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C-Ethynylpyrroles: synthesis and reactivity

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Main methods for the synthesis of C-ethynylpyrroles were systematically surveyed and described. The reaction mechanisms behind these methods are considered. The reactivity of C-ethynylpyrroles is discussed, with a main focus on cycloaddition and intramolecular cyclization reactions involving the ethynyl substituent to form new pyrrole systems.
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I. Introduction

Pyrrole structures are components of many biologically important natural compounds, such as chlorophyll, haemoglobin, vitamin B_{12}, alkaloids, *etc*., involved in the bioconversion of solar energy, oxygen transfer processes and other life supporting reactions.[1] C-Ethynyl derivatives occupy an important place among representatives of the pyrrole series. Due to the simultaneous presence of such highly reactive moieties as the pyrrole ring and the carbon – carbon triple bond, these compounds can be successfully used for the synthesis of various functionalized pyrroles, as well as conjugated and combined heterocyclic systems. This is why C-ethynylpyrroles have attracted keen attention.

A large amount of data has been accumulated on the methods for the synthesis of C-ethynylpyrroles and their reactions.[2] However, to date there are no reviews on this subject. Hence, in the present review we include not only the studies published in the past two decades, when the chemistry of ethynylpyrroles was extensively developed, but also earlier publications in this area. The aim of the systematic analysis of advances in this area of chemistry of heterocyclic compounds is to consider all known synthetic approaches to C-ethynylpyrroles and summarize the data on their reactivity.

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An analysis of the methods for the synthesis of C-ethynylpyrroles published in the literature shows that they are based either on transformations of functional substituents in the heterocycle or on the introduction of an available ethynyl group into the pyrrole nucleus. Some methods for the synthesis of C-ethynylpyrroles involve the simultaneous construction of the pyrrole ring. In the present review, the data are successively considered according to these approaches.

The reactivity of C-ethynylpyrroles and their application as building blocks in the synthesis of functionalized pyrrole-containing systems are determined primarily by the presence of the acetylenic substituent. Hence, in the present review we consider the reactions of C-ethynylpyrroles proceeding mainly at the acetylenic group: reactions with the participation of the acetylenic hydrogen atom and the addition to the triple bond, including the cycloaddition and intramolecular cyclization.

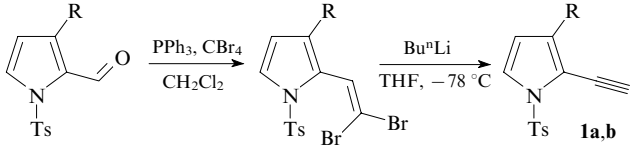
II. Methods for the synthesis of C-ethynylpyrroles

1. Methods based on transformations of functional substituents attached to the pyrrole ring

The transformation of a substituent attached to the pyrrole ring is one of conventional approaches to the synthesis of C-ethynylpyrroles that still retains its importance.

Thus, ethynylpyrroles **1a**,**b** containing the terminal triple bond were synthesized by the Corey – Fuchs reaction of N-substituted pyrrole-2-carbaldehydes, triphenylphosphine and CBr_4 followed by the elimination of the bromine molecule in the reaction with Bu^nLi (Scheme 1).[3, 4]

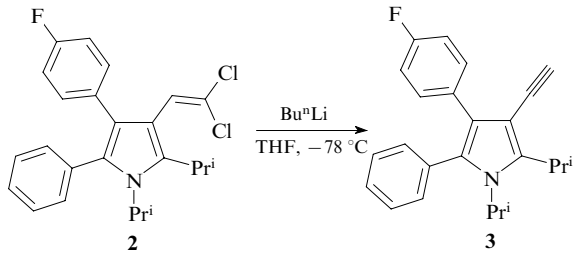
Scheme 1



R = H (**a**), Ph (**b**); Ts is *p*-toluenesulfonyl

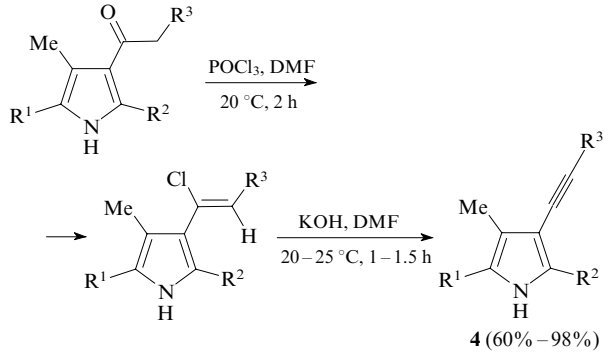
Under the same conditions, the removal of the chlorine molecule from 3-(2,2-dichloroethenyl)pyrrole **2** gives rise to 3-ethynylpyrrole **3** (Scheme 2).[5]

Scheme 2



A large series of ethynylpyrroles **4** were synthesized by the transformation of 3-acylpyrroles unsubstituted at the nitrogen atom with the Vilsmeier complex to form 3-(1-chloroethenyl)pyrroles followed by the elimination of HCl in a basic medium (Scheme 3).[6–12]

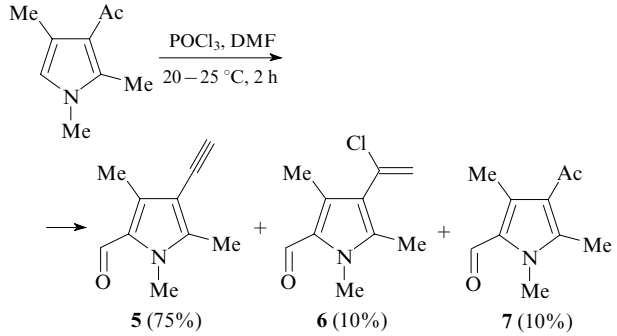
Scheme 3



R^1 = H, Me, CHO, CO_2Et, CO_2Bn; R^2 = H, Me, CHO, CO_2Et; R^3 = H, Me, Ph, n-$C_{16}H_{33}$

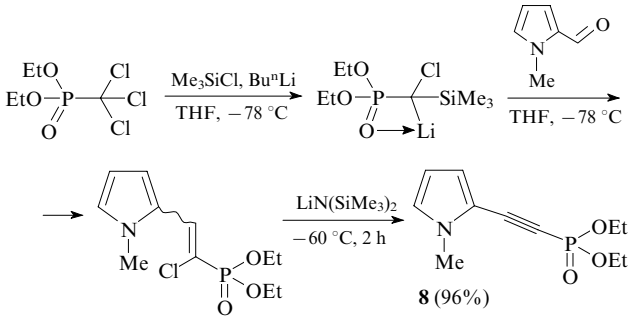
The treatment of 3-acetyl-1,2,4-trimethylpyrrole with the Vilsmeier reagent results both in the formylation at the 5-position of the pyrrole ring and the transformation of the acetyl group into the ethynyl one. This gives a mixture of 3-ethynyl- (**5**), 3-(1-chloroethenyl)- (**6**) and 3-acetyl-1,2,4-trimethylpyrrole-5-carbaldehydes (**7**) (Scheme 4).[13] The yield of ethynylpyrrole **5** can be increased by means of the quantitative dehydrohalogenation (EtONa, EtOH, 10 min) of chloroethenyl derivative **6**. The heating of the latter under reflux in DMF with an aqueous solution of potassium carbonate affords a mixture of pyrroles **5** and **7** in 75% and 25% yields, respectively.

Scheme 4



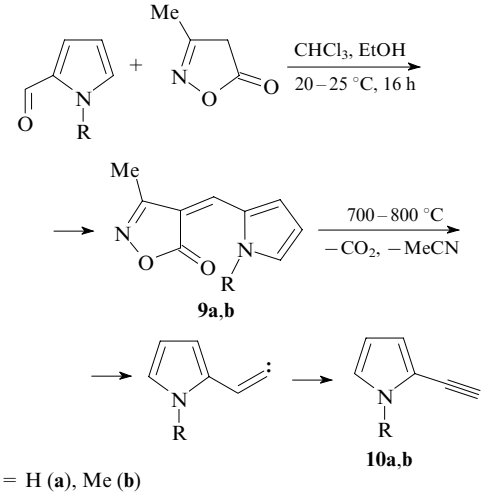
Ethynylpyrrole **8** was synthesized by the one-pot method from $(EtO)_2P(O)CCl_3$ and 1-methylpyrrole-2-carbaldehyde. The synthesis involves the Peterson olefination to form the chloroethenylphosphonate intermediate followed by its dehydrochlorination with lithium hexamethyldisilazide (Scheme 5).[14]

Scheme 5



The pyrolysis of ethenylpyrroles **9a**,**b**, which are produced by the reactions of the corresponding pyrrole-2-carbaldehydes with methylisoxazolone, provides an efficient route to 2-ethynylpyrroles **10a**,**b** (in 95% and 84% yields, respectively). Apparently, the reaction proceeds through the intermediate formation of carbene (Scheme 6).[15]

Scheme 6

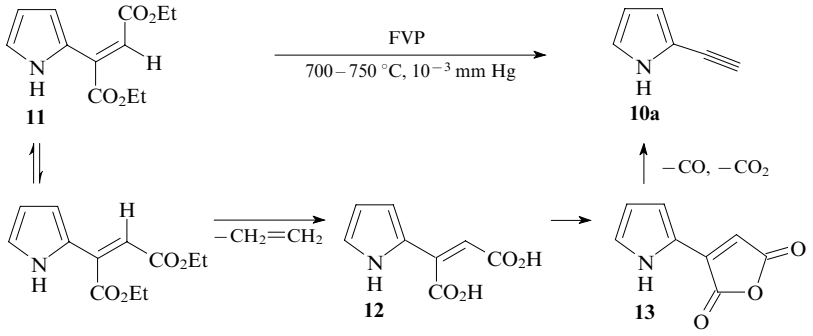


R = H (**a**), Me (**b**)

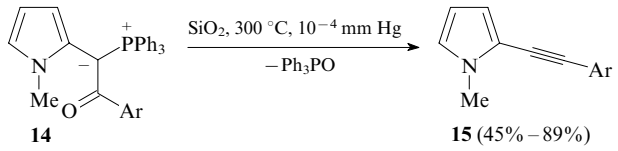
Flash vacuum pyrolysis (FVP) of 2-(1,2-diethoxycarbonylethenyl)pyrrole **11** affords 2-ethynylpyrrole **10a** as the major product.[16] The sequence of transformations involves, apparently, the *E*–*Z* isomerization of alkene **11** accompanied by the elimination of ethylene from one or both ester groups, the thermal dehydration of diacid **12** to form anhydride **13** and the elimination of CO and CO_2 from the latter compound (Scheme 7). This scheme was confirmed by the pyrolysis of maleic acid **12** by itself and its anhydride **13** (which was synthesized by the dehydration or mild thermolysis of diacid **12**). Under similar conditions, both reactions give 2-ethynylpyrrole **10a**.[16, 17]

The thermal fragmentation of π-excessive heteroaroylmethylenephosphoranes **14** is accompanied by the elimination of triphenylphosphine oxide to form arylethynylpyrroles **15** in good yield (Scheme 8).[18] The fragmentation of phosphoranes under electron impact also gives ions corresponding to pyrroles **15**.

Scheme 7

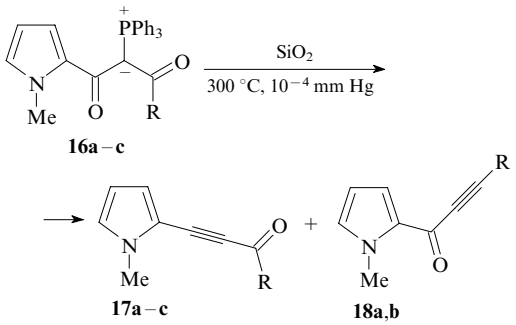


Scheme 8



Ar = Ph, 2-pyrrolyl, 2-thienyl (Th), 2-furyl (Fu)

Scheme 9



R = Me (**a**), Ph (**b**), OEt (**c**)

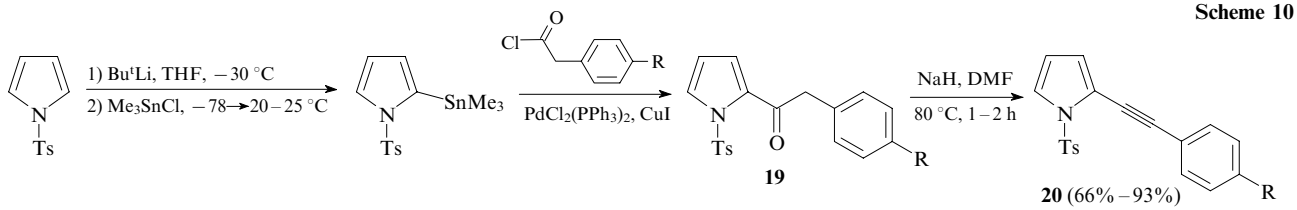
Under similar conditions, phosphoranes containing two carbonyl groups [α-acetyl- (**16a**) and α-benzoyl-α-(*N*-methylpyrrol-2-ylcarbonyl)methylenephosphoranes (**16b**)] are transformed into isomeric pyrroles **17a**,**b** and **18a**,**b** in a ratio of 1 : 1 (for **16a**) and 1 : 3 (for **16b**). By contrast, phosphorane **16c** containing the ethoxycarbonyl group is selectively transformed into pyrrolylpropynoate **17c** in 86% yield (Scheme 9).[18]

The treatment of *N*-toluenesulfonylpyrroles **19** with sodium hydride afforded 2-phenylethynylpyrroles **20**. The presence of the *N*-tosyl protecting group is a necessary condition for the reaction to be efficient (Scheme 10).[19]

The unusual anionic domino process based on the Bu^{n}Li-induced rearrangement of 3-(1-methylpyrrol-2-yl)-3-methylsulfanyl-2-(2-bromophenyl)acrylonitrile **21** (the product of the base-catalyzed condensation of nitrile **22** with 1-methylpyrrole-2-carbodithioate followed by the S-methylation of enethiolate with methyl iodide) was described in the literature. This transformation gives ethynylpyrrole **23** in good yield (Scheme 11).[20]

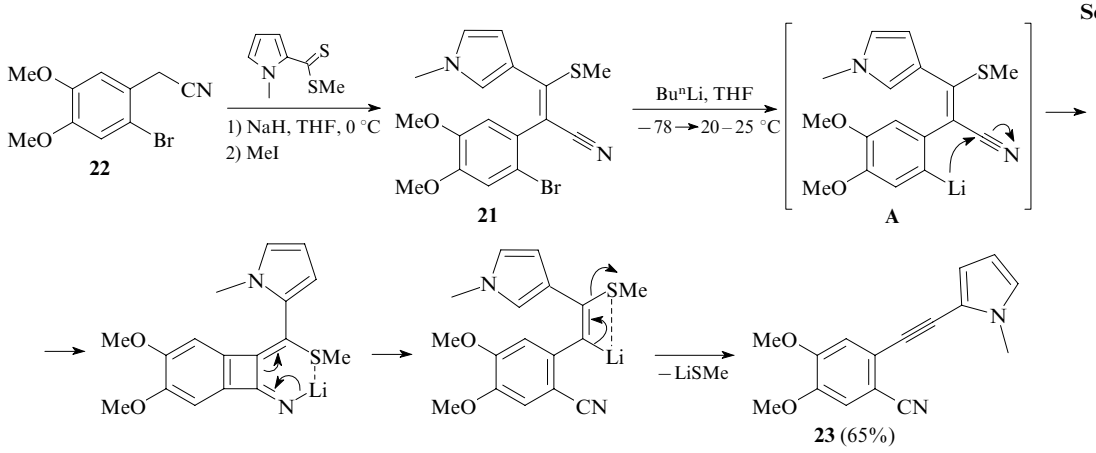
The proposed mechanism of the rearrangement involves a series of cascade reactions: the bromine–lithium exchange reaction, the fragmentation of the intermediate **A** accompanied by the intramolecular transfer of the nitrile group and the elimination of lithium methanethiolate.

Scheme 10



R = H, Me, OMe, Cl

Scheme 11

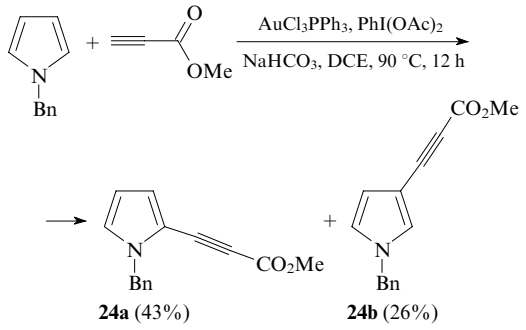


2. Insertion of the ethynyl group into the pyrrole ring

The direct ethynylation of the unfunctionalized pyrrole ring with electron-deficient acetylene was recently reported.[21] The reaction is mediated by the Au-catalyzed C–H-activation of aromatic and acetylenic moieties.

Thus, in the presence of $AuCl_3PPh_3$ (5 mol.%) and $PhI(OAc)_2$ (1.5 equiv.), *N*-benzylpyrrole reacts with methyl propynoate to form a mixture of 2- and 3-ethynyl-*N*-benzylpyrroles **24a**,**b** (Scheme 12).

Scheme 12



DCE is 1,2-dichloroethane

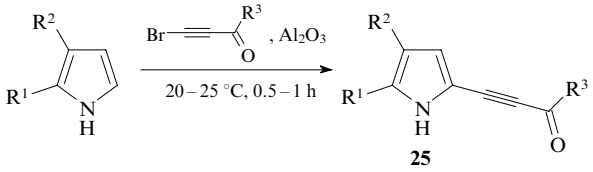
Two possible pathways proposed by Haro and Nevado involve the formation of the Au^I acetylene complex **A** as the first step (Scheme 13). According to the first pathway, this complex is oxidized in the presence of $PhI(OAc)_2$ to form the Au^{III} acetylene intermediate **B**, and the reaction of the latter with pyrrole proceeds *via* the electrophilic aromatic substitution to give the intermediate **C**. The reductive elimination gives rise to a new $C(sp_2)-C(sp)$ bond and the formation of ethynylpyrrole.

According to an alternative pathway, the complex **A** is supposed to react with $PhI(OAc)_2$ to form the electrophilic ethynyliodonium complex **D** followed by the addition of pyrrole. The vinyl intermediate **E** is transformed into ethynylpyrrole *via* β-elimination (see Scheme 13).

It should be emphasized that only *N*-benzylpyrrole is involved in this reaction. Although this method holds promise, it cannot be considered as a preparative procedure because it is nonselective and requires the use of a 1.5-fold excess of the oxidant [$PhI(OAc)_2$].

In the past years, the direct ethynylation of pyrroles with ethynyl halides or pseudohalides, which is sometimes called in the literature as the 'inverse Sonogashira reaction', has attracted great attention.[22] Initially, we suggested this name in the study,[23] in which we described for the first time the reaction of pyrroles with electrophilic haloacetylenes on aluminium oxide in the absence of solvents or specially added catalysts and bases (Scheme 14, for the complete scheme of the synthesis see below).

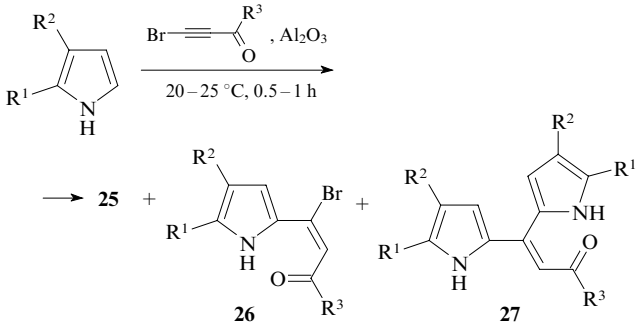
Scheme 14



It should be admitted that this name is not an apt one because the chemical essence of this type of ethynylation has nothing in common with the palladium-catalyzed Sonogashira cross-coupling.

This reaction is the first example of the ethynylation of pyrroles, which proceeds in the absence of transition metals, bases and solvents.[23–28] It should be emphasized that this type of cross-coupling does not take place in the absence of Al_2O_3 (or in a Al_2O_3–solvent suspension). In addition to 2-(2-acylethynyl)pyrroles **25**, these reactions afford products of another type (Scheme 15).

