Divergent Synthesis of Densely Substituted Arenes and Pyridines *via* Cyclotrimerization Reactions of Alkynyl Triazenes

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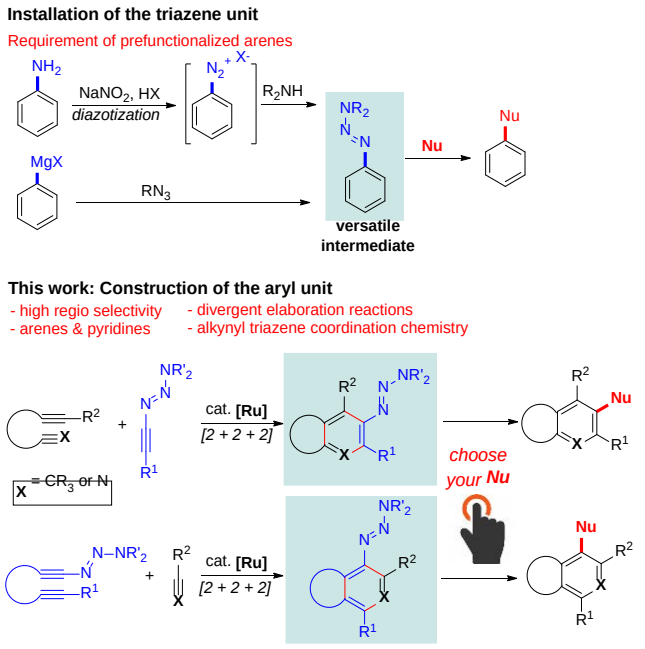
ABSTRACT: Densely functionalized fused aromatic triazenes can be prepared by [2 + 2 + 2] cyclotrimerization reactions of 1-alkynyl triazenes. The Cp*Ru-catalyzed cyclization proceeds well both with simple alkynyl triazenes and tethered 1-diynyl triazenes. Attractively, the methodology can be extended to pyridine synthesis by replacing an alkyne with a nitrile. The reaction is regioselective and yields the sterically more hindered product. The triazene group precisely installed on the synthesized aryl and pyridyl ring is a highly versatile moiety, which is effortlessly converted into the most important and frequently used functional aryl substituents, including fluorides. It is also suited for intramolecular transformations to afford a variety of valuable heterocycles. The coordination chemistry of alkynyl triazenes and Cp*RuCl was studied, and led to the structural characterization of a Cp*RuCl(η^2-alkyne) complex, a Cp*RuCl(η^4-cyclobutadiene) complex, and an unusual dinuclear Ru complex with a bridging tetramethylfulvene ligand. Complexes of this type are potentially involved in catalyst deactivation pathways.

Introduction

Aryl triazenes have garnered great attention over the last decades. Some triazenes display valuable biological activities and for instance are used as anti-cancer agents.[1,2] A very large portion of their high synthetic value stems from their unique property as a stable aryl diazonium surrogate. In this respect, they represent a platform intermediate that can be easily transformed into many functional groups. Synthetic applications range from natural product synthesis,[3] heterocycle synthesis,[4,5] linkers in solid-phase synthesis,[6] to materials.[7] The aryl diazonium functionality is revealed under acidic conditions and can be elaborated into numerous functional groups upon interception with nucleophiles.[1,8-11] However, the synthetic access to such aryl triazenes requires an already appropriately functionalized aryl precursor (Scheme 1). The most frequently used procedure involves the diazotization of an aniline substrate and its subsequent coupling to a secondary amine.[12] Alternative methods use aryl magnesium salts and azides[13] or aminodiazotates[14] as partners. The requirement of a functionalized substrate limits exploitation of the triazene platform, particularly if the targeted functionalized substrate is not available or features a complex substitution pattern. For further exploitation of the synthetic potential of aryl triazenes, complementary methods without the requirement of pre-functionalized arenes would be highly desirable.

Scheme 1: Access to Aryl & Heteroaryl Triazenes and their use as Versatile Platform Intermediates.



Transition-metal catalyzed [2 + 2 + 2] cyclotrimerizations are a powerful tool to construct complex densely substituted arenes from three simple alkynes.[15-19] Replacement of an alkyne by a nitrile opens an attractive avenue to highly valued pyridines.[20-22] Fueled by our recently reported access to 1-alkynyl triazenes,[14] the reactivity profile of this particular alkyne having properties related to ynamides[23f] was explored.[23] Intrigued by the compatibility of 1-alkynyl triazenes with Ru^{II}-catalysts for

enantioselective [2 + 2] cycloadditions,[23c] we investigated the possibility to prepare highly elaborated aryl and heteroaryl triazenes by Ru-catalyzed cyclotrimerization reactions (Scheme 1). Noteworthy, combined with nitriles, the reactions would provide a unique access to 3-triazenyl-substituted pyridines. Subsequent elaboration of the triazene unit would enable a general divergent functionalization strategy targeting the 3-position of pyridines. Frequently, functionalizations of the 3-position of pyridines are sluggish and challenging for S_EAr as well as S_NAr-type reactions.[24]

In general, the envisioned bicyclic arenes and pyridines with a triazenyl group are highly valuable scaffolds. Such fused aryl and pyridyl systems are frequently occurring motifs in natural products and biologically active molecules (Figure 1).[25] The regioselectively installed triazenyl moiety can be easily elaborated by a myriad of methods, offering late stage functional group modifications on these important frameworks in a divergent fashion. Besides the introduction of many different nucleophiles, the triazenyl unit can as well engage in intramolecular cyclizations to deliver several heterocyclic systems.[4,5]

