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Regioselective Iron-Catalyzed Decarboxylative Allylic Etherification

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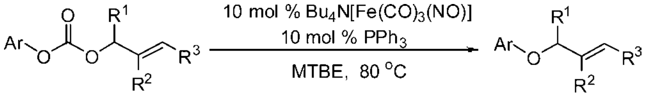
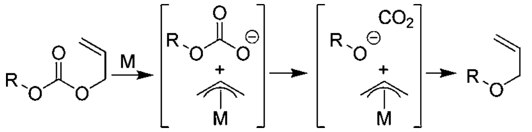
ABSTRACT



An anionic iron complex catalyzes the decarboxylative allylation of phenols to form allylic ethers in high yield. The allylation is regioselective rather than regiospecific. This suggests that the allylation proceeds through π-allyl iron intermediates in contrast to related allylations of carbon nucleophiles that have been proposed to proceed via σ-allyl complexes. Ultimately, iron catalysts have the potential to replace more expensive palladium catalysts that are typically utilized for decarboxylative couplings.

Decarboxylative allylation reactions are a powerful method for the allylation of a wide variety of nucleophiles under neutral conditions.[1] A remaining issue with decarboxylative allylations is their reliance on relatively expensive platinum group metals. For instance, decarboxylative etherification has been reported to occur with Pd,[2] Rh,[2c] and more recently Ru-based catalysts.[3,4] A single example of nickel-catalyzed decarboxylative etherification has also been reported. However, the specific reaction conditions and yield were not included in that report.[2c] Herein we report that similar transformations can be effected with simple, inexpensive iron-based catalysts (Scheme 1).

Scheme 1



The first palladium-catalyzed decarboxylative etherification was reported in 1981 and Larock later generalized the transformation into a useful method.[2b] Initial attempts at enantioselective coupling were not fruitful (<23% ee);[2c] however, these reactions provided the foundation for the recent enantioselective Ru-catalyzed decarboxylative etherification.[3]

In looking to utilize catalysts other than standard platinum group metals for decarboxylative etherification, we were drawn to the seminal iron-catalyzed allylic alkylations of Roustan[5] and more recently Plietker.[6] More specifically, Plietker has used phosphine and *N*-heterocyclic carbene-modified versions of the Hieber anion to form electrophilic allyl species from allylic carbonates. However, Plietker has

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(1) (a) Shimizu, I.; Yamada, T.; Tsuji, J. *Tetrahedron Lett.* **1980**, 3199. (b) Tsuda, T.; Chujo, Y.; Nishi, S.-i.; Tawara, K.; Saegusa, T. *J. Am. Chem. Soc.* **1980**, *102*, 6381. (c) Rayabarapu, D. K.; Tunge, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 13510. (d) Waetzig, S. R.; Rayabarapu, D. K.; Weaver, J. D.; Tunge, J. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 4977. (e) Waetzig, S. R.; Tunge, J. A. *J. Am. Chem. Soc.* **2007**, *129*, 4138. (f) Weaver, J. D.; Tunge, J. A. *Org. Lett.* **2008**, *10*, 4657. (g) Mohr, J. T.; Behenna, D. C.; Harned, A. W.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 6924. (h) Trost, B. M.; Bream, R. N.; Xu, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 3109.

(2) (a) Guibe, F.; M'Leux, Y. S. *Tetrahedron Lett.* **1981**, *22*, 3591. (b) Larock, R. C.; Lee, N. H. *Tetrahedron Lett.* **1991**, *32*, 6315. (c) Consiglio, G.; Scalone, M.; Rama, F. *J. Mol. Catal.* **1989**, *50*, L11. (d) Tsuji, J.; Sato, K.; Okumoto, H. *J. Org. Chem.* **1984**, *49*, 1341. (e) Backvall, J.-E.; Nordberg, R. E.; Vagberg, J. *Tetrahedron Lett.* **1983**, *24*, 411.

(3) Austeri, M.; Linder, D.; Lacour, J. *Chem.—Eur. J.* **2008**, *14*, 5737.

