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Iron-Catalyzed 1,4-Addition of α-Olefins to Dienes

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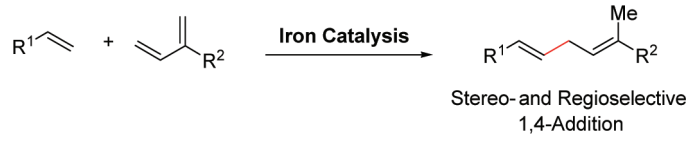
ABSTRACT



A new intermolecular, stereo- and regioselective iron-catalyzed 1,4-addition of α-olefins to 1,3-dienes using as low as 1 mol % of an iminopyridine−ferrous chloride complex was developed. Importantly, both double bonds of the linear 1,4-diene addition products are obtained with absolute stereocontrol.

Iron catalysis has the potential to form valuable carbon−carbon bonds starting from simple starting materials such as hydrocarbons.[1] In this communication we present a functional-group-tolerant, stereo- and regioselective iron-catalyzed 1,4-addition reaction of α-olefins to 1,3-dienes (eq 1). Previously, in the 1960's, Hata investigated the addition of butadiene and isoprene to ethylene and propylene in an autoclave at >500 psi catalyzed by an $Fe(acac)_3/Et_3Al$ mixture.[2] Using the same $Fe(acac)_3/Et_3Al$ mixture but in the presence of 2,2′-bipyridine, Takacs observed formal [4 + 4] ene reactions with 1,3-dienes.[3] The iron-diimine-catalyzed dimerization of 1,3-dienes to afford cyclooctadienes and vinyl cyclohexenes was developed by tom Dieck in the 1980's.[4] Within the past 5 years, Fürstner has shown that a well-defined anionic iron(0) complex, supported by a cyclopentadienyl ligand, can catalyze intramolecular ene reactions,[5] intramolecular cycloadditions, and cycloisomerizations.[6] In 2006, Chirik demonstrated the intramolecular [2 + 2] cycloaddition of 1,6-dienes catalyzed by a redox-active bisiminopyridine−iron complex.[7]

We have investigated iminopyridine-ligated iron complexes that provide access to linear 1,4-diene products that cannot be obtained with tom Dieck's or Takacs' catalysts or by any other hydrovinylation reaction reported to date.[8] Our 1,4-addition reaction complements the functional-group-tolerant cobalt-catalyzed 1,4-hydrovinylation reaction, pioneered by Hilt, which typically affords branched 1,4-dienes.[9] Notable features of the carbon−carbon bond-forming reaction presented herein include the regioselective introduction of prenyl and geranyl substituents, the stereospecific formation of (*E*)-trisubstituted double bonds, and the functionalization of unactivated commodity chemicals using a simple low-valent iron catalyst.

The readily available iron(II) complex **1**·$FeCl_2$ shown in eq 1 can be reduced in situ with activated magnesium metal

(1) For recent reviews of iron catalysis, see: (a) Bolm, C.; Legros, J.; Le Paih, J.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217. (b) Enthaler, S.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3317. (c) Correa, A.; Mancheno, O. G.; Bolm, C. *Chem. Soc. Rev.* **2008**, *37*, 1108. (d) Sherry, B. D.; Fürstner, A. *Acc. Chem. Res.* **2008**, *41*, 1500.

(2) (a) Hata, G. *J. Am. Chem. Soc.* **1964**, *86*, 3903. (b) Hata, G.; Aoki, D. *J. Org. Chem.* **1967**, *32*, 3754. (c) Hata, G.; Miyake, A. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 2762. For related publications, see: (d) Iwamoto, M.; Yuguchi, S. *J. Org. Chem.* **1966**, *31*, 4290. (e) Iwamoto, M.; Yuguchi, S. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 2001.

(3) (a) Takacs, J. M.; Anderson, L. G.; Madhavan, G. V. B.; Creswell, M. W.; Seely, F. L.; Devroy, W. F. *Organometallics* **1986**, *5*, 2395. (b) Takacs, J. M.; Anderson, L. G.; Madhavan, G. V. B.; Seely, F. L. *Angew. Chem., Int. Ed.* **1987**, *26*, 1013. (c) Takacs, J. M.; Anderson, L. G.; Newsome, P. W. *J. Am. Chem. Soc.* **1987**, *109*, 2542. (d) Takacs, J. M.; Myoung, Y.-C.; Anderson, L. G. *J. Org. Chem.* **1994**, *59*, 6928. (e) Takacs, J. M.; Newsome, P. W.; Kuehn, C.; Takusagawa, F. *Tetrahedron* **1990**, *46*, 5507.

