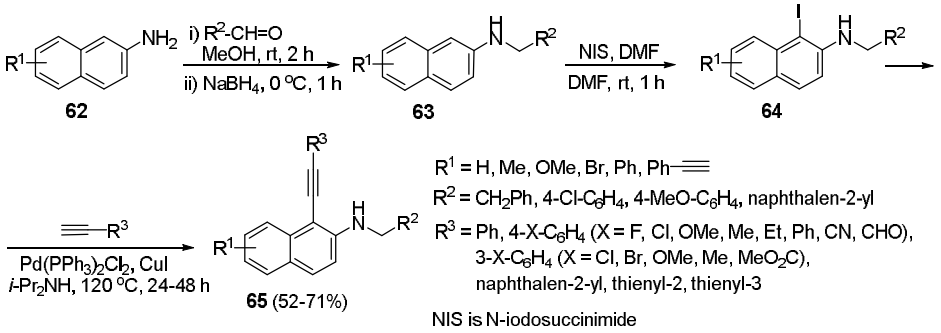
Scheme 17. Synthesis of *N*-methyl-1-(phenylethynyl)naphthalen-2-amine.

The synthesis of a wide series of 1-alkynyl-*N*-alkylnaphthalen-2-amines **65** from β-naphthylamines **62**, including the Schiff reaction and subsequent reduction of azomethines, iodination of *N*-alkylamino derivatives **63** and, finally, the catalytic coupling of iodides **64** with arylacetylenes, has been described (Scheme 18).[44]

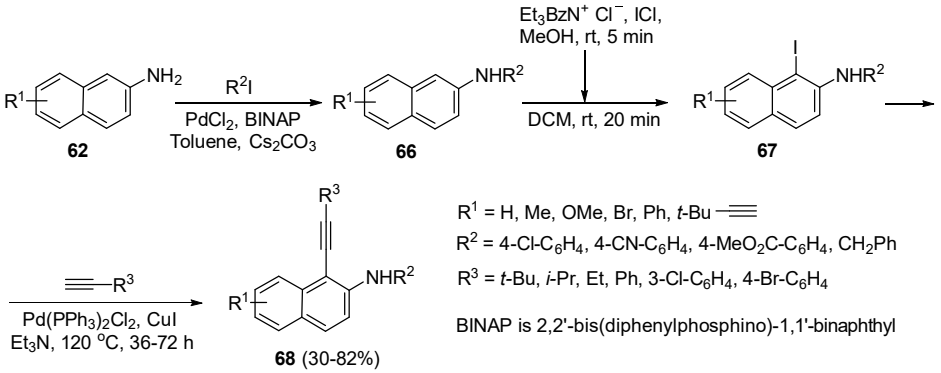
A similar synthetic method was proposed for compounds **68**,[45] with the only difference that in the first step the *N*-arylation of β-naphthylamines **62** was performed by the Buchwald-Hartwig coupling with aryl iodides (Scheme 19).[45] Three-step synthesis included catalytic of *N*-arylation of compounds **62**, *ortho*-iodination of arylamines **66** and, finally, Sonogashira coupling of the resulting iodides **67** with 1-alkynes.

In some cases, to perform effective coupling with 1-alkynes, the unsubstituted amino group of 1-iodonaphthalen-2-amines was pre-protected by *N*-acylation. For example, the synthesis of 1-(trimethylsilylethynyl)naphthylamine **71** was preceded by two successive steps of *N*-acetylation and *N*-tosylation of amine **69** (Scheme 20).[46] Protected iodide **70** was then coupled with trimethylsilylacetylene to

give compound **71**. Desilylation of the latter and double Sonogashira coupling of the resulting 1-alkyne **72** with 1,2-diiodo-4,5-dimethylbenzene produced *ortho*-dialkynylbenzene **73**. Its deacylation afforded compound **74**, which was used in the synthesis of diaza[7]helicene (see Scheme 62).



Scheme 18. Synthesis of *N*-alkyl-1-(alkynyl)naphthalen-2-amines from naphthalen-2-amine.



Scheme 19. Synthetic approach to *N*-aryl-1-(alkynyl)naphthalen-2-amines.

Treatment of iodide **75** with but-3-yn-1-ol in a standard catalytic system gave alkynyl derivative **76** in good yield (Scheme 21).[47] The latter was then converted to sulfamide **77**.

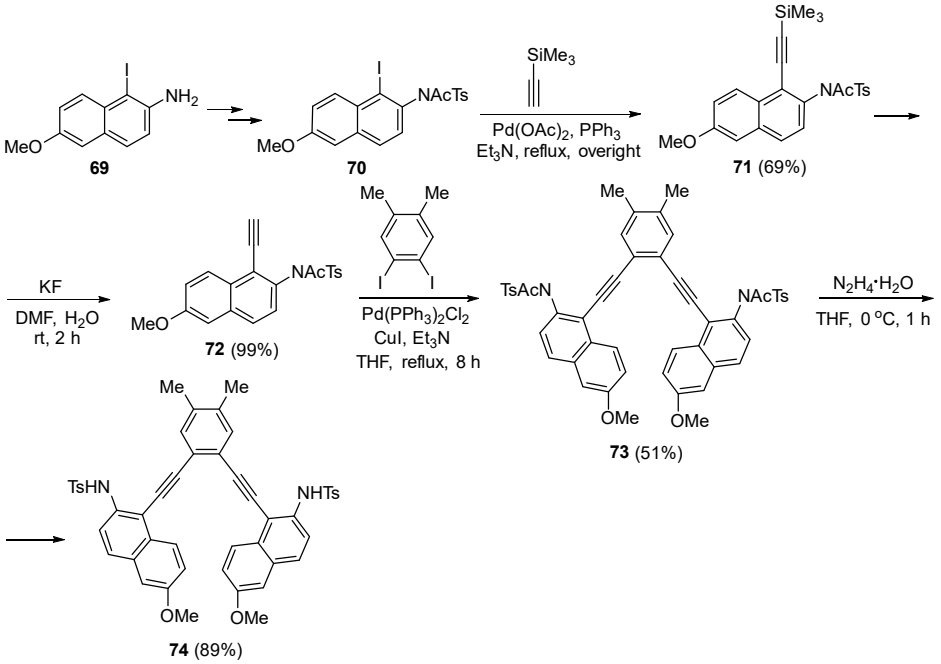
An efficient catalytic approach to the synthesis of *N*,*N*-dialkyl-2-alkynylanilines, including preparation of 4-(1-(phenylethynyl)naphthalen-2-yl)morpholine **79** from 1-iodonaphthalene **78**, was developed by using Pd-catalyzed norbornene-mediated three-component reactions of haloarenes, alkoxyamines (BzO-NR_2), and alkynes (Scheme 22).[48] During this transformation, one C–N and one C–C bond were formed in a one-pot manner from readily available starting materials (aryliodide, Favorskii alcohol and morpholino benzoate).

A plausible catalytic cycle for the above process is shown in Scheme 23. The reaction is initiated by oxidative addition of 2-iodonaphthalene **78** to the Pd(0) species producing intermediate **I**. Subsequent insertion of norbornene into Pd–Ar bond of **I** leads to intermediate **II**. The C–H activation with palladacycle **III** formation then occurs. Further oxidative addition of $BzONR_2$ towards **III** affords palladium species **IV**. The latter undergoes reductive elimination to yield **V**. Resulting from norbornene molecule release, a new intermediate **VI** undergoes ligand exchange and β-C elimination to yield the final product **79**.

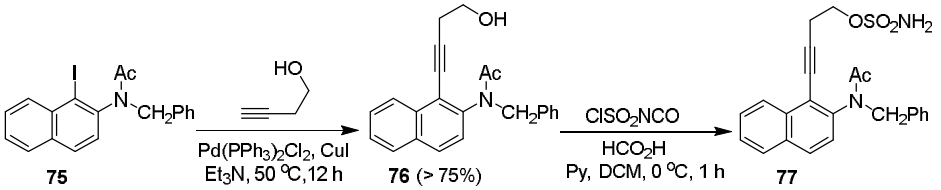
1.3. Synthesis of 3-alkynylnaphthalen-2-amines

Apparently, this is synthetically less available group of *ortho*-amino(alkynyl)naphthalenes. There are only two reports on the synthesis of the title compounds. 2-Amino-3-(4-methyl-3-oxopent-1-yn-1-yl)naphthalene-1,4-dione **83** was obtained by the Sonogashira reaction of 2-bromo-1,4-naphthoquinone **80**

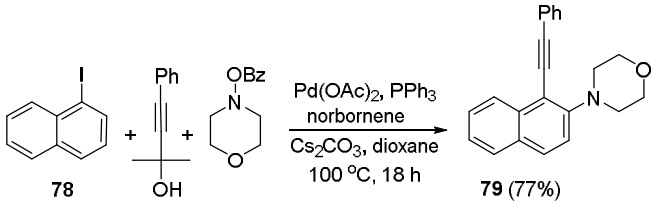
with acetylenic alcohol (Scheme 24).[49] Product **81** was further subjected to oxidative amination, which made it possible to obtain 2-amino-3-ethynylnaphthalene-1,4-dione **82**. The latter was converted to ketone **83** by oxidation with chromium(VI) oxide in the presence of pyridine (Collins reagent).



Scheme 20. Synthesis of *ortho*-dialkynylbenzene **74**.

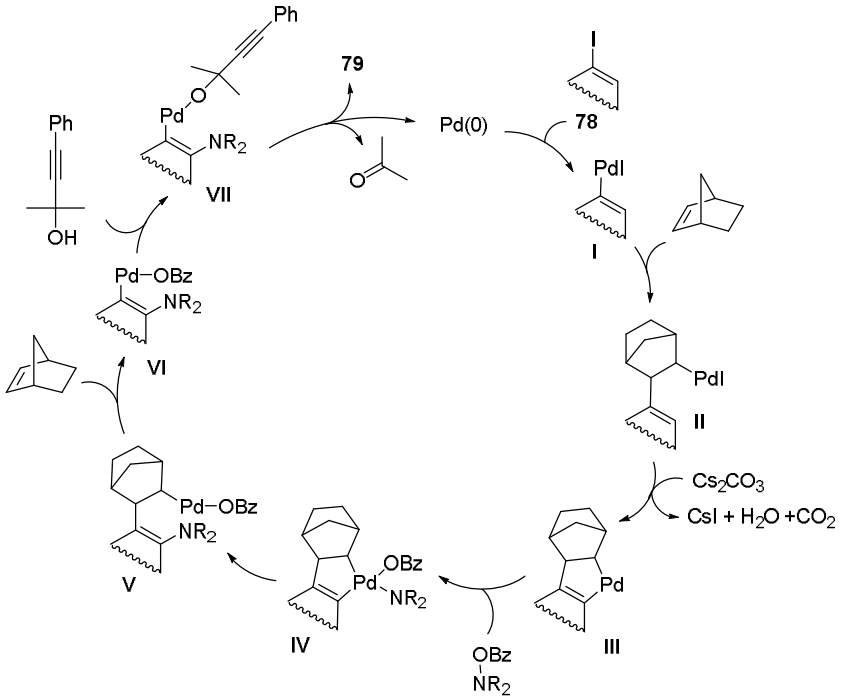


Scheme 21. Synthesis of sulfamide **77**.

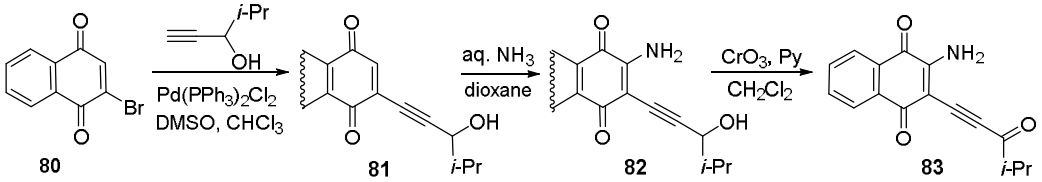


Scheme 22. Three-component synthesis of 4-(1-(phenylethynyl)naphthalen-2-yl)morpholine.

