

Metal-Catalyzed C-H Bond Activation of 5-Membered Carbocyclic Rings: A Powerful Access to Azulene, Acenaphthylene and Fulvene Derivatives

Xinzhe Shi, Arpan Sasmal, Jean-François Soulé, Henri Doucet

▶ **To cite this version:**

Xinzhe Shi, Arpan Sasmal, Jean-François Soulé, Henri Doucet. Metal-Catalyzed C-H Bond Activation of 5-Membered Carbocyclic Rings: A Powerful Access to Azulene, Acenaphthylene and Fulvene Derivatives. Chemistry - An Asian Journal, 2018, 13 (2), pp.143-157. 10.1002/asia.201701455 . hal-01709529

HAL Id: hal-01709529

https://univ-rennes.hal.science/hal-01709529

Submitted on 9 Mar 2018

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Metal-catalyzed C-H bond functionalization of 5-membered carbocyclic rings: A powerful access to azulenes, acenaphthylenes and fulvenes derivatives

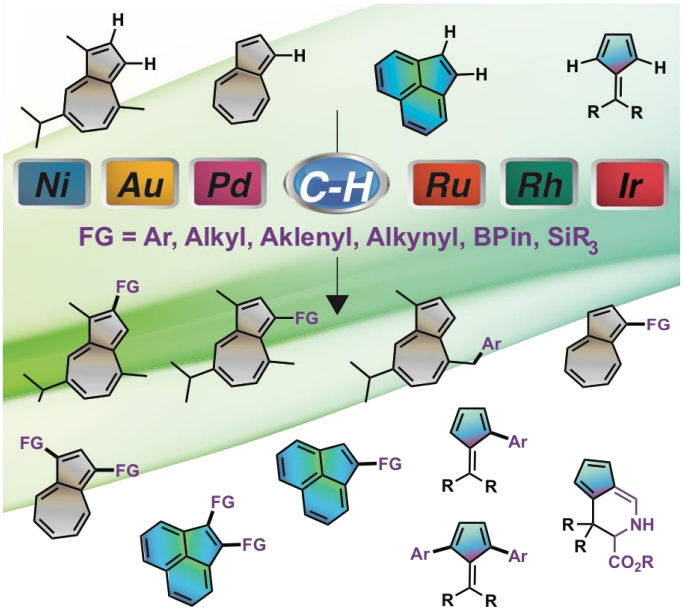
Xinzhe Shi,[a] Arpan Sasmal,[a] Jean-François Soulé,[a]* Henri Doucet[a]*

[a] X. Shi, A. Sasmal, Dr. J-F. Soulé, Dr. H. Doucet

Institut des Sciences Chimiques de Rennes, UMR 6226 CNRS-Université de Rennes 1 "Organométalliques, Matériaux et Catalyse", Campus de Beaulieu, 35042 Rennes, France.

Tel: +(33) 0223233206; +(33) 0223236384.

E-mail: jean-francois.soule@univ-rennes1.fr, henri.doucet@univ-rennes1.fr



Abstract: Azulenes, acenaphthylenes and fulvenes derivatives exhibit important physical properties useful in material chemistry and also biological properties. Since a two decades, the metal-catalyzed functionalization of such compounds, *via* the C-H bond activation of their 5-membered carbocyclic ring, proved to be a very convenient method for the synthesis of a wide variety of azulene, acenaphthylene and fulvene derivatives. For such reactions, there is no need to prefunctionalize the 5-membered carbocyclic rings. In this review, the progress in the synthesis of azulene, acenaphthylene and fulvene derivatives *via* the metal-catalyzed C-H bond activation of their 5-membered carbocyclic ring are summarized.

Accepted Manuscript

1. Introduction

2. Functionalization of azulenes

2.1 Arylation

2.2 Alkylation

2.3 Alkenylation

2.4 Alkynylation

2.5 Propargylation

2.6 Carbonylation

2.7 Borylation

2.8 Silylation

3. Functionalization of acenaphthylenes

3.1 Arylation

3.2 Alkylation

3.3 Alkynylation

4. Functionalization of fulvenes

4.1 Arylation

4.2 Annulation/isomerization

5. Conclusions and perspectives

6. References

1. Introduction

Azulenes, acenaphthylenes and fulvenes, which contain a 5-membrered carbocyclic ring, exhibit important physical and biological properties.[1] Azulene and also guaiazulene that feature the azulene skeleton (Fig. 1)[2] are constituents of pigments in the lactarius indigo mushrooms, and are also present in some corals. Guaiazulene is used as a cosmetic color additive, as a drug against ulcer, provides anti-inflammatory and pain relief benefits, and it also exhibits antioxidant and antiviral properties. It is also employed as a fragrance in some formulations, because of its rose-like scent. Acenaphthylenes derivatives are also useful structures. They have been employed as ligands, and can be easily transformed into acenaphthene derivatives.[3] Fulvenes are on the borderline between true aromatic compounds and conjugated dienes, and exhibit high polar character and charge transfer properties.[4] Some fulvene derivatives also display useful biological properties such as Iorfulvene, which is currently

Accepted Manuscript

evaluated against castration-resistant prostate cancer.[4c] They also exhibit important photophysical properties with possible photovoltaic applications.[4d,4e] Moreover, fulvenes are also often employed as ligands in organometallic chemistry.[4b] As a result, there is a continuing interest in the development of effective and simple methods to access azulene, acenaphthylene and fulvene derivatives.

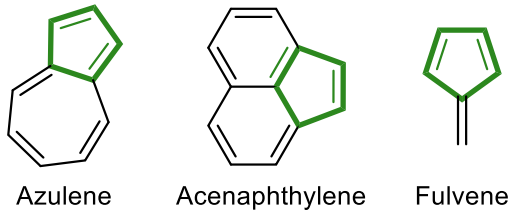


Figure 1

One of the most promising methods allowing the functionalization of azulenes, acenaphthylenes and fulvenes, is the metal-catalyzed C–H bonds activation/functionalization reaction. In recent years, several examples of such metal-catalyzed functionalization have been reported, providing simpler accesses to a wide variety of derivatives of such compounds. Moreover, in several cases, such as the alkynylation of azulenes or acenaphthylenes or the propargylation of azulenes, there are currently no alternative methods to metal-catalyzed C–H bonds activation/functionalization.

The metal-catalyzed functionalization of (hetero)aromatic C-H bonds has been covered in the last years by several reviews.[5] However, to the best of our knowledge, there is no review focusing on the catalyzed functionalization of the 5-membred ring of azulenes, acenaphthylenes and fulvenes. In this review, we summarize the developments concerning the intermolecular metal-catalyzed functionalization, *via* a C-H bond activation, of the 5-membred ring of azulenes, acenaphthylenes and fulvenes. In the first part, the synthesis of azulene derivatives *via* C-H functionalization shall be reviewed. In the second part, the metal-catalyzed C1- and/or C2-(hetero)arylations, -alkylations or -alkynylations of acenaphthylenes will be discussed. In the third part, the rare examples of Ag- and Pd-catalyzed functionalization of the 5-membred ring of fulvenes will be described. In the conclusion, the remaining challenges in the field are evoked.

2. Functionalization of azulenes

From the non-benzenoid aromatic compounds, azulene and guaiazulene, which are commercially available, several examples of metal-catalyzed functionalizations, *via* a C-H bond activation, have been described (Fig. 2). Both C1- and C2-positions of azulenes and C2- and C3-positions of guaiazulene

Accepted Manuscript

have been functionalized. In most cases, C-C bonds were formed *via* Pd- or Au-catalyzed arylations, Au- or Ni-catalyzed alkylations, Rh-catalyzed alkenylations, Ru- or Au-catalyzed propargylations reactions, or Pd-catalyzed carbonylations, but some Ir-catalyzed borylation and silylation reactions have also been reported.

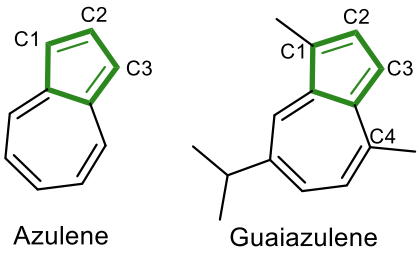
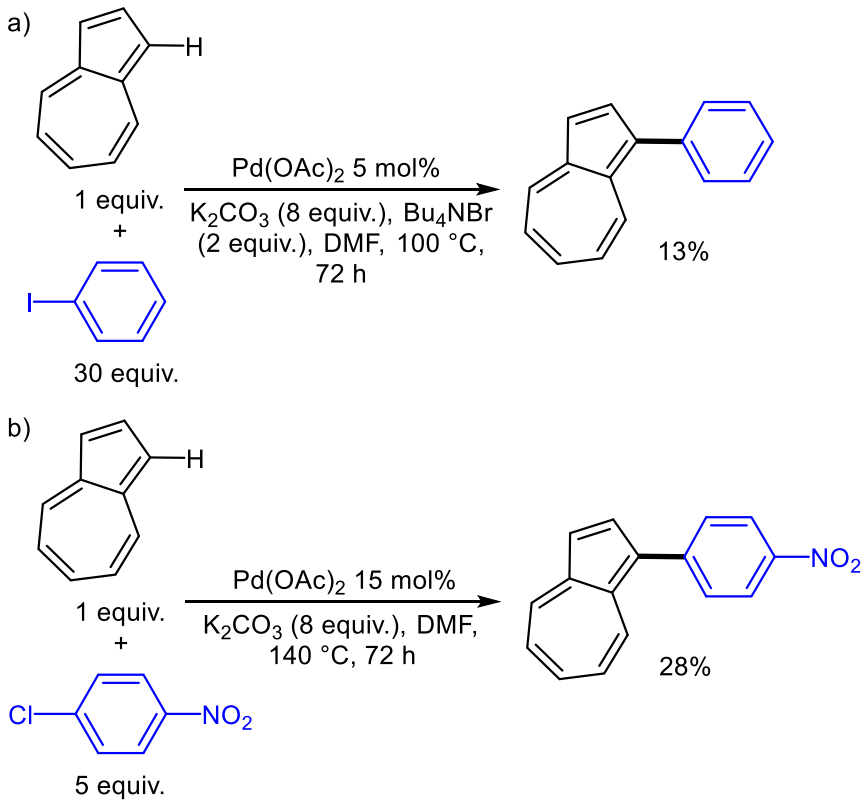


Figure 2

2.1 Arylation

The first example of metal-catalyzed functionalization of the 5-membered ring of azulene, *via* a C-H bond activation, was reported in 1997 by Dyker et al. (Scheme 1).[6] The reaction of azulene with 5 equiv. of iodobenzene using 5 mol% $Pd(OAc)_2$ catalyst and K_2CO_3 as base, gave the C1-arylated azulene in only 5% yield; whereas the use of 30 equiv. of iodobenzene gave 13% of this coupling product (Scheme 1, a). From azulene and 5 equiv. of 4-chloronitrobenzene, under quite similar reaction conditions, 1-(4-nitrophenyl)azulene was obtained in a higher 28% yield (Scheme 1, b).

Accepted Manuscript

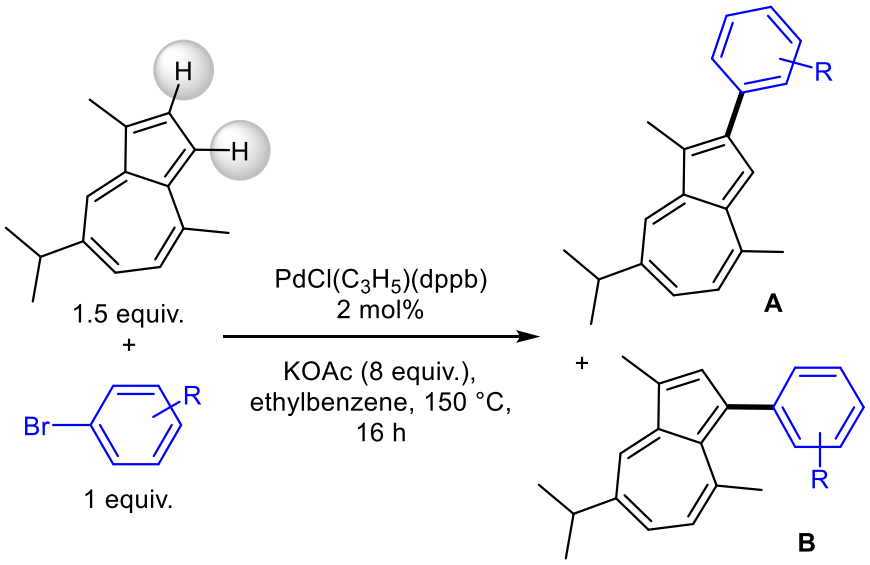


Scheme 1. Pd-catalyzed arylations at C1-position of azulene with aryl halides

Then, a few groups extended the arylation of azulenes using modified reaction conditions.[7-9] The Pd-catalyzed direct arylation of guaiazulene with a variety of aryl bromides has been reported by our group in 2013 (Schemes 2 and 3).[7] Both sp^2 and sp^3 C-H bonds of guaiazulene have been functionalized, as the nature of the cation of the base was found to allow the control of the regioselectivity of the arylation, giving rise to C2- or C3-arylated guaiazulenes and also to 4-benzylguaiazulenes. The coupling of guaiazulene with 4-bromobenzonitrile using 2 mol% $PdCl(C_3H_5)$(dppb) as catalyst, DMA as solvent and KOAc as base afforded a mixture of the C2- and C3-arylated guaiazulenes **A** and **B** in 15:85 ratio; whereas, the use of a less polar solvent such as ethylbenzene gave a mixture of **A** and **B** in a 53:47 ratio (Scheme 2). Better regioselectivities in favor of the formation of the C2-arylated guaiazulene were observed with 3- or 4-bromotoluene or bromobenzene to give the derivatives **A** in 54-56% yields. In both cases, the first step of the catalytic cycle is certainly the oxidative addition of the aryl bromide to a Pd(0) species to afford a Pd(II) intermediate. The arylation which takes place, in DMA, at the electron-rich guaiazulene C3-position suggests an electrophilic aromatic substitution mechanism from an electrophilic cationic Pd-species, although a concerted-metallation-deprotonation mechanism could not be ruled out. The non-polar solvent ethylbenzene certainly favors the formation of neutral Pd-species

Accepted Manuscript

and therefore Heck type mechanism with the formation of a Pd-C bond at guaiazulene C3-position and arylation at C2-position.



