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Cyclization of *ortho*-ethynylbiaryls as an emerging versatile tool for the construction of polycyclic arenes †

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Cyclization and cycloisomerization of *ortho*-aryl(ethynyl)arenes provide an easy direct access to fused polycyclic aromatic carbo- and heterocycles. This methodology has demonstrated an impressive progress in the recent years. The goal of this review is to give a comprehensive outlook on the synthetic potential, scope, limitations, and mechanistic aspects of the cyclization reactions. The material is arranged according to the activation method that can be used to induce cyclization: pyrolysis, metal catalysis, electrophilic activation, radical induction, base catalysis. Particular attention is paid to the specificity of *ortho*-ethynylbiaryls with a heterocyclic central core.
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1. Introduction

First reported by Fujiwara in 2000,[1–3] the Pd^{II}-catalyzed insertion of alkynes into $C_{Ar}-H$ bonds of arenes (so called hydroarylation of the triple bond) has been widely developed further for the construction of carbo- and heterocycles, in particular, in an intramolecular version. Although the first attempts on cyclization of *ortho*-alkynylbiphenyls under flash vacuum pyrolysis (FVP) conditions were done in 1974,[4,5] the work of Fürstner on $PtCl_2$-catalyzed synthesis of phenanthrenes from alkynylated biphenyl derivatives published in 2002 (Ref. 6) paved the way for a rapid growth of related metal-catalyzed cyclizations. Since then, late transition metal catalysis has been the most common approach to perform these reactions. Meanwhile, other methods of activation, *i.e.* by electrophiles including Brønsted acids, base catalysis, and radical induction, present valuable alternative methodologies.

Hydroarylation of alkynes and related cyclization reactions have been a subject of several previous reviews;[7–16] however, these papers mainly discuss intermolecular reactions between arenes and alkynes or intramolecular reactions of substrates with at least one atom linking an aryl ring and a triple bond. Only fragmental and particular aspects of intramolecular cyclizations of *ortho*-ethynylbiaryls were covered. The vast amount of relevant literature that has appeared during the past few years necessitates a review of this subject to provide a systematic outlook on its features and scope.

Our review comprehensively covers all types of cyclizations employing *ortho*-ethynylbiaryls as starting material, and is organized by the type of the activation method applied. Historically the first pyrolytic technique is given at the beginning. The reactions of *ortho*-ethynylbiaryls with a central heterocyclic core are described in a separate Section as we believe that presentation of the effect of ring

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size, number, type and position of heteroatoms on the activity of substrates and the reaction outcome is more important in this case. Reactions with no change in the substrate molecular formula are mentioned as 'cycloisomerization' to emphasize their specificity.

The synthetic potential, substrate scope and limitations, functional group tolerance, and mechanistic issues of the cyclization reactions are discussed; however, the details of seemingly contradictory mechanisms given in some original articles have been omitted to prevent confusion. We aim to present flexibility of this transformation and its exceptional value and current relevance for the chemistry community. The review covers original articles which have been published mainly through the last 10 – 15 years, up to the middle of 2018.

Abbreviations

AIBN — azobisisobutyronitrile,
(*R*)-BINAP — (*R*)-(+)-(1,1′-binaphthalene-2,2′-diyl)-bis(diphenylphosphine),
BrettPhos — 2-(dicyclohexylphosphino)-3,6-dimethoxy-2′,4′,6′-triisopropyl-1,1′-biphenyl,
t-ButylXPhos — 2-di-*tert*-butylphosphino-2′,4′,6′-triisopropyl-1,1′-biphenyl,
Cod — cycloocta-1,5-diene,
Cp* — pentamethylcyclopentadiene,
Cy — cyclohexyl,
p-Cymene — 1-isopropyl-4-methylbenzene,
DBU — 1,8-diazabicyclo[5.4.0]undec-7-ene,
DCE — 1,2-dichloroethane,
DDQ — 2,3-dichloro-5,6-dicyano-1,4-benzoquinone,
DFT — density functional theory,
D-*i*-Prpf — 1,1′-bis(diisopropylphosphino)ferrocene,
DMA — *N*,*N*-dimethylacetamide,
Dppf — 1,1 -bis(diphenylphosphino)ferrocene,
(*R*)-DTBM-SegPhos — [(4*R*)-(4,4′-bi-1,3-benzodioxole)-5,5′-diyl]bis[bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphine],
FVP — flash vacuum pyrolysis,
IPr — 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene,
JohnPhos — 2-(di-*tert*-butylphosphino)biphenyl,
KIE — kinetic isotope effect,
Me_4Bu^tXPhos — 2-di-*tert*-butylphosphino-3,4,5,6-tetramethyl-2′,4′,6′-triisopropyl-1,1′-biphenyl,
$NaBAr^F_4$ — sodium tetrakis[3,5-bis(trifluoromethyl)-phenyl]borate,
NIS — *N*-iodosuccinimide,
NMP — *N*-methyl-2-pyrrolidone,
OFET — organic field effect transistor,
(*S*,*S*)-Ph-BPE — (+)-1,2-bis((2*S*,5*S*)-2,5-diphenylphospholano)ethane,
Phth — phthaloyl,
Selectfluor — *N*-chloromethyl-*N*′-fluorotriethylenediammonium bis(tetrafluoroborate),
TBP — 2,4,6-tri(*tert*-butyl)pyridine,
TBS — tributylsilyl,
TFA — trifluoroacetic acid,
TFAA — trifluoroacetic anhydride,
TFE — 2,2,2-trifluoroethanol,
TfOH — trifluoromethanesulfonic acid,
TFP — tris(2-furanyl)phosphine,
Th — thiophenyl,
TIPS — triisopropylsilyl,
TIPS-EBX — 1-[(triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one,
Tp — tris(1-pyrazolyl)borate,
p-TSA — *p*-toluenesulfonic acid,
XPhos — 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl.

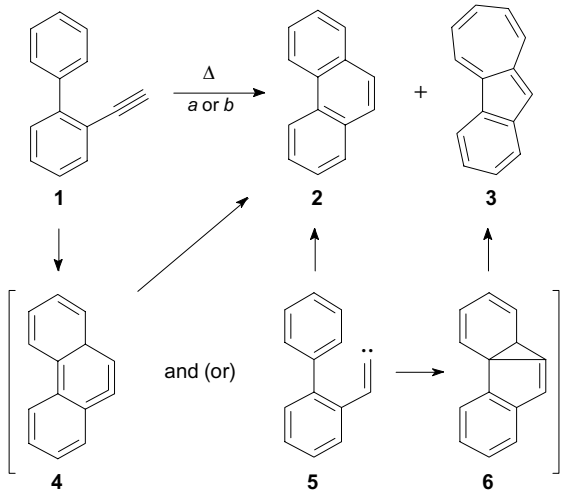
2. Pyrolysis

In 1974, Brown and coworkers reported a first example of flash vacuum pyrolysis (FVP) of 2-ethynylbiphenyl **1** leading to phenanthrene **2** (Scheme 1 *a*).[4, 5] The second product was benzo[*a*]azulene **3**, which was considered as a compelling evidence for generation of the carbene intermediate **5** and its trapping by the adjacent phenyl ring. Vinylidene **5** could undergo direct insertion into an aromatic C – H bond to form phenanthrene **2** or, alternatively, its addition to an aromatic double bond would lead to benzazulene **3** through a putative intermediate **6**. Phenanthrene **2** could also arise in this reaction *via* the known thermal azulene-to-naphthalene rearrangement.[17] Later, thermal ring closure of ethynylbiphenyl **1** to phenanthrene **2** was studied by DFT calculations, and a competitive route *via* electrocyclic closure to a cyclic allene (isophenanthrene **4**) was predicted to be nearly isoenergetic to a vinylidene pathway.[18] However, free energy estimates at 625 °C favour the 1,2-H-shift to vinylidene **5** because of its lower entropic cost. Alternative transformations of vinylidene **5** to phenanthrene **2**, which can take place instead of C – H insertion, were also calculated.[18]

This transformation could be easier performed under conditions of microwave flash pyrolysis on graphite. The reaction of ethynylbiphenyl **1** carried out with graphite at 300 °C/150 W gave phenanthrene **2** in 94% yield along with benzazulene **3** (< 1%) and anthracene (6%, as secondary product from **3**) (Scheme 1 *b*).[19]

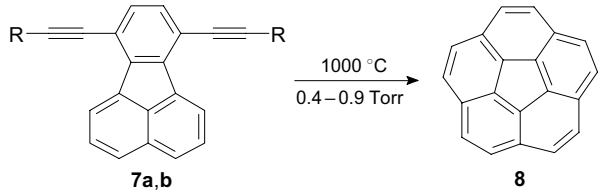
Since the pioneering work of Brown, a great interest to cyclization of *ortho*-ethynylbiphenyls has been prompted by its outstanding potential to construct complex fused systems. Synthetic routes to corannulene, the smallest bowl-shaped polycyclic hydrocarbon fragment of C_{60} with fullerene-like curvature, were elaborated by Scott *et al.*[20,21] Unfortunately, 7,10-diethynylfluoranthene **7a** suffers polymerization under FVP conditions because of extremely low volatility requiring strong heating (1000 °C); hence, the yield of corranulene **8** was *ca.* 10% (Scheme 2). At lower

Scheme 1



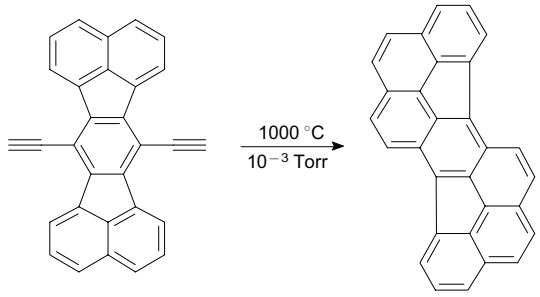
(*a*) 700 °C, 0.2 mm: **2** : **3** = 72 : 28 (99%); (*b*) 300 °C, MW (150 W), graphite: **2** (94%), **3** (< 1%), anthracene (6%)

Scheme 2



7a,**b** **8**

R = H (**a**, 10%), TMS (**b**, 36%)

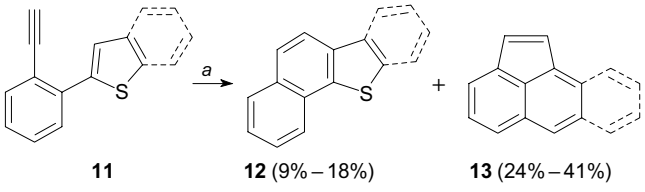


9 **10** (20%)

temperatures, an isomer with only one side closed was obtained. Better yield of **8** was obtained from trimethylsilyl-substituted precursor **7b**.[22] FVP of diethynyl compound **9** led to hepta[5][5]circulene **10**, a subunit of C_{70} fullerene, in 20% yield.[23]

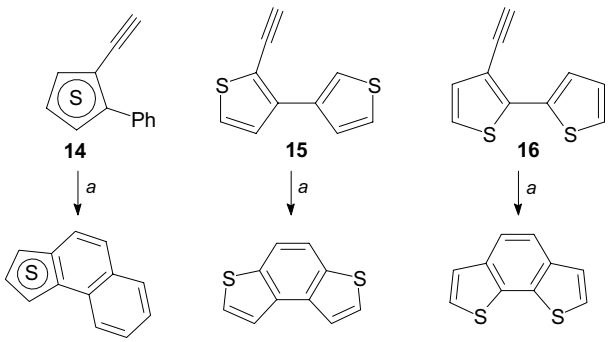
Thiophene ring was attempted in FVP cyclization in both roles: as a central core and as an aromatic counterpart to the triple bond. Upon harsh pyrolytic conditions, desulfurized products (acenaphthylenes **13**) were predominantly obtained when 2-(2-ethynylphenyl)(benzo)thiophenes **11** were used as starting compounds; minor amounts of naphthothiophenes **12** also formed (Scheme 3).[24] In contrast, cyclizations of three isomeric *ortho*-ethynyl(phenyl)thiophenes **14**, as well as reactions of ethynyl(thiophenyl)thiophenes **15** and **16**, smoothly occurred to give fused polycycles **17** – **19** in high yields regardless the position of the sulfur atom. Thiophenes with two *ortho*-ethynyl(phenyl) moieties required higher vacuum (0.01 Torr), because of the lower volatility, to provide acceptable yields of the corresponding pentacyclic products.

Scheme 3



11 **12** (9% – 18%) **13** (24% – 41%)

(*a*) 800 – 1000 °C, 0.1 Torr



14 **15** **16**

17 (76% – 86%) **18** (98%) **19** (63%)

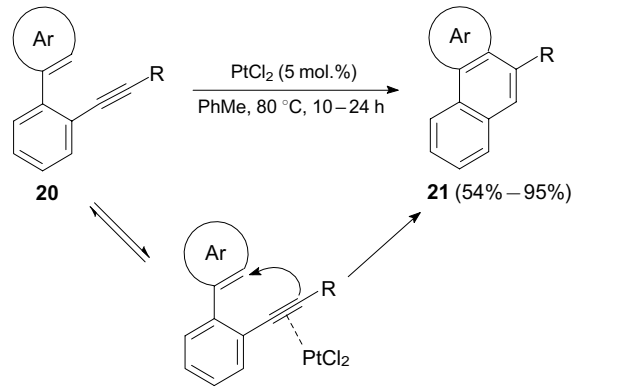
(*a*) 1000 °C, 0.1 Torr

3. Metal catalysis

3.1. Platinum

The fundamental work of Fürstner considered the effect of various metal catalysts and structure factors on cyclization of *ortho*-ethynylbiaryls **20** (Scheme 4).[6,25] Among a set of different metal species (Pt^{II}, Ga^{III}, In^{III}, Au^{III}, Ru^{III}, Rh^{III}), $PtCl_2$ and $AuCl_3$ proved to be the best catalysts in terms of efficiency and practical convenience. The use of $PtCl_2$ (5 mol.%) in toluene at 80 °C was accepted as the optimal conditions, and this has been widely employed in a subsequent work (see below). Various substituents in starting biphenyls **20** were tolerated to provide high yields of phenanthrenes **21**, though the phenyl ring undergoing cyclization maintained electron-rich or neutral character. Pyrrole and thiophene can successfully replace this phenyl ring; however, $PtCl_2$ was effective only for such compounds with terminal triple bond (R = H) whereas heteroaryl substrates with internal alkyne moiety required the use of either $GaCl_3$ or $InCl_3$ for productive cyclization (see Scheme 68, Section 3.4). A pronounced preference for 6-*endo*-*dig* cyclization to give phenanthrenes over the conceivable 5-*exo* mode was established for $PtCl_2$-catalyzed reactions. $PtCl_2$ exhibits high affinity for π-bonds and acts as a soft Lewis acid. The subsequent attack of the activated triple bond on the adjacent aryl ring proceeds in a manner similar to Friedel – Crafts type aromatic substitution; the empirical data gathered from this and the following work correspond to this interpretation.

Scheme 4



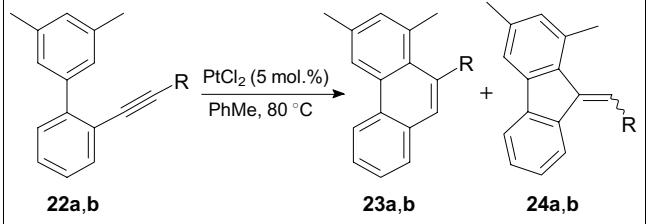
20 **21** (54% – 95%)

Ar = 2-$MeOC_6H_4$, 3-$MeOC_6H_4$, 3,5-$Me_2C_6H_3$, 3,5-$(MeO)_2C_6H_3$, Ph, 1-Naph, pyrrol-2-yl, *N*-methylindol-2-yl; R = H, Me, Ph;
Ar = 2-Th, pyrrol-1-yl; R = H

The only exception was compound **22a** possessing an electron-withdrawing ester group at the triple bond, which enforced the 5-*exo*-*dig* pathway to form 9-benzylidenefluorene **24a** predominantly (Scheme 5).[6,25] Likewise, the *p*-anisyl derivative **22b** gave a mixture of both possible isomers **23b** and **24b** in a 3 : 2 ratio.

Mechanism of cyclization of *ortho*-ethynylbiphenyls upon treatment with transition and non-transition metal salts and complexes was thoroughly studied using DFT

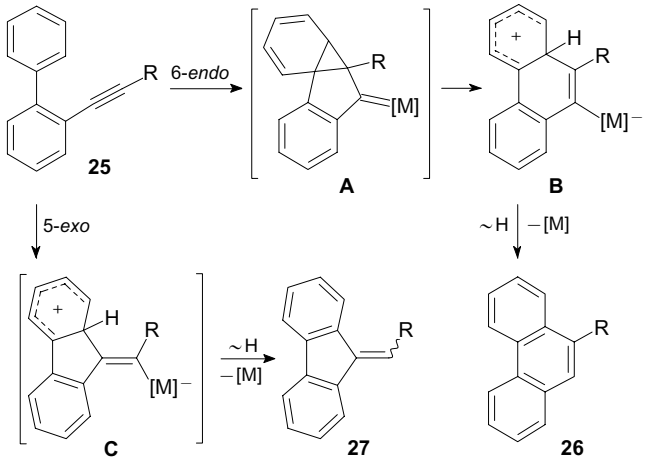
Scheme 5



22a,**b** **23a**,**b** **24a**,**b**

R = CO_2Me (**a**), 4-$MeOC_6H_4$ (**b**); **23a** : **24a** = 5 : 95 (73%^{GC}), **23b** : **24b** = 60 : 40 (100%^{GC})

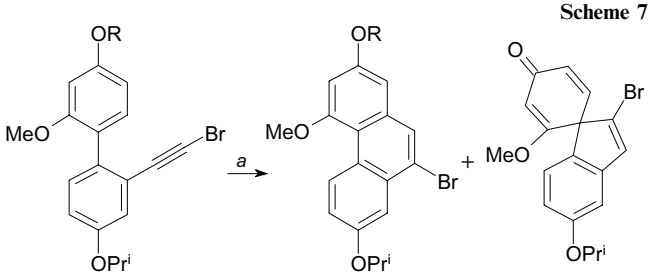
Scheme 6



calculations (Scheme 6).[26] Recently it was refined for compounds **25** possessing a fragment of propiolic acid (R = CO_2Me) taking into account the possible involvement of the ester group in the intramolecular proton transfer.[27] The reaction can proceed in either 6-*endo* or 5-*exo* fashion; the choice between the two modes depends on the type of catalyst and the structure of substrate. As a rule, the metal – cyclopropane – carbene intermediate **A** arises on the way to phenanthrene **26**. Opening of the cyclopropane bond of **A** gives Wheland-type intermediate **B**, which finally undergoes two consecutive 1,2-H shifts. Formation of fluorene **27** starts directly with the five-membered intermediate **C**. In this case, the calculated energy barriers of the rate-determining first step were lower, although phenanthrene **26** is significantly more stable than isomeric fluorene **27**. The ester group at the triple bond reduces the barrier of 5-*exo*-cyclization [26] and facilitates H-migration in the final steps.[27] All these factors favour fluorene **27** that is consistent with the experimental data (see Scheme 5).

$PtCl_2$ was reported to be ineffective for cyclization of haloalkynes where Au^I or In^{III} catalysts are preferable (see Scheme 33, Section 3.2).[25] At the same time, electron-rich bromoalkynes **28a,b** afforded phenanthrenes **29a,b** even by $PtCl_2$-catalysis (Scheme 7).[28] The *ortho*-cyclization to **29** was accompanied by unexpected 1,2-migration of the bromine atom (it usually proceeds by Au^I catalysis, see Section 3.2), but in addition, a concomitant 5-*endo-dig ipso*-cyclization to form spiro derivative of cyclohexadienone **30** took place.[29] The two branches of the reaction pathway could be switched by using different catalysts. Thus, pivaloyl-substituted **29b** was preferentially obtained with $PtCl_2$ (63% yield) from **28b**; however, the same starting

Scheme 7



28a – c **29a**,**b** **30**

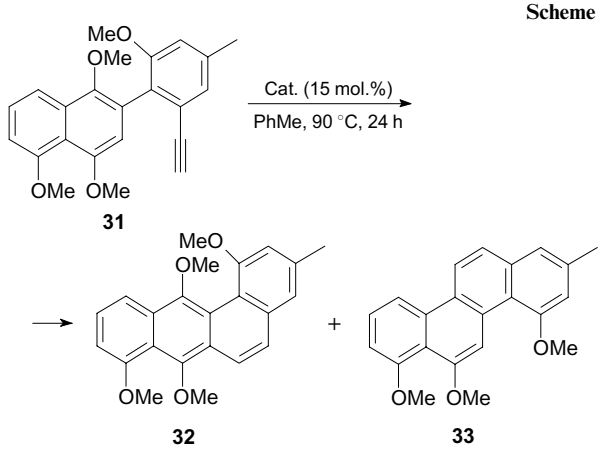
(*a*) Cat., PhMe, 80 °C

Compounds **28**	R	Catalyst	Yield (%)	
			compounds **29**	compound **30**
a	CH_2OMe	$PtCl_2$	9	49
a	CH_2OMe	$InCl_3$	–	–
b	$C(O)Bu^t$	$PtCl_2$	63	–
b	$C(O)Bu^t$	$InCl_3$	–	83
c	H	$PtCl_2$	–	72
c	H	$InCl_3$	–	82

compound afforded spiro product **30** with $InCl_3$ (83% yield). Compound **28c**, with a free hydroxy group, was transformed to spiro compound **30** with both $InCl_3$ and $PtCl_2$.

Another option for the *ipso*-attack was demonstrated in the reaction of the sterically encumbered compound **31** (Scheme 8).[30] Upon $PtCl_2$-catalysis, starting naphthalene **31** provided a mixture of benzo[*a*]anthracene **32** obtained through an ordinary cyclization on the unsubstituted *ortho*-position of naphthalene, and chrysene **33** resulted from *ipso*-substitution of the methoxy group at the opposite *ortho*-position. Replacement of Pt^{II} for Au^{III} gave almost the same yields of both products.

Scheme 8

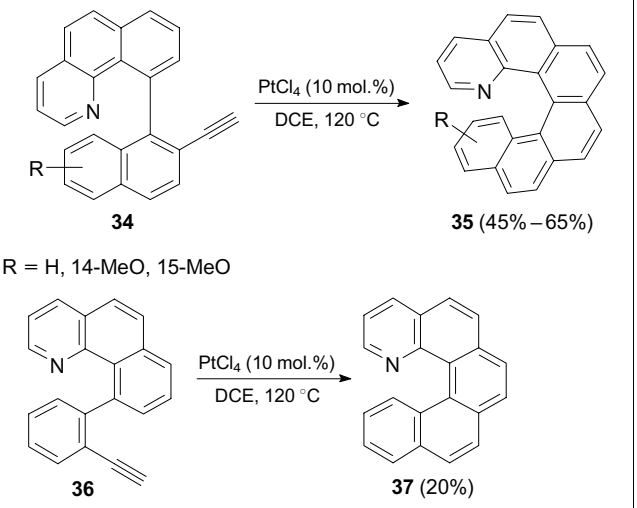


31 **32** **33**

Catalyst	Yield (%)	
	compound **32**	compound **33**
$PtCl_2$	61	23
$AuCl_3$	56	31

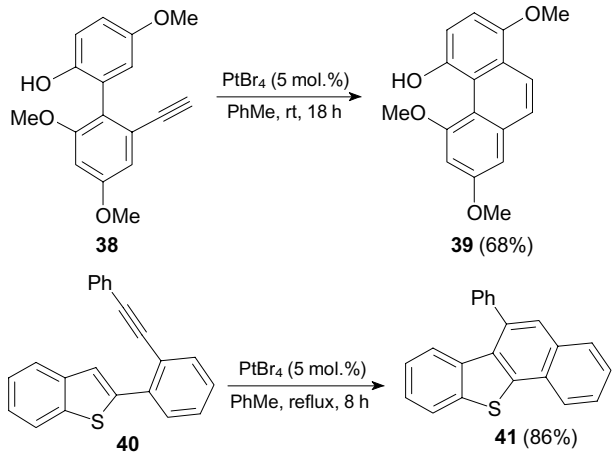
Not only Pt^{II} but also Pt^{IV} salts can catalyze cycloisomerization. 1-Aza[6]helicenes **35** were prepared from 10-(2-ethynylnaphth-1-yl)benzo[*h*]quinolines **34** using $PtCl_4$ since attempts with $PtCl_2$, Au, In, Ga, and Ru catalysts failed, likely due to the presence of pyridine functionality (Scheme 9).[31] Later this procedure was adapted for the synthesis of 1-aza[5]helicene **37** from pyridine derivative **36**.[32]

Scheme 9



$PtBr_4$ allowed the synthesis of phenanthrene **39** from sterically encumbered biphenyl **38** even at room temperature (Scheme 10, top line).[33] Cyclization of 2-(2-(phenylethynyl)phenyl)benzo[*b*]thiophene **40** was performed with high yield of product **41** using $PtBr_4$ in refluxing toluene (Scheme 10, bottom line).[34]

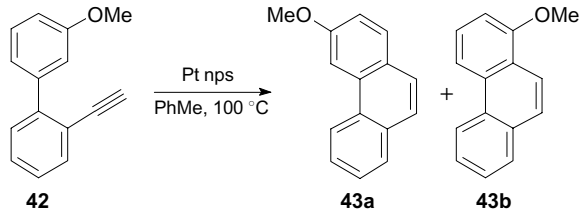
Scheme 10



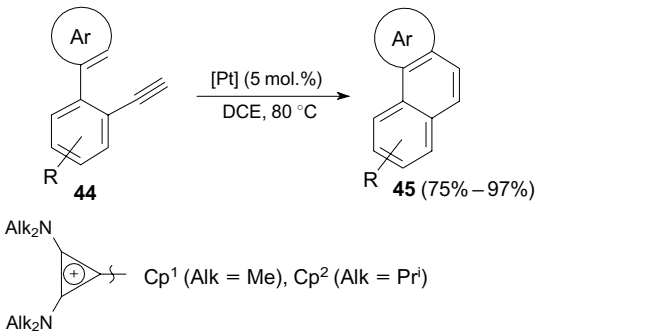
Platinum nanoparticles were applied as a heterogeneous catalyst with comparable yield and selectivity relative to $PtCl_2$ (Scheme 11).[35] A mixture of regioisomeric products **43a**,**b** was obtained from biphenyl **42** with *meta*-methoxy substituted ring undergoing cyclization.

The strong π-acceptor character of cyclopropenylidene-stabilized phosphenium ligands (Cp^1 and Cp^2) substantially increases the intrinsic π-acidity of Pt and enhances its ability to activate π-systems toward nucleophilic attack (Scheme 12).[36,37] As a result, a remarkable acceleration of 6-*endo*-*dig* cyclization was observed for *ortho*-ethynylbiaryls

Scheme 11



Scheme 12



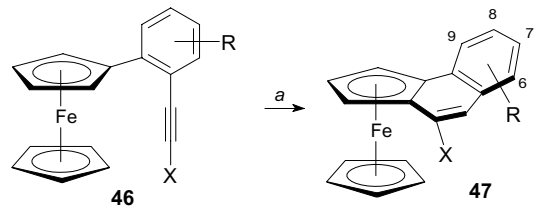
[Pt] = $Cp^{\ddagger}_3PPtCl_3(ClO_4)_2$, $Ag[CB_{11}H_6Cl_6]$ or $Cp^2PX_2PtCl_3$ [X = 3,5-$(CF_3)_2C_6H_3$], $AgSbF_6$; Ar = 4-TMS-C_6H_4, 3,5-$(MeO)_2C_6H_3$, 3,5-$Me_2C_6H_3$, 3,4,5-$(MeO)_3C_6H_2$, 1-Naph, phenanthren-9-yl, acenaphthylen-5-yl, dibenzo[*b*,*d*]furan-4-yl, benzothiophen-3-yl, 5-chlorothiophen-2-yl; R = H, OH, OMe, OBn, Cl, F, CO_2Me, CF_3, OTBS

44: high yields of phenanthrenes **45** were achieved within 15 – 90 min [*cf.* 10 – 24 h with $PtCl_2$ (see Scheme 4)]. Perfect functional group tolerance expands the substrate scope to various biphenyls and heterocyclic compounds **44**. Only strongly coordinating functionalities such as thioether group were found to interfere with the activity of the catalytic system.

Enantioselective cycloisomerization of ethynyl(ferrocenyl)benzene derivatives **46** was achieved using a chiral cationic platinum catalyst (Scheme 13).[38] The worst *ee* value (18%) was observed for trifluoromethyl-substituted substrate while for other terminal alkynes *ee* was >75%. Introduction of ethoxycarbonyl group to the triple bond required heating and had a drastic effect on both the yield of **47** and the enantioselectivity.

Meanwhile, it is $PtCl_2$ that is the most used catalyst to perform cyclization probably due to an attractive combina-

Scheme 13



(*a*) $PtCl_2$(cod) (10 mol.%), (*S*,*S*)-Ph-BPE (10 mol.%), $AgBF_4$ (20 mol.%), DCE, rt, 15 – 24 h; X = H, R = H, 7-MeO, 7-Me, 7-Cl, 7-F, 7-F_3C, 8-Cl, 7,8-$(CH)_4$ (62% – 97%, 18% – 97% *ee*); X = CO_2Et, R = H (35%, 36% *ee*, at 80 °C)

tion of high activity and availability. Application of $PtCl_2$ for the synthesis of various fused polycyclic systems (phenanthrenes, chrysenes, helicenes, pyrenes, coronenes, *etc.*) is described in the examples below. As a rule, the number of triple bonds as well as the number of aromatic rings involved in cyclization has no noticeable effect on the outcome of the reaction. A more pronounced impact is observed for substituents in both aryl rings of biphenyl system. Reaction conditions which were optimized by Fürstner (see Scheme 4) can be referred to as the standard ones and they are generally used only with slight alterations in the temperature regime (in certain cases heating to 120 °C was needed) and catalyst loading (up to 10 mol.% – 20 mol.%).

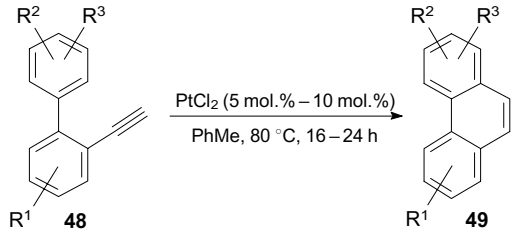
Similarly to the above mentioned examples of biphenyls with electron-neutral or electron-rich aryl rings, electron-deficient substrates **48** were annulated using $PtCl_2$ (Scheme 14).[39] A series of fluoro-, chloro- and acetyl-substituted phenanthrenes **49** with various position of these groups was prepared in this manner, albeit in moderate yields. A comparable result was obtained for the bromo(methoxy)-substituted biphenyl **48** (see Scheme 14, bottom line).[40]

Several tylophora alkaloids were synthesized using $PtCl_2$-catalyzed annulation of alkynylated biphenyls **50** as a key step to construct a phenanthrene core of **51** (Scheme 15).[41]

Both 1-naphthyl- **52** and 2-naphthyl- **54** *ortho*-ethynylbenzenes delivered benzannulated phenanthrenes **53** and **55** under standard conditions (Scheme 16).[42–44] In contrast to the substrate **52** with R^1 = OMe ($R^2 - R^4$ = H) providing 80% yield of the corresponding benzo[*c*]phenanthrene **53**, compound with R^1 = Me was completely inactive.[42] Steric hindrance caused by the methyl group also suppressed reactions of this substrate with $InCl_3$ or $PdCl_2(PhCN)_2/2\,AgBF_4$, and even electrophilic cyclization upon treatment with TfOH or TFA (see Section 4.2). Cyclization on 2-naphthyl ring of **54** occurred with high regioselectivity (> 20 : 1) to give chrysene **55** in 85% yield.[44]

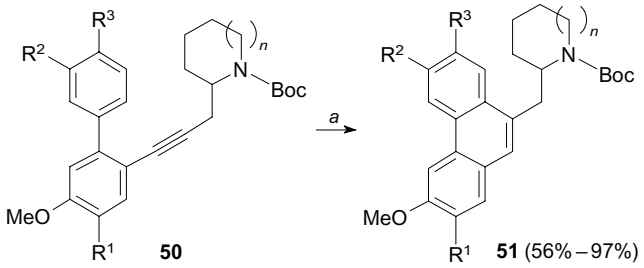
Bischrysenes **57** were synthesized in a similar manner from bis(biaryl)diynes **56** (Scheme 17).[45–48] This strategy is applicable to larger polycyclic aromatic hydrocarbons containing up to six Clar sextets[49] (phenanthren-2-yl, phenanthren-9-yl, chrysen-2-yl groups instead of naphthyl were successfully introduced).[45] However, the $PtCl_2$-catalyzed aromatization of bis((2-(chrysen-5-yl)phenyl)diyne failed while the use of ICl effected the electrophilic cyclization smoothly to give the desired iodinated compound in 83% yield.[45]

Scheme 14



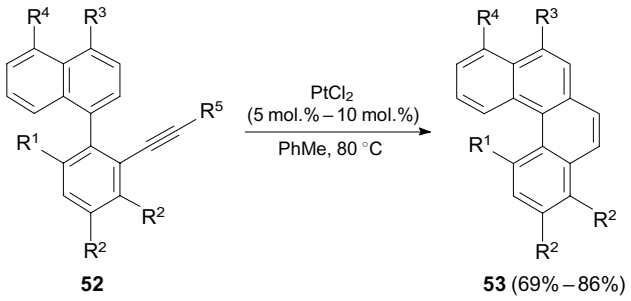
48: R^1 = H, F, Cl; R^2 = H, 4-F; R^3 = Ac (43% – 60%); R^1 = H, R^2 = 2-Br, R^3 = 3-MeO (68%)

Scheme 15

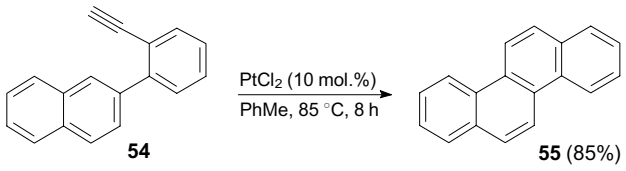


(*a*) $PtCl_2$ (5 mol.%), PhMe, 80 °C; *n* = 0, 1; R^1, R^2, R^3 = H, OMe; $R^2 + R^3 = OCH_2O$

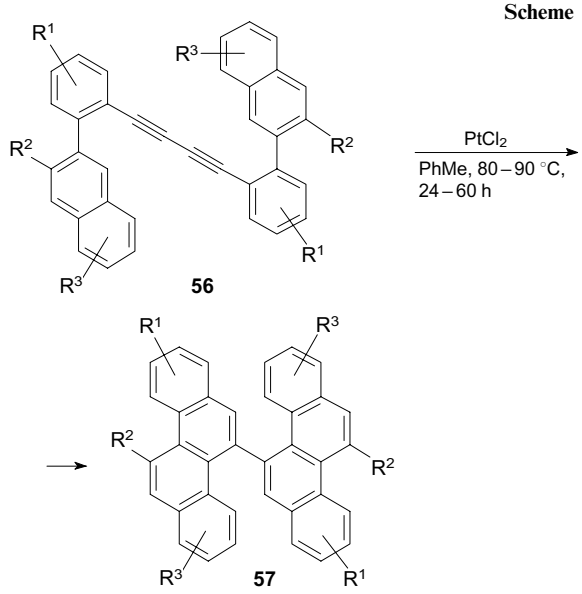
Scheme 16



R^1, R^2 = H, OMe; R^3 = H, Me; R^4 = H; $R^3 + R^4 = (CH_2)_2$; R^5 = H, TMS



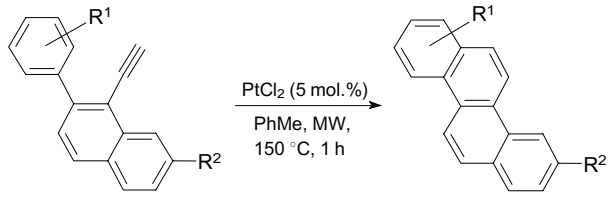
Scheme 17



R^1, R^3 = H, Bu^t; R^2 = H, Br ($PtCl_2$ 10 mol.%) (70% – 88%);
$R^1 = C_{12}H_{25}$, R^2 = H, R^3 = CHO ($PtCl_2$ 30 mol.%) (48%);
$R^1 = R^2$ = H, $R^3 = CH_2OAc$ ($PtCl_2$ 25 mol.%) (33%)

Electron-deficient chrysenes **59** were synthesized from substrates **58** with *ortho*-aryl(ethynyl) fragment located at the naphthyl ring (Scheme 18).[50] Use of microwave conditions was reasoned by the example of the naphthalene **58** derivative (R^1 = 4-CF_3, R^2 = F, TMS-terminated triple bond): refluxing for 65 h gave only 58% conversion to the desilylated chrysene **59**, while higher temperature under microwave heating allowed to get 71% of **59** within 1 h. The lowest yield (31%) was obtained from nitrile **58** (R^1 = 3-CN, R^2 = H), while other substrates **58** provided not less than 51% yield of **59**.

Scheme 18

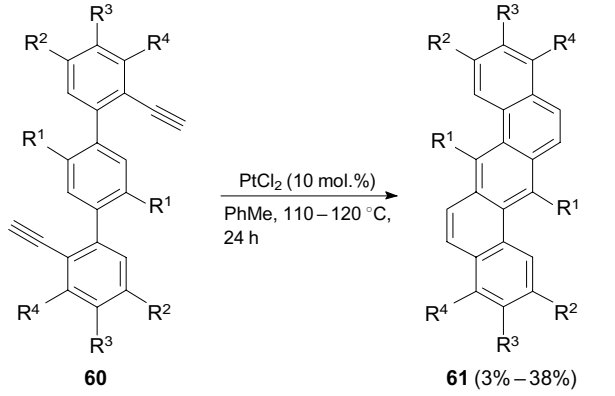


58 **59** (31% – 83%)

R^1 = 4-CF_3, 4-CO_2Me, 2-F, 3-CN; R^2 = H, F, OMe

Dibenzo[*a*,*h*]anthracene framework can be constructed in two ways. The first one consists in double cyclization on the central ring of *para*-terphenyl system (Scheme 19), and the second implies isomeric position of two alkyne moieties at the central ring (Scheme 20). Quite expected in the first case, the yield of dibenzo[*a*,*h*]anthracene **61** with bulkier *ortho*-tolyl groups at the core (R^1 = 2-MeC_6H_4, R^2 = R^4 = H, R^3 = Bu^t, 27%)[51] was slightly lower than that with methyl groups instead (R^1 = Me, 26% – 38%)[52] (see Scheme 19). The TMS-substituted terphenyl **60** (R^1 = Me, R^2 = R^4 = H, R^3 = TMS) gave almost no product **61** (3%) probably due to desilylation and/or related side reactions.[52]

Scheme 19

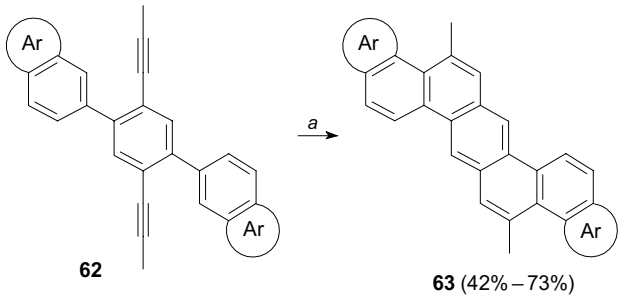


60 **61** (3% – 38%)

R^1 = 2-MeC_6H_4, Me; R^2 = H, Me, $OC_{10}H_{21}$; R^3 = H, TMS, Bu^t; R^4 = H, Me

On the other hand, dibenzo[*a*,*h*]anthracenes **63** can be obtained from 1,4-diaryl-2,5-dipropynylbenzenes **62** (see Scheme 20).[53,54] Aromatic counterparts for the cyclization vary from 2-naphthyl to extended polyaromatic systems with up to five rings (picen-3-yl).[54] Platinum catalyst provided excellent regioselectivity and satisfactory efficiency through attack on the more hindered carbon atom of the 2-naphthyl and other fused aromatic arrays (due to the large HOMO orbital coefficients of these carbon atoms). An opposite regioselectivity was observed for ruthenium catalysis in that the less hindered aryl carbon was the preferable site for attack (see Scheme 77, Section 3.4).

Scheme 20

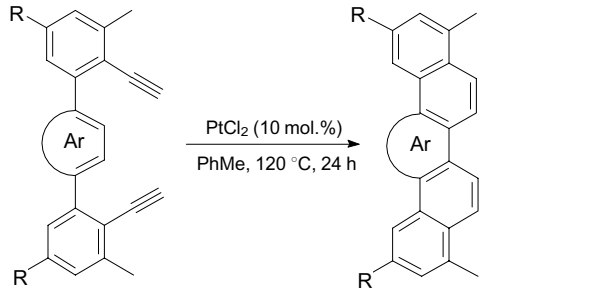


62 **63** (42% – 73%)

(*a*) $PtCl_2$ (20 mol.%), CO, PhMe, 80 – 90 °C, 12 h

Double annulation on the same side of the central ring of diethynylterphenyl **64** is determined by structure limitations (Scheme 21). The reaction proceeded smoothly whether the core is phenyl or thiophenyl moiety to give picenes **65**.[52]

Scheme 21



64 **65** (51% – 73%)

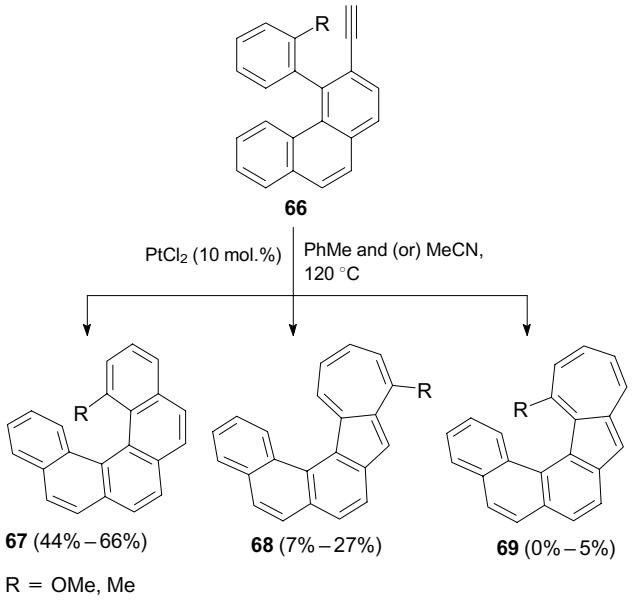
Ar = 2,3-$Me_2C_6H_2$, thiophene-2,5-diyl; R = H, Me, $OC_{10}H_{21}$

1-Substituted [5]helicenes **67** were isolated as major products of the cyclization of *ortho*-aryl(ethynyl)phenanthrenes **66** with $PtCl_2$ in toluene (Scheme 22).[55] The formation of minor products, azulene derivatives **68** and **69** [their appearance was explained by an alternative cleavage of the cyclopropane ring in a metal carbene intermediate of type **A** (see Scheme 6)], could be diminished by using AuCl/$AuCl_3$ or by switching solvent from toluene to acetonitrile. The highest yields of phenanthrenes **67** were achieved in a 1 : 1 toluene/acenonitrile mixture; the yields of azulenes did not exceed 8%.

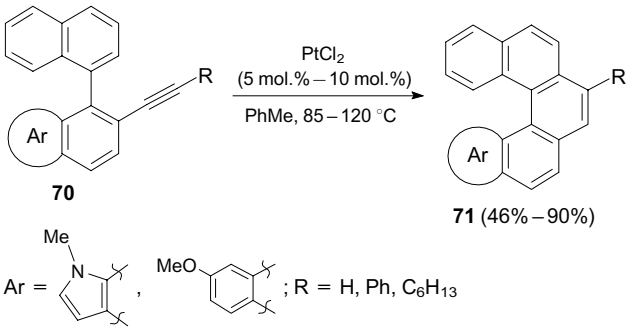
Effect of the substituent at the triple bond was observed in the course of cyclization to [5]helicene derivatives **71** (Scheme 23).[56 – 58] Higher yields (75% – 90%) were obtained for oct-1-ynyl (R = C_6H_{13}) and ethynyl substituted compounds **70** (Ar = $MeOC_6H_3$) than for the naphthalene with phenyl group at the alkyne terminus (46%).