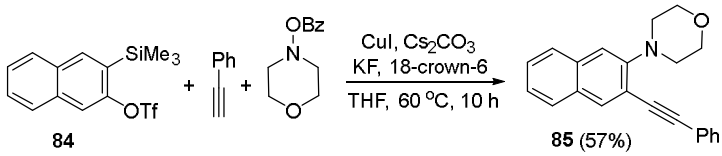
4-(3-(Phenylethynyl)naphthalen-2-yl)morpholine **85** was synthesized similarly to isomeric compound **32** (see Scheme 10) starting from 3-(trimethylsilyl)naphthalen-2-yl trifluoromethanesulfonate **84** (Scheme 25).[33]



Scheme 23. Proposed mechanism for the transformation **78→79.**



Scheme 24. Synthesis of 2-amino-3-(4-methyl-3-oxopent-1-yn-1-yl)naphthalene-1,4-dione.



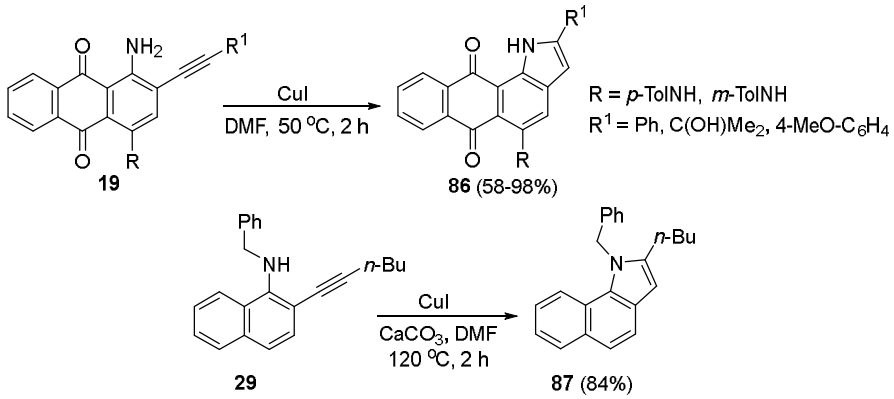
Scheme 25. Synthesis of 4-(3-(phenylethynyl)naphthalen-2-yl)morpholine.

3. Heterocyclizations of *ortho*-amino(alkynyl)naphthalenes

The currently known heterocyclizations of *ortho*-amino(alkynyl)naphthalenes can be divided into three main groups. The heterocyclizations that make up the first of them proceed with the participation of only the amino group and the C≡C bond, leading to the pyrrole ring closure. In some cases, side substituents at the C≡C bond or at the nitrogen atom are involved in heterocyclization, resulting in the formation of 6- or 7-membered heterocycles. The third group of heterocyclizations is based on the transformations involving the second reagent, a source of additional C, P, S or O ring atoms in the polynuclear reaction product. There are also rare examples of heterocyclizations, which are realized due to the structural peculiarities of the *ortho*-amino(alkynyl)naphthalene substrate and do not have a general character.

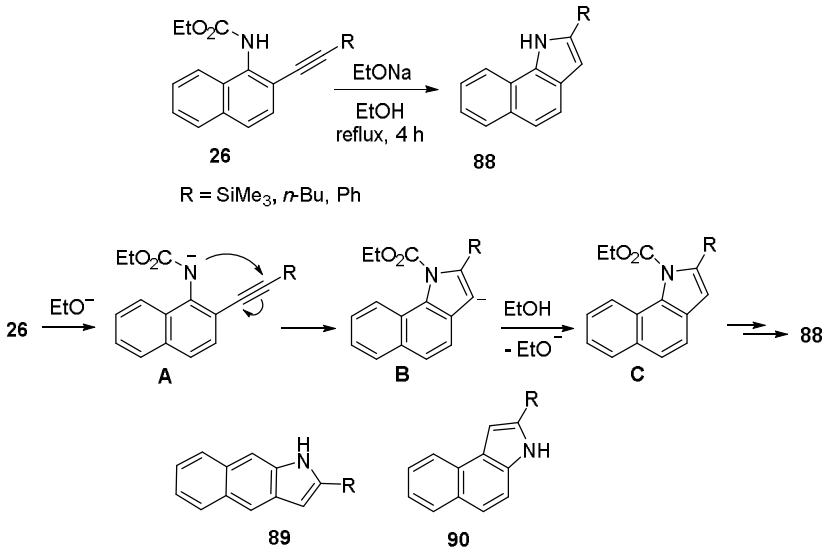
3.1. Heterocyclizations of 2-alkynylnaphthalen-1-amines

Hydroamination of multiple C–C bonds is a fundamental atom-economical process often used in the synthesis of nitrogen heterocycles. The reaction proceeds as a nucleophilic attack on the C=C or C≡C bond, and therefore electron-deficient alkenes and alkynes undergo hydroamination more easily than others. Hydroamination reactions are facilitated by activation of multiple bonds by Lewis acids (including transition metal complexes) as well as by an increase in the nucleophilicity of the amino group (for example, by its deprotonation). A typical example of such transformation is the Cu(I)-catalyzed cyclization of 1-amino-2-alkynylanthraquinones **19** into 1*H*-naphtho[2,3-*g*]indole-6,11-diones **86** (Scheme 26).[26-28] When heated with copper iodide in the presence of $CaCO_3$, *N*-benzyl-2-(hex-1-yn-1-yl)naphthalen-1-amine **29** underwent heterocyclization forming 1-benzyl-2-butyl-1*H*-benzo[*g*]indole **87**.[32]



Scheme 26. Cu-Catalyzed cyclizations of 2-alkynylnaphthalen-1-amines into benzo[*g*]indoles.

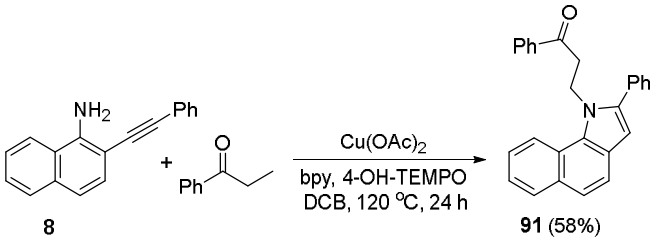
Cyclization of ethyl(2-alkynylnaphthalen-1-yl)carbamates **26** into 1*H*-benzo[*g*]indoles **88** was promoted by heating with sodium ethoxide (Scheme 27).[31]



Scheme 27. Base-induced cyclization of 2-alkynylnaphthalen-1-amines into benzo[*g*]indoles.

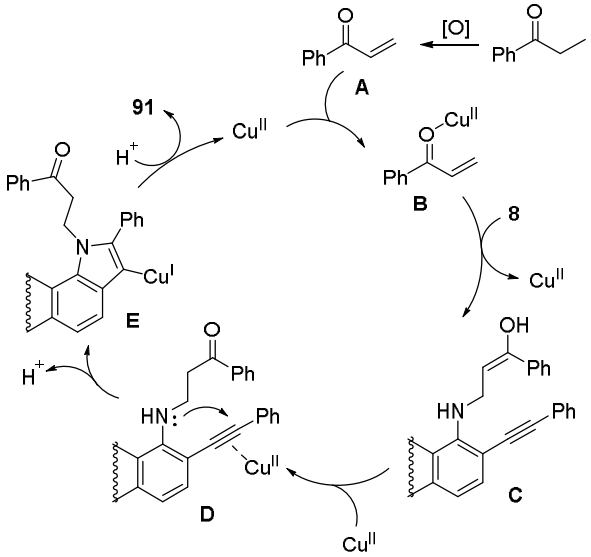
The nucleophilic 5-*endo-dig* cyclization of the intermediate *N*-anion **A** (**A**→**B**→**C**) was accompanied by the *N*-deacylation process and, in the case of the trimethylsilyl derivative, also desilylation. Similarly, isomeric to compounds **26** ethyl (3-bromonaphthalen-2-yl)- and ethyl (1-bromonaphthalen-2-yl)carbamates were converted into 1*H*-benzo[*f*]indole **89** and 3*H*-benzo[*e*]indole **90**, respectively (Scheme 27).

The interaction of 2-(phenylethynyl)naphthalen-1-amine **8** with propiophenone in the presence of copper acetate, 4-OH-TEMPO and 2,2′-bipyridine proceeded as a cascade process dehydrogenation/aza-Michael reaction/intramolecular hydroamination, leading to the formation of benzo[*g*]indole **91** (Scheme 28).[21] A proposed mechanism of this transformation is shown in Scheme 29. Initially, propiophenone is transformed into enone **A** through a Cu-catalyzed oxidative dehydrogenation reaction, followed by copper-promoted nucleophilic attack of **8** to form the key intermediate **C**. Next, Cu(II)-assisted 5-*endo-dig* cyclization of intermediate **C** provides species **E.** Finally, protonation of the latter leads to the formation of the desired product **91** along with the release of catalytically active Cu(II).



bpy - 2,2'-bipyridine
4-OH-TEMPO - 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl
DCB - *o*-dichlorobenzene

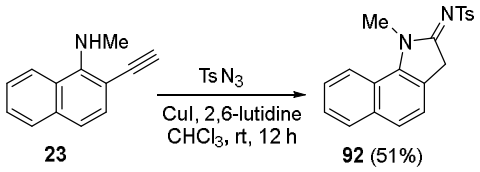
Scheme 28. Cu-Catalyzed cyclization/*N*-alkylation of 2-alkynylnaphthalen-1-amines.



Scheme 29. Proposed mechanism for the transformation **8**→**91**.

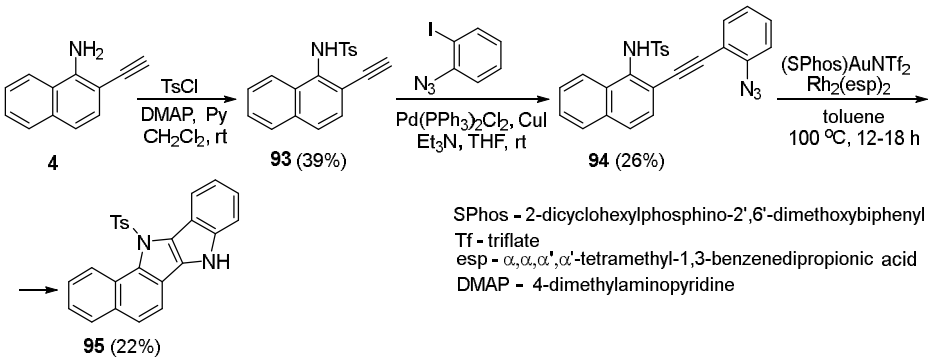
2-Ethynyl-*N*-methylnaphthalen-1-amine **23** reacted with tosyl azide in the presence of CuI, forming *N*-(1-methyl-1,3-dihydro-2*H*-benzo[*g*]indol-2-ylidene)tosylamide **92** in 51% yield (Scheme 30).[29] Presumably, this cascade process includes Cu-catalyzed [3+2]-cycloaddition of tosyl azide to the activated

C≡C bond, the release of a nitrogen molecule from the triazole intermediate to form ketimine, and intramolecular nucleophilic attack of the methylamino group on the ketimine group.

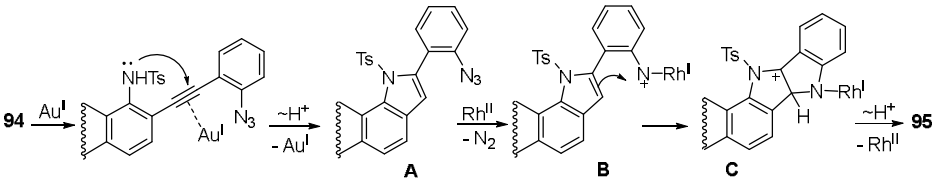


Scheme 30. Cu-Catalyzed [3+2]-cycloaddition of tosyl azide/heterocyclization of 2-ethynyl-*N*-methylnaphthalen-1-amine.

N-(2-((2-Azidophenyl)ethynyl)]naphthalen-1-yl)tosylamide **94**, prepared by the coupling of alkyne **93** with 1-azido-2-iodobenzene, underwent cascade cyclization into 12-tosyl-7,12-dihydrobenzo[*g*]indolo[3,2-*b*]indole **95** using relay catalysis with Au(I)/Rh(II) complexes (Scheme 31).[18] Control experiments showed that Au(I) is an effective catalyst for the initial cyclization of the naphthylamine fragment to benzoindole **A**, while the second cyclization **A→B→C**, in which the azide fragment is involved, is catalyzed by rhodium(II) (Scheme 32).