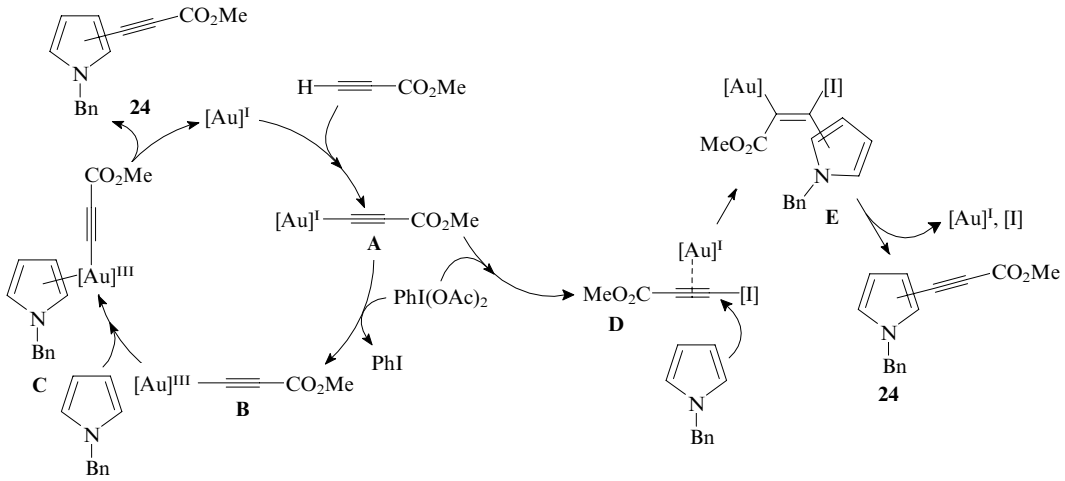
Scheme 15



R^1 = H, Ph, 4-$Me_2NC_6H_4$, 4-$MeOC_6H_4$, 4-ClC_6H_4, 4-PhC_6H_4; R^2 = H, Ph; R^1-R^2 = $(CH_2)_4$; R^3 = Ph, 2-Th

The reaction mechanism involves the addition and elimination steps. Intermediates, 2-(2-acyl-1-bromoethe-

Scheme 13

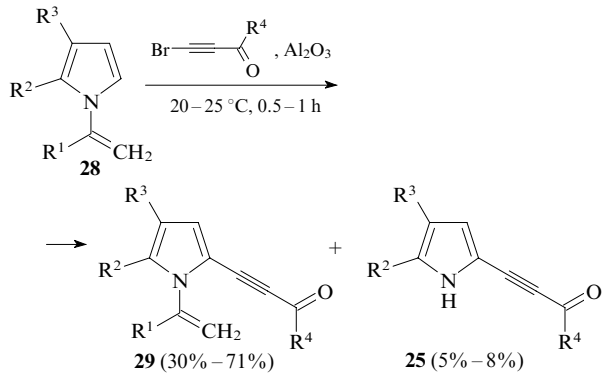


nyl)pyrroles **26**, were isolated from the reaction mixture and were transformed on Al_2O_3 into the corresponding ethynylpyrroles **25**.[24, 25]

2-Acyl-1,1-bis(pyrrol-2-yl)ethenes **27** are generated as by-products of the cross-coupling apparently as a result of the exchange of bromine atom in intermediates **26** for the second pyrrole molecule.[23–25] Their yields, which are usually not higher than 20%, are substantially increased (to 40%) in the presence of an excess of pyrrole, at elevated temperature or at longer reaction times.

In the reactions with acylbromoacetylenes on Al_2O_3, *N*-vinyl- and *N*-isopropenylpyrroles **28** are regioselectively transformed into 2-acylethynylpyrroles **29** (Scheme 16).[25, 29]

Scheme 16

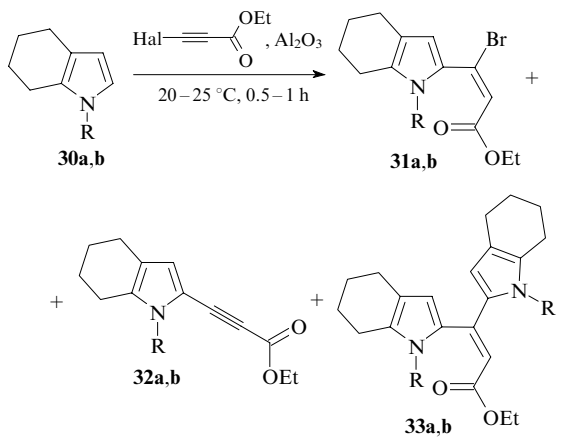


R^1 = H, Me; R^3 = H: R^2 = H, Ph; R^2–R^3 = $(CH_2)_4$; R^4 = Ph, 2-Th

The ethynylation of *N*-isopropenylpyrroles **28** (R^1 = Me) is accompanied by the deisopropenylation yielding small amounts of *N*-H-pyrroles **25**. This is apparently due to the HBr-catalyzed hydrolysis of the *N*-isopropenyl group both in the starting compounds and the end products, because Al_2O_3 always contains water of hydration.[29]

Under similar conditions, ethyl bromopropynoate reacts with 4,5,6,7-tetrahydroindole (**30a**) on aluminium oxide to give ethyl 3-bromo-3-(4,5,6,7-tetrahydroindol-2-yl)propenoate (**31a**) as the major intermediate (Scheme 17).[25, 30] In the presence of a larger amount of Al_2O_3 (a 50-fold mass excess), intermediate **31a** was not detected, and the reaction produced ethyl 3-(4,5,6,7-tetrahydroindol-2-yl)propynoate (**32a**) and ethyl 3,3-bis(4,5,6,7-tetrahydroindol-2-yl)acrylate

Scheme 17



R = H (**a**), CH=CH$_2$ (**b**); Hal = Br, I

(**33a**) (in a 38 : 62 ratio). The addition of K_2CO_3 to aluminium oxide leads to an increase in the percentage of propynoate **32a** in the reaction mixture to 58% (the preparative yield is 46%), whereas the percentage of acrylate **33a** decreases to 34%.

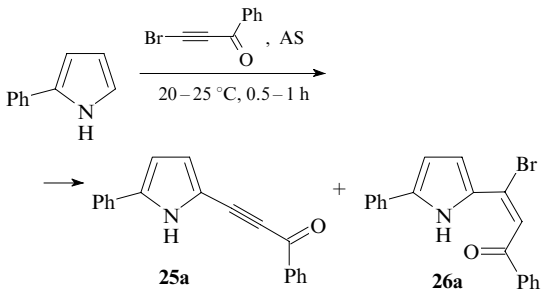
Unlike ethyl bromopropynoate, ethyl iodopropynoate selectively reacts with 4,5,6,7-tetrahydroindole (**30a**) in the presence of a 10- or 50-fold excess of aluminium oxide to form acrylate **33a** in 79% yield (see Scheme 17).

The reaction of *N*-vinyl-4,5,6,7-tetrahydroindole (**30b**) with both bromopropynoate and iodopropynoate (in the presence of a 50-fold mass excess of Al_2O_3) gives mainly the cross-coupling product, ethyl 3-(1-vinyl-4,5,6,7-tetrahydroindol-2-yl)propynoate (**32b**) (see Scheme 17).

As mentioned above, this type of cross-coupling was performed for the first time on aluminium oxide. This gave rise to a question whether Al_2O_3 is a unique medium for this reaction or other oxides and salts can also stimulate this process.

To answer this question, we studied the reaction of 2-phenylpyrrole with benzoylbromoacetylene on different metal oxides and salts in the absence of solvents (Scheme 18).[31]

Scheme 18



AS = MgO, CaO, ZnO, BaO, Al_2O_3, TiO_2, ZrO_2, $CaCO_3$, $ZrSiO_4$

It appeared that, depending on the active surface used, this reaction affords either cross-coupling product **25a** or the product of the addition of 2-phenylpyrrole to the triple bond of acetylene (**26a**). The activity of metal oxides in the ethynylation reaction decreases in the following series (the percentage of benzoylethynylpyrrole **25a** in the reaction mixture is given in parentheses): ZnO (81), BaO (73), Al_2O_3 (71), MgO (69), CaO (50). The oxides SiO_2,[32] TiO_2 and ZrO_2 and the salts $CaCO_3$ and $ZrSiO_4$ are inert with respect to ethynylation but facilitate the formation of exclusively 2-(2-benzoyl-1-bromoethenyl)-5-phenylpyrrole (**26a**); in the presence of ZrO_2, the yield of this product reaches 60%.[25, 31]

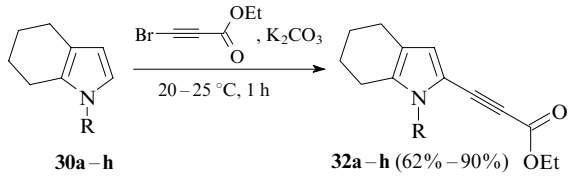
According to the X-ray diffraction data, after chromatography on alumina, 2-(2-benzoylethynyl)-5-phenylpyrrole (**25a**) crystallizes in two visually discernible forms (prisms and needles), which are *cis* and *trans* rotamers that differ in the mutual arrangement of the nitrogen atom and the carbonyl group.[25, 33] The prisms that are formed in an insignificant amount are less stable and are partially transformed into needles during the recrystallization. Apparently, this is the first example of the experimentally observed hindered rotation about the C(sp)–C(sp$_2$) bond.

A study of the above-mentioned series of the surfaces for the ethynylation of 4,5,6,7-tetrahydroindole (**30a**) with ethyl bromopropynoate showed that the oxides CaO, MgO, ZnO and BaO have higher activity than aluminium oxide.[34] The

best results were achieved with the use of potassium carbonate as the active medium. In the latter case, the selective formation of cross-coupling product **32a** was observed (yield 90%).

Under these conditions, other N-derivatives of 4,5,6,7-tetrahydroindole **31b–h** are also selectively ethynylated with bromopropynoate at the 2-position to form propynoates **32a–h** (Scheme 19).[25,35] In solvents (diethyl ether, chloroform), this reaction does not proceed either in the presence or in the absence of K_2CO_3. The regioselectivity of the ethynylation is not disturbed even by such bulky substituents as CH(Me)OPr^i and CH(Me)OBu^n, although the reactants have to be in contact with each other for a much longer time (12 h *vs* 1 h) and the portionwise addition of bromopropynoate to the reaction mixture is required. Evidently, the low reaction rate is due to the steric shielding of the 2-position of the pyrrole ring by the substituent R.

Scheme 19

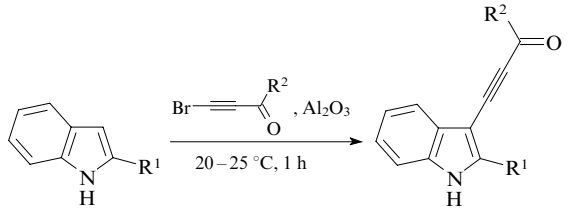


30a–h **32a–h** (62%–90%)

R = H (**a**), CH=CH$_2$ (**b**), Et (**c**), Bn (**d**), CH(Me)OPr^i (**e**), CH(Me)OBu^n (**f**), (CH$_2$)$_2$SEt (**g**), (CH$_2$)$_2$SPr^n (**h**)

Indoles (benzopyrroles) **34a**,**b** smoothly react with benzoylbromoacetylene on aluminium oxide, resulting in the chemo- and regioselective formation of 3-benzoylethynylindoles **35a**,**b** (R^2 = Ph, Scheme 20).[25,36] This is the first example of the direct ethynylation of the indole nucleus. The reaction with bromopropynoate gives the corresponding ethynylation products **36a**,**b** (R^2 = OEt) in 17% and 12% yields, respectively (see Scheme 20).[25,37]

Scheme 20



34a,**b** **35a**,**b**; **36a**,**b**

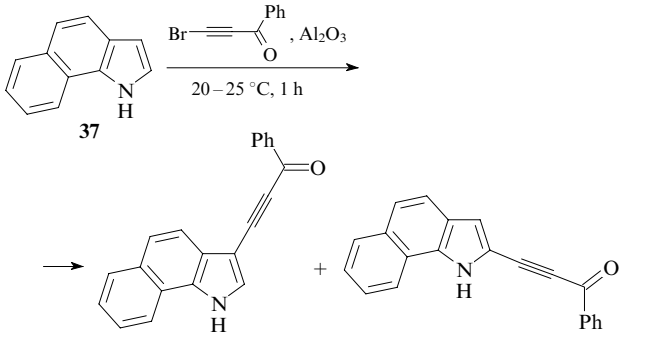
R^1 = H (**a**), Me (**b**); R^2 = Ph (**35**), OEt (**36**)

Under similar conditions, benz[*g*]indole (**37**) reacts with benzoylbromoacetylene to form a mixture of the corresponding 3- and 2-ethynyl derivatives in a total yield of 45% (Scheme 21).[25,36]

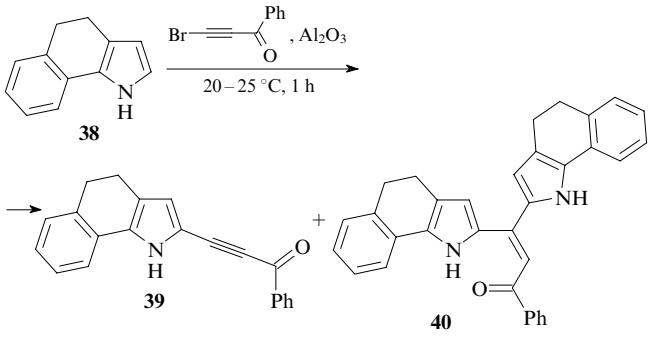
Formally being a substituted pyrrole, 4,5-dihydrobenzo[*g*]indole (**38**) readily reacts with benzoylbromoacetylene on aluminium oxide to form 2-ethynyl derivative **39** in 68% yield (Scheme 22). This reaction also produced bis(dihydrobenzo[*g*]indolyl)ethene **40** in 9% yield.[25,36]

The above-considered new version of the ethynylation of the pyrrole ring acquired a particular importance since the classical transition metal-catalyzed cross-coupling reactions, including the Sonogashira reaction, are not suitable for the preparation of ethynylpyrroles containing acceptor groups at the triple bond.[38–41]

Scheme 21



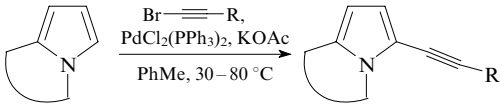
Scheme 22



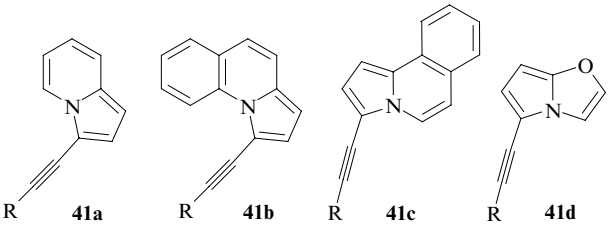
Several examples of the reactions of unfunctionalized pyrroles with haloacetylenes in the presence of transition metals were reported.[42]

Thus, the transition metal-catalyzed direct ethynylation of electron-rich N-fused heterocycles with haloacetylenes was carried out for the first time in 2007 (Scheme 23).[43] It was shown that ethynyl derivatives of indolizine (**41a**), pyrroloquinoline (**41b**), pyrroloisoquinoline (**41c**) and pyrroloxazole (**41d**) can be regioselectively synthesized from the corresponding heterocyclic systems in the presence of $PdCl_2(PPh_3)_2$ and KOAc in toluene.

Scheme 23



41a–d (50%–90%)



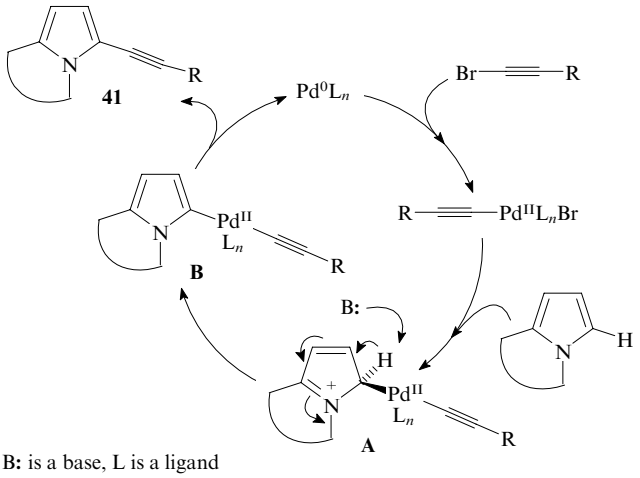
for **41a**: R = Bu^n, Ph, $SiMe_3$;

for **41b**: R = CO_2Et, , $C_6H_4CO_2Et$-4, 2-naphthyl (Naph), $SiMe_3$;

for **41c**: R = Bu^n, Ph, $SiMe_3$, CO_2Et, ; for **41d**: R = Ph

The proposed mechanism of the direct Pd-catalyzed C–H-ethynylation of the above-mentioned heterocycles (Scheme 24) involves the nucleophilic attack of ethynylpalladium on the most electron-rich atom C(2) of the pyrrole ring to form the iminium intermediate **A**. The deprotonation of the latter gives the Pd^{II} intermediate **B**, and the subsequent reductive elimination affords ethynylpyrroles **41**.

Scheme 24

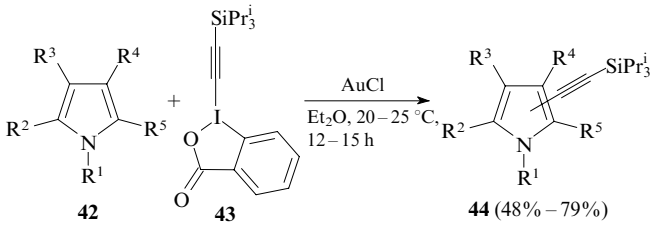


B: is a base, L is a ligand

The ethynylation of substituted pyrroles **42** was performed with the use of the benziodoxolone derivative of hypervalent iodine **43** instead of bromoacetylenes.[44] The reaction proceeds under mild conditions (at room temperature) in the presence of catalytic amounts of AuCl to form 2- or 3-ethynylpyrroles **44** in good yields (Scheme 25). However, this method is limited to the synthesis of ethynylpyrroles containing the triisopropylsilyl group at the C≡C bond.

The pathway of this reaction can be controlled by blocking the 2 (or 3) positions of the pyrrole ring or inserting a bulky substituent at the nitrogen atom.

