CHEMISTRY
A European Journal

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Divergent Iron-Catalyzed Couplings of O-Acyloximes with Silyl Enol Ethers

Authors: Hai-Bin Yang and Nicklas Selander

To be cited as: *Chem. Eur. J.* 10.1002/chem.201605636

Link to VoR: http://dx.doi.org/10.1002/chem.201605636

Supported by
ACES

WILEY-VCH

10.1002/chem.201605636

COMMUNICATION

WILEY-VCH

Divergent Iron-Catalyzed Couplings of *O*-Acyloximes with Silyl Enol Ethers

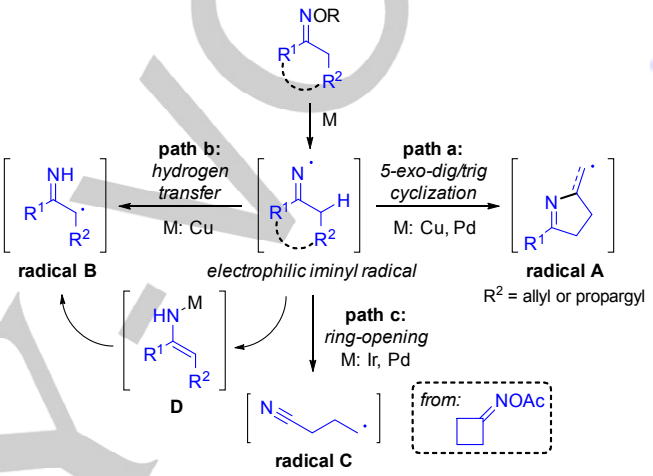
Hai-Bin Yang and Nicklas Selander*[a]

Abstract: An iron-catalyzed coupling reaction of *O*-acyloxime/*O*-benzoyl amidoximes with silyl enol ethers is reported. The protocol provides access to functionalized pyrroles, 1,6-ketonitriles, pyrrolines and imidazolines via carbon-centered radicals generated from an initially formed iminyl radical. The intramolecular cyclization and ring-opening processes of the iminyl radical take place preferentially over a 1,3-hydrogen transfer, providing insights into iron-catalyzed reactions with oxime derivatives. The cheap and environmentally friendly iron catalyst, the broad substrate scope and functional group compatibility make this protocol useful for synthesis of valuable nitrogen-containing products.

Transitional metal-catalyzed cross-coupling reactions are pivotal for the construction of new C–C and C–X bonds. This research area has for long been dominated by precious metals, *e.g.* palladium.[1] Compared with precious metals, iron is advantageous in catalysis in terms of low cost and low toxicity. Furthermore, the broad spectrum of oxidation states (-2 to +5) of iron provides a rich reactivity platform which is useful for the development of new transformations.[2] In contrast to Pd-catalysis, where the electrophilic cross-coupling partners are typically activated via a two-electron oxidative addition, Fe-catalysis often involves radical species and single electron transfer (SET) mechanisms.[3]

As a part of our interest in the applications of N–O bond-containing substrates we envisaged that oxime esters would serve as viable electrophilic partners for iron-catalysis by reduction of the N–O bond. Iminyl radicals are useful intermediates[4] that can be generated from oxime esters by heat,[5] transition metals[6] or photo irradiation.[7] As the heat-induced activation of oxime esters usually requires harsh conditions[5a,5c-e] or toxic reagents (*e.g.* Bu_3SnH/AIBN)[5h-i] and photo irradiation typically requires more complex oxime ester derivatives (*e.g.* O–Ar or O_2C–Ar groups),[7a-c] transition metal catalysis is an attractive alternative.

Iminyl radicals[8] are reactive electrophilic species that can be transformed into carbon-centered radicals via three different pathways (Scheme 1 path a-c). In path a, the iminyl radical is added to a tethered alkene[5e-h,7a-b] or alkyne[5a] in a 5-*exo-trig* or 5-*exo-dig* cyclization to form radical **A**.[9] In path b, the electrophilic iminyl radical can abstract a hydrogen atom *via* an intramolecular 1,3-hydrogen transfer process to form the stabilized radical **B**.[6b,d] The radical intermediate **B** may also be formed via a metal-coordinated enamine intermediate (**D**). In the third pathway, c, the release of ring-strain in a cyclobutanone-derived *O*-acyloxime generates cyano-substituted radical **C**.[7j,10]



Scheme 1. Divergent reaction modes of iminyl radicals

Unlike heat- or photo-induced generation of iminyl radicals, transition metals can interact with the reactive radicals **A**-**C** above to improve the reaction selectivity.[11] Thus, it is highly desirable to develop a united transition metal-catalyzed methodology to understand the competitive relationship between the three different reaction modes, hitherto unexplored by a single catalytic protocol.