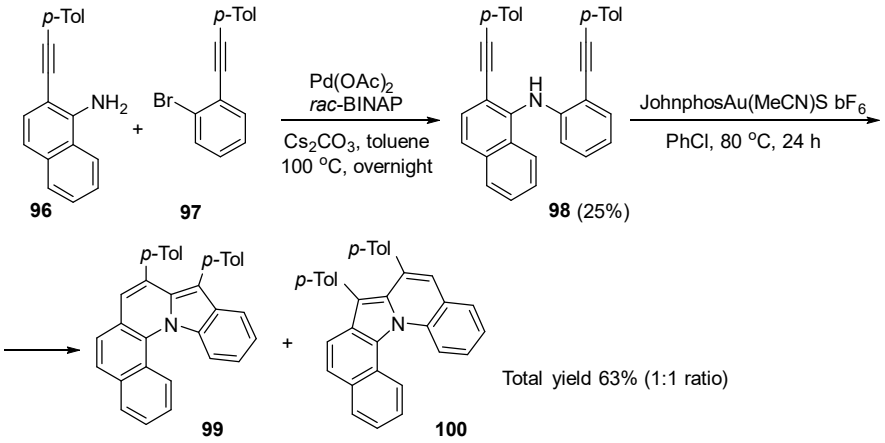


Scheme 31. Synthesis and cascade Au/Rh-catalyzed cyclization of tosylamide **94**.



Scheme 32. Proposed mechanism for the transformation **94→95**.

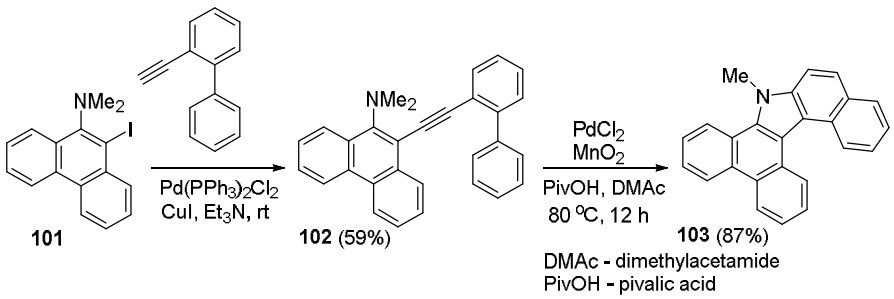
On heating in chlorobenzene in the presence of Johnphos-coordinated gold(I) complex, 2-(*p*-tolylethynyl)-*N*-(2-(*p*-tolylethynyl)phenyl)naphthalen-1-amine **98,** prepared by the Buchwald-Hartwig reaction of amine **96** and bromide **97**, underwent cascade heterocyclization forming a mixture of isomeric aza[5]helicenes **99** and **100**, derivatives of benzo[*h*]indolo[1,2-*a*]quinoline and benzo[6,7]indolo[1,2-*a*]quinoline (Scheme 33).[50] The reaction apparently starts with the Au-catalyzed 5-*endo-dig* cyclization of one of the *ortho*-aminoarylacetylene fragments resulting in the pyrrole ring closure. The subsequent 6-*endo-dig* cycloisomerization, in which Johnphos plays a crucial role, is accompanied by the migration of the *p*-tolyl substituent.



Johnphos is 2-(di-*tert*-butylphosphino)biphenyl

Scheme 33. Au-Catalyzed heterocyclization of compound **98** into isomeric aza[5]helicenes **99** and **100**.

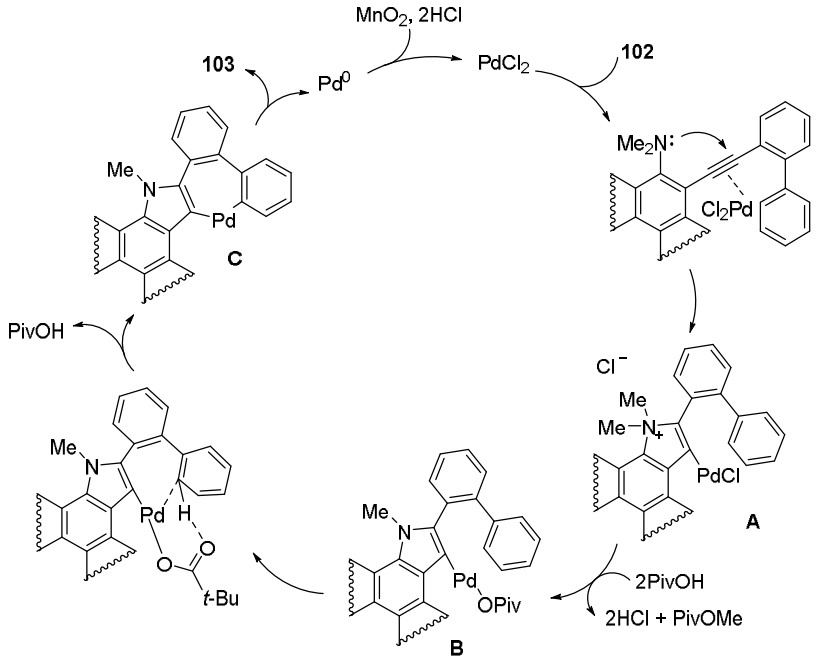
10-((1,1'-Biphenyl)-2-ylethynyl)-*N*,*N*-dimethylphenanthren-9-amine **102**, synthesized from iodide **101**, was cyclized to 7-methyl-7*H*-tribenzo[*a*,*c*,*g*]carbazole **103** using the $PdCl_2/MnO_2$/PivOH oxidative catalytic system (Scheme 34).[51] The catalytic cycle (Scheme 35) includes a nucleophilic attack of the dimethylamino group on the C≡C bond activated by coordination with $PdCl_2$. The resulting intermediate **A** loses one of the *N*-methyl groups under the action of pivalic acid and exchanges the chloride ligand for the pivalate in the palladium coordination sphere. The next key step is cyclopalladation, leading to the formation of intermediate **C**. The process is completed by reductive elimination of Pd(0), giving a polynuclear product, hetero[5]helicene **103**. Palladium(0) is oxidized by MnO_2 in the presence of HCl to catalytically active palladium chloride.



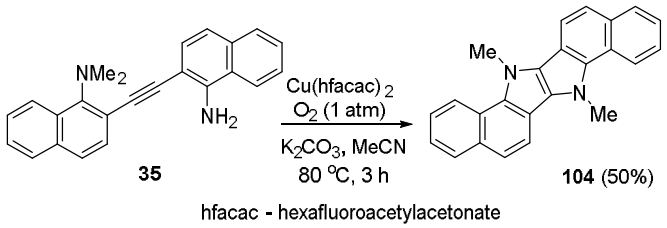
Scheme 34. Synthesis and heterocyclization of compound **102** into aza[5]helicene **103**.

Upon heating in the $Cu(hfacac)_2/O_2/K_2CO_3$/MeCN system, 2-((1-aminonaphthalen-2-yl)ethynyl)-*N*,*N*-dimethylnaphthalen-1-amine **35** was transformed into 7,14-dimethyl-7,14-dihydrobenzo[*g*]benzo[6,7]indolo[3,2-*b*]indole **104** in 50% yield (Scheme 36).[35] In the authors' opinion, this heterocyclization can proceed according to one of the mechanisms shown in Scheme 37. At first, one-electron oxidation of the *N*,*N*-dimethylamino group with a copper salt gives the radical cation **A**. The primary amino group of the latter in the presence of a copper complex is oxidized with oxygen to form the aniline-copper radical **B** and H_2O_2 molecules. The resonance structure of **B** is the Cu-nitrenoid complex **C**. The role of K_2CO_3 is to decompose the H_2O_2 molecule, whose presence is undesirable for less stable radical **B** or **C**. Then, the intermolecular transfer of the *N*-methyl group from the *N*,*N*-dimethylamine fragment of radical-cation **B** to the N-Cu radical in intermediates **B** or **C** affords intermediate **D**. The latter undergoes intramolecular radical addition to the C≡C bond, giving the product **104** *(path a)*. On the other hand, intramolecular radical addition

to the alkyne fragment in species **B** or **C** can occur before the transfer of *N*-methyl to form salt **E**, which subsequently undergoes intermolecular transfer of one of the *N*-methyl groups giving rise to product **104** (*path b*).



Scheme 35. Proposed mechanism for the transformation **102**→**103**.

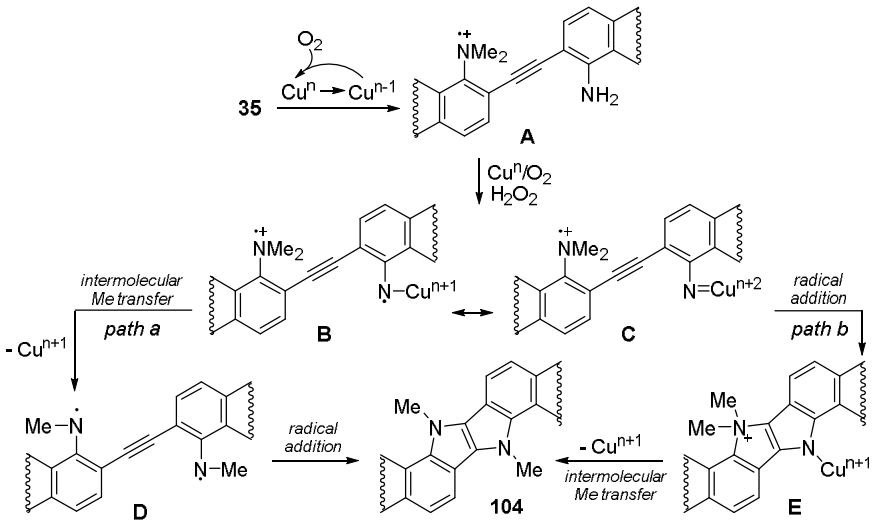


Scheme 36. Cascade heterocyclization/methyl migration of 2-((1-aminonaphthalen-2-yl)ethynyl)-*N*,*N*-dimethylnaphthalen-1-amine.

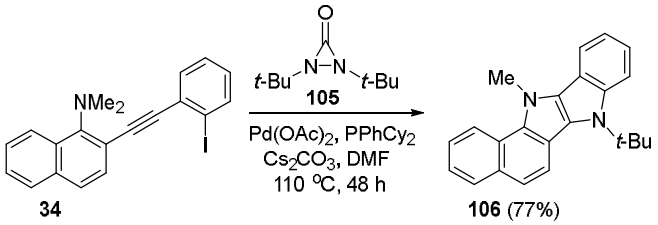
Another benzo[*g*]benzo[6,7]indolo[3,2-*b*]indole derivative **106** was synthesized by Pd-catalyzed reaction of alkyne **34** with 1,2-di-*tert*-butyldiaziridin-3-one **105** (Scheme 38).[34] The catalytic cycle, proposed by the authors, differs from that shown in Scheme 37. This cascade process starts with the oxidative addition of Pd(0) to the C–I bond to form complex **A** (Scheme 39). The triple bond activated by coordination with Pd(II) undergoes nucleophilic aminopalladation, giving dimethylammonium intermediate **B**. *N*-Demethylation of the latter leads to palladacycle **C**. Oxidative addition of intermediate **C** to diaziridinone **105** gives complex **D**, which, eliminating the *t*-BuNCO molecule, is converted into Pd(IV)-nitrene derivative **E**. Insertion of an unsaturated nitrene ligand into the C–Pd bond and reductive elimination of Pd(0) complete the heterocyclization process.

A similar transformation involving alkyne **34** and methyl (2-diazo-2-phenyl)acetate, leading to the formation of methyl 12-methyl-7-phenyl-7,12-dihydrobenzo[*g*]indeno[1,2-*b*]indole-7-carboxylate **107**

(Scheme 40), was described by the same authors.[52] In this case, the transformation proceeds through intermediate carbene complexes of palladium.



Scheme 37. Proposed mechanism for the transformation **35**→**104**.



