Highly Regioselective Allylic Substitution Mediated by Chiral Rhenium Complexes

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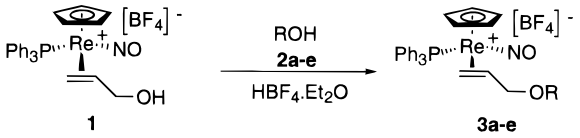
Summary: The nucleophilic addition of alcohols, thiols, allylsilane, or triphenylphosphine on an allylic alcohol complexed to a chiral rhenium salt leads, in the presence of an acid, to the corresponding ethers, thioethers, 1,5-diene, and phosphonium salt in high yields. The high regioselectivity of these reactions is unambiguously established using a deuterated ligand.

Addition of nucleophiles on transition metal π-complexes of unsaturated ligands is an efficient method for carbon−carbon or carbon−heteroatom bond formation.[1] For allylic substitution, various transition metals have been used, such as Pd, Pt, Mo, Rh, Ru, Ni, Co, W, and Fe.[2] For most of these complexes, the regio- and stereoselectivity are strongly dependent on the nature of the metal, the ligands, and the nucleophiles. Extensive studies have been carried out, in particular on π-allyl complexes of palladium, which are used in organic synthesis both as stoichiometric reagents and as catalysts.[2] Furthermore, they have been successfully extended to asymmetric synthesis mainly using chiral, nonracemic ligands.[3]

Another possible approach involves chirality at the metal center. Faller *et al.* have studied in detail molybdenum complexes of this type: nucleophilic addition gave interesting results in terms of regioselectivity, stereoselectivity, and asymmetric synthesis.[4] Gladysz *et al.* have reported the preparation of the first chiral rhenium complex with the chirality centered at the metal atom,[5] and they have extensively studied the properties of such complexes.[6] Starting from the same intermediate, we recently prepared several chiral rhenium complexes of unsaturated alcohols and performed a variety of transformations on the appending functionalities (oxidation of alcohol, Wittig reaction, reduction, ...),[7] indicating that such a complex acted as an efficient protecting group of the CC double or triple bond. The π-allyl system is another example of a useful ligand, but in the case of rhenium derivatives very few complexes have been reported until now. Starting from a *neutral* rhenium complex, Sutton *et al.* recently isolated a π-allyl derivative and studied its reactivity with various nucleophiles.[8] We report here that *cationic* rhenium complexes also activate allylic substitution on the ligand and, therefore, promote nucleophilic substitutions *under acidic conditions*. Furthermore, we demonstrate on a simple model that such chiral rhenium complexes offer very interesting and new possibilities for regiocontrolled allylic substitutions under mild conditions, and we discuss the mechanism of these reactions.

Scheme 1



1 3a-e

Table 1. Reaction of Complex 1 with Alcohol in the Presence of HBF_4·Et_2O

nucleophile	product	yield (%)
$CH_3C{\equiv}CCH_2OH$	**3a**	80
$HC{\equiv}CCH_2OH$	**3b**	87
$HC{\equiv}CCH(Me)OH$	**3c**	81
nBuOH	**3d**	81
$H_2C{=}CHCH_2OH$	**3e**	76

The addition of a catalytic amount (20%) of HBF_4·Et_2O to a CH_2Cl_2 solution of the known chiral cationic rhenium complex **1**[7] and primary or secondary alcohols **2a**−**e** led to the corresponding complexed unsaturated ethers **3a**−**e** in very good yields (Scheme 1, Table 1).[9] In the case of unsaturated nucleophiles, it is noteworthy that the unsymmetrical unsaturated ethers **3a**−**c** are formed with selective coordination of the CC double bond, without any shift of the organometallic unit.

This substitution has been extended to several other nucleophiles (Scheme 2). The reaction of **1** with allyl mercaptan, butanethiol, and thiophenol led to the corresponding complexed thioethers **4a**−**c** in 82, 86, and

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(1) Harrington, P. J. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds; Pergamon: New York, 1995; Chapter 8.2, pp 797−904.

(2) For some examples, see the following. Palladium: Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1989,** *28*, 1173−1192. von Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 566−568. Trost, B. M.; Organ, M. G.; O'Doherty, G. A. *J. Am. Chem. Soc.* **1995**, *117*, 9662−9670. Molybdenum: Faller, J. W.; Linebarrier, D. *Organometallics* **1988**, *7*, 1670−1672. Trost, B. M.; Merlic, C. A. *J. Am. Chem. Soc* **1990**, *112*, 9590−9600. Iron: Enders, D.; Jandeleit, B.; Raabe, G. *Angew. Chem., Int. Ed. Engl.* **1994,** *33*, 1949−1951. Enders, D.; Von Berg, S.; Jandeleit, B. *Synlett* **1996,** 18−20.