Scheme 25



R^1 = H, Me, $SiPr^i_3$; R^2 = H, Me, Et, Ph; R^3 = H, Ac; R^4, R^5 = H, Me

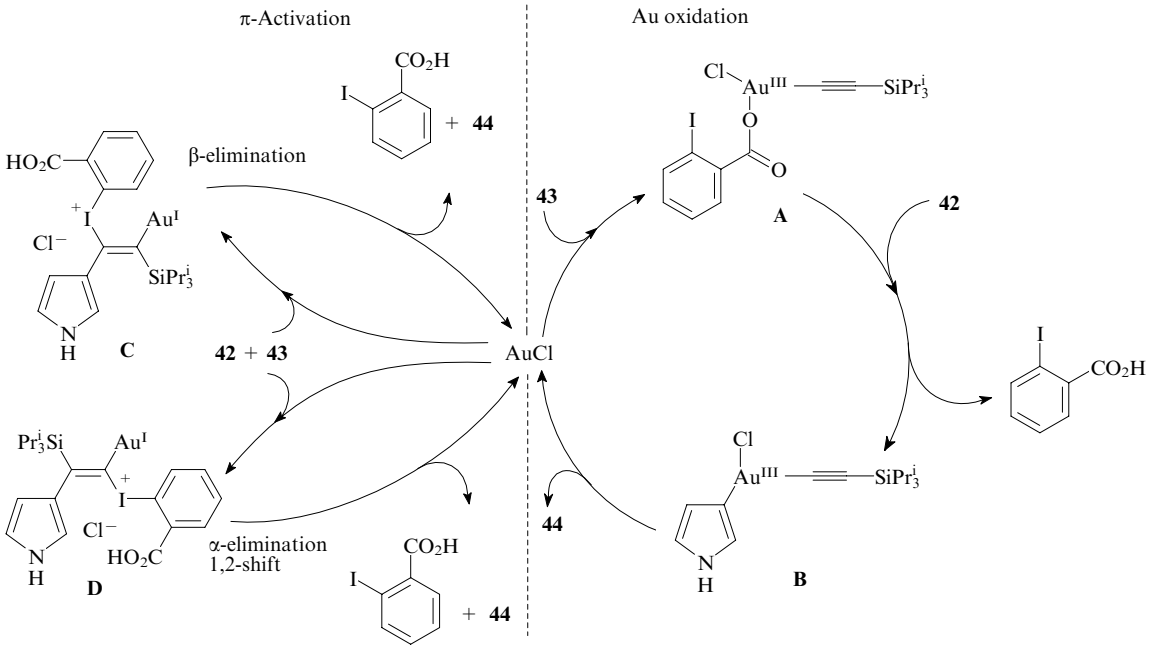
Thus, pyrrole gives exclusively 2-ethynylpyrrole, the ethynylation of *N*-methylpyrrole affords, along with the major 2-ethynyl derivative, a large amount of 3-ethynylpyrrole (25%), whereas *N*-(triisopropylsilyl)pyrrole undergoes only 3-ethynylation.

Two reaction mechanisms were proposed by Brand *et al.*[44] (Scheme 26). According to one mechanism, the initial oxidation of a gold(I) salt with a derivative of hypervalent iodine **43** to the Au^{III} acetylene complex **A** is followed by the metallation of pyrrole giving the complex **B** and by reductive elimination. According to an alternative mechanism, the Au^I-catalyzed addition of pyrrole to the triple bond of the complex **A** gives the vinyl complex of gold **C** or **D** and is accompanied, depending on the regioselectivity of the addition, by either β-elimination or α-elimination and the 1,2-shift.

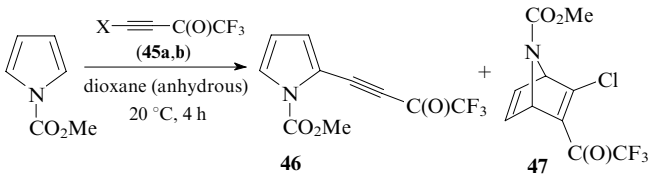
The reaction of *N*-methoxycarbonylpyrrole with chlorotrifluoroacetylacetylene (**45a**) giving 2-ethynylpyrrole **46** and unstable bicyclic compound **47** (Scheme 27) was described in 2009.[45]

As opposed to chloride **45a**, the reaction of bromide **45b** with *N*-methoxycarbonylpyrrole is exothermic and produces exclusively 2-ethynylpyrrole **46** without traces of the corresponding [4 + 2]-cycloadduct **47**.

Scheme 26



Scheme 27

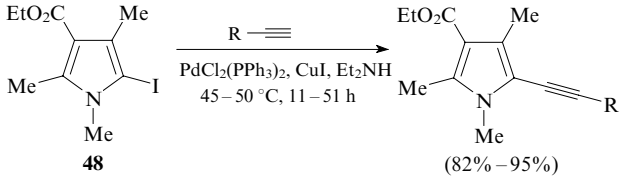


X	Yield, %	
	46	**47**
Cl	19	62
Br	78	0

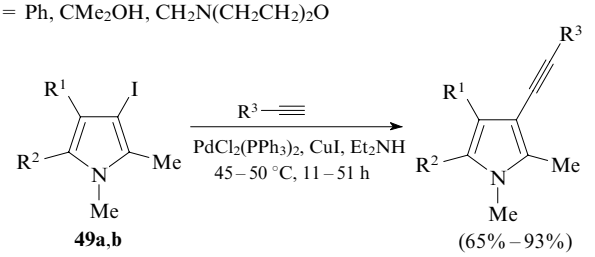
The ethynyl substituent can be introduced into the pyrrole ring also using the cross-coupling of halopyrroles with terminal acetylenes in the presence of palladium catalysts (Sonogashira reaction and its modifications[46]). This reaction was employed to synthesize various pyrrole-containing building blocks for the design of natural compounds,[47–56] pharmaceuticals[57,58] and high-tech materials.[59–62] According to a typical procedure, halopyrroles are treated with terminal acetylenes in the presence of palladium catalysts, such as the triphenylphosphine complex of Pd^0 or the combined palladium copper catalytic system $PdCl_2(PPh_3)_2$–CuI, and bases (for example, potassium carbonate, secondary or tertiary amines) in an inert medium. Iodopyrroles are most commonly used as halopyrroles, although bromo and chloro derivatives of pyrrole are also active is some cases.

In the series of pyrroles, the Sonogashira reaction was carried out for the first time[63,64] with 2-iodo (**48**) and 3-iodo derivatives (**49a**,**b**) (Scheme 28).[64]

Scheme 28



R = Ph, CMe_2OH, $CH_2N(CH_2CH_2)_2O$



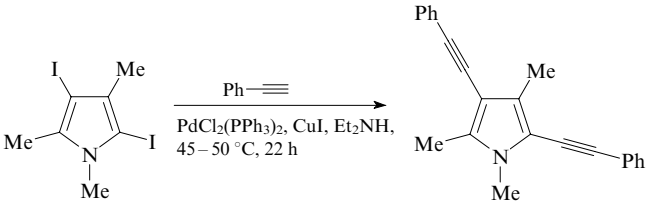
R^1 = CO_2Et, R^2 = Me (**a**); R^1 = Me, R^2 = CO_2Et (**b**);
R^3 = Ph, CMe_2OH, $CH_2N(CH_2CH_2)_2O$

3-Iodopyrrole **49b** is less reactive than 2-iodopyrrole **48**. However, the presence of the electron-withdrawing ethoxycarbonyl group in the 4-position adjacent to the iodine atom increases the activity of the compound due to which iodopyrrole **49a** reacts with acetylenes more vigorously compared to compounds **48** and **49b**.

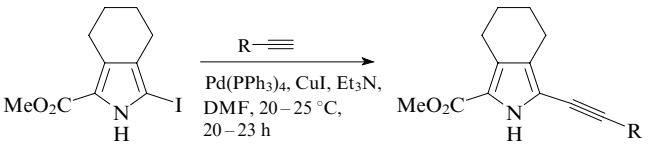
Under similar conditions, 2,4-diiodo-substituted pyrrole **50** was successfully involved in the reaction with phenylacetylene producing 1,2,4-trimethyl-3,5-bis(phenylethynyl)-pyrrole (**51**) (Scheme 29).[64]

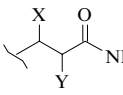
The same catalytic system was used for the preparation of ethynylpyrrole **52** (R = Ph) from 2-iodopyrrole **53** and phenylacetylene (Scheme 30). However, this compound was obtained in rather low yield (25%).[53] This reaction gives 1,4-diphenylbutadiyne as the major product, which is formed through the oxidative dimerization of phenylacetylene. The optimal conditions for the ethynylation were found by varying the catalytic system, the ratio of the reactants and the solvent: the $Pd(PPh_3)_4$–CuI–Et_3N catalyst, the iodopyrrole **53**–phenylacetylene molar ratio is 1 : 1.1, DMF as the solvent and an inert atmosphere. The yield of the cross-coupling product sharply decreases (from 89% to 21%) in the presence of oxygen.

Scheme 29



Scheme 30

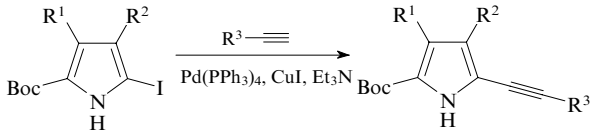


R = Ph,  [X = H, Me, CH(OMe)Me, CH(OBn)Me; Y = H, Me]

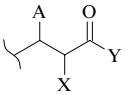
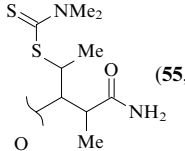
The same conditions proved to be suitable for the synthesis of ethynylpyrroles **52** containing amide substituents. The yields of compounds **52** were >85%, and an insignificant amount of the dimerization product of acetylene was found (see Scheme 30).

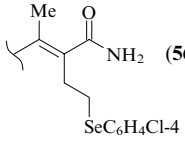
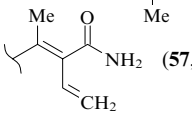
The Sonogashira cross-coupling is the key step in the synthesis of precursors of phytochrome and phytocyanin, *viz.*, compounds **54**,[47,48,53,54] **55**,[53] **56** and **57**[52] (Scheme 31).

Scheme 31



R^1 = $(CH_2)_2CO_2Me$, R^2 = Me; R^1–R^2 = $(CH_2)_4$;

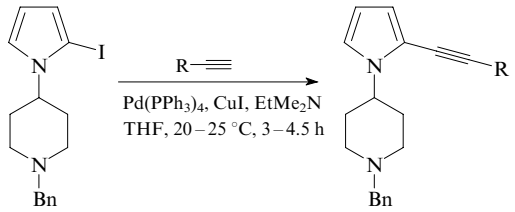
R^3 =  (**54**, yield 88%–93%)  (**55**, 37%),

 (**56**, 85%–95%),  (**57**, 85%–95%);

A = H, Me, CH(OMe)Me, CH(OBn)Me; X = H, Me;
Y = NH_2, NHBn, OH; Boc is *tert*-butoxycarbonyl

The introduction of the acetylenic moiety into 1-(*N*-benzylpiperidine-4-yl)-2-iodopyrrole under the conditions of the Sonogashira reaction resulted in the selective formation of ethynylpyrroles **58** (Scheme 32).[58]

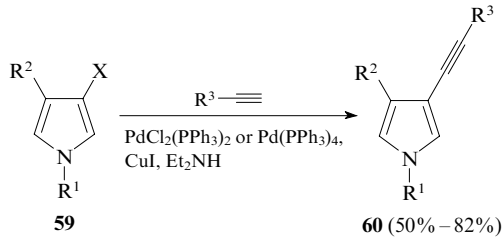
Scheme 32



R = Ph, $SiMe_3$

The palladium-catalyzed cross-coupling was used for the transformation of N-protected pyrroles **59** into ethynylpyrroles **60** (Scheme 33).[65,66] The latter were synthesized in good yields by the reaction of halopyrroles **59** with various terminal acetylenes in the presence of CuI as the cocatalyst and diethylamine as the base. The active Pd^0 catalyst was generated *in situ* from $PdCl_2(PPh_3)_2$ and CuI in diethylamine.

Scheme 33



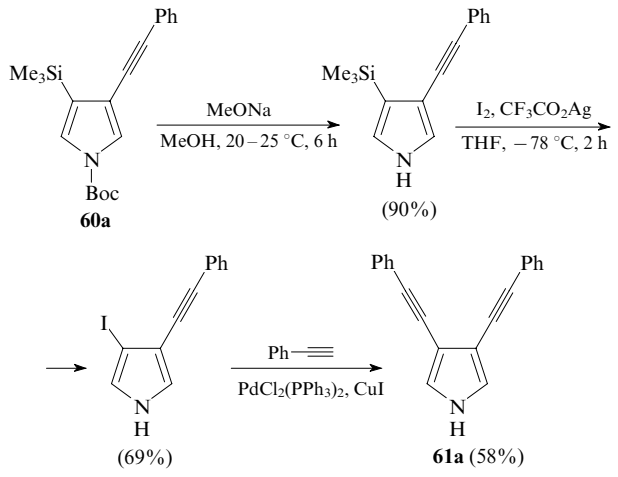
X = Br, I; R^1 = Boc, $SiPr^i_3$, SO_2NMe_2; R^2 = Me, $SiMe_3$;

R^3 = $SiMe_3$, $(CH_2)_2OH$, , Ph

Using $Pd(PPh_3)_4$ as the catalyst, which was generated *in situ* from triphenylphosphine and palladium on carbon, the reaction mixture was heated to reflux, resulting in a substantial decrease in the yields of the target products, from 83%–92% (Ref. 66) to 56%–82%.[65]

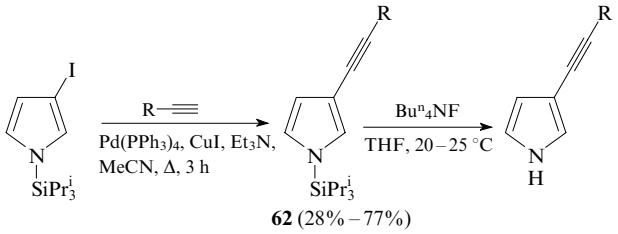
The second ethynyl group was introduced at the 4-position of 3-ethynylpyrrole derivative **60a** using the following sequence of transformations: the removal of the Boc protecting group, the iodination in the presence of silver trifluoroacetate and the palladium-catalyzed cross-coupling with phenylacetylene. This reaction afforded 3,4-bis(phenylethynyl)pyrrole (**61a**) (Scheme 34).[66]

Scheme 34



The cross-coupling of 1-(triisopropylsilyl)-3-iodopyrrole with various acetylenes to form 3-ethynylpyrroles **62** can be easily performed in the presence of $Pd(PPh_3)_4$ (either *ex situ* or generated *in situ* from PPh_3 and Pd/C) or $PdCl_2(PPh_3)_2$ (Scheme 35).[67] The triisopropylsilyl group is easily removed using tetra-n-butylammonium fluoride.

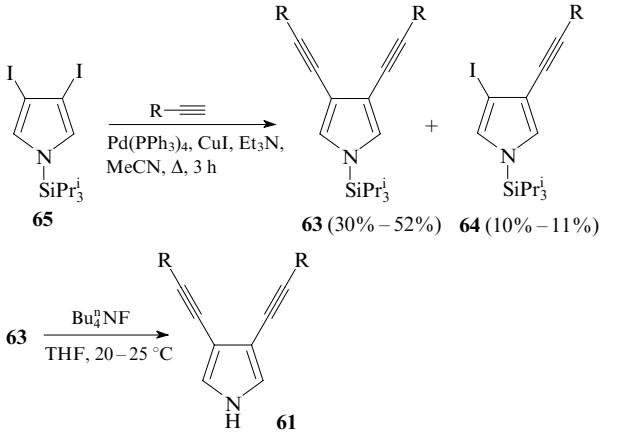
Scheme 35



R = Pr^n, n-C_5H_{11}, $SiMe_3$, Ph

3,4-Diacetylene pyrroles **63** were synthesized according to a similar procedure. In addition to these compounds, small amounts of monocoupling products **64** were detected in the reaction mixtures (Scheme 36).[67]

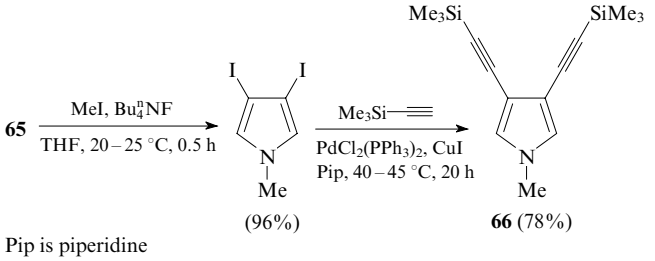
Scheme 36



R = Pr^n, n-C_5H_{11}, $SiMe_3$, Ph

l-(Triisopropylsilyl)-3,4-diiodopyrrole (**65**) was used also for the synthesis of 3,4-diethynyl-1-methylpyrrole **66** (Scheme 37).[68]

Scheme 37

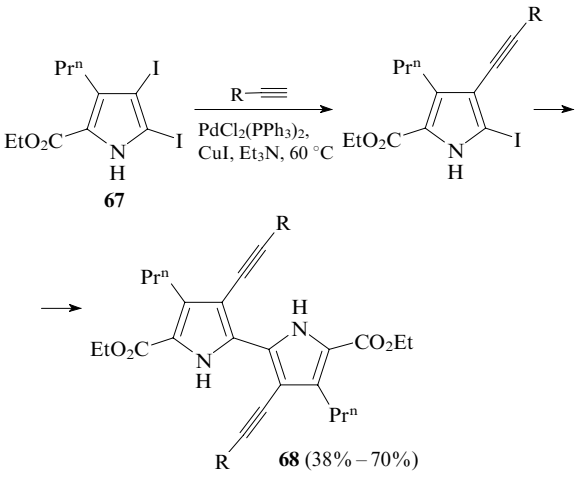


Pip is piperidine

The Sonogashira reaction of 2,3-diiodopyrrole **67** produced[69] 2,2′-bipyrroles **68** containing 3,3′-ethynyl groups (Scheme 38). In the authors' opinion, the first step of this

reaction involves the replacement of the iodine atom at the 3-position of compound **67** by the ethynyl group followed by the dimerization. Apparently, the ethynyl group at the 3-position facilitates the cross-coupling in bipyrrole due to the complexation with the palladium catalyst, resulting in its close approach to the reaction centre C(2)–I.[69]

Scheme 38

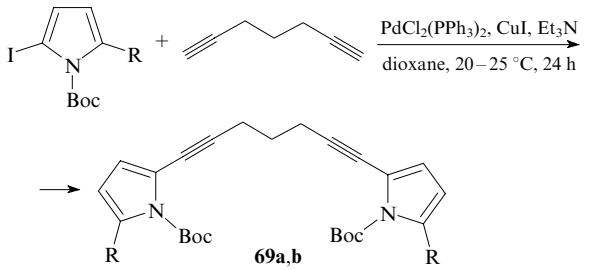


R = SiMe$_3$, CH$_2$OH, (CH$_2$)$_2$OH, Ph

The reaction of hepta-1,6-diyne with 1-*tert*-butoxycarbonyl-2-iodopyrrole and its 5-phenyl derivative produces diynes **69a**,**b** containing terminal pyrrole rings (Scheme 39).[70]

The Sonogashira reaction was also used for the synthesis of the precursor of chlorin (compound **70**) and for the introduction of ethynyl functional groups as auxochromic groups at the 3- and 13-positions of chlorins **71a**–**d** (Scheme 40).[71]

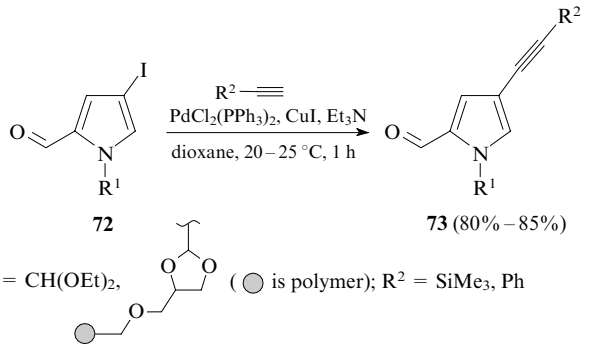
Scheme 39



R = H (**a**, 85%), Ph (**b**, 81%)

The PdCl$_2$(PPh$_3$)$_2$- and CuI-catalyzed cross-coupling of 4-iodopyrrole-2-carbaldehydes **72**, including immobilized derivatives, with trimethylsilylacetylene[72,73] or phenylacetylene[73,74] affords 4-ethynylpyrrole-2-carbaldehydes **73** (Scheme 41).

