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Iron-Catalyzed [2π + 2π] Cycloaddition of α,ω-Dienes: The Importance of Redox-Active Supporting Ligands

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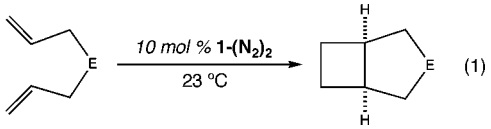
The metal-catalyzed [2π + 2π] cycloaddition of olefins to form cyclobutanes is an attractive transformation for the direct construction of strained four-membered rings.[1] While thermally forbidden,[2] photochemical methods,[3] use of strained olefins, activated π-systems (e.g., allenes), and transition metal reagents have all been employed to circumvent the constraints of orbital symmetry.[1] Examples of metal catalyzed [2π + 2π] cycloadditions have broadened the scope of this transformation to include styrene derivatives[4] and the conversion of bis(enones) into bicyclo[3.2.0] ring systems.[5] Here we describe the iron-catalyzed synthesis of a family of bicyclo-[0.2.3]heptane derivatives via intramolecular [2π + 2π] cycloaddition of the corresponding α,ω-dienes. A key feature of the catalytic cycle is the redox activity of the supporting bis(imino)-pyridine ligand.

Recently our laboratory described the synthesis of the bis(imino)-pyridine iron bis(dinitrogen) complexes, (^{i}PrPDI)Fe(N_2)$_2$ (^{i}PrPDI = 2,6-(2,6-^{i}Pr$_2$C$_6$H$_3$NCR)$_2$C$_5$H$_3$N; R = Me, **1-(N$_2$)$_2$**, R = Ph, **2-(N$_2$)$_2$)**, that serve as efficient precursors for the catalytic hydrogenation of olefins, alkynes,[6] and aryl azides.[7] More detailed computational, spectroscopic, and structural studies established a two electron reduced bis(imino)pyridine ligand, suggesting Fe(II) rather than Fe(0) as the active species.[8] As part of our continuing effort to expand the role of inexpensive and relatively nontoxic iron catalysts in organic synthesis, the construction of small rings via the cyclization of α,ω-dienes was explored.

Inspired by the work with group 3 transition metal and lanthanide catalysts,[9] the cyclization of 1,5-hexadiene was attempted. Stirring the diolefin with 10 mol % of **1-(N$_2$)$_2$** under 0.5 atm of H_2 yielded a mixture of methylenecyclopentane as well as the hydrogenation products, methylcyclopentane and *n*-hexane (see Supporting Information). The selectivity of the catalytic reaction was improved and formed only methylenecyclopentane when the iron dihydrogen complex (^{i}PrPDI)Fe(η^2-H_2) (**1-(H$_2$)**) was employed as the precatalyst. Attempts to extend the scope of the catalytic cyclization to 1,6-heptadiene produced a different result. In this case, cyclization with 10 mol % **1-(N$_2$)$_2$** with 0.5 atm H_2 yielded *n*-heptane and a new alkane, identified as the cis isomer of bicyclo[0.2.3]heptane, arising from intramolecular [2π + 2π] cycloaddition of the two terminal olefins (eq 1).

The observation of efficient α,ω-diene cycloaddition to yield the corresponding bicycle prompted investigation into the scope of the catalytic C−C bond-forming reaction. Table 1 reports a family of diolefins that undergo [2π + 2π] cycloaddition at 23 °C using **1-(N$_2$)$_2$** as the catalyst precursor. Typically the catalytic reactions were conducted with 10 mol % of **1-(N$_2$)$_2$**, and the conversion was monitored by ^{1}H NMR spectroscopy. Alternatively, catalytic turnover was accomplished by in situ activation of air-stable **1-Br$_2$** with $NaBEt_3H$, obviating the synthesis of sensitive



(1)

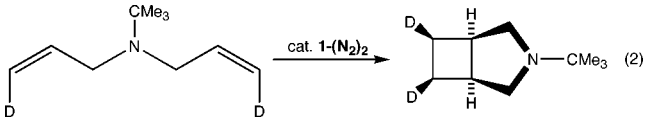
Table 1. [2π + 2π] Cycloaddition of α,ω-Dienes[a]

