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Fe-Catalyzed Allylic C−C-Bond Activation: Vinylcyclopropanes As Versatile a1,a3,d5-Synthons in Traceless Allylic Substitutions and [3 + 2]-Cycloadditions

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Ⓢ *Supporting Information*

ABSTRACT: The low-valent iron complex $Bu_4N[Fe(CO)_3(NO)]$ (*TBAFe*) catalyzes the allylic C−C-bond activation of electron-poor vinyl cyclopropanes to generate synthetically useful a1,a3,d5-synthons which are prone to undergo multiple consecutive reactions. The versatility of this approach is demonstrated by a traceless allylic substitution and a formal [3 + 2] cycloaddition to give either functionalized acyclic products or densely substituted cyclopentanes and pyrrolidines in high yields and regioselectivities.

Within the past years our group and others have shown that the electron-rich ferrate $Bu_4N[Fe(CO)_3(NO)]$ (*TBAFe*) is a versatile electron-transfer catalyst that can be employed in various transformations like allylic substitutions,[1] transesterifications,[2] or hydrosilylations.[3] Although the former transformation is performed under neutral and salt-free conditions the degree of atom economy in transition metal catalyzed allylic substitutions in general can be improved through the use of strained vinyl-substituted rings like vinyloxiranes,[4] vinylaziridines,[5] or vinylcyclopropanes.[6,7]

We envisioned this strategy to be attractive in order to push the limits in Fe-catalyzed allylic substitution chemistry. In particular the activation of a C−C-bond appeared to be of interest from both a catalytic and synthetic point of view. The selective catalytic activation of a carbon−carbon single bond is a scientific task that has attracted considerable interest in the past decade.[8] The working catalytic systems are mainly based on rhodium,[9] ruthenium,[10] nickel,[11] and palladium.[12] However, systems that employ inexpensive and readily abundant metals such as iron have only scarcely been investigated. Iron salts were shown to act as Lewis acid catalysts[13−15] leading to stabilized carbenium ions which can be trapped in Friedel−Craft type reactions (eqs 1 and 2, Figure 1). Furthermore, ferric chloride catalyzes the DDQ/$TMSN_3$ mediated formation of amides under oxidative conditions (eq 2, Figure 1).[16] In the field of photocatalysis, $[Cp(CO)_2FeMe]$ allows for a σ-bond metathesis between alkylsilanes and alkylnitriles via the cleavage of a C−CN bond (eq 3, Figure 1).[17] The catalytic activation of vinylcyclopropanes (VCPs) by a Lewis acid[18] or nucleophilic noble metal catalysts based on Pd,[7a−e] Ir,[7e] Rh,[7f,g] Ru,[7h] and Ni[7i,j] is a literature precedent. Fürstner was able to show that low-valent ferrates generated in situ by treating $Fe(acac)_3$ with alkyl Grignard reagents are potent catalysts for the addition of hard nucleophiles into the π-bond of a VCP (eq 4, Figure 1).[19]

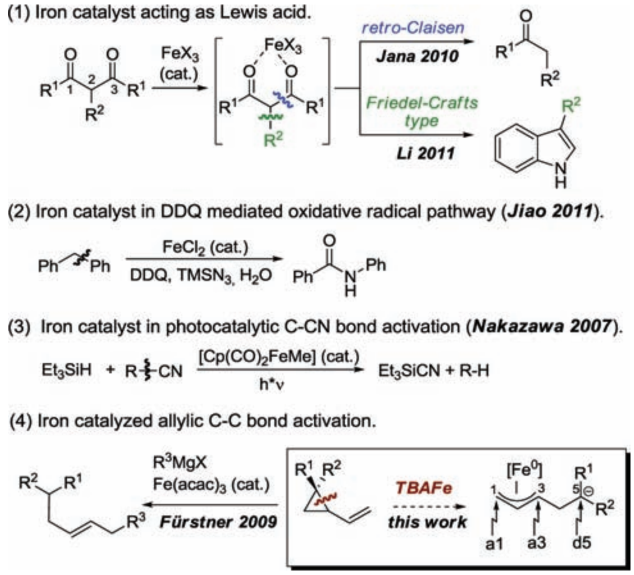

Figure 1. Iron-catalyzed C−C bond activations.