Herein, we report on the iron-catalyzed coupling of *O*-acyloximes/*O*-benzoylamidoximes with silyl enol ethers[12] via the three radical intermediates **A**-**C** above. Silyl enol ethers are useful reaction partners as they react rapidly[13] with the electrophilic carbon-centered radicals. Thus, the competing self-condensation[6d] and hydrolysis[14] of *α*-iminyl radicals can be avoided. Furthermore, the coupling with *α*-iminyl radicals provides access to pyrroles via an intramolecular condensation of the 1,4-ketoimine product. Although the synthesis of biologically relevant pyrrole derivatives has extensively been explored,[15] the synthesis of unprotected electron-rich pyrroles, amenable for *N*-functionalization,[16] remains challenging.

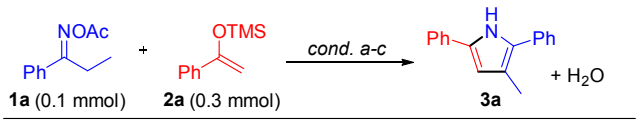
We began our studies with *O*-acyloxime **1a** and silyl enol ether **2a**. With 20 mol% of CuCl in 1,4-dioxane at 100 °C, pyrrole **3a** was formed in 25% yield by ^{1}H NMR. Further screening of metal salts and reaction conditions (see the Supporting Information), pointed towards $FeCl_2$ as a better catalyst for this transformation (57% yield).[17] Improved yields were obtained in MeCN; pyrrole **3a** was obtained in 83% yield using 5 mol % $FeCl_2$ at 80 °C (Table 1). It should be pointed out that oxime esters have previously been used as (N_1+C_2) synthons in

[a] Dr. H.-B. Yang, Dr. N. Selander
Department of Organic Chemistry, Stockholm University
Arrhenius Laboratory, SE-106 91 Stockholm (Sweden)
E-mail: nicklas.selander@su.se

Supporting information for this article is given via a link at the end of the document.

cyclizations with electron-deficient unsaturated substrates through metal-coordinated enamine intermediates, however not with electron-rich alkenes.[18] In comparison, our method allows for the synthesis of a variety of pyrrole derivatives.

Table 1: Representative screening data

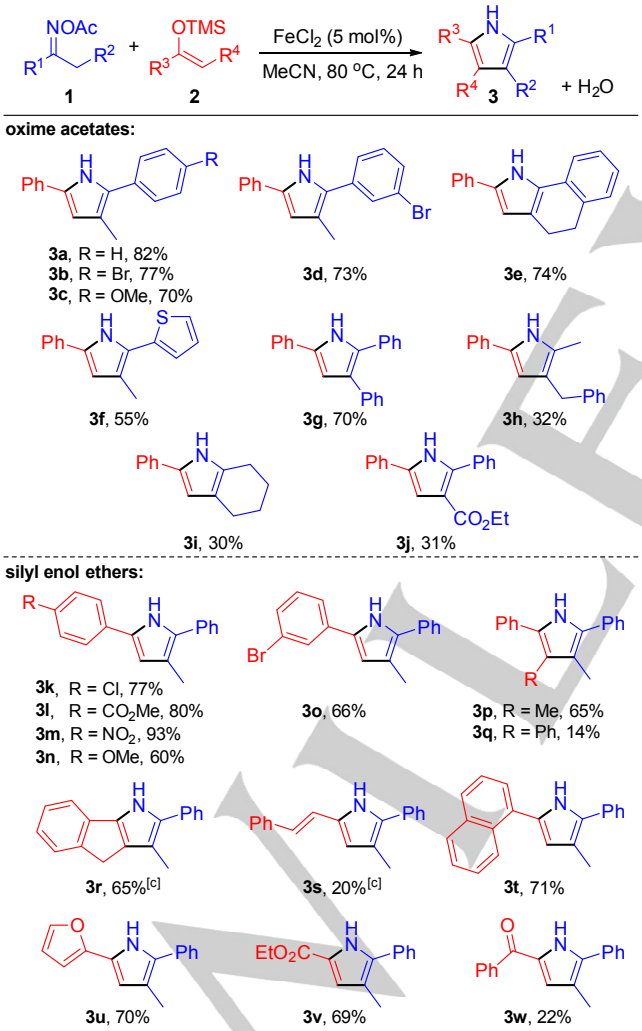


1a (0.1 mmol) **2a** (0.3 mmol) **3a**

a)	CuCl (20 mol%), 1,4-dioxane (1 mL), 100 °C / 24 h	25%
b)	$FeCl_2$ (20 mol%), 1,4-dioxane (1 mL), 100 °C / 24 h	57%
***c*)**	**$FeCl_2$ (5 mol%), MeCN (1 mL), 80 °C / 24 h**	**83% (82% isol.)**