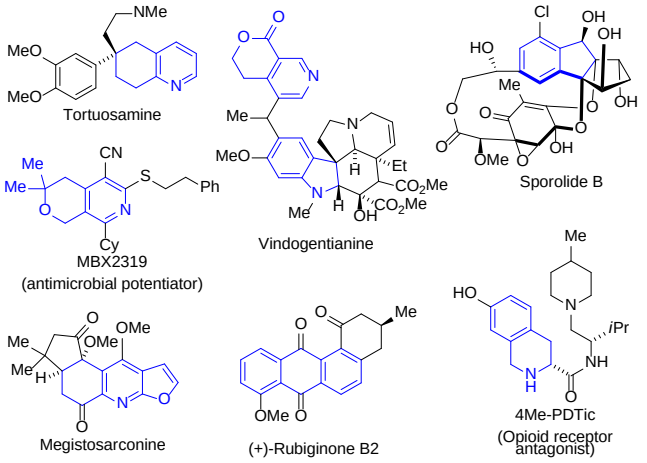
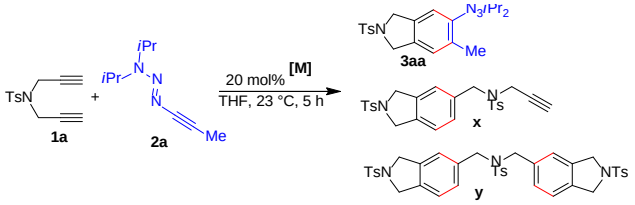


Figure 1. Selected examples of fused-arene and fused-pyridine heterocyclic compounds and natural products.

Results and Discussion

We first conducted a compatibility check to gauge the stability of the alkynyl triazene in the presence of the most common cyclotrimerization catalysts.[16-19] For this purpose, the synthesis of isoindoline **3aa** from the reaction between diyne **1a** and alkynyl triazene **2a** was targeted (Table 1). Under Ni^0 catalysis,[17] the alkynyl triazene is unstable and decomposes without formation of a defined product (Entry 1). Along the same lines, Fe^{II} and Pd^0 were not competent for the envisioned cyclotrimerization.[18] Again, decomposition of **2a** was observed (Entries 2 and 3). In contrast, different Rh^I catalysts were able to effect the cyclization,[19] giving desired **3aa** in 15-35% yield (Entries 4-6). However, in all three cases, homotrimerization of **1a** could not be mitigated and was the major reaction pathway. Gratifyingly, exposure of the substrates to Cp*Ru(cod)Cl, a Ru^{II} complex introduced by Yamamoto[16] for [2 + 2 + 2] cycloadditions, provided **3aa** at ambient temperature in 50 % yield (Entry 7). The formation of di- and trimerization products **x** and **y** from the tethered diyne **1a** could be effectively suppressed in this case by its slow addition to the reaction mixture. Ruthenium complexes lacking the Cp* ligand were not competent for the cyclization (Entries 8 and 9). The usage of $[Cp^*RuCl_2]_2$ improved the yield of **3aa** to 74 % (Entry 10). With prolongation of the addition period of **1a**, this complex allowed for a full and clean conversion of **2a** to **3aa** with a reduced catalyst loading (Entry 13).

Table 1: Optimization of the Fused Aryl Triazene Formation[a]



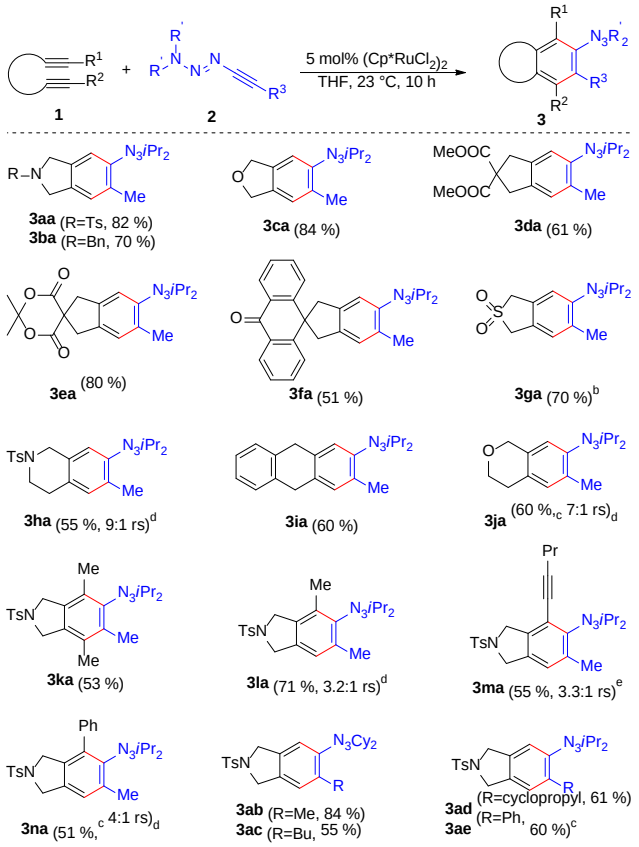
Entry	[M]	% conv.[b]	% **3aa**[b]	% **x+y**[b]
1[c]	$Ni(cod)_2$ / xantphos	>95	-	-
2	$FeCl_2$ / dppe / Zn	34	<5	<5
3[c,d]	$Pd_2(dba)_3$ / PPh_3	65	<5	<5
4	$[Rh(cod)_2]BF_4$ / binap	47	35	61
5	$[Rh(cod)_2]BF_4$ / Segphos	25	15	60
6	$Rh(PPh)_3Cl$	26	20	75
7	Cp*RuCl(cod)Cl	68	50	4
8	$[(Cymene)RuCl_2]_2$	<5	<5	40
9	$[Ru(cod)Cl_2]_n$	0	-	-
10	$(Cp^*RuCl_2)_2$	94	74	12
11[e]	$(Cp^*RuCl_2)_2$	80	64	-
12[f]	$(Cp^*RuCl_2)_2$	47	30	-
13[e,g]	$(Cp^*RuCl_2)_2$	>95	82[h]	-

[a] Conditions: 0.1 mmol **2a**, 20 mol% **[M]**, 30 mol% additive(s), slow addition of **1a** over 5 h, 0.1 M in THF. [b] Determined by ^{1}H-NMR with an internal standard; conversion of **2a**. [c] PhMe was used as solvent. [d] 110 °C. [e] With 5 mol% cat. [f] With 2.5 mol% cat. [g] Slow addition of **1a** over 10 h. [h] Isolated yield.