[6]Helicene framework of **75** can be easily achieved either by double[59] or monoannulation[60,61] of variously constructed substrates **72** – **74** (Scheme 24). Regardless of which diastereomeric form of **72** (R^1 = Me) (or a mixture of

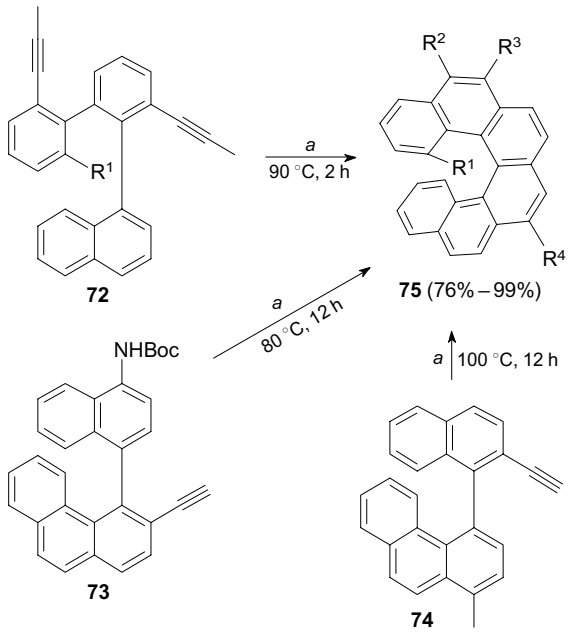
Scheme 22



Scheme 23



Scheme 24

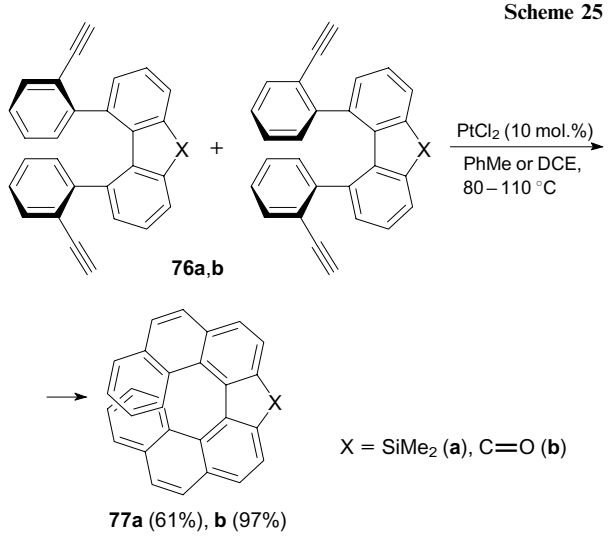


(*a*) $PtCl_2$ (10 mol.%), PhMe; R^1 = H, OMe; R^2 = H, NHBoc; R^3 = H, Me; R^4 = H, Me

both) was taken into the reaction, the final product **75** was a racemic mixture of two axial enantiomers.[59]

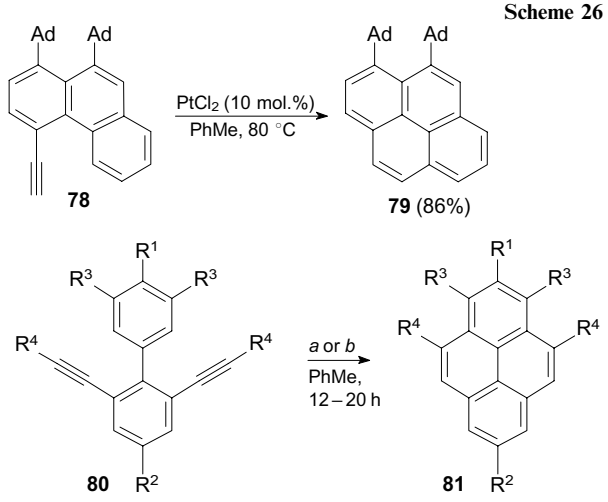
Pt-catalyzed double cyclization of alkynes was applied for the construction of two twisted phenanthrene moieties. The resulting [7]helicene-like structures **77a,b** were obtained from unseparable mixtures of two conformers of 1,9-bis-(2-ethynylphenyl)dibenzosilole[62] **76a** and fluorenone[63] **76b** (Scheme 25). Racemic **77a**,**b** can be separated to enatiomerically pure (*P*)- and (*M*)-isomers by using preparative HPLC on a chiral stationary phase.

Scheme 25



Pyrene system can be formed *via* either monocyclization of 4-ethynylphenanthrene or double cyclization of bis(*ortho*-ethynyl)biphenyl.[64] In that way adamantyl-substituted[65] **79** and alkoxy-substituted[66] pyrenes **81** were prepared in high yields from the corresponding substrates **78** and **80** with terminal triple bonds (Scheme 26). Aryl-substituted diynes **80** demonstrated poor reactivity, and low yields of the corresponding pyrenes **81** were observed even with 1 equiv. of $PtCl_2$ at higher temperature.[67,68] Introduction of more electron-deficient aryl group (**80**,

Scheme 26

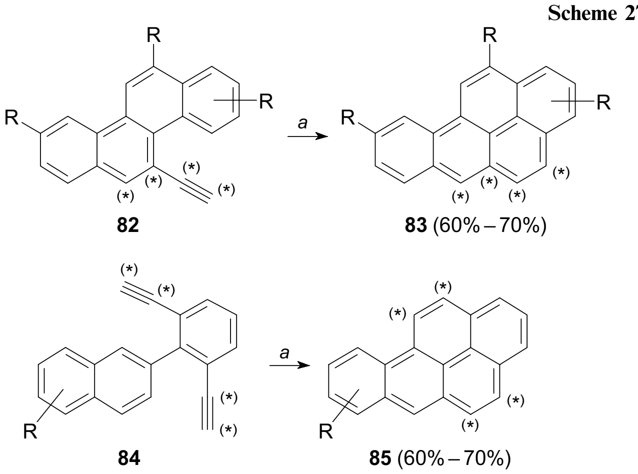


(*a*) $PtCl_2$ (10 mol.%), 80 °C; R^1, R^2 = OBu, OMe, OBn; R^3 = H, $CH_2NH(Boc)$; R^4 = H (62% – 78%);
(*b*) $PtCl_2$ (1 equiv.), 110 °C; R^1 = R^2 = R^3 = H, R^4 = Ph (13%); R^1 = R^2 = H, R^3 = Me, R^4 = 2-Br-4-MeC_6H_3 (28%)

R^4 = 4-FC_6H_4) resulted in a mixture of unidentified side products.[67]

Facile cyclization of *ortho*-aryl(ethynyl) fragment enabled direct access to benzo[*a*]pyrenes **83** and **85** in four or five steps from simple starting material (Scheme 27).[69] The key annulation step was accomplished with $PtCl_2$ for monoethynylated chrysenes **82** or for 2-(2,6-diethynylphenyl)naphthalenes **84** including their $^{13}C_4$-labelled analogues.

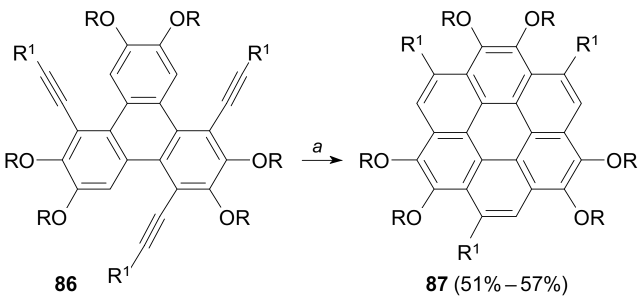
Scheme 27



(*a*) $PtCl_2$ (10 mol.%), PhMe, 80 °C, 12 h; R = H, OMe

Triple cyclization of 1,4,8-tris(arylethynyl)triphenylenes **86** with three alkyne units attached on two benzene rings required 20 mol.% of $PtCl_2$ and prolonged heating to furnish coronenes **87** (Scheme 28).[70] Aryl groups at the triple bond did not interfere with the reaction (*cf.* Scheme 26), and moderate yields were thus obtained.

Scheme 28

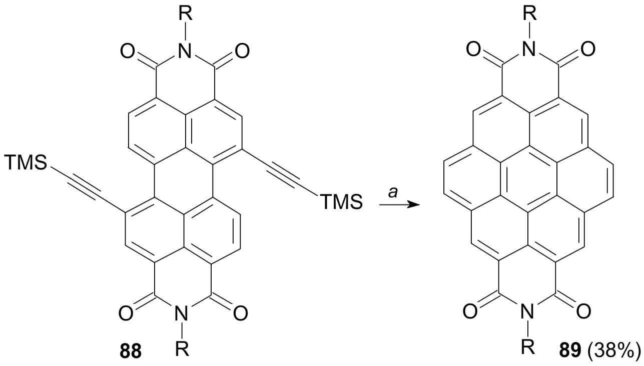


(*a*) $PtCl_2$ (20 mol.%), PhMe, 90 °C, 48 h;
R = Bu^n; R^1 = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$

Base catalysis is the method of choice for the synthesis of coronene derivatives similar to coronene tetracarboxydiimide **89** (Scheme 29) (*cf.* compound **379**, Scheme 127, Section 6). However, it is suitable only for substrates bearing at least one methylene group in the α-position to the triple bond, hence in the case of bis(trimethylsilylethynyl)-substituted perylene **88** the application of DBU failed.[71] Instead, $PtCl_2$-catalyzed cyclization of **88** run albeit the TMS groups were removed during this process.

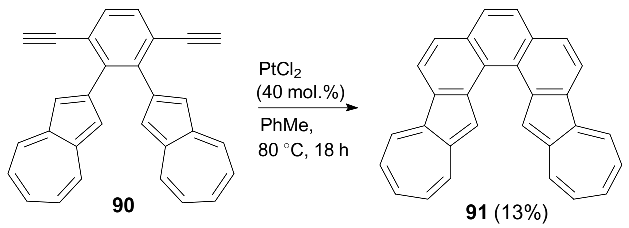
Almost all the examples described above deal with biphenyls, that is, an aromatic ring engaged in cyclization is a free or substituted benzene ring. Recently, double cyclization onto five-membered moieties of azulene fragments of **90** was accomplished using $PtCl_2$ to give diazulenophenanthrene **91** (Scheme 30).[72]

Scheme 29



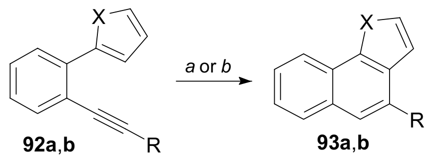
(*a*) $PtCl_2$ (20 mol.%), PhMe, 90 °C, 48 h; R = 2,6-$Pr^i_2C_6H_3$

Scheme 30



Feasibility to employ a heterocyclic ring as a counterpart to a triple bond was described in the first work of Fürstner (pyrrole and thiophene rings, see Scheme 4). A comparison of several metal catalysts was made for the cyclization of *ortho*-alkynyl(pyrrolyl)benzenes **92a** (Scheme 31).[73] The best result for propynyl-substituted substrate (R = Me) was achieved with $PtCl_2$ (94%), while for the compound bearing R = C_6H_{13}, with $AuCl_3$ (97%); $[Rh(CO)_2Cl]_2$ provided 75% – 80% yields of final benzo[*g*]indoles **93a**. Silver trifluoroacetate allowed realizing cyclization at room temperature albeit with equimolar catalyst loading.

Scheme 31



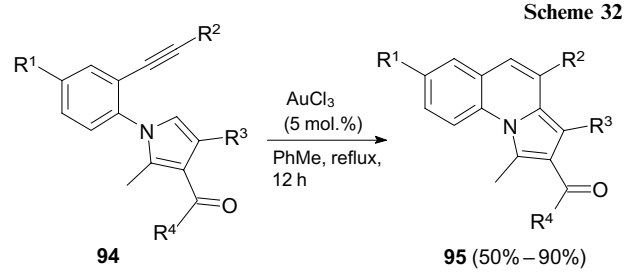
(*a*) $[Rh(CO)_2Cl]_2$ (10 mol.% – 13 mol.%), or $PtCl_2$ (9 mol.% – 13 mol.%), or $AuCl_3$ (10 mol.%), PhMe, 90 – 130°C; or $Ag(OCOCF_3)$ (1.1 equiv), $MeNO_2$, rt: X = NMe, R = Me, n-C_6H_{13} (**a**, 69% – 97%);
(*b*) $PtCl_2$ (5 mol.% – 15 mol.%), acetone, reflux, 8 – 80 h:
X = O, R = H (90%), Me (10%), TMS (0%) (**b**)

A high yield of naphtho[1,2-*b*]furan **93b** (R = H) was obtained in $PtCl_2$-catalyzed cyclization of 2-(2-ethynylphenyl)furan **92b** (see Scheme 31).[74] Trimethylsilyl-substituted analogue failed to react under these conditions, while the reaction of methyl-substituted compound was very sluggish, leading to the corresponding **93b** in only 10% yield after 80 h.

3.2. Gold

In the first work of Fürstner,[6] both $PtCl_2$ and $AuCl_3$ showed comparable results in the cyclization of *ortho*-ethynylbiphenyls; however, examples of Au^{III}-catalyzed reactions are quite rare. Intramolecular hydroarylation of a triple bond by a pyrrole ring was realized in **94** with $AuCl_3$ (Scheme 32).[75] This catalyst proved to be more effective than $FeCl_3$ or silver and indium triflates. Variously substituted pyrrolo[1,2-*a*]quinolines **95** were obtained in 70% – 90% yields from substrates **94** with arylethynyl fragment (R^2 = Ar) while only 50% – 53% yields were observed for alkynyl-substituted compounds (R^2 = Alk).

Scheme 32



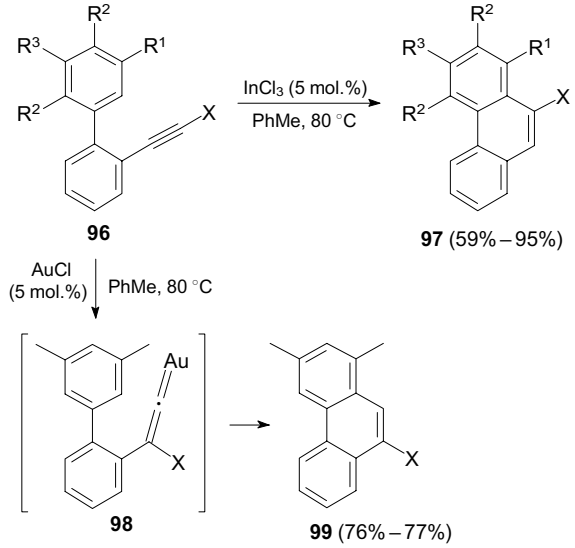
94 **95** (50% – 90%)

R^1 = H, F, Cl, Me; R^2 = XC_6H_4 (X = H, 4-MeO, 4-Br, 4-Cl, 4-Me, 4-CO_2Et, 3-NO_2), Cy, C_6H_{13}; R^3 = Ph, 4-ClC_6H_4, 4-$MeOC_6H_4$, 2-Fu, 2-Th, 2-Naph; R^4 = Me, Ph, OEt

In contrast, Au^I salts and complexes have found extremely wide application. AuCl and $InCl_3$ were utilized for cyclization of biaryls **96** with a haloalkyne unit since such compounds reacted poorly with $PtCl_2$ under the standard conditions (Scheme 33).[25] While $InCl_3$ was found to effect the desired transformation in good to excellent yields of products **97** and high selectivity, AuCl caused formation of isomeric halophenanthrenes **99**. This outcome could be explained by assuming the formation of a gold vinylidene intermediate **98** *via* a concomitant 1,2-halide shift.[26,76]

The same correlation between Au^I and In^{III} catalysts with respect to 1,2-migration was discovered for the cyclization of *ortho*-(arylselanylethynyl)biphenyls **100** (Scheme 34).[77] $In(OTf)_3$ allowed for retention of selanyl

Scheme 33

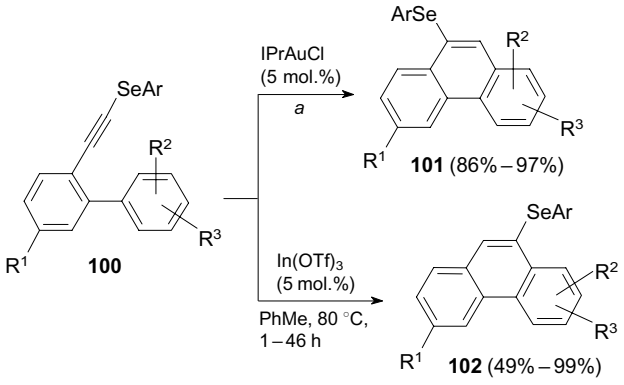


96 **97** (59% – 95%)

98 **99** (76% – 77%)

97: X = Cl, Br; R^1 = H, Me, $(CH_2)_2$NPhth; R^2 = H, OMe; R^3 = Me, OMe; **99**: X = Br, I; R^1 = R^3 = Me, R^2 = H

Scheme 34

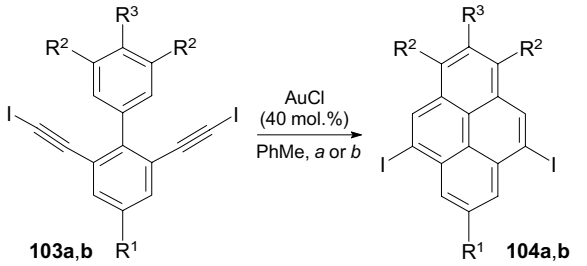


(*a*) $AgSbF_6$ (5 mol.%), CH_2Cl_2, rt or PhMe, 80 °C, 0.25 – 10 h; Ar = Ph, 4-$MeOC_6H_4$; R^1 = H, OMe, Cl; R^2, R^3 = H, Me, OMe, F

group in resulting phenanthrenes **102**, while AuCl or IPrAuCl/$AgSbF_6$ promoted its 1,2-migration to give isomeric products **101**. Gold-catalyzed reactions were faster and generally took only 0.25 – 2 h for the full conversion of substrates. Particularly, the electron-deficient biphenyl **100** (R^1 = H; R^2, R^3 = 3,5-F_2) produced the corresponding phenanthrene **101** with Au^I within 10 h in 86% yield; with In^{III} only 49% yield of **102** was obtained after 46 h, even if 10 mol.% of catalyst was used. The Au^I-catalyzed reaction of dimethoxy-substituted biphenyl **100** [R^1 = H; R^2, R^3 = 3,5-$(MeO)_2$] surprisingly produced only product **102** with retention of selanyl group position in 36% yield.

Later this idea was used for a twofold cyclization of diynes **103a** (Ref. 78) and **103b** (Ref. 66) in the synthesis of substituted iodopyrenes **104a**,**b**, albeit moderate yields were obtained with 40 mol.% catalyst loading (Scheme 35).

Scheme 35



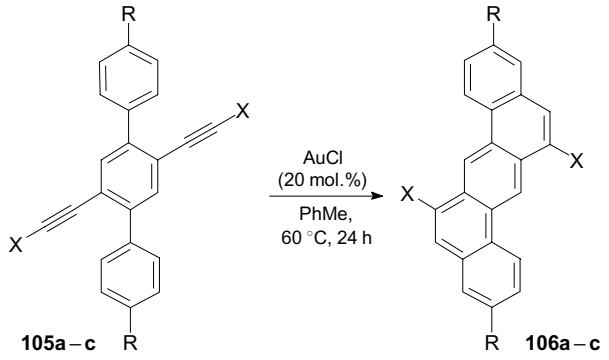
103a,**b** **104a**,**b**

(*a*) 60 °C, 16 h: R^1 = R^2 = H, R^3 = Bu^t (**a**, 45%); (*b*) rt, 16 h: R^1 = CH_2OTBDMS, R^2 = CH_2NHBoc, R^3 = H (**b**, 38%)

Different halogen atoms at the triple bond displayed unequal activity in Au-catalyzed cyclization of terphenyls **105** (Scheme 36).[79] Cycloisomerization of bromo-derived terphenyl **105a** gave the best yield (49%) of anthracene **106a** at 60 °C (only 6%^{NMR} at rt, 32% – 35%^{NMR} at 80 – 110 °C). Replacement of the bromine atoms by the iodine ones in compounds **105** led to a drastic improvement, as transformation to **106b**,**c** occurred in high yields at 60 °C.

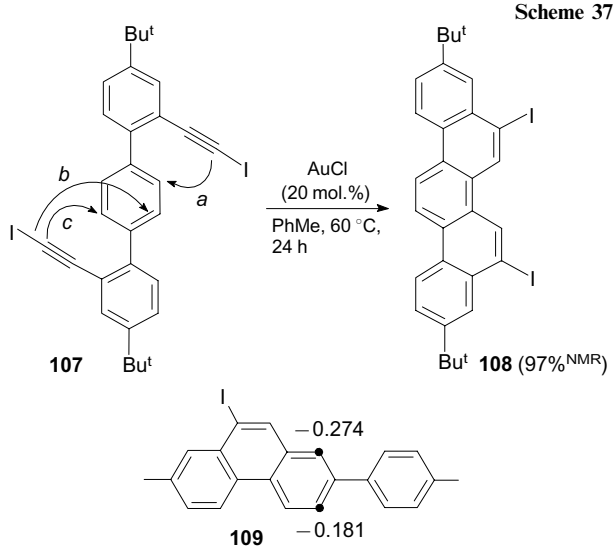
Regioselectivity of double cyclization was investigated for bis(iodoethynyl)-substituted terphenyl **107**, which might give two products (Scheme 37).[79] The initial cyclization (see Scheme 37 *a*) gives a phenylphenanthrene intermediate, which yields either picene or dibenzo[*a*,*h*]anthracene by attack at the opposite positions (see Scheme 37 *b* or *c*,

Scheme 36



X = Br, R^1 = n-C_6H_{13} (**a**, 49%);
X = I, R^1 = n-C_6H_{13} (**b**, 84%), Bu^t (**c**, 92%)

Scheme 37

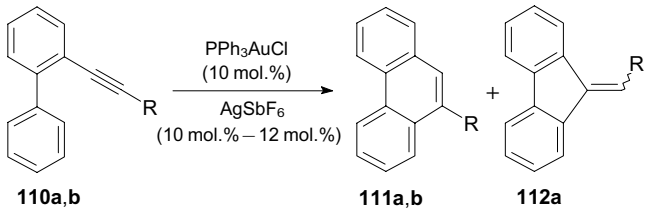


respectively; the latter process is more sterically favourable). However, only trace amount of dibenzo[*a*,*h*]anthracene was observed, while NMR yield of picene **108** was 97%. The charge densities estimated from the DFT calculations for model phenylphenanthrene **109** supported the experimental results, therefore the selective formation of picene **108** occurs under electronic but not steric control.

Au-catalyzed cyclizations of *ortho*-ethynylbiaryls without a halogen atom at the triple bond are usually performed using Au^I-complexes (the simplest one is Ph_3PAuCl) with silver salts as additives. Silver salts, being inactive themselves as reported numerously [however, examples of silver-catalyzed cyclizations have also been described (see Section 3.4)], increase the catalytic activity of Au^I complexes. For example, 6-*endo-dig* cyclization by $Ph_3PAuCl/AgSbF_6$ delivered phenanthrenes **111a**,**b**[80,81] though fluorene **112a** was additionally obtained[80] as a minor product through 5-*exo-dig* cyclization of **110a** (Scheme 38).

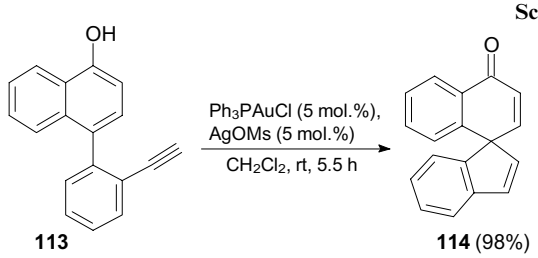
For an appropriate substrate bearing hydroxy or alkoxy group (*cf.* compounds **28**, Scheme 7), *ipso*-cyclization can be performed as a target reaction under gold catalysis to afford a derivative of spirocyclohexadienone. In this way, naphthol **113** was quantitatively transformed to spiro compound **114** using Ph_3PAuCl (Scheme 39).[82] Anion MsO^- from silver salt is proposed to assist elimination of a proton from the hydroxy group.

Scheme 38



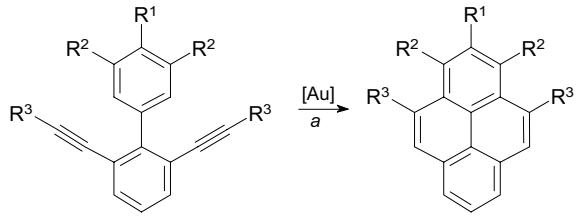
R = Bu^n: DCE, 40 °C, 90 h, **111a** : **112a** = 5 : 1 (57%);
R = Ph: PhMe, 110 °C, 12 h, **111b** (63%)

Scheme 39



Cationic Au^I complexes with Buchwald-type biarylphosphine ligands efficiently catalyzed double hydroarylation of dialkynylbenzenes **115** into pyrenes **116**; (*tert*-butylXPhos)$AuNTf_2$ was the best one (Scheme 40).[83] Au^ICl complexes bearing the same biarylphosphine ligands failed to promote the hydroarylation. The reaction proceeded more easily with electron-donating aryl groups at the triple bonds [the best yield (96%) for R^3 = 4-$MeOC_6H_4$]; as a rule, higher reaction temperature provided better yields. The reactions of **115** ($R^1 = R^2 = H$) with terminal or trimethylsilyl-substituted ethynyl groups suffered formation of byproducts to afford pyrenes **116** in low yields (16% – 30% at 80 °C, 18% – 42% at 150 °C).

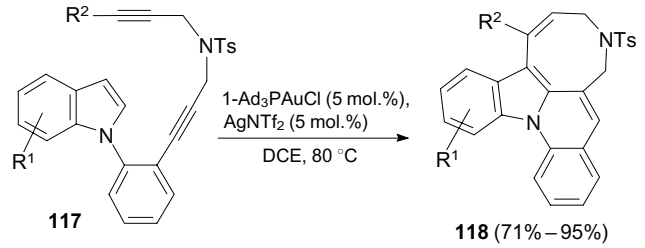
Scheme 40



(*a*) [Au] = (*t*-butylXPhos)$AuNTf_2$ (5 mol.% – 20 mol.%), DCE, 80 °C or *p*-xylene, 150 °C, 24 h; R^1 = H, Bu^t; R^2 = H, Me;
R^3 = H, Me, TMS, Ph, 4-$MeOC_6H_4$, 4-ClC_6H_4

Sequential 6-*endo*/8-*endo* cyclization of indoles **117** bearing diyne in a side chain proceeded smoothly with gold catalyst to give indolizine derivatives **118** in high yields (Scheme 41).[84] However, introduction of electron-withdrawing nitro group in the indole fragment reduced the activity of **117** as much as only trace amount of target product was detected. Replacement of indole by pyrrole afforded the corresponding product in 67% yield (R^2 = Me). This reaction also tolerated other sulfonyl groups at the nitrogen atom, *i.e.* SO_2Ph, SO_2Bn, SO_2Me, and the oxygen atom and methylene group were successfully

Scheme 41

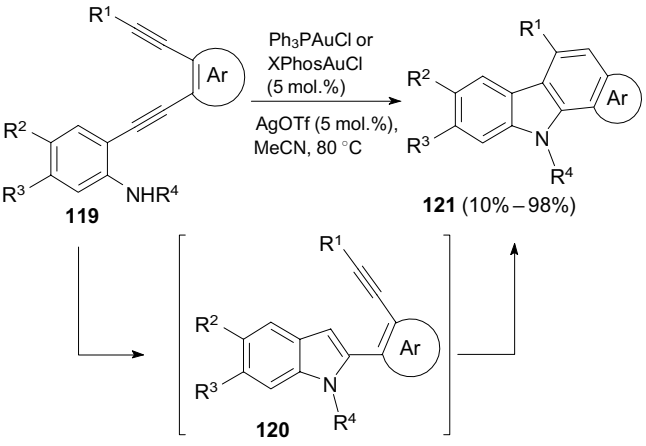


R^1 = H, F, Cl, Br, Me, OMe; R^2 = Me, Et, Ph

introduced instead of sulfamide linker between two alkyne moieties.

Gold-catalyzed tandem transformation *via* 5-*endo-dig* hydroamination and subsequent 6-*endo-dig* hydroarylation of diynes **119** led to aryl-annulated[*a*]carbazoles **121** and their heterocyclic derivatives (Scheme 42).[85] The electronic influence of diyne substituents in the cascade cyclization can be diminished by using a gold catalyst with bulky biaryl phosphine ligands. Predominantly high yield of **121** (not less than 68%) sharply decreased in two cases: for the *ortho*-cyanophenyl group at the triple bond (10%, R^1 = 2-NCC_6H_4; but 79% when R^1 = 3-NCC_6H_4) and for pyridine tether between two alkynyl fragments [Ar = pyridine-2,3-diyl, 15%; 40% with $NaAuCl_4$ (20 mol.%)[86]]. The formation of 2-(2-ethynylaryl)indole intermediate **120** was supported by the quantitative cyclization of an isolated compound **120** (R^1 = Ph, $R^2 - R^4$ = H) under the same conditions.

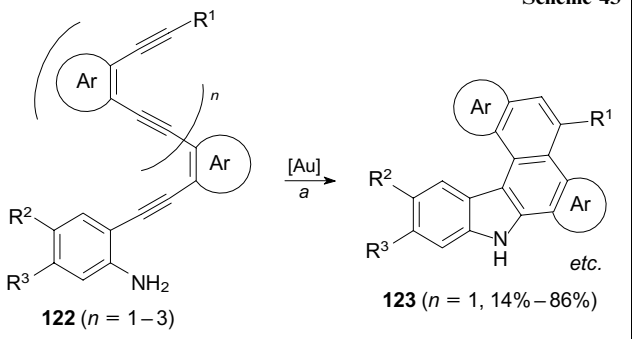
Scheme 42



R^1 = XC_6H_4 (X = H, CF_3, CN, Cl, Me, OMe), 3-Th, cyclopentyl, Cy, Pr^n; R^2 = H, Me, CO_2Me; R^3 = H, Cl, CF_3; R^4 = H, Me, Boc; Ar = *o*-phenylene, pyridine-2,3-diyl, furan-2,3-diyl

Later this strategy was extended to a cascade cyclization of tri- and even tetra- and pentaynes **122** (Scheme 43).[87] Slightly altered conditions resulted in target polycyclic compounds **123** in high yields ($\geqslant$47%) with exception of substrates **122** (n = 1) bearing R^1 = H (a mixture of unidentified products was observed) and R^1 = Bu^t (only double cyclization occurred). As in the previous case (see Scheme 42), the cyano group (**122**, R^2 = CN, n = 1) significantly decreased the reactivity to afford the tricyclization product **123** in only 14% yield, probably, due to coordination ability of gold catalysts towards the nitrile functionality; however, introduction of R^1 = 4-NCC_6H_4 in **122** did not affect the reaction (77% yield).

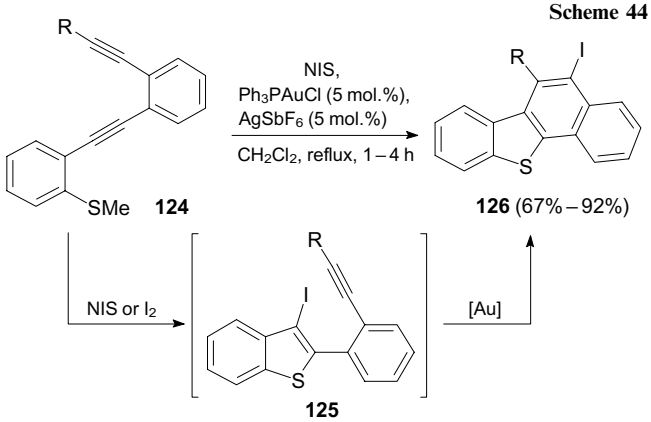
Scheme 43



(*a*) [Au] = JohnPhosAuCl or XPhosAuCl (5 mol.% – 20 mol.%); $AgBF_4$ (5 mol.% – 20 mol.%), AcOH or EtOH, 80 °C; R^1 = 4-XC_6H_4 (X = H, CN, Cl, Me, OMe), Cy, Pr^n; R^2 = H, Me, Cl, CN; R^3 = H, Cl; Ar = *o*-phenylene, thiophene-2,3-diyl

2-[(2-Ethynylphenyl)ethynyl]thioanisoles **124** were converted in a similar way to benzo[*b*]naphtho[2,1-*d*]thiophenes **126** (Scheme 44).[88] In contrast to analogous anilines with alkyl- and aryl groups at the distal triple bond (**196**, see Scheme 100), where both steps could be performed with iodine without a metal catalyst, only an aryl-substituted thioanisole **124** (R = Ph) gave final naphthothiophene **126** with I_2, while an alkyl-substituted substrate (R = Pr^n) furnished monocyclized benzothiophene **125** under the same conditions. This corresponds to a lesser tendency to electrophilic substitution of a more aromatic thiophene ring than that of a pyrrole ring. Subsequent 6-*endo* iodoarylation of **125** was accomplished with Au^I catalyst. In a one-pot fashion NIS/Ph_3PAuCl/$AgSbF_6$ system [NIS was found to be more effective than iodine (higher yields and shorted reaction time)] afforded iodinated naphthothiophenes **126** in high yields.

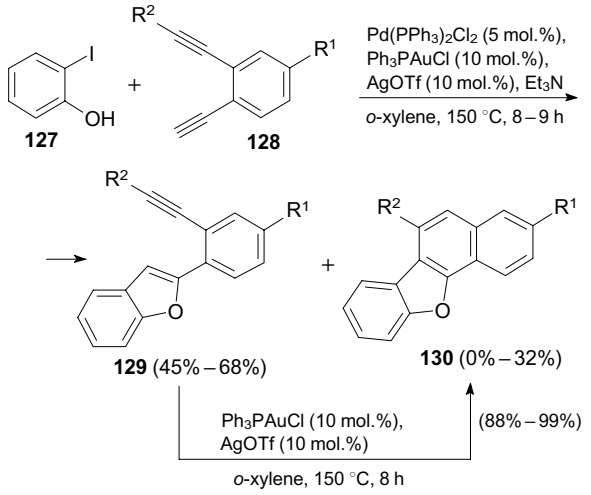
Scheme 44



R = Pr^n, n-C_5H_{11}, XC_6H_4 (X = H, 4-MeO, 2-Me, 3-Me, 4-Me, 4-Cl, 4-Br, 4-F_3C)

Similar strategy was utilized in the synthesis of furan-based polycycles **130** (Scheme 45).[89] Treatment of 2-iodophenol **127** and diyne **128** with Pd/Au catalytic system triggered a cascade of the Sonogashira coupling, 5-*endo-dig* cyclization of *ortho*-alkynylphenol and 6-*endo-dig* cyclization of 2-(2-alkynylphenyl)benzofuran; however, a mixture of two products, the target tetracycle **130** and the

Scheme 45



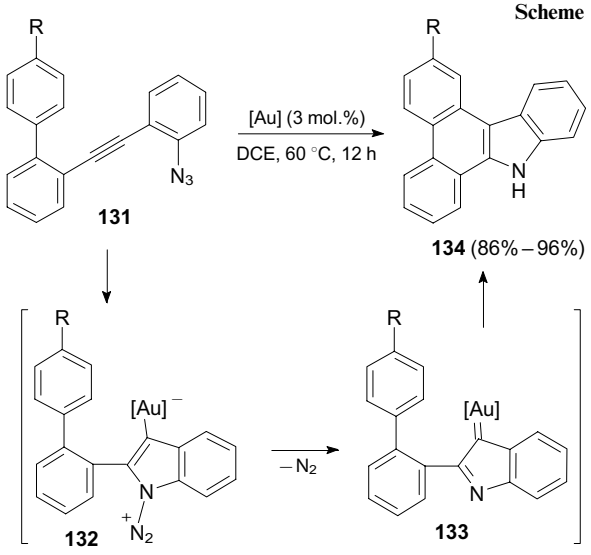
R^1 = H, Me; R^2 = Bu, 3-Th, 3-Py, 4-XC_6H_4 (X = H, Me, F, MeO, CN, Cl)

intermediate benzofuran **129** thus formed with the latter being the major one. For pyridine-substituted substrate, the final cyclization did not occur and only benzofuran **129** (R^1 = H, R^2 = pyridin-3-yl) was obtained in 54% yield. The base, which is necessary for the Sonogashira coupling, suppressed the Au-catalyzed cyclization, whereas isolated benzofurans **129** were converted into target products **130** in excellent yields. Thus, the full cascade is more efficient in a two-step procedure that removes base. With this fact in hand, the method was applied to perform tricyclization of a substrate with R^2 = 2-(*p*-tolylethynyl)phenyl.

Au^I-activation of the alkyne moiety of diarylacetylenes **131** enables nucleophilic attack of tethered azide fragment to generate α-imino gold carbenoid species **133** after extrusion of N_2 from **132** (Scheme 46).[90] Subsequently, this carbenoid intermediate **133** can be captured by the adjoining phenyl ring through formal electrophilic aromatic substitution followed by 1,3-H shift. In this manner, polycyclic indole derivatives **134** were obtained in high yields.

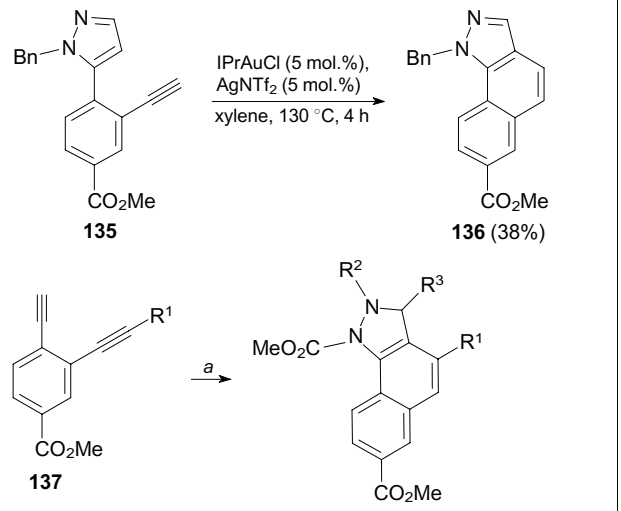
Beside phosphine ligands, *N*-heterocyclic carbenes may form active gold complexes to trigger cyclization, for

Scheme 46



R = H, OMe, Cl; [Au] = JohnPhosAu(CH_3CN)SbF_6

Scheme 47

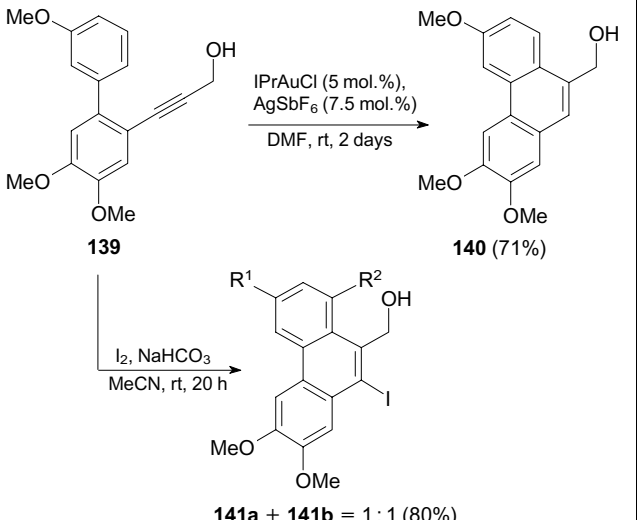


(*a*) $R^2NHNHCO_2Me$, R^3CHO, IPrAuCl (5 mol.%), $AgNTf_2$ (5 mol.%), AcOH, 35 – 80 °C; R^1 = Pr^n, Ph, 4-$MeOC_6H_4$, 2-Th; R^2 = 4-$MeOC_6H_4CH_2$

example, IPrAuCl catalyzed annulation on pyrazole ring of **135** into tricyclic **136** (Scheme 47).[91] Although the yield is moderate, this catalytic system can be employed in acetic acid media for the one-pot reaction involving initial pyrazoline ring formation to get benzo[*g*]indazole derivatives **138** from diynes **137**.

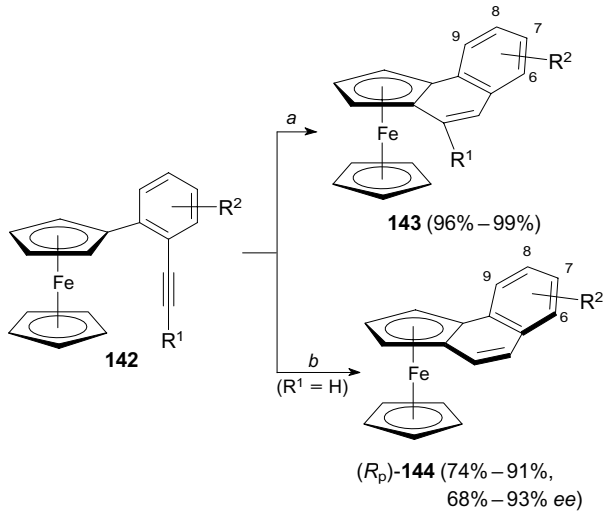
A precursor of (−)-cryptopleurine **140** was synthesized *via* regioselective IPrAuCl-catalyzed cyclization of **139** in good yield (Scheme 48);[92] conversely, the use of $PtCl_2$ produced a complex mixture. To compare, iodocyclization upon treatment of **139** with iodine proceeded unselectively leading to a nearly equimolar mixture of two regioisomers **141a**,**b**.

Scheme 48



a: R^1 = H, R^2 = OMe; **b**: R^1 = OMe, R^2 = H

Scheme 49



(*a*) IPrAuSbF$_6$ (5 mol.%), CH_2Cl_2, rt, 0.5 – 2 h; (*b*) L(AuCl)$_2$ (10 mol.%), AgSbF$_6$ (20 mol.%), PhMe, 0 °C, 3 – 15 h; L = (*R*)-DTBM-SegPhos;
143: R^1 = XC_6H_4 (X = H, 4-F, 4-Cl, 3-Cl, 2-Cl, 4-Br, 4-Ac, 4-O_2N, 4-MeO_2C, 4-Me, 3-Me, 2-Me, 4-MeO, 4-Bu^t), 3,4,5-$(MeO)_3C_6H_2$, Cy, cyclohex-1-enyl, 1-Naph, 2-Th, benzofuran-2-yl, TMS, H;
R^2 = H, 7-Cl, 7-Me, 8-F_3C;
144: R^2 = H, 7-MeO, 8-MeO, 6-F, 7-F, 8-F, 9-F, 8-Me, 7,8-F_2, 7,8-O$(CH_2)_2$O, 8,9-$(CH)_4$

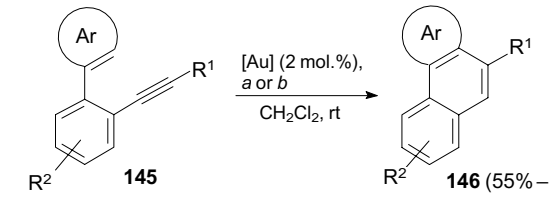
IPrAuCl was inactive towards 2-arylethynyl-1-ferrocenylbenzenes, however, slight alteration of counterion in IPrAuSbF$_6$ effected a racemic cyclization of **142** (Scheme 49).[93] Electronic nature of a substituent at the triple bond had no notable effect on the reaction as electron-donating and electron-withdrawing aryl rings, heterocycles and alkyl groups were well tolerated providing products **143** in quantitative yields.

Enantioselective approach to (*R*p)-planar-chiral ferrocenes **144** from *ortho*-ethynylaryl ferrocenes **142** was developed through the Au^I-catalyzed cycloisomerization in the presence of chiral bidentate phosphine under very mild conditions (see Scheme 49).[94] Substituents in various positions of the phenyl ring, regardless of their electronic nature, were successfully introduced to afford tricyclic ferrocenes. $PtCl_2$ (at 100 °C) was mentioned to perfectly catalyze the racemic cycloisomerization while chiral platinum catalysts turned out to be less effective in this work. However, suitable conditions for Pt-catalyzed enantioselective cyclization of similar ferrocenes were found in the aforementioned work (see Scheme 13).