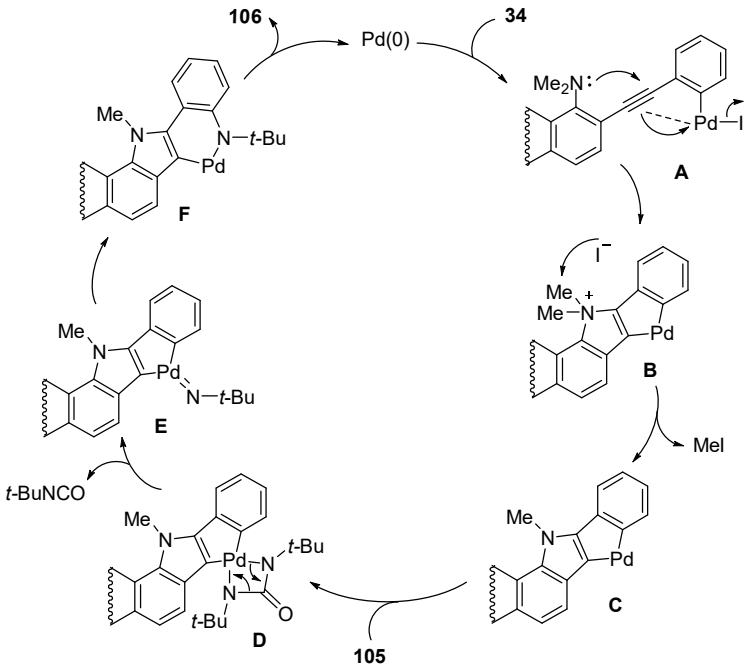
Scheme 38. Cascade Pd-catalyzed heterocyclization of compound **34** with 1,2-di-*tert*-butyldiaziridin-3-one.

As mentioned above, in the series of iodine derivatives of the proton sponge, a change in the protocol for the isolation of the Sonogashira reaction products (see Scheme 12), namely the replacement of the extraction of the reaction mixture by evaporation in a porcelain cup, resulted in several heterocyclizations with the participation of the C≡C bond and 1-NMe_2 group.[37,53] These include: i) a cyclization of alkynes **37a,b** and **43** (R=Ar) into isomeric 1*H*-benzo[*g*]indoles **108** and **110**, respectively, with [1,3]-migration of the *N*-methyl group into the newly formed pyrrole ring; ii) a similar cyclization of alkyne **37c** into 1*H*-benzo[*g*]indole **109** with a loss of the *N*-methyl group; iii) pyrrole-ring closure with a loss of the *N*-methyl group and alkynylation of the newly formed pyrrole ring at position 3 (transformation **42**→**111**) (Scheme 41).

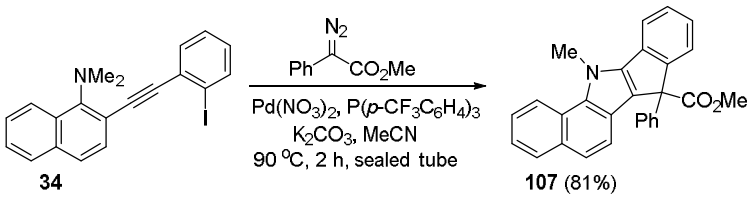
It was also shown that heating 2-(phenylethynyl)-1,8-bis(dimethylamino)naphthalene **36a** with palladium and (or) copper salts leads to the formation of a mixture of heterocyclic products **108**, **112**, **113** and **114** (Scheme 42).[37]

Proposed mechanisms for the formation of heterocyclization products **108**-**113** are shown in Scheme 43. In most cases, the reactions occur in parallel, but under certain conditions, one of the above products becomes predominant or even the only one. All transformations, except for **37**→**114**, start with a nucleophilic attack of the dimethylamino group on the adjacent Pd^{2+}-activated C≡C bond, followed by 5-*endo*-*dig* cyclization to cationic intermediate **II**. The latter either undergoes methyl 1,3-migration, forming benzo[*g*]indoles **108**, **110**, or is demethylated by the action of iodide ion, giving product **112**. Some evidence for the porcelain catalysis was obtained for rearrangement **37**→**108**. The intermediate palladium complex **III** is also able to dimerize,

forming compound **113**, and to enter a transmetalation reaction with (phenylethynyl)copper, giving product **111**.



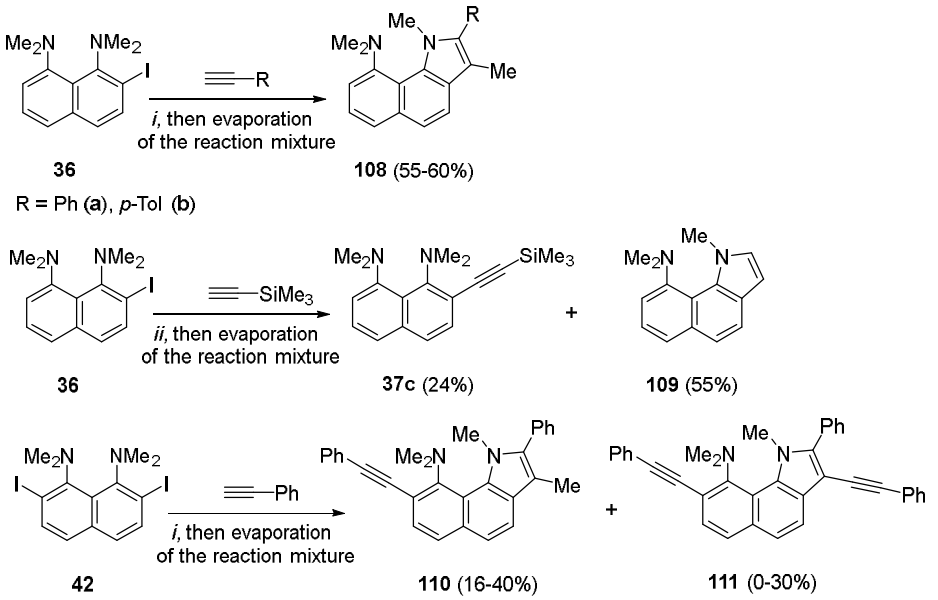
Scheme 39. Proposed mechanism for the transformation **34**→**106**.



Scheme 40. Cascade Pd-catalyzed heterocyclization of compound **34** with methyl (2-diazo-2-phenyl)acetate.

The formation of 3-aroylbenzo[*g*]indole **114** is the result of Cu-catalyzed oxidative transformation (Scheme 44). Initially, the oxidation/deprotonation of the dimethylamino group gives the iminium intermediate **I**, which then undergoes nucleophilic attack from the C≡C bond, leading to the pyrrole ring closure and the formation of species **II**. The process is completed by its deprotonation and the interaction of the resulting carbene **III** with atmospheric oxygen.

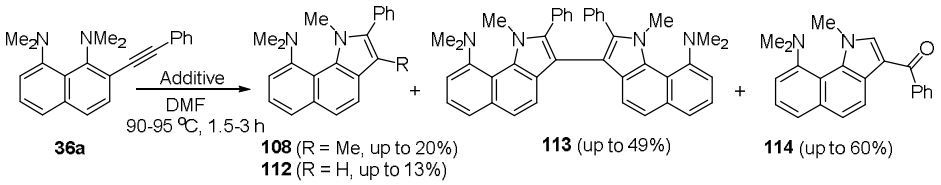
In contrast to the reaction of 2-ethynyl derivative of the proton sponge **38** with 1-iodonaphthalene, shown in Scheme 13, the Sonogashira coupling of 2-ethynyl- **38** and 2,7-diethynyl-1,8-bis(dimethylamino)naphthalenes **44** with 1,8-diiodonaphthalene resulted in the formation of *N*,*N*,7-trimethyl-7*H*-acenaphtho[1,2-*b*]benzo[*g*]indol-8-amines **116** and **117**, respectively (Scheme 45).[38] In the case of compound **38**, *N*,*N*,1,3-tetramethyl-1*H*-benzo[*g*]indol-9-amine **115** was also formed as a minor product. Clearly, in the course of the reaction, the initial product of the C-C coupling **I** undergoes oxidative addition of Pd(0) (Scheme 46). The C≡C bond of the resulting aryl-palladium complex **II** is activated to nucleophilic attack by the NMe_2 group, which leads to the pyrrole ring closure and the formation of palladacycle **III**. Reductive elimination of Pd(0) and S_N2 *N*-demethylation completes the process.



i - Pd_2dba_3, PPh_3, CuI, K_2CO_3, DMF, 60-65 °C, 8-10 h

ii - Pd_2dba_3, PPh_3, CuI, Et_3N, 50-60 °C, 8 h

Scheme 41. Heterocyclizations of alkynyl derivatives of the proton sponge during isolation from the reaction mixture.



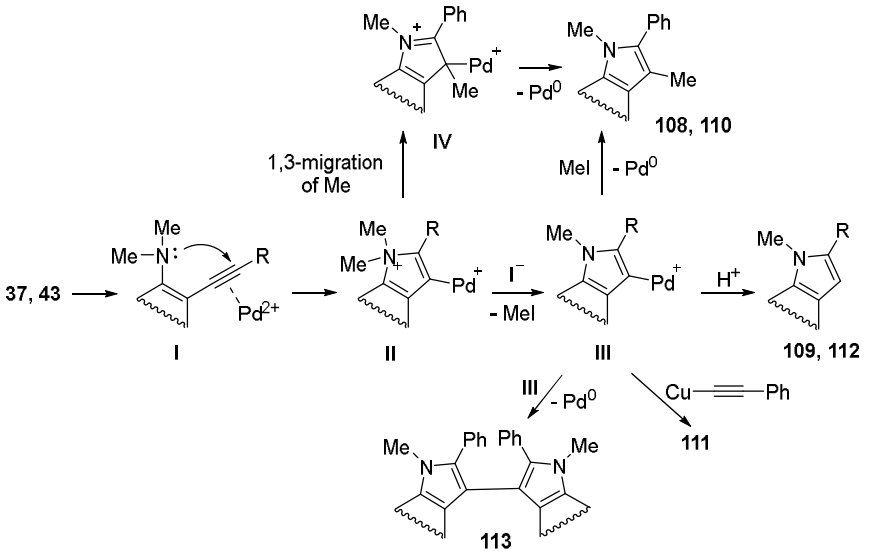
Additive: Pd_2dba_3, PPh_3, CuI, K_2CO_3, porcelain shards, air; CuI, air; $PdCl_2$, CuI, argon

Scheme 42. Pd- and(or) Cu-Catalyzed heterocyclizations of 2-(phenylethynyl)-1,8-bis(dimethylamino)naphthalene.

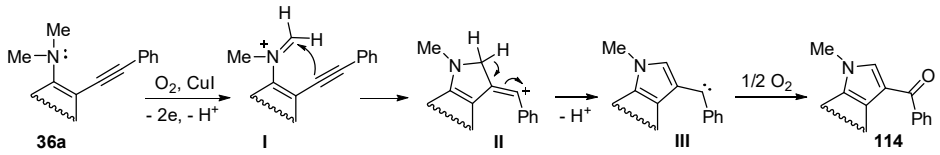
It was also shown that proton sponge-based 1,4-diaryl-1,3-butadiyne **46**, when heated with CuI in aniline, forms 2,2'-bibenzo[*g*]indole **118** in 57% yield (Scheme 47).[39] Under the same conditions, isomeric diyne **52** was cyclized into 2,5-diarylpyrrole **119**.