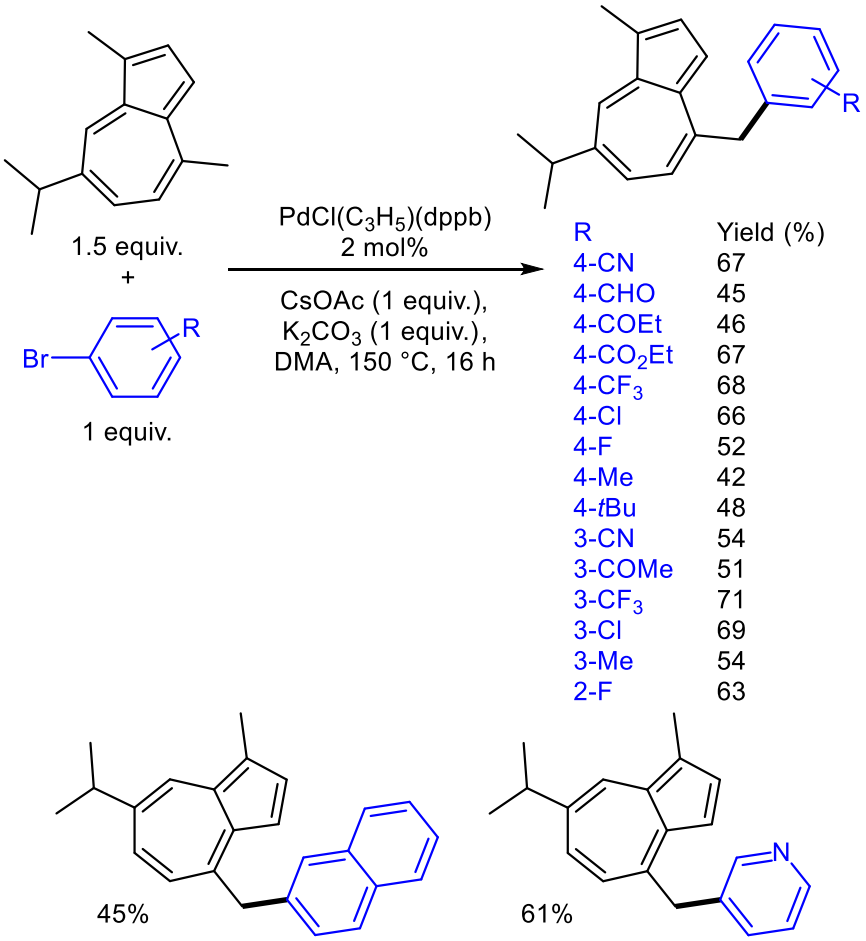
R	ratio **A**:**B**	Yield of **A** (%)
4-CN	53:47	38
4-CN	15:85	51 of **B***
4-Cl	77:23	53
4-F	77:23	51
4-Me	70:30	56
3-Me	76:24	54
H	75:25	56
3-Me	37:63	38 of **B***

* DMA as the solvent

Scheme 2. Pd-catalyzed arylations C2- or C3- positions of guaiazulene with aryl bromides

The use of a mixture of CsOAc/K_2CO_3 as base led to a complete modification of the regioselectivity of the arylation with an exclusive sp^3 C-H bond functionalization at C4-Me of guaiazulene to give 4-benzylguaiazulenes (Scheme 3).[7] This sp^3 C-H bond functionalization reaction tolerates various substituents such as formyl, acetyl, propionyl, ester, fluoro, trifluoromethyl, fluoro or even chloro on the aryl bromide and *N*-containing aryl bromides. Such 4-benzylguaiazulenes likely result from the formation of an allyl-Pd intermediate. The higher base concentration in solution due to the better solubility of CsOAc compared to KOAc might favor this reaction pathway.

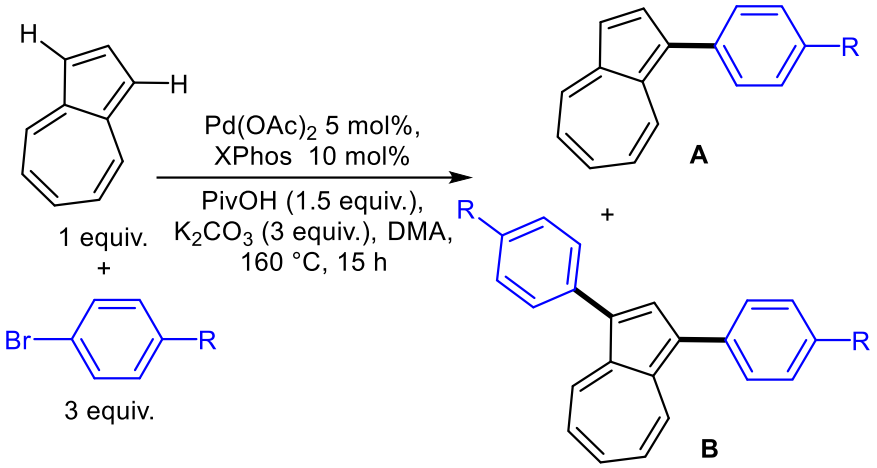
Accepted Manuscript



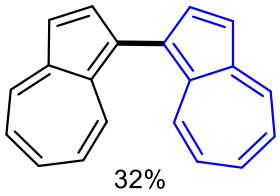
Scheme 3. Pd-catalyzed arylations at C4-Me of guaiazulene with aryl bromides

In 2016, Murai, Takai et al. reinvestigated the palladium-catalyzed direct arylation of azulenes (Scheme 4).[8] They succeeded to obtain better yields than Dyker (see scheme 1) in mono-C1-arylated azulenes using 5 mol% $Pd(OAc)_2$ associated to 10 mol% XPhos ligand as catalytic system and a mixture of PivOH and K_2CO_3 as base. The higher yields obtained using this procedure are probably due to the use of this mixture as base, which promotes concerted metallation deprotonation mechanism.[5p] Moreover, the addition of 3 equiv. of aryl bromide, 5 mol% catalyst and 10 mol% ligand to the reaction mixture after 8 h provided the C1,C3-diarylated azulenes in 51-62% yields. The reaction of azulene with 1-iodoazulene, under similar reaction conditions gave 1,1'-biazulene in 32% yield.

Accepted Manuscript



R	Yield in **A** (%)	Yield in **B** (%)
Me	39	26
OMe	35	32
H	43	31
CF_3	36	34
OMe*	8	51
H*	5	62
CF_3*	12	58
CN*	0	0



32%

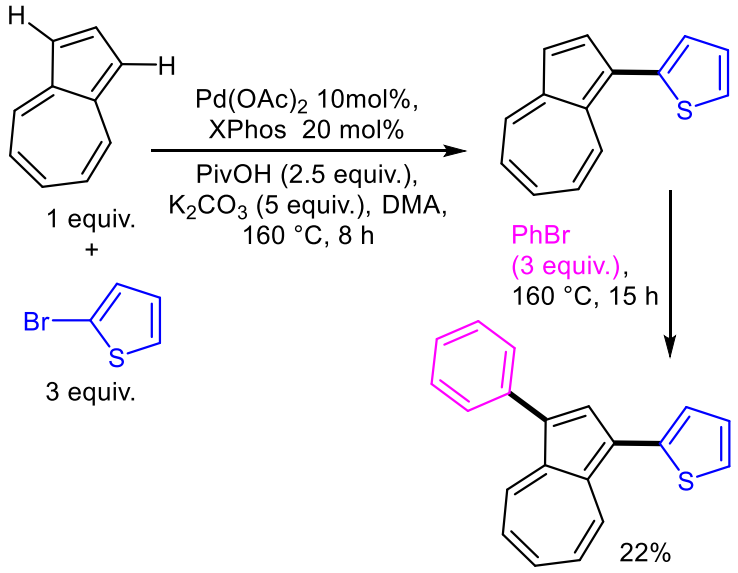
From 1-iodoazulene (5 equiv.), PivOH (2.5 equiv), K_2CO_3 (5 equiv).

*: PivOH (3 equiv), K_2CO_3 (6 equiv). After 8 h, additional ArBr (3 equiv), $Pd(OAc)_2$ (5 mol%), XPhos (10 mol%) were added and the reaction was stirred for 8 h.

Scheme 4. Pd-catalyzed arylations at C1-position of azulene with aryl bromides

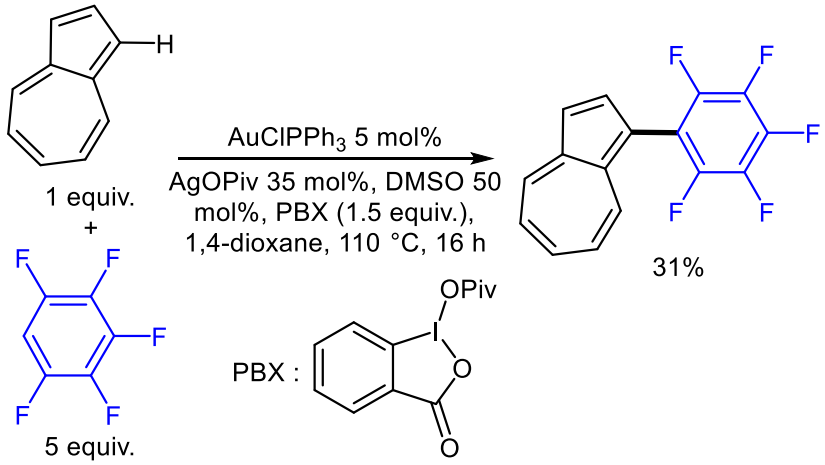
This group also prepared an unsymmetrically substituted 1,3-diarylazulene under slightly modified reaction conditions.[8] The one pot treatment of azulene with 2-bromothiophene (3 equiv.) followed by coupling with bromobenzene (3 equiv.) furnished 1-phenyl-3-(2-thienyl)azulene in 22% yield (Scheme 5).

Accepted Manuscript



Scheme 5. Pd-catalyzed arylations at C1- and C3-positions of azulene with (hetero)aryl bromides

In 2015, the gold-catalyzed oxidative cross-coupling of azulene with pentafluorobenzene *via* a double C−H bond activation has been described by Larrosa et al. (Scheme 6).[9] $AuClPPh_3$ (5 mol%) was employed as catalyst and 1-pivaloyloxy-1,2-benziodoxol-3(1*H*)-one (PBX) as the oxidant, affording 1-(perfluorophenyl)azulene, which was contaminated by traces of 1-iodo-3-(perfluorophenyl)azulene, in 31% yield. For this coupling, an excess of pentafluorobenzene (5 equiv.) was employed. The mechanism was not elucidated, but the substrate scope of such couplings appears to be consistent with Au(I) and Au(III) C−H bond activation steps.

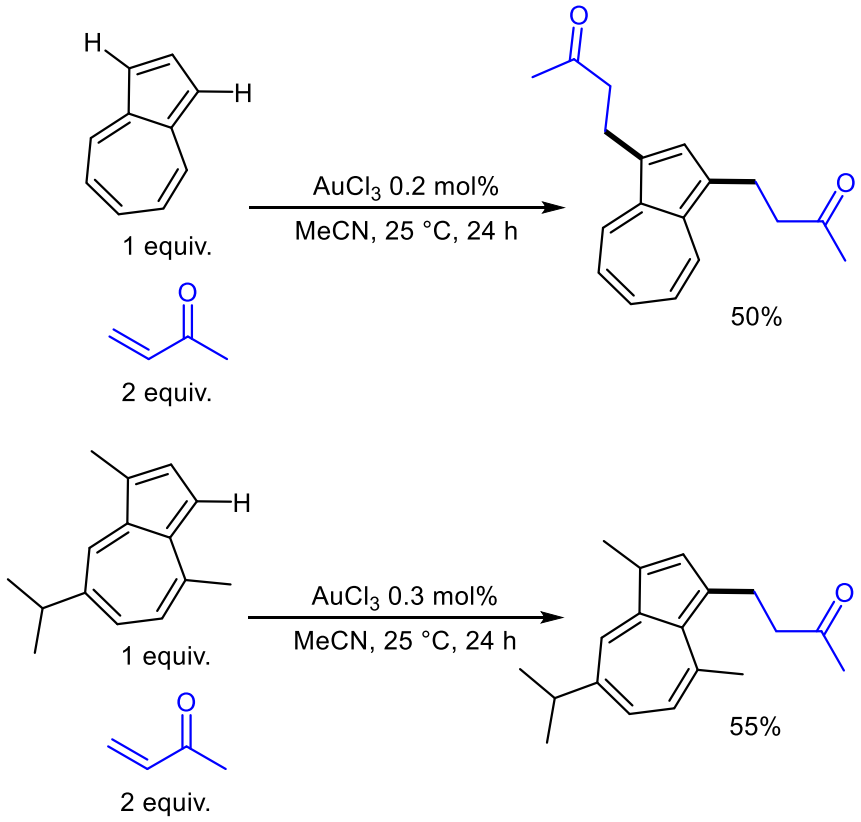


Scheme 6. Au-catalyzed arylation at C1-position of azulene with pentafluorobenzene

2.2 Alkylation

Accepted Manuscript

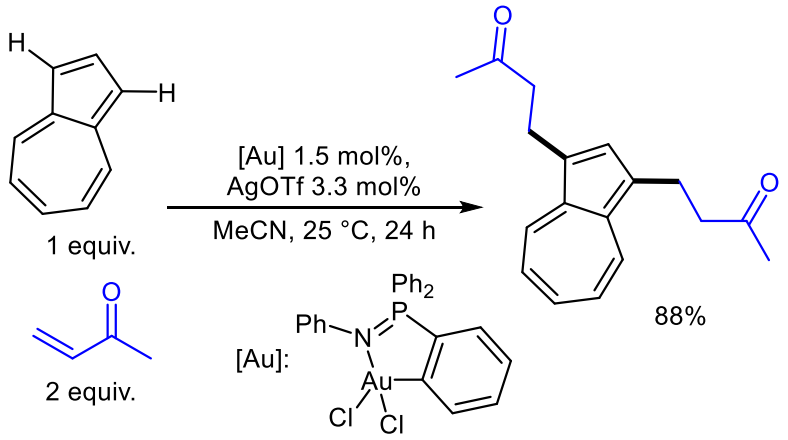
In 2003, Dyker, Hashmi et al. reported the $AuCl_3$ catalyzed addition of azulene and guaiazulene to methyl vinyl ketone at room temperature in moderate yields (Scheme 7).[10] According to the authors, such reactions probably proceed *via* Michael-type addition; however, they could not rule out a C-H bond activation step of the azulenes by the gold catalyst.