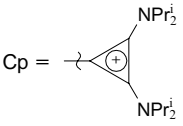
Cyclopropenylidene-stabilized phosphenium ligands mentioned above for the platinum complex (see Scheme 12) were successfully employed for the gold one. These ligands enhance the π-acidity of Au^I thus increasing the catalytic activity. High yields of cyclization products **146** were obtained for diversely substituted substrates **145** using low catalyst loading (2 mol.%) under mild reaction conditions (Scheme 50). Most work was done with terminal alkynes,[95,96] though methyl group at the triple bond was also tolerated.[97] This methodology was utilized for the synthesis of several sterically hindered naturally occurring phenanthrenes.[95,96]

Superior catalytic efficiency was achieved using cationic imidazolinio- and amidiniophosphine ligands in the Au-

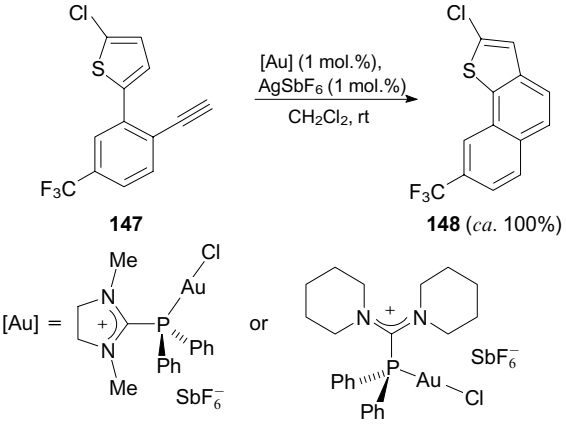
Scheme 50



(*a*) [Au] = (CpPL$_2$AuNTf$_2$)BF$_4$, L = Ph, Ad; R^1 = Me; R^2 = H;
Ar = pyrrol-1-yl; (*b*) [Au] = (Cp$_2$PLAuCl)(BF$_4$)$_2$, AgSbF$_6$ (2 mol.%), L = Ph, *o*-biphenyl; R^1 = H, R^2 = H, OH, OMe, Me, Ph, F, CO_2Me;
Ar = 2-XC_6H_4 (X = Ph, Pr^i, Bu^t, Me, OMe), 2,5-$(MeO)_2C_6H_3$, 2,3,4-$(MeO)_3C_6H_2$, 2-Fu, 3-Fu, 5-methyl-2-furyl, benzofuran-2-yl;



Scheme 51

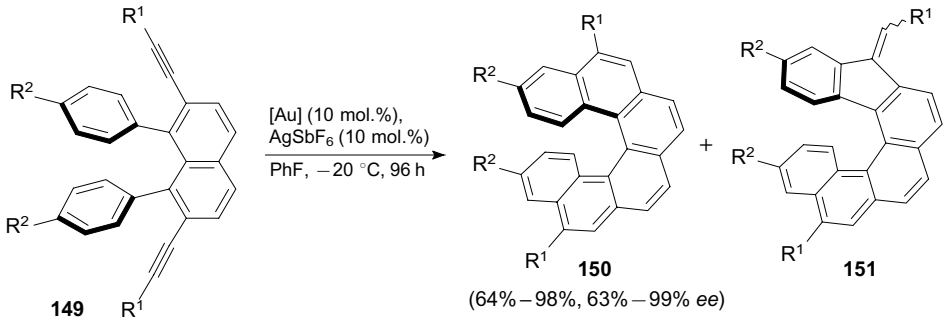


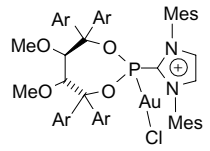
catalyzed hydroarylation of **147** into naphtho[1,2-*b*]thiophene **148** (Scheme 51).[98] Just 1 mol.% of Au-catalyst promoted almost full conversion of substrate **147** within 10 min at room temperature.

Beneficial design of chiral cationic phosphonite ligand for Au^I-complex allowed for highly enantio- and regioselective synthesis of [6]helicenes **150** (along with minor amounts of 5-*exo*-cyclization products **151**, Scheme 52).[99] The lowest value of *ee* (63%) was observed for methyl-capped alkyne **149**, while in other cases the level of *ee* was maintained over 81%. Among two sequential cyclizations the latter one serves as the enantio-determining step of the whole process.

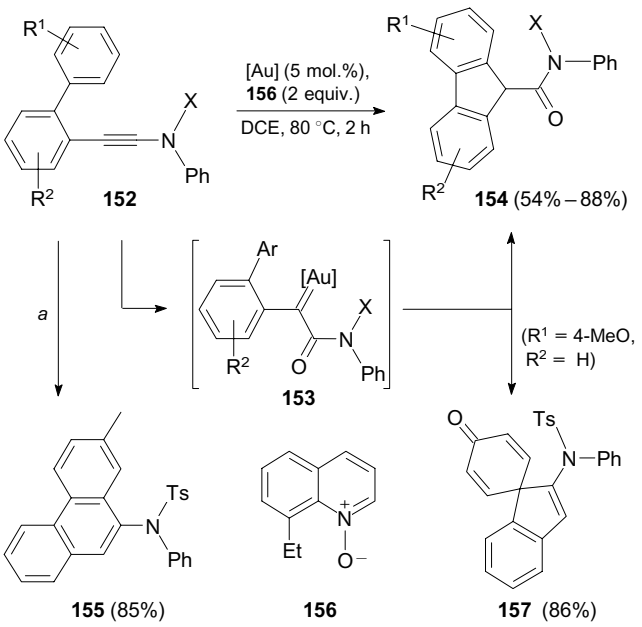
Using an oxidant as an additive to an Au-catalyst may lead to the formation of α-oxo gold carbenoid from the triple bond of *ortho*-alkynylbiphenyl followed by trapping this carbenoid by an aryl ring in a 5-*exo*-*dig* mode. This strategy was demonstrated in the synthesis of fluorenes **154** from ynamides **152** (Scheme 53).[100] Fluorenes **154** were generally obtained in high yields, except for the *p*-methoxy-substituted biphenyl **152** where spiro compound **157** formed through *ipso*-cyclization. The phenanthrene **155** was obtained in 85% yield from the corresponding ynamide **152** without addition of *N*-oxide **156**, indicating that the gold-catalyzed 6-*endo*-*dig* cycloisomerization can be suppressed by an oxidant. The use of bulky phosphine ligand prevented the overoxidation of the carbene centre of **153**, while the corresponding 1,2-diketones were the major pro-

Scheme 52



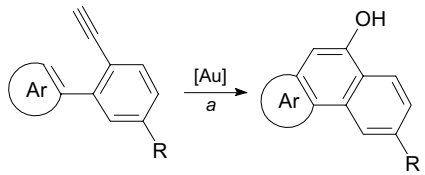
[Au] =  ; R^1 = Me, 4-XC_6H_4 (X = H, Me, F, Cl, OBn, OMe, TMS, CH_2OTIPS); R^2 = H, Ph, OMe; Ar = 4-$F_3CC_6H_4$

Scheme 53



[Au] = BrettPhosAuNTf$_2$; R^1 = H, 4-Me, 3-Me, 4-MeO, 3,5-Me_2; R^2 = H, 3-Me, 4-Me, 3-F, 4-F, 3-Cl; X = Ts, 4-$MeOC_6H_4SO_2$; (*a*) [Au] (5 mol.%), DCE, 80 °C, 10 h; R^1 = 4-Me, R^2 = H

Scheme 54



(*a*) [Au] = $Me_4Bu^tXPhosAuCl$ (2 mol.%), $NaBAr^F_4$ (3 mol.%), 2,6-dichloropyridine *N*-oxide (1.2 equiv.), DCE, 50 °C, 11 – 37 h; Ar = XC_6H_4 (X = H, 4-F, 4-Cl, 4-OMe, 3-Me), benzothiophen-2-yl; R = H, 3-F

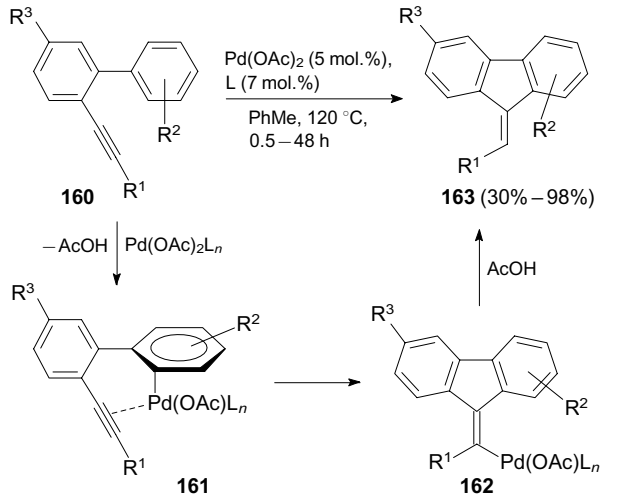
ducts using less sterically hindered phosphine gold complexes (PAr_3, PEt_3 *etc.*).[100]

Under similar conditions terminal alkynes **158** were converted into phenanthrenols **159** (Scheme 54).[101] In contrast to the previous case, α-oxo gold carbenoid formed with the inverse orientation of a carbene centre and a carbonyl group with respect to an aryl ring of **158**. As a result, 6-*endo*-cyclization followed by aromatization occurred to afford phenanthrenes **159**; both electron-withdrawing and electron-donating substituents were tolerated.

3.3. Palladium

The main advantage of Pd-catalysis for the cyclization of *ortho*-alkynyl biphenyls is a feasibility to realize 5-*exo*-*dig* annulation in contrast to the majority of aforementioned works where 6-*endo* fashion was the exclusive or predominant reaction pathway. This delivers a central fluorene fragment, as was first shown by Gevorgyan.[102] Biphenyls **160** were converted to benzylidenefluorenes **163** in high yields (mostly >77%) upon catalysis with $Pd(OAc)_2$ (Scheme 55). Electron-withdrawing substituents at both

Scheme 55



L = d-i-Prpf; R^1 = 4-XC_6H_4 (X = H, Me, OMe, NO_2, CN, CF_3), CO_2Et, 3-Py; R^2 = H, 4-CF_3, 4-CO_2Me, 3,5-F_2, 3,5-$(CF_3)_2$, 2-F-5-Me, 2,5-Me_2, 4-F-2-Me; R^3 = H, CF_3, OMe

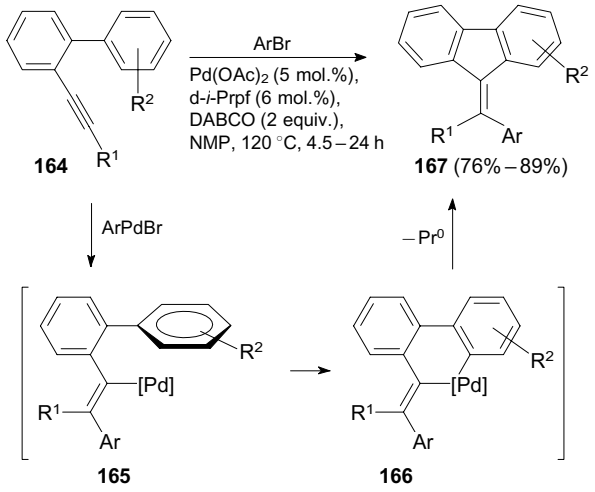
the triple bond and aromatic ring of **160** did not interfere with the reaction and even accelerated it compared to compounds bearing electron-neutral groups; moderate yields were obtained for the sterically hindered substrates with a methyl group at the *ortho*-position [**160**, R^2 = 2,5-Me_2 (30%); 4-F-2-Me (47%)]. Cyclizations of all compounds **160** proceeded with high *cis*-selectivity. These observations along with kinetic isotope effect (KIE) measurements [significant intramolecular KIE was found for this reaction ($k_H/k_D = 3.5$) and for similar processes (see Schemes 62, 158), while the inverse KIE ($k_H/k_D < 1$) was reported for the electrophilic cyclization mechanism (see Schemes 13, 158)] assume the most probable mechanism involving the C–H activation motif.[103] Initial *ortho*-palladation of **160** gives **161**, which, upon migratory insertion to a triple bond, produces vinylpalladium species **162**, which differs from the previously described Pt-catalyzed transformations. Protiodepalladation of **162** furnishes **163** and regenerates the catalyst.

Later this catalytic system was successfully applied for the cyclization accompanied by arylation (Scheme 56).[104] As proposed, arylethynyl fragment of **164** underwent carbopalladation followed by *ortho*-C–H activation of the adjacent aromatic ring in **165** to form a six-membered palladacycle **166**, which produced a five-membered ring of **167** after reductive elimination of Pd^0. As in the previous reaction, one stereoisomer **167** formed in all cases, and electron-deficient substrates reacted faster, meanwhile the whole transformation appeared to be quite general with respect to both *ortho*-alkynylbiaryl and aryl halide used.

Similar arylation/cyclization sequence of 1-(*ortho*-ethynylaryl)triazoles **168** proceeded stereoselectively depending on the substituent at the triple bond (Scheme 57).[105] According to the plausible mechanism (the same as in Scheme 56), initial carbopalladation of the triple bond of **168** by ArPdX occurs as *syn*-addition producing vinylpalladium species like **165**. It is the case for arylethynyl-substituted aryltriazoles **168**, which afforded fused triazoles **169**. For alkynyl-substituted substrates, *anti*-carbopalladation may account for the inverse configuration of the exocyclic double bond in products **170**. The reaction tolerated various substituents in starting compounds, but surprisingly hex-1-ynyl **168** ($R^1 = Bu^n$) furnished ketones **171**, which was explained by easy allylic oxidation of α-methylene group during the reaction. Meanwhile, there were no oxidants in the reaction mixtures. As an alternative to Pd-catalyst, $Ni(cod)_2$ acted in the same way providing comparable yields of indoline-fused triazoles.

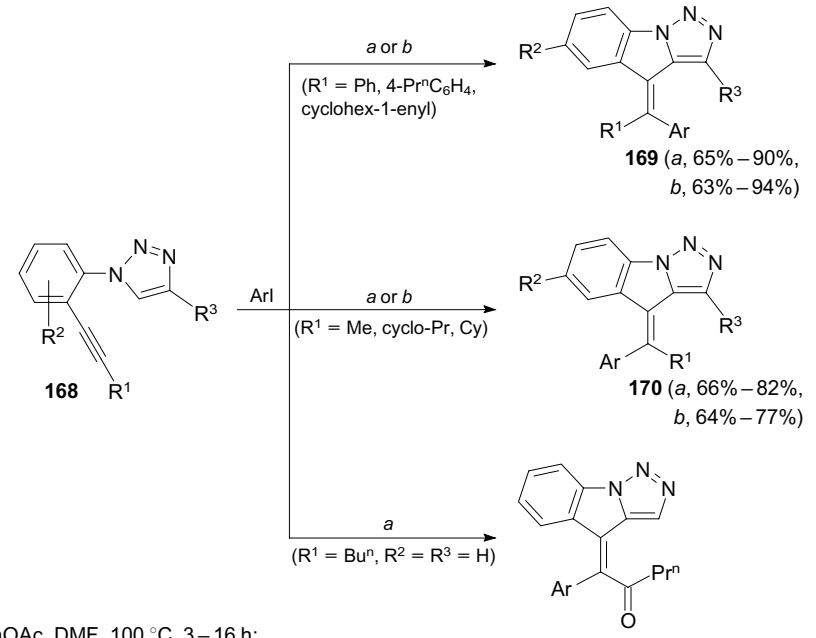
Double cyclization of bis(*o*-biaryl)alkynes **172** was accomplished using $PdCl_2$ in the presence of oxidant

Scheme 56



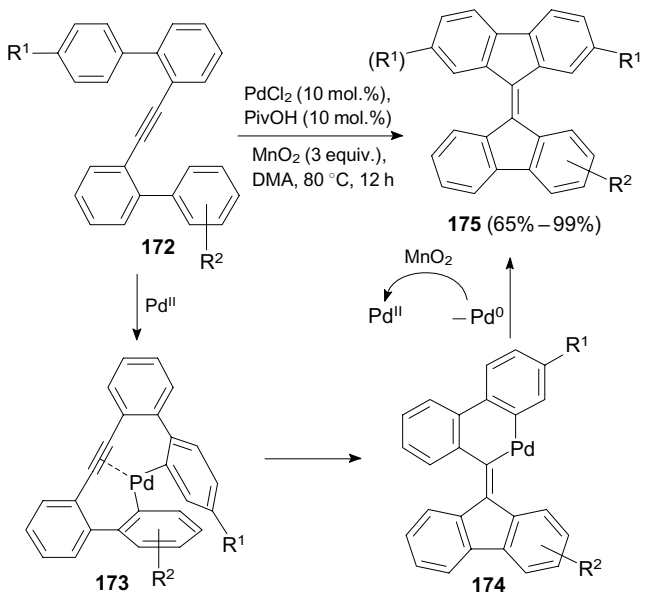
$R^1 = XC_6H_4$ (X = H, 4-Me, 2-Me, 4-MeO, 4-F_3C), 3-Py;
R^2 = H, 2-Cl, 4-MeO, 4-F_3C, 3,5-F_2; Ar = Ph, 3-MeC_6H_4, 4-$F_3CC_6H_4$

Scheme 57



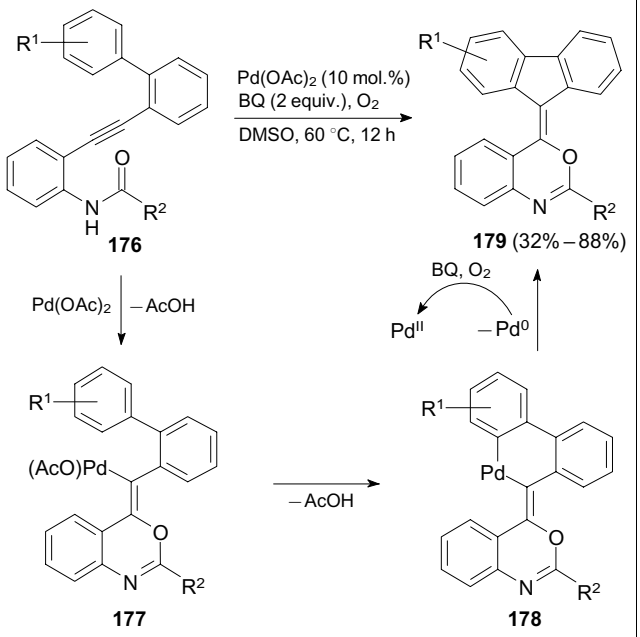
(*a*) $Pd(PPh_3)_4$ (5 mol.%), NaOAc, DMF, 100 °C, 3 – 16 h;
(*b*) $Ni(cod)_2$ (10 mol.%), K_2CO_3, DMF, 100 °C, 16 h;
R^2 = H, Me, F, CF_3; R^3 = H, CH_2OH, Bu^n, Ph;
Ar = XC_6H_4 (X = H, Me, OMe, CF_3, NH_2), 3,4,5-$(MeO)_3C_6H_2$, 2-Th

Scheme 58



R^1 = H, R^2 = H, 4-CHO, 4-CO_2Me, 4-F, 4-OMe, 4-NPh_2, 4-Me, 3-Me, 2-Me; ArR^2 = 2-Naph, benzofuran-2-yl, benzothiophen-2-yl; R^1 = R^2 = 4-OMe (*cis* : *trans* = 1 : 1.1), 4-CF_3 (*cis* : *trans* = 1.5 : 1), 4-Me (*cis* : *trans* = 1 : 1)

Scheme 59



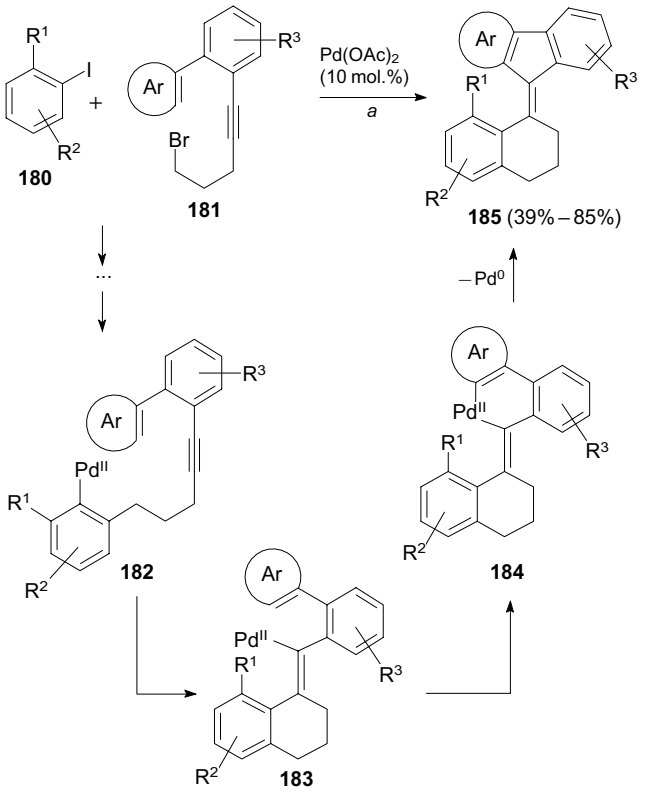
R^1 = H, 4-F, 2-Cl, 4-Cl, 4-MeO, 4-Me, 3-Me, 2-Me; R^2 = XC_6H_4 (X = 2-Me, 3-Me, 4-Me, 4-Et, 4-MeO, 4-Cl, 2-F_3C, 3-Me_2N), 2-Naph, 2-Th, CH═CHPh, Bu^t

(MnO_2) and pivalic acid in DMA to furnish 9,9′-bifluorenylidenes **175** in good yields (Scheme 58).[106] Disubstituted compounds **172** ($R^1 \neq H$) gave mixtures of *cis*- and *trans*-isomers (in *ca.* 1 : 1 ratio at 80 °C), but when the reaction was carried out at room temperature for a prolonged time, *cis*-isomer formed predominantly and could be isomerized to *trans*-isomer upon heating, which suggests a *cis*-manner of the initial annulation. A plausible mechanism involves biarylpalladium intermediate **173** formation *via* alkyne-directed dual C – H activation. Intramolecular alkyne carbopalladation affords the six-membered palladacycle **174**, which after the reductive elimination gives the corresponding product **175** and the Pd^0 species. As proposed, MnO_2 acts as an oxidant for regeneration of the active $PdCl_2$ catalyst while PivOH accelerates the *ortho*-C – H bond cleavage, as without these additives the reaction is almost inefficient.

ortho-C – H-Activation may occur after carbopalladation of the triple bond as observed in many examples. In the course of cyclization of amides **176** to fluorenylidenebenzoxazines **179**, the palladium-activated triple bond is attacked by the amide oxygen atom to form 1,3-oxazine and vinylpalladium moieties of **177** (Scheme 59).[107] Palladium activation of aromatic C – H bond in **177** occurred to provide the six-membered palladacycle **178**, similar to aforementioned ones, which underwent reductive elimination of Pd^0. To regenerate an active catalyst in this case, the oxidative benzoquinone (BQ)/O_2 system was used. High yields of products (> 58%) were obtained for most *ortho*-ethynylanilides **176** with exception of dimethylamino- and trifluoromethyl-substituted benzamides and cinnamamide (32% – 35%).

A cascade of Pd-catalyzed C – H activations was implemented in the synthesis of tetrasubstituted alkenes **185** from starting iodoarenes **180** and alkynes **181** (Scheme 60).[108] The final steps (formation of intermediate **182** assisted by

Scheme 60



(*a*) PPh_3 (20 mol.%), norbornene (2 equv.), Cs_2CO_3, MeCN, 90 °C, 24 h; Ar = pyrrol-1-yl, indol-1-yl, 2-Fu, 2-Th, Ph, 3-MeO_2C-1-Me-pyrrol-4-yl; R^1 = Me, OMe, CF_3; R^2 = H, 4-NO_2, 5-F, 3-Cl; R^3 = H, F_2, 2-Cl, 2-NO_2

norbornene is not detailed here)[108] occurred as a carbopalladation/aromatic C–H-activation/reductive elimination sequence to construct a product of formal 5-*exo*-cyclization of the triple bond to the aromatic ring (intermediates **183**, **184**). The reaction tolerated various heterocycles as aromatic counterparts; in almost all cases a single isomer formed; however, acid catalyzed and/or light-driven isomerization was observed for several products.

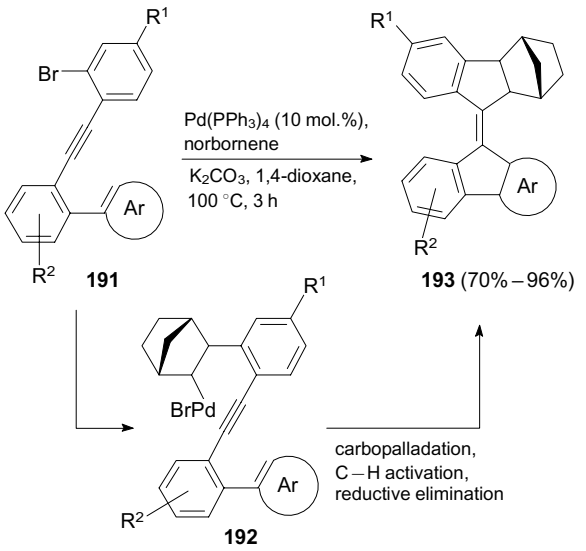
Provided a haloarene as a starting compound, Pd^0 complex can be used to promote cyclization *via* initial oxidative insertion into C–Hal bond. The subsequent steps, the same as in the previous examples, lead through formation of a palladacycle to a fluorene based product. In this manner (intermediates **187**–**189**) *N*-(2-bromobenzyl)-propargylamines **186** were converted to tetrasubstituted alkenes **190** in high yields and as single isomers for thiophene-containing substrates (Scheme 61).[109]

Later the same authors expanded their method to the synthesis of norbornene-fused olefins **193** (Scheme 62).[110] The aromatic moiety of *ortho*-alkynylbiaryl **191** involved in cyclization may be represented as a variously substituted phenyl ring or as a heterocycle providing high yields of **193**, as a rule. The proposed mechanism resembles the aforementioned one with the difference in the carbopalladation of norbornene to form intermediate **192** after oxidative addition of Pd^0 to **191**.

The presence of *ortho*-halogen atom in the aryl ring excludes a Pd-catalyzed C–H activation step from the whole transformation. Instead of that, a C–Hal bond in *ortho*-alkynyl(2-haloaryl)arene allows for oxidative insertion of Pd^0 followed by carbopalladation of the adjacent triple bond in a 5-*exo*-mode. The fluorenylidene palladium intermediate thus formed can intercept a nucleophile, *e.g.*, *via* cross-coupling with arylboronic acid.[111, 112] This strategy was demonstrated in the synthesis of diaryldibenzofulvenes **195** from biphenyls **194** (Scheme 63).[113]

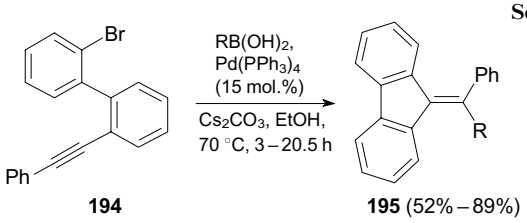
On the other hand, in contrast to exclusive 5-*exo*-pathway mentioned before, a Pd-catalyzed cyclization of halo-substituted *ortho*-alkynylbiaryls may proceed in a 6-*endo* fashion. Treatment of alkynes **196** with $PdCl_2$ and $CuCl_2$ gave benzo[*a*]carbazoles **198** in good yields (Scheme 64)[114] (see Scheme 42 for the similar Au^I-catalyzed reactions). In the first step formation of chloroindole **197** occurs upon $CuCl_2$ treatment even without Pd-source. The second step could be promoted by either Pd^{II} [$Pd(Cl/Br/I)_2$, $Pd(OAc)_2$] or Pt^{II} ($PtCl_2$) implying possible coordination of metal to the triple bond followed by intramolecular Friedel–Crafts

Scheme 62



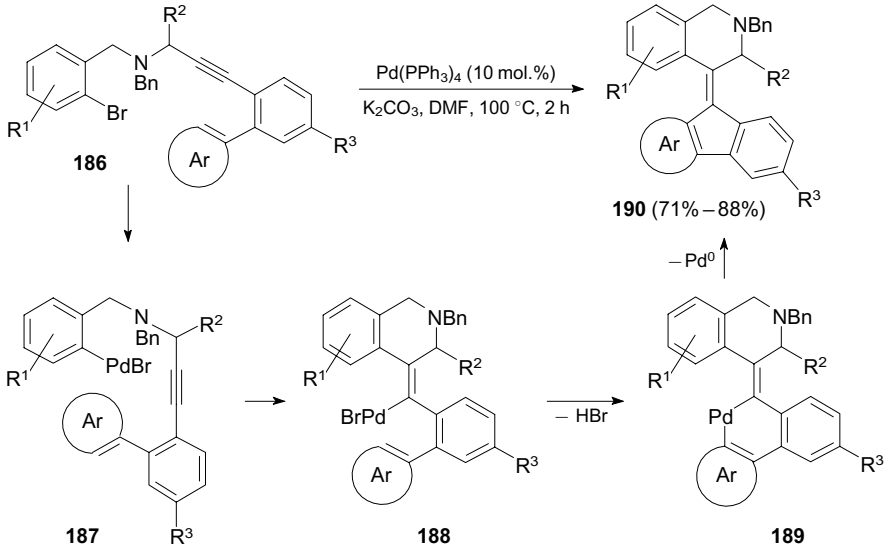
R^1 = H, Me, Cl, CO_2Me, NO_2; R^2 = H, Me, NO_2;
Ar = XC_6H_4 (X = H, 4-MeO, 4-Cl, 3-Cl, 4-F), 2-Fu, 3-Th, pyrrol-1-yl, indol-1-yl

Scheme 63



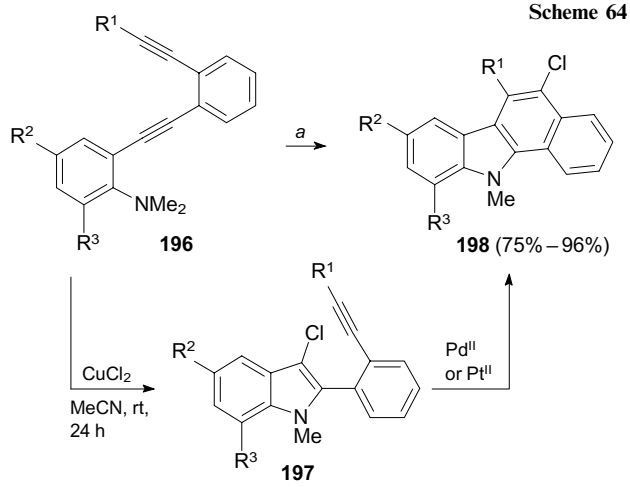
R = Ph, 1-Naph, 4-NCC_6H_4

Scheme 61



R^1 = H, 4,5-$(MeO)_2$; R^2 = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-ClC_6H_4, 1-Naph, 2-Th, *N*-ethylcarbazol-3-yl, 3-Fu, Pr^i; R^3 = H, Me; Ar = Ph, 3-Th

Scheme 64

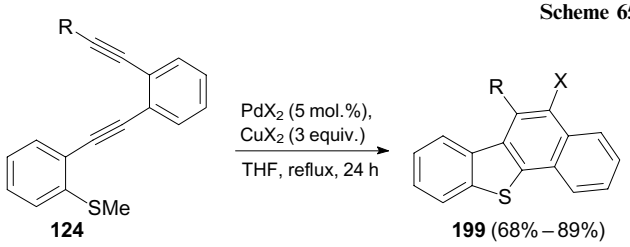


(*a*) $PdCl_2$ (10 mol.%), $CuCl_2$ (2 equiv.), THF, reflux, 1 h;
R^1 = Pr^n, Bu^i, XC_6H_4 (X = H, 4-MeO, 2-Me, 3-Me, 4-Me, 4-Cl, 4-Br, 4-F_3C, 4-O_2N); R^2 = H, Me, CO_2Me; R^3 = H, Me;
197: R^1 = Pr^n, Ph, R^2 = R^3 = H (88% – 93%)

type substitution of a halogen atom. Various groups at the alkyne moiety were tolerated with one exception of bulky *tert*-butyl group (**196**, R^1 = Bu^t) where only chloroindole **197** was obtained in 95% yield which was transformed into the corresponding benzocarbazole **198** in 40% yield upon prolonged heating (72 h).

Similar transformation was realized for thioanisole-based diynes **124** to produce naphthothiophenes **199**, albeit with longer heating (Scheme 65)[88] (for the preparation of analogous iodinated naphthothiophenes, see Scheme 44). Gold catalyst ($Ph_3PAuCl/AgSbF_6$) was found to be less efficient in these reactions. Under these conditions, *tert*-butyl substituted thioanisole **124** (R = Bu^t) afforded only monocyclization product as an analogous aniline **196** in the above example (see Scheme 64).

Scheme 65

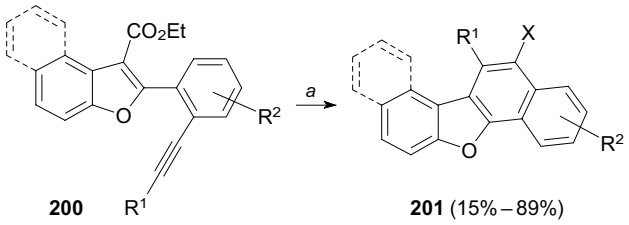


X = Cl, Br; R = Pr^n, n-C_5H_{11}, YC_6H_4 (Y = H, 4-MeO, 2-Me, 3-Me, 4-Me, 4-Cl, 4-Br, 4-F_3C)

The same catalytic system promoted decarboxylative annulation of benzofurans **200** into products **201** (Scheme 66).[115] The first step is proposed as halopalladation of the triple bond to generate a vinylpalladium intermediate, which underwent coupling with Cu-moiety formed after decarboxylation. However, this transformation is quite similar to the aforementioned synthesis of benzo[*a*]carbazoles **198**; therefore, similar reaction pathway could not be excluded in that case. Substrates **200** with alkyl groups at the triple bond gave moderate yields (42% – 64%); the worst result (15%) was obtained for the hydroxymethyl group.

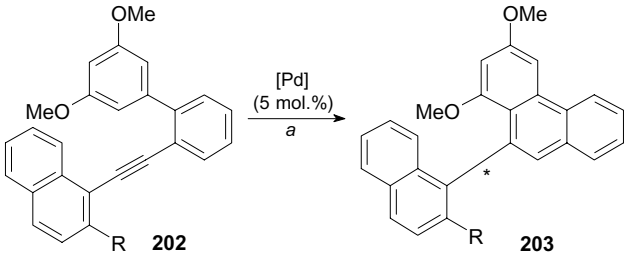
A rare example of Pd^{II}-catalyzed 6-*endo*-cyclization of a substrate **202** without a halogen atom was described in the

Scheme 66



(*a*) PdX_2 (10 mol.%), CuX_2, PhH, 100 °C, 4 – 30 h;
X = Cl, Br; R^1 = XC_6H_4 (X = H, 4-Me, 2-Me, 4-MeO, 4-O_2N), n-C_8H_{17}, n-C_5H_{11}, CH_2OH, 2-Th, 2-cyclohexenyl; R^2 = H, OMe, F

Scheme 67



(*a*) [Pd] = $[Pd(MeCN)_4](BF_4)_2$, (*R*)-BINAP (10 mol.%), DCE, 60 °C, 6 h;
203: R = Me (86%, 53% *ee*), OMe (66%, 59% *ee*)

synthesis of axially chiral compounds **203** (Scheme 67).[116] Asymmetric induction was driven by a chiral ligand used as an additive.

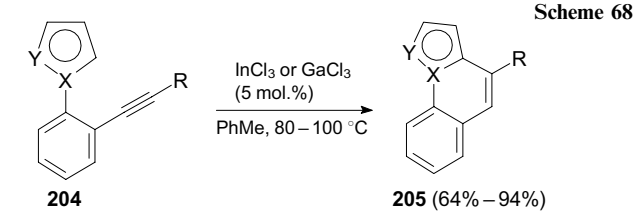
3.4. Other metals

Complexes and salts of metals, other than the above mentioned Pt, Au, and Pd, have found modest application. In most cases coordination of a metal centre to a triple bond triggers 6-*endo*-*dig* cyclization on an aryl ring in electrophilic substitution mode as with $PtCl_2$. Meanwhile, for ruthenium and tungsten catalysts, formation of vinylidene intermediates, as with AuCl, is proposed.

$InCl_3$ and $GaCl_3$ were found to be effective in cases where employment of $PtCl_2$ failed, in particular, the difference was observed for the cyclization of *ortho*-ethynyl(heteroaryl)benzenes **204** (Scheme 68).[25] $PtCl_2$ catalyzed cyclization of terminal triple bonds (see Scheme 4) but led to only <40% conversion of alkynes with R = C_6H_{13}. In contrast, the use of $InCl_3$ or $GaCl_3$ provided high yields of the corresponding tricyclic compounds **205**.

As mentioned above (see Schemes 33, 34), the useful correlation between In^{III} and Au^I catalysts was found for the annulation of *ortho*-ethynylbiaryls with a halogen atom (Br, I) or SePh group at the triple bond. $InCl_3$ turned out to

Scheme 68

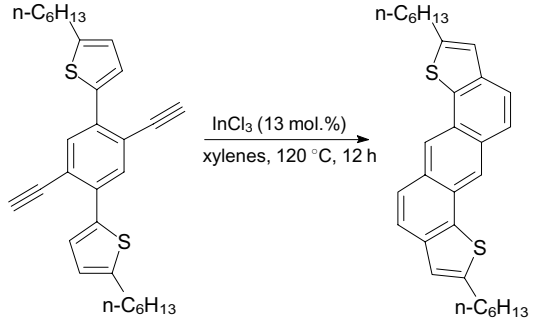


X = C, Y = S; R = Ph; X = N, Y = CH; R = Me, Ph, C_6H_{13}, TMS

perfectly catalyze ordinary 6-*endo*-cyclization while Au^I promotes concomitant 1,2-migration of an alkyne substituent. $InCl_3$ was employed in the total synthesis of the aporphine alkaloid *O*-methyldehydroisopiline [**99**, X = Br, $R^1 = (CH_2)_2NPhth$, $R^2 = R^3 = OMe$ using 1 equiv. of $InCl_3$, see Scheme 33].[117]

Cyclization of 2,5-diethynyl-*para*-phenylene **206** onto thiophene rings was realized by treatment with $InCl_3$; double annulation gave target pentacyclic compound **207** in high yield (Scheme 69).[118]

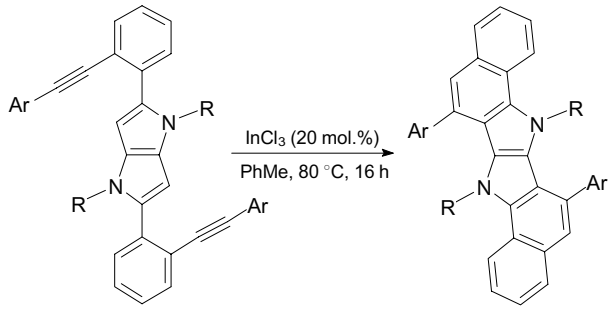
Scheme 69



206 **207** (90%)

Indolo[3,2-*b*]indoles **209** were prepared *via* $InCl_3$-catalyzed double cyclization of peripheral 2-ethynylphenyl moieties onto central pyrrolo[3,2-*b*]pyrrole core of **208** (Scheme 70).[119] The most notable feature is that ethynyl substituents were terminated with phenyl rings bearing strong electron-withdrawing groups, however, excellent yields of products **209** were obtained.

Scheme 70

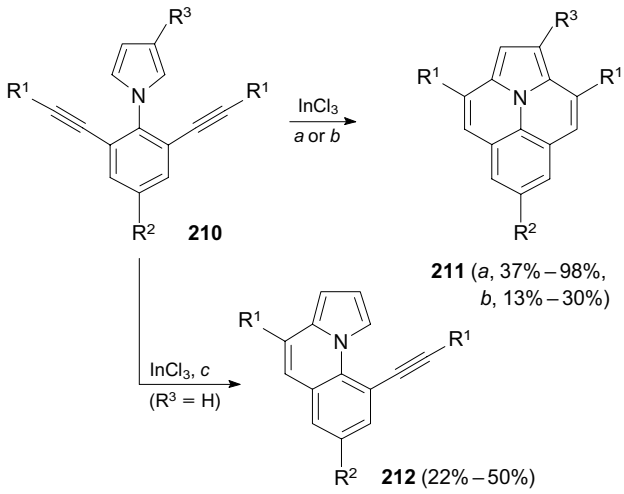


208 **209** (75% – 99%)

R = 3,5-$Bu^t_2C_6H_3$; Ar = 4-XC_6H_4 [X = CF_3, CN, NO_2, SF_5, $SO_2N(CH_2CH_2)_2O$, OMe], 3,5-$(F_3C)_2C_6H_3$

Ullazine core of **211** may be assembled by the twofold cyclization starting from *N*-(2,6-diethynylphenyl)pyrroles **210** (Scheme 71). Large catalyst load (60 mol.%) was used (Scheme 71 *a*), and even 2 equiv. of $InCl_3$ was needed for the substrate with a carbonyl group (R^3 = CHO), which obviously deactivates the pyrrole ring towards electrophiles.[120,121] The lowest yields of **211** (along with some amounts of monocyclized products) were observed for 4-[bis(4-hexyloxyphenyl)amino]phenylethynyl- (37%) and dodec-1-ynyl-substituents (40%) at the alkyne moieties while in other cases yields were not less than 73%.

Scheme 71

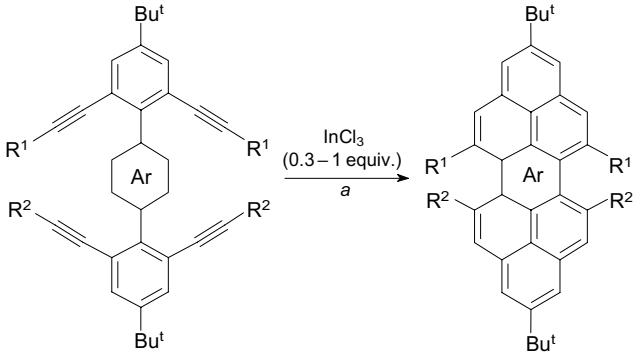


(*a*) $InCl_3$ (60 mol.%), PhMe, 100 – 110 °C, 24 h: $R^1 = C_{10}H_{21}$, Ph, 4-$HexOC_6H_4$, 2,4-$(HexO)_2C_6H_3$, 4-(4-$HexOC_6H_4)_2NC_6H_4$; R^2 = H, Cl, Br; R^3 = H; $InCl_3$ (2 equiv.), *o*-xylene, reflux, 24 h: R^1 = Ph, R^2 = H, R^3 = CHO; (*b*) $InCl_3$ (1 – 2 equiv.), *o*-$Cl_2C_6H_4$, MW, 130 °C, 20 min; R^1 = Ph; R^2 = H, Me, F; R^3 = H; (*c*) $InCl_3$ (30 mol.%), *o*-$Cl_2C_6H_4$, MW, 90 °C, 20 min; R^1 = Ph; R^2 = H, Me, F; R^3 = H

Using advantages of microwave heating allowed for running the cyclization of **210** in a selective way.[122] The monoannulation to **212** was achieved after 20 min using 30 mol.% of $InCl_3$ at 90 °C (Scheme 71 *c*) while bisannulation to **211** required 1 – 2 equiv. of $InCl_3$ at 130 °C for the same time (*b*) providing, however, lower yields than the reaction under conventional heating (*a*). For the synthesis of azaullazines with the central pyridine core harsher conditions were needed (see Scheme 140).

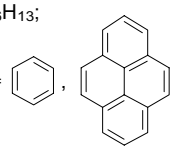
Two- or fourfold benzannulations to construct peropyrenes, teropyrenes **214**, as well as chiral peropyrenes, were achieved using $InCl_3$ (Scheme 72).[123] As reported, In^{III}

Scheme 72



213 **214** (52% – 91%)

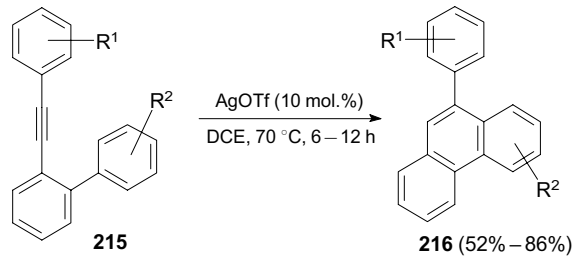
(*a*) PhMe or xylenes, 80 – 150 °C, 2 – 36 h; R^1, R^2 = 4-XC_6H_4 (X = OC_6H_{13}, CF_3, Bu^t), 5-hexylthiophen-2-yl, 3,5-Bu^t_2-4-$MeOC_6H_2$, n-C_6H_{13};

Ar = 

catalysts exhibited higher catalytic ability for this transformation than Au^{I} and Au^{III} catalysts. Compared to a Brønsted acid activation, which is effective only for similar substrates with electron-rich alkyne substituents (see Scheme 111), $InCl_3$ tolerates even electron-deficient arylethynyl groups and alkyl substituents in **213**. However, fourfold cyclization of substrates **213** with four *p*-trifluoromethylphenyl groups failed, and only partly cyclized products were observed.

