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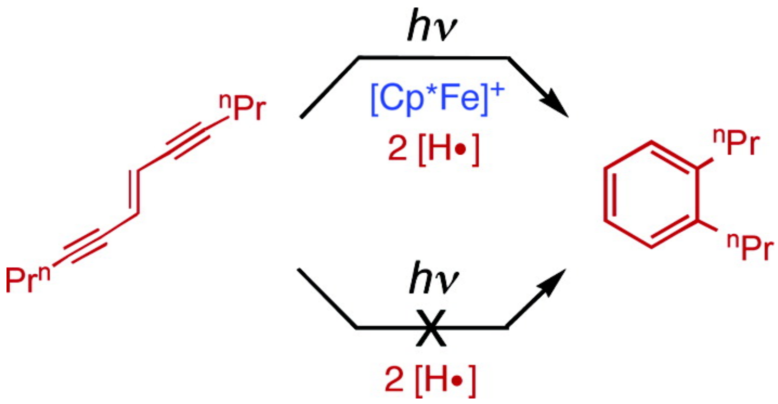

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A Transition-Metal-Catalyzed Enediyne Cycloaromatization

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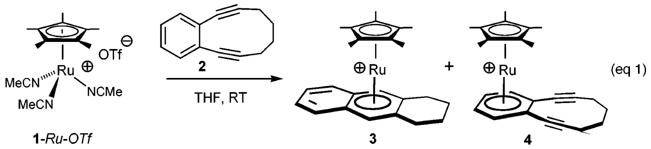
The controlled cycloaromatization of conjugated enediynes is an important and challenging problem,[1] which has led to the development of stoichiometric metal-based triggering mechanisms.[2] A key design requirement of this approach is metal coordination by judiciously placed heteroatoms within the enediyne framework. A fundamentally different cyclization trigger involves the room temperature reaction of $[(\eta^5\text{-}C_5Me_5)Ru(CH_3CN)_3]OTf$ (**1**-Ru-OTf)[3] with either benzannelated or alicyclic enediynes which lack heteroatoms.[4,5] For example, reaction of **1**-Ru-OTf with **2** led to a small amount of the cyclized complex **3**, with noncyclized ruthenium−arene **4** as the major product (eq 1).[4a]



We were intrigued by the possibility that the readily available iron complex $[(\eta^5\text{-}C_5Me_5)Fe(CH_3CN)_3]PF_6$ (**1**-Fe)[6] may function as a cycloaromatization trigger without competitive binding to the arene (e.g., to form the iron analogue of **4**). Despite the structural and electronic similarity of **1**-Ru and **1**-Fe, these complexes display remarkably different reactivity patterns. Of particular note, **1**-Ru, *but not* **1**-Fe, readily undergoes ligand substitution reactions with arenes at room temperature to afford η^6-arene complexes.[7] In addition, the lower "areneophilicity" of **1**-Fe suggested that photoinduced arene dissociation from the $[(\eta^5\text{-}C_5Me_5)Fe]$ cation would be irreversible, thereby facilitating dissociation and isolation of the cycloaromatized organic product.[8]

Here we report that **1**-Fe does indeed trigger cycloaromatization of acyclic and alicyclic enediynes, and that photochemical liberation of the arene ligand from iron is significantly more effective than in the case of ruthenium. These observations have led to the development of iron−arene complexes as air-stable reagents for the room temperature cycloaromatization of enediynes, the first demonstration of a transition-metal-catalyzed enediyne cycloaromatization reaction, and a novel method for cycloaromatization of *trans*-enediynes that are normally inert toward both thermal and photochemical cyclization.

Initial attempts at utilizing **1**-Fe as a trigger for cycloaromatization of either **2** or the nonbenzannelated enediyne (*Z*)-dodeca-4,8-diyn-6-en (**5**-*Z*)[9] appeared to fail due to the poor solubility and/or instability of **1**-Fe in THF.[10] In an effort to avoid the use of THF solvent and efficiently trap the presumed metal−biradical intermediate, both 1,4-cyclohexadiene and the more sterically hindered γ-terpinene (1-isopropyl-4-methyl-1,4-cyclohexadiene) were examined as potential H-atom donors in acetone solvent.[11]