Scheme 7. Au-catalyzed alkylations at C1-position of azulene with methyl vinyl ketone

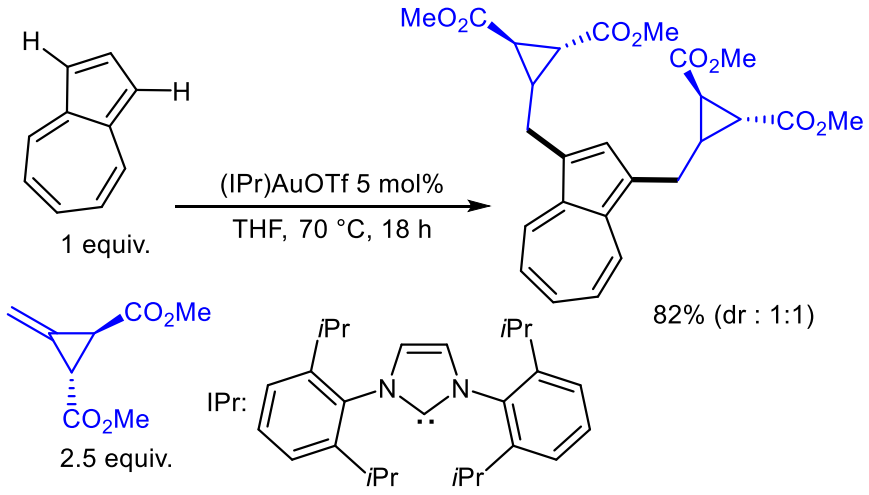
Four years later, Contel, Urriolabeitia et al. obtained a higher yield of 88% for the addition of azulene to methyl vinyl ketone using an organogold(III) iminophosphorane complexe as catalyst (Scheme 8).[11] They were not able to isolate a reaction intermediate to demonstrate that the reaction takes place by electrophilic C-H activation. However, as their cycloaurated complexes are much less acidic than $AuCl_3$, they assumed that a cyclometalated gold(III) cationic derivatives might be the catalytically active species in this addition reaction. The reaction would proceed *via* an electrophilic gold C-H bond activation of azulene as a first step.

Accepted Manuscript



Scheme 8. Au-catalyzed alkylation of azulene with methyl vinyl ketone

Widenhoefer et al. reported in 2016 that a cationic gold complex containing a *N*-heterocyclic carbene ligand catalyzes the intermolecular hydroarylation of a disubstituted methylenecyclopropane derivative with azulene (Scheme 9).[12] They didn't succeed to obtain the mono-alkylated azulene, but in the presence of 2.5 equiv. of the methylenecyclopropane derivative, the bis-alkylated azulene was obtained in good yield as a mixture of diastereoisomers (1:1). According to the authors, the selectivity of the reaction is consistent with a mechanism involving outer-sphere addition of the arene to a cis π-methylenecyclopropane complex, followed by protodeauration.

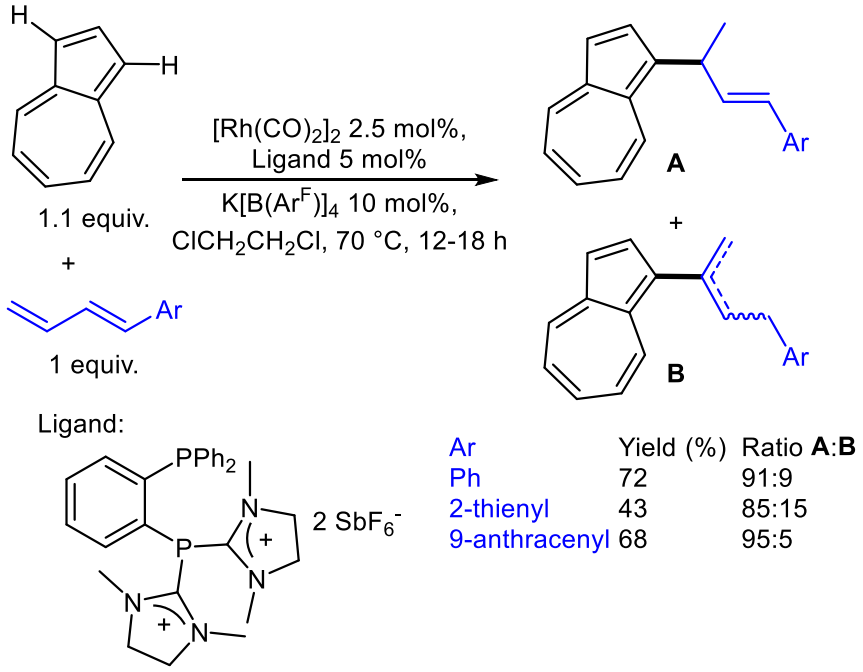


Scheme 9. Au-catalyzed alkylation of azulene with a methylenecyclopropane

The preparation of allyl-substituted azulenes by reaction of azulenes with conjugated dienes, catalyzed by a rhodium catalyst, has been described by Alcarazo et al. in 2017 (Scheme 10).[13] They obtained the desired hydroarylation products **A** in moderate to good yields and regioselectivities. However, in all cases, traces of other isomers (**B**) were observed by GC/MS or ^{1}H NMR analysis of the crude mixtures.

Accepted Manuscript

For such reactions, the use of 10 mol% of $KB(Ar^F)_4$ (potassium tetrakis(pentafluorophenyl)borate) as additive was crucial. This additive increases the solubility of the catalyst in the reaction medium by anion exchange.

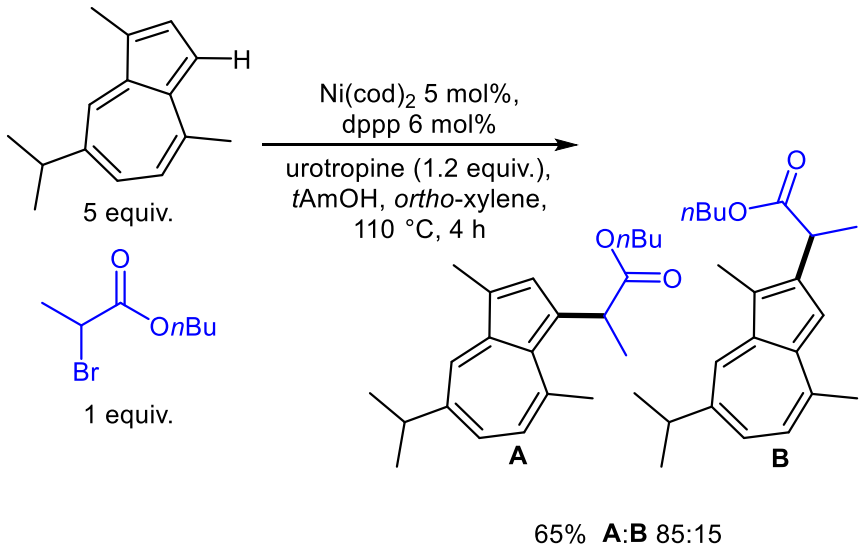


Ar	Yield (%)	Ratio **A**:**B**
Ph	72	91:9
2-thienyl	43	85:15
9-anthracenyl	68	95:5

Scheme 10. Rh-catalyzed alkylations of azulene with conjugated dienes

Hirano, Miura et al. developed in 2013 a nickel-catalyzed direct alkylation of electron-rich heterocycles with α-bromocarbonyl compounds (Scheme 11).[14] They extended their procedure to guaiazulene using *n*-butyl 2-bromopropanoate as alkyl source. The reaction was successful, but a mixture of two regioisomers was formed in a 85:15 ratio. The alkylation at position 1 was favored. For this coupling, the authors postulated an homolytic radical aromatic substitution mechanism. A single electron transfer from a Ni(I) species would give an alkyl radical intermediate with the generation of a Ni(II) complex. Then, addition of this alkyl radical intermediate to azulene proceeds through a SOMO/HOMO interaction, with the formation of a C-C bond.

Accepted Manuscript



Scheme 11. Ni-catalyzed alkylation of azulene with a 2-bromopropanoate

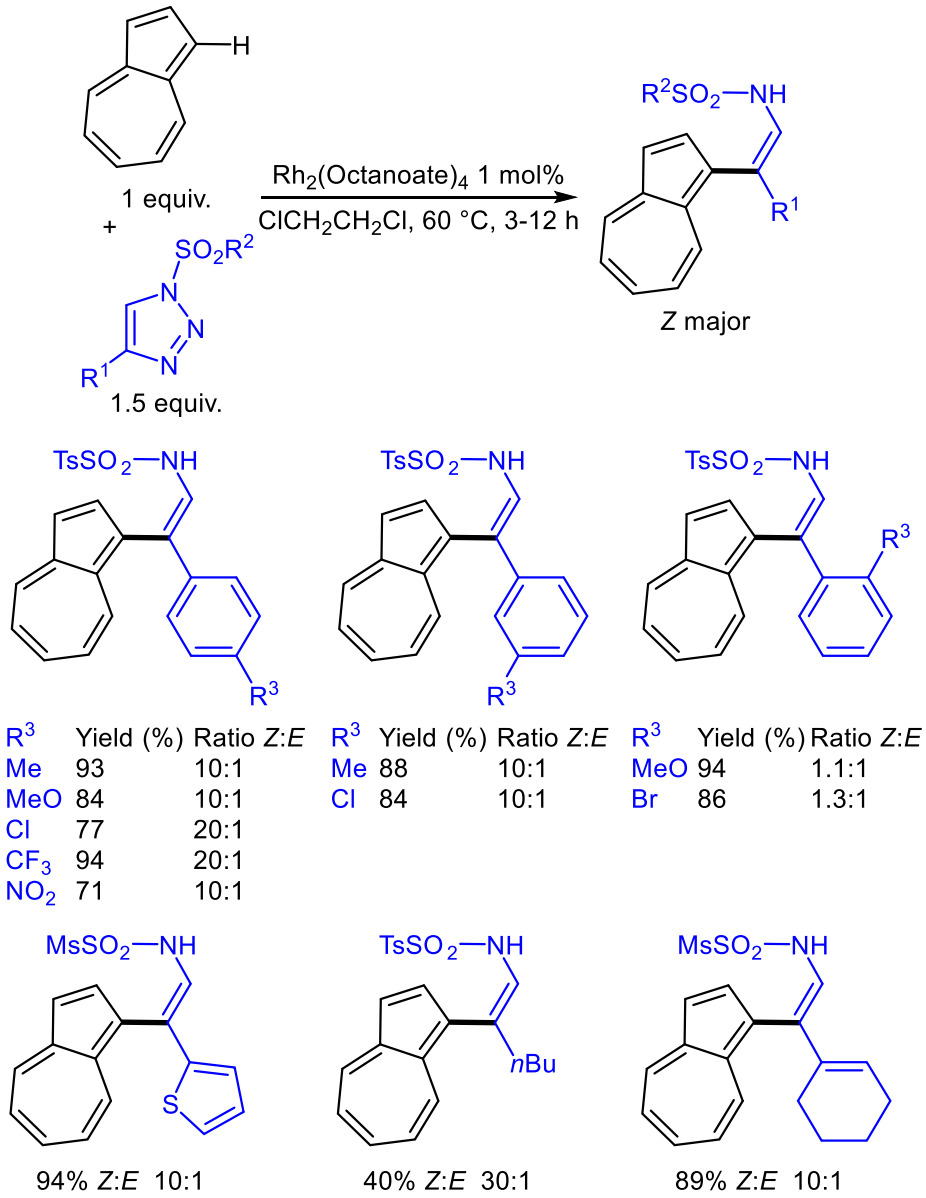
2.3 Alkenylation

In 2014, Lee et al. developed a rhodium-catalyzed stereoselective *N*-sulfonylaminoalkenylation of azulenes using *N*-sulfonyl-1,2,3-triazoles as coupling partners (Scheme 12).[15a] With 1 mol% Rh_2(Octanoate)$_4$ catalyst in CH_2Cl_2 at 60 °C under air, the (*Z*)-*N*-sulfonylaminoalkenylated azulenes were stereoselectively obtained in high yields. The electronic variation of substituents on the aryl moiety of 4-aryl-1-tosyl-1,2,3-triazoles had little effect on the stereoselectivity and yield. In contrast, introduction of bromo- or methoxy-substituents at *ortho*-position on the triazole phenyl ring decreased the stereoselectivities due to steric reasons. The reactivity of guaiazulene was similar to azulene (Scheme 13, a). Under the same reaction conditions, guaiazulene gave exclusively the (*Z*)-stereoisomers of the 3-alkenylated guaiazulenes (Scheme 13, a). A possible mechanism for this reaction was reported. First, a reversible ring-chain tautomerization of *N*-sulfonyl-1,2,3-triazole would provide an α-diazo imine. The reaction of this α-diazo imine with Rh(II) would give an α-imino Rh(II) carbenoid, with the liberation of N_2. Then, the nucleophilic addition of azulene to the electrophilic carbene center of this Rh intermediate affords a Rh-bound zwitterionic intermediate. Anionic rhodium would release an electron pair, which moves into the imine moiety, making the nitrogen atom basic enough to abstract an allylic proton and to afford the alkenylated azulene with regeneration of the Rh(II) catalyst.

To demonstrate the synthetic potential of these *N*-sulfonylaminoalkenylated azulenes, this group also developed a synthetic method to prepare azulen-1-yl ketones *via* the oxidative cleavage of the C=C double bond of these 1-alkenylazulenes (Scheme 13, b).[15b] For this C=C bond cleavage, a mixture of the

Accepted Manuscript

1-alkenylazulenes and Cs_2CO_3 was heated at 70 °C in toluene under air and natural sunlight. The azulene-1-yl ketones were obtained in high yields.



R^3	Yield (%)	Ratio *Z*:*E*
Me	93	10:1
MeO	84	10:1
Cl	77	20:1
CF_3	94	20:1
NO_2	71	10:1

R^3	Yield (%)	Ratio *Z*:*E*
Me	88	10:1
Cl	84	10:1

R^3	Yield (%)	Ratio *Z*:*E*
MeO	94	1.1:1
Br	86	1.3:1

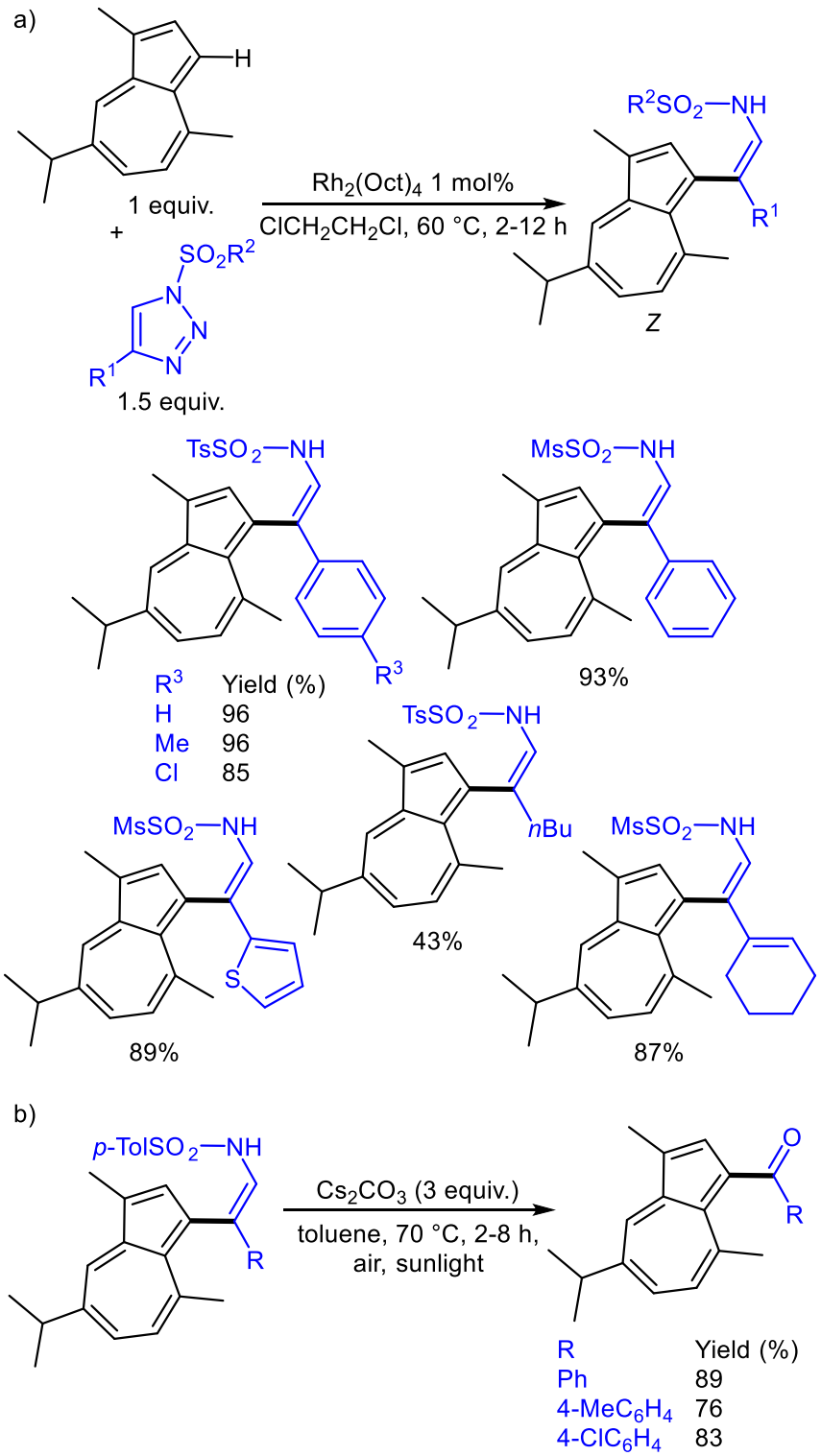
94% *Z*:*E* 10:1

40% *Z*:*E* 30:1

89% *Z*:*E* 10:1

Scheme 12. Rh-catalyzed alkenylations of azulene with *N*-sulfonyl-1,2,3-triazoles