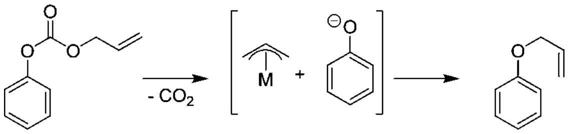
(4) Other related catalytic allylations of phenols: (a) Lopez, F.; Ohmura, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 3426. (b) Evans, P. A.; Leahy, D. K. *J. Am. Chem. Soc.* **2000**, *122*, 5012.

(5) (a) Roustan, J. J.; Merour, J. Y.; Houlihan, F. *Tetrahedron Lett.* **1979**, *39*, 3721. (b) Ladoulis, S. J.; Nicholas, K. M. *J. Organomet. Chem.* **1985**, *265*, C13. (c) Xu, Y.; Zhou, B. *J. Org. Chem.* **1987**, *52*, 974. (d) Zhou, B.; Xu, Y. *J. Org. Chem.* **1988**, *53*, 4419. (e) Eberhardt, U.; Mattern, G. *Chem. Ber.* **1988**, *121*, 1531.

10.1021/ol902291z

not investigated the loss of CO_2 from such allylic carbonates as a method for decarboxylative coupling reactions. Thus, we chose to investigate the decarboxylative allylic etherification using iron catalysts. To begin, we compared a small variety of catalysts for their ability to effect the decarboxylative allylation of phenols (Table 1). Here the qualitative rate of decarboxylative allylation, as catalyzed by PPh_3-modified $Bu_4N[Fe(CO)_3NO)]$ (**1**) in methyl *tert*-butyl ether (MTBE), was compared with those of more standard Pd and Ru catalysts.[1,7] These studies show that the order of reactivity is Pd > Ru > Fe. While the iron catalyst was not the most active, iron is ca. 10 000 times less expensive than either ruthenium or palladium.[8] Thus, the scope of the iron-catalyzed decarboxylative etherification was worthy of further investigation.

Table 1. Catalyst Comparison

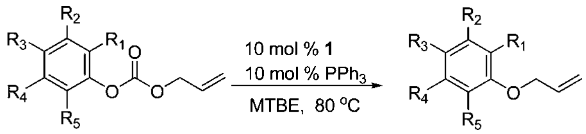


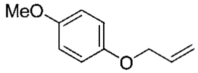
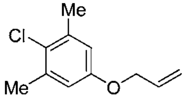
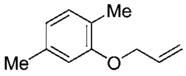
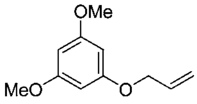
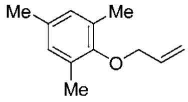
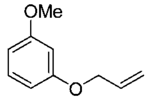
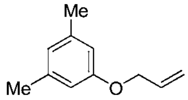
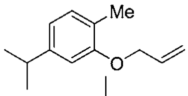
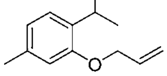
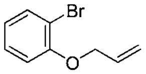
catalyst	solv	temp, °C	time	yield, %
10 mol % of **1**, 12 mol % of PPh_3	MTBE	80	24 h	98
1.25 mol % of $[Cp^*RuCl]_4$, 5 mol % of bpy	CH_2Cl_2	50	14 h	96
5 mol % of $Pd(PPh_3)_4$	CH_2Cl_2	rt	<15 min	98

As can be seen from Table 2, a variety of phenols undergo decarboxylative allylation in high yield. In particular, the reaction is effective for nearly any substitution pattern about the phenol; even sterically demanding *ortho*-substituted phenolates undergo allylation, albeit at a reduced rate (entries 3, 5, 8, and 9). In addition, allyl ethers of electron-rich phenols like **3e** undergo exclusive *O*-allylation. Related palladium-catalyzed allylations of 3,5-dimethoxyphenol are often plagued by the formation of *C*-allylated products.[9] Lastly, aryl halides are tolerated (entries 2 and 10). These functional groups have the potential to interfere with the analogous palladium-catalyzed reactions.

