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Redox-Active Triazolium-Derived Ligands in Nucleophilic Fe-Catalysis – Reactivity Profile and Development of a Regioselective *O*-Allylation

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Triazolium-derived *N*-heterocyclic carbene (aNHC) ligands, which are readily accessible by deprotonation of the corresponding triazolium salts, proved to be versatile ligands in diverse allylic substitution reactions. The corresponding triazolium salts are formed from azides and alkynes through the application of 1,3-dipolar cycloaddition and *N*-alkylation reactions. The unique property of these ligands is to be zwitterionic in their liberated form and to act as strong redox-active σ-donor ligands. By virtue of these qualities, these ligands enable the development of an unprecedented Fe-catalyzed regioselective aryloxylation of allylic carbonates.

Introduction

Heteroatom-stabilized singlet carbenes have evolved into privileged ligands for organometallic chemistry and catalysis.[1] The most prominent example for this class of ligands are certainly the *N*,*N*-heterocyclic carbenes in which the lone pair of electrons of the carbene carbon atom occupies the exocyclic position whereas, the remaining (empty) π-orbital is stabilized by the adjacent lone electron pairs of the (electronegative) *N*-atoms. Depending on the electronic properties of the *N*-substituent *N*,*N*-heterocyclic carbenes are often categorized as strong σ-donor and poor π-acceptor ligands [Equation (1), Figure 1]. Upon changing one of the nitrogen atoms to a carbon atom, the situation changes drastically. Instead of deprotonating an imidazolium salt, the generation of the carbene is performed using strong alkyllithium bases. The resulting (carbanionic) carbene might be regarded as being one of the strongest σ-donor ligands. The negative charge is transferred to the metal center [Equation (2), Figure 1]. Recently this concept was extended to triazolium-based ligands,[2] in which one of the backbone atoms is a quaternary ammonium cation. The implementation of an electron sink leads to carbenes with ylide-like structures that bind to the metal center in a dual fashion. Either the electron density is shifted to the metal or back donation of one-electron from the metal to the ligand leads to a metal–ligand double bond. Hence, this ligand motif might be regarded as a redox-active abnormal *N*-heterocyclic carbene (aNHC) [Equation (3), Figure 1].[3]

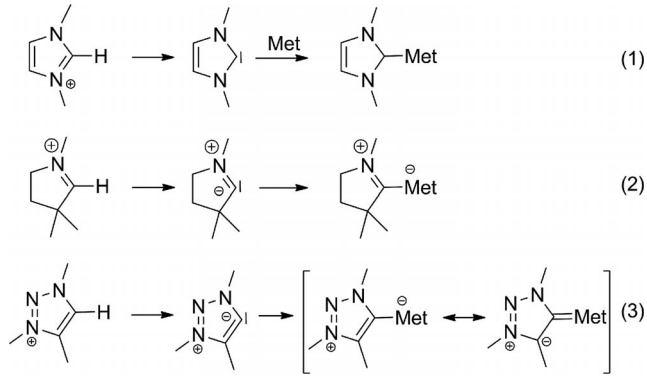

Figure 1. *N*,*N*-heterocyclic carbenes, *N*-heterocyclic carbenes and triazolium-based carbenes – generation and binding properties.

Whereas, *N*-heterocyclic carbene ligands are frequently used in homogeneous catalysis, the latter two carbene ligand classes have only very recently been employed in homogeneous catalysis.[4]

Within the past five years the Plietker group[5] has been involved in the development of catalytic transformations using electron-rich ferrates like $Bu_4N[Fe(CO)_3(NO)]$ (TBAFe).[6] The redox-active nitrosyl ligand in this complex was identified as being essential to retaining catalytic activity throughout the reaction. Furthermore, *N*-heterocyclic carbene ligands were found to significantly increase the reactivity of the catalytic systems.[7] The Sarkar group, on the other hand, was able to showcase triazolium-based carbene ligands as suitable ligands for Pd- or Cu-catalyzed transformations.[8] With regard to the unique properties of triazolium-based aNHCs we wondered in which way these ligands might influence the catalytic outcome of TBAFe-catalyzed

