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Substituent effects on the amination of racemic allyl carbonates using commercially available chiral rhodium catalysts

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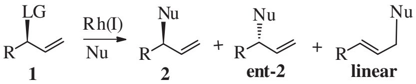
ABSTRACT

In the presence of commercially available chiral rhodium catalysts, a competitive benzylamination of racemic allyl carbonates, substituted with *p*-X-Ph groups, shows that the reaction proceeds faster with substituents (X) that are more electron-withdrawing. Mechanistic implications of these results are discussed.

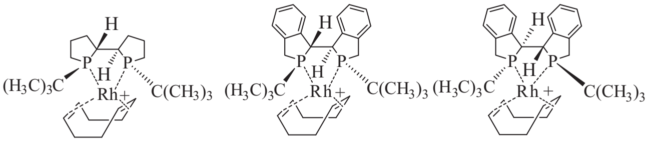
Transition-metal-catalyzed asymmetric allylic substitution reactions continue to receive considerable attention with complexes of palladium,[1a–c] iridium,[1d] and rhodium[2] serving as important tools in synthesis. Madrahimov and Hartwig recently conducted mechanistic studies of iridium-catalyzed allylic substitution reactions that give products with overall retention of configuration as a result of two steps that occur with inversion of configuration.[1d] They concluded that factors controlling the enantioselectivity of these reactions are not the same as those of other metal ions such as palladium.

In the presence of Rh(I) catalysts, allylic substitution reactions often proceed with high regioselectivity.[3] Thus, substrates with secondary allylic leaving groups yield mostly branched substitution products whereas those with primary allylic leaving groups generate linear substitution products in high yields. A variety of compounds containing secondary allylic carbonates have been alkylated,[4] aminated,[5] and etherified[4h,6a,b] in excellent yields and high regioselectivities using rhodium catalysts. Allylic acetates have also been substituted with malonates using chiral[6c] and achiral[6d] rhodium catalysts.

The stereochemistry of rhodium-catalyzed allylic substitution reactions has also been examined. Chiral substrates **1** generally react with nucleophiles in the presence of an achiral catalyst to give branched products **2** with retention of stereochemical configuration in high yields relative to enantiomer **ent-2** and linear structural isomers (Eq. 1).[4g–i,5a–d,6b,7] Interestingly, when Vrieze et al.[5d] reacted one equivalent of the racemic substrate rac-1 (R = CH_2Ph; LG = OCO_2CH_3) with one-half equivalent of $PhCH_2NH_2$ in the presence of the commercially available chiral rhodium catalyst, (*S*,*S*,*R*,*R*)-Tangphos-Rh (A in Fig. 1), they obtained a 36% yield (50% is theoretical) of unreacted **ent-1** in 99% ee and a 50% yield of **2** (R = CH_2Ph; Nu = $NHCH_2Ph$) in 99% ee. These results demonstrate a kinetic resolution of **rac-1** in which **ent-1** reacts slower than **1** due to a 'mismatch' with



(1)



(S,S,R,R)-Tangphos-Rh
(A)

(R,R,S,S)-Duanphos-Rh
(B)

(S,S,R,R)-Duanphos-Rh
(**ent-B**)

Figure 1. Rh(I) catalysts commercially available as BF_4^- salts.

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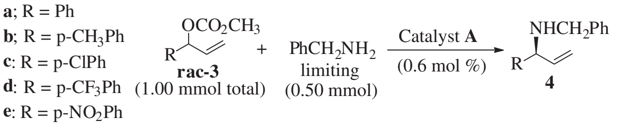
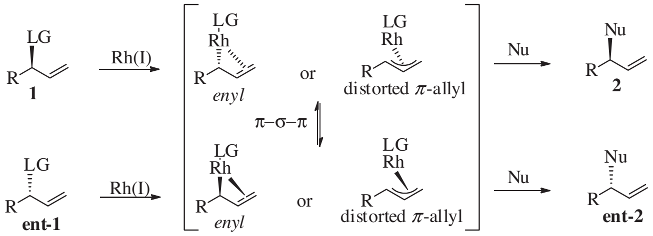
chiral catalyst **A**. On the other hand, **1** is 'matched' with **A** and reacts faster with $PhCH_2NH_2$ giving **2** almost quantitatively with retention of configuration.[5d]

Evans and co-workers have proposed a σ,π-coordinated (enyl)[8] or distorted π-allyl intermediate to account for the high regioselectivity and stereospecificity of rhodium-catalyzed allylic substitution reactions (Scheme 1).[4b,h] This mechanism explains the high yields of **2**, provided that the enyl intermediate undergoes a relatively slow π–σ–π rearrangement or metal–metal displacement. In this study, we aim to better understand this mechanism by determining substituent effects on the benzylamination of allyl carbonates using Rh(I) chiral catalysts.