Silver salts have been widely used as cocatalysts in gold-promoted reactions, however, there are several examples of employing them as the prime catalysts. AgOTf was reported to perfectly catalyze a common cyclization of *ortho*-alkynylbiphenyls **215** (Scheme 73).[124] Electron-deficient aryl ring ($R^2 = CO_2Me$) suppressed the cyclization, while neutral and electron-rich substrates furnished phenanthrenes **216** in high yields. Other silver sources ($AgNO_3$, AgOAc) appeared less effective as yields were not over 20%.

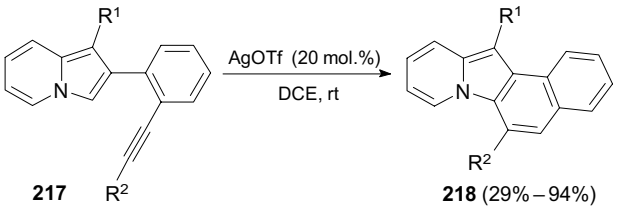
Scheme 73



215: R^1 = H, 4-Et, 4-Me, 4-Bu^t, 4-Bu^n, 3-Me, 3-OMe; R^2 = 4-OMe, 4-Me, 4-Et, 4-OPr^i, 3,4-$(OMe)_2$, 4-CH_2O(4-FC_6H_4), 4-CH_2OPh, 2-Ph

Ag^{I}-catalyzed hydroarylation runs smoothly for 2-(2-ethynylphenyl)indolizines **217** (Scheme 74).[125] Modest yields (29% – 40%) of benzo[*e*]pyrido[1,2-*a*]indoles **218** were obtained with substrates **217** having an alkylethynyl unit even at 60 °C. AgOTf provided the best result compared to $Bi(OTf)_3$, $In(OTf)_3$, and TfOH. Similar iodinated products could be prepared *via* I_2-mediated cyclization of indolizines (see Scheme 98).

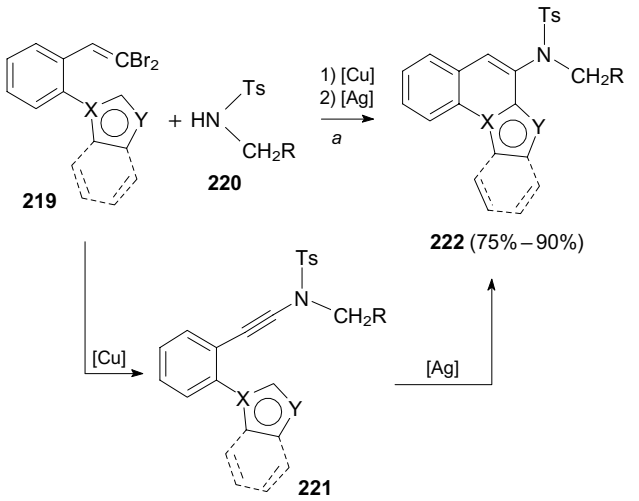
Scheme 74



R^1 = CO_2Et, CO_2Me; R^2 = XC_6H_4 (X = H, 4-Me, 4-MeO, 3-MeO, 4-Ph, 4-$NCCH_2$), 2-Me-4-$MeOC_6H_3$, 3,5-$(MeO)_2C_6H_3$, 1-Naph, 6-MeO-2-naphthyl, 3-Th, Bu^n, cyclo-C_5H_{11}

Cyclization of ynamides onto pyrrole or thiophene ring of **221** with AgOTf as catalyst is a second step in transformation of dibromides **219** into pyrrolo-, indolo[1,2-*a*]quinolines and naphtho[2,1-*b*]thiophenes **222** (Scheme 75).[126] Triflates of other metals (Zn, Yb, In) showed less catalytic activity in this reaction (yields not over 63%). Intermediate ynamides **221** can be isolated and

Scheme 75

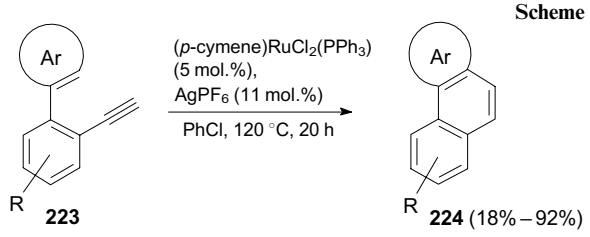


(*a*) 1) CuI (3 mol.%), 1,10-phenanthroline (5 mol.%), Cs_2CO_3, THF, rt; 2) AgOTf (5 mol.%); X = N, Y = CH (pyrrol-1-yl, indol-1-yl); X = C, Y = S (3-Th); R = Pr^n, 4-ZC_6H_4 (Z = H, Cl, Br, Me, MeO), 3-Py, 2-Th; **221**: R = Ph, X = N, Y = CH (pyrrol-1-yl) (89%)

the hydroarylation can be performed separately. Simultaneous addition of both Cu^{I} and Ag^{I} catalysts to the starting compounds afforded the ynamide and only trace amount of final fused product, while addition of silver triflate after the formation of ynamide led to the target tricyclic compound. Tosyl group on the nitrogen atom of **220** was successfully replaced by the mesyl group in several cases but other electron-withdrawing groups (Boc, $COCF_3$, Ac) inhibited the reaction, even when the temperature and catalyst loading increased.

Ruthenium complexes also effectively convert 2-ethynylbiaryls into phenanthrenes. Catalytic system [(*p*-cymene)$RuCl_2(PPh_3)$]/$AgPF_6$ in chlorobenzene at 120 °C was found as the optimal one for a wide range of biphenyls and heterocyclic substrates **223**; the latter, as a rule, gave higher yields of products **224** (Scheme 76).[127] Interestingly, *ortho*-ethynyl(thiophen-2-yl)benzenes **223** provided 72% – 90% yields, while 3-aryl-2-ethynylthiophenes **463** (see Scheme 156) gave only 44% – 49%. The electron-donating methoxy group on the central phenyl ring at the *para*-position to the ethynyl fragment (**223**, R^1 = H) negatively affected the cyclization efficiency, thus a complex mixture of products (18% yield of target **224**) was obtained. In all cases, the annulation proceeded selectively in a 6-*endo*-mode. Based on several control experiments and the DFT

Scheme 76

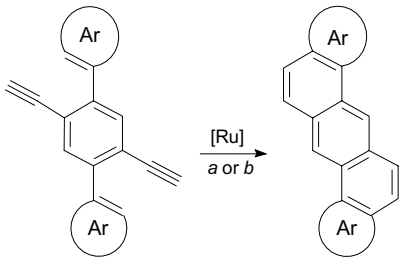


Ar = XC_6H_4 (X = H, OMe, Cl, F, CO_2Me), 5-Y-thiophen-2-yl (Y = H, Me, Cl, Ac), 5-Me-furan-2-yl, *N*-Boc-pyrrol-2-yl, indol-2-yl, benzofuran-2-yl, benzothiophen-2-yl; R = H, OMe, F

calculations, the electrophilic cyclization involving a π-alkyne complex and subsequent consecutive 1,2-H shifts was assumed as the most probable mechanism; however, a distinctive pathway *via* a ruthenium-vinylidene intermediate was proposed for similar cyclizations.[54, 128, 129]

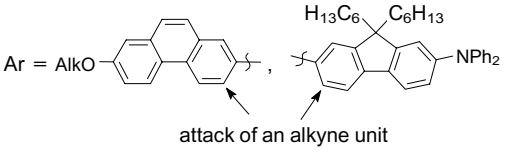
Ruthenium-catalyzed double cyclizations of biphenyls[53, 54] and heterocycle-containing[127, 129] analogues **225** to form polyarenes **226** were reported as well (Scheme 77). The regioselectivity of annulation onto the phenanthrenyl substituents was opposite compared to that of $PtCl_2$/CO-catalyzed reaction of similar substrates (see Scheme 20). Here attack occurred at the less sterically hindered position of phenanthrene fragment, which was attributed to the steric effect of the bulky ruthenium ligands (see Scheme 77, bottom line).

Scheme 77



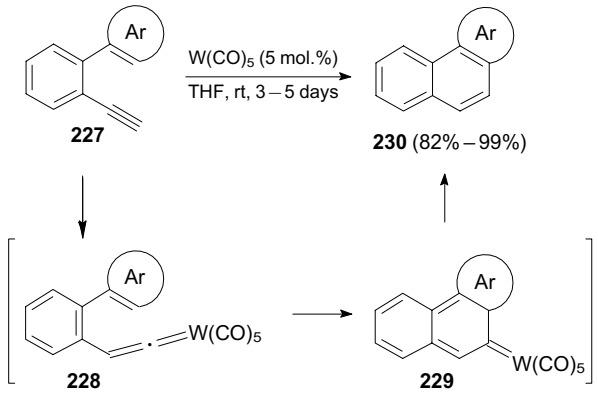
225 **226** (58% – 83%)

(*a*) [Ru] = $TpRuPPh_3(CH_3CN)_2PF_6$ (or SbF_6) (10 mol.% – 20 mol.%), DCE, 80 °C, 12 – 24 h; Ar = Ph, 4-$(Ph_2N)C_6H_4$, 4-$AlkOC_6H_4$, 3-Th; (*b*) [Ru] = [(*p*-cymene)$RuCl_2(PPh_3)$] (10 mol.%), $AgPF_6$ (22 mol.%), PhCl, 120 °C, 20 h; Ar = 6-Bu^t-benzofuran-2-yl;



For $W(CO)_5$-catalyzed cyclization, formation of tungsten vinylidene intermediate is accepted as a key step. Complex **228** formed from *ortho*-ethynyl(heteroaryl)benzenes **227** underwent electrocyclization to give a metallocarbene intermediate **229**, which gave product **230** by 1,2-H migration with aromatization (Scheme 78).[130] A catalytic amount of $W(CO)_5$ was sufficient to smoothly

Scheme 78

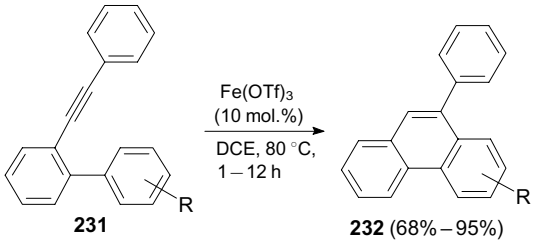


Ar = 2-Th, 3-Th, *N*-methylpyrrol-2-yl, 2-Fu (1 equiv. of Cat. used)

transform thiophenyl and pyrrolyl substrates **227** while 100 mol.% of catalyst was needed to achieve good yield of furan-fused naphthalene.

Electron-deficient arylethynylbiphenyls **231** were engaged in cyclization by $Fe(OTf)_3$ to form phenanthrenes **232**, albeit the lack of the electron density in the arylethynyl fragment (4-$O_2NC_6H_4$ instead of Ph) suppressed the reaction (Scheme 79).[131] 6-*endo*-Cyclization of substrate **231** with donating methoxy group (R = OMe) was accompanied by minor 5-*exo*-cyclization (9-benzylidene-2-methoxyfluorene was obtained in 11% yield).

Scheme 79

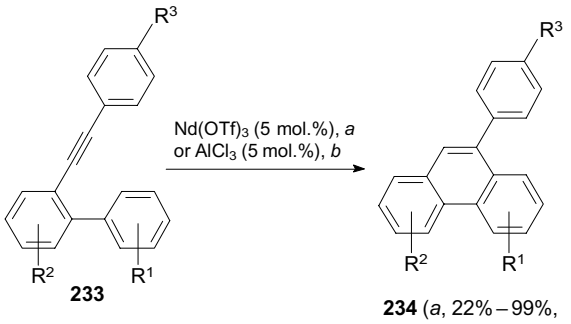


231 **232** (68% – 95%)

R = 4-CN, 4-CO_2Me, 4-NO_2, 4-CF_3, 4-OMe, 3,5-F_2, H

Neodymium triflate[132] and $AlCl_3$ (Ref. 133) were used for the synthesis of phenanthrenes **234** (Scheme 80). Both catalysts work only for substrates **233** with electron-rich aryl rings at the triple bond. In both cases cyclization of (4-alkoxyphenylethynyl)biphenyls **233** proceeded quantitatively while the lowest yields were obtained from chloro-substituted compound **233** ($R^1 = R^2 = H$, $R^3 = Cl$): 22% [$Nd(OTf)_3$] and 41% ($AlCl_3$). Electron-withdrawing R^1 groups in the biphenyl moiety had no significant effect on the reaction outcome.

Scheme 80

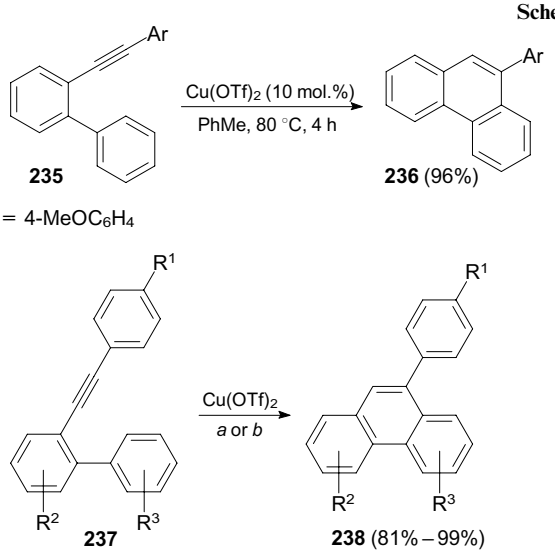


234 (*a*, 22% – 99%, *b*, 40% – 98%)

(*a*) $MeNO_2$, 115 °C, 10 – 72 h; (*b*) CH_2Cl_2, rt – reflux, 2 – 72 h; R^1 = 4-CN, 4-CO_2Me, 4-NO_2, 4-Br, 4-Ac, H, 4-OMe, 4-OH, 2-Me; R^2 = H, 4-Me, 5-Me, 4-Cl; R^3 = H, OMe, OEt, Me, Et, Cl

$Cu(OTf)_2$ was reported to efficiently catalyze common thermal cycloisomerization of biphenyl **235** into phenanthrene **236** (Scheme 81, top line).[134] Interestingly, it was also used as a catalyst in photocyclization of *ortho*-aryl(arylethynyl)benzenes **237** into compounds **238**, which did not take place under dark conditions, as reported (Scheme 81, bottom line). Photoactivation could be performed using visible light in the presence of a photosensitizer Eosin Y (Ref. 135) or under UV irradiation.[136] In the former case,

Scheme 81



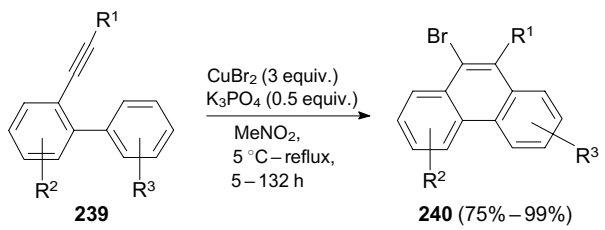
(*a*) CH_2Cl_2, rt, 0.5 – 18 h, *hν*; (*b*) Eosin Y, CH_2Cl_2/MeCN, 20 – 90 °C, 1.5 – 5 days, visible light; R^1 = H, Me, Et, OMe, Ac, Cl; R^2 = H, Cl, Me, CO_2Me; R^3 = H, Me, CO_2Me, Ac, CN, CF_3, NO_2, Br

the reaction took 1.5 – 5 days to reach completion, and electron-deficient substrates required heating at 60 – 90 °C. The UV irradiation (254 nm) dramatically increased the reaction rate even at room temperature for variously substituted biphenyls **237**. Different mechanisms were proposed for these processes involving single electron transfer from the excited Eosin Y to the copper – alkyne complex followed by electrophilic cyclization under visible light, or UV-induced photo-6π-electrocyclization of triene system formed after coordination of copper to the triple bond.

Thermal cyclization of similar biphenyls **239** upon treatment with $CuBr_2$ led to 9-bromophenanthrenes **240** (Scheme 82).[137] For highly electron-deficient substrates refluxing in $MeNO_2$ was necessary, while for electron-rich compounds excellent yields were obtained at room temperature or even at 5 °C. Large excess of copper bromide was used because of its noncatalytic behaviour in this reaction as a bromine source; the addition of a base allowed preventing formation of byproduct without a bromine atom. The electrophilic cyclization of alkyne moiety activated by $CuBr_2$ coordination was assumed as a key step in this transformation.

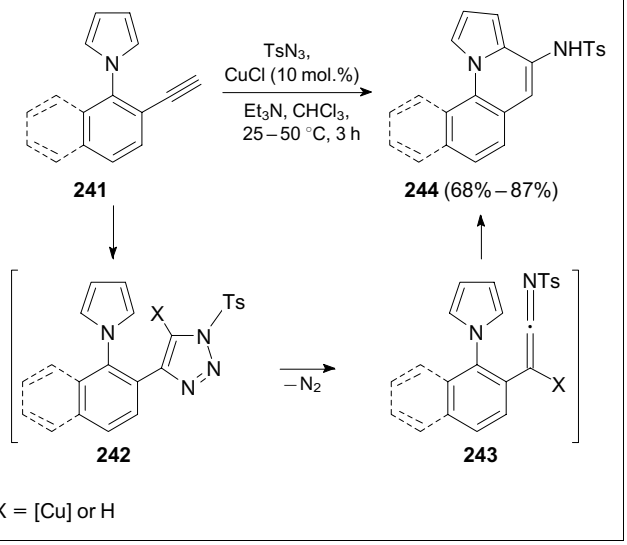
Cu^I catalyzed the reaction between 1-(2-ethynylphenyl)-pyrrole **241** and *p*-toluenesulfonyl azide to produce pyrrolo[1,2-*a*]quinoline derivative **244**, as well as its benzofused analogue (Scheme 83).[138] The cyclization is proposed to

Scheme 82



R^3 = 4-XC_6H_4 (X = H, Me, Et, OMe, Cl, Br, NO_2, Ph), Bu^t, TMS; R^2 = H, Cl, Me, OMe, CO_2Me; R^3 = H, Me, OMe, Ph, Br, I, Ac

Scheme 83



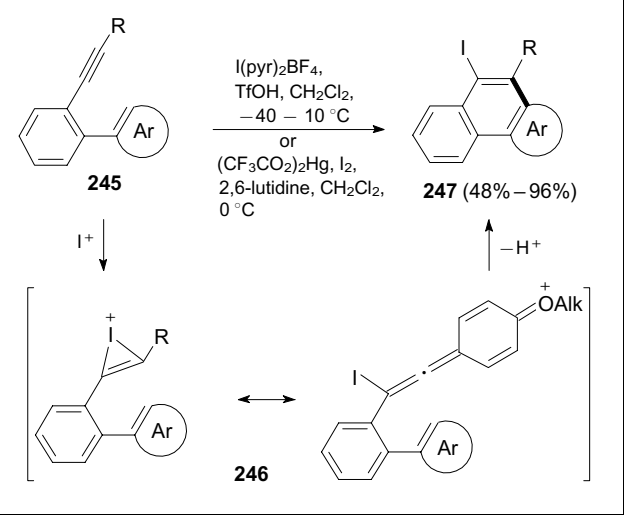
proceed through a ketenimine intermediate **243**, which is generated *in situ* from the triazole cycloadduct **242** upon release of N_2. Thus, the formation of six-membered ring proceeds through attack of the α-pyrrole carbon atom to the imine carbon atom.

4. Electrophilic activation

4.1. Iodine-based electrophiles

In the first work on electrophilic cyclization of *ortho*-ethynylbiaryls, $I(pyr)_2BF_4$ was treated with 2 equiv. of TfOH to liberate free $I^+BF_4^-$, a source of electrophilic iodine.[139] Later cation I^+ was generated *in situ* by reaction of $(CF_3CO_2)_2Hg$ with I_2 in the presence of 2,6-lutidine, which proved to be operationally simpler (Scheme 84).[140, 141] As a result, iodinated polycyclic arenes **247** were obtained in high yields from biaryls **245**. This reaction requires stoichiometric amount of I^+ precursor since it proceeds through electrophilic attack at the triple bond followed by 6-*endo*-*dig* cyclization on aryl ring in a Friedel – Crafts type manner. The presence of electron-donating *para*-alkoxy groups on the phenylethynyl fragment of substrates **245** was found crucial to successful cyclization, which is consistent with the proposed mecha-

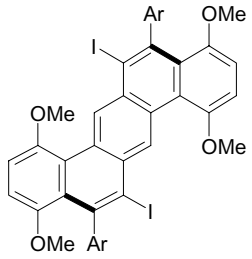
Scheme 84



nism through the cation **246**; no target products were observed when R = Ph, C_6H_{13}.

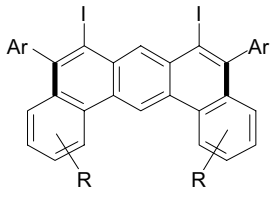
Among symmetric systems containing two *ortho*-aryl(ethynyl) fragments, the best results of iodocyclization were achieved for substrates with *para*- and *meta*-positions of these moieties at the central benzene ring, which provided dibenzo[*a*,*h*]anthracene **248**[140] and dibenzo[*a*,*j*]anthracenes **249**,[140, 142, 143] respectively, in high yields (the new C – C bonds are marked in bold). The substrate with *ortho*-located phenyl groups undergoing cyclization was recovered after treatment with mercury(II) trifluoroacetate and I_2; surprisingly, replacement of mercury salt by AgOTf led to helicene **250** without any iodine atom, albeit in only 20% yield, moreover, in the absence of iodine no helicene formed at all.[140]

Structures 248 – 251



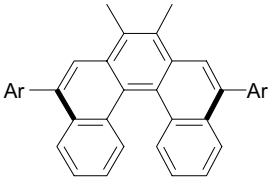
248 (96%)

Ar = 4-($C_{12}H_{25}O$)C_6H_4



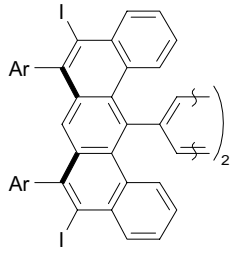
249 (54% – 99%)

Ar = 4-($C_{12}H_{25}O$)C_6H_4, 3,4-($C_6H_{13}O$)$_2C_6H_3$;
R = C_6H_{13}, $C_{12}H_{25}$, benzo[*b*]-thiophene-2,3-diyl



250 (20%)

Ar = 4-$BuOC_6H_4$



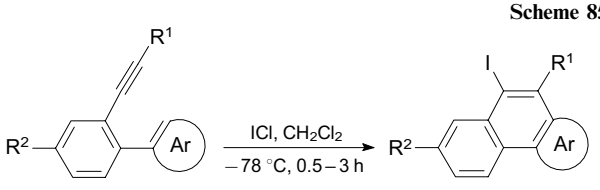
251 (58%)

Ar = 4-$Bu^tC_6H_4$

The I(pyr)$_2BF_4$/TfOH system was also used to perform fourfold cyclization in the synthesis of precursor **251** for hexa-*peri*-hexabenzocoronene.[144]

Larock suggested[145-147] ICl as more active and convenient reagent to perform iodocyclization of variously substituted *ortho*-ethynylbiaryls **252** to give **253**

Scheme 85



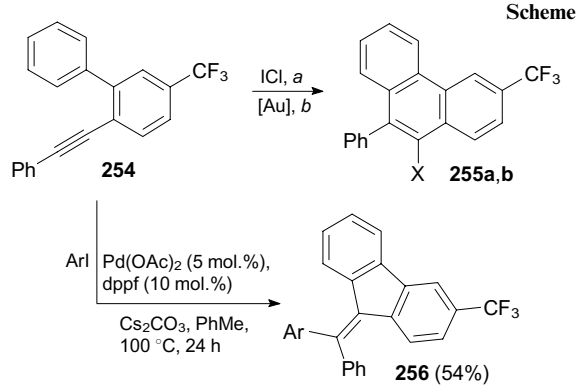
252 **253** (50% – 99%)

R^1 = 4-XC_6H_4 (X = H, Me, Bu^n, OMe, NO_2, CO_2Et), 2-Th, 3-Th, cyclohex-1-enyl, CH_2TMS, CH_2OH; R^2 = H, NO_2;
Ar = 4-YC_6H_4 (Y = H, CHO, NO_2), benzofuran-3-yl, 2-Naph, 3-Th, benzothiophen-3-yl; R^2 = CO_2Me (25 °C, 5 h)

(Scheme 85).[148, 149] In comparison to the abovementioned reactions, *para*-alkoxy groups on phenylethynyl moiety were not needed, and even electron-deficient compounds **252** were amenable to ICl, albeit within longer reaction time (3 – 5 h). Only alkynes with R^1 = Bu^n or TMS appeared resistant to cyclization by ICl, and addition of halogen atoms to the triple bond occurred instead. A system I_2/$NaHCO_3$ can also be employed as the electrophile, but the reaction took 24 h at room temperature to afford the corresponding product **253**.

ICl proved to be comparable in efficiency with metal catalysts. By the example of biphenyl **254**, three main pathways of cyclization were explored (Scheme 86).[150] Iodinated phenanthrene **255a** was assembled *via* an ICl-induced 6-*endo*-*dig* cyclization. Alternatively, annulation under gold catalysis delivered phenanthrene **255b** in the same yield. Arylative Pd-catalyzed 5-*exo*-*dig* cyclization afforded single stereoisomer of fluorene **256**.

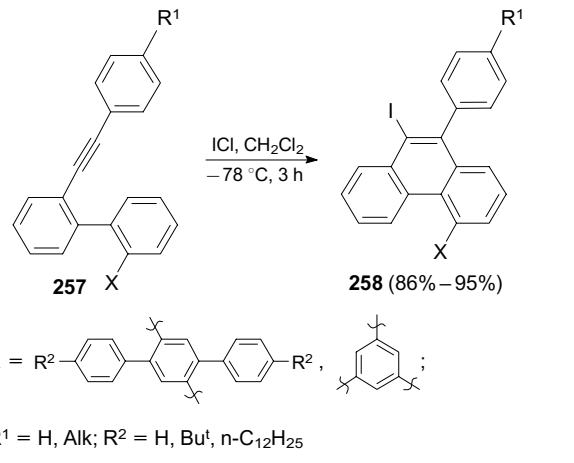
Scheme 86



(*a*) CH_2Cl_2, 0 °C, 0.5 h; (*b*) (2,6-$Bu^t_2C_6H_3O)_3$PAuCl (5 mol.%), $AgBF_4$ (10 mol.%), PhMe, 100 °C, 3 h; Ar = 4-(MeO_2C)C_6H_4;
255: X = I (**a**, 91%), H (**b**, 91%)

Two- and threefold iodocyclizations were realized for compounds **257** bearing two or three 2′-(arylethynyl)biphen-2-yl fragments at the central benzene ring, respectively (Scheme 87).[151, 152] Simultaneous annulations occurred smoothly to give bis- and tris(phenanthren-4-yl)benzenes **258** in high yields.

Scheme 87

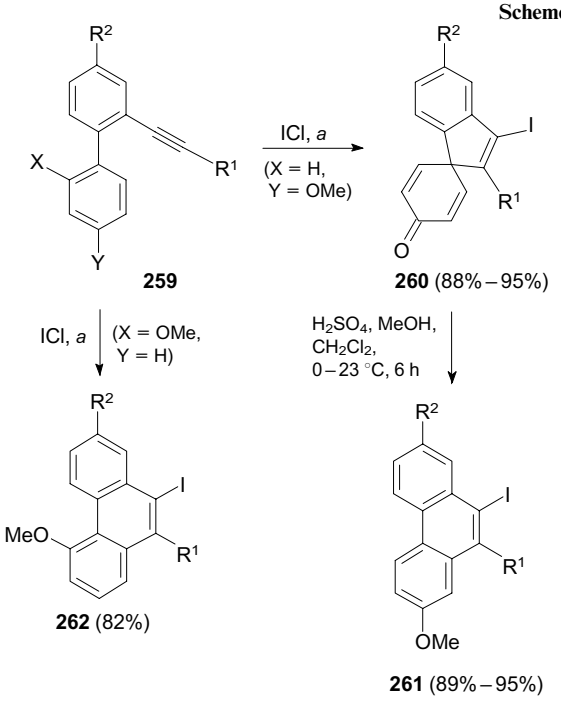


257 **258** (86% – 95%)

R^1 = H, Alk; R^2 = H, Bu^t, n-$C_{12}H_{25}$

For substrates **259** with *para*-methoxy group on the phenyl ring undergoing cyclization (X = H, Y = OMe), treatment with ICl led to alternative *ipso*-cyclization[29] to give spirocyclohexadienones **260** (Scheme 88).[153] In acidic alcoholic medium these spiro compounds transformed to 9-iodophenanthrenes **261** (the same products could be anticipated, if the ICl-induced 6-*endo*-*dig* cyclization were to take place) through a selective 1,2-migration of the alkenyl group. Thus, the apparent restriction turned into an advantage of obtaining two different structures from the one substrate. The *ipso*-chemoselectivity seems to be inherent to *para*-methoxy-substituted compounds, since 2′-methoxy-2-(arylethynyl)biphenyl **259** (X = OMe, Y = H) gave only corresponding iodophenanthrene **262**; however, the possibility that *ipso*-cyclization also actually occurred, but products suffered rapid rearrangement under the reaction conditions, could not be excluded.

Scheme 88

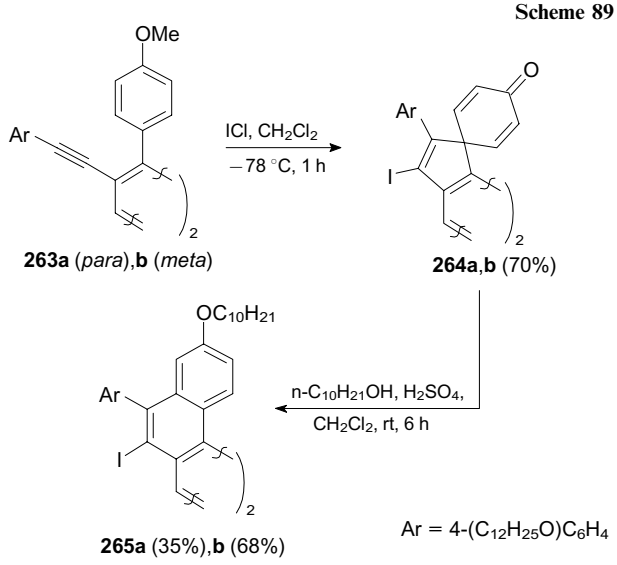


(*a*) CH_2Cl_2, −78 °C, 2 h; **261**: R^1 = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 2-Th, 2-Fu, benzofuran-2-yl, benzo[*b*]thiophen-2-yl, n-C_6H_{13}; R^2 = H, OMe; **262**: R^1 = 4-$MeOC_6H_4$, R^2 = OMe

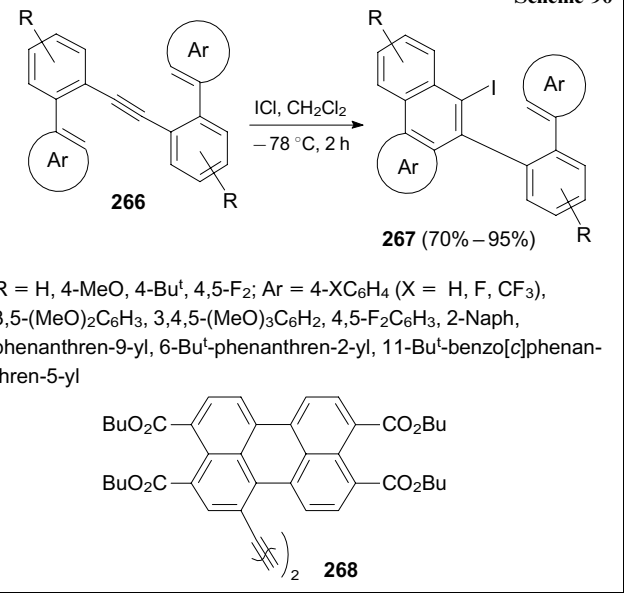
Replacement of methanol by other alcohols might produce arene with alkoxy group other than that in starting compound. This was used for the synthesis of decyl ethers **265a**,**b** from both *para*- (Ref. 154) and *meta*- (Ref. 143) bis[*ortho*-(arylethynyl)(4-methoxyphenyl)]benzenes **263a**,**b** *via* spiro derivatives **264a**,**b** (Scheme 89).

ICl successfully induced cyclizations of symmetrical bis(2-biphenyl)acetylenes **266** with electron-donating and electron-withdrawing groups,[153, 155] and of analogous compounds with extended aromatic systems[156] to produce iodinated products **267** (Scheme 90). Ethynylene-linked di(perylene tetraester) **268** was subjected to ICl at room temperature and afforded the iodocyclization product with moderate stability in air, which was immediately used further.[157] However, an analogous di(perylene diimide)

Scheme 89



Scheme 90

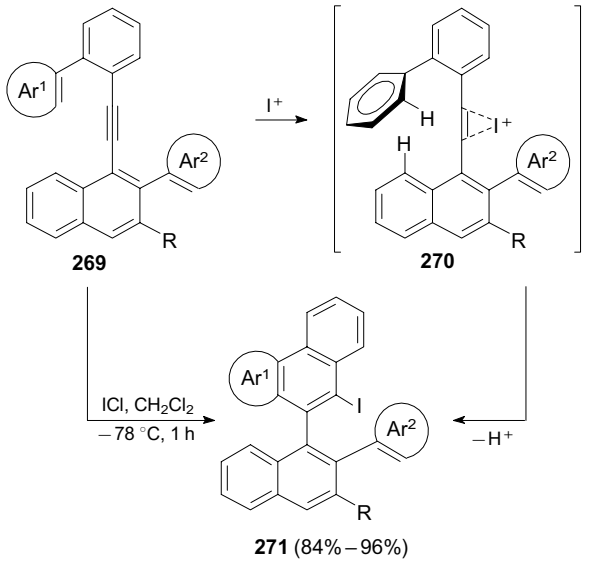


was completely inert to ICl, which was likely attributed to its more electron-deficient character.

Formation of an iodonium ion through the addition of I^+ to the triple bond is sensitive to steric factors in case of unsymmetrical sterically encumbered substrates. The I^+-induced annulation of *ortho*-aryl(arylethynyl)naphthalenes **269** could afford either the substituted iodochrysene, or iodophenanthrene, or a mixture of both (Scheme 91).[158] Only iodophenanthrene derivatives **271** formed in high yields. The observed regioselectivity is likely due to less steric congestion upon coordination of I^+ to the alkyne away from the naphthyl moiety in **270**.

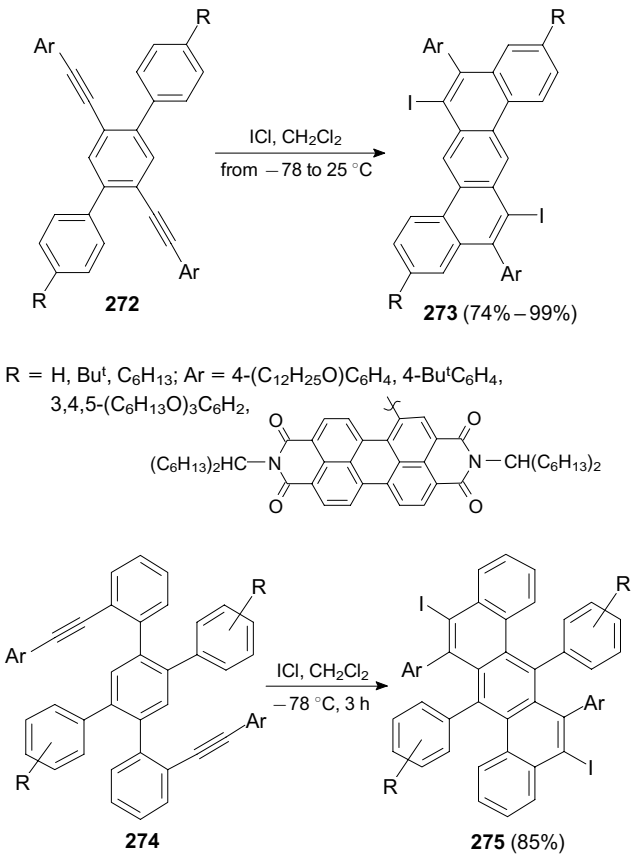
ICl is commonly used to achieve dibenzoanthracenes **273** and **275** *via* double electrophilic cyclization of various terphenyls **272** and **274** with *para*-alkoxyphenyl[154, 159] or *para*-alkylphenyl[160 – 162] groups on ethynyl terminus, and even with fragment of perylene diimide[163] (Scheme 92). Reactions proceed smoothly in high yields for various positions of ethynyl fragments in substrates, either on the central core in **272** or on pendant phenyl rings in **274**.

Scheme 91



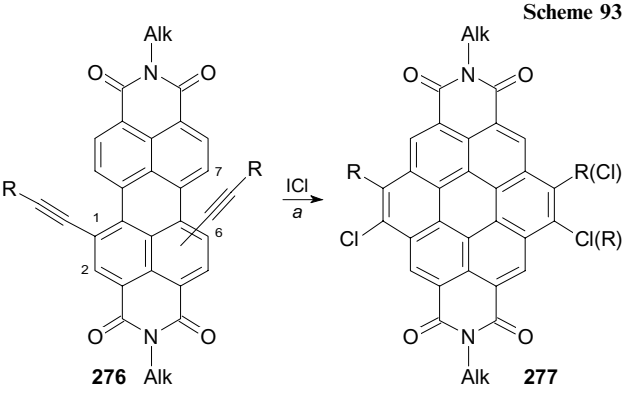
R = H, Me; Ar^1 = Ph, 3,5-$(MeO)_2C_6H_3$, 2-Th; Ar^2 = Ph, 2-MeC_6H_4, 4-MeC_6H_4, 4-FC_6H_4, 4-NCC_6H_4, 2-Naph, 2-Py, 5-pyrimidyl

Scheme 92



ortho-Ethynylbiaryls with perylene diimide core feature an unusual halogen change when treated with ICl. A mixture of isomeric 1,6- and 1,7-diethynylperylenes **276** produced chlorocoronenes **277** instead of or in addition to

Scheme 93

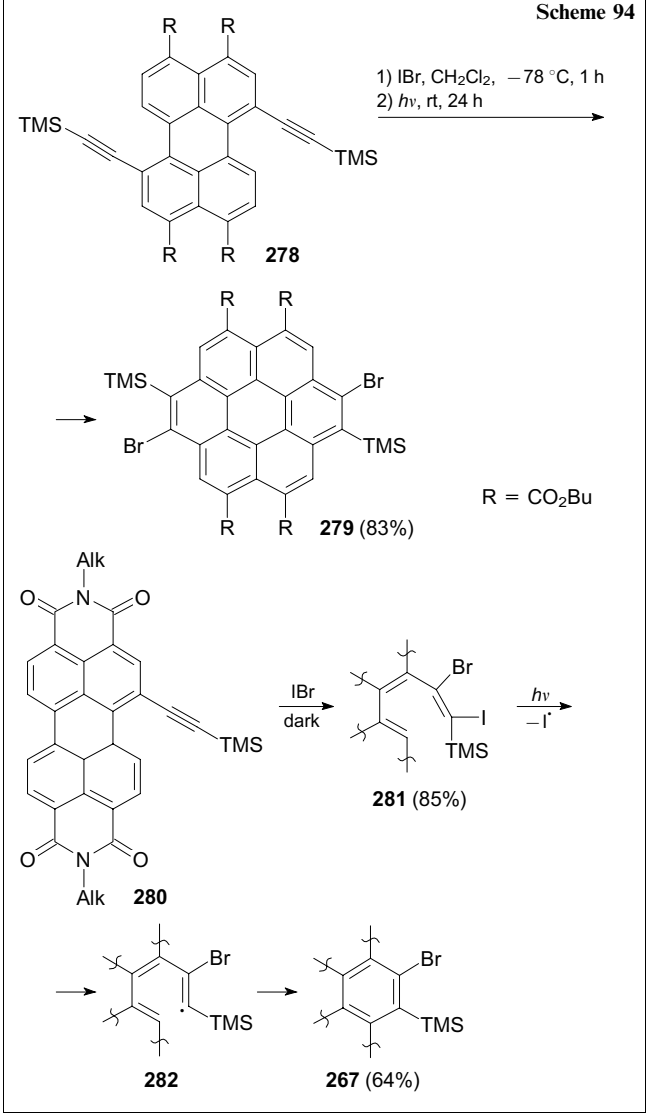


(*a*) CH_2Cl_2, from −78 °C to 30 °C, *hν*; R = TMS (88%), n-$C_{10}H_{21}$ (28%), 4-$(C_{12}H_{25}O)C_6H_4$ (60%); Alk = $CH(C_6H_{13})_2$

expected iodinated derivatives irrespectively of the substituents at the triple bonds (Scheme 93).[164] Exposing the reaction to sunlight improved the yield of **277** (R = TMS) from 40% to 88%.

The similar result was obtained using IBr for the cyclization of perylene **278**: only dibromocoronene tetraester **279** was obtained in 83% yield (Scheme 94).[165] No

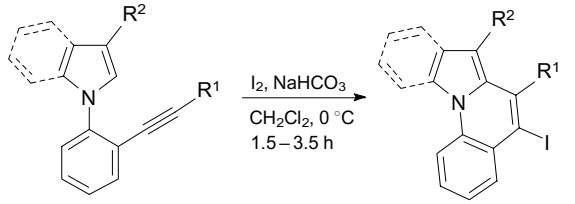
Scheme 94



stable cyclization product was observed under dark conditions, likely due to the lack of electron density in the core of perylene tetracarboxylic acid that impedes an electrophilic substitution. The plausible mechanism was studied on mono(trimethylsilylethynyl)perylene diimide **280**. In the dark, an addition of IBr to the triple bond of **280** occurred to give **281**, which underwent radical annulation through **282** to form final **283** upon exposure to the day light at room temperature.

Molecular iodine may serve as an iodinating cyclization reagent; it is often used in the presence of a base to prevent the involvement of resulting HI in side reactions, in particular, acid-catalyzed 6-*endo*-cyclization to non-iodinated product. Cyclization of *N*-(2-ethynylphenyl)pyrroles **284** by $I_2/NaHCO_3$ smoothly gave 5-iodopyrrolo[1,2-*a*]quinolines **285** in higher yields for aryl than for alkyl groups at the triple bond (Scheme 95).[166] Only 4-nitrophenyl group at the alkyne terminus provided an inseparable mixture of products. Among analogous indoles **284**, which were subjected to iodine to get 5-iodoindolo[1,2-*a*]quinolines **285**, 3-methyl-substituted compounds showed better results (79% – 92%) than those without a methyl group (70% – 75%).

Scheme 95

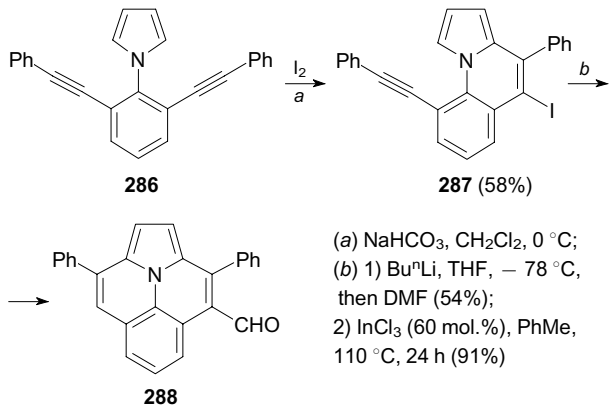


284 **285** (70% – 93%)

R^1 = XC_6H_4 (X = H, 4-Me, 4-Et, 4-Bu^n, 4-MeO, 4-Me_2N, 4-Ph, 3-Me, 2-Me, 3-MeO), 6-MeO-2-naphthyl, 3-Th, anthracen-9-yl, Bu^n, Bu^t, Cy, cyclo-C_5H_{11}, cyclo-Pr, CH_2OH, CH_2OPh; R^2 = H, Me

I_2-Induced monocyclization of *N*-[2,6-di(phenylethynyl)phenyl]pyrrole **286** was implemented as the first step in the synthesis of 3,9-diphenyllullazine-4-carbaldehyde **288** (Scheme 96).[121] Annulation of the remaining alkyne fragment in **287** was accomplished with $InCl_3$ after replacement of the iodine atom by the carbonyl group (compare with the $InCl_3$-catalyzed syntheses of ullazines, see Scheme 71).