With these reaction conditions in hand, we continued to investigate the substrate scope with respect to various oxime acetates and silyl enol ethers. Propiophenone-derived *O*-acyloximes provided pyrroles **3a**-**3d** in high yields (70-82%), regardless of the electronic character of the aryl group (Table 2).

Table 2: Substrate scope for pyrroles[a,b]

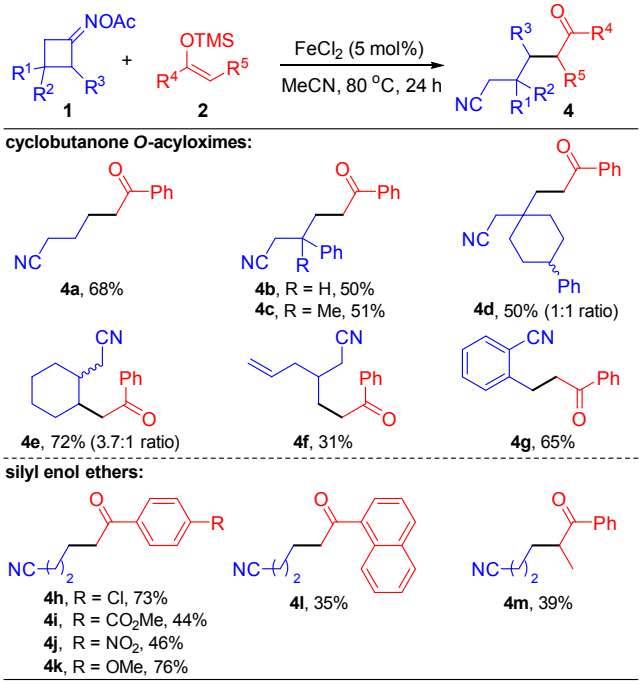


[a] Reaction conditions: **1** (0.20 mmol), **2** (0.60 mmol) and $FeCl_2$ (5 mol%) were stirred in MeCN (2.0 mL) under Ar for 24 h at 80 °C. [b] Isolated yields. [c] Yields were determined by ^{1}H NMR using CH_2I_2 as an internal standard. For some oxime derivatives, an *E*/*Z* mixture was used, see the SI.

A cyclic *O*-acyloxime provided the fused pyrrole **3e** in 74% yield and the thiophene-substituted oxime derivative gave the corresponding pyrrole **3f** in 55% yield. The highly conjugated pyrrole **3g** was obtained in 70% yield for the diphenyl-substituted *O*-acyloxime. When non-conjugated *O*-acyloximes were applied, lower yields were observed; pyrroles **3h**-**i** were however isolated in respectable yields. For compound **3h**, two carbon-centered radicals can be formed. As expected, the more stable secondary radical determined the regiochemical outcome.[19] The method is also applicable for the hitherto unexplored ester-substituted oxime derivative to yield pyrrole **3j** in 31%. With respect to the nucleophilic component, substituted acetophenone-derived silyl enol ethers led to the formation of pyrroles **3k**-**o** in 60-93% yield. Electron-poor silyl enol ethers performed better than the electron-rich counterparts. Furthermore, di-substituted silyl enol ethers ($R^4 \neq H$) were applied in the reaction to yield the tetra-substituted pyrroles **3p**-**r**. For the methyl substituted pyrrole **3p**, a yield of 65% was obtained, whereas the diphenyl-substituted silyl enol ether resulted in a low yield, 14% of **3q**, likely due to the extended conjugation. Products **3r** and **3s**, formed from the corresponding cyclic and alkenyl-derived silyl enol ethers were unfortunately not stable upon concentration; the yields, 65% and 20% respectively were determined by ^{1}H NMR. The naphthyl- and furyl-substituted pyrroles **3t**-**u** were obtained in good yields. Notably, the method also provides access to the ester- and keto-functionalized pyrroles **3v**-**w** by employing the less explored electron-poor silyl enol ethers (Table 2).