The diazonium salt **120** prepared by diazotization of the amine **15f** in the presence of hydrochloric acid underwent rapid cyclization to the alkylidene derivative of 3*H*-benzo[g]indazol-6,9-dione **122** (Scheme 48).[54] Dilution of the reaction mixture with water immediately after completion of diazotization led to the pyridazine ring closure and the formation of benzo[*h*]cinnoline-4,7,10(1*H*)-trione **121**. It is quite obvious that in the first case heterocyclization is initiated by the nucleophilic attack of the chloride ion on the C(β) atom of the triple bond, while a water molecule attacks the C(α) atom. The vicinal amino(alkynyl) derivatives of anthraquinone enter similar transformations.[55-57]

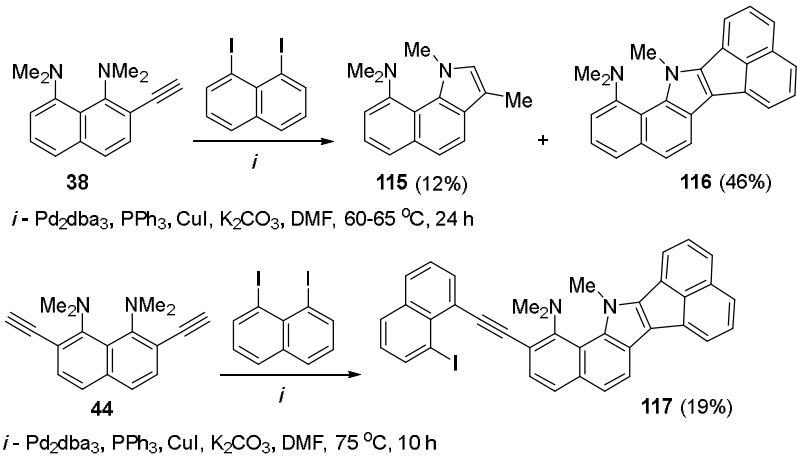
Azide **123**, obtained by successive diazotization of aminoanthraquinone **19** and interaction of the corresponding diazonium salt with sodium azide, was cyclized to 6*H*-anthra[1,9-*cd*]isoxazol-6-one **124** upon heating in toluene (Scheme 49).[26-28]



Scheme 43. Proposed mechanisms for the formation of heterocyclization products **108**-**113**.



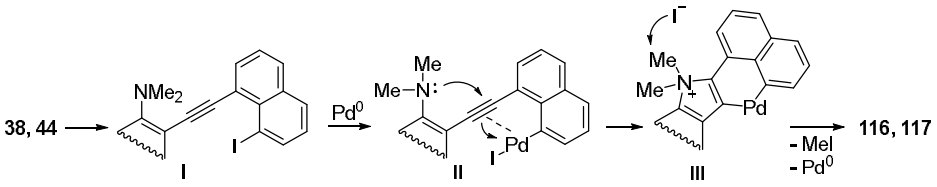
Scheme 44. A proposed mechanism for the transformation **36a**→**114**.



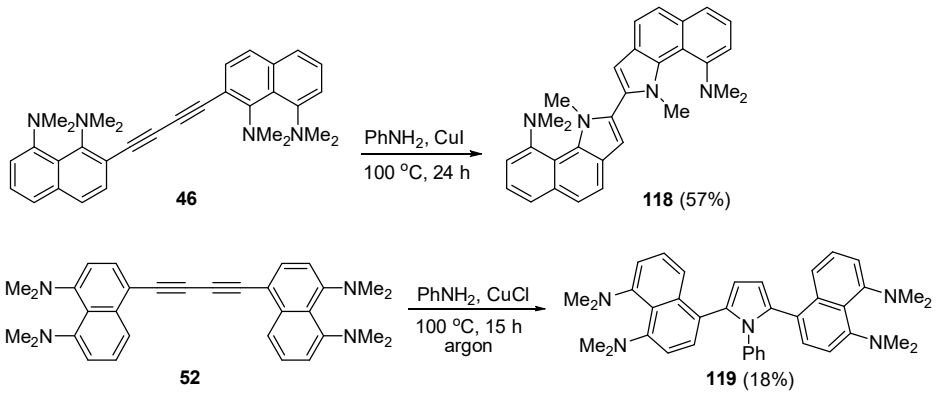
Scheme 45. Heterocyclizations of ethynyl derivatives of the proton sponge with 1,8-diiodonaphthalene.

In the presence of hydrohalic acids, vicinal amino(alkynyl) derivatives of naphthoquinone **125** were cyclized to benzo[*h*]quinoline-7,10-diones **126** in 65-90% yields (Scheme 50).[49] The reaction starts with the conjugated addition of the HX molecule to the alkynylketone fragment (**125**→**A**), which leads to a change in

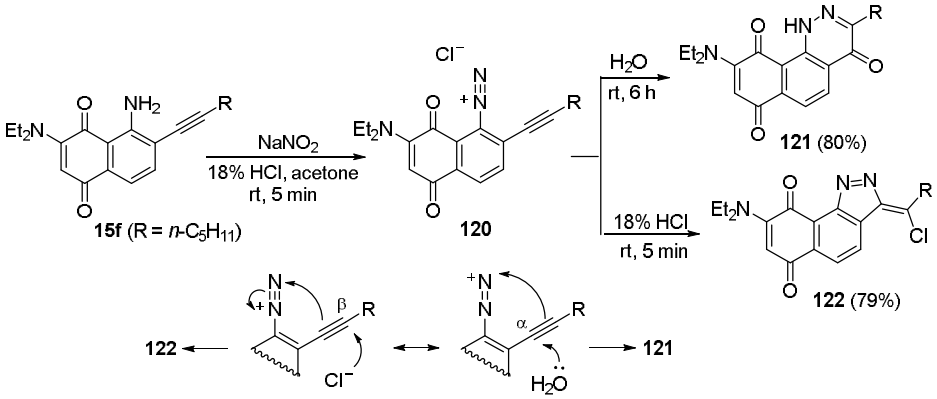
the geometry of the unsaturated side substituent and promotes further heterocyclization. The intramolecular nucleophilic attack of the amino group on the carbonyl in intermediate **B** leads to the pyridine ring closure.



Scheme 46. Proposed mechanism for the transformations **38**→**116** and **44**→**117**.



Scheme 47. Different reactivity of isomeric proton sponge-based 1,4-diaryl-1,3-butadiynes in the CuCl/aniline medium.

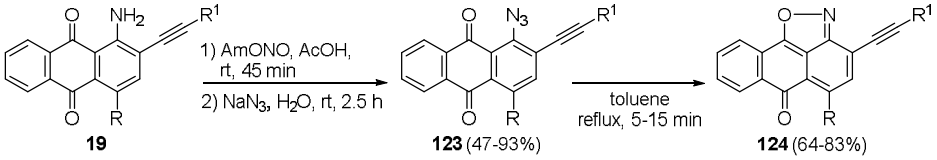


Scheme 48. Heterocyclizations of 8-amino-7-alkynylnaphthalene-1,4-dione **15f** under diazotization conditions.

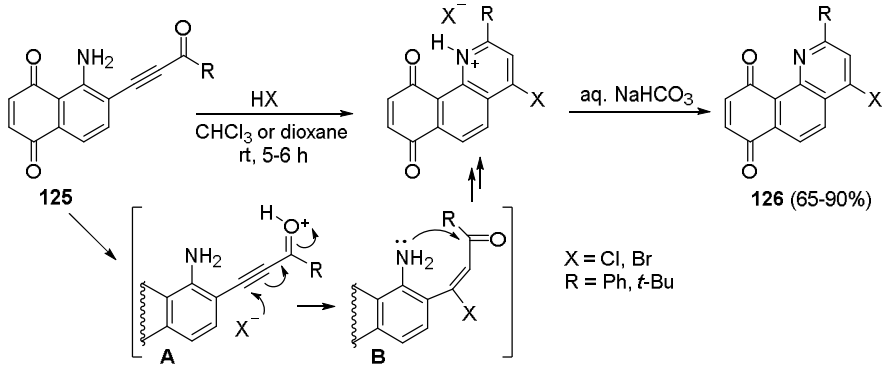
Interestingly, similar cyclization also occurs under the action of nucleophilic reagents, *e.g.* secondary amines, leading to the formation of 4-aminobenzo[*h*]quinoline-7,10-diones **127** (Scheme 51).[25]

When heated in the presence of catalytic amounts of silver nitrate and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 2-(phenylethynyl)naphthalen-1-amine **8** reacted with carbon dioxide, giving 4-hydroxy-3-phenylbenzo[*h*]quinolin-2(1*H*)-one **128** in quantitative yield (Scheme 52).[58] The mechanism of this heterocyclization includes: i) intermediate formation of carbamate **A**; ii) 6-*exo*-*dig* cyclization with the

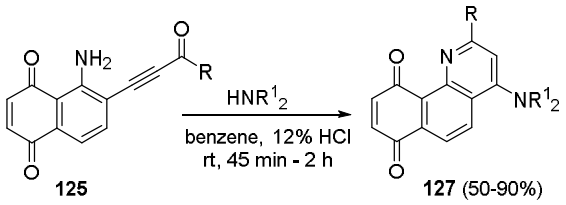
participation of carboxylate oxygen and a C≡C bond activated by coordination with silver nitrate; iii) the oxazine ring opening in intermediate **B**; iv) cyclization of isocyanate **C** to benzoquinoline **D** and, finally, tautomerization.



Scheme 49. Thermal heterocyclization of azide **123** into 6*H*-anthra[1,9-*cd*]isoxazol-6-one **124**.



Scheme 50. Acid-catalyzed cyclization of ynones **125** into benzo[*h*]quinoline-7,10-diones **126**.

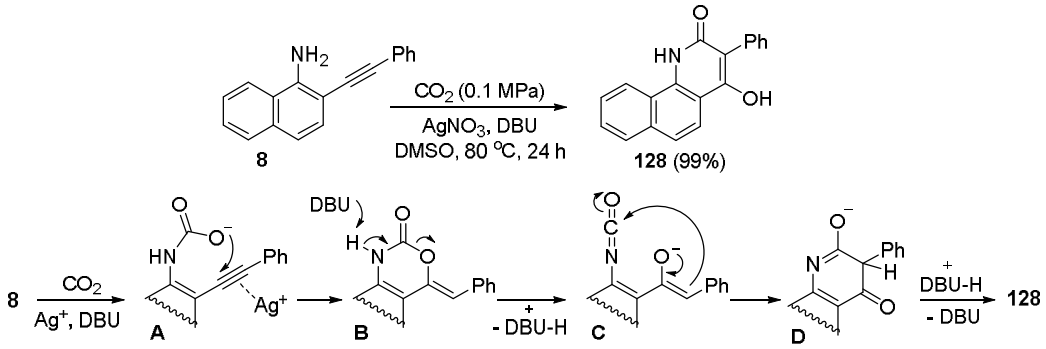


Scheme 51. Cyclization of ynones **125** into benzo[*h*]quinoline-7,10-diones **127** induced by nucleophilic addition of an amine to the C≡C bond.

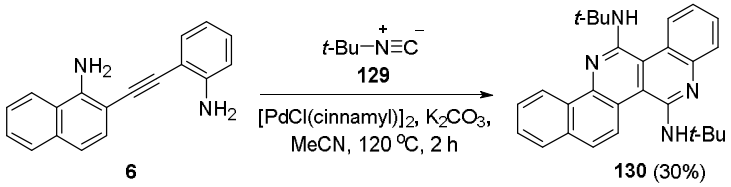
Pd-Catalyzed heterocyclization involving 2-((2-aminophenyl)ethynyl)naphthalen-1-amine **6** and two molecules of *tert*-butyl isocyanide **129** was accompanied by the closure of two pyridine rings at once, leading to the formation of benzo[*c*]naphtho[1,2-*h*][2,6]naphthyridine **130** (Scheme 53).[20]

According to the authors,[20] the interaction of starting compounds **6** and **129** in the presence of a palladium catalyst and a base gives rise to complex **A** (Scheme 54). Insertion of an isonitrile ligand into the Pd–N bond and a 1,3-H shift affords the imidoylpalladium intermediate **B**, which is rapidly converted to intermediate **C** *via* a second aminopalladation. Subsequent *anti*-carbopalladation yields the key binuclear complex Pd(II) **D**. Insertion of a second molecule of isonitrile **129** and a 1,3-H shift leads to intermediate **E**. The latter reacts with complex **C** in such a way that one Pd(II) from **E** is transferred to **C** with the formation of a seven-membered cyclic one-nuclear complex Pd(II) **F** and a three-nuclear intermediate product **G** (the

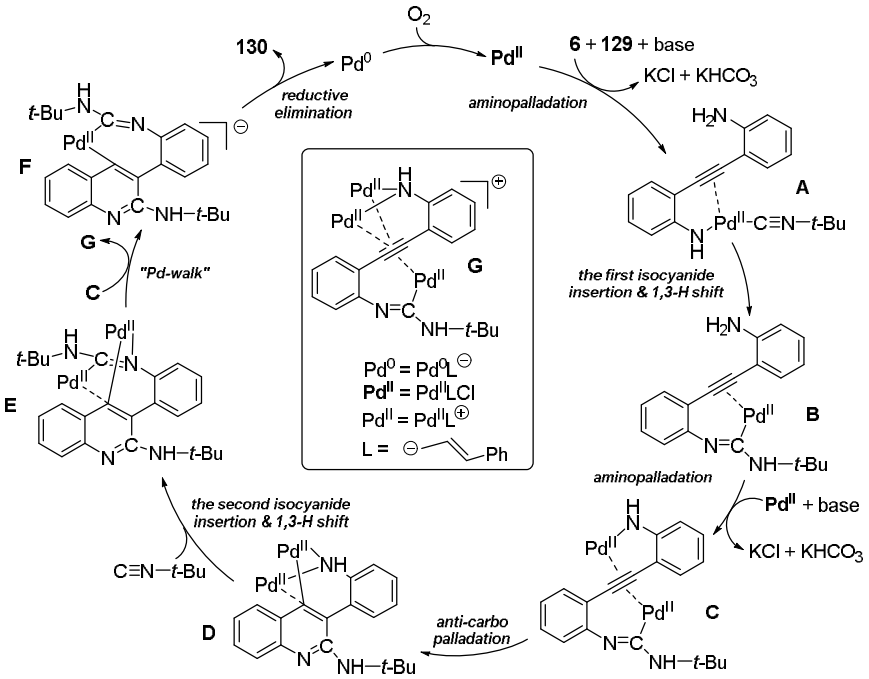
authors call this process “Pd-walk”). Reductive elimination of Pd(0) from complex **F** provides quinoline **130**. Finally, the Pd(0) particles are re-oxidized to the catalytically active Pd(II) species with atmospheric oxygen.