Scheme 96

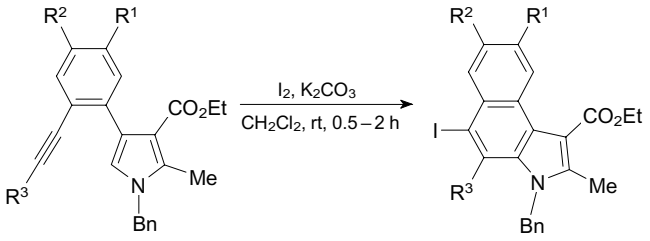


286 **287** (58%) **288**

(*a*) $NaHCO_3$, CH_2Cl_2, 0 °C;
(*b*) 1) Bu^{n}Li, THF, – 78 °C, then DMF (54%);
2) $InCl_3$ (60 mol.%), PhMe, 110 °C, 24 h (91%)

2-Ethynylphenyl fragment may also be located on the C(3) atom of a pyrrole ring to allow iodocyclization on the activated C(2) atom. 3*H*-Benzo[*e*]indoles **290** were obtained in high yields despite the presence of electron-withdrawing ethoxycarbonyl group on the pyrrole ring of **289** (Scheme 97).[167] Upon acid catalysis with HI or TsOH, non-iodinated benzo[*e*]indole (R^1 = R^2 = H, R^3 = Ph) was isolated in only 41% yield to compare with 93% of **290** using I_2/K_2CO_3.

Scheme 97

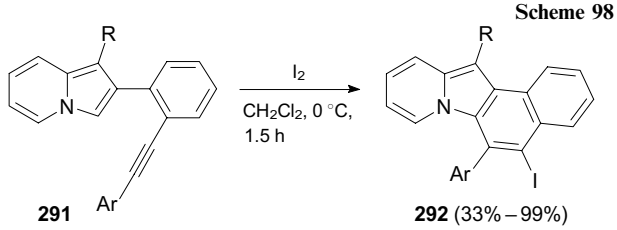


289 **290** (61% – 96%)

R^1 = H, OMe, F; R^2 = H, OMe; R^3 = XC_6H_4 (X = H, 4-Me, 3-Me, 4-Cl, 2-Cl, 4-F), Bu^n

2-(2-Ethynylphenyl)indolizines **291** smoothly furnished 5-iodobenzo[*e*]pyrido[1,2-*a*]indoles **292** with I_2 (5 equiv.); addition of $NaHCO_3$ enabled the amount of iodine to be reduced to 2 – 3 equiv. with no loss in yield (with NIS and ICl poor results were obtained) (Scheme 98).[168] In general, high yields (> 65%) were obtained for various substituents in substrates **291**, but introducing a methyl group instead of alkoxycarbonyl group in the pyrrole ring decreased the yield of the corresponding **292** to 33%.

Scheme 98

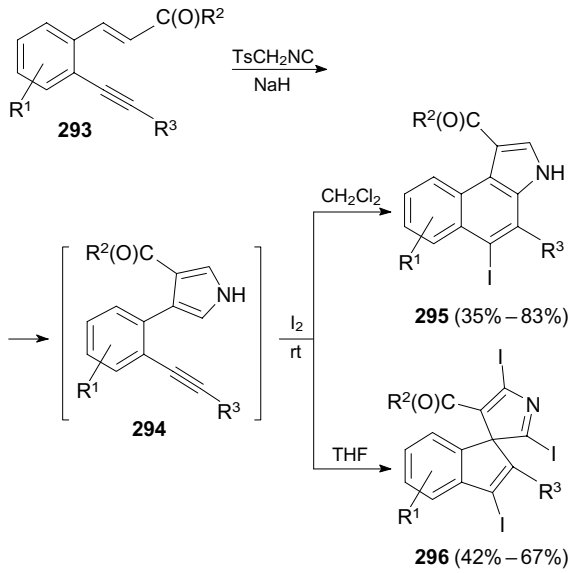


291 **292** (33% – 99%)

R = CO_2Alk, Me; Ar = XC_6H_4 (X = H, 4-Me, 4-F, 3-MeO, 4-Ph, 4-MeO, 4-$NCCH_2$), 2-Me-4-$MeOC_6H_3$, 3,5-$(MeO)_2C_6H_3$, 3-Th, 1-Naph, 6-MeO-2-naphthyl

An unusual solvent-dependent regioselective iodocyclization of 3-(2-ethynylphenyl)pyrroles **294** generated *in situ* from alkyne-tethered chalcones/cinnamates **293** and tosylmethyl isocyanide upon treatment with NaH was reported (Scheme 99).[169] Formation of pyrrole **294** in the first step was confirmed by isolation of one such compound in high yield. The subsequent cyclization proceeded in 6-*endo-dig* and 5-*endo-dig* mode with benzo[*e*]indoles **295** as the major products when the reaction was performed in CH_2Cl_2, while spiro[indene-1,3′-pyrroles] **296** predominated in THF. The increased amount of iodine (4 equiv.) favoured the latter pathway through an electrophilic bisiodination of intermediate pyrrole, which occurred before the cyclization as it was shown by control experiments. Using $PtCl_2$ (5 mol.%) or Ph_3PAuCl (1 mol.%) instead of iodine only pyrrole **294** was obtained and no cyclization took place.

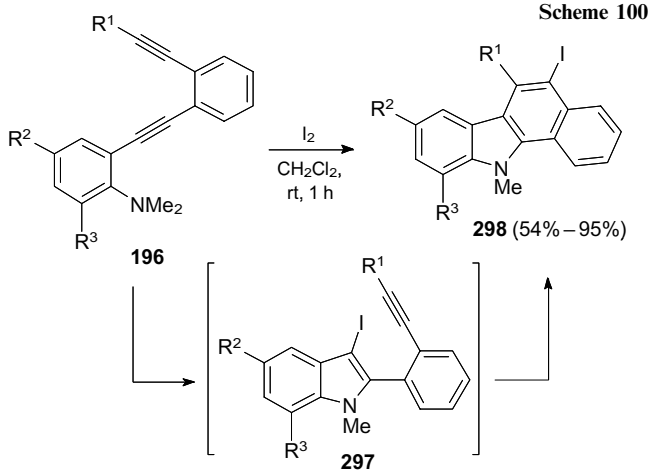
Scheme 99



R^1 = H, Me, Cl; R^2 = EtO, XC_6H_4 (X = H, Me, OMe, Cl, Br); R^3 = YC_6H_4 (Y = H, 4-Me, 3-Me, 4-MeO, 4-Cl, 4-Br, 4-F), 2-Th, Pr^n, cyclo-Pr; **294**: R^1 = H, R^2 = EtO, R^3 = 4-ClC_6H_4 (90%)

Cyclization on the C(3) atom of the pyrrole ring could also be realized with iodine. On the way from anilines **196** to benzo[*a*]carbazoles **298**, iodine promoted a cascade of two cyclizations: the first one to form indole ring of **297** and the second one as electrophilic 6-*endo* iodoarylation of the triple bond (Scheme 100).[170] Various substituents were tolerated with an exception of *tert*-butyl group at the triple bond, which inhibited the final transformation. Anilines bearing electron-withdrawing group (R^2 = CO_2Me) required refluxing in THF for 48 h to complete the second iodocyclization. With an isolated indole **297** (R^1 = Pr^n, R^2 = R^3 = H) other catalytic systems were tested and showed comparable results [$Pd(OAc)_2$ (86%), Ph_3PAuCl (80%), Ph_3PAuCl_3 (60%), $AuCl_3$ (68%), ICl (85%)]. Starting from aniline **196** with NIS or $I(pyr)_2BF_4$ only indole **297** was obtained, but addition of $Pd(OAc)_2$ or Ph_3PAuCl to the reaction mixture provided full conversion to the target carbazole **298** as well. This is quite expected as examples of gold and palladium catalyzed reactions were described for these and similar compounds (see Schemes 42, 64).

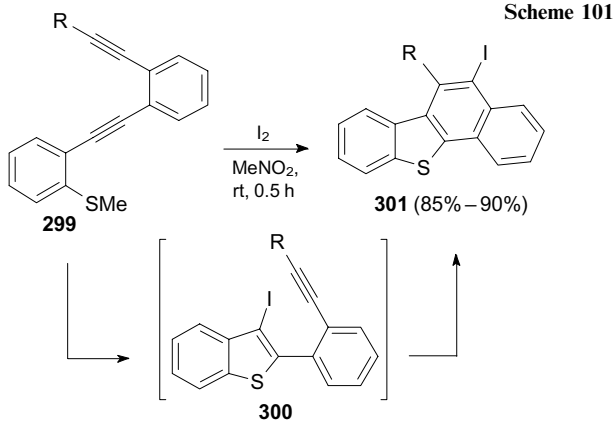
Scheme 100



R^1 = Pr^n, Bu^i, XC_6H_4 (X = H, 4-MeO, 2-Me, 3-Me, 4-Me, 4-Cl, 4-Br, 4-F_3C, 4-O_2N); R^2 = H, Me, CO_2Me; R^3 = H, Me

Replacement of NMe_2 moiety by SMe in **299** could give benzo[*b*]naphtho[2,1-*d*]thiophenes **301** (Scheme 101).[34] The solvent strongly affected the outcome of the reaction, *i.e.* in CH_2Cl_2, MeCN, and $MeNO_2$ the target compound **301** (R = Ph) formed within 20 min in 84% – 90% yields, while in toluene, THF, and MeOH within 5 h only intermediate iodobenzothiophene **300** was obtained (65% – 85%), which could be fully converted to **301** on treatment with I_2 in nitromethane. Thioanisole with an alkyl group at the triple bond (**299**, R = Cy) gave a complex mixture with a trace amount of naphthothiophene even in nitromethane. Later this problem was solved using gold catalysis (Scheme 44).

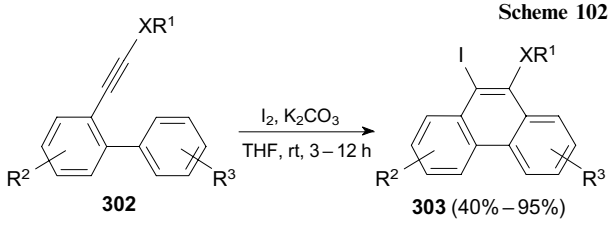
Scheme 101



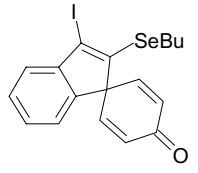
R = 4-XC_6H_4 (X = OMe, CN, Me, F), 3-Th

Arylethynyl sulfides and selenides **302** were converted to chalcogen-substituted phenanthrenes **303** with I_2 in the presence of a base (Scheme 102).[171] *ortho*-Cyclization on *para*-methoxyphenyl ring of **302** (R^3 = 4-MeO) accompanied by *ipso*-cyclization provided a mixture of the corresponding phenanthrene **303** and cyclohexadienone **304** in a ratio of 1 : 1.6. Substrates with electron-withdrawing groups (NO_2, CO_2R, Cl) on the distal phenyl ring were inert to iodine as well as compounds with other groups on the ethynyl moiety (TMS, $PO(OEt)_2$, CH_2OH, CHO). When a

Scheme 102



X = Se, S; R^1 = Me, Et, Bu^n, Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-FC_6H_4, 4-ClC_6H_4, 1-Naph; R^2 = H, Me, OMe, F; R^3 = H, Me, OMe

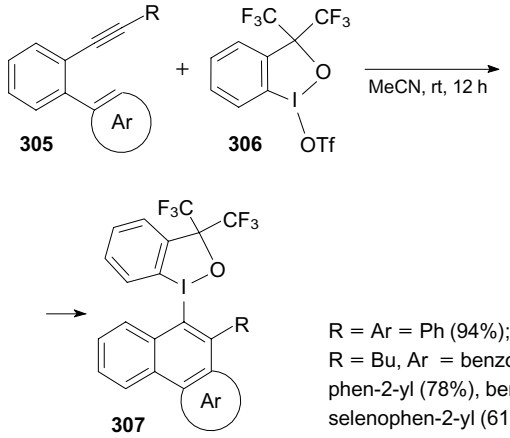


304 (53%) + **303** (33%), if R^3 = 4-MeO

phenyl tellurium group was introduced at the triple bond of **302**, a replacement of TePh for I occurred instead of cyclization.[171]

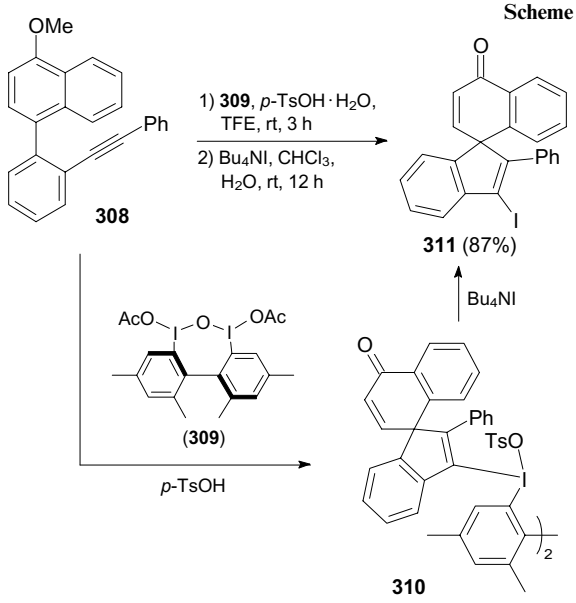
Trivalent iodine compound, benziodoxole **306**, was successfully utilized as an electrophilic reagent to induce cyclization of 2-(phenylethynyl)biphenyl **305** (Scheme 103).[172] The I^{III} centre of **306**, upon dissociation of the triflate anion, activates the triple bond in the same way as an iodine cation. The resulting cyclization product resists further reactions because of the stabilizing effect of the benziodoxole moiety. Benzothiophene and benzoselenophene rings also acted as nucleophiles allowing facile preparation of heteroaryl-λ^3-iodanes **307**.

Scheme 103



Spiro-cyclization on the methoxy-substituted naphthyl ring of **308** was performed using a hypervalent iodine compound **309** (Scheme 104).[173] *ipso*-Cyclization occurred in the course of formation of bisiodonium compound **310** [ordinary hypervalent iodine compounds, *e.g.* $PhI(OAc)_2$, $PhI(OCOCF_3)_2$, PhI(OH)OTs were ineffective], and then anionic nucleophile I^- from inorganic salt replaced aryliodonio group to give target spiro compound **311**.

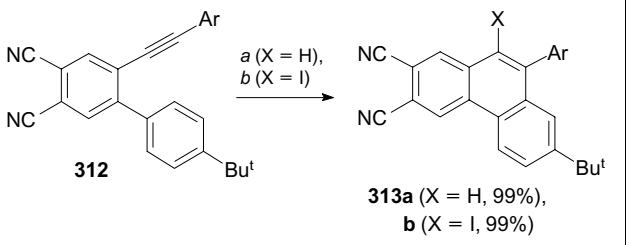
Scheme 104



4.2. Other electrophiles

Among other electrophiles used to trigger cyclization, note Brønsted acids that allow getting cycloisomerization products without additional groups or atoms, as with transition metal catalysis. This method excels due to simplicity of experimental procedure (no need in inert atmosphere and low temperature) and high efficiency. Quantitative yield of the corresponding phenanthrenes **313a**,**b** was obtained from biphenyl **312** both *via* TFA- and ICl-induced cyclization, respectively (Scheme 105).[174]

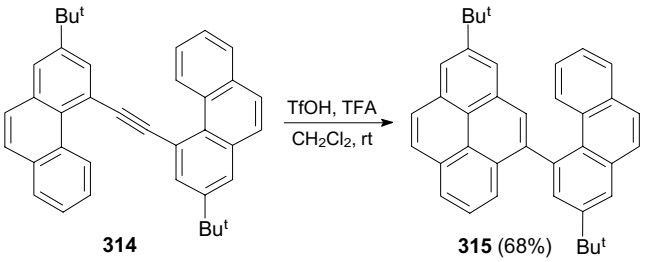
Scheme 105



(*a*) TFA, DCE, 60°C, 3 h; (*b*) ICl, CH_2Cl_2, −78 °C, 1 h;
Ar = 4-(n-$C_6H_{13}O$)C_6H_4

The Brønsted acid catalysis is extremely attractive when the use of ICl does not give the expected results. Treatment of bis[2-(*tert*-butyl)phenanthren-4-yl]acetylene **314** with ICl led to the exclusive 1,2-addition of halogen atoms to the triple bond, while 6-*endo*-cyclization run in a TFA (20 equiv.)/TfOH (1 equiv.) mixture to give pyrene **315** in 68% yield (Scheme 106).[175]

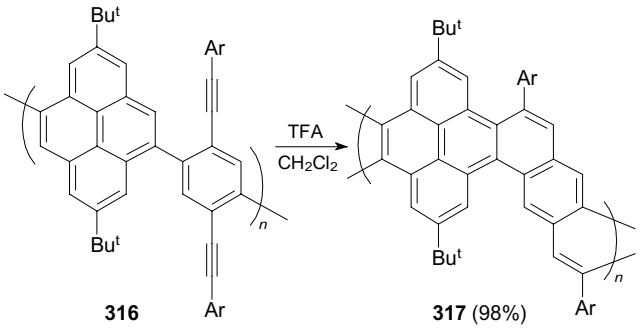
Scheme 106



TFA was also successfully employed to form a central anthracene fragment in the synthesis of ladder-conjugated polymer **317** from polyalkyne **316** (Scheme 107).[176]

The strong difference in acidity of commonly used TFA and TfOH can be conveniently used in synthesis. The active electron-rich terphenyls **318** were successfully annulated by TFA to provide dibenzo[*a*,*h*]anthracenes **319** (Scheme 108).[140,177] The refluxing conditions were needed for substrates **318** with Ar = 4-$Bu_2NC_6H_4$ as protonation of amino groups occurred initially.[177] In contrast, TFA-catalyzed cyclization of 1,4-di(thiophen-2-yl)benzenes **318** failed, but it was realized with TfOH.[140] The acid-promoted cyclization of *ortho*-oriented analogue of **318** (2,3-diaryl-1,4-diethynylbenzene) stopped after monoannulation even with TfOH.[140] This work disclosed that the halogenated solvents such as CH_2Cl_2 and DCE are preferable for the acid-catalyzed cyclization, because the reaction does not run in hydrocarbon and ethereal solvents.[140]

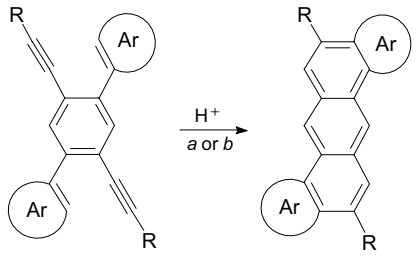
Scheme 107



316 **317** (98%)

Ar = 4-Bu^{t}C$_6$H$_4$

Scheme 108

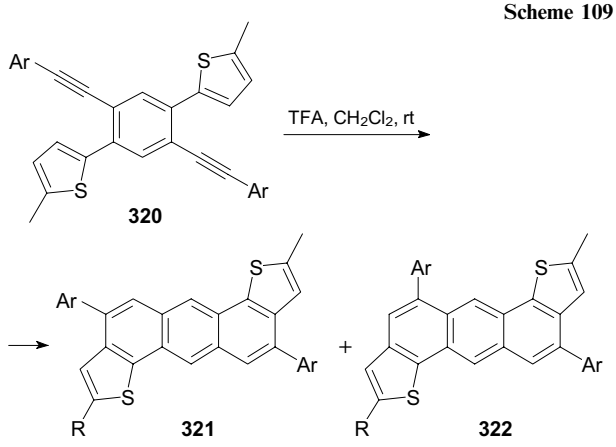


318 **319** (51% – 99%)

(*a*) TFA, CH_2Cl_2, 25 – 40 °C: R = 4-XC$_6$H$_4$ (X = NBu$_2$, OC$_{12}$H$_{25}$, OBu^n), Ar = X$_2$C$_6$H$_3$ (X = H, Me, OMe), dibenzo[*b*,*d*]thiophen-4-yl; (*b*) TfOH, CH_2Cl_2, rt: R = 4-Bu$_2$NC$_6$H$_4$, Ar = 2-Th

Cyclization onto 5-methylthiophen-2-yl moiety in **320** was possible with TFA but provided mixture of products **321** and **322**, which differ in the position of the aryl group (Scheme 109).[140] The rearrangement product **322** was proposed to form *via* an acid-catalyzed 1,2-migration of the phenyl ring in 'normal' product **321** through a phenonium ion stabilized by the *para*-alkoxy group. For the analogues of **320** with *meta*-orientation of two *ortho*-aryl(ethynyl) fragments [1,5-di(arylethynyl)-2,4-di(thiophen-2-yl)benzenes] the 'normal'/rearrangement product ratio was *ca.* 6 : 1.[140] The same aryl migration in anthracenes **319** (see Scheme 108) occurred only upon heating with difluoroacetic acid at 135 °C.[140]

Scheme 109



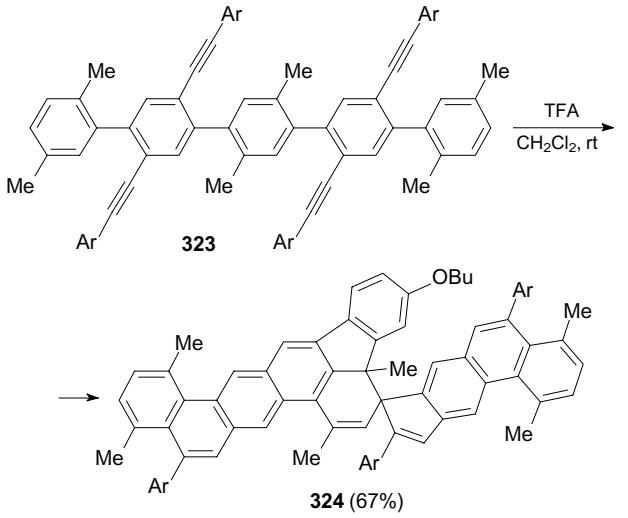
320

321 : **322** = 5 : 6 (83%)

Ar = 4-(C$_{12}$H$_{25}$O)C$_6$H$_4$

Extraordinary example of cyclization was demonstrated for tetraethynyl-substituted *p*-quinquephenyl **323** (Scheme 110).[141] The major isolable product of TFA-catalyzed reaction was unsymmetrical compound **324**. The spiro linkage of **324** presumably formed after one of the central arylethynyl moieties was successfully cyclized. The vinyl carbocation generated from the other central arylethynyl moiety then attacked the *ipso*-position to create a spiro linkage instead of *ortho*-cyclization to produce a six-membered ring. The corresponding spiro intermediate was trapped by the pendant alkoxyphenyl moiety. Obviously, this phenomenon was caused by the cyclization of two arylethynyl moieties onto the same backbone aryl ring. However, treatment of **323** with $(CF_3CO_2)_2Hg/I_2$/2,6-lutidine gave no product of such type (see Section 4.1), and fourfold normal iodocyclization occurred. Moreover, more sterically encumbered quinquephenyl [Ar = 2,6-Me$_2$-4-(C$_8$H$_{17}$O)C$_6$H$_2$, OAlk instead of Me groups] also produced 'normal' product even with trifluoroacetic acid.

Scheme 110



323

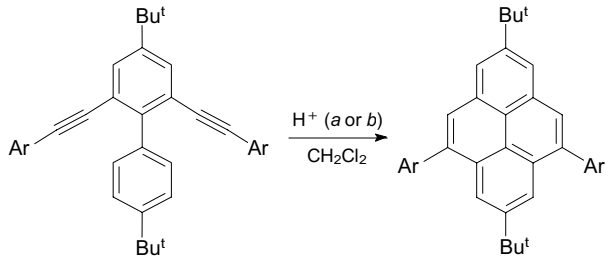
324 (67%)

Ar = 4-BuOC$_6$H$_4$

Sequential cyclization of several triple bonds can be realized *via* increasing the acidity of a medium. In that way pyrenes **326** (and similar pero- and teropyrenes) were synthesized stepwise from diethynylbiaryls **325** when weaker TFA promoted monoannulation and then stronger TfOH cyclized the remaining alkyne (Scheme 111 *a*).[178] Using only TfOH led to side products and lower yields. The following work revealed that the slow addition of diluted TfOH resulted in good yields and clean reactions as well (Scheme 111 *b*).[179,180] The poly(*para*-phenylene) substrate **327** was transformed into narrow strips of graphene (graphene nanoribbons) **328** using TFA/TfOH sequence.[181]

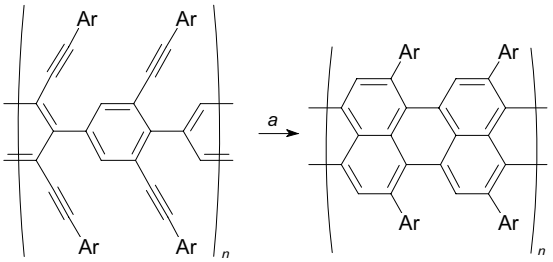
Recently this stepwise approach was applied for the synthesis of twisted and thus axially chiral tetraaryl peropyrenes **331** (Scheme 112).[182] Treatment of tetraalkynes **329** with TFA resulted in the bis-cyclization which occurred on the same side of the molecule to make a picene derivative **330** (the kinetic preference for this *syn*-cyclization path was supported by DFT calculations). The remaining two benzannulations were accomplished using dilute TfOH.

Scheme 111



325 **326** (49% – 61%)

(*a*) 1) TFA, rt; 2) TfOH, 0 °C; Ar = 4-ROC_6H_4 (R = Me, C_6H_{13}, $C_{10}H_{21}$); (*b*) TfOH, from 0 °C to rt; Ar = 5-hexylthiophen-2-yl



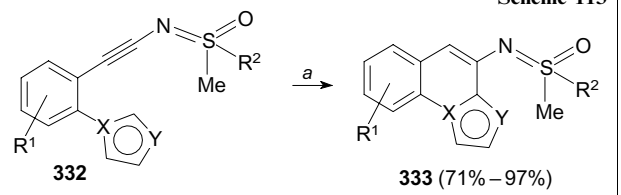
327 **328** (87%)

(*a*) 1) TFA, CH_2Cl_2, rt; 2) TfOH, CH_2Cl_2, −40 °C; Ar = 4-$C_8H_{17}OC_6H_4$

N-Alkynylated sulfoximines **332** underwent acid-promoted cyclization under mild reaction conditions affording naphtho[2,1-*b*]thiophenes or pyrrolo[1,2-*a*]quinolines **333** in high yields (Scheme 113).[183] Trifluoromethanesulfonic imide (Tf_2NH) was found to be the best catalyst in comparison to TfOH and TFA. Variation of the substitution pattern as well as the type of heterocyclic core almost did not influence the outcome of the process. Similar Ag^I-catalyzed cyclization of *N*-alkynylated sulfonamides was described above (see Scheme 75, Section 3.4).

Much weaker acetic acid was reported to promote hydroarylation of 2-ethynylphenyl-substituted pyrazoles and isoxazoles **336** generated *in situ* from alkyne-tethered chalcones **334** and $XHNH_2$ (**335**) to give 1*H*-benzo[*g*]indazoles and naphtho[2,1-*d*]isoxazoles **337**, respectively (Scheme 114).[184] Both steps were implemented in a one-pot fashion, and no iodinated product was observed even when 10 equiv. of iodine were used in the reaction. Thus, iodine only oxidized an initially formed pyrazoline

Scheme 113

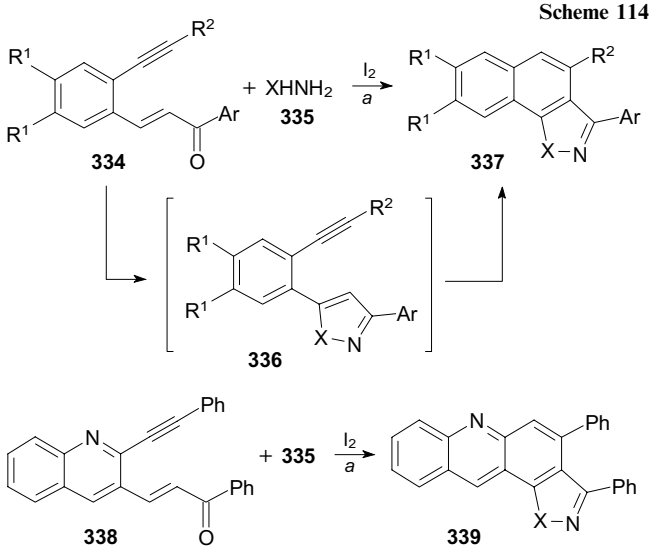


332 **333** (71% – 97%)

(*a*) Tf_2NH (10 mol.%), CH_2Cl_2, −20 °C, 2 h; X = N, Y = CH; X = C, Y = S; R^1 = H, Me, OMe; R^2 = XC_6H_4 (X = H, 4-Cl, 4-Br, 3-Br, 3-MeO)

(if hydrazine was used); this was confirmed by carrying out the reaction with DDQ as an oxidant. Subsequent cyclization of isolated pyrazole **336** (R^1 = OMe, R^2 = 4-$MeOC_6H_4$, Ar = 4-BrC_6H_4, X = PhN) in AcOH led to the corresponding benzoindazole **337** (upon treatment by I_2 the corresponding 5-iodobenzoindazole formed in 85% yield). A chalcone with Ar = 4-$O_2NC_6H_4$ gave final products neither with hydrazine, nor with hydroxylamine. The methodology was also extended to the synthesis of

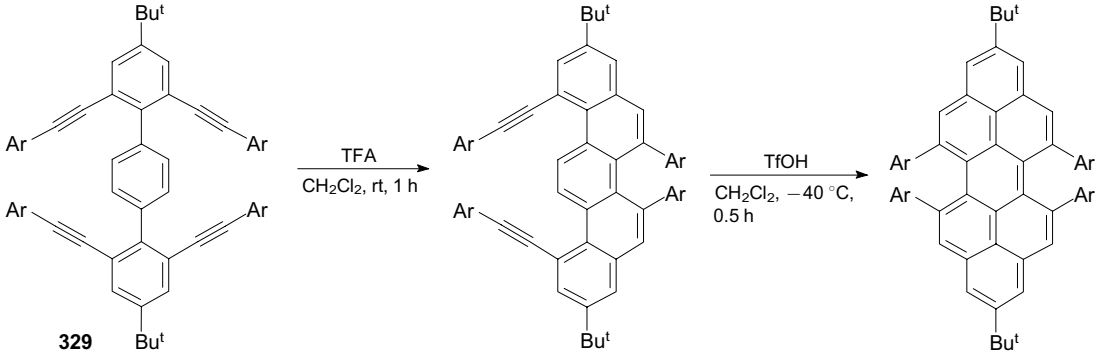
Scheme 114



339: X = PhN (58%), O (55%)

(*a*) AcOH, reflux, 8 h; **335**: R^3NHNH_2 (R^3 = H, Ph, 4-BrC_6H_4), $NH_2OH \cdot HCl$ (add. NaOAc); Ar = Ph, 4-$MeOC_6H_4$, 4-BrC_6H_4; R^1 = MeO, H; R^2 = Ph, 4-$MeOC_6H_4$, Bu^n; **337**: X = R^3N (60% – 73%), O (52% – 59%)

Scheme 112



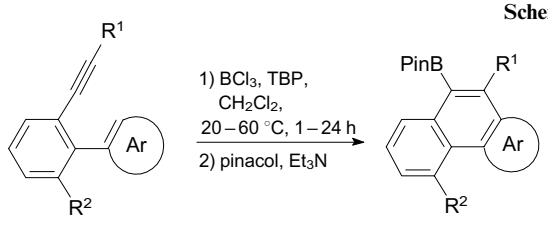
329 **330** (94% – 97%) (*P*,*P*) + (*M*,*M*)-**331** (28% – 40%)

Ar = 4-ROC_6H_4 (R = Me, C_6H_{13}, C_8H_{17}, $C_{10}H_{21}$)

quinoline-fused indazoles and benzo[*d*]isoxazoles **339** from the corresponding substrates **338**.

Electrophiles other than Brønsted acids usually grant a heteroatom moiety to a final structure like the iodine compounds. BCl_3 induced borylative cyclization of *ortho*-ethynylbiaryls **340** to polycycles **341** under mild conditions (Scheme 115).[185] Both phenyl- and pyrrolyl-substituted compounds **340** were amenable to this reagent though the latter substrate reacted faster at lower temperature (20 °C, 1 h *vs.* 60 °C, 24 h) with a comparable yield.

Scheme 115

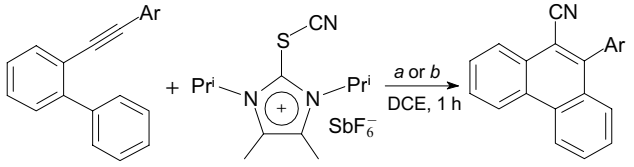


340 **341** (58% – 60%)

R^1 = C_6H_{13}, 4-MeC_6H_4; R^2 = H, Br; Ar = Ph, pyrrol-1-yl

On the other hand, boron-based Lewis acid may assist cyclization without incorporating the boron atom into a product. Imidazolium thiocyanate **342** activated *via* coordination of $B(C_6F_5)_3$ or BCl_3 at the nitrogen atom of the cyano group implemented electrophilic addition to the triple bond of **235** with subsequent cyclization to form **343** (Scheme 116).[186] This reaction was carried out to study chlorocyanation of alkynes; however, it represents a valuable example of cyclization with simultaneous cyanation excluding unpleasant cyanogen chloride as a CN^+ precursor.

Scheme 116



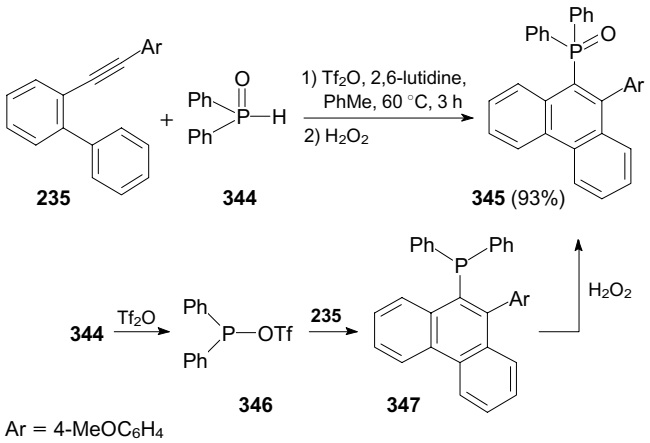
235 **342** **343** (*a*, 55%, *b*, 53%)

(*a*) $B(C_6F_5)_3$; (*b*) BCl_3; Ar = 4-$MeOC_6H_4$

The electrophilic phosphorus-based reagent **346** was obtained *in situ* from diphenylphosphine oxide **344** with Tf_2O/2,6-lutidine system (Scheme 117).[187] Addition of **346** to the triple bond of ethynylbiphenyl **235** triggered phosphinative cyclization on the pendant aryl moiety delivering phosphine **347**, which was treated with H_2O_2 to form more stable phosphine oxide **345**.

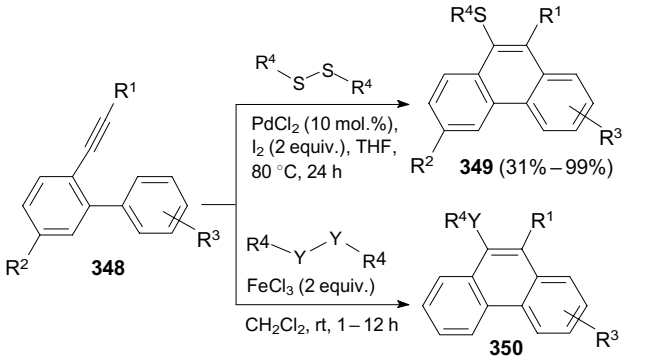
Formal sulfenylative cyclization was implemented *via* palladium-catalyzed iodine-mediated electrophilic annulation of *ortho*-alkynylbiphenyls **348** with disulfides (Scheme 118).[188] 9-Sulfenylphenanthrenes **349** were obtained using a variety of alkyl and aryl sulfides in 75% – 99% yields; moderate yields were observed when alkyne substrate **348** had electron-deficient groups. Iodocyclization products were not detected even when carrying out the reaction in the absence of disulfide. Thus iodine did not serve as an electrophile but likely converted disulfide $R^4_2S_2$ to an active R^4SI reagent. The reaction ran even

Scheme 117



Ar = 4-$MeOC_6H_4$

Scheme 118



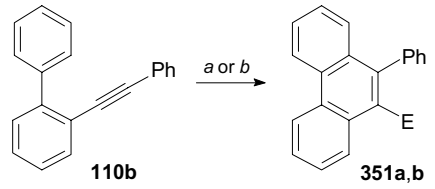
349: R^1 = Ph, 2-MeC_6H_4, 4-MeC_6H_4, 4-ClC_6H_4, 3-$F_3CC_6H_4$, 2-Th, C_6H_{13}; R^2 = H, Me, F; R^3 = H, 4-Me, 3-Me, 3,4-Cl_2; R^4 = Me, Cy, Bn, XC_6H_4 (X = H, 4-Me, 4-Cl, 4-F, 3-F, 4-O_2N);
350: Y = Se (49% – 99%), S (26% – 37%); R^1 = Ph, 2-Naph, 4-ClC_6H_4; R^2 = H; R^3 = H, 4-Me, 4-MeO, 4-Cl; R^4 = Ph, 4-MeC_6H_4, 4-FC_6H_4

without $PdCl_2$, albeit in lower yield, implying that it may occur either as R^4S^+-induced electrophilic cyclization or as palladium-catalyzed annulation (see Section 3.3).

Selenium-containing phenanthrenes **350** (Y = Se) could be accessed *via* a similar strategy using $FeCl_3$ instead of $PdCl_2/I_2$ system (see Scheme 118).[171] According to the plausible mechanism, the iron(III) coordination to one selenium atom activates the other one towards nucleophilic attack by the alkyne with subsequent electrophilic cyclization on the aromatic ring. When the reaction was carried out using disulfides, 9-sulfenylphenanthrenes **350** (Y = S) were obtained in poor yields (26% – 37%) after 12 h, while cyclization with diselenides completed within 1 h. *ortho*-Ethynylbiphenyls **348** having groups other than aryl at the alkyne terminus, such as SeBu, I, TMS, $PO(OEt)_2$, CH_2OH, CHO, failed to give the desired products under the standard reaction conditions and only decomposition of the starting material was observed.

Excellent yield of the sulfur-containing phenanthrene **351a** was obtained in 30 min using *para*-nitrobenzenesulfenyl chloride (Scheme 119).[146] Bromophenanthrene **351b** was isolated in 86% yield after stirring the substrate **110b** with a mixture of NBS and silica gel for 6 days. Meanwhile, these electrophiles have not found further application.

Scheme 119



(*a*) 4-$O_2NC_6H_4SCl$, CH_2Cl_2, rt, 0.5 h; (*b*) NBS, silica gel, CH_2Cl_2, rt, 6 days; **351**: E = 4-$O_2NC_6H_4S$ (**a**, 92%), Br (**b**, 86%)

5. Radical induction

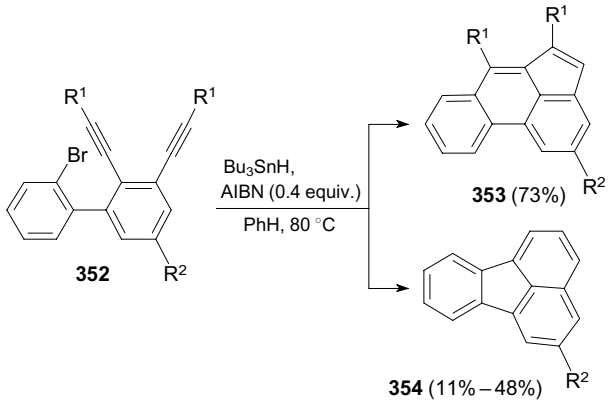
Cyclization of *ortho*-alkynylbiphenyls can be performed with participation of radical species. This strategy is not as widespread as metal catalysis, but high efficiency and selectivity can be achieved in radical-induced reactions as well. Some mechanisms of the following transformations are disputable and contradictory to some extent, and therefore we do not highlight all of them here.

Generation of a radical centre in **352** was possible due to the bromine atom adjacent to the phenyl ring bearing an alkynyl fragment (Scheme 120).[189] In the presence of tributyltin hydride and AIBN, this radical trigger causes the formation of acephenanthrylene **353** *via* 6-*endo*-cyclization followed by a 5-*endo* ring closing of bis(phenylethynyl)-substituted substrate **352** (R^1 = Ph). Biphenyls **352** with terminal alkyne moieties (R^1 = H) suffered hydrostannylation of the triple bonds and afforded fluoranthenes **354** in low yields. Substrates with R^1 = TMS, Bu^n yielded no identifiable cyclization products.

Later, radical cyclization was performed with the same reagents Bu_3SnH/AIBN for substrates **355** having no halogen atoms (Scheme 121).[190] As proposed, 6-*endo*-cyclization of the tributyltin vinyl radical generated after radical attack on the triple bond is terminated by oxidative aromatization with AIBN, a commonly used radical initiator, as an oxidant. The reaction is fully compatible with acceptor and donor aryl and alkyl substituents at the alkyne fragment of **355** and provided phenanthrenes **357** after acid hydrolysis of the initially formed Bu_3Sn-derivatives **356**.

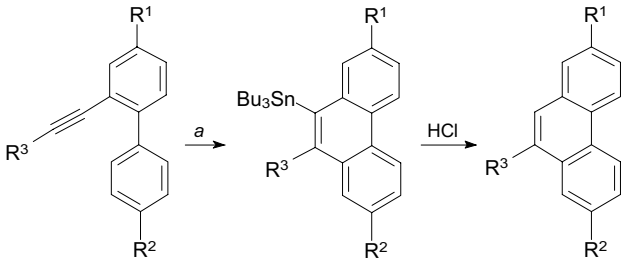
Photoactivation of *ortho*-alkynylbiphenyls **358a – c** in methylcyclohexane solution produced complex product mixtures with poor mass balance (Scheme 122).[191] Upon irradiation of biphenyl **358d** in methanol, four primary products **360 – 363** were observed, and three of them were isolated in modest yields. These results can be attributed to the photocyclization yielding the putative isophenanthrene (cyclic allene) intermediate **359** having either biradicaloid or

Scheme 120



353: R^1 = Ph, R^2 = Bu^t; **354**: R^1 = H, R^2 = Bu^t, CH_2OMe, OMe

Scheme 121

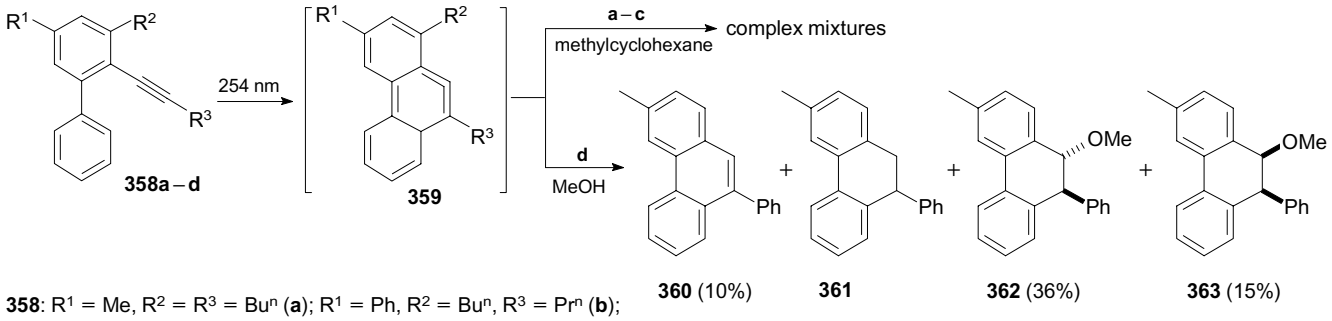


(*a*) Bu_3SnH (1.2 equiv.), AIBN (1 equiv.), PhMe, 110 °C;
R^1 = H, Me; R^2 = H, F, Me; R^3 = 4-XC_6H_4 (X = H, Me, F, CN, CF_3, OMe, Ac), 2-Th, 1-Naph, benzothiophen-2-yl, 4-Py, Bu^n

zwitterionic character. Phenanthrene formation does not occur *via* a unimolecular sigmatropic hydrogen shift, but rather by protonation or hydrogen abstraction mechanisms involving the solvent. However, the low quantum yields were measured for these photocyclization processes. Thus, the obvious inefficiency limits the preparative utility of these reactions.