Accepted Manuscript

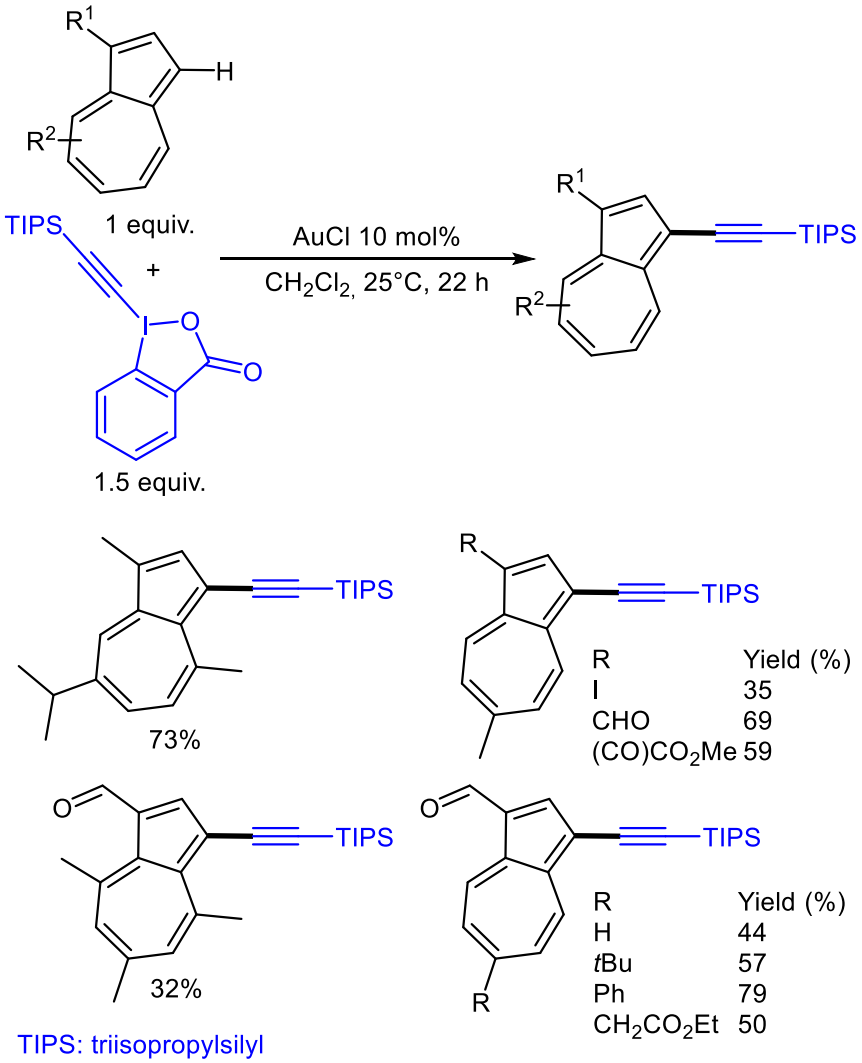


Scheme 13. Rh-catalyzed alkenylations of guaiazulene with *N*-sulfonyl-1,2,3-triazoles

2.4 Alkynylation

Accepted Manuscript

The synthesis of alkynylated azulenes *via* purely organic chemistry has not been reported. Very recently, Tolnai, Novak et al. developed a procedure for the alkynylation of azulenes (Scheme 14).[16] For this reaction, they employed an hypervalent iodonium reagent associated to 10 mol% AuCl as catalyst with CH_2Cl_2 as the solvent. Guaiazulene gave regioselectively the 3-alkynylated guaiazulene in 73% yield. They also employed several azulene derivatives containing formyl, iodo, alkyl or phenyl substituents. For example, some 1-formylazulenes were alkynylated at position 3 in 32-79% yields.



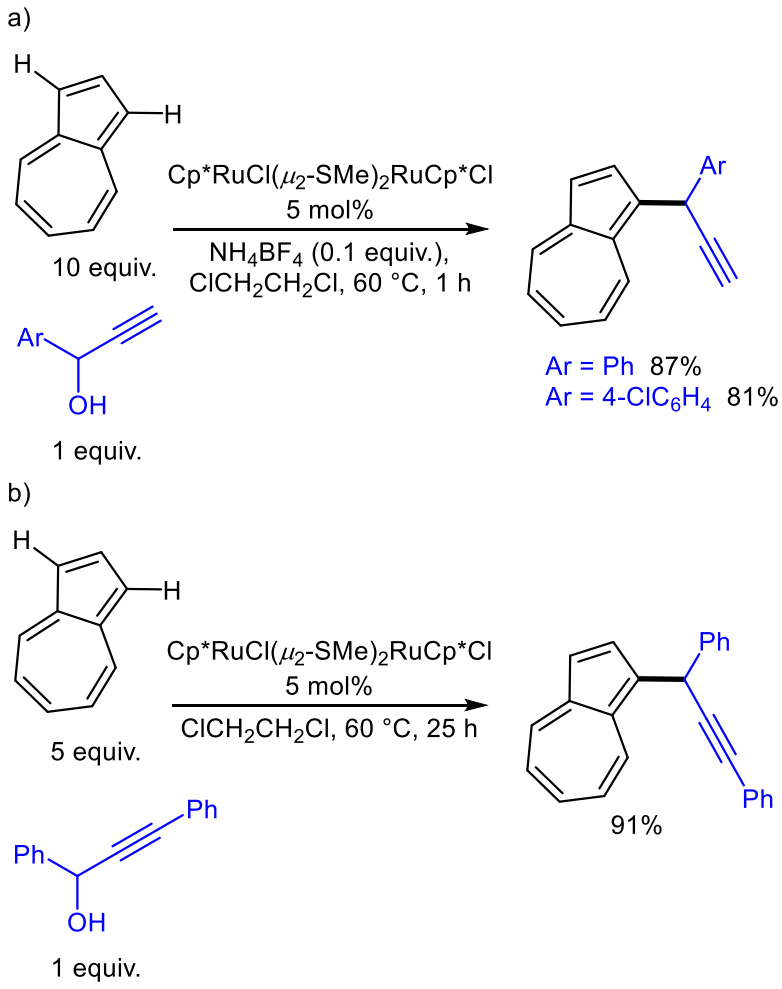
Scheme 14. Au-catalyzed alkynylations of azulenes

2.5 Propargylation

The introduction of propargyl units on azulenes *via* organic chemistry has not been described. The ruthenium-catalyzed propargylation of azulene with propargylic alcohols has been reported by Hidai, Uemura et al. in 2002 (Scheme 15, a).[17a,17b] The reaction proceeds *via* the formation of an allenylidene

Accepted Manuscript

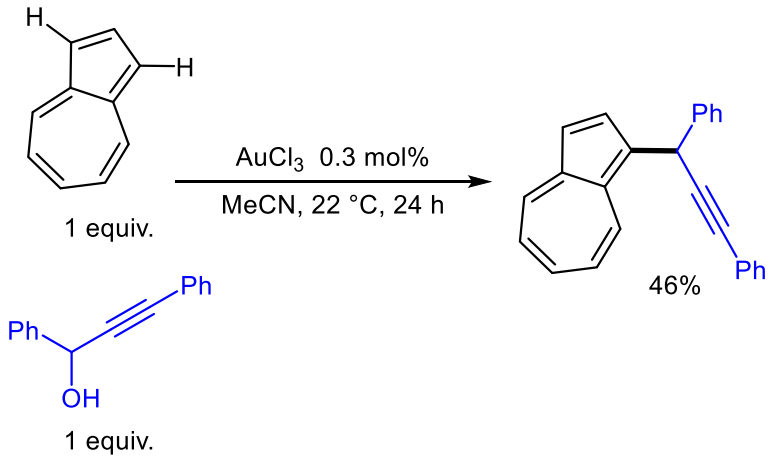
ruthenium complex to afford 1-(1-arylprop-2-yn-1-yl)azulenes in good yields. The mono-propargylation was observed; however, it should be mentioned that, a huge excess of azulene (10 equiv.) was employed. One year later, they extended this reaction to an internal acetylene derivative (Scheme 15, b).[17c] According to the authors, the reaction with the propargyl alcohols containing an internal acetylene unit (Scheme 15, b) may proceed *via* a (η-propargyl)ruthenium species. An electrophilic attack of the (η-propargyl)ruthenium complexes on azulene would afford the propargylated azulene. Conversely, the propargylation of azulene with the propargyl alcohols containing terminal acetylenes (Scheme 15, a) would proceed *via* an electrophilic attack of the cationic Cγ atom in the allenylidene intermediate. It should be mentioned that the introduction of propargyl units on azulenes *via* organic chemistry has not been described.



Scheme 15. Ru-catalyzed propargylations of azulene with propargyl alcohols

Accepted Manuscript

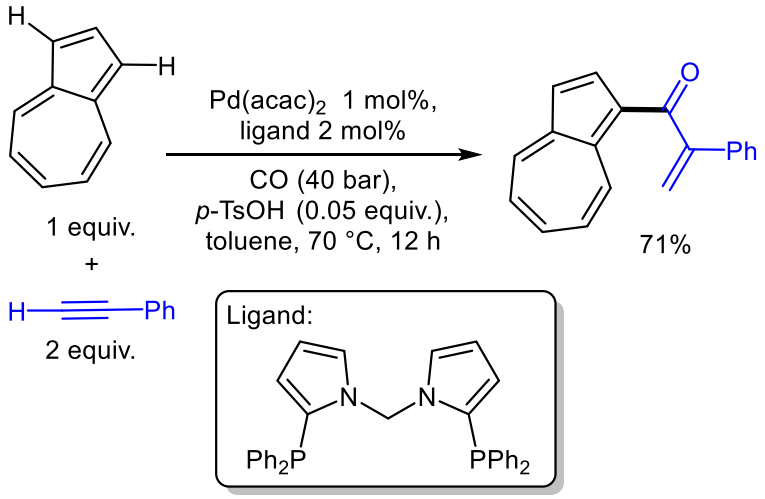
In 2006, Dyker et al. reported that a low loading of $AuCl_3$ using acetonitrile as the solvent at 22 °C also promotes the 1-propargylation of azulene (Scheme 16).[18] The mono-propargylation product was obtained in 46% yield from an equimolar mixture of azulene and the propargyl alcohol derivative.



Scheme 16. Au-catalyzed propargylation of azulene with a propargyl alcohol

2.6 Carbonylation

Very recently, Beller et al. reported the Pd-catalyzed Markovnikov carbonylation of phenylacetylene with azulene to give the corresponding branched α,β-unsaturated ketone in 71% yield and excellent regioselectivity (branched/linear 99:1) (Scheme 17).[19] This C-H carbonylation reactions regioselectively occurred at position 1 on azulene. For this reaction, which was conducted under 40 bars of CO, $Pd(acac)_2$ complex was associated to the diphosphine ligand [bis(2-(diphenylphosphanyl)-1*H*-pyrrol-1-yl)methane] as catalyst.