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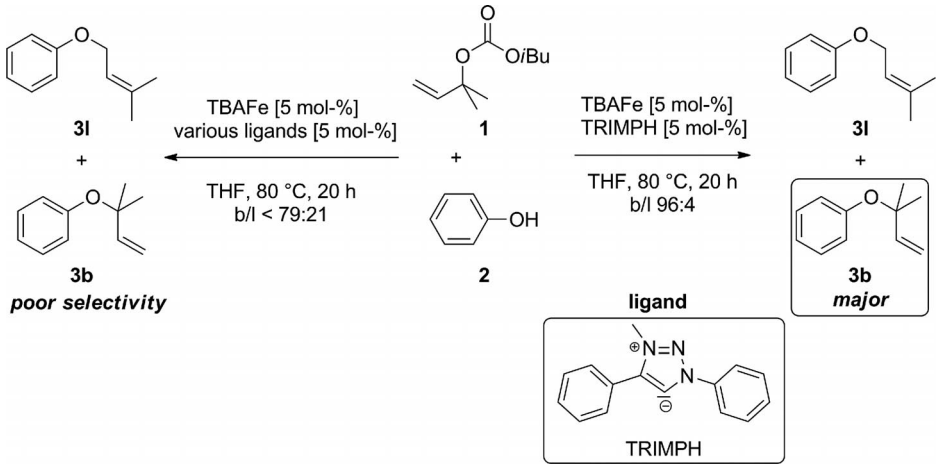
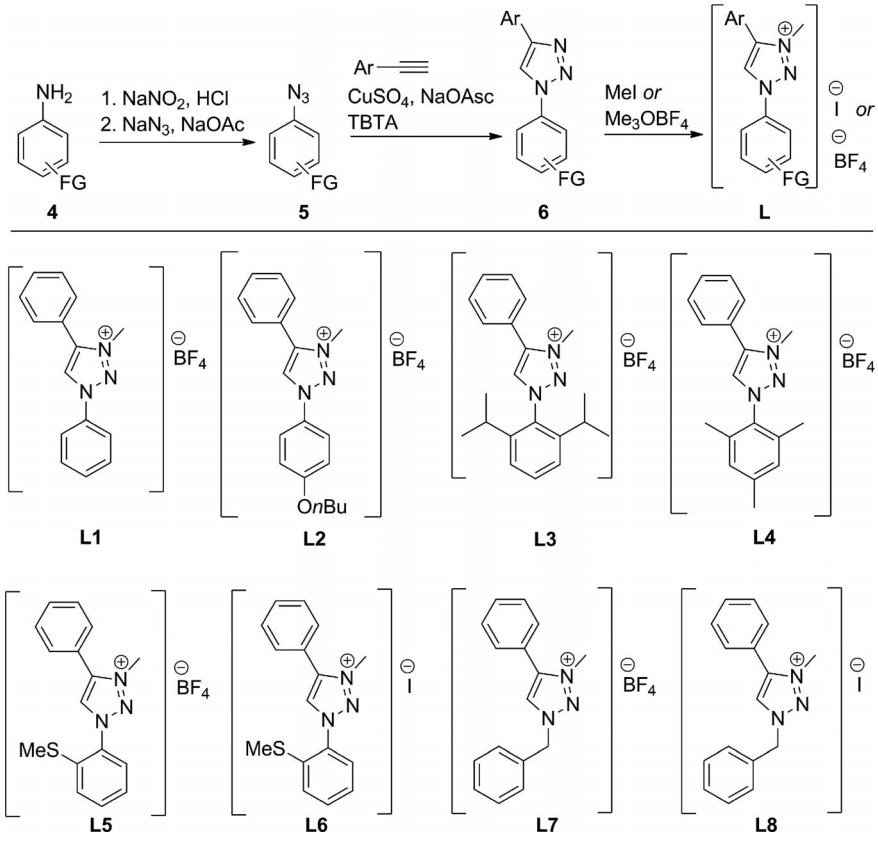


Scheme 1. Regioselective Fe-catalyzed allylic aryloxyallylation.