The scope of the reaction was subsequently evaluated with the optimized condition (Scheme 2). A series of 1,6-diynes containing typical hetero atom or carbon tethers reacted well, forming the desired arenes **3aa**-**3ga** in good yields. Notably, basic nitrogen atoms (**3ba**) caused no problem. The use of 1,7-diynes allowed the construction of larger ring systems such as tetrahydroisoquinoline **3ha**, 5,10-dihydroanthracene **3ia** and isochroman **3ja**. Despite considerable distance of the heteroatom in the tether, the cyclotrimerization proceeds in a regioselective manner. The triazenyl group is preferentially placed *meta* to benzylic nitrogen or oxygen atom. Using a diyne with two internal alkynes (R^1, R^2 = Me) provided hexa-substituted arene **3ka**. Unsymmetrical diyne substrates reacted and gave arene products **3la**-**3na**. Remarkably, the R^1 substituent is preferentially placed *ortho* to the triazenyl group. This seems to be counterintuitive since the triazenyl group is sterically more demanding than the methyl residue. The regioselectivity is contrasting with the usually observed *meta*-selectivity for these constellations,[16b] which may be explained by the electronic influence of the triazenyl moiety on the alkyne. Concerning the alkynyl triazene, its isopropyl groups can be swapped for bulkier cyclohexyl substituents (**3ab**), maintaining efficiency of the transformation. Moreover, the cyclization proceeded as well with alkynes having

larger substituents R^3 such as butyl (**3ac**), cyclopropyl (**3ad**) and phenyl (**3ae**).

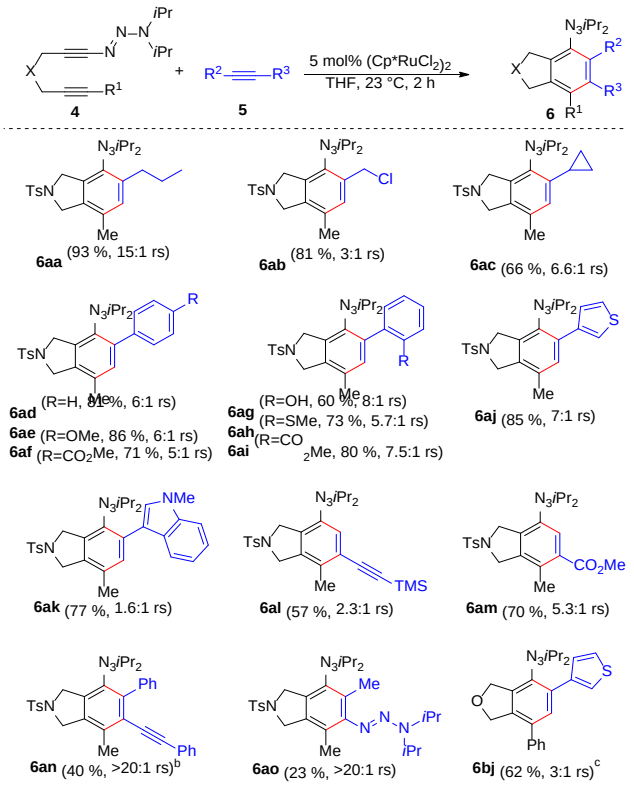
Scheme 2: Scope for the Ru-Catalyzed Synthesis of Aryl Triazenes.[a]



[a] Conditions: 0.1 mmol **2**, 0.15 mmol **1**, 5 mol% $(Cp^*RuCl_2)_2$, 0.1 M in THF, isolated yields. [b] 0.15 mmol **1g**, 0.1 mmol **2a**, 5 mol% $(Cp^*RuCl_2)_2$, at 60 °C for 18 h. [c] 10 mol% $(Cp^*RuCl_2)_2$. [d] Ratio of regioisomers determined by ^{1}H NMR. [e] Ratio determined from isolated isomers.

After developing a catalytic system for the installation of the triazenyl group distal to the ring fusion, it piqued our interest to examine the possibility to access arenes having this versatile group proximal to the ring fusion. This maneuver would further enhance the synthetic utility of the methodology in complex molecule synthesis. We conceived that a related [2 + 2 + 2] cycloaddition between a tethered 1-diynyl triazene **4** and an alkyne **5** would suit well this purpose (Scheme 3). To our delight, the same catalyst, $[Cp^*RuCl_2]_2$, allowed conversion of 1-(1,6-diynynl) triazene **4a** and pent-1-yne into aryl triazene **6aa** in 93 % in less than two hours. Notably, **6aa** is formed in a highly regioselective manner, giving preferentially the *ortho*-isomer in a 15:1 ratio. A variety of terminal alkynes readily participated and provided arenes **6** in good yields and regioselectivities. For instance, ethynyl cyclopropane delivered aryl cyclopropane **6ac** in high regioselectivity. 3-Chloro prop-1-yne reacted smoothly to give **6ab**, albeit with reduced regioselectivity. A range of aryl acetylenes were found to be competent substrates providing *ortho*-triazenyl biphenyls in good yields and regioselectivities. Variations of the steric and electronic parameters of the aryl groups, including a potentially catalyst poisoning 2-thioanisyl unit, had little impact on yields and regio-control of the cyclotrimerization (**6ae-6ai**). Heteroaryl alkynes also underwent cyclization. 3-Ethynyl thiophene gave product **6aj** in good yield and the typical regioselectivity of 7:1. The related 3-ethynyl (*N*-methyl)indole delivered arene **6ak** with a lower selectivity. Surprisingly, two alkynes – TMS-1,3-diyne and methyl propiolate – caused a reversal of the regioselectivity. In these two cases, *meta*-substituted aryl triazene **6al** and **6am** were majorly formed. Concerning internal alkynes, diphenyl diacetylene reacted highly regioselectively and gave **6an**. The combination of **4a** with triazene **2a** gave unique *bis*-triazenyl arene **6ao**. A diyne with an oxygen tether and a phenyl group at R^1 was also tolerated and provided *para*-triazenyl biphenyl **6bj**.

Scheme 3: [2 + 2 + 2] Cyclotrimerizations with 1-Diynyl Triazenes.[a]

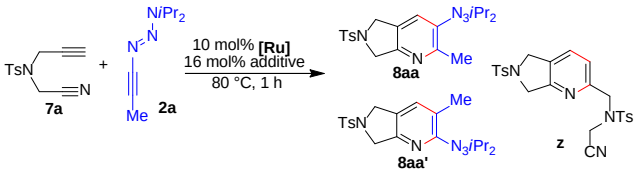


[a] Conditions: 0.1 mmol **4**, 0.15 mmol **5**, 5 mol% $(Cp^*RuCl_2)_2$, 0.1 M in THF, isolated yields, ratio of regioisomers determined by ^{1}H-NMR. [b] 60 °C, 20 h. [c] 80 °C, 4 h.