Attempted cycloaromatization of the benzannelated enediyne **2** in acetone-d_6, containing 1,4-cyclohexadiene and **1**-Fe, again led to no observable reaction at room temperature and only decomposition of **1**-Fe at elevated temperatures. However, in acetone-d_6 containing 1,4-cyclohexadiene, **5**-*Z* underwent a rapid (30 min) reaction with **1**-Fe to give **6**-Fe in 92% yield[12] (Scheme 1). In a similar fashion, an acetone solution containing the alicyclic enediyne **7**, **1**-Fe, and γ-terpinene led to an 82% yield of the tetrasubstituted arene complex **8**-Fe. Despite the fact that **1**-Ru reacts with γ-terpinene to give $\{(\eta^5\text{-}C_5Me_5)Ru[\eta^6\text{-(3-isopropyltoluene)}]\}PF_6$,[11] the reactions of **1**-Ru with enediynes **5**-*Z* and **7** proceed in the presence of γ-terpinene to give the desired arene complexes in 82% (**6**-Ru) and 78% (**8**-Ru) yield.

The development of a catalytic system requires in situ liberation of the arene ligand from the metal−arene product. Photochemical decomplexation studies on metal−arenes **6** and **8** were carried out utilizing a medium pressure 500W Hanovia light source (Scheme 1). Photolysis of **6**-Fe in acetonitrile-d_3 solution at 25 °C for 24 h led to quantitative conversion to 1,2-di(*n*-propyl)benzene (**9**) and formation of $[(\eta^5\text{-}C_5Me_5)Fe(CD_3CN)_3]PF_6$ (**1**-Fe-d, 92%). A similar experiment, involving photolysis of **6**-Ru in acetonitrile-d_3, required 48 h to give both **9** and $[(\eta^5\text{-}C_5Me_5)Ru(CD_3CN)_3]PF_6$ (**1**-Ru-d) in 98% yield at 91% conversion.[13] Continued irradiation had no effect on the percent conversion, suggesting that a photostationary state had been established. This was supported by the observation that photolysis of **1**-Ru (0.014 mmol) and *o*-xylene (0.071 mmol) in acetonitrile-d_3 generated the η^6-*o*-xylene complex in a maximum yield of 9%. Similar irradiation of an acetonitrile-d_3 solution of **1**-Fe and *o*-xylene failed to generate an iron−arene complex, even after 5 days. When acetone was employed as the solvent, no photochemical decomplexation occurred with **6**-Ru; however, photolysis of **6**-Fe in acetone at 25 °C for 24 h gave **9** in 95% yield. The differences in arene ligand dissociation for iron and ruthenium were even more pronounced for the tetrasubstituted arene complexes **8**. Photolysis of **8**-Fe in acetonitrile-d_3 for 132 h led to nearly quantitative formation of **10** and an 87% yield of **1**-Fe-d, whereas arene decomplexation from **8**-Ru was only 50% complete after 156 h of irradiation. Photochemical dissociation of the arene ligand from **6**-Fe indicated that arene complexes may serve as air-stable reagents for enediyne cycloaromatization, and that transition-metal-catalyzed cycloaromatizations may be feasible under photochemical conditions.[14,15] When an acetone-d_6 solution containing a substoichiometric amount of **6**-Fe (0.005 mmol, 0.017 M), **5**-*Z* (0.018 mmol), and γ-terpinene (0.090 mmol) was irradiated at 23 °C for 144 h, the free arene **9** was generated in 91% yield (TON > 3; Scheme 2). Consistent with the previous results of Bergman,[9] photolysis of a similar reaction mixture, but with no **6**-Fe present, failed to generate arene product.

The well-established photochemical interconversion of *cis*- and *trans*-enediynes[16] suggested that room temperature photolysis of the *trans*-enediyne, (*E*)-dodeca-4,8-diyn-6-en (**5**-*E*), in the presence of **6**-Fe would also lead to the formation of arene **9**. The *trans*-enediyne **5**-*E* (0.026 mmol) was therefore photolyzed (144 h) in the presence of **6**-Fe (0.007 mmol, 0.021 M) and 1,4-cyclohexadiene (0.14 mmol) to give 3.1 turnovers and an 83% yield of **9**.