Next, we investigated the effect of ring-strain by employing cyclobutanone-derived *O*-acyloximes. In contrast to the pyrrole formation (Table 2) where the iminyl radical is converted into a carbon-centered radical through a hydrogen transfer process, the cyclobutanone oxime derivatives underwent a selective ring-opening. The resulting radical then coupled with the silyl enol ether to yield the useful 1,6-ketonitrile building blocks **4** (Table 3).[20] With the non-substituted cyclobutanone-derived *O*-acyloxime, 1,6-ketonitrile **4a** was obtained in 68% yield, without traceable amounts of the cyclobutane-fused pyrrole.[10] Moderate yields, around 50%, were obtained for ketonitriles **4b**-**d** from 3-mono and 3,3-disubstituted cyclobutanone *O*-acyloximes respectively. The opening of a 2,3-disubstituted cyclobutanone-derived oxime acetate proceeded efficiently with a selective cleavage to provide ketonitrile **4e** in 72% yield (~4:1 isomeric mixture). Interestingly, ketonitrile **4f** was obtained in 31% yield, indicating that the ring-opening process is preferred over a 5-*exo-trig* cyclization with the allyl moiety. Furthermore, we were able to use the previously unexplored benzene-fused cyclobutanone derivative. The ring-opening yielded the more stable benzylic radical for the selective formation of ketonitrile **4g** in 65% yield.[19] Various *para*-substituted phenyl silyl enol ethers gave the corresponding 1,6-ketonitriles **4h**-**k** in moderate to good yields. Lower yields (35-39%) were obtained with the naphthyl-substituted silyl enol ether and a non-terminal coupling partner (**4l**-**m**). The lower yields of the 1,6-ketonitriles (*c.f.* Table 2) is a consequence of the more reactive non-stabilized radical[19] formed in the ring-opening process, making competitive hydrogen abstraction processes inevitable.

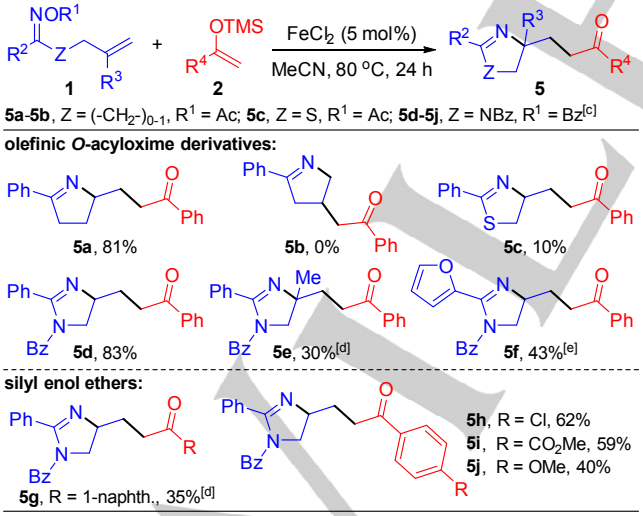
Table 3: Substrate scope for 1,6-ketonitriles[a,b]



[a] Reaction conditions: **1** (0.20 mmol), **2** (0.60 mmol) and $FeCl_2$ (5 mol%) were stirred in MeCN (2.0 mL) under Ar for 24 h at 80 °C. [b] Isolated yields. For some oxime derivatives, an *E*/*Z* mixture was used, see the SI.

We then investigated the possibility of an intramolecular C-N bond-formation taking place in favor of a 1,3-hydrogen transfer path for the iminyl radical. For a *γ*,*δ*-unsaturated oxime derivative, pyrroline **5a** was formed in 81% yield, without traces of the corresponding allyl-substituted pyrrole (Table 4).

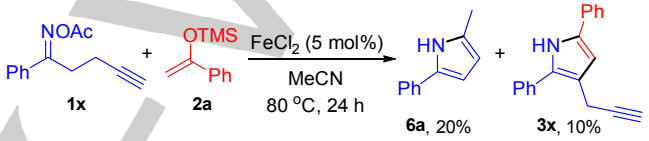
Table 4: Substrate scope for pyrrolines and thio-/aza-derivatives[a,b]



[a] Reaction conditions: **1** (0.20 mmol), **2** (0.60 mmol) and $FeCl_2$ (5 mol%) were stirred in MeCN (2.0 mL) under Ar for 24 h at 80 °C. [b] Isolated yields. [c] The *O*-acetylamidoxime derivatives were synthetically inaccessible. [d] Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. [e] Performed on a 0.10 mmol scale. For some oxime derivatives, an *E*/*Z* mixture was used, see the SI.