The complementary activation of a VCP using a metal-centered nucleophilic ferrate with generation of an intermediate allyl-Fe complex, which might be regarded as an a1,a3,d5-synthon, however has not been reported yet but would open up new perspectives for synthetic applications.[20]

Herein we report that the nucleophilic ferrate $Bu_4N[Fe(CO)_3(NO)]$ (*TBAFe*) is an efficient catalyst for this particular allylic C−C-bond activation. The synthetic versatility of the intermediate allyl metal complexes is demonstrated in a formal traceless allylic substitution and a [3 + 2]-cycloaddition (Scheme 1).

We initiated our studies by focusing on the traceless allylic substitution reaction. The carbanion of the allyl-Fe intermediate, which is formed upon Fe-mediated C−C-bond scission, reacts as a base and generates a new nucleophilic species which in turn attacks the allyl metal a1,a3-acceptor to give the corresponding homologation product (Scheme 1). In order to trigger the proton shift, a sufficient difference in the pK_a values of the primary formed carbanion and the pronucleophile is a prerequisite. As a consequence acidic pronucleophiles were chosen as coupling partners. After an

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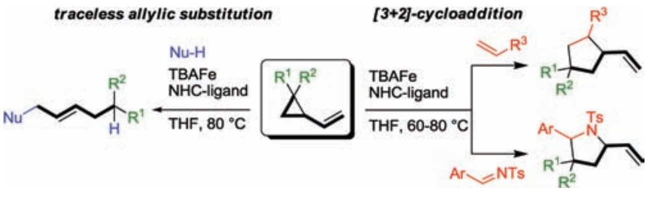
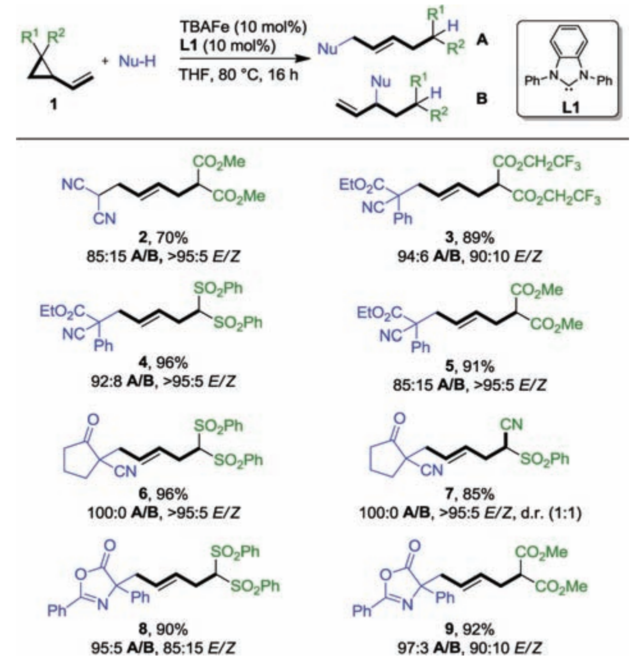
Scheme 1. Fe-Catalyzed Traceless Allylic Substitution and [3 + 2]-Cycloaddition of VCPs



optimization of solvent and ligands,[21] we were pleased to find that TBAFe and NHC-ligand **L1** in THF combine to a potent catalytic system for this transformation. The desired substitution products were obtained in good to excellent yields and regioselectivities in favor of the linear substitution products **A** (Table 1).