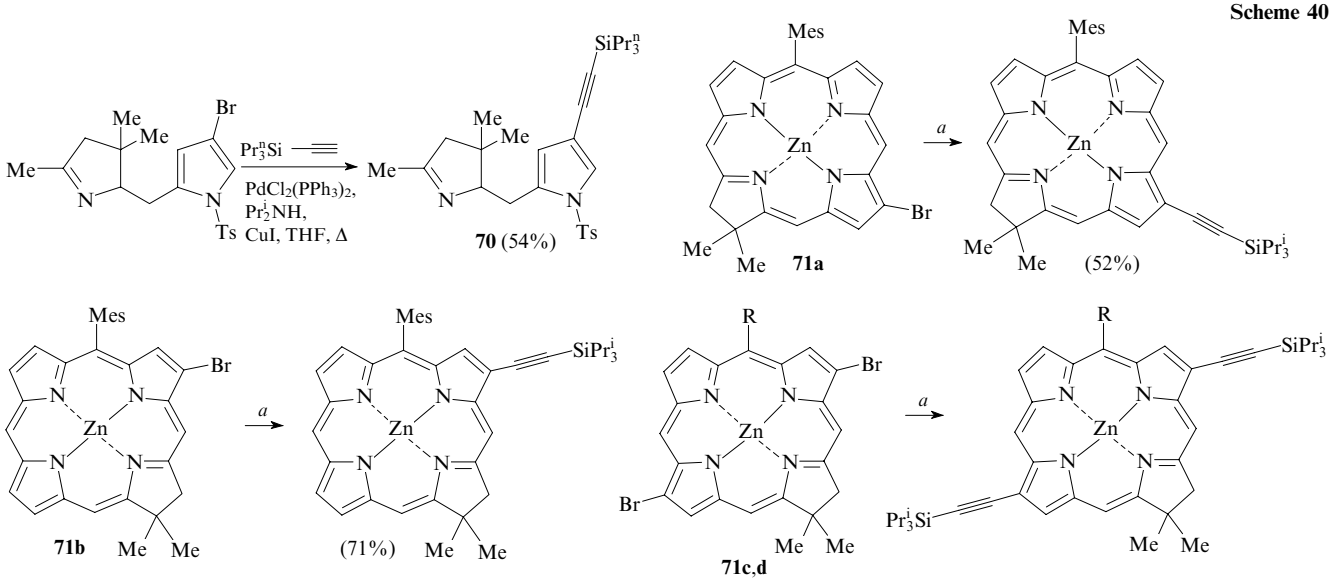
Scheme 41



R^1 = CH(OEt)$_2$, (● is polymer); R^2 = SiMe$_3$, Ph

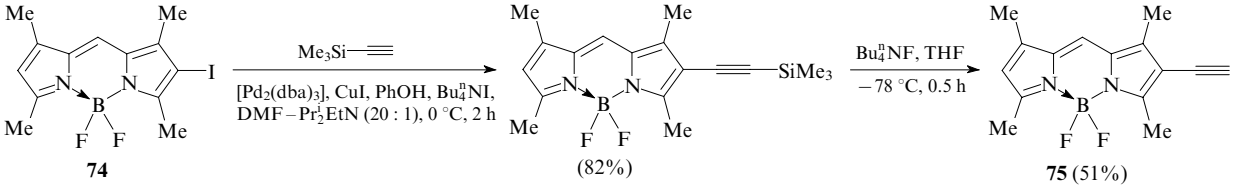
Tri-*n*-butyl (propyn-1-yl)tin was also employed for the synthesis of ethynylpyrroles. For example, 4-(propyn-1-yl)pyrrole-2-carbaldehyde was prepared by the palladium-catalyzed cross-coupling of this compound with 4-iodopyrrole-2-carbaldehyde (Scheme 42).[75]

Scheme 40

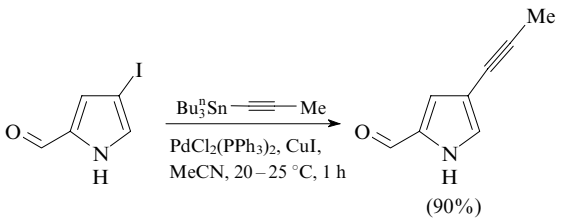


(*a*) Pr$^i_3$SiC≡CH, Pd$_2$(dba)$_3$, P(Tol-*o*)$_3$, PhMe–Et$_3$N (5 : 1), 60°C; Mes is mesityl (2,4,6-trimethylphenyl), dba is dibenzylideneacetone, *o*-Tol is *o*-tolyl; R = H (**71c**, yield 53%), Mes (**71d**, 75%)

Scheme 43



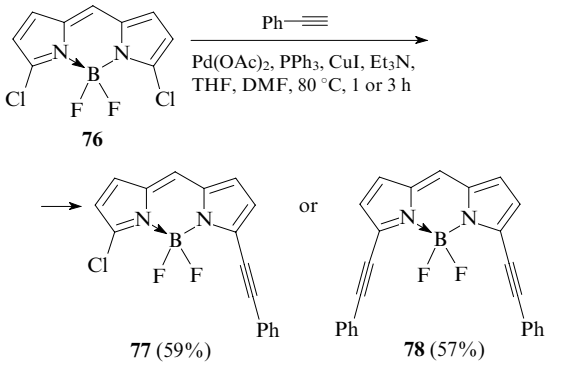
Scheme 42



The application of the Sonogashira reaction for the modification of the boradiazaindacene unit of fluorophores of the BODIPY family (boron-dipyrromethene) with acetylenic substituents as bathochromic groups was reported. For example, the reaction of iodide **74** with trimethylsilylacetylene followed by the desilylation affords ethynyl derivative **75** (Scheme 43).[60]

The reaction of 3,5-dichloro-BODIPY (**76**) with phenylacetylene (1 equiv.) proceeds regioselectively to form the 3-ethynyl derivative of difluoroboradiazaindacene **77** in 1 h (Scheme 44). An increase in the reaction time to 3 h and the use of a larger amount of phenylacetylene resulted in the formation of 3,5-diethynylboradiazaindacene **78**.[62]

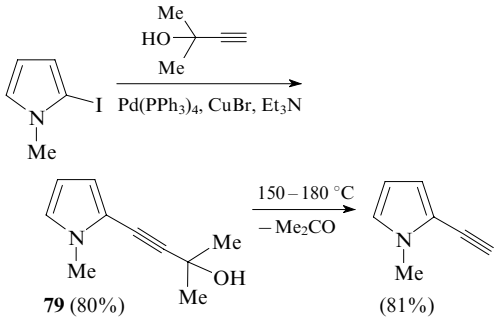
Scheme 44



The Sonogashira cross-coupling is, as a rule, not used for the synthesis of pyrrole derivatives containing the terminal acetylene group starting from halopyrroles and acetylene, because the latter is a bifunctional reagent. Such ethynylpyrroles are most commonly synthesized by the reactions of pyrrole derivatives of tertiary acetylenic alcohols or trimethylsilylacetylene with catalytic amounts of an alkali.

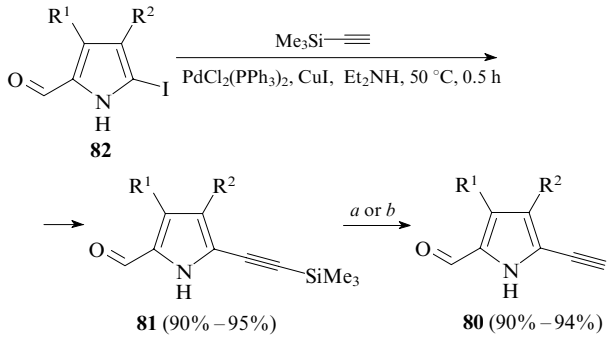
Thus, 1-methylpyrrole containing the terminal acetylene group at the 2-position was synthesized by the base-catalyzed cleavage of ethynylpyrrole **79**, which can be easily prepared by the Pd–Cu-catalyzed cross-coupling of 2-iodo-1-methylpyrrole with 2-methylbut-3-yn-2-ol (Scheme 45).[63, 64, 76]

Scheme 45



2-Ethynylpyrroles **80** were prepared by the desilylation of trimethylsilylethynylpyrroles **81**, which are products of the $PdCl_2(PPh_3)_2$–CuI-catalyzed cross-coupling of iodopyrrolecarbaldehydes **82** with trimethylsilylacetylene, using sodium hydroxide[77] or Bu^n_4NF (Refs 78–81) (Scheme 46).

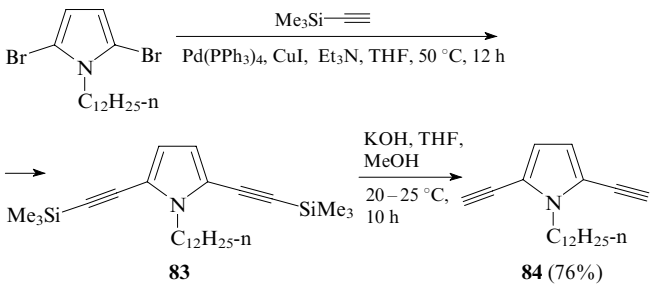
Scheme 46



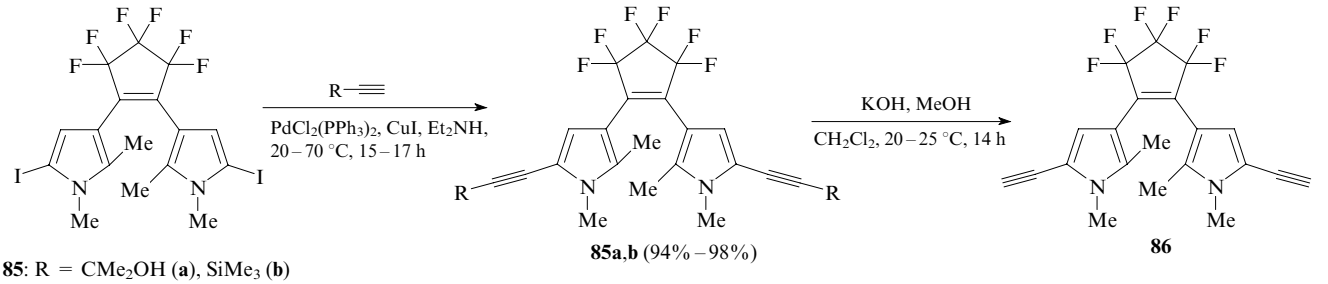
(*a*) NaOH, MeOH–H_2O, 20–25 °C, 0.5 h;
(*b*) Bu^n_4NF, THF, 20–25 °C, 1 h;
R^1 = Me, Et; R^2 = Me, Et, $(CH_2)_nCO_2Me$ (n = 2, 3)

The desilylation of 2,5-bis(trimethylsilylethynyl)pyrrole **83**, which is generated by the cross-coupling reaction of 2,5-dibromo-1-dodecylpyrrole with trimethylsilylacetylene, in the presence of KOH affords diethynylpyrrole **84** (Scheme 47).[82]

Scheme 47



Scheme 48

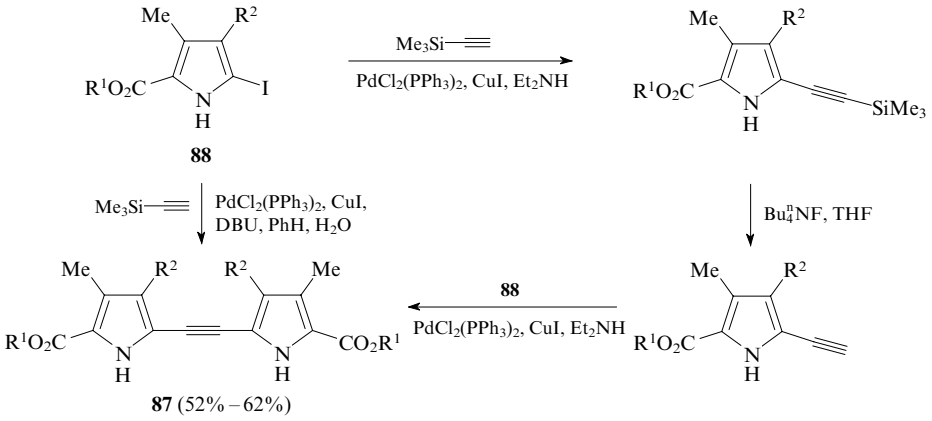


85: R = CMe_2OH (**a**), $SiMe_3$ (**b**)

85a,b (94%–98%)

86

Scheme 49



88

87 (52%–62%)

R^1 = Me, Bn; R^2 = Me, Et

The cleavage of tertiary acetylenic alcohol **85a** or trimethylsilylacetylene derivative **85b** gave di(ethynylpyrrolyl)ethene **86**. Starting compounds **85a**,**b** were prepared in quantitative yield by the reaction of 1,2-bis(2-iodo-1,5-dimethylpyrrol-4-yl)perfluorocyclopentene with 2-methylbut-3-yn-2-ol or trimethylsilylacetylene (Scheme 48).[83, 84]

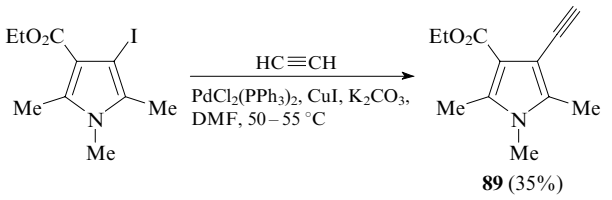
Bis(5-alkoxycarbonylpyrrol-2-yl)acetylenes **87** are important intermediates in the synthesis of porphyrin analogues because they contain a two-carbon bridge between the pyrrole rings. These compounds were synthesized by the reaction of 5-iodopyrrole-2-carboxylates **88** with trimethylsilylacetylene in the presence of palladium(0) and copper(I) at room temperature (Scheme 49). The three-step (cross-coupling–desilylation–cross-coupling) and one-step (using the double Sonogashira coupling of 2-iodopyrrole and trimethylsilylacetylene) methods were developed for the synthesis of such bispyrroles. In the latter case, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) serves as the base.[85, 86]

Under these conditions, the reaction with the use of 2-bromo-1-tosylpyrrole as the starting compound produces bis(pyrrolyl)acetylene in low yield (8%).[87]

However, the reaction of trimethylsilylacetylene gives only trimethylsilyl derivatives. On the other hand, the base-catalyzed cleavage of α-acetylenic alcohols (reverse Favorsky reaction) requires severe conditions (strong alkali, high temperature) and cannot be applied to the synthesis of unstable acetylenic compounds.

For this reason, 3-ethynylpyrrole **89** was synthesized by the reaction of ethyl 3-iodo-1,2,5-trimethylpyrrole-4-carboxylate with acetylene in the presence of catalytic amounts of $PdCl_2(PPh_3)_2$, CuI and an excess of K_2CO_3 instead of usual di- and trialkylamines (Scheme 50).[88]

Scheme 50

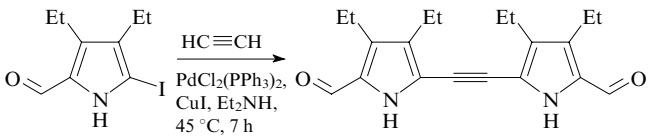


89 (35%)

To provide a high concentration of acetylene, dimethylformamide (in a relatively high amount), which has a high boiling point and absorbs a considerable amount of acetylene, was employed as the solvent. An excess of acetylene is necessary for the suppression of the competitive reaction of the starting iodide with ethynylpyrrole **89** that is formed in the reaction.

Meanwhile, the use of acetylene in the synthesis of ethynylpyrroles can give rise to side reactions giving diacetylenes and dipyrroles. For example, the intermediate for the preparation of acetylene-cumulene porphycene, bis(pyrrolyl)acetylene **90a**, is generated by bubbling acetylene through a solution of 3,4-diethyl-2-iodopyrrole-5-carbaldehyde (**82a**) in diethylamine in the presence of dichlorobis(triphenylphosphine)palladium(II) and copper(I) iodide (Scheme 51).[89]

Scheme 51

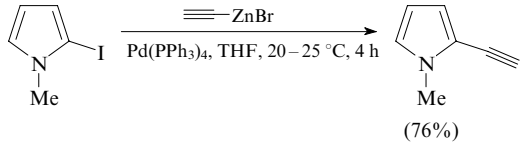


82a

90a (22%)

The cross-coupling of iodopyrroles with ethynylmagnesium and ethynylzinc bromides has a considerable advantage for the selective synthesis of pyrroles containing the terminal acetylene group. For example, 2-ethynyl-1-methylpyrrole is selectively produced by the Pd-catalyzed coupling of 2-iodo-1-methylpyrrole with ethynylzinc bromide (Scheme 52).[90]

Scheme 52

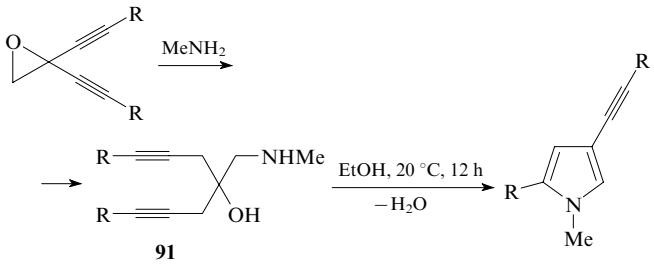


It should be noted that the Pd–Cu-catalyzed cross-coupling of halopyrroles with acetylenes is limited to pyrroles containing electron-withdrawing substituents and their N-substituted representatives. In addition, this reaction is apparently inapplicable to electron-deficient acetylenes (examples of the cross-coupling of pyrroles with acetylenes containing electron-withdrawing substituents are unknown).[41]

3. Synthesis of C-ethynylpyrroles with the simultaneous construction of the pyrrole ring

Several methods for the synthesis of C-ethynylpyrroles with the simultaneous construction of the pyrrole ring were described in the literature. For example, it was shown[91,92] that diacetylenic amino alcohols **91**, which are produced by the reaction of diacetylenic epoxides with amines, are unstable and, under mild conditions, undergo cyclization to ethynylpyrroles (Scheme 53).

Scheme 53

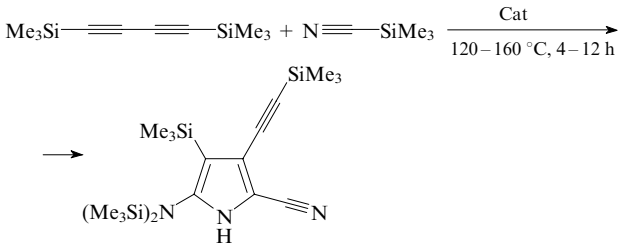


R = H, Me, Ph

The cycloaddition of 1,3-diphenylazaallyllithium (**92**) to 1,4-diphenylbut-1-en-3-yne or 1,4-diphenylbuta-1,3-diyne affords 3-ethynylpyrrolidine **93** or 3-ethynyl-2,5-dihydropyrrole **94**, respectively (Scheme 54).[93,94] When heated under reflux in xylene (6 h) in the presence of chloranil, both pyrrolidine **93** and dihydropyrrole **94** are transformed into 3-phenylethynylpyrrole **95**.[93,94] The treatment of pyrrole **95** with methyl sulfate or benzyl bromide gives its *N*-methyl or *N*-benzyl derivatives.

3-(Trimethylsilylethynyl)pyrrole **96** was synthesized from 1,4-bis-(trimethylsilyl)butadiyne and trimethylsilyl cyanide in the presence of various palladium compounds: $PdCl_2$, $Pd(OAc)_2$, $Pd(CN)_2$, $PdCl_2(PhCN)_2$, $PdCl_2(PPh_3)_2$, Pd black, 10% Pd/C (Scheme 55).[95] The reaction is apparently catalyzed by the palladium isonitrile or cyanide complex, which acts like a metal carbene complex.