(3) Frost, C. G.; Howarth, J.; Williams, J. M., Jr. *Tetrahedron: Asymmetry* **1992**, *3*, 1089−1122. Trost, B. M. *Acc. Chem. Res.* **1996**, *29*, 355−364 and references cited therein.

(4) Faller, J. W *Inorg. Chem.* **1980**, *19*, 2857−2859. Faller, J. W.; Chao, K.-H. *J. Am. Chem. Soc.* **1983**, *105*, 3893−3898. Faller, J. W.; Lambert, C.; Mazzieri, M. R. *J. Organomet. Chem.* **1990**, *383*, 161−177.

(5) Tan, W.; Lin, G. Y.; Wong, W. K.; Kiel, W. A.; Wong, V. K.; Gladysz, J. A. *J. Am. Chem. Soc.* **1982**, *104*, 141−152.

(6) (a) Wang, Y.; Agbossou, F.; Dalton, D. M.; Liu, Y.; Arif, A. M.; Gladysz, J. A. *Organometallics* **1993**, *12*, 2699−2713. (b) Peng, T. S.; Wang, Y.; Arif, A. M.; Gladysz, J. A. *Organometallics* **1993**, *12*, 4535−4544. (c) Johnson, T. J.; Arif, A. M.; Gladysz, J. A. *Organometallics* **1994**, *13*, 3182−3193. (d) Wang, Y.; Gladysz, J. A. *J. Org. Chem.* **1995**, *60*, 903−909.

(7) Legoupy, S.; Crévisy, C.; Guillemin, J.-C.; Grée, R. *Tetrahedron Lett.* **1996**, *37*, 1225−1228.

(8) Batchelor, R. J.; Einstein, F. W. B.; He, Y.; Sutton, D. *J. Organomet. Chem.* **1994**, *468*, 183−191. He, Y.; Batchelor, R. J.; Einstein, F. W. B.; Sutton, D. *J. Organomet. Chem.* **1996**, *509*, 37−48. See also: Krivykh, V. V.; Gusev, O. V.; Rybinskaya, M. I. *J. Organomet. Chem.* **1989**, *362*, 351−362.

(9) These reactions have been performed with racemic complexes. However, for clarity, only one enantiomer is shown in the schemes. The resolution of such rhenium complexes has been reported: Agbossou, F.; O'Connor, E. J.; Garner, C. M.; Quiros Mendez, N.; Fernandez, J. M.; Patton, A. T.; Ramsden, J. A.; Gladysz, J. A. *Inorg. Synth.* **1992,** *29*, 211−225.

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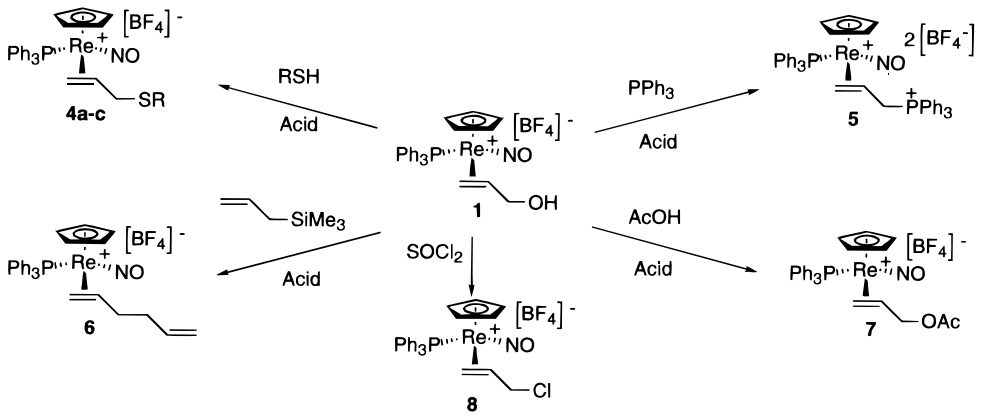
Scheme 2