However, for the *β*,*γ*-unsaturated oxime acetate, a complex mixture was obtained as the formation of **5b** would require the disfavored 5-*endo*-cyclization. The scope of the method was further expanded to thiohydroximic acid[21] and amidoxime[22] derivatives. Although thiazoline derivative **5c** was obtained in only 10% yield (due to hydrolysis), imidazoline **5d** could be obtained in 83% yield using the *O*-benzoylamidoxime derivative. A methyl group on the alkene moiety lowered the efficiency, providing **5e** in 30% yield along with a comparable amount of a aminooxygenated byproduct.[23] The furyl-substituted imidazoline **5f** was obtained in 43% yield. Furthermore, upon variation of the silyl enol ether, imidazolines **5g-j** were obtained in acceptable yields, demonstrating that iron catalysis is useful for the generation of amidinyl radicals and biologically relevant imidazoline motifs.[24]

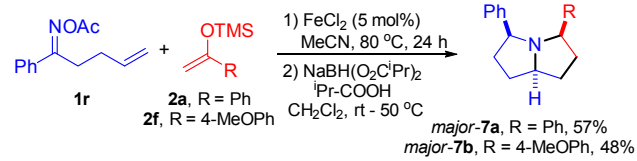
Upon subjecting oxime acetate **1x** to the standard conditions we observed a mixture of products. Pyrrole **6a** was obtained in 20% NMR-yield along with 10% of **3x**, demonstrating the competitive pathways of the 5-*exo*-*dig* cyclization and the 1,3-hydrogen transfer of the iminyl radical for an intermolecular coupling reaction (Scheme 2).



Scheme 2. Competitive 5-*exo*-*dig* cyclization vs. hydrogen transfer/coupling

The addition of TEMPO to the presented reactions (Tables 2-4) did not result in any traces of products **3**-**5**. Instead, we were able to isolate TEMPO coupling products (See the Supporting Information). Thus, we propose a mechanism involving iminyl radicals (*c.f.*, Scheme 1). In this process, the applied iron catalyst first cleaves the N–O bond, and turns over by forming the keto group after reaction with the silyl enol ether.

Our method was applied for the synthesis of the biologically important pyrrolizine skeleton.[7a,25] In a two-step reaction, oxime acetate **1r** was converted into pyrrolizine derivatives **7a-b** in 57% and 48% yield (major diastereomers), respectively through an iron-catalyzed coupling/reduction sequence.[26] The sterically hindered reagent $NaBH(O_2C^iPr)_3$ led to an improved diastereoselectivity (~2.5:1) for the formation of **7** (Scheme 3).[27]



Scheme 3. Synthesis of the pyrrolizine skeleton

In summary, the iron-catalyzed reaction of silyl enol ethers and oxime esters was demonstrated in three different reaction modes of iminyl radicals for the synthesis of pyrroles, 1,6-ketonitriles and imidazolines. Our studies show that the intramolecular cyclization and ring-opening take place in favor of reactions proceeding via a 1,3 hydrogen transfer. These results are important for the further development of iron-catalyzed coupling reactions via radical intermediates.

Acknowledgements

Financial support from the Swedish Research Council, VR (621-2012-2981), the Carl Trygger foundation and the Wenner-Gren Foundations is gratefully acknowledged.

Keywords: acyloximes•iron•pyrroles•radicals•silyl enol ethers

[1] For selected recent reviews on Pd-catalyzed coupling reactions, see; a) F.-S. Han, *Chem. Soc. Rev.* **2013**, *42*, 5270; b) C. E. I. Knappke, A. Jacobi von Wangelin, *Chem. Soc. Rev.* **2011**, *40*, 4948.

[2] a) I. Bauer, H.-J. Knölker, *Chem. Rev.* **2015**, *115*, 3170; b) A. A. O. Sarhan, C. Bolm, *Chem. Soc. Rev.* **2009**, *38*, 2730; c) B. Plietker, *Iron-catalysis in Organic Synthesis.* Wiley-VCH: Weinheim, **2008**; d) D. Bézier, J.-B. Sortais, C. Darcel, *Adv. Synth. Catal.* **2013**, *355*, 19; e) W. M. Czaplik, M. Mayer, J. Cvengroš, A. Jacobi von Wangelin, *ChemSusChem* **2009**, *2*, 396; f) G. Cera, L. Ackermann, *Top Curr Chem* **2016**, *374*, 57; g) T. C Atack, R. M. Lecker, S. P. Cook, *J. Am. Chem. Soc.* **2014**, *136*, 9521; h) A. Guérinot, J. Cossy, *Top Curr Chem* **2016**, *374*, 49.