Scheme 52. Ag-Catalyzed cyclizations of 2-(phenylethynyl)naphthalen-1-amine with carbon dioxide.

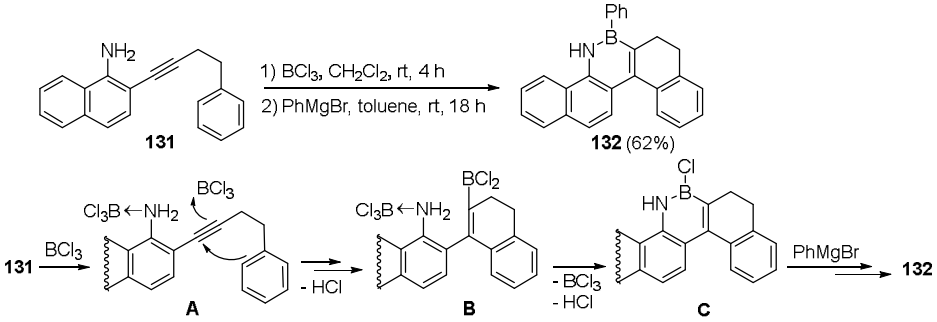


Scheme 53. Cascade Pd-catalyzed heterocyclization of 2-((2-aminophenyl)ethynyl)naphthalen-1-amine with *tert*-butyl isocyanide.



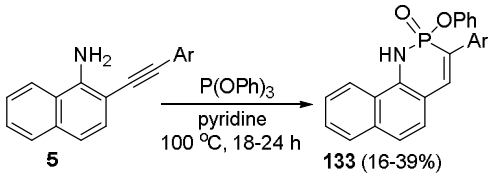
Scheme 54. Proposed mechanism for the transformation **6**→**130**.

Boron chloride-initiated cascade cyclization of 2-(4-phenylbut-1-yn-1-yl)naphthalen-1-amine **131** to 6-phenyl-5,6,7,8-tetrahydrodinaphtho[2,1-*c*:2',1'-*e*][1,2]azaborinine **132** has been described (Scheme 55).[59] The reaction starts with the coordination of BCl_3 at the amino group. The second BCl_3 molecule then activates the triple bond, promoting nucleophilic attack of the aromatic ring and 6-*endo-dig* carbocyclization. The product of these transformations, intermediate **B**, loses the BCl_3 molecule, forming an intramolecularly a new B–N bond. The resulting azaborinine **C** upon treatment with phenylmagnesium bromide gives compound **132**.



Scheme 55. Cyclization of 2-(4-phenylbut-1-yn-1-yl)naphthalen-1-amine **131** into dinaphtho[2,1-*c*:2',1'-*e*][1,2]azaborinine **132**.

Heating of alkynes **5** with $P(OPh)_3$ in pyridine led to their cyclization to the corresponding phosphinimidates, which were then hydrolyzed with a minimum amount of water to form 3-aryl-2-phenoxy-1*H*-naphtho[2,1-*e*][1,2]azaphosphine-2-oxides **133** (Scheme 56).[19] The authors consider these P,N-heterocycles as a new class of promising fluorescent sensors. Compounds **133** demonstrated bright fluorescence with an emission maximum adjusted by varying the aryl substituent (λ_{em}=441-493 nm, Φ_F=0.19-0.93). Molecules **133** are prone to dimerization due to the formation of N–H…O=P hydrogen bonds.

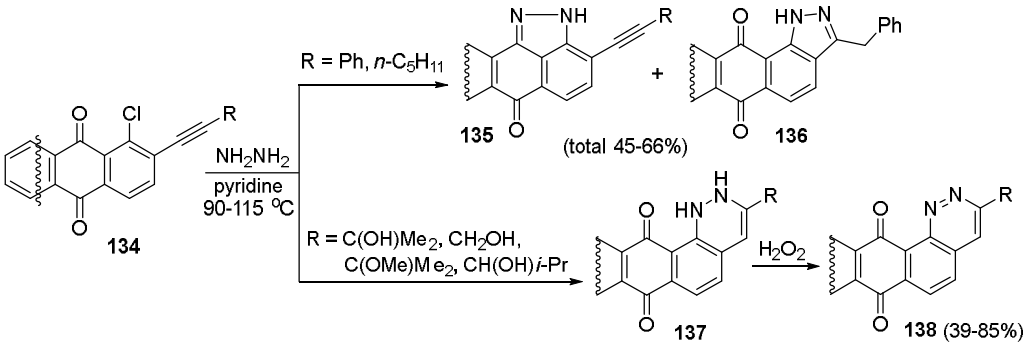


Ar = 3,4-$(CN)_2C_6H_3$, 4-CNC_6H_4, 4-$CF_3SO_2C_6H_4$, 4-$CH_3SO_2C_6H_4$, 4-$CF_3C_6H_4$, 4-$MeOC_6H_4$

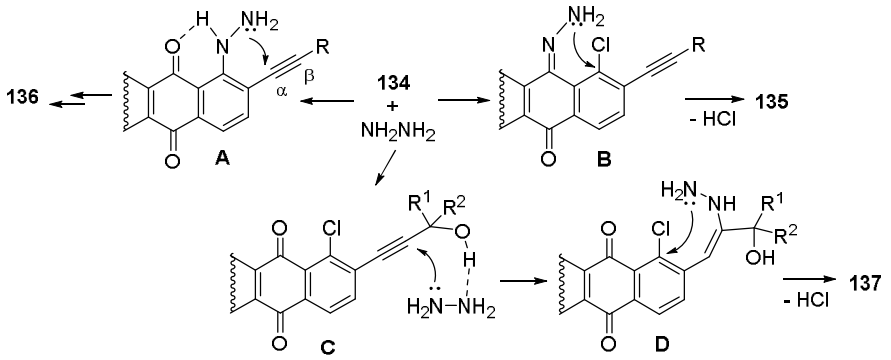
Scheme 56. Synthesis of naphtho[2,1-*e*][1,2]azaphosphines from 1-amino-2-alkynylnaphthalenes.

Heating anthraquinones **134** with hydrazine in a pyridine solution, depending on the substituent R at the C≡C bond, resulted in the formation of either fused pyrazoles **135** and **136** or dihydropyridazines **137** (Scheme 57).[60]

Compound **137** were then oxidized into pyridazines **138**. Although the authors did not discuss the mechanism of transformations, it can be assumed that pyrazole **136** is formed by replacing chlorine with a hydrazino group (intermediate **A**) and subsequent nucleophilic 5-*exo-dig* cyclization (Scheme 58). Pyrazole **135** appears to be the product of the initial formation of hydrazone **B** and subsequent aminodehalogenation. It was noted that the formation of dihydropyridazine **137** is facilitated by the hydroxy group in the R substituent due to hydrogen bonding. In this case, the most probable intermediate is enhydrazine **D**, whose geometry favors further intramolecular nucleophilic substitution of chlorine.



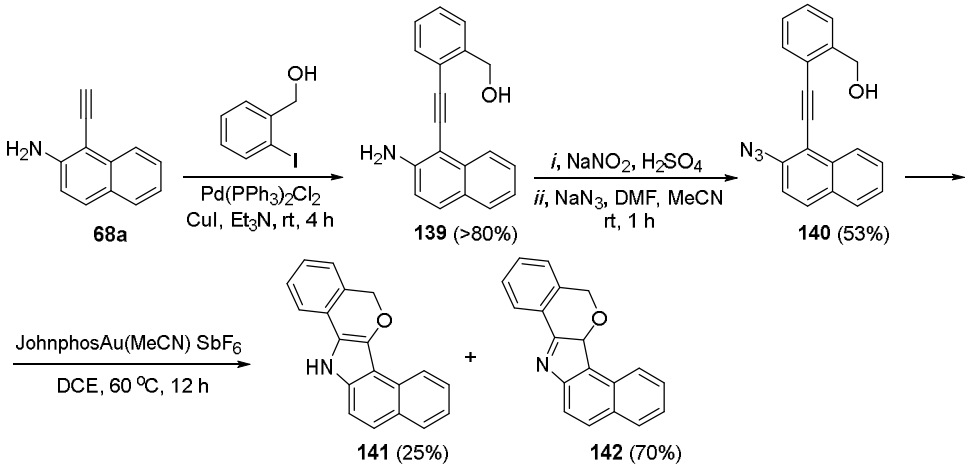
Scheme 57. Dual reactivity of 1-chloro-2-ethynylanthracene-9,10-dione towards hydrazine.



Scheme 58. Proposed mechanisms for the formation of compounds **135-137**.

3.2. Heterocyclizations of 1-alkynylnaphthalen-2-amines

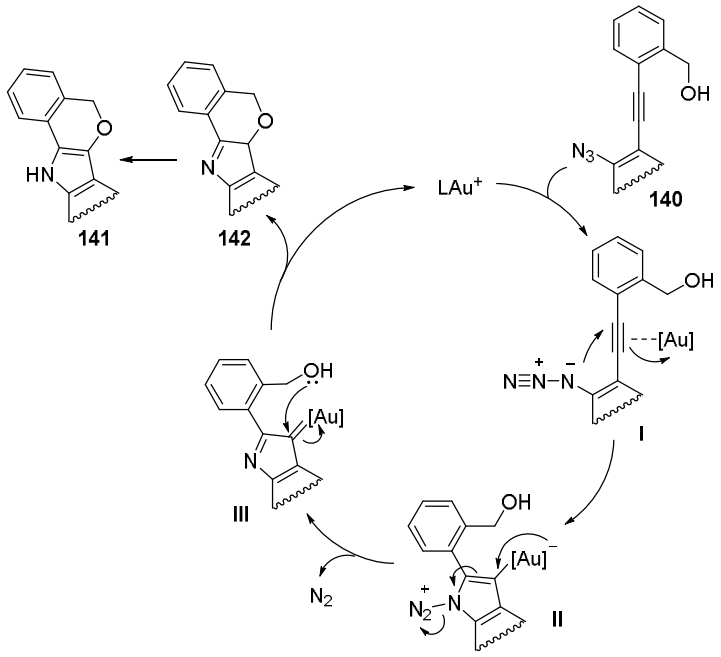
Heterocyclizations of 1-alkynylnaphthalen-2-amines are not so diverse. For example, an atom-economical approach to the fused indoles **141** and **142** starting from 1-ethynylnaphthalen-2-amine **68a** has been developed (Scheme 59).[61]



Scheme 59. Four-steps synthesis of benzo[*e*]isochromeno[4,3-*b*]indoles from 1-ethynylnaphthalen-2-amine.