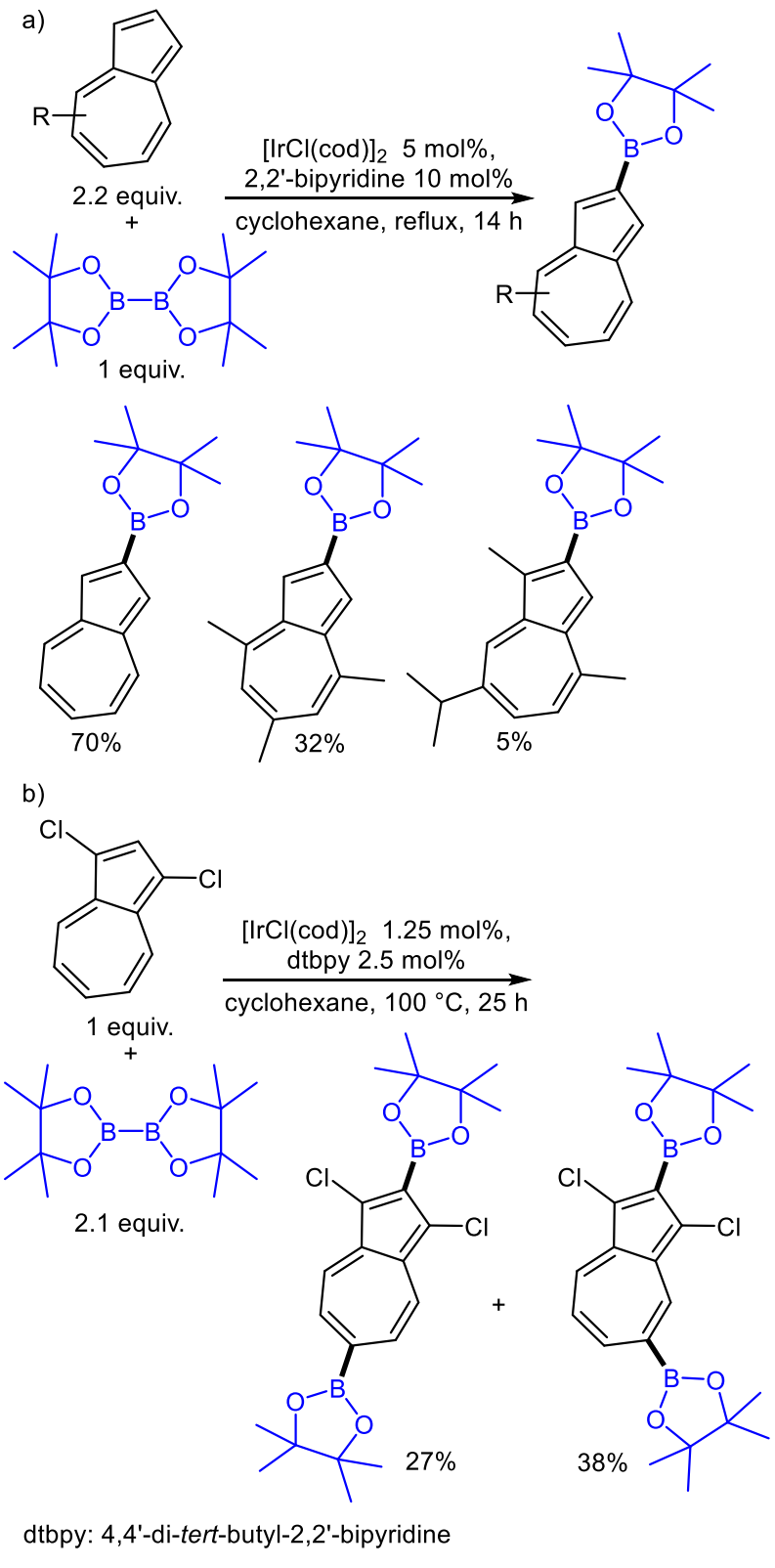
Scheme 17. Pd-catalyzed carbonylation of azulene with phenylacetylene and carbon monoxide

Accepted Manuscript

2.7 Borylation

Murafuji, Sugihara et al. described in 2003 that 4,4,5,5-tetramethyl-1,3,2-dioxaborolanyl group could be directly introduced at the 2-positions of azulenes with high regioselectivities, *via* iridium-catalyzed C−H bond activation reactions (Scheme 18, a).[20a] The formation of small amounts of C1-borylated azulenes was also observed. The site selectivity appears to be governed by the formation of a π complex between the azulene five-membered ring and iridium in preference to the azulene seven-membered ring. Then, the more electron-poor 2-position in the azulene five membered ring is borylated. The substrate scope appears to be very limited. Steric effect is an important factor, as azulenes bearing methyl groups at 1- or 4-positions such as guaiazulene are converted into the 2-borylated products in low yields, and 1,3-di-*tert*-butylazulene was recovered. Moreover, 6-formylazulene, 6-(hydroxymethyl)azulene and 1-(trifluoroacetyl)azulene resulted in the recovery of the starting azulenes. This group also studied the Ir-catalyzed polyborylation of azulenes.[20b] Azulene reactivity was found to decrease in the following order: 2-position > 1,3-positions > 6-position > 5,7-positions. In most cases, they obtained mixtures of polyborylated azulenes in low to moderate yields (Scheme 18, b).

Accepted Manuscript

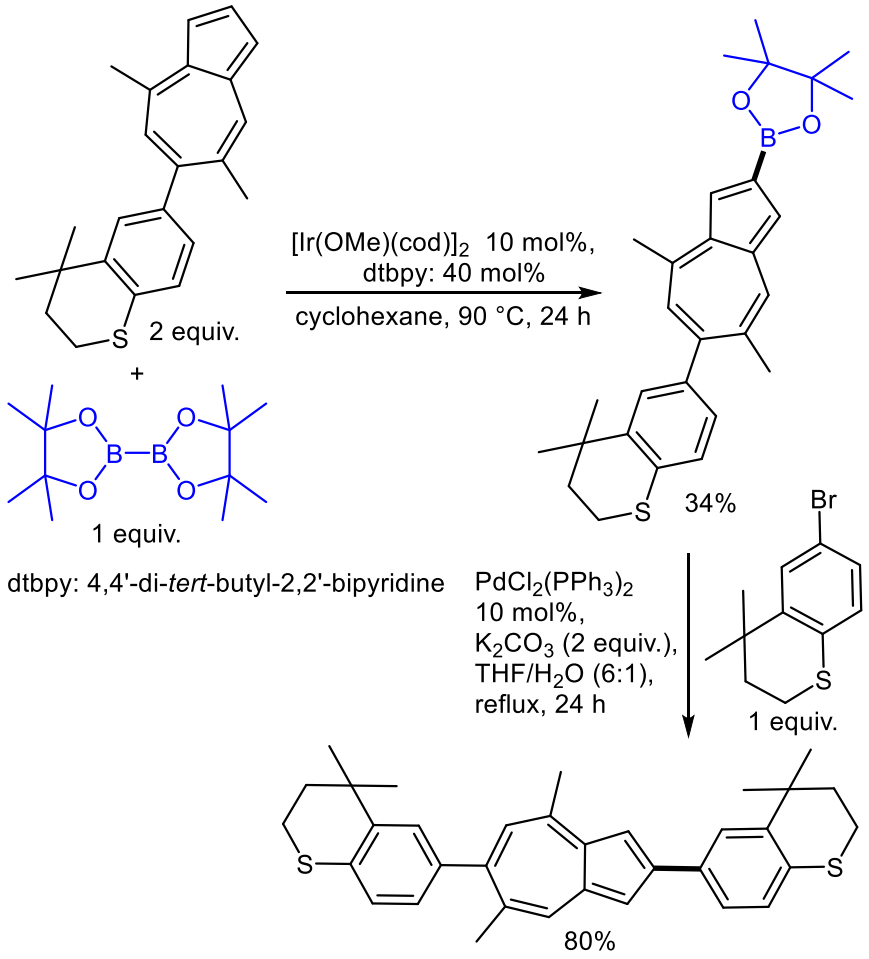


dtbpy: 4,4'-di-*tert*-butyl-2,2'-bipyridine

Scheme 18. Ir-catalyzed borylation at C2-position of an azulene

Accepted Manuscript

Although iridium-catalyzed borylation of azulene affords moderate yields in 2-borylated azulenes, it was employed in 2014 by Venkataraman, Campos et al. for the synthesis of azulene derivatives to study the effects of quantum interference through single-molecule conductance measurements.[21] The reaction of a 4,7-dimethyl-6-arylazulene with bis(pinacolato)diboron in the presence of an iridium catalyst gave the 2-borylated azulene in 34% yield (Scheme 19). Then, a Suzuki-coupling reaction with an aryl bromide provides the 2-arylated azulene in 80% yield. Murafuji, Tsunashima et al. also employed this synthetic pathway in 2015 to prepare a 2-(2-pyridyl)azulene derivative;[22a] and very recently, Murai, Takai et al. also employed this methodology for the access to azulene-fused linear polycyclic aromatic hydrocarbons with small bandgap.[22b]

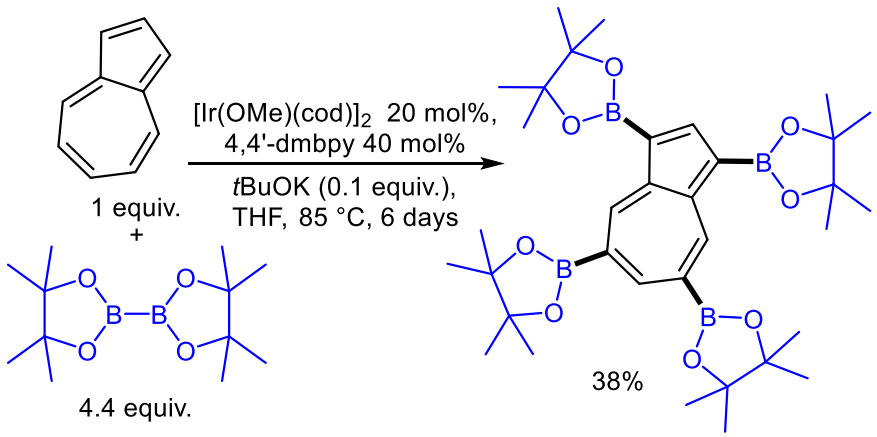


Scheme 19. Ir-catalyzed borylation at C2-position of an azulene followed be Suzuki coupling

In 2015, Scott et al. studied the iridium-catalyzed tetra-borylation of azulene.[23] They discovered that the products of kinetically controlled borylations can be equilibrated by running the reaction for a long time at 85 °C in the presence of *t*BuOK as base and high catalyst loadings. When 4.4 equiv. of $B_2(pin)_2$ are

Accepted Manuscript

used under these equilibrating conditions, 1,3,5,7-tetraborylation can be achieved in 38% yield (Scheme 20).



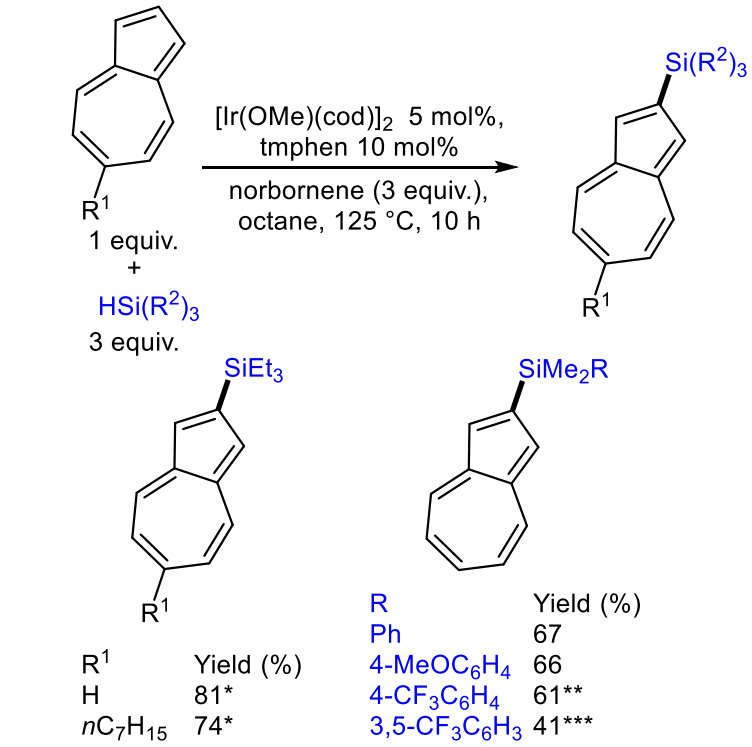
4,4'-dmbpy: 4,4'-dimethyl-2,2'-bipyridine

Scheme 20. Ir-catalyzed polyborylation of azulene

2.8 Silylation

The iridium-catalyzed C2-silylation of azulene derivatives has been described in 2015 by Murai, Takai et al. (Scheme 21).[24] The reaction of 3 equiv. of triethylsilane with azulene using 5 mol% of $[Ir(OMe)(cod)]_2$ associated to a phenanthroline ligand as catalytic system and 3,3-dimethyl-1-butene as hydrogen acceptor gave the 2-silylated azulene in 81% yield. The reaction is not limited to the use of triethylsilane, as with a set of dimethyl(aryl)silanes, they also obtained the 2-silylated azulenes in good yields. In several cases, norbornene was used as hydrogen acceptor. On the contrary, dihydrosilanes, including Et_2SiH_2, Ph_2SiH_2, and $PhMeSiH_2$, were not applicable. The use of $[Rh(OMe)(cod)]_2$ in place of the iridium catalyst was also ineffective.

Accepted Manuscript



R^1	Yield (%)
H	81*
nC_7H_{15}	74*

R	Yield (%)
Ph	67
4-$MeOC_6H_4$	66
4-$CF_3C_6H_4$	61**
3,5-$CF_3C_6H_3$	41***

tmphen: 3,4,7,8-tetramethyl-1,10-phenanthroline

*: 3,3-dimethyl-1-butene instead of norbornene, cyclohexane, 100 °C, 4 h

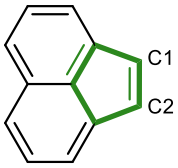
**: 24 h

***: 150 °C, 24 h

Scheme 21. Ir-catalyzed silylations at C2-position of azulenes

3. Functionalization of acenaphthylenes

Acenaphthylene is a commercially available compound (Fig. 3). The extent of aromaticity of the five-membered ring in the acenaphthylene molecule is very small,[3b] and both C1- and C2-positions of acenaphthylene can be functionalized *via* Pd- or Rh-catalyzed coupling reactions. However, so far, only a few examples of arylations and two examples of Pd-catalyzed alkylation and alkynylation of acenaphthylene have been reported.



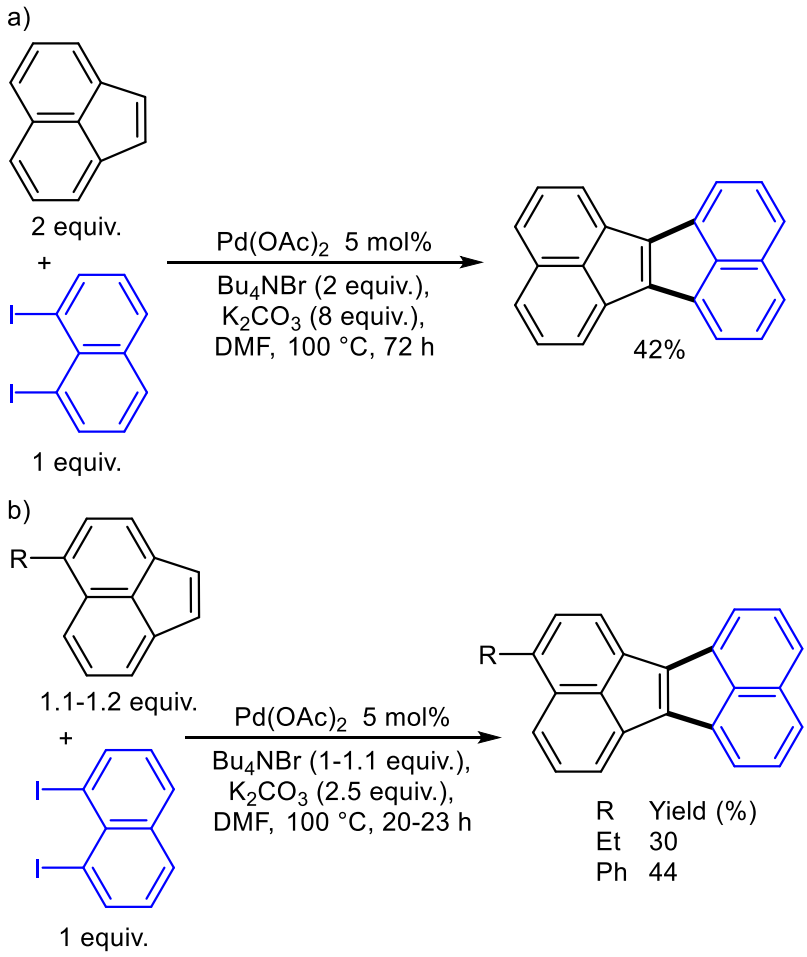
Acenaphthylene

Figure 3

Accepted Manuscript

3.1 Arylation

The first example of Pd-catalyzed direct arylation of acenaphthylene was reported in 1991 by Dyker (Scheme 22, a).[25,26] The reaction of 1,8-di(iodo)naphthalene with acenaphthylene in the presence of 5 mol% $Pd(OAc)_2$ / Bu_4NBr as catalytic system gave acenaphtho[1,2-*a*]acenaphthylene in 42% yield; whereas, without Bu_4NBr, the yield was only 29%. In 1999, Nakayama et al. employed Dyker's procedure to prepare 5-substituted acenaphtho[1,2-*a*]acenaphthylenes (Scheme 22, b).[27] Both ethyl- and phenyl-substituents were tolerated affording the coupling products in 30% and 44% yields, respectively.