Scheme 55



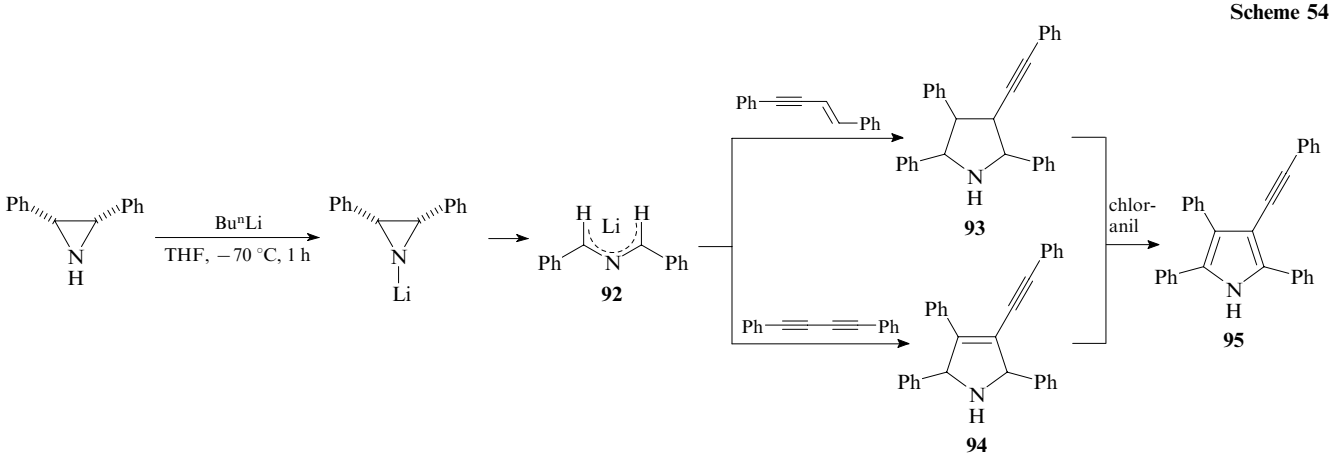
96 (55%–84%)

Cat = $PdCl_2$, $Pd(OAc)_2$, $Pd(CN)_2$, $PdCl_2(PPh_3)_2$, Pd (black), Pd/C

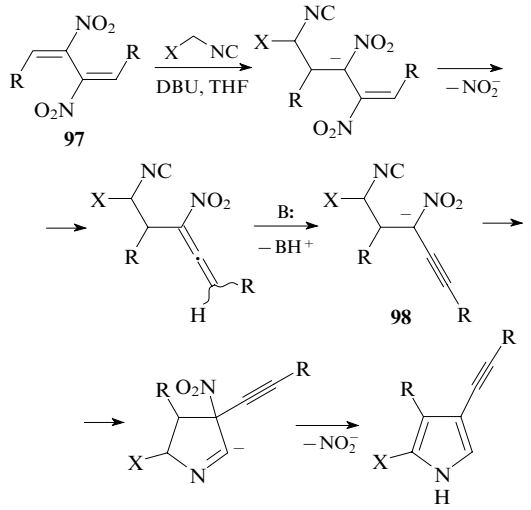
1,4-Disubstituted 2,3-dinitrobuta-1,3-dienes **97** react with isocyanides XCH_2NC (X = Ts, Boc) in the presence of DBU to form 2,3-disubstituted 4-ethynylpyrroles in 37%–76% yields (Scheme 56).[96] The reaction mechanism involves the base-induced formation of the isocyanide anion, the addition of the latter to the double bond of butadiene **97**, the elimination of NO_2^- and the cyclization of anion **98** followed by aromatization.

The domino reaction of imine **99** with difluorocarbene in the presence of dimethyl acetylenedicarboxylate produces 5-ethynyl-2-fluoropyrrole **100** (Scheme 57).[97] The reaction apparently begins with the attack of difluorocarbene on the electron pair of the nitrogen atom to form intermediate unstable azomethine ylide.

Scheme 54



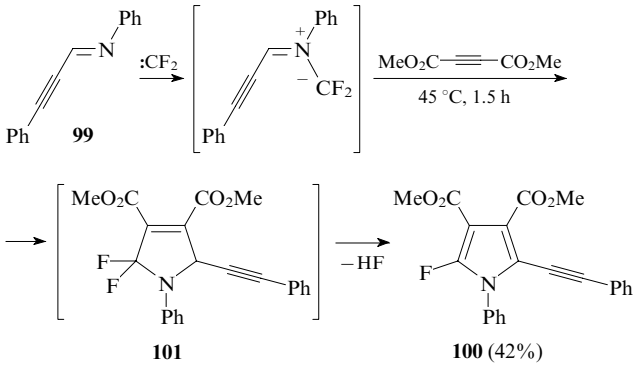
Scheme 56



R = Et, cyclo-C_6H_{11}, Ph, 2-MeC_6H_4, 4-MeC_6H_4, 4-$MeOC_6H_4$, 1-Naph, 2-Th

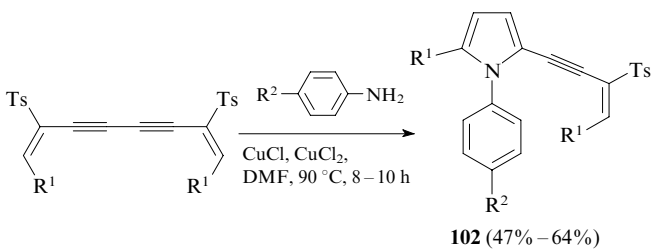
The 1,3-dipolar cycloaddition of the latter to dimethyl acetylenedicarboxylate is accompanied by dehydrofluorination of ethynyldifluorodihydropyrrole **101**. The modified method for the generation of difluorocarbene using active lead instead of lead powder for the reduction of dibromodifluoromethane makes it possible to reduce the reaction time (1.5 h *vs* 25 h) and increase the yield of ethynylpyrrole (42% *vs* 11%).

Scheme 57



1-Aryl-2-ethynylpyrroles **102** are produced by the treatment of 1,8-disubstituted 2,7-bis(*p*-toluenesulfonyl)octa-1,7-diene-3,5-diynes with aniline derivatives in the presence of CuCl (1.6 equiv.) and $CuCl_2$ (0.16 equiv.) in DMF (Scheme 58).[98, 99]

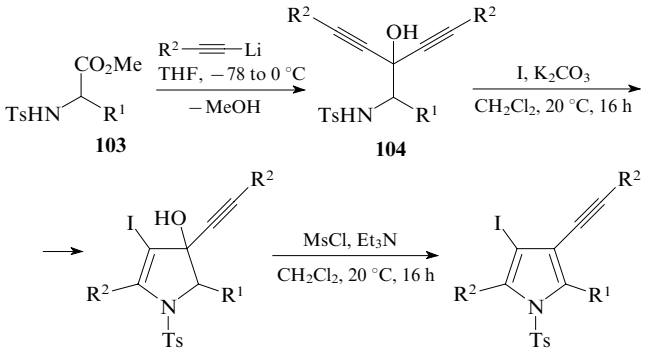
Scheme 58



R^1 = Ph, 3-$MeOC_6H_4$, 4-$MeOC_6H_4$, 4-BrC_6H_4, 2-Naph;
R^2 = H, Me, OMe, F, Br

In the presence of an excess of lithium acetylenides, α-amino acid esters **103** containing a substituted amino group are transformed into compounds **104**, and the iodination of the latter at the triple bond results in their cyclization to hydroxydihydropyrroles **105**. The dehydration of the latter in the presence of methanesulfonyl chloride and Et_3N gives rise to ethynylpyrroles **106** (Scheme 59).[100] At R^1 = Pr^i, the dehydration is already observed in the step of cyclization of compounds **104** to pyrroles.

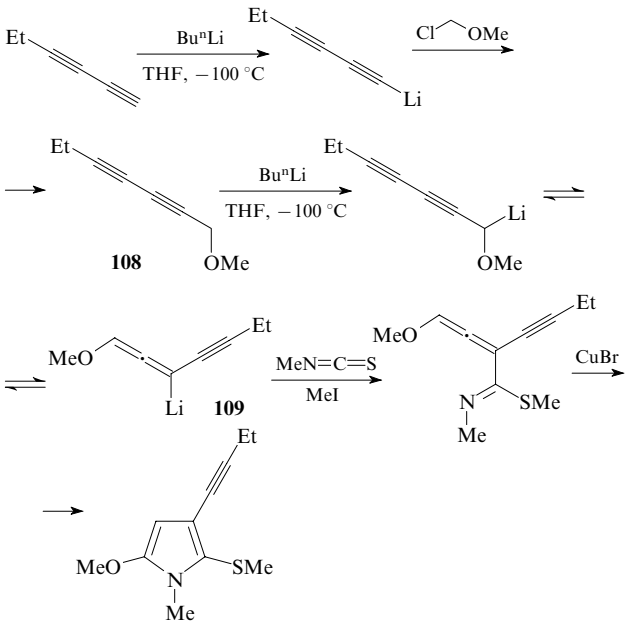
Scheme 59



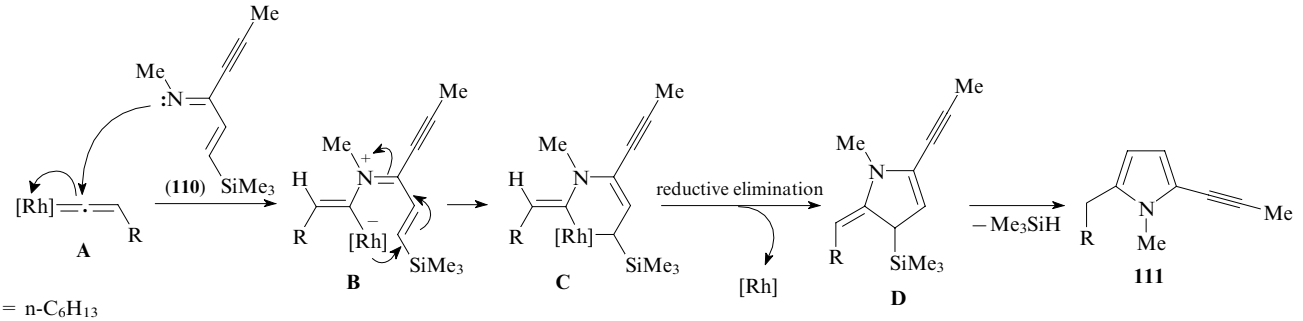
R^1 = Me, Pr^i; R^2 = Bu^n, Ph; Ms is methanesulfonyl

3-(But-1-yn-1-yl)-2-methylsulfanyl-5-methoxypyrrole (**107**) was synthesized from hexa-1,3-diyne and methyl isothiocyanate in one preparative step (Scheme 60).[101] 1-Methoxyhepta-2,4-diyne (**108**), which is required for the formation of the pyrrole ring, can be easily produced from 1-lithiohexa-1,3-diyne and methoxychloromethane. The deprotonation of heptadiyne **108** with Bu^nLi followed by the reaction of compound **109** with isothiocyanate and methyl iodide give the corresponding imidothiolate, and, in the presence of catalytic amounts of CuBr, the latter undergoes cyclization to 3-(but-1-yn-1-yl)pyrrole **107**.

Scheme 60



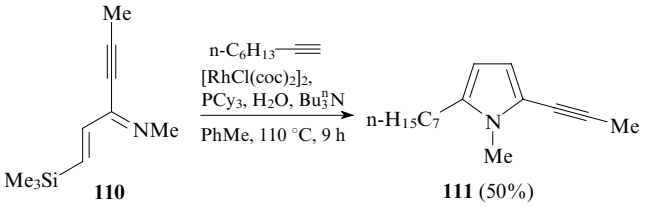
Scheme 62



R = n-C_6H_{13}

The treatment of a mixture of β-trimethylsilyl-substituted α,β-unsaturated imine **110** and oct-1-yne with catalytic amounts of the rhodium catalyst $[RhCl(coc)_2]_2$ and tricyclohexylphosphine produced 5-(propyn-1-yl)pyrrole **111** ([4 + 1]-cycloaddition product) (Scheme 61).[102]

Scheme 61



coc is cyclooctene; Cy is cyclohexyl

The reaction apparently proceeds as the nucleophilic addition of imine **110** (through the nitrogen atom) to the carbene carbon atom of the rhodium complex **A** (generated *in situ* from terminal alkyne) followed by the cyclization of the zwitterionic intermediate **B** to the metallacycle **C** (Scheme 62). Then the reductive elimination (through the formation of enamine **D**), the isomerization of the double bond and the desilylation give pyrrole **111**.

III. Reactions of C-ethynylpyrroles

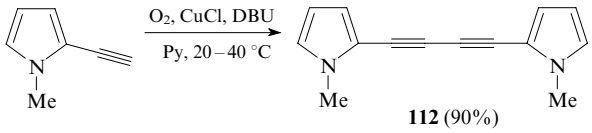
C-Ethynylpyrroles are involved in the following reactions typical of acetylenic compounds: the substitution of a hydrogen atom leaving the triple bond intact and the addition at the acetylenic moiety, including the cycloaddition and intramolecular cyclization.

1. Reactions leaving the triple bond intact

Among these reactions are, in particular, the oxidative coupling involving two acetylenic moieties.

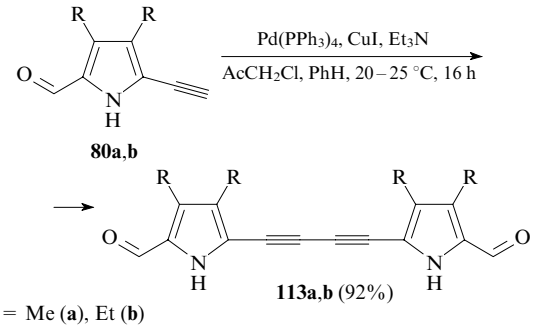
Unlike other hetarylacetylenes (2-furyl-, 2- and 3-thienylacetylenes), 2-ethynyl-1-methylpyrrole does not undergo dimerization under usual conditions [O_2, CuCl, pyridine (Py), 20 – 40 °C]. Thus, more than 90% of the starting compound is recovered from the reaction even after the prolonged bubbling of oxygen at 50 °C. However, in the presence of catalytic amounts of DBU, which efficiently deprotonates the terminal carbon atom, the dimerization readily proceeds under mild conditions. Thus, in the presence of 1 mol.% CuCl and 2 mol.% DBU, 2-ethynyl-1-methylpyrrole is rapidly and almost quantitatively transformed into conjugated dipyrrolylidiyne **112** (Scheme 63).[103]

Scheme 63



The oxidative coupling of 5-ethynyl-3,4-dimethylpyrrole-2-carbaldehyde (**80a**) and its 3,4-diethyl analogue **80b** in the presence of the $Pd(PPh_3)_4$ – CuI system, chloroacetone and triethylamine affords 1,4-bis(3,4-dialkyl-5-formylpyrrol-2-yl)butadiynes **113a**,**b** (Scheme 64).[77, 78]

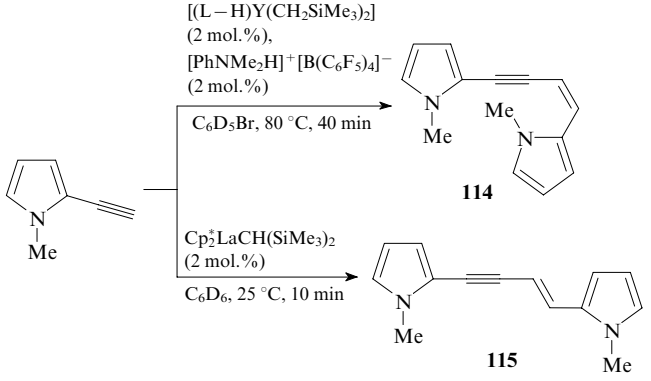
Scheme 64



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

The yttrium dialkyl complex $[(L-H)Y(CH_2SiMe_3)_2]$ activated with $[PhNMe_2H]^+[B(C_6F_5)_4]^-$ catalytically dimerizes 2-ethynyl-1-methylpyrrole to *Z*-enyne **114** at a high rate and with absolute selectivity. The corresponding *E*-enyne **115** was synthesized in the presence of the perme-

Scheme 65

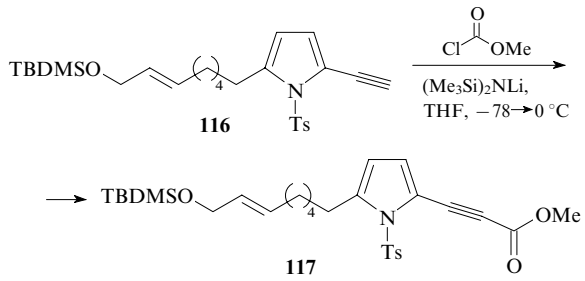


L is 1,4,6-trimethyl-*N*-(2-pyrrolidinoethyl)-1,4-diazepane-6-amine, Cp* is pentamethylcyclopentadienyl

thyllanthanocene catalyst $Cp^*_2LaCH(SiMe_3)_2$ (Scheme 65).[104]

The deprotonation of compound **116** with lithium hexamethyldisilazide followed by the reaction of the intermediate carbanion with methyl chloroformate afforded pyrrolylpropynoate **117** serving as an intermediate in the synthesis of roseophilin (Scheme 66).[105]

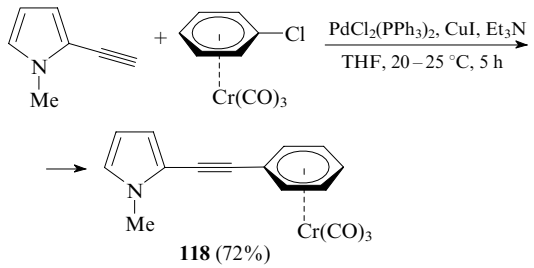
Scheme 66



TBDMS is *tert*-butyldimethylsilyl

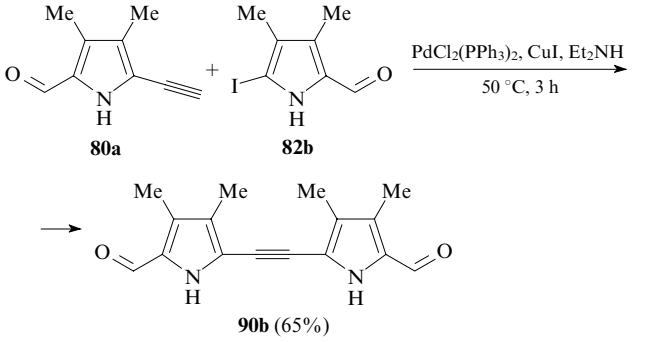
C-Ethynylpyrroles are often used as an acetylenic component in the Sonogashira reaction. Thus, 2-ethynyl-1-methylpyrrole is involved in the Pd–Cu-catalyzed cross-coupling with (tricarbonyl)(η^6-chlorobenzene)chromium to form complex **118**. The latter is employed as a precursor for the design of organometallic materials for nonlinear optics (Scheme 67).[106]

Scheme 67



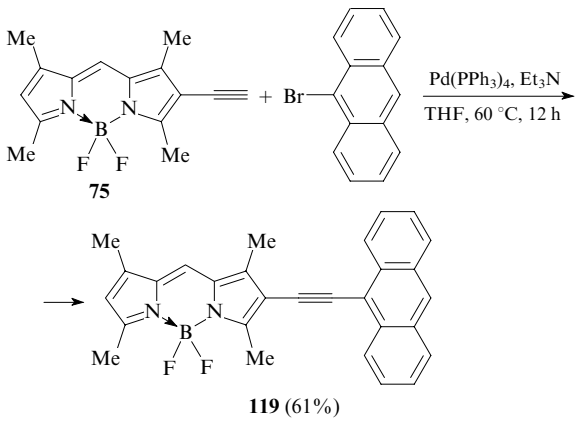
Acetylenic dipyrroledialdehyde **90b** used as the building block in the synthesis of the porphyrin isomer porphycene is produced by the reaction of ethynylpyrrolecarbaldehyde **80a** with iodopyrrolecarbaldehyde **82b** (Scheme 68). An attempt to perform the direct synthesis of compound **90b** by means of the double coupling reaction of the corresponding iodo-substituted aldehyde with acetylene resulted in the formation of the target product in low yield (9%).[77, 78]

Scheme 68



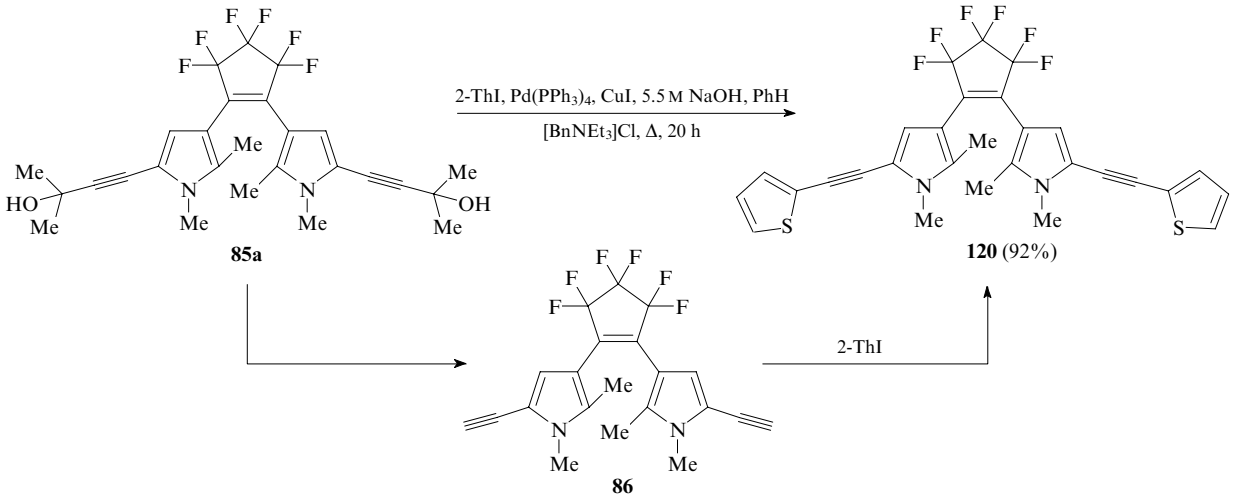
The cross-coupling of ethynyldifluoroboradiazaindacene **75** with 9-bromoanthracene affords functionalized BODIPY fluorophore **119** (Scheme 69).[60]

Scheme 69



Photoswitchable dipyrrolylethene **120** was synthesized[83] by the modified Sonogashira reaction performed under phase transfer conditions. Thus, dipyrrolylethene **120** was prepared by heating under reflux a mixture of alkynylpyrrole **85a** with 2-iodothiophene in the presence of benzyltriethylammonium chloride (as the phase transfer reagent),

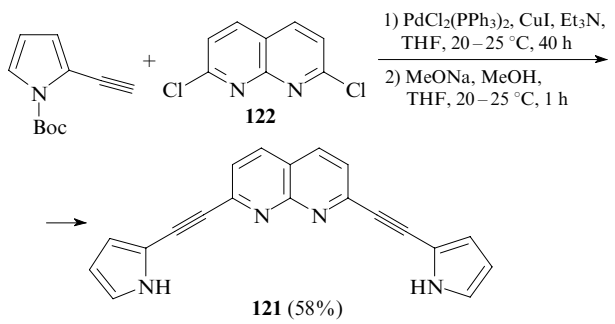
Scheme 70



5.5 M NaOH aqueous solution (as the base) and the $Pd(PPh_3)_4$–CuI catalytic system (Scheme 70). Compound **120** is apparently generated by the reaction of dipyrrolylethene **86** containing terminal alkynyl groups with iodothiophene.