[3] a) C. W. Cheung, F. E. Zhurkin, X. Hu, *J. Am. Chem. Soc.* **2015**, *137*, 4932; b) S. L. Daifuku, J. L. Kneebone, B. E. R. Snyder, M. L. Neidig, *J. Am. Chem. Soc.* **2015**, *137*, 11432; c) T. Hatakeyama, T. Hashimoto, Y. Kondo, Y. Fujiwara, H. Seike, H. Takaya, Y. Tamada, T. Ono, M. Nakamura, *J. Am. Chem. Soc.* **2010**, *132*, 10674; d) R. Martin, A. Fürstner, *Angew. Chem.* **2004**, *116*, 4045*; Angew. Chem. Int. Ed.* **2004**, *43*, 3955.

[4] For selected recent reviews, see; a) J. C. Walton, *Acc. Chem. Res.* **2014**, *47*, 1406; b) M. Minozzi, D. Nanni, P. Spagnolo, *Chem. Eur. J.* **2009**, *15*, 7830; c) M. Kitamura, K. Narasaka, *Bull. Chem. Soc. Jpn.* **2008**, *81*, 539; d) S. Z. Zard, *Chem. Soc. Rev.* **2008**, *37*, 1603; e) H. Huang, J. Cai, G.-J. Deng, *Org. Biomol. Chem.* **2016**, *14*, 1519.

[5] a) Y. Cai, A. Jalan, A. R. Kubosumi, S. L. Castle, *Org. Lett.* **2015**, *17*, 488; b) S. J. Markey, W. Lewis, C. J. Moody, *Org. Lett.* **2013**, *15*, 6306; c) F. Portela-Cubillo, J. S. Scott, J. C. Walton, *J. Org. Chem.* **2009**, *74*, 4934; d) F. Portela-Cubillo, J. S. Scott, J. C. Walton, *Chem. Commun.* **2008**, 2935; e) F. Portela-Cubillo, J. S. Scott, J. C. Walton, *J. Org. Chem.* **2008**, *73*, 5558; f) M. Yoshida, M. Kitamura, K. Narasaka, *Bull. Chem. Soc. Jpn.* **2003**, *76*, 2003; g) F. Gagosz, S. Z. Zard, *Synlett* **1999**, 1978; h) J. Boivin, A.-C. Callier-Dublanchet, B. Quiclet-Sire, A.-M. Schiano, S. Z. Zard, *Tetrahedron* **1995**, *51*, 6517; i) A.-C. Callier-Dublanchet, B. Quiclet-Sire, S. Z. Zard, *Tetrahedron Lett.* **1995**, *36*, 8791.

[6] a) N. J. Race, A. Faulkner, M. H. Shaw, J. F. Bower, *Chem. Sci.* **2016**, *7*, 1508; b) J. Ke, Y. Tang, H. Yi, Y. Li, Y. Cheng, C. Liu, A. Lei, *Angew. Chem.* **2015**, *127*, 6704*; Angew. Chem. Int. Ed.* **2015**, *54*, 6604; c) A. Faulkner, N. J. Race, J. S. Scott, J. F. Bower, *Chem. Sci.* **2014**, *5*, 2416; d) L. Ran, Z.-H. Ren, Y.-Y. Wang, Z.-H. Guan, *Green Chem.* **2014**, *16*, 112; e) W. Du, M.-N. Zhao, Z.-H. Ren, Y.-Y. Wang, Z.-H. Guan, *Chem. Commun.* **2014**, *50*, 7437; f) M.-N. Zhao, H. Liang, Z.-H. Ren, Z.-H. Guan, *Synthesis* **2012**, *44*, 1501; g) Y. Koganemaru, M. Kitamura, K. Narasaka, *Chem. Lett.* **2002**, 784; h) T. Nishimura, S. Uemura, *J. Am. Chem. Soc.* **2000**, *122*, 12049.