(4) (a) tom Dieck, H.; Dietrich, J. *Chem. Ber.-Recueil* **1984**, *117*, 694. (b) tom Dieck, H.; Dietrich, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 781.

(5) Fürstner, A.; Martin, R.; Majima, K. *J. Am. Chem. Soc.* **2005**, *127*, 12236.

(6) Fürstner, A.; Majima, K.; Martin, R.; Krause, H.; Kattnig, E.; Goddard, R.; Lehmann, C. W. *J. Am. Chem. Soc.* **2008**, *130*, 1992.

(7) Bouwkamp, M. W.; Bowman, A. C.; Lobkovsky, E.; Chirik, P. J. *J. Am. Chem. Soc.* **2006**, *128*, 13340.

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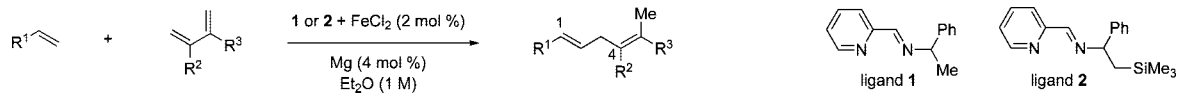
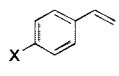
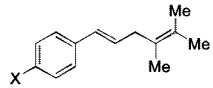
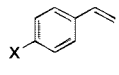
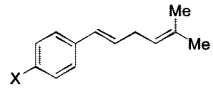
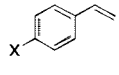
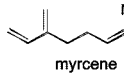
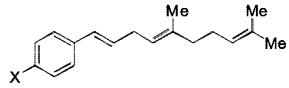
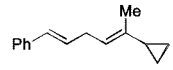
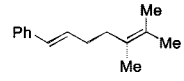
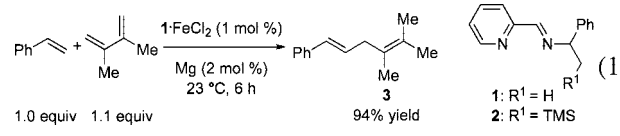
Table 1. Iron-Catalyzed 1,4-Addition of Olefins to 1,3-Dienes

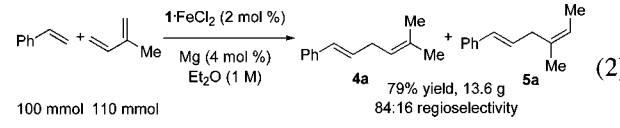


entry	alkene	diene	product	X	ligand	yield	regioselectivity[a]	1-*E*/*Z*	4-*E*/*Z*
1				H (**3**)	1	94[b]	–	>99:1	–
2				F (**4b**)		86	–	>99:1	–
3				Cl (**4c**)		78	–	>99:1	–
4				OAc (**4d**)		85	–	>99:1	–
5				CF_3 (**4e**)		90	–	>99:1	–
6				^{t}Bu (**4f**)		92	–	>99:1	–
7		 isoprene		H (**4a**)	2	60[c]	90:10	>99:1	–
8				F (**4g**)		74[c]	91:9	>99:1	–
9		 myrcene		H (**4h**)	2	66[d]	93:7	>99:1	>99:1
10				OMe (**4i**)		51[d]	96:4	>99:1	>99:1
11				**4j**	1	77	>98:2	>99:1	>99:1
12				**4k**	1	79[e]	–	>99:1	–

[a] Regioisomeric ratio as described (eq 2). [b] 1 mol % **1**·$FeCl_2$ used. [c] 20 mol % **2**·$FeCl_2$ used. [d] 10 mol % **2**·$FeCl_2$ used. [e] 5 mol % **1**·$FeCl_2$ used.