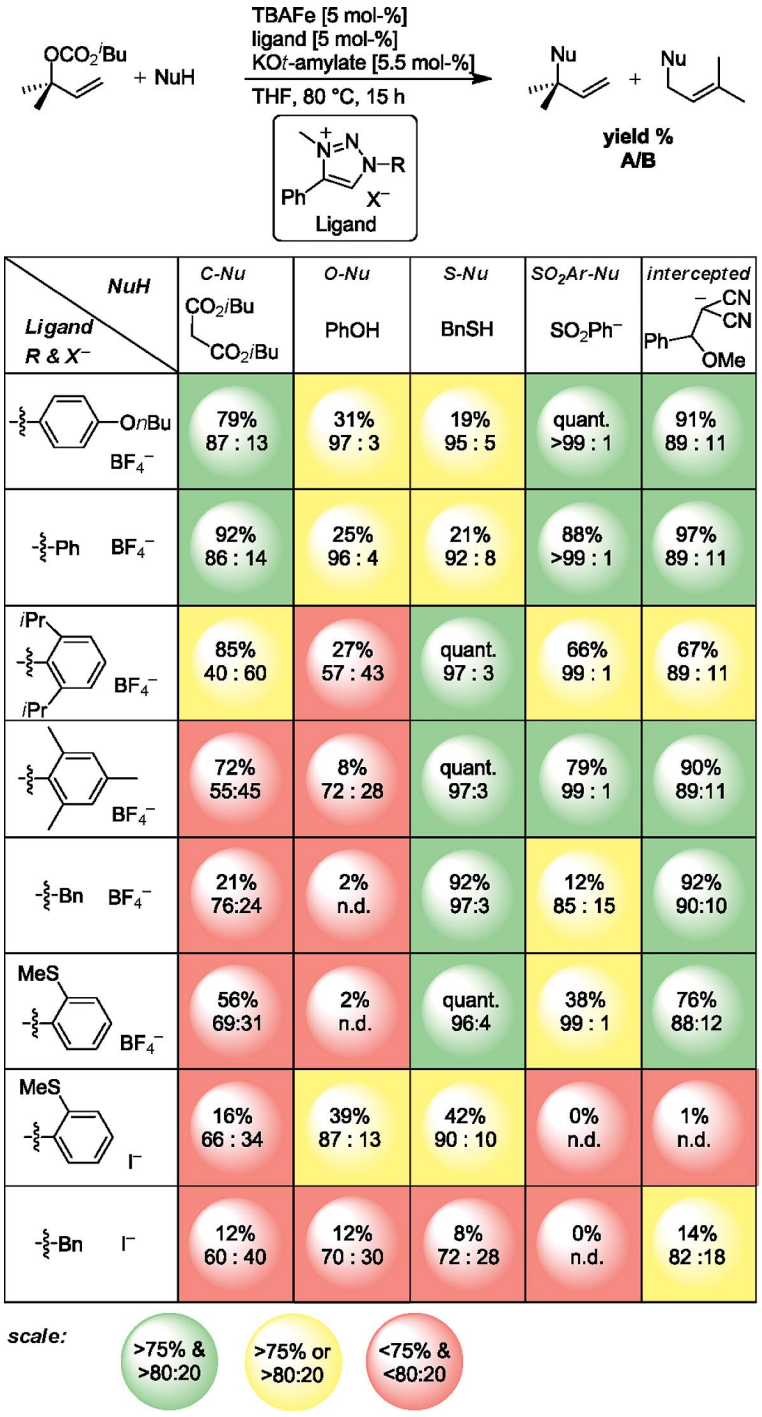
transformations such as allylic substitutions with special emphasis on problematic cases such as *O*-allylations. Herein, we summarize the results of this study which led to the development of a regioselective Fe-catalyzed *O*-allylation of phenols.[9] Whereas *N*,*N*-heterocyclic carbene ligands like SIMES [1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene] did not show any preference with regard to regioselectivity, the corresponding triazolium-based ligand TRIMPH (*tri*azolium *m*ethyl *ph*enyl) enabled selective *ipso*-substitution (Scheme 1).