	E	time (min)	conversion (%)	TOF (h^{-1})	ΔG° (kcal/mol)	ΔH° (kcal/mol)	ΔS° (eu)
1	CH_2	300	92	1.8	−9.4	−13.2	−12.6
2	$SiMe_2$	300	0	0	−6.2	−10.9	−15.8
3	NH[b]	300	0	0	−11.4	−15.3	−12.7
4	N−Bn	26	90	21[c]	−14.0	−17.4	−11.3
5	N-^{t}Bu	<5	>95	>240[d]	−18.3	−21.0	−9.5
6	NBoc	300	24	0.5	−15.5	−18.6	−10.3
7	$C(CO_2Et)_2$	141	>95	4	−16.3	−19.1	−9.4

[a] Conditions: 0.5 mL of a 0.010 M C_6D_6 solution of **1-(N$_2$)$_2$**, 10 equiv of substrate, 23 °C. [b] Stoichiometric reaction (vide infra). [c] 90% conversion; diminishes after 26 min owing to product inhibition (see text). [d] >95% in <5 min.

1-(N$_2$)$_2$. The yields did not change when the reactions were conducted in the dark, suggesting thermal processes.

The stereochemistry of the catalytic [2π + 2π] reactions was also investigated with the cyclization of (*Z*,*Z*)-^{t}BuN(CH_2CH═CHD)$_2$. Exposure of the labeled substrate to 10 mol % of **1-(N$_2$)$_2$** produced no isotopic scrambling affording only one isotopomer of the cyclized product (eq 2). The converse experiment with the (*E*,*E*) diolefin yielded the complimentary isotopomer.



(2)

The iron catalyst is tolerant of amine and ester functional groups as evidenced by facile cyclizations of diallyl-*tert*-butylamine and diethyldiallylmalonate (entries 5 and 7, respectively). *N*-Boc and benzyl-protected amines also undergo efficient conversion to the corresponding bicycle. Also presented in Table 1 are the DFT-computed thermodynamic values for each reaction; all of the [2π + 2π] cycloadditions to cis products (observed) are spontaneous. Some substrates, such as E = $SiMe_2$ and those with internal olefins (allyl-*tert*-butylcrotylamine or *tert*butyldicrotylamine), were not successfully cyclized even though the reaction is thermodynamically favorable.

Monitoring the [2π + 2π] cyclization reactions by ^{1}H NMR spectroscopy provided insight into the relative rates of conversion for the series of amine substrates. In the case where E = N^{t}Bu, the iron bis(dinitrogen) complex, **1-(N$_2$)$_2$** was recovered at the completion of catalysis. For E = NBn, the bis(imino)pyridine iron

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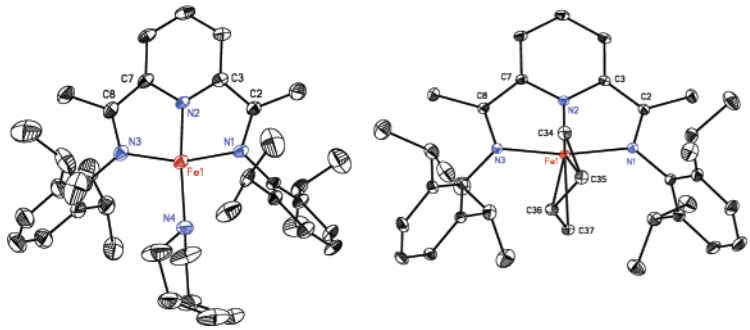
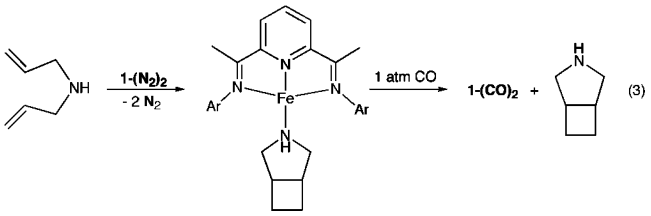