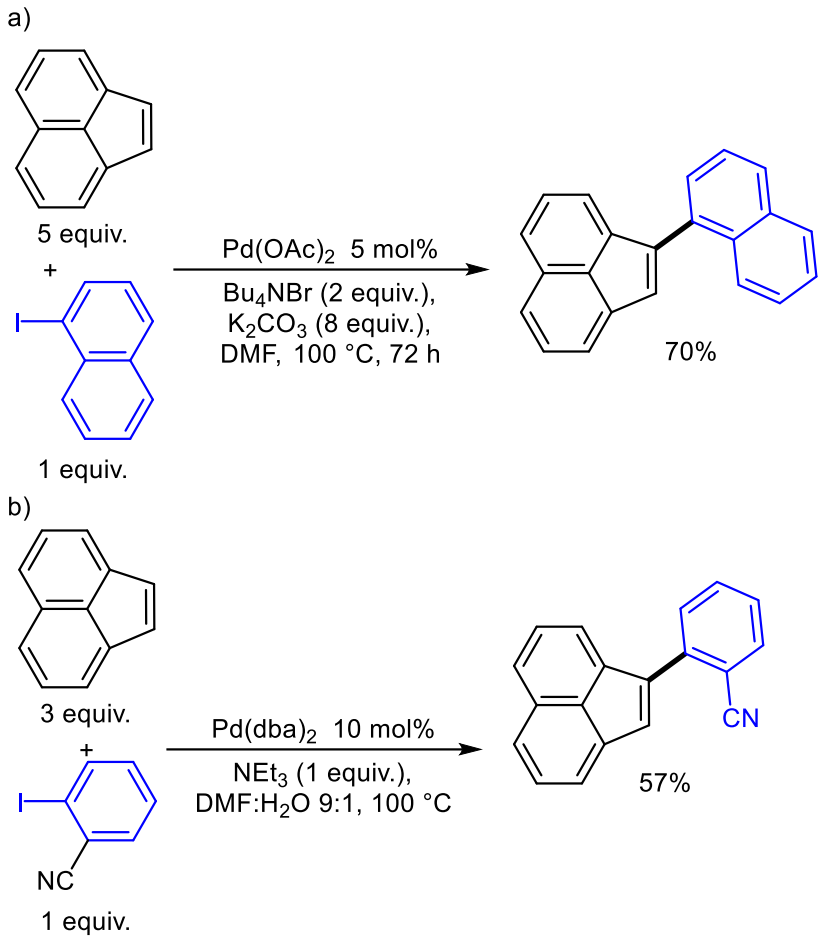


Scheme 22. Pd-catalyzed arylations of acenaphthylenes with an aryl iodide

Dyker also studied the C1-arylation of acenaphthylene.[26] Under the same reaction conditions he employed in scheme 22, top, but using 5 equiv. of acenaphthylene with 1 equiv. of 1-iodonaphthalene as aryl source, 1-(naphthalen-1-yl)acenaphthylene was formed in 70% yield (Scheme 23, a). More recently, he reported that the reaction of acenaphthylene with 9-bromoanthracene, under similar reaction condition, allows the preparation of 9-(acenaphthylen-1-yl)anthracene in 84% yield.[28] Larock et al. also

Accepted Manuscript

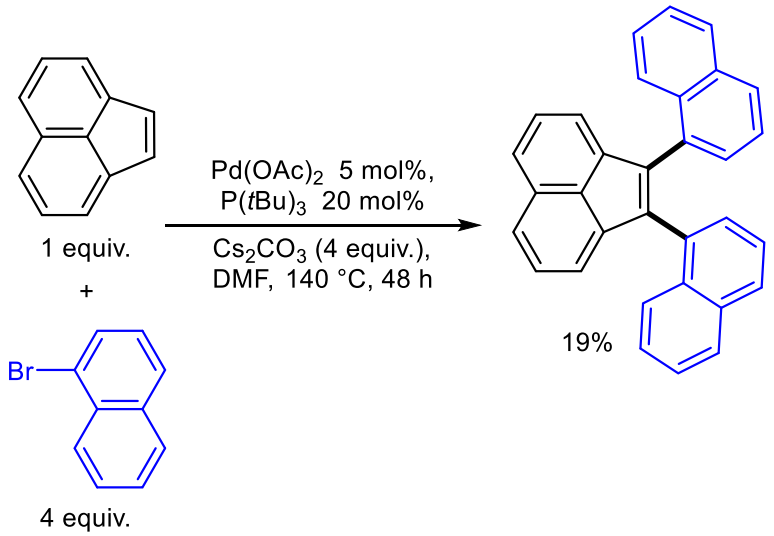
reported a procedure for the C1-arylation of acenaphthylene (Scheme 23, b).[29] They employed $Pd(dba)_2$ as catalyst and NEt_3 as base, and obtained 1-(2-cyanophenyl)acenaphthylene in 57% yield.



Scheme 23. Pd-catalyzed arylations of acenaphthylene with aryl iodides

In 2007, Dyker et al. also reported that the one pot Pd-catalyzed 1,2-diarylation of acenaphthylene proceeds in 19% yield in the presence of a large excess (4 equiv.) of 1-bromonaphthalene as aryl source (Scheme 24).[30] For this reaction $Pd(OAc)_2$ was associated to the electron-rich phosphine ligand P(*t*Bu)$_3$.

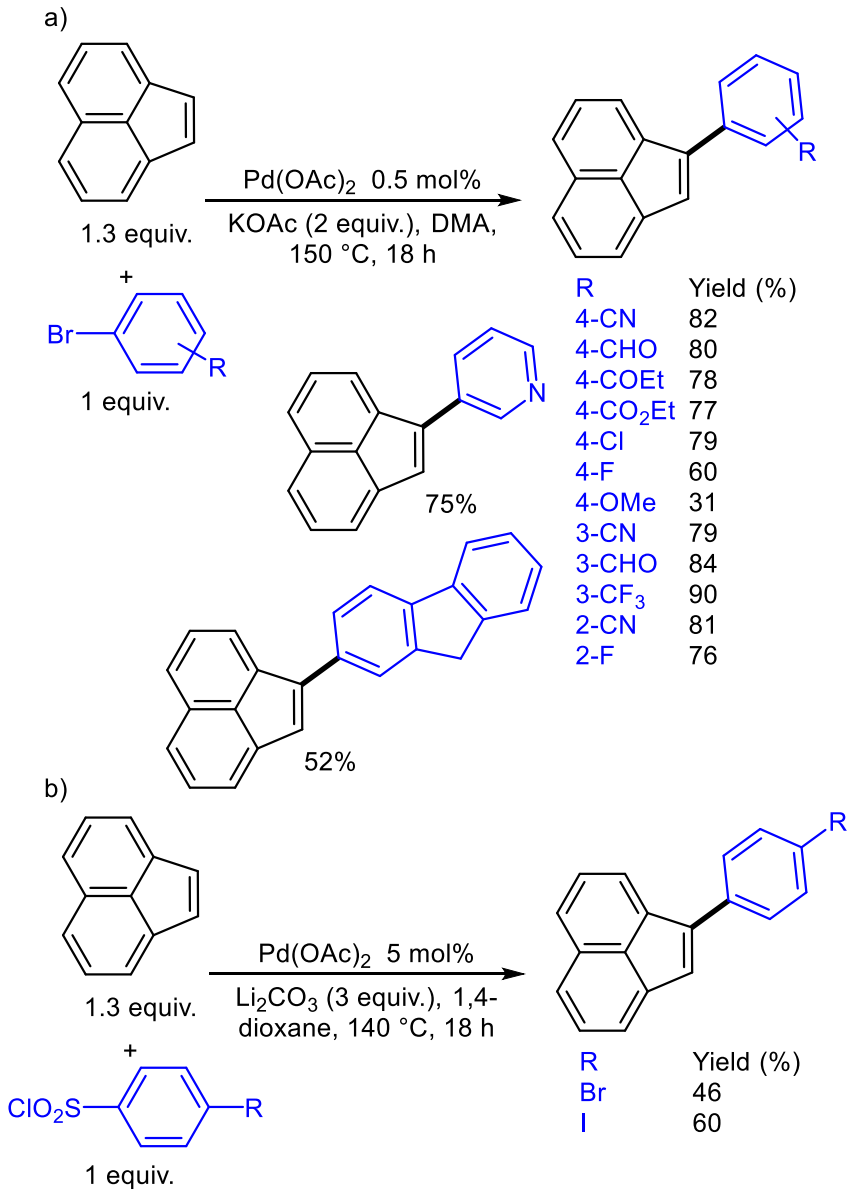
Accepted Manuscript



Scheme 24. Pd-catalyzed diarylation of acenaphthylene with an aryl bromide

Very recently, our group reinvestigated the Pd-catalyzed direct arylation of acenaphthylene.[31] We demonstrated that this reaction can be performed using either aryl bromides or benzenesulfonyl chlorides as aryl sources in the presence of phosphine-free $Pd(OAc)_2$ catalyst without additives. First, we described the C1-arylation of acenaphthylene with a wide variety of aryl bromides using only 0.5 mol% $Pd(OAc)_2$ catalyst, KOAc base in DMA. The reaction afforded regioselectively the C1-arylated acenaphthylenes in high yields (Scheme 25, a). Our group also investigated the coupling of acenaphthylene with 4-bromo- and 4-iodo-benzenesulfonyl chlorides (Scheme 25, b). Using 5 mol% $Pd(OAc)_2$ catalyst, Li_2CO_3 base in 1,4-dioxane, the C1-arylated acenaphthylenes were obtained in satisfactory yields without cleavage of the C-Br and C-I bonds, allowing further transformations.

Accepted Manuscript



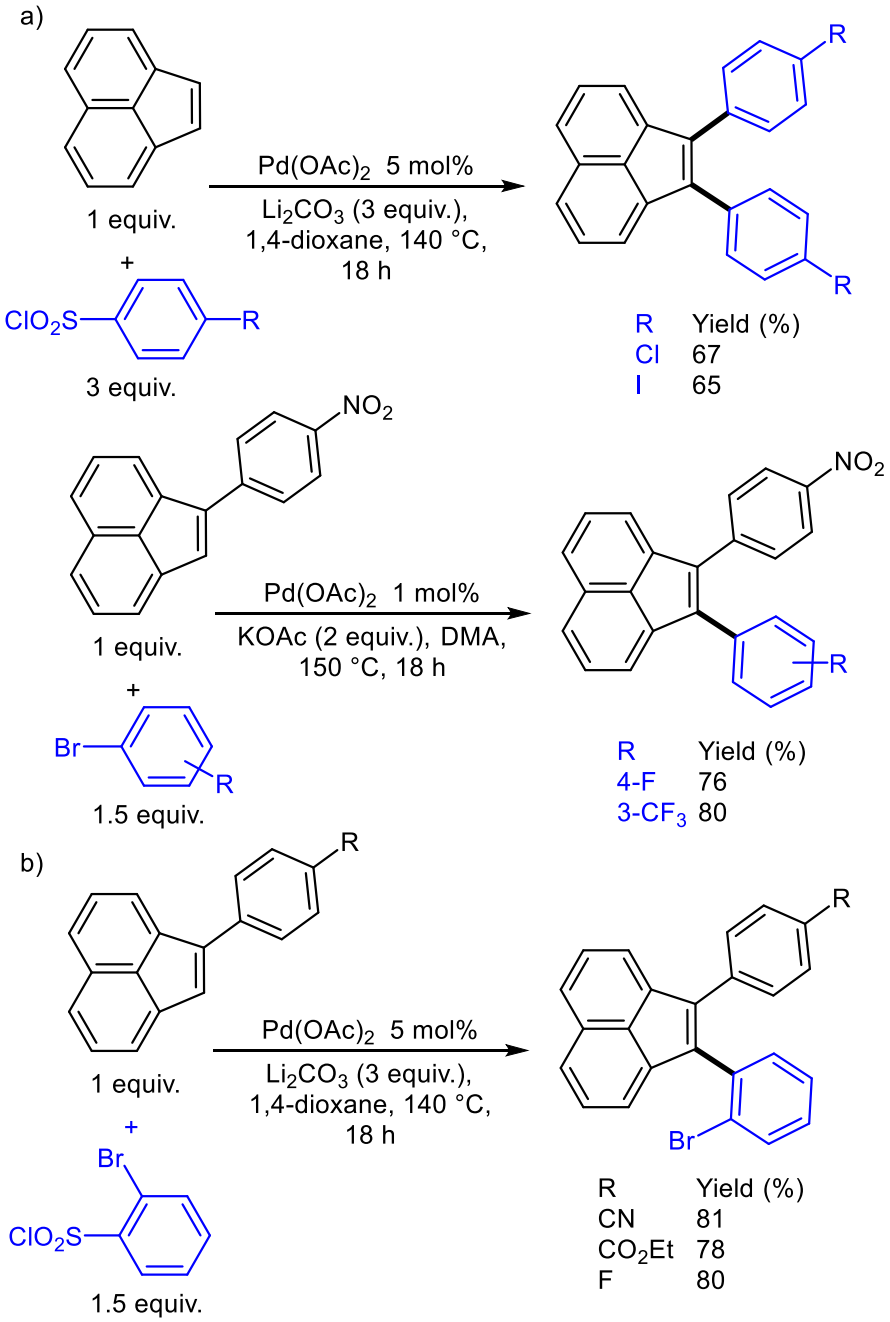
Scheme 25. Pd-catalyzed arylations of acenaphthylene with aryl bromides or benzenesulfonyl chlorides

Our group also reported that, under the same reaction conditions than for C1-arylation of acenaphthylene, but with 3 equiv. of benzenesulfonyl chlorides, the one-pot preparation of symmetrical 1,2-diarylacenaphthylenes proceeds in quite good yields using chloro-, fluoro- or trifluoromethyl-substituted benzenesulfonyl chlorides (Scheme 26, a).[31] Moreover, from 4-iodobenzenesulfonyl chloride, the acenaphthylene derivative containing two 4-iodobenzene units at C1 and C2 positions was obtained in 65% yield.