to catalyze carbon−carbon bond formation between styrene and 2,3-dimethylbutadiene to afford 1,4-diene **3** in 94% yield after 6 h at 23 °C. Control experiments showed that the presence of iron, together with reducing agent and ligand, is essential for productive catalysis. A 1:1 complex of ferrous chloride and iminopyridine ligand[10] (for X-ray, see Supporting Information) is responsible for the exclusive formation of the intermolecular addition product **3**, with no traces of diene dimerization or subsequent observable double bond isomerization. A selection of 18 other complexes derived from bidentate nitrogenous ligands afforded the desired linear 1,4-diene **3** in less than 50% yield, provided significant amounts of diene dimerization products as observed by tom Dieck,[4a] or gave double bond isomerization to form a conjugated 1,3-diene subsequent to addition (see Supporting Information). As shown in Table 1, 2,3-dimethylbutadiene can be added to electron-rich and -poor styrenes bearing various functional groups such as ethers, an ester, and halides. This practical procedure can be scaled to 100 mmol using 2 mol % of catalyst, 100 mL of solvent, and commercially available styrene and isoprene (eq 2).





Although the reaction shown in eq 2 afforded 1,4-addition product in 79% yield, two regioisomeric products were obtained due to bond formation at either of the two different olefin termini of isoprene. The regioselectivity in favor of prenylation product **4a** induced by ligand **1** was 86:14. The introduction of a prenyl group upon 1,4-addition to isoprene is synthetically useful,[11] but control over regioselectivity is challenging. To increase the regioselectivity, we evaluated different iminopyridine ligands and found a strong dependence of the regioselectivity on the ligand. The highest ratio of 10:1 in favor of the desired linear 1,4-diene product was observed with the trimethylsilyl-substituted ligand **2** (Table 1). Methyl substitution at the 6-position of the pyridyl ligand

(8) For hydrovinylation reactions of olefins, including 1,3-dienes, see: (a) RajanBabu, T. V. *Chem. Rev.* **2003**, *103*, 2845. (b) Bogdanovi, B.; Pauling, H.; Wilke, G.; Meister, B.; Henc, B. *Angew. Chem., Int. Ed.* **1972**, *11*, 1023. (c) Zhang, A. B.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2006**, *128*, 54. (d) Shirakura, M.; Suginome, M. *J. Am. Chem. Soc.* **2008**, *130*, 5410. (e) Saha, B.; Smith, C. R.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2008**, *130*, 9000.

(9) (a) Hilt, G.; du Mesnil, F. X.; Lüers, S. *Angew. Chem., Int. Ed.* **2001**, *40*, 387. (b) Hilt, G.; Lüers, S. *Synthesis* **2002**, 609. (c) Hilt, G.; Lüers, S.; Schmidt, F. *Synthesis* **2004**, 634. The functional-group-tolerant Co-catalyzed 1,4-hydrovinylation typically affords the branched 1,4-dienes; if acrylates are used as enes, linear 1,4-diene products are observed, see ref 9c.

(10) Gibson, V. C.; O'Reilly, R. K.; Wass, D. F.; White, A. J. P.; Williams, D. J. *Dalton Trans.* **2003**, 2824. For a related review of bisiminopyridine−iron complexes, see: (b) Gibson, V. C.; Redshaw, C.; Solan, G. A. *Chem. Rev.* **2007**, *107*, 1745.

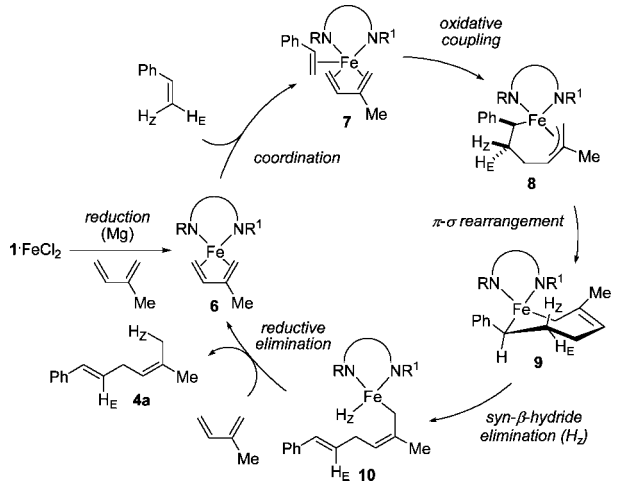
can invert the regioselectivity to 16:84 to afford **5a** as the major isomer (see Supporting Information). Substitution of the 1,3-diene starting material with substituents larger than methyl, such as that in the commodity chemical myrcene, increased the regioselectivity to up to >20:1 (entry 10, **4i**). Using this procedure, the geranyl substituent can be introduced regioselectively. A diene with branched substitution afforded a single regioisomer as determined by ^{1}H NMR (entry 11, **4j**). Although the regioselectivity was increased using ligand **2**, higher catalyst loadings were required to achieve full conversion of starting material.