Despite being an efficient strategy to access substituted fused pyridines, the scope of the cyclotrimerization between two alkynes and one nitrile is less broad compared to the parent reaction. In this aspect, reports on cyclizations involving tethered alkynyl nitriles are limited to nickel(0),[21a] iron(II)[21b] and cobalt(I)[21c-g] based systems, and they are largely met with regioselectivity issues. To explore this underdeveloped area, we investigated the feasibility of pyridine cyclization with alkynyl triazene **2a** and tethered nitrile **7a** (Table 2). The envisioned cyclization proceeded with very poor efficiency with the previously used $(Cp^*RuCl_2)_2$ (Entry 1). We switched to the cationic $Cp^*Ru(MeCN)_3PF_6$ complex in combination with halide additives (Entries 2-5). No reactivity was observed in the absence of additives, while switching the counter ion to iodide substantially improved the reactivity, presumably by a better coordination involvement of the nitrile group of **7a**. Notably only pyridine **8aa** without traces of the isomer **8aa'** was formed in 43 %

yield. Besides the desired pyridine, 28 % of homocyclization product **z** was observed. Switching the solvent from THF to dioxane and increasing the temperature to 100 °C reduced this by-product slightly while increasing the yield of pyridine **8aa** to 71 % (Entry 8).

Table 2: Optimization of the Ru-Catalyzed Synthesis of Pyridyl Triazenes.[a]

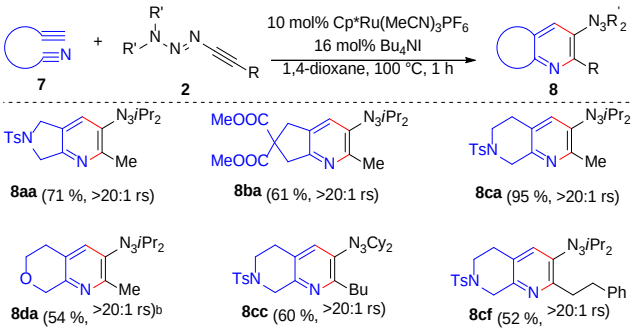


Entry	[Ru]	Additive	Solvent	% **8aa**[b]	% **z**[b]
1	$(Cp^*RuCl_2)_2$	-	THF	8	8
2	$Cp^*Ru(MeCN)_3PF_6$	-	THF	-	<5
3	$Cp^*Ru(MeCN)_3PF_6$	Bu_4NCl	THF	6	9
4	$Cp^*Ru(MeCN)_3PF_6$	Bu_4NBr	THF	11	16
5	$Cp^*Ru(MeCN)_3PF_6$	Bu_4NI	THF	43	28
6	$Cp^*Ru(MeCN)_3PF_6$	Bu_4NI	Dioxane	53	30
7	$Cp^*Ru(MeCN)_3PF_6$	Bu_4NI	MeCN	<5	<5
8	$Cp^*Ru(MeCN)_3PF_6$	Bu_4NI	Dioxane	71[c,d]	21

[a] Conditions: 0.15 mmol **7a**, 0.1 mmol **2a**, 10 mol% **[Ru]**, 0.1 M in solvent. [b] Determined by ^{1}H-NMR with an internal standard, **8aa**:**8aa'** >20:1. [c] At 100 °C. [d] Isolated yield.

The optimized conditions were subsequently utilized to prepare a small set of bicyclic pyridines (Scheme 4). Besides the classical malonate tether (**8ba**), we were pleased that the method is as well useful to access fused nitrogen- and oxygen containing six-membered fused pyridines such as **8ca** and **8da**. Alkynyl triazene **2** with longer alkyl chains engaged as well in the heterotrimerization and yielded pyridines **8cc** and **8cf**. In all cases, the pyridines are remarkably formed as single regio-isomers possessing their triazenyl group in the *meta*-position.

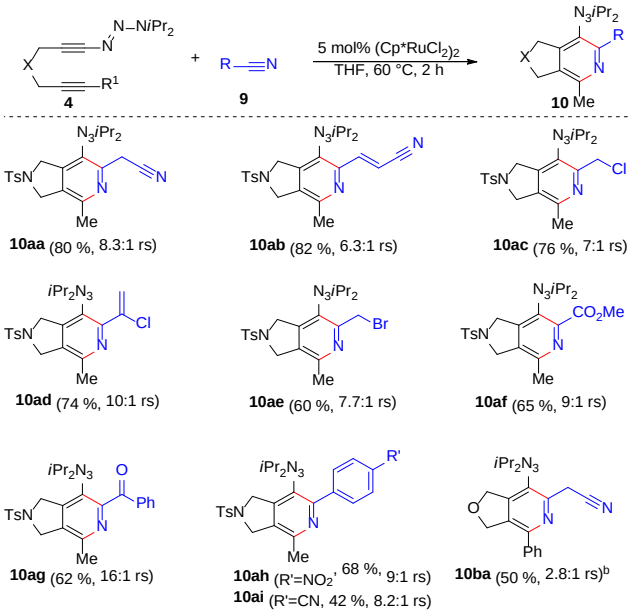
Scheme 4: Synthesis of 3-Triazenyl Pyridines with Tethered Nitriles.[a]



[a] Conditions: 0.1 mmol **2**, 0.15 mmol **7**, 10 mol% $Cp^*Ru(MeCN)_3PF_6$, 16 mol% $(Bu_4N)I$, 0.1 M in 1,4-dioxane, isolated yields. [b] with 20 mol% $Cp^*Ru(MeCN)_3PF_6$, 32 mol% $(Bu_4N)I$.