[7] a) S.-H. Cai, J.-H. Xie, S. Song, L. Ye, C. Feng, T.-P. Loh, *ACS Catal.* **2016**, *6*, 5571; b) J. Davies, S. G. Booth, S. Essafi, R. A. W. Dryfe, D. Leonori, *Angew. Chem.* **2015**, *127*, 14223*; Angew. Chem. Int. Ed.* **2015**, *54*, 14017; c) H. Jiang, X. An, K. Tong, T. Zheng, Y. Zhang, S. Yu, *Angew. Chem.* **2015**, *127*, 4127*; Angew. Chem. Int. Ed.* **2015**, *54*, 4055; d) R. T. McBurney, J. C. Walton, *J. Am. Chem. Soc.* **2013**, *135*, 7349; e) R. T. McBurney, A. M. Z. Slawin, L. A. Smart, Y. Yu, J. C. Walton, *Chem. Commun.* **2011**, *47*, 7974; f) R. Alonso, P. J. Campos, M. A. Rodríguez, D. Sampedro, *J. Org. Chem.* **2008**, *73*, 2234; g) F. Portela-Cubillo, J. Lymer, E. M. Scanlan, J. S. Scott, J. C. Walton, *Tetrahedron* **2008**, *64*, 11908; h) F. Portela-Cubillo, E. M. Scanlan, J. S. Scott, J. C. Walton, *Chem. Commun.* **2008**, 4189; i) R. Alonso, P. J. Campos, B. García, M. A. Rodríguez, *Org. Lett.* **2006**, *8*, 3521; j) J. Boivin, E. Fouquet, S. Z. Zard, *Tetrahedron Lett.* **1991**, *32*, 4299.

[8] Y.-J. Chi, H.-T. Yu, *Comp. Theor. Chem.* **2013**, *1005*, 75.

[9] a) Y. Guindon, B. Guérin, S. R. Landry, *Org. Lett.* **2001**, *3*, 2293; b) M.-H. Le Tadic-Biadatti, A.-C. Callier-Dublanchet, J. H. Horner, B. Quiclet-Sire, S. Z. Zard, M. Newcomb, *J. Org. Chem.* **1997**, *62*, 559.

[10] T. Nishimura, T. Yoshinaka, Y. Nishiguchi, Y. Maeda, S. Uemura, *Org. Lett.* **2005**, 7, 2425.

[11] a) U. Jahn, *Radicals in Synthesis III,* Springer: Berlin, Heidelberg, **2012**; b) R. Poli, *Eur. J. Inorg. Chem.* **2011**, 1513; c) M. T. Lemaire, *Pure Appl. Chem.* **2004**, *76,* 277.

[12] For selected recent articles on the addition of radicals to siliyl enol ethers, see; a) T. Amaya, Y. Maegawa, T. Masuda, Y. Osafune, T. Hirao, *J. Am. Chem. Soc.* **2015**, *137*, 10072; b) N. Matsuda, K. Hirano, T. Satoh, M. Miura, *Angew. Chem.* **2012**, *124,* 11997*; Angew. Chem. Int. Ed.* **2012**, *51*, 11827; c) H.-Y. Jang, J.-B. Hong, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2007**, *129*, 7004.

[13] a) N. Arai, K. Narasaka, *Chem. Lett.* **1995**, *24*, 987; b) Y. Kohno, K. Narasaka, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 322; c) P. Renaud, *Tetrahedron Lett.* **1990**, *31*, 4601.

[14] M. Bingham, C. Moutrille, S. Z. Zard, *Heterocycles* **2014**, *88*, 953.

[15] a) G. M. Torres, J. S. Quesnel, D. Bijou, B. A. Arndtsen, *J. Am. Chem. Soc.* **2016**, *138*, 7315; b) G.-Q. Chen, X.-N. Zhang, Y. Wei, X.-Y. Tang, M. Shi, *Angew. Chem.* **2014***, 126,* 8632*; Angew. Chem. Int. Ed.* **2014**, *53*, 8492; c) J. Xuan, X.-D. Xia, T.-T. Zeng, Z.-J. Feng, J.-R. Chen, L.-Q Lu, W.-J. Xiao, *Angew. Chem.* **2014***, 126,* 5759*; Angew. Chem. Int. Ed.* **2014**, *53*, 5653; d) S. Rakshit, F. W. Patureau, F. Glorius, *J. Am. Chem. Soc.* **2010**, *132*, 9585.

[16] a) H. McNab, L. Hill, S. Imam, W. O'Neill, *Synthesis* **2009**, 2535; b) O. Flögel, J. Dash, I. Brüdgam, H. Hartl, H.-U. Reißig, *Chem. Eur. J.* **2004**, *10*, 4283.

[17] M.-N. Zhao, Z.-H. Ren, L. Yu, Y.-Y. Wang, Z.-H. Guan, *Org. Lett.* **2016**, *18*, 1194.