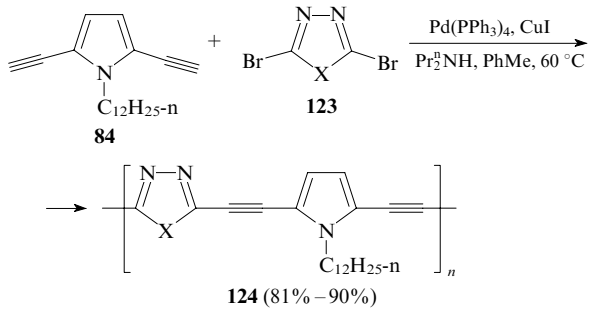
2,7-Bis(pyrrol-2-ylethynyl)-1,8-naphthyridine (**121**), which is a glucopyranoside receptor, was synthesized by the cross-coupling of *N*-*tert*-butoxycarbonyl-2-ethynylpyrrole (2 equiv.) with 2,7-dichloro-1,8-naphthyridine (**122**) followed by the removal of the N-protecting group (Scheme 71).[59, 61]

Scheme 71



The polycondensation of diethynylpyrrole **84** with dibromo derivatives of azoles **123** catalyzed by the $Pd(PPh_3)_4$–CuI system affords photoluminescent π-conjugated copolymers **124**. The latter contain electron-withdrawing (1,3,4-thiadiazole or 4-alkyl-1,2,4-triazole) and electron-donating (*N*-dodecylpyrrole) groups (Scheme 72).[82, 107]

Scheme 72



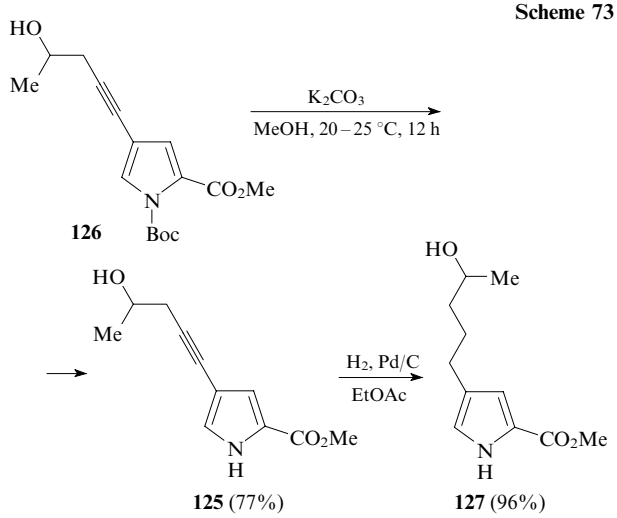
X = S, $NC_{12}H_{25}$-n

2. 1,2-Addition reactions

Yet another important synthetic application of ethynylpyrroles is based on addition reactions to the triple bond. One of these reactions is the catalytic reduction of the acetylenic moiety by hydrogen, which can occur either partially or completely depending on the reaction conditions.

For example, 4-(4-hydroxypent-1-yn-1-yl)pyrrole-2-carboxylate **125**, which is formed after the removal of the protecting group from the nitrogen atom in compound **126**, is easily reduced with hydrogen in the presence of Pd/C under atmospheric pressure to form 4-(4-hydroxypentyl)-pyrrole-2-carboxylate **127**, which is the key intermediate in the synthesis of the alkaloid monomorine (Scheme 73).[49]

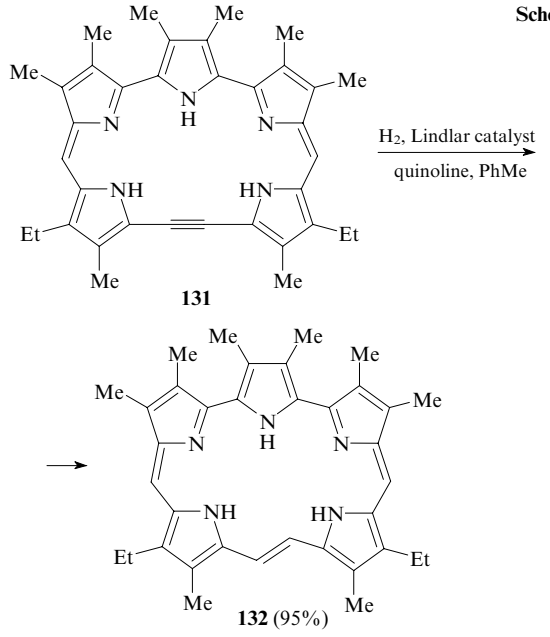
Scheme 73



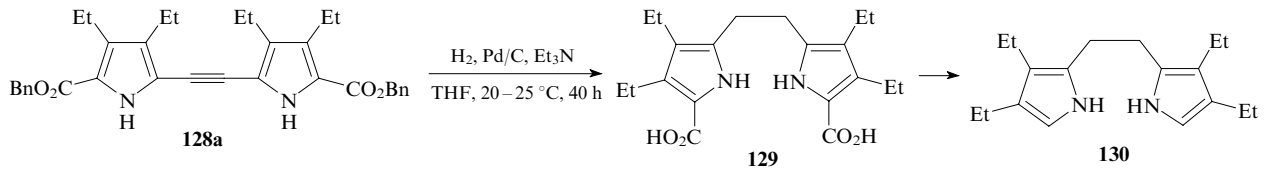
The catalytic hydrogenation of bis(5-benzyloxycarbonylpyrrol-2-yl)acetylene **128a** in the presence of 10% Pd/C in THF with the addition of triethylamine affords dicarboxylic acid **129** containing the reduced triple bond, which is rapidly decarboxylated to 1,2-dipyrrolylethane **130** (Scheme 74).[108]

The selective catalytic hydrogenation of the ethynyl group of macrocyclic compound **131** under mild conditions

Scheme 75



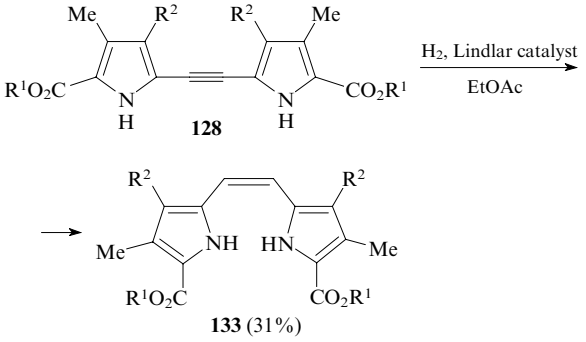
Scheme 74



in the presence of the Lindlar catalyst ($Pd/PbO/CaCO_3$) provides a simple route to sapphirine isomer **132** (Scheme 75).[109]

The reaction of dipyrrolylacetylenes **128** in the presence of the same catalyst but in the absence of quinoline gave dipyrrolylethenes **133** (Scheme 76).[86] The stereoselective synthesis of *cis*-ethenes **133** was performed also with the use of triethylsilane as the reducing agent.[86] The reduction was carried out under the following conditions:[110] Et_3SiH, $PdCl_2(dppf)$, dppf, CH_2Cl_2, 20–25 °C [dppf is 1,1′-bis(diphenylphosphino)ferrocene].

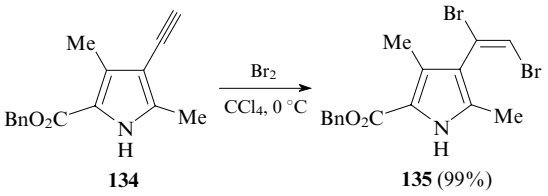
Scheme 76



R^1 = Me, Bn; R^2 = Me, Et

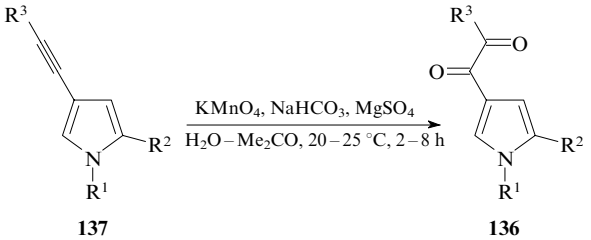
The transformation of the ethynyl group into the dibromovinyl group in compound **134** was used to prepare porphyrin precursor, compound **135** (Scheme 77).[111]

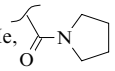
Scheme 77

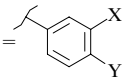


The oxidation of alkynylpyrroles **137** with potassium permanganate is a key step in the synthesis of compounds **136**, which are used for the prevention and treatment of Alzheimer's disease (Scheme 78).[112]

Scheme 78

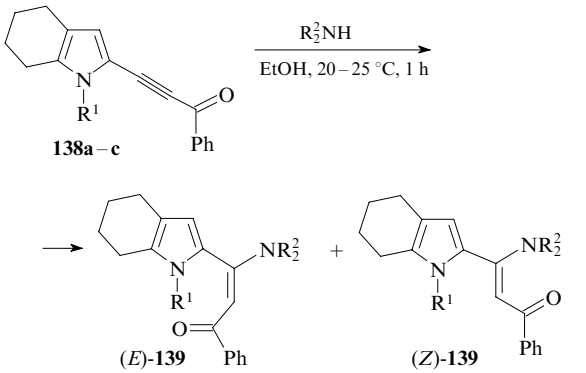


R^1 = H, Et, $SiPr^i_3$, CH_2CF_3, Boc; R^2 = H, C(O)H, C(O)Cl, SO_2Me, CO_2Et, CN, C(O)N(Me)OMe, ;

R^3 =  (X = Br, Y = F; Y = H: X = Br, OMe, NHBoc)

The reactions of 3-(4,5,6,7-tetrahydroindol-2-yl)prop-2-yn-1-ones **138a–c** with dimethyl- and diethylamines proceed smoothly and stereoselectively at room temperature to give 3-dialkylamino-3-(4,5,6,7-tetrahydroindol-2-yl)-1-phenylprop-2-en-1-ones **139** exclusively (for tetrahydroindole **138a**) or mainly as *E* isomers (Scheme 79).[113]

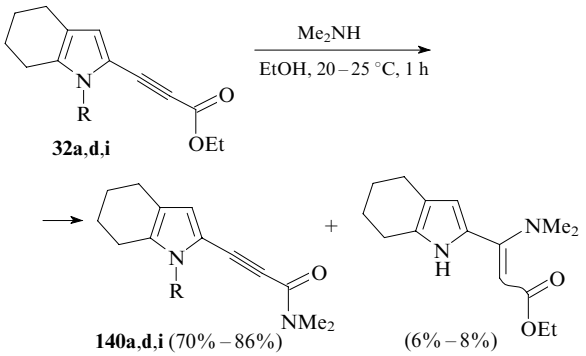
Scheme 79



R^1 = H (**a**), Me (**b**), Bn (**c**); R^2 = Me, Et

Unlike 3-(4,5,6,7-tetrahydroindol-2-yl)prop-2-yn-1-ones **138**, tetrahydroindolylpropynoates **32a**,**d**,**i** are easily transformed into *N,N*-dimethyl-3-(4,5,6,7-tetrahydroindol-2-yl)propynamides **140a**,**d**,**i** by the reactions with dimethylamine performed under similar conditions (at room temperature, for 1 h).[113] Despite a large excess of dimethylamine, the triple bond in the product remains intact. The formation of the addition product in small amounts was observed by ^1H NMR spectroscopy only in the reaction with propynoate **32a** (Scheme 80).

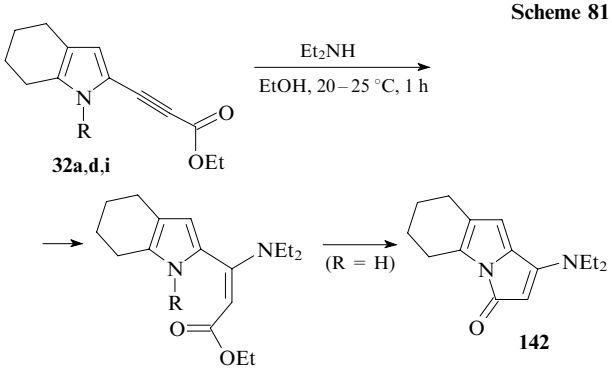
Scheme 80



R = H (**a**), Bn (**d**), Me (**i**)

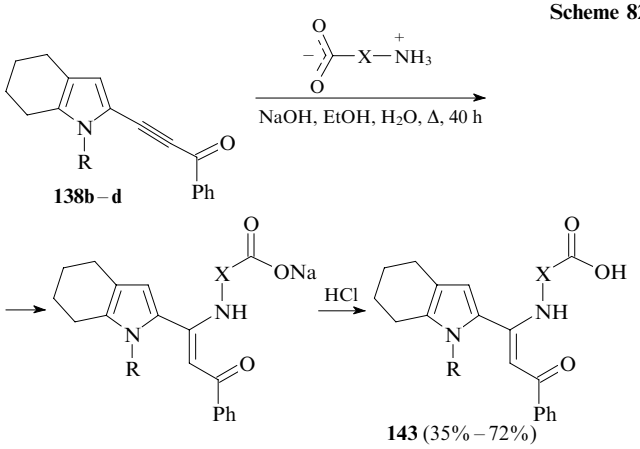
Diethylamine reacts with propynoates **32a**,**d**,**i** as the hydroaminating agent to form *E* isomers of adducts **141a**,**d**,**i** (Scheme 81).[113]

Scheme 81



R = H (**a**), Bn (**d**), Me (**i**)

Scheme 82



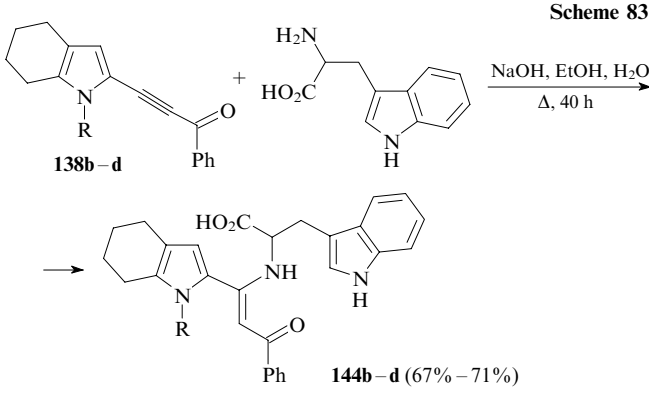
R = Me (**b**), Bn (**c**), CH=CH$_2$ (**d**); X = CH$_2$, (CH$_2$)$_2$, (CH$_2$)$_3$, CH(Bn)

The reaction of propynoate **32a** with diethylamine is accompanied by the intramolecular cyclization of primary adduct **141a** to hydrogenated pyrroloindole **142** (1 : 1 ratio). After the separation of the mixture of these products on Al_2O_3, adduct **141a** undergoes complete cyclization to give compound **142** (see Scheme 81).[113]

Therefore, tetrahydroindolylpropynoates **32** react with dimethylamine and diethylamine in a different way. Thus, the reactions with dimethylamine produce propynamides **140**, whereas diethylamine adds to the triple bond. This unexpected difference in the reactivity of dimethyl- and diethylamines towards propynoates **32** is attributed to the different steric characteristics of these amines because their basicity and nucleophilicity are almost identical. It is quite possible that this is due to the difference in the conditions used in the reactions with amines.

The nucleophilic addition of the simplest amino acids (glycine, β-alanine, γ-aminobutyric acid and phenylalanine) to the triple bond of 2-(benzoylethynyl)tetrahydroindoles **138b–d** affords new amino acids **143** containing the tetrahydroindole moiety.[114] The reaction is performed by heating under reflux in the presence of NaOH followed by the treatment with an aqueous HCl solution (Scheme 82). In the absence of NaOH, the addition of amino acids to the triple bond of ethynyltetrahydroindoles **138** does not take place. The role of the base is apparently to convert amino acids from the zwitterionic form into salts containing a free amino group, which are then react with compounds **138** as nucleophiles to form the corresponding salts. The latter are transformed into amino acids **143** by the treatment with an aqueous HCl solution. The reaction is regio- and stereoselective. In all cases, only *Z* isomers are produced.