Next, we aimed to broaden the application potential further by permutation of the nitrogen atom's position in the arising pyridine products. To realize this goal, triazenyl diyne **4** was combined with a variety of nitriles with synthetically valuable functional groups (Scheme 5).[22] The standard catalyst $[Cp^*RuCl_2]_2$ was found to cleanly catalyze the reaction between **4a** and malonitrile, selectively forming pyridine **10aa** in 80% yield. The transformation is characterized by a good regioselectivity of 8.3:1 placing the triazenyl moiety *meta* to the pyridine nitrogen atom. Notably, no second [2 + 2 + 2] with the remaining nitrile group of **10aa** was observed. Additionally, nitriles bearing attractive functionalities such as fumaronitrile, chloro- and bromoacetonitrile as well as chloroacrylonitrile provided the desired pyridine products **10ab**-**10ae** in good yields and regioselectivities. Mander's reagent reacted to give methylester substituted pyridine **10af**. Nitriles bearing electron-withdrawing groups like benzoyl cyanide, *p*-nitro benzonitrile and 1,4-dicyano benzene were also found to be competent reaction partners, giving 2-acylated, 2-arylated pyridines respectively. 2-Phenyl pyridine **10ba** was also generated from phenyl substituted diyne **4b**.

Scheme 5: Scope for the Synthesis of Pyridyl Triazenes from Nitriles[a]

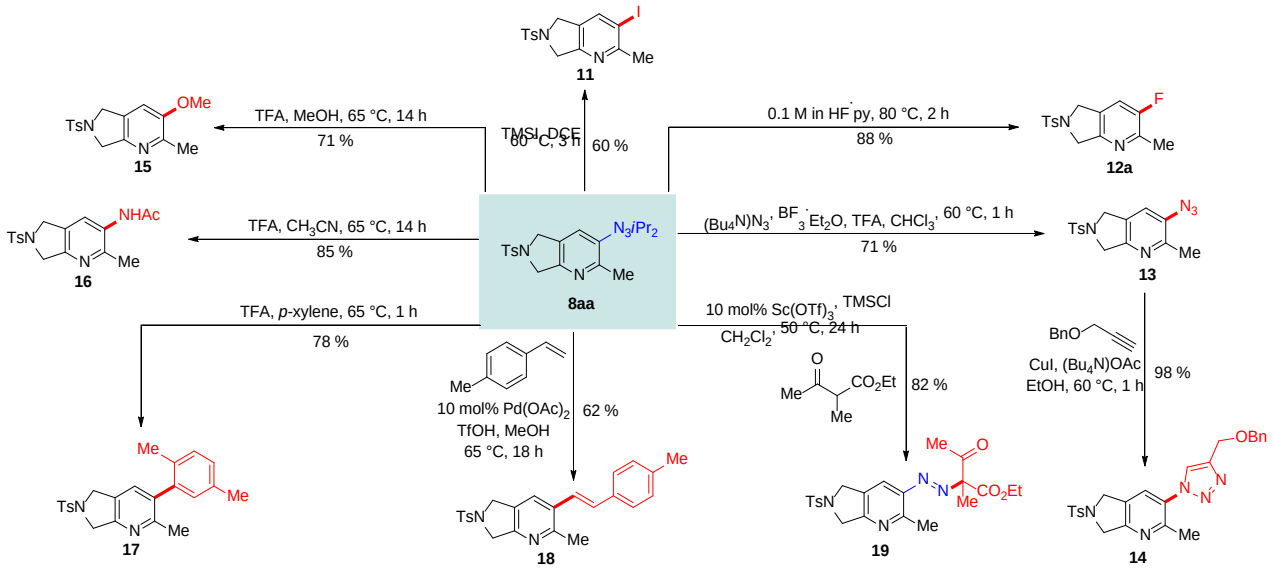


[a] Conditions: 0.1 mmol **4**, 0.15 mmol **9**, 5 mol% $(Cp^*RuCl_2)_2$, 0.1 M in THF; isolated yields, regioisomeric ratio determined by ^{1}H-NMR. [b] 10 mol% $(Cp^*RuCl_2)_2$, 80 °C, 4 h.

Elaboration of the triazenyl group

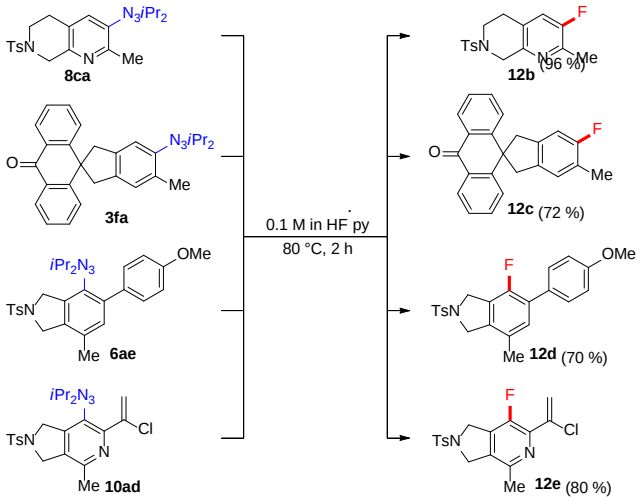
Aryl triazenes are a highly versatile group that can be converted into a wide-ranging array of synthetically highly relevant functional groups.[9-11] However, much less is known regarding the reactivity profile of pyridyl triazenes. Therefore, we opted for pyridine **8aa** as a representative case for a basic and coordinating heterocycle and embarked to map its reactivity profile (Scheme 6). Many functionalizations operate under acidic conditions *via* protonation of the triazenyl group forming a diazonium intermediate. The presence of the basic pyridine nitrogen usually renders the reaction more delicate. We concluded that if they are successful with **8aa**, it is fair to assume a very high chance of success with less challenging substrates. Replacing the triazenyl groups by halides was realized by the treatment of **8aa** with trimethylsilyl iodide to provide iodo pyridine **11**.[9g] Highly valuable 3-fluoro pyridine **12a** was cleanly formed by exposure of **8aa** to HF·pyridine.[9i] Moreover, transformation of the triazenyl group into an azide functionality proceeded well with a soluble azide source under acidic conditions.[10c] The obtained pyridyl azide **13** can be further converted to triazole **14** by Cu-catalyzed click reaction. Oxygen nucleophiles can be introduced by protonating the triazenyl group with TFA in the presence of an alcohol, e.g. 3-methoxypyridine **15**. In analogy, the introduction of nitrogen nucleophiles is feasible *via* the Ritter reaction. For instance, protonation in acetonitrile as the solvent gave rise to 3-acetamido pyridine **16**. Replacing the solvent by an aromatic hydrocarbon such as *p*-xylene allowed for a Friedel-Crafts reaction to give phenyl pyridine **17**. Complementary aromatic triazenes can take over the role of the electrophilic partner for palladium-catalyzed cross-coupling reactions.[11] In this respect, a Heck-reaction with 4-methyl styrene using triflic acid as additive delivered styryl pyridine **18** in good yield. Besides transformations involving a complete loss of all triazenyl nitrogen atoms, the intermediate pyridyl diazonium species can be utilized. For instance, $Sc(OTf)_3$-catalyzed azo coupling with a beta-ketoester gave azo product **19** in 82 % yield.[10a]