At the first step of the synthesis, the Sonogashira coupling of compound **68a** with (2-iodophenyl)methanol gave the corresponding alkynyl derivative **139**. Its sequential diazotization and treatment with sodium azide afforded (2-((2-azidonaphthalen-1-yl)ethynyl)phenyl)methanol **140**. Being heated in the presence of the gold complex, the latter was transformed into benzo[*e*]isochromeno[4,3-*b*]indoles **141** and **142** (Scheme 59).

The putative mechanism of this heterocyclization is shown in Scheme 60. Initial 5-*endo-dig* nucleophilic cyclization of the Au(I)-activated alkyne moiety with tethered azide gives intermediate **II**, which, after extrusion of N_2, is transformed into α-imino gold carbenoid species **III**. Subsequently, intermediate **III** is captured by the nucleophilic hydroxyl group through a stepwise formal O−H insertion reaction to generate the corresponding polycyclic product **142**.



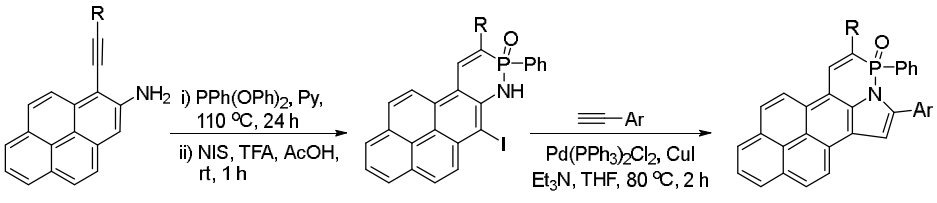
Scheme 60. Proposed mechanism for the formation of compounds **141** and **142**.

A straightforward method for the preparation of fused phosphorus- and nitrogen-containing heterocyclic pyrenes **143** and **144** has been described (Scheme 61).[43] $PPh(OPh)_2$-Mediated cyclization of 1-alkynylpyren-2-amines **59** followed by iodination of the resulting PN-heterocycle gave 6-iodo-8-phenyl-7*H*-pyreno[1,2-*e*][1,2]azaphosphinine 8-oxides **143** in good yields. Finally, a one-pot sequential Sonogashira coupling/5-*endo-dig* cyclization using the appropriate arylacetylene provided PN-heterocycles **144**. The latter exhibited intriguing redox properties and showed strong photoluminescence with a wide range of tunable emission colors, with λ_{em} ranging from blue at 459 nm to red at 622 nm in CH_2Cl_2 solution.

A new diaza[7]helicene (7,12-dihydrodibenzo[*a,g*]benzo[4,5]indolo[2,3-*c*]carbazole derivative) **145** was synthesized from aromatic enediyne **74** by catalytic domino cyclodehydrogenation in the presence of $Pd(OAc)_2$ and O_2 (Scheme 62).[46]

Palladium-catalyzed domino carbonylative cyclization of 1-(phenylethynyl)-2-(tosylamino)naphthalene **146** with alkene-tethered indole **147** into benzo[*g*]indole derivative **148** has been reported (Scheme 63).[62] By using benzene-1,3,5-triyl triformate (TFBen) as the CO source, this domino reaction proceeded smoothly with the consecutive formation of three C–C bonds and one C–I bond as shown in Scheme 64. Initially, the catalytically active Pd(0) species undergoes oxidative addition with iodide **147** to form Ar-Pd(II) complex **I**.

Regioselective intramolecular insertion of the C=C bond into the C–Pd bond of **I** leads to intermediate **II**. Then, CO is released from TFBen and inserted to **II** producing acyl-Pd(II) complex **III**. Subsequently, coordination of **III** with the triple bond of **146** facilitates the nucleophilic attack of the amino group, leading to the formation of the key intermediate **V** under the assistance of Na_2CO_3. Finally, reductive elimination of Pd(0) affords the target product **148**.

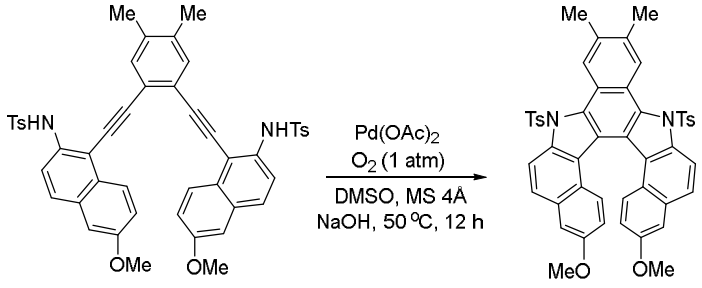


59 **143** (62-81%) **144** (63-87%)

R = *n*-Bu, 3,5-$(CF_3)_2$-C_6H_3
Ar = Ph, 4-Ph_2N-C_6H_4

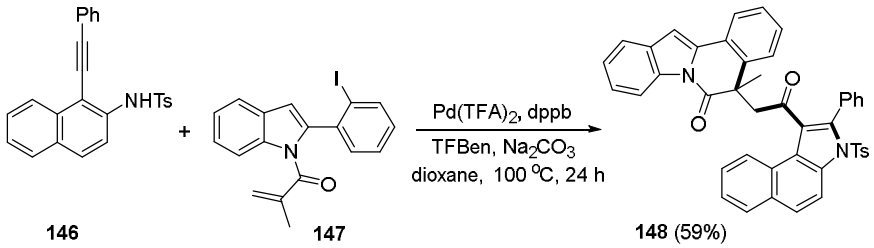
TFA is trifluoroacetic acid

Scheme 61. Synthesis of PN-heterocycles from 1-alkynylpyren-2-amines.



74 **145** (47%)

Scheme 62. Synthesis of diaza[7]helicene **145** from diyne **74**.



146 **147** **148** (59%)

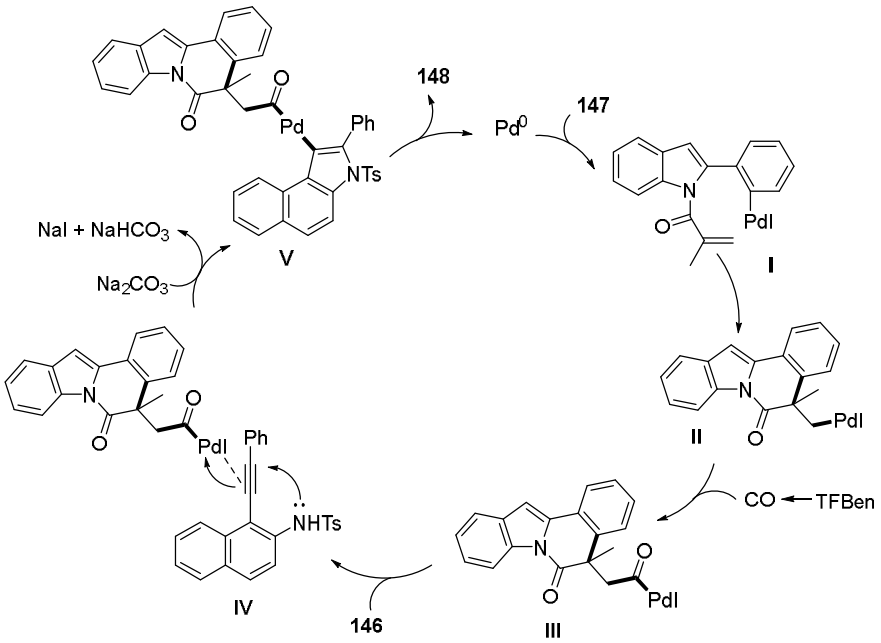
TFBen is benzene-1,3,5-triyl triformate
dppb is 1,4-bis(diphenylphosphino)butane

$Pd(TFA)_2$ is bis(2,2,2-trifluoroacetoxy)palladium

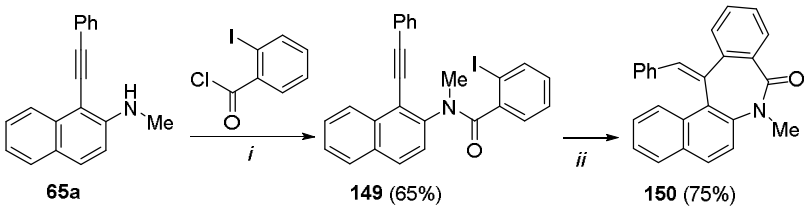
Scheme 63. Pd-Catalyzed domino carbonylative cyclization of sulfonamide **146** with alkene-tethered indole **147**.

N-Methyl-1-(phenylethynyl)naphthalen-2-amine **65a** was acylated with 2-iodobenzoyl chloride under the phase transfer catalysis conditions (in the presence of tetrabutylammonium hydrogen sulfate (TBAHS) and potash in the CH_2Cl_2-H_2O system) to form amide **149** (Scheme 65).[30] Under the same conditions, isomeric

2-alkynylnaphthalen-1-amine **24** did not enter the acylation reaction, which is associated with the steric factor (acylation of the *peri*-amino group is sterically hindered). Pd-Catalyzed intramolecular coupling involving C–I and C≡C bonds of **149** resulted in heterocyclization and formation of 13-benzylidene-7-methyl-7,13-dihydro-8*H*-benzo[*e*]naphtho[2,1-*b*]azepin-8-one **150**. The key steps of this transformation are oxidative addition with the formation of the Ar-Pd-I intermediate and subsequent electrophilic 7-*exo*-*dig* cyclization.



Scheme 64. Proposed mechanism for the formation of compound **148.**

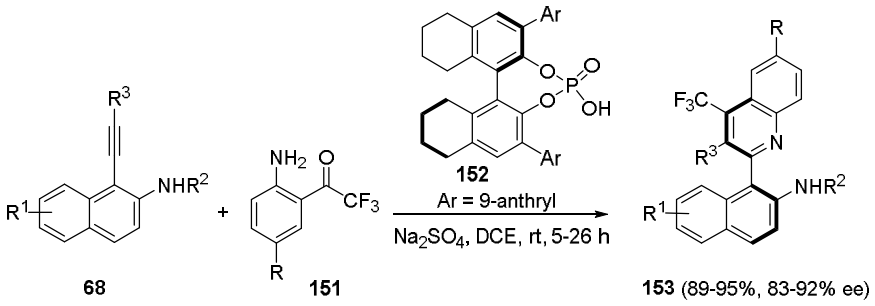


Scheme 65. Pd-Catalyzed cyclization of compound **149** into benzo[*e*]naphtho[2,1-*b*]azepine **150**.

The construction of axially chiral *N*-heterobiaryls is of great interest because of their using as organocatalysts, chiral ligands and biologically active molecules. Asymmetric heteroannulation of 1-alkynyl-2-aminonaphthalenes **68** with 2-(trifluoroacetyl)anilines **151** in the presence of a chiral phosphoric acid ester **152** led to 2-(naphthalen-1-yl)quinolines **153** in high yields and enantioselectivity (up to 95% yield, 92% *ee*) (Scheme 66).[44] The resulting compounds are new representatives of chiral biaryl *N*,*N*-ligands.

A plausible reaction pathway of this transformation is shown in Scheme 67. The dual hydrogen-bonding between *ortho*-alkynyl-naphthylamine **68** and phosphoric acid **152** is the pivotal interaction to form the complex **I**. The activated alkyne undergoes a concerted 1,5-H transfer to form the key vinylidene *ortho*-quinone methide intermediate **II**. Association with *ortho*-trifluoroacetyl aniline **151** results in a

stabilized complex **III**, which features an additional hydrogen-bonding with acid **152**. Subsequently, the attack of *ortho*-trifluoroacetyl aniline **151** to the intermediate **II** give rise to enamine specie **IV**. The acid-catalyzed intramolecular nucleophilic attack of the enamine on the carbonyl group, followed by dehydration, affords the desired axially chiral product **153**. Clearly, chiral phosphoric acid **152** plays an important role in the asymmetric induction by creating an appropriate chiral environment in the final cyclization process.