Results and Discussion

Compared to the NHC-ligands, the synthesis of aNHC-ligands is straightforward and modular. Huisgen [3+2]-cycloaddition using Sharpless conditions between an alkyne and an azide yields the corresponding triazole, which upon methylation at *N*-3 gives the corresponding triazolium salt. At the outset of our studies we prepared different triazolium-based ligands following a recently published procedure[8] (Scheme 2).



Scheme 2. Triazolium-based carbene ligand library.



Scheme 3. Carbene ligand screening in Fe-catalyzed allylic substitutions.

This set of triazolium-salts was subsequently deprotonated using KO*t*-amylate as a base and the liberated ligands were employed in various allylic alkylation reactions (Scheme 3).

C-,[7h] *O*-,[10] *S*- (sulfenylation[11] and sulfonation[12]) and the intercepted allylation[13] were selected. All reactions have literature precedence and allow for direct comparison. In the allylation of *C*-nucleophiles, ligands **L1** and **L2** gave results we had seen previously with the sterically hindered SIBU [1,3-bis(*tert*-butyl)-4,5-dihydroimidazol-2-ylidene] ligand. Ligands **L3**–**L8** gave only low regioselectivity and poor to moderate yields. The allylation of phenols proceeded in only moderate yields. However, excellent regioselectivity was observed for the first time when ligands **L1** and **L2** were used. In the allylic sulfenylation very good selectivity was observed in almost all cases. Ligand **L8** proved to be inferior resulting in poor selectivity and almost no catalytic turnover. Furthermore, ligands **L1** and **L2** displayed what appears to be poor reactivity. These trends are contrary to the ones observed for *O*-allylation. It is pos-

sible that the more sterically encoumbered ligands **L3**–**L6** are not directly involved. Allylic sulfonation followed the same trends observed for *C*-allylation. We have previously employed phosphane-based ligands in this reaction; triazole ligands could be an alternative in this case.

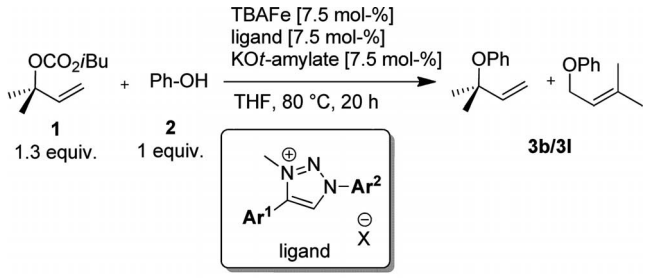
The intercepted allylation was rather insensitive to the choice of ligand. Only the use of iodide salts **L6** and **L8** resulted in inhibition of the reaction. This is probably a result of the iodide counterion, rather than the ligands themselves. Overall, it must be noted that triazole-based carbenes can serve as potent ligands in a number of allylic alkylation reactions. Ligands **L1** and **L2** appear to be generally applicable and should be included when screening ligand effects in transition metal-catalyzed reactions. In general, a preference for the formation of the *ipso*-substitution product was observed in these iron-catalyzed allylation reactions. This was previously obtained only when employing sterically demanding *tert*-butyl-substituted NHC-ligands.[7h] Furthermore, the substitution pattern at the *N*-substituent was found to have a strong impact on conversion rate and chemoselectivity. As can be seen from this screening, the nature of the counter anion plays an important role in the catalytic conversion;[14] the use of tetrafluorborate salts significantly enhanced reactivity. Only in one instance was an increase in reactivity observed. The *O*-allylation proceeded in slightly better yield when using ligand **L6** possessing an iodide counterion when compared to ligand **L5** which possesses the BF_4^- counterion. However, a slightly decreased selectivity was observed.