Scheme 6: Synthetic Transformations of Pyridyl Triazene 8aa



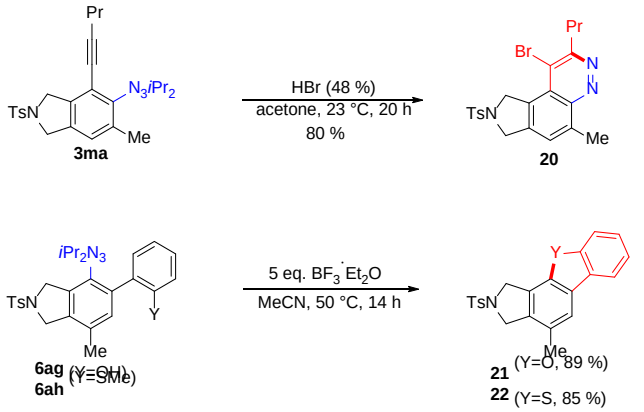
In order to gauge the generality and robustness of the product derivatizations, selected members from different product categories were treated with HF·pyridine under the aforementioned conditions (Scheme 7). All triazenyl groups were efficiently converted to the corresponding aryl fluorides **12b**-**12e** in 70-96 % yield.

Scheme 7: Exemplary Fluorinations of Aryl and Pyridyl Triazenes.



In addition to transformations of the triazenyl group with external nucleophiles, appropriate *ortho*-substituents allow for rich cyclization chemistry and provide rapid access to synthetically useful heterocycles (Scheme 8)[4,5]. For examples, *ortho*-alkynyl triazene **3ma** was converted into bromo cinnoline **20** by exposure to aqueous HBr.[5i] A smooth ring closure to dibenzofuran **21** was achieved from phenol **6ag**.[5k] In close analogy, thioanisole **6ah** formed dibenzothiophene **22** under acidic conditions.[5e]

Scheme 8: Use of the Triazene Handle for the Formation of Heterocycles.

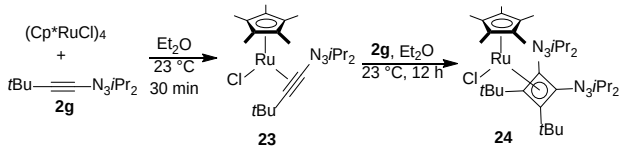


Coordination chemistry of alkynyl triazenes

The cyclotrimerization reactions described above require a coordination of the alkynyl triazene to the Cp*Ru fragment at some stage during the catalytic cycle. So far, the coordination chemistry of alkynyl triazenes is completely unexplored, and it was not clear if binding to a late transition-metal complex such as Cp*RuCl would occur *via* its triple bond or *via* its triazene group. In order to gain further insight, we studied reactions of the tetramer $(Cp^*RuCl)_4$, a common precursor for the Cp*RuCl fragment, with alkynyl triazenes. First investigations were performed with alkynyl triazene **2g** (Scheme 9). We expected that the bulky *tert*-butyl group next to the triple bond would favor the coordination of the triazene function. However, when the reaction mixture was analyzed by ^{13}C NMR spectroscopy (CD_2Cl_2), the data indicated the formation of a η^2-bound alkyne complex (**23**). Characteristic deshielded signals were observed for alkyne C atoms, which appeared at 143.4 and 154.6 ppm, respectively. For comparison, the corresponding C_{sp} resonances for alkyne **2g** are found at 84.3 and 88.5 ppm ($CDCl_3$).[14] The strong deshielding of the ^{13}C NMR signals suggested that that the alkyne acts as a four electron donor in this complex.[26]

Complexes of the formula (cyclopentadienyl) RuCl(η^2-alkyne) are notoriously difficult to isolate.[27] Common problems are facile decomplexation of the weakly bound alkyne ligand, and follow-up reaction such as [2 + 2] cycloadditions. Both types of problems were encountered during our investigations, and we were not able to synthesize the adduct **23** on a preparative scale in pure form. However, we did manage to obtain single crystals of complex **23** by storing a saturated solution of the complex in diethyl ether at –20 °C.

Scheme 9. Reaction of $(Cp^*RuCl)_4$ with Alkynyl Triazene 2g.



The molecular structure of complex **23** was determined by X-ray diffraction, and a graphic representation is shown in Figure 2a.[28] As already indicated by the NMR data, the alkynyl triazene is bound via the triple bond to the Cp*RuCl fragment. The coordination to the Ru leads to an elongation of the triple bond: for complex **23**, a C1-C2 distance of 1.274(5) Å is observed, where as a value of 1.2033(14) Å is found for *t*BuCCN$_3$Me$_2$, a close analogue of **2g**.[14] Furthermore, one can observe a strong bending away from linearity, with a C1-C2-C3 angle of only 141.3 °.