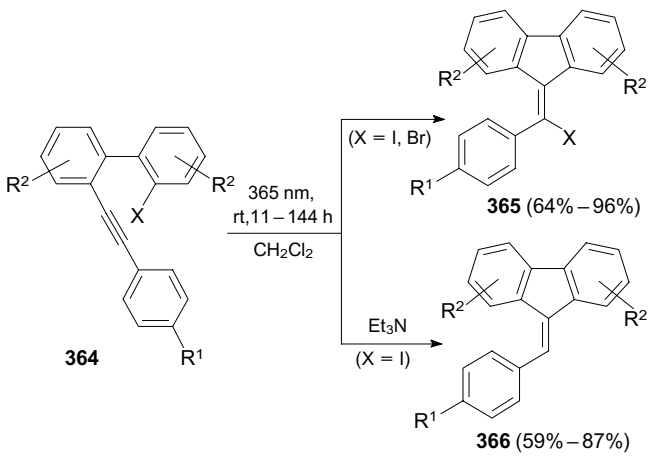
Recently, photoinduced cyclization of halo-*ortho*-alkynylbiphenyls **364** to arylidenefluorenes was reported to proceed as haloarylation to **365** or hydroarylation to **366** depending on the presence of triethylamine (Scheme 123).[192] Haloarylation tolerated variously substi-

Scheme 122



358: R^1 = Me, R^2 = R^3 = Bu^n (**a**); R^1 = Ph, R^2 = Bu^n, R^3 = Pr^n (**b**); R^1 = Me, R^2 = R^3 = Ph (**c**); R^1 = Me, R^2 = H, R^3 = Ph (**d**)

Scheme 123

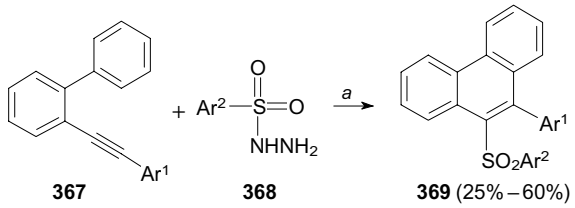


R^1 = H, Me, OMe, Cl, CN; R^2 = H, OMe, NMe_2

tuted substrates, while electron-deficient compounds (R^1 = Cl, CN) were inactive in hydroarylation. However, introduction of donor groups into biphenyl system diminished the negative effect of electron-withdrawing groups in phenylethynyl fragment and corresponding fluorenes **366** were obtained in 70% – 85% yields. Both iodides and bromides were active in haloarylation but the latter showed no activity in hydroarylation. Experimental data proved the possibility of both homolytic and heterolytic C – X bond cleavage in the excited state of **364**.

Unsymmetrical phenanthrene-based diaryl sulfones **369** were obtained *via* $Cu(OTf)_2$-catalyzed radical cyclization of *ortho*-ethynylbiphenyls **367** in the presence of arenesulfonyl hydrazides **368** and di-*tert*-butyl peroxide (Scheme 124).[193] Di-*tert*-butyl peroxide likely generated sulfonyl radicals from hydrazides **368**; the subsequent radical addition to the activated triple bond of **367** initiated annulation to a 6-membered ring. A wide number of arenesulfonyl hydrazides **368** was successfully tested, but benzylsulfonyl hydrazide did not work in this reaction.

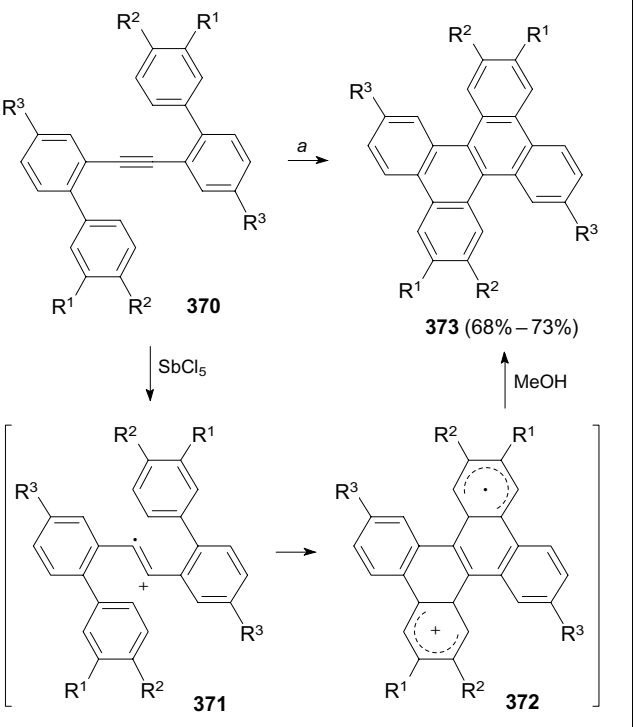
Scheme 124



(*a*) $Cu(OTf)_2$ (10 mol.%), $(Bu^tO)_2$ (6 equiv.), DCE, 100 °C; Ar^1 = 4-XC_6H_4 (X = H, Cl, F, Me, MeO); Ar^2 = YC_6H_4 (Y = H, 4-Me, 4-Bu^t, 4-MeO, 4-F, 4-Cl, 4-Br, 4-F_3C, 3-Br, 2-Cl)

Unusual tandem radical-electrophilic mechanism of cyclization was proposed for the transformation of bis(biaryl)acetylenes **370** to dibenzo[*g*,*p*]chrysenes **373** (Scheme 125).[194] A PM3 calculation showed that the highest occupied molecular orbital of **370** is localized on the central diphenylacetylene fragment, suggesting that the initial one-electron oxidation by $SbCl_5$ occurs at the triple bond. The radical cation **371** thus formed undergoes radical and electrophilic cyclizations onto two phenyl rings in **372**

Scheme 125



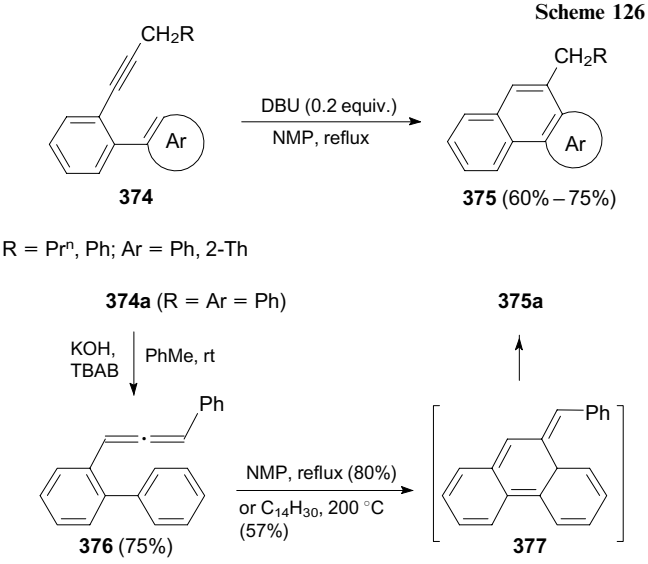
(*a*) 1) $SbCl_5$, CH_2Cl_2, rt, 1 h; 2) MeOH; R^1 = OMe, OC_6H_{13}; R^2 = H, OMe, OC_6H_{13}; R^3 = H, $O(CH_2)_2OMe$

delivering dibenzo[*g*,*p*]chrysenes **373** after quenching the reaction with methanol. If there was R^1 = H, dimerization at these free positions occurred.

6. Base catalysis

The first report on base-catalyzed cycloisomerization in the synthesis of coronene derivatives (see Scheme 127) was published in 1998.[195] Strong non-nucleophilic bases, such as DBU, are commonly used in this method. The plausible reaction pathway was studied and supported experimentally later by Burton for the cyclization of *ortho*-alkynyl(phenyl)-benzenes **374** to phenanthrenes **375** (Scheme 126).[196] An allene intermediate was proposed as a result of base-induced

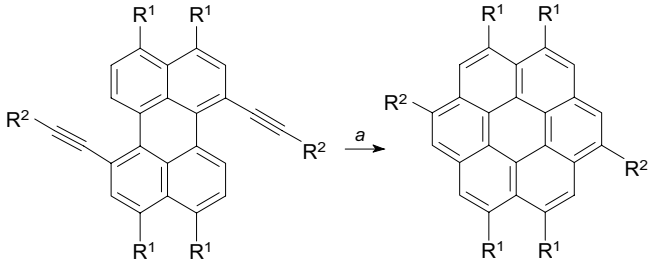
Scheme 126



isomerization of the initial acetylene. Allene **376** was indeed isolated upon treatment of acetylene **374a** with KOH as a base. Subsequent heating in either NMP or tetradecane converted allene **376** into phenanthrene **375a** *via* 6π-electrocyclization into **377** followed by isomerization/aromatization in comparable total yield. Thus, the presence of at least one methylene group at the triple bond is crucial for this type of cyclization. Thiophene ring in **374** was used as an aromatic counterpart as well.[197]

Base-catalyzed cyclization of *ortho*-alkynylbiaryls has found wide applicability for the synthesis of coronene derivatives as the presence of long alkyl chains ensures higher solubility and better physical properties of the polycyclic products. Heating of bis(alkynyl)-substituted perylene-3,4,9,10-tetracarboxydiimides [195, 198 – 205] or corresponding tetraesters[206] **378** with DBU provided coronenes **379** in various yields (Scheme 127).

Scheme 127



(*a*) DBU, PhMe, 90 – 110°C; $R^1 + R^1 = -C(O)-NX-C(O)-$ (X = Alk, Ar); $R^1 = CO_2Alk$; R^2 = Alk, $(CH_2)_{2-3}Y$ (Y = OAr, OC(O)Ar, *N*-piperidyl)

Perylenes **378** with R^2 = Ph, Bu^t did not undergo the base-catalyzed cyclization that corresponds to the above mentioned mechanism because a propargyl – allenyl isomerization is not possible for such substrates.[198] However, DBU-assisted cyclization of perylene with an aryl group at the triple bonds (**378**, $R^1 = Pr^n$, R^2 = 4-ClC_6H_4, see Scheme 127) was reported to yield 74% of the corresponding coronene.[207] This result seems quite surprising as the way how cycloisomerization occurs is not clear.

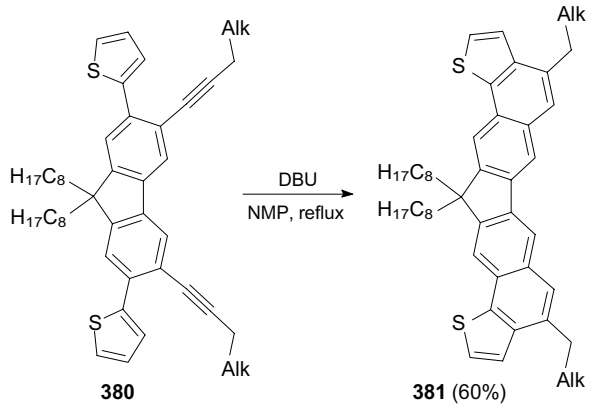
Since the work of Burton,[197] thiophene ring has been used in base-induced cyclizations for the construction of semiconducting conjugated thiophene-based polymers. Monomer precursor **381** was obtained *via* double benzannulation of **380** allowing for predefined position of large alkyl chains in the final compound (Scheme 128).[208]

Catalytic system DBU/NMP was more effective for the cyclization on thiophene rings in the syntheses of polycyclic thienoacenes **383** and **384** than $PtCl_2$/toluene (the new C – C bonds are marked in bold).[209] Only 28% yield of **383** and almost no **384** was observed after heating the corresponding substrates in toluene with $PtCl_2$, which is likely ascribed to the low solubility of reaction intermediates in hot toluene. Microwave heating in NMP with DBU allowed getting target products in 56% – 60% yields. $PtCl_2$ was suitable only for the annulation of the smallest compound **382**.

Selenophene ring of **385** can be involved in cyclization as shown in the synthesis of pentacyclic **386** albeit in only 20% yield (Scheme 129).[210]

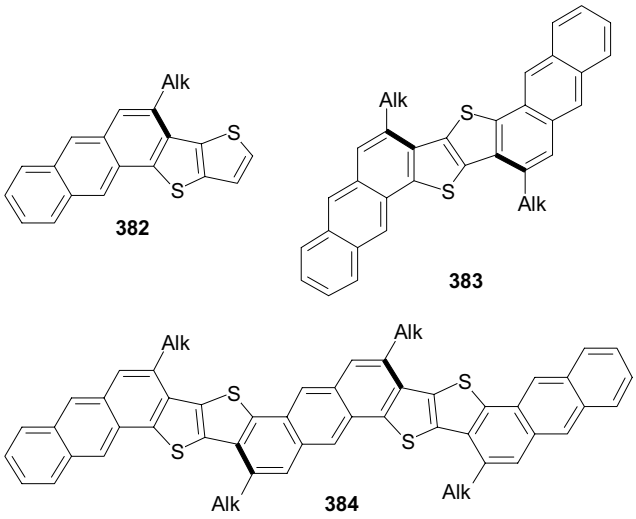
This strategy is also applicable for the synthesis of bisindoloanthracene **388**, which was obtained *via* double cyclization of hex-1-ynyl groups onto indole rings of **387**

Scheme 128



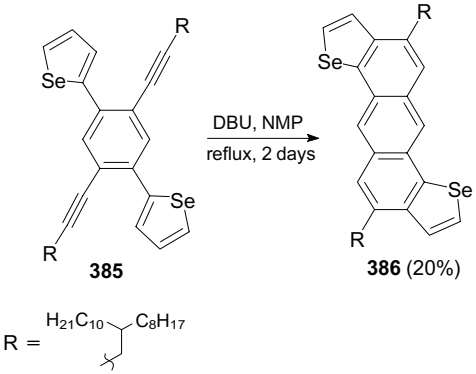
Alk = $CH(C_8H_{17})(C_{10}H_{21})$

Structures 382 – 384



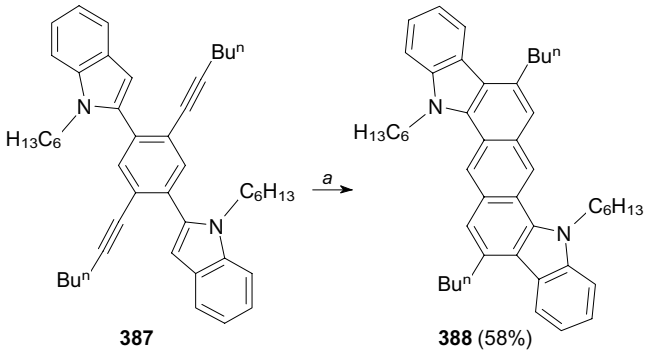
382: $PtCl_2$, PhMe, 100 °C (43%); **383**, **384**: DBU, NMP, 250 °C, MW (56% – 60%); Alk = $CH_2CH(C_2H_5)(C_4H_9)$, $CH_2CH(C_6H_{13})(C_8H_{17})$, $CH_2CH(C_8H_{17})(C_{10}H_{21})$

Scheme 129



(Scheme 130).[211] The final compound exhibits bright luminescence with high quantum yield and was used for the fabrication of sky-blue OLED.

Scheme 130



387 **388** (58%)

(*a*) DBU, NMP, reflux, 3 h

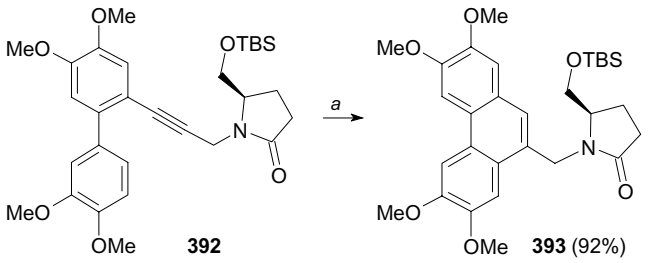
The selectivity of cyclization of **389** to biscarbazoloanthracene **390** as the major product is notable as this aromatic compound is less stable than isomeric **391** due to steric interactions which twist the aromatic skeleton (Scheme 131).[212] However, it is consistent with the results of DFT calculations which revealed lower activation energy barrier for the electrocyclization of intermediate allene to the 3,4-bond of the carbazole, rather than the 2,3-bond.

DBU-promoted annulation was efficiently used in the synthesis of tylophorine alkaloid for the construction of the central phenanthrene core of **393** from the precursor **392** (Scheme 132).[213]

7. Cyclization of *ortho*-aryl(ethynyl)heteroarenes

Various heterocycles were mentioned above as an aromatic counterpart to a triple bond in the cyclizations of *ortho*-ethynyl(heteroaryl)benzenes. In this role, a heterocyclic ring does not affect much the reaction outcome compared to that for similar biphenyls. But a central heterocyclic core has a significant effect on the activity of the substrate. That is a ground to describe reactions of *ortho*-aryl(ethynyl)heteroarenes in this separate section.

Scheme 132



392 **393** (92%)

(*a*) DBU, NMP, reflux, 3h

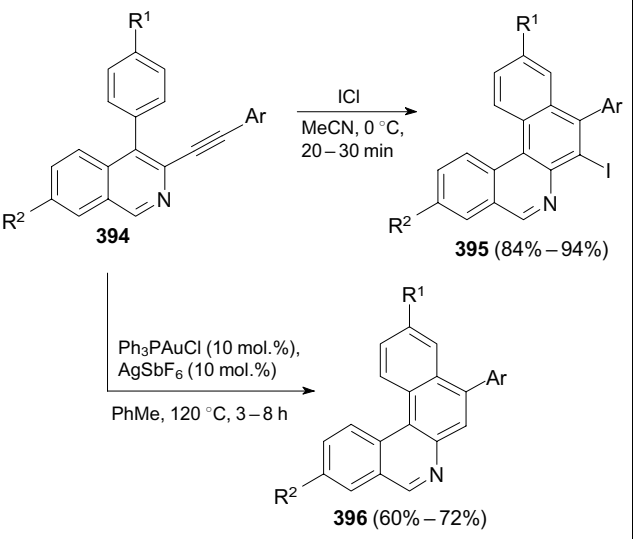
7.1. Six-membered heterocycles

Widely used aromatic six-membered heterocycles are limited to nitrogen-containing ones, therefore this section describes transformations of pyridine, pyrimidine and pyrazine derivatives. Research into the cyclization of such *ortho*-aryl(ethynyl)heteroarenes has begun only in last years. The structural similarity to biphenyls is obvious, and general principles and catalytic systems to perform cyclization are the same as for biphenyls; however, the number and position of heteroatoms strongly affect the behaviour of the substrate and the outcome of the cyclization.

Pyridines bearing an alkynyl moiety in the *ortho*-position to the nitrogen atom resemble carbocyclic analogues in their activity in cyclization. Hydroarylation of 4-aryl-3-arylethynylisoquinolines **394** could be performed either by Au-catalysis or by electrophilic activation with ICl to produce benzo[*a*]phenanthridines **396** or their iodinated derivatives **395**, respectively (Scheme 133).[214]

In contrast, cycloisomerization of 4-alkynyl-3-arylpyridines **397** failed upon heating with $Pt^{II/IV}$ and $Au^{I/III}$

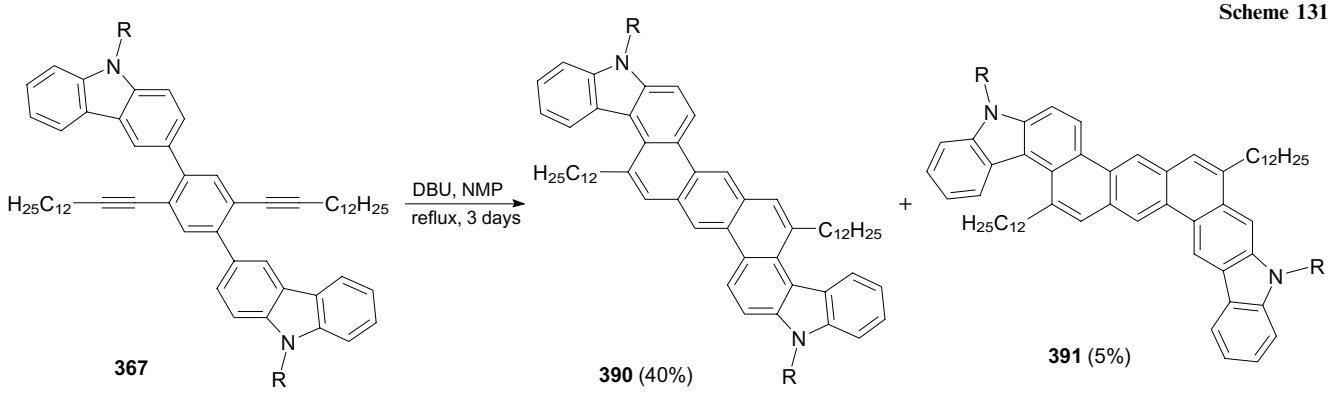
Scheme 133



394 **395** (84% – 94%) **396** (60% – 72%)

Ar = 4-$R^1C_6H_4$, R^1 = H, Me, Bu^t, OMe; R^2 = H, F, OMe

Scheme 131

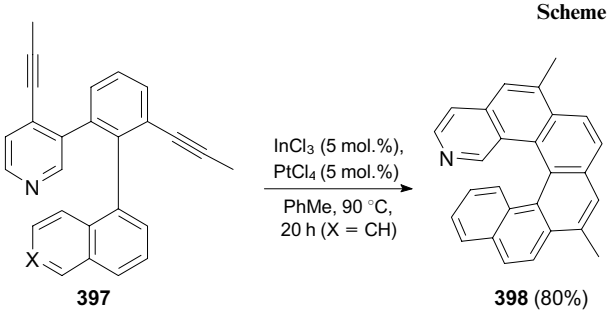


367

R = $CH_2CH(Et)(Bu)$

390 (40%) **391** (5%)

Scheme 134

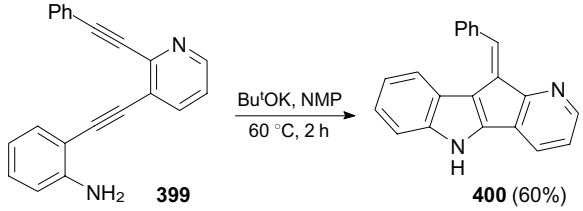


X = CH, N

catalysts (Scheme 134).[215] Treatment of **397** (X = N) with ICl provided addition of halogen atoms to both triple bonds. Only $PtCl_4/InCl_3$ catalytic system allowed the double cyclization of pyridine **397** (X = CH) into target 2-aza[6]helicene **398** in 80% yield.

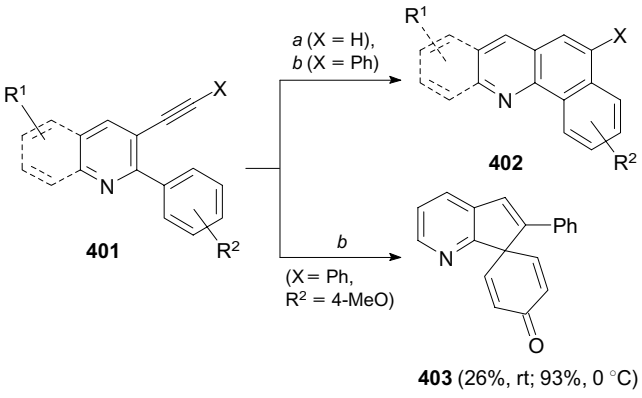
An interesting example of base-promoted transformation was reported for 2,3-diethynylpyridine **399** upon treatment with Bu^{t}OK in NMP (Scheme 135).[86] The single (*E*)-isomer of product **400** formed in 60% yield through a probable cascade 5-*endo*-*dig*/5-*exo*-*dig* cyclization. Final step could proceed in a 6-*endo* mode when XPhosAuCl catalyst is used (cyclization of **119** to **121**, see Scheme 42, Section 3.2), albeit in low yield, while analogous carbocyclic substrates provided high yields of the corresponding products under the same conditions.[85,86]

Scheme 135



2-Aryl-3-ethynylpyridines **401** could be easily cyclized to benzo[*h*]quinolines **402**, moreover, the substituent at the triple bond governs a choice between transition metal or Brønsted acid catalysis: $PtCl_2$ is favourable for terminal alkynes, while TfOH excels with phenylethynyl-substituted heterocycles (Scheme 136).[216] Various substituents in aryl fragments were tolerated. Compounds **401** appeared less reactive than carbocyclic analogues as reaction with trifluoroacetic acid failed even upon heating. Moreover, higher temperature and longer time were needed to convert quinolines compared to pyridines. For the methoxy-substituted pyridine **401** (R^2 = 4-MeO), a competing *ipso*-cyclization was observed as well, which predominated as the reaction temperature decreased, and spiro compound **403** was obtained in 93% yield at 0 °C.

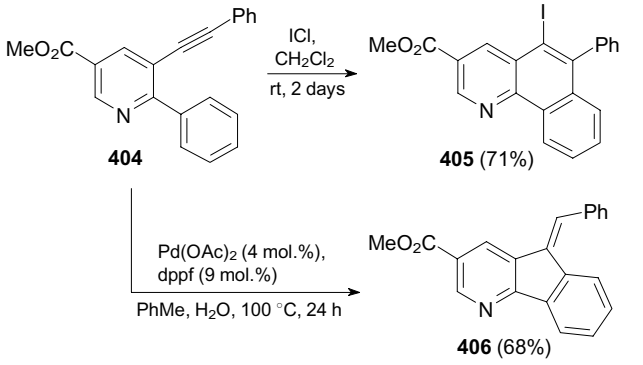
Scheme 136



(*a*) $PtCl_2$ (10 mol.%), PhMe, 110 °C or PhCl, 130 °C, 20 – 48 h;
(*b*) TfOH, rt, 15 min – 1 h; R^1 = H, 6-Me, 6-MeO, 8-MeO;
R^2 = H, 2-Me, 4-Et, 4-F_3C, 4-F, 4-Cl, 3-Cl, 4-MeO, 4-Me_2N, 3,5-Me_2
402: X = H (54% – 80%), Ph (65% – 97%)

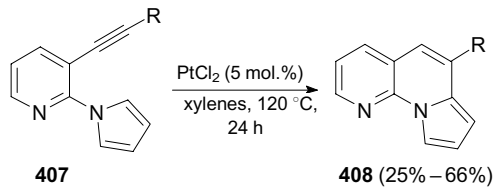
The possibility of Pd-catalyzed selective 5-*exo*-cyclization of 2-aryl-3-ethynylpyridine core of **404** was shown in the synthesis of 4-azafluorene **406** (Scheme 137).[217] An alternative 6-*endo* mode of electrophilic cyclization with ICl led to the expected benzo[*h*]quinoline **405**.

Scheme 137

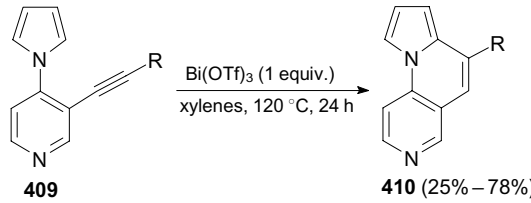


Isomeric 3-alkynyl-2-(pyrrol-1-yl)pyridines **407** and 3-alkynyl-4-(pyrrol-1-yl)pyridines **409** demonstrated different reactivity upon treatment with $PtCl_2$ (Scheme 138). While substrates **407** gave cyclization products **408** in good yields, compounds **409** were completely inert to $PtCl_2$, and only the use of stoichiometric amount of $Bi(OTf)_3$ provided pyrrolo[1,2-*a*][1,6]naphthyridines **410** in the yields up to 78%.[218] Generally, higher yields were obtained for arylalkynes, especially for electron-rich ones; alkylethynyl-sub-

Scheme 138



R = Bu^n, Cy, 3-Th, XC_6H_4 (X = H, 4-Me, 3-Me, 2-F, 4-F, 4-MeO, 3-MeO, 4-Bu^t), 2-Me-4-MeOC_6H_3

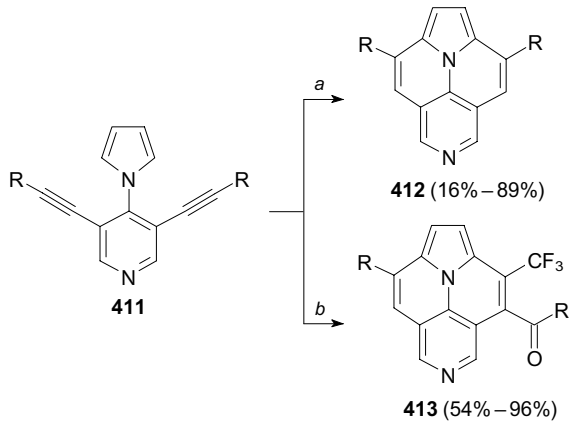


R = 1-Naph, 3-Th, XC_6H_4 (X = H, 4-Me, 3-Me, 4-F_3C, 4-MeO, 4-Pr^n, 4-C_6H_{13}, 4-Bu^t), 2-Me-4-MeOC_6H_3

stituted **409** gave target products only in trace amounts. Electrophilic activation with Brønsted acids (TFA, *p*-TSA) was much less effective for both isomers (yields < 28%).

At the same time, the best results for double cyclization of 3,5-dialkynyl-4-(pyrrol-1-yl)pyridines **411** into aza-ullazines **412** were achieved with *p*-TSA (Scheme 139).[219] With electron-deficient and *ortho*-substituted arylalkynes or alkylalkynes **411**, the yields decreased to 16% – 40%. Later, similar cyclization of **411** accompanied with simultaneous alkynyl – carbonyl metathesis [after initial trifluoroacetylation of the pyrrole C(2) atom] to form **413** was realized using TFAA and copper(II) carbonate hydroxide.[220] However, this reaction did not run for alkylethynyl-substituted pyridines.

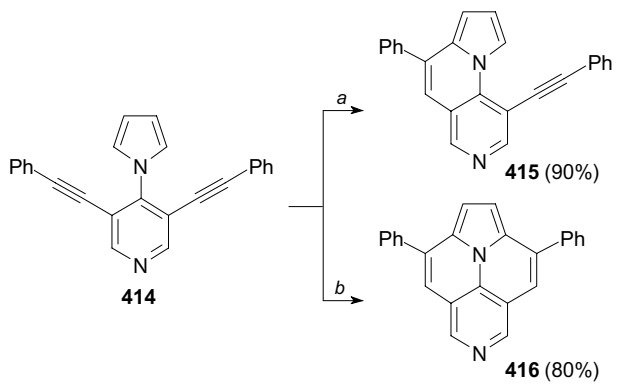
Scheme 139



(*a*) *p*-TSA, xylenes, 120 °C, 24 h;
(*b*) TFAA (15 equiv.), $Cu_2(OH)_2CO_3$, K_2CO_3, $C_6H_4Cl_2$, 170 °C, 1 h;
412: R = XC_6H_4 (X = H, 4-Me, 2-MeO, 4-MeO, 4-Bu^t, 4-$H_{13}C_6$, 4-F, 4-F_3C), 1-Naph, C_6H_{13};
413: R = YC_6H_4 (Y = H, 4-Me, 3-Me, 4-Bu^t, 4-Ph, 4-MeO, 4-F, 2-F, 3-Cl), 2-Me-4-$MeOC_6H_3$

The cyclization of similar pyrrolopyridine **414** could be done in a selective way as mono- or bisannulation to form **415** or **416**, respectively, by adjusting the reaction temperature and amount of $InCl_3$ as catalyst under microwave irradiation (Scheme 140).[122] Harsher conditions and larger catalyst loadings were needed compared to benzene analogues **210** (see Scheme 71) due to the electron-deficient

Scheme 140

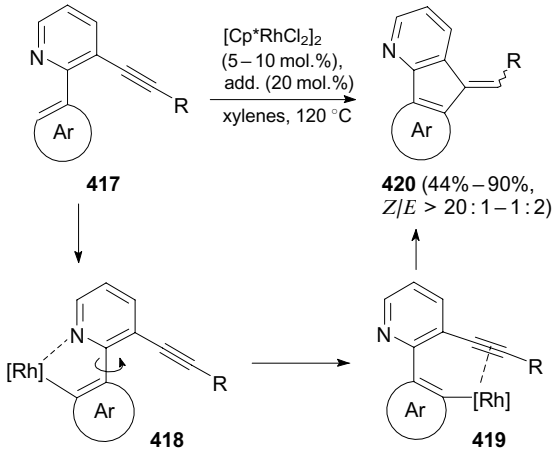


(*a*) $InCl_3$ (2 equiv.), *o*-$Cl_2C_6H_4$, MW, 160 °C, 5 min;
(*b*) $InCl_3$ (3 equiv.), *o*-$Cl_2C_6H_4$, MW, 180 °C, 20 min

character of the pyridine ring and probable coordination of metal centre to the nitrogen atom.

Position of the nitrogen atom strongly affects the success of Rh^{III}-catalyzed cyclization of *ortho*-aryl(ethynyl)-pyridines. 4-Azafluorenes[221] and their heterocyclic analogues[222] **420** were successfully obtained from 3-alkynyl-2-(hetero)arylpyridines **417** (Scheme 141), while the reactions of three regioisomeric *ortho*-aryl(ethynyl)pyridines and *ortho*-(phenylethynyl)biphenyl under the same conditions did not proceed at all (see Section 3.4 for Rh-catalyzed cyclizations of biphenyls). These results imply that the coordination of a metal centre to the nitrogen atom assists C(sp^2) – H bond cleavage on the adjacent (hetero)aryl ring in **418**. 'Rollover' *via* rotation around the single bond between aryl rings affords Rh-alkyne complex **419**, and subsequent intramolecular 5-*endo*-carbometallation gives the final fluorene derivative. Irrelevance of electrophilic Friedel – Crafts type substitution pathway was confirmed as the use of standard catalysts ($PtCl_2$, $InCl_3$, Ph_3PAuCl/$AgBF_4$) failed for these substrates.

Scheme 141

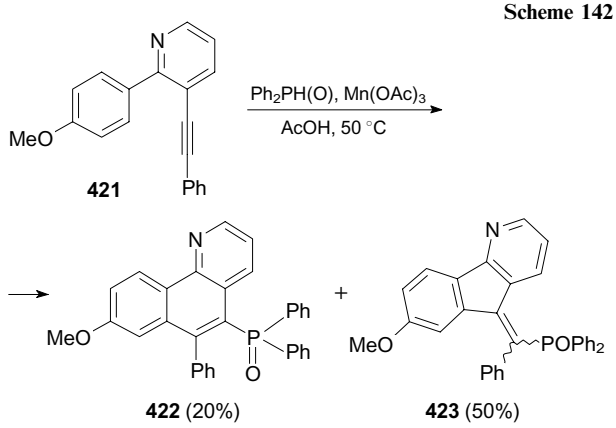


Ar = XC_6H_4 (X = H, 2-Me, 4-Me, 4-MeO, 4-Ac, 4-Cl, 4-F);
R = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-FC_6H_4, Bu^n; add. = $Cu(OAc)_2$;
Ar = 2-Fu, 3-Fu, benzofuran-2-yl, 3-Th, 2-Th, pyrrol-1-yl, indol-1-yl;
R = Ph; add. = NaOPiv

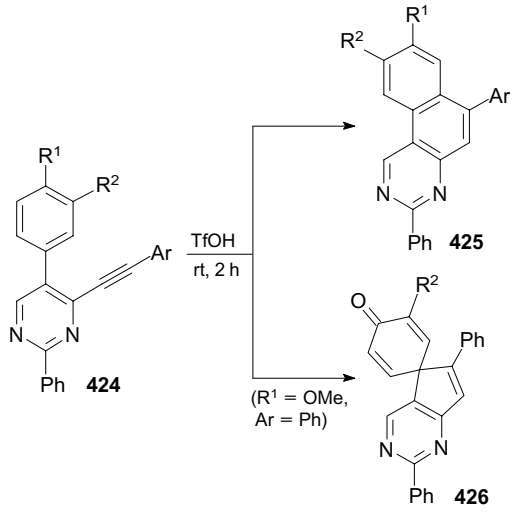
Radical induction was employed for the annulation of 2-(4-methoxyphenyl)-3-(phenylethynyl)pyridine **421** upon treatment with phosphinoyl radical $Ph_2PO^{\bullet}$ generated from diphenylphosphine oxide and $Mn(OAc)_3$ (Scheme 142).[223] Two alternative pathways of radical addition to the triple bond of **421** gave two products of cyclization: compound **423** with the central five-membered ring as the major one along with phenanthrene **422** as a minor product.

Cycloisomerization of 5-aryl-4-(arylethynyl)pyrimidines **424** in TfOH smoothly gave benzo[*f*]quinazolines **425** in excellent yields except for electron-deficient substrates (Scheme 143).[224] Nitro group in phenylethynyl fragment suppressed the reaction, and when $R^1 = NO_2$ the yield of quinazoline **425** decreased significantly. Alternative spirocyclic compounds **426** were obtained from methoxy-substituted pyrimidines **430** (R^1 = OMe, R^2 = H, OMe) as well. Concentrated sulfuric acid was also used instead of TfOH albeit the results were not equal, *e.g.* pyrimidine **424** with R^1 = Cl (R^2 = H, Ar = Ph) afforded spiro compound **426** in 82% yield. DFT calculations and NMR analysis sup-

Scheme 142



Scheme 143

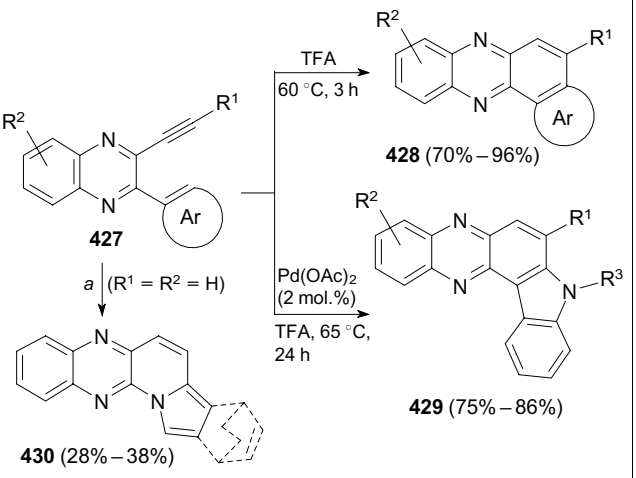


425: R^1 = H, Me, Cl; R^2 = H; Ar = Ph, 4-$MeOC_6H_4$ (95 – 98%); $R^1 = R^2$ = OMe (87%, 0 °C); $R^2 = NO_2$, R^2 = H, Ar = Ph (20%, 50 °C, 24 h); **426**: R^2 = H (98%), OMe (65%)

ported the mechanism including initial protonation of the triple bond followed by electrophilic attack on the aryl ring which might proceed either at the *ortho*- or at the *ipso*-position if there are $+M$ donor groups in the *para*-position (R^1 = OMe, Cl). In the latter case the nucleophilic substitution of R^1 group by water molecule is assumed to finalize the transformation instead of the proposed earlier elimination of a methyl cation.[225, 226]

The reported data on cyclization of 2-aryl-3-ethynylquinoxalines are contradictory. In one case, the reaction of **427** was carried out with trifluoroacetic acid and palladium acetate, and the necessity of the metal catalyst was emphasized (Scheme 144).[227] Various substituents were tolerated except electron-withdrawing groups in the aryl fragment (Ar = 4-$O_2NC_6H_4$, 4-$F_3CC_6H_4$, 4-$MeO_2CC_6H_4$), as only enols formed *via* hydration of the triple bond instead of corresponding phenazines **428**. On the other hand, similar substrates **427** were converted to indolophenazines **429** in TFA without any additives.[228] This discrepancy is unlikely to follow from the difference in the aryl fragments since, as shown above, the nature of this aryl ring has no significant effect on the cyclization. Indium-catalyzed cyclization of

Scheme 144

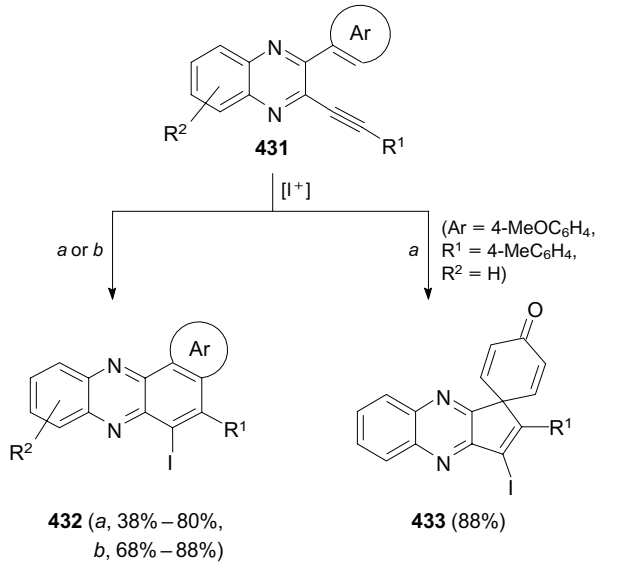


(*a*) $InCl_3$ (10 mol.%), PhMe, 100 – 110 °C, 2 – 3 h;
428: R^1 = XC_6H_4 (X = H, 4-Me, 4-Et, 4-Bu^t, 4-Me_2N, 2-F, 4-F, 4-F_3C, 2-MeO, 4-MeO), cyclo-Pr, Cy, Bu, CH_2OPh, $(CH_2)_2Ph$, 3-Th; R^2 = H, 6-Me, 6-Cl; Ar = Ph, 4-MeC_6H_4, 4-EtC_6H_4, 3,5-$(MeO)_2C_6H_3$, 3,4,5-$(MeO)_3C_6H_2$, 3-Th;
429: R^1 = Ph, Bu, C_5H_{11}, C_6H_{13}; R^2 = H, 6,7-Me_2; R^3 = H, Me, Et, Bn

ethynylquinoxalines **427** onto pyrrole ring proceeded typically to form adducts **430** albeit in moderate yields.[229]

Electrophilic activation by ICl (Ref. 225) or I_2 (Ref. 230) allowed cyclization of 2-aryl-3-ethynylquinoxalines **431** into iodobenzo[*a*]phenazines **432** (Scheme 145). Quinoxaline **431** bearing Ar = 4-MeC_6H_4 (R^1 = 4-MeC_6H_4,

Scheme 145

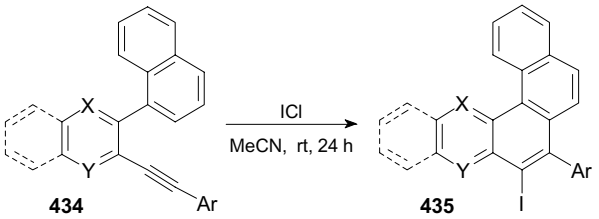


(*a*) ICl, CH_2Cl_2, rt, 48 – 72 h; R^1 = 4-XC_6H_4 (X = Me, MeO, CF_3); R^2 = H; Ar = Ph, 4-MeC_6H_4, 3-MeC_6H_4, 4-$MeOC_6H_4$, 1-Naph, 2-Naph; (*b*) I_2, $NaHCO_3$, CH_2Cl_2, rt, 4 – 26 h; R^1 = YC_6H_4 (Y = H, 2-Me, 3-Me, 4-Me, 4-Et, 4-Bu^t, 2-F, 4-F, 4-F_3C, 2-MeO, 4-MeO, 4-Me_2N), cyclo-Pr, Cy, Bu, 3-Th; R^2 = H, 6-Me; Ar = 3-Th, Ph, 3,5-$(MeO)_2C_6H_3$, 2,5-$(MeO)_2C_6H_3$, 3,4,5-$(MeO)_3C_6H_2$

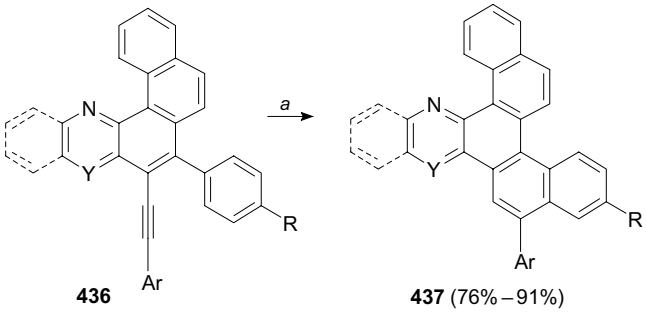
R^2 = H) afforded a mixture of the corresponding phenazine **432** and minor amount of its iodomethyl derivative.[225] As in the reaction of pyrimidines **424** (see Scheme 143), the alternative *ipso*-cyclization to **433** was the major transformation for the *para*-methoxy-substituted quinoxaline **431** (Ar = 4-$MeOC_6H_4$) upon treatment with ICl;[225] however, only standard 6-*endo*-annulation product was reported for the reaction of similar quinoxaline **431** [Ar = 3,4,5-$(MeO)_3C_6H_2$] with I_2.[230]

Recently, ICl was utilized for the synthesis of fused naphthoazines **435** with the best result observed for methoxyphenyl-substituted quinoxaline **434** (X = Y = N) (Scheme 146).[231] *para*-Tolylethynylquinoxalines **436** obtained from **435** *via* Sonogashira coupling smoothly underwent TFA-mediated annulation to form S-shaped double 1,4-diaza[4]helicenes **437**. However, the corresponding derivative of pyridine-based [4]helicene remained intact even after prolonged refluxing in TFA.