Table 1. Fe-Catalyzed Traceless Allylic Substitution of VCPs[a]

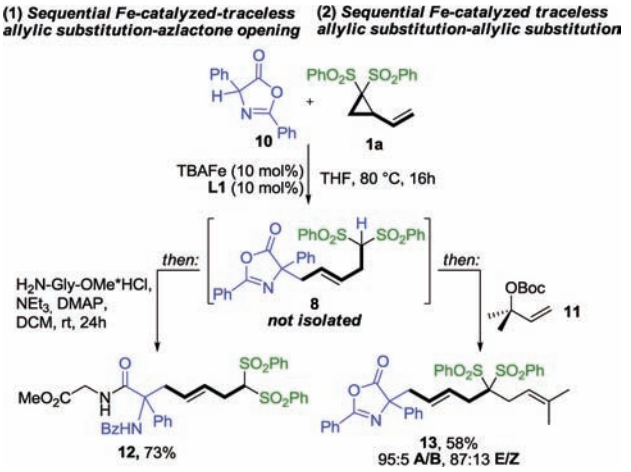


[a] The reactions were performed on a 0.2 mmol scale, using vinylcyclopropane (1 equiv), pronucleophile (1.5 equiv), TBAFe (10 mol %), and **L1** (10 mol %) in THF (0.4 M) at 80 °C.

A variety of pronucleophiles such as malodinitrile, a cyanophenyl ester, cyanocyclopentanone, or a phenylazlactone were successfully employed in this transformation giving rise to polyfunctional products in good to excellent yields. In general *E*-configured double bonds were formed with high selectivity. However, a drop in *E*/*Z* ratio was observed for azlactone **8**. Interestingly, in the presence of malodinitrile the minor isomer **2B** was not isolated as the anticipated branched product, but rather as the cyclic enamine resulting from a subsequent cyclization.[22]

In order to underline the synthetic usefulness of this transformation, vinylcyclopropane **1a** was employed in two different sequential transformations: an Fe-catalyzed traceless allylic substitution followed by a ring opening of the azlactone by an amino acid (eq 1, Scheme 2) and a traceless allylic substitution followed by a standard allylic substitution (eq 2, Scheme 2). Without isolation of intermediate **8**, the addition of methyl glycinate delivered, under standard coupling conditions,[23] functionalized dipeptide **12** in good overall yield. In contrast, the addition of allyl carbonate **11** to the reaction mixture triggers a second Fe-catalyzed process leading to the allylic substitution product **13** in good regioselectivity and a reasonable 58% isolated yield.

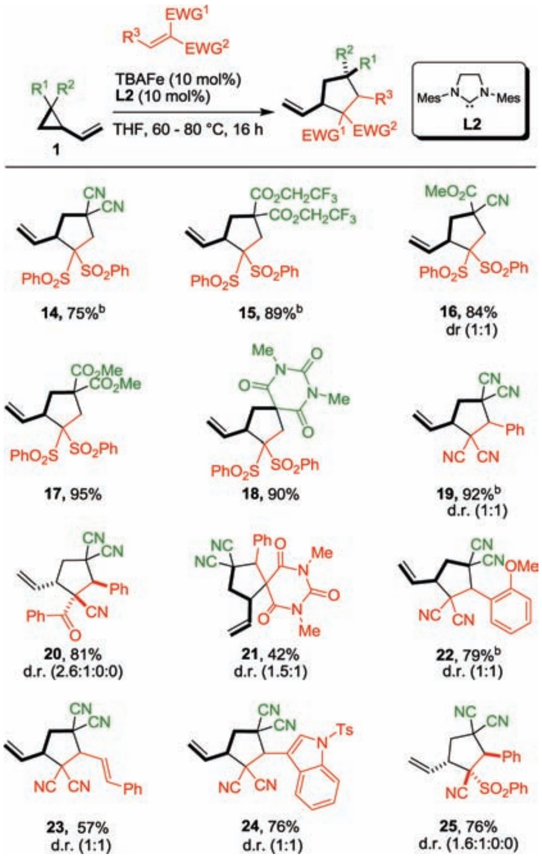
Scheme 2. Sequential Fe-Catalyzed Transformations of VCPs



We subsequently turned our attention toward the elaboration of the second reaction manifold, the formal [3 + 2]-cycloaddition. In this case the carbanion of the allyl-Fe intermediate, formed upon Fe-mediated C−C-bond scission, reacts as a d5-synthon in a Michael addition thus generating a new carbanion that adds onto the allyl Fe-moiety to form a five-membered ring (Scheme 1).