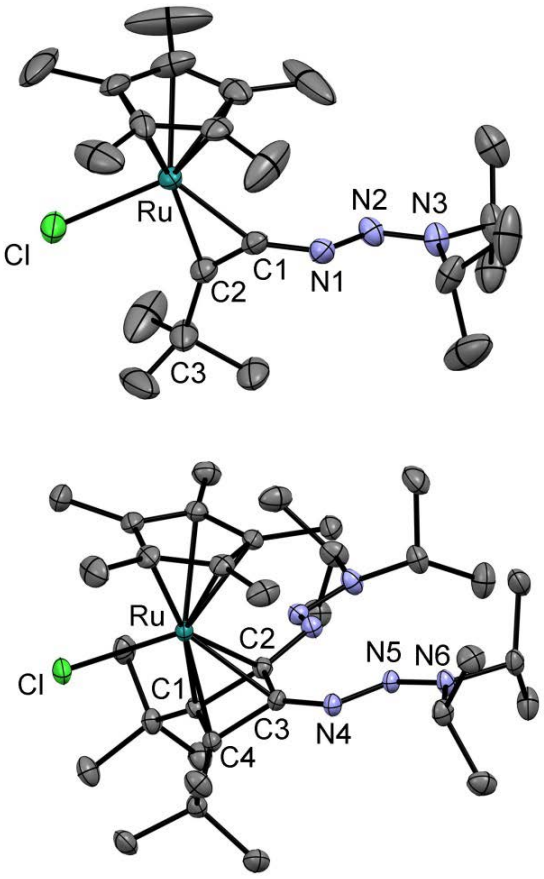
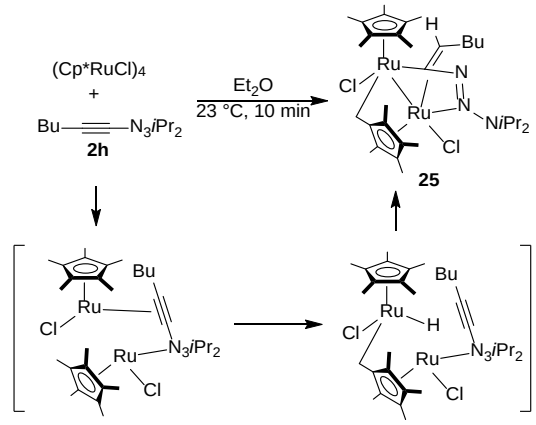


Figure 2. Molecular structures of complex **23** (a) and **24** (b) in the crystal. Hydrogen atoms are omitted for clarity. The ellipsoids are at 50% probability. Selected bond lengths (Å) and angles (°): **23**: Ru-Cl 2.413(2), Ru-C1 2.040(5), Ru-C2 2.061(3), C1-C2 1.274(5), C1-N1 1.382(6), N1-N2 1.276(17), N2-N3 1.342(9), C1-C2-C3 141.3, C2-C1-N1 147.4; **25**: Ru-Cl 2.4217(5), Ru-C1 2.1698(17), Ru-C2 2.1978(17), Ru-C3 2.1792(17), Ru-C4 .21450(17), C3-N4 1.392(2), N4-N5 1.279(2), N5-N6 1.325(2).

The reaction between $(Cp^*RuCl)_4$ and an excess of alkyne **2g** resulted in the formation of the cyclobutadiene complex **24**, which was isolated in 71 % yield (Scheme 9). A crystallographic analysis[25] revealed that the alkynyl triazene had undergone a head-to-head dimerization, as it is often observed for Cp*RuCl(cyclobutadiene) complexes.[27b,29] The Ru-Cl bond distance (2.413(2) Å), as well as the distances between the carbon atoms of the cyclobutadiene ring and the Ru center ($Ru\text{-}C_{av.}$ = 2.17 Å) are within the expected range. The planes defined by the triazene groups are nearly coplanar with the plane defined by the cyclobutadiene ring. This structural feature suggests that there is electronic communication between the triazene groups and the four-membered ring. Changing the substituent on the alkynyl triazene from *tert*-butyl to a less bulky *n*-butyl group had a pronounced effect of the outcome of the reaction. When $(Cp^*RuCl)_4$ was mixed with triazene **2h**, we were not able to detect a simple adduct of type Cp*RuCl(**2h**). Instead, dinuclear complex **25** was found (Scheme 10).

Scheme 10. Reaction of $(Cp^*RuCl)_4$ with Alkynyl Triazene 2h.



The solid state structure of complex **25** is depicted in Figure 3.[28] A peculiar feature of **25** is the presence of a bridging, $\eta^1:\eta^5$-bound tetramethylfulvene ligand.[30] Furthermore, one can observe a metalated vinyl triazene ligand. The latter also acts as a bridging ligand, with coordination to the Cp*RuCl centers via the vinyl group and the central N3 atom of the triazene function. A plausible mechanism for the formation of **25** involves coordination of two Cp*RuCl fragments to one alkynyl triazene (Scheme 10). The simultaneous complexation to the same alkyne promotes an oxidative addition of the Cp* methyl group, resulting in the formation of a hydride complex. Insertion of the triple bond into to the Ru-H bond then gives complex **25**. It should be noted that complex **25** was only isolated in modest yield, and we were not able to identify other reaction products. Although an X-ray crystal structure of **25** was obtained, isolation of pure **25** on a preparative scale failed due to its lability in solution. Still, the formation of complex **25** is evidence that the organometallic chemistry of alkynyl triazenes can be quite distinct from the one of 'normal' alkynes.