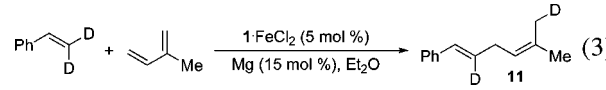
The geometry of both double bonds of the 1,4-diene products was controlled, and all addition products were observed as single double bond isomers. Importantly, the trisubstituted double bond that is generated upon 1,4-addition is formed as its *E*-isomer exclusively (entries 9−11); trisubstituted double bonds with three alkyl substituents are otherwise difficult to form as *E*-isomers with high selectivity.[12] The aliphatic α-olefin allylbenzene afforded a single addition product after double bond transposition (entry 12, **4k**). Addition of olefins to 1-substituted 1,3-dienes afforded addition products, albeit in lower yields. Overall, the iminopyridine iron complexes control stereo- and regioselectivity and afford linear 1,4-diene addition products selectively over potential dimerization, isomerization, or branched products.

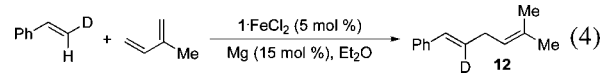
Although 1,4-addition reactions proceeded with aliphatic α-olefins, product mixtures were generally observed. In addition to the desired linear 1,4-dienes, branched 1,4-dienes[9] and dienes resulting from double bond isomerization subsequent to addition were detected. Therefore, the presented addition reaction is currently limited to styrene derivatives and selected aliphatic α-olefins (e.g., **4k**, Table 1).

A mechanistic hypothesis that is consistent with our experimental observations is detailed in Scheme 1. We propose formation of iron(II) alkyl allyl complex **8** after reduction[13] of the Fe(II) complex **1**·$FeCl_2$ and oxidative coupling with styrene. We cannot yet rationalize the influence of the catalyst on the regioselectivity that may be determined during oxidative coupling. A $\pi-\sigma$ rearrangement to form the seven-membered η^1-allyl ferracycle **9**, in which the phenyl substituent is pseudoequatorial, positions only one β-hydride (H_z) *syn* to iron. Hence, β-hydride elimination can only afford a single double bond isomer and delivers the 1,2-disubstituted *E* double bond as part of the iron(II) alkyl hydride **10**. Assuming that subsequent reductive elimination proceeds without $\sigma-\pi-\sigma$ rearrangement of **10**, the new trisubstituted double bond is formed with *E* geometry stereospecifically. To substantiate the assumption that stereospecific reductive elimination from **10** is faster than isomerization, we designed two deuterium-labelingexperiments. The deuterium atoms of β,β-dideuterostyrene and (*E*)-β-deuterostyrene in the 1,4-addition reactions to isoprene were observed exclusively at the positions indicated in **11** and **12**, respectively, consistent with our mechanistic hypothesis (eqs 3 and 4).

Scheme 1. Proposed Catalytic Cycle for 1,4-Addition to Dienes







In conclusion, we have developed an intermolecular iron-catalyzed 1,4-addition of α-olefins to 1,3-dienes using readily available iminopyridine−ferrous chloride complexes. Importantly, both regioselectivity and double bond geometry of the addition products can be controlled. Furthermore, synthetically useful products such as prenyl- and geranyl-substituted molecules are synthesized from simple commodity chemicals.

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Supporting Information Available: Detailed experimental procedures and spectroscopic data for all new compounds, as well X-ray data in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) *Isoprenoids Including Carotenoids and Steroids*; Cane, D. E., Ed.; *Comprehensive Natural Products Chemistry*; Barton, D., Nakanishi, K., Eds.; Elsevier: Oxford, 1999; Vol. 2.
(12) Yu, J. S.; Kleckley, T. S.; Wiemer, D. F. *Org. Lett.* **2005**, *7*, 4803.
(13) A related (1,2-diimine)iron(diene) complex was obtained similarly: Bart, S. C.; Hawrelak, E. J.; Lobkowsky, E.; Chirik, P. J. *Organometallics* **2005**, *24*, 5518.