The fact that arene dissociation from the $[(\eta^5\text{-}C_5Me_5)Ru]$ cation is reversible, unlike the iron analogue, imposes an inherent limitation

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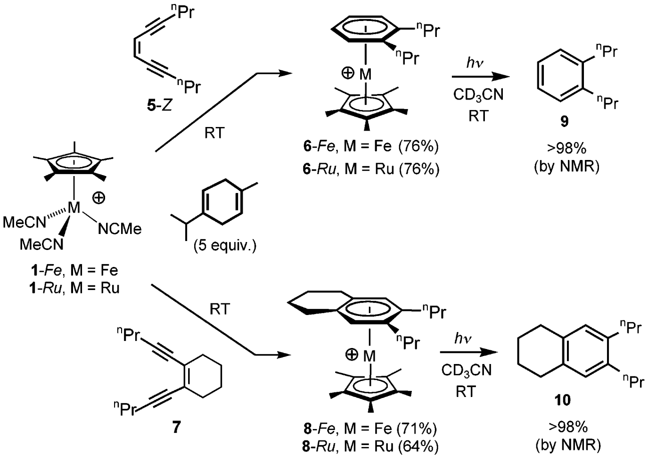
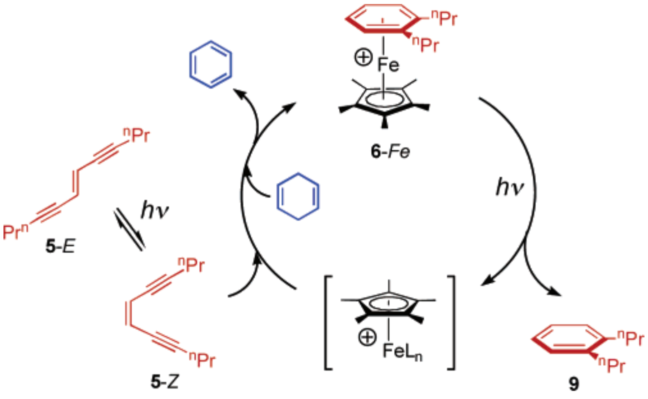
Scheme 1



(Isolated yields are given in parentheses)

Scheme 2



on its use in catalytic enediyne cyclizations. Furthermore, arene ligand dissociation in the ruthenium system fails in neat acetone, and added acetonitrile inhibits reaction of the [(η^5-C$_5$Me$_5$)Ru] cation with enediynes. Despite these limitations, photolysis (144 h) of an acetone-d_6 solution containing acetonitrile-d_3 (0.05 mmol), **1**-Ru (0.005, 0.017 M), **5**-*Z* (0.02 mmol), and 1,4-cyclohexadiene (0.10 mmol) led to a 74% yield of **9**.

The catalytic cycle in Scheme 2 represents the first transition-metal-catalyzed Bergman cycloaromatization reaction. Catalysis is currently limited primarily by the slow arene dissociation step. It is therefore anticipated that improved catalysts will be achieved by modification of the ancillary ligand on iron or the use of metals that bind less strongly to the arene products. The tandem use of a metal and light promises to dramatically expand the scope of enediyne cycloaromatization by circumventing the previous stereochemical requirement of a *cis*-enediyne geometry.[17]

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Supporting Information Available: Experimental and spectroscopic details of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) When an acetone/THF solvent mixture was employed in order to improve the solubility of **1**-Fe, there was once again no observable reaction with **2**. However, in an acetone-d_6/THF-d_8 solvent mixture, **1**-Fe and **5**-*Z* underwent a slow conversion to **6**-Fe-d_2 over the course of 3 days in 39% yield at 75% conversion.

(11) In the absence of an enediyne, both 1,4-cyclohexadiene and γ-terpinene underwent reaction with **1**-Ru at room temperature in acetone to form the corresponding η^6-benzene and η^6-cymene complexes in nearly quantitative yield. Significantly, **1**-Fe failed to undergo reaction with either H-atom donor at room temperature.

(12) Yield was determined by integration of the ^{1}H NMR spectrum. Isolated yields are given in Scheme 1 and in the Supporting Information.

(13) Initial dissociation of arene from **6**-Ru was observed to occur faster than that for **6**-Fe, which is consistent with Mann's determination that the quantum yield for arene dissociation from [(η^5-C$_5$Me$_5$)Ru] is greater than that for [(η^5-C$_5$Me$_5$)Ru]: Schrenk, J. L.; McNair, A. M.; McCormick, F. B.; Mann, K. R. *Inorg. Chem.* **1986**, *25*, 3501.

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