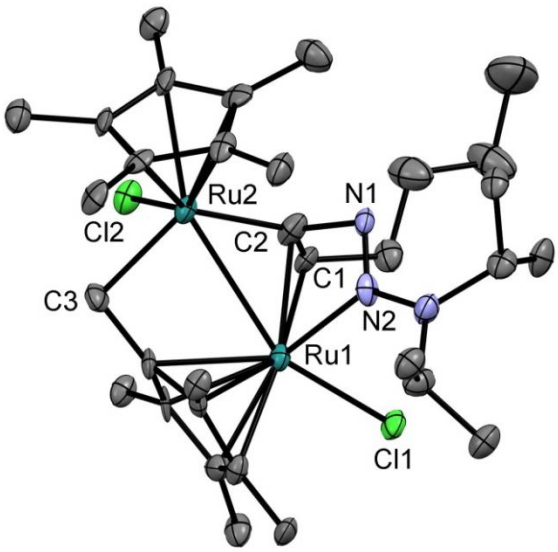
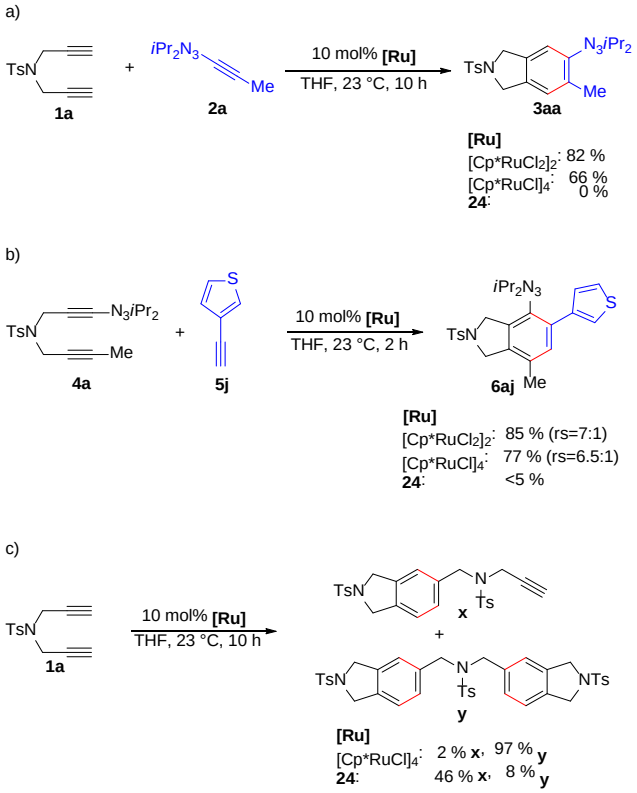


Figure 3. Molecular structure of complex **25** in the crystal. Hydrogen atoms and solvent molecules are omitted for clarity. The ellipsoids are at 50% probability. Selected bond lengths (Å) and angles (°): Ru1-Cl1 2.407(2), Ru1-N2 2.144(8), Ru1-C1 2.356(11), Ru1-C2 2.211(11), Ru2-Cl2 2.455(3), Ru2-C3 2.134(10), Ru2-C2 2.044(11), Ru1-Ru2 3.0094(11).

Investigation of potential catalyst deactivation pathways

The rapid formation of ruthenium complexes **24** and **25** with alkynyl triazenes raises the question of their bearing on the cyclotrimerization catalysis. In this respect, a set of control experiments using ruthenium complex **24** was conducted (Scheme 11). Exposure of **1a** and **2a** towards complex **24** did not yield any cyclotrimerization product. In comparison, both $[Cp^*RuCl_2]_2$ and $[Cp^*RuCl]_4$ efficiently catalyze the formation of **3aa**. This outcome was confirmed by the attempted reaction between alkynyl triazene **4a** and alkyne **5j**. $[Cp^*RuCl_2]_2$ and $[Cp^*RuCl]_4$ reliably provided arene **6aj** in comparable yields and regioselectivity, whereas complex **24** was catalytically inactive. In a last simplified control, diyne **1a** without any additional alkyne was exposed to the different ruthenium complexes. As expected $[Cp^*RuCl]_4$ formed double [2 + 2 + 2] trimer **y** in almost quantitative yield. Exposure of **1a** to complex **24** gave moderate yields of dimerization product **x** and a small amount of trimer **y**. It indicates that the cyclobutadiene ligand of **24** can dissociate over time. To some degree, **24** is capable of reentering a productive catalytic cycle.



Scheme 11: Assessment of the Catalytic Competence of Ruthenium Complex 24.

Due to difficulties to prepare complex **25** on a preparative scale, we have not performed control experiments with this complex. Nevertheless, it is conceivable that dimeric complexes of this type are involved in catalyst deactivation. If this was the case, prevention of the initial steps of the deactivation pathway, namely the putative C-H activation of the methyl group of the Cp* ligand, may allow for improved methods with lower catalyst loadings.

Conclusion

In summary, we have reported the cyclotrimerization of 1-alkynyl triazenes for the convenient access to densely functionalized aryl and pyridyl triazenes. These findings significantly expand the synthetic utility of alkynyl triazenes and highlight their compatibility with transition metal catalysts, especially ruthenium. The Cp*Ru-catalyzed [2 + 2 + 2] cyclotrimerization proceeds well both with simple alkynyl triazenes and tethered 1-diynyl triazenes. Attractively, the methods could be extended to pyridine synthesis by replacing an alkyne with a nitrile. Generally, the reactions are characterized by a very pronounced regioselectivity induced by the triazenyl group and notably yield the sterically more hindered product. The precisely installed triazene group of the formed aromatic ring is a highly versatile moiety which is smoothly converted into the most important functional aryl substituents, including fluorides. This makes the method extremely useful for divergent functionality manipulations on these bicyclic motifs. Moreover, such triazenes engage equally well in intramolecular transformation to afford a variety of valuable heterocycles. Investigations of the largely unknown coordination chemistry of alkynyl triazenes revealed not only a rare Cp*RuCl(η^2-alkyne) complex, but as well unusual addi-

tional complexes. These species may be linked to catalyst deactivation and can provide some guidance to design even better performing catalysts.

ASSOCIATED CONTENT

Supporting Information

Synthetic procedures, characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

This work is supported by the EPFL and the Swiss National Science Foundation (No 200021_157085). We thank Dr. R. Scopelliti and Dr. F. Fadaei Tirani for X-ray crystal structure analyses.

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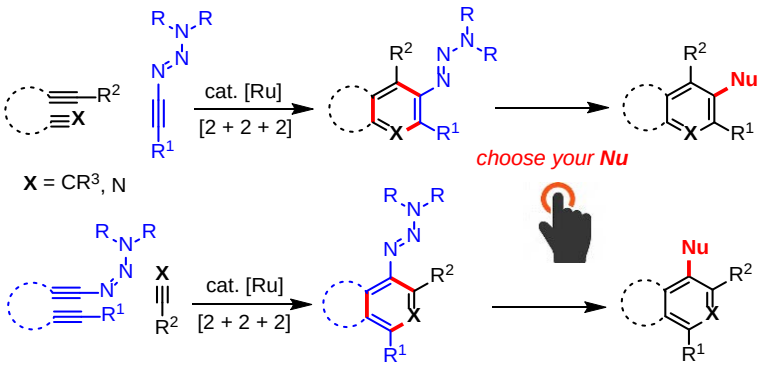
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