Performing this transformation under the conditions that proved successful for the traceless allylic substitution gave only moderate conversions; however, good yields of the desired cycloaddition products were obtained using mesityl substituted NHC-ligand **L2** (Table 2).[20] First the scope of vinylcyclopropanes was investigated using 1,1-bis(phenylsulphonyl)-ethylene as a Michael acceptor. To our delight different VCPs can be employed in this cycloaddition giving rise to vinylcyclopentanes **14**−**18** in good to excellent yields. Competing side reactions like dimerization of the starting material or formation of the corresponding seven-membered rings were not observed. Functional groups such as esters, nitriles, or amides on the VCPs are tolerated. Whereas a Meldrum acid derived VCP was unreactive, barbiturate-derived VCP gave rise to spiro compound **18** in a 90% yield. Further studies focused on the application of different activated olefins in the [3 + 2]-cycloaddition using malononitrile-derived VCP as a coupling partner. A variety of Michael acceptors are reactive, yielding densely substituted carbocycles in good to excellent yields albeit with low diastereoselectivities (**19**, **21**−**24**) (Table 2). The transformation displays a broad functional group tolerance. Esters, sulfones, nitriles, amides, and ketones are successfully employed; even heterocycles such as indoles **24** are tolerated. The use of an extended Michael acceptor yields only the 1,4-addition product **23**. Interestingly, for some unsymmetrically substituted Michael acceptors a moderate stereoselective bias could be observed during product formation (**20**, **25**) generating only two out of four possible diastereoisomers.

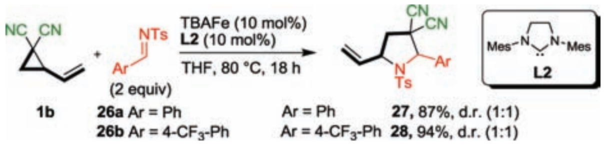
Table 2. Fe-Catalyzed [3 + 2]-Cycloaddition of VCPs[a]



[a] The reactions were performed on a 0.2 mmol scale, using vinylcyclopropane (1 equiv), Michael acceptor (1.25 equiv), TBAFe (10 mol %), and **L2** (10 mol %) in THF at 80 °C unless noted otherwise. [b] Reaction run at 60 °C.

Finally, we wondered whether we could extend this method toward electron-deficient π-bonds of imines. Whereas *N*-Ph and *N*-Boc protected imines gave no or an undefined reaction, we were pleased to find that *N*-tosyl arylimines are good coupling partners for this transformation. In two test experiments **1b** was coupled with **26a** and **26b** under the standard reaction conditions to the corresponding pyrrolidines **27** and **28** in good yields, albeit with low diastereoselectivity (Scheme 3). Unfortunately aldehydes were not applicable toward the reaction conditions.

Scheme 3. Fe-Catalyzed VCP Activation towards Pyrrolidines



In summary we report the allylic C–C-bond activation in the presence of the low-valent iron (-II) complex Bu$_4$N[Fe(CO)$_3$(NO)] (TBAFe). The intermediate allyl Fe-complex was employed as an a1,a3,d5-synthon in a traceless allylic substitution and a [3 + 2]-cycloaddition with activated olefins and imines giving rise to densely substituted vinylcyclopentanes or -pyrrolidines. Both reaction manifolds display a broad functional group tolerance. The advantages of the present catalytic system were demonstrated in sequential iron-catalyzed transformations. Apart from the synthetic usefulness of the multifunctional products, the activation of electron-poor allylic C–C bonds opens up new perspectives in the field of low-valent Fe catalysis. Future studies will focus on the activation of other strained ring systems such as cyclobutanes as well as vinyl oxiranes and aziridines.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed experimental procedures and characterization of all reported 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 interest.

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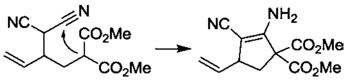
(21) See Supporting Information for details.

(22) The branched isomer **2B** cyclizes spontaneously to the corresponding enamine:



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