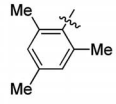
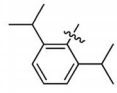
This latter transformation is remarkable since both our and Tunge's group[11] have observed that the use of *O*-nucleophiles in allylic substitutions using TBAFe is problematic with regards to regioselectivity. However, excellent regioselectivity was observed using ligands **L1** and **L2**. These observations appeared to be an important starting point for filling this gap in Fe-catalyzed regioselective allylic substitutions. From the data set shown above it is obvious that steric hindrance at the *N*-aromatic substituent disfavors the *ipso*-substitution pathway (**L3** and **L4**). The absence of a substituent at the *o*,*o*-position seems to favour a high degree of regioselectivity. This is complementary to the allylic alkylation of C-nucleophiles where *ipso*-substitution is greatly enhanced with increased steric bulk. In order to showcase the interplay of electronic parameters and the counter anion effect, different triazolium cations were used in aryloxyallylation reactions using either their iodide or tetrafluorborate salts (Table 1).

As can be seen from these results, little or no effect on the reaction was attributable to *para*-substitution. The most remarkable changes were achieved using *o*,*o*-substituents (vide supra). Furthermore, the counter anion had a significant influence on the yield. In general, triazolium iodide salts were less suitable as ligand precursors. Based on these results, ligand **L1** was chosen for subsequent screenings to evaluate reaction scope and limitations (Table 2). A variety of different phenol derivatives were allylated in moderate to excellent yields and with excellent regioselectivity throughout. An array of functional groups were found to be tolerated and even *ortho*-substituents did not inhibit the reaction. Introduction of an acyl group or a bromide resulted in diminished yields albeit with retention of excellent regioselectivity (Table 2, Entries 5 and 8). In addition, no formation of product was observed when using highly acidic pentafluoro-substituted phenol (Table 2, Entry 10).

Tunge was able to show that TBAFe in the presence of a phosphane ligand allows for efficient decarboxylative aryloxyallylation.[15] However, the regioselective course of this transformation points to that of a π-allyl mechanism. Hence, independent of the structure of the starting material, a clear preference for the formation of the linear product was observed. Furthermore, a fast [3,3]-sigmatropic re-

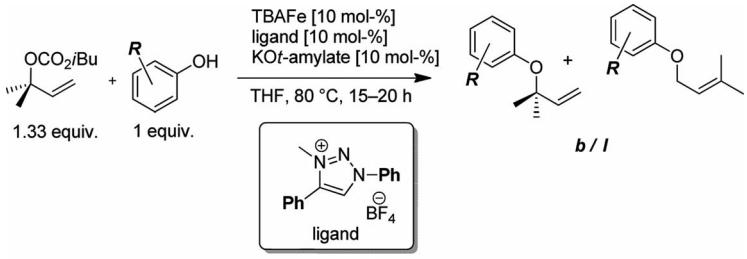
Table 1. Variation of the ligand.

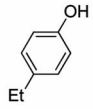
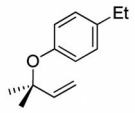
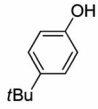
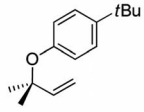
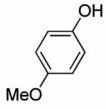
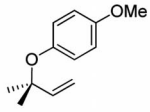
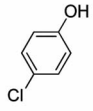
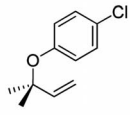
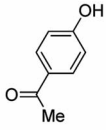
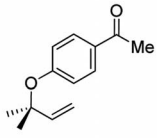
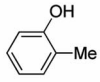
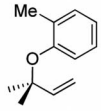
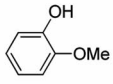
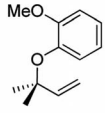
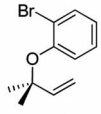
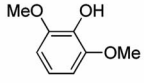
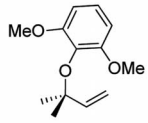
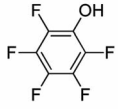
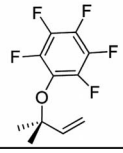