Scheme 146



X = CH, N, Y = N, Ar = Ph, 4-$MeOC_6H_4$ (47% – 71%);
X = N, Y = CH, Ar = Ph (35%, CH_2Cl_2, 48 h)



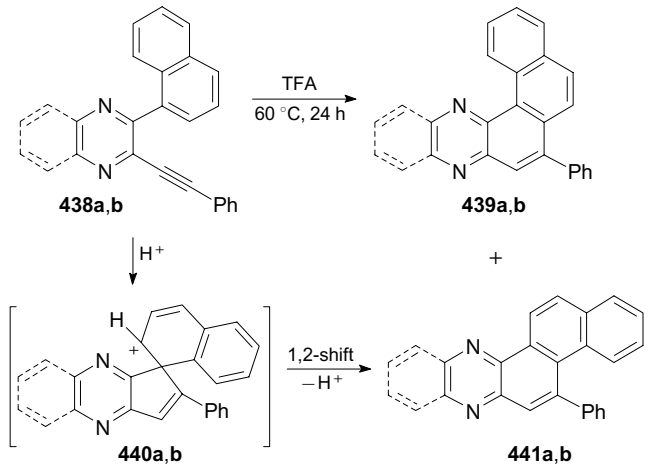
(*a*) TFA, 60 °C, 3 h; R = H, MeO; Ar = 4-MeC_6H_4

In contrast to the ICl-mediated reaction of azines **434** (see Scheme 146), TFA-induced cyclization of similar substrates **438a**,**b** produced the expected 1,4-diaza[4]helicenes **439a**,**b** along with the isomeric naphtho[2,1-*f*]quinoxalines **441a**,**b** (Scheme 147).[231] While the structure of the former products is consistent with the regioselectivity of ordinary electrophilic aromatic substitution, the latter compounds likely formed *via* an *ipso*-attack at the naphthalene moiety followed by isomerization of intermediate cation **440** and subsequent deprotonation (see Scheme 147).

7.2. Five-membered heterocycles

Among all five-membered heterocycles, *ortho*-alkynyl(aryl)thiophenes have received considerable attention as products of their cyclization (thienoacenes) are one of the most frequent molecular units found in organic materials (for OFET devices, solar cells *etc.*)[232 – 234] owing to their outstanding optoelectronic properties. First examples of cyclization on the central thiophene core were performed

Scheme 147

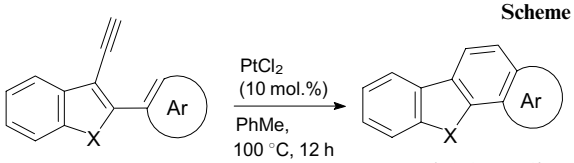


pyrazine: **439a** (53%) + **441a** (36%);
quinoxaline: **439b** : **441b** = 1.8 : 1 (87%)

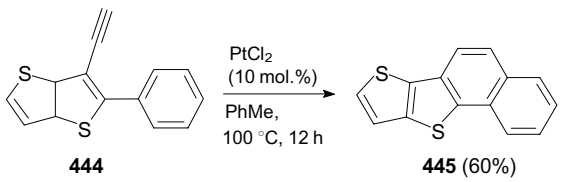
under FVP conditions in 1999 (compounds **14** – **16**, see Scheme 3).[24] Harsh conditions limit wide application of this technique, and two other methods are most often used for the cyclization of *ortho*-aryl(ethynyl)thiophenes with comparable success: transition metal (Pt or Au) and base (DBU) catalysis. Although a five-membered central ring presets a longer distance between an aromatic ring and an ethynyl substituent in comparison to a six-membered core, cyclization of thiophenes usually proceeds smoothly under standard conditions equally good for both 2-alkynyl-3-aryl- and regioisomeric 3-alkynyl-2-arylthiophenes.

Benzofused thiophenes and furans **442** were cyclized by $PtCl_2$ providing tetracyclic compounds **443** in good yields (Scheme 148).[235] Similarly, naphtho[1,2-*b*]thieno[2,3-*d*]thiophene (**445**) was obtained from 3-ethynyl-2-phenylthieno[3,2-*b*]thiophene (**444**) in 60% yield.[235]

Scheme 148

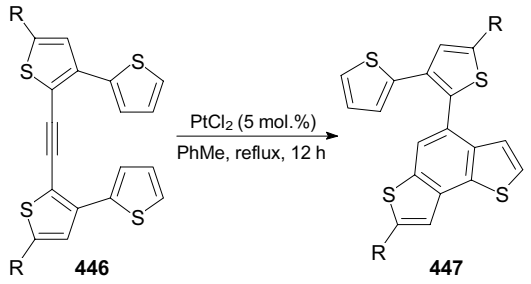


X = S, O; Ar = Ph, 4-BrC_6H_4, 4-FC_6H_4, 5-hexylthiophen-2-yl, 5-hexylfuran-2-yl, 2-Th, 3-Th



ortho-Alkynyl(thiophenyl)thiophenes **446** successfully underwent cyclization on treatment with $PtCl_2$ and were used for the synthesis of tetrathienonaphthalene-based polymers for OFET devices (Scheme 149).[236] In this work the subsequent oxidative coupling between the distal thiophene ring and the central benzene ring of **447** to form

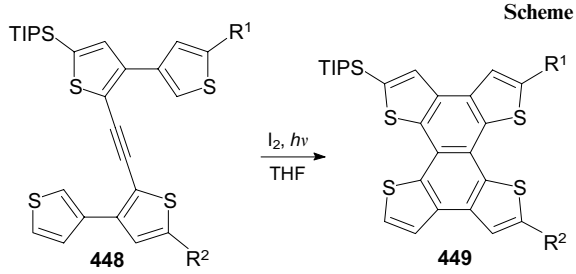
Scheme 149



447: R = $C_{15}H_{25}$ (67%), TIPS (73%)

naphthalene core was done under the conditions of Scholl oxidation with DDQ. However, it is possible to perform double cyclization of bis(thiophenyl)acetylenes in a one-pot fashion using photoirradiation with an excess amount of iodine. Acetylenes **448** were transformed into tetrathienonaphthalenes **449** in this manner in high yields (Scheme 150).[237] The first step is likely an electrophilic monocyclization mediated by iodine while the photoirradiation promotes the second electrocyclization followed by aromatization.

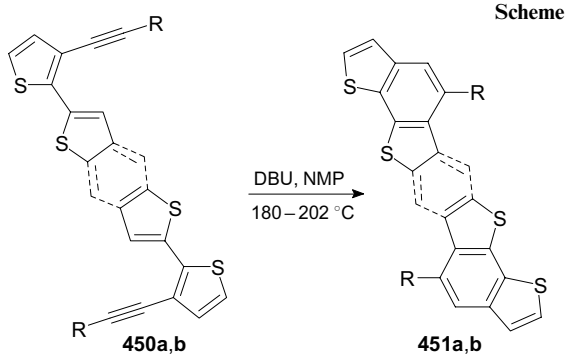
Scheme 150



R^1 = H, R^2 = TIPS (86%); R^1 = TIPS, R^2 = H (73%)

Basic catalysis was successfully used to carry out biscyclization of thieno[3,2-*b*]thiophene **450a** (Scheme 151).[238] Refluxing of **450a** with DBU in NMP provided the target hexacycle **451a** in high yield. Later similar transformation was performed for analogous benzofused dithiophene **450b** furnishing ladder-type heptacycle **451b**.[239] Inverse position of alkynyl and aryl substituents at terminal thiophene rings in regioisomer of **450b** did not affect the reaction outcome, as the corresponding isomer of **451b** was obtained in 63% yield.[239]

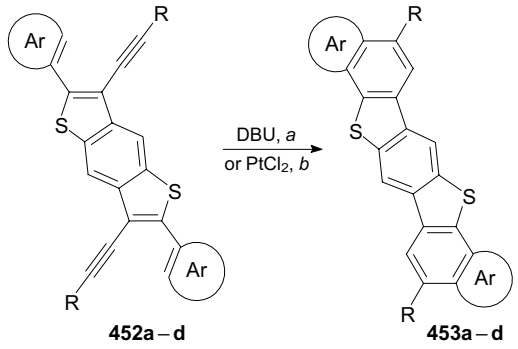
Scheme 151



thieno[3,2-*b*]thiophene: R = $C_{14}H_{29}$ (**a**, 78%);
benzo[1,2-*b*:4,5-*b*′]dithiophene: R = $C_{10}H_{21}$ (**b**, 53%)

Besides, alkynyl groups could be attached to thiophene rings of the central benzodithiophene fragment without loss of reactivity; compare **450b** (see Scheme 151) and **452a** (Scheme 152).[239] Greater influence on the reaction was observed when comparing isomeric terminal thiophene rings of **452a**,**b**: cyclization onto the C(2) atom of thiophen-3-yl substituent gave twice lower yield than cyclization on the C(3) atom of thiophen-2-yl substituent [**453b** (35%) *vs*. **453a** (65%), see Scheme 152].

Scheme 152

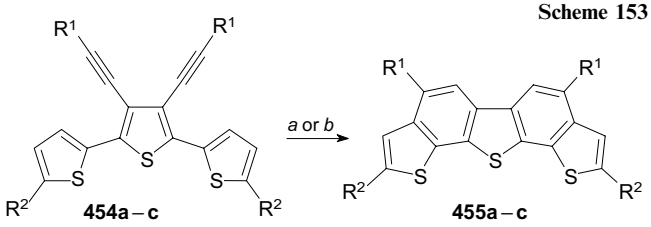


(*a*) NMP, 180 °C: R = $C_{10}H_{21}$; Ar = 2-Th (**a**, 65%), 3-Th (**b**, 35%); (*b*) PhMe, 80 °C: R = H, Ar = 4-($H_{13}C_6O$)C_6H_4 (**c**, 45%), 4-(TIPSO)C_6H_4 (**d**, 51%)

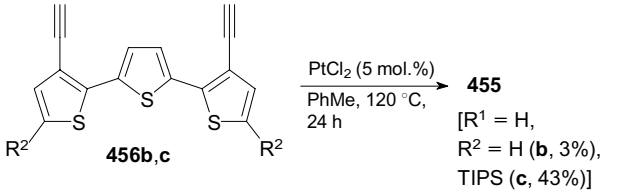
Mechanism of base-catalyzed cyclization implies initial propargyl – allenyl isomerization of alkynyl substituent followed by electrocyclization/aromatization (see Scheme 126), which determines suitable substrates bearing a substituent with at least one methylene group at the triple bond. Therefore, cyclization of similar benzodithiophenes **452c**,**d** with unsubstituted ethynyl groups was realized with $PtCl_2$ (see Scheme 152).[240]

Similarly, DBU-assisted double cyclization of dialkynyl-substituted thiophenes **454a** afforded ethene-bridged terthiophenes **455a** in good yields while substrate with trimethylsilylethynyl groups (R^1 = TMS) gave only complex mixture under these conditions (Scheme 153).[241] In con-

Scheme 153



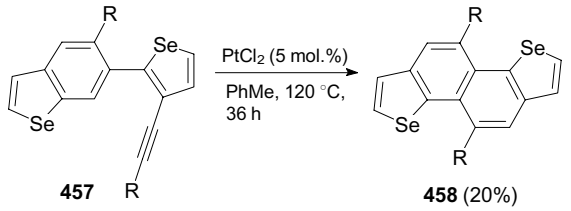
(*a*) DBU, NMP, 190 °C, 24 h; R^1 = Bu, C_6H_{13}, Oct; R^2 = H (**a**, 56% – 70%); (*b*) $PtCl_2$ (5 mol.%), PhMe, 120 °C, 24 h; R^1 = H; R^2 = H (**b**, 9%), TIPS (**c**, 20%)



trast, cyclization of ethynyl-substituted thiophenes **454b**,**c** was accomplished with $PtCl_2$, albeit in poor yields, which could be attributed to low reactivity of the β-position of thiophene ring towards electrophilic aromatic substitution (about mechanism of Pt-catalyzed cyclization see Section 3.1). Thiophenes **456b**,**c**, regioisomers of **454b**,**c**, furnished terthiophenes **455b**,**c** in similar yields.

A single example of cyclization of *ortho*-aryl(ethynyl)selenophene was executed under $PtCl_2$ catalysis though a triple bond of **457** has an alkyl group; the yield of the resulting naphthodiselenophene **458** was only 20% (Scheme 154).[242]

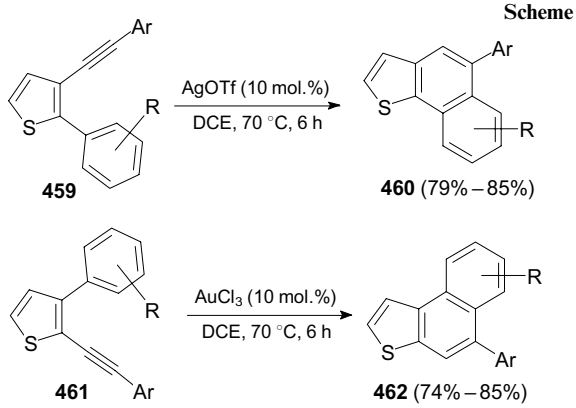
Scheme 154



R = $C_{12}H_{25}$

Ag-catalyzed cyclization was used in the synthesis of naphtho[1,2-*b*]thiophenes **460** from 2-aryl-3-(arylethynyl)thiophenes **459** (Scheme 155).[124] Interestingly, isomeric substrates [3-aryl-2-(arylethynyl)thiophenes **461**] were inactive with AgOTf, and corresponding naphtho[2,1-*b*]thiophenes **462** were obtained using Au^{III} catalysis under the same conditions.

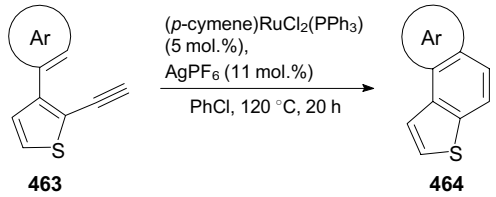
Scheme 155



Ar = 4-XC_6H_4 (X = H, Bu^t, Me, MeO);
R = 4-Me, 4-Et, 4-MeO, 4-F, 2-Ph

Ruthenium catalyst was less effective for the cyclization of 3-aryl-2-ethynylthiophenes **463** (Scheme 156) compared

Scheme 156

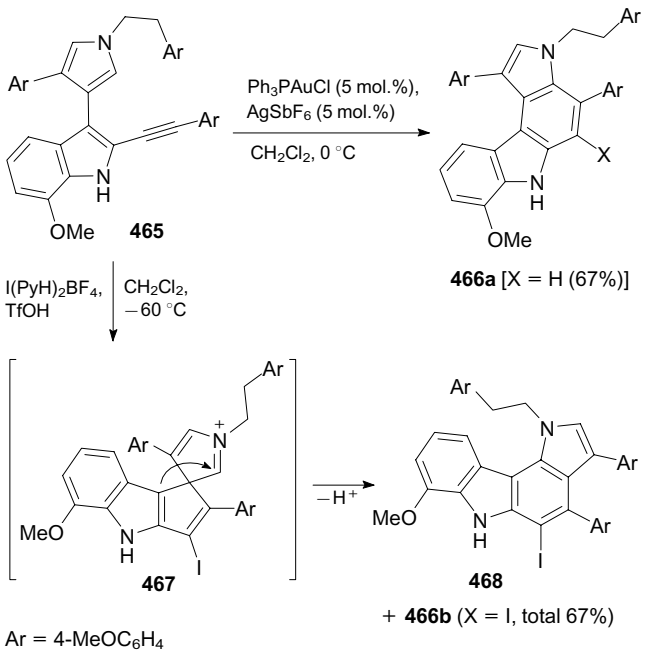


Ar = 3-Th (44%), 4-$MeOC_6H_4$ (49%)

to that of similar *ortho*-ethynyl(thiophen-2-yl)benzenes **223** (see Scheme 76).[127] Moderate yields of naphthothiophene and benzodithiophene **464** were obtained in this way.

Cyclization on pyrrole ring was realized in the synthesis of dictyodendrin analogues. While Au-catalyzed reaction of **465** provided the expected product of 6-*endo*-cyclization **466a**, electrophilic activation by I^+ revealed the tendency of this heteroarene to undergo unusual skeletal rearrangement (Scheme 157).[243] In addition to the major product **466b**, isomer **468** was obtained as a result of a competing 5-*endo*-*ipso*-cyclization enabled by resonance stabilization of intermediate cation **467**, which generates **468** by a Wagner – Meerwein-like rearrangement. However, treatment of **465** with either I_2/K_2CO_3 or ICl led to instantaneous decomposition.

Scheme 157

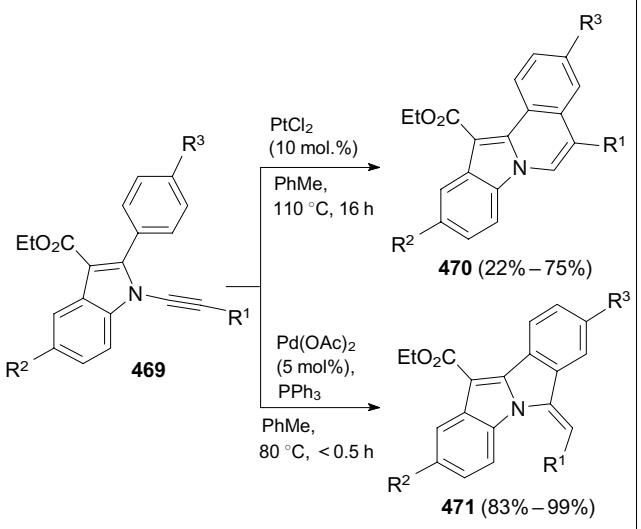


Ar = 4-$MeOC_6H_4$

The cyclization mode of *N*-alkynyl indoles **469** depends on the catalyst used (Scheme 158).[244] The $PtCl_2$-catalyzed reaction led to 6-*endo*-*dig* cycloisomerization into **470**, while $Pd(OAc)_2$ promoted 5-*exo*-*dig* mode to form 5-membered products **471**. In general, the first reaction took longer time and gave lower yields than the second one. Moreover, for ynamines **469** containing thiophene at the triple bond or the bromine atom as R^3 group, the desired products **470** were obtained in 22% and 27% yields, respectively, even after 36 h. Study of the kinetic isotope effect for both cyclizations revealed a significant value of KIE ($k_H/k_D = 2.86$) for the second process and the inverse ratio for the first one ($k_H/k_D = 0.50$); the same phenomenon as in the previous work on biphenyls (see Scheme 55). That is consistent with a mechanism involving electrophilic aromatic substitution for Pt-catalyzed cyclization and aromatic C – H activation pathway for Pd-catalyzed reaction.

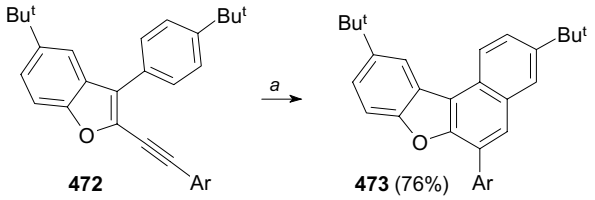
Furan and thiophene cores were employed in cascade Au^I-catalyzed cyclizations of polyynes **119** and **122**, respectively (see Schemes 42, 43, Section 3.2). For 3-aryl-2-(arylethynyl)benzofuran **472**, the 6-*endo*-cyclization induced by $PtCl_2$ was accompanied by 1,2-aryl shift (Scheme 159).[245] A mixture of two cyclic products in a ratio of 10 : 1 was obtained. Although the structure of the

Scheme 158



R^1 = XC_6H_4 (X = H, 4-Me, 4-CO_2Me, 4-CHO, 4-CF_3, 4-F, 2-OMe, 3-OMe, 3-Cl), n-C_6H_{13}, 2-Th, 2-Naph; R^2 = H, OMe, CF_3; R^3 = H, OMe, Br

Scheme 159



(*a*) $PtCl_2$ (10 mol.%), PhMe, 80 °C, 12 h; Ar = 4-$Ph_2NC_6H_4$

minor isomer was not established, the main product was confirmed to be benzonaphthofuran **473** using X-ray diffraction analysis.

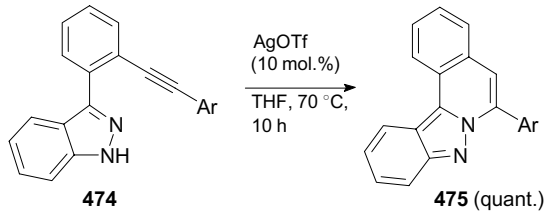
8. Amination

Reactions described in this Section differ from the previously mentioned ones in that the formation of a new C – N bond, rather than C – C bond, occurs, and, therefore, they present amination rather than arylation of a triple bond. However, from the formal point of view, given the nitrogen atom included in an aromatic ring, these reactions can be considered as cyclizations of *ortho*-ethynyl(heteroaryl) fragment. Reactive compounds may be converted in this manner under non-catalytic conditions although standard catalysts facilitate these cyclizations in the same way as ordinary carbocyclizations.

Upon treatment with catalytic amount of AgOTf, indazole derivative **474** smoothly cyclized to indazolo[3,2-*a*]isoquinoline **475** (Scheme 160).[246] The cyclization was suggested to proceed *via* nucleophilic attack of the pyrazole nitrogen atom at the silver-activated triple bond.

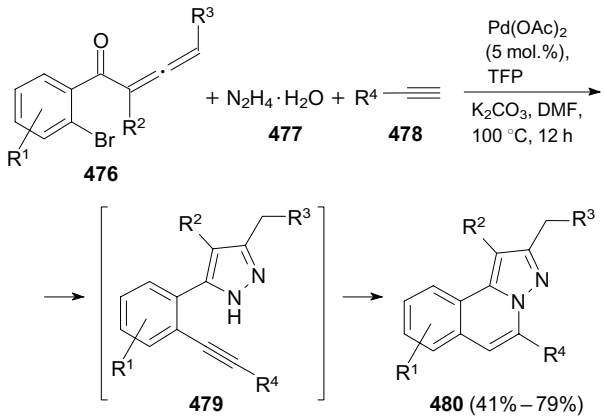
Pyrazolo[5,1-*a*]isoquinolines **480** were obtained *via* the one-pot three-component cascade reaction between allenes **476**, hydrazine **477** and alkynes **478** (Scheme 161).[247] The plausible mechanism includes palladium-catalyzed 6-*endo*-*dig* cyclization of alkyne moiety on the pyrazole ring of intermediate **479**. Separately prepared pyrazole **479** ($R^1 - R^3$ = H, R^4 = Ph) being subjected to the standard reaction conditions underwent hydroamination into corresponding **480** in 82% yield. The electronic nature of the substrates did not show any obvious effect on the yield of the products.

Scheme 160



Ar = 4-MeC_6H_4

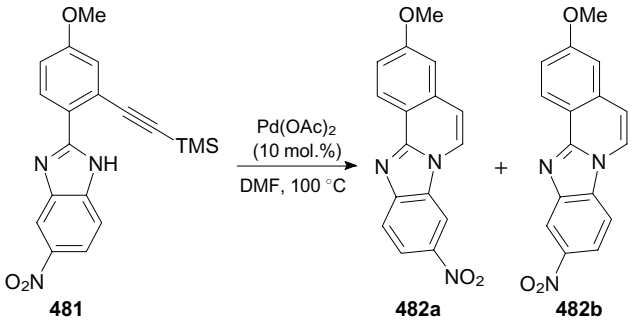
Scheme 161



R^1 = H, Cl, F, OMe, Me, CF_3, CH_2OCH_2; R^2, R^3 = H, Me, Et; R^4 = XC_6H_4 (X = H, 4-Cl, 4-F, 4-MeO, 3-Me), Bn

Benzoannulation of *ortho*-ethynyl(imidazolyl)benzene **481** by treatment with $Pd(OAc)_2$ provided a mixture of isomeric benzimidazo[2,1-*a*]isoquinolines **482a,b** (Scheme 162).[248] This reaction proceeded in a 6-*endo*-mode at the nitrogen atom of the imidazole fragment.

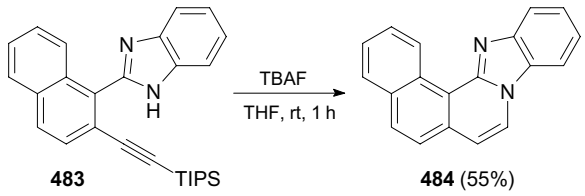
Scheme 162



Similar benzimidazole **483** with TIPS group at the alkyne terminus gave pentacyclic heteroarene **484** by desilylative cyclization merely with TBAF at room temperature (Scheme 163).[249]

Buildup of imidazolyl fragment at the *ortho*-position to the ethynyl group is often performed *in situ* using 2-ethy-

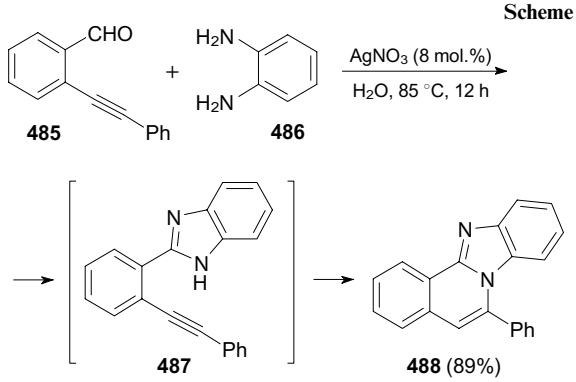
Scheme 163



nylbenzaldehyde and diamine as starting material. Among such examples, only the reactions where intermediate *ortho*-ethynyl(imidazolyl)benzene was isolated are mentioned below.

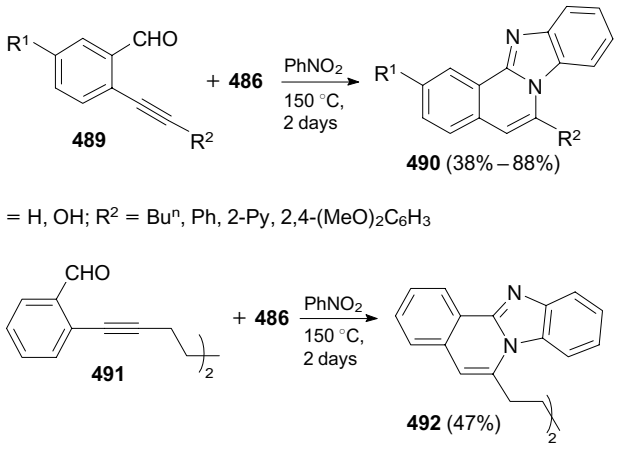
Cyclization onto imidazole ring of **487** occurred with $AgNO_3$ to give 6-phenylbenzo[4,5]imidazo[2,1-*a*]isoquinoline **488** (Scheme 164).[250] The obscure way how 'auto-oxidation' of the initially formed imidazoline occurred without any oxidant in the reaction mixture was not commented. During the optimization of the reaction conditions, intermediate benzoimidazole **487** (20% – 45%) was isolated along with cyclization product **488** (35% – 72%; the total yield of both compounds was > 100% in some cases), when the reaction between *ortho*-alkynylbenzaldehyde **485** and diamine **486** was carried out in CH_2Cl_2, DCE, toluene, DMSO, DMF and even EtOH. Surprisingly, only final **488** was obtained in 89% yield in water despite the poor solubility of reactants. Replacement of water by D_2O did not affect the reaction outcome, therefore the role of water is not clear. However, extremely wide substrate scope was reported for the whole transformation with yields of imidazoisoquinoline derivatives similar to **488** not less than 65%.

Scheme 164



In contrast to the example mentioned above, the same process was realized without any catalyst to give benzo[4,5]imidazo[2,1-*a*]isoquinolines **490** and **492** in good yields (Scheme 165)[251] [in this manner compound **488** (see Scheme 164) was obtained in 83% yield]. Cyclization proceeded under conditions of oxidative condensation of aldehydes **489**, **491** with *ortho*-phenylene diamine (**486**) in nitrobenzene. Interestingly, substrates with a furyl substituent at the triple bond gave completely different products (isoindolo[2,1-*a*]quinoxalines) by a reaction involving the furan ring.[251]

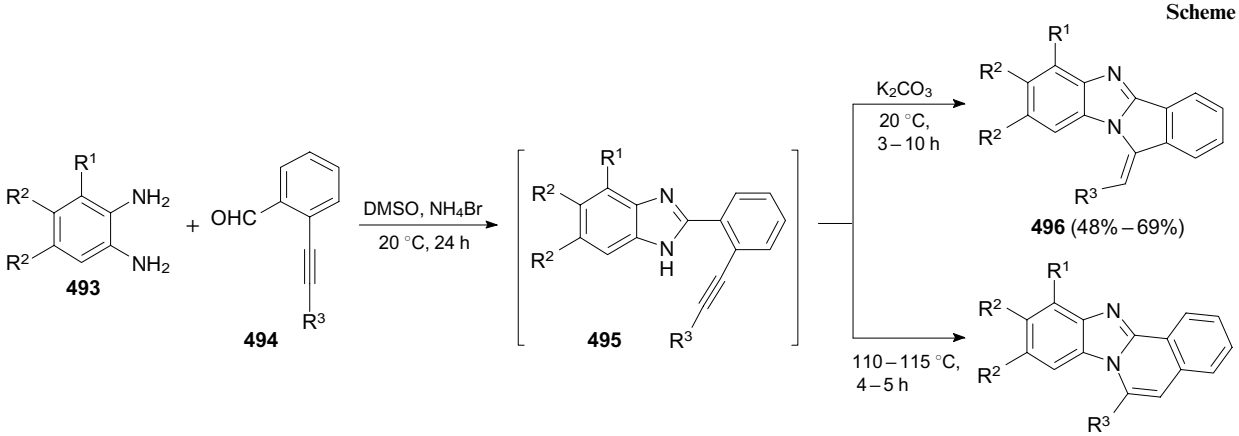
Scheme 165



R^1 = H, OH; R^2 = Bu^n, Ph, 2-Py, 2,4-$(MeO)_2C_6H_3$

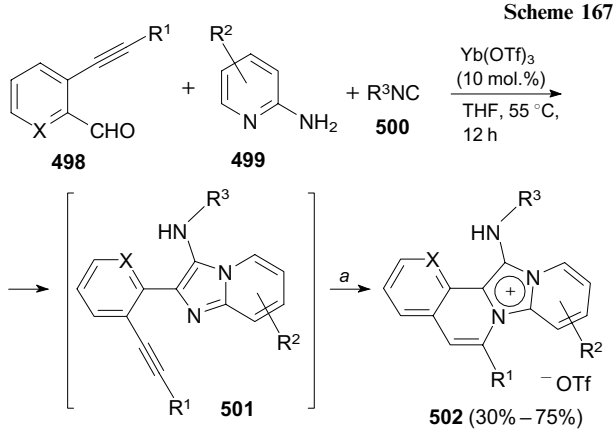
Regioselective annulation on imidazole ring was realized by simply adjusting the reaction conditions without a metal catalyst. Upon addition of K_2CO_3 at room temperature, after the reaction between starting *o*-diaminobenzenes **493** and aldehydes **494** finished, intermediate benzimidazoles **495** underwent 5-*exo* and 6-*endo*-cyclization to produce mixtures of isoindolo[2,1-*a*]benzimidazoles **496** [selectively (*Z*)-isomers] and benzimidazo[2,1-*a*]isoquinolines **497**, respectively, with **496** as the major one in a (2.9 – 13) : 1 ratio (Scheme 166, isolated yields are given).[252] Without a base, at higher temperature only benzimidazo[2,1-*a*]isoquinolines **497** formed. These results were supported by DFT calculations for the cyclization of corresponding *N*-anions generated from **495**, which showed that 6-*endo-dig* cyclization is thermodynamically more favourable than 5-*exo-dig* cyclization. However, the latter process is characterized by lower activation barrier.

Scheme 166



R^1, R^2 = H, Me; R^3 = Ph, 4-$Bu^tC_6H_4$, 2-Th

Scheme 167

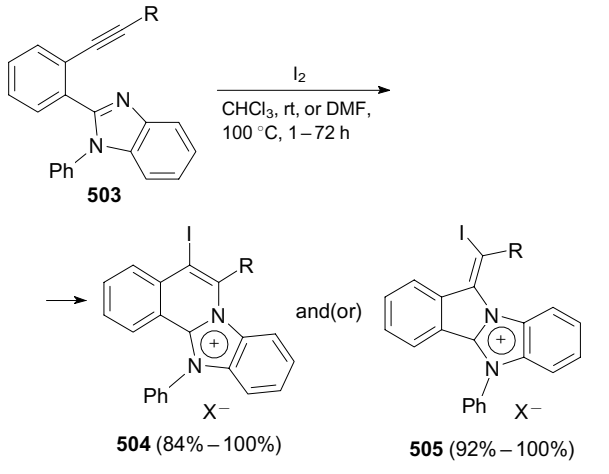


(*a*) AgOTf (1 equiv.), THF, 55°C, 1 h; X = CH, N; R^1 = YC_6H_4 (Y = H, 2-Me, 3-Me, 4-Me, 4-MeO, 4-F), 3-Th, Bu^n; R^2 = H, F, Cl, Br, Me, CN; R^3 = ZC_6H_4 [Z = OMe, F, NO_2, Cl, $O(CH_2)_2O$], Cy, C_8H_{17}, CH_2CO_2Et

Cyclization with the participation of the nitrogen atom of imidazo[1,2-*a*]pyridine moiety was reported (Scheme 167).[253] The impossibility of hydrogen shift in **501** accounts for the formation of quaternary ammonium cation of **502**. Optimization of the cyclization conditions was done for the isolated compound **501** (X = CH, R^1 = Ph, R^2 = H, R^3 = 4-$MeOC_6H_4$). Equimolar amount of silver triflate was required to achieve reasonable yield of target product. Moderately polar solvents (CH_2Cl_2, DCE, MeCN, alcohols) facilitated the reaction, with THF being the best one, while only 31% yield was obtained in toluene. The cyclization step can be realized in a one-pot fashion through addition of silver triflate to the reaction mixture upon completion of the first step — Groebke – Blackburn – Bienaymé three-component reaction. Various substituents in all substrates **498** – **500** were tolerated. Only *tert*-butyl group at the triple bond (R^1 = Bu^t) inhibited cyclization probably due to the steric hindrance.

The reaction of 2-(2-alkynylphenyl)benz[*d*]imidazoles **503** with molecular iodine afforded organic salts with six- **504** or five-membered **505** rings (Scheme 168).[254] The products were obtained with triiodide as a counteranion; however, compounds with iodide were also obtainable under certain conditions. The cyclization was proposed to start with coordination of I_2 to the triple bond to give an iodonium cation. The selectivity of subsequent annulation *via* nucleophilic attack of the nitrogen atom depends on the alkyne substituent. 6-Membered rings (isoquinoline derivatives **504**) were formed from compounds bearing aryl groups (R = Ar), which can stabilize positive charge in the benzylic position, whereas 5-membered ones (isoindole derivatives **505**) were obtained from compounds with hydrogen or alkyl substituents (R = H, CMe_2OH), because in this case stabilization is more effective in the α-position to the central phenyl ring.

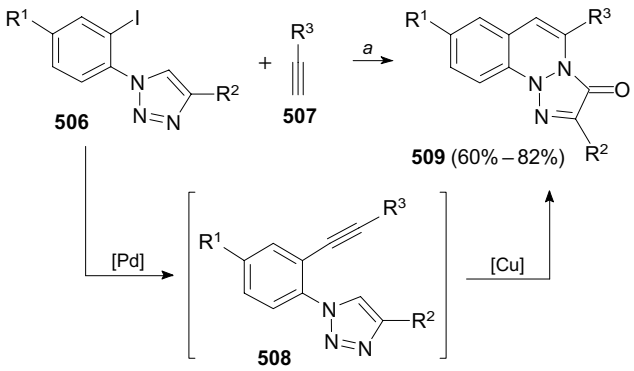
Scheme 168



X = I or I_3; **504**: R = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$; **505**: R = H, CMe_2OH

Triazolocinnolinones **509** were obtained *via* copper-catalyzed cyclization of 1-(2-ethynylphenyl)triazoles **506** accompanied by oxidation under air (Scheme 169).[255] Optimization of reaction conditions enabled the Sonogashira coupling between 1-aryl-1,2,3-triazole **506** and alkyne **507** to form ethynylated intermediate **508** and its subsequent annulation in a one-pot fashion by addition of cyclization reagents after evaporation of triethylamine. Using phenylacetylene (**507**, R^3 = Ph) the second step did not proceed and only intermediate **508** was isolated.

Scheme 169

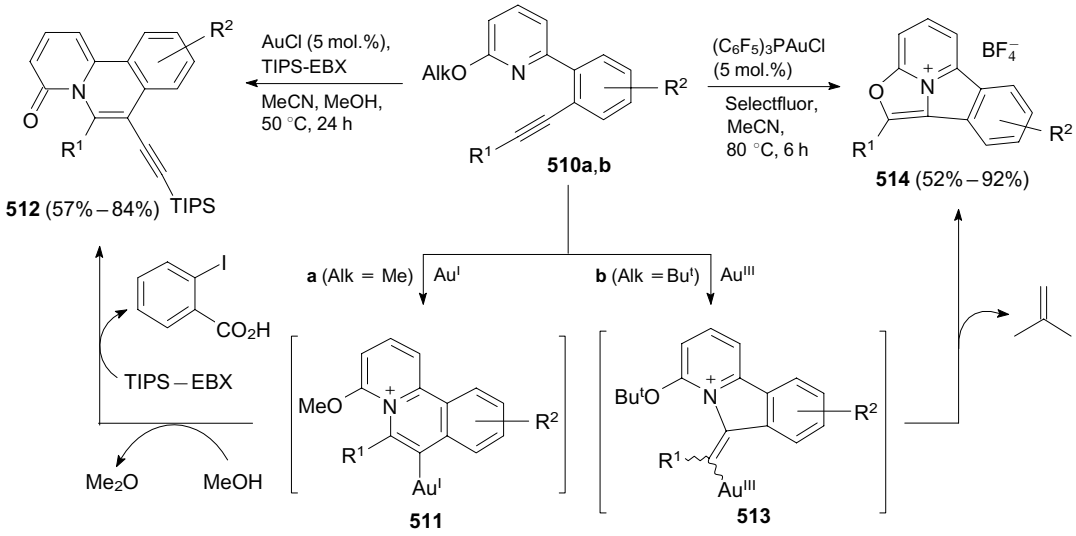


(*a*) 1) $Pd(PPh_3)_2Cl_2$ (2 mol.%), CuI (2 mol.%), Et_3N, 50 °C, 6 h; 2) $Cu(OAc)_2$ (1 equiv.), NaOAc, $(Ph_2P)_2CH_2$, PivOH, PhMe, 120 °C, 12 h, under air; R^1 = H, Me, CN, CO_2Me, Cl; R^2 = XC_6H_4 (X = H, 4-Me, 3-MeO, 4-F, 2-F_3C), 1-Naph, 2-Th, 2-Py, n-C_8H_{17}, cyclo-Pr, Bu^n, $(CH_2)_2OH$; R^3 = Bu^n, n-C_5H_{11}, CH_2OH, $(CH_2)_2OH$, CH_2OMe, Cy, cyclo-Pr, $(CH_2)_2NHTs$

Even the pyridine nitrogen atom can be involved in cyclization on the triple bond, moreover, neutral polycyclic compounds can be formed under oxidative conditions. 6-*endo*-Cyclization of 2-(2-alkynylphenyl)pyridines **510a** to pyrido[2,1-*a*]isoquinolines **512** was implemented with AuCl/TIPS-EBX system (Scheme 170, left).[256] According to the proposed mechanism, activation of the alkyne moiety in **510a** by coordination of Au^I (Au^{III} salts and phosphine/NHC-ligated gold complexes proved to be ineffective) enables nucleophilic attack of the pyridine nitrogen atom to generate a vinyl – gold intermediate **511** *via* annulation to the six-membered ring. The presence of TIPS-EBX allowed for alkynylation of the demethylated complex **511** to get **512**, while in its absence the C(7) unsubstituted pyrido[2,1-*a*]isoquinolin-4-one formed. Instead of TIPS, TBDMS and TBDPS groups may be introduced, but reaction with Ph-EBX failed.

Interestingly, the same starting compounds **510b** underwent transformation into pyridinium-oxazoles **514** *via*

Scheme 170



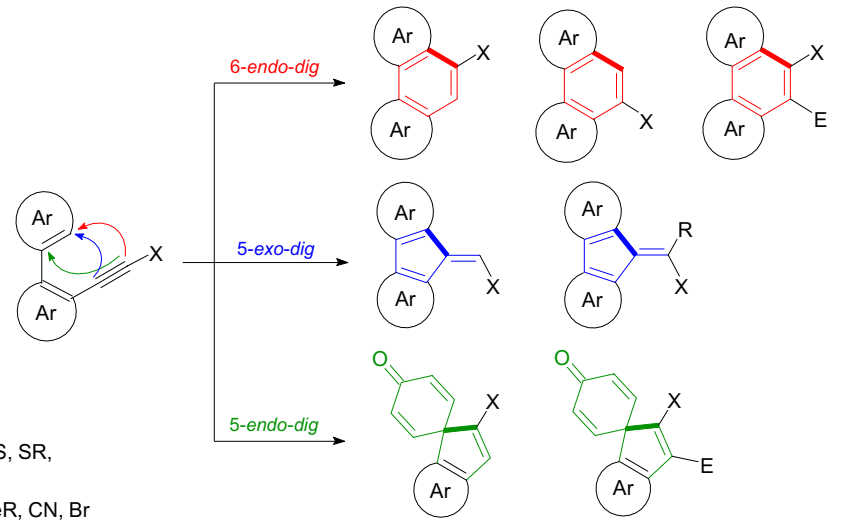
512: R^1 = Ph, 2-Naph, phenanthren-9-yl, Bu^n, n-C_6H_{13}, Cy, cyclo-C_5H_{11}, cyclohex-1-enyl, $CyCH_2$, 4-MeC_6H_4, 4-$MeOC_6H_4$, 3-ClC_6H_4, 3,5-$(MeO)_2C_6H_3$; R^2 = Me, Cl, 3,5-$(MeO)_2$; **514**: R^1 = XC_6H_4 (X = H, Me, Pr^i, C_5H_{11}, OMe, OBu, F, Cl, NMe_2, COBu), 1-Naph, 2-Naph, phenanthren-9-yl, 1-pyrenyl; R^2 = Me, Cl, F

5-*exo*-cyclization into **513** catalyzed by gold as well (see Scheme 170, right).[257] The replacement of the methoxy group by the *tert*-butoxy group in pyridine **510** increased the reaction efficiency and selectivity. Electron-deficient Au^I complex supposed to be oxidized by Selectfluor into Au^{III} species able to activate the alkyne towards nucleophilic attack of the pyridine nitrogen atom. However, the reasons for the different regioselectivity of cyclization compared to the aforementioned example (see Scheme 170, left) are not clear. Without Selectfluor, the pyrido[2,1-*a*]isoquinolin-4-one (the same as formed from **510a** with AuCl without TIPS-EBX) and 6-arylidenepyrido[2,1-*a*]isoindol-4-one were obtained only. Substrates **510b** with alkynyl groups failed to give the desired products.