[18] a) X. Tang, Z. Zhu, C. Qi, W. Wu, H. Jiang, *Org. Lett.* **2016**, *18*, 180; b) H. Huang, J. Cai, L. Tang, Z. Wang, F. Li, G.-J. Deng, *J. Org. Chem.* **2016**, *81*, 1499; c) M. Zheng, P. Chen, W. Wu, H. Jiang, *Chem. Commun.* **2016**, *52*, 84; d) H. Jiang, J. Yang, X. Tang, J. Li, W. Wu, *J. Org. Chem.* **2015**, *80*, 8763; e) X. Tang, L. Huang, J. Yang, Y. Xu, W. Wu, H. Jiang, *Chem. Commun.* **2014**, *50*, 14793; f) Q. Wu, Y. Zhang, S. Cui, *Org. Lett.* **2014**, *16*, 1350; g) Y. Wei, N. Yoshikai, *J. Am. Chem. Soc.* **2013**, *135*, 3756; h) Z.-H. Ren, Z.-Y. Zhang, B.-Q. Yang, Y.-Y. Wang, Z.-H. Guan, *Org. Lett.* **2011**, *13*, 5394. For a relevant example of pyrrole synthesis, see: i) X. Tang, L. Huang, C. Qi, W. Wu, H. Jiang *Chem. Commun.* **2013**, *49*, 9597.

[19] a) J. Z. Hioe, H. Zipse, *Radical Stability−Thermochemical Aspects. In Encyclopedia of Radicals in Chemistry, Biology and Materials*;, Wiley:, Chichester, **2012**; b) A. S. Menon, D. J. Henry, T. Bally, L. Radom, *Org. Biomol. Chem.* **2011**, *9*, 3636; c) M. L. Coote, C. Y. Lin, A. L. J. Beckwith, A. A. Zavitsas, *Phys. Chem. Chem. Phys.* **2010**, *12*, 9597.

[20] a) J. Streuff, M. Feurer, P. Bichovski, G. Frey, U. Gellrich, *Angew. Chem.* **2012***, 124,* 8789*; Angew. Chem. Int. Ed.* **2012**, *51*, 8661; b) F. F. Fleming, L. A. Funk, R. Altundas, V. Sharief, *J. Org. Chem.* **2002**, *67*, 9414.

[21] B. C. Lemercier, J. G. Pierce, *Org. Lett.* **2014**, *16*, 2074.

[22] D. Gennet, S. Z. Zard, H. Zhang, *Chem. Commun.* **2003**, 1870.

[23] S. Sanjaya, S. Chiba, *Org. Lett.* **2012**, *14*, 5342.

[24] M. E. Giusepponi, C. Cifani, M. V. Micioni Di Bonaventura, L. Mattioli, A. Hudson, E. Diamanti, F. Del Bello, M. Giannella, V. Mammoli, C. D. Paoletti, A. Piergentili, M. Pigini, W. Quaglia, *ACS Med. Chem. Lett.* **2016**. 7, 956.

[25] a) J. Robertson, K. Stevens, *Nat. Prod. Rep.* **2014**, *31*, 1721; b) K. M. G. O'Connell, M. Díaz-Gavilán, W. R. J. D. Galloway, D. R. Spring, *Beilstein J. Org. Chem.* **2012**, *8*, 850.

[26] A. Faulkner, J. S. Scott, J. F. Bower, *J. Am. Chem. Soc.* **2015**, *137*, 7224.

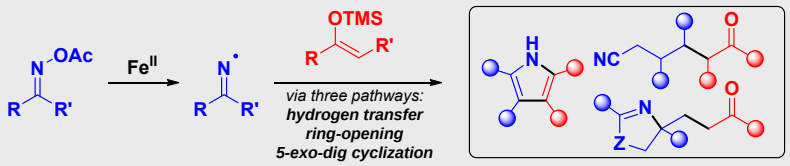
[27] S. Nawaz Khan, S.-Y. Bae, H.-S. Kim, *Tetrahedron Lett.* **2005**, *46*, 7675.

10.1002/chem.201605636

WILEY-VCH

Entry for the Table of Contents (Please choose one layout)
Layout 2:

COMMUNICATION



*Hai-Bin Yang, Nicklas Selander**

Page No. – Page No.
Divergent Iron-Catalyzed Couplings of *O*-Acyloximes with Silyl Enol Ethers

An iron-catalyzed coupling reaction of *O*-acyloxime/*O*-benzoyl amidoximes with silyl enol ethers is reported. The protocol provides access to functionalized pyrroles, 1,6-ketonitriles, pyrrolines and imidazolines via carbon-centered radicals generated from an initially formed iminyl radical. The intramolecular cyclization and ring-opening processes of the iminyl radical take place preferentially over a 1,3-hydrogen transfer, providing insights into iron-catalyzed reactions with oxime derivatives. The cheap and environmentally friendly iron catalyst, the broad substrate scope and functional group compatibility make this protocol useful for synthesis of valuable nitrogen-containing products.