Scheme 83



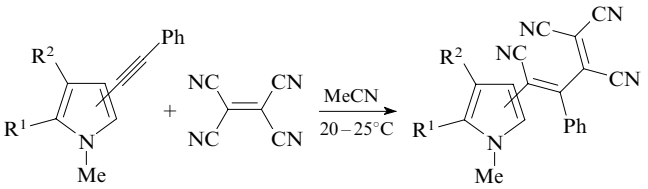
R = Me (**b**), Bn (**c**), CH=CH$_2$ (**d**)

As was shown by the reaction of 2-benzoylethynyl-4,5,6,7-tetrahydroindoles **138b–d** with tryptophan, this method can be applied for the synthesis of amino acids **144b–d**, which simultaneously contain the tetrahydroindole and indole substituents (Scheme 83).[114]

3. Cycloaddition involving the triple bond

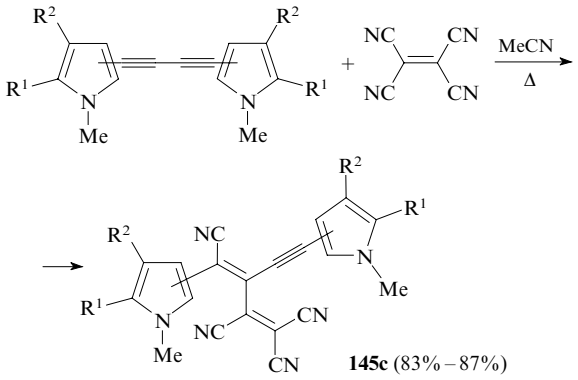
The reactions of 2- and 3-(phenylethynyl)pyrroles with tetracyanoethylene at room temperature produce 2-butadienyl derivatives of pyrroles **145a**,**b** (Scheme 84).[115]

Scheme 84



145a,**b** (83%–85%)

R^1, R^2 = Me, CO$_2$Et; isomers: 2 (**a**), 3 (**b**)



145c (83%–87%)

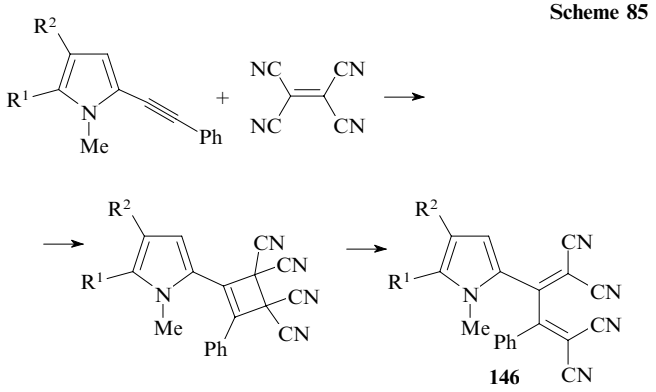
R^1, R^2 = Me, CO$_2$Et

In the case of butadiynediyldipyrrole, despite more severe reaction conditions (heating under reflux in acetonitrile), one of the triple bonds remains intact. In our opinion, the structure of compounds **145a–c** proposed by the authors [115] is doubtful. Based on the literature data on similar reactions,[116, 117] the reaction under consideration occurs most likely as the [2 + 2]-cycloaddition followed by the opening of the four-membered ring to form butadienylpyrroles **145a** (Scheme 85).

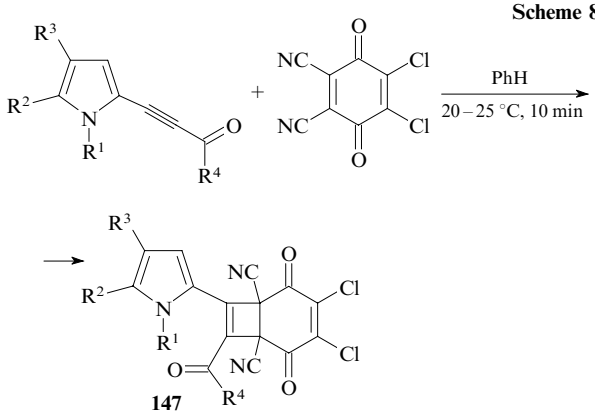
The [2 + 2]-cycloaddition of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone to 2-ethynylpyrroles affords functionalized bicyclic octadienediones **147** bound to pyrrole systems. The reaction proceeds in acetone or benzene at room temperature for 5–10 min and gives products in quantitative yields (Scheme 86). This reaction is the first example of the non-photochemical [2 + 2]-cycloaddition of the ethylene group to the triple bond.[118]

Meanwhile, in methanol, tetrahydroindolylpropynoate **32a** [R^1 = H, R^2–R^3 = (CH$_2$)$_4$, R^4 = OEt in Scheme 86] was unexpectedly transformed into dihydrofuranone **148** in 52% yield (Scheme 87). Isomeric dihydrofuranone **149** and bicycloheptadienone **150** were isolated in smaller amounts.[119] When considering possible schemes of the formation of these compounds, [2 + 2]-cycloadduct **147a**

Scheme 85



Scheme 86

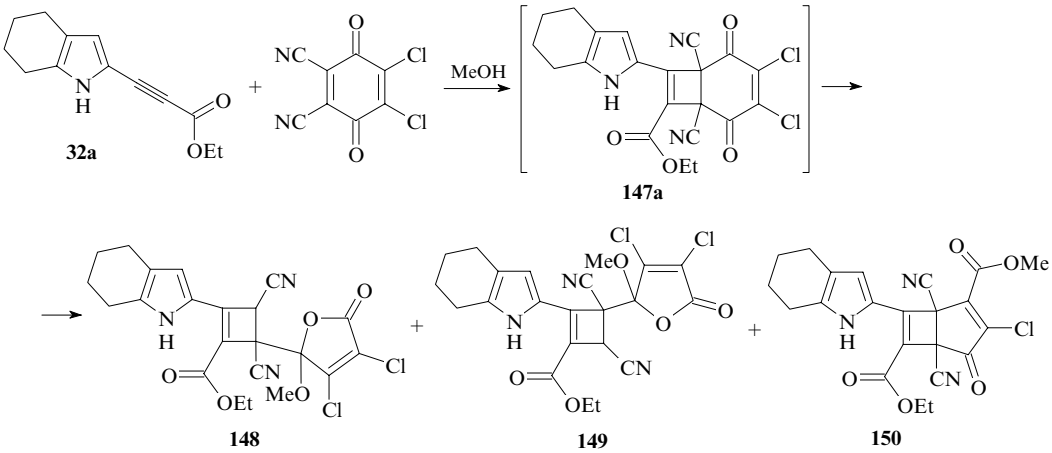


R^1 = H, Me, Bn; R^3 = H: R^2 = Ph, 4-ClC_6H_4; R^2–R^3 = $(CH_2)_4$; R^4 = OEt, Ph, 4-$O_2NC_6H_4$

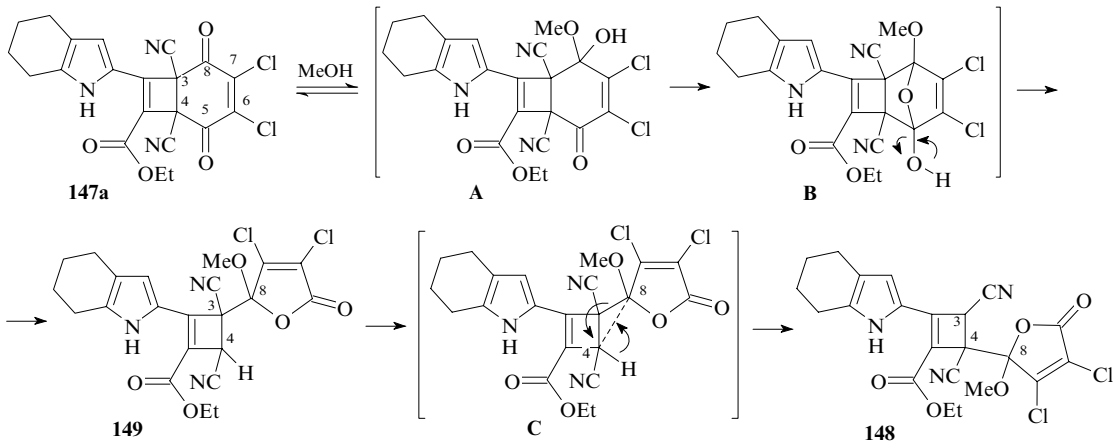
was postulated as an intermediate. Actually, the treatment of the latter with methanol (20–25 °C, 24 h or 55–56 °C, 15 min) afforded the same products.[120] The monitoring of the reaction (by ^{1}H NMR spectroscopy) showed that a large amount of dihydrofuranone **149** that was present at the onset of the rearrangement decreased and the ratio changed towards isomer **148**, *i.e.*, isomer **149** is apparently the kinetic reaction product, whereas isomer **148** is the thermodynamic product. This is confirmed by the fact that almost pure (98%) isomer **148** was isolated by the fractionation of a mixture of isomers **148** and **149** (1 : 8 ratio) using column chromatography (SiO_2, CH_2Cl_2).[119]

The formation of dihydrofuranones **148** and **149** is apparently a typical domino process. This process is initiated by the addition of methanol to the carbonyl group adjacent to the 3-position of cyclobutene (Scheme 88). Then the hydroxyl group in hemiacetal **A** attacks the opposite carbonyl function [at the C(5) atoms] followed by the breaking of the C(4)–C(5) bond in the intermediate **B**. This process is accompanied by the simultaneous proton transfer from the hydroxy group to the carbon atom C(4) and the formation of labile (kinetic) isomer **149**. The latter (as follows from the experimental data) is rearranged to more stable (thermodynamic) isomer **148**.[119]

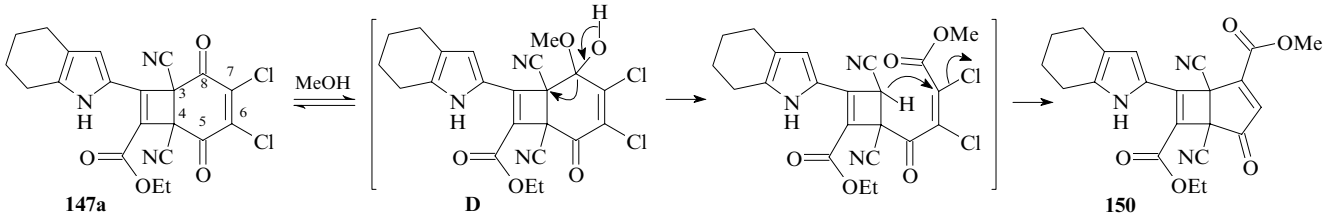
Scheme 87



Scheme 88



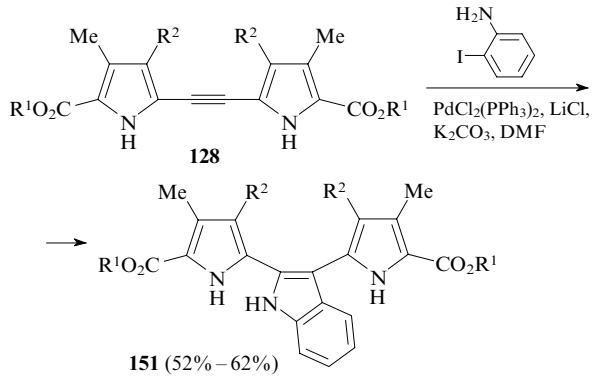
Scheme 89



Apparently, the first step of the rearrangement of bicyclo[4.2.0]octadienedione **147a** into bicyclo[3.2.0]heptadienone **150** involves the addition of alcohol to the same carbonyl group of quinone (Scheme 89) followed by the cleavage of the C(3)–C(8) bond in hemiacetal **D** with the simultaneous proton transfer from the hydroxy group to the C(3) atom and the formation of an ester functional group. This is followed by the proton abstraction from the 3-position accompanied by the nucleophilic attack on the opposite C–Cl bond and elimination of HCl. The final step of the reaction involves the cyclization to bicycloheptadienone **150**.[119]

The palladium-catalyzed heteroannulation of dipyrrolylacetylenes **128** with iodoaniline (Larock indole synthesis) affords 2,3-dipyrrolylindoles **151** capable of the selective binding of fluoride ions (Scheme 90).[86]

Scheme 90

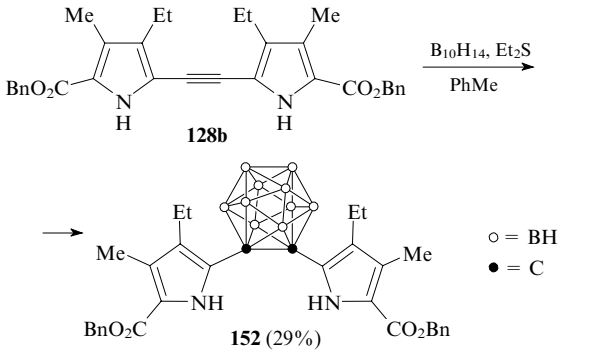


R^1 = Me, Bn; R^2 = Me, Et

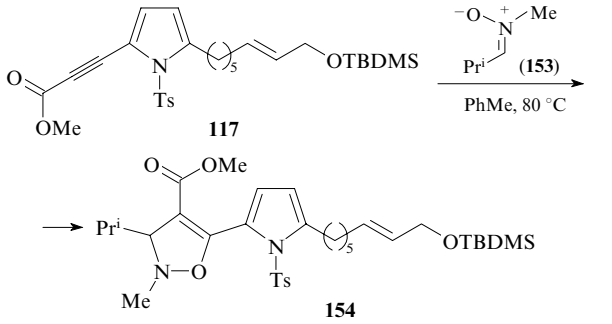
The reaction of dipyrrolylacetylene **128b** (R^1 = Bn, R^2 = Et) with decaborane and diethyl sulfide in toluene gave *ortho*-carborane cluster **152** exhibiting fluorescence with high quantum yield (Scheme 91).[86]

The 1,3-dipolar cycloaddition of nitrone **153** to pyrrolylpropynoate **117** affords isoxazoline **154** serving as an intermediate in the synthesis of roseophilin (Scheme 92).[105]

Scheme 91



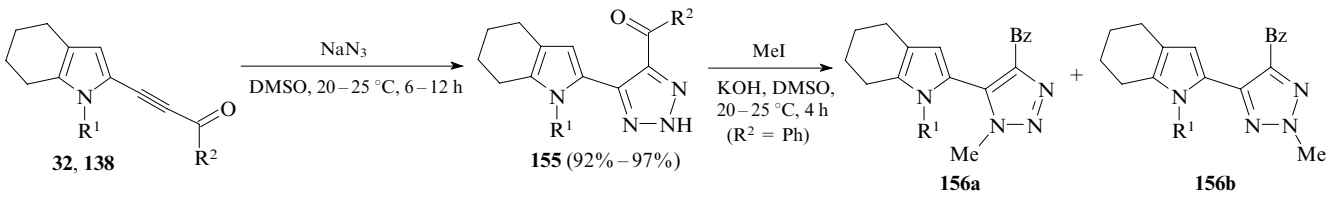
Scheme 92



Conjugates of 4,5,6,7-tetrahydroindoles with 1,2,3-triazoles functionalized by an ester or benzoyl group (compounds **155**) were synthesized by the 1,3-dipolar cycloaddition of the azide anion to the C≡C bond of tetrahydroindolylpropynoates **32** and 2-benzoylethynyltetrahydroindoles **138** (Scheme 93).[121] The alkylation of compounds **155** (R^2 = Ph) affords a mixture of two possible regioisomers: N(1)- (**156a**) and N(2)-substituted (**156b**) 1,2,3-triazoles in a ratio of ~1 : 1.

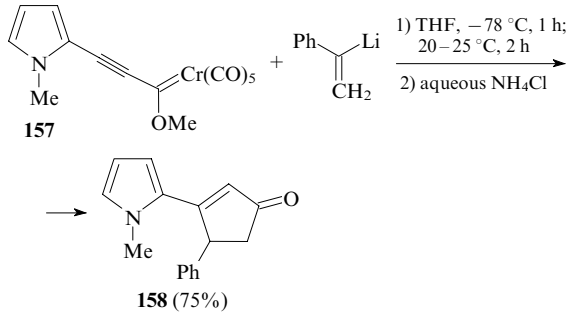
Ethynylpyrrolecarbene complex **157**, which can be easily prepared from ethynylpyrrole and $Cr(CO)_6$, reacts with α-styryllithium to form cyclopentenone **158** (Scheme 94).[122]

Scheme 93



R^1 = H, Me, Bn, CH=CH_2; R^2 = OEt, Ph

Scheme 94

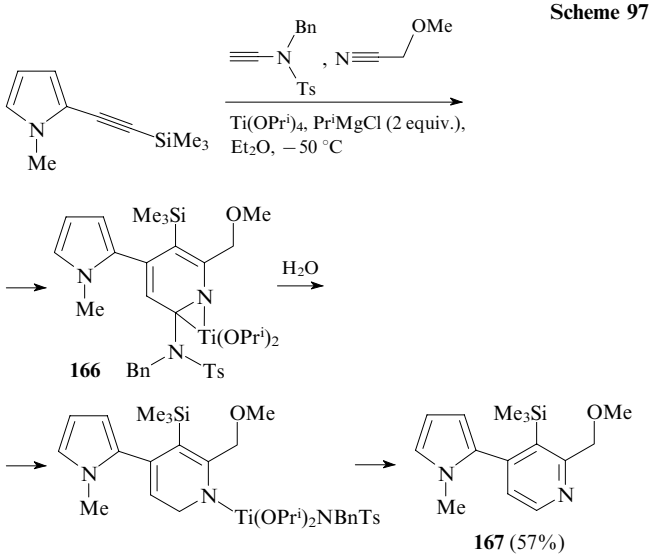


The treatment of pyrrolylethynyl vinyl sulfones **102** with a large excess of lithium hexamethyldisilazide results in their transformation into butadiynylpyrroles **159**, and the reaction of the latter with anilines produces tetraaryl-2,2′-bipyrroles **160** (Scheme 95).[98] After the heating with Na_2S in DMF, butadiynylpyrrole **159a** ($Ar^1 = Ar^2 = Ph$) forms 1,2-diphenyl-5-(5-phenyl-2-thienyl)pyrrole (**161**).[98]

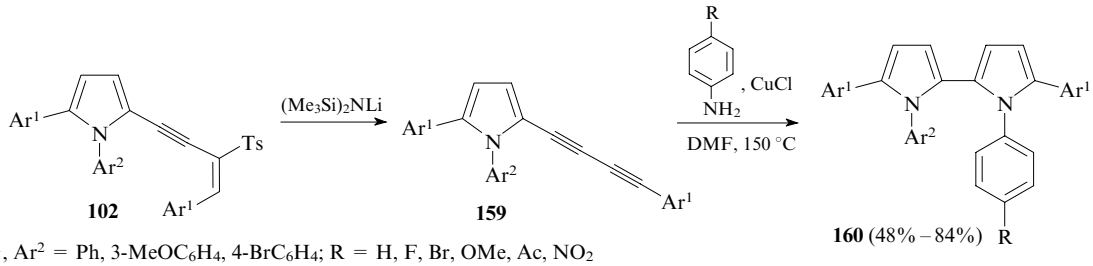
The reaction of heptadiynyldipyrroles **69a**,**b** with the complex (η^2-propene)$Ti(OPr^i)_2$ generated *in situ* from $Ti(OPr^i)_4$ and 2 equiv. of Pr^iMgCl, followed by the treatment with $PhPCl_2$ gave 2,5-bis(*N*-*tert*-butoxycarbonylpyrrol-2-yl)phospholes **162a**,**b**. The treatment of products **162a**,**b** with sodium methoxide afforded 2,5-bis(pyrrol-2-yl)phospholes **163a**,**b** (Scheme 96).[70] Compounds **163** are easily oxidized by hydrogen peroxide or *m*-chloroperoxybenzoic acid to give phosphine oxides **164a**,**b**, whereas these compounds are transformed into phosphine sulfides **165a**,**b** by the treatment with elemental sulfur.