88% yield, respectively.[10] The formation of thioethers (and not of ethers) is the first indication that the mechanism must involve a nucleophilic attack of the reagent on the ligand of complex **1**. The phosphonium salt **5**, which is a potential substrate for Wittig reactions, was formed in the reaction of complex **1** with triphenylphosphine in the presence of 1 equiv of $HBF_4 \cdot Et_2O$ (60% yield). A carbon−carbon bond has also been formed by reacting **1** with allylsilane, yielding the 1,5-hexadiene complex **6** in a 74% yield. The allyl acetate complex **7** was similarly prepared in a 63% yield by reaction of complex **1** with acetic acid in the presence of a catalytic amount of $HBF_4 \cdot Et_2O$.[11]

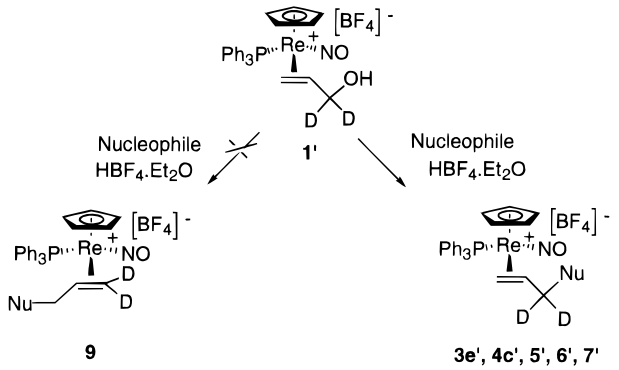
Carbon−halide bonds have also been formed: reaction of complex **1** with $SOCl_2$ (Scheme 2) in CH_2Cl_2 at room temperature gave the allyl chloride complex **8** (79% yield). It is interesting to note that previous attempts to directly complex allyl chloride were unsuccessful,[12] and thus **8** is the first example of an allyl halide coordinated to this organometallic unit.

We performed detailed mechanistic studies in order to characterize the regioselectivity as well as the effect of the acid and the leaving group on the reaction efficiency.

The nucleophilic substitution is dependent on the nature of the acid, and the formation of **3a**−**e** can be best achieved using catalytic amounts of $HBF_4 \cdot Et_2O$. Alternatively, $BF_3 \cdot Et_2O$ gave equivalent results, while replacement by $SnCl_4$ led to lower yield; no reaction was observed using camphorsulfonic acid or Amberlyst 15.

Different leaving groups can be used. For example, the acetate complex **7** reacted with allyl alcohol in the presence of small amounts of $HBF_4 \cdot Et_2O$, leading to complex **3e** in an 86% yield. Similarly, the butyl ether complex **3d** and allyl alcohol gave **3e** in the presence of $HBF_4 \cdot Et_2O$ (95% yield) or $BF_3 \cdot Et_2O$ (87% yield). However, when the sulfide complex **4b** was used, no nucleophilic substitution was observed in the presence of either allyl alcohol or allyl mercaptan. This result can be correlated with the poor leaving group properties of thiols.

Scheme 3[a]



[a] *3e′*, Nu = $OCH_2CH{=}CH_2$; **4c′**, Nu = SPh; **5′**, Nu = $^{+}PPh_3(BF_4)^{-}$; **6′**, Nu = $CH_2CH{=}CH_2$; **7′**, Nu = OAc.

The regioselectivity of these substitution reactions was clearly established using isotopic labeling. The complex **1′**, prepared starting from the allyl alcohol-1,1-d_2,[13] participated in nucleophilic substitution with allyl alcohol, thiophenol, triphenylphosphine, allyltrimethylsilane, and acetic acid. *In each case, we observed by ^1H and ^{13}C NMR spectroscopy only the signals corresponding to the products **3e′**, **4c′**, **5′**, **6′**, and **7′**, respectively, bearing the two deuterium atoms on the sp^3 carbon* (Scheme 3). The 1,1-dideuterioallyl chloride complex **8′** was similarly obtained using $SOCl_2$. Since none of the corresponding regioisomers **9** were detected by high-field NMR, these results demonstrate the very high regioselectivity (≥96%) of these reactions.

It is generally accepted that allylic substitution on transition metal complexes usually occurs via π-allyl complex intermediates.[1] In most cases, the major product is the one corresponding to the nucleophilic attack on the less substituted carbon, but nucleophilic substitutions can also occur at the more substituted carbon.[3] In the complex **1′**, the presence of the two hydrogens on the sp^2 carbon and two deuterium atoms on the sp^3 carbon should lead to a π-allyl complex intermediate which is almost symmetric. So, the regioselectivity cannot be explained simply by the steric hindrance introduced by a substituent on the π-allyl system. Thus, two different mechanisms can be considered in order to explain our results. In the first one, the reaction does not proceed via a π-allyl complex intermediate but is better represented by an S_N2 type reaction (Scheme 4, path a).