Carbonates **rac-3** with electron-donating and electron-withdrawing substituents[9] were reacted competitively with benzylamine[10] in the presence of catalyst A (Eq. 2). [11] To a mixture containing 0.200 mmol of each of the five carbonates **rac-3a–e** (i.e., 1.00 mmol total) were added 0.500 mmol of benzylamine and a THF solution of **A** (Eq. 2). Given the 2:1 mole ratio of **rac-3** to benzylamine, the carbonates are forced to compete for benzylamine, the limiting reagent. The extent of reaction was then determined from the crude reaction mixture using C-13 NMR. Although the integrals of carbon peaks are normally unreliable for making quantitative comparisons, the integrals of one of the vinyl carbons in carbonates **rac-3** are almost identical as shown in Figure 2a inset for an equimolar solution of the five carbonates before reaction. The NMR spectrum of the same vinyl carbon after reaction of an equimolar mixture of **rac-3** with one-half equivalent of benzylamine (Fig. 2b) shows the presence of both unreacted carbonates and product amines **4**. As expected, the peaks for **4** are at lower chemical shifts. It is clear from the integrations of these signals that the allylic substitution reaction goes faster as the substituents become more electron-withdrawing. Not surprising, the Hammett type plot in Figure 3 shows a good correlation between the negative logarithms of the unreacted carbonate integrals in Figure 2b and σ with ρ = +0.36. If the reaction rate depends upon the concentration of carbonate, which is likely, these integrals underestimate the relative reactivities of the carbonates because the more reactive a carbonate, the faster its concentration would decrease with time.



(2)



Scheme 1. Proposed mechanism for the transformation of **1** to **2** (and **ent-1** to **ent-2**) regioselectively and with retention of configuration.[4j]

We next investigated the stereochemistry of the reaction of the five carbonates of **rac-3** separately with one-half equivalent of benzylamine in the presence of rhodium catalysts. In Table 1 are the % ee's of the recovered carbonates when catalyst **A** is used, which range in value from 42 to 49% and have the R absolute configuration based upon their optical rotations. Stereochemical data are also given in Table 1 for amines **4** formed in this reaction using

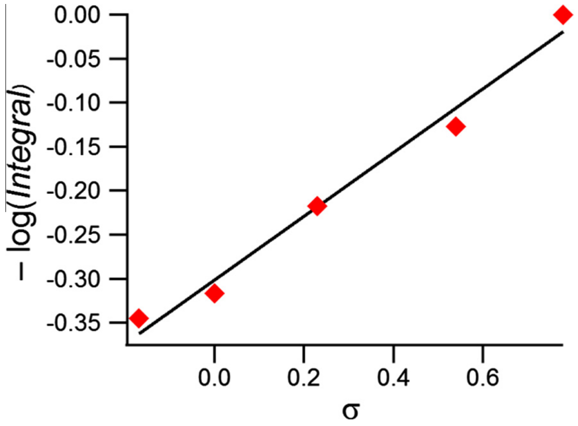


Figure 3. A Hammett type plot using the integrals of one of the vinyl carbons in the carbonate NMR spectra in Figure 2b. [−log (*integral*) = (0.36 ± 0.03)σ − (0.30 ± 0.01); R^2 = 0.98].

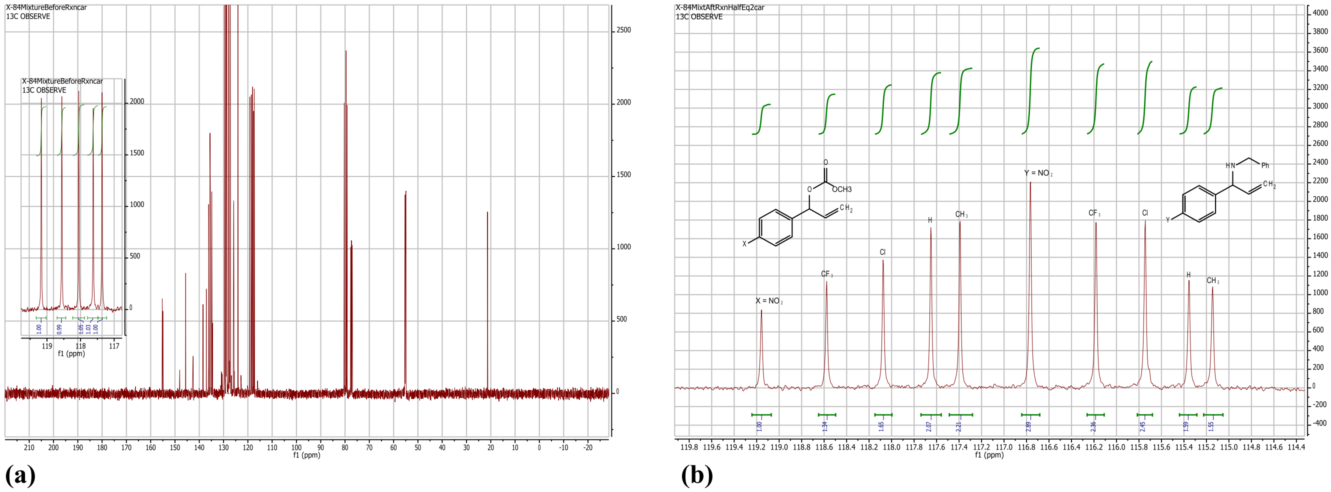


Figure 2. (a) C-13 NMR spectrum of an equimolar mixture of **rac-3a–e** with an inset of the region where one of the vinyl carbons in the five carbonates gives peaks. (b) Partial C-13 NMR spectrum of products from the reaction in Eq. 2 which is an expansion of the inset in (a) along with the peaks from the same carbon in amines **4** at slightly lower chemical shifts.