We also described the synthesis of non-symmetrical 1,2-diarylacenaphthylenes from 1-arylacenaphthylenes using both aryl bromides and benzenesulfonyl chlorides as aryl sources, under

Accepted Manuscript

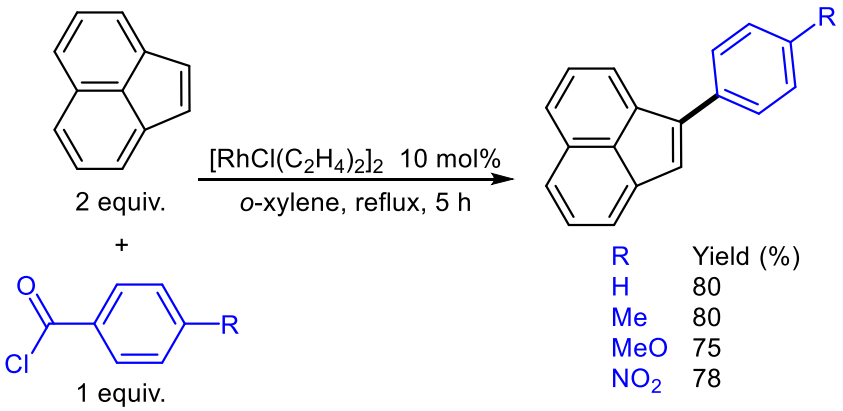
similar reaction conditions than for the C1-arylations of acenaphthylene.[31] The reaction of 4-fluorobromobenzene or 3-(trifluoromethyl)bromobenzene with a C1-arylated acenaphthylene using 1 mol% $Pd(OAc)_2$ catalyst, afforded the 1,2-diarylacenaphthylenes in 76% and 80% yield, respectively (Scheme 26, middle). 2-Bromobenzenesulfonyl chloride was also successfully employed as aryl source for the C2-arylation of 1-arylacenaphthylenes, allowing to prepare 1,2-diarylacenaphthylenes, without cleavage of the C-Br bonds (Scheme 26, b). From these compounds, an intramolecular Pd-catalyzed direct arylation provides the corresponding dibenzo[*j*,*l*]fluoranthenes.



Scheme 26. Pd-catalyzed arylations of acenaphthylenes with aryl bromides

Accepted Manuscript

The metal-catalyzed direct arylation of acenaphthylene is not limited to palladium catalysis. Miura et al. described in 2004, the reaction of benzoyl chlorides with acenaphthylene in the presence of 1 mol% $[RhCl(C_2H_4)_2]_2$ in refluxing *o*-xylene (Scheme 27).[32] They obtained the 1-arylacenaphthylenes in 75-80% yields. Both electron-rich and electron-deficient benzoyl chlorides were tolerated.

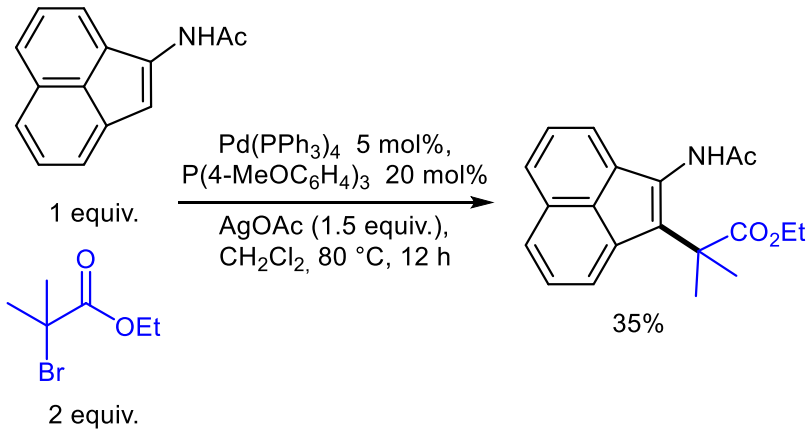


Scheme 27. Rh-catalyzed arylations of acenaphthylene with benzoyl chlorides

3.2 Alkylation

Only one example of metal-catalyzed C2-alkylation of an acenaphthylene derivative, *via* a C-H bond activation, has been reported so far. Xu, Loh et al. reported in 2016 the coupling of *N*-(acenaphthylen-1-yl)acetamide with ethyl 2-bromo-2-methylpropanoate in the presence of a palladium catalyst (Scheme 28).[33] The regioselective functionalization of the C-H bond on the 5-membered ring was observed affording the 2-alkylated *N*-(acenaphthylen-1-yl)acetamide in 35% yield. A mechanism was proposed, which involved the formation of an enolate radical, generated *via* Pd-catalyzed C–Br bond cleavage of ethyl 2-bromo-2-methylpropanoate. This enolate radical would react at the C2-position of the acenaphthylene derivative. Then, the new radical intermediate could react with a Pd(I) species. Finally, the reductive elimination takes place to afford C2-alkylated acenaphthylene and release Pd(0) catalyst in the presence of AgOAc.

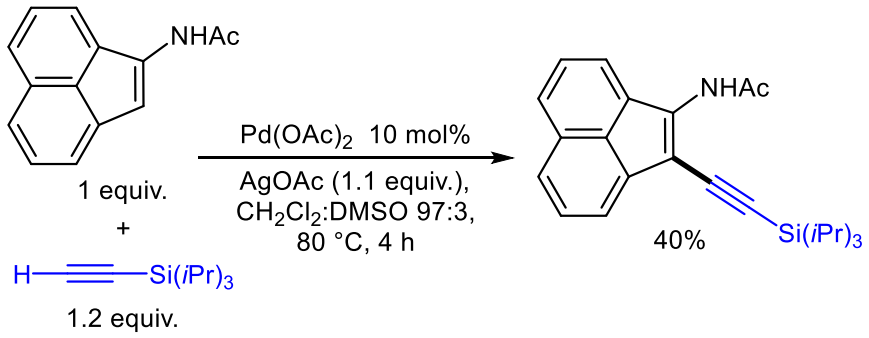
Accepted Manuscript



Scheme 28. Pd-catalyzed alkylation of an acenaphthylene

3.3 Alkynylation

In 2014, Xu, Loh et al. reported the first method allowing to introduce an alkynyl unit on an acenaphthylene. They discovered that the Pd-catalyzed alkynylation of *N*-(acenaphthylen-1-yl)acetamide with tri(isopropyl)silylacetylene, can be promoted by 10 mol% $Pd(OAc)_2$ catalyst and AgOAc as base, (Scheme 29).[34] The 5-membered ring of this acenaphthylene derivative was alkynylated in moderate yield, but without desilylation.

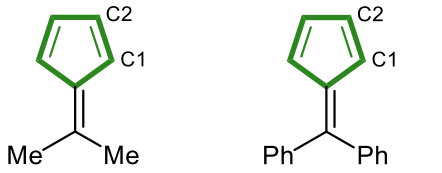


Scheme 29. Pd-catalyzed alkynylation of an acenaphthylene

4. Functionalization of fulvenes

Only a few fulvene derivatives such as 6,6-diphenylfulvene and 6,6-dimethylfulvene, are commercially available (Fig. 4). The metal-catalyzed C-H bond functionalization of fulvenes has attracted less attention than the C-H bond functionalization of azulenes or acenaphthylenes, as only Pd-catalyzed C1-arylation reactions and Ag-catalyzed annulation/isomerization reactions have been reported.

Accepted Manuscript



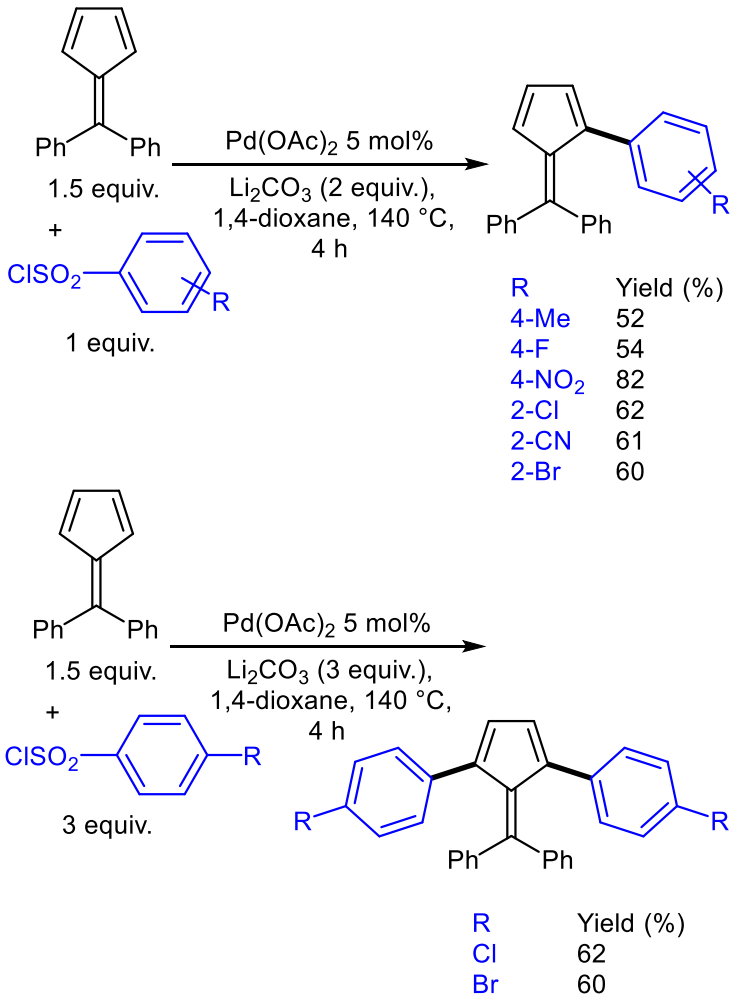
6,6-Dimethylfulvene 6,6-Diphenylfulvene

Figure 4

4.1 Arylation

The only examples of metal-catalyzed direct arylations of a fulvene derivative were reported in 2017 by our group (Scheme 30).[35] We observed that the nature of the aryl source is very important for such reactions. The reaction of 6,6-diphenylfulvene with aryl bromides gave low yields of C1-arylated fulvenes; whereas, the use of benzenesulfonyl chlorides in the presence of $Pd(OAc)_2$ catalyst and Li_2CO_3 base afforded regioselectively the desired products in good yields. We also reported that using an excess of benzenesulfonyl chlorides, the formation of C1,C4-diarylated fulvenes proceeded in good yields. This protocol was applicable to a range of functions on the benzenesulfonyl chloride, including reactive ones such as cyano or bromo substituents.

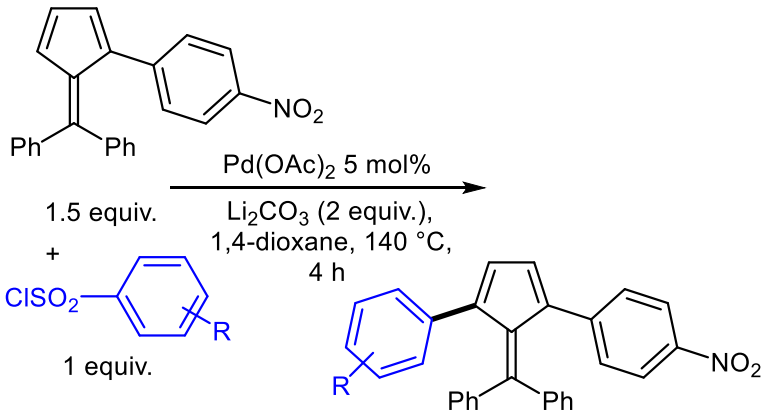
Accepted Manuscript



Scheme 30. Pd-catalyzed arylations of a fulvene with benzenesulfonyl chlorides

Such Pd-catalyzed direct arylations also allowed the synthesis of 1,4-diarylated fulvenes containing two different aryl groups *via* successive couplings. Using a set of benzenesulfonyl chlorides and ((2-(4-nitrophenyl)cyclopenta-2,4-dien-1-ylidene)methylene)dibenzene, under the same reaction conditions than for the first arylation, good to high yields of 1,4-diarylated fulvenes were obtained (Scheme 31).[35] The reaction tolerated both electron–withdrawing and electron-donating substituents on the benzenesulfonyl chloride. The reaction with 2-bromobenzenesulfonyl chloride gave the 1,4-diarylated fulvene, again without cleavage of the C-Br bond.

Accepted Manuscript



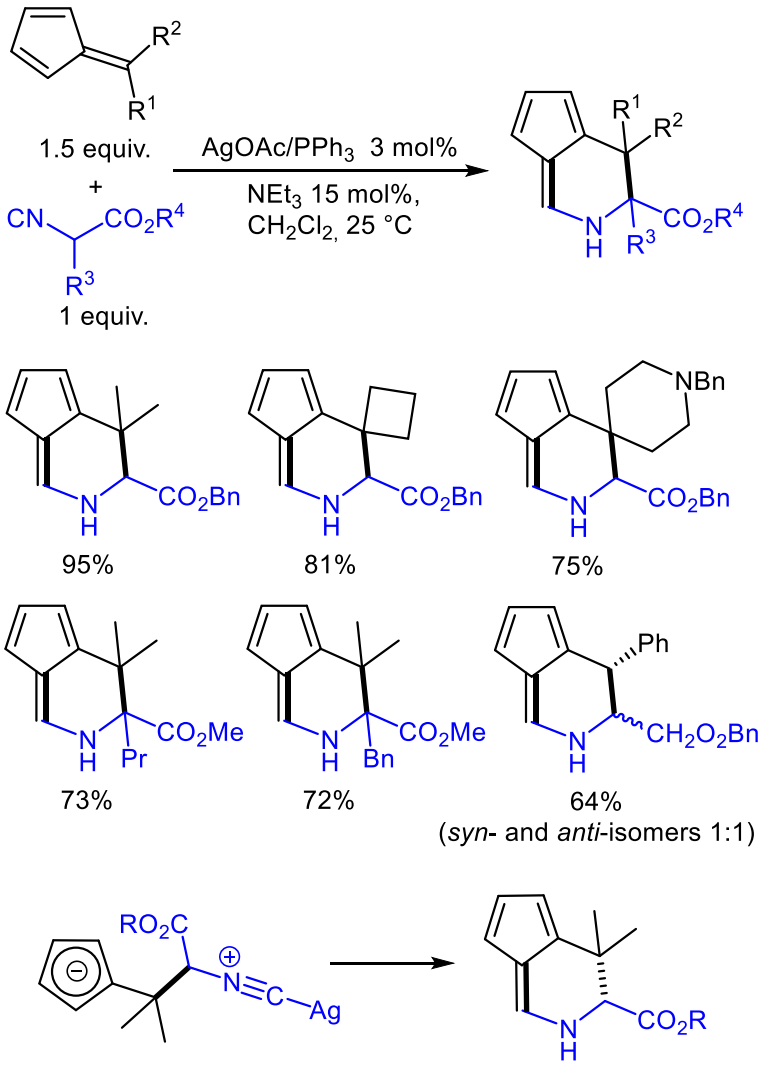
R	Yield (%)
4-Me	82
4-F	56
4-Cl	80
4-CF_3	86
2-CN	81
2-Br	78
2-Cl	74

Scheme 31. Pd-catalyzed arylations of fulvenes with benzenesulfonyl chlorides

4.2 Annulation/isomerization

Wang et al. described in 2015 the Ag(I)-catalyzed tandem [6+3] cycloaddition/isomerization of isocyanoacetates with fulvenes affording dihydropyridines (Scheme 32).[36] Using 3 mol% AgOAc/PPh_3 as the catalyst and Et_3N as the base at room temperature in dichloromethane, the tandem cycloaddition/isomerization products were obtained in high yields. The use of other silver salts, such as $AgNO_3$, Ag_2CO_3 and $AgClO_4$, also afforded the cycloaddition/isomerization products, but in slightly lower yields. Variation of the substituent on the ester group had almost no influence on the reaction. They also found that fulvene derivatives bearing different ring sizes gave similar yields. From unsymmetrical fulvenes this annulation reaction generated a tertiary center. The cycloadducts were produced in good yields as an equimolar mixture of the *syn*- and *anti*-isomers. They also studied the asymmetric version of this reaction using AgOAc associated to a chiral ligand, but a moderate enantiomeric excess of 28% was obtained. A catalytic cycle was proposed. With the aid of the base in the presence of Ag(I), metalation and deprotonation of the isocyanoacetates occurs. A nucleophilic attack on fulvene delivers a zwitterionic intermediate (See scheme 32 bottom left). Then, intramolecular cyclization followed by protonation/isomerization gave the dihydropyridines derivative and regenerates the catalyst.