	1-(HNC_6H_{10})	1-(C_4H_6)
Fe(1)-N(1)	1.910(3)	2.0049(7)
Fe(1)-N(2)	1.819(3)	1.8411(7)
Fe(1)-N(3)	1.921(4)	1.9656(7)
Fe(1)-N(4)	2.031(3)	
N(1)-C(2)	1.360(5)	1.3324(11)
N(3)-C(8)	1.372(5)	1.3718(11)
C(2)-C(3)	1.412(6)	1.4219(12)
C(7)-C(8)	1.389(6)	1.4136(12)
N(2)-C(3)	1.360(5)	1.3718(11)
N(2)-C(7)	1.386(5)	1.3768(11)

Figure 1. ORTEP representation of **1-(HNC_6H_{10})** (left) and **1-(C_4H_6)** (right) at 30 % probability. Hydrogen atoms are omitted for clarity. Selected distances (Å) are also included.

benzylamine complex, **1-($BnNC_6H_{10}$)**, was identified following turnover. Diallyamine, the least hindered in the series, produced only stoichiometric [$2\pi + 2\pi$] cyclization, cleanly affording **1-(HNC_6H_{10})** upon addition to **1-(N_2)$_2$** (eq 3). Liberation of free azobicyclo[0.2.3]heptane was accomplished by exposure to 1 atm of carbon monoxide. Thus, product inhibition dictates the rate of catalytic turnover, where the less substituted and hence more nucleophilic azabicycles coordinate more tightly and inhibit conversion. It should also be noted that the most facile cycloadditions were observed for the most thermodynamically favored cases, consistent with the Thorpe−Ingold effect.[10]



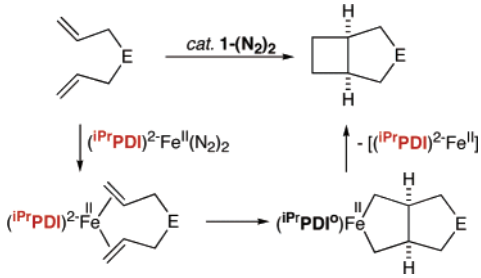
Red brown **1-(HNC_6H_{10})** was characterized by X-ray diffraction (Figure 1). Both the metrical parameters and NMR spectroscopic data are analogous to the *N*,*N*-(dimethylamino)pyridine iron compound, **1-DMAP**,[8a] where computational, spectroscopic, and structural data established an intermediate spin ($S_{Fe} = 1$) ferrous center complexed by a bis(imino)pyridine dianion, [^{i}PrPDI]$^{2-}$.

To gain further insight into the mechanism of the cyclization reaction and in particular, the nature of the α,ω-diene intermediate, **1-(N_2)$_2$** was treated with a diolefin unlikely to undergo intramolecular [$2\pi + 2\pi$] cycloaddition. For this reason, 1,3-butadiene was added to **1-(N_2)$_2$** and yielded a red, diamagnetic solid identified as the iron-butadiene compound, **1-(C_4H_6)**. The solid-state structure (Figure 1, right) reveals a rare example of *trans*-butadiene coordination[11] in addition to a two electron reduced bis(imino)pyridine chelate. These data support an Fe(II) complexed by [^{i}PrPDI]$^{2-}$ rather than an Fe(0) ion with a neutral chelate.[8]

The proposed mechanism (Scheme 1) for the catalytic [$2\pi + 2\pi$] cycloaddition involves initial substitution of the N_2 ligands by the diene. Based on the properties of **1-(C_4H_6)**, the oxidation states of the iron are maintained as ferrous throughout the process. Following C−C coupling to form the metallocycle, formal reductive elimination yields the observed bicycle and regenerates the iron diene complex. The redox activity of the [^{i}PrPDI] ligand preserves the ferrous oxidation state throughout the cycle and may prevent complications from Fe(0) precipitation that are observed with other (e.g., Ni) metallocycles.[12]

In summary, we have discovered an efficient method for the synthesis of cyclobutanes via iron-catalyzed [$2\pi + 2\pi$] cycloaddition that takes advantage of the unique electronic structure of bis(imino)pyridine iron compounds.

Scheme 1



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Supporting Information Available: Additional experimental, computational, and crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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