Next, the regioselectivity of the allylation was investigated (Table 3). In all cases, the cinnamyl carbonates preferentially formed the linear allylic ethers in good yield (entries 2−7). Here, one can also see that the reaction is compatible with electron-withdrawing groups on the phenol like CF_3 and CO_2Me. To investigate the regiospecificity of the allylation, the product of the reaction of a cinnamyl carbonate was compared to that derived from a 1-phenylallyl carbonate (entries 7 and 8). As can be seen, both substrates provided the linear product exclusively as judged by ^1H NMR spectroscopy. Thus, the reaction with aryl-substituted allylic carbonates is regioselective. Moreover, subjecting the branched allyl phenyl ether, (1-phenoxyallyl)benzene, to the catalytic reaction conditions resulted in no isomerization to the linear allyl ether **3r**. Thus, the observed regioselectivity is a kinetic selectivity and not simply the result of equilibration to the more stable linear product. Next, we investigated the coupling of crotyl alcohol, which provided the branched allylation product with moderate regiocontrol and high yield (entry 9). The isomeric branched carbonate also produced the branched allylic ether selectively (entry 10). While the regiochemical outcome slightly depends on the regiochemistry of the

Table 2. Scope of Phenols



entry	time	product		yield (%)
1	12 h		**3b**	99
2	12 h		**3c**	92
3	12 h		**3d**	82
4	24 h		**3e**	96
5	48 h		**3f**	85
6	12 h		**3g**	92
7	24 h		**3h**	93
8	24 h		**3i**	89
9	24 h		**3j**	98
10	72 h		**3k**	85

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(6) (a) Plietker, B. *Angew. Chem., Int. Ed.* **2006**, *45*, 1469. (b) Plietker, B. *Angew. Chem., Int. Ed.* **2006**, *45*, 6053. (c) Plietker, B.; Dieskau, A. *Eur. J. Org. Chem.* **2009**, 775. (d) Plietker, B.; Dieskau, A.; Mows, K.; Jatsch, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 198.

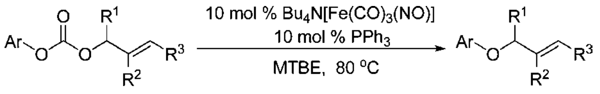
(7) Burger, E. C.; Tunge, J. A. *Org. Lett.* **2004**, *6*, 2603. (b) Burger, E. C.; Tunge, J. A. *Chem. Commun.* **2005**, 2835.

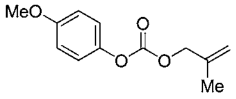
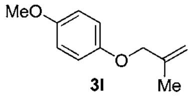
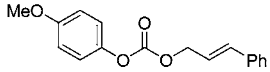
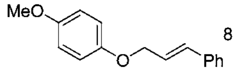
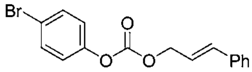
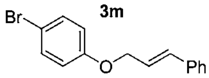
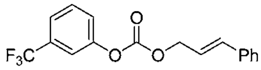
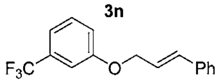
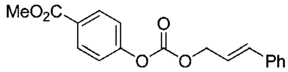
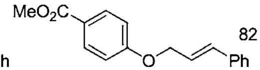
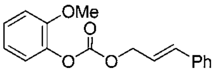
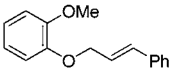
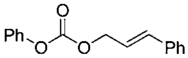
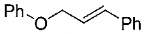
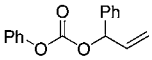
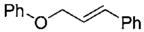
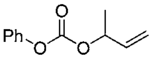
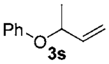
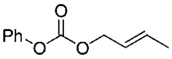
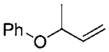
(8) Approximate market prices 10/2/09: Pd ($292/oz), Ru ($90/oz), Fe ($0.01/oz) .

(9) (a) Satoh, T.; Ikeda, M.; Miura, M.; Nomura, M. *J. Org. Chem.* **1997**, *62*, 4877. (b) Kuntz, E.; Amgoune, A.; Lucas, C.; Godard, G. *J. Mol. Catal. A* **2006**, *244*, 124.

(10) He, S.; Kozmin, S. A.; Rawal, V. H. *J. Am. Chem. Soc.* **2000**, *122*, 190.