Entry[a]	Ar^1	Ar^2	Ligand	X$^\ominus$	**b** / **l**[b]	Yield (%)[c]
1			**L9**	I	95:5	41
2			**L1**	BF_4	95:5	>98
3			**L10**	I	96:4	53
4			**L2**	BF_4	95:5	58
5			**L11** **L12**	I	95:5	33
6			**L13**	I	98:2	56
7			**L14**	BF_4	93:7	78
8			**L15**	I	88:12	46
9			**L16**	I	70:30	49
10			**L4**	BF_4	77:23	96
11			**L3**	BF_4	68:32	23

[a] Reactions were performed using 0.375 mmol PhOH and 0.5 mmol carbonate, TBAFe (7.5 mol-%), and ligand (7.5 mol-%) in THF (0.5 mL) at 80 °C for 20 h, ligands were deprotonated using KO^{t}amylate solution in PhMe (7.5 mol-%). [b] Determined by GC. [c] GC yield using *n*-dodecane as an internal standard.

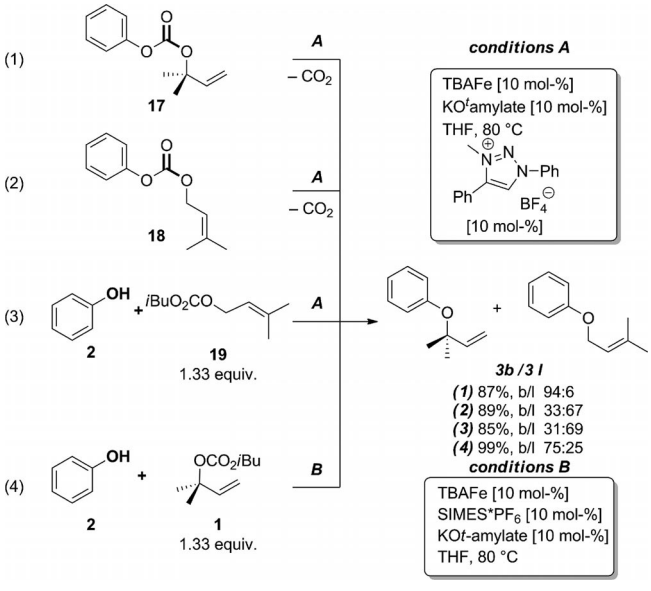
Table 2. Substrate scope for phenols.



Entry[a]	Ar-OH	Product		b / l[b]	Yield (%)[c]
1			**7**	95:5	88
2			**8**	>95:5	99
3			**9**	>95:5	82
4			**10**	>95:5	92
5			**11**	>95:5	37
6			**12**	95:5	99
7			**13**	>95:5	80
8			**14**	>95:5	49[e]
9			**15**	>95:5	86
10			**16**	n.d.	n.r.[e]

[a] Reactions were performed using 0.375 mmol PhOH and 0.5 mmol carbonate, TBAFe (10 mol-%), and ligand (10 mol-%) in THF (0.5 mL) at 80 °C, the ligand was deprotonated using KO*t*-amylate solution in PhMe (10 mol-%). [b] Determined by integration of the crude NMR spectra. [c] Isolated yields. [d] Determined by GC. [e] 13 mol-% catalyst were used.

arrangement of the *ortho*-allyl phenol derivatives was reported for allyl ethers of the general type shown above. We wondered if the decarboxylative reaction pathway would also lead to a linear or rearranged product. If *ipso*-selectivity would be observed, a different mechanistic manifold for this type of transformation should be operative using the catalyst system reported here. Very much to our delight, the course of the reaction was mainly determined by the original structure of the employed carbonate [Equations (1) and (2), Scheme 4]. Starting from branched carbonate **17**, branched product **3b** was obtained in high yields with excellent regioselectivity. Subjecting the regioisomeric linear carbonate to the standard reaction conditions led to a mixture of regioisomers with the linear product being the major product. Moreover, identical regioselectivities were observed for the intermolecular case [Equation (3), Scheme 4]. In order to exemplify the TRIMPH-ligand effect, we finally performed the aryloxylation using SIMES as the NHC-ligand [Equation (4), Scheme 4], under otherwise identical conditions. Under these conditions, the branched product was formed as the major product in excellent yields. However, the regioselectivity by no means matched that obtained when using ligand **L1**. Interestingly, use of the *tert*-butyl-substituted NHC-ligand SIBU resulted in very low conversion under these reaction conditions.