The four-component coupling reaction, which involves two acetylene derivatives, (*N*-methylpyrrol-2-yl)trimethylsilylacetylene and (*N*-benzyl-*N*-*p*-toluenesulfonylamino)ace-

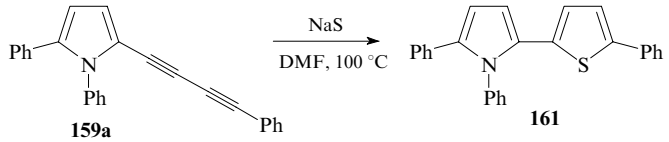
Scheme 97



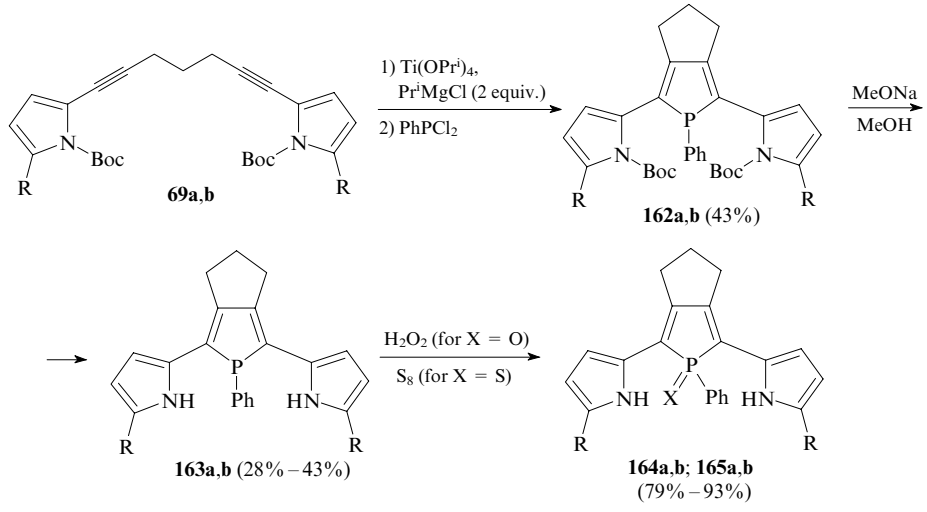
Scheme 95



Ar^1, Ar^2 = Ph, 3-$MeOC_6H_4$, 4-BrC_6H_4; R = H, F, Br, OMe, Ac, NO_2



Scheme 96

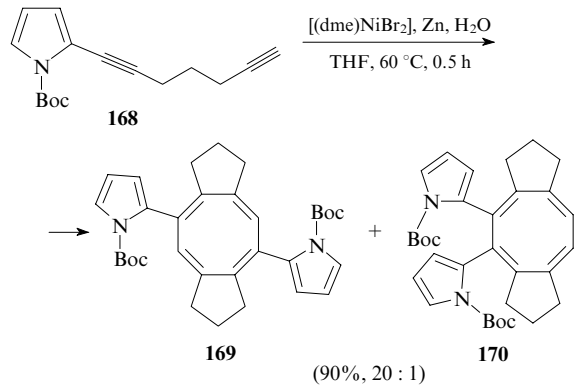


R = H (**a**), Ph (**b**); X = O (**164**), S (**165**)

tylene, methoxyacetonitrile and the titanium reagent, selectively produces titanated pyridine **166**, and the latter is transformed into substituted pyrrolylpyridine **167** after the treatment with water (Scheme 97).[123]

The formation of four C–C bonds and three rings in one step is observed in the Ni^0-catalyzed [2+2+2+2]-cycloaddition of pyrrole **168** containing internal and terminal alkynyl groups. This reaction produced functionalized cyclooctatetraenes **169** and **170** (Scheme 98).[124] The reaction is almost selective. Thus, cycloadduct **170** was detected in an insignificant amount.

Scheme 98

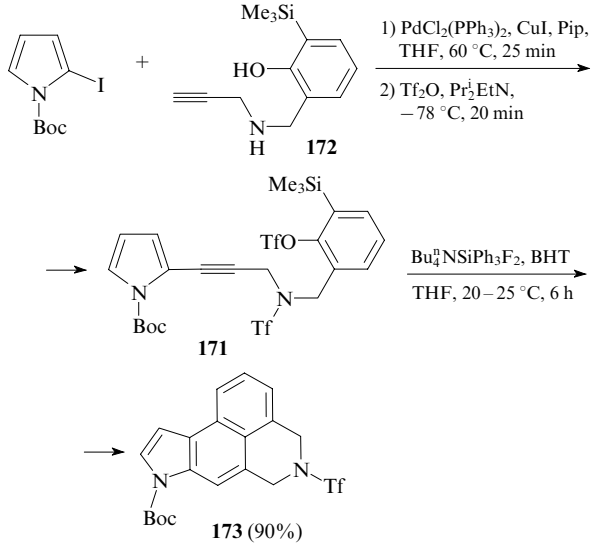


dme is dimethoxyethane

4. Annulation reactions

The intramolecular [4+2]-cycloaddition of functionalized ethynylpyrrole **171**, which was prepared from *N*-Boc-pyrrol-2-yl iodide and terminal acetylene **172**, affords fused polycyclic aromatic compound **173** in high yield (Scheme 99).[125]

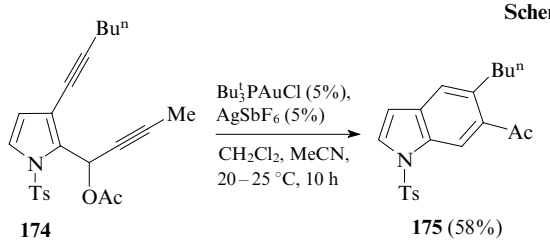
Scheme 99



BHT is 2,6-di(*tert*-butyl)-4-methylphenol,
Tf is trifluoromethanesulfonate

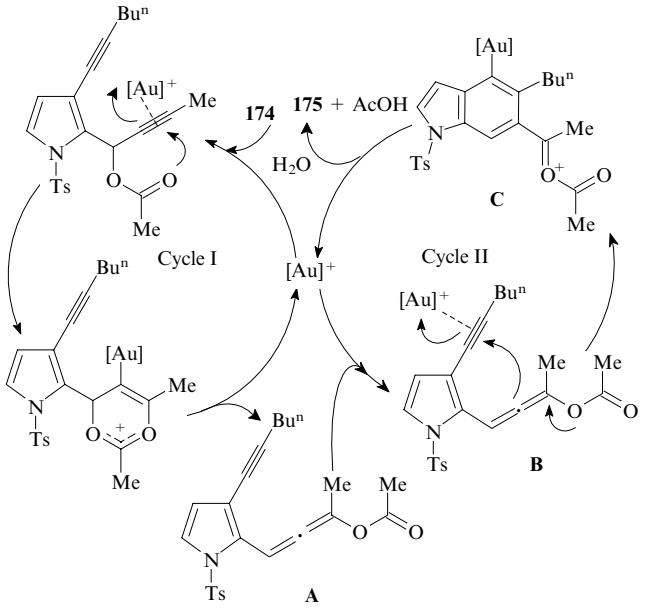
In the presence of gold salt as a catalyst, dialkynylpyrrole **174** undergoes cyclization to acetylindole **175** (Scheme 100).[126]

Scheme 100



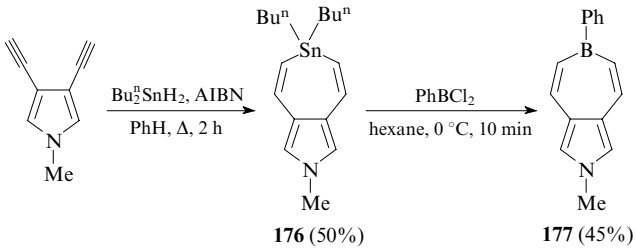
The proposed mechanism of this transformation involves the coordination of metal to dialkynylpyrrole **174** to form allene **A** *via* the [3,3]-sigmatropic rearrangement (cycle I) (Scheme 101). The activation of the triple bond of the compound **A** that remained intact with AuCl induces the 6-*endo-dig* cyclization of allenylacetate **B** (cycle II) to indole **C.** The hydrolysis of the latter gives acetylindole **175**. Silver salts do not catalyze this rearrangement.

Scheme 101



The hydrostannylation of 3,4-diethynyl-1-methylpyrrole followed by the treatment of the resulting bicyclic compound **176** with $PhBCl_2$ gave 5-methyl-1-phenylpyrrolo[3,4-*d*]-borepine (**177**) (Scheme 102).[68]

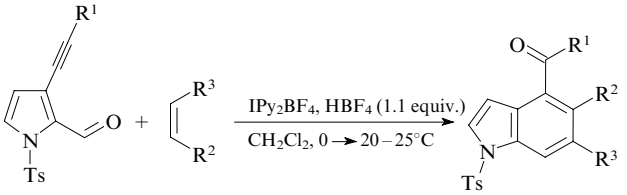
Scheme 102



AIBN is azobis(isobutyronitrile)

The benzannulation of 3-alkynylpyrrole-2-carbaldehydes **178a**,**b** with alkenes, enamines or enol ethers catalyzed by the iodonium salt afforded indole derivatives **179** (Scheme 103).[127, 128]

Scheme 103



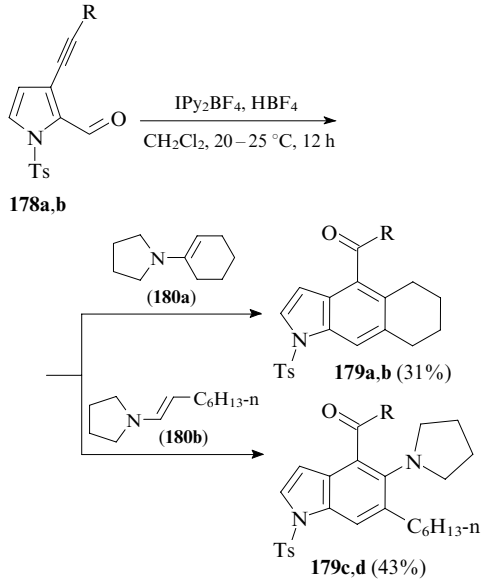
178a,**b** **179** (31–72%)

R^1 = Bu^n (**178a**), Ph (**178b**); R^3 = Ph: R^2 = H, Me;
R^2 R^3 is cyclopentene, cyclohexene, indene, 1,2-dihydronaphthalene, 1-cyclohexenylpyrrolidine, 2,3-dihydropyran

Indoles **179** were regioselectively generated from *N*-tosyl-substituted 3-alkynylpyrrole-2-carbaldehydes **178a**,**b** and the corresponding alkenes by the treatment with the IPy_2BF_4–HBF_4 system. Alkyl- and aryl-substituted alkenes, as well as cycloalkenes, such as 2,3-dihydropyran, indene and 1,2-dihydronaphthalene, were used as the starting reactants.

The structures of the reaction products of aldehydes **178** with enamines, which were synthesized from aldehydes and ketones, depend on the nature of enamine. Thus, the reaction of enamine **180a**, which was prepared from pyrrolidine and cyclohexanone, with compounds **178a**,**b** produces indoles **179a**,**b**, whereas under similar conditions, enamine **180b** prepared from hexanal is transformed into indoles **179c**,**d** containing functional groups of the starting enamine in the indole ring (Scheme 104).[127, 128]

Scheme 104



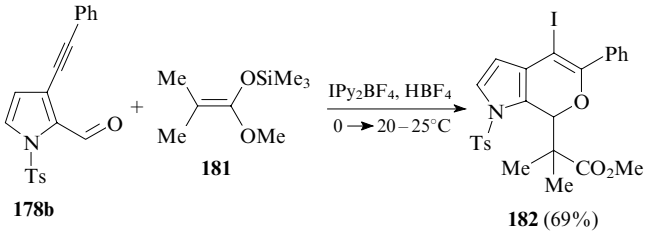
178a,**b** **179a**,**b** (31%) **179c**,**d** (43%)

R = Bu^n (**178a**, **179a**, **179c**), Ph (**178b**, **179b**, **179d**)

In the presence of the benziodonium salt as the catalyst, 3-ethynylpyrrole-2-carbaldehyde **178b** reacts with silyl ketene acetal **181** to form 1,7-dihydropyrano[3,4-*b*]pyrrole **182** (Scheme 105).[127, 128]

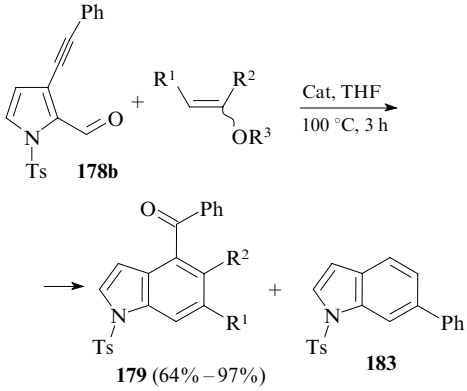
In order to develop the catalytic version of the synthesis of indole from 3-ethynylpyrrolecarbaldehyde **178b,** the reaction of the latter compound with enol ethers was studied in the presence of catalysts of different types: $Cu(OTf)_2$, $AuBr_3$ and $AgNTf_2$. In all cases, the corresponding benzoylindoles **179** were prepared in good yields (Scheme 106).[129]

Scheme 105



178b **181** **182** (69%)

Scheme 106



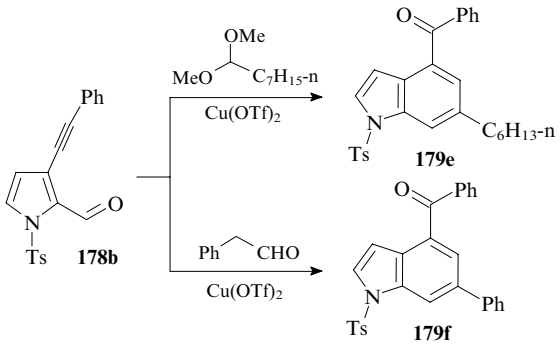
178b **179** (64%–97%) **183**

R^2 = H: R^1 = H, n-C_6H_{13}, Ph; R^1–R^2 = $(CH_2)_4$; R^3 = Me, Bu^n

Attempts to synthesize decarbonylated indole did not give satisfactory results. For example, the reaction of ethynylpyrrole **178b** with β-methoxystyrene in the presence of the $Cu(NTf_2)_2$–H_2O system produced the corresponding indole **179** (R^1 = Ph, R^2 = H, R^3 = Me in Scheme 103) in 49% yield, whereas decarbonylated indole **183** was obtained in a yield of $<20\%$.[129]

Benzoylindoles were synthesized also with the use of 2-phenylacetaldehyde and dimethoxyoctane. Their reactions with ethynylpyrrolecarbaldehyde **178b** are catalyzed by $Cu(OTf)_2$ to give indoles **179e**,**f** in 79% and 53% yields, respectively (Scheme 107).[129]

Scheme 107



178b **179e** **179f**

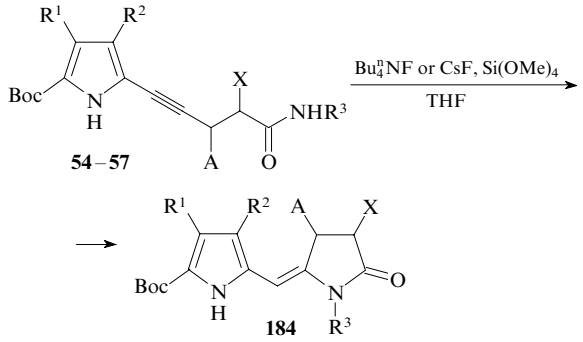
5. Intramolecular cyclization of acetylenic substituents

Under particular conditions, ethynylpyrroles can be transformed into cyclic compounds. Hence, these compounds can be considered as key building blocks for the synthesis of complex polycyclic systems, many of which are analogues of natural structures having biological activity.

For example, ethynylpyrroles **54**–**57**, which were synthesized by the Sonogashira reaction from halopyrroles and acetylenic amides, undergo 5-*exo-dig* cyclization to dihy-

dropyrromethenones **184** (Scheme 108).[47–55] The reaction is usually performed in the presence of Bu^n_4NF. It was shown that the $CsF-Si(OMe)_4$ system can also be employed as the catalyst, and it was hypothesized that the active catalyst for this reaction can include the pentacoordinate silicon atom that is formed by the nucleophilic attack of the F anion on $Si(OMe)_4$.[49]

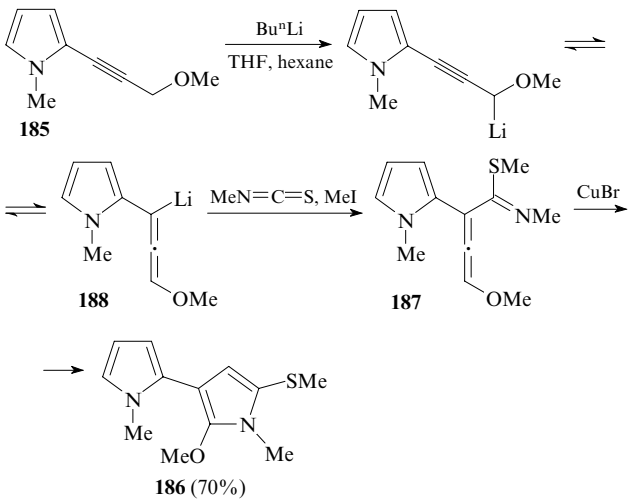
Scheme 108



$R^1 = (CH_2)_2CO_2Me$, $R^2 = Me$; $R^1-R^2 = (CH_2)_4$; $R^3 = H$, Bn; A = H, Me, CH(OMe)Me, CH(OBn)Me; X = H, Me

The one-pot assembly of 1,1′,2,5-tetrasubstituted 3,2′-bipyrrole **186** containing alkoxy and alkylsulfanyl groups was performed based on ethynylpyrrole **185** (Scheme 109).[130] The precursor of product **186**, azatriene **187**, is generated by the addition of methyl isocyanate to lithium derivative **188** followed by the methylation of the adduct with MeI. The final step of the process was carried out in the presence of catalytic amounts of CuBr.

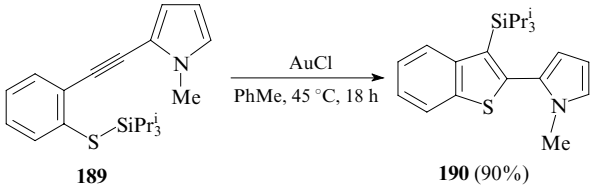
Scheme 109



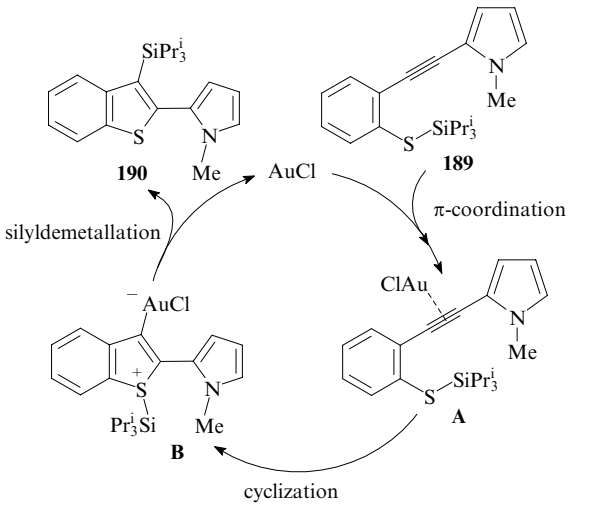
The AuCl-catalyzed cyclization of 2-phenylethynylpyrrole **189**, which contains the triisopropylsilylsulfanyl group in the *ortho* position of the benzene ring, to 3-(triisopropylsilyl)-2-(pyrrol-2-yl)benzo[*b*]thiophene **190** proceeds as the *trans*-addition to the S–Si bond, the so-called thiosilylation (Scheme 110).[131]

The mechanism of the cyclization of ethynylpyrrole **189** is shown in Scheme 111. Gold(I) chloride acts as a Lewis acid and is involved in the coordination to the acetylenic group to form the intermediate **A**.

Scheme 110



Scheme 111



The subsequent intramolecular nucleophilic attack of the sulfur atom on the electron-deficient triple bond results in the formation of the silylsulfonium intermediate **B**. The 1,3-migration of the silyl group and the subsequent elimination of AuCl (silyldemetallation) afford product **190**.[131]

* * *

Therefore, as can be seen from the above-considered data, there is a considerable progress in the synthesis of C-ethynylpyrroles and the use of these compounds for the preparation of various functionalized pyrroles. Along with the improvement of the known methods for the synthesis based on the reactions of halopyrroles with terminal acetylenes, new preparative approaches are being developed with the goal of synthesizing C-ethynylpyrroles from the most readily available compounds. In particular, great attention is given to the development of reactions of unfunctionalized pyrroles with haloacetylenes, which open up facile and efficient routes to groups of difficult to access or unknown C-ethynylpyrroles containing acceptor substituents at the triple bond. It should be emphasized that the introduction of such substituents into the ethynyl moiety of C-ethynylpyrroles fundamentally extends their scope for the synthesis of various compounds and the possible areas of their application. There are considerable prospects of the use of these systems as basic pyrrole building blocks for the design of conjugated and fused heterocyclic compounds.

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