However, due to the chirality at the metal center, the resulting regioselectivity could also be explained by a

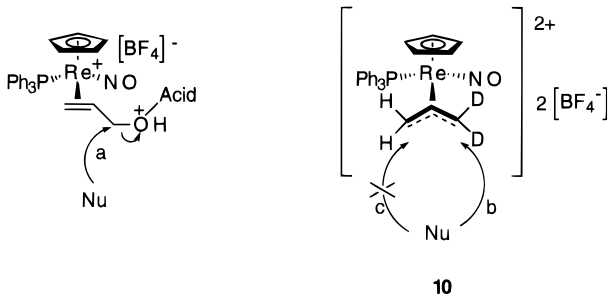
(10) (a) No product was obtained using phenol or allyl amine as nucleophile. (b) The ^1H NMR data of product **4a**−**c** clearly show that there is no bond-shift to the sulfur atom.

(11) Complex **7** can also be obtained starting from complex **1** with acetic anhydride and pyridine (yield, 71%).

(12) Legoupy, S.; Crévisy, C.; Guillemin, J.-C.; Grée, R. unpublished results.

(13) Casey, C. P.; Vosejpka, P. C.; Underiner, T. L.; Slough, G. A. Z.; Gavney, J. A., Jr. *J. Am. Chem. Soc.* **1993**, *115*, 6680−6688.

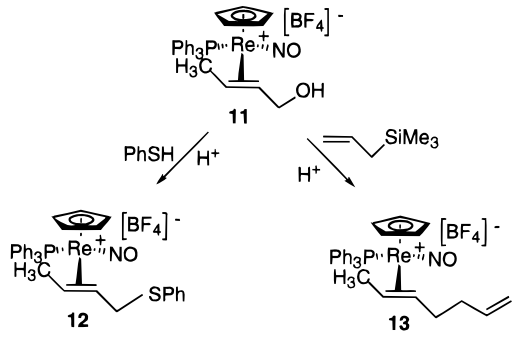
Scheme 4



cationic π-allyl intermediate.[8] On complexes such as **1**, Gladysz *et al.* have demonstrated conformational preferences of the π-ligands: the unsubstituted part of the double bond is on the side of the bulky triphenylphosphine.[6a,b] The ^{1}H NMR spectrum of complex **1** is in good agreement with that structure: for instance the coupling constants with the phosphorus atom (J_{PH} = 11.2 and 6.6 Hz and J_{CP} = 5.7 Hz) were only observed with the methylene group. The aforementioned regioselectivity could then be explained by a (*bicationic!*) π-allyl type intermediate **10** provided that (i) there is no rotation of the ligand during the protonation step and the departure of the leaving group, (ii) there is no isomerization of the π-allyl ligand in this intermediate, and (iii) the regioselectivity is controlled by the differences in the steric and electronic effects between the PPh_3 and NO ligands in **10** (Scheme 4, path b and not c). It is important to point out that previous studies on closely related molybdenum complexes give good support for such a mechanism, indicating that the NO ligand plays a key role in this process.[4]

Preliminary results indicate that this nucleophilic substitution can be extended to other complexes. For instance, the crotyl alcohol derivative **11** readily reacts with thiophenol and allyltrimethylsilane as nucleophiles (Scheme 5). The spectroscopic data of the observed

Scheme 5



products, the thioether **12** and the 1,5-diene **13**, respectively, are consistent with crotyl structures. The substitution is again completely regioselective, since attempts to detect in the crude reaction mixture traces of products corresponding to an allylic rearrangement were unsuccessful.

To conclude, the allylic function of these rhenium complexes is strongly activated toward nucleophilic substitution under acidic conditions. Furthermore, the very high regioselectivity of this new process has been attributed to a particular reactivity of these chiral complexes. Extention of these reactions and further applications in synthesis are under active investigations.

Acknowledgment. We gratefully acknowledge Dr. P. Guenot (CRMPO) for performing the mass spectral experiments.

Supporting Information Available: Text giving experimental details and ^{1}H, ^{13}C, and ^{31}P NMR data (8 pages). Ordering information is given on any current masthead page.

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