Scheme 4. Scope and limitations of Fe-catalyzed aryloxy allylation – the carbonate scope.

The analysis of CO frequencies of carbonyl containing iridium complexes featuring SIMES and structurally analogous triazole-ligand has recently been reported by Terashima et al. and suggests that the triazole ligands are the stronger σ-donor ligands.[16] When ligated to iron, in the present case, this would aid nucleophilic attack onto the allyl carbonate. However, it would also result in a reduction in leaving group ability. Consistent with previous reports of redox-participation,[3a] electron transfer from the iron center to the ligand could result in formal reduction of the ligand thus rendering the oxidized iron a better leaving group. Interestingly, it has been observed that the addition of catalytic amounts of triazole derived aNHC-ligands resulted in improved reactivities and γ-selectivities in alkyl-Grignard-mediated alkyl–allyl cross-coupling reactions.[17] This is consistent with selective S_N2' allylation of the iron center by the allyl carbonate in the present case.

Conclusions

In the present manuscript we report a regioselective Fe-catalyzed aryloxy allylation of allylic carbonates using triazolium-derived aNHC-ligands. Contrary to the use of phosphane or NHC-ligands, the TRIMPH-ligand allows for regioselective preparation of allyl aryl ethers in good to excellent yields in favor of the *ipso*-substitution product. Consequently, this approach complements existing methodology developed by Tunge and co-workers. Although, the reason for this unexpected regioselectivity remains elusive, the unusual electronic properties of aNHC-ligands that enable electron shifts from the metal to the ligand seem to be of key importance in the transformation. It is our hope that this ligand motif will allow further broadening of the scope of TBAFe-catalyzed transformations.

Experimental Section

General Procedure for Fe-Catalyzed Allylation of Phenols: Ligand **L1** (12.1 mg, 0.0375 mmol, 10 mol-%) was weighed into a dried Schlenk tube (20 mL size) equipped with a PTFE-lined screw-cap under an atmosphere of dry N_2. Freshly distilled anhydrous THF (500 μL) was added followed by the addition of KO*t*-amylate (24 μL, 1.7 M sol. in PhMe). The mixture was stirred for 20 min at r.t. To the solution was then added $Bu_4N[Fe(CO)_3(NO)]$ (15.5 mg, 0.0375 mmol, 10 mol-%) while maintaining an N_2 atmosphere. The reaction mixture was then heated to 80 °C for 1 h (reduced times led to decreased conversion). The mixture was cooled to room temperature prior to the addition of the appropriate allyl-carbonate (0.5 mmol, 1.33 equiv.) and phenol (0.375 mmol, 1.0 equiv.). *n*-Dodecane was added as a standard prior to GC analysis for screening reactions. Decarboxylative allylation was carried out on a 0.375 mmol scale following the above protocol.

Supporting Information (see footnote on the first page of this article): Experimental procedures for the preparation of the triazolium salts, spectroscopic data for novel triazolium salts and for all allylated phenols.

Acknowledgments

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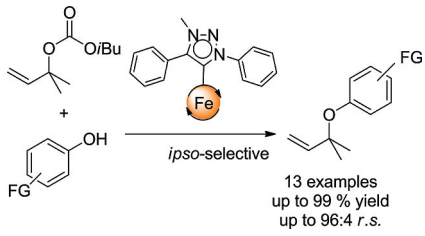
Triazolium-derived *N*-heterocyclic carbene ligands, generated by deprotonation of corresponding triazolium salts, are versatile ligands in diverse allylic substitution reactions. The corresponding triazolium salts are zwitterionic in their liberated form and act as strong redox-active σ-donor ligands thus enabling an unprecedented Fe-catalyzed regioselective aryloxylation of allylic carbonates.



Keywords: Iron / Carbene ligands / Allylation / Regioselectivity