Accepted Manuscript



Scheme 32. Ag-catalyzed cycloaddition/isomerization of isocyanoacetates with fulvenes

5. Conclusions and perspectives

Since the seminal report by Dyker in 1991 on the Pd-catalyzed direct arylation of acenaphthylene, the knowledge concerning the metal-catalyzed functionalization of C-H bond of the 5-membered carbocyclic rings of azulenes and acenaphthylenes has been widely extended; whereas, relatively few examples using fulvenes have been reported. Initially, Pd-complexes were the most commonly employed catalysts for such functionalizations and allowed the formation of C-C bonds with aryl, alkynes, alkenes or alkyls. Then, several examples of C-C bond formation using Au, Ni, Rh and also Ru catalysts have been described. Moreover, since 2014, examples of Ir-catalyzed borylations and silylations have been reported. A wide variety of functionalized azulenes and acenaphthylenes can now be obtained *via* these C-H bond activation reactions. C-H bond functionalization reaction for the

Accepted Manuscript

introduction of substituents on such compounds is very attractive, as no prior functionalization is required, reducing the number of steps to prepare the target compounds. In the near future, the metal-catalyzed C-H bond functionalization of such arenes will certainly drastically modify the synthetic pathways for the preparation of these compounds. However, many challenges remain, as regioselectivity issues were observed for some reactions, as in several cases moderate yields were obtained, and as only a few results with acenaphthylenes and especially fulvenes have been reported. In most cases, more efficient catalysts permitting lower catalyst loadings need to be found in order to provide more economically attractive procedures. Finally, concerning catalytic cycles, a large number of interrogations are not addressed concerning the various mechanisms involved. Moreover, in recent years, a few examples of C-H bonds functionalizations of azulenes *via* visible-light driven reactions using metal-free conditions have been described.[37] They might also provide attractive procedures for the functionalization of such compounds.

6. Acknowledgements

We thank CEFIPRA for providing financial support to A. S.

7. References

1. a) M. Gordon, *Chem. Rev.* **1952**, *52*, 127-200; b) A. B. Skov, S. L. Broman, A. S. Gertsen, J. Elm, M. Jevric, M. Cacciarini, A. Kadziola, K. V. Mikkelsen, M. B. Nielsen, *Chem. Eur. J.* **2016**, *22*, 14567-14575; c) H. Xin, X. Gao, *ChemPlusChem* **2017**, *82*, 945-956; d) P. Preethalayam, K. S. Krishnan, S. Thulasi, S. S. Chand, J. Joseph, V. Nair, F. Jaroschik, K. V. Radhakrishnan, *Chem. Rev.* **2017**, *117*, 3930-3989; e) H. Xin, X. Gao, *ChemPlusChem* **2017**, *82*, 945-956.
2. a) V. B. Mochalin, Y. N. Porshnev, *Russ. Chem. Rev.* **1977**, *46*, 530-547; b) K. Hafner, K.-P. Meinhardt, *Org. Synth.* **1984**, *62*, 134; c) S. E. Estdale, R. Brettle, D. A. Dunmur, C. M. Marson, *J. Mater. Chem.* **1997**, *7*, 391-401; d) A. L. Crombie, J. L. Kane, Jr., K. M. Shea, R. L. Danheiser, *J. Org. Chem.* **2004**, *69*, 8652-8667; e) S. Carret, A. Blanc, Y. Coquerel, M. Berthod, A. E. Greene, J.-P. Deprés, *Angew. Chem. Int. Ed.* **2005**, *44*, 5130-5133; f) F. Wang, T. T. Lin, C. He, H. Chi, T. Tang, Y.-H. Lai, *J. Mater. Chem.* **2012**, 22, 10448-10451.
3. a) S. Fukumoto, T. Nakagawa, S. Kawai, T. Nakashima, T. Kawai, *Dyes Pigm.* **2011**, *89*, 297-304; b) For a study on the aromaticity of the five-membered ring of acenaphthylene: S.

Accepted Manuscript

Radenkovic, J. Durdevic, P. Bultinck, *Phys. Chem. Chem. Phys.* **2012**, *14*, 14067-14078; c) C. Lambruschini, L. Banfi, G. Guanti, *Chem. Eur. J.* **2016**, *22*, 13831-13834.

4. a) E. D. Bergmann, *Chem. Rev.* **1968**, *68*, 41-84; b) A. Z. Kreindlin, M. I. Rybinskaya, *Russ. Chem. Rev.* **2004**, *73*, 417-432; c) M. S. Butler, *Nat. Prod. Rep.* **2008**, *25*, 475-516; d) A. J. Peloquin, R. L. Stone, S. E. Avila, E. R. Rudico, C. B. Horn, K. A. Gardner, D. W. Ball, J. E. B. Johnson, S. T. Iacono, G. J. Balaich, *J. Org. Chem.* **2012**, *77*, 6371-6376; e) N. P. Godman, G. J. Balaich, S. T. Iacono, *Chem. Commun.* **2016**, *52*, 5242-5245; f) H. Hopf, M. S. Sherburn, Cross Conjugation: Modern Dendralene, Radialene and Fulvene Chemistry, Wiley-VCH, 2016.

5. a) L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem. Int. Ed.* **2009**, *48*, 9792-9826; b) B.-J. Li, S.-D. Yang, Z.-J. Shi, *Synlett* **2008**, 949-957; c) F. Kakiuchi, T. Kochi, *Synthesis* **2008**, 3013-3039; d) G. P. McGlacken, L. M. Bateman, *Chem. Soc. Rev.* **2009**, *38*, 2447-2464; e) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2009**, *48*, 5094-5115; f) F. Bellina, R. Rossi, *Tetrahedron* **2009**, *65*, 10269-10310; g) T. Satoh, M. Miura, *Synthesis* **2010**, 3395-3409; h) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147-1169; i) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315-1345; j) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord, F. Glorius, *Angew. Chem. Int. Ed.* **2012**, *51*, 10236-10254; k) J. Wencel-Delord, F. Glorius, *Nat. Chem.* **2013**, *5*, 369-375; l) R. Rossi, F. Bellina, M. Lessi, C. Manzini, *Adv. Synth. Catal.* **2014**, *356*, 17-117; m) K. Yuan, J.-F. Soulé, H. Doucet, *ACS Catal.* **2015**, *5*, 978-991; n) M. R. Yadav, R. K. Rit, M. Shankar, A. K. Sahoo, *Asian J. Org. Chem.*, **2015**, *4*, 846–864; o) L. Theveau, C. Schneider, C. Fruit, C. Hoarau, *ChemCatChem* **2016**, *8*, 3183-3194; p) C. B. Bheeter, L. Chen, J.-F. Soulé, H. Doucet, *Cat. Sci. Technol.* **2016**, *6*, 2005-2049; q) R. Rossi, M. Lessi, C. Manzini, G. Marianetti, F. Bellina, *Tetrahedron* **2016**, *72*, 1795-1837; r) A. Skhiri, R. Ben Salem, J.-F. Soulé, H. Doucet *ChemCatChem* **2017**, *9*, 2895-2913.

6. G. Dyker, S. Borowski, J. Heiermann, J. Körning, K. Opwis, G. Henkel, M. Köckerling, *J. Organomet. Chem.* **2000**, *606*, 108-111.

7. L. Zhao, C. Bruneau, H. Doucet, *Chem. Commun.* **2013**, *49*, 5598-5600.

8. M. Murai, M. Yanagawa, M. Nakamura, K. Takai, *Asian J. Org. Chem.* **2016**, *5*, 629-635.

9. X. C. Cambeiro, N. Ahlsten, I. Larrosa, *J. Am. Chem. Soc.* **2015**, *137*, 15636-15639.

10. G. Dyker, E. Muth, A. S. K. Hashmi, L. Ding, *Adv. Synth. Catal.* **2003**, *345*, 1247-1252.

11. a) D. Aguilar, M. Contel, R. Navarro, E. P. Urriolabeitia, *Organometallics* **2007**, *26*, 4604-4611; see also: b) D. Aguilar, M. Contel, R. Navarro, T. Soler, E. P. Urriolabeitia, *J. Organomet. Chem.* **2009**, *694*, 486-493.

Accepted Manuscript

12. J. C. Timmerman, W. W. Schmitt, R. A. Widenhoefer, *Org. Lett.* **2016**, *18*, 4966-4969.
13. L. Gu, L. M. Wolf, A. Zielinski, W. Thiel, M. Alcarazo, *J. Am. Chem. Soc.* **2017**, *139*, 4948-4953.
14. A. Nakatani, K. Hirano, T. Satoh, M. Miura, *Chem. Eur. J.* **2013**, *19*, 7691-7695.
15. a) S. Park, W.-S. Yong, S. Kim, P. H. Lee, *Org. Lett.* **2014**, *16*, 4468-4471; b) S. Park, W. H. Jeon, W.-S. Yong, P. H. Lee, *Org. Lett.* **2015**, *17*, 5060-5063.
16. A. Szekely, A. Peter, K. Aradi, G. L. Tolnai, Z. Novak, *Org. Lett.* **2017**, *19*, 954-957.
17. a) Y. Nishibayashi, M. Yoshikawa, Y. Inada, M. Hidai, S. Uemura, *J. Am. Chem. Soc.* **2002**, *124*, 11846-11847; see also: b) Y. Inada, M. Yoshikawa, M. D. Milton, Y. Nishibayashi, S. Uemura, *Eur. J. Org. Chem.* **2006**, 881-890; c) Y. Nishibayashi, Y. Inada, M. Yoshikawa, M. Hidai, S. Uemura, *Angew. Chem., Int. Ed.* **2003**, *42*, 1495-1498.
18. J. Liu, E. Muth, U. Floerke, G. Henkel, K. Merz, J. Sauvageau, E. Schwake, G. Dyker, *Adv. Synth. Catal.* **2006**, *348*, 456-462.
19. J. Liu, H. Li, R. Dühren, J. Liu, A. Spannenberg, R. Franke, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2017**, *56*, 11976-11980.
20. a) K. Kurotobi, M. Miyauchi, K. Takakura, T. Murafuji, Y. Sugihara, *Eur. J. Org. Chem.* **2003**, 3663-3665; b) M. Fujinaga, T. Murafuji, K. Kurotobi, Y. Sugihara, *Tetrahedron* **2009**, *65*, 7115-7121.
21. J. Xia, B. Capozzi, S. Wei, M. Strange, A. Batra, J. R. Moreno, R. J. Amir, E. Amir, G. C. Solomon, L. Venkataraman, L. M. Campos, *Nano Lett.* **2014**, *14*, 2941-2945.
22. a) K. Ninomiya, Y. Harada, T. Kanetou, Y. Suenaga, T. Murafuji, R. Tsunashima, *New J. Chem.* **2015**, *39*, 9079-9085; b) M. Murai, S. Iba, H. Ota, K. Takai, *Org. Lett.* **2017**, DOI: 10.1021/acs.orglett.7b02729
23. H. Nishimura, M. N. Eliseeva, A. Wakamiya, L. T. Scott, *Synlett* **2015**, *26*, 1578-1580.
24. M. Murai, K. Takami, H. Takeshima, K. Takai, *Org. Lett.* **2015**, *17*, 1798-1801.
25. G. Dyker, *Tetrahedron Lett.* **1991**, *32*, 7241-7242.
26. G. Dyker, *J. Org. Chem.* **1993**, *58*, 234-238.
27. Y. Sugihara, H. Takeda, J. Nakayama, *Eur. J. Org. Chem.* **1999**, 597-605.
28. M. Pillekamp, A. Aniol, J. Heppekausen, S. Neukirchen, S. Seel, I. M. Oppel, G. Dyker, *Synlett* **2009**, 133-137.
29. A. A. Pletnev, Q. Tian, R. C. Larock, *J. Org. Chem.* **2002**, *67*, 9276-9287.
30. G. Dyker, K. Merz, I. M. Oppel, E. Muth, *Synlett* **2007**, 897-900.

Accepted Manuscript

31. X. Shi, T. Roisnel, J.-F. Soulé, H. Doucet, *Org. Chem. Front.* **2017**, in press.
32. T. Sugihara, T. Satoh, M. Miura, M. Nomura, *Adv. Synth. Catal.* **2004**, *346*, 1765-1772.
33. R. Ding, Z.-D. Huang, Z.-L. Liu, T.-X. Wang, Y.-H. Xu, T.-P. Loh, *Chem. Commun.* **2016**, *52*, 5617-5620.
34. Y.-H. Xu, Q.-C. Zhang, T. He, F.-F. Meng, T.-P. Loh, *Adv. Synth. Catal.* **2014**, *356*, 1539-1543.
35. M. Brahim, H. Ben Ammar, V. Dorcet, J.-F. Soulé, H. Doucet, *Org. Lett.* **2017**, *19*, 2584-2587.
36. Z.-L. He, C.-J. Wang, *Chem. Commun.* **2015**, *51*, 534-536.
37. a) J. Davies, T. D. Svejstrup, D. Fernandez Reina, N. S. Sheikh, D. Leonori, *J. Am. Chem. Soc.* **2016**, *138*, 8092-8095; b) A. U. Meyer, A. Wimmer, B. Koenig, *Angew. Chem., Int. Ed.* **2017**, *56*, 409-412.

Accepted Manuscript