9. Conclusion

We have demonstrated intensely expanding applications of the cyclization of *ortho*-ethynylbiaryls as a general and versatile tool for the synthesis of polycyclic aromatic hydrocarbons (PAHs) and their heterocyclic analogues. The method features ultimate atom-efficiency and high selectivity, easy availability of starting compounds, operational simplicity, and late-stage applicability. The extremely broad scope of catalysts and stoichiometric reagents allows finding the optimal conditions for cyclization of almost every substrate, whether it is biphenyl or heteroaryl, electron-rich or electron-deficient compound with either terminal or substituted triple bond. This strategy can serve to merge two aromatic rings in one step, and given all the variety of reaction conditions, three main pathways can be underlined: 6-*endo-dig ortho*-cyclization (accompanied with 1,2-migration of an alkyne substituent in certain cases) to give phenanthrenes, 5-*exo-dig ortho*-cyclization to form 9-methylidenefluorenes, and 5-*endo-dig ipso*-cyclization of substrates bearing *para*-alkoxy group or halogen atom to produce spiro derivatives of cyclohexadienone (Scheme 171). The two first processes can be considered as cycloisomerization since no changes in the substrate composition occur; meanwhile, new functionalities can be intro-

Scheme 171



Ar = phenyl, heteroaryl;
X = H, Ar, Alk, Hal, TMS, SR, SeR, CO_2R, N(EWG)R;
E = I, BR_2, PR_2, SR, SeR, CN, Br

duced in the resulting products using appropriate reagents and/or additives. The selectivity may be tuned by choosing a catalyst or through slight alterations in the substrate structure that offers a unique opportunity for accessing various aromatic scaffolds.

Strongly pronounced advantages of the cyclization of *ortho*-ethynylbiaryls pave the way for intense research into related reactions and expanding the scope of its application. The rapidly growing number of studies on this topic, especially over the last years, allows us to anticipate that intriguing contributions in the field have yet to be made. Theoretical and experimental studies on mechanisms of cyclization seem relevant as it would assist a right choice of optimal conditions (activation method, catalyst, solvent *etc*.). The design of new catalysts which require lower loading and/or effectively induce cyclization of inactive compounds would be highly desirable from a practical point of view. We dare to foresee that cascade reactions including cyclization of *ortho*-aryl(ethynyl) fragment as a key step to gain complex structures from simple precursors will be developed extensively. The area of cyclization of *ortho*-ethynyl-(hetero)arylheteroarenes will undoubtedly be filled with novel examples as heterocyclic products thus obtainable are very relevant molecules for the development of valuable drugs and new organic materials.

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References

1. C.Jia, W.Lu, J.Oyamada, T.Kitamura, K.Matsuda, M.Irie, Y.Fujiwara. *J. Am. Chem. Soc*., **122**, 7252 (2000)
2. C.Jia, D.Piao, J.Oyamada, W.Lu, T.Kitamura, Y.Fujiwara. *Science*, **287**, 1992 (2000)
3. C.Jia, T.Kitamura, Y.Fujiwara. *Acc. Chem. Res*., **34**, 633 (2001)
4. R.F.C.Brown, K.J.Harrington, G.L.McMullen. *J. Chem. Soc. Chem. Commun*., 123 (1974)
5. R.F.C.Brown, F.W.Eastwood, K.J.Harrington, G.L.McMullen. *Aust. J. Chem*., **27**, 2393 (1974)
6. A.Fürstner, V.Mamane. *J. Org. Chem*., **67**, 6264 (2002)
7. G.Zimmermann. *Eur. J. Org. Chem*., 457 (2001)
8. C.Nevado, A.M.Echavarren. *Synthesis,* 167 (2005)
9. Y.Yamamoto, I.D.Gridnev, N.T.Patil, T.Jin. *Chem. Commun*., 5075 (2009)
10. D.M.Hitt, J.M.O'Connor. *Chem. Rev*., **111**, 7904 (2011)
11. P.de Mendoza, A.M.Echavarren. In *Modern Gold Catalyzed Synthesis*. (Eds A.S.K.Hashmi, F.D.Toste). (Wiley-VCH, 2012). P. 135
12. Y.Yamamoto. *Chem. Soc. Rev*., **43**, 1575 (2014).
13. V.P.Boyarskiy, D.S.Ryabukhin, N.A.Bokach, A.V.Vasilyev. *Chem. Rev.,* **116**, 5894 (2016)
14. E.Aguilar, R.Sanz, M.A.Fernández-Rodríguez, P.García-García. *Chem. Rev*., **116**, 8256 (2016)
15. Y.Yamamoto, A.I.Almansour, N.Arumugam, R.S.Kumar. *ARKIVOC*, 9 (2016)
16. S.B.Alyabyev, I.P.Beletskaya. *Russ. Chem. Rev*., **87**, 984 (2018)
17. E.Heilbronner, P.A.Plattner, K.Wieland. *Experientia*, **3**, 70 (1947)
18. I.D.Mackie, R.P.Johnson. *J. Org. Chem*., **74**, 499 (2009)
19. H.Y.Cho, A.Ajaz, D.Himali, P.A.Waske, R.P.Johnson. *J. Org. Chem*., **74**, 4137 (2009)
20. L.T.Scott, M.M.Hashemi, D.T.Meyer, H.B.Warren. *J. Am. Chem. Soc*., **113**, 7082 (1991)
21. L.T.Scott, P.-C.Cheng, M.M.Hashemi, M.S.Bratcher, D.T.Meyer, H.B.Warren. *J. Am. Chem. Soc*., **119**, 10963 (1997)
22. H.-J.Kniilker, A.Braier, D.J.Brucher, P.G.Jones, H.Piotrowski. *Tetrahedron Lett*., **40**, 8075 (1999)
23. M.Matsuda, H.Matsubara, M.Sato, S.Okamoto, K.Yamamoto. *Chem. Lett*., **25**, 157 (1996)
24. K.Imamura, D.Hirayama, H.Yoshimura, K.Takimiya, Y.Aso, T.Otsubo. *Tetrahedron Lett*., **40**, 2789 (1999)
25. V.Mamane, P.Hannen, A.Fürstner. *Chem. – Eur. J*., **10**, 4556 (2004)
26. E.Soriano, J.Marco-Contelles. *Organometallics*, **25**, 4542 (2006)
27. B.Michelet, G.Thiery, C.Bour, V.Gandon. *J. Org. Chem*., **80**, 10925 (2015)
28. N.Katsuki, S.Isshiki, D.Fukatsu, J.Okamura, K.Kuramochi, T.Kawabata, K.Tsubaki. *J. Org. Chem*., **82**, 11573 (2017)
29. C.R.Reddy, S.K.Prajapti, K.Warudikar, R.Ranjan, B.B.Rao. *Org. Biomol. Chem*., **15**, 3130 (2017)
30. K.J.Ngwira, A.L.Rousseau, M.M.Johnson, C.B.de Koning. *Eur. J. Org. Chem*., 1479 (2017)
31. M.Weimar, R.Correa da Costa, F.-H.Lee, M.J.Fuchter. *Org. Lett*., **15**, 1706 (2013)
32. R.Pollice, M.Bot, I.J.Kobylianskii, I.Shenderovich, P.Chen. *J. Am. Chem. Soc*., **139**, 13126 (2017)
33. D.K.Winter, M.A.Endoma-Arias, T.Hudlicky, J.A.Beutler, J.A.Porco. *J. Org. Chem*., **78**, 7617 (2013)
34. G.Ferrara, T.Jin, Md.Akhtaruzzaman, A.Islam, L.Han, H.Jiang, Y.Yamamoto. *Tetrahedron Lett*., **53**, 1946 (2012)
35. C.A.Witham, W.Huang, C.-K.Tsung, J.N.Kuhn, G.A.Somorjai, F.D.Toste. *Nat. Chem*., **2**, 36 (2010)
36. J.Carreras, M.Patil, W.Thiel, M.Alcarazo. *J. Am. Chem. Soc*., **134**, 16753 (2012)
37. A.Kozma, T.Deden, J.Carreras, C.Wille, J.Petuskova, J.Rust, M.Alcarazo. *Chem. Eur. J*., **20**, 2208 (2014)
38. T.Shibata, N.Uno, T.Sasaki, K. S. Kanyiva. *J. Org. Chem*., **81**, 6266 (2016)
39. H.Sharma, T.W.Sanchez, N.Neamati, M.Detorio, R.F.Schinazi, X.Cheng, J.K.Buolamwini. *Bioorg. Med. Chem. Lett*., **23**, 6146 (2013)
40. R.Yamano, J.Hara, K.Murayama, H.Sugiyama, K.Teraoka, H.Uekusa, S.Kawauchi, Y.Shibata, K.Tanaka. *Org. Lett*., **19**, 42 (2017)
41. A.Fürstner, W.J.Kennedy. *Chem. – Eur. J*., **12**, 7398 (2006)
42. J.Storch, J.Cermak, J.Karban. *Tetrahedron Lett*., **48**, 6814 (2007)
43. P.F.Thomson, D.Parrish, P.Pradhan, M.K.Lakshman. *J. Org. Chem*., **80**, 7435 (2015)
44. T.-L.Wu, H.-H.Chou, P.-Y.Huang, C.-H.Cheng, R.-S.Liu. *J. Org. Chem*., **79**, 267 (2014)
45. T.-A.Chen, R.-S.Liu. *Chem. – Eur. J.,* **17**, 8023 (2011)
46. J.Liu, B.-W.Li, Y.-Z.Tan, A.Giannakopoulos, C.Sanchez-Sanchez, D.Beljonne, P.Ruffieux, R.Fasel, X.Feng, K.Müllen. *J. Am. Chem. Soc*., **137**, 6097 (2015)
47. G.M.Paterno, Q.Chen, X.-Y.Wang, J.Liu, S.G.Motti, A.Petrozza, X.Feng, G.Lanzani, K.Müllen, A.Narita, F.Scotognella. *Angew. Chem., Int. Ed*., **56**, 6753 (2017)
48. D.M.Coles, Q.Chen, L.C.Flatten, J.M.Smith, K.Müllen, A.Narita, D.G.Lidzey. *Nano Lett*., **17**, 5521 (2017)
49. M.Solà. *Front. Chem.,* **1**, 22 (2013)
50. L.Eccleshare, S.Selzer, S.Woodward. *Tetrahedron Lett*., **58**, 393 (2017)
51. J.Liu, P.Ravat, M.Wagner, M.Baumgarten, X.Feng, K.Müllen. *Angew. Chem., Int. Ed*., **54**, 12442 (2015)
52. K.Kitazawa, T.Kochi, M.Nitani, Y.Ie, Y.Aso, F.Kakiuchi. *Chem. Lett*., **40**, 300 (2011)
53. B.S.Shaibu, S.-H.Lin, C.-Y.Lin, K.-T.Wong, R.-S.Liu. *J. Org. Chem*., **76**, 1054 (2011)
54. T.-A.Chen, T.-J.Lee, M.-Y.Lin, S.M.A.Sohel, E.W.-G.Diau, S.-F.Lush, R.-S.Liu. *Chem. – Eur. J*., **16**, 1826 (2010)

55. K.Yamamoto, M.Okazumi, H.Suemune, K.Usui. *Org. Lett.*, **15**, 1806 (2013)
56. K.Usui, K.Yamamoto, T.Shimizu, M.Okazumi, B.Mei, Y.Demizu, M.Kurihara, H.Suemune. *J. Org. Chem.*, **80**, 6502 (2015)
57. M.Frigoli, J.Marrot, P.L.Gentili, D.Jacquemin, M. Vagnini, D.Pannacci, F.Ortica. *ChemPhysChem*, **16**, 2447 (2015)
58. Y.Li, J.Waser. *Angew. Chem., Int. Ed.*, **54**, 5438 (2015)
59. J.Storch, J.Sykora, J.Cermak, J.Karban, I.Cisarova, A.Ruzicka. *J. Org. Chem.*, **74**, 3090 (2009)
60. M.W.van der Meijden, E.Gelens, N.Murillo Quirûs, J.D.Fuhr, J.E.Gayone, H. Ascolani, K.Wurst, M.Lingenfelder, R.M.Kellogg. *Chem. – Eur. J.*, **22**, 1484 (2016)
61. M.W.van der Meijden, T.Balandina, O.Ivasenko, S.De Feyter, K.Wurst, R.M.Kellogg. *Chem. – Eur. J.*, **22**, 14633 (2016)
62. H.Oyama, K.Nakano, T.Harada, R.Kuroda, M.Naito, K.Nobusawa, K.Nozaki. *Org. Lett.*, **15**, 2104 (2013)
63. H.Oyama, M.Akiyama, K.Nakano, M.Naito, K.Nobusawa, K.Nozaki. *Org. Lett.*, **18**, 3654 (2016)
64. J.M.Casas-Solvas, J.D.Howgego, A.P.Davis. *Org. Biomol. Chem.*, **12**, 212 (2014)
65. K.Yamamoto, N.Oyamada, S.Xia, Y.Kobayashi, M.Yamaguchi, H.Maeda, H.Nishihara, T.Uchimaru, E.Kwon. *J. Am. Chem. Soc.*, **135**, 16526 (2013)
66. D.B.Walker, J.Howgego, A.P.Davis. *Synthesis*, 3686 (2010)
67. M.M.Machuy, C.Würtele, P.R.Schreiner. *Synthesis*, **44**, 1405 (2012)
68. F.Eisenhut, T.Lehmann, A.Viertel, D.Skidin, J.Krüger, S.Nikipar, D.A.Ryndyk, C.Joachim, S.Hecht, F.Moresco, G.Cuniberti. *ACS Nano*, **11**, 12419 (2017)
69. A.Wu, D.Xu, D.Lu, T.M.Penning, I.A.Blair, R.G.Harvey. *Tetrahedron*, **68**, 7217 (2012)
70. D.Wu, H.Zhang, J.Liang, H.Ge, C.Chi, J.Wu, S.H.Liu, J.Yin. *J. Org. Chem.*, **77**, 11319 (2012)
71. C.L.Eversloh, C.Li, K.Müllen. *Org. Lett.*, **13**, 4148 (2011)
72. A.Shiotari, T.Nakae, K.Iwata, S.Mori, T.Okujima, H.Uno, H.Sakaguchi, Y.Sugimoto. *Nature Commun.*, **8**, 16089 (2017)
73. J.W.Dankwardt. *Tetrahedron Lett.*, **42**, 5809 (2001)
74. B.Martín-Matute, C.Nevado, D.J.Cárdenas, A.M.Echavarren. *J. Am. Chem. Soc.*, **125**, 5757 (2003)
75. S.Sarkar, K.Bera, S.Jalal, U.Jana. *Eur. J. Org. Chem.*, 6055 (2013)
76. G.Huang, B.Cheng, L.Xu, Y.Li, Y.Xia. *Chem. – Eur. J.*, **18**, 5401 (2012)
77. W.Lim, Y.H.Rhee. *Eur. J. Org. Chem.* 460 (2013)
78. D.Lorbach, M.Wagner, M.Baumgarten, K. Müllen. *Chem. Commun.*, **49**, 10578 (2013)
79. T.Nakae, R.Ohnishi, Y.Kitahata, T.Soukawa, H.Sato, S.Mori, T.Okujima, H.Uno, H.Sakaguchi. *Tetrahedron Lett.*, **53**, 1617 (2012)
80. T.Shibata, Y.Ueno, K.Kanda. *Synlett*, **2006**, 411 (2006)
81. C.Xie, Y.Zhang, Y.Yang. *Chem. Commun.*, 4810 (2008)
82. W.-T.Wu, R.-Q.Xu, L.Zhang, S.-L.You. *Chem. Sci.*, **7**, 3427 (2016)
83. T.Matsuda, T.Moriya, T.Goya, M.Murakami. *Chem. Lett.*, **40**, 40 (2011)
84. R.Liu, Q.Wang, Y.Wei, M.Shi. *Chem. Commun.*, **54**, 1225 (2018)
85. K.Hirano, Y.Inaba, N.Takahashi, M.Shimano, S.Oishi, N.Fujii, H.Ohno. *J. Org. Chem.*, **76**, 1212 (2011)
86. K.Hirano, Y.Inaba, T.Watanabe, S.Oishi, N.Fujii, H.Ohno, *Adv. Synth. Catal.*, **352**, 368 (2010)
87. K.Hirano, Y.Inaba, K.Takasu, S.Oishi, Y.Takemoto, N.Fujii, H.Ohno. *J. Org. Chem.*, **76**, 9068 (2011)
88. C.-C.Chen, C.-M.Chen, M.-J.Wu. *J. Org. Chem.*, **79**, 4704 (2014)
89. P.M.Byers, J.I.Rashid, R.K.Mohamed, I.V.Alabugin. *Org. Lett.*, **14**, 6032 (2012)
90. J.Cai, B.Wu, G.Rong, C.Zhang, L.Qiu, X.Xu. *Org. Lett.*, **20**, 2733 (2018)
91. Y.Suzuki, S.Oishi, Y.Takei, M.Yasue, R.Misu, S.Naoe, Z.Hou, T.Kure, I.Nakanishi, H.Ohno, A.Hirasawa, G.Tsujimoto, N.Fujii. *Org. Biomol. Chem.*, **10**, 4907 (2012)
92. A.Stoye, T.Opatz. *Eur. J. Org. Chem.*, 2149 (2015)
93. P.-C.Zhang, Y.Wang, D.Qian, W.Li, J.Zhang. *Chin. J. Chem.*, **35**, 849 (2017)
94. A.Urbano, G.Hernandez-Torres, A.M.del Hoyo, A.Martinez-Carrion, M.C.Carreno. *Chem. Commun.*, **52**, 6419 (2016)
95. J.Carreras, G.Gopakumar, L.Gu, A.Gimeno, P.Linowski, J.Petuskova, W.Thiel, M.Alcarazo. *J. Am. Chem. Soc.,* **135**, 18815 (2013)
96. G.Mehler, P.Linowski, J.Carreras, A.Zanardi, J.W.Dube, M.Alcarazo. *Chem. Eur. J.*, **22**, 15320 (2016)
97. J.Petuškova, H.Bruns, M.Alcarazo. *Angew. Chem. Int. Ed.*, **50**, 3799 (2011)
98. E.Haldón, Á.Kozma, H.Tinnermann, L.Gu, R.Goddard, M.Alcarazo. *Dalton Trans.*, **45**, 1872 (2016)
99. E.González-Fernández, L.D.M.Nicholls, L.D.Schaaf, C.Farès, C.W.Lehmann, M.Alcarazo. *J. Am. Chem. Soc.*, **139**, 1428 (2017)
100. F.Pan, S.Liu, C.Shu, R.-K.Lin, Y.-F.Yu, J.-M.Zhou, L.-W.Ye. *Chem. Commun.*, **50**, 10726 (2014)
101. H.-B.Ling, Z.-S.Chen, F.Yang, B.Xu, J.-M.Gao, K.Ji. *J. Org. Chem.*, **82**, 7070 (2017)
102. N.Chernyak, V.Gevorgyan. *J. Am. Chem. Soc.*, **130**, 5636 (2008)
103. E.M.Simmons, J.F.Hartwig. *Angew. Chem., Int. Ed.*, **51**, 3066 (2012)
104. N.Chernyak, V.Gevorgyan. *Adv. Synth. Catal.*, **351**, 1101 (2009)
105. G.C.Senadi, W.-P.Hu, S.S.Kumar Boominathan, J.-J.Wang. *Adv. Synth. Catal.*, **355**, 3679 (2013)
106. J.Zhao, N.Asao, Y.Yamamoto, T.Jin. *J. Am. Chem. Soc.*, **136**, 9540 (2014)
107. Z.-J.Cai, F.-H.Li, S.-Y.Wang, S.-J.Ji. *Org. Lett.*, **18**, 4810 (2016)
108. H.Liu, M.El-Salfiti, M.Lautens. *Angew. Chem., Int. Ed.*, **51**, 9846 (2012)
109. K.Naveen, A.Nandakumar, P.T.Perumal. *Synthesis*, **47**, 1633 (2015)
110. K.Naveen, S.A.Nikson, P.T.Perumal. *Adv. Synth. Catal.*, **359**, 2407 (2017)
111. C.H.Oh, Y.M.Lim. *Tetrahedron Lett.*, **44**, 267 (2003)
112. D.Zhu, Y.Wu, B.Wu, B.Luo, A.Ganesan, F.-H.Wu, R.Pi, P.Huang, S.Wen. *Org. Lett.*, **16**, 2350 (2014)
113. T.Morishita, H.Yoshida, J. Ohshita. *Chem. Commun.*, **46**, 640 (2010)
114. C.-C.Chen, L.-Y.Chin, S.-C.Yang, M.-J.Wu. *Org. Lett.*, **12**, 5652 (2010)
115. X.-C.Huang, F.Wang, Y.Liang, J.-H.Li. *Org. Lett.*, **11**, 1139 (2009)
116. N.Kadoya, M.Murai, M.Ishiguro, J.Uenishi, M.Uemura. *Tetrahedron Lett.*, **54**, 512 (2013)
117. A.Fürstner, V.Mamane. *Chem. Commun.*, 2112 (2003)
118. C.Quinton, M.Suzuki, Y.Kaneshige, Y.Tatenaka, C.Katagiri, Y.Yamaguchi, D.Kuzuhara, N.Aratani, K.Nakayama, H.Yamada. *J. Mater. Chem. C*, **3**, 5995 (2015)
119. R.Stezycki, M.Grzybowski, G.Clermont, M.Blanchard-Desce, D.T.Gryko. *Chem. – Eur. J.*, **22**, 5198 (2016)
120. J.H.Delcamp, A.Yella, T.W.Holcombe, M.K.Nazeeruddin, M.Grätzel *Angew. Chem. Int. Ed.*, **52**, 376 (2013)
121. N.A.Drigo, S.Paek, A.J.Huckaba, P.A.Schouwink, N.Tabet, M.K.Nazeeruddin. *Chem. – Eur. J.*, **23**, 17209 (2017)
122. P.Pierrat, S.Hesse, C.Cebrián, P.C.Gros. *Org. Biomol. Chem.*, **15**, 8568 (2017)

123. W.Yang, R.R.Kazemi, N.Karunathilake, V.J.Catalano, M.A.Alpuche-Aviles, W.A.Chalifoux. *Org. Chem. Front.*, 5, 2288 (2018)
124. R.K.Saunthwal, A.K.Danodia, K.M.Saini, A.K.Verma. *Org. Biomol. Chem.*, **15**, 6934 (2017)
125. Y.Jung, I.Kim. *Org. Lett.*, **17**, 4600 (2015)
126. S.E.Kiruthika, A.Nandakumar, P.T.Perumal. *Org. Lett.*, **16**, 4424 (2014)
127. Y.Yamamoto, K.Matsui, M.Shibuya. *Chem. Eur. J.*, **21**, 7245 (2015)
128. C.A.Merlic, M.E.Pauly. *J. Am. Chem. Soc.*, **118**, 11319 (1996)
129. H.-C.Shen, J.-M.Tang, H.-K.Chang, C.-W.Yang, R.-S.Liu. *J. Org. Chem.*, **70**, 10113 (2005)
130. K.Maeyama, N.Iwasawa, *J. Org. Chem.*, **64**, 1344 (1999)
131. K.Komeyama, R.Igawa, K.Takaki. *Chem. Commun.*, **46**, 1748 (2010)
132. D.Xu, R.Jin, W.Liu, F.Ba, Y.Li, A.Ding, H.Guo. *Tetrahedron Lett.*, **57**, 3235 (2016)
133. Y. Li, Y.Wang, D.Xu, R.Jin, G.Gu, H.Guo. *Synlett*, **28**, 2159 (2017)
134. Y.-L.Wang, W.-M.Zhang, J.-J.Dai, Y.-S.Feng, H.-J.Xu. *RSC Adv.*, **4**, 61706 (2014)
135. R.Jin, Y.Chen, W.Liu, D.Xu, Y.Li, A.Ding, H.Guo. *Chem. Commun.*, **52**, 9909 (2016)
136. R.Jin, J.Chen, Y.Chen, W.Liu, D.Xu, Y.Li, A.Ding, H.Guo. *J. Org. Chem.,* **81**, 12553 (2016)
137. W.Liu, J.Chen, R.Jin, D.Xu, Y.Li, F.Ba, G.Gu, Y.Kuang, H.Guo. *Org. Chem. Front.*, **3**, 852 (2016)
138. S.Hwan Cho, S.Chang. *Angew. Chem., Int. Ed.*, **47**, 2836 (2008)
139. M.B.Goldfinger, T.M.Swager. *J. Am. Chem. Soc.*, **116**, 7895 (1994)
140. M.B.Goldfinger, K.B.Crawford, T.M.Swager. *J. Am. Chem. Soc.*, **119**, 4578 (1997)
141. M.B.Goldfinger, K.B.Crawford, T.M.Swager. *J. Org. Chem.*, **63**, 1676 (1998)
142. H.-B.Chen, J.Yin, Y.Wang, J.Pei. *Org. Lett.,* **10**, 3113 (2008)
143. J.M.W.Chan, J.R.Tischler, S.E.Kooi, V.Bulović, T.M.Swager. *J. Am. Chem. Soc.*, **131**, 5659 (2009)
144. T.Dumslaff, B.Yang, A.Maghsoumi, G.Velpula, K.S.Mali, C.Castiglioni, S.De Feyter, M.Tommasini, A.Narita, X.Feng, K.Müllen. *J. Am. Chem. Soc.*, **138**, 4726 (2016)
145. T.Yao, M.A.Campo, R.C.Larock. *Org. Lett.*, **6**, 2677 (2004)
146. T.Yao, M.A.Campo, R.C.Larock. *J. Org. Chem.*, **70**, 3511 (2005)
147. J.P.Waldo, X.Zhang, F.Shi, R.C.Larock. *J. Org. Chem.*, **73**, 6679 (2008)
148. M.Tobisu, T.Takahira, A.Ohtsuki, N.Chatani. *Org. Lett.,* **17**, 680 (2015)
149. C.T.Bui, B.L.Flynn. *Mol. Divers.*, **15**, 83 (2011)
150. O.V.Zatolochnaya, V.Gevorgyan. *Org. Lett.*, **15**, 2562 (2013)
151. X.Feng, W.Pisula, K.Müllen. *J. Am. Chem. Soc.*, **129**, 14116 (2007)
152. X.Feng, J.Wu, M.Ai, W.Pisula, L.Zhi, J.P.Rabe, K.Müllen. *Angew. Chem. Int. Ed.*, **46**, 3033 (2007)
153. C.-W.Li, C.-I.Wang, H.-Y.Liao, R.Chaudhuri, R.-S.Liu. *J. Org. Chem.,* **72**, 9203 (2007)
154. J.M.W.Chan, S.E.Kooi, T.M.Swager. *Macromolecules*, **43**, 2789 (2010)
155. R.Chaudhuri, M.-Y.Hsu, C.-W.Li, C.-I.Wang, C.-J.Chen, C.K.Lai, L.-Y.Chen, S.-H.Liu, C.-C.Wu, R.-S.Liu. *Org. Lett.*, **10**, 3053 (2008)
156. T.-A.Chen, R.-S.Liu. *Org. Lett.*, **13**, 4644 (2011)
157. Y.Li, C.Wang, C.Li, S.D.Motta, F.Negri, Z.Wang. *Org. Lett.*, **14**, 5278 (2012)
158. R.K.Mohamed, S.Mondal, J.V.Guerrera, T.M.Eaton, T.E.Albrecht-Schmitt, M.Shatruk, I.V.Alabugin. *Angew. Chem., Int. Ed.,* **55**, 12054 (2016)
159. Y.Long, H.Chen, Y.Yang, H.Wang, Y.Yang, N.Li, K.Li, J.Pei, F.Liu. *Macromolecules,* **42**, 6501 (2009)
160. J.Liu, A.Narita, S.Osella, W.Zhang, D.Schollmeyer, D.Beljonne, X.Feng, K.Müllen. *J. Am. Chem. Soc.*, **138**, 2602 (2016)
161. J.Liu, S.Osella, J.Ma, R.Berger, D.Beljonne, D.Schollmeyer, X.Feng, K.Müllen. *J. Am. Chem. Soc.*, **138**, 8364 (2016)
162. H.-H.Hseuh, M.-Y.Hsu, T.-L.Wu, R.-S.Liu. *J. Org. Chem.*, **74**, 8448 (2009)
163. Z.Zhang, T.Lei, Q.Yan, J.Pei, D.Zhao. *Chem. Commun.*, **49**, 2882 (2013)
164. Q.Yan, K.Cai, C.Zhang, D.Zhao. *Org. Lett.*, **14**, 4654 (2012)
165. W.Mao, J.Zhang, X.Li, C.Li, H. Tian. *Chem. Commun.*, **53**, 5052 (2017)
166. A.K.Verma, S.P.Shukla, J.ingh, V.Rustagi. *J. Org. Chem.*, **76**, 5670 (2011)
167. G.M.Martins, G.Zeni, D.F.Back, T.S.Kaufman, C.C.Silveira. *Adv. Synth. Catal.*, **357**, 3255 (2015)
168. Y.Jung, I.Kim. *Asian J. Org. Chem.*, **5**, 147 (2016)
169. X.Zhang, C.Feng, T.Jiang, Y.Li, L.Pan, X.Xu. *Org. Lett.*, **17**, 3576 (2015)
170. C.-C.Chen, S.-C.Yang, M.-J.Wu. *J. Org. Chem.*, **76**, 10269 (2011)
171. T.B.Grimaldi, G.Lutz, D.F.Back, G.Zeni. *Org. Biomol. Chem.*, **14**, 10415 (2016)
172. B.Wu, J.Wu, N.Yoshikai. *Chem. Asian J.*, **12**, 3123 (2017)
173. T.Dohi, D.Kato, R.Hyodo, D.Yamashita, M. Shiro, Y.Kita. *Angew. Chem., Int. Ed.*, **50**, 3784 (2011)
174. H.Suzuki, N.Kobayashi, M.Kimura. *Asian J. Org. Chem.*, **5**, 506 (2016)
175. A.Mukherjee, K.Pati, R.-S.Liu. *J. Org. Chem.*, **74**, 6311 (2009)
176. X.Shen, Y.Wu, L.Bai, H.Zhao, X.Ba. *J. Polym. Sci. Pol. Chem.*, **55**, 1285 (2017)
177. J.D.Tovar, T.M.Swager. *J. Organomet. Chem.*, **653**, 215 (2002)
178. W.Yang, J.H.S.K.Monteiro, A.de Bettencourt-Dias, V.J.Catalano, W.A.Chalifoux. *Angew. Chem., Int. Ed.*, **55**, 10427 (2016)
179. W.Yang, J.H.S.K.Monteiro, A.de Bettencourt-Dias, W.A.Chalifoux. *Can. J. Chem.*, **95**, 341 (2017)
180. W.Yang, W.A.Chalifoux. *Synlett*, **28**, 625 (2017)
181. W.Yang, A.Lucotti, M.Tommasini, W.A.Chalifoux. *J. Am. Chem. Soc.*, **138**, 9137 (2016)
182. W.Yang, G.Longhi, S.Abbate, A.Lucotti, M.Tommasini, C.Villani, V.J.Catalano, A.O.Lykhin, S.A.Varganov, W.A.Chalifoux. *J. Am. Chem. Soc.*, **139**, 13102 (2017)
183. R.Pirwerdjan, P.Becker, C.Bolm. *Org. Lett.*, **18**, 3307 (2016)
184. S.Akbar, K.Srinivasan. *Eur. J. Org. Chem.*, 1663 (2013)
185. A.J.Warner, J.R.Lawson, V.Fasano, M.J.Ingleson. *Angew. Chem., Int. Ed.*, **54**, 11245 (2015)
186. A. G.Barrado, A.Zielinski, R.Goddard, M. Alcarazo. *Angew. Chem., Int. Ed.*, **56**, 13401 (2017)
187. Y.Unoh, K.Hirano, M. Miura. *J. Am. Chem. Soc.*, **139**, 6106 (2017)
188. B.-L.Hu, S.-S.Pi, P.-C.Qian, J.-H.Li, Xi.-G.Zhang. *J. Org. Chem.*, **78**, 1300 (2013)
189. J.L.Scott, S.R.Parkin, J.E.Anthony. *Synlett*, 161 (2004)
190. K.Pati, C.Michas, D.Allenger, I.Piskun, P.S.Coutros, G.dos Passos Gomes, I.V.Alabugin. *J. Org. Chem.*, **80**, 11706 (2015)
191. F.D.Lewis, P.C.Karagiannis, M.C.Sajimon, K.S.Lovejoy, X.Zuo, M.Rubin, V.Gevorgyan. *Photochem. Photobiol. Sci.*, **5**, 369 (2006)
192. D.Xu, R.Rios, F.Ba, D.Ma, G.Gu, A.Ding, Y.Kuang, H.Guo. *Asian J. Org. Chem.*, **5**, 981 (2016)
193. R.Fu, W.-J.Hao, Y.-N.Wu, N.-N.Wang, S.-J.Tu, G.Li, B.Jiang. *Org. Chem. Front.*, **3**, 1452 (2016)
194. S.Yamaguchi, T.M.Swager. *J. Am. Chem. Soc.*, **123**, 12087 (2001)
195. U.Rohr, P.Schlichting, A.Böhm, M.Gross, K.Meerholz, C.Bräuchle, K.Müllen. *Angew. Chem., Int. Ed.*, **37**, 1434 (1998)
196. Y.Wang, D.J.Burton. *Org. Lett.,* **8**, 5295 (2006)

197. Y.Wang, D.J.Burton. *J. Fluor. Chem.,* **128**, 1052 (2007)
198. U.Rohr, C.Kohl, K.Müllen, A.van de Craats, J.Warman. *J. Mater. Chem.,* **11**, 1789 (2001)
199. M.Franceschin, A.Alvino, G.Ortaggi, A.Bianco. *Tetrahedron Lett.*, **45**, 9015 (2004)
200. F.Nolde, W.Pisula, S.Müller, C.Kohl, K. Müllen. *Chem. Mater.*, **18**, 3715 (2006)
201. M.Franceschin, A.Alvino, V.Casagrande, C.Mauriello, E.Pascucci, M.Savino, G.Ortaggi, A.Bianco. *Bioor. Med. Chem.*, **15**, 1848 (2007)
202. A.Zesheng, Y.Junsheng, B.Domercq, S.C.Jones, S.Barlow, B.Kippelen, S.R.Marder. *J. Mater. Chem.*, **19**, 6688 (2009)
203. A.J.Pollard, E.W.Perkins, N.A.Smith, A.Saywell, G.Goretzki, A.G.Phillips, S.P.Argent, H.Sachdev, F.Müller, S.Hüfner, S.Gsell, M.Fischer, M.Schreck, J.Osterwalder, T.Greber, S.Berner, N.R.Champness, P.H.Beton. *Angew. Chem., Int. Ed.*, **49**, 1794 (2010)
204. M.Franceschin, A.Rizzo, V.Casagrande, E.Salvati, A.Alvino, A.Altieri, A.Ciammaichella, S.Iachettini, C.Leonetti, G.Ortaggi, M.Porru, A.Bianco, A.Biroccio. *ChemMedChem.*, **7**, 2144 (2012)
205. K.-Q.Zhao, L.-L.An, X.-B.Zhang, W.-H.Yu, P.Hu, B.-Q.Wang, J.Xu, Q.-D.Zeng, H.Monobe, Y.Shimizu, B.Heinrich, B.Donnio. *Chem. – Eur. J.*, **21**, 10379 (2015)
206. Z.Zhu, J.-Q.Xu, C.-C.Chueh, H.Liu, Z.Li, X.Li, H.Chen, A.K.-Y.Jen. *Adv. Mater.*, **28**, 10786 (2016)
207. I.-H.Lee, Y.-M.Jeon, M.-S.Gong. *Synthetic Met.*, **158**, 532 (2008)
208. C.-H.Lee, Y.-Y.Lai, F.-Y.Cao, J.-Y.Hsu, Z.-L.Lin, U-S.Jeng, C.-J.Su, Y.-J.Cheng. *J. Mater. Chem. C*, **4**, 11427 (2016)
209. J.Shao, X.Zhao, L.Wang, Q.Tang, W.Li, H.Yu, H.Tian, X.Zhang, Y.Geng, F.Wang. *Tetrahedron Lett.,* **55**, 5663 (2014)
210. Y.-Y.Lai, H.-H.Chang, Y.-Y.Lai, W.-W.Liang, C.-E.Tsai, Y.-J.Cheng. *Macromolecules*, **48**, 6994 (2015)
211. K.Ivaniuk, V.Cherpak, P.Stakhira, Z.Hotra, B.Minaev, G.Baryshnikov, E.Stromylo, D.Volyniuk, J.V.Grazulevicius, A.Lazauskas, S.Tamulevicius, B.Witulski, M.E.Light, P.Gawrys, R.J.Whitby, G.Wiosna-Salyga, B.Luszczynska. *J. Phys. Chem. C*, **120**, 6206 (2016)
212. G.V.Baryshnikov, P.Gawrys, K.Ivaniuk, B.Witulski, R.J.Whitby, A.Al-Muhammad, B.Minaev, V.Cherpak, P.Stakhira, D.Volyniuk, G.Wiosna-Salyga, B.Luszczynska, A.Lazauskas, S.Tamulevicius, J.V.Grazulevicius. *J. Mater. Chem. C*, **4**, 5795 (2016)
213. Q.-X.Lin, T.-L.Ho. *Tetrahedron*, **69**, 2996 (2013)
214. A.K.Mandadapu, M.D.Dathi, R.K.Arigela, B.Kundu. *Tetrahedron*, **68**, 8207 (2012)
215. J.Storch, J.Čermák, J.Karban, I.Císařová, J.Sýkora. *J. Org. Chem.*, **75**, 3137 (2010)
216. A.N.Shestakov, A.S.Pankova, M.A.Kuznetsov. *Chem. Heterocyclic Compd.*, **53**, 1103 (2017)
217. C.R.Reddy, S.A.Panda, M.D.Reddy. *Org. Lett.*, **17**, 896 (2015)
218. A.Flader, S.Parpart, P.Ehlers, P.Langer. *Org. Biomol. Chem.*, **15**, 3216 (2017)
219. S.Boldt, S.Parpart, A.Villinger, P.Ehlers, P.Langer. *Angew. Chem., Int. Ed.*, **56**, 4575 (2017)
220. S.Parpart, S.Boldt, P.Ehlers, P.Langer. *Org. Lett.*, **20**, 122 (2018)
221. T.Shibata, S.Takayasu, S.Yuzawa, T.Otani. *Org. Lett.*, **14**, 5106 (2012)
222. T.Shibata, S.Takayasu. *Heteroatom Chem.*, **25**, 379 (2014)
223. D.-P.Li, X.-Q.Pan, L.-T.An, J.-P.Zou, W.Zhang. *J. Org. Chem.*, **79**, 1850 (2014)
224. A.N.Shestakov, A.S.Pankova, P.Golubev, A.F.Khlebnikov, M.A.Kuznetsov. *Tetrahedron*, **73**, 3939 (2017)
225. A.V.Gulevskaya. *Eur. J. Org. Chem.*, 4207 (2016)
226. X.Zhang, R.C.Larock. *J. Am. Chem. Soc.*, **127**, 12230 (2005)
227. S.Kumar, R.K.Saunthwal, M.Mujahid, T.Aggarwal, A.K.Verma. *J. Org. Chem.*, **81**, 9912 (2016)
228. K.S.Kumar, B.Bhaskar, M.S.Ramulu, N.P.Kumar, M.A.Ashfaq, M.Pal. *Org. Biomol. Chem.*, **15**, 82 (2017)
229. M.Kojima, H.Hayashi, T.Aotake, S.Ikeda, M.Suzuki, N.Aratani, D.Kuzuhara, H.Yamada. *Chem. Asian J.*, **10**, 2337 (2015)
230. S.Kumar, M.Mujahid, A.K.Verma. *Org. Biomol. Chem.*, **15**, 4686 (2017)
231. A.V.Gulevskaya, E.A.Shvydkova, D.I.Tonkoglazova. *Eur. J. Org. Chem.*, 5030 (2018)
232. H.Dong, X.Fu, J.Liu, Z.Wang, W.Hu. *Adv. Mater.*, **25**, 6518 (2013)
233. A.P.Kulkarni, C.J.Tonzola, A.Babel, S.A.Jenekhe. *Chem. Mater.*, **16**, 4556 (2004)
234. C.Wang, H.Dong, W.Hu, Y.Liu, D.Zhu. *Chem. Rev.*, **112**, 2208 (2012)
235. Y.Li, G.Gryn ova, F.Saenz, X.Jeanbourquin, K.Sivula, C.Corminboeuf, J.Waser. *Chem. – Eur. J.*, **23**, 8058 (2017)
236. S.-L.Chang, C.-W.Lu, Y.-Y.Lai, J.-Y.Hsu, Y.-J.Cheng. *Org. Lett.*, **18**, 368 (2016)
237. C.Dou, S.Saito, L.Gao, N.Matsumoto, T.Karasawa, H.Zhang, A.Fukazawa, S.Yamaguchi. *Org. Lett.*, **15**, 80 (2013)
238. R.Rieger, D.Beckmann, W.Pisula, M.Kastler, K.Müllen. *Macromolecules*, **43**, 6264 (2010)
239. Y.-L.Chen, J.-Y.Hsu, F.-Y.Lin, Y.-Y.Lai, H.-C.Chou, Y.-J.Cheng. *J. Org. Chem.*, **81**, 2534 (2016)
240. C.-H.Wang, R.-R.Hu, S.Liang, J.-H.Chen, Z.Yang, J.Pei. *Tetrahedron Lett.,* **46**, 8153 (2005)
241. K.Mitsudo, H.Sato, A.Yamasaki, N.Kamimoto, J.Goto, H.Mandai, S.Suga. *Org. Lett.*, **17**, 4858 (2015)
242. C.-E.Tsai, R.-H.Yu, F.-J.Lin, Y.-Y.Lai, J.-Y.Hsu, S.-W.Cheng, C.-S.Hsu, Y.-J.Cheng. *Chem. Mater.,* **28**, 5121 (2016)
243. P.Buchgraber, M.M.Domostoj, B.Scheiper, C.Wirtz, R.Mynott, J.Rust, A.Fürstner. *Tetrahedron,* **65**, 6519 (2009)
244. K.Alam, S.W.Hong, K.H.Oh, J.K.Park. *Angew. Chem., Int. Ed.*, **56**, 13387 (2017)
245. A.Baralle, H.Yorimitsu, A.Osuka. *Chem. – Eur. J.*, **22**, 10768 (2016)
246. J.Zhao, P.Li, C.Wu, H.Chen, W.Ai, R.Sun, H.Ren, R.C.Larock, F.Shi. *Org. Biomol. Chem.*, **10**, 1922 (2012)
247. X.Fan, M.Yan, Y.Wang, X.Zhang. *J. Org. Chem.*, **80**, 10536 (2015)
248. Q.Sun, E.J.LaVoie. *Heterocycles*, **43**, 737 (1996)
249. Y.Ano, M.Tobisu, N.Chatani. *Synlett*, **23**, 2763 (2012)
250. V.Rustagi, R.Tiwari, A.K.Verma. *Eur. J. Org. Chem.*, 4590 (2012)
251. G.Dyker, W.Stirner, G.Henkel. *Eur. J. Org. Chem.*, 1433 (2000)
252. V.D.Gvozdev, K.N.Shavrin, E.G.Baskir, M.P.Egorov, O.M.Nefedov. *Mendeleev Commun.*, **27**, 231 (2017)
253. H.Zhou, W.Wang, O.Khorev, Y.Zhang, Z.Miao, T.Meng, J.Shen. *Eur. J. Org. Chem.*, 5585 (2012)
254. S.Matsumoto, S.Kikuchi, N.Norita, H.Masu, M.Akazome. *J. Org. Chem.*, **81**, 5322 (2016)
255. A.Kumar, D.Kumar Tiwari, B.Sridhard, P.R.Likhar. *Org. Biomol. Chem.*, **16**, 4840 (2018)
256. P.S.Shinde, A.C.Shaikh, N.T.Patil. *Chem. Commun.*, **52**, 8152 (2016)
257. A.C.Shaikh, D.S.Ranade, P.R.Rajamohanan, P.P.Kulkarni, N.T.Patil. *Angew. Chem., Int. Ed.*, **56**, 757 (2017)