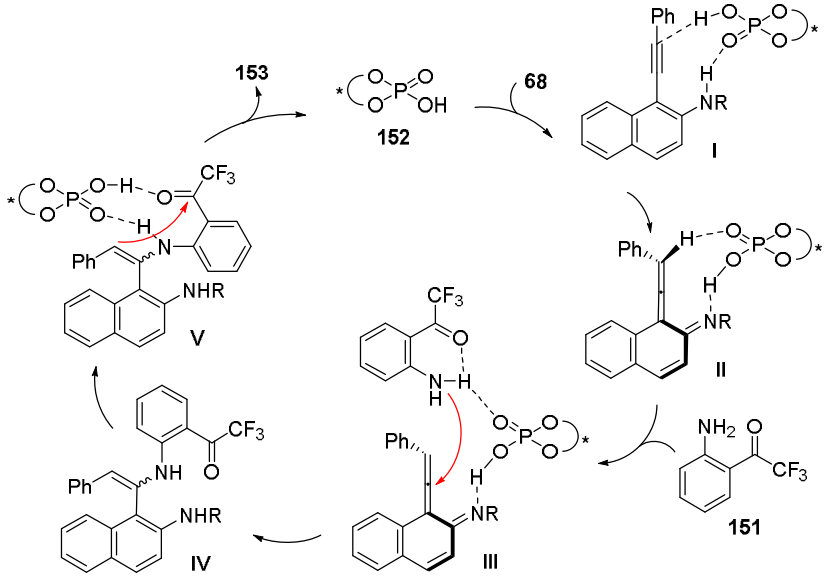
R = H, Hal, Me, Et, OMe, CF_3

R^1 = H, Me, OMe, Br, Ph, Ph–≡

R^2 = CH_2Ph, 4-Cl-C_6H_4, 4-MeO-C_6H_4, naphthyl-2

R^3 = Ph, 4-X-C_6H_4 (X = F, Cl, OMe, Me, Et, Ph, CN, CHO),
3-X-C_6H_4 (X = Cl, Br, OMe, Me, MeO_2C),
naphthyl-2, thienyl-2, thienyl-3

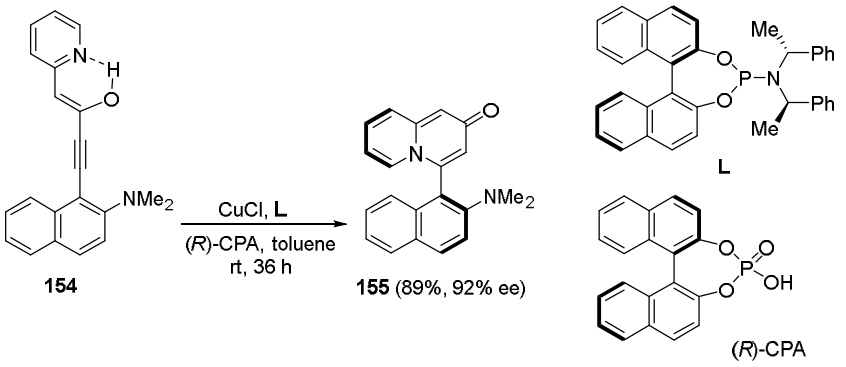
Scheme 66. Stereoselective synthesis of axially chiral 2-(naphthalen-1-yl)quinolines from compounds **68**.



Scheme 67. Proposed mechanism for the formation of compounds **153.**

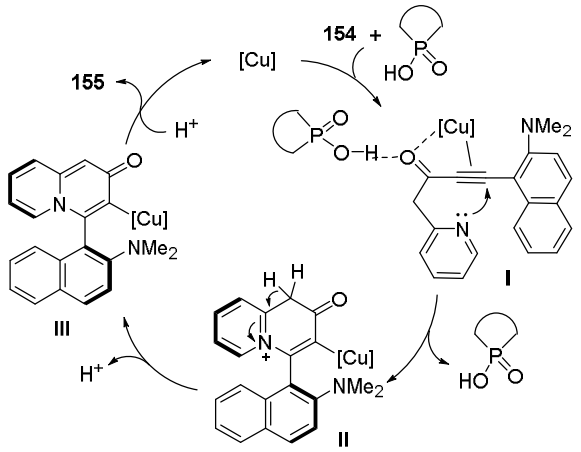
The enantioselective synthesis of axially chiral naphthylquinolizone **155** through an intramolecular atroposelective cycloisomerization of alkyne **154** in the presence of CuCl, chiral phosphoric acid ester

(*R*)-CPA and phosphoramidite ligand **L** has also been reported (Scheme 68).[63] Mechanistic studies demonstrated that Brønsted acid plays a significant role in promoting the reaction by changing the enol/keto ratio of the substrate.



Scheme 68. Enantioselective synthesis of axially chiral naphthylquinolizone **155**.

A proposed mechanism of this transformation is outlined in Scheme 69. First, substrate **154** coordinating with CPA increases the *ketone*/*enol* ratio *via* the hydrogen-bonding interactions. The CPA hydrogen-bonded to the carbonyl as well as coordination with Cu(I) in **I** makes the C≡C bond more electrophilic and facilitates the intramolecular nucleophilic addition of the pyridine aza group to the alkyne giving chiral intermediate **II**. Subsequent proton transfer affords product **155** and regenerates the copper catalyst.



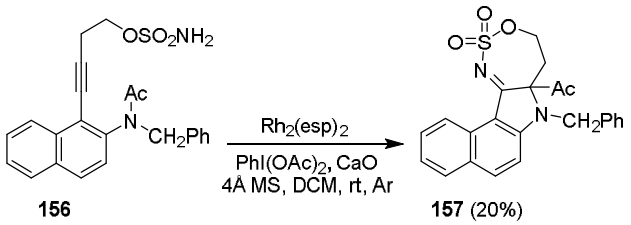
Scheme 69. Proposed mechanism for the formation of compound **155.**

A $Rh_2(esp)_2$-catalyzed cascade heterocyclization of alkyne-tethered sulfamate **156** in the presence of $PhI(OAc)_2$ oxidant provided facile access to 7,7a,8,9-tetrahydrobenzo[*e*][1,2,3]oxathiazepino[5,4-*b*]indole derivative **157** (Scheme 70).[47] The reaction is initiated by a Rh-promoted nitrene/alkyne metathesis under oxidative conditions (**156→A→B**) to form α-imino metal carbene intermediate **B**, followed by a formal carbene insertion reaction of the amide C–N bond and [1,2]-acyl shift (Scheme 71).

3.3. Heterocyclizations of 3-alkynylnaphthalen-2-amines

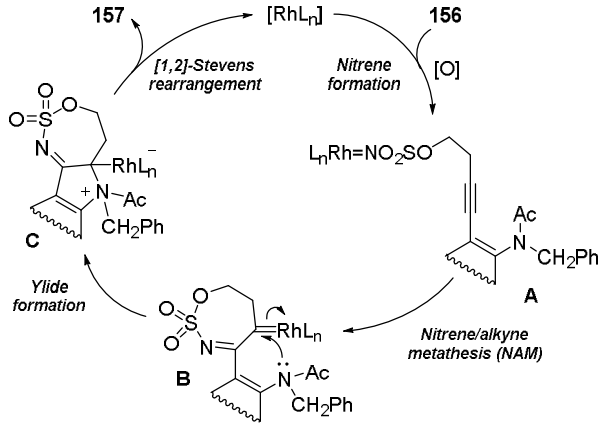
There is only one example of title transformations. Like naphthoquinone derivatives **125** (Scheme 50), in the presence of hydrohalic acids, 6-amino-5-chloro-7-(4-methyl-3-oxopent-1-yl-1-yl)naphthalen-1,4-dione

158 and 2-amino-3-(4-methyl-3-oxopent-1-yn-1-yl)naphthalen-1,4-dione **83** underwent cyclization into benzo[*g*]quinolinediones **159** and **161**, respectively (Scheme 72).[49] Upon treatment with aqueous $NaHCO_3$ salts **159** were transformed into the corresponding bases **160**.

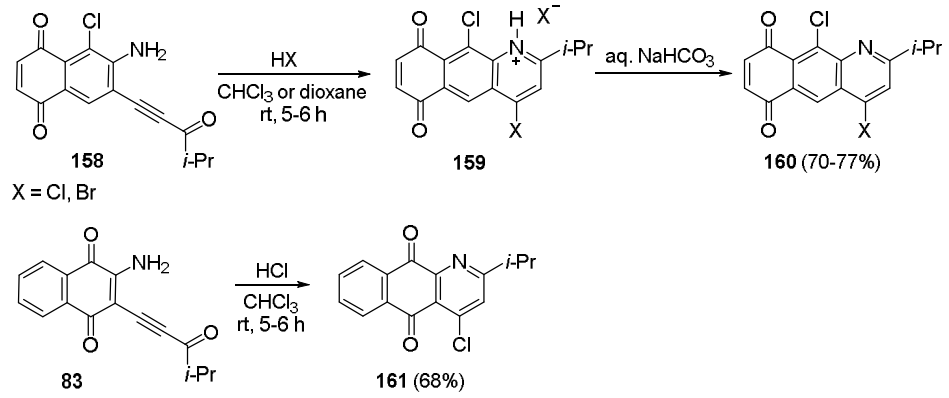


156 **157** (20%)

Scheme 70. Cascade heterocylization of sulfamate **156** into benzo[*e*][1,2,3]oxathiazepino[5,4-*b*]indole **157**.



Scheme 71. Proposed mechanism for the transformation **156**→**157**.



Scheme 72. Acid-induced heterocyclizations of 3-alkynylnaphthalen-2-amines into benzo[*g*]quinolines.

4. Conclusions

Heterocyclization of *ortho*-amino(alkynyl)naphthalenes, which are readily available *via* the Sonogashira coupling, is a valuable strategy for the synthesis of condensed *N*-heterocycles. In this regard, intramolecular transition metal-catalyzed or base-induced hydroamination of the C≡C bond of

ortho-amino(alkynyl)naphthalenes leading to the pyrrole ring closure as well as cascade processes, in which hydroamination is one of the key steps, seem to be particularly fruitful. These transformations allow to obtain benzo[*g*]indoles, benzo[*g*]indolo[3,2-*b*]indoles, benzo[*h*]indolo[1,2-*a*]quinolines, benzo[6,7]indolo[1,2-*a*]-quinolines, tribenzo[*a,c,g*]-carbazoles, acenaphtho[1,2-*b*]benzo[*g*]indoles and dibenzo[*a,g*]benzo[4,5]indolo[2,3-*c*]-carbazoles. Heterocyclizations, in which a side substituent at the triple bond or at the nitrogen atom takes part, are also useful in accessing fused *O,N*- and *O,S,N*-heterocycles such as benzo[*h*]quinolines, benzo[*g*]quinolines, benzo[*e*]isochromeno[4,3-*b*]indoles and benzo[*e*][1,2,3]oxathiazepino[5,4-*b*]indoles. An important feature of heterocyclizations of another type is the participation in the process of the second reagent, which serves as a source of an additional ring carbon or heteroatom (N, P, B) in the polynuclear reaction product-derivative of benzo[*g*]benzo[6,7]indolo[3,2-*b*]indole, benzo[*g*]indeno[1,2-*b*]indole, benzo[*c*]naphtho[1,2-*h*][2,6]naphthyridine, dinaphtho[2,1-*c*:2',1'-*e*][1,2]azaborinine, naphtho[2,1-*e*][1,2]azaphosphine, pyreno[1,2-*e*][1,2]azaphosphinine or benzo[*e*]naphtho[2,1-*b*]azepine. Most of the methods developed in this area date back to the last decade. The design of new versatile reagents for such transformations is of particular interest in the synthesis of heterocyclic compounds of new types with different ring sizes and different combinations of ring heteroatoms. There are a few examples of the synthesis based on initial transformations of the NH_2 group and subsequent heterocyclizations giving rise to benzo[*h*]cinnoline, benzo[*g*]indazole and anthra[1,9-*cd*]isoxazoles. Several reported heterocyclizations of *ortho*-amino(alkynyl)naphthalenes, which do not have a general character as synthetic methods, provide quinolines, naphtho[2,3-*g*]indazoles, naphtho[2,3-*h*]cinnolines, and dibenzo[*cd,g*]indazoles.

The specificity of 2-alkynyl- and 2,7-dialkynyl-1,8-bis(dimethylamino)naphthalenes noted in the Introduction and their increased tendency to heterocyclization with pyrrole ring closure, which is often accompanied by migration of the *N*-methyl group, is clearly due to the strong steric hindrance of these compounds. To some extent, similar behavior is also observed in the case of 1-(dimethylamino)-2-alkynylnaphthalenes.

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