Table 3. Scope of Allyl Electrophiles

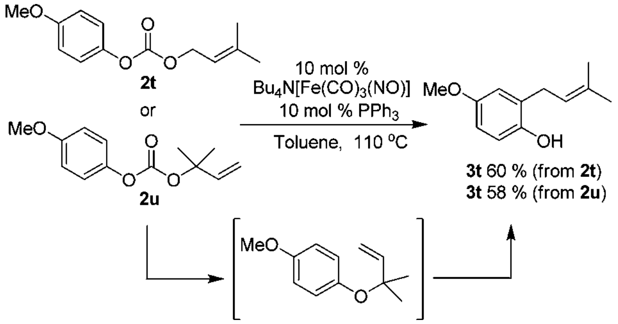


entry	substrate	product	yield (%) (l:b)
1		 **3l**	96[a]
2		 **3m**	81 (>95:5)
3		 **3n**	83 (80:20)
4		 **3o**	83 (80:20)
5		 **3p**	82 (>95:5)
6		 **3q**	84 (>95:5)
7		 **3r**	87 (>95:5)
8		 **3r**	99 (>95:5)
9		 **3s**	95 (25:75)
10		 **3s**	99 (30:70)

starting allyl ester, the reaction is not strongly regiospecific. Thus, the decarboxylative etherfication is best referred to as a regioselective reaction, where the position of the oxygen nucleophile in the product is independent of the position of the leaving group in the reactant. This is an interesting observation since Xu[5c,d] and more recently Plietker[6] have shown that the analogous iron-catalyzed allylation of carbon nucleophiles is a regiospecific process, with nucleophilic attack occurring to preserve the regiochemistry present in the reactant. Thus, it appears that **1** catalyzes decarboxylative etherification through the intermediacy of π-allyl iron complexes, while allylic alkylation occurs through σ-allyl iron complexes.[2b,3]

Lastly, we investigated decarboxylative prenylation reactions, since prenyl aryl ethers are excellent precursors to biologically active chromans.[11] Interestingly, the decarboxylative prenylation reaction provided the 2-prenyl phenol **3t** in moderate yield (Scheme 2). Thus, under the reaction

Scheme 2. Decarboxylative Allylation/Claisen Rearrangement



conditions *C*-allylation product is produced rather than the *O*-allylation product. Once again, the regiochemistry of allylation is independent of the starting regioisomer of the allylic ester (**2t** vs. **2u**). Next, we were curious whether product **3t** arose from direct *C*-allylation of the phenolate or via a tandem *O*-allylation/Claisen rearrangement reaction.[1d,e,10] The mechanism of the transformation appears to be the latter, since the *O*-allylated product was directly observed by ^{1}H NMR spectroscopy of the reaction mixture at intermediate reaction times. Moreover, the *O*-allylated product was observed to convert to the *C*-allylated product **3t** slowly as the reaction progressed.

While the yield of **3t** is only moderate, our decarboxylative allylation is more straightforward than that for some related *C*-prenylations. For instance, Nicolaou has utilized propargylation followed by Lindlar reduction and Claisen rearrangement to control the regiochemistry of formal *C*-allylation of phenols.[11] Lastly, it is noteworthy that attempts to utilize Pd(PPh$_3$)$_4$ to catalyze decarboxylative etherification of **2t** led to quantitative elimination, forming 4-methoxyl phenol and isoprene. Thus, in this instance there is both an economic and a synthetic advantage to utilizing an iron catalyst for decarboxylative etherification.

In conclusion, an iron-catalyzed decarboxylative allylation of phenolates was developed. The yields of the reaction are generally high and the iron catalyst often provides chemo- and regioselectivities that complement those of more standard palladium catalysts. Ultimately, the results presented herein show that decarboxylative coupling can be accomplished with an inexpensive iron catalyst. We are currently investigating extensions to other decarboxylative allylations.

Acknowledgment. We thank the National Science Foundation (CHE-0548081) for funding.

Supporting Information Available: Experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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[11] (a) Nicolaou, K. C.; Sasmal, P. K.; Xu, H.; Namoto, K.; Ritzen, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 4225. (b) Nicolaou, K. C.; Sasmal, P. K.; Xu, H. *J. Am. Chem. Soc.* **2004**, *126*, 5493. (c) Nicolaou, K. C.; Xu, H.; Wartmann, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 756. (d) Nicolaou, K. C.; Lister, T.; Denton, R. M.; Gelin, C. F. *Tetrahedron* **